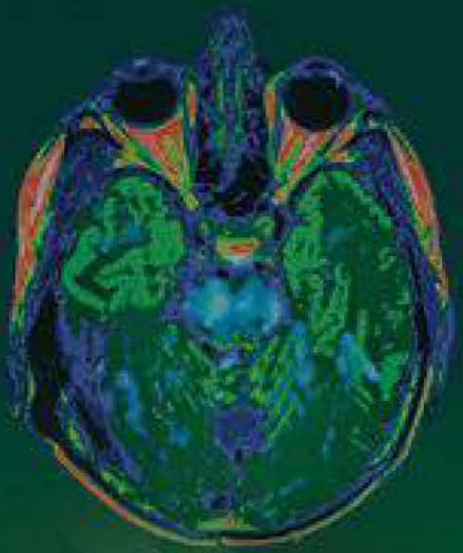
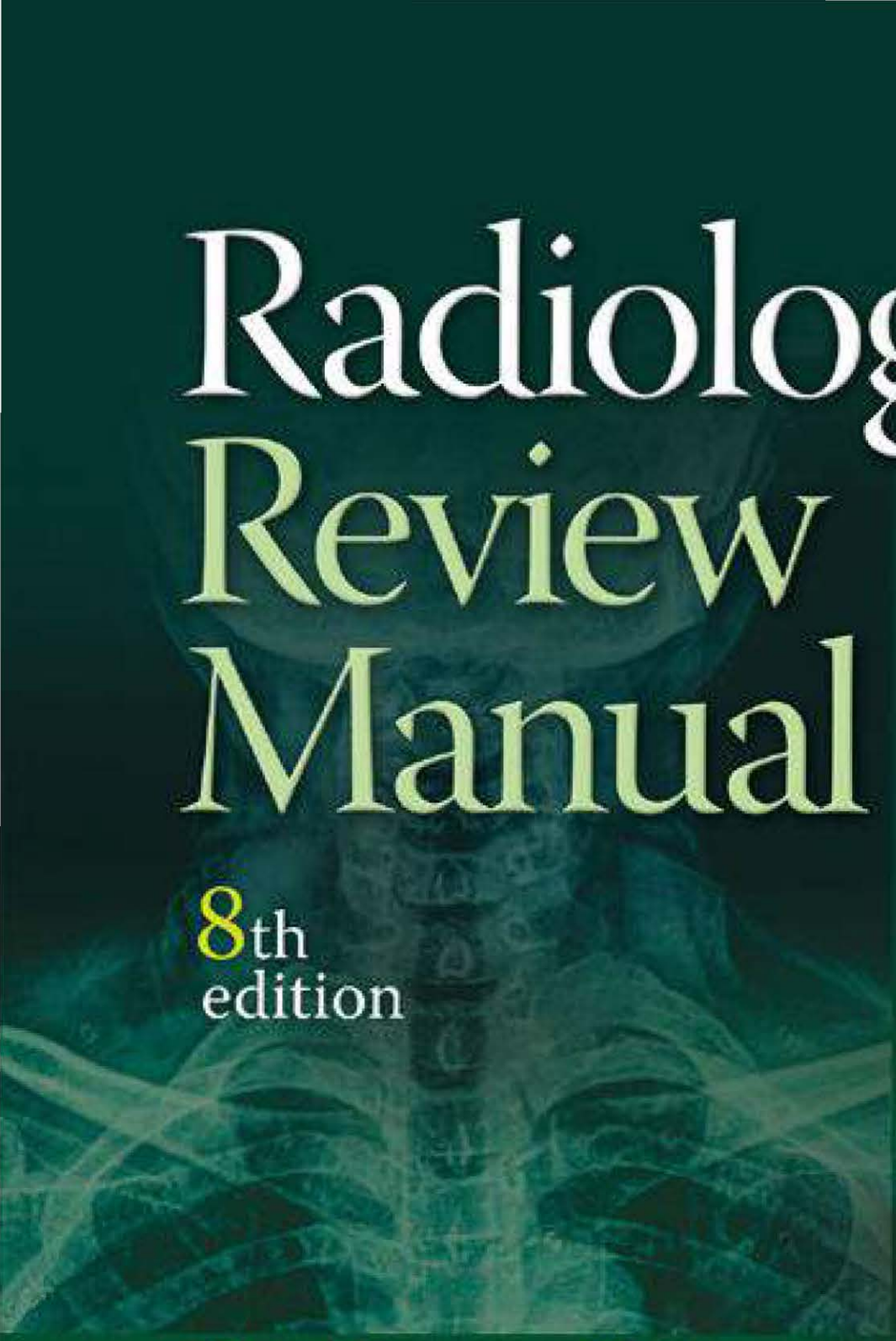
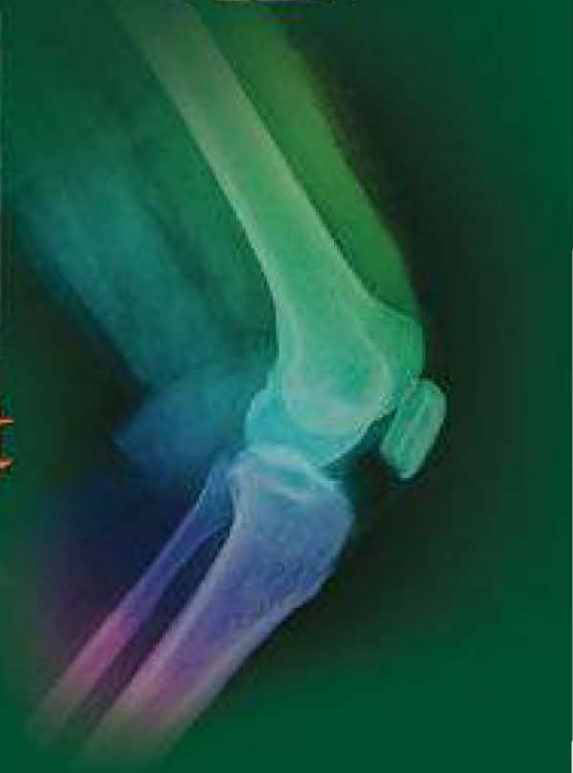
Radiology Review Manual

8th edition







Wolfgang Dähnert

Wolters Kluwer

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8th edition

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“If a little knowledge is dangerous, where is the man who has so much to be out of danger!”

T.H. Huxley, 1825–1895 from Elementary Instruction in Physiology published in 1877

“It is the tragedy of the world that no one knows what he doesn’t know — and the less a man knows, the more sure he is that he knows everything”

Joyce Cary, British author 1888–1957

“Nothing in the world can take the place of persistence.

Talent will not; nothing is more common than unsuccessful men with talent. Genius will not; unrewarded genius is almost a proverb.

Education will not; the world is full of educated derelicts.

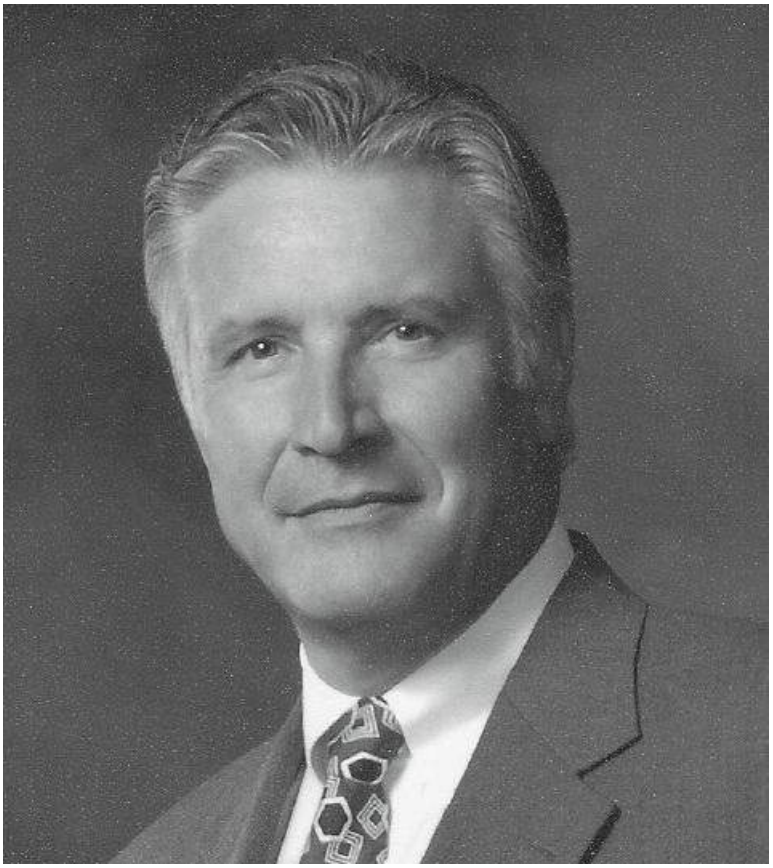
Persistence and determination alone are omnipotent."

Calvin Coolidge 1872–1933

Vice President 1921–1923

President 1923–1929

About the Author



Wolfgang Dähnert, M.D.

Wolfgang Dähnert was born in Hamburg, Germany. After graduating from the Wilhelm-Gymnasium High School in Braunschweig, Lower Saxony, in 1966 he enlisted into the German Air Force for four years. After his discharge from the armed services he studied medicine at the Heinrich-Heine Universität in Düsseldorf, North Rhine-Westphalia, for his preclinical years and at the Johannes-Gutenberg Universität in Mainz, Rhineland-Palatinate, for his clinical years. He graduated from medical school in 1975 and received his doctor of medicine degree shortly thereafter based on his dissertation "Pulse Flow Photocytometry of Prostate Punch Biopsies". A one-year rotating internship in urology, internal medicine and sports medicine at the Johannes-Gutenberg Universität and at the municipal Dr. Horst Schmidt Klinik in Wiesbaden was followed by a one-year residency in general surgery at the Deutsches Rotes Kreuz Krankenhaus in Mainz, Germany. In 1978 he switched to begin a residency in radiology at the municipal and teaching hospital in Darmstadt, Hesse, under the directorship of Prof. H.K. Deininger. He continued his education in diagnostic

and therapeutic radiology at the Johannes-Gutenberg Universität in Mainz under the directorship of Prof. Manfred Thelen and Prof. Rolf W. Günther receiving his German certification for radiology in 1982. Dr. Dähnert started a 2-year fellowship in ultrasound and computed tomography at the Johns Hopkins Hospital in Baltimore in 1984 under the leadership of Roger Sanders / Ulrike Hamper and Stanley Siegelman / Elliot Fishman and was appointed Clinical Instructor in 1986. In 1985 he sat for the federal licensing exam, and in 1987 took his oral exam in diagnostic radiology in Louisville, Kentucky. The American Board of Radiology had approved a 2-year fellowship program for him in lieu of a residency in radiology. The foundation of Radiology Review Manual was laid during the three years at Hopkins while preparing for the ABR exam. Between 1987 and 1989 he worked as Assistant Professor of Radiology in ultrasound at Thomas Jefferson Hospital in Philadelphia under Barry Goldberg. During this period in Philadelphia Radiology Review Manual was taken to fruition culminating in the publication of its first edition in 1991. Dr. Dähnert joined Clinical Diagnostic Radiology & Nuclear Medicine in Phoenix, AZ, in 1989 as director of ultrasound. This group practice of approximately 25 mostly fellowship-trained radiologists served three center city hospitals and their affiliated residency program in radiology, the latter at St. Joseph's Hospital and Medical Center, before it ceased operations in 2006 brought about by a fiscally unsustainable management style and culture. In September of 2004 Dr. Dähnert relocated to Green Bay, Wisconsin, joining a group of eight radiologists as part of a multispecialty group practice at Aurora BayCare Medical Center, the northern hub of Aurora Health Care, one of Wisconsin's largest private-sector employers.

PREFACE

Since the first publication of Radiology Review Manual in 1990 momentous changes have occurred in radiology. We have progressed from films developed in the dark-room to images on a computer screen. We have gone from an initially voluntary lifetime certificate of qualification to a never-ending process of proving to the public that our knowledge, skills, and clinical ability in the area of radiology has kept apace with the times. The first ABR Core Examination took place in October 2013. It tests knowledge and comprehension of anatomy, pathophysiology, physics and all aspects of diagnostic radiology including breast, cardiac, gastrointestinal, interventional, musculoskeletal, neuroradiology, nuclear, pediatric, reproductive/endocrinology, thoracic, urinary, vascular, computed tomography, magnetic resonance, radiography/fluoroscopy, ultrasound, physics, safety and radioisotope safety. The first Certifying Examination was in fall 2015.

Given the predominant practice pattern in the United States I estimate that General Radiology makes up at least 10% to 20% of the work a radiologist with subspecialty training is asked to perform. This is true for the vast majority of radiology practices, with the possible exception of those practices that employ more than 20 radiologists. Our clinical colleagues expect from us a depth of medical knowledge and familiarity with all imaging modalities suitable to address their clinical questions, regardless of our favored subspecialty. To remain relevant to them we need to stay current at their level.

Commensurate with an explosion of knowledge in medicine the number of pages for this volume have more than doubled, while radiologists have been squeezed between knowing more and reading faster. Radiology Review Manual has developed over the years from a simple preparatory text for the “oral boards” to something that has kept pace with my own growth in radiology. Since 1987 and between editions I have never stopped working on this book: new (eg, genetic) insights were added, variations in categorizations amended, words tweaked, numbers changed, and statements clarified. It is my humble attempt to put into a single reference much of the information that is or could be relevant to my practice and, hopefully, also yours. The decision for inclusions or omissions herein have always been governed by my own practical needs. We have conducted a survey among radiology residents to help us with the decision what topics to delete in an effort to diminish the number of pages. The results showed such a wide variation in opinions that I didn’t have the guts to wield the eraser at all. A single author book does not require collaboration, and thankfully I didn’t have to defend this decision.

The popularity of the “green giant” or the “green bible”, as it has been dubbed by residents, and the continued impressive number of sales and several translations into other languages confirms the usefulness of this type of publication. The outline style chosen for the sake of conserving space provides only an extract of information and may, at times, jeopardize the intended meaning of statements without any prior background knowledge of the subject. Accordingly, be careful, this book is not intended for the uninitiated.

How to use this book:

I have selected one of many possible ways to organize a book of this size and scope with the intent

to cover all modalities and provide room for growth and change over time. The material is presented anatomically from head to heel (when possible) to avoid duplications and save space. Systemic diseases have been forced into this topographical scheme rather than occupying a separate section. Departing from prior editions, NUC imaging findings are now relegated to the respective entity. A general section has been introduced that also includes some aspects about techniques in nuclear medicine in addition to contrast media, statistics, sedation, analgesia, and local anesthesia. As in the 6th edition I hope we can again use the inside of the cover pages to provide immediate access for accepted therapies of contrast reactions.

The organization within the individual chapters follows the practical approach of reading images. Often the initial step of image interpretation is to scrutinize for a radiologic pattern that may help suggest the disease process at hand. Therefore, differential diagnoses of radiologic patterns are presented in the first section of a chapter. Occasionally, important clinical signs and their differential diagnoses, relevant to the practice of radiology, are included in the first portion of a chapter as well. Lists of differential diagnoses can be presented in many fashions. There is no right or wrong way, but there certainly is a chaotic versus an organized approach. Accordingly, an attempt is made to categorize differential diagnostic considerations or etiologies of certain diseases in a manner digestible for recapitulation. It is a common experience that this is not always possible, logically satisfactory, or complete.

The majority of this book deals with disease entities presented in the last section of a chapter. The disease entities are presented in alphabetical order and headed by their most commonly used name with other designations listed below. Not infrequently and without explanations name switches occur from one publication to another. As a radiologic diagnosis should be entertained in context with its probability to be correct, percentages in regard to frequency of signs and symptoms are included liberally, often giving the lowest and the highest number found in the literature. The truth may be somewhere in between for nonselected patient populations, and occasionally a third number is provided between the high and low number as the most frequently cited. I had to arbitrate choices when different or contradictory results are found in the literature – unfortunately, an occurrence not at all infrequent.

This latest edition includes text on a gray background to guide the reader toward an emphatic statement made by a speaker or author on a particular topic.

These two sections in each chapter are separated by a few pages of functional, anatomic, or embryologic aspects. Mnemonics (which I personally abhor) have been liberally added. The index, which selectively refers to those pages with significant information, concludes the manual and is usually the starting point for many. The index also includes so-called “buzz words” that are miraculously attached to diseases.

Acknowledgement:

Various sources are responsible for the content: individuals (named in prior editions), ACR syllabi, handouts from various CME courses, major textbooks, hand-written notes taken during lectures, feed-back from board examinees and most importantly the journals dedicated to imaging with brilliant review articles, in particular the practice-oriented publication of Radiographics. Accordingly, the material in this book is a compilation and extraction of other’s work presented from my perspective of relevance and perhaps with omissions of my ignorance. Our radiologic ancestors, mentors, teachers and scientists alike, throughout the world deserve our admiration and gratitude for the collective knowledge passed on to us for the benefit of our profession and our

patients. I realize, in retrospect, that the omission of references may present a problem when certain statements appear unlikely and their verification has to be left to the user. For my defense, I can say that I have tried to extract all data as diligently as possible.

I sincerely hope that Radiology Review Manual will serve you in your preparation for the board exam, in teaching situations, and particularly in your daily work assignments — the way it continues to help me.

Green Bay, August 2016

CONTENTS

ABBREVIATIONS

√	radiologic sign
•	clinical sign, symptom
=	equals, is
≠	is not
@	at anatomic location of
/	or, per
+	and, plus, with
±	with or without
<	less than
>	more than, over
›	separation of points
»	method
◊	important comment
→	leads to, is followed by
←	due to, 2° to, caused by
↑	increased
⇑	much increased
↓	decreased
⇓	much decreased
↔	unchanged
~	about, approximately
÷	ratio
1°	primary
2°	secondary
2-D	two-dimensional
3-D	three-dimensional
5-HIAA	5-hydroxyindole acetic acid

aa.	**arteries**
AAA	abdominal aortic aneurysm
AAAs	abdominal aortic aneurysms
ABC	aneurysmal bone cyst
ABER	abduction + external rotation
ABO	blood group
ABR	American Board of Radiology

AC	abdominal circumference
ACA	anterior cerebral artery
ACE	angiotensin I–converting enzyme
ACEI	angiotensin-converting enzyme inhibitor
ACL	anterior cruciate ligament
aCom	anterior communicating artery
ACR	American College of Radiology
ACTH	adrenocorticotropic hormone
ADC	apparent diffusion coefficient
ADH	antidiuretic hormone; atypical ductal hyperplasia
ADPKD	adult polycystic kidney disease
AF-AFP	amniotic fluid alpha-fetoprotein
AFI	amniotic fluid index
AFP	alpha-fetoprotein
AICA	anterior inferior cerebellar artery
AIDS	acquired immune deficiency syndrome
AIP	acute interstitial pneumonia
AJCC	American Joint Committee on Cancer
ALARA	as low as reasonably achievable
AlkaPhos	alkaline phosphatase
ALL	acute lymphoblastic leukemia
ALPSA	**a**nterior **l**abroligamentous **p**eriosteal **s**leeve **a**vulsion
ALSA	aberrant left subclavian artery
ALT	alanine aminotransferase
AMA	antimitochondrial antibody
AML	acute myeloblastic leukemia; angiomyolipoma
aML	anterior mitral valve leaflet
AMLs	angiomyolipomas
ANA	antinuclear antibodies
ANCA	antineutrophil cytoplasmic autoantibodies
Angio	angiography
ANT	anterior
Ao	aorta
AP	anteroposterior; arterial phase; alkaline phosphatase
APA	aldosterone producing adenoma
aPL-ab	antiphospholipid antibody
approx.	approximately
APUD	amine precursor uptake and decarboxylation
APUDomas	endocrine cells tumors
APVR	anomalous pulmonary venous return

APW	absolute percentage washout
ARA-C	arabinoside C
ARDS	acute respiratory distress syndrome
ARF	acute renal failure
AS	aortic stenosis
ASA	acetylsalicylic acid
ASD	atrial septal defect
ASH	asymmetric septal hypertrophy
AST	aspartate aminotransferase
ATN	acute tubular necrosis
ATP	adenosine triphosphate
AV	arteriovenous; atrioventricular
AVF	arteriovenous fistula
AVM	arteriovenous malformation
AVMs	arteriovenous malformations
AVN	avascular necrosis
AVNA	atrioventricular node artery
Ba	barium
BAH	bilateral adrenal hyperplasia
BAL	bronchoalveolar lavage
BALT	bronchus-associated lymphoid tissue
BCG	bacille Calmette-Guérin
BCNU	bis-chloronitrosourea
BDI	basion-dens interval
BE	barium enema
BF	blood flow
b.i.d.	*bis in die*, Latin = twice per day
BIDA	butyl iminodiacetic acid
BI-RADS	Breast Imaging Reporting and Data System
BIH	benign intracranial hypertension
BKG	background
BKG_{counts}	background counts
BLC	biceps-labral complex
BLL	benign lymphoepithelial lesions
BMD	bone marrow density
BOOP	bronchiolitis obliterans organizing pneumonia
BP	blood pressure
BPD	biparietal diameter
BPH	benign prostatic hyperplasia

bpm	beats per minute
BPP	biophysical profile
Bq	Becquerel (1 Bq = one nucleus decays per sec)
BRCA	breast cancer suppressor gene
BSA	body surface area
BSO	bilateral salpingo-oophorectomy
Bx	biopsy
Ca	calcium
Ca2+	calcium ion
c-ANCA	cytoplasmic pattern of antineutrophil cytoplasmic autoantibodies
CA-125	cancer antigen 125
CABG	coronary artery bypass grafting
CAD	coronary artery disease
CADASIL	cerebral autosomal dominant arteriopathy with subcortical infarcts and leukoencephalopathy
CAM	cystic adenomatoid malformation
CBD	common bile duct
CBF	cerebral blood flow
cBPD	corrected biparietal diameter
CBV	cerebral blood volume
CC	craniocaudad
CCA	common carotid artery
CCK	cholecystokinin
CCMC	common carpometacarpal joint
CCNU	1-(2-Chloroethyl)-3-cyclohexyl-1-nitrosourea
CD4	specialized lymphocyte responsible for cell-mediated immunity
CDC	Center for Disease Control
CDH	Congenital Diaphragmatic Hernia
CEA	carcinoembryonic antigen
CECT	contrast-enhanced computed tomography
CEMR	contrast-enhanced MR
CF	cystic fibrosis
CFI	color flow imaging
CFTR	cystic fibrosis transmembrane regulator gene
cGy	centigray = rad
CHAOS	Congenital high airway obstruction syndrome
CHD	common hepatic duct; congenital heart defect
CHF	congestive heart failure
CLL	chronic lymphatic leukemia

cm	centimeter
cm^2	square centimeter
cm^3	cubic centimeters
CMC	carpometacarpal
CME	continuing medical education
CML	chronic myelogenous leukemia
CMV	Cytomegalovirus
CN	cranial nerve
CNS	central nervous system
CO	carbon monoxide
CoA	coarctation of aorta
COPD	chronic obstructive pulmonary disease
COW	circle of Willis
CP	cerebellopontine
CPA	cerebellopontine angle
CPAP	continuous positive airway pressure
CPD	cardiopulmonary disease
CPDN	cystic partially differentiated nephroblastoma
cpm	counts per min
CPPD	calcium pyrophosphate dihydrate
CPR	cardiopulmonary resuscitation
cps	counts per sec
cRCC	conventional renal cell cancer; cystic renal cell cancer
CRF	chronic renal failure
CRL	crown rump length
CRT	cathode ray tube
CSF	cerebrospinal fluid
CSI	chemical shift imaging
CST	contraction stress test
C/T	cardiothoracic ratio
CT	computed tomography
CTA	computed tomography angiogram
CVA	cerebrovascular accident
CVC	central venous catheter
CVJ	craniovertebral junction
CVS	chorionic villus sampling
CWP	coal worker's pneumoconiosis
Cx	complication
CXR	chest x-ray
CXRs	chest x-rays

d	day(s)
D5W	solution of 5% dextrose in water
DCBE	double-contrast barium enema
DCIS	ductal carcinoma in situ
DDH	developmental dysplasia of hip
DDx	differential diagnosis
DES	diethylstilbestrol
DEXA	dual energy X-ray absorptiometry
DFSP	dermatofibrosarcoma protuberans
DIC	disseminated intravascular coagulation
DIDA	diethyl iminodiacetic acid
DIP	desquamative interstitial pneumonia; distal interphalangeal
DISH	diffuse idiopathic skeletal hyperostosis
DISIDA	diisopropyl iminodiacetic acid
dist	distal
DIT	diiodotyrosine
DLCL	diffuse large cell lymphoma
D_LCO	diffusion capacity of lung for carbon monoxide
DMSA	dimercaptosuccinic acid
DORV	double outlet right ventricle
DPLD	diffuse parenchymal lung disease
DSA	digital subtraction angiography
DTPA	diethylenetriamine pentaacetic acid
DVT	deep vein thrombosis
DWI	diffusion weighted images
Dx	diagnosis
dz	disease
EAC	external auditory canal
EBV	Epstein-Barr virus
EC-cells	enterochromaffin cells
ECA	external carotid artery
ECD	endocardial cushion defect; ethyl cysteinate dimer
ECF	extracellular fluid
ECG	electrocardiogram
ECHO	echocardiogram; enteric cytopathic human orphan (virus)
ECMO	extracorporeal membrane oxygenation
EDD	enddiastolic diameter
EDTA	ethylenediaminetetraacetic acid

EDV	enddiastolic volume
EEG	electroencephalogram
EF	ejection fraction
EFW	estimated fetal weight
EG	eosinophilic granuloma
eg	exempli gratia
EGA	estimated gestational age
EHDP	ethylene hydroxydiphosphonate
EKG	electrocardiogram
ELISA	enzyme-linked immunosorbent assay
EMA	epithelial membrane antigen
ENT	ear, nose and throat
ErbB	epidermal growth factor receptor gene
ERC	endoscopic retrograde cholangiography
ERCP	endoscopic retrograde cholangiopancreatography
ERPF	effective renal plasma flow
ERV	expiratory reserve volume
ESD	endsystolic diameter
esp.	especially
ESR	erythrocyte sedimentation rate
EtOH	ethanol
ESV	end-systolic volume
F	female; fluorine
Fab	fragment antigen binding
FAI	femoroacetabular impingement
FAP	familial adenomatous polyposis
FDA	Federal Drug Administration
FDG	fluorodeoxyglucose
Fe^{2+}	ferrous ion
Fe^{3+}	ferric state
FEV	forced expiratory volume
FEV_1	FEV at 1 sec
FEV_3	FEV at 3 sec
FHM	fetal heart motion
FIGO	Fédération Internationale de Gynécologie et d'Obstétrique
FISH	fluorescence in situ hybridization
FK-506	code number for tacrolimus
FL	femur length
FLAIR	fluid-attenuated inversion recovery sequence

FLASH	fast low-angle shot
FN	false negative
FNAB	fine needle aspiration biopsy
FNH	follicular nodular hyperplasia
FOOSH	fall on outstretched hand
FP	false positive
Fr	French = unit of linear measure of circumference (1 F = 1/3 mm ≈ 1 mm in diameter)
FRC	functional residual capacity
FS	fractional shortening
FSE	fast spin echo
FSH	follicle stimulating hormone
FVC	forced vital capacity
FWHM	full-width at half-maximum
Fx	fracture
GA	gestational age
GB	gallbladder
GBM	glioblastoma multiforme
GCT	giant cell tumor; granulosa cell tumor
GCTs	giant cell tumors
Gd	gadolinium
GDA	gastroduodenal artery
GE	gastroesophageal
GER	gastroesophageal reflux
GERD	gastroesophageal reflux disease
GFR	glomerular filtration rate
GH	growth hormone
GHA	glucoheptonate
GI	gastrointestinal
GIST	gastrointestinal stromal tumor
GMP	guanosine monophosphate
GMRH	germinal matrix–related hemorrhage
GN	glomerulonephritis
GNRH	gonadotropin releasing hormone
GRASS	gradient recalled acquisition in steady state
GRE	gradient refocused echo
GS	gestational sac
GSV	great saphenous vein
GnRH	gonadotropin releasing hormone

GU	genitourinary
Gy	1 gray = absorption of 1 joule of ionizing radiation by 1 kilogram of matter = 1 J • kg^{-1} = 1 m2 • sec^{-2}
γGT	gamma-glutamyltransferase
HAART	highly active antiretroviral therapy
HAGL	humeral avulsion of the glenohumeral ligament
Hb	hemoglobin
HBME-1	mouse monoclonal antibody to mesothelioma
HBP	high blood pressure
HBV	hepatitis B virus
HC	head circumference
HCC	hepatocellular carcinoma
HCCs	hepatocellular carcinomas
hCG	human chorionic gonadotropin
HCl	hydrochloric acid
Hct	hematocrit
HD	Hodgkin disease
HELLP	hemolysis, elevated liver enzymes, low platelets
Hg	mercury
HHV_8	human herpes virus type 8
HIAA	hydroxyindole acetic acid
HIDA	hepatic 2,6-dimethyl iminodiacetic acid
HIE	hypoxic ischemic encephalopathy
Histo	histology
HIV	human immunodeficiency virus
HL	Hodgkin lymphoma
HLA	human leukocyte antigen
HMB-45	monoclonal antibody against human melanoma black
HMPAO	hexamethylpropyleneamine oxime = exametazime
HNP	herniated nucleus pulposus
HOCM	hypertrophic obstructive cardiomyopathy; high-osmolar contrast media
HPF	high power field (400 x magnification)
HPO	hypertrophic pulmonary osteoarthropathy
HPS	hypertrophic pyloric stenosis
HPT	hyperparathyroidism
HPV	human papilloma virus
hr	hour(s)
HRCT	high-resolution CT
HRT	hormone replacement therapy

HSA	human serum albumin
HSG	hysterosalpingography
HSV	herpes simplex virus
HTN	hypertension
HU	Hounsfield unit
HV	hepatic vein
HypoPT	hypoparathyroidism
Hx	history
IAA	interruption of aortic arch
IAC	internal auditory canal
ICA	internal carotid artery
ICBT	intercostal bronchial trunk a.
ICP	intracranial pressure
IDA	iminodiacetic acid
IDC	invasive ductal carcinoma
IDDM	insulin-dependent diabetes mellitus
IDM	infant of diabetic mother
ie	id est
IgA	Immunoglobulin A
IgE	Immunoglobulin E
IgG	Immunoglobulin G
IGL	inferior glenohumeral ligament
IGHLC	inferior glenohumeral labroligamentous complex
IGL	inferior glenohumeral ligament
IgM	immunoglobulin M
IHSS	idiopathic hypertrophic subaortic stenosis
IIP	idiopathic interstitial pneumonia
ILC	invasive lobular carcinoma
IM	intramuscular
IMA	inferior mesenteric artery
IMH	intramural hematoma
IMV	inferior mesenteric vein
In	indium
inf	inferior
intermed	intermediate
IPF	idiopathic pulmonary fibrosis
IPH	idiopathic pulmonary hemosiderosis; intraparenchymal hemorrhage
IPMT	intraductal papillary mucinous tumor
IQ	intelligence quotient

IR	inversion recovery
IRP	international reference preparation
IRU	inferior radioulnar joint
IRV	inspiratory reserve volume
IS	iliosacral; international standard
IU	international unit = amount of a substance, based on measured biological activity or effect
IUD	intrauterine device
IUGR	intrauterine growth retardation
IUP	intrauterine pregnancy
IV	intravenous
IVC	inferior vena cava
IVDA	intravenous drug abuse
IVH	intraventricular hemorrhage
IVP	intravenous pyelogram
IVS	intraventricular septum
IVU	intravenous urogram
JAA	juxtaposition of atrial appendages
KCC	Kulchitsky cell carcinoma
kDa	atomic weight in terms of kilodaltons
keV	1 kiloelectron volt = 1.60217646 × 10-16 joules
kV	kilovolt
kVp	kilovolt peak
KUB	kidney + ureter + bladder on one film
L	left
L-DOPA	3-(3,4-dihydroxyphenyl)-levo-alanin
LA	left atrium
LAD	left anterior descending
LAO	left anterior oblique
LAT	lateral
LATS	long-acting thyroid stimulating
lbs	pounds (*Libra pondo*, Latin)
LCA	left coronary artery
LCH	Langerhans cell histiocytosis
LCIS	lobular carcinoma in situ
LCL	lateral collateral ligament
LCx	left circumflex coronary artery

LDH	lactate dehydrogenase
LE	lupus erythematosus
LES	lower esophageal sphincter
LFTs	liver function tests
LGA	large for gestational age
LGE	late gadolinium-induced enhancement
LH	luteinizing hormone
LHBB	long head of biceps brachii
LHRH	luteinizing hormone releasing hormone
lig.	ligament
ligg.	ligaments
LIP	lymphocytic interstitial pneumonitis
LL	lower lobes
LLL	left lower lobe
LLQ	left lower quadrant
LM	left main coronary artery; lateromedial
LMP	last menstrual period
Lnn	lymph nodes
LOCM	low-osmolar contrast media
LPA	left pulmonary artery
LPD	lymphoproliferative disease
LPO	left posterior oblique
LPV	left portal vein
L/S	Lecithin-Sphingomyelin (ratio)
LSA	left subclavian artery
LSD	lysergic acid diethylamide
LUL	left upper lobe
LUQ	left upper quadrant
LV	left ventricle
LVEF	left ventricular ejection fraction
LVET	left ventricular ejection time
LVFT1	left ventricular fast filling time
LVOT	left ventricular outflow tract
LVPW	left ventricular posterior wall

M	male
m	meter
m.	muscle
MA	menstrual age
MAA	macroaggregated albumin

MAG	mercaptoacetyltriglycine
MAI	Mycobacterium avium intracellulare
MALT	mucosa-associated lymphoid tissue
Mammo	mammography
max.	maximum
MBC	maximum breathing capacity
MBq	mega Becquerel = 106 Bq
MCA	middle cerebral artery
MCDK	multicystic dysplastic kidney
mCi	millicurie (1 mCi = 3.7×10^7 disintegrations per sec)
MCP	metacarpophalangeal
MCL	medial collateral ligament
MDMA	3,4-methylenedioxymethamphetamine
MDP	methylene diphosphonate
MEA	multiple endocrine adenomas
MED	medial
MELAS	**M**itochondrial myopathy, **E**ncephalopathy, **L**actic acidosis, **A**nd **S**trokelike episodes
MEN	multiple endocrine neoplasms
mEq	milliequivalent
mets	metastases
MFH	malignant fibrous histiocytoma
MGL	middle glenohumeral ligament
mGy	absorbed energy of ionizing radiation (1 Gy = 1 J • kg^{-1} = 1 m^2 • sec^{-2})
MHA	microhemagglutination assay
MIBG	metaiodobenzylguanidine
MIBI	methoxyisobutylisonitril
min.	minimum
min	minute(s)
MIP	maximum intensity projection
MIT	monoiodotyrosine
mIU	1 • 10^{-6} IU
ML	middle lobe
MLCN	multilocular cystic nephroma
MLO	mediolateral oblique
mm.	muscles
MMAA	mini-microaggregated albumin colloid
MMFR	maximal midexpiratory flow rate
mo	month(s)
MoM	multiple of mean

MPA	main pulmonary artery
MPS	mucopolysaccharidosis
MPV	main portal vein
MR	magnetic resonance
MRA	magnetic resonance angiography
MRCP	magnetic resonance cholangiopancreatography
MRV	magnetic resonance venography
MS-AFP	maternal serum - fetoprotein
mSv	millisievert (1 Sv = 1 J/kg)
MT	metatarsal
MTP	metatarsophalangeal
MTT	mean transit time
MUGA	multiple gated acquisition
MV	mitral valve
MVA	motor vehicle accident
MVC	motor vehicle collision
Myelo	myelography
NASCET	North American symptomatic endarterectomy trial
N.B.	nota bene
NCCT	noncontrast CT
NECT	nonenhanced computed tomography
NF1	neurofibromatosis type 1
NG	nasogastric
NHL	non-Hodgkin lymphoma
NIDDM	non-insulin dependent diabetes mellitus
nn.	nerves
NMLE	non-masslike enhancement
NOS	not otherwise specified
npl	neoplasm
NPO	nulla per os
NPV	negative predictive value
NRC	Nuclear Regulatory Commission
NSAID	nonsteroidal antiinflammatory drug
NSAIDs	nonsteroidal antiinflammatory drugs
NSIP	nonspecific interstitial pneumonia
NST	nonstress test
NTD	neural tube defect
NTDs	neural tube defects
NUC	nuclear medicine

OB	**obstetrical**
OB-US	obstetrical ultrasound
OBL	oblique
OEIS	omphalocele, (bladder) exstrophy, imperforate anus, spinal defects
OFD	occipitofrontal diameter
OHSS	ovarian hyperstimulation syndrome
OI	osteogenesis imperfecta
OIH	orthoiodohippurate
OKC	odontogenic keratocyst
P	phosphorus
p-ANCA	perinuclear antineutrophil cytoplasmic autoantibodies
PA	posteroanterior; pulmonary artery
PACs	premature atrial contractions
PAH	para-aminohippurate; precapillary pulmonary arterial hypertension
PALM	premature with accelerated lung maturity
PAP	primary atypical pneumonia; pulmonary alveolar proteinosis
PAPVR	partial anomalous pulmonary venous return
PAS	periodic acid Schiff
PASH	pseudoangiomatous stromal hyperplasia
Path	pathology
PAVM	pulmonary arteriovenous malformation
PAWP	pulmonary artery wedge pressure
PBF	pulmonary blood flow
PCA	posterior cerebral artery
PCKD	polycystic kidney disease
PCL	posterior cruciate ligament
pCom	posterior communicating artery
PCP	Pneumocystis carinii pneumonia
PCWP	pulmonary capillary wedge pressure
PD	posterior descending artery
PDA	patent ductus arteriosus
PE	pulmonary embolism
PEEP	positive end expiratory pressure
PEP	preejection period
PET	positron emission tomography, pancreatic endocrine tumor
PFT	pulmonary function tests
pHPT	primary hyperparathyroidism
PHPV	persistent hyperplastic primary vitreous

PHypoPT	pseudohypoparathyroidism
PICA	posterior inferior cerebellar artery
PID	pelvic inflammatory disease
PIE	pulmonary infiltrate with eosinophilia; pulmonary interstitial emphysema
PIOPED	prospective investigation of pulmonary embolus detection
PIP	proximal interphalangeal
PIPIDA	paraisopropyl iminodiacetic acid
PLCH	pulmonary Langerhans cell histiocytosis
PLSA	posterolateral segment artery
pML	posterior mitral valve leaflet
PMMA	polymethylmethacrylate
PMN	polymorphonuclear
PMNs	polymorphonuclears
PMT	photomultiplier tube
PNET	primitive neuroectodermal tumor
PNST	peripheral nerve sheath tumor
PO	*per os*, Latin = by mouth
pO_2	oxygen pressure
POST	posterior
PPD	purified protein derivative
PPG	photoplethysmography
PPHypoPT	pseudopseudohypoparathyroidism
ppm	parts per million
PPROM	preterm premature rupture of membranes
PPV	positive predictive value; positive-pressure ventilation
pRCC	papillary renal cell cancer
preval	prevalence
p.r.n.	*pro re nata*, Latin = as the circumstance arises
PS	pulmonary stenosis
PSA	prostate-specific antigen
PSS	progressive systemic sclerosis
PSV	peak systolic velocity
PTA	percutaneous transluminal angioplasty
PTC	percutaneous transhepatic cholangiography
PTH	parathyroid hormone
pTL	posterior tricuspid valve leaflet
PTU	propylthiouracil
PV	portal vein; pulmonary valve
PVC	polyvinyl chloride
PVCs	premature ventricular contractions

PVH	pulmonary venous hypertension
PVL	periventricular leukomalacia
PVNS	pigmented villonodular synovitis
PVP	portal venous phase
PVR	pulse volume recording; postvoid residual
PYP	pyrophosphate
QPS	quantitative perfusion SPECT
R	right
RA	rheumatoid arthritis; right atrium
RAA	right aortic arch; right atrial appendage
rad	radiation absorbed dose, in 1975 replaced by gray (Gy)
RAIU	radioactive iodine uptake
RAO	right anterior oblique
Rb	Rubidium
RB-ILD	respiratory bronchiolitis-associated interstitial lung disease
RBC	red blood cell
RBCs	red blood cells
RCA	right coronary artery
RCC	renal cell carcinoma
RCCs	renal cell carcinomas
RDS	respiratory distress syndrome
rel.	relative
RES	reticuloendothelial system
RHV	right hepatic vein
RI	resistive index
RIBA	recombinant immunoblot assay
RIND	reversible ischemic neurologic deficit
RISA	radioiodine serum albumin
RLAT	right lateral
RLL	right lower lobe
RLQ	right lower quadrant
RML	right middle lobe
RMS	root mean square
ROC	receiver operating characteristic
ROI	region of interest
ROIs	regions of interest
RPF	renal plasma flow
RPO	right posterior oblique

RPV	right portal vein
RPW	relative percentage washout
RSV	respiratory syncytial virus
RTA	renal tubular acidosis
RUL	right upper lobe
RUQ	right upper quadrant
RV	residual volume; right ventricle
RVOT	right ventricular outflow tract
RVT	renal vein thrombosis
Rx	therapy
S1Q3T3	prominent S wave in lead I + Q wave and inverted T wave in lead III
S/P	status post
SAE	subcortical arteriosclerotic encephalopathy
SAG	sagittal
SAH	subarachnoid hemorrhage
SBE	subacute bacterial endocarditis
SBFT	small bowel follow-through
SBO	small bowel obstruction
SCC	squamous cell carcinoma
SCBE	single-contrast barium enema
SCLC	small cell lung cancer
SCMM	sternocleidomastoid muscle
S/D	systolic / diastolic (ratio)
SD	standard deviation
SDS	summed difference score
SE	spin echo
Sens	sensitivity
SGA	small for gestational age
SGL	superior glenohumeral ligament
sHPT	secondary hyperparathyroidism
SI	signal intensity
SIJ	sacroiliac joint
SIS	Second International Standard
SLAP	superior labral tear from anterior to posterior
SLE	systemic lupus erythematosus
SMA	superior mesenteric artery
SMV	superior mesenteric vein
Sn	stannum
SNHL	sensorineural hearing loss

SOB	shortness of breath
S/P	status post
Specif	specificity
SPECT	single photon emission
SPIO	superparamagnetic iron oxide
SQ	subcutaneous
SRS	summed rest score
SSS	summed stress score
STH	somatotrophic hormone
STIR	short tau inversion recovery
supp	suppositorium, suppository
Surg	surgery
SUV	standardized uptake values
SVC	superior vena cava
SVCs	superior venae cavae
T1WI	T1-weighted image
T2WI	T2-weighted image
TAH	total abdominal hysterectomy
TAPVR	total anomalous pulmonary venous return
TB	tuberculosis
TBG	thyroxin-binding globulin
Tc	Technetium
TCC	transitional cell carcinoma
TDLU	terminal ductal lobular unit
TDLUs	terminal ductal lobular units
TE	echo time
TEF	tracheoesophageal fistula
TGA	transposition of great arteries
TGV	transposition of great vessels
tHPT	tertiary hyperparathyroidism
TIA	transitory ischemic attack
TIAs	transitory ischemic attacks
TLC	total lung capacity
Tm	transport maximum across tubular cells
T_{max}	time to maximum peak
TMB-IDA	2,4,6-trimethylbromo-acetanilide iminodiacetic acid
TN	true negative
TNF	tumor necrosis factor
TNM	tumor nodes metastasis

TOA	tuboovarian abscess
TOF	tetralogy of Fallot; time of flight
TORCH	toxoplasmosis, rubella, cytomegalovirus, herpes virus
TP	true positive
TPN	total parenteral nutrition
TPROM	term premature rupture of membranes
TR	repetition time
TRH	thyrotropin-releasing hormone
TRV	transverse
TSC	tuberous sclerosis
TSH	thyroid-stimulating hormone
TURP	transurethral resection of prostate
TV	tidal volume
UA	umbilical artery
UCL	ulnar collateral ligament
uE3	unconjugated estriol
UGI	upper gastrointestinal series
UICC	Union Internationale Contre le Cancer
UIP	usual interstitial pneumonia
UL	upper lobe
UPJ	ureteropelvic junction
URI	upper respiratory infection
US	ultrasound
USA	United States of America
USP	United States Pharmacopoeia
USP XX	United States Pharmacopoeia, 20th edition
UTI	urinary tract infection
UTIs	urinary tract infections
UVJ	ureterovesical junction
Uvol	urine volume
VACTERL	vertebral, **a**norectal, **c**ardiovascular, **t**racheo-**e**sophageal fistula, **r**enal, **l**imb anomalies
VC	vital capacity
VCUG	voiding cystourethrogram
VDRL	venereal disease research laboratory
vHL	Von Hippel-Lindau disease
VIP	vasoactive intestinal peptides
VMA	vanillylmandelic acid

VP	ventriculoperitoneal
V/Q	ventilation perfusion
VR	Virchow-Robin space
vs.	versus
VSD	ventricular septal defect
VSDs	ventricular septal defects
VUR	vesicoureteral reflux
vv.	venae, veins
WAGR	Wilms tumor, aniridia, genital abnormalities, mental retardation
WBC	white blood cell
WBCs	white blood cells
WDHA	watery diarrhea, hypokalemia, achlorhydria
WDHH	watery diarrhea, hypokalemia, hypochlorhydria
WM	white matter
wk	week(s)
w/o	without
WPW	Wolff-Parkinson-White
wt/vol	weight/volume percent = amount of solute in g per amount of solution in mL
XGP	xanthogranulomatous pyelonephritis
YS	yolk sac
yr	year(s)

TREATMENT OF ADVERSE CONTRAST REACTIONS[1]

PRINCIPLES OF TREATMENT

1. Give high doses of oxygen
2. Infuse physiologic fluids
3. Establish adequate airway
4. Monitor heart rate & blood pressure

◊ No therapeutic role in acute adverse reaction: antihistamines, H_2 antagonists, corticosteroids

VASOVAGAL REACTION

- **hypotension** (systolic blood pressure < 80 mmHg) **with** sinus **bradycardia** (pulse < 60 bpm)
- dizziness, diaphoresis
- loss of consciousness

⇒ Monitor vital signs

⇒ Leg elevation > 60° + Trendelenburg position

⇒ Secure airway + **O_2** 6–10 L/min

⇒ Secure IV access + rapid IV infusion of isotonic Ringer's lactate / normal saline

if symptoms persist, add:

⇒ **atropine** slowly IV 0.6–1.0 mg

⇒ Repeat atropine every 3–5 min slowly IV up to a total dose of 0.04 mg/kg (3 mg) in adults [pediatric: 0.02 mg/kg IV; starting dose: min. 0.1 mg, max. 0.6 mg; may repeat to total dose of 2 mg]

DERMAL CONTRAST REACTION

- hives = urticaria
- itching = pruritus
- flushing
- facial angioedema (= nonpruritic SQ edema of eyelid / peroral)

Mild Urticaria

⇒ Discontinue injection if not completed

⇒ No treatment needed in most cases

⇒ H_1-antihistamine, ie

diphenhydramine (Benadryl®) PO/IM/IV 25–50 mg

or

hydroxyzine (Vistaril®) PO/IM/IV 25–50 mg

Severe Urticaria

add H_2-antihistamine:

⇒ **cimetidine** (Tagamet®) 300 mg PO / slowly IV (diluted in 20 mL D5W solution)

[pediatric: 5–10 mg/kg diluted in 20 mL D5W solution]
or
ranitidine (Zantac®) 50 mg PO / slowly IV (diluted in 20 mL D5W solution)

if widely disseminated:
⇒ IV line started + kept open (with normal saline / Ringer's lactate)
⇒ **epinephrine IV** (1÷10,000) IV slowly over 2–5 min 1.0 mL (= 0.1 mg) if no cardiac contraindication

NAUSEA / VOMITING

may be the 1st signs of a more severe reaction
⇒ watch patient closely

RESPIRATORY DISTRESS

- wheezing (inconsequential)
- bronchoconstriction (life-threatening)
- laryngeal edema (life-threatening)

Facial / Laryngeal Edema

⇒ **epinephrine SQ** (1÷1,000) 0.1–0.2 mL (= 0.1–0.2 mg)
or – if patient hypotensive –
epinephrine (1÷10,000) slowly IV 1.0 mL (= 0.1 mg)
Repeat after 15 min up to a maximum of 1.0 mg
⇒ **O_2** 6–10 L/min (via mask)
monitor: ECG; O_2 saturation (pulse oximeter); BP

If not responsive to therapy:
⇒ Seek assistance (CODE team)
⇒ Consider intubation

Bronchospasm (isolated)

⇒ **O_2** 6–10 L/min (by mask, not nasal prongs)
monitor: ECG; O_2 saturation (pulse oximeter); BP
⇒ β_2-agonist metered dose inhaler in 2–3 deep inhalations: **metaproterenol** (Alupent®) / **terbutaline** (Brethaire®) / **albuterol** (Proventil®)
NOT: diphenhydramine as it thickens secretions

If unrelieved
with normal blood pressure + stable bronchospasm
⇒ **epinephrine SQ** (1÷1,000) 0.1–0.2 mL (= 0.1–0.2 mg); may give 0.3 mg
[pediatric: 0.01 mg/kg up to 0.3 mg max.]
with decreased blood pressure + progressive bronchospasm
⇒ **epinephrine IV** (1÷10,000) slowly over 2–5 min IV 1.0 mL (= 0.1 mg)
[pediatric: 0.01 mg/kg IV]
Repeat after 15 min up to a maximum of 1.0 mg

Alternatively

⇒ **aminophylline** 6 mg/kg IV in D5W over 15–20 min (loading dose); then 0.4–1.0 mg/kg/hr

Cx: hypotension, cardiac arrhythmia

or

terbutaline 0.25–0.50 mg IM/SQ

⇒ 200–400 mg hydrocortisone IV

if unsuccessful, may require intubation

if anxiety exacerbates bronchospasm, sedation with 5–10 mg Demerol IV

⇒ Call for assistance (CODE team) for severe bronchospasm / if O_2 saturation persists < 88%

TREATMENT OF ADVERSE CONTRAST REACTIONS[2]

ANAPHYLACTOID REACTION

= acute rapidly progressing generalized systemic reaction characterized by multisystem involvement

- tachycardia (pulse > 100 bpm)
- hypotension (systolic blood pressure < 80 mmHg)
- dizziness, diaphoresis
- loss of consciousness

Hypotension with Tachycardia

⇒ leg elevation > 60° + Trendelenburg position
⇒ monitor: ECG; pulse oximeter; BP
⇒ **O_2** 6–10 L/min (via mask, not nasal prongs)
⇒ rapid IV infusion of isotonic Ringer's lactate / normal saline
⇒ suction as needed

if poorly responsive to fluid therapy add vasopressors
⇒ call CODE
⇒ **epinephrine IV** (1÷10,000) slowly over 2–5 min IV 1.0 mL (= 0.1 mg);
[pediatric: 0.02 mg/kg IV; starting dose of min. 0.1 mg to max. 0.6 mg; may repeat to 2 mg total dose]
repeat after 15 min up to a maximum of 1.0 mg (titrated to effect)
⇒ dopamine

if still poorly responsive:
⇒ transfer to ICU

in adults without IV access:
⇒ **epinephrine SQ** (1÷1,000) 0.3 mL (= 0.3 mg)

in infants / children:
⇒ epinephrine SQ (1÷1,000) with body weight determining the correct dose

Seizure / Convulsion

⇒ protect patient from injury
⇒ monitor airway from obstruction by tongue
⇒ suction as needed
⇒ **O_2** 6–10 L/minute (by mask)

if uncontrolled:
⇒ **diazepam** (Valium®) 5.0 mg / **midazolam** (Versed®) 2.5 mg IV
⇒ monitor: ECG, O_2 saturation (pulse oximeter), BP

if longer effect needed:
⇒ obtain consultation

⇒ **phenytoin** (Dilantin®) infusion 15–18 mg/kg at 50 mg/minute
⇒ consider CODE for intubation

Pulmonary Edema

⇒ Elevate torso
⇒ Apply rotating tourniquets for venous compression
⇒ **O_2** 6–10 L/minute (via mask)
⇒ **furosemide** (Lasix®) 40 mg IV, slow push
⇒ Consider morphine
⇒ Transfer to ICU
⇒ Corticosteroids optional

SEVERE HYPERTENSION

⇒ monitor: ECG, pulse oximeter, BP
⇒ IV fluids very slowly to maintain venous access
⇒ **nitroglycerin** 0.4 mg tablet sublingual; may repeat x 3; topical 1–2" strip of 2% ointment
⇒ **sodium nitroprusside** arterial line (infusion pump necessary to titrate)
⇒ transfer to ICU

for pheochromocytoma:

⇒ **phentolamine** (Regitin®)
Adult dose: 5.0 mg IV; Pediatric dose: 1.0 mg IV

ANGINA

⇒ **O_2** 6–10 L/min (via mask, not nasal prongs)
⇒ IV fluids, very slowly
⇒ **nitroglycerin** 0.4 mg, sublingually; may repeat q 15 minutes
⇒ **morphine** 2 mg IV

AIR EMBOLISM

- air hunger, dyspnea, expiratory wheezing, cough
- chest pain, pulmonary edema, tachycardia, hypotension
- stroke ← decreased cardiac output / paradoxical air embolism / pulmonary AVM / R-to-L intracardiac shunt

Rx: ⇒ 100% **O_2** administration
⇒ left lateral decubitus position

CONTRAST EXTRAVASATION

= escape of contrast material from vascular lumen + infiltration of interstitial tissue during injection

Incidence: 0.1–0.4%; no direct correlation with injection flow rate (although frequent with power injectors)

Risk: fragile veins, IV catheter indwelling for many days, multiple puncture attempts during IV placement

Effect: (a) acute inflammatory response (peaking in 24–48 hrs) related to hyperosmolality of

contrast material

(b) compartment syndrome

(c) ulceration + tissue necrosis (as early as 6 hours)

(d) fibrosis

(e) muscle atrophy

- may be asymptomatic; edema, erythema
- swelling, tightness, tenderness, stinging, burning pain

Evaluate for:

(1) Skin injury (blanching, discoloration)
(2) Nerve compromise
(3) Vascular compromise

Dx: (1) Palpate catheter venipuncture site during initial seconds of injection
(2) Ask patient to report any sensation of pain / swelling at injection site

Severe Cx (uncommon): compartment syndrome, skin ulceration, tissue necrosis

Rx: (1) Elevation of affected extremity above heart → decrease capillary hydrostatic pressure
(2) Cold compress → decreases cellular uptake
(3) Warm compress → vasodilatation promotes absorption
(4) Discharge with instructions to watch for symptoms that indicate a need for surgical evaluation
(5) Surgical consultation if
› extravasation > 50 mL
› ↑ in swelling / pain after 2–4 hours
› ↓ in capillary refill time
› change in sensation (paresthesia) in affected limb
› skin ulceration / blistering
(5) Documentation in medical record
(6) Notification of referring physician
(7) 24-hour follow up (phone call, examination)

MUSCULOSKELETAL SYSTEM

DIFFERENTIAL DIAGNOSIS OF MUSCULOSKELETAL DISORDERS

UNIVERSAL DIFFERENTIAL DIAGNOSIS

mnemonic: VINDICATE

Vascular and cardiac
Infectious, **I**nflammatory
Neoplasm
Drugs
Iatrogenic, **I**diopathic, **I**ntoxication
Congenital
Autoimmune, **A**llergic
Trauma
Endocrine and metabolic

DIAGNOSTIC GAMUT OF BONE DISORDERS

Conditions to be considered = "dissect bone disease with a DIATTOM"

Dysplasia + **D**ystrophy
Infection
Anomalies of development
Tumor + tumorlike conditions
Trauma
Osteochondritis + ischemic necrosis
Metabolic disease

Dysplasia = disturbance of bone growth
Dystrophy = disturbance of nutrition

LIMPING CHILD

Limping Child at 1–4 Years

A. CONGENITAL
   1. Developmental dysplasia of hip
B. TRAUMATIC
   1. Toddler's fracture
   2. Nonaccidental trauma
   3. Other fractures
   4. Foreign body
C. INFLAMMATORY
   1. Diskitis

2. Septic arthritis
3. Osteomyelitis
4. Transient synovitis of hip

Limping Child at 4–10 Years

A. TRAUMATIC
B. INFLAMMATORY
   1. Septic arthritis
   2. Osteomyelitis
   3. Transient synovitis of hip
   4. Diskitis
   5. Juvenile rheumatoid arthritis
C. VASCULAR
   1. Legg-Perthes disease

Limping Child at 10–15 Years

A. TRAUMATIC
   1. Stress fracture
   2. Osteochondritis dissecans
   3. Osgood-Schlatter disease
B. INFLAMMATORY
   1. Juvenile rheumatoid arthritis
   2. Ankylosing spondylitis
   3. Septic arthritis
   4. Osteomyelitis
C. HORMONAL
   1. Epiphyseolysis of femoral head

DELAYED BONE AGE

A. CONSTITUTIONAL
   1. Familial
   2. IUGR
B. METABOLIC
   1. Hypopituitarism
   2. Hypothyroidism
   3. Hypogonadism (Turner syndrome)
   4. Cushing disease, steroid therapy
   5. Diabetes mellitus
   6. Rickets
   7. Malnutrition
   8. Irradiation of brain (for cerebral tumor / ALL)
C. SYSTEMIC DISEASE
   1. Congenital heart disease
   2. Renal disease
   3. GI disease: celiac disease, Crohn disease, ulcerative colitis

4. Anemia
5. Bone marrow transplantation (< 5 years of age)

D. SYNDROMES
1. Trisomies
2. Noonan disease
3. Cornelia-de-Lange syndrome
4. Cleidocranial dysplasia
5. Lesch-Nyhan disease
6. Metatropic dwarfism

UPTAKE PATTERN IN BONE LESIONS

Superscan

Cause:

A. METABOLIC
1. Renal osteodystrophy
2. Osteomalacia
√ randomly distributed focal sites of intense activity
= Looser zones = pseudofractures
= Milkman fractures (most characteristic)
3. Hyperparathyroidism
√ focal intense uptake ← site of brown tumors
4. Hyperthyroidism
→ rate of bone resorption > rate of bone formation (= decrease in bone mass)
• hypercalcemia (occasionally)
• elevated alkaline phosphatase
√ radiographically NOT visible
√ susceptible to fracture

B. Widespread bone lesions
1. Diffuse skeletal metastases: prostate, breast, multiple myeloma, lymphoma, lung, bladder, colon, stomach (most frequent)
2. Myelofibrosis / myelosclerosis
3. Aplastic anemia, leukemia
4. Waldenström macroglobulinemia
5. Systemic mastocytosis
6. Widespread Paget disease

√ diffusely increased activity in bones: particularly prominent in axial skeleton, calvarium, mandible, costochondral junctions (= "rosary beading"), sternum (= "tie sternum"), long bones
√ increased metaphyseal + periarticular activity
√ increased bone-to-soft-tissue ratio
√ "absent kidney" sign = little / no activity in kidneys but good visualization of urinary bladder
√ femoral cortices become visible

CAVE: scan may be interpreted as normal, particularly in patients with poor renal function!

Hot Bone Lesions

mnemonic: NATI MAN

Neoplasm
Arthropathy
Trauma
Infection
Metastasis
Aseptic **N**ecrosis

Long Segmental Diaphyseal Uptake

A. BILATERALLY SYMMETRIC
   1. Hypertrophic pulmonary osteoarthropathy
   2. Thigh / shin splints = mechanical enthesopathy
   3. Ribbing disease
   4. Engelmann disease = progressive diaphyseal dysplasia

B. UNILATERAL
   1. Inadvertent arterial injection
   2. Melorheostosis
   3. Chronic venous stasis
   4. Osteogenesis imperfecta
   5. Vitamin A toxicity
   6. Osteomyelitis
   7. Paget disease
   8. Fibrous dysplasia

Doughnut Sign of Bone Lesion

= radiotracer accumulation at periphery of bone lesion with little activity at its center

1. Aneurysmal bone cyst
2. Giant cell tumor
3. Chondrosarcoma
4. Telangiectatic osteosarcoma

Photon-deficient Bone Lesion

= decreased radiotracer uptake

A. Interruption of blood flow in local bone
   = vessel trauma or vascular obstruction by thrombus / tumor
   1. Early osteomyelitis
   2. Radiation therapy
   3. Posttraumatic aseptic necrosis
   4. Sickle cell crisis

B. Replacement of bone by destructive process
   1. Metastases (most common cause): central axis skeleton > extremity, most commonly in carcinoma of kidney + lung + breast + multiple myeloma

2. Primary bone tumor (exceptional)

mnemonic: HM RANT

Histiocytosis X
Multiple myeloma
Renal cell carcinoma
Anaplastic tumors (reticulum cell sarcoma)
Neuroblastoma
Thyroid carcinoma

Radionuclide Uptake in Benign Bone Lesions

A. NO TRACER UPTAKE
   1. Bone island
   2. Osteopoikilosis
   3. Osteopathia striata
   4. Fibrous cortical defect
   5. Nonossifying fibroma

B. INCREASED TRACER UPTAKE
   1. Fibrous dysplasia
   2. Paget disease
   3. Eosinophilic granuloma
   4. Melorheostosis
   5. Osteoid osteoma
   6. Enchondroma
   7. Exostosis

BONE SCLEROSIS

Diffuse Osteosclerosis

mnemonic: 5 M'S To PROoF

Metastases
Myelofibrosis
Mastocytosis
Melorheostosis
Metabolic: hypervitaminosis D, fluorosis, hypothyroidism, phosphorus poisoning
Sickle cell disease
Tuberous sclerosis
Pyknodysostosis, Paget disease
Renal osteodystrophy
Osteopetrosis
Fluorosis

Acquired Syndromes with Increased Bone Density

1. Renal osteodystrophy
2. Osteoblastic metastases
3. Paget disease of bone

4. Erdheim-Chester disease
5. Myelofibrosis
6. Sickle cell disease

Constitutional Sclerosing Bone Disease

1. Progressive diaphyseal dysplasia
2. Infantile cortical hyperostosis
3. Melorheostosis
4. Osteopathia striata
5. Osteopetrosis
6. Osteopoikilosis
7. Pachydermoperiostosis
8. Pyknodysostosis
9. Van Buchem disease
10. Williams syndrome

Sclerosing Bone Dysplasia

Endochondral bone formation:

primary spongiosa forms at 7th week of embryogenesis → resorption around 9th week with conversion into secondary spongiosa → osteoclastic remodeling into trabeculae + medullary cavity

Target sites for endochondral bone formation:

tubular + flat bones, vertebrae, skull base, ethmoids, ends of clavicle

Intramembranous ossification:

= transformation of mesenchymal cells into cortical bone without intervening cartilaginous matrix beginning at 9th week of fetal life to beyond closure of growth plates

Target sites for intramembranous bone formation:

cortex of tubular + flat bones, calvaria, upper facial bones, tympanic temporal bone, vomer, medial pterygoid process

A. DYSPLASIA OF ENDOCHONDRAL OSSIFICATION (PRIMARY SPONGIOSA)
   = failure in resorption + remodeling of primary immature spongiosa by osteoclasts
   √ accumulation of calcified cartilage matrix packing the medullary cavity
   1. Osteopetrosis
   2. Pyknodysostosis

B. DYSPLASIA OF ENDOCHONDRAL OSSIFICATION (SECONDARY SPONGIOSA)
   = errors in resorption + remodeling of secondary spongiosa
   √ focal densities / striations along trabecular bone
   1. Osteopoikilosis
   2. Osteopathia striata

C. DYSPLASIA OF INTRAMEMBRANOUS OSSIFICATION
   = disequilibrium between periosteal bone formation + endosteal bone resorption
   1. Progressive diaphyseal dysplasia
   2. Hereditary multiple diaphyseal sclerosis
   3. Hyperostosis corticalis generalisata
   4. Diaphyseal dysplasia with anemia

5. Oculodento-osseous dysplasia
6. Trichodento-osseous dysplasia
7. Kenny-Caffey syndrome

D. MIXED SCLEROSING DYSPLASIAS = OVERLAP SYNDROME

(a) predominantly endochondral disturbance

1. Dysosteosclerosis
2. Metaphyseal dysplasia (Pyle disease)
3. Craniometaphyseal dysplasia
4. Frontometaphyseal dysplasia

(b) predominantly intramembranous defects

1. Melorheostosis
2. Craniodiaphyseal dysplasia
3. Lenz-Majewski hyperostotic dwarfism
4. Progressive diaphyseal dysplasia

Nonhereditary Sclerosing Dysplasia

1. Intramedullary osteosclerosis
2. Melorheostosis
3. Overlap syndromes
   = disorder of endochondral + intramembranous ossification
   Combination: melorheostosis + osteopoikilosis + osteopathia striata

Solitary Osteosclerotic Lesion

A. DEVELOPMENTAL

1. Bone island

B. VASCULAR

1. Old bone infarct
2. Aseptic / ischemic / avascular necrosis

C. HEALING BONE LESION

(a) trauma: callus formation in stress fracture
(b) benign tumor: fibrous cortical defect / nonossifying fibroma; brown tumor; bone cyst
(c) malignant tumor: lytic metastasis after radiation, chemotherapy, hormone therapy

D. INFECTION / INFLAMMATION
(low-grade chronic infection / healing infection)

1. Osteoid osteoma
2. Chronic / healed osteomyelitis: bacterial, tuberculous, fungal
3. Sclerosing osteomyelitis of Garré
4. Granuloma
5. Brodie abscess

E. BENIGN TUMOR

1. Osteoma
2. Osteoblastoma
3. Ossifying fibroma
4. Healed fibrous cortical defect
5. Enchondroma / osteochondroma

F. MALIGNANT TUMOR
   1. Osteoblastic metastasis: prostate, breast
   2. Lymphoma
   3. Sarcoma: osteo-, chondro-, Ewing sarcoma

G. OTHERS
   1. Sclerotic phase of Paget disease
   2. Fibrous dysplasia

Cortical Sclerotic Lesion in Child

1. Osteoid osteoma
2. Stress fracture
3. Chronic osteomyelitis
4. Healed fibrous cortical defect

Multiple Osteosclerotic Lesions

A. FAMILIAL
   1. Osteopoikilosis
   2. Enchondromatosis = Ollier disease
   3. Melorheostosis
   4. Multiple osteomas: associated with Gardner syndrome
   5. Osteopetrosis
   6. Pyknodysostosis
   7. Osteopathia striata
   8. Chondrodystrophia calcificans congenita
   9. Multiple epiphyseal dysplasia = Fairbank disease

B. SYSTEMIC DISEASE
   1. Mastocytosis = urticaria pigmentosa
   2. Tuberous sclerosis

Bone-within-bone Appearance

= endosteal new bone formation

1. Normal
   (a) thoracic + lumbar vertebrae (in infants)
   (b) growth recovery lines (after infancy)
2. Infantile cortical hyperostosis (Caffey)
3. Sickle cell disease / thalassemia
4. Congenital syphilis
5. Osteopetrosis / oxalosis
6. Radiation
7. Acromegaly
8. Paget disease
9. Gaucher disease

mnemonic: BLT PLT RSD RSD

Bismuth ingestion

Lead ingestion

Thorium ingestion
Petrosis (osteopetrosis)
Leukemia
Tuberculosis
Rickets
Scurvy
D toxicity (vitamin D)
RSD (reflex sympathetic dystrophy)

Dense Metaphyseal Bands

mnemonic: DENSE LINES
D-vitamin intoxication
Elemental arsenic + heavy metals: lead, bismuth, phosphorus
Normal variant
Systemic illness
Estrogen to mother during pregnancy
Leukemia
Infection (TORCH), **I**diopathic hypercalcemia
Never forget healed rickets
Early hypothyroidism (cretinism)
Scurvy, congenital **S**yphilis, **S**ickle cell disease
also: methotrexate therapy

OSTEOPENIA

= decrease in bone quantity maintaining normal quality
√ increased radiolucency of bone:
√ vertical striations in vertebral bodies
√ accentuation of tensile + compressive trabeculae of proximal femur
√ reinforcement lines (= bone bars) crossing marrow cavity about knee
√ cortical resorption of 2nd metacarpal:
√ measuring outer cortical diameter (W) and width of medullary cavity (m) at mid portion of bone and reporting combined cortical thickness (CCT = W + m)
√ subperiosteal tunneling

Categories:

A. DIFFUSE OSTEOPENIA
1. Osteoporosis = decreased osteoid production
2. Osteomalacia = undermineralization of osteoid
3. Hyperparathyroidism
4. Multiple myeloma / diffuse metastases
5. Drugs
6. Mastocytosis
7. Osteogenesis imperfecta

B. REGIONAL OSTEOPENIA

Osteoporosis

= reduced bone mass of normal composition secondary to
(a) osteoclastic resorption (85%): trabecular, endosteal, intracortical, subperiosteal
(b) osteocytic resorption (15%)

Prevalence: 7% of all women aged 35–40 years;
12% for males + females aged 50–79 years;
◊ Most common of all metabolic bone disorders; 14 million worldwide by 2020

Classification:

(a) Primary / involutional osteoporosis ← cumulative bone loss as people age and undergo sex hormone changes
1. Type I (postmenopausal) osteoporosis
= accelerated trabecular bone resorption ← estrogen deficiency
Fracture pattern: spine and wrist
2. Type II (senile) osteoporosis
= proportionate loss of cortical and trabecular bone
Fracture pattern: hip, proximal humerus, tibia, pelvis

(b) Secondary osteoporosis (in 20–30%) = consequence of various medical conditions / use of certain medications

Etiology:

A. CONGENITAL DISORDERS
1. Osteogenesis imperfecta
◊ The only osteoporosis with bending of bones!
2. Homocystinuria

B. IDIOPATHIC (bone loss begins earlier + proceeds more rapidly in women)
1. Juvenile osteoporosis: < 20 years
2. Adult osteoporosis: 20–40 years
3. Postmenopausal osteoporosis: > 50 years
(40–50% lower trabecular bone mineral density in elderly than in young women)
4. Senile osteoporosis: > 60 years
progressively decreasing bone density at a rate of 8% (3%) in females (males) per year

C. NUTRITIONAL DISTURBANCES scurvy; calcium deficiency; protein deficiency (nephrosis, chronic liver disease, alcoholism, anorexia nervosa, kwashiorkor, starvation, malnutrition, malabsorption)

D. ENDOCRINOPATHY Cushing disease, hypogonadism (Turner syndrome, eunuchoidism), hyperthyroidism, hyperparathyroidism, acromegaly, Addison disease, diabetes mellitus, pregnancy, paraneoplastic phenomenon in liver tumors

E. RENAL OSTEODYSTROPHY
decrease / same / increase in spinal trabecular bone; rapid loss in appendicular skeleton

F. IMMOBILIZATION = disuse osteoporosis

G. COLLAGEN DISEASE, RHEUMATOID ARTHRITIS

H. BONE MARROW REPLACEMENT infiltration by lymphoma / leukemia (ALL), multiple myeloma, diffuse metastases, marrow hyperplasia ← hemolytic anemia

I. DRUG THERAPY
corticosteroids, heparin (15,000–30,000 U for > 6 months), methotrexate, excessive alcohol consumption, smoking, Dilantin, aromatase inhibitors, gonadotropin-releasing hormone antagonist

J. RADIATION THERAPY

K. LOCALIZED OSTEOPOROSIS
immobilization / disuse, Sudeck dystrophy, transient osteoporosis of large joints, regional migratory osteoporosis of lower extremities

- serum calcium, phosphorus, alkaline phosphatase frequently normal
- hydroxyproline may be elevated during acute stage

Significant predictors of osteoporotic fractures:

1. Age
2. History of fracture
3. Failed chair test (= inability to rise from a chair in 3 successions without using arms)
4. Fall within past 12 months

Clinical manifestation:

(1) Vertebral compression fracture (HALLMARK)
(2) Femoral fracture: neck + intertrochanteric region
(3) Fracture of distal radius (Colles) and tibia

Technique of Bone Densitometry:

(1) **Single-Photon Absorptiometry** measures primarily cortical bone of appendicular bones, single-energy ^{125}I radioisotope source
Site: distal radius (= wrist bone density), os calcis
Dose: 2–3 mrem
Precision: 1–3%

(2) **Dual-Photon Absorptiometry** radioactive energy source with 2 photon peaks; should be reserved for patients < 65 years of age because of interference from osteophytosis + vascular calcifications
Site: vertebrae, femoral neck
Dose: 5–10 mrem
Precision: 2–4%

(3) **Single X-ray Absorptiometry**
= area projectional technique for quantitative bone density measurement
Site: distal radius, calcaneus
Dose: low
Precision: 0.5–2%

(4) **Dual Energy X-ray Absorptiometry (DXA / DEXA)**
= quantitative digital radiography
◊ Most widely used & most precise technique!
◊ Standard of reference for diagnosis of osteoporosis in conjunction with *Fracture Risk Assessment Tool* at http://www.shef.ac.uk/FRAX/ for results of a 10-year probability of a major osteoporotic fracture in hip, spine, proximal humerus, distal

forearm

Technique:

» mobile x-ray source composed of 2 different photon energy levels (constant + pulsed) moves together with detection system
» rectilinear / fan-beam scanners
» attenuation values of soft tissues are subtracted, leaving only the attenuation values of bone
» lateral scanning of spine increases accuracy without superimposition of posterior elements + marginal osteophytes + vascular calcifications

Advantage:

(1) low radiation dose with higher radiation flux than radioisotope source of dual-photon absorptiometry
(2) uses sites where osteoporotic fractures occur
(3) low cost; ease of use; rapidity of measurement

Limitation of 2-dimensional (areal) technique:

(1) no distinction between cortical + trabecular bone
(2) no discrimination between changes secondary to bone geometry + increased bone density
(3) regulatory oversight for ionizing radiation

Site: (a) lumbar spine (L1–L4)
(b) proximal femur (total hip, femoral neck, trochanter, Ward area)
(c) calcaneus (95% trabecular bone)
(d) forearm (suboptimal ← mostly cortical bone)

Dose: < 3 mrem

Precision: 1–2%

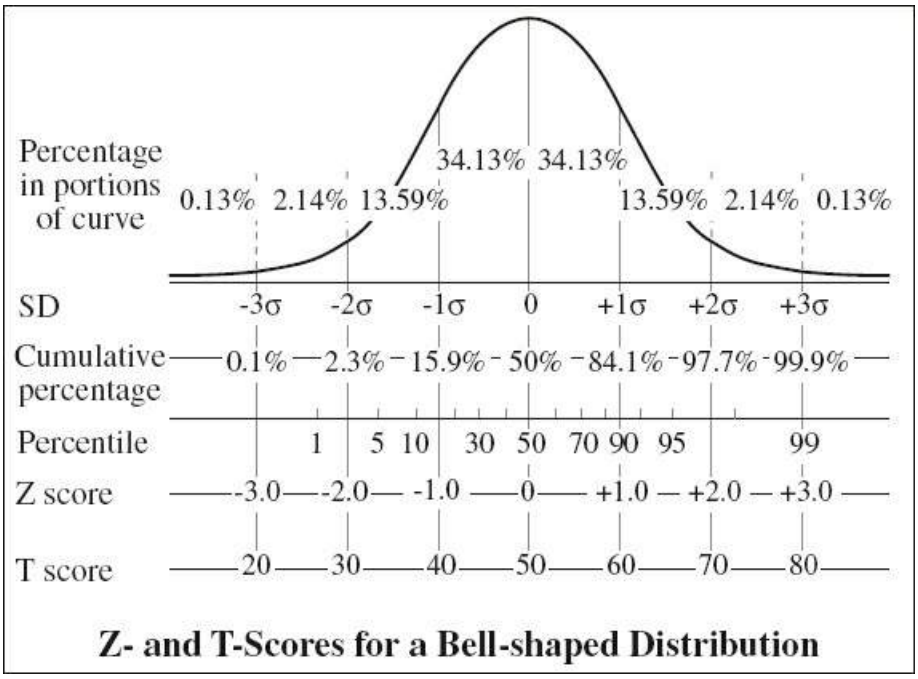
Data collected:

BMD (bone marrow density) value (g/cm^2)
T-score = how far is the score from the mean of 50 with a SD of 10 compared with young adults 20–30 years of age (= peak of bone mass)
Z-score = location of a score compared to age-matched + gender-matched controls in a distribution with a mean of 0 and a SD of 1.0; particularly important in patients aged > 75 years

Interpretation:

normal (≥ –1.0); osteopenia (< –1.0 but > –2.5); osteoporosis (≤ –2.5); severe osteoporosis (≤ –2.5 with a fragility fracture)

Pitfalls:



Z- and T-Scores for a Bell-shaped Distribution

› weekly phantom calibration to detect scanner drift
› improper patient positioning (decentering of lumbar spine, abduction / external rotation of hip)
› improper numbering of vertebrae, placement of intervertebral markers, detection of bone edges
› blurring / irregular contour of bone margins ← patient motion
› anatomic artifacts from
(a) superimposed disease: degenerative disk disease, compression fracture, postsurgical defect, overlying atherosclerotic calcifications
(b) implanted devices: stent + vena cava filter, GI barium, hardware, vertebroplasty cement
(c) external objects: piercing, bra clips, metallic buttons
◊ Results from different scanners not interchangeable ← differences in scanners and software programs

(5) **Quantitative Computed Tomography**
= determines true volumetric density (mg/cm^3) by providing separate estimates of trabecular + cortical bone BMD over 2–4 vertebrae (T12–L4)
• high-turnover cancellous bone is important for vertebral strength and has high responsiveness
• trabecular bone + low-turnover compact bone can be measured separately
Advantage:
› allows separate analysis of trabeculae + cortices
› selective assessment of metabolically active trabecular bone in center of vertebral body
› better sensitivity than projectional methods (DXA)
› exclusion of structures not contributing to spine mechanical resistance

Disadvantage:
› high radiation dose
› poor precision limited to longitudinal assessment
› high costs
› high degree of operator dependence
› need for considerable amount of space
› limited scanner access

Pitfalls affecting measurements:
myelofibrosis + hematopoietic disorders + fat

Technique:
» use of low-dose commercial CT scanner
» compared to external bone mineral reference phantom that is scanned simultaneously with patient to calibrate CT attenuation measurements
» 10-mm–thick section with gantry angle correction through center of vertebral body
» results expressed as absolute values / Z and T scores

Site: vertebrae L1–L3, other sites

Use: assessment of vertebral fracture risk; measurement of age-related bone loss; follow-up of osteoporosis + metabolic bone disease

(a) single energy: 300–500 mrem; 6–25% precision
(b) dual energy: 750–800 mrem; 5–10% precision

◊ Most sensitive technique!

(6) **Peripheral Quantitative CT**

= exact 3-dimensional localization of target volumes with multisection data acquisition capability covering a large volume of bone

Site: distal radius

(7) **Quantitative Heel Ultrasound**

= determines US stiffness index(SI) using formula

SI = 0.67 • BUA [dB/MHz] + 0.28 • SOS [m/s] – 420 SOS = speed of sound BUA = broadband ultrasound attenuation for 200–600 kHz

as a risk assessment independent from DEXA

◊ Fracture risk increases with decrease in SI

Precision: 2.2%

Disadvantage: lack of sensitivity, equipment drift

Location: axial skeleton (lower dorsal + lumbar spine), proximal humerus, neck of femur, wrist, ribs

Radiographs:

◊ Radiographs: insensitive prior to bone loss of 25–30%
◊ Bone scans do NOT show a diffuse increase in activity
√ increased radiolucency = decreased number + thickness of trabeculae = osteopenia ("poverty of bone"):
√ relatively prominent primary trabeculae ← initially selective loss of secondary trabeculae
√ juxtaarticular osteopenia with trabecular bone predominance (eg, distal radius + proximal femur):
√ accentuation of compressive + tensile trabeculae

√ sparsely trabeculated region in inferomedial femoral neck between converging primary and secondary compressive groups = **Ward triangle**

◊ Trabecular bone responds to metabolic changes faster than cortical bone

√ cortical thinning (endosteal + intracortical + periosteal resorption):

√ scalloping of inner cortical margin

√ widening of marrow canal

√ prominent longitudinal cortical striations = tunneling

√ irregular definition of outer bone surface

◊ Most specific finding of high bone turnover

√ delayed fracture healing with poor callus formation (DDx: abundant callus formation in osteogenesis imperfecta + Cushing syndrome)

Cx: fracture for 1÷2 women + 1÷4 men > age 50 years

(1) Fractures at sites rich in labile trabecular bone (eg, vertebrae, wrist) in postmenopausal osteoporosis

(2) Fractures at sites containing cortical + trabecular bone (eg, hip) in senile osteoporosis

Rx: calcitonin, sodium fluoride, diphosphonates, parathyroid hormone supplements, estrogen replacement

Osteoporosis of Spine

Clinical manifestation:

- vertebral compression fracture occurring
  (a) spontaneously
  (b) during lifting / bending / coughing
  (c) load simply caused by muscle contraction
- progressive loss of stature → shortening of paraspinal musculature requiring prolonged active contraction for maintenance of posture → pain from muscle fatigue

Location: thoracolumbar junction (T12, L1), midthoracic area (T7, T8)

√ diminished radiographic density

√ vertical striations = rarefaction of trabeculae ← marked thinning of secondary horizontal (transverse) trabeculae + relative accentuation of primary vertical trabeculae along lines of stress

√ accentuation of endplates

√ "picture framing" (= accentuation of cortical outline with preservation of external dimensions ← endosteal + intracortical resorption

√ <u>anterior wedge fracture</u> resulting in spinal deformity:

√ kyphosis ← multiple fractures in 20–30%

◊ The greater the degree of osteoporosis the greater the number of fractures!

√ "dowager's hump"

√ reduction in thoracic and abdominal space →

- impaired pulmonary function
- protuberant abdomen
- alteration in body shape

√ <u>endplate fracture</u> = compression deformity with reduction in mid height + protrusion of intervertebral disks:

√ biconcavity of vertebra
√ Schmorl nodes

√ crush fracture = reduction of overall height of a vertebra relative to adjacent vertebrae:
√ height loss > 4 mm (posterior height is normally 1–3 mm more than anterior height for thoracic vertebra)
√ decreased height of vertebrae → loss of body height
√ absence of osteophytes

MR:
√ heterogeneously hyperintense SI on T1WI:
√ focal fatty marrow usually has a round morphology
√ round lesions coalesce to involve entire vertebral body
√ variable T2 signal intensity

Osteoporosis of Appendicular Skeleton

@ Hand (on industrial hard-copy film)
√ corticomedullary index = evaluation of cortical thickness of 2nd metacarpal bone
Digital X-ray Radiogrammetry (DXR)
= digitized PA radiograph with automatic segmentation of cortex + medulla of midshafts of 2nd + 3rd + 4th metacarpal bones → average cortical thickness + average bone width in region of interest
Advantage: high reproducibility; capacity to predict future fracture; widely available; inexpensive; low radiation dose

@ Femur
√ Singh classification system = trabeculae in proximal femur disappear in predictable sequence

@ Calcaneus
√ Jhamaria index = lateral radiograph of calcaneus

Osteomalacia

= accumulation of excessive amounts of uncalcified osteoid with bone softening + insufficient mineralization of osteoid due to
(a) high remodeling rate: excessive osteoid formation + normal / little mineralization
(b) low remodeling rate: normal osteoid production + diminished mineralization

Etiology:
(1) dietary deficiency of vitamin D3 + lack of solar irradiation
(2) deficient metabolism of vitamin D:
› chronic renal tubular disease
› chronic administration of phenobarbital (alternate liver pathway)
› diphenylhydantoin (interferes with vitamin D action on bowel)
(3) decreased absorption of vitamin D:
› malabsorption syndromes (most common)
› partial gastrectomy (self-restriction of fatty foods)
(4) diminished deposition of calcium in bone
› diphosphonates (for treatment of Paget disease)

Histo: excess of osteoid seams + decreased appositional rate

- bone pain / tenderness; muscular weakness
- serum calcium slightly low / normal
- decreased serum phosphorus
- elevated serum alkaline phosphatase

√ uniform osteopenia
√ fuzzy indistinct trabecular detail of endosteal surface
√ coarsened frayed trabeculae decreased in number + size
√ thin cortices of long bone
√ bone deformity from softening:
  √ hourglass thorax
  √ bowing of long bones
  √ acetabular protrusion
  √ buckled / compressed pelvis
  √ biconcave vertebral bodies
√ increased incidence of insufficiency fractures
√ pseudofractures = Looser zones
√ mottled skull

Localized / Regional Osteopenia

1. Disuse osteoporosis / atrophy
   Etiology: local immobilization secondary to
   (a) fracture (more pronounced distal to fracture site)
   (b) neural paralysis
   (c) muscular paralysis
2. Reflex sympathetic dystrophy = Sudeck dystrophy
3. Regional migratory osteoporosis, transient regional osteoporosis of hip
4. Rheumatologic disorders
5. Infection: osteomyelitis, tuberculosis
6. Osteolytic tumor
7. Lytic phase of Paget disease
8. Early phase of bone infarct and hemorrhage
9. Burns + frostbite

Bone Marrow Edema

= hypointense on T1WI + hyperintense on T2WI relative to fatty marrow

1. Trauma
   (a) "bone bruise"
   (b) radiographically occult acute fracture
   (c) recent surgery
2. Infection = osteomyelitis
3. Aseptic arthritis
4. Osteonecrosis = early stage of AVN
5. Neuropathic osteoarthropathy
6. Reflex sympathetic dystrophy (some cases)
7. Transient osteoporosis of hip

8. Infiltrative neoplasm

Transverse Lucent Metaphyseal Lines

mnemonic: LINING

Leukemia
Illness, systemic (rickets, scurvy)
Normal variant
Infection, transplacental (congenital syphilis)
Neuroblastoma metastases
Growth lines

Frayed Metaphyses

mnemonic: CHARMS

Congenital infections (rubella, syphilis)
Hypophosphatasia
Achondroplasia
Rickets
Metaphyseal dysostosis
Scurvy

MYELOPROLIFERATIVE DISORDERS

= autonomous clonal disorder initiated by an acquired pluripotential hematopoietic stem cell

Types:

1. Polycythemia vera
2. Chronic granulomatous / myelogenous leukemia
3. Essential idiopathic thrombocytopenia
4. Agnogenic myeloid metaplasia (= primary myelofibrosis + extramedullary hematopoiesis in liver + spleen)

Pathophysiology:

› self-perpetuating intra- and extramedullary hematopoietic cell proliferation without stimulus
› trilinear panmyelosis (RBCs, WBCs, platelets)
› myelofibrosis with progression to myelosclerosis
› myeloid metaplasia = extramedullary hematopoiesis (normocytic anemia, leukoerythroblastic anemia, low platelet count, reticulocytosis, normal / reduced WBC count)

BONE TUMOR

Role of Radiologist

1. Is there a lesion?
2. Is it a bone tumor?
3. Is the tumor benign or malignant?
4. Is a biopsy necessary?
5. Is histologic diagnosis consistent with radiographic image?

Assessment of Bone Tumor

A systematic approach is imperative for assessment of a bone tumor with attention to size, number, and location of lesions; margins and zone of transition; periosteal reaction; matrix mineralization; soft-tissue component.

1. **Age** (and gender) of patient
2. Precise tumor **location**
   (a) transverse: medullary, cortical, juxtacortical
   (b) longitudinal: epi-, meta-, diaphyseal
3. Pattern of **bone destruction / aggressiveness**
   (a) nonaggressive
      √ well-defined sharp margins
      √ smooth solid-appearing periosteal reaction
   (b) aggressive infiltrative osseous process
      √ broad zone of transition
      √ poorly defined borders
      √ disrupted / "sunburst" appearance
      DDx: destructive metabolic / infectious process
4. Lesion **matrix**
   √ "rings-and-arcs" appearance = chondral origin
   √ opaque cloud-like matrix = osseous mineralization
   √ osteolytic lesion → FEGNOMASHIC
   √ CT for cortical continuity / disruption

Action Following Bone Tumor Assessment

A. BENIGN
   1. Diagnosis certain: no further work-up necessary
   2. Asymptomatic lesion with highly probable benign diagnosis may be followed clinically
   3. Symptomatic lesion with highly probable benign diagnosis may be treated without further work-up

B. CONFUSING LESION
   not clearly categorized as benign or malignant; needs staging work-up

C. MALIGNANT: needs staging work-up

Staging work-up:

Bone scan: identifies polyostotic lesions (eg, multiple myeloma, metastatic disease, primary osteosarcoma with bone-forming metastases, histiocytosis, Paget disease)

Chest CT: identifies metastatic deposits + changes further work-up and therapy

Local staging with MR imaging:
   (1) Margins: encapsulated / infiltrating
   (2) Compartment: intra- / extracompartmental
   (3) Intraosseous extent + skip lesions
   (4) Soft-tissue extent (DDx: hematoma, edema)
   (5) Joint involvement

(6) Neurovascular involvement

Local assessment with CT imaging:

√ matrix / rim calcifications

VESSEL AND NERVE INVOLVEMENT

√ tumor encasement of neurovascular bundle by

– 180–360° = indicates infiltration by tumor

– 90–180° = indeterminate for infiltration by tumor

– 0–90° = infiltration by tumor unlikely

Tumorlike Conditions

1. Solitary bone cyst
2. Juxtaarticular ("synovial") cyst
3. Aneurysmal bone cyst
4. Nonossifying fibroma; cortical defect; cortical desmoid
5. Eosinophilic granuloma
6. Reparative giant cell granuloma
7. Fibrous dysplasia (monostotic; polyostotic)
8. Myositis ossificans
9. "Brown tumor" of hyperparathyroidism
10. Massive osteolysis

Pseudomalignant Appearance

1. Osteomyelitis
2. Aggressive osteoporosis

Pattern of Bone Tumor Destruction / Aggressiveness

A. GEOGRAPHIC BONE DESTRUCTION

Cause: (a) slow-growing usually benign tumor

(b) rarely malignant: plasma cell myeloma, metastasis

(c) infection: granulomatous osteomyelitis

√ well-defined smooth / irregular margin

√ narrow zone of transition

B. MOTH-EATEN BONE DESTRUCTION

Cause: (a) rapidly growing malignant bone tumor

(b) osteomyelitis

√ less well-defined / demarcated lesional margin

√ broad zone of transition

mnemonic: H LEMMON

Histiocytosis X

Lymphoma

Ewing sarcoma

Metastasis

Multiple myeloma

Osteomyelitis

Neuroblastoma

C. PERMEATIVE BONE DESTRUCTION
Cause: aggressive bone tumor with rapid growth potential (eg, Ewing sarcoma)
√ poorly demarcated lesion imperceptibly merging with uninvolved bone
√ broad zone of transition

Size, Shape, and Margin of Bone Tumors

◊ Primary malignant tumors are larger than benign tumors
√ elongated lesion (= greatest diameter of > 1.5 times the least diameter): Ewing sarcoma, histiocytic lymphoma, chondrosarcoma, angiosarcoma
√ sclerotic margin (= reaction of host tissue to tumor)

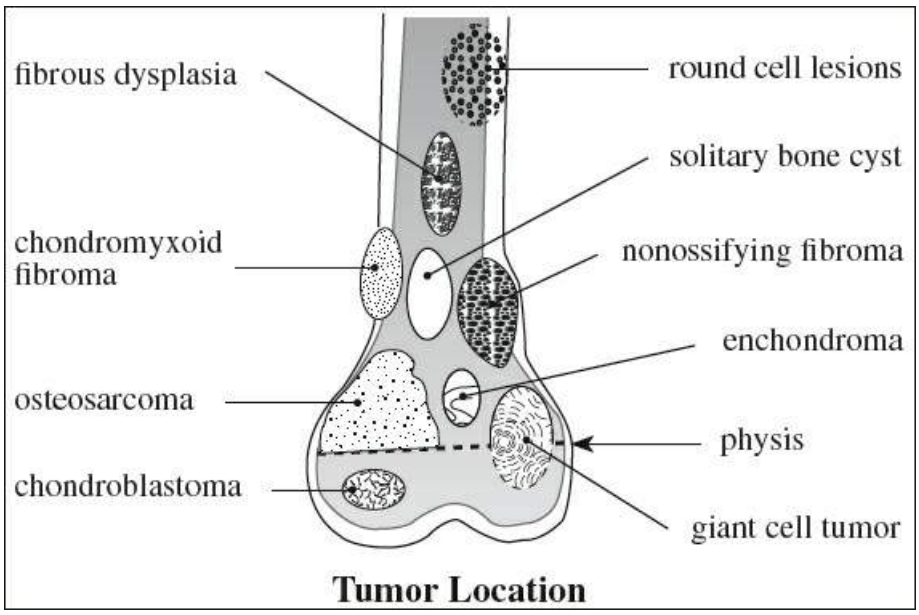
Tumor Position in Transverse Plane

A. CENTRAL MEDULLARY LESION
1. Enchondroma
2. Solitary bone cyst

B. ECCENTRIC MEDULLARY LESION
1. Giant cell tumor
2. Osteogenic sarcoma, chondrosarcoma, fibrosarcoma
3. Chondromyxoid fibroma

C. CORTICAL LESION
1. Nonossifying fibroma
2. Osteoid osteoma

D. PERIOSTEAL / JUXTACORTICAL LESION
1. Juxtacortical chondroma / osteosarcoma
2. Osteochondroma
3. Parosteal osteogenic sarcoma



Tumor Location

Tumor Position in Longitudinal Plane

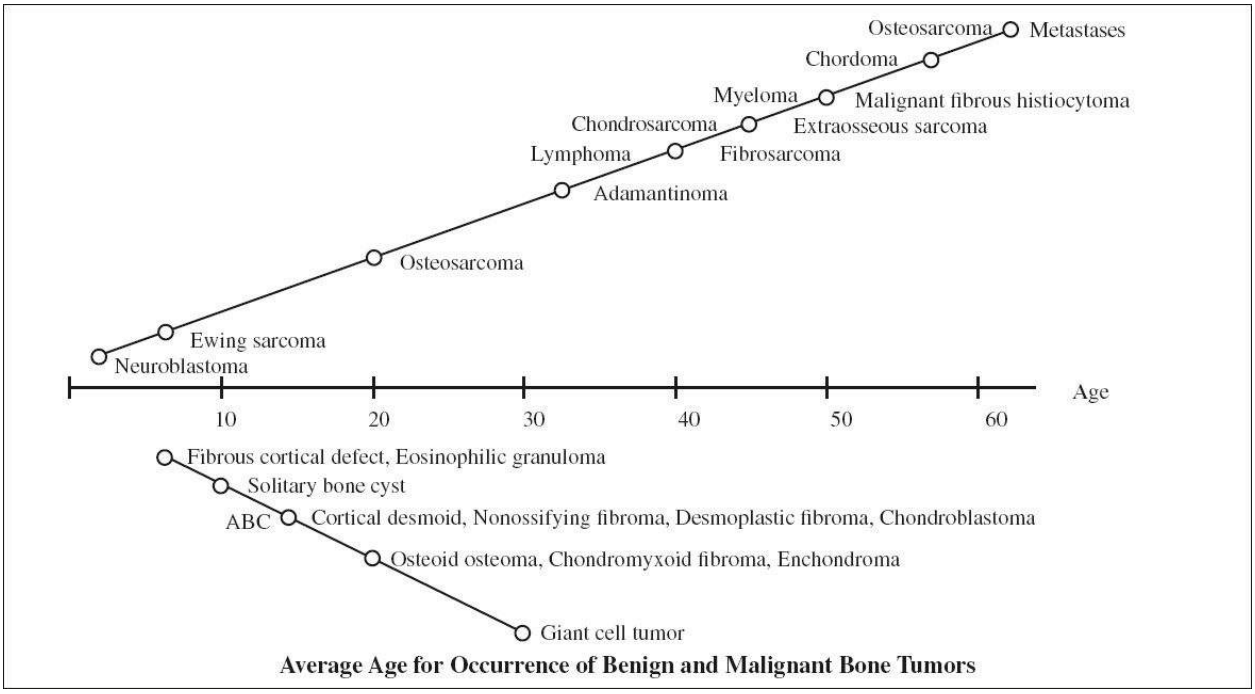
A. EPIPHYSEAL LESION
   1. Chondroblastoma (prior to closure of growth plate)
   2. Intraosseous ganglion, subchondral cyst
   3. Giant cell tumor (originating in metaphysis)
   4. Clear cell chondrosarcoma
   5. Fibrous dysplasia
   6. Abscess

   mnemonic: CAGGIE
      Chondroblastoma
      Aneurysmal bone cyst
      Giant cell tumor
      Geode
      Infection
      Eosinophilic granuloma
         [after 40 years of age throw out "CEA" and insert metastases / myeloma]

B. METAPHYSEAL LESION
   1. Nonossifying fibroma (close to growth plate)
   2. Chondromyxoid fibroma (abutting growth plate)
   3. Solitary bone cyst
   4. Osteochondroma
   5. Brodie abscess
   6. Osteogenic sarcoma, chondrosarcoma

C. DIAPHYSEAL LESION
   1. Round cell tumor (eg, Ewing sarcoma)
   2. Nonossifying fibroma
   3. Solitary bone cyst
   4. Aneurysmal bone cyst
   5. Enchondroma
   6. Osteoblastoma
   7. Fibrous dysplasia

   mnemonic: FEMALE
      Fibrous dysplasia
      Eosinophilic granuloma
      Metastasis
      Adamantinoma



Average Age for Occurrence of Benign and Malignant Bone Tumors

Leukemia, **L**ymphoma
Ewing sarcoma

Tumors Localizing to Hematopoietic Marrow

1. Metastases
2. Plasma cell myeloma
3. Ewing sarcoma
4. Histiocytic lymphoma

Diffuse Bone Marrow Abnormalities in Childhood

A. REPLACED BY TUMOR CELLS
   (a) metastatic disease
      1. Neuroblastoma (in young child)
      2. Lymphoma (in older child)
      3. Rhabdomyosarcoma (in older child)
   (b) primary neoplasm
      1. Leukemia

B. REPLACED BY RED CELLS
   = red cell hyperplasia = reconversion
   (a) severe anemia: sickle cell disease, thalassemia, hereditary spherocytosis
   (b) chronic severe blood loss
   (c) marrow replacement by neoplasia
   (d) treatment with granulocyte-macrophage colony stimulating factor

C. REPLACED BY FAT
   1. Myeloid depletion = aplastic anemia

D. REPLACED BY FIBROUS TISSUE

1. Myelofibrosis

Incidence of Bone Tumors

◊ 80% of bone tumors are correctly determined on the basis of age alone!

Most Frequent Benign Bone Tumor

1. Osteochondroma 20–30%
2. Enchondroma 10–20%
3. Simple bone cyst 10–20%
4. Osteoid osteoma
5. Nonossifying fibroma
6. Aneurysmal bone cyst 5%
7. Fibrous dysplasia
8. Giant cell tumor

Most Frequent Malignant Bone Tumor

A. Bone malignancy
   1. Metastasis
B. Primary bone malignancy
   1. Multiple myeloma
   2. Osteosarcoma
   3. Chondrosarcoma
   4. Ewing sarcoma
C. Primary bone malignancy in children & adolescents
   1. Osteosarcoma
   2. Ewing sarcoma

Sarcomas by Age

mnemonic: **E**very **O**ther **R**unner **F**eels **C**rampy **P**ain **O**n **M**oving

Ewing sarcoma	0–10 years
Osteogenic sarcoma	10–30 years
Reticulum cell sarcoma	20–40 years
Fibrosarcoma	20–40 years
Chondrosarcoma	40–50 years
Parosteal sarcoma	40–50 years
Osteosarcoma	60–70 years
Metastases	60–70 years

EWING SARCOMA FAMILY

1. Ewing sarcoma of bone
2. Extraskeletal Ewing sarcoma
3. Primitive neuroectodermal tumor
4. Askin tumor

Malignancy with Soft-tissue Involvement

mnemonic: **M**y **M**other **E**ats **C**hocolate **F**udge **O**ften
Metastasis
Myeloma
Ewing sarcoma
Chondrosarcoma
Fibrosarcoma
Osteosarcoma

Tumor Matrix of Bone Tumors

Cartilage-forming Bone Tumors

√ centrally located ringlike / flocculent / flecklike radiodensity

A. BENIGN
   1. Enchondroma
   2. Parosteal chondroma
   3. Chondroblastoma
   4. Chondromyxoid fibroma
   5. Osteochondroma

B. MALIGNANT
   1. Chondrosarcoma
   2. Chondroblastic osteosarcoma

Bone-forming Tumors

√ inhomogeneous / homogeneous radiodense collections of variable size + extent

A. BENIGN
   1. Osteoma
   2. Osteoid osteoma
   3. Osteoblastoma
   4. Ossifying fibroma

B. MALIGNANT
   1. Osteogenic sarcoma

Fibrous Connective Tissue Tumors

A. BENIGN FIBROUS BONE LESIONS
   (a) cortical
      1. Benign cortical defect
      2. Avulsion cortical irregularity
   (b) medullary
      1. Herniation pit
      2. Nonossifying fibroma
      3. Ossifying fibroma
      4. Congenital generalized fibromatosis
   (c) corticomedullary
      1. Nonossifying fibroma
      2. Ossifying fibroma
      3. Fibrous dysplasia

4. Cherubism
5. Desmoplastic fibroma
6. Fibromyxoma
7. Benign fibrous histiocytoma

B. MALIGNANT
1. Fibrosarcoma

Tumors of Histiocytic Origin

A. LOCALLY AGGRESSIVE
1. Giant cell tumor
2. Benign fibrous histiocytoma

B. MALIGNANT
1. Malignant fibrous histiocytoma

Tumors of Fatty Tissue Origin

A. BENIGN
1. Intraosseous lipoma
2. Parosteal lipoma

B. MALIGNANT
1. Intraosseous liposarcoma

◊ Lipomas follow the SI of subcutaneous fat in all sequences!

Tumors of Vascular Origin

< 1% of all bone tumors

A. BENIGN
1. Hemangioma
2. Glomus tumor
3. Lymphangioma
4. Cystic angiomatosis
5. Hemangiopericytoma

B. MALIGNANT
1. Malignant hemangiopericytoma
2. Angiosarcoma = hemangioendothelioma

Metastatic sites: lung, brain, lymph nodes, other bones

Tumors of Neural Origin

A. BENIGN
1. Solitary neurofibroma
2. Neurilemmoma

B. MALIGNANT
1. Neurogenic sarcoma = malignant schwannoma

Bone Tumors with Fluid-Fluid Levels

1. Aneurysmal bone cyst
2. Telangiectatic osteosarcoma
3. Giant cell tumor

4. Chondroblastoma
5. Fibrous dysplasia

Round Cell Tumor

Location: arises in midshaft
√ osteolytic lesion
√ reactive new bone formation
√ NO tumor new bone
mnemonic: LEMON
Leukemia, **L**ymphoma
Ewing sarcoma, **E**osinophilic granuloma
Multiple myeloma
Osteomyelitis
Neuroblastoma

INTRAOSSEOUS LESION

Bubbly Bone Lesion

mnemonic: FOGMACHINES
Fibrous dysplasia, **F**ibrous cortical defect
Osteoblastoma
Giant cell tumor
Myeloma (plasmacytoma), **M**etastases from kidney, thyroid, breast
Aneurysmal bone cyst / **A**ngioma
Chondromyxoid fibroma, **C**hondroblastoma
Hyperparathyroid brown tumor, **H**emangioma, **H**emophilia, **H**istiocytosis X
Infection (Brodie abscess, Echinococcus, coccidioidomycosis)
Nonossifying fibroma
Eosinophilic granuloma, **E**nchondroma, **E**pithelial inclusion cyst
Solitary bone cyst
mnemonic: FEGNOMASHIC
Fibrous dysplasia
Enchondroma / **E**osinophilic granuloma
Giant cell tumor
Nonossifying fibroma
Osteoblastoma
Metastasis, **M**yeloma
Aneurysmal bone cyst
Simple bone cyst
Hyperparathyroidism
Infection
Chondroblastoma, **C**hondromyxoid fibroma

Infectious Bubbly Lesion

1. Brodie abscess (Staph. aureus)

2. Coccidioidomycosis
3. Echinococcus
4. Atypical mycobacterium
5. Cystic tuberculosis

Blowout Lesion

A. METASTASES
   Carcinoma of thyroid, kidney, breast
B. PRIMARY BONE TUMOR
   1. Fibrosarcoma
   2. Multiple myeloma (sometimes)
   3. Aneurysmal bone cyst
   4. Hemophilic pseudotumor

Nonexpansile Well-demarcated Bone Defect

Unilocular Well-demarcated Bone Defect

1. Fibrous cortical defect
2. Nonossifying fibroma
3. Simple unicameral bone cyst
4. Giant cell tumor
5. Brown tumor of HPT
6. Eosinophilic granuloma
7. Enchondroma
8. Epidermoid inclusion cyst
9. Posttraumatic / degenerative cyst
10. Pseudotumor of hemophilia
11. Intraosseous ganglion
12. Histiocytoma
13. Arthritic lesion
14. Endosteal pigmented villonodular synovitis
15. Fibrous dysplasia
16. Infectious lesion

Multilocular Well-demarcated Bone Defect

1. Aneurysmal bone cyst
2. Giant cell tumor
3. Fibrous dysplasia
4. Simple bone cyst

Expansile Unilocular Well-demarcated Osteolysis

1. Simple unicameral bone cyst
2. Enchondroma
3. Aneurysmal bone cyst
4. Juxtacortical chondroma
5. Nonossifying fibroma

6. Eosinophilic granuloma
7. Brown tumor of HPT

Poorly Demarcated Osteolytic Lesion

Osteolytic Lesion <u>without</u> Periosteal Reaction

A. NONEXPANSILE
   1. Metastases from any primary neoplasm
   2. Multiple myeloma
   3. Hemangioma

B. EXPANSILE
   1. Chondrosarcoma
   2. Giant cell tumor
   3. Metastasis from kidney / thyroid

Osteolytic Lesion <u>with</u> Periosteal Reaction

1. Osteomyelitis
2. Ewing sarcoma
3. Osteosarcoma

Mixed Sclerotic and Lytic Lesion

Mixed Bone Lesion <u>without</u> Sequestrum

1. Osteomyelitis
2. Tuberculosis
3. Ewing sarcoma
4. Metastasis
5. Osteosarcoma

Mixed Bone Lesion <u>with</u> Button Sequestrum

√ bone opacity surrounded by a well-defined lucent area

common:

1. Osteomyelitis
2. Eosinophilic granuloma
3. Fibrosarcoma, desmoplastic fibroma, MFH
4. Lymphoma

uncommon:

partially calcified intraosseous lipoma, tuberculous osteitis, radiation necrosis, metastatic carcinoma, fibrous dysplasia, dermoid & epidermoid cyst, hemangioma, meningioma

Trabeculated Bone Lesion

1. Giant cell tumor: delicate thin trabeculae
2. Chondromyxoid fibroma: coarse thick trabeculae
3. Nonossifying fibroma: lobulated
4. Aneurysmal bone cyst: delicate, horizontally oriented trabeculae

5. Hemangioma: striated radiating trabeculae

Lytic Bone Lesion Surrounded by Marked Sclerosis

mnemonic: BOOST

Brodie abscess
Osteoblastoma
Osteoid osteoma
Stress fracture
Tuberculosis

Multiple Lytic Lesions

mnemonic: FEEMHI

Fibrous dysplasia
Enchondromas
Eosinophilic granuloma
Metastases, **M**ultiple myeloma
Hyperparathyroidism (brown tumors), **H**emangiomas
Infection

Multiple Lytic Lesions in Child

1. Histiocytosis X
2. Metastatic neuroblastoma / leukemia
3. Fibrous dysplasia
4. Enchondromatosis
5. Rare: cystic angiomatosis, multifocal osteomyelitis

Lytic Bone Lesion in Patient < 30 Years of Age

mnemonic: CAINES

Chondroblastoma
Aneurysmal bone cyst
Infection
Nonossifying fibroma
Eosinophilic granuloma
Solitary bone cyst

Lytic Bone Lesion on Both Sides of Joint

mnemonic: SAC

Synovioma
Angioma
Chondroid lesion

Multiple Bone Lesions with Soft-tissue Tumor

1. Neurofibromatosis & fibroxanthomas
2. Maffucci syndrome = enchondromatosis & hemangioma
3. Mazabraud syndrome = fibrous dysplasia & myxoma
4. Metastases

(a) Multiple myeloma
(b) Malignant melanoma
(c) Lymphoma

Osteoblastic Bone Lesion

A. BENIGN
   1. Bone island
   2. Osteoma
   3. Osteoid osteoma

B. MALIGNANT
   1. Osteosarcoma
   2. Parosteal sarcoma

Widespread Osteosclerotic Lesions

1. Metastases: prostate, breast, lung, bladder, pancreas, stomach, colon, carcinoid, brain
2. Paget disease
3. Sarcoma
4. Myelofibrosis
5. Mastocytosis

BONE OVERGROWTH

Bone Overdevelopment

1. Marfan syndrome
2. Klippel-Trénaunay syndrome
3. Nerve territory-oriented macrodactyly
   (a) Macrodystrophia lipomatosa
   (b) Fibrolipomatous hamartoma with macrodactyly

Erlenmeyer Flask Deformity

= expansion of distal end of long bones, usually femur

1. Gaucher disease, Niemann-Pick disease
2. Hemolytic anemia: thalassemia, sickle cell
3. Osteopetrosis
4. Heavy metal poisoning
5. Metaphyseal dysplasia = Pyle disease
6. Rickets
7. Fibrous dysplasia
8. Down syndrome
9. Achondroplasia
10. Rheumatoid arthritis
11. Hypophosphatasia
12. Leukemia

mnemonic: TOP DOG
Thalassemia

Osteopetrosis
Pyle disease
Diaphyseal aclasis
Ollier disease
Gaucher disease

PERIOSTEAL REACTION / PERIOSTITIS

1. Trauma, hemophilia
2. Infection
3. Inflammatory: arthritis
4. Neoplasm
5. Congenital: physiologic in newborn
6. Metabolic: hypertrophic osteoarthropathy, thyroid acropachy, hypervitaminosis A
7. Vascular: venous stasis

Solid Periosteal Reaction

= reaction to periosteal irritant
√ even + uniform thickness > 1 mm
√ persistent + unchanged for weeks
Patterns:
(a) thin: eosinophilic granuloma; osteoid osteoma
(b) dense undulating: vascular disease
(c) thin undulating: pulmonary osteoarthropathy
(d) dense elliptical: osteoid osteoma; long-standing malignant disease (with destruction)
(e) cloaking: storage disease; chronic infection

Interrupted Periosteal Reaction

= pleomorphic, rapidly progressing process undergoing constant change
(a) buttressing = periosteal bone formation merges with underlying cortex: eosinophilic granuloma
(b) laminated = "onion skin": acute osteomyelitis; malignant tumor (osteosarcoma, Ewing sarcoma)
(c) radiating spicules = "sunburst": osteosarcoma; Ewing sarcoma; chondrosarcoma; fibrosarcoma; leukemia; metastasis; acute osteomyelitis
(d) perpendicular spicules = "hair-on-end": Ewing sarcoma
(e) amorphous: malignancy (deposits may represent extension of tumor / periosteal response); osteosarcoma
(f) Codman triangle: hemorrhage; malignancy (osteosarcoma, Ewing sarcoma); acute osteomyelitis; fracture
[Ernest Armory Codman (1869–1940), orthopedic surgeon at Massachusetts General Hospital, Harvard Medical School]

Symmetric Periosteal Reaction in Adulthood

1. Venous stasis (lower extremity)
2. Hypertrophic osteoarthropathy
3. Pachydermoperiostosis
4. Thyroid acropachy
5. Fluorosis
6. Rheumatoid arthritis
7. Psoriatic arthritis
8. Reiter syndrome
9. Idiopathic-degenerative

Periosteal Reaction in Childhood

(a) benign

1. Physiologic (up to 35%): symmetric involvement of diaphyses during first 1–6 months of life
2. Nonaccidental trauma = battered child syndrome
3. Infantile cortical hyperostosis: < 6 months of age
4. Hypervitaminosis A
5. Scurvy
6. Osteogenesis imperfecta
7. Congenital syphilis

(b) malignant

1. Multicentric osteosarcoma
2. Metastases from neuroblastoma + retinoblastoma
3. Acute leukemia

mnemonic: PERIOSTEAL SOCKS

Physiologic, Prostaglandin
Eosinophilic granuloma
Rickets
Infantile cortical hyperostosis
Osteomyelitis
Scurvy
Trauma
Ewing sarcoma
A-hypervitaminosis
Leukemia + neuroblastoma
Syphilis
Osteosarcoma
Child abuse
Kinky hair syndrome
Sickle cell disease

Periosteal Reaction in Infant

› before 6 months of age

1. Infantile cortical hyperostosis

2. Physiologic
3. Extracorporeal membrane oxygenation

› after 6 months of age

1. Hypervitaminosis A
2. Scurvy
3. Rickets

› anytime during infancy

1. Nonaccidental trauma
2. Syphilis
3. Metastatic neuroblastoma / leukemia
4. Prostaglandin therapy: within 40 days
5. Sickle cell dactylitis

DDx: motion artifact

Enthesopathy

[*en*, Greek = in; *thesis*, Greek = position]

Enthesis = osseous attachment of tendon composed of 4 zones, ie, tendon itself + unmineralized fibrocartilage + mineralized fibrocartilage + bone

Cause:

1. Degenerative disorder
2. Seronegative arthropathies: ankylosing spondylitis, Reiter disease, psoriatic arthritis
3. Diffuse idiopathic skeletal hyperostosis
4. Acromegaly
5. Rheumatoid arthritis (occasionally)

Location: at site of tendon + ligament attachment

√ bone proliferation (enthesophyte)
√ calcification of tendon + ligament
√ erosion

BONE TRAUMA

Childhood Fractures

1. Greenstick fracture
2. Bowing fracture
3. Traumatic epiphyseolysis
4. Battered child syndrome
5. Epiphyseal plate injury

Pseudarthrosis in Long Bones

1. Nonunion of fracture
2. Fibrous dysplasia
3. Neurofibromatosis
4. Osteogenesis imperfecta
5. Congenital: clavicular pseudarthrosis

Exuberant Callus Formation

1. Steroid therapy / Cushing syndrome
2. Neuropathic arthropathy
3. Osteogenesis imperfecta
4. Congenital insensitivity to pain
5. Paralysis
6. Renal osteodystrophy
7. Multiple myeloma
8. Battered child syndrome

EPIPHYSIS

Premature Epiphyseal Ossification

@ Proximal femoral and humeral epiphyses
   1. Jeune asphyxiating thoracic dysplasia
   2. Ellis-van Creveld chondroectodermal dysplasia

Epiphyseal / Apophyseal Lesion

1. Chondroblastoma
2. Brodie abscess
3. Fungal / tuberculous infection
4. Langerhans cell histiocytosis
5. Osteoid osteoma
6. Chondromyxoid fibroma
7. Enchondroma
8. Bone cyst
9. Foreign-body granuloma

mnemonic: ICEBAGS

Infection
Chondroblastoma (age <40)
Eosinophilic granuloma
Brown tumor
Aneurysmal bone cyst
Giant cell tumor
Subchondral cyst

Subarticular Lesion

(a) T2 hypo- to isointense matrix
   1. Giant cell tumor

(b) T2 hyperintense matrix
   2. Solitary subchondral cyst
   3. Intraosseous ganglion
   4. Brodie abscess
   5. Clear cell chondrosarcoma

Stippled Epiphyses

1. Normal variant
2. Avascular necrosis
3. Hypothyroidism
4. Chondrodysplasia punctata
5. Multiple epiphyseal dysplasia
6. Spondyloepiphyseal dysplasia
7. Hypoparathyroidism
8. Down syndrome
9. Trisomy 18
10. Fetal exposure to warfarin / hydantoin
11. Homocystinuria (distal radial + ulnar epiphyses = PATHOGNOMONIC)
12. Zellweger cerebrohepatorenal syndrome

Physeal / Metaphyseal Widening & Irregularity

1. Rickets
2. Hypophosphatasia
3. Metaphyseal chondroplasia

Epiphyseal Overgrowth

1. Juvenile rheumatoid arthritis
2. Hemophilia
3. Healed Legg-Perthes disease
4. Tuberculous arthritis
5. Pyogenic arthritis (chronic)
6. Fungal arthritis
7. Epiphyseal dysplasia hemimelica
8. Fibrous dysplasia of epiphysis
9. Winchester syndrome

Epiphyseolysis

= SLIPPED EPIPHYSIS (zone of maturing hypertrophic cartilage affected, NOT zone of proliferation)

1. **Idiopathic / juvenile epiphyseolysis**
   Age: 12–15 years (? puberty-related hormonal dysregulation)
   • adiposogenital type; tall stature
2. Renal osteodystrophy
3. Hyperparathyroidism in chronic renal disease
4. Hypothyroidism
5. Radiotherapy

JOINTS

Approach to Arthritis

mnemonic: ABCDE'S

Alignment
Bone mineralization
Cartilage loss
Distribution
Erosion
Soft tissues

Signs of Arthritis

Prevalence of arthritis: 15% of population in USA

Conventional x-ray:

√ narrowing of radiologic joint space:
  (a) uniform = inflammatory arthritis
  (b) nonuniform = degenerative arthritis

√ evidence of disease on both sides of joint:
  √ osteopenia
  √ subchondral sclerosis
  √ erosion
  √ subchondral cyst formation
  √ malalignment

√ joint effusion

√ joint bodies

NUC:

√ increase in regional blood flow (active disease)

√ distribution of disease

MR:

√ bone marrow edema = predictor of erosions

√ Gd-DTPA enhancement of synovium (active disease)

√ radiographically occult extraarticular inflammation = tenosynovitis + enthesitis

√ irregularity + narrowing of articular cartilage

Classification of Arthritides

A. SEPTIC ARTHRITIS
   1. Tuberculous
   2. Pyogenic
   3. Lyme arthritis
   4. Fungal arthritis: Candida, Coccidioides immitis, Blastomyces dermatitidis, Histoplasma capsulatum, Sporothrix schenckii, Cryptococcus neoformans, Aspergillus fumigatus

   N.B.: Tuberculous + fungal arthritis show *Phemister triad* (1) prominent osteoporosis, (2) slower rate of destruction, and (3) less joint narrowing than a pyogenic infection

B. COLLAGEN / COLLAGEN-LIKE DISEASE
   1. Rheumatoid arthritis
   2. Ankylosing spondylitis
   3. Psoriatic arthritis

4. Rheumatic fever
5. Sarcoidosis

C. BIOCHEMICAL ARTHRITIS
1. Gout
2. Chondrocalcinosis
3. Ochronosis
4. Hemophilic arthritis

D. DEGENERATIVE JOINT DISEASE = Osteoarthritis

E. TRAUMATIC
1. Secondary osteoarthritis
2. Neurotrophic arthritis
3. Pigmented villonodular synovitis

F. ENTEROPATHIC ARTHROPATHY
(a) INFLAMMATORY BOWEL DISEASE
1. Ulcerative colitis (in 10–20%)
2. Crohn disease (in 5%): peripheral arthritis increases with colonic disease
3. Whipple disease (in 60–90% transient intermittent polyarthritis: sacroiliitis, spondylitis)

◊ Resection of diseased bowel is associated with regression of arthritic symptomatology!

(b) INFECTIOUS BOWEL DISEASE
Infectious agents: Salmonella, Shigella, Yersinia

(c) after intestinal bypass surgery

Spondyloarthritis with Positive HLA-B 27 Histocompatibility Complex

1.	Ankylosing spondylitis	95%
2.	Reiter disease	80%
3.	Arthropathy of inflammatory bowel disease	75%
4.	Psoriatic spondylitis	70%
5.	Normal population	10%

Monoarthritis

Destructive Monoarthritis

◊ Any destructive monoarthritis should be regarded as infection until proved otherwise!

A. SEPTIC ARTHRITIS

B. Monoarticular presentation of a systemic arthritis
1. Rheumatoid arthritis
2. Gout
3. Amyloidosis
4. Seronegative arthritis

C. Joint tumor
1. PVNS
2. Synovial chondromatosis
3. Articular hemangioma

Nonseptic Monoarthritis

1. Gout
2. Milwaukee shoulder
3. Rapidly destructive articular disease
4. Amyloid arthropathy
5. Hemophilic arthropathy
6. Primary synovial osteochondromatosis
7. Pigmented villonodular synovitis
8. Neuropathic arthropathy
9. Foreign-body synovitis

Arthritis without Demineralization

1. Gout
2. Neuropathic arthropathy
3. Psoriasis
4. Reiter disease
5. Pigmented villonodular synovitis

mnemonic: PONGS

Psoriatic arthritis
Osteoarthritis
Neuropathic joint
Gout
Sarcoidosis

Arthritis with Demineralization

mnemonic: HORSE

Hemophilia
Osteomyelitis
Rheumatoid arthritis, Reiter disease
Scleroderma
Erythematosus, systemic lupus

Deforming Nonerosive Arthropathy

1. Collagen-vascular disease, especially SLE
2. Rheumatoid arthritis (rare)
3. Rheumatic fever (Jaccoud arthritis) (rare)

Arthritis with Periostitis

1. Juvenile rheumatoid arthritis
2. Psoriatic arthritis
3. Reiter syndrome
4. Infectious arthritis

Premature Osteoarthritis

mnemonic: COME CHAT

Calcium pyrophosphate dihydrate arthropathy
Ochronosis
Marfan syndrome
Epiphyseal dysplasia
Charcot joint = neuroarthropathy
Hemophilic arthropathy
Acromegaly
Trauma

Synovial Disease with Decreased Signal Intensity

= blooming" artifact of low SI on gradient-echo pulse sequences ← magnetic susceptibility artifact of hemosiderin

1. Pigmented villonodular synovitis
2. Rheumatoid arthritis
3. Hemophiliac arthropathy
4. Synovial hemangioma

Chondrocalcinosis

mnemonic: WHIP A DOG
Wilson disease
Hemochromatosis, **H**emophilia, **H**ypothyroidism, 1° **H**yperparathyroidism (15%), **H**ypophosphatasia, Familial **H**ypomagnesemia
Idiopathic (aging)
Pseudogout (CPPD)
Arthritis (rheumatoid, postinfectious, traumatic, degenerative), **A**myloidosis, **A**cromegaly
Diabetes mellitus
Ochronosis
Gout

mnemonic: 3 C's

Crystals	CPPD, sodium urate (gout)
Cations	calcium (any cause of hypercalcemia), copper, iron
Cartilage degeneration	osteoarthritis, acromegaly, ochronosis

Subchondral Cyst

= SYNOVIAL CYST = SUBARTICULAR PSEUDOCYST
= NECROTIC PSEUDOCYST = GEODES

Etiology: bone necrosis allows pressure-induced intrusion of synovial fluid into subchondral bone; in conditions with synovial inflammation

Cause by mnemonic: COORS
CPPD
Osteoarthritis
Osteonecrosis
Rheumatoid arthritis
Synovial tumor

√ size of cyst usually 2–35 mm
√ may be large + expansile (especially in CPPD)
DDx: (1) Giant cell tumor
(2) Pigmented villonodular synovitis
(3) Metastasis
(4) Intraosseous ganglion
(5) Brown tumor of hemophilia

Periarticular Calcified Mass

1. Calcinosis of chronic renal failure = uremic tumoral acalcinosis = secondary tumoral calcinosis = tumoral calcification
2. Tumoral calcinosis

Periarticular Cyst

= cyst located in the vicinity of a synovial joint

1. Ganglion
   = mucin-containing cyst arising from tendon sheath / joint capsule / bursa / subchondral bone lined by flat spindle-shaped cells
2. Synovial cyst
   = cyst continuous with joint capsule lined by synovial cells (term is used by some synonymously with ganglion)
3. Meniscal cyst
   = associated with meniscal tear, in > 90% of a tear with horizontal component
4. Bursa
   = synovial lining, forms in area of friction, may communicate with joint

Loose Intraarticular Bodies

1. Osteochondrosis dissecans
2. Synovial osteochondromatosis
3. Chip fracture from trauma
4. Severe degenerative joint disease
5. Neuropathic arthropathy

Rice Bodies

= subset of loose bodies as a nonspecific response to chronic synovial inflammation resembling polished rice

1. Rheumatoid arthritis
2. Juvenile rheumatoid arthritis
3. Tuberculous arthritis

Pathogenesis:
(1) microinfarction of synovium / detachment of hypertrophied synovium → sloughed synovium falls into joint space → coated with fibrinogen
(2) precipitate of fibrin + fibronectin / core of mononuclear cells, blood cells and amorphous material

MRI:

√ well-defined nodules of intermediate SI on T1WI + relatively low intensity on T2WI

DDx:

(1) Synovial osteochondromatosis (monoarticular, large joint, hyperintense cartilage components on T2WI)

(2) Pigmented villonodular synovitis (monoarticular, large joint, hemosiderin deposition)

Intraarticular Mass

A. PROLIFERATIVE SYNOVIAL PROCESS
   1. Lipoma arborescens
   2. Synovial osteochondromatosis
   3. Pigmented villonodular synovitis
   4. Rheumatoid arthritis

B. INFECTIOUS GRANULOMATOUS DISEASE
   1. Tuberculous arthritis
   2. Coccidioidomycosis arthritis

C. DEPOSITION DISEASE
   1. Gout
   2. Amyloid arthropathy

D. VASCULAR MALFORMATION
   1. Synovial hemangioma
   2. Arteriovenous malformation

E. MALIGNANCY
   1. Synovial chondrosarcoma
   2. Synovial sarcoma
   2. Synovial metastasis: primary lung cancer

F. Peculiar joint anatomy
   1. Cyclops lesion

Intraarticular Process with Cortical Erosion

1. Pigmented villonodular synovitis
2. Synovial osteochondromatosis
3. Rheumatoid arthritis
4. Gout
5. Synovial hemangioma
6. Lipoma arborescens

Erosions of DIP Joints

1. Inflammatory osteoarthritis
2. Psoriatic arthritis
3. Gout
4. Multicentric reticulohistiocytosis
5. Hyperparathyroidism
6. Frostbite
7. Septic arthritis

Articular Disorders of Hand and Wrist

1. **Osteoarthritis** = degenerative joint disease
   = abnormal stress with minor + major traumatic episodes
   Target areas: DIP, PIP, 1st CMC, trapezioscaphoid; bilateral symmetric / asymmetric
   √ joint space narrowing
   √ subchondral eburnation
   √ marginal osteophytes + small ossicles
   √ radial subluxation of 1st metacarpal base
   ◊ Radiocarpal joint normal unless history of trauma
2. **Erosive osteoarthritis** = inflammatory osteoarthritis
   Age: predominantly middle-aged / postmenopausal women
   • acute inflammatory episodes
   Target areas: DIP, PIP, 1st CMC, trapezioscaphoid; bilateral symmetric / asymmetric
   √ central erosions combined with osteophytes = subchondral "gull wing" erosions
   √ joint space narrowing + sclerosis
   √ rare ankylosis
3. **Psoriatic arthritis**
   = rheumatoid variant / seronegative spondyloarthropathy; peripheral manifestation in monoarthritis / asymmetric oligoarthritis / symmetric polyarthritis
   Target areas: all hand + wrist joints (commonly distal); bi- / unilateral asymmetric polyarticular changes
   √ "mouse ears" marginal erosions
   √ intraarticular osseous excrescences
   √ new bone formation ± fusion
   √ osteoporosis may be absent
4. **Rheumatoid arthritis**
   = synovial proliferative granulation tissue = *pannus*
   Target areas: PIP (early in 3rd), MCP (earliest changes in 2nd + 3rd), all wrist joints (early in RC, IRU), ulnar styloid; both hands in relative symmetric fashion
   √ fusiform soft-tissue swelling
   √ regional periarticular osteoporosis
   √ diffuse loss of joint space
   √ marginal + central poorly defined erosions
   √ joint deformities
5. **Gouty arthritis**
   • monosodium urate crystals in synovial fluid
   • asymptomatic periods from months to years
   Target areas: commonly CCMC + all hand joints
   √ development of chronic tophaceous gout = lobulated soft-tissue masses
   √ well-defined eccentric erosions with overhanging edge (often periarticular) + sclerotic margins
   √ preservation of joint spaces
   √ absence of osteoporosis
   √ most extensive changes in common carpometacarpal compartment:
   √ scalloped erosions of bases of ulnar metacarpals

6. **Calcium pyrophosphate dihydrate crystal deposition disease = CPPD**
   Target areas: MCP (2nd, 3rd), radiocarpal; bilateral symmetric / asymmetric changes
   √ chondrocalcinosis + periarticular calcifications:
      √ calcification of triangular fibrocartilage
   √ "degenerative changes" in unusual locations:
      √ narrowing ± obliteration of space between distal radius and scaphoid ± fragmentation of surfaces
      √ scapholunate separation
      √ destruction of trapezioscaphoid space
   √ no erosions
   √ + large osteophytes = hemochromatosis
7. **SLE**
   = myositis, symmetric polyarthritis, deforming nonerosive arthropathy, osteonecrosis
   Target areas: PIP, MCP
   √ reversible deformities
8. **Scleroderma** = progressive systemic sclerosis (PSS)
   Target areas: DIP, PIP, 1st CMC
   √ tuft resorption
   √ soft-tissue calcifications

Arthritis Involving Distal Interphalangeal Joints

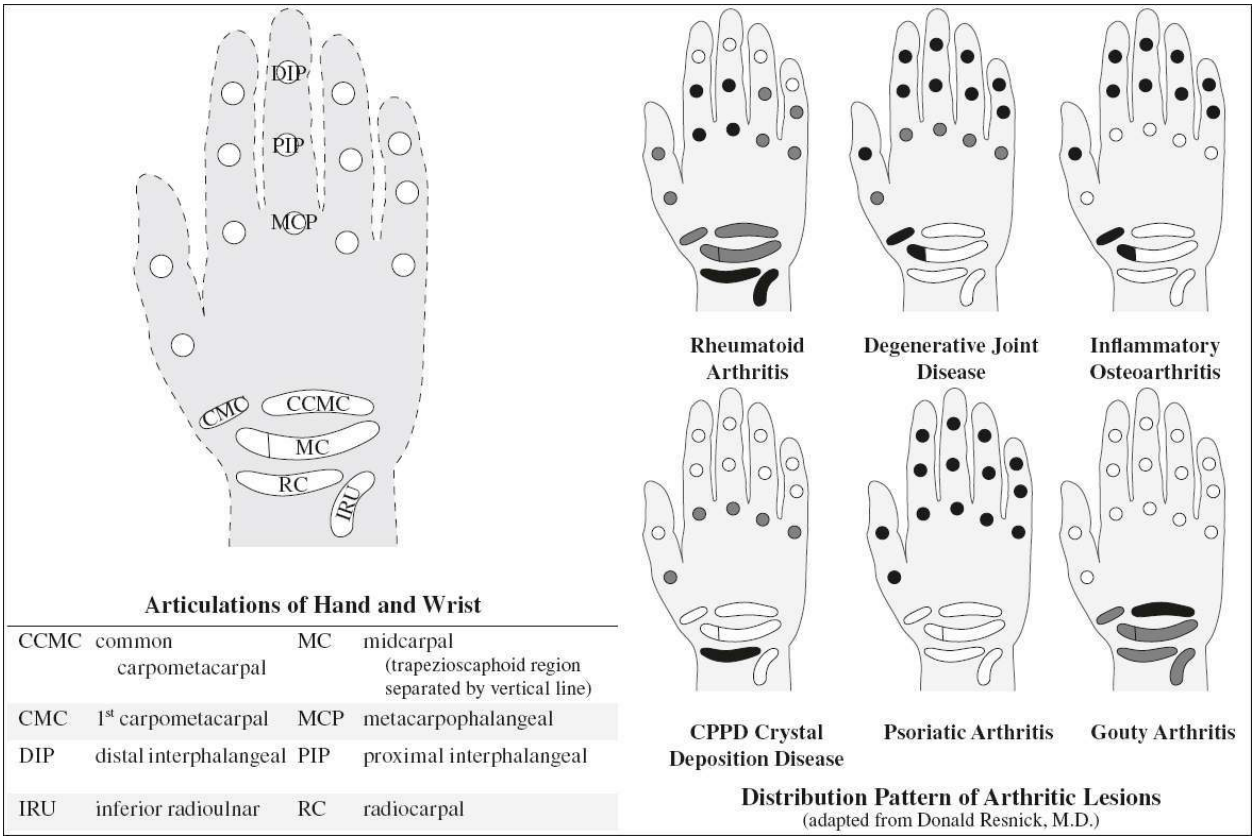
mnemonic: "POEM"
Psoriatic arthritis
Osteoarthritis
Erosive osteoarthritis
Multicentric reticulohistiocytosis

Ankylosis of Interphalangeal Joints

mnemonic: "S - Lesions"
1. P**s**oriatic arthritis
2. Ankylo**s**ing spondylitis
3. Ero**s**ive osteoarthritis
4. **S**till disease

Arthritis of Interphalangeal Joint of Great Toe

1. Psoriatic arthritis



Articulations of Hand and Wrist

CCMC	common carpometacarpal	MC	midcarpal (trapezioscaphoid region separated by vertical line)
CMC	1st carpometacarpal	MCP	metacarpophalangeal
DIP	distal interphalangeal	PIP	proximal interphalangeal
IRU	inferior radioulnar	RC	radiocarpal

Distribution Pattern of Arthritic Lesions
(adapted from Donald Resnick, M.D.)

2. Reiter disease
3. Gout
4. Degenerative joint disease

RIBS

Thoracic Deformity

Pectus Carinatum = Pigeon Breast

= anterior displacement of sternum

Frequency: 1÷1500 live births; in 25% familial

In > 30% associated with: scoliosis

Types:

(a) chondrogladiolar deformity = protrusion of middle + lower sternum
[*gladiolus*, Latin, diminutive for *gladius* = sword]

(b) chondromanubrial deformity (Currrarino-Silverman syndrome) = protrusion of manubrium + upper sternum
[*manubrium*, Latin = a handle]

• shortness of breath, exercise intolerance

√ increase in AP diameter

√ pectus index (TRV diameter ÷ AP diameter of chest): < 1.42–1.98

Pectus Excavatum = Funnel Chest

= posterior depression of sternum with reduction of prevertebral space compressing heart against spine

Frequency: 1÷400 to 1÷1000 live births; M÷F = 4÷1

Cause: rapid misdirected growth of lower costal cartilages

◊ Most common congenital deformity of the sternum

◊ Most frequently an isolated anomaly (45% familial)!

May be associated with:

prematurity, homocystinuria, Marfan syndrome, Poland syndrome, Noonan syndrome, fetal alcohol syndrome, congenital heart disease

In > 20% associated with: scoliosis

• decreased total lung capacity

• decreased cardiac stroke volume

√ depressed position of sternum (LATERAL)

√ indistinct right heart border mimicking right middle lobe process (FRONTAL) = leftward displacement + axial rotation of heart

√ decreased heart density (FRONTAL)

√ leftward displacement of heart mimicking cardiomegaly (FRONTAL)

√ horizontal course of posterior portion of ribs

√ accentuated downward course of anterior portions of ribs (FRONTAL)

CT:

√ pectus index (TRV diameter ÷ AP diameter of chest): > 2.56 ± 0.35

Rx: surgical correction with pectus index > 3.25

Barrel Chest

= large sagittal diameter of thorax

Cause: COPD, emphysema

√ lateral segments of ribs elongated + straight pointing vertical (FRONTAL)

√ square shape on cross section (CT)

Congenital Rib Anomalies

Prevalence: 1.4%

1. **Cervical rib** (0.2–1–8%)

   M< F

   • usually asymptomatic

   • thoracic outlet syndrome (due to elevation of floor of scalene triangle with decrease of costoclavicular space):

   ◊ 10–20% of symptomatic patients have a responsible cervical rib

   ◊ 5–10% of complete cervical ribs cause symptoms

   May be associated with: Klippel-Feil anomaly

   √ uni- / bilateral

   √ may fuse with first ribs anteriorly

   √ adjacent transverse process angulated inferiorly

   Cx: aneurysmal dilatation of subclavian a.

   DDx: elongated transverse process of 7th cervical vertebra; hypoplastic 1st thoracic rib

2. **Forked / bifid rib** (0.6%) = duplication of anterior portion

Location: 4th rib (most often)
May be associated with: Gorlin basal cell nevus syndrome
◊ A single bifid rib is most commonly a normal incidental finding!

3. **Rib fusion** (0.3%)
   May be associated with: vertebral segmentation anomalies
   Location: 1st + 2nd rib / several adjacent ribs
   Site: posterior / anterior portion
4. **Bone bridging** = focal joining by bone outgrowth
   Cause: congenital / posttraumatic
   Location: anywhere along one pair of ribs / several adjacent ribs
   √ complete bridging / pseudarthrosis
5. **Rudimentary / hypoplastic rib** (0.2%)
   Location: 1st rib (usually)
   √ transverse process angulated superiorly
   DDx: cervical rib
6. **Pseudarthrosis of 1st rib** (0.1%)
   √ radiolucent line through mid portion with dense sclerotic borders
7. **Intrathoracic / pelvic rib** (rare)
8. **Abnormal number of ribs**
   (a) supernumerary: trisomy 21, VATER syndrome
   (b) 11 pairs: normal individuals (5–8%); trisomy 21 (33%); cleidocranial dysplasia; camptomelic dysplasia

Short Ribs

1. Thanatophoric dysplasia
2. Jeune asphyxiating thoracic dysplasia
3. Ellis-van Creveld chondroectodermal dysplasia
4. Short rib-polydactyly syndromes (Saldino-Noonan, Majewski, Verma-Naumoff)
5. Achondroplasia
6. Achondrogenesis
7. Mesomelic dwarfism
8. Spondyloepiphyseal dysplasia
9. Enchondromatosis

Rib Lesions

A. BENIGN RIB TUMOR
   1. Fibrous dysplasia (most common benign lesion)
      √ predominantly posterior / lateral location
      √ expansile remodeling of protracted length of bone
      √ typical ground-glass appearance
   2. Enchondroma (2nd most common)
      √ at costochondral junction
      √ high SI on T2WI + lobulated contour
   3. Osteochondroma / exostosis (8%):
      √ at costochondral / costovertebral junction

Associated with: spontaneous hemothorax

4. Langerhans cell histiocytosis (eosinophilic granuloma)
   - age < 30 years
   √ "black hole" on CT of lower density
   √ aggressive features like periostitis + cortical breakthrough + soft-tissue mass
5. Benign cortical defect
6. Hemangioma of bone
7. Giant cell tumor
   √ low to intermediate SI on T1WI + T2WI
8. Aneurysmal bone cyst
   √ lobulated septated mass with thin well-defined rim of low SI + fluid levels
9. Osteoblastoma
10. Osteoid osteoma
11. Chondroblastoma
    √ at costovertebral / costochondral junction
12. Enostosis = bone island (0.4%)
13. Paget disease
14. Brown tumor of HPT
15. Xanthogranuloma
16. Nonossifying fibroma = fibroxanthoma
    √ eccentric intracortical location, smaller in size
    √ spontaneous regression with age

B. PRIMARY MALIGNANT RIB TUMOR
1. Chondrosarcoma (33%)
2. Plasmacytoma
3. Lymphoma
4. Osteosarcoma (1.3%)
5. Fibrosarcoma
6. Primitive neuroectodermal tumor / Askin tumor

C. SECONDARY MALIGNANT RIB TUMOR
› *in adult:* 1. Metastasis (most common malignant lesion)
2: Multiple myeloma
3: Desmoid tumor
› *in adult:* 1. Ewing sarcoma (most common malignant rib tumor of children and adolescents)
2: Metastatic neuroblastoma

D. TRAUMATIC RIB DISORDER
1. Healing fracture
2. Radiation osteitis

DDx: pulmonary nodule

E. AGGRESSIVE GRANULOMATOUS INFECTIONS
= osteomyelitis

Expansile Rib Lesion

mnemonic: O FEEL THE CLAMP

Osteochondroma (25% of all benign rib tumors)
Fibrous dysplasia
Eosinophilic granuloma
Enchondroma (7% of all benign rib tumors)
Lymphoma / **L**eukemia
Tuberculosis
Hematopoiesis
Ewing sarcoma
Chondromyxoid fibroma
Lymphangiomatosis
Aneurysmal bone cyst
Metastases
Plasmacytoma

Abnormal Rib Shape

Rib Notching on Inferior Margin

= minimal concave scalloping / deep ridges along the neurovascular groove with reactive sclerosis

◊ Minor undulations in the inferior ribs are normal!

◊ The medial third of posterior ribs near transverse process of vertebrae may be notched normally!

A. ARTERIAL
Cause: intercostal aa. function as collaterals to descending aorta / lung
(a) Aorta: coarctation (usually affects ribs 4–8; rare before age 8 years), thrombosis
(b) Subclavian artery: Blalock-Taussig shunt
(c) Pulmonary artery: pulmonary stenosis, tetralogy of Fallot, absent pulmonary artery

B. VENOUS
Cause: enlargement of intercostal veins
(a) AV malformation of chest wall
(b) Superior vena cava obstruction

C. NEUROGENIC
1. Intercostal neuroma
2. Neurofibromatosis type 1
3. Poliomyelitis / quadriplegia / paraplegia

D. OSSEOUS
1. Hyperparathyroidism
2. Thalassemia
3. Melnick-Needles syndrome

Unilateral Rib Notching on Inferior Margin

1. Postoperative Blalock-Taussig shunt (subclavian to pulmonary artery)
2. Coarctation between origin of innominate a. + L subclavian a.
3. Coarctation proximal to aberrant subclavian a.

Rib Notching on Superior Margin

1. Rheumatoid arthritis
2. Scleroderma
3. Systemic lupus erythematosus
4. Hyperparathyroidism
5. Restrictive lung disease
6. Marfan syndrome

Dysplastic Twisted Ribbon Ribs

1. Osteogenesis imperfecta
2. Neurofibromatosis

Bulbous Enlargement of Costochondral Junction

1. Rachitic rosary
2. Scurvy
3. Achondroplasia
4. Hypophosphatasia
5. Metaphyseal chondrodysplasia
6. Acromegaly

Wide Ribs

1. Marrow hyperplasia (anemias)
2. Fibrous dysplasia
3. Paget disease
4. Achondroplasia
5. Mucopolysaccharidoses

Slender Ribs

1. Trisomy 18 syndrome
2. Neurofibromatosis

Dense Ribs

1. Tuberous sclerosis
2. Osteopetrosis
3. Mastocytosis
4. Fluorosis
5. Fibrous dysplasia
6. Chronic infection
7. Trauma
8. Subperiosteal rib resection

Hyperlucent Ribs

Congenitally Lucent Ribs

1. Osteogenesis imperfecta
2. Achondrogenesis
3. Hypophosphatasia
4. Camptomelic dysplasia

Acquired Lucent Ribs

1. Cushing disease
2. Acromegaly
3. Scurvy

CLAVICLE

Absence of Outer End of Clavicle

1. Rheumatoid arthritis
2. Hyperparathyroidism
3. Posttraumatic osteolysis
4. Metastasis / multiple myeloma
5. Cleidocranial dysplasia
6. Gorlin basal cell nevus syndrome

Penciled Distal End of Clavicle

mnemonic: SHIRT Pocket

Scleroderma
Hyperparathyroidism
Infection
Rheumatoid arthritis
Trauma
Progeria

Destruction of Medial End of Clavicle

mnemonic: MILERS

Metastases
Infection
Lymphoma
Eosinophilic granuloma
Rheumatoid arthritis
Sarcoma

SHOULDER

Shoulder Instability

= recurrent subluxation / dislocation of humeral head out of the glenoid socket during activities causing symptoms

Stabilizer: inferior glenohumeral ligament-labrum complex = IGHLC (most important); anterior labrum-ligament complex

Lesions after first anterior dislocation:

(1) traumatic, unidirectional, Bankart, surgical (TUBS)

Age: < 40 years

- fall on outstretched hand (FOOSH)

√ capsulolabral avulsion (Bankart lesion / its variants)
√ anterior-inferior instability

(2) **a**traumatic, **m**ultidirectional, **b**ilateral, **r**esponding to rehabilitation, **i**nferior capsular shift (AMBRI)
Age: > 40 years
√ tear of supraspinatus tendon (33%)
√ fracture of greater tuberosity (33%)
√ subscapularis avulsion from humerus (33%)

Instability lesions:
√ detachment of anteroinferior labrum:
√ scapular periosteum disrupted = Bankart lesion:
√ without bone fragment = soft Bankart
√ with bone fragment = osseous Bankart
√ scapular periosteum intact:
√ labrum displaced = ALPSA
√ labrum not displaced = Perthes lesion
√ fractured articular cartilage = GLAD
√ avulsion of humeral detachment of inferior glenohumeral ligament = HAGL
√ detachment of posterior labrum

Fluid in Subcoracoid Bursa

1. Isolated subcoracoid bursitis
2. Inadvertent injection of contrast material into bursa
3. Posttraumatic inflammatory response with tears of rotator cuff + rotator interval

WRIST

Carpal Angle

= angle of 130° formed by tangents to proximal row of carpal bones

A. DECREASED CARPAL ANGLE (< 124°)
1. Turner syndrome
2. Hurler syndrome
3. Morquio syndrome
4. Madelung deformity

B. INCREASED CARPAL ANGLE (> 139°)
1. Down syndrome
2. Arthrogryposis
3. Bone dysplasia with epiphyseal involvement

HAND

Axiality: determined after limb extension at right angle to long axis of body

preaxial = lateral (radial) aspect of upper limb or medial (tibial) aspect of lower limb

postaxial = medial (ulnar) aspect of upper limb or lateral (fibular) aspect of lower limb

Metacarpal Sign

= relative shortening of 4th + 5th metacarpals

√ tangential line along heads of 5th + 4th metacarpals intersects 3rd metacarpal

1. Idiopathic
2. Pseudo- and pseudopseudohypoparathyroidism
3. Basal cell nevus syndrome
4. Multiple epiphyseal dysplasia
5. Beckwith-Wiedemann syndrome
6. Sickle cell anemia
7. Juvenile chronic arthritis
8. Gonadal dysgenesis: Turner + Klinefelter syndrome
9. Ectodermal dysplasia = Cornelia de Lange syndrome
10. Hereditary multiple exostoses
11. Peripheral dysostosis
12. Melorheostosis

mnemonic: **P**ing **P**ong **I**s **T**ough **T**o **T**each

Pseudohypoparathyroidism
Pseudopseudohypoparathyroidism
Idiopathic
Trauma
Turner syndrome
Trisomy 13–18

Brachydactyly

= shortening / broadening of metacarpals ± phalanges

1. Idiopathic
2. Trauma
3. Osteomyelitis
4. Arthritis
5. Turner syndrome
6. Osteochondrodysplasia
7. Pseudohypoparathyroidism, Pseudopseudohypoparathyroidism
8. Mucopolysaccharidoses
9. Cornelia de Lange syndrome
10. Basal cell nevus syndrome
11. Hereditary multiple exostoses

Clinodactyly

= curvature of finger in mediolateral plane

1. Normal variant
2. Down syndrome
3. Multiple dysplasia
4. Trauma, arthritis, contracture

Polydactyly

Frequently associated with:

1. Carpenter syndrome
2. Ellis-van Creveld syndrome
3. Meckel-Gruber syndrome
4. Polysyndactyly syndrome
5. Short rib-polydactyly syndrome
6. Trisomy 13

Syndactyly

= osseous ± cutaneous fusion of digits

1. Apert syndrome
2. Carpenter syndrome
3. Down syndrome
4. Neurofibromatosis
5. Poland syndrome
6. Others

FINGER

Benign Lesion of Finger

(a) cartilage matrix
1. Enchondroma
2. Enchondromatosis
3. Periosteal / juxtacortical chondroma
4. Chondromyxoid fibroma
5. Chondroblastoma

(b) bone matrix
1. Osteochondroma
2. Hereditary multiple exostoses
3. Subungual exostosis
4. Florid Reactive Periostitis
5. Bizarre parosteal osteochondromatous proliferation
6. Osteoid osteoma
7. Aneurysmal bone cyst
8. Giant cell tumor

(b) mimics of primary osseous lesion
1. Glomus tumor
2. Epidermal inclusion cyst
3. Systemic disease: sarcoidosis, tophaceous gout, brown tumor of hyperparathyroidism, rheumatoid arthritis ± pressure erosion from overlying rheumatoid nodule
4. Infection

Lucent Lesion in Finger

A. BENIGN TUMOR
1. Enchondroma
2. Epidermoid inclusion cyst
3. Giant cell tumor
4. Reparative granuloma
5. Sarcoidosis
6. Glomus tumor (rare)

others: aneurysmal bone cyst, brown tumor, hemophilic pseudotumor, solitary bone cyst, osteoblastoma

B. MALIGNANT PRIMARY TUMOR (exceedingly rare)

(a) osseous malignancy
1. Chondrosarcoma
   ◊ Most common primary malignant bone tumor of the hand!
2. Osteosarcoma
3. Fibrosarcoma
4. Hemangioendotheliosarcoma
5. Ewing sarcoma

(b) nail bed malignancy

1. Squamous cell carcinoma
2. Malignant melanoma

C. MALIGNANT SECONDARY TUMOR
1. Metastasis from lung > genitourinary tract > breast

mnemonic: GAMES PAGES
Glomus tumor
Arthritis (gout, rheumatoid)
Metastasis (lung, breast)
Enchondroma
Simple cyst (inclusion)
Pancreatitis
Aneurysmal bone cyst
Giant cell tumor
Epidermoid
Sarcoid

Dactylitis

= expansion of bone with cystic changes
1. Tuberculous dactylitis (= spina ventosa)
2. Pyogenic / fungal infection
3. Syphilitic dactylitis
4. Sarcoidosis
5. Hemoglobinopathies
6. Hyperparathyroidism
7. Leukemia

Resorption of Terminal Tufts

A. TRAUMA
1. Amputation
2. Burns, electric injury
3. Frostbite
4. Vinyl chloride poisoning

B. NEUROPATHIC
1. Congenital indifference to pain
2. Syringomyelia
3. Myelomeningocele
4. Diabetes mellitus
5. Leprosy

C. COLLAGEN-VASCULAR DISEASE
1. Scleroderma
2. Dermatomyositis
3. Raynaud disease

D. METABOLIC
1. Hyperparathyroidism

E. INHERITED

1. Familial acroosteolysis
2. Pyknodysostosis
3. Progeria = Werner syndrome
4. Pachydermoperiostosis

F. OTHERS
1. Sarcoidosis
2. Psoriatic arthropathy
3. Epidermolysis bullosa

Subungual Tumors

A. Benign solid tumor
1. Glomus tumor
2. Subungual exostosis
3. Soft-tissue chondroma
4. Keratoacanthoma
5. Hemangioma
6. Lobular capillary hemangioma

B. Benign cystic lesion
1. Epidermal cyst
2. **Mucoid cyst**
= cyst containing hyaluronic acid + related to osteoarthritis of DIP joint

C. Malignant tumor
1. Squamous cell carcinoma
2. Malignant melanoma

Acroosteolysis

1. Acroosteolysis: (a) acquired
(b) familial
2. Massive osteolysis
3. Essential osteolysis
4. Ainhum disease

Acquired Acroosteolysis

mnemonic: PETER's DIAPER SPLASH

Psoriasis, **P**orphyria
Ehlers-Danlos syndrome
Thrombangiitis obliterans
Ergot therapy
Raynaud disease
Diabetes, **D**ermatomyositis, **D**ilantin therapy
Injury (thermal + electrical burns, frostbite)
Arteriosclerosis obliterans
PVC (polyvinyl chloride) worker
Epidermolysis bullosa
Rheumatoid arthritis, **R**eiter syndrome

Scleroderma, **S**arcoidosis
Progeria, **P**yknodysostosis
Leprosy, **L**esch-Nyhan syndrome
Absence of pain
Syringomyelia
Hyperparathyroidism
also in: yaws; Kaposi sarcoma; pachydermoperiostosis

√ lytic destructive process involving distal + middle phalanges
√ NO periosteal reaction
√ epiphyses resist osteolysis until late

Acroosteosclerosis

= focal opaque areas + endosteal thickening

1. Incidental in middle-aged women
2. Rheumatoid arthritis
3. Sarcoidosis
4. Scleroderma
5. Systemic lupus erythematosus
6. Hodgkin disease
7. Hematologic disorders

Fingertip Calcifications

1. Scleroderma / CREST syndrome
2. Raynaud disease
3. Systemic lupus erythematosus
4. Dermatomyositis
5. Calcinosis circumscripta universalis
6. Hyperparathyroidism

HIP

Snapping Hip Syndrome

A. INTRAARTICULAR
   1. Osteocartilaginous bodies
B. EXTRAARTICULAR = tendon slippage
   1. Fascia lata / gluteus maximus over greater trochanter
   2. Iliopsoas tendon over iliopectineal eminence
   3. Long head of biceps femoris over ischial tuberosity
   4. Iliofemoral ligament over anterior portion of hip capsule

Increase in Teardrop Width

√ increase in distance between teardrop + femoral head
Cause: hip joint effusion
√ increase in mediolateral size of teardrop
Cause: hip dysplasia, chronic hip joint effusion during skeletal maturation

Protrusio Acetabuli

= acetabular floor bulging into pelvis
√ center-edge angle of Wiberg of > 40°
√ medial wall of acetabulum projecting medially to ilioischial line by > 3 mm (in males) / > 6 mm (in females)
√ crossing of medial + lateral components of pelvic "teardrop" (U-shaped radiodense area medial to hip joint)
Anatomy:
(a) lateral aspect = articular surface of acetabular fossa
(b) medial aspect = anteroinferior margin of quadrilateral surface of ilium)
√ obscured "teardrop" sign = pelvic teardrop obscured by femoral head

A. UNILATERAL
1. Tuberculous arthritis
2. Trauma
3. Fibrous dysplasia

B. BILATERAL
1. Rheumatoid arthritis
2. Paget disease
3. Osteomalacia

mnemonic: PROT
Paget disease
Rheumatoid arthritis
Osteomalacia (HPT)
Trauma

Pain with / after Hip Prosthesis

= pain in groin / thigh after hip arthroplasty
Prevalence of pain: 40%; ~ 120,000 hip arthroplasties per year in USA

1. Postoperative hematoma
Incidence: 1.7% (within first 2 weeks)
Cx: wound dehiscence, infection
2. Heterotopic ossification
Incidence: 50–60% (within 8 weeks after surgery)
Risk factors: male gender, DISH, history of heterotopic ossification, osteoarthritis with preexisting heterotopic bone, ankylosing spondylitis
• loss of motion ← ossifications bridging the joint
3. Trochanteric bursitis
4. Prosthetic / periprosthetic / cement fracture
• audible crack during tapping of stem (intraoperative!)
Incidence: in up to 18%
Predisposition: osteoporosis, osteolysis, stress shielding (= bone resorption due to decreased stress to bone) typically at base of greater trochanter and calcar
5. Dislocation
Risk factors: component malposition, imbalance of tissue tension, implant design, surgical approach, extent of surgical soft-tissue dissection, small femoral

head, failure of abductor mechanism

(a) posterior joint instability disruption of posterior joint capsule + short external rotator muscles / muscle atrophy

(b) anterior joint instability excessive acetabular cup anteversion > 30° → impingement of femoral neck onto posterior rim of acetabular component → creation of posterior lever mechanism forcing femoral head out anteriorly

6. Synovitis
   (a) nonspecific mechanical irritation
      √ small amount of joint fluid without debris
      √ thin synovial lining
   (b) polyethylene wear-induced = polymeric debris
      √ slowly progressive typically bulky osteolysis
      √ expansion of hip pseudocapsule by thick + particulate-appearing synovitis
   (c) adverse local tissue reaction (metal hypersensitivity, metallosis)
      √ synovial thickness > 7 mm
   (d) infection *(see below)*
7. Iliopsoas impingement syndrome & tendinopathy
   Incidence: 4.3%
   Cause:
      (a) idiopathic
      (b) prominent oversized / malpositioned acetabular component
      (c) retained cement
      (d) excessively long iliac screws
      (e) femoral head larger than native head
   √ gluteus medius and minimus tendon thickening / tear
8. **Aseptic loosening**
   = complete loss of implant fixation
   Frequency: 50% of prostheses after 10 years; 30% require revision
   Cause:
      (a) mechanical wear + tear of components
      (b) small-particle disease
         Path: particulate debris incites inflammatory / immune reaction → unsuccessful enzymatic destruction of debris → cytokines and proteolytic enzymes damage bone and cartilage → osteolysis
         Histo: synovium-like pseudomembrane of histiocytes (95% of specimens), giant cells (80%), lymphocytes and plasma cells (25%), neutrophils (< 10%)
   √ thin and enlarging > 2 mm radiolucent area around component / between cement mantle + bone
   √ NEW radiolucent area < 2 mm
   √ increasing osteolysis (due to particulate debris with foreign body granuloma)
   √ increasingly wide / asymmetric periprosthetic radiolucency
   √ endosteal scalloping around femoral stem
   √ pedestal formation = bone sclerosis distal to prosthetic tip in medullary canal ← micromotion

√ bead shedding = punctate pieces of metal around in-growth component
√ fractured cement mantle
√ fractured acetabular cup screw
√ newly tilted / migrated acetabular cup
√ rotated / migrated / toggled femoral stem:
  √ subsidence (= distal migration) of prosthesis (up to 5 mm is normal for noncemented femoral component in first few months)
  √ "sinking" of femoral flange into lesser trochanter
√ contrast medium between points of fixation
√ motion of components on stress views / fluoroscopy
√ inflammatory benign solid soft-tissue mass / pseudotumor around metal-on-metal implants

Rx: 30% require single-stage revision arthroplasty

9. **Infection of Hip Prosthesis** (= septic loosening)

Frequency: 0.3–1.7–9.0%; < 2% of primary arthroplasties; < 5% of revisions

Organism: Staphylococcus epidermidis (31%), Staphylococcus aureus (20%), Streptococcus viridans (11%), Escherichia coli (11%), Enterococcus faecalis (8%), group B streptococcus (5%)

Time of onset: ⅓ within 3 months, ⅓ within 1 year, ⅓ > 1 year

Path: bacteria bind to implant

Histo: neutrophils present in large numbers

Rx: excisional arthroplasty + protracted course of antimicrobial therapy + revision arthroplasty

• clinical signs of infection often absent

Plain film:
  √ "aggressive" osteolysis with ill-defined margins ← particulate debris with foreign body granuloma / abscess
  √ periostitis = periosteal new bone (100% specific, 16% sensitive for infection)
  √ periarticular fluid collection with irregular walls communicating with joint (CT arthrography) and sinus track to skin

NUC (83% sensitive, 88% specific): *(see below)*

PET:
  √ NO advantage over bone marrow imaging as a combination of ^{111}In-labeled leukocytes and ^{99m}Tc sulfur colloid

Arthrography:
  √ irregularity of joint pseudocapsule
  √ filling of nonbursal spaces / sinus tracts / abscess cavities

Aspiration of fluid under fluoroscopy (12–93% sensitive, 83–92% specific for infection):
  • joint aspiration: high number of FP + FN
  √ injection of contrast material to confirm intraarticular location

Evaluation of Total Hip Arthroplasty

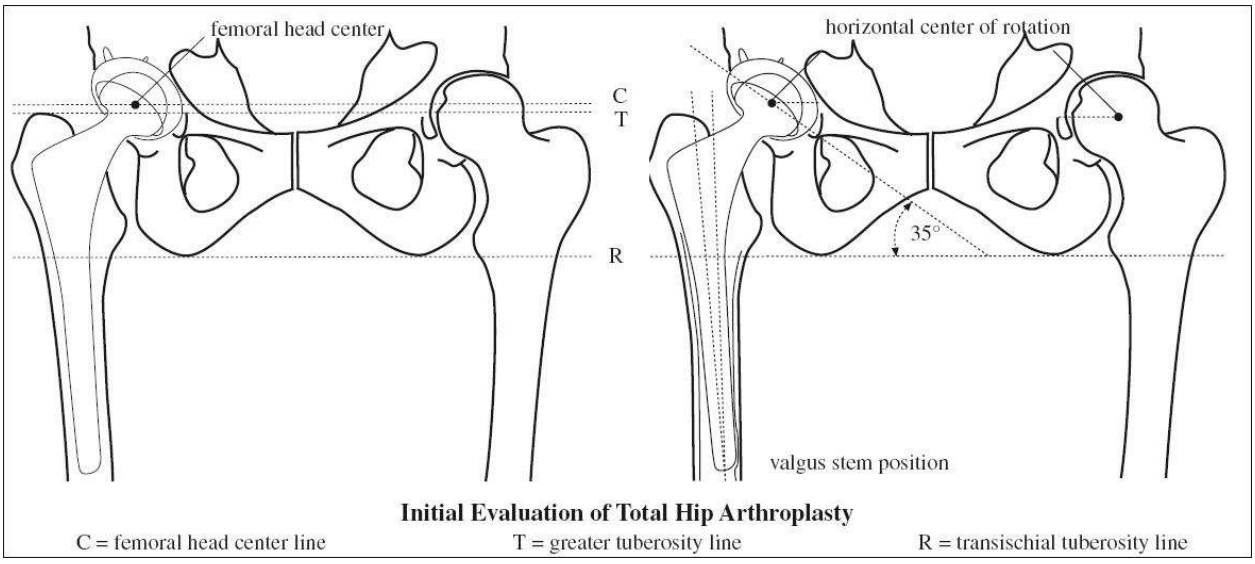
MEASUREMENTS

Reference line: transischial tuberosity line (R)

1. Leg length = vertical position of acetabular component

= comparing level of greater / lesser tuberosity (T) with respect to line R
High placement: shorter leg, less effective muscles crossing the hip joint
Low placement: longer leg, muscles stretched to point of spasm with risk of dislocation

2. Vertical center of rotation
   = distance from center of femoral head (C) to line R
3. Horizontal center of rotation
   = distance from center of femoral head (C) to teardrop / other medial landmark
   Lateral position: iliopsoas tendon crosses medial to femoral head center of rotation increasing risk of dislocation
4. Lateral acetabular inclination = horizontal version
   = angle of cup in reference to line R (40° ± 10° desirable)
   Less angulation: stable hip, limited abduction
   Greater angulation: risk of hip dislocation
5. Acetabular anteversion (15° ± 10° desirable)
   = lateral radiograph of groin
   Retroversion: risk of hip dislocation
6. Varus / neutral / valgus stem position
   Varus position: tip of stem rests against lateral endosteum, increased risk for loosening
   Valgus position: tip of stem rests against medial endosteum, not a significant problem
7. Femoral neck anteversion works synergistically with acetabular anteversion, true angle assessed by CT
8. Cup overhang > 12 mm associated with iliopsoas impingement, assessed by CT



9. Unfavorable position of screw tip eg, abutting the L5 nerve root in sciatic notch

Type of Hip Prosthesis

A. Hemiprosthesis
   √ preservation of acetabular cartilage + subchondral bone plate

√ only femoral stem is fixed by
(a) bone cement (polymethylmethacrylate)
(b) press-fit / in-growth with textured surface facilitating in-growth of trabecular bone

1. Unipolar head
= 1 articulation between metal implant head + native acetabular cartilage
2. Bipolar head
= 2 articulations to improve range of motion:
(a) between inner head + liner of bipolar head
(b) between bipolar head (shell) + acetabulum
√ smooth outer surface
√ slightly greater than hemispheric shape
√ no screw holes

B. Total prosthesis (mostly for treatment of arthritis)
√ acetabulum reamed
1. Conventional
√ screw holes in acetabular cup
2. Resurfacing = replacing articulating surfaces of hip joint and removing very little bone
√ small acetabular cup in pelvic socket
√ femoral head component seated with a pegged stem inside a preserved femoral neck

Radiographic Findings in Total Hip Arthroplasty

A. NORMAL
√ irregular cement-bone interface
= normal interdigitation of PMMA (polymethylmethacrylate) with adjacent bone remodeling providing a mechanical interlock
◊ PMMA is not a glue!
√ thin lucent line along cement-bone interface
= 0.1–1.5-mm thin connective tissue membrane ("demarcation") along cement-bone interface accompanied by thin line of bone sclerosis

B. ABNORMAL
√ wide lucent zone at cement-bone interface
= ≥ 2-mm lucent line along bone-cement interface due to granulomatous membrane
Cause: component loosening ± reaction to particulate debris (eg, PMMA, polyethylene)
√ lucent zone at metal-cement interface along proximal lateral aspect of femoral stem
= suboptimal metal-cement contact at time of surgery / loosening
√ well-defined area of bone destruction (= histiocytic response, aggressive granulomatous disease)
Cause: granulomatous reaction as response to particulate debris / infection / tumor
√ asymmetric positioning of femoral head within acetabular component
Cause: acetabular wear / dislocation of femoral head / acetabular disruption / liner displacement / deformity

√ cement fracture
Cause: loosening

Scintigraphy for Prosthetic Failure

√ increased uptake of bone agent, ^{67}Gallium, ^{111}Indium-labeled leukocytes, complementary technetium-labeled sulfur colloid + combinations

(1) ***Bone Scintigraphy*** (high NPV):
› negative
√ periprosthetic uptake indistinguishable from surrounding nonarticular bone = no prosthetic abnormality (= high NPV)
› positive for infection / loosening:
√ diffuse intense uptake around femoral component (= generalized osteolysis unreliable in separating infection from loosening)
√ diffuse periprosthetic uptake favors infection
√ focal uptake at distal tip of femoral component in > 1 year old prosthesis = aseptic loosening
› nonspecific:
√ periprosthetic activity generally decreases with time:
√ variable uptake patterns in 1st year after implantation
√ persistent uptake > 1 year is frequent in cementless / porous-coated hip replacements

(3) ***Sequential bone/gallium scintigraphy*** (60–80% accurate, modest improvement over bone scintigraphy alone):
› negative for infection:
√ gallium distribution normal regardless of findings on bone imaging
√ spatially congruent distribution of both radiotracers + gallium intensity less than bone tracer
› inconclusive:
√ spatially congruent radiotracer distribution + similar uptake intensity for both radiotracers
› positive for infection:
√ spatially incongruent distribution of the 2 radiotracers
√ gallium uptake intensity exceeds that of bone agent

(4) ***Labeled leukocyte scintigraphy***:
› positive for infection:
√ intensity exceeds that of a reference point
√ activity outside normal distribution

(5) ***Combined labeled leukocyte–marrow scintigraphy*** = WBC/sulfur colloid scintigraphy (study of choice):
Accuracy: 88–98%
Concept: ^{99m}Tc-sulfur colloid maps aberrantly located normal bone marrow as a point of reference for leukocyte tracer
› positive for infection:
√ labeled leukocyte activity without corresponding sulfur colloid activity ← osteomyelitis stimulates WBC uptake + depresses sulfur colloid uptake

› negative for infection:
√ spatially congruent distribution of both radiotracers / any other pattern of uptake

KNEE

Bone Contusion Pattern

√ edema of mid portion of lateral femoral condyle
Cause: **pivot shift injury** = valgus load + external rotation of tibia / external rotation of femur applied to various states of flexion (noncontact injury)
Predisposed: skier, football player
Associated with injury of:
(1) anterior cruciate lig. (midsubstance > femoral attachment > tibial attachment site)
(2) posterior joint capsule + arcuate ligament
(3) posterior horn of lateral / medial meniscus
(4) medial collateral ligament

√ ± edema of posterior patellar surface
Cause: dashboard injury = force upon anterior proximal tibia with knee in flexed position
Associated with:
(1) rupture of posterior cruciate lig. (midsubstance > femoral attachment > tibial attachment site)
(2) tear of posterior joint capsule
(3) fracture / osteochondral injury of patella
(4) injury of hip

√ "kissing" bone contusion pattern = anterior aspect of tibial plateau + anterior aspect of femoral condyle
Cause: **hyperextension injury** = direct force upon anterior tibia while foot is planted / indirect force of forceful kicking motion
Associated with:
(1) injury to posterior / anterior cruciate lig.
(2) meniscal injury
(3) dislocation of knee
(4) popliteal neurovascular injury
(5) complete disruption of posterolateral complex

√ edema in lateral aspect of femoral condyle ← direct blow

√ small area of edema in medial femoral condyle ← avulsive stress to medial collateral ligament
Predisposed: football player
Cause: **clip injury** = pure valgus stress with knee in mild flexion
Associated with injury of:
(1) medial collateral ligament (at femoral attachment site
(2) anterior cruciate ligament
(3) medial meniscus
(4) combination of all three = methyl triad

√ anterolateral aspect of lateral femoral condyle

√ inferomedial aspect of patella
Predisposed: teenaged / young adult athletes with shallow trochlear groove
Cause: **lateral patellar dislocation** = twisting motion with knee in flexion + quadriceps contraction
Associated with injury of:
(1) medial retinaculum
(2) medial patellofemoral ligament (near femoral attachment site) most important stabilizing structure)
(3) medial patellotibial ligament

Double PCL sign on MRI
1. Bucket-handle tear of medial / lateral meniscus
2. Ligament of Humphrey
3. Torn ACL
4. Fracture fragments
5. Osteophyte
6. Loose body

Absent bow-tie sign
1. Bucket-handle tear of medial meniscus
2. Congenitally hypoplastic / ring-shaped meniscus
3. Small meniscus in child / petite adult
4. Partial meniscectomy
5. Arthritic degeneration

Unique Tibial Lesions
1. Fibrous dysplasia
2. Ossifying fibroma
3. Adamantinoma

Tibiotalar Slanting
= downward slanting of medial tibial plafond
1. Hemophilia
2. Still disease
3. Sickle cell disease
4. Epiphyseal dysplasia
5. Trauma

FOOT

Abnormal Foot Positions
A. FOREFOOT
1. **Varus** = adduction
= axis of 1st metatarsal deviated medially relative to axis of talus
2. **Valgus** = abduction

= axis of 1st metatarsal deviated laterally relative to axis of talus

3. **Inversion** = supination
   = inward turning of sole of foot
4. **Eversion** = pronation
   = outward turning of sole of foot

B. HINDFOOT

talipes = any deformity of the ankle and hindfoot
[*talus*, Latin = ankle; *pes*, Latin = foot]

1. Equinus
   = hindfoot abnormality with reversal of calcaneal pitch so that the heel cannot touch the ground
2. Calcaneal foot
   = very high calcaneal pitch so that forefoot cannot touch the ground
3. Pes planus = flatfoot
   = low calcaneal pitch + (usually) heel valgus + forefoot eversion
4. Pes cavus
   = high calcaneal pitch (fixed high arch)

Clubfoot = Talipes Equinovarus

Common severe congenital deformity characterized by

- equinus of heel (reversed calcaneal pitch)
- heel varus (talocalcaneal angle of almost zero on AP view with both bones parallel to each other)
- metatarsus adductus (axis of 1st metatarsal deviated medially relative to axis of talus)

1. Arthrogryposis multiplex congenita
2. Chondrodysplasia punctata
3. Neurofibromatosis
4. Spina bifida
5. Myelomeningocele

Rocker-bottom Foot = Vertical Talus

√ vertically oriented talus with increased talocalcaneal angle on lateral view
√ dorsal navicular dislocation at talonavicular joint
√ heel equinus
√ rigid deformity

Associated with: Arthrogryposis multiplex congenita; spina bifida; trisomy 13–18

Talar Beak = Hypertrophied Talar Ridge

1. Talocalcaneal type of tarsal coalition
2. Diffuse idiopathic skeletal hyperostosis (DISH)
3. Acromegaly
4. Rheumatoid arthritis

Heel Pad Thickening

= heel pad thickening > 25 mm (normal < 21 mm)

mnemonic: MAD COP

Myxedema
Acromegaly
Dilantin therapy
Callus
Obesity
Peripheral edema

Soft-tissue Masses of Foot + Ankle

A. NONTUMORAL
   (a) synovial proliferations
      1. Pigmented villonodular synovitis (PVNS)
      2. Giant cell tumor (GCT) of tendon sheath
   (b) posttraumatic
      1. Plantar fasciitis
   (c) inflammatory
   (d) uncertain origin
      1. Ganglion cyst
      2. Epidermoid cyst
      3. Morton neuroma
      4. Florid reactive periostitis
      6. Rheumatoid nodules
B. BENIGN TUMORS
   1. Plantar fibromatosis
   2. Deep fibromatosis
   3. Infantile digital fibromatosis
   4. Hemangioma
   5. Nerve sheath tumor
   6. Lipoma, angiolipoma

SOFT TISSUES

Categories of Soft-tissue Masses

A. Neoplastic
   Incidence: 300÷100,000 / year; benign÷malignant = 100÷1
   (a) benign (most frequent)
      1. Lipoma
      2. Hemangioma
      3. Desmoid tumor
      4. Ganglion cyst
      5. Pigmented villonodular synovitis
      6. Neurofibroma (5%)
      7. Lipoblastoma
   (b) malignant
      Frequency: 1% of all cancers in adults, increasing with age

1. Malignant fibrous histiocytoma
2. Liposarcoma

B. Inflammatory
C. Traumatic
D. Vascular

Superficial Soft-tissue Mass

A. MESENCHYMAL TUMOR
   (a) cutaneous
      1. Dermatofibrosarcoma protuberans
   (b) subcutaneous
      1. Lipoma / liposarcoma
      2. Angioma (hemangioma, lymphangioma, mixed)
      3. Peripheral nerve sheath tumor
      4. Malignant fibrous histiocytoma
      5. Leiomyosarcoma
      6. Epithelioid sarcoma
   (c) fascial
      1. Nodular fasciitis
      2. Fibromatosis

B. SKIN APPENDAGE LESION
   1. Epidermal inclusion cyst
   2. Pilomatricoma
   3. Eccrine cystadenoma / hydrocystoma
      = cystic ectasia of dermal portion of eccrine duct
   4. Cylindroma (head, neck, scalp in women)
   5. Syringoma (eyelids, upper cheek)

C. METASTATIC TUMOR
   ◊ 5–10% of all cancer patients develop skin metastases
   1. Carcinoma
      mnemonic: BLOCK
         Breast
         Lung
         Ovary
         Colon
         Kidney
   2. Melanoma (in 30% of melanoma patients)
   3. Myeloma (in < 5% of multiple myeloma patients)

D. OTHER TUMORS & TUMORLIKE LESION
   1. Myxoma
      √ homogeneous fluidlike signal intensity
   2. Lymphoma
   3. Granuloma annulare

E. INFLAMMATORY LESION
   1. Cellulitis

= inflammation / infection of cutis + subcutis without gross suppuration
√ thickened skin with reticulated fluidlike SI

2. Fasciitis
   = inflammation / infection of fascia
   √ fascial thickening + enhancement
3. Adenitis
   √ intermediate SI on non–fat-suppressed T2WI
4. Abscess
   = confined focal collection of pus or necrotic tissue + WBCs + bacteria
   √ fluidlike signal intensity + rim of enhancement
5. Phlegmon
   = poorly defined region with edema-like pattern and indistinct margins

Histologic Classification of Soft-tissue Lesions

A. FATTY
   1. Lipoma
   2. Angiolipoma
   3. Liposarcoma

B. FIBROUS
   1. Fibroma
   2. Nodular fasciitis
   3. Aggressive fibromatosis / desmoid
   4. Fibrosarcoma

C. MUSCLE
   (a) skeletal muscle tumor
      1. Rhabdomyoma
      2. Rhabdomyosarcoma
   (b) smooth muscle tumor
      1. Leiomyoma
      2. Leiomyosarcoma

D. VASCULAR
   1. Hemangioma
   2. Kaposiform hemangioendothelioma
   3. Kaposi sarcoma
   4. Hemangiopericytoma
   5. Hemangiosarcoma
   6. Glomus tumor
   7. Myopericytoma

E. LYMPH
   1. Lymphangioma
   2. Lymphangiosarcoma
   3. Lymphadenopathy in lymphoma / metastasis

F. SYNOVIAL
   1. Nodular synovitis
   2. Pigmented villonodular synovitis

3. Synovial sarcoma

G. NEURAL
1. Neurofibroma
2. Neurilemmoma
3. Ganglioneuroma
4. Malignant neuroblastoma
5. Neurofibrosarcoma

H. CARTILAGE AND BONE
1. Myositis ossificans
2. Extraskeletal osteoma
3. Extraskeletal / soft-tissue chondroma
4. Mesenchymal chondrosarcoma
5. Extraskeletal osteosarcoma

I. UNCERTAIN DIFFERENTIATION
1. Intramuscular myxoma
2. Ossifying fibromyxoid tumor
3. Synovial sarcoma
4. Primitive neuroectodermal tumor
5. Extraskeletal Ewing sarcoma

Most Frequent Benign Soft-tissue Tumors

8 pathologic diagnoses make up 70% of all benign tumors!

1. Lipoma 16%
2. Fibrous histiocytoma 13%
3. Nodular fasciitis 11%
4. Neurogenic neoplasm 10%
5. Hemangioma 7%
6. Fibromatosis 7%
7. PVNS / giant cell tumor of tendon sheath 4%
8. Ganglion cyst

Most Frequent Malignant Soft-tissue Tumors

7 pathologic diagnoses make up 80% of all malignant tumors!

1. Undifferentiated pleomorphic sarcoma (= malignant fibrous histiocytoma) 29%
2. Liposarcoma 14%
3. Nonspecific spindle cell sarcoma 12%
4. Leiomyosarcoma 8%
5. Malignant peripheral nerve sheath tumor 6%
6. Dermatofibroma protuberans 6%
7. Synovial sarcoma 5%

Fat-containing Soft-tissue Masses

A. BENIGN LIPOMATOUS TUMORS
1. Lipoma
2. Intra- / intermuscular lipoma

3. Synovial lipoma
4. Lipoma arborescens = diffuse synovial lipoma
5. Neural fibrolipoma = fibrolipomatous tumor of nerve
6. Macrodystrophia lipomatosa

B. LIPOMA VARIANTS
1. Lipoblastoma
2. Lipomatosis
   (a) Madelung disease
   (b) Mediastinal lipomatosis
   (c) Pancreatic lipomatosis
   (d) Pelvic lipomatosis
3. Hibernoma

C. MALIGNANT LIPOMATOUS TUMOR
1. Liposarcoma

D. OTHER FAT-CONTAINING TUMORS
1. Hemangioma
2. Elastofibroma dorsi

E. LESIONS MIMICKING FAT-CONTAINING TUMORS
1. Myxoid tumors: intramuscular myxoma, extraskeletal myxoid chondrosarcoma, myxoid malignant fibrous histiocytoma
2. Neural tumors: neurofibroma, neurilemmoma, malignant schwannoma
   √ 73% have tissue attenuation less than muscle
3. Hemorrhage

Benign Fibrous Soft-Tissue Tumors

So-called Fibrohistiocytic Tumors

1. Benign fibrous histiocytoma
2. Diffuse-type giant cell tumor
3. Malignant fibrous histiocytoma

Benign Myofibroblastic Proliferations

1. Nodular fasciitis
2. Proliferative fasciitis / myositis
3. Fibroma of tendon sheath
4. Keloid and hypertrophic scar
5. Elastofibroma

Musculoskeletal Fibromatoses

= wide range of clinicopathologic conditions with benign proliferation of fibrous tissue characterized by infiltrative growth pattern and tendency to recur locally

SUPERFICIAL FASCIAL FIBROMATOSES

1. Palmar fibromatosis (Dupuytren disease)
2. Plantar fibromatosis (Ledderhose disease)
3. Penile fibromatosis (Peyronie disease)

4. **Knuckle pads**
   = focal fibrous thickening dorsally at PIP / MCP joint
5. Juvenile aponeurotic fibroma
6. Infantile digital fibromatosis

Deep Musculoaponeurotic Fibromatoses

1. Desmoid-type fibromatosis
2. Abdominal wall fibromatosis
3. Mesenteric fibromatosis
4. Retroperitoneal fibromatosis
5. Pelvic fibromatosis
6. Gardner syndrome fibromatosis

Childhood Fibromatosis

1. Fibromatosis colli
2. Lipofibromatosis
3. Calcifying aponeurotic fibroma
4. Inclusion body fibromatosis
5. Infantile myofibromatosis
5. Juvenile aponeurotic fibroma
6. Infantile digital fibromatosis

Cystlike T2-hyperintense Soft-tissue Lesions on MRI

Cause: (a) true cyst
(b) internal tumor necrosis
(c) high extracellular water content = edema
(d) extracellular matrix of high water + protein content = myxoid stroma

A. TRULY CYSTIC LESION
   1. Synovial cyst
   2. Ganglion cyst
   2. Distended bursa
   3. Postsurgical collection + hematoma
   4. Skin appendage: eg, epidermal inclusion cyst
   5. Lymphatic malformation
   6. Hydatid cyst

B. BENIGN SOLID LESION
   1. Myxoma
   2. Peripheral nerve sheath tumor
   3. Vascular lesions: hemangioma, vascular malformation
   4. Glomus tumor

C. MALIGNANT SOLID LESION
   1. Malignant fibrous histiocytoma = undifferentiated pleomorphic sarcoma
   2. Myxoid sarcoma:
      › myxofibrosarcoma
      › myxoid liposarcoma
      › extraskeletal myxoid chondrosarcoma

3. Synovial sarcoma
4. Metastasis

Myxomatous Lesions of Soft Tissue

= tumor with abundance of extracellular mucoid material
√ mimicker of cysts ← high water content

A. BENIGN
   1. Intramuscular myxoma
      √ perilesional edema + rim of fat
   2. Synovial cyst
      √ communication with joint / tendon sheath
   3. Bursa
   4. Soft-tissue ganglion
      √ communication with joint / tendon sheath
   5. Benign peripheral nerve sheath tumor: neurofibroma, schwannoma
      √ "entering-and-exiting-nerve" sign

B. MALIGNANT
   1. Myxoid liposarcoma
      √ intralesional fat
   2. Myxoid leiomyosarcoma
   3. Myxoid chondrosarcoma
      √ internal chondroid matrix
   4. Ossifying fibromyxoid tumor
      √ incomplete peripheral ossification
   5. Myxofibrosarcoma

C. SYNDROMES
   1. Mazabraud syndrome

Extraskeletal Osseous + Cartilaginous Tumors

A. OSSEOUS SOFT-TISSUE TUMORS
   √ cloudlike "cumulus" type of calcification
   1. Myositis ossificans
   2. Fibrodysplasia ossificans progressiva
   3. Soft-tissue osteoma
   4. Extraskeletal osteosarcoma
   5. Myositis ossificans variants
      (a) Panniculitis ossificans
      (b) Fasciitis ossificans
      (c) Fibroosseous pseudotumor of digits

B. CARTILAGINOUS SOFT-TISSUE TUMORS
   √ arcs and rings, spicules and floccules of calcification
   1. Synovial osteochondromatosis
   2. Soft-tissue chondroma
   3. Extraskeletal chondrosarcoma

DDx:

(1) Synovial sarcoma
(2) Benign mesenchymoma
= lipoma with chondroid / osseous metaplasia
(3) Malignant mesenchymoma
= 2 or more unrelated sarcomatous components
(4) Calcified / ossified tophus of gout
(5) Ossified soft-tissue masses of melorheostosis
(6) Tumoral calcinosis
(7) **Pilomatricoma** = calcifying epithelioma of Malherbe
• lesion arises from hair matrix cells with slow growth confined to the subcutaneous tissue of the face, neck, upper extremities
√ central sandlike calcifications (84%)
√ peripheral ossification (20%)

Soft-tissue Uptake of Bone Agents

A. Physiologic
1. Breast
2. Kidney: accentuated uptake with dehydration, antineoplastic drugs, gentamicin
3. Bowel: surgical diversion of urinary tract

B. Faulty preparation with radiochemical impurity
(a) free pertechnetate (TcO_4^-)
Cause: introduction of air into the reaction vial
√ activity in mouth (saliva), salivary glands, thyroid, stomach (mucus-producing cells), GI tract (direct secretion + intestinal transport from gastric juices), choroid plexus
(b) ^{99m}Tc-MDP colloid
Cause: excess aluminum ions in generator eluate / patient ingestion of antacids; hydrolysis of stannous chloride to stannous hydroxide, excess hydrolyzed technetium
√ diffuse activity in liver + spleen

C. Neoplastic condition
(a) benign tumor
1. Tumoral calcinosis
2. Myositis ossificans
(b) primary malignant neoplasm
1. Extraskeletal osteosarcoma / soft-tissue sarcoma: bone forming
2. Neuroblastoma (35–74%): calcifying tumor
3. Breast carcinoma
4. Meningioma
5. Bronchogenic carcinoma (rare)
6. Pericardial tumor
(c) metastases with extraosseous activity
1. to liver: mucinous carcinoma of colon, breast carcinoma, lung cancer, osteosarcoma
mnemonic: LE COMBO

Lung cancer
Esophageal carcinoma
Colon carcinoma
Oat cell carcinoma
Melanoma
Breast carcinoma
Osteogenic sarcoma

2. to lung: 20–40% of osteosarcomas metastatic to lung demonstrate ^{99m}Tc-MDP uptake
3. Malignant pleural effusion, ascites, pericardial effusion

D. Inflammation
1. Inflammatory process (abscess, pyogenic / fungal infection):
   (a) adsorption onto calcium deposits
   (b) binding to denatured proteins, iron deposits, immature collagen
   (c) hyperemia
2. Crystalline arthropathy (eg, gout)
3. Dermatomyositis, scleroderma
4. Radiation: eg, radiation pneumonitis
5. Necrotizing enterocolitis
6. Diffuse pericarditis
7. Bursitis
8. Pneumonia

E. Trauma
1. Healing soft-tissue wounds
2. Rhabdomyolysis:
   crush injury, surgical trauma, electrical burns, frostbite, severe exercise, alcohol abuse
3. Intramuscular injection sites:
   especially Imferon® (= iron dextran) injections with resultant chemisorption; meperidine
4. Ischemic bowel infarction (late uptake)
5. Hematoma: soft tissue, subdural
6. Heterotopic ossification
7. Myocardial contusion, defibrillation, unstable angina pectoris
8. Lymphedema

F. Metabolic
1. Hypercalcemia (eg, hyperparathyroidism):
   (a) uptake enhanced by alkaline environment in stomach (gastric mucosa), lung (alveolar walls), kidneys (renal tubules)
   (b) uptake with severe disease in myocardium, spleen, diaphragm, thyroid, skeletal muscle
2. Diffuse interstitial pulmonary calcifications: hyperparathyroidism, mitral stenosis
3. Amyloid deposits

G. Ischemia / necrosis with dystrophic soft-tissue calcifications

@ Spleen: infarct (sickle cell anemia in 50%), microcalcifications ← lymphoma, thalassemia major, hemosiderosis, glucose-6-phosphate-dehydrogenase deficiency

@ Liver: massive hepatic necrosis
@ Heart: transmural myocardial infarction, valvular calcification, amyloid deposition
@ Muscle: traumatic / ischemic skeletal muscle injury
@ Brain: cerebral infarction (damage of blood-brain barrier)
@ Kidney: nephrocalcinosis
@ Vessels: calcified wall, calcified thrombus

Soft-tissue Calcification

Metastatic / Metabolic Calcification

= deposit of calcium salts in normal tissue
(1) as a result of elevation of Ca x P product above 60–70
(2) with normal Ca x P product after renal transplant

Location: lung (alveolar septa, bronchial wall, vessel wall), kidney, gastric mucosa, heart, peripheral vessels

Cause:

(a) Skeletal deossification
1. 1° HPT
2. Ectopic HPT production (lung / kidney tumor)
3. Renal osteodystrophy + 2° HPT
4. Hypoparathyroidism
5. Prolonged immobilization

(b) Massive bone destruction
1. Widespread bone metastases
2. Plasma cell myeloma
3. Leukemia

(c) Hypercalcemia
1. Primary hyperparathyroidism
2. Hypervitaminosis D
3. Milk-alkali syndrome
4. Sarcoidosis
5. Hydroxyapatite deposition disease
6. IV administration of calcium salts

(d) Idiopathic hypercalcemia

(e) Hyperuricemia
1. Tophaceous gout

Dystrophic Calcification

= deposit of calcium salts in tissue damaged by injury / inflammation (with local electrolyte / enzyme alterations) in presence of normal serum Ca + P level

Cause:

(a) Metabolic disorder without hypercalcemia
1. Renal osteodystrophy with 2° HPT
2. Hypoparathyroidism
3. Pseudohypoparathyroidism

4. Pseudopseudohypoparathyroidism
5. Gout
6. Pseudogout = chondrocalcinosis
7. Ochronosis = alkaptonuria
8. Diabetes mellitus

(b) Connective tissue disorder
1. Scleroderma = progressive systemic sclerosis
2. Dermato- and polymyositis
3. Systemic lupus erythematosus
4. Mixed connective tissue disorders

(c) Trauma
1. Neuropathic calcifications
2. Frostbite
3. Myositis ossificans progressiva

(d) Infestation
1. Cysticercosis
2. Dracunculosis (guinea worm)
3. Loiasis
4. Bancroft filariasis
5. Hydatid disease
6. Leprosy

(e) Vascular disease
1. Atherosclerosis
2. Media sclerosis (Mönckeberg)

DDx of Soft-Tissue Calcifications

Metastatic Calcifications	*Dystrophic Calcifications*	*Calcinosis*
Hyperpara-thyroidism	Soft-tissue tumor: lipoma, sarcomas (synovial, osteo~, chondro~)	Idiopathic tumoral calcinosis
Hypopara-thyroidism	Inherited disorder: Ehlers-Danlos, pseudoxanthoma	Calcinosis interstitialis universalis
Milk-alkali syndrome	Parasitic infection	Calcinosis in SLE, scleroderma, juvenile dermatomyositis
Excessive vitamin D	Tophaceous gout	
Sarcoidosis		
Paraneoplastic hypercalcemia		
Destructive bone disease		

3. Venous calcifications
4. Tissue infarction (eg, myocardial infarction)

(f) Miscellaneous
1. Ehlers-Danlos syndrome
2. Pseudoxanthoma elasticum
3. Werner syndrome = progeria
4. Calcinosis (circumscripta, universalis, tumoral calcinosis)

(g) Neoplastic disease
1. Synovial sarcoma
2. Osteosarcoma
3. Chondrosarcoma
4. Necrotic tumor

(h) Degenerative disease
1. Calcium pyrophosphate deposition disease
2. Calcific tendonitis (in 3% of adults)
Location: shoulder > hip > elbow > wrist > knee
3. Calcific bursitis

(i) Metaplasia
1. Synovial osteochondromatosis

GENERALIZED CALCINOSIS

(a) Collagen vascular disorders
1. Scleroderma
2. Dermatomyositis

(b) Idiopathic calcinosis universalis

Idiopathic Calcification

1. Tumoral calcinosis
   - normal calcium + elevated phosphate levels

Interstitial Calcinosis

Calcinosis Circumscripta

- firm white commonly ulcerating dermal papules / plaques / subcutaneous nodules extruding a chalky white material of hydroxyapatite

1. Acrosclerosis: granular deposits around joints of fingers and toes, fingertips
2. Scleroderma + CREST syndrome: acrosclerosis and absorption of ends of distal phalanges
3. Dermatomyositis: extensive subcutaneous deposits
4. Varicosities: particularly in calf
5. 1° Hyperparathyroidism: infrequently periarticular calcinosis
6. Renal osteodystrophy with 2° hyperparathyroidism: extensive vascular deposits even in young individuals
7. Hypoparathyroidism: occasionally around joints; symmetrical in basal ganglia
8. Vitamin D intoxication: periarticular in rheumatoid arthritis (puttylike); calcium deposit in tophi

Calcinosis Universalis

= progressive disease of unknown origin
Age: children + young adults
Associated with: poly- and dermatomyositis
√ diffuse plaque- / sheetlike calcium deposits in skin and subcutis; sometimes in tendons + muscles + fascia
√ NO true bone formation

Soft-tissue Ossification

= formation of trabecular bone

1. Myositis ossificans progressiva / circumscripta
2. Paraosteoarthropathy
3. Soft-tissue osteosarcoma
4. Parosteal osteosarcoma
5. Posttraumatic periostitis = periosteoma
6. Surgical scar
7. Severely burned patient

Connective Tissue Disease

= CTD = [COLLAGEN VASCULAR DISEASE]

= heterogeneous group of immunologically mediated systemic inflammatory disorders that may affect various organs but share a number of clinical + laboratory features

- Features:
  (a) relatively specific: arthritis, myositis, Raynaud phenomenon with digital ulceration, tethered skin in extremities + trunk, malar rash sparing nasolabial folds, morning stiffness
  (b) relatively nonspecific: polyarthralgias (most common initial symptom), myalgias, mottling of extremities, muscle weakness + tenderness
- Laboratory findings:
  (a) relatively specific: ANA in peripheral rim / nucleolar pattern, anti-DNA, elevated muscle enzyme
  (b) relatively nonspecific: ANA in homogeneous pattern, anti-single-stranded DNA, positive rheumatoid factor

Types and most distinctive features:

1. Rheumatoid arthritis positive rheumatoid factor, prominent morning stiffness, symmetric erosive arthritis
2. Systemic lupus erythematosus malar rash, photosensitivity, serositis, renal disorders with hemolytic anemia, leukopenia, lymphopenia, thrombocytopenia, positive ANA
3. Sjögren syndrome dry eyes + mouth, abnormal Schirmer test
4. Progressive systemic sclerosis
   Raynaud phenomenon, skin thickening of distal extremities proceeding to include proximal extremities + chest + abdomen, positive ANA in a nucleolar pattern
5. Polymyositis, dermatomyositis heliotrope rash over eyes, proximal muscle weakness, elevated muscle enzymes, inflammation at muscle biopsy
6. Mixed connective tissue disease

Thoracic imaging pattern: *(see table)*

Muscle

MR signal intensity of normal muscle:

√ higher than water + lower than fat on T1WI

√ much lower than water + fat on T2WI

Intramuscular Mass

A. NEOPLASM

B. INFECTION / INFLAMMATION

1. Intramuscular abscess
2. Focal myositis = benign inflammatory pseudotumor
3. Necrotizing fasciitis
4. Sarcoidosis

√ nodules with central star-shaped area of fibrosis surrounded by granuloma

C. MYONECROSIS

1. Sickle cell crisis
2. Poorly controlled diabetes
3. Compartment syndrome
4. Crush injury
5. Severe ischemia
6. Intraarterial chemotherapy
7. **Rhabdomyolysis** = severe muscle injury with loss of integrity of muscle cell membranes

Cause: trauma, severe exercise, ischemia, burn, toxin, IV heparin therapy, autoimmune inflammation

Frequency of Thoracic CT Findings of Connective Tissue Disease

	Mixed Connective Tissue Disease	*Dermatomyositis Polymyositis*	*Progressive Systemic Sclerosis*	*Juvenile Idiopathic Arthritis*	*Systemic Lupus Erythematosus (SLE)*
Ground-glass opacity	+++	+++	+++	+++	+++
Septal thickening	++	++	++	++	++
Honeycombing	+++	+	++++	+	+
Consolidation	+	+++	+	+	++++
Crazy paving	—	—	—	—	++
Pulmonary nodules	—	—	—	++	—
Pleural / pericardial effusions	++	—	+	++++	++++
Progressive ↓ of lung volume	+	+	+	++	++
Pulmonary embolism	—	—	—	—	+
MPA dilatation	+	+	++	+	+

Pulmonary Manifestations of Collagen Vascular Disease

Type	*UIP*	*NSIP*	*COP*	*LIP*	*DAD*	*Hemorrhage*	*Airway disease*
Rheumatoid arthritis	+++	++	++	+	+	–	+++
Progressive systemic sclerosis	+	+++	+	–	+	–	–
Dermato- / polymyositis	+	+++	+++	–	++	–	–
Sjögren syndrome	++	++	–	++	+	–	+
Mixed connective tissue disease	+	++	+	–	–	–	–
Systemic lupus erythematosus	+	++	+	+	++	+++	–

COP = Crytpogenic Organizing Pneumonia, DAD = Diffuse Alveolar Damage, LIP = Lymphocytic Interstitial Pneumonia, NSIP = Nonspecific Interstitial Pneumonia, UIP = Usual Interstitial Pneumonia

Thoracic Manifestations of Collagen Vascular Disease						
	Ankylosing Spondylitis	*Dermatomyositis Polymyositis*	*Progressive Systemic Sclerosis*	*Rheumatoid Arthritis*	*Sjögren Syndrome*	*Systemic Lupus Erythematosus (SLE)*
Pulmonary fibrosis	occasional	common	frequent	frequent	occasional	occasional
Pleural disease	—	—	—	frequent	—	frequent
Diaphragm weakness	—	frequent	—	—	—	frequent
Aspiration pneumonia	—	frequent	frequent	—	—	—
Bronchiectasis	—	—	—	occasional	common	—
Apical fibrosis	frequent	—	—	—	—	—
Bronchiolitis obliterans	—	—	—	common	—	—
BOOP	—	common	—	common	—	—

Cx: renal damage from myoglobulinemia, tetany, compartment syndrome

D. TRAUMA
   1. Intramuscular hematoma (eg, severe muscle strain, laceration, contusion, spontaneous)
   2. Myositis ossificans traumatica

Muscle Edema

√ muscle hyperintensity on STIR images

A. INFLAMMATION
   1. Dermatomyositis
   2. Polymyositis
   4. Radiation therapy: straight sharp margins, involves muscle + subcutaneous fat
   5. Early stage of myositis ossificans

B. CELLULAR INFILTRATE
   1. Lymphoma

C. INFECTION
   1. Bacterial / infectious myositis
      (a) direct extension from adjacent infection (eg, osteomyelitis, subcutaneous abscess)
      (b) hematogenous
   2. Inclusion body myositis (probably due to paramyxovirus infection) resembling polymyositis

D. RHABDOMYOLYSIS
   1. Sport / electric injury
   2. Diabetic muscular infarction
   3. Focal nodular myositis
   4. Metabolic myopathy: eg, phosphofructokinase deficiency, hypokalemia, alcohol overdose
   5. Viral myositis

E. TRAUMA
   1. **Subacute muscle denervation**
      Time of onset: 2–4 weeks after denervation
      Mechanism:
      spinal cord injury, poliomyelitis, peripheral nerve injury / compression (ganglion cyst, bone spur), Graves disease, neuritis

2. Muscle contusion (from direct blow)
3. **Muscle strain** (= injury at musculotendinous junction from overly forceful muscle contraction)
   Predilection for: hamstring, gastrocnemius m., biceps brachii m.)
4. **Delayed-onset muscle soreness**
   = overuse injury becoming symptomatic hours / days after overuse episode
5. **Compartment syndrome**
   = increased pressure within indistensible space of confining fascia leading to venous occlusion, muscle + nerve ischemia, arterial occlusion, tissue necrosis
   Cause: trauma, burns, heavy exercise, extrinsic pressure, intramuscular hemorrhage
   • severe pain
   • dysfunction of sensory + motor nerves passing through affected compartment
   Rx: urgent fasciotomy
6. Sickle cell crisis

Fatty Infiltration of Muscle

1. Chronic stage of muscle denervation (eg, poliomyelitis, stroke, peripheral nerve injury)
2. Chronic disuse (eg, chronic tendon tear, severe osteoarthritis)
3. Late stage of severe muscle injury
4. Long-term high-dose corticosteroid medication affecting truncal muscles

MUSCULOSKELETAL INFECTION

At risk: IV drug abuse, HIV, sickle cell disease, diabetes, peripheral vascular disease, immunocompromised, cancer, alcoholism, organ transplants

1. **Cellulitis**
   = acute infection of dermis + SQ tissue
   • pain, erythema, edema, warmth
   CT:
   √ skin thickening
   √ septation of SQ fat
   √ thickening of underlying superficial fascia
   Dx: clinical assessment
   DDx: heart failure
2. Necrotizing fasciitis
3. Soft-tissue abscess
   Cause: methicillin-resistant S. aureus (MRSA, 51%)
   √ well-demarcated fluid collection with peripheral pseudo-capsule showing rim enhancement
   DDx: cellulitis, fasciitis (no rim enhancement)
4. Infectious myositis
5. Osteomyelitis
6. Septic arthritis
7. Septic bursitis

TENDON

MRI Spectrum of Tendon Pathology

1. Tendinosis
   √ fusiform thickening of tendon + ↑ SI on PDWI + T1WI
   √ ↑ SI on T2WI ← severe intrasubstance degeneration
2. Tenosynovitis
   √ fluid + synovial proliferation within tendon sheath
3. Peritendinosis
   √ fluid in adjacent soft tissues
4. Tendon rupture
   (a) partial rupture
      √ focal areas of fiber discontinuity often outlined by fluid
   (b) complete rupture
      √ complete fiber discontinuity (= disruption) of tendon
      √ fluid outlining retracted proximal + distal stumps
5. Tendon entrapment
6. Tendon instability: subluxation / dislocation

Tendon Rupture

Location: quadriceps, Achilles tendon, rotator cuff, biceps brachii

Cause:

A. Traumatic

B. Spontaneous

= rupture during movement and activity that usually does not damage the musculotendinous unit

Risk factors: hyperparathyroidism, chronic renal failure, gout, Reiter syndrome, obesity, leukemia, rheumatoid arthritis, diabetes mellitus, systemic lupus erythematosus, infection, metabolic diseases, psoriasis, steroid abuse / injections, Marfan syndrome, tumors, immobilization

Classification and findings on MR:

(a) partial tear
   √ increased signal within tendon on T1WI + T2WI with extension to surface of tendon
   √ focal / diffuse enlargement or atrophy
   √ partial disruption of tendon fibers
   √ focal intratendinous fluid
   √ tendon enhancement

(b) complete tear
   √ discontinuity + separation of torn ends of tendon
   √ interposed edema + hemorrhage

FIXATION DEVICES

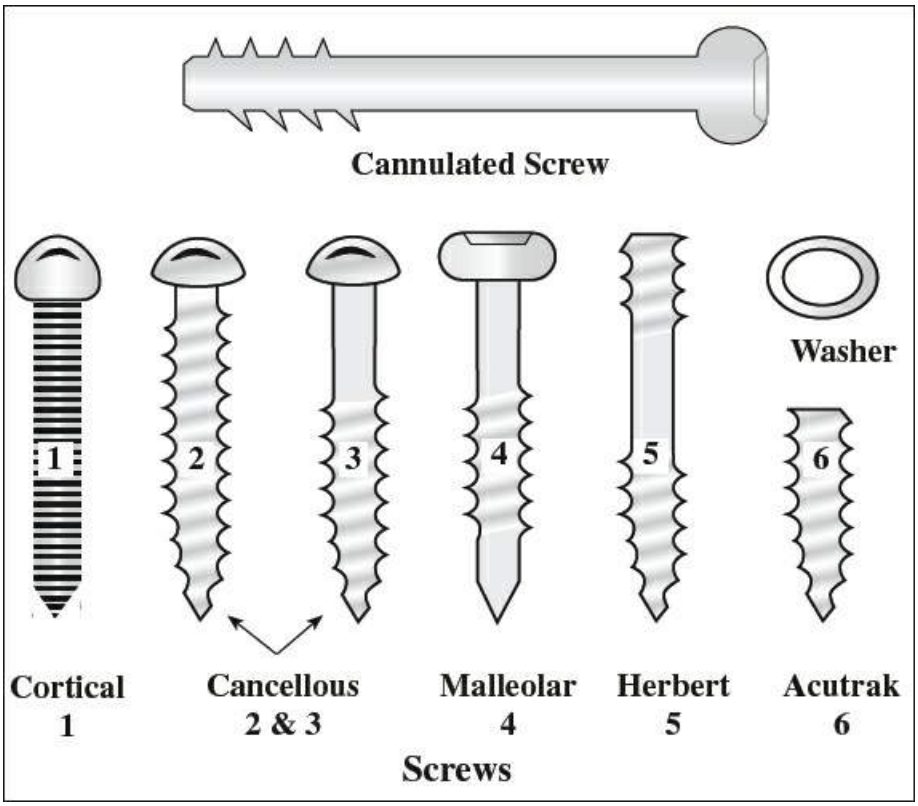
Internal Fixation Devices

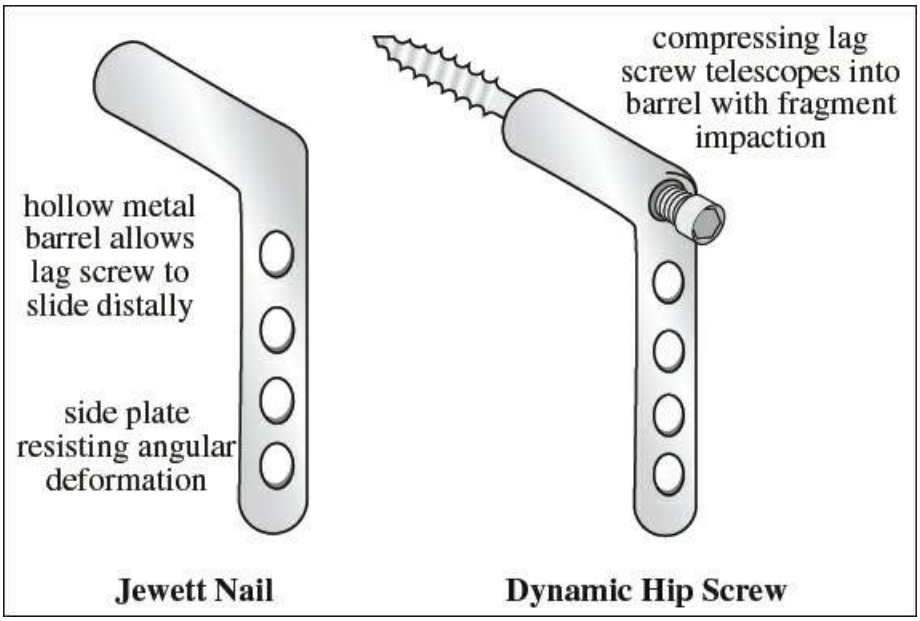
A. Screws

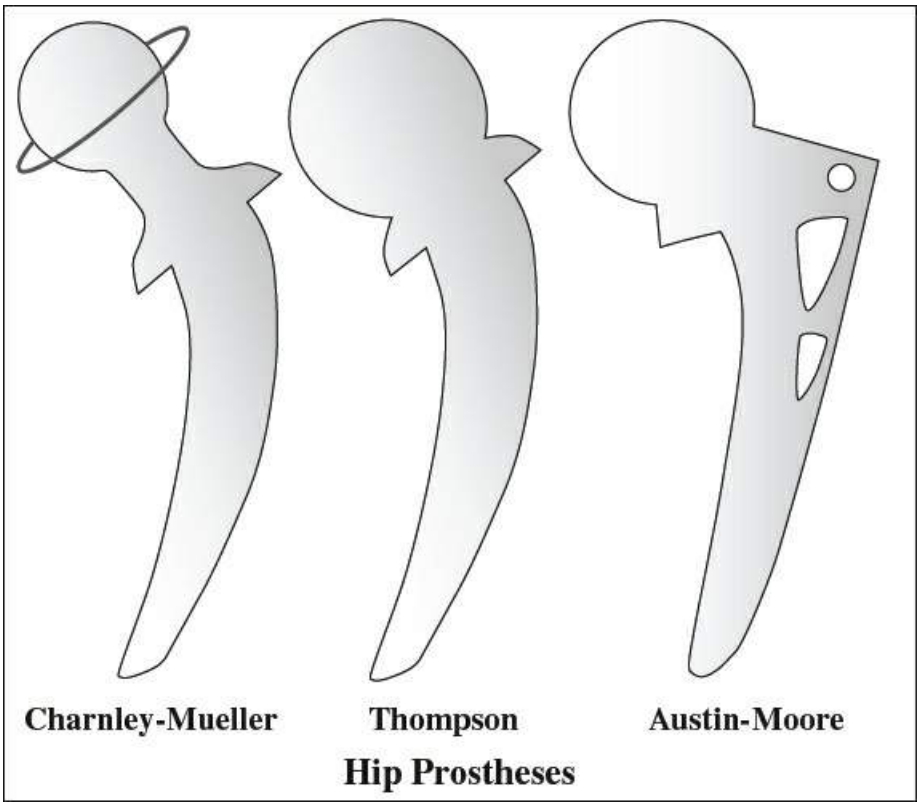
1. Cannulated screw = hollow shaft screw inserted over guide pin (K-wire = Kirschner wire)
   Use: fracture of femoral neck
2. Cortical screw = shallow finely threaded over entire length, blunt tip
   Use: fixation of plates anchored in bone cortex
3. Cancellous screw = wide thread diameter with varying length of smooth shank between head + threads
   Use: compression across fracture site anchored in soft medullary bone
4. Malleolar screw = partially threaded
5. Herbert screw = cannulated screw threaded on both ends with wider pitch of proximal portion causing fragment compression, no screw head
   Use: scaphoid + other carpal bone fractures
6. Interference screw = short, fully threaded, cancellous thread pattern, self-tapping tip, recessed head
   Use: within tunnel holding bone graft of ACL and PCL reconstruction
7. Acutrak screw = cannulated screw fully threaded with variable thread pitch causing fragment compression, submerged without screw head
   Use: scaphoid fracture
8. Dynamic hip screw = lag screw telescopes (= free to slide) within hollow metal barrel of angular side plate allowing impaction of fracture without perforation of subarticular cortex
   Use: intertrochanteric, subtrochanteric, subcapital fracture
9. Knowles pin
   Use: proximal femoral neck fracture with tenuous blood supply
10. Radiolucent absorbable polycarbonate screw = "stealth hardware"

B. Washer
   1. Flat washer = increase surface area over which force is distributed
   2. Serrated washer = spiked edges used for affixing avulsed ligaments / small avulsion fractures

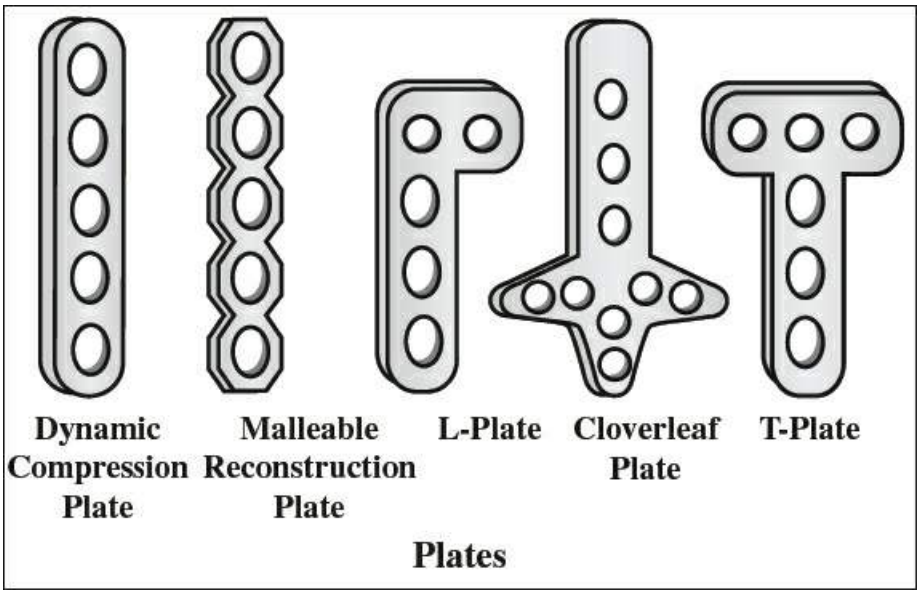
C. Plates
   › compression plate
   Use: compression of tension side of stable fractures
   › neutralization plate = protects fracture from bending, rotation + axial-loading forces
   › buttress plate = support of unstable fractures in compression / axial loading
   1. Straight plate
      (a) straight plate with round holes
      (b) dynamic compression plate (DCP) = oval holes
      (c) tubular plate = thin pliable plate with concave inner surface
      (d) reconstruction plate = thin pliable / malleable plate to allow bending, twisting, contouring
   2. Special plates
      T-shaped, L-shaped, Y-shaped, cloverleaf, spoon, cobra, condylar blade plate, dynamic compression screw system


Cannulated Screw
Washer
1
2
3
4
5
6
Cortical
1
Cancellous
2 & 3
Malleolar
4
Herbert
5
Acutrak
6
Screws

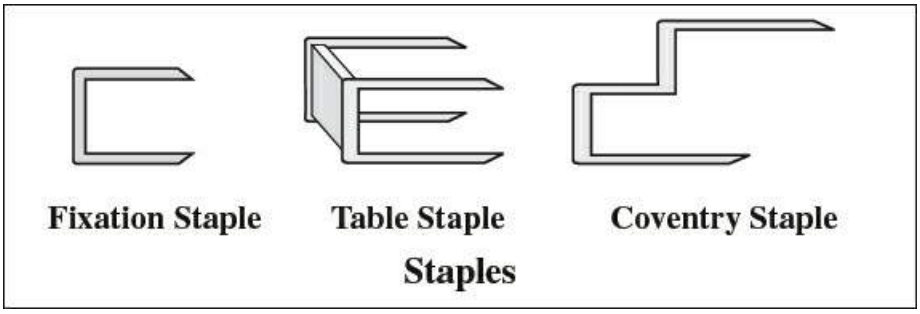

compressing lag screw telescopes into barrel with fragment impaction
hollow metal barrel allows lag screw to slide distally
side plate resisting angular deformation
Jewett Nail
Dynamic Hip Screw

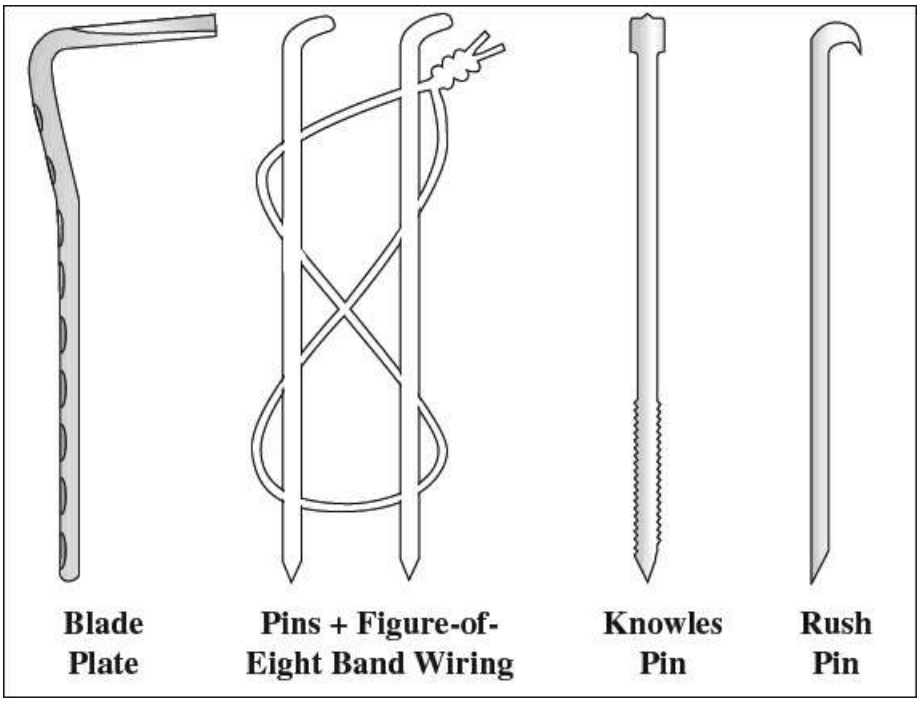


Hip Prostheses



Plates





D. Staples
Fixation = bone = epiphyseal = fracture staples with smooth / barbed surface
› Coventry = stepped osteotomy staple
› stone = table staple

E. Wires
1. K wire (= Kirschner wire) = unthreaded segments of extruded wire of variable thickness
Use: temporary fixation
2. Cerclage wiring = wire placed around bone
Use: fixation of comminuted patellar fracture, holding bone grafts in position
3. Tension band wiring = figure-of-eight wire placed on tension side of bone
Use: olecranon / patellar fractures

External Fixation Devices

= smooth / threaded pins / wires attached to an external frame

(a) unilateral pin = enters bone only from one side
1. Steinmann pin = large-caliber wire with pointed tip

2. Rush pin = smooth intramedullary pin
3. Schanz screw = pin threaded at one end to engage cortex, smooth at other end to connect to external fixation device
4. Knowles pin (for femoral neck fracture)

(b) transfixing pin = passes through extremity supported by external fixation device on both ends

Intramedullary Fixation Devices

Use: diaphyseal long bone fractures

(a) nail / pin= driven into bone without reaming

(b) rod = solid / hollow device with blunted tip driven into reamed channel (reaming disrupts blood supply and may decrease the rate of fracture healing)

(c) interlocking nail = accessory pins / screws / deployable fins placed to prevent rotation

1. Rush pin = beveled end + hooked end
   Use: fibular shaft / tubular bone fractures
2. Ender nail = chisel-like end + oval in cross section; usually 3–4 at a time pushed through a cortical hole up or down the shaft across fracture under fluoroscopic control
   Use: humeral shaft
3. Sampson rod = slightly curved rigid rod with fluted surface
4. Küntscher nail = cloverleaf in cross section with rounded tip
   Use: tibial / femoral shaft fracture
5. Zickel nail
   Use: subtrochanteric fracture

ANATOMY AND METABOLISM OF BONE

BONE MINERALS

Bone composition: highly metabolic tissue consisting of type I collagen (40%) + hydroxyapatite (45%) + water (15%)

Bone mass: function of

(a) peak bone mass attained in 3rd decade of life influenced by dietary calcium intake during adolescence, sex hormone status (male > female), nutrition, physical activity, genetic factors (Blacks > Whites > Asians)

(b) rate of age-related bone loss = endosteal + Haversian resorption + loss of cancellous bone (particularly in vertebrae) without replacement by new bone

Bone resorption: in the elderly due to

(a) estrogen deficiency = rate increased at menopause

(b) diminished fractions of bioavailability for testosterone

(c) vitamin D insufficiency → secondary hyperparathyroidism

(d) declining levels of physical activity

(e) reduced serum levels of insulin-like growth factors

Calcium

A. 99% in bone

B. serum calcium

(a) protein-bound fraction (albumin)

(b) ionic (pH-dependent) 3% as calcium citrate / phosphate

Absorption: facilitated by vitamin D

Excretion: related to dietary intake; > 500 mg/24 hours (= hypercalciuria)

Phosphorus

Absorption: requires sodium; decreased by aluminum hydroxide gel in gut

Excretion: increased by estrogen, parathormone decreased by vitamin D, growth hormone, glucocorticoids

BONE MARROW

4th largest organ, 5% of body weight

Components: trabeculae, hematopoietic cells, fat cells, stroma, and RES cells, sinusoids

(a) **Red marrow**

= hematopoietically active (by EGA of 20 weeks) with a rich + extensive vascular supply, composed of erythrocyte + leukocyte + platelet precursors

› in adolescence: 40% fat, 40% water, 20% protein

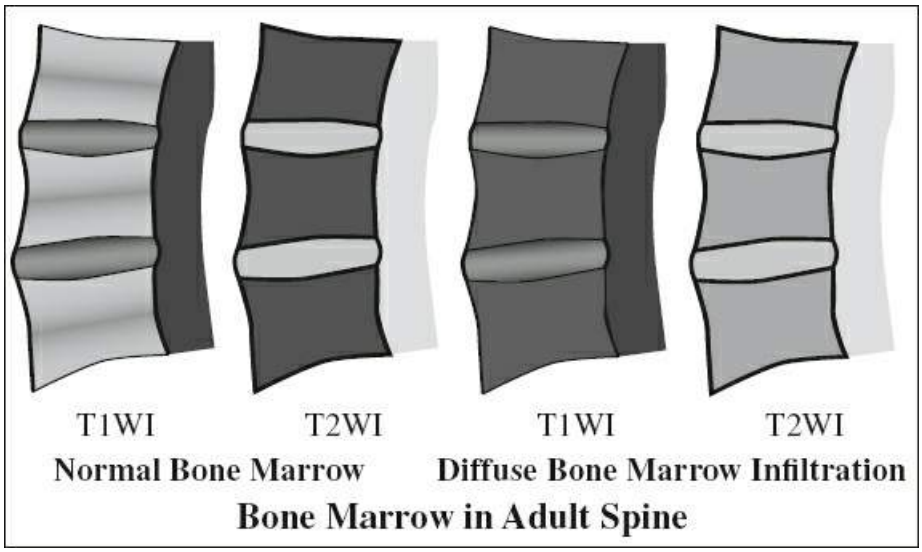
› at age 70: 60% fat, 30% water, 10% protein

(b) **Yellow / fatty marrow**

with a sparse vascular network

› composed of 80% fat, 15% water, 5% protein

Distribution: conversion from red to fatty marrow throughout life



@ birth: marrow contains primarily hematopoietically active cells

@ 1 year: 1st conversion in phalanges of feet

@ puberty: conversion in diaphyses of long bones

@ 1st 2 decades: conversion begins in appendicular skeleton progressing to axial skeleton; conversion in long bones begins in diaphysis > distal metaphysis > proximal metaphysis

@ 3rd decade: residual red marrow remains in skull, spine, flat bones (clavicle, sternum, scapula, ribs), proximal 25–30% of humerus and femur; acetabulum superiorly + medially > ilium > around sacroiliac joints

NUC:

(1) Labeled leukocyte scintigraphy

(2) Bone marrow scintigraphy

MR:

Anatomic sites for MRI marrow screening:

› spine (SAG images)

› pelvis + femora (COR images)

√ red marrow:

√ iso- / slightly hyperintense compared with muscle on T1WI + T2WI (longer T1 relaxation time)

√ hypointense compared with fatty marrow (shorter T2 relaxation time)

√ yellow marrow:

√ isointense compared with subcutaneous fat on T1WI (relatively short T1 relaxation time compared with water)

√ T2-iso- / hypointense compared with subcutaneous fat

√ hyperintense compared with muscle on T2WI (long T2 relaxation time compared with water)

◊ Differences in SI are maximized on T1WI but diminished on T2WI

◊ Marrow signal iso- / hypointense to muscle + disk on T1WI in adults is abnormal!
◊ After 10 years of age red marrow is hyperintense to muscle on T1WI
◊ Fat-suppressed T2-FSE and STIR are very sensitive for pathology!

Bone Marrow Reconversion

= reversal of yellow to red marrow

1. Obesity
2. Pulmonic pathology
3. Smoking
4. High altitude
5. High-performance athletes
6. GCSF (granulocyte stimulating factor)

Parathormone Function		
	PTH Action	*Net Effect*
Principal function:	phosphate diuresis resorption of Ca + P from bone	Serum: increase in Ca decrease in P
Secondary function:	resorption of Ca from gut reabsorption of Ca from renal tubule	Urine: increase in Ca increase in P

HORMONES

Parathormone

= key modulator of calcium homeostasis

Origin: chief cells of 4 parathyroid glands

Major stimulus: low levels of serum calcium ions (action requires vitamin D presence)

Target organs:

BONE: mobilization of calcium at bone surface ← ↑ in osteoclastic activity

KIDNEY: (a) ↑ renal tubular absorption of calcium
(b) ↓ tubular reabsorption of phosphate (+ amino acids) = phosphaturia
(c) ↑ hydroxylation of 25-OH vitamin D *(see below under vitamin D metabolism)*

GUT: ↑ absorption of calcium + phosphorus

Major function:

- increase of serum calcium levels
- increase in serum alkaline phosphatase (50%)

Vitamin D Metabolism

required for

(1) adequate calcium absorption from gut
(2) synthesis of calcium-binding protein in intestinal mucosa
(3) parathormone effect (→ stimulation of osteoclastic + osteocytic resorption of bone)

Biochemistry:

inactive form of vitamin D3 present through diet / exposure to sunlight (photoconversion of 7-dehydrocholesterol in skin to cholecalciferol)

› vitamin D3 is converted into **25-OH-vitamin D3** by liver

› 25-OH-vitamin D3 is converted into **1,25-OH vitamin D3** (biologically most active form = hormone) by kidney

(a) ↑ intestinal absorption of calcium

(b) binds to intranuclear receptors within bone → production of mediators for calcium mobilization + mineralization of organic matrix

Stimulus for conversion: (1) Hypophosphatemia
(2) PTH elevation

Action:

(a) BOWEL: (1) ↑ absorption of calcium from bowel
(2) increased absorption of phosphate from distal small bowel

(b) BONE: (1) proper mineralization of osteoid
(2) mobilization of calcium + phosphate (potentiates parathormone action)

(c) KIDNEY: (1) ↑ absorption of calcium from renal tubule
(2) ↑ absorption of phosphate from renal tubule

(d) CELL: binds to receptor on nucleus → activation of genes involved in calcium homeostasis

Calcitonin

secreted by parafollicular cells of thyroid

Major stimulus: increase in serum calcium

Target organs:

(a) BONE: (1) inhibits parathormone-induced osteoclasis by reducing number of osteoclasts
(2) enhances deposition of calcium phosphate; responsible for sclerosis in renal osteodystrophy

(b) KIDNEY: inhibits phosphate reabsorption in renal tubule

(c) GUT: increases excretion of sodium + water into gut

Major function: decreases serum calcium + phosphate

PHYSIS

= Growth Plate

Four distinct zones of cartilage in longitudinal layers

(1) Germinal zone = small cells
adjacent to epiphyseal ossification center

(2) Zone of proliferation = flattened cells
arranged in columns

(3) Zone of hypertrophy = swollen vacuolated cells
(a) zone of maturation
(b) zone of degeneration
(c) zone of provisional calcification

(4) Zone of primary and secondary spongiosa

NORMAL SHOULDER JOINT ANATOMY

Acromion Types

Normal anatomic variants can cause compression with an increased incidence of rotator cuff tears with type II and type III acromions according to cadaveric studies

Suprascapular Nerve

= mixed motor and sensory peripheral nerve

Origin: upper trunk of brachial plexus (roots of C5 and C6, variably from C4)

Course: deep to omohyoid m. and trapezius m. → *suprascapular notch* (beneath superior transverse scapular ligament) → supraspinatus fossa → around scapular spine → *spinoglenoid notch* → infraspinatus fossa

Innervation:

(a) supraspinatus m. (motor); glenohumeral joint + acromioclavicular joint + rotator cuff + posterior $^{2}/_{3}$ of joint capsule (sensory)

(b) infraspinatus m. (motor)

Rotator Cuff Muscles

mnemonic: SITS

Supraspinatus
Infraspinatus
Teres minor
Subscapularis

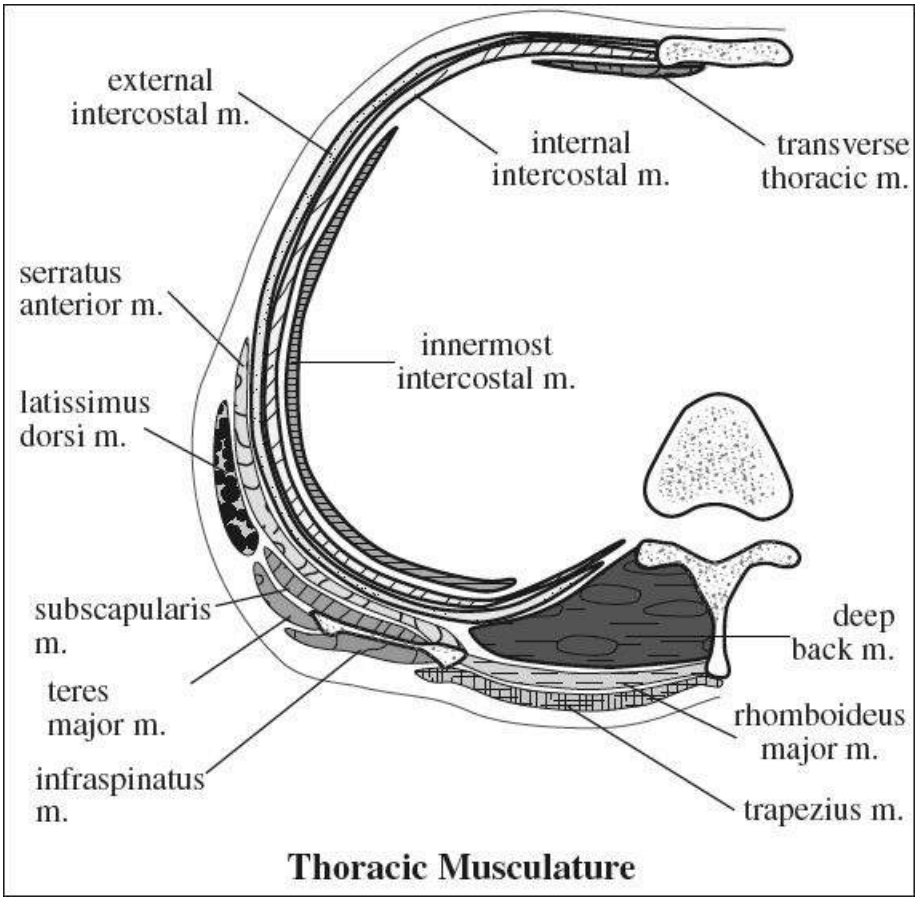
Glenoid Labrum

= 4-mm–wide triangular fibrocartilaginous rim (= extension of the glenoid fossa) with considerable variation in shape

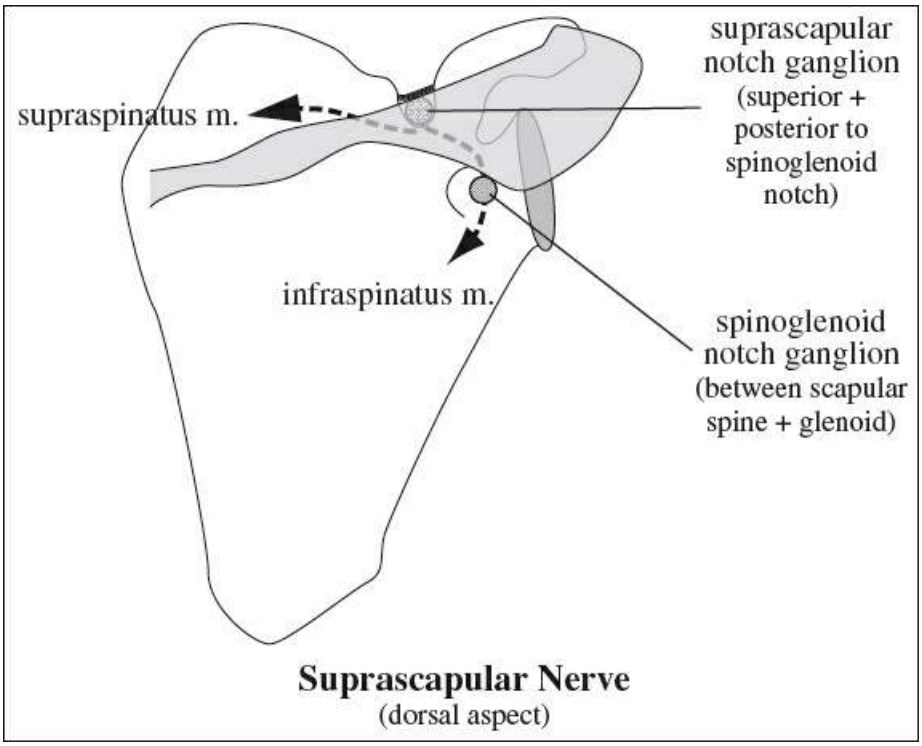
Function: stabilizes glenohumeral joint by deepening and increasing surface area of glenoid fossa and providing attachment for glenohumeral ligaments and tendon of long head of biceps

√ low SI on all pulse sequences; susceptible to magic angle artifact at 55°

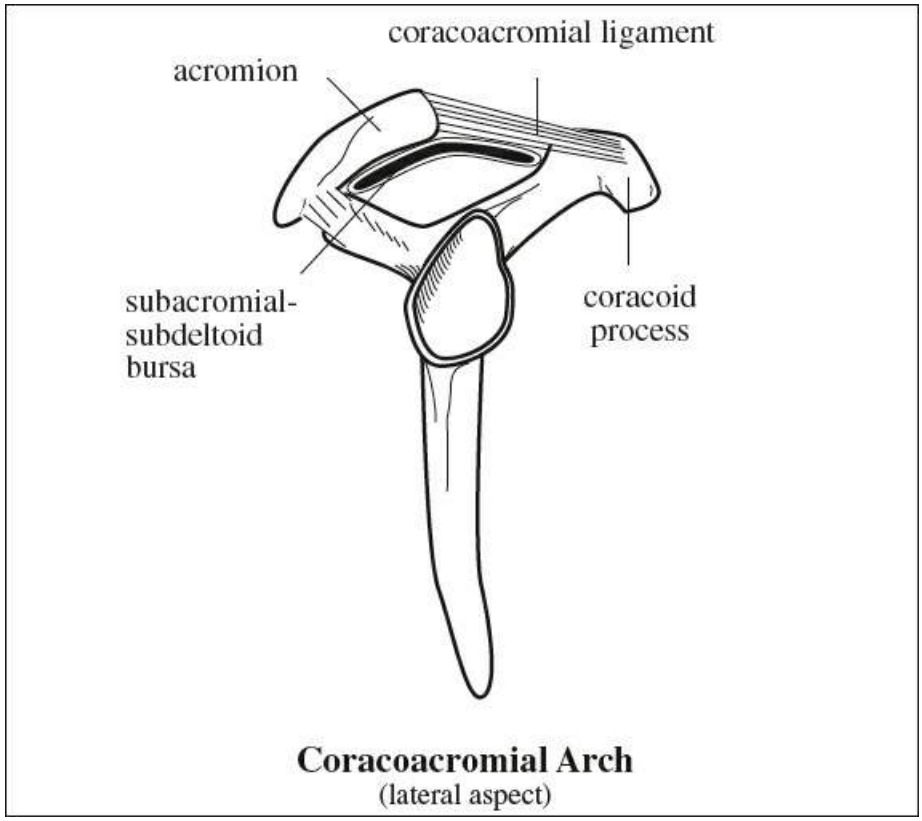
√ variations in attachment above epiphyseal line (= junction of upper + middle thirds of glenoid body fossa): limited to sector from 11 to 3 o'clock (anterior = 3 o'clock, posterior 9 o'clock, superior 12 o'clock, inferior 6 o'clock):



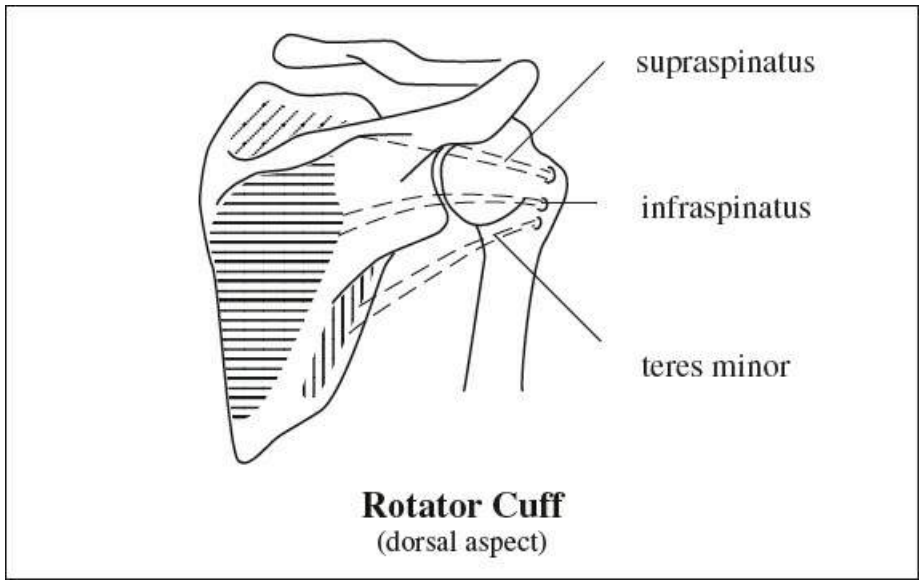
Thoracic Musculature



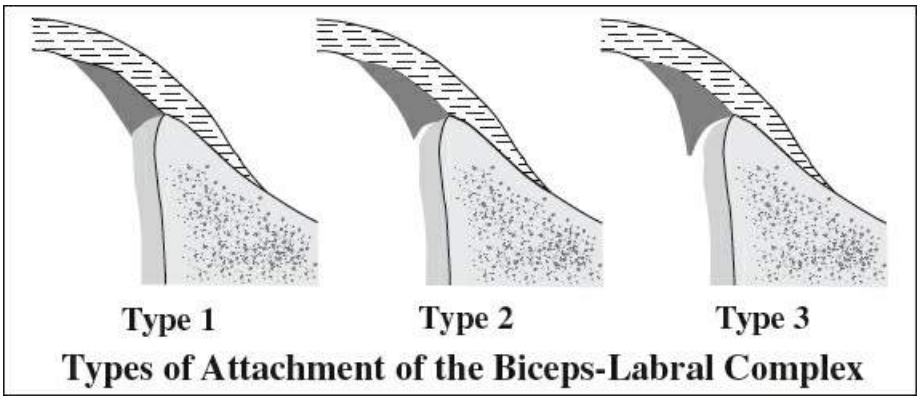
Suprascapular Nerve
(dorsal aspect)



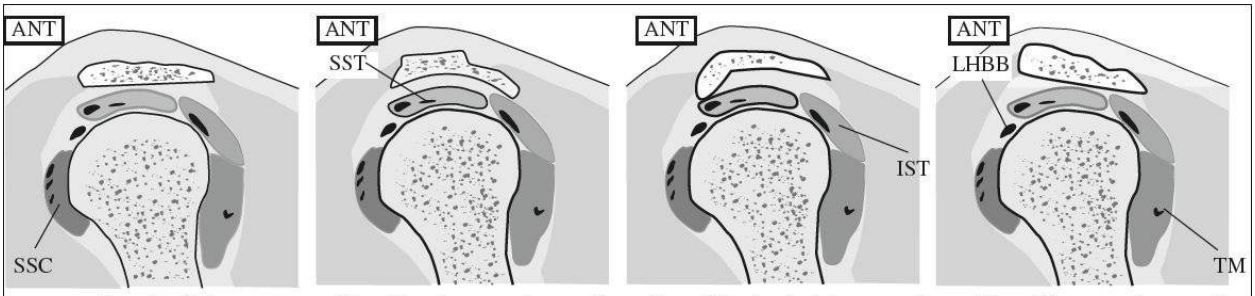
Coracoacromial Arch
(lateral aspect)



Rotator Cuff
(dorsal aspect)



Types of Attachment of the Biceps-Labral Complex



Acromion Types

(on sagittal view of shoulder)

IST = infraspinatus, LHBB = long head of biceps brachii tendon, SSC = subscapularis, SST = supraspinatus, TM = teres minor

Muscle Attachments of Shoulder

Name of Muscle	*Origin*	*Insertion*
Deltoid	lateral third of clavicle	deltoid tuberosity of humerus
	lateral border of acromion	deltoid tuberosity of humerus
	lower part of spinous process of scapula	deltoid tuberosity of humerus
Subscapularis	medial ²/₃ of costal surface of scapula	superior aspect of lesser tubercle of humerus
Pectoralis major		
› clavicular portion	medial half of clavicle	crest of greater tubercle of humerus
› sternocostal portion	manubrium + corpus of sternum	crest of greater tubercle of humerus
› abdominal portion	anterior sheath of rectus abdominis	crest of greater tubercle of humerus
Pectoralis minor	2nd / 3rd–5th ribs	superomedial aspect of coracoid process
Biceps brachii		
› long head	supraglenoid tubercle of scapula	tuberosity of radius
› short head	tip of coracoid process	tuberosity of radius
Coracobrachialis	tip of coracoid process	medial surface of middle third of humerus
Supraspinatus	supraspinatus fossa of scapula	greater tubercle of humerus, highest facet
Infraspinatus	infraspinatus fossa of scapula	greater tubercle of humerus, middle facet
Teres minor	upper ²/₃ of lateral border of scapula	greater tubercle of humerus, lower facet
Teres major	dorsum of inferior angle of scapula	inferior crest of lesser tubercle of humerus

- √ occasionally partially deficient anterosuperiorly
- √ labrum continuous with glenoid articular cartilage inferior to epiphyseal line
- √ triangular / rounded shape on cross-sectional image:
  - √ round / cleaved / flat larger anterior labrum
  - √ flat / round smaller posterior labrum

√ blends superiorly with biceps tendon

Superior Sublabral Sulcus / Recess

= variations in depth of sulcus between osseous glenoid rim + labrum

Location: 12 o'clock position at the site of biceps tendon attachment (in sagittal plane); NOT posterior to labral attachment of long head of biceps

Size: consistently 1–2 mm wide throughout its length

Types of attachment of biceps-labral complex (BLC):

(1) BLC firmly adherent to superior pole of glenoid without sulcus / sublabral foramen

(2) small sulcus = BLC attached several mm medially; hyaline cartilage beneath labrum; may be continuous with sublabral foramen which is anterior to BLC

(3) deep probe-patent sulcus = meniscoid labrum with large sulcus between labrum and hyaline cartilage

√ may be continuous with sublabral foramen

√ best visualized on oblique coronal CT / MR

DDx: type II SLAP lesion (more lateral in oblique coronal plane)

Biceps Brachii

= muscle with 2 separate origins

Short Head of Biceps Brachii Muscle

Function: ineffectual elevator of the arm

Origin: apex of coracoid process (together with coracobrachialis tendon)

Course: extraarticular

Insertion: radial tuberosity (conjoined distal tendon of the short and long head)

Long Head of Biceps Brachii Muscle

Function: ineffectual elevator of the arm

Origin: supraglenoid tubercle of scapula ± posterosuperior glenoid labrum

Course: traverses rotator interval + descends through intertubercular sulcus (bicipital groove)

Insertion: radial tuberosity (conjoined distal tendon of the short and long head)

Tendon of Long Head of Biceps Brachii

√ attached to anterosuperior aspect of glenoid rim with fibers to

(a) anterosuperior labrum (biceps-labral complex)

(b) posterosuperior labrum (biceps-labral complex)

(c) supraglenoid tubercle

(d) base of coracoid process

√ exits joint through intertubercular groove

√ secured to intertubercular groove by transverse lig.

√ surrounded by slinglike band of CHL superiorly and superior GHL anteriorly

Coracohumeral Ligament

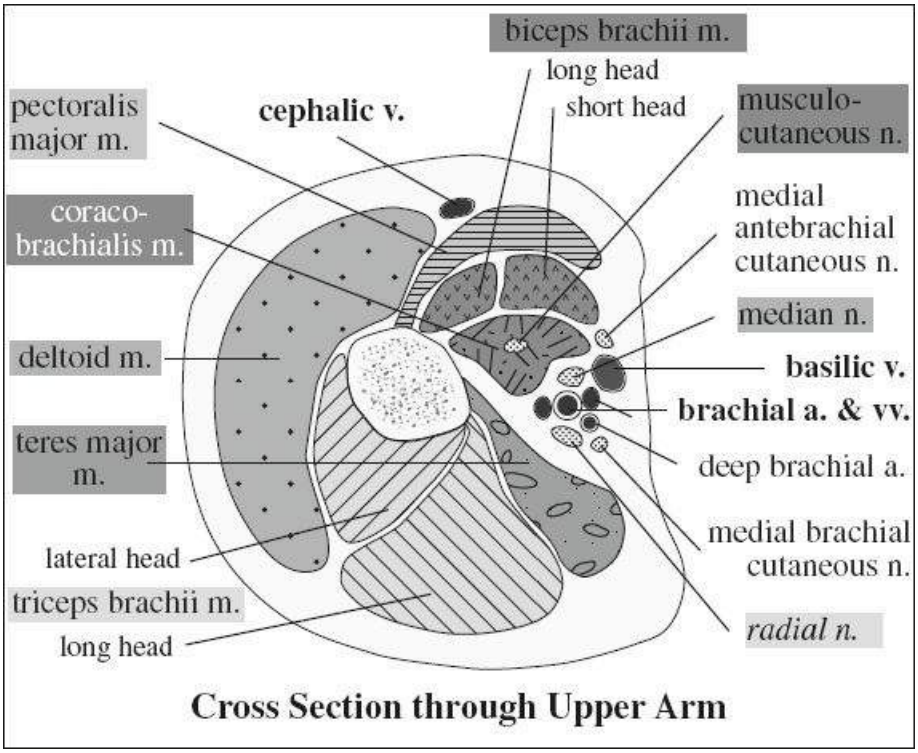
= most superficial capsular structure of rotator interval blending with fibers of subscapularis + supraspinatus tendons at their insertions forming roof of rotator interval with

(a) larger (lateral) band
Insertion: greater tuberosity + fibers of supraspinatus tendon
(b) smaller (medial) band crosses over biceps tendon + forms anterior covering around biceps tendon blending with fibers of subscapularis tendon
Insertion: proximal aspect of lesser tuberosity

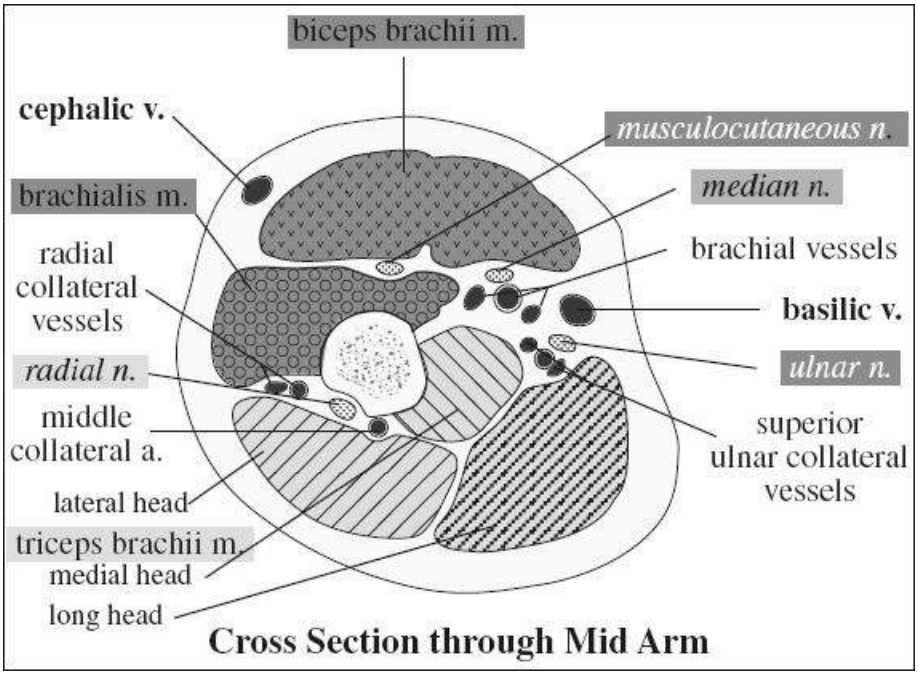
Origin: lateral aspect of base of coracoid process

Course: runs parallel to superior glenohumeral lig. posteriorly + laterally to fuse with joint capsule

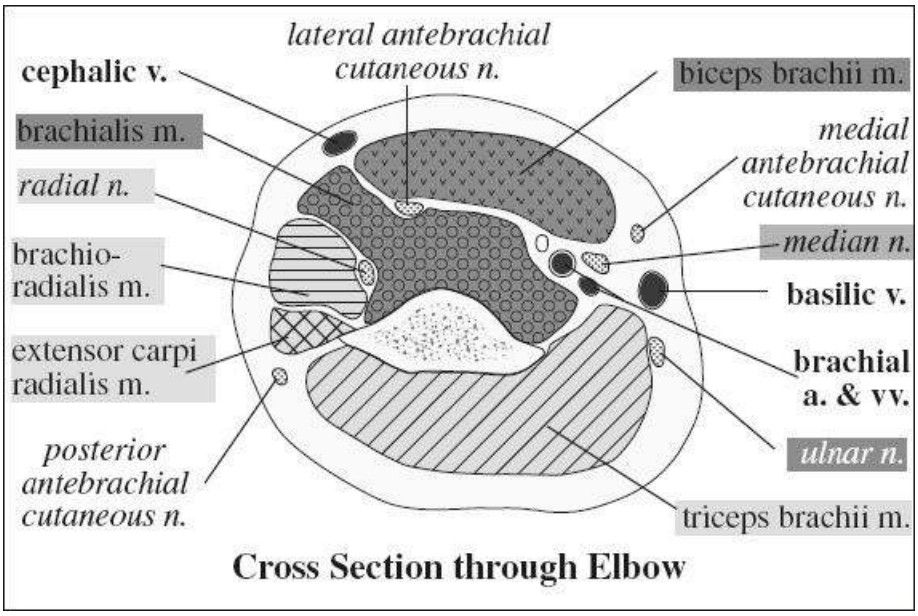
Variations of insertion:
(a) into rotator interval
(b) to supraspinatus tendon / subscapularis tendon
(c) to supraspinatus + subscapularis tendons



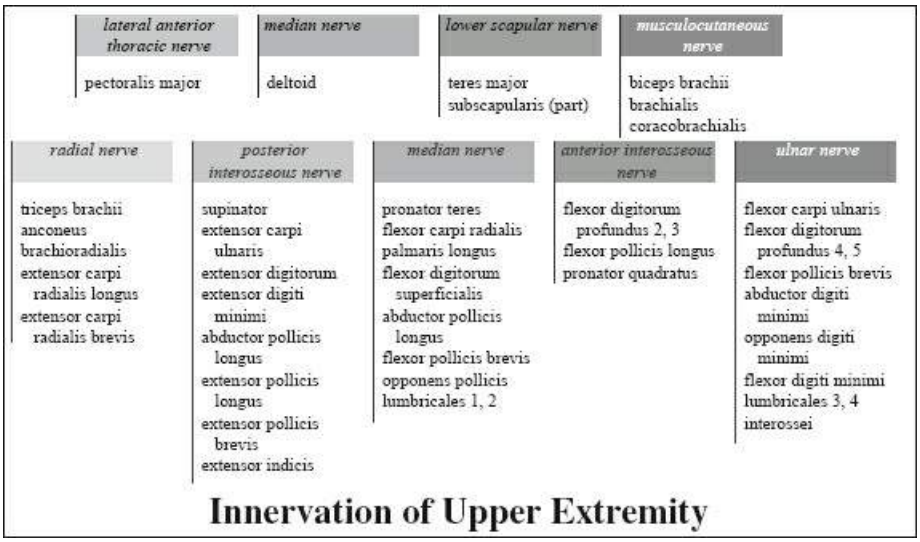
Cross Section through Upper Arm



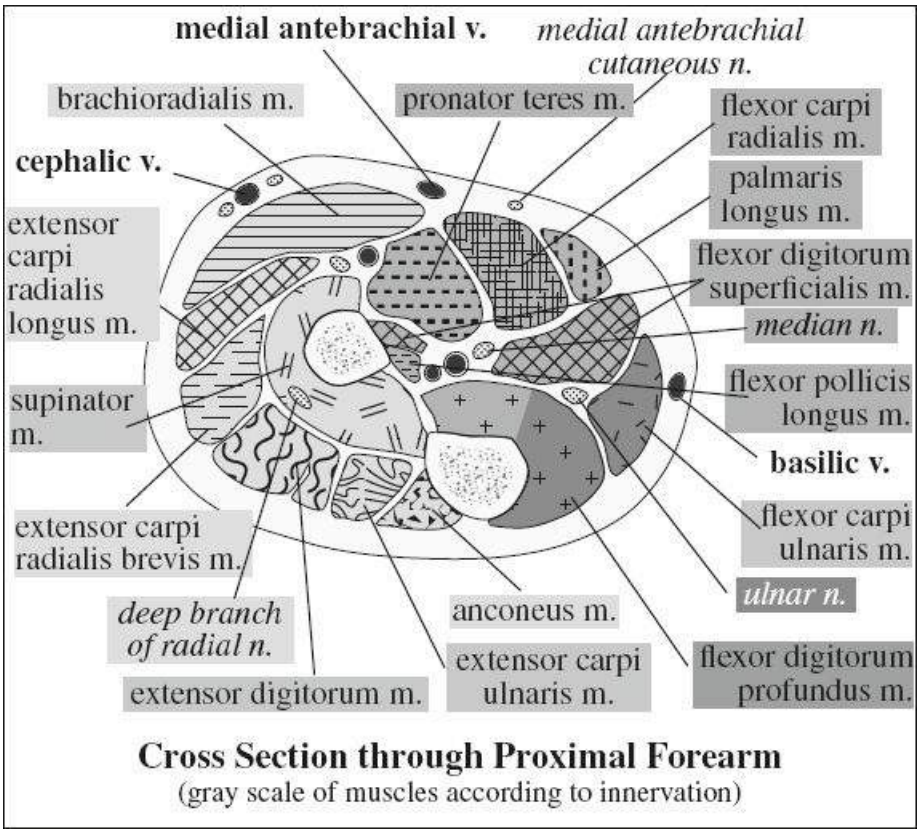
Cross Section through Mid Arm



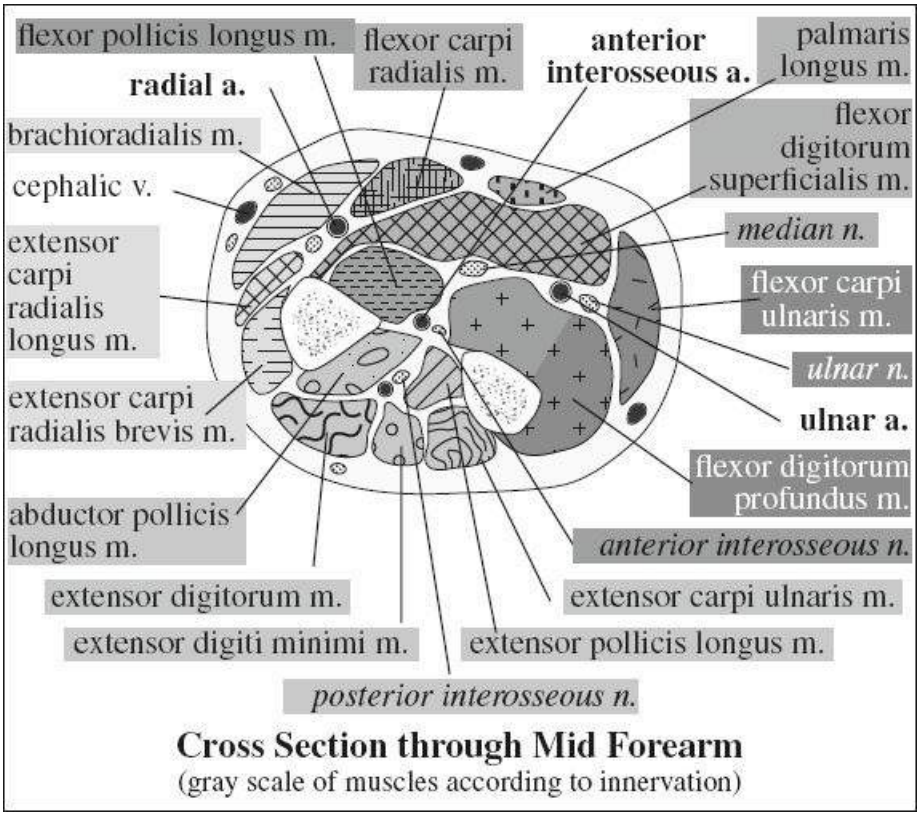
Cross Section through Elbow



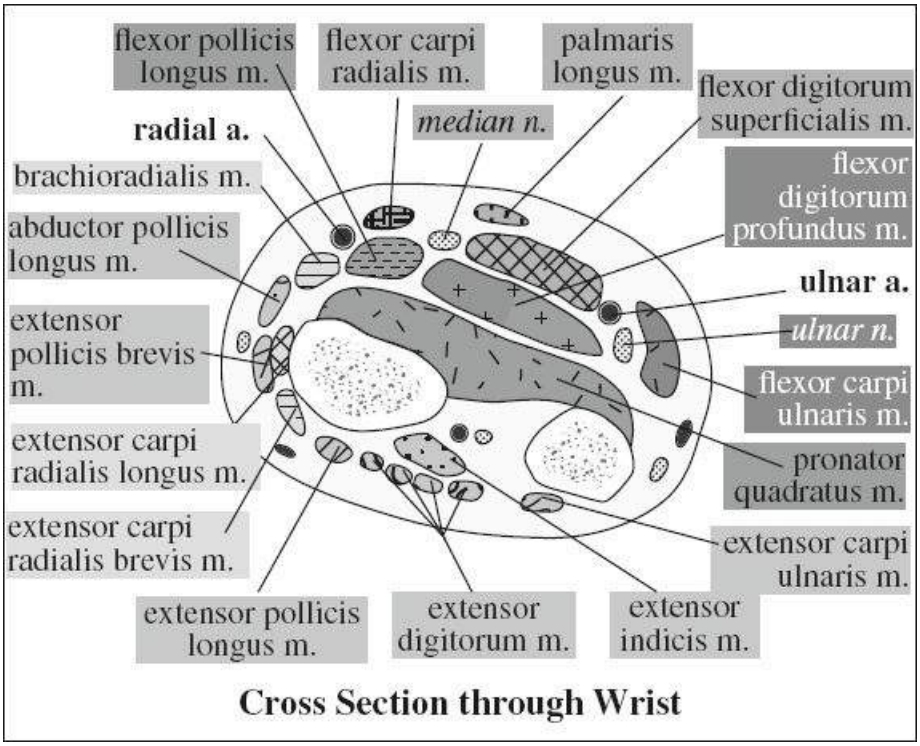
Innervation of Upper Extremity



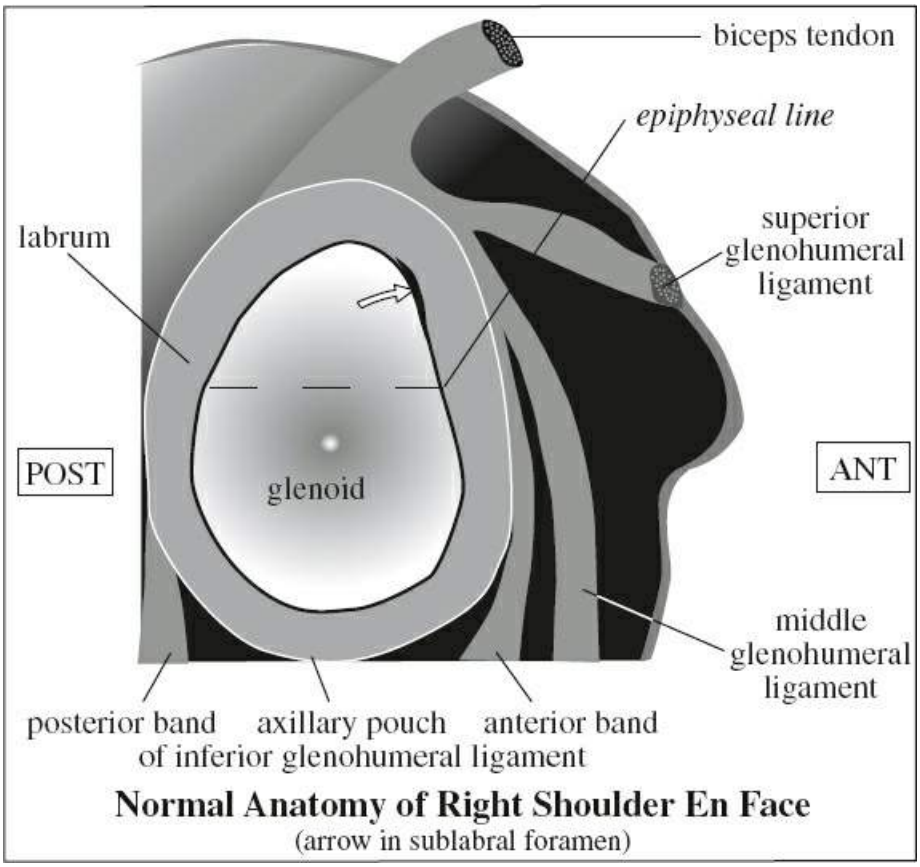
Cross Section through Proximal Forearm
(gray scale of muscles according to innervation)



Cross Section through Mid Forearm
(gray scale of muscles according to innervation)

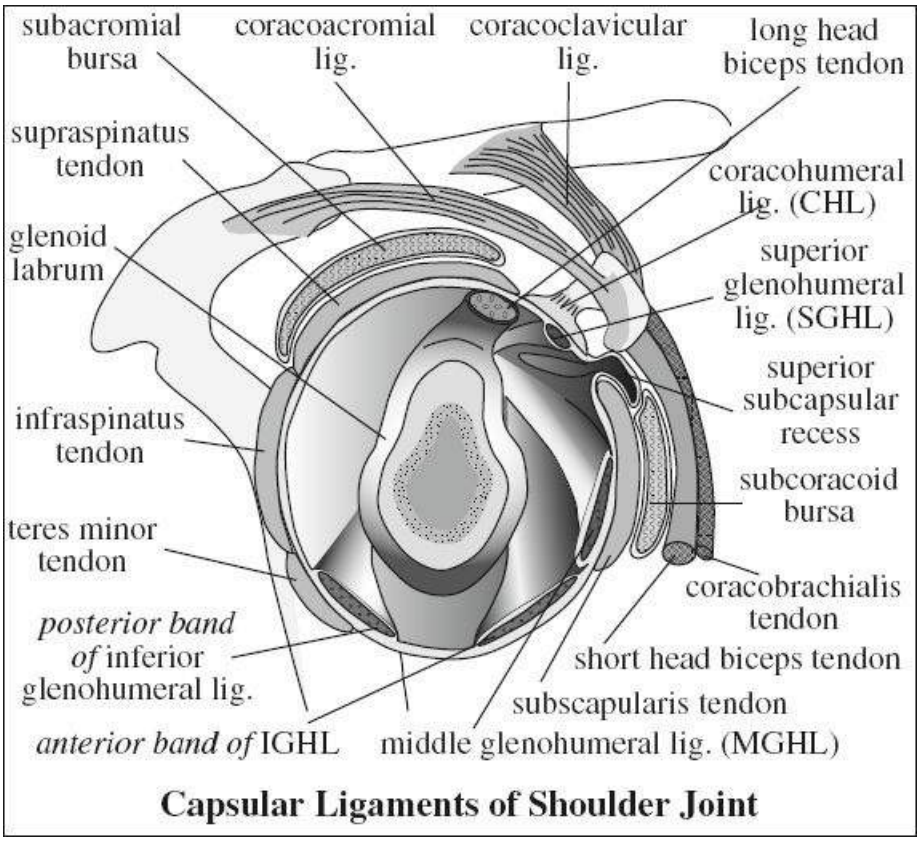


Cross Section through Wrist



Normal Anatomy of Right Shoulder En Face
(arrow in sublabral foramen)

Buford Complex



Capsular Ligaments of Shoulder Joint

Coracoacromial Ligament

= strong triangular fibrous band that extends from coracoid process to acromion forming protective arch superficial to rotator cuff

Rotator Interval

= triangular space between superior border of subscapularis tendon + anterior border of supraspinatus tendon

= portion of glenohumeral joint capsule that is not reinforced by overlying rotator cuff muscles

Apex: combined fibers from subscapularis tendon with contributions from supraspinatus tendon and CHL + posterior lamina of tendon of pectoralis major muscle ("transverse ligament") bridging bicipital groove

Base: coracoid process with origin of coracohumeral lig. medially

Content: intraarticular portion of long biceps tendon, coracohumeral ligaments

Glenohumeral Ligaments

= thickened collagenous bands of joint capsule functioning as shoulder stabilizers

Superior Glenohumeral Ligament (SGHL)

= most consistently identified capsular ligament

Function: passive restraint to inferior translation of adducted shoulder

Origin: superior glenoid tubercle (= upper pole of glenoid cavity) just anterior to origin of biceps tendon and base of coracoid process

Course: passes between supraspinatus + subscapularis in plane perpendicular to middle glenohumeral ligament + parallel to coracoid process
Insertion: lesser tuberosity at bicipital groove
√ merges with coracohumeral ligament in rotator cuff interval
√ best visualized on transverse CT / MR

Middle Glenohumeral Ligament (MGHL)
= varies most in size + attachment; may be absent
Function: limits anterior translation with external rotation + moderate abduction
Origin: medially on scapular neck / superior portion of anterior glenoid rim
Course: obliquely from superomedial to inferolateral
Insertion: medial from lesser tuberosity at anterior aspect of anatomic neck
• taught during external rotation
√ blends into capsular sheath of subscapularis tendon
√ may be thick + cordlike
√ best visualized on sagittal / transverse CT / MR

Inferior Glenohumeral Ligament (IGHL)
= important stabilizer of anterior shoulder joint
Function: resists anteroinferior glenohumeral translation
Course: from anteroinferior labrum to humeral metaphysis
• ligament + labrum function as single unit
= **inferior glenohumeral labral-ligamentous complex** *(IGHLC)*
• taught during ABER position
√ attaches to inferior $^{2}/_{3}$ of the circumference of the entire labrum for a variable distance
√ forms sleeve of continuous tissue with glenoid rim, capsule, periosteum, humeral metaphysis
√ best visualized on MR arthrography / joint effusion
Parts:
1. Anterior band of IGHL = thickened anterior-superior extent of ligament
◊ Critical to passive joint stabilization!
2. Axillary pouch
3. Posterior band of IGHL (usually thinner)

Normal Anatomic Variants of Shoulder

Sublabral Foramen = Sublabral Hole
= sublabral hole between labrum + glenoid
Prevalence: 12% of individuals
Location: 2 o'clock position anterior to biceps tendon attachment
√ may coexist with sublabral recess
DDx: labral tear (isolated tears are rare in this region)

Buford Complex
= cordlike thickening of middle glenohumeral ligament directly attaching to anterosuperior glenoid + absence of anterosuperior labrum

Prevalence: 1.5% of individuals
Location: 2 o'clock position anterior to biceps tendon attachment
√ course of middle glenohumeral ligament can be followed on serial images from origin to insertion
√ may coexist with sublabral recess
DDx: displaced anterosuperior labral fragment

Cysts and Bursae of Shoulder

1. Subacromial-subdeltoid bursa
2. Superior subscapular recess / subscapularis bursa
   Location: between subscapularis muscle + anterior surface of scapula with extension above superior margin of subscapularis tendon
   (a) **Foramen of Weitbrecht**
   = opening between SGHL and MGHL
   (b) **Foramen of Rouvière**
   = opening between MGHL and IGHL
3. Subcoracoid bursa
   Location: between anterior surface of subscapularis muscle + coracoid process with extension along merged tendons of coracobrachialis m. + short head of biceps
   √ no communication with glenohumeral joint
   √ ± communication with subacromial-subdeltoid bursa
   √ often associated with rotator cuff + interval tears
4. AC joint cyst
5. Glenoid labral cyst

ELBOW

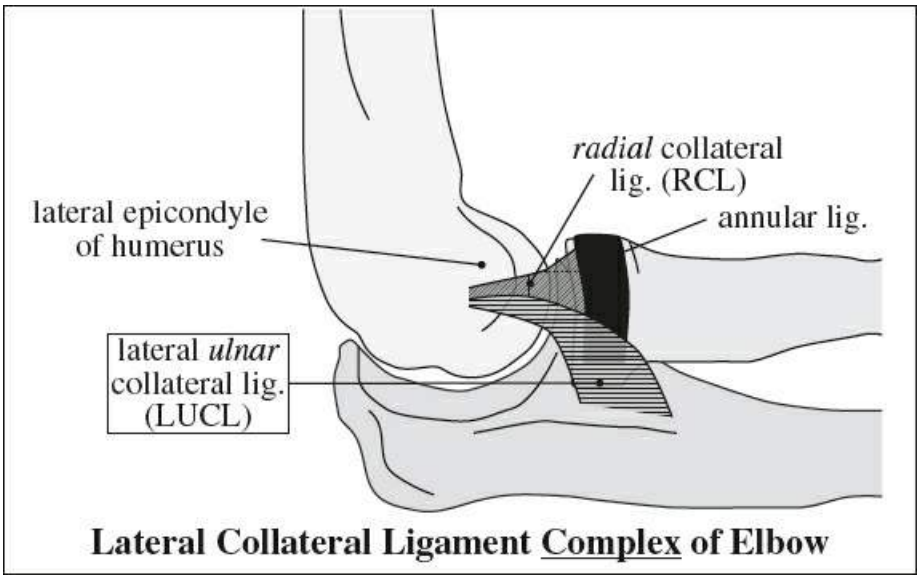
Elbow Joint Stabilizers

A. Medial / (ulnar) collateral ligament complex (MCL)
   Origin: anteroinferior margin of medial epicondyle
   (a) anterior bundle (functionally important): inserts on sublime tubercle (= anteromedial aspect of coronoid process) – resists valgus forces
   (b) posterior bundle
   (c) transverse (oblique) bundle = Cooper lig.
B. Lateral / radial collateral ligament complex
   Origin: inferior margin of lateral epicondyle
   1. Radial collateral ligament (RCL)
      Insertion: on annular ligament
   2. Lateral ulnar collateral ligament (LUCL): functionally important – resists varus forces
      Insertion: distal to tubercle of crista supinatoris ulnae
   3. Annular ligament

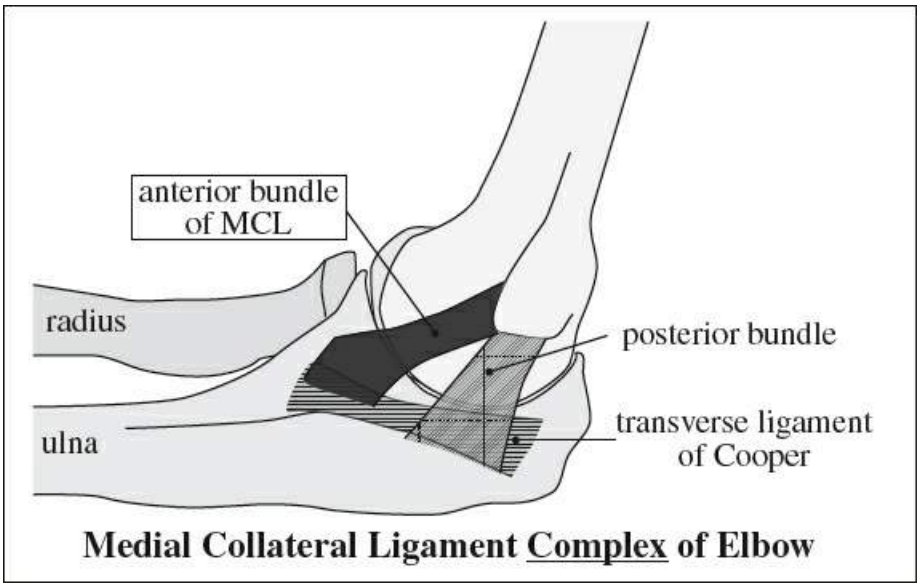
Functionally primary stabilization:

1. Ulnohumeral articulation
2. Anterior bundle of MCL
3. LUCL

Functionally secondary stabilization:

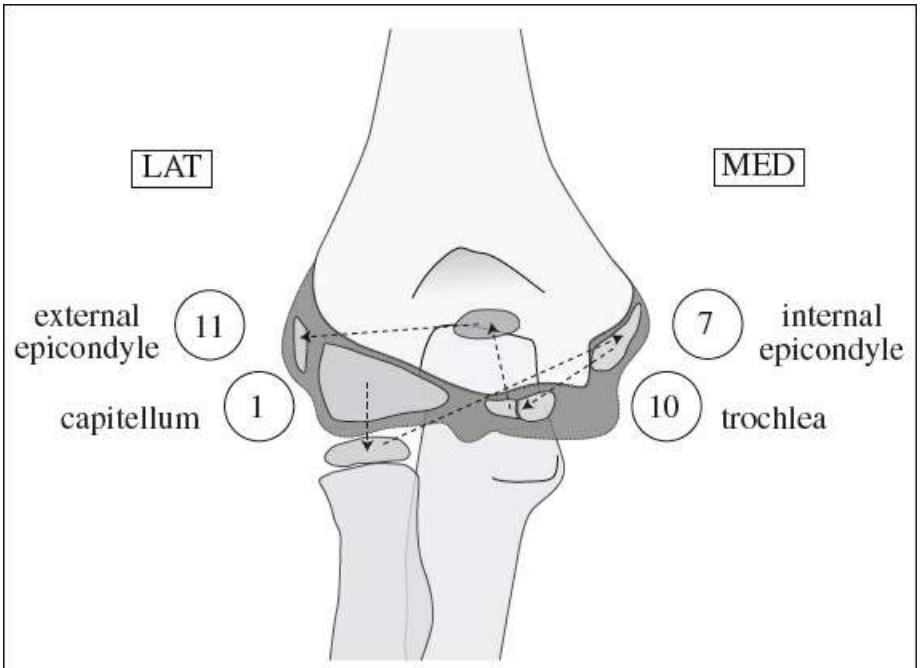


Lateral Collateral Ligament Complex of Elbow



Medial Collateral Ligament Complex of Elbow

Occurrence of Bone Centers at Elbow		
mnemonic: CRITOE		
Capitellum	**1** yr	(M 1–11 m, F 1–26 m)
Radial head	4 yrs	(3–6 yrs)
Internal (medial) humeral epicondyle	**7** yrs	(M 5–8 yrs, F 7–9 yrs)
Trochlea	**10** yrs	(M 7–11 yrs, F 8–13 yrs)
Olecranon	10 yrs	(9–10 yrs)
External (lateral) humeral epicondyle	**11** yrs	(F 8–11 yrs, M 9–13 yrs)



Occurrence of Bone Centers in Elbow *(numbers in years)*
mnemonic: "Nelson's X: 1, 7, 10, 11 years"

1. Radiocapitellar articulation
2. Common flexor-pronator tendon
3. Common extensor tendon
4. Joint capsule

Cysts and Bursae of Elbow

1. Olecranon bursa
2. Medial + lateral epicondylar bursa
3. Cubital tunnel bursa
4. Biceps tendon bursa
   (a) Bicipitoradial bursa
   Location: lateral to biceps insertion
   • posterior interosseous nerve compression
   (b) Interosseous bursa
   Location: medial to biceps insertion
   • median nerve compression
5. Ganglion

CARPAL BONES

mnemonic: **S**ome **L**overs **T**ry **P**ositions **T**hat **T**hey **C**an't **H**andle

proximal row	*distal row*
Scaphoid	**T**rapezium

Lunate	**T**rapezoid
Triquetrum	**C**apitate
Pisiform	**H**amate

◊ Remember that trapezium comes before trapezoid in the dictionary as well!

◊ Spaces between carpal bones: ≤ 3 mm wide (internal comparison with capitolunate joint)

Scaphoid

[*scaphion*, Greek = boat]

◊ The largest bone of proximal carpal row!

Function: acts as an intercalated segment between lunate proximally + trapezium and trapezoid distally

Division: proximal third; middle third with waist; distal third with tuberosity on palmar surface

Blood supply: branches of radial artery enter bone near midportion / waist dorsally → perfusion of mid to proximal 70–80% of scaphoid + proximal pole supplied by end artery in retrograde fashion

Lunate

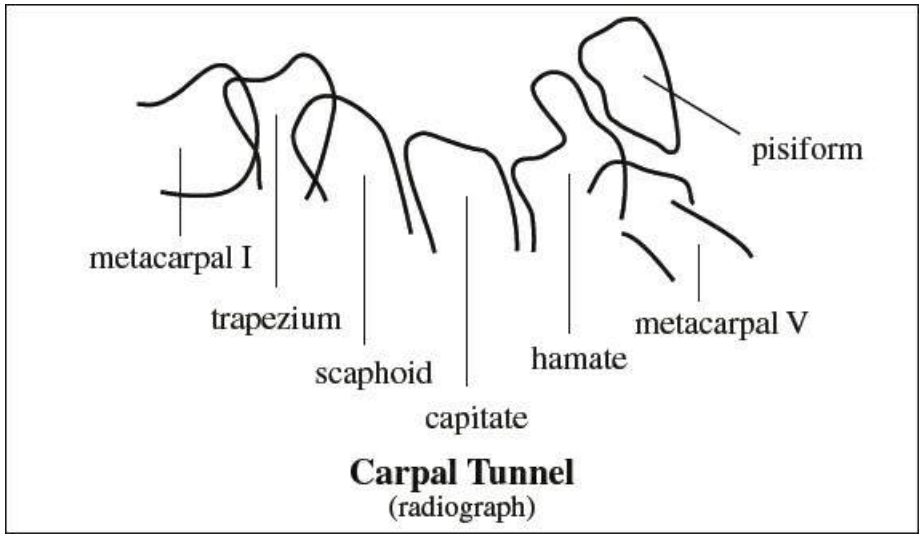
[*luna*, Latin = moon]

= moon-shaped configuration on LAT view

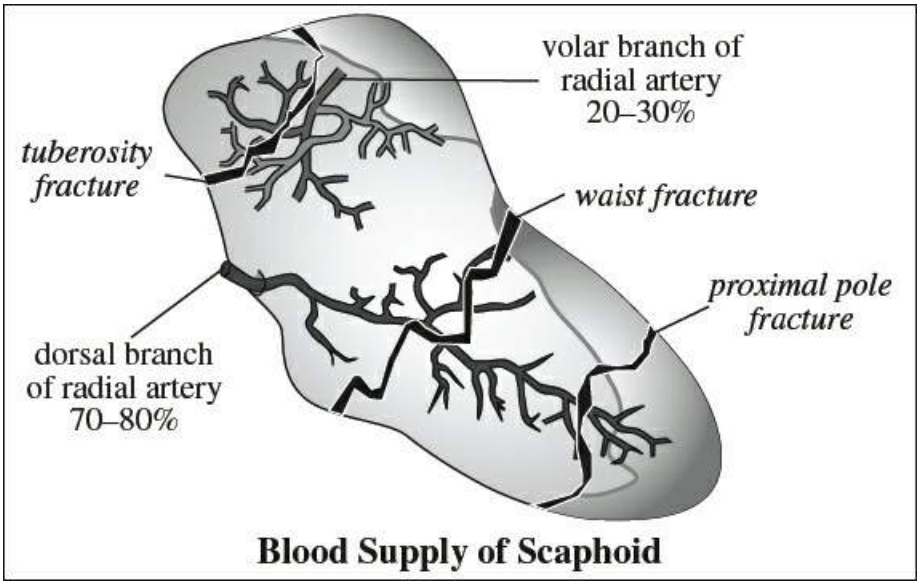
Parts: body, volar pole, dorsal pole

Function: acts as keystone of proximal carpal row

Blood supply: single vessel (20%); 2 nonarticular nutrient arteries with consistent intraosseous anastomosis (80%)



Carpal Tunnel
(radiograph)



Blood Supply of Scaphoid

Carpal Bone Blood Supply

◊ Blood vessels frequently enter distal half of bone putting proximal bone at risk for avascular necrosis!

Single arterial supply	scaphoid, capitate, lunate (in 20%)
Two nutrient arteries without intraosseous anastomosis	trapezoid, hamate
Two nutrient arteries with intraosseous anastomosis	trapezium, triquetrum, pisiform, lunate (in 80%)

Ulnar Variance

= HULTEN VARIANCE = RADIOULNAR INDEX
= relative lengths of distal articular surfaces of radius and ulna

Definition:

» neutral = both surfaces at same level = equal length of ulna + radius
» positive = ulnar surface distal to radial surface = long ulna
◊ Gymnasts have a predilection for a positive ulnar variance!
Risk: (1) ulnar impaction (→ chondral fibrillation, chondromalacia, degenerative arthritis)
(2) ligamentous and carpal disturbances (→ TFCC tear, focal chondral lunate injury)
» negative = ulnar surface proximal to radial surface = short ulna
◊ Most children aged 12–16 years have a negative ulnar variance!

Effect of wrist position:

(a) increase of ulnar variance
1. maximum forearm pronation
2. firm grip

(b) decrease of ulnar variance
1. maximum forearm supination

2. cessation of grip

Radiographic standard view of unloaded wrist: posteroanterior, neutral forearm rotation, elbow flexed 90°, shoulder abducted 90°

Guyon Canal

[Jean Casimir Félix Guyon (1831–1920), 1st French chair in urology at University of Paris]

= canalis nervi ulnaris = loge de Guyon (French)

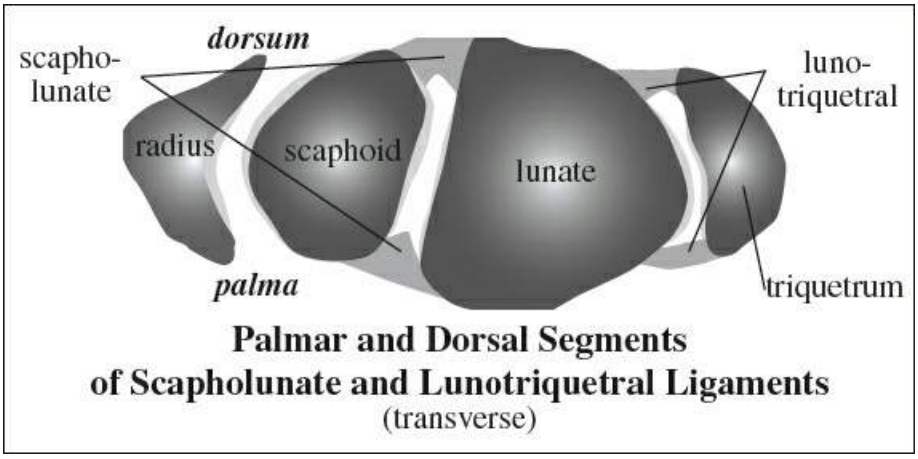
= small superficial tunnel-like structure at base of *hypothenar*

Floor: depression between pisiform + hook of hamate

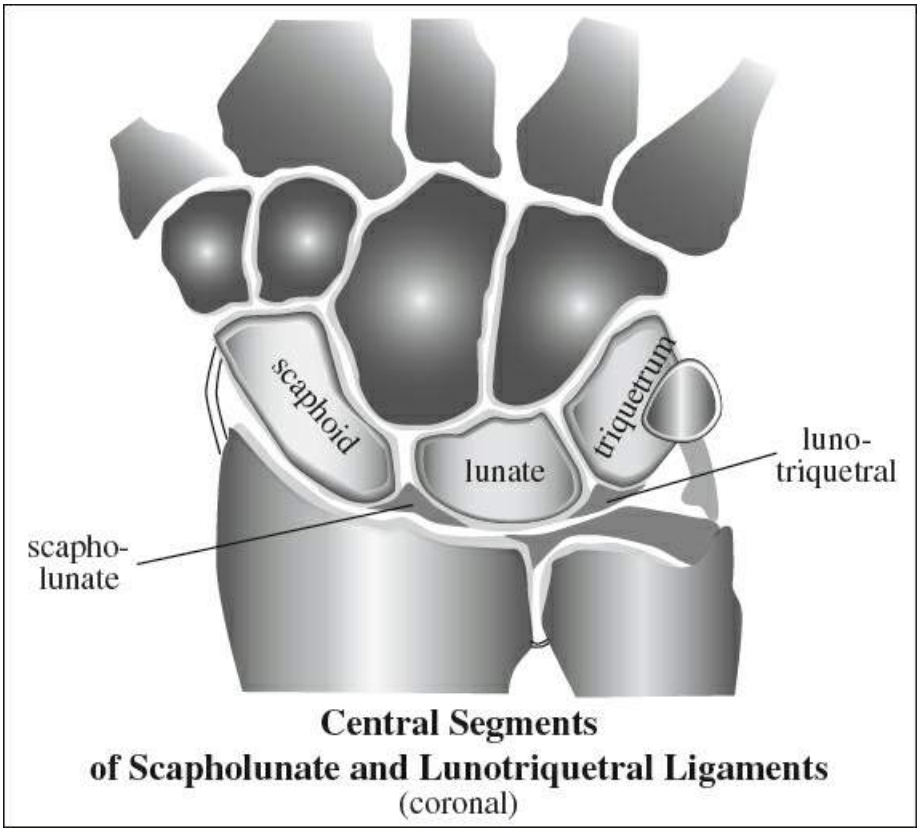
Roof: volar carpal ligament and pisohamate ligament; retinaculum flexorum manus; flexor carpi ulnaris m.

Contents: ulnar nerve with bifurcation into superficial and deep branches; ulnar artery

Clinical significance: site for compression injury by anomalous muscle, ganglion, hamate fracture



Palmar and Dorsal Segments of Scapholunate and Lunotriquetral Ligaments
(transverse)



Central Segments
of Scapholunate and Lunotriquetral Ligaments
(coronal)

Important Stabilizing Wrist Ligaments

◊ Important for carpal stability!

A. Intrinsic = between carpal bones
   1. Scapholunate lig.
   2. Lunotriquetral lig.

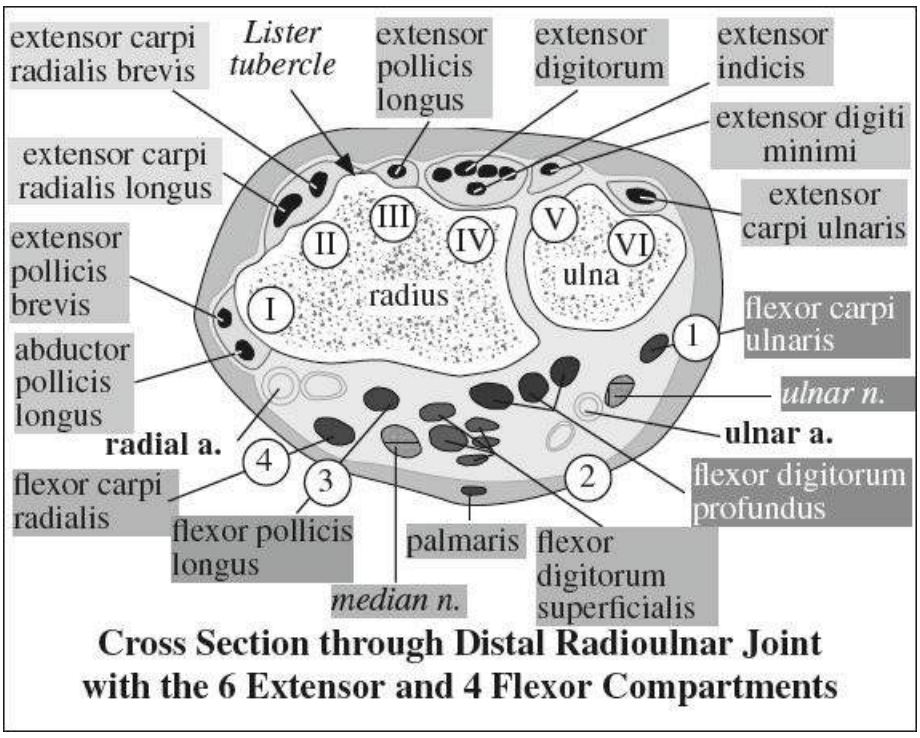
B. Extrinsic = between carpal + metacarpal bones or between carpal bones + radius / ulna
   (a) Palmar: carpal stability
      1. Radial collateral lig.
      2. Radiolunotriquetral lig. (RLTL): preventing ulnar translation
      3. Radioscaphocapitate lig. (RSCL): keeps scaphoid in position
   (b) Dorsal radiocarpal ligg.: prevent perilunate instability + volar intercalated segment instability
   (c) Dorsal intercarpal ligg.: prevent perilunate instability + dorsal intercalated segment instability

HIP

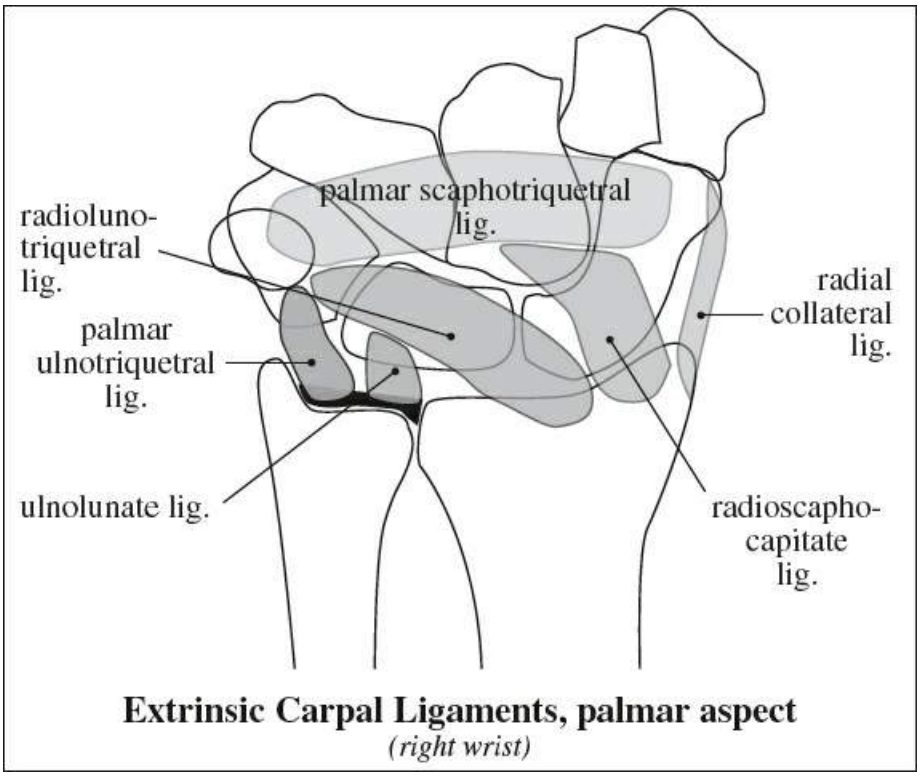
Cysts and Bursae of Hip

1. Iliopsoas bursa
   Location: surrounds iliopsoas tendon
   √ largest bursa in body
   √ communication with hip in 15%

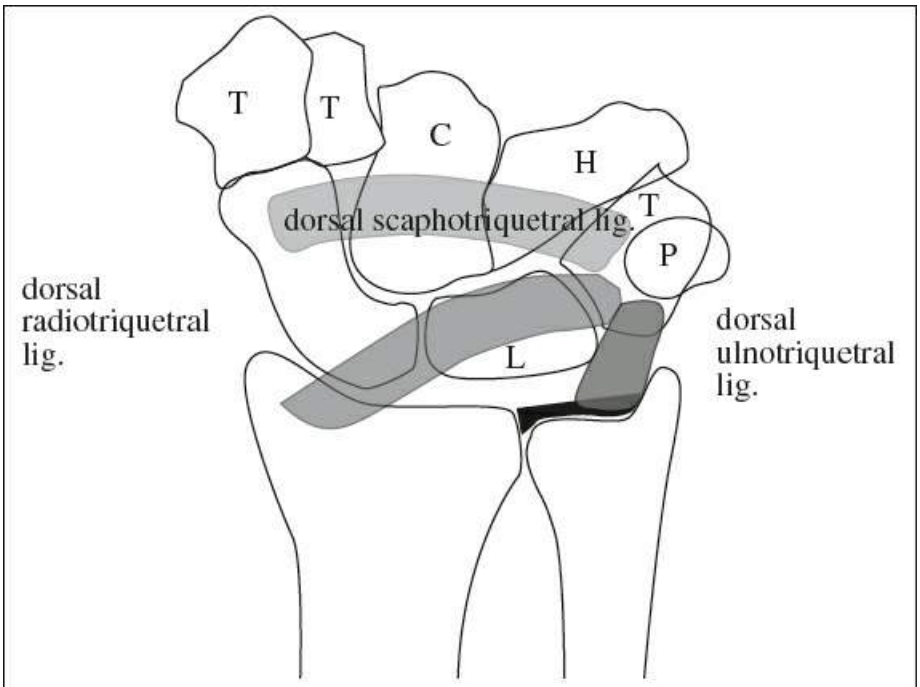
2. Greater trochanteric bursae
   (a) Trochanteric bursa
   Location: covers posterior facet, beneath gluteus maximus muscle + iliotibial tract
   (b) Subgluteus medius bursa



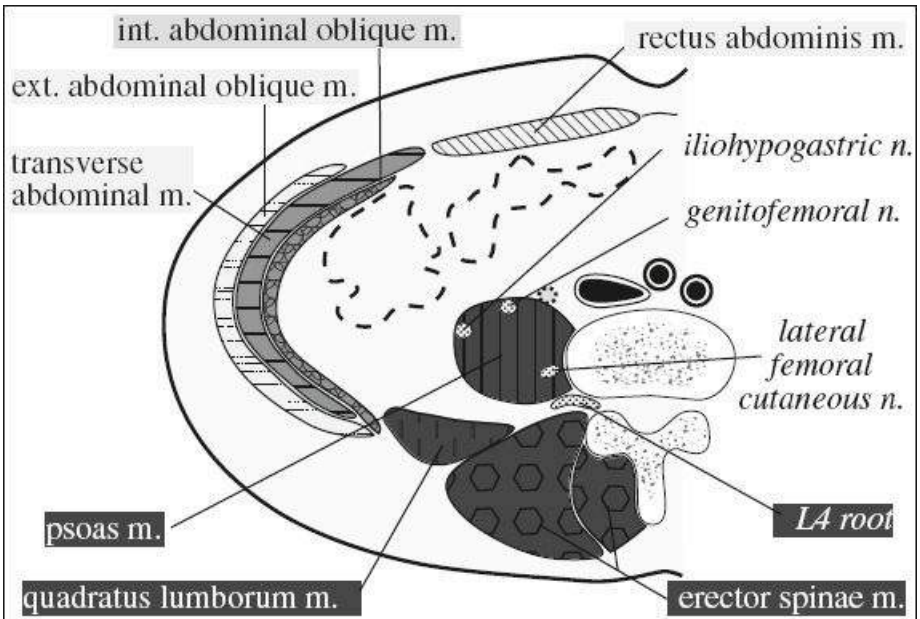
Cross Section through Distal Radioulnar Joint with the 6 Extensor and 4 Flexor Compartments



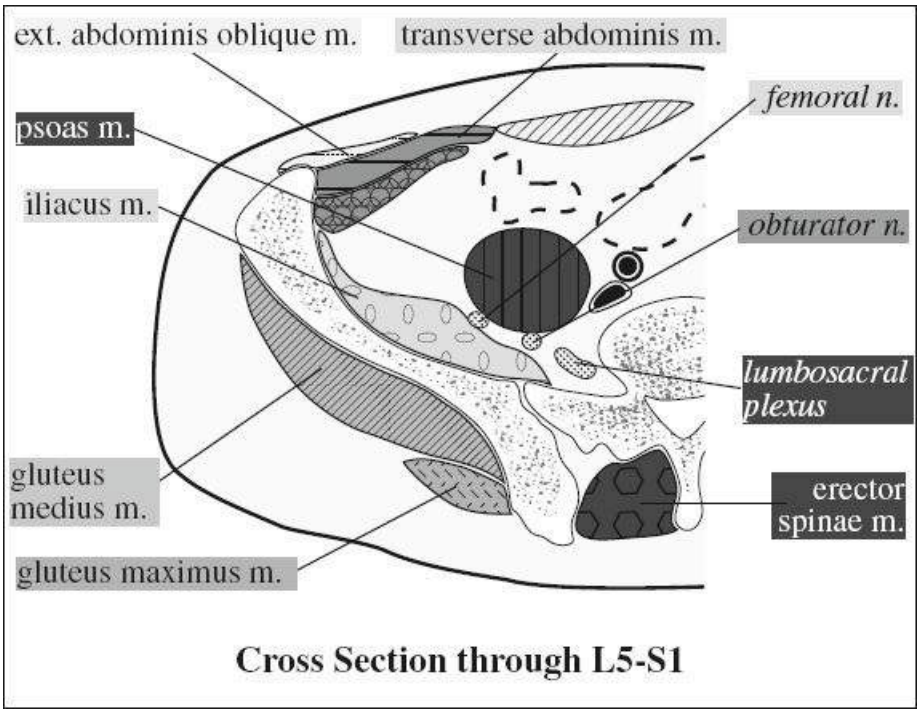
Extrinsic Carpal Ligaments, palmar aspect
(right wrist)



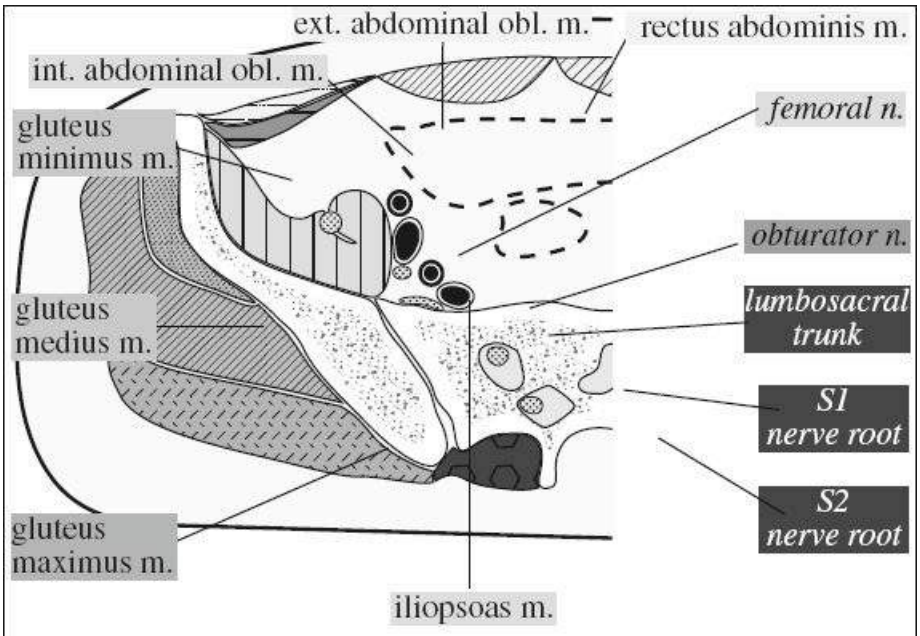
Extrinsic Carpal Ligaments, dorsal aspect
(right wrist with abbreviations of carpal bones)



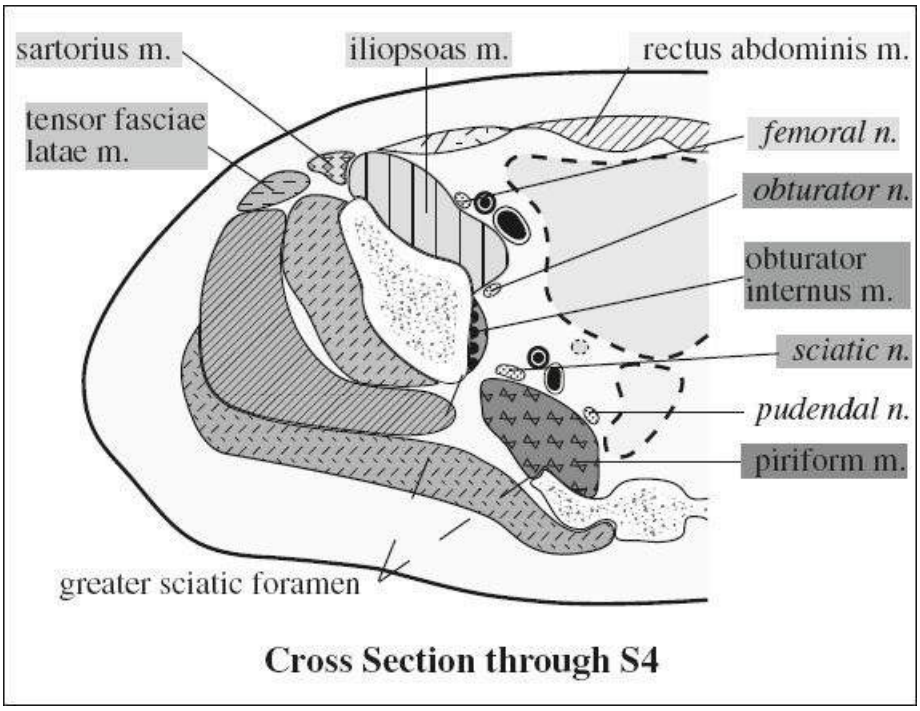
Cross Section through L4-5



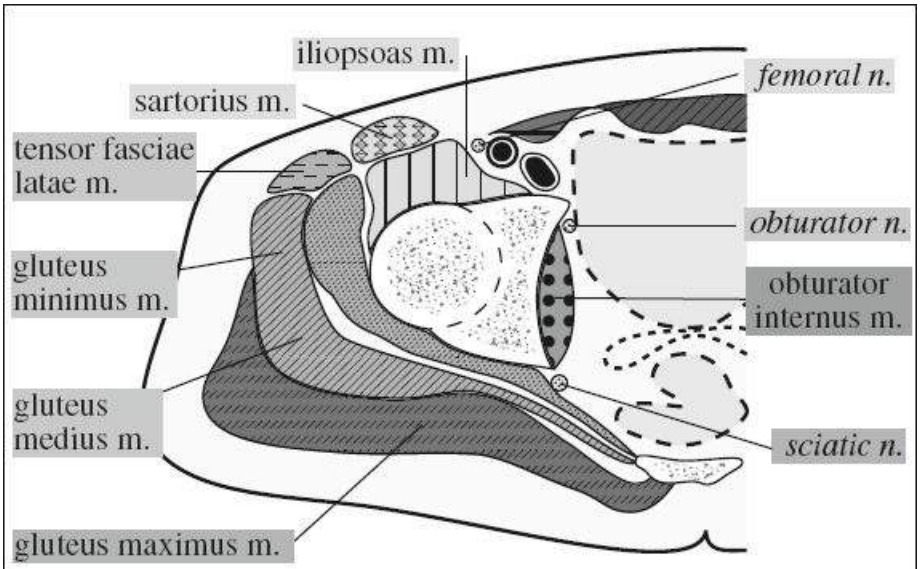
Cross Section through L5-S1



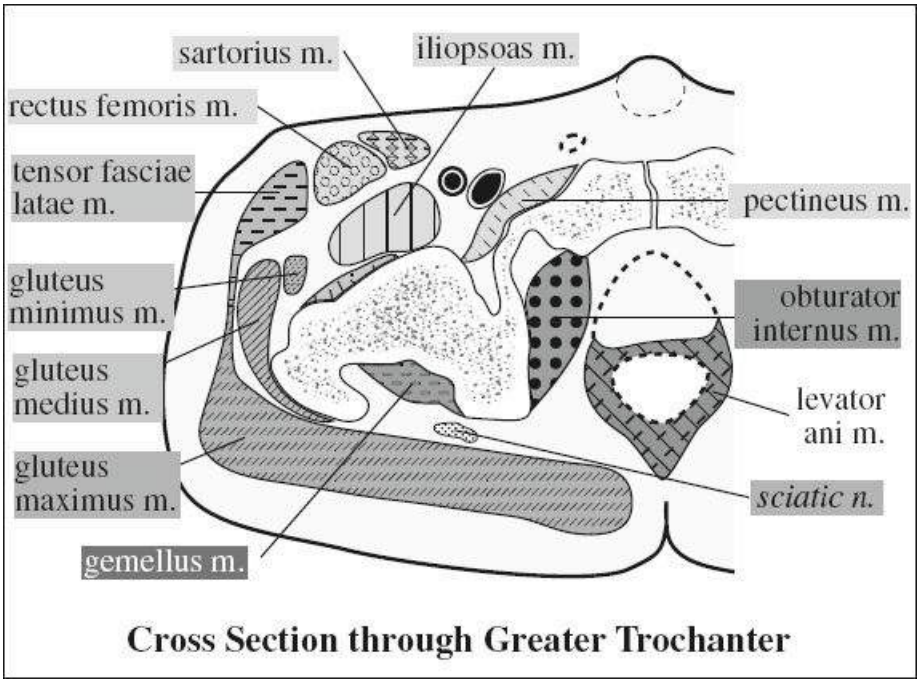
Cross Section through S1-2



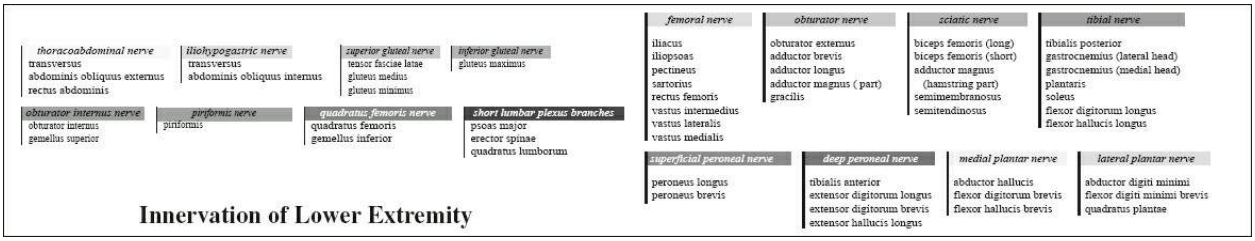
Cross Section through S4



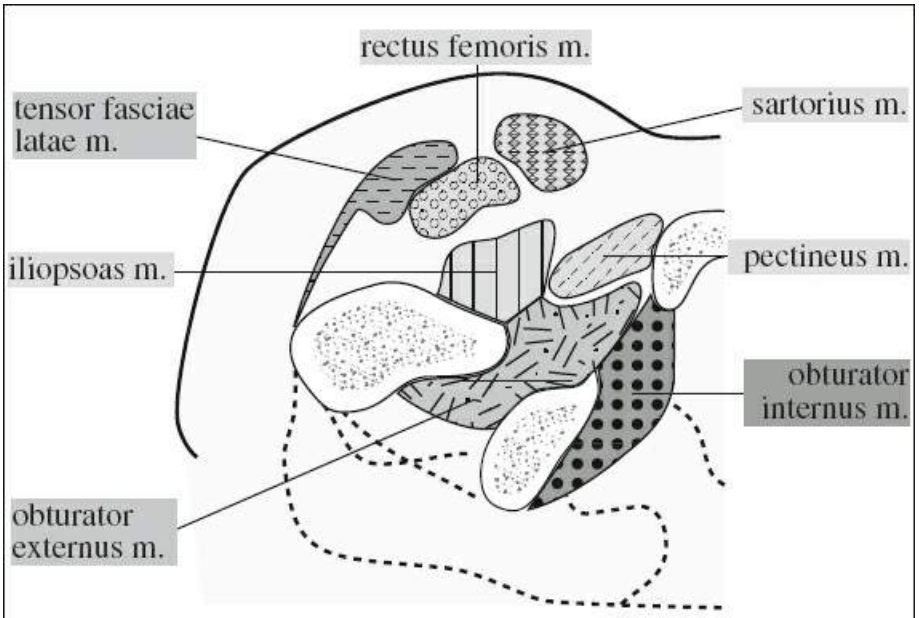
Cross Section through Acetabular Roof



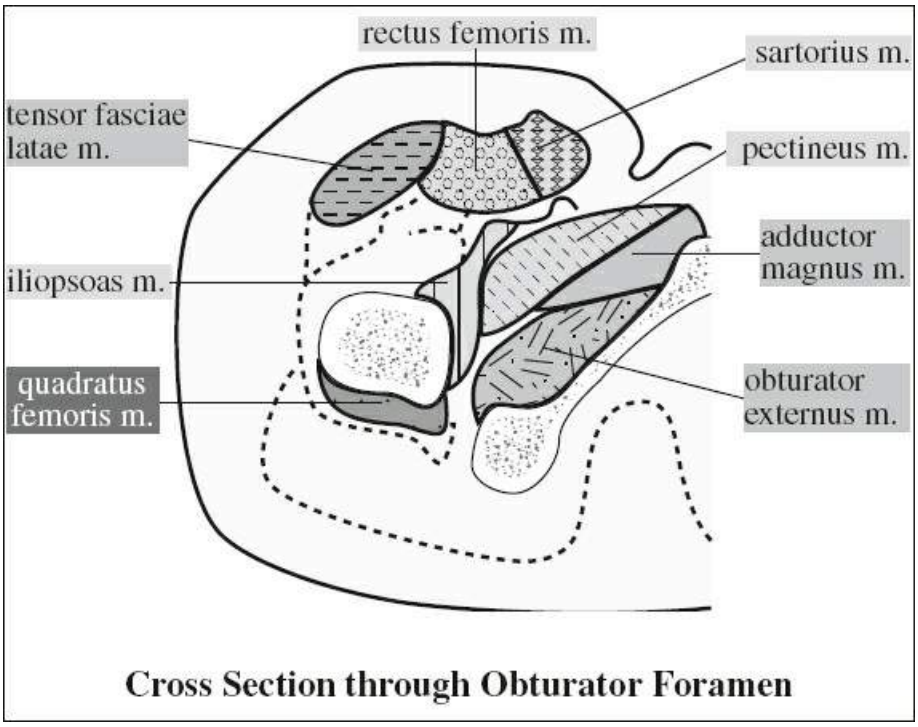
Cross Section through Greater Trochanter



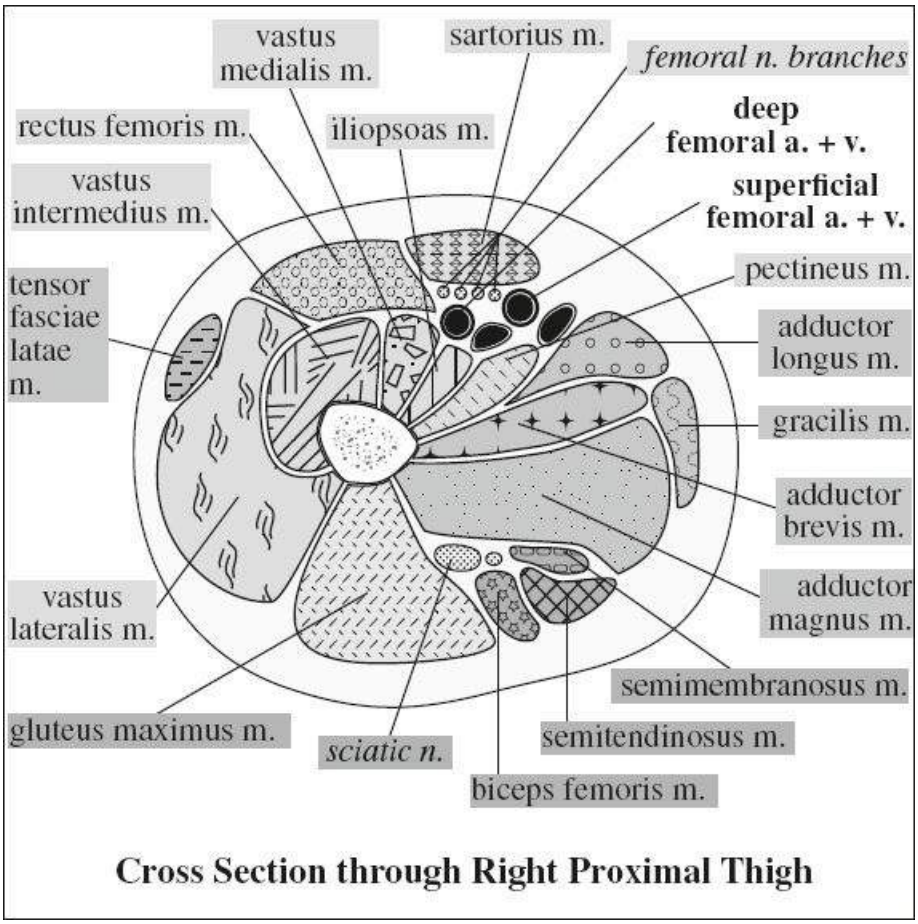
Innervation of Lower Extremity



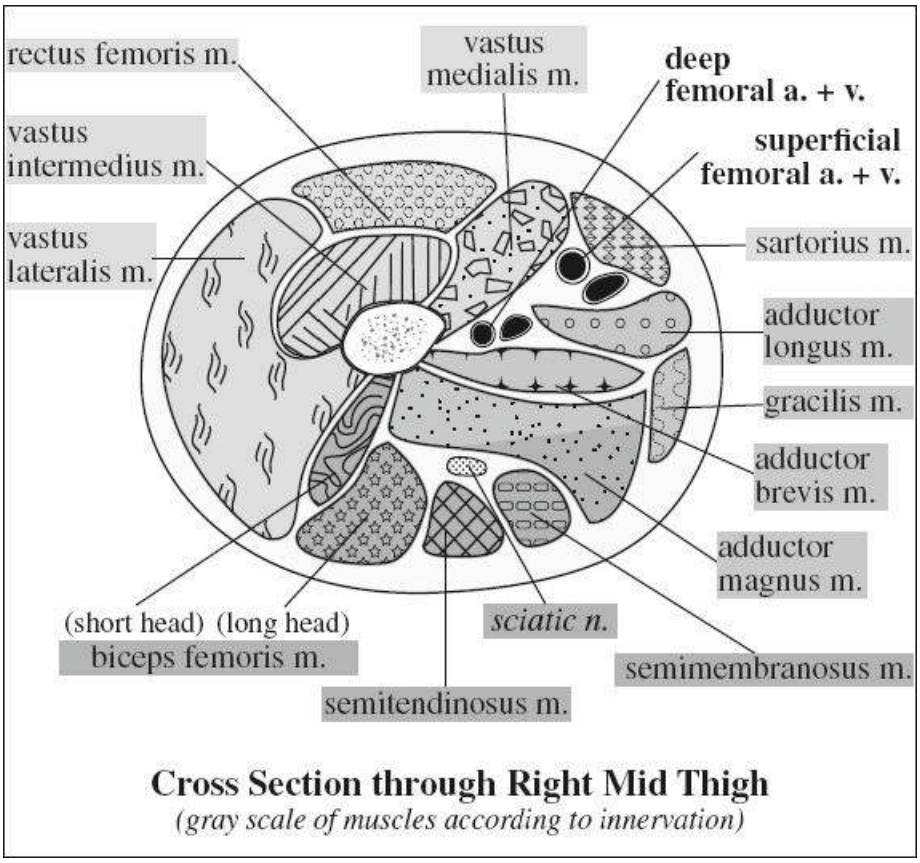
Cross Section through Minor Trochanter



Cross Section through Obturator Foramen

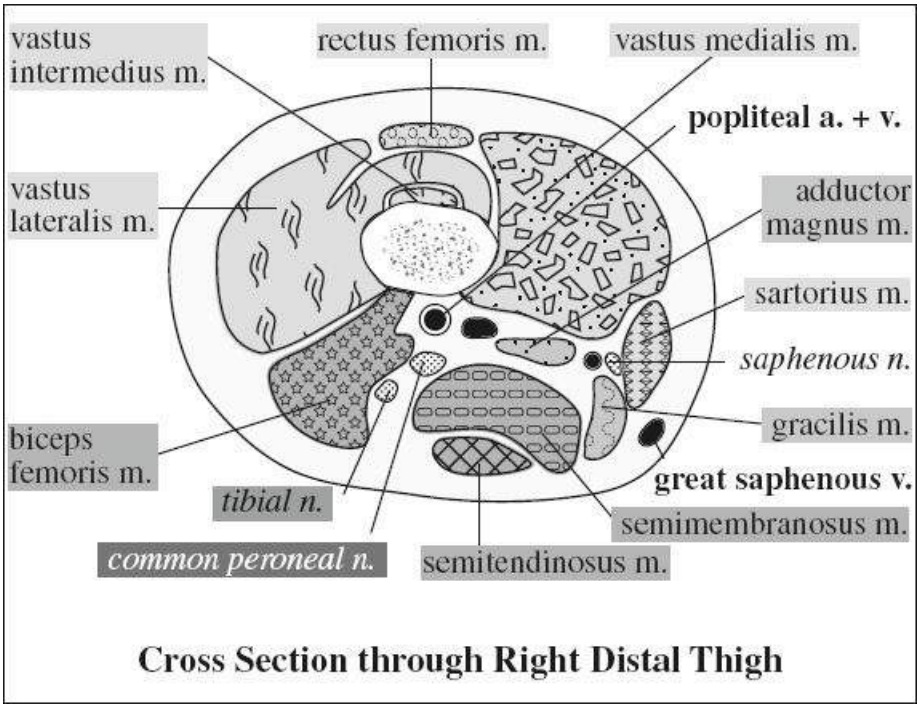


Cross Section through Right Proximal Thigh

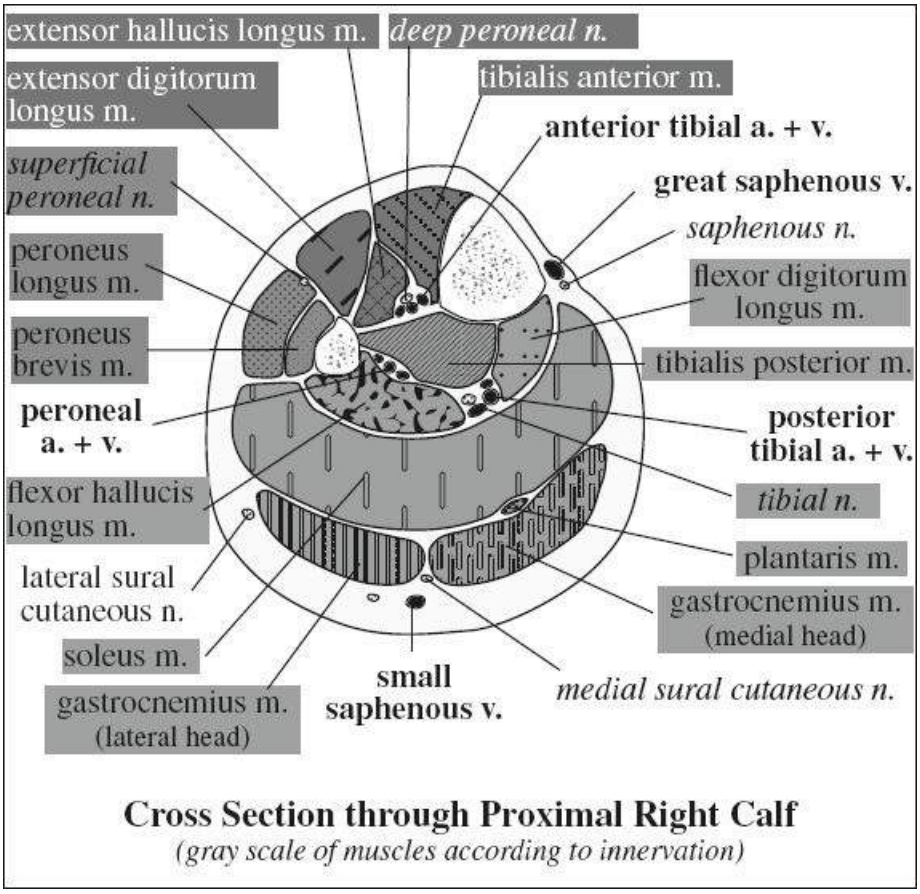


Cross Section through Right Mid Thigh

(gray scale of muscles according to innervation)

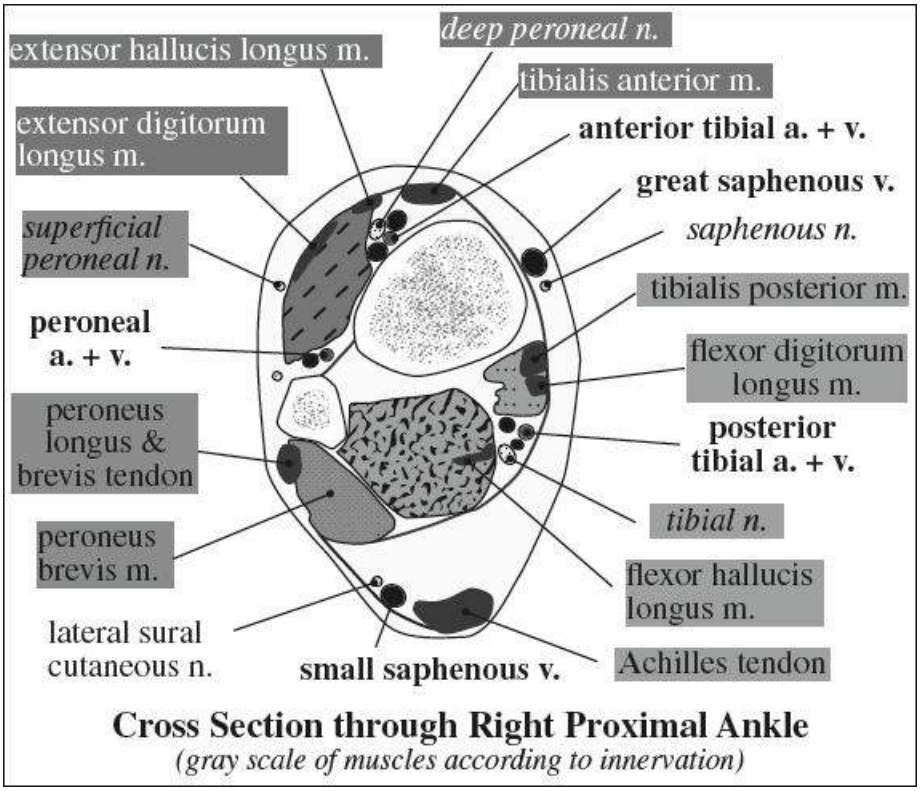


Cross Section through Right Distal Thigh



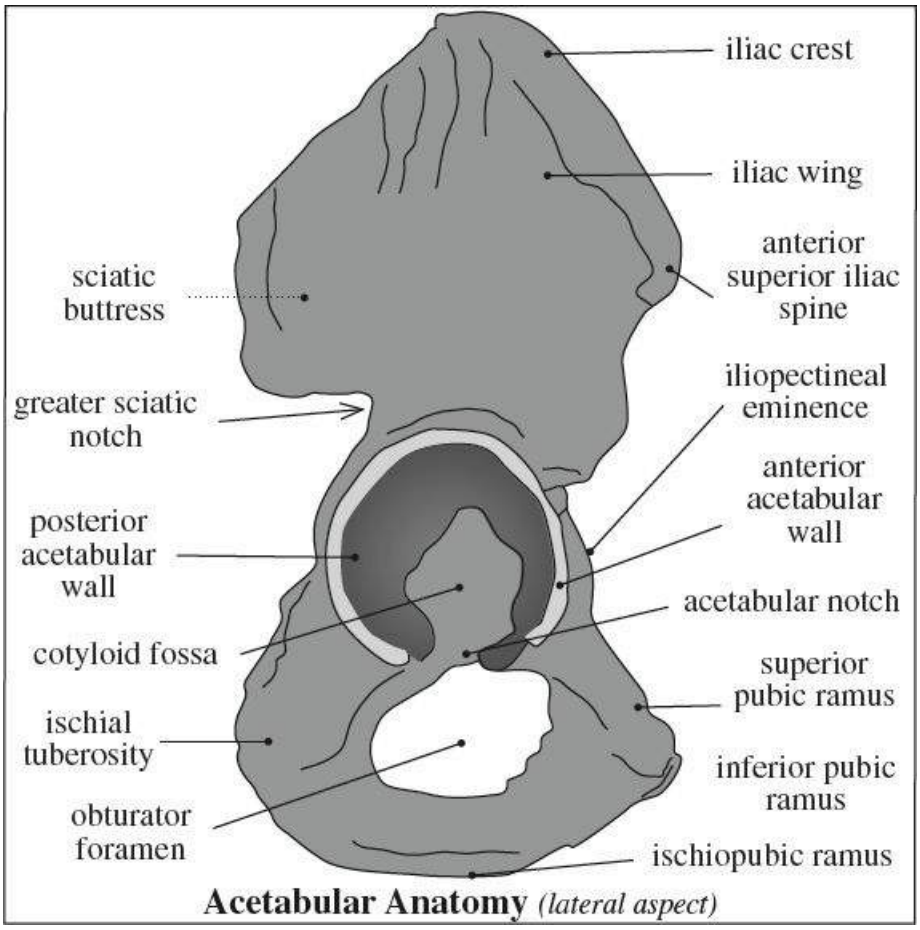
Cross Section through Proximal Right Calf

(gray scale of muscles according to innervation)

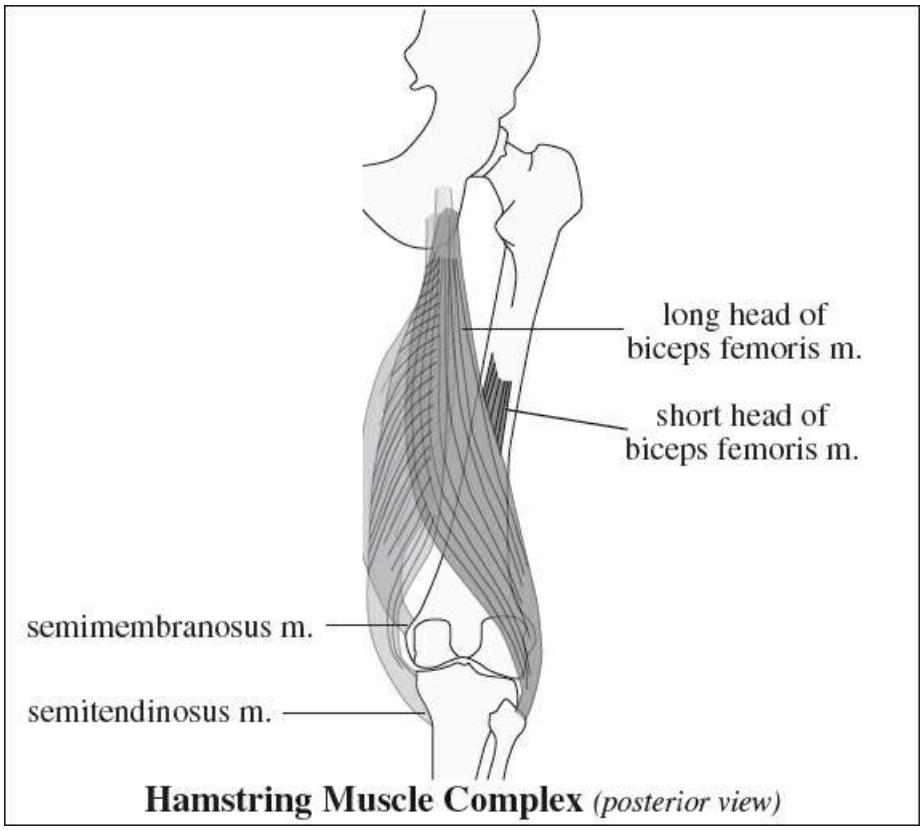


Cross Section through Right Proximal Ankle

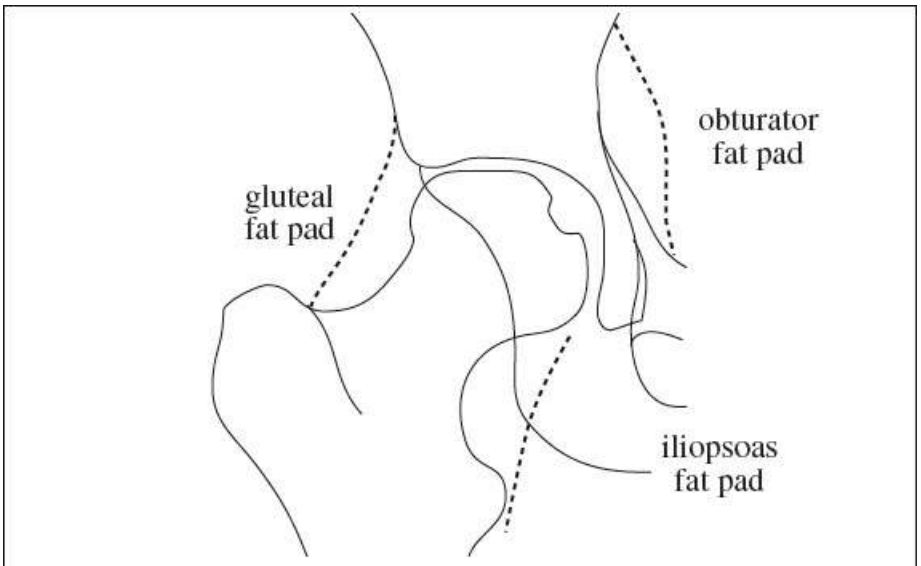
(gray scale of muscles according to innervation)



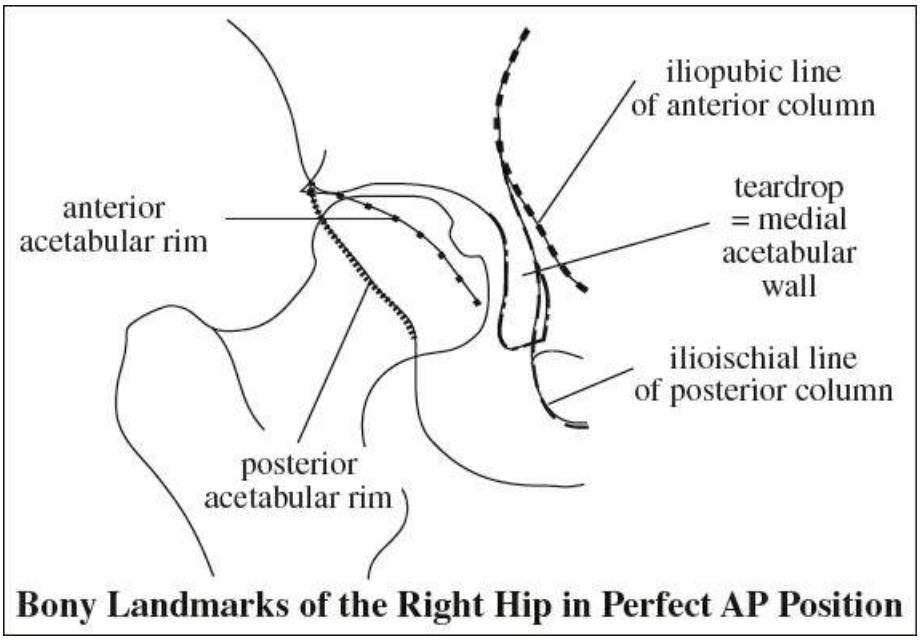
Acetabular Anatomy *(lateral aspect)*



Hamstring Muscle Complex *(posterior view)*

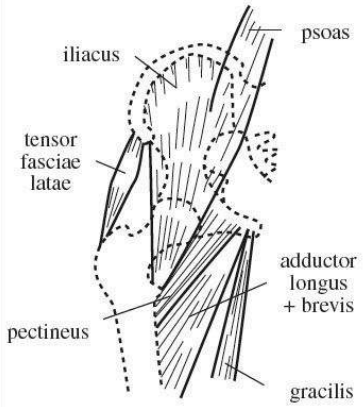


Fat Pads of the Right Hip in Perfect AP Position



Bony Landmarks of the Right Hip in Perfect AP Position

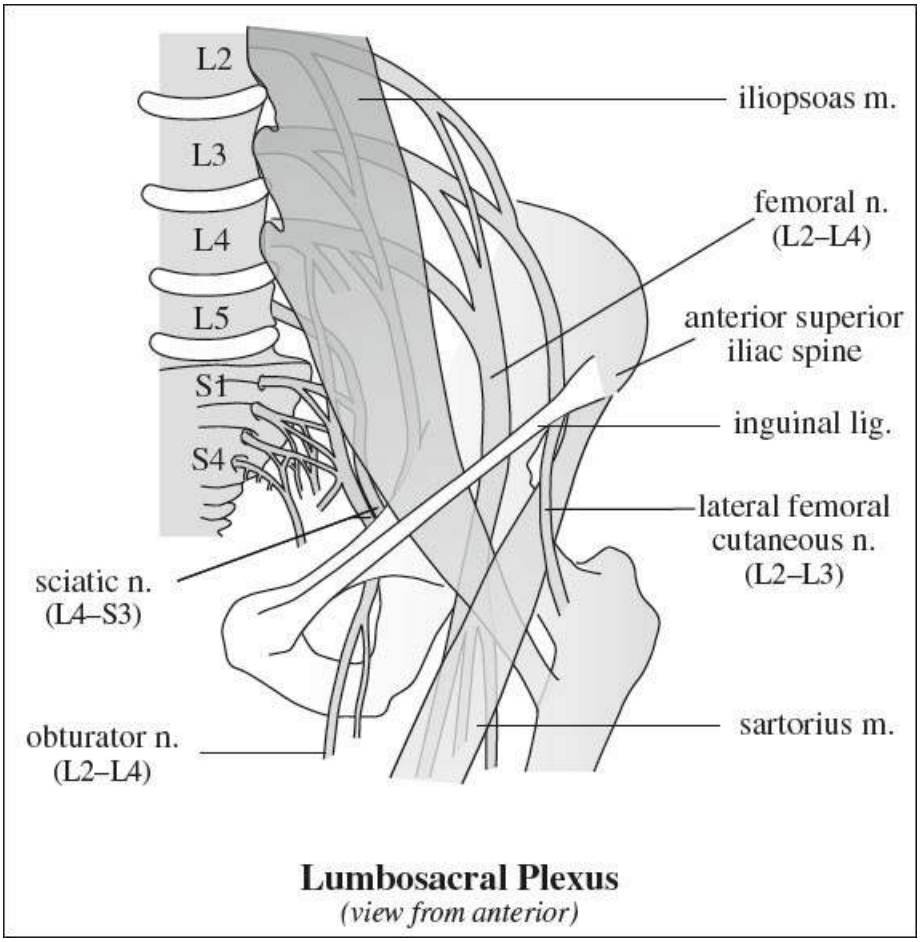
Innervation of Pelvis & Thigh Muscles	
Supplying Nerve	*Muscles Innervated*
Sacral plexus	piriformis, inferior gemellus, superior gemellus,obturator internus, quadratus femoris
Femoral nerve	iliopsoas, pectineus, quadriceps (rectus femoris, vastus lateralis, vastus medialis, vastus intermedius), sartorius
Obturator nerve	adductor brevis, adductor longus, anterior head of adductor magnus (also supplied by sciatic nerve), obturator externus, gracilis
Sciatic nerve	
› tibial division	long head of biceps femoris, semitendinosus, semimembranosus, adductor magnus
› peroneal division	short head of biceps femoris
Superior gluteal n.	gluteus medius, gluteus minimus, tensor fasciae latae
Inferior gluteal n.	gluteus maximus



Hip Flexors

Muscle Attachments of Thigh

Name of Muscle	*Origin*	*Insertion*
Gracilis	inferior pubic ramus	pes anserinus
Semimembranosus	ischial tuberosity	medial tibial condyle
Semitendinosus	ischial tuberosity	pes anserinus
Biceps femoris		
› long head	ischial tuberosity	fibular head
› short head	lateral linea aspera	fibular head
Adductor		
› longus	superior pubic ramus	medial linea aspera
› magnus	inferior pubic ramus	medial linea aspera
Sartorius	anterior superior iliac spine	pes anserinus
Quadriceps		
› rectus	anterior inferior iliac spine	patellar tendon
› vastus lateralis	greater trochanter	patellar tendon
› vastus medialis	medial intertrochanteric line	patellar tendon
Iliopsoas		
› iliacus	ilium	lesser trochanter
› psoas	lumbar spine	lesser trochanter
Tensor fasciae latae	anterior superior iliac spine	anterolateral tibia



Lumbosacral Plexus
(view from anterior)

Location: covers superior portion of lateral facet, beneath lateral portion of gluteus

medius m.

(c) Subgluteus minimus bursa

Location: covers superomedial portion of anterior facet, beneath + medial to gluteus minimus m.

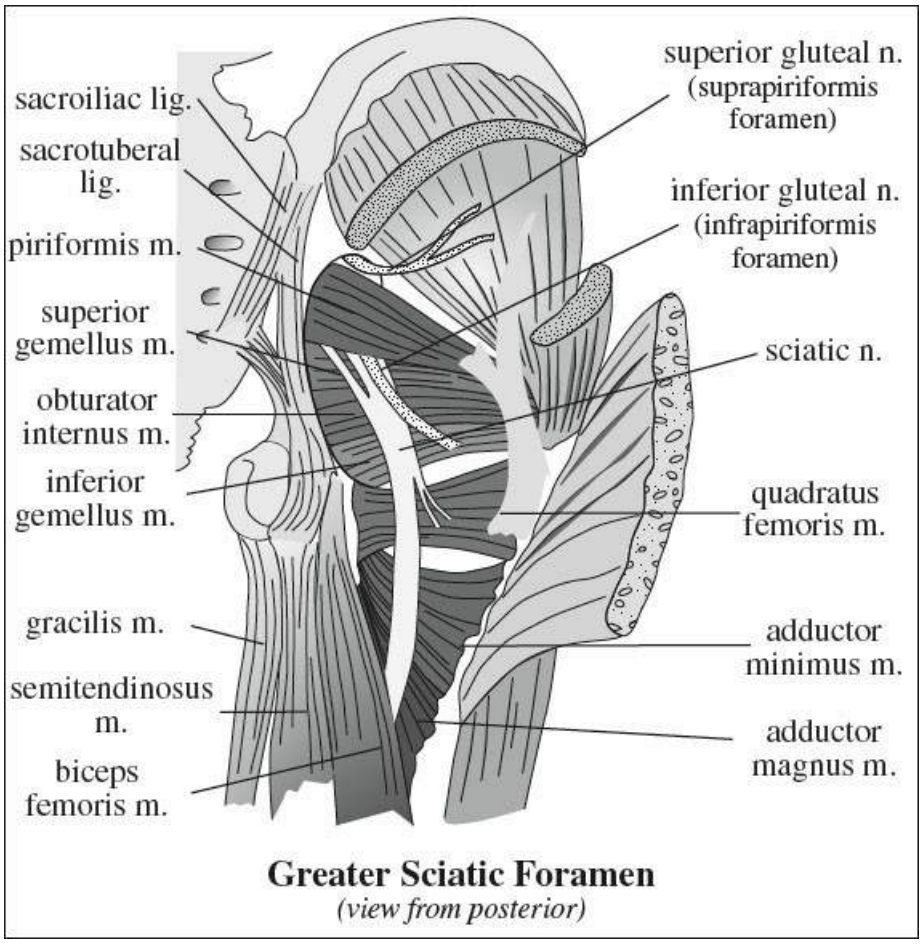
3. Ischiotrochanteric bursa
4. Obturator externus bursa

Location: posteroinferior communication of hip joint capsule

5. Ischial bursa (= weaver's bottom)
6. Paralabral cyst

Iliotibial Tract

Function: primary stabilizing structure of anterolateral knee together with lateral capsular ligaments



Greater Sciatic Foramen
(view from posterior)

Consists of:

1. Distal extension of superficial + deep layers of fascia lata
2. Tensor fasciae latae
3. Gluteus maximus m.
4. Gluteus medius m.

Insertion:

(a) supracondylar tubercle of lateral femoral condyle
(b) intermuscular septum of distal femur (deep component)
(c) **Gerdy Gerdy**, Pierre Nicolas (1797–1856), surgeon in Paris tubercle (main site of superficial component) = anterolateral tubercle of tibia
[Pierre Nicolas Gerdy (1797–1856), surgeon in Paris]
(d) patella + patellar ligament

Hamstring Muscle Complex

◊ Most frequently injured muscle!

(a) medial hamstring

Function: flexion + medial rotation of knee joint as thigh is swung forward and hip extended

1. Semimembranosus m.

Origin: superolateral aspect of ischial tuberosity (beneath semitendinosus m.)
Course: medial + anterior to other hamstring muscles with connections to tendons of adductor magnus m. + long head of biceps m.
Insertion: via 5 tendinous arms on
› medial tibial condyle (anterior[1] + direct[2] + inferior[3] arm) deep to tibial collateral ligament
› posterior oblique lig. (capsular[4] arm)
› arcuate lig. (oblique popliteal lig.[5])
Innervation: single branch off tibial division of sciatic n.

2. Semitendinosus m.

Origin: inferomedial impression of upper portion of ischial tuberosity *conjoined with* long head of biceps femoris m.
Insertion: Gerdy tubercle *conjoined* with gracilis m.
Innervation: tibial n. (2 separate branches)

(b) lateral hamstring

Function: flexion + lateral rotation of knee joint

3. Biceps femoris m.

Insertion: head of fibula, lateral condyle of tibia, fascia of leg
(a) long head
Origin: medial facet of ischial tuberosity
Innervation: tibial portion of sciatic n.
(b) short head (does not cross 2 joints, may be absent)
Origin: lateral linea aspera + lateral supracondylar line + intermuscular septum
Used as: landmark to distinguish between proximal and distal hamstring injuries
Innervation: peroneal division of sciatic n.

KNEE

Knee Extensors

= quadriceps muscle consisting of

1. Vastus medialis m.
2. Vastus lateralis m.

3. Vastus intermedius m.
4. Rectus femoris m.

Insertion: combined as quadriceps tendon on patella

Pes Anserinus

[*pes*, Latin = foot; *anser*, Latin = goose]

= tendinous configuration of 3 flexors + medial rotators of knee joint attaching inferomedially to tibial tuberosity

mnemonic: **S**ay GraceSe before eating goose

Sartorius tendon (anterior)

Gracilis tendon (middle)

Semitendinosus tendon (posterior)

Patella Alta

= high-riding patella as normal anatomic variant

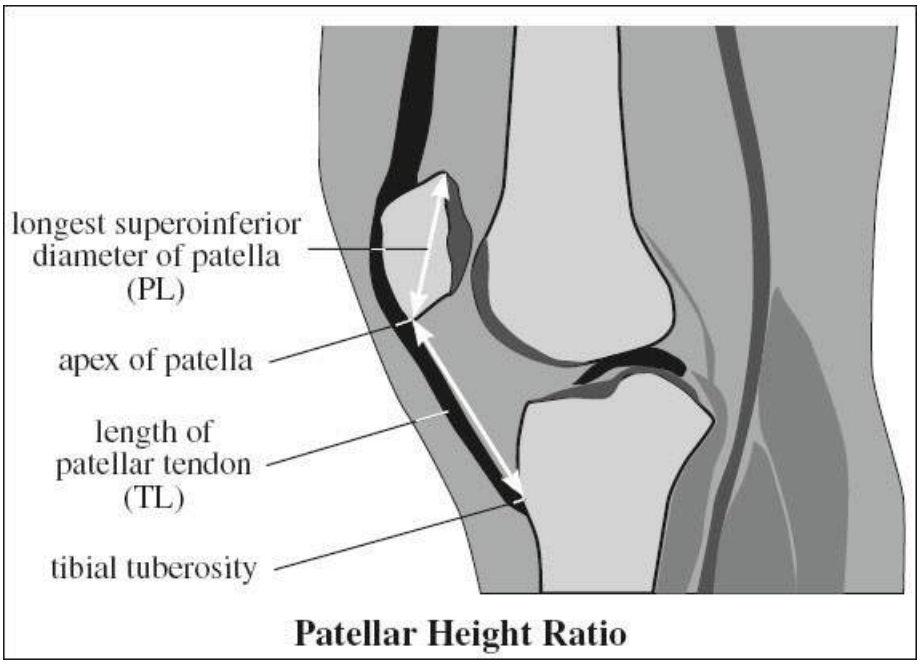
Cause: patellar tendon too long → reduced patellar contact area → patellar dislocation

◊ High-riding patella in 25% of patients with acute patellar dislocation

• mostly asymptomatic

MR measurement:

patellar height ratio (Insall-Salvati index) = TL÷PL = patellar tendon length (TL) divided by superoinferior diameter of patella (PL) 1.1 ± 0.1 = normal; >1.3(M) or >1.5 (F) = patella alta; <0.74 (M) or <0.79 (F) = patella baja (infera)



Cruciate Ligaments

◊ Both cruciate ligaments are intracapsular but extrasynovial!

Anterior Cruciate Ligament (ACL)

Function: limits anterior tibial translation
Origin: inner face of lateral femoral condyle
Insertion: noncartilaginous region of anterior aspect of intercondylar eminence of tibia
Anatomy: several distinct bundles of fibers
(1) large posterior bulk = spiraling together at femoral origin
(2) small anteromedial bundle diverging at tibial insertion

√ thin solid taut dark band (sagittal MR with knee in extension) almost parallel to intercondylar roof (= Blumensaat line):
√ with knee extension posterolateral band taut
√ with increasing flexion:
anteromedial band becomes more taut + posterolateral band more lax

√ thin hypointense band parallel to inner aspect of lateral femoral condyle + fanlike configuration toward tibial spine (coronal MR)

√ thin ovoid hypointense band proximally, elliptical configuration distally with higher intensity (axial MR)

√ greater SI than posterior cruciate ligament (due to anatomy)

Posterior Cruciate Ligament (PCL)

Function: limits posterior tibial translation
Origin: in a depression posterior to intercondylar region of tibia below joint surface
Insertion: most distal + anterior aspect of inner face of medial femoral condyle

√ thick dark band slightly posteriorly convex (arclike course on sagittal MR with knee in extension)

√ medial to ACL (coronal MR)

Collateral Ligaments of Knee Joint

Medial (Tibial) Collateral Ligament

Origin: just distal to adductor tubercle of femur
Insertion: anteromedial face of tibia distal to level of tibial tubercle about 5 cm below joint line

(a) deep portion:
› meniscofemoral ligament
› meniscotibial ligaments

(b) superficial portion
› vertical band from femoral epicondyle to pes anserinus
› posterior oblique ligament = posterior oblique band from femoral epicondyle to semimembranosus tendon

√ deep and superficial dark bands separated by a thin bursa + fatty tissue (on coronal MR)

Lateral (Fibular) Collateral Ligament

Origin: lateral aspect of lateral femoral condyle
Insertion: styloid process of fibular head

√ bicipital tendon + iliotibial band join lateral collateral lig.

Arcuate Complex

Function: provides posterolateral stabilization
Consists of: lateral (fibular) collateral ligament
+ biceps femoris tendon
+ popliteus muscle and tendon
+ popliteal meniscal ligament
+ popliteal fibular ligament
+ oblique popliteal ligament
+ arcuate ligament
+ fabellofibular ligament
+ lateral gastrocnemius muscle

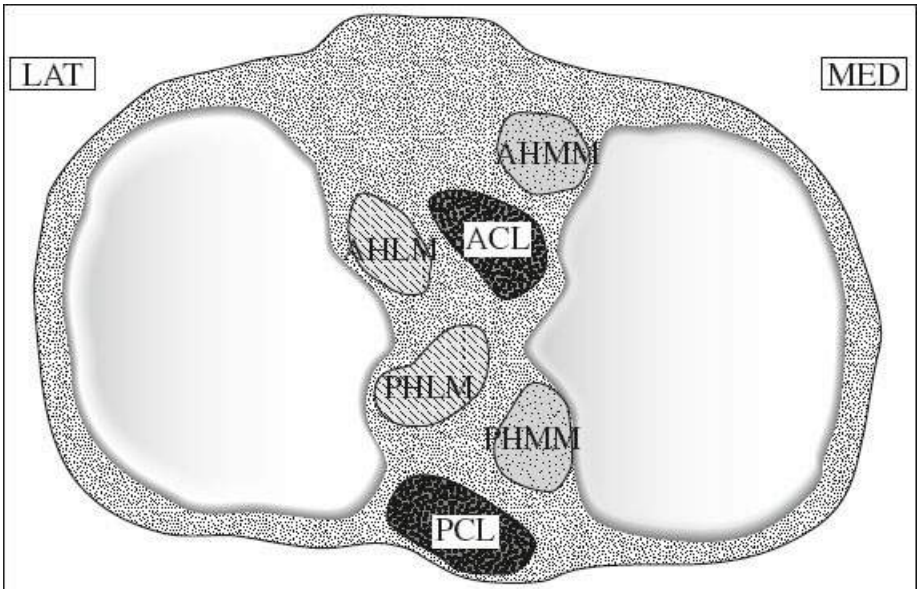
Posteromedial Corner of Knee

1. Semimembranosus tendon
   Attachment: infraglenoid tubercle of posteromedial tibia; posterior joint capsule; posterior horn of medial meniscus
2. Posterior joint capsule
3. Posterior oblique ligament

Menisci

= wedge-shaped semilunar fibrocartilaginous structures
Function: absorb shock, distribute axial load, assist in joint lubrication, facilitate nutrient distribution
Margin: (a) superior concave surface conforming to femoral condyle → increase in contact area
(b) inferior flat base that attaches to central tibial plateau via anterior + posterior root ligament anchors → maintain normal meniscal position + biomechanical function
(c) thick peripheral portion
(d) tapered central free edge
Composition: collagen bundles oriented in
(1) circumferential (longitudinal) type I collagen bundles parallel to long axis of meniscus → hoop strength resisting axial load + preventing meniscal extrusion
(2) radial thin fibers perpendicular to longitudinal bundles forming a lattice → tying bundles together + providing structural support
Subdivision into thirds:
» anterior horn
» meniscal body
» posterior horn
Attachment:
» posterior root
» anterior root
@ lateral meniscus (LM)
√ striated / comb-like appearance of anterior horn ← intimate association between anterior root of lateral meniscus + ACL insertion site
@ medial meniscus (MM)

√ anomalous insertion paralleling ACL → mimicks MM tear
√ anterior root may insert along anterior margin of tibia → mimicks MM subluxation



Attachment of Cruciate Ligaments and Menisci on Tibial Plateau

ACL	anterior cruciate ligament
AHMM	anterior horn of medial meniscus
AHLM	anterior horn of lateral meniscus
PCL	posterior cruciate ligament
PHMM	posterior horn of medial meniscus
PHLM	posterior horn of lateral meniscus

√ peripheral attachment to deep fibers of medial collateral ligament → meniscus less mobile

Imaging:

› on sagittal images of menisci:
√ "bow-tie" structure peripherally
√ opposing triangles centrally
√ posterior horn larger than anterior horn for MM
√ anterior + posterior horns of similar size + shape for LM
› on coronal images:
√ triangular shape through body of meniscus
√ wedge-shaped through horn of meniscus
› on axial images:
√ open C-shaped configuration of medial meniscus
√ increase in width from anterior to posterior

Variants mimicking a tear:

1. **Transverse meniscal (geniculate) ligament** (83–90%)
= thin fibrous band that connects and stabilizes the anterior horns of the menisci

√ overrides superior aspect of menisci before completely fusing to menisci
DDx: anterior root tear
Dx: Trace cross section of transverse ligament through infrapatellar fat pad on more central SAG images!

2. **Meniscofemoral ligaments** (MFL) in 89–93%
   (a) **Wrisberg** ligament
   √ posterior to posterior cruciate ligament
   (b) **Humphrey** ligament
   √ anterior to posterior cruciate ligament
   mnemonic: **under** the **hump** (of the PCL)
   Origin: superior + medial aspect of posterior horn of lateral meniscus
   Insertion: lateral aspect of medial femoral condyle
   Function: assist PCL + help control mobility of posterior horn of lateral meniscus during knee flexion + extension
   √ demonstrated in ⅓ of cases on SAG images; usually limited to single most medial image!
3. **Popliteomeniscal fascicles** (visualized in 90%)
   (a) anteroinferior fascicle = floor of popliteal hiatus
   (b) posterosuperior fascicle = roof of popliteal hiatus
   = synovial-lined fibrous bands that attach to posterior horn of lateral meniscus + help form popliteal hiatus
   Function: stabilize posterior horn
4. **Popliteal hiatus**
   = separates lateral meniscus from joint capsule
   √ above posterior aspect of lateral meniscus on most superficial SAG slice!
   √ popliteal tendon moves behind + inferior to meniscus on adjacent deeper SAG sections!
5. **Oblique meniscomeniscal ligament** (1–4%)
   = connects meniscal horns in X-wise fashion on AXIAL image
   (a) medial oblique meniscomeniscal ligament
   √ anterior horn of medial meniscus to posterior horn of lateral meniscus
   (b) lateral oblique meniscomeniscal ligament
   √ anterior horn of lateral meniscus to posterior horn of medial meniscus
   √ traverses intercondylar fossa between ACL and PCL

Anatomic Variants of Menisci

1. **Diskoid meniscus**
   = abnormally shaped enlarged meniscus with further central extension onto tibial articular surface
   Prevalence: 1.5–3% for lateral meniscus; 0.12–0.3% for medial meniscus
   Side: lateral÷medial meniscus = 10÷1
   Age: children, adolescents
   √ body of meniscus measures ≥ 15 mm on midline coronal image
   √ ≥ 3 bow-tie shapes on contiguous sagittal (4-mm-thick) sections
   √ diffuse intrameniscal signal intensity ← increased meniscal vascularity

2. **Meniscal flounce**
   = rippled appearance of free nonanchored inner edge of medial meniscus
   Prevalence: 0.2–0.3% of asymptomatic knees
3. Meniscal ossicle (rare)
   Cause: developmental, degenerative, posttraumatic
   Location: posterior horn of MM
   √ calcification on radiograph mimicks loose body
   √ increased signal intensity can mimic a tear
4. Chondrocalcinosis
   Prevalence: 5– 15% (increasing with age)
   √ calcifications on radiograph
   √ increased signal intensity → lowers sensitivity and specificity for detection of meniscal tear

Posterolateral Corner Structures

= arcuate complex

1. Fibular collateral ligament
2. Arcuate ligament
3. Popliteus musculotendinous complex
4. Popliteofibular ligament
5. Fabellofibular ligament
6. Posterolateral capsule

Popliteus Musculotendinous Complex

Origin: posteromedial tibial surface proximal to soleal line forming floor of popliteal fossa

Course: forms long strong **popliteal tendon** that passes underneath posterolateral joint capsule + arcuate ligament (extracapsular); enters knee through popliteal hiatus posteroinferiorly behind posterior horn of lateral meniscus; passes beneath lateral collateral ligament + tendon of biceps femoris
= *intracapsular – extraarticular – extrasynovial*

Attachment: popliteal notch on lateral aspect of lateral femoral condyle; anteroinferior to proximal attachment of lateral collateral ligament on lateral epicondyle

Function: in non–weight-bearing state primary internal rotator of tibia on femur; in weight-bearing state external rotator of femur on leg

√ fluid-filled popliteus bursa surrounds popliteus muscle and tendon

Fibular Collateral Ligament

= (TRUE) LATERAL COLLATERAL LIGAMENT

Origin: lateral femoral epicondyle

Attachment: lateral aspect of fibular head + neck anterior and distal to fibular styloid process; often conjoined insertion with biceps femoris tendon

Function: simple passive restraint

√ extracapsular WITHOUT meniscal attachment

Arcuate Ligament

= Y-shaped inconstant thickening of posterolateral capsule
(a) lateral limb inserts into posterolateral joint capsule
(b) medial limb extends medially over popliteus muscle to oblique popliteal ligament

Popliteofibular Ligament

= attachment of popliteus tendon to fibular head
Origin: popliteus tendon near myotendinous junction
Attachment: posterior aspect of fibular styloid process posteromedial to the biceps insertion
Function: one of the strongest lateral stabilizers in knee

Fabella (present in 20%)

= sesamoid bone in lateral head of gastrocnemius muscle
Function: anchors fabellofibular ligament

FABELLOFIBULAR LIGAMENT (present in 40%)

Origin: fabella
Attachment: styloid process of fibular head posterior to arcuate ligament + lateral to popliteofibular ligament / to lateral femoral condyle (in absence of fabella)

Cysts and Bursae of the Knee

1. Suprapatellar bursa
2. Popliteal bursa
3. Pes anserine bursa
4. Semimembranosus-tibial collateral ligament bursa
5. Prepatellar bursa
6. Infrapatellar bursa
7. Tibial collateral ligament bursa
8. Tibiofibular joint cyst
9. Popliteus bursa
10. Meniscal cyst
11. Cruciate ligament cyst
12. Ganglion (mucinous degeneration of ACL)

ANKLE & FOOT

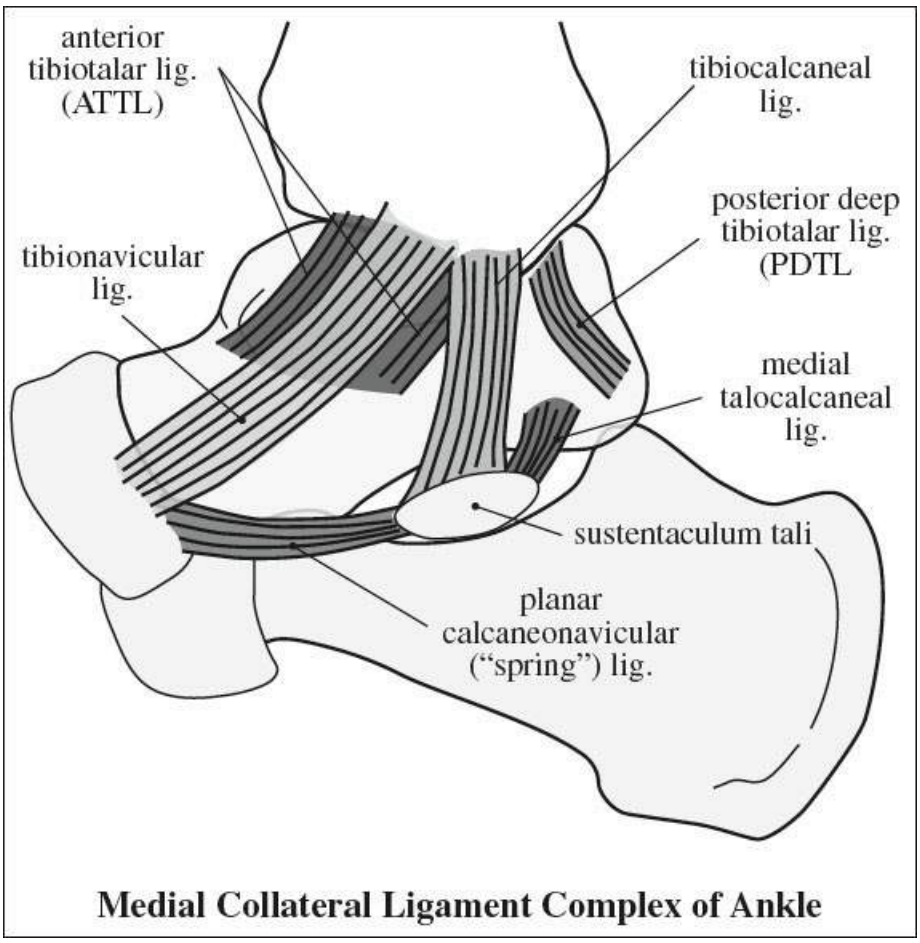
Ligamentous Stabilizers of Ankle

Deltoid Ligament

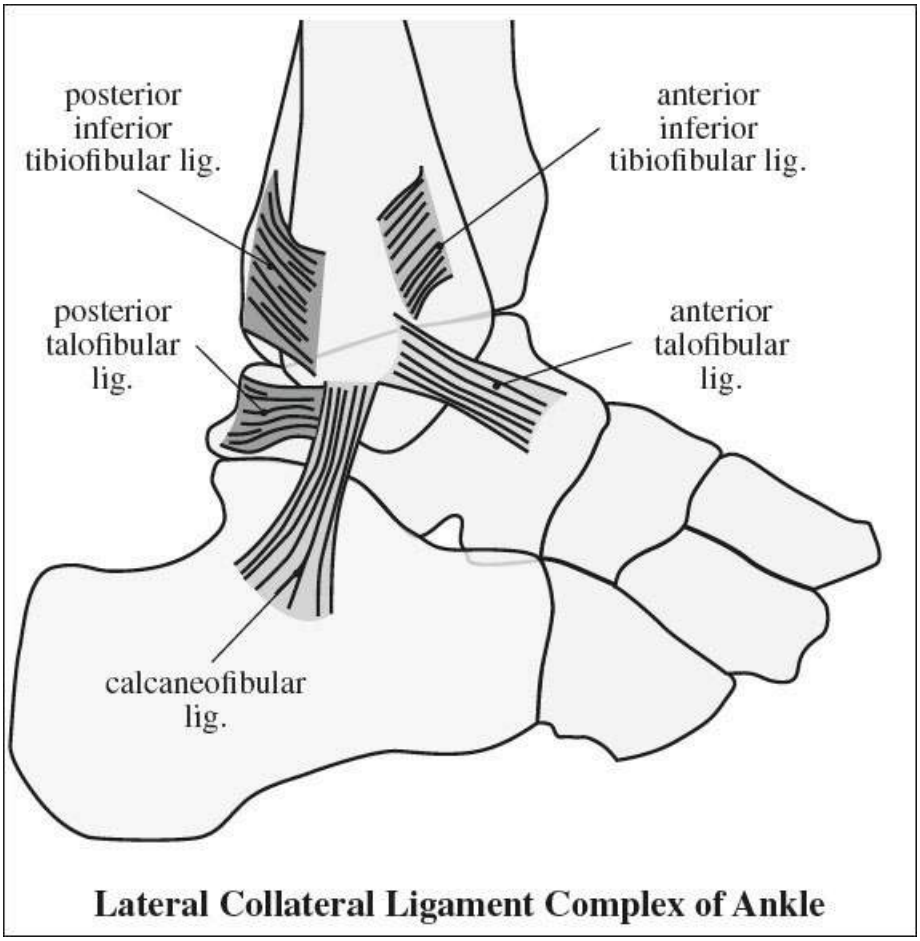
= MEDIAL COLLATERAL LIGAMENT OF ANKLE
Function: main stabilizer against valgus force / pronation force / rotational force on talus
Components:
(a) superficial layer:
Origin: anterior colliculus of medial malleolus
1. Tibiocalcaneal ligament

Distal attachment: calcaneus

2. Tibionavicular ligament
   Distal attachment: os naviculare
3. Posterior superficial tibiotalar ligament
   Distal attachment: talus
4. Tibiospring ligament
   Distal attachment: joins superomedial oblique band of spring lig. proper (= calcaneonavicular lig.)
   Function: stabilizer for talocalcaneonavicular joint + medial plantar arch



Medial Collateral Ligament Complex of Ankle



Lateral Collateral Ligament Complex of Ankle

(b) deep layer = intraarticular, covered by synovium
Origin: intercollicular (= malleolar) groove + posterior colliculus of medial malleolus

1. Anterior tibiotalar ligament (ATTL)
2. Posterior deep tibiotalar ligament (PDTL)

Deltoid ligament rupture is rare without additional injuries to the ankle ← uncommon occurrence of eversion ankle sprains and due to intrinsic thickness of the ligament.

Lateral Collateral Ligament Complex (LCL)

◊ 85% of all ankle sprains involve these ligaments!

1. Anterior talofibular ligament (ATFL)
2. Posterior talofibular ligament (PTFL)

The anterior talofibular ligament is the weakest and most frequently injured among the 3 components of the lateral collateral ligament complex.

3. Calcaneofibular ligament (CFL)

In inversion sprains, the calcaneofibular ligament is usually sequentially torn after the anterior talofibular ligament. If the anterior talofibular ligament is normal, then an isolated tear of the CFL is unlikely.

Syndesmotic Ligament Complex

binding tibia + fibula

1. Anterior-inferior tibiofibular (AITFL)
   Attachment: slightly above talofibular ligaments = above level of talotibial joint line
   ◊ One of the most commonly injured ligaments in the ankle!
2. Posteroinferior tibiofibular (PITFL)
3. Transverse tibiofibular ligament
4. Interosseous membrane

Anterior Ankle Tendons

Anterior Tibialis

= most medial and largest extensor of ankle with appearance of tendon at junction of middle to distal ⅓

Function: 80% of foot dorsiflexion; helps support longitudinal arch; aids in foot supination and inversion

Origin: proximal third of lateral tibia, lateral tibial condyle, interosseous membrane, deep fascia, intermuscular septum

Insertion: bifid = medial cuneiform (dominant slip) + 1st metatarsal base (thin slip)

Tendon fixation: superior + inferior extensor retinaculum (with oblique superomedial and oblique inferomedial bands)

Extensor Hallucis Longus

Function: extension of hallux

Origin: middle half of fibula + interosseous membrane; becomes tendinous at distal ⅓ of tibia

Insertion: dorsomedial surface of distal phalangeal base of hallux

Course: descends vertically between anterior tibial and extensor digitorum longus muscles deep to superior + inferior extensor retinaculi

Extensor Digitorum Longus

Function: extension of phalanges; contributes to foot dorsiflexion

Origin: lateral tibial condyle, proximal ¾ of anterior fibula, interosseous membrane, deep fascia, intermuscular septa

Insertion: dorsal aspect of middle + distal phalanges of 2nd through 5th digits

Course: behind superior extensor retinaculum

Posterior Ankle Tendons

Achilles Tendon

Size: 7 mm in AP thickness (largest tendon of the body)

Origin: gastrocnemius + soleus muscle

√ surrounded by loose paratenon without tendon sheath

Plantaris Tendon

√ parallels Achilles tendon anteromedially

Insertion: Achilles tendon. calcaneus, plantar fascia

Medial Flexor Tendons

Posterior Tibialis Tendon

Function: plantar flexion + inversion of foot; support for medial longitudinal arch of the foot

Size: twice the size of flexor digitorum longus tendon

Course: posterior + beneath medial malleolus (used as pulley) + flexor retinaculum; continues medial to subtalar joints

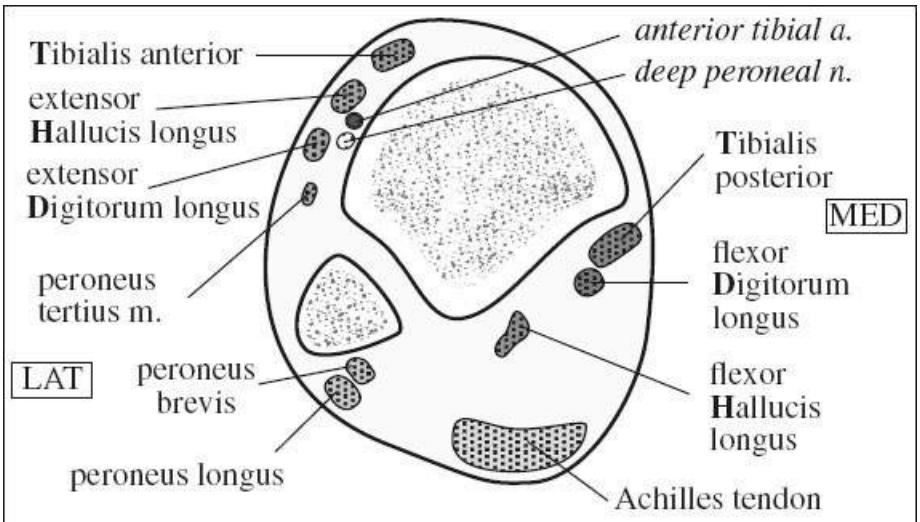
(a) largest anterior tendon component

Insertion: navicular tuberosity + plantar capsule of navicular-cuneiform joint + plantar aspect of medial cuneiform bone

Variation: ossified accessory navicular bone (in 25%) embedded into tendon

(b) deep middle (tarsometatarsal) tendon component

Insertion: 2nd and 3rd cuneiform bones + cuboid bone + 2nd to 4th (± 5th) metatarsal bases



Cross Section through Ankle

mnemonic for posterior tendons: "**T**om, **D**ick and **H**arry from medial to lateral"

Tibialis posterior
Digitorum longus (flexor)
Hallucis longus (flexor)

mnemonic for anterior ankle compartment - medial to lateral:

"**T**he **H**ospitals **A**re **N**ot **D**irty **P**laces"

Tibialis anterior tendon (extensor)
Hallucis longus (extensor)
Artery (anterior tibial)
Nerve (deep peroneal)
Digitorum longus (extensor)
Peroneus tertius

mnemonic for peroneus tendons at the ankle:

"**P**eroneus **L**ongus is **P**osterior and **L**ateral from peroneus brevis"

(c) posterior tendon component

Origin: proximal tendon

Insertion: anterior aspect of sustentaculum tali

Tendon sheath: ends 1–2 cm proximal to navicular insertion

Flexor Digitorum Longus Tendon

Course: pierces medial intermuscular septum in medial-to-lateral direction; travels obliquely superficial (plantar) to flexor hallucis longus tendon; receives insertion of quadratus plantae muscle as it splits into four separate tendons giving rise to lumbrical muscles

Insertion: bases of 2nd – 5th distal phalanges

Flexor Hallucis Longus Tendon

Course: groove beneath posterior process of talus, beneath sustentaculum tali; pierces medial inter- muscular septum in medial-to-lateral direction; courses through fibro-osseous tunnel between tibial + fibular sesamoid bones of great toe

Insertion: base of distal phalanx of hallux

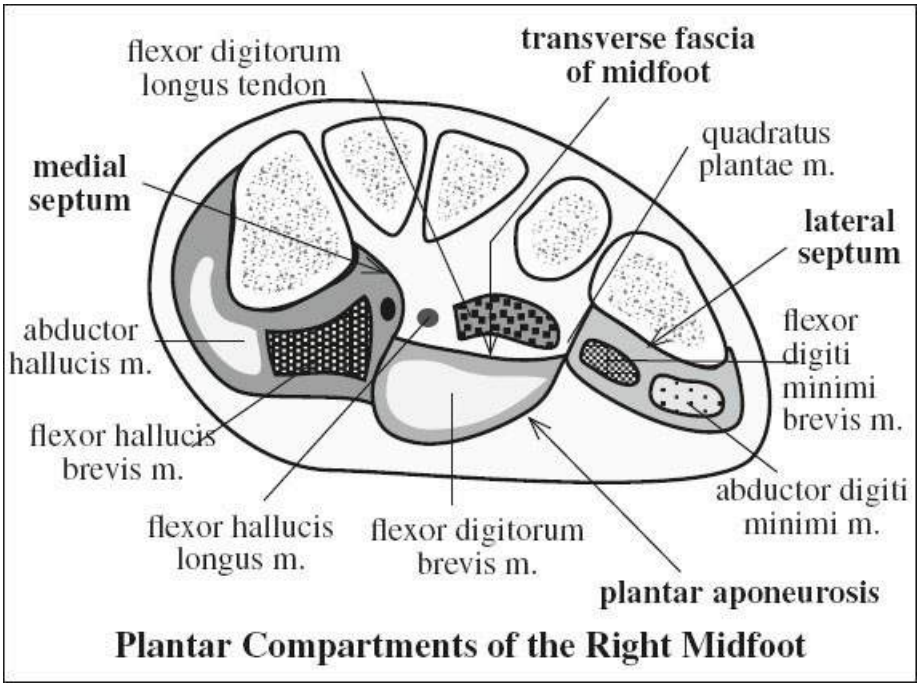
Flexor digitorum and hallucis longus tendons cross at the level of the navicular bone forming the master knot of Henry!

Peroneus Longus Tendon

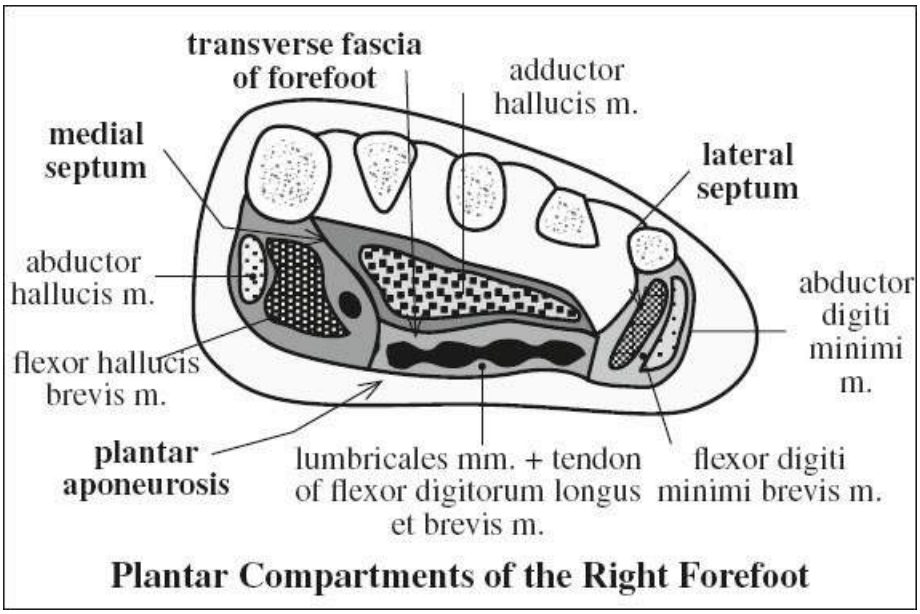
The peroneus longus tendon is located posterolateral to peroneus brevis tendon in retromalleolar groove!

Function: plantar flexion of 1st ray of foot + ankle and eversion of ankle; important stabilizer of ankle

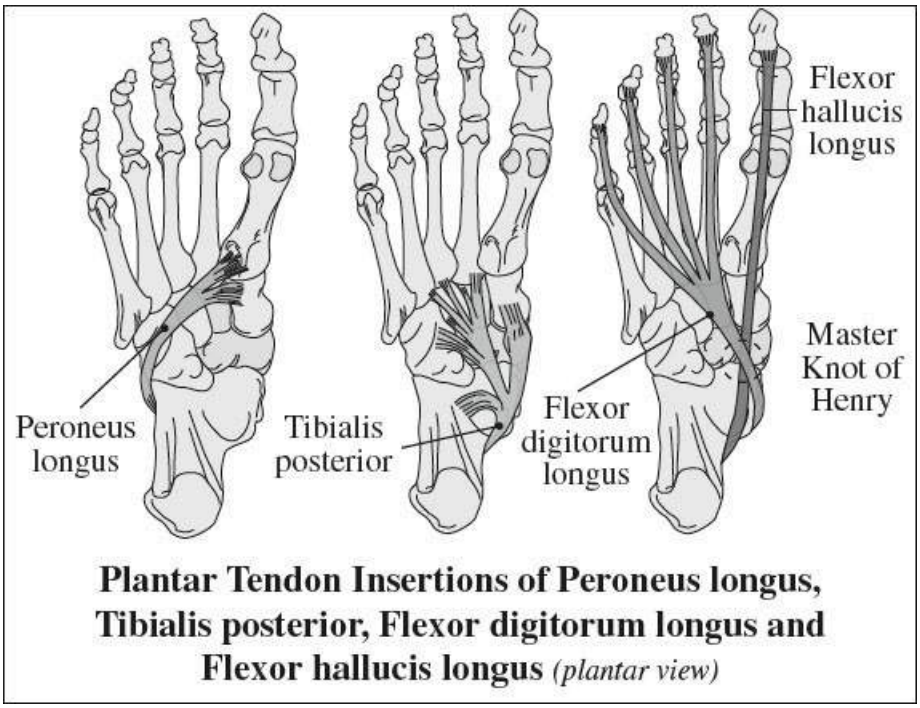
Insertion: fan-shaped onto lateral tubercle at base of 1st MT + plantar aspect of 1st cuneiform bone + base of 2nd MT bone + 1st dorsal interosseous muscle



Plantar Compartments of the Right Midfoot



Plantar Compartments of the Right Forefoot



Plantar Tendon Insertions of Peroneus longus, Tibialis posterior, Flexor digitorum longus and Flexor hallucis longus *(plantar view)*

Course: posterior to lateral malleolus in retromalleolar groove; posterolateral to peroneus brevis tendon; beneath cuboid bone through cuboid fibro-osseous tunnel / groove; oblique anteromedial orientation while crossing plantar aspect of foot

Variant: os peroneum (20%) = accessory ossicle embedded in peroneus longus tendon at level of calcaneocuboid joint

N.B.: Tenosynovial effusion within plantar peroneus longus tendon sheath is uncommon

Fluid in plantar peroneus longus tendon sheath is highly suggestive of tenosynovitis!

Cysts and Bursae of the Ankle and Foot

1. Malleolar bursa
2. Retrocalcaneal bursa
3. Tendo-Achilles bursa
4. Tarsal tunnel ganglion
5. Sinus tarsi bursa
6. Intermetatarsal bursae

Foot Compartments

(a) medial compartment
Border: medial septum (extending from plantar aponeurosis to navicular bone, medial cuneiform bone, plantar surface of 1st metatarsal bone)
Content: abductor hallucis muscle + flexor hallucis brevis muscle + flexor hallucis longus tendon

(b) lateral compartment
Border: lateral septum (extending from plantar aponeurosis to medial surface of 5th metatarsal bone)
Content: abductor muscle + short flexor muscle + opponens muscle of 5th toe

(c) central compartment
Border: medial + lateral septa; communicates directly with posterior compartment of calf; subdivided by horizontal septa: adductor hallucis muscle separated from quadratus plantae muscle
Content: flexor digitorum brevis m. + flexor digitorum longus tendon + quadratus plantae muscle + lumbricales mm. + adductor hallucis muscle

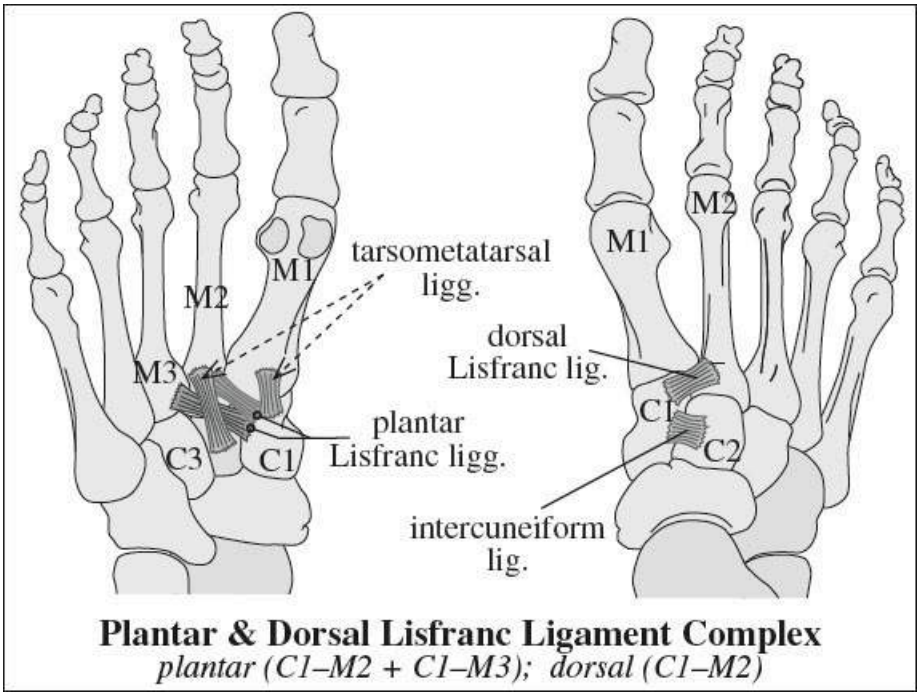
(d) deep subcompartment
Border: transverse fascia of forefoot; separated from quadratus plantae muscle
Content: adduct hallucis muscle

Lisfranc Joint Complex

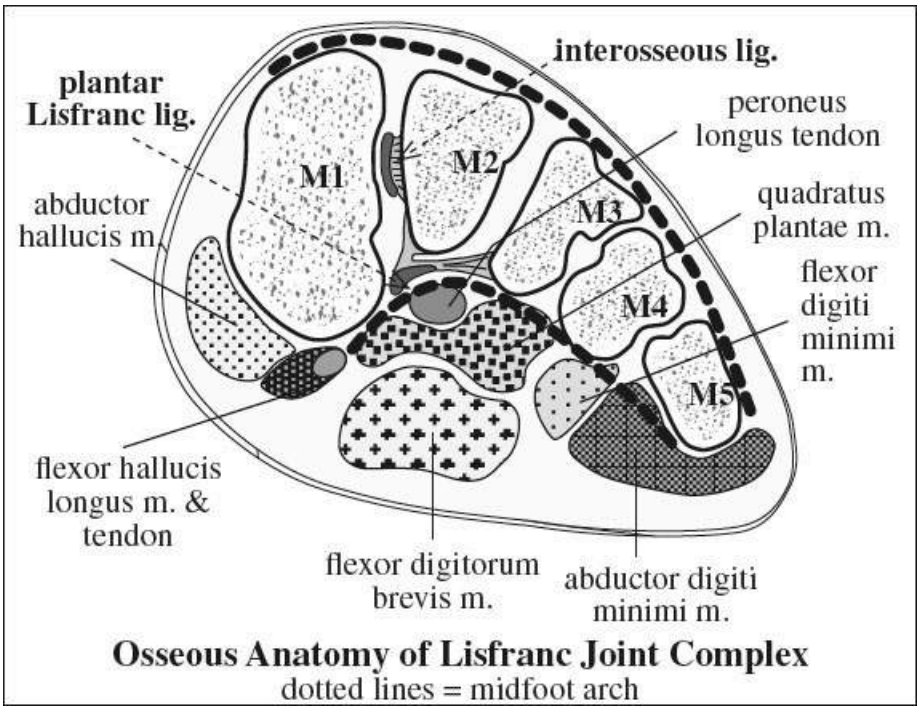
= articulation between nine bones of forefoot and midfoot:
- 5 metatarsals (M1–M5) → contribute to plantar arch (M2–M4 bases of trapezoidal morphology at cross section and M2 base representing osseous "keystone")
- 3 cuneiforms (C1–C3)
- cuboid

Three separate synovial articulations:
- lateral column = most mobile articulation of M4 + M5 with cuboid
- middle column = most rigid articulations of M2 + M3 with C2 + C3
- medial column = rigid articulation between C1 and M1

Location of Common Synovial Recesses and Bursae		
Joint	*Recess or Bursa*	*Location*
Shoulder	Subscapularis	between scapula + subscapularis muscle, extending above + (sometimes) anterior to subscapularis tendon
	Subacromial-subdeltoid	between deltoid muscle + joint capsule, extending underneath acromion + coracoacromial ligament
	Subcoracoid	between anterior surface of subscapularis tendon + coracoid
Elbow	Olecranon	posterior to olecranon process of ulna
	Bicipitoradial	between distal biceps tendon + proximal radius
Hip	Trochanteric	between gluteus maximus / iliotibial tract + posterior facet of greater trochanter
	Iliopsoas	between anterior aspect of hip joint + iliopsoas tendon
	Obturator externus	between superior margin of obturator externus + posteroinferior hip joint capsule
Knee	Gastrocnemius-semimembranosus	posteromedial knee, extending between distal tendon of semimembranosus + proximal tendon of medial head of gastrocnemius
	Suprapatellar	between posterior surface of patella + prefemoral fat pad
	Prepatellar	subcutaneous tissues anterior to patella
	Pes anserine	deep to distal tendons of sartorius, gracilis, semitendinosus as they insert on medial aspect of proximal tibia
Ankle & foot	Retrocalcaneal	between Achilles tendon + posterosuperior surface of calcaneus
	Intermetatarsal	between metatarsal heads



Plantar & Dorsal Lisfranc Ligament Complex
plantar (C1–M2 + C1–M3); dorsal (C1–M2)



Osseous Anatomy of Lisfranc Joint Complex
dotted lines = midfoot arch

Talus

= 2nd largest tarsal bone; ²/₃ of surface covered with articular cartilage

› head of talus

Anterior articulation: Talonavicular joint

Inferior articulation: Anterior talocalcaneal (subtalar) joint

› neck of talus

Inferior surface: tarsal canal opening laterally into sinus tarsi

› talar body

Inferior (subtalar) articulations:

(1) Posterior (lateral) facet: larger articulation

(2) Middle (medial) facet: sustentaculum

Superior articulation: talar dome / trochlea

(1) tibiotalar joint

Lateral articulation: fibula

(1) posterior facet of posterior talocalcaneal (subtalar) joint

› posterior process

(a) medial tubercle

(b) lateral tubercle

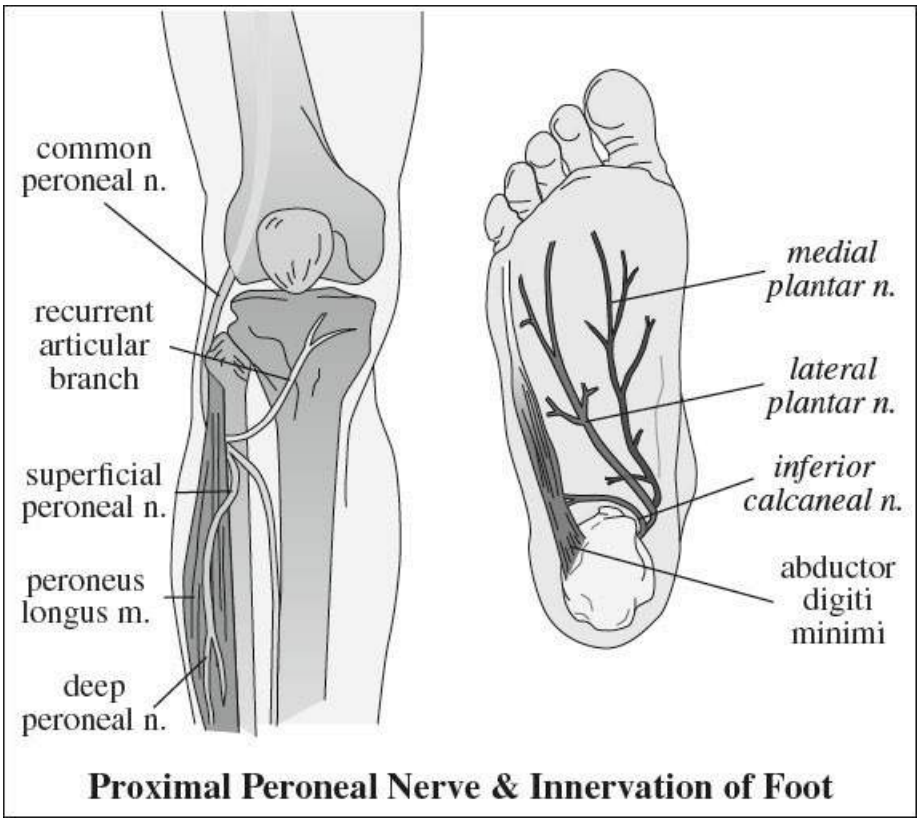
» elongated = Stieda process

» nonfused = os trigonum (prevalence of 2–50%)

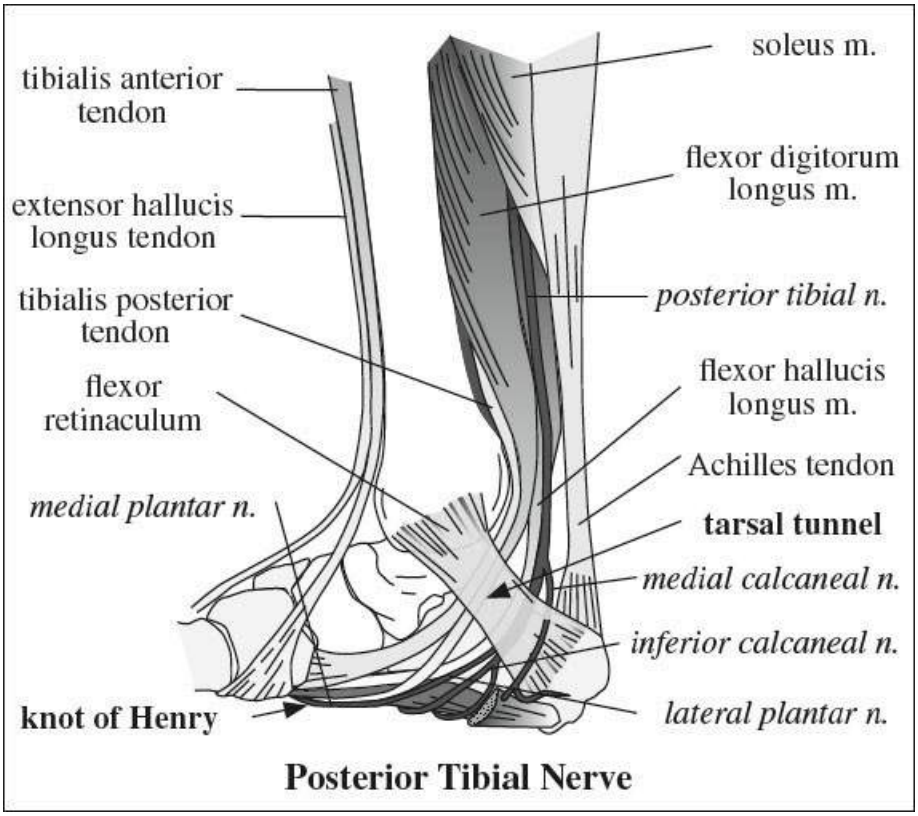
(c) groove between both: for flexor hallucis longus tendon

Blood supply:

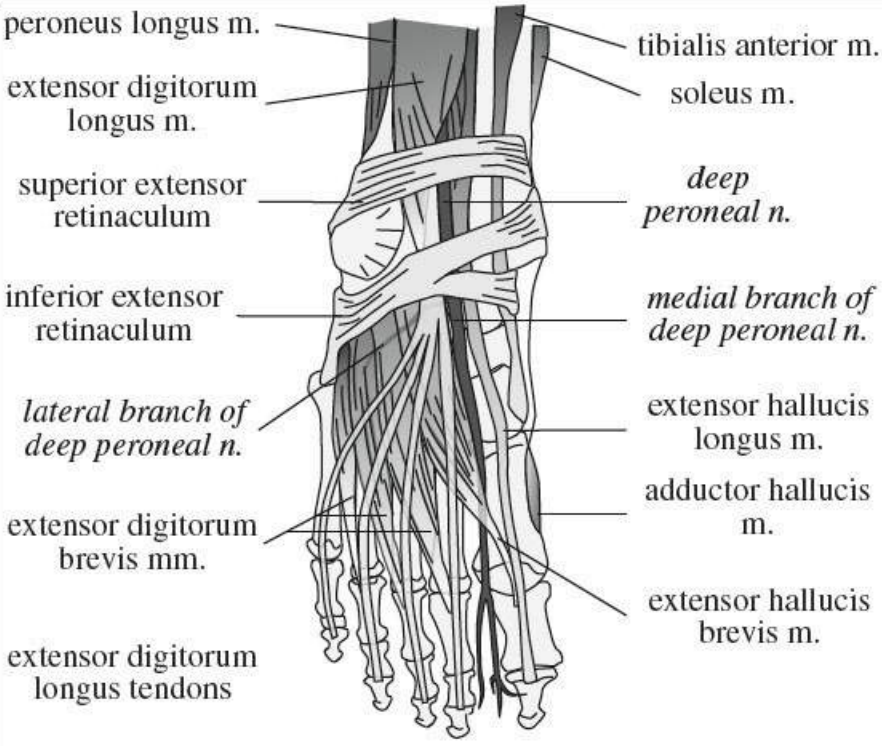
(1) Anterior tibial (dorsalis pedis) artery



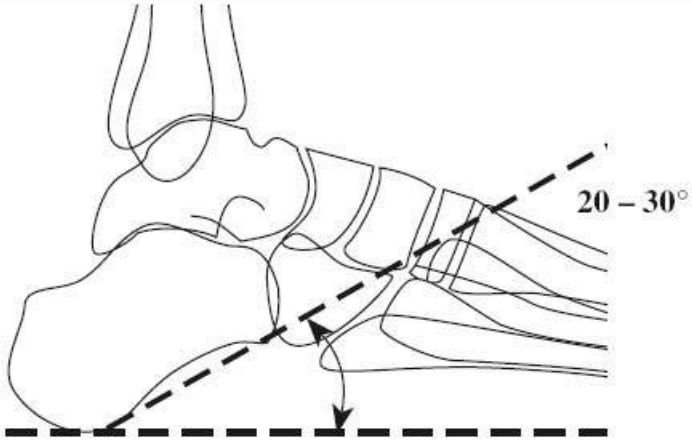
Proximal Peroneal Nerve & Innervation of Foot



Posterior Tibial Nerve

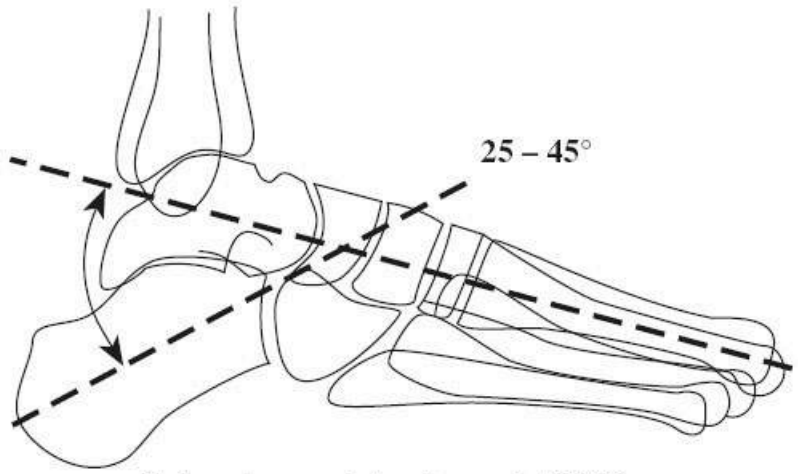


Distal Peroneal Nerve



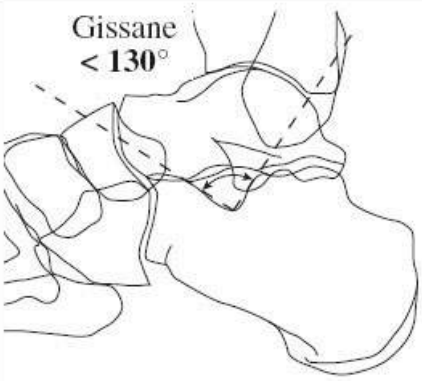
Calcaneal Pitch
= Calcaneal Inclination Angle

= determines longitudinal arch of foot;
angle between line drawn along the inferior border of calcaneus connecting the anterior and posterior prominences + line representing the horizontal surface



Talocalcaneal Angle on LAT View

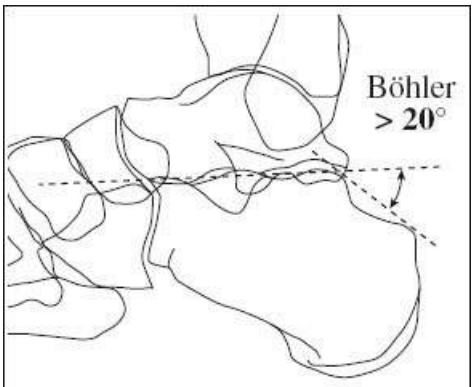
= angle between lines drawn through mid-transverse planes of talus + calcaneus; the midtalar line parallels the longitudinal axis of the first metatarsal



Angle of Gissane

[William Gissane (1898–), trauma surgeon in Birmingham, England]

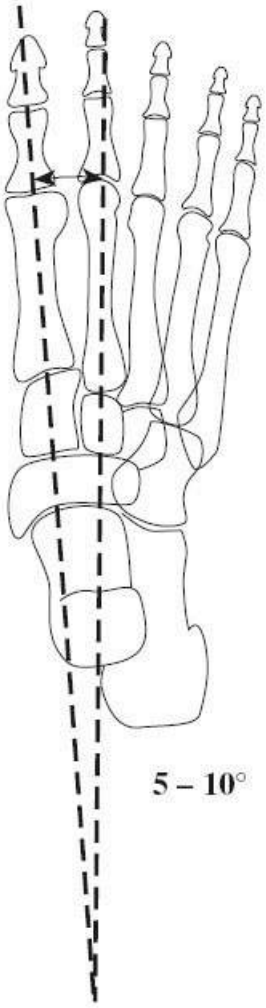
= formed by intersection of downward + upward slopes of calcaneal superior surface, located inferior to lateral process of talus



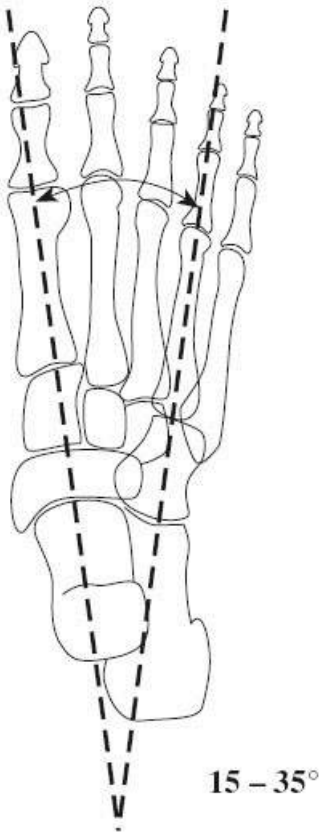
Angle of Böhler

[Lorenz Böhler (1885–1973), trauma surgeon in Vienna, Austria]

= formed by intersection of (a) a line from the highest point of posterior calcaneal tuberosity to the highest point of posterior facet and (b) a line from highest point of anterior process to the highest point of posterior facet



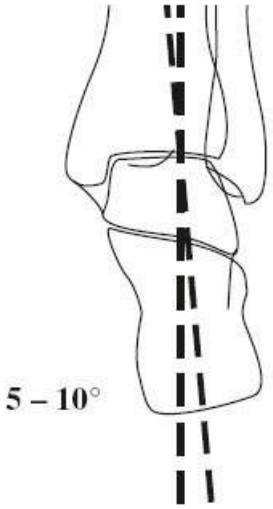
Intermetatarsal Angle
= amount that 1st + 2nd metatarsals diverge from each other



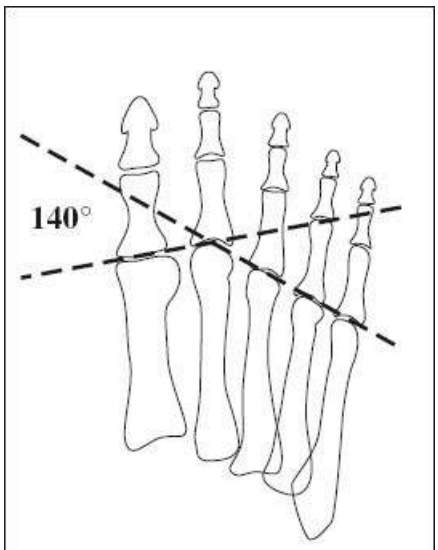
Talocalcaneal Angle on AP View

= KITE ANGLE

= the midtalar and midcalcaneal lines parallel the 1^{st} + 4^{th} metatarsals; angle is greater in infants



Heel Valgus
cannot be measured directly on radiographs but inferred from the talocalcaneal angle and estimated on coronal CT sections

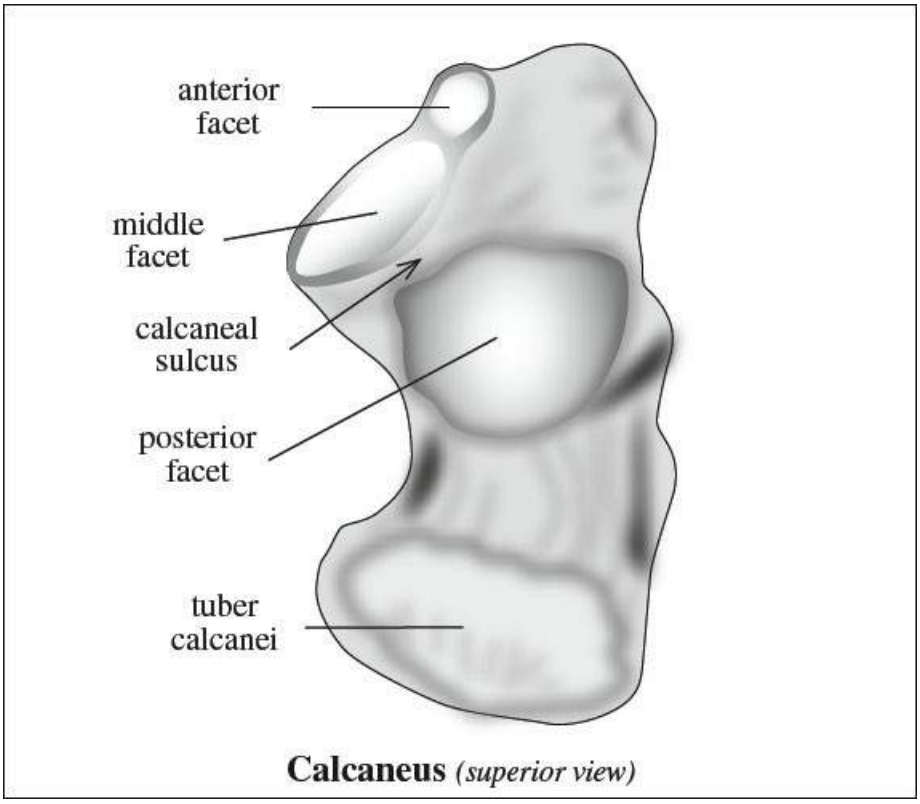


Angle of Metatarsal Heads
= obtuse angle formed by lines tangential to metatarsal heads

(2) Posterior tibial artery → artery of tarsal canal
(3) Peroneal a. → peroneal perforating branch / lateral tarsal artery → tarsal sinus artery

Calcaneus

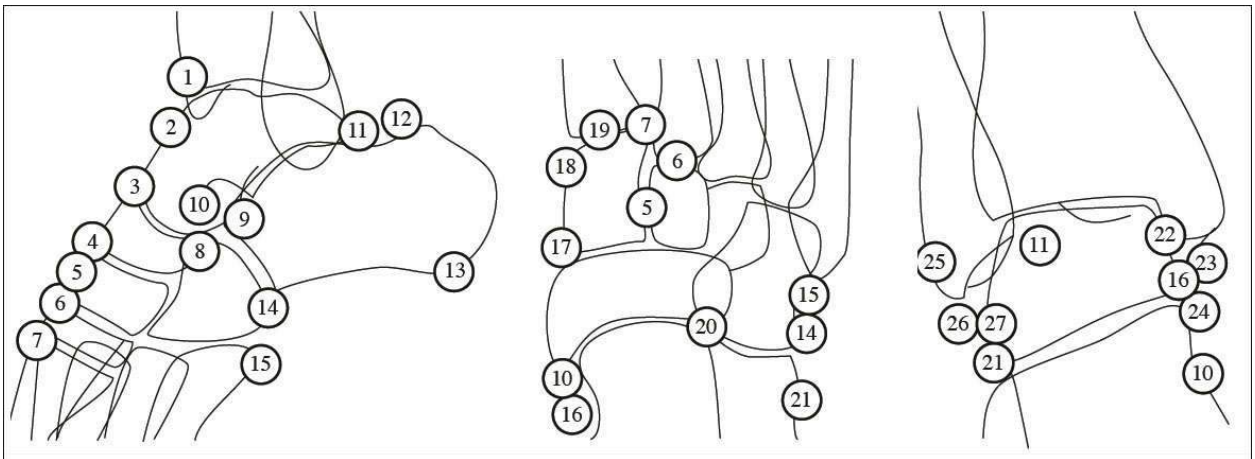
Articulations:
(a) superiorly – subtalar joint:
(1) Anterior talar facet
› supported by calcaneal beak
› articulates with anterior talar facet
(2) Middle talar facet
› articulates with middle talar facet
› supported by sustentaculum tali
calcaneal sulcus = groove between middle and posterior facet
sinus tarsi = canal between calcaneal sulcus and talus
(3) Posterior talar facet
thalamic portion = condensed cortical bone inferior to posterior facet
(b) anteriorly – calcaneocuboid joint
(4) triangular cuboidal facet
Lateral surface: flat + subcutaneous
› peroneal tubercle (centrally located)
» centrally = attachment of calcaneofibular ligament centrally
» anterosuperiorly = attachment of lateral talocalcaneal ligament



Calcaneus *(superior view)*

Medial surface:

› talar support by
  » interosseous lig. + medial talocalcaneal lig.
› *sustentaculum tali* at anterior aspect of medial surface
  » groove inferior to sustentaculum transmits tendon of flexor hallucis longus
› neurovascular bundle



Accessory Ossicles of the Foot

1	Os talotibiale	10	Os tibiale externum	19	Os cuneometatarsale I plantare
2	Os supratalare	11	Trigonum	20	Cuboides secundarium
3	Os supranaviculare	12	Os accessorium supracalcaneum	21	Os trochleare calcanei
4	Os infranaviculare	13	Os subcalcis	22	Sesamoid talus – int. malleolus
5	Os intercuneiforme	14	Os peroneum	23	Os subtibiale
6	Os cuneometatarsale II dorsale	15	Os vesalianum	24	Os sustentaculi
7	Os intermetatarsale	16	Talus accessorius	25	Os retinaculi
8	Secondary cuboid	17	Os cuneonaviculare mediale	26	Os subfibulare
9	Calcaneus secundarius	18	Sesamum tibiale anterius	27	Talus secundarius

BONE AND SOFT-TISSUE DISORDERS

ACHONDROGENESIS

= autosomal recessive lethal chondrodystrophy characterized by extreme micromelia, short trunk, large cranium

Triad: (1) severe short-limb dwarfism
(2) lack of vertebral calcification
(3) large head with normal / decreased calvarial ossification

Birth prevalence: 2.3÷100,000

Path: disorganization of cartilage

A. TYPE I = Parenti-Fraccaro disease
= defective enchondral + membranous ossification
√ complete lack of ossification of calvarium + spine + pelvis
√ absent sacrum + pubic bone
√ extremely short long bones without bowing: especially femur, radius, ulna
√ thin ribs with multiple fractures (frequent)

B. TYPE II = Langer-Saldino disease
= defective enchondral ossification only
√ good ossification of skull vault
√ nonossification of lower lumbar vertebrae + sacrum
√ short + stubby horizontal ribs without fractures

• often subcutaneous edema
√ irregular flared metaphyses: esp. humerus
√ short trunk with narrow chest + protruding abdomen
√ redundant soft tissues
√ polyhydramnios (common)
√ increase in HC÷AC ratio

Prognosis: lethal often in utero / within few hours or days after birth (← respiratory failure)

DDx: often confused with thanatophoric dwarfism

ACHONDROPLASIA

Heterozygous Achondroplasia

◊ Prototype of rhizomelic dwarfism!

= autosomal dominant / sporadic (80%) disease with quantitatively defective endochondral bone formation; related to advanced paternal age; epiphyseal maturation + ossification unaffected

Prevalence: 1÷26,000–66,000 births; M < F ◊ Most common of lethal bone dysplasias!

• normal intelligence + motor function
• neurologic defects
• classically circus dwarfs

@ Skull
- flat nasal bridge (= hypoplastic base of skull)
- macrocephaly + brachycephaly with enlarged bulging forehead (= nonprogressive hydrocephalus)
- relative prognathism

√ large calvarium with frontal bossing
√ depression of nasion
√ broad mandible
√ constricted basicranium + small foramen magnum:
  √ communicating hydrocephalus caused by obstruction of basal cisterns + aqueduct

Cx: apnea + sudden death ← compression of spinal cord and lower brain stem

@ Chest
√ anteroposterior narrowing of chest
√ short anteriorly flared concave ribs
√ squaring of inferior scapular margin

@ Spine
√ hypoplastic bullet- / wedge-shaped vertebra:
  √ rounded anterior beaking of vertebra in upper lumbar spine (DDx: Hurler disease)
  √ decreased vertebral height
√ scalloped posteriorly concave vertebral margin
√ scoliosis:
  √ thoracolumbar angular kyphosis (gibbus)
  √ exaggerated sacral lordosis
√ stenosis of lumbar spine:
  √ narrowing of interpedicular space ← laminar thickening
  √ ventrodorsal narrowing of spine ← short pedicles
  √ bulging / herniation of intervertebral disks
√ wide intervertebral foramina

@ Pelvis
- protuberant abdomen; prominent buttocks
- rolling gait from backward tilt of pelvis and hip joints

√ square flattened iliac bones = tombstone configuration
√ "champagne glass"-shaped pelvic inlet
√ lack of flaring of iliac wings
√ horizontal acetabula (= flat acetabular angle)
√ small sacrosciatic notch

@ Extremities
- trident hand = separation of 2nd + 3rd digit and inability to approximate 3rd + 4th finger; short stubby limbs + fingers
- limited range of motion of elbow

√ predominantly rhizomelic micromelia of long bones (ie, femur, humerus):
  √ "trumpet" appearance of long bones = shortening with disproportionate metaphyseal flaring (= actually normal width of metaphysis)
  √ short femoral necks
  √ limb bowing

√ "ball-in-socket" epiphysis = broad V-shaped distal femoral metaphysis in which epiphysis is incorporated
√ high position of fibular head (= disproportionately long fibula)
√ short ulna with thick proximal + slender distal end
√ brachydactyly (short tubular bones of hand + feet), especially short proximal + middle phalanges

OB-US (diagnosable > 21st–27th week GA):
√ shortening of proximal long bones: femur length < 99th percentile between 21 and 27 weeks MA
√ increased BPD, HC, HC÷AC ratio
√ decreased FL÷BPD ratio
√ normal mineralization, no fractures
√ normal thorax + normal cardiothoracic ratio
√ three-pronged (= trident) hand = 2nd + 3rd + 4th finger of similarly short length without completely approximating each other (= PATHOGNOMONIC)

Cx: (1) Hydrocephalus + syringomyelia (small foramen magnum)
(2) Recurrent ear infection (poorly developed facial bones)
(3) Neurologic complications (compression of spinal cord, lower brainstem, cauda equina, nerve roots): → apnea and sudden death
(4) Crowded dentition + malocclusion

Prognosis: long life
DDx: various mucopolysaccharidoses

Homozygous Achondroplasia

= hereditary autosomal dominant disease with severe features of achondroplasia (= disproportionate limb shortening, more marked proximally than distally)
Risk: marriage of two achondroplasts to each other
√ large cranium with short base + small face
√ flattened nose bridge
√ short ribs with flared ends
√ hypoplastic vertebral bodies
√ decreased interpedicular distance
√ short squared innominate bones
√ flattened acetabular roof
√ small sciatic notch
√ short limb bones with flared metaphyses
√ short, broad, widely spaced tubular bones of hand
Prognosis: often stillborn; lethal in neonatal period (← respiratory failure)
DDx: thanatophoric dysplasia

Pseudoachondroplasia

= part of osteochondroplasias
Prevalence: 4÷1,000,000
Etiology: mutation of genes encoding for cartilage oligomeric matrix protein (COMP) on

chromosome 19 (closely related to multiple epiphyseal dysplasia)

Age at presentation: 2–4 years

- normal facial features and intelligence
- mean adult height 118 (range, 82–130) cm
- disturbance of gait; joint laxity

@ Skull: normal

@ Spine
  - √ persistent oval-shaped vertebral bodies
  - √ anterior beaking, platyspondyly, scoliosis
  - √ odontoid dysplasia
  - √ disk space widening

@ Extremities
  - √ short long bones with flared metaphyses
  - √ small irregular flared epiphyses with delayed development
  - √ coxa vara = medial beaking of proximal femoral neck (CHARACTERISTIC)
  - √ genu valgum, genu varum, genu recurvatum
  - √ shortening + widening of phalanges and metacarpals + metatarsals

@ Pelvis
  - √ widened triradiate cartilage

Cx: premature osteoarthritis

DDx: (1) Achondroplasia (large head with prominent frontal region + depressed bridge of nose, normal epiphyses, trident hands)

(2) Multiple epiphyseal dysplasia (near normal pelvis)

(3) Spondyloepiphyseal dysplasia congenita (hip joints more affected + near normal extremities)

(4) Diastrophic dwarfism (joint contractures and scoliosis at birth / in early infancy)

(5) Metatropic dwarfism (dumbbell-shaped long bones + flattened vertebrae in infancy, less epiphyseal involvement)

ACROOSTEOLYSIS, FAMILIAL

dominant inheritance

Age: onset in 2nd decade; M÷F = 3÷1

- sensory changes in hands + feet
- destruction of nails; joint hypermobility
- swelling of plantar of foot with deep wide ulcer + ejection of bone fragments

@ Skull
  - √ wormian bones
  - √ craniosynostosis
  - √ basilar impression
  - √ protuberant occiput
  - √ resorption of alveolar processes + loss of teeth

@ Spine
  - √ spinal osteoporosis ± fracture

√ kyphoscoliosis + progressive decrease in height

DDx: Hyperparathyroidism

ACROMEGALY

Etiology: excess growth hormone ← eosinophilic adenoma / hyperplasia in anterior pituitary

• gigantism in children: advanced bone age + excessive height (DDx: Sotos syndrome of cerebral gigantism = large skull, mental retardation, cerebral atrophy, advanced bone age)

√ osseous enlargement (phalangeal tufts, vertebrae)

√ flared ends of long bone

√ cystic changes in carpals, femoral trochanters

√ osteoporosis

@ Hand

• spadelike hand

√ widening of terminal tufts

@ Skull

√ prognathism (= elongation of mandible) in few cases

√ sellar enlargement + erosion

√ enlargement of paranasal sinuses: large frontal sinuses (75%)

√ calvarial hyperostosis: especially inner table

√ enlarged occipital protuberance

@ Vertebrae

√ posterior scalloping in 30% ← pressure of enlarged soft tissue

√ anterior new bone

√ loss of disk space (weakening of cartilage)

@ Soft tissue

√ heel pad > 25 mm

@ Joints

√ premature osteoarthritis (commonly knees)

ACTINOMYCOSIS

= chronic suppurative infection characterized by formation of multiple abscesses, draining sinuses, abundant granulation tissue ← mucosal disruption + low tissue oxygen tension

Organism: Actinomyces israelii / naeslundii / odontolyticus / viscosus / meyeri / gerencseriae / eriksonii, gram-positive non–acid-fast anaerobic pleomorphic small branching filamentous bacterium with proteolytic activity, superficially resembling the morphology of a hyphal fungus (Gömöri methenamine silver stain-positive filaments); closely related to mycobacteria

◊ Actinomycotic infections are polymicrobial!

Pathogenesis: trauma / surgery / foreign body → disruption of mucosal barrier → bacterial entry into deep tissues → <u>fibrotic lesion</u> spreading beyond fascial planes → <u>abscess formation</u> centrally → <u>draining sinus tracts</u> extending from abscess to skin / adjacent organs

Spread:

(a) contiguous: production of proteolytic enzymes allow crossing of normal anatomic barriers

(b) hematogenous

No lymphatic spread ← size of organism!

Histo: (a) mycelial form in tissue as yellow tangled filaments of actinomyces = diagnostic sulfur granules seen as round / oval horseshoe-shaped basophilic masses with a radiating fringe of eosinophilic clubs

(b) rod-shaped bacterial form = opportunistic pathogens that normally inhabit oropharynx (dental caries, gingival margins, tonsillar crypts) + GI tract + female genital tract

At risk: very poor dental hygiene, immunosuppressed patient, prolonged use of IUD, bisphosphonate therapy

Location: mandibulofacial > intestinal > lung

Clinical types:

(1) Mandibulo- / cervicofacial actinomycosis (50–65%)

Origin: odontogenic

At risk: poor dental hygiene, recent dental extraction, dental caries, oromaxillofacial trauma, chronic tonsillitis, otitis, mastoiditis, osteonecrosis from irradiation / bisphosphonate therapy

• draining cutaneous sinuses

• "sulfur granules" in sputum / exudate = colonies of organisms arranged in circular fashion = mycelial clumps with thin hyphae 1–2 mm in diameter

√ destruction of mandible (most frequent bone involved) around tooth socket = osteomyelitis of mandible

Site: angle of jaw, submandibular region, cheek, submental space, masticator space, temporomandibular joint

√ no new-bone formation

√ spread into soft tissues at angle of jaw + into neck ignoring normal fascial planes

√ no / few reactive regional lymph nodes

– acute form:

√ soft-tissue swelling / painful pyogenic abscess / mass

– subacute to chronic form:

√ painless indurated mass ± spread to skin often accompanied by draining sinus tracts

(2) Pleuropulmonary / thoracic actinomycosis (15–30%)

Cause: (a) aspiration of infected material from oropharynx

(b) hematogenous spread

(c) direct extension into mediastinum from cervicofacial infection (extremely rare)

(d) transdiaphragmatic / retroperitoneal spread

Predisposed: alcoholics

Histo: masses of PMN leukocytes containing round actinomycotic / sulfur granules surrounded by a rim of granulation tissue

@ Lung

• draining chest wall sinuses ← spread through fascial planes

Predisposed: areas of parenchymal destruction and bronchiectasis ← prior TB / other organisms (= tendency of actinomyces for invasion of devitalized tissue)

√ enhancing extensive transfissural chronic segmental airspace consolidation:
√ hypoattenuating areas + peripheral enhancement (= lung necrosis)
√ often adjacent pleural thickening
Site: usually unilateral + lower lobe predominance
√ multiple small cavitary lesions with ringlike enhancement (= abscesses)
√ fibrotic pleuritis
√ chronic pleural effusion / empyema (in > 50%)
√ rarely acute airspace pneumonia ← postobstructive endobronchial actinomycosis
DDx: carcinoma, TB, bacterial / fungal pneumonia

@ Vertebra + ribs
√ destruction of vertebra with preservation of disk + small paravertebral abscess without calcification (DDx to tuberculosis: disk destroyed, large abscess with calcium)
√ thickening of cervical vertebrae around margins
√ destruction / thickening of ribs

(3) Abdominopelvic / ileocecal / abdominal actinomycosis (20%)
Cause: appendicitis, colonic diverticulitis; penetrating trauma, gut surgery; prolonged IUD use > 2 years (25% of IUDs become eventually colonized with serious infections in 2–4%)
Location: initially localized to cecum / appendix
• fever, leukocytosis, mild anemia
• weight loss, nausea, vomiting, lower abdominal pain
• chronic sinus in groin, vaginal discharge
• yellow / brown sulfur granules on cervical Papanicolaou smear
√ concentric bowel wall thickening:
√ adjacent cystic / solid mass
√ surrounding invasive soft-tissue strands
√ strong enhancement of solid portions ← extensive dense fibrosis = hallmark of actinomycosis
√ fold thickening + ulcerations (resembling Crohn disease)
√ rupture of abdominal viscus (usually appendix)
√ fistula formation
√ rarely regional lymphadenopathy
√ usually no / minimal ascites
Cx: (1) abscess in liver (15%), retroperitoneum, psoas muscle, pelvis, tuboovarian abscess (containing yellow "sulfur granules" = 1–2-mm colony of gram-positive bacilli)
(2) hydronephrosis ← compression of ureter by pelvic abscess

(4) Mixed organs (10%)
@ Tubular bones of hands
√ destructive lesion of mottled permeating type
√ cartilage destruction + subarticular erosive defects in joints (simulating TB)
@ CNS (2–3%), skin, pericardium

Dx: anaerobic culture; species-specific antibodies

Rx: high doses of penicillin G + surgical débridement
DDx: malignancy, chronic granulomatous disease (TB, fungal infection)

ADAMANTINOMA

= (MALIGNANT) ANGIOBLASTOMA
= rare locally aggressive / low-grade malignancy of bone
Risk factors for malignant course:
male sex, young age at presentation, short duration of symptoms, pain at initial presentation, local recurrence
Histo: zonal architecture of neoplastic epithelial cells (reactive to cytokeratins) concentrated centrally in osteofibrous stroma that forms peripherally columnar cells in a palisade pattern; prominent vascularity; resembles ameloblastoma of the jaw
Age: 25–50 (range, 3–74) years, commonest in 2 nd –3 rd decade
Prevalence: < 0.5% of malignant bone tumors
• frequently history of trauma; local swelling ± pain
Location: middle ⅓ of tibia (90%), fibula, ulna, carpals, metacarpals, humerus, shaft of femur
Size: average length of 10 cm
√ eccentric round osteolytic lesion with sclerotic margin
√ multiple additional foci (= multicentricity) in continuity with major lesion (CHARACTERISTIC) in 27%
√ longitudinally oriented along anterior tibial diaphysis
√ narrow zone of transition, may show mottled density
√ slight bone expansion (frequent)
√ cortical breakthrough in 15%
√ synchronous fibular involvement in 5–10%
MR:
√ intermediate signal intensity relative to muscle on T1WI
√ intensity similar to fat on T2WI
√ marked homogeneous enhancement
Prognosis: tendency to recur after local excision (19%); after several recurrences pulmonary metastases may develop; 13% mortality rate
DDx: fibrous dysplasia (in child < 10 years of age, painless enlargement of tibia, anterior bowing, pathologic fracture, eccentric bubbly cortical lucency and expansion with spontaneous regression)

AINHUM DISEASE

= DACTYLOLYSIS SPONTANEA
[ainhum, Brazilian tribal language = fissure, saw, sword]
Etiology: unknown
Histo: hyperkeratotic epidermis with fibrotic thickening of collagen bundles below; chronic lymphocytic inflammatory reaction may be present; arterial walls may be thickened with narrowed vessel lumina
Frequency: up to 2%
Age: usually in males in 4th + 5th decades; Blacks (West Africa) + their American descendants;

M > F

- deep soft-tissue groove forming on medial aspect of plantar surface of proximal phalanx with edema distally
- painful ulceration may develop

Location: mostly 5th / 4th toe (rarely finger); near interphalangeal joint; mostly bilateral

√ sharply demarcated progressive bone resorption of distal / middle phalanx with tapering of proximal phalanx to complete autoamputation (after an average of 5 years)

√ osteoporosis

Rx: early surgical resection of groove with Z-plasty

DDx: (1) Neuropathic disorders (diabetes, leprosy, syphilis)
(2) Trauma (burns, frostbite)
(3) Acroosteolysis from inflammatory arthritis, infection, polyvinyl chloride exposure
(4) Congenitally constricting bands in amniotic band syndrome

AMYLOIDOSIS

= extracellular deposition of a chemically diverse group of protein polysaccharides in body tissues (abnormal folding + assembly of β2-microglobulin); tends to form around capillaries + endothelial cells of larger blood vessels causing ultimately vascular obliteration with infarction

β_2-microglobulin = low-molecular-weight serum protein not filtered by standard dialysis membranes

Incidence: 6–10÷100,000 annually in USA + western Europe

Path: stains with Congo red

At risk: patients on long-term hemodialysis

- bone pain (eg, shoulder pain)
- periarticular rubbery soft-tissue swelling + stiffness (shoulders, hips, fingers):
  - carpal-tunnel syndrome (commonly bilateral)
- Bence-Jones protein (without myeloma)

Amyloid Arthropathy

= synovial-articular pattern of amyloidosis

Associated with: chronic hemodialysis, plasma cell dyscrasia, rheumatoid arthritis, familial Mediterranean fever, chronic osteomyelitis

Location: cervical spine, hip, shoulder, elbow, knee, wrist; bilateral

√ juxtaarticular soft-tissue masses (amyloid deposited in synovium, joint capsule, tendons, ligaments) ± extrinsic osseous erosion

√ mild periarticular osteopenia

√ subchondral cysts + well-defined sclerotic margin

√ joint effusion

√ joint space preserved until late in course of disease

√ subluxation of proximal humerus + femoral neck

MR:

√ extensive deposition of abnormal soft tissue of low to intermediate SI on T1WI + T2WI covering synovial membrane, filling subchondral defects, extending into periarticular

tissue
√ low SI on T1WI + T2WI subjacent to vertebral endplates in lower cervical > thoracic / lumbar spine
√ joint effusion
DDx: inflammatory arthritis, PVNS

Diffuse Amyloid Marrow Deposition

√ generalized osteoporosis
√ coarse trabecular pattern (DDx: sarcoidosis)
√ pathologic collapse of vertebral body may occur

Amyloidoma

= localized destructive lesion of amyloidosis (rarest form)
Location: appendicular > axial skeleton
√ focal medullary lytic lesion with endosteal scalloping (± secondary invasion + erosion of articular bone)
Cx: pathologic fracture

ANEURYSMAL BONE CYST

= expansile pathologically benign lytic lesion of bone containing thin-walled cystic cavities filled with chronic blood products; name derived from roentgen appearance
Incidence: 1.4–2.3% of primary bone tumors
Etiology:
(a) primary ABC (65–99%):
› local circulatory disturbance ← trauma
› improper repair of traumatic subperiosteal hemorrhage
(b) secondary ABC (29–35%) hemorrhage into a preexisting bone lesion → venous obstruction / arteriovenous fistula:
› common: giant cell tumor (19–39%), osteoblastoma, angioma, chondroblastoma
› uncommon: fibrous dysplasia, fibrous histiocytoma, chondromyxoid fibroma, xanthoma (= nonossifying fibroma), eosinophilic granuloma, telangiectatic osteosarcoma, metastatic carcinoma, solitary bone cyst
Histo: lack of anaplasia
(a) "intraosseous arteriovenous malformation" with cystic honeycombed spaces filled with blood separated by spindle cell stroma + osteoclast-like giant cells and osteoid / bone production; mineralized chondroidlike material in 1/3; areas of free hemorrhage
(b) solid variant of ABC in 5–7%: proliferation of spindle cells
Types:
1. INTRAOSSEOUS ABC
= primary cystic / telangiectatic tumor of giant cell family, originating in bone marrow cavity, slow expansion of cortex; rarely related to history of trauma
2. EXTRAOSSEOUS ABC
= posttraumatic hemorrhagic cyst; originating on surface of bones, erosion through cortex into marrow

Peak age: peak age 16 (range, 10–30) years; in 75% < 20 years; F > M
- pain of relatively acute onset with rapid increase of severity over 6–12 weeks; ± history of trauma
- neurologic signs (radiculopathy to quadriplegia) if in spine

Location:
- @ spine (3–20%): thoracic (34%), lumbar (31%), cervical spine (22%), sacrum (13%); involvement of posterior elements with extension into vertebral body (75%); may involve two contiguous vertebrae (25%) / intervertebral disk / ribs / paravertebral soft tissues
- @ long bones: eccentric in metaphysis of femur, tibia, humerus, fibula
- @ pelvis

√ purely lytic eccentric radiolucency
√ aggressive expansile ballooning lesion of "soap-bubble" pattern + thin internal septations + trabeculations
√ rapid progression within 6 weeks to 3 months
√ sclerotic inner portion
√ almost invisible thin cortex (CT shows integrity)
√ tumor respects epiphyseal plate
√ no periosteal reaction (except when fractured)

CT:
- √ "blood-filled sponge" = fluid-fluid / hematocrit levels ← blood sedimentation (in 10–35%)
- √ ± mineralized chondroidlike material when abundant

MR:
- √ multiple cysts of different SI representing different stages of blood by-products:
  - √ heterogeneous fluid-fluid levels within loculations ← hemorrhage with sedimentation
  - √ ↑ signal intensity on T1WI ← methemoglobin
- √ low-SI rim ← intact thickened periosteal membrane
- √ heterogeneous enhancement:
  - √ smooth enhancement of internal septa

NUC:
- √ "doughnut" sign = moderate to intense radiotracer accumulation at lesion periphery (64%)

Angio:
- √ hypervascularity in lesion periphery (in 75%)

Prognosis: 20–30% recurrence rate

Rx: preoperative embolotherapy; complete resection; radiation therapy (subsequent sarcoma possible)

Cx: (1) Pathologic fracture (frequent)
(2) Extradural block with paraplegia

DDx: (1) Giant cell tumor (particularly in spine)
(2) Hemorrhagic cyst (end of bone / epiphysis, not expansile)
(3) Enchondroma
(4) Metastasis (renal cell + thyroid carcinoma)
(5) Plasmacytoma
(6) Chondro- and fibrosarcoma

(7) Fibrous dysplasia
(8) Hemophilic pseudotumor
(9) Hydatid cyst

ANGIOMATOSIS

= diffuse infiltration of bone / soft tissue by hemangiomatous / lymphangiomatous lesions
Age: first 3 decades of life
May be associated with:
chylothorax, chyloperitoneum, lymphedema, hepatosplenomegaly, cystic hygroma

A. OSSEOUS ANGIOMATOSIS (30–40%)
- indolent course

Location: femur > ribs > spine > pelvis > humerus > scapula > other long bones > clavicle
√ osteolysis with honeycomb / latticework ("hole-within-hole") appearance
√ may occur on both sides of joint
DDx: solitary osseous hemangioma

B. CYSTIC ANGIOMATOSIS
= extensive involvement of bone
Histo: endothelium-lined cysts in bone
Peak age: 10–15 years (range, 3 months to 55 years)
Location: long bones, skull, flat bones
√ size of 1–2 mm to several cm
√ multiple osteolytic metaphyseal lesions with fine sclerotic margins + relative sparing of medullary cavity
√ may show overgrowth of long bone
√ endosteal thickening
√ sometimes associated with soft-tissue mass ± phleboliths
√ chylous pleural effusion suggests fatal prognosis
DDx: (other polyostotic diseases like) histiocytosis X, fibrous dysplasia, metastases, Gaucher disease, congenital fibromatosis, Maffucci syndrome, neurofibromatosis, enchondromatosis

C. SOFT-TISSUE ANGIOMATOSIS (60–70%)
= VISCERAL ANGIOMATOSIS
- poor prognosis

D. ANGIOMATOUS SYNDROMES
Maffucci, Osler-Weber-Rendu, Klippel-Trénaunay-Weber, Kasabach-Merritt, Gorham

ANGIOSARCOMA

= aggressive vascular malignancy, frequently with local recurrence + distant metastases; M÷F = 2÷1
Origin: endothelial + mesenchymal cells
Histo: vascular channels surrounded by hemangiomatous / lymphomatous cellular elements with high degree of anaplasia
Associated with: **Stewart-Treves syndrome** = angiosarcoma with chronic lymphedema developing in postmastectomy patients

Location: skin (33%); soft tissue (24%); bone (6%): tibia (23%), femur (18%), humerus (13%), pelvis (7%)
◊ Most commonly in right atrium > retroperitoneum (IVC)
√ heterogeneously enhancing mass expanding involved vessel
DDx: hemangioendothelioma, hemangiopericytoma

Soft-Tissue Angiosarcoma

Risk factors: chronic lymphedema, previous radiation therapy, foreign bodies, immunosuppression
Associated with: NF1, Klippel-Trénaunay-Weber syndrome, Maffucci syndrome
Age: any age; peak incidence in 7th decade
MR:
√ intermediate signal intensity on T1WI
√ areas of high SI on T1WI ← hemorrhage
√ high SI on T2WI (← tumor necrosis + methemoglobin)
√ aggressive infiltration of adjacent tissue
√ intratumoral low SI on all pulse sequences ← high flow
√ intratumoral high SI on T2WI ← low flow
√ contrast enhancement ± central areas of necrosis

ANTERIOR TIBIAL BOWING

= WEISMANN-NETTER SYNDROME
[Robert-Julius Weismann-Netter (1894–1980)]
= congenital painless nonprogressive bilateral anterior leg bowing
Age: beginning in early childhood
• may be accompanied by mental retardation, goiter, anemia
√ anterior bowing of tibia + fibula, bilaterally, symmetrically at middiaphysis
√ thickening of posterior tibial + fibular cortices
√ minor radioulnar bowing
√ kyphoscoliosis
√ extensive dural calcification
DDx: Luetic saber shin (bowing at lower end of tibia + anterior cortical thickening)

APERT SYNDROME

= ACROCEPHALOSYNDACTYLY TYPE I
[Eugène Charles Apert (1868–1940), médecin des hôpitaux Hôtel-Dieu and at the Hôpital des Enfants-Malades]
Frequency: 5.5÷1,000,000 neonates
Etiology: autosomal dominant with incomplete penetrance; sporadic (in majority)
Associated with CNS anomalies:
megalocephaly, gyral abnormalities, hypoplastic white matter, heterotopic gray matter, frontal encephalocele, corpus callosal agenesis, Kleeblattschädel, cleft palate, ventriculomegaly (? related to skull base hypoplasia, rarely progressive)
• IQ varies depending on CNS anomalies (in 50% normal)

- otitis media (high prevalence)
- bifid uvula
- conductive hearing loss (common ← external + middle ear malformations)

@ Skull
- downturned mouth

√ brachycephalic skull (← coronal craniosynostosis) + flat occiput

√ widened metopic + sagittal sutures extending from glabella to posterior fontanel (closing between 2–4 years)

√ hypoplastic / retruded midface:

√ hypertelorism

√ shallow orbits with proptosis

√ underdeveloped paranasal sinuses

√ underdeveloped maxilla with prognathism

√ high pointed arch of palate

√ prominent vertical crest in middle of forehead (← increased intracranial pressure)

√ V-shaped anterior fossa ← elevation of lateral margins of lesser sphenoid

√ ± enlargement of sella

√ stylohyoid ligament calcification (38–88%)

√ cervical spine fusion (in up to 71%), commonly of 5th and 6th vertebrae

√ choanal stenosis

@ Hand & feet

√ severe symmetric syndactyly = fusion of distal portions of phalanges, metacarpals / carpals (most often of 2nd, 3rd + 4th digit)

√ absence of middle phalanges

√ missing / supernumerary carpal / tarsal bones

√ pseudarthroses

@ GU (10%)
- cryptorchidism

√ hydronephrosis

√ polycystic kidneys (rare)

√ bicornuate uterus (rare)

ARTERIOVENOUS FISTULA OF BONE

Etiology: (a) acquired (usually gunshot wound)
(b) congenital AVF

Location: lower extremity most frequent

√ soft-tissue mass

√ presence of large vessels

√ phleboliths (DDx: long-standing varicosity)

√ accelerated bone growth

√ cortical osteolytic defect (= large-vessel pathway into medulla)

√ increased bone density

ARTHROGRYPOSIS

= ARTHROGRYPOSIS MULTIPLEX CONGENITA
= nonprogressive congenital syndromic complex characterized by poorly developed + contracted muscles, deformed joints with thickened periarticular capsule and intact sensory system

Pathophysiology:
congenital / acquired defect of motor unit (anterior horn cells, nerve roots, peripheral nerves, motor end plates, muscle) early in fetal life with immobilization of joints at various stages in their development

Cause: ? neurotropic agents, toxic chemicals, hard drugs, hyperthermia, neuromuscular blocking agents, mytotic abnormalities, mechanical immobilization

Frequency: 0.03% of newborn infants; 5% risk of recurrence in sibling

Path: diminution in size of muscle fibers + fat deposits in fibrous tissue

Associated with:
(1) neurogenic disorders (90%)
(2) myopathic disorders
(3) skeletal dysplasias
(4) intrauterine limitation of movement (myomata, amniotic band, twin, oligohydramnios)
(5) connective tissue disorders

Distribution: all extremities (46%), lower extremities only (43%), upper extremities only (11%); peripheral joints >> proximal joints; symmetrical

• clubfoot; claw hand; congenital dislocation of hip
• diminished muscle mass; skin webs
√ flexion + extension contractures
√ osteopenia ± pathologic fractures
√ congenital dislocation of hip
√ carpal coalition
√ vertical talus
√ calcaneal valgus deformity

ASPHYXIATING THORACIC DYSPLASIA

= JEUNE DISEASE
= autosomal recessive dysplasia characterized by short narrow thorax and short limbs

Prevalence: 1÷100,000 to 1÷130,000 live births

Associated with: renal anomalies (hydroureter), PDA

• respiratory distress ← reduced thoracic mobility (abdominal breathing) + frequent pulmonary infections
• progressive renal failure + hypertension

@ Chest
  √ markedly narrow + elongated bell-shaped chest:
    √ chest diameter significantly decreased compared with that of the abdomen
    √ short horizontal ribs + flared irregular bulbous costochondral junction
  √ normal size of heart leaving little room for lungs
  √ "handle-bar clavicles" = horizontal clavicles at level of C6
@ Pelvis

√ trident morphology of acetabular roof ← retardation of ossification of triradiate cartilage
√ small iliac wings flared + shortened in cephalocaudal diameter ("wineglass" pelvis)
√ narrow sacrosciatic notches
√ short ischial + pubic bones
√ reduced acetabular angle + acetabular spurs
√ premature ossification of capital femoral epiphysis

@ Extremities
√ metaphyseal irregularity
@ thigh & arm
√ rhizomelic brachymelia (humerus, femur) = long bones shorter + wider than normal
√ proximal humeral + femoral epiphyses ossified at birth (frequently)
@ hand & foot
√ postaxial hexadactyly (occasionally)
√ shortening of distal phalanges
√ cone-shaped epiphyses

@ Visceral involvement
√ nephronophthisis (= medullary cystic renal disease) = enlarged kidneys with linear streaking on nephrogram → progressive renal failure (in adulthood)
√ pancreatic cysts
√ intrahepatic bile duct dilatation
√ intestinal malrotation
√ situs anomalies

OB-US:
√ proportionate shortening of long bones
√ small thorax with decreased circumference
√ increased cardiothoracic ratio
√ occasionally polydactyly
√ polyhydramnios

Prognosis: neonatal death in 80% (respiratory failure + infections)
DDx: Ellis-van Creveld syndrome

AVASCULAR NECROSIS

= AVN = OSTEONECROSIS = ASEPTIC NECROSIS
= consequence of reduced / completely interrupted blood supply to bone with death of cellular elements

Terminology (now often used interchangeably):
(1) Osteonecrosis = ischemic bone death ← sepsis
(2) Ischemic necrosis / avascular necrosis / aseptic necrosis = necrosis of epiphyseal + subarticular bone
(3) Bone infarction = necrosis of metaphyseal + diaphyseal bone

Cause: [common causes are underlined]
◊ NO predisposing factors in 25%!
A. Trauma / thermal injury → interruption of arteries
√ typically unilateral

@ Femoral head:
1. Femoral neck fracture (60–75%)
2. Dislocation of hip joint (25%)
3. Slipped capital femoral epiphysis (15–40%)

@ Carpal scaphoid:
4–6 months after fracture (in 10–15%), in 30–40% of nonunions of scaphoid fracture
Site: proximal fragment (most common)

@ humeral head (infrequent)
@ talus (after talar neck fracture)

B. Nontraumatic
√ bilateral (in 70–80%)
(a) Occlusion / embolization of artery
1. Thrombus: thromboembolic disease, sickle-cell disease (SS + SC hemoglobin), polycythemia rubra vera, pheochromocytoma (microscopic thrombotic disease)
2. Nitrogen bubbles: Caisson disease, astronauts
3. Fat: pancreatitis (intramedullary fat necrosis from circulating lipase), alcoholism
4. Thromboembolism, arteriosclerosis
5. Pregnancy

(b) Vessel wall disease:
1. Collagen-vascular disease: SLE, rheumatoid arthritis, polyarteritis nodosa, sarcoidosis
2. Infectious vasculitis
3. Arteriosclerosis

(c) Vascular compression by abnormal deposition of:
1. Fat: corticosteroid therapy (eg, renal transplant, Cushing disease), diabetes
2. Blood: hemophilia, trauma (fractures, dislocations)
3. Inflammatory cells: osteomyelitis, infection, Langerhans cell histiocytosis
4. Tumor cells: leukemia, lymphoma
5. Edema: radiation therapy, hypothyroidism, frostbite
6. Substances: Gaucher disease (vascular compression by lipid-filled histiocytes), gout

(d) Direct cell toxicity
1. Drug therapy: immunosuppressives, cytotoxics, biphosphonates
2. Radiation therapy

(e) Idiopathic
1. Spontaneous osteonecrosis of knee
2. Legg-Calvé-Perthes disease
3. Freiberg disease (repetitive microtrauma)
4. Hypopituitarism

mnemonic: PLASTIC RAGS x 2
Pancreatitis, **P**regnancy
Legg-Perthes disease, **L**upus erythematosus
Alcoholism, **A**therosclerosis
Steroids, **S**ickle-cell disease
Trauma, **T**hermal injury

Idiopathic (Legg-Perthes disease), **I**nfection
Caisson disease, **C**ollagen disease (SLE)
Rheumatoid arthritis, **R**adiation treatment
Alcoholism, **A**myloid
Gaucher disease, **G**out
Sickle cell disease, **S**pontaneous osteonecrosis of knee

mnemonic: GIVE INFARCTS
Gaucher disease
Idiopathic (Legg-Calvé-Perthes, Köhler, Chandler)
Vasculitis (SLE, polyarteritis nodosa, rheumatoid arthritis)
Environmental (frostbite, thermal injury)
Irradiation
Neoplasia (-associated coagulopathy)
Fat (prolonged corticosteroid use increases marrow)
Alcoholism
Renal failure + dialysis
Caisson disease
Trauma (femoral neck fracture, hip dislocation)
Sickle cell disease

Path:

(a) Stage of cell death: cellular ischemia / anoxia → death of hematopoietic cells (in 6–12 hours) > adipocytes > bone cells = osteoclasts and osteoblasts + osteocytes (in 12–48 hours)
  ◊ Chondrocytes are adapted to relatively low oxygen tension and do not become devitalized!

(b) Stage of ↑ vascularity / reparative phase (osteoclasis): trabecular resorption ← inflammatory fibrovascular infiltration + proliferation ← hyperemia mixed with areas of relatively increased trabecular density ← osteonecrosis

(c) Stage of substitution / reactive phase (= osteogenesis): mesenchymal cells differentiate to osteoblasts on surface of dead trabeculae synthesizing new bone layer → trabecular thickening + osteoclastic resorption of devitalized bone (= creeping zone of substitution)
  @ metadiaphyseal osteonecrosis: rim of sclerosis is frequently of undulating / serpentine morphology
  @ epiphyseal osteonecrosis: increased bone resorption at junction of reactive zone and subchondral bone plate + weight-bearing → early fracture of overlying cartilage

Age: 4th–6th decades of life; M÷F = 4–8÷1

- asymptomatic (majority of patients)
- reduced range of motion; pain ← increase in intramedullary pressure ← medullary bone marrow edema

Location: femoral head (most common), humeral head, femoral condyles, proximal tibia, distal femoral metadiaphysis, distal tibial metadiaphysis, scaphoid, lunate, talus

Radiography (positive only after several months of symptoms):
  √ preservation of joint space (DDx: arthritis)
  √ patchy areas of lucency and sclerosis:
    √ dense osteonecrotic bone ← lack of resorption relative to healthy osteopenic bone + new

bone laid down over necrotic trabeculae:
- √ sclerosis of serpentine / undulating morphology characteristically about lesion rim (more common in metadiaphyseal lesions)
- √ early areas of articular collapse (in epiphyseal osteonecrosis) typically at junction of serpentine sclerotic rim and articular surface

√ radiolucent rim around area of osteonecrosis ← absorption around necrotic bone:
- √ "crescent" sign = crescentic subchondral lucency = subchondral structural collapse of necrotic segment parallel to articular surface in weight-bearing portion with separation from overlying cartilage and attached subchondral bone plate (in epiphyseal osteonecrosis)

√ later findings:
- √ flattening of articular surface ← articular fragmentation + progressive articular collapse, secondary osteoarthritis
- √ increased bone density ← compression of osseous trabeculae ← microfracture of nonviable bone + calcification of dendritic marrow + creeping substitution = deposition of new bone

CT (less sensitive than MRI / NUC):

◊ May be utilized for staging of known disease

√ staging upgrades in 30% compared with plain films

√ serpentine / undulating sclerotic margin (late stage)

√ useful for detecting location of articular collapse + extent in epiphyseal osteonecrosis!

NUC (80–85% sensitivity in early stages):

◊ Bone marrow imaging (with radiocolloid) more sensitive than bone imaging (with diphosphonates)

◊ More sensitive than plain films in early AVN ← evidence of ischemia seen as much as 1 year earlier

◊ Less sensitive than MR except for SPECT

Technique: imaging improved with double counts, pinhole collimation

√ diffuse increased radionuclide activity in epiphyseal involvement with articular collapse + 2ndary osteoarthritis

√ very early: cold = photopenic defect on bone scan (blood flow, blood pool, static phase) + bone marrow scan ← interrupted blood supply

√ late: "doughnut" sign = cold spot surrounded by increased radionuclide uptake ← chronic reparative processes:
- (a) capillary revascularization + new-bone synthesis
- (b) degenerative osteoarthritis

MR:

MRI Classification of Aseptic Necrosis
(Mitchell Classification)

Stage	*T1*	*T2*	*Analogous to*
A	high	intermediate	fat
B	high	high	subacute blood
C	low	high	fluid/edema
D	low	low	fibrous tissue

Cx: Malignant transformation to sarcoma (exceedingly rare, exclusive to metaphysis / metadiaphysis): malignant fibrous histiocytoma (69%), osteosarcoma (17%), angiosarcoma (9%)

Cortical Infarction

◊ Requires compromise of
(a) nutrient artery and (b) periosteal vessels!

Age: particularly in childhood where periosteum is easily elevated by edema

√ avascular necrosis = osteonecrosis

√ osteochondrosis dissecans

Cx: (1) Growth disturbances
√ cupped / triangular / coned epiphyses
√ "H-shaped" vertebral bodies
(2) Fibrosarcoma (most common), malignant fibrous histiocytoma, benign cysts
(3) Osteoarthritis

Medullary Infarction

◊ Nutrient artery is the sole blood supply for diaphysis!

Location: distal femur, proximal tibia, iliac wing, rib, humerus

(a) Acute phase:
√ NO radiographic changes without cortical involvement
√ area of rarefaction
√ infarcted area T1 hypointense + T2 hyperintense
√ bone marrow scan: diminished uptake in medullary RES for long period of time
√ bone scan: photon-deficient lesion within 24–48 hours; increased uptake after collateral circulation established

(b) Healing phase (complete healing / fibrosis / calcification):
√ demarcation by zone of serpiginous / linear calcification + ossification parallel to cortex
√ dense bone indicating revascularization
√ focal lesion with fatty marrow SI centrally + surrounding hypointense rim (= reactive / sclerotic bone)

Avascular Necrosis / Adult Osteonecrosis of Hip

Incidence: 10,000–20,000 new cases annually in USA

◊ Involvement of one hip increases risk to contralateral hip to 70%!

Age: 20–50 years

Zonal anatomy (from articular surface to center of head):
› zone of cell death
› reactive interface / creeping zone of substitution
› zone of reinforcing trabecular bone
› zone of reactive marrow
› zone of normal marrow

Classification (Steinberg):

Stage 0 = normal
Stage I = normal / barely detectable trabecular mottling; abnormal bone scan / MRI
Stage IIA = focal sclerosis + osteopenia
Stage IIB = distinct sclerosis + osteoporosis + early "crescent" sign
Stage IIIA = subchondral undermining ("crescent" sign) + cyst formation
Stage IIIB = mild alteration in femoral head contour / subchondral fracture + normal joint space
Stage IV = marked collapse of femoral head + significant acetabular involvement
Stage V = joint space narrowing + acetabular degenerative changes

- hip / groin / thigh / knee pain; limited range of motion

MR (90–100% sensitive, 85% specific for symptomatic disease):
Prevalence of clinically occult disease: 6%

◊ MR imaging changes reflect the death of marrow fat cells (not death of osteocytes with empty lacunae)!
◊ Sagittal images particularly useful!

⇒ EARLY AVN:

The early standard MRI may be normal ← lack of edema / hemorrhage / bone marrow response while Gd-enhancement shows devascularized areas

√ decreased Gd-enhancement on short-inversion-recovery (STIR) images (very early)
√ bone marrow edema: extensive even when area of infarction is small (early)
√ low-SI band with sharp inner interface + blurred outer margin on T1WI within 12–48 hours (= mesenchymal + fibrous repair tissue, amorphous cellular debris, thickened trabecular bone) seen as
(a) band extending to subchondral bone plate
(b) complete ring (less frequent)
√ "double-line" sign on T2WI (in 80%) [MORE SPECIFIC] = juxtaposition of inner hyperintense band (vascularized granulation tissue) + outer hypointense band (chemical shift artifact / fibrosis and sclerosis)

⇒ ADVANCED AVN:
√ "pseudohomogeneous edema pattern" = large inhomogeneous areas of mostly decreased SI on T1WI
√ hypo- to hyperintense lesion on T2WI
√ contrast-enhancement of interface + surrounding marrow + within lesion

⇒ SUBCHONDRAL FRACTURE:
√ predilection for anterosuperior portion of femoral head (SAG images!)
√ cleft of low SI running parallel to the subchondral bone plate within areas of fatlike SI on T1WI
√ hyperintense band (= fracture cleft filled with articular fluid / edema) within the intermediate- or low-signal-intensity of necrotic marrow on T2WI
√ lack of enhancement within + around fracture cleft

⇒ COLLAPSE OF ARTICULAR SURFACE:

√ focal depression of subchondral bone with low SI on T2WI = fibrotic changes in infarcted bone marrow
√ loss of normal spherical contour of bone
√ incongruity of articular surfaces
Predisposition: increased thickness of reparative zone, increasing volume of joint effusion, presence of prominent surrounding edema, patient age > 40 years, body mass index ≥ 24 kg/m^2

Cx: early osteoarthritis through collapse of femoral head + joint incongruity in 3–5 years if left untreated
Best predictor: volume of femoral head involved; collapse in 43–87% with > 25–50% + in 0–5% with < 25–30% involvement of femoral head volume

Rx: (1) core decompression (for grade 0–II): most successful with < 25% involvement of femoral head
(2) osteotomy (for grade 0–II)
(3) arthroplasty / arthrodesis / total hip replacement (for grade > III)

DDx: (1) Transient osteoporosis of the hip = bone marrow edema syndrome (marked diffuse increased SI on long repetition time images + diffuse contrast enhancement, no reactive interface)
(2) Subchondral epiphyseal insufficiency fracture (low SI band in superolateral femoral head convex toward articular surface; speckled / linear hypointense areas, focal depression of epiphyseal contour)
(3) Spondyloarthropathy

Blount Disease

[Walter Putnam Blount (1900–1992), professor of orthopedics at Marquette Medical School, Milwaukee, Wisconsin]
= TIBIA VARA
= avascular necrosis of medial tibial condyle
Age: > 6 years
• limping, lateral bowing of leg
√ medial tibial condyle enlarged + deformed (DDx: Turner syndrome)
√ irregularity of metaphysis (medially + posteriorly prolonged with beak)

Calvé-Kümmel-Verneuil Disease

= VERTEBRAL OSTEOCHONDROSIS = VERTEBRA PLANA
= avascular necrosis of vertebral body
Age: 2–15 years
√ uniform collapse of vertebral body into flat thin disk
√ increased density of vertebra
√ neural arches NOT affected
√ disks are normal with normal intervertebral disk space
√ intravertebral "vacuum cleft" sign (PATHOGNOMONIC)
DDx: eosinophilic granuloma, metastatic disease

Freiberg Disease

[Albert Henry Freiberg (1868–1940), orthopedic surgeon in Cincinnati, Ohio]
= osteochondrosis of head of 2nd (3rd / 4th) metatarsal
Age: 10–18 years; M÷F = 1÷3
• metatarsalgia, swelling, tenderness
Early:
√ flattening, increased density, cystic lesions of metatarsal head
√ widening of metatarsophalangeal joint
Late:
√ osteochondral fragment
√ sclerosis + flattening of metatarsal head
√ increased cortical thickening

Kienböck Disease

= LUNATOMALACIA
[Robert Kienböck (1871–1953), radiologist in Vienna, Austria]
= avascular necrosis of lunate bone
Predisposed: individuals engaged in manual labor with repeated / single episode of trauma
Age: 20–40 year old males
Associated with: ulna minus variant (short ulna) in 75%
• progressive pain + soft-tissue swelling of wrist
Location: uni- > bilateral (usually right hand)
Classification (Lichtman):

Stage I	=	normal radiographs + abnormal MRI
Stage II	=	increased radiographic density with preservation of normal lunate shape
Stage IIIA	=	lunate sclerosis + collapse on radiographs
Stage IIIB	=	+ diminished carpal height and flexion of scaphoid
Stage IV	=	+ extensive carpal degenerative changes

Radiographs:
√ initially normal radiograph
√ osteonecrotic fracture of carpal lunate
√ increased density + altered shape + collapse of lunate
CT:
√ coronal fracture creating a dorsal and volar half
√ multiple lunate fragments
MR:
√ diffusely decreased T1 SI involving entire lunate
√ variable T2 / STIR signal intensity
Cx: scapholunate dissociation, ulnar deviation of triquetrum, degenerative joint disease in radiocarpal / midcarpal compartments
Rx: ulnar lengthening / radial shortening, lunate replacement

Köhler Disease

[Alban Köhler (1874–1947), radiologist in Wiesbaden, Germany and co-founder of Deutsche

Röntgengesellschaft in Berlin]
= avascular necrosis of tarsal scaphoid
Age: 3–10 years; boys
√ irregular outline
√ fragmentation
√ disklike compression in AP direction
√ increased density
√ joint space maintained
√ decreased / increased uptake on radionuclide study

Legg-Calvé-Perthes Disease

= COXA PLANA
[Arthur Thornton Legg (1874–1939), orthopedic surgeon in Boston]
[Jacques Calvé (1875–1954), orthopedic surgeon at Fondation Franco-Americaine de Berck, France]
[Georg Clemens Perthes (1869–1927), head of the surgical clinic in Tübingen, Germany]
= idiopathic avascular necrosis of femoral head in children; one of the most common sites of AVN; in 10–15% almost always metachronously bilateral
Incidence: 1÷10,000 children; increased with lower socioeconomic status, low birth weight, delayed skeletal maturation
Age: (a) 2–12 (peak, 5–6) years: M÷F = 3–5÷1
(b) adulthood: Chandler disease
Cause: trauma in 30% (subcapital fracture, epiphyseolysis, esp. posterior dislocation), closed reduction of congenital hip dislocation, prolonged interval between injury and reduction
Pathophysiology:
insufficient femoral head blood supply (epiphyseal plate acts as a barrier in ages 4–10; ligamentum teres vessels become nonfunctional; blood supply is from medial circumflex artery + lateral epiphyseal artery only); articular cartilage continues to grow ← supplied with nutrients from synovium
Stages:
I = histologic + clinical diagnosis without radiographic findings
II = sclerosis ± cystic changes with preservation of contour + surface of femoral head
III = loss of structural integrity of femoral head
IV = in addition loss of structural integrity of acetabulum

Radiographic Findings in Legg-Calvé-Perthes Disease (*Catterall Classification*)		
Group	*Radiographic Findings*	*Epiphyseal Involvement*
I	√ anterior portion of epiphysis involved √ NO metaphyseal reaction / sequestrum / subchondral fracture	< 25%
II	√ more extensive involvement of anterior portion of epiphysis √ sequestrum √ anterolateral metaphyseal reaction √ subchondral fracture line NOT extending to apex of epiphysis	< 50%
III	√ entire epiphysis dense √ diffuse metaphyseal reaction + widening of neck √ subchondral fracture line posteriorly	most
IV	√ epiphyseal flattening / mushrooming / collapse √ extensive metaphyseal reaction √ posterior remodeling of posterior head	total

- 1 week–6 months (mean 2.7 months) duration of symptoms prior to initial presentation: limp, knee pain
- decreased range of hip motion concerning abduction and internal rotation

NUC (may assist in early diagnosis):

√ decreased uptake (early) in femoral head = interruption of blood supply

√ increased uptake (late) in femoral head

(a) revascularization + bone repair

(b) degenerative osteoarthritis

√ increased acetabular activity associated with degenerative joint disease

X-RAY:

Early signs:

√ femoral epiphysis smaller than on contralateral side (96%) = epiphyseal growth deficit

√ sclerosis of femoral head epiphysis ← sequestration + compression (82%)

√ slight widening of joint space ← thickening of cartilage, failure of epiphyseal growth, presence of joint fluid, joint laxity (60%)

√ ipsilateral bone demineralization (46%)

√ alteration of pericapsular soft-tissue outline ← atrophy of ipsilateral periarticular soft tissues (73%)

√ radiolucency of lateral + medial metaphyseal areas of femoral neck

N.B.: NEVER destruction of articular cortex as in bacterial arthritis

Late signs:

√ delayed osseous maturation of a mild degree

√ "radiolucent crescent line" of subchondral fracture = small archlike subcortical lucency (32%)

√ subcortical fracture on anterior articular surface (best seen on frog leg view)
√ lateral subluxation of femoral head = lateral collapse of ossific nucleus
√ femoral head fragmentation
√ femoral neck cysts (from intramedullary hemorrhage in response to stress fractures)
√ loose bodies (only found in males)

Regenerative signs:
√ coxa plana = flattened collection of sclerotic fragments (over 18 months)
√ coxa magna = remodeling of femoral head to become wider + flatter in mushroom configuration to match widened metaphysis + epiphyseal plate

CT:
√ loss of "asterisk" sign (= starlike pattern of crossing trabeculae in center of femoral head) with distortion of asterisk and extension to surface of femoral head

MR (gold standard):
√ "asterisk" sign of marrow edema = normal marrow SI of femoral epiphysis replaced by low T1-SI + high T2-SI
√ low signal intensity on T1WI and T2WI = necrotic portion of superior epiphysis
√ "double-line" sign (80%) = sclerotic nonsignal rim between necrotic + viable bone edged by a hyperintense rim of granulation tissue
√ "crescent" sign ← subchondral fracture
√ prominent involvement of anterosuperior + lateral femoral head (often best seen on SAG images)
√ thickening of epiphyseal cartilage
√ synovial hypertrophy, joint effusion
√ fluid within fracture plane
√ absent enhancement of femoral head epiphysis
√ early increased diffusivity in affected femoral epiphysis
√ hip joint incongruity: lateral femoral head uncovering, labral inversion, femoral head deformity

NUC (3-phase bone scan):
√ initially no uptake of radiopharmaceutical on early dynamic images
√ increased activity in lateral pillar ← revascularization phase
√ increased activity at epiphyseal base near physis ← transphyseal neovascularization

US:
√ joint effusion, synovitis

Cx: severe degenerative joint disease in early adulthood

Rx: bed rest, abduction bracing (to reduce stress on infarcted head), physical therapy

Metadiaphyseal Osteonecrosis

√ well-defined serpentine hypointense rim surrounding a central region of fat SI on T1WI
√ "double line" sign = bands of low + high SI that course together in parallel surrounding a central region of low SI (= necrotic bone) on T2WI (virtually PATHOGNOMONIC)

Panner Disease

[Hans Jessen Panner (1871–1930), head of roentgenological clinic at Rikshospitalet, Copenhagen, Denmark]

(NOT osteonecrosis)
= benign self-limited disorder of fragmented ossification in epiphysis of humeral capitellum
Age: children 7–12 years of age

Preiser Disease

[Georg Karl Felix Preiser (1876–1913), orthopedic surgeon in Hamburg, Germany]
= nontraumatic spontaneous osteonecrosis of entire scaphoid

Scaphoid Osteonecrosis

= OSTEONECROSIS OF PROXIMAL POLE OF SCAPHOID
Cause: fracture through waist / proximal pole and nonunion
Incidence of proximal pole osteonecrosis:
(a) in > 60% of fracture nonunions of proximal $^{1}/_{3}$ of scaphoid
(b) in ~ 20% of midscaphoid fractures
X-RAY:
√ increased density of proximal scaphoid fracture fragment compared with distal scaphoid / adjacent carpal bones
√ often sclerotic rounded fracture margins (= nonunion)
√ frequently surrounding lucencies (= cysts)
NUC (bone scan):
√ decreased uptake in proximal pole
CT:
√ increased sclerosis + lack of normal trabeculae in proximal third of scaphoid
MR:
√ homogeneously decreased SI (≤ SI of skeletal muscle) at T1WI in proximal pole of scaphoid (71% sensitive, 74% specific)
√ < 20% enhancement in proximal pole (86% sensitive, 96% specific)
√ complete absence of enhancement in proximal pole (54–76% sensitive)
Cx: scaphoid nonunion advanced collapse (= persistent fracture nonunion, radioscaphoid joint space narrowing, sclerosis, osteophytes, potentially proximal pole collapse)

Spontaneous Osteonecrosis of Knee

= SONK
Cause: ? meniscal tear (78%), trauma with resultant microfractures, vascular insufficiency, degenerative joint disease, severe chondromalacia, gout, rheumatoid arthritis, joint bodies, intraarticular steroid injection (45–85%)
Age: 7th decade (range, 13–83 years)
• acute onset of pain
Location: weight-bearing medial condyle more toward epicondylus (95%), lateral condyle (5%), may involve tibial plateau
√ radiographs usually normal (within 3 months after onset)
√ positive bone scan within 5 weeks (most sensitive)
√ flattening of weight-bearing segment of medial femoral epicondyle
√ radiolucent focus in subchondral bone + peripheral zone of osteosclerosis
√ horizontal subchondral fracture (within 6–9 months) + osteochondral fragment

√ periosteal reaction along medial side of femoral shaft (30–50%)
Cx: osteoarthritis

Talar Avascular Necrosis

◊ Fractures involving the talar body have a higher prevalence of AVN
Risk of AVN:
(a) nondisplaced fracture
– talar neck fracture (Hawkins type I) 0–15%
(b) fracture with dislocation / subluxation of:
› subtalar joint (Hawkins type II) 20–50%
› ankle + subtalar joints (Hawkins type III) almost 100%
› subtalar + tibiotalar + talonavicular joints (Hawkins type IV fracture) 100%
√ increase in talar dome opacity / sclerosis
√ deformity + articular collapse + bone fragmentation
√ absent Hawkins sign = thin subchondral radiolucent line along talar dome (← disuse osteopenia) indicates an adequate blood supply

BASAL CELL NEVUS SYNDROME

= NEVOID BASAL CELL CARCINOMA (BCC) SYNDROME = GORLIN-GOLTZ SYNDROME
= syndrome of autosomal dominant inheritance characterized by
(1) multiple cutaneous basal cell carcinomas during childhood
(2) odontogenic keratocysts of mandible
(3) ectopic calcifications
(4) skeletal anomalies (midface hypoplasia, frontal bossing, prognathism)
Mean age: 19 years
• up to hundreds of skin-colored pink / tan dome-shaped papules resembling benign nevi; aggressive after puberty; may metastasize
Distribution: nose, mouth, chest, back; affected by solar + ionizing radiation
• shallow pitlike defects in palms + soles = deficient stratum corneum (85%)
• mental retardation
Genetics: mutation of patched 1 (PTCH) gene that codes for regulatory receptor in the important Sonic hedgehog signaling pathway + acts as a tumor suppressor gene in BCC + medulloblastoma
Association: high incidence of medulloblastoma in children (4–5%); ovarian fibroma (in 17%); cardiac fibroma (in 14%)
√ multiple aggressive uni- / multiloculated mandibular > maxillary cystic lesions = odontogenic keratocyst / keratocystic odontogenic tumor (in 75%)
√ anomalies of upper 5 ribs:
√ forked = bifid rib (most commonly 4th rib) in 26%
√ agenesis / supernumerary ribs
√ fusion of adjacent ribs
√ hypo- / dysplastic distorted splayed ribs
√ bifid spinous processes, spina bifida
√ scoliosis (cervical + upper thoracic)

√ hemivertebrae + block vertebrae
√ Sprengel deformity (scapula elevated, hypoplastic, bowed)
√ deficiency of lateral clavicle
√ brachydactyly
√ extensive early calcification of falx + tentorium (65%)
√ ectopic calcifications of subcutaneous tissue, ovaries, sacrotuberous ligaments, mesentery
√ bony bridging of sella turcica
√ macrocephaly

BATTERED CHILD SYNDROME

= CAFFEY-KEMPE SYNDROME = CHILD ABUSE = PARENT -INFANT TRAUMATIC STRESS SYNDROME = NON-ACCIDENTAL TRAUMA
◊ Most common cause of serious intracranial injuries in children < 1 year of age; 3rd most common cause of death in children after sudden infant death syndrome + true accidents
Prevalence: 1.7 million cases reported + 833,000 substantiated in USA in 1990 (45% neglected, 25% physically abused, 16% sexually abused children); resulting in 2,500–5,000 deaths per year; 5–10% of children seen in emergency rooms
Age: usually < 2 years
• skin burns, bruising, lacerations, hematomas (SNAT = suspected nonaccidental trauma)
@ Skeletal trauma (50–80%)
Site: multiple ribs, costochondral / costovertebral separation, acromion, skull, anterior-superior wedging of vertebra, tibia, metacarpus
Unusual sites: transverse fracture of sternum, lateral end of clavicles, scapula, vertebral compression, vertebral fracture dislocation, disk space narrowing, spinous processes
Other clues: bilateral acute fractures, fractures of lower extremities in children not yet walking
√ multiple asymmetric fractures in different stages of healing (repeated injury = HALLMARK)
√ exuberant callus formation at fracture sites
√ avulsion fracture of ligamentous insertion; frequently seen without periosteal reaction
@ Epiphysis
√ separation of distal epiphysis
@ Metaphysis
√ marked irregularity + fragmentation of metaphyses (DDx: osteochondritis stage of congenital syphilis; infractions of scurvy)
√ "corner" fracture (11%) = "bucket-handle" fracture = avulsion of an arcuate metaphyseal fragment overlying the lucent epiphyseal cartilage
Cause: sudden twisting motion of extremity (periosteum easily pulled away from diaphysis but tightly attached to metaphysis)
Location: knee, elbow, distal tibia, fibula, radius, ulna
@ Diaphysis
√ isolated spiral fracture (15%) of diaphysis ← external rotatory force applied to femur / humerus

√ extensive periosteal reaction from large subperiosteal hematoma apparent after 7–14 days following injury (DDx: scurvy, copper deficiency)
√ cortical hyperostosis extending to epiphyseal plate (DDx: not in infantile cortical hyperostosis)

@ Head trauma (13–25%)
◊ Most common cause of death + physical disability!
(1) Impact injury with translational force: skull fracture (flexible calvaria + meninges decrease likelihood of skull fractures), subdural hematoma, brain contusion, cerebral hemorrhage, infarction, generalized edema
(2) Whiplash injury with rotational force: shearing injuries + associated subarachnoid hemorrhage
• bulging fontanels, convulsions
• ocular lesions, retinal detachment

Skull film (associated fracture in 1%):
√ linear fracture > comminuted fracture > diastases (conspicuously absent)

CT:
√ subdural hemorrhage (most common): interhemispheric location most common
√ subarachnoid hemorrhage
√ epidural hemorrhage (uncommon)
√ cerebral edema: focal, multifocal, diffuse
√ acute cerebral contusion as ovoid collection of intraparenchymal blood with surrounding edema

MR:
◊ More sensitive in identifying hematomas of differing ages
√ white matter shearing injuries as areas of prolonged T1 + T2 at corticomedullary junction, centrum semiovale, corpus callosum

@ Visceral trauma (3%)
◊ Second leading cause of death in child abuse
Cause: crushing blow to abdomen (punch, kick)
Age: often > 2 years
√ small bowel / gastric rupture
√ hematoma of duodenum / jejunum
√ contusion / laceration of lung, pancreas, liver, spleen, kidneys
√ traumatic pancreatic pseudocyst

Cx: (1) Brain atrophy (up to 100%)
(2) Infarction (50%)
(3) Subdural hygroma
(4) Encephalomalacia
(5) Porencephaly

DDx: normal periostitis of infancy, long-term ventilator therapy in prematurity, osteogenesis imperfecta, congenital insensitivity to pain, infantile cortical hyperostosis, Menkes kinky hair syndrome, Schmid-type chondrometaphyseal dysplasia, scurvy, congenital syphilitic metaphysitis

BENIGN CORTICAL DEFECT

= developmental intracortical bone defect

Age: usually 1st–2nd decade; uncommon in boys < 2 years of age; uncommon in girls < 4 years of age

• asymptomatic

Site: metaphysis of long bone

√ well-defined intracortical round / oval lucency

√ usually < 2 cm long

√ sclerotic margins

Cx: pathologic / avulsion fracture following minor trauma (infrequent)

Prognosis: (1) Spontaneous healing resulting in sclerosis / disappearance

(2) Ballooning of endosteal surface of cortex = fibrous cortical defect

(3) Medullary extension resulting in nonossifying fibroma

BIZARRE PAROSTEAL OSTEOCHONDROMATOUS PROLIFERATION

= NORA LESION

= benign exophytic surface lesion of bone

Cause: ? reactive mass of heterotopic mineralization arising from periosteum of intact cortex without involvement of medullary canal

Location: small tubular bones of hands + feet; proximal and middle phalanges (92%); metacarpal bones (8%)

Site: diaphyses + metaphyses of phalanges

• painless progressive swelling of digit

• ± limited motion in proximity to a joint

√ well-marginated ossified broad-based lesion arising from bone cortex, usually without cortical erosion

√ cortical + medullary discontinuity from underlying host bone

√ periosteal reaction usually absent

MR:

√ uniformly enhancing T1-hypointense mass

√ mass of hyperintensity on T2WI

Rx: surgical excision with wide margins in symptomatic patient

Prognosis: 55% recurrence rate within 2 years of excision

DDx: osteochondroma (cortical + medullary continuity between host bone and mass)

BONE CONTUSION

= BONE BRUISE

= acute bone injury in children

Path: subcortical trabecular microfractures → intraosseous hemorrhage + edema without cortical fracture line

• chronic pain ← persistently elevated intraosseous pressure

Radiograph / CT:

√ invisible

MR (fat-suppression!):

√ high T2 signal intensity = marrow edema + hemorrhage

Prognosis: healing in 12–16 weeks (much longer than for a typical cortical fracture)

Cx: insufficiency fracture ← return to normal physical activity before complete healing

BONE ISLAND

= ENOSTOSIS = ENDOSTEOMA = COMPACT ISLAND
= FOCAL SCLEROSIS = SCLEROTIC BONE ISLAND
= CALCIFIED MEDULLARY DEFECT
= focal lesion of densely sclerotic (compact) bone nesting within spongiosa

Age: any age (mostly 20–80 years of age); grows more rapidly in children

Histo: nest of lamellar compacted bone with haversian system embedded within medullary canal

Pathogenesis: ? misplaced cortical hamartoma, ? developmental error of endochondral ossification as a coalescence of mature bone trabeculae with failure to undergo remodeling; not inherited

• asymptomatic

Location: ilium + proximal femur (88–92%), ribs, spine (1–14%), humerus, phalanges (not in skull)

Size: usually 2–10 mm; lesion > 2 cm in longest axis = giant bone island

√ round / oval / oblong solitary osteoblastic lesion with abrupt transition to surrounding normal trabecular bone:
  √ "brush border" = "thorny radiations" = sharply demarcated margins with feathery peripheral radiations (HALLMARK) blending with trabeculae of surrounding spongiosa
  √ long axis of bone island parallels long axis of bone

√ may demonstrate slow growth / decrease in size (32%)

√ NO involvement of cortex / radiolucencies / periosteal reaction

MR:
  √ low signal intensity at T1WI and T2WI

NUC:
  √ may show activity on bone scan (< 10%), esp. if large

Prognosis: may increase to 8–12 cm over years (40%); may decrease / disappear

DDx: (1) Osteoblastic metastasis (aggressive, break through cortex, periosteal reaction)
(2) Low-grade osteosarcoma (cortical thickening, extension beyond medullary cavity)
(3) Osteoid osteoma (pain relieved by aspirin, nidus)
(4) Benign osteoblastoma
(5) Involuted nonossifying fibroma replaced by dense bone scar
(6) Eccentric focus of monostotic fibrous dysplasia
(7) Osteoma (surface lesion)

BRUCELLOSIS

= multisystemic zoonosis of worldwide distribution; endemic in Middle East (Arabian Peninsula), South and Central America, Mediterranean region (Spain, Italy)

Organism: small gram-negative nonmotile, nonsporing, aflagellate, nonencapsulated

coccobacilli: Brucella abortus, B. suis, B. canis, B. melitensis

Mode of transmission:
handling contaminated animal products (in excreta of infected animals like urine, stool, milk, products of conception) or consuming dairy products from unpasteurized milk

Histo: small intracellular pathogens cause small noncaseating granuloma within RES

Location: commonest site of involvement is reticuloendothelial system; musculoskeletal system

• 1–3 weeks between initial infection + symptoms
  ◊ Radiologic evidence of disease in 69% of symptomatic sites!

@ Brucellar spondylitis (53% = most common site)
  Age: 40 years is average age at onset
  • pain, localized tenderness, radiculopathy, myelopathy
  Location: lumbar (71%) > thoracolumbar (10%) > lumbosacral (8%) > cervical (7%) > thoracic (4%)
  (a) focal form
    √ bone destruction at diskovertebral junction (anterior aspect of superior endplate)
    √ associated with bone sclerosis + anterior osteophyte formation + small amount of gas
  (b) diffuse form: entire vertebral endplate / whole vertebral body affected with spread to adjacent disks + vertebral bodies
    √ bone destruction associated with sclerosis
    √ small amount of disk gas (25–30%)
    √ facet joint involvement
    √ obliteration of paraspinal muscle-fat planes
    √ paraspinal abscess (smaller than in TB)
    √ no / minimal epidural extension
    DDx: TB (paraspinal abscess, gibbus)

@ Extraspinal disease
  (a) Brucellar synovitis (81%)
    Location: knee > sacroiliac joint > shoulder > hip > sternoclavicular joint > ankle > elbow
    Site: organism localized in synovial membrane
    • serosanguinous sterile joint effusion
    √ bilateral sacroiliitis
  (b) Brucellar destructive arthritis (9%)
    √ indistinguishable from tuberculous / pyogenic arthritis
  (c) Brucellar osteomyelitis (2%)
    • pain, tenderness, swelling
  (d) Brucellar myositis (2%)

Dx: serologic tests (enzyme-linked immunosorbent assay, counterimmunoelectrophoresis, rose bengal plate test

Rx: combination of aminoglycosides + tetracyclines

DDx: fibrous dysplasia, benign tumor, osteoid osteoma

CAISSON DISEASE

= DECOMPRESSION SICKNESS = THE BENDS

Etiology: during too rapid decompression (= reduction of surrounding pressure ← ascent from dive, exit from caisson / hyperbaric chamber, ascent to altitude) nitrogen bubbles form (nitrogen is more soluble in fat of panniculus adiposus, spinal cord, brain, bones containing fatty marrow)

- "the bends" = local pain in knee, elbow, shoulder, hip
- neurologic symptoms: paresthesia, major cerebral / spinal involvement
- "chokes" = substernal discomfort + coughing ← embolization of pulmonary vessels

Location: mostly in long tubular bones of lower extremity (distal end of shaft + epiphyseal portion); symmetrical lesions

√ early: area of rarefaction
√ healing phase: irregular new-bone formation with greater density
√ peripheral zone of calcification / ossification
√ ischemic necrosis of articular surface → secondary osteoarthritis

CALCIUM PYROPHOSPHATE DIHYDRATE DEPOSITION DISEASE

= CPPD = PSEUDOGOUT = FAMILIAL CHONDROCALCINOSIS
= metabolic arthropathy characterized by deposition of calcium pyrophosphate dihydrate crystals in articular + periarticular tissues
◊ Most common crystalline arthropathy

Chondrocalcinosis = term for intra-articular calcifications with involvement of hyaline articular cartilage and fibrocartilage

Types:
1. Osteoarthritic form (35–60%)
2. **Pseudogout** = acute synovitis (10–20%) mimicking gout attack
3. Rheumatoid form (2–6%)
4. Pseudoneuropathic arthropathy (2%)
5. Asymptomatic with tophaceous pseudogout (common)

Associated with: hyperparathyroidism, hypothyroidism, hemochromatosis, hypomagnesemia

Prevalence: widespread in older population; increasing with age; M÷F = 3÷2

- calcium pyrophosphate crystals in synovial fluid + within leukocytes (characteristic weakly positive birefringent rhomboid foci)
- acute / subacute / chronic joint inflammation

√ polyarticular chondrocalcinosis (in fibro- and hyaline cartilage)
√ large subchondral cyst (HALLMARK)
√ numerous intraarticular bodies (fragmentation of subchondral bone)
√ coalescing CPPD crystals → tophus-like deposits (rare) → significant articular destruction

Site: involvement of tendons, bursae, pinnae of the ear

- painful mass

√ joint space narrowing + extensive subchondral sclerosis
◊ CPPD arthropathy resembles osteoarthritis!

@ Hand

Distribution: 1 CMC; 2nd + 3rd MCP joints; bilateral symmetric

√ resembling degenerative joint disease (without DIP and PIP involvement)
√ small hook-like osteophytes at radial aspect of metacarpal heads 2 & 3

@ Wrist

Distribution: triangular fibrocartilage in distal radioulnar joints bilaterally, proximal carpal row joints at lunotriquetral + scapholunate ligaments

√ calcification (chondrocalcinosis) of triangular fibrocartilage

√ extensive narrowing / obliteration of joint space between distal radius + scaphoid → destruction of trapezioscaphoid space:

√ incorporation of scaphoid into articular surface of radius

√ prominent cysts

√ scapholunate separation (= ligament tear) → scapholunate advanced collapse (SLAC

@ Knee

Distribution: especially meniscus + cartilage of patellofemoral joint

√ medial femorotibial + patellofemoral compartments commonly involved simultaneously (as in osteoarthritis) but with greater osseous destruction + fragmentation

√ disproportionate narrowing of patellofemoral joint

@ Spine

√ chondrocalcinosis / calcifications of outer fibers of annulus fibrosus of lumbar spine resembling syndesmophytes; NEVER in nucleus pulposus

DDx: ochronosis (in nucleus pulposus)

√ vertical radiodense line in symphysis pubis

Other locations:

› pelvis (sacroiliac joint, symphysis)

› shoulder (glenoid), hip (labrum), elbow, ankle, acromioclavicular joint

CAMPTOMELIC DYSPLASIA

= sporadic / autosomal recessive dwarfism

Prevalence: 0.05÷10,000 births

Associated with:

1. Hydrocephalus (23%)
2. Congenital heart disease (30%): VSD, ASD, tetralogy, AS
3. Hydronephrosis (30%)

• pretibial dimple

√ macrocephaly, cleft palate, micrognathia (90–99%)

@ Chest & spine

√ absence / hypoplasia of scapula (92%)

√ narrow bell-shaped chest

√ hypoplastic vertebral bodies + nonmineralized pedicles (especially lower cervical spine)

@ Pelvis

√ vertically narrowed iliac bones

√ vertical inclination of ischii

√ wide symphysis

√ narrow iliac bones with small wings

√ shallow acetabulum

@ Extremities (lower extremity more severely affected)

√ dislocation of hips + knees

√ anterior bowing (= campto) of long bones: marked in tibia + moderate in femur

√ hypoplastic fibula
√ small secondary ossification center of knee
√ small primary ossification center of talus
√ clubfoot

OB-US:
√ bowing of tibia + femur
√ decreased thoracic circumference
√ hypoplastic scapulae
√ ± cleft palate

Prognosis: death usually < 5 months of age (within first year in 97%) ← respiratory insufficiency

CARPAL TUNNEL SYNDROME

= entrapment syndrome caused by chronic pressure on the median nerve within the carpal tunnel

Etiology:
(a) intrinsic: flexor tendon tendinitis or tenosynovitis, infiltrative disorder, mass, cyst, muscle hypertrophy (from repetitive wrist / finger flexion), anomalous origin of lumbrical muscles
(b) extrinsic: mass, carpal instability, Kienböck disease

Pathogenesis: probably ischemia with venous congestion (stage 1), nerve edema from anoxic damage to capillary endothelium (stage 2), impairment of venous and arterial blood supply (stage 3)

• nocturnal hand discomfort
• weakness, clumsiness, finger paresthesias

MR:
√ "pseudoneuroma" of median nerve = swelling of median nerve proximal to carpal tunnel
√ swelling of nerve within carpal tunnel
√ increased signal intensity of nerve on T2WI
√ volar bowing of flexor retinaculum
√ swelling of tendon sheath ← tenosynovitis
√ mass(es) within carpal tunnel
√ marked enhancement ← nerve edema ← breakdown of blood-nerve barrier
√ no enhancement (= ischemia) provoked by wrist held in an extended / flexed position

CARPENTER SYNDROME

= ACROCEPHALOPOLYSYNDACTYLY TYPE 2

autosomal recessive

• retardation; hypogonadism
√ patent ductus arteriosus
√ acro(oxy)cephaly
√ brachymesophalangia
√ soft-tissue syndactyly (hands + feet)
√ preaxial polysyndactyly of feet

CEREBROCOSTOMANDIBULAR SYNDROME

= rare bone disorder of uncertain transmission
• respiratory distress ← flail chest and airway abnormalities
√ 11 pairs of ribs:
  √ abnormal costovertebral articulations
  √ posterior ossification gaps resembling fractures
√ microcephaly
√ micrognathia
√ congenital heart disease
DDx: multiple fractures

CHONDROBLASTOMA

= CODMAN TUMOR = BENIGN CHONDROBLASTOMA = CARTILAGE-CONTAINING GIANT CELL TUMOR
= benign cartilaginous tumor with predilection for growing skeleton
Frequency: 1% of primary bone neoplasms (700 cases in world literature)
Age: peak in 2nd decade (range, 8–59 years); 10–26 years (90%); M÷F = 2÷1; occurs before cessation of enchondral bone growth
Path: derived from primitive cartilage cells
Histo: polyhedral chondroblasts + reactive multinucleated giant cells + nodules of pink amorphous material (= chondroid) = epiphyseal chondromatous giant cell tumor (resembles chondromyxoid fibroma); "chicken wire" calcification of matrix = pericellular deposition of calcification is virtually PATHOGNOMONIC
• symptomatic for months to years prior to treatment
• mild joint pain, tenderness, swelling (joint effusion)
• limitation of motion
Location:
(a) long bones (80%): proximal femur + greater trochanter (23%), distal femur (20%), proximal tibia (17%), proximal humerus (17%)
  ◊ ²/₃ in lower extremity, 50% about knee
  ◊ may occur in apophyses (minor + greater trochanter, patella, greater tuberosity of humerus)
(b) flat bones: near triradiate cartilage of innominate bone, rib (3%), vertebral body & posterior elements (1.4%)
(c) short tubular bones of hand + feet
Site: eccentric medullary, subarticular location with open growth plate (98% begin within epiphysis); tumor growth may continue to involve metaphysis (50%) + rarely diaphysis
√ oval / round eccentrically placed lytic lesion of epiphysis
√ 1–4 cm in diameter occupying < ½ of epiphysis
√ well-defined sclerotic margin, lobulated in 50%
√ stippled / irregular calcifications in 25–30–50% (cartilaginous clumps better visualized by CT)
√ intact scalloped cortical border
√ thick periosteal reaction in metaphysis (50%) / joint involvement
√ periostitis of adjacent metaphysis / diaphysis (30–50%)

√ growth plate open in majority of patients

MR:

◊ MR tends to overestimate extent + aggressiveness ← large area of reactive edema!

√ intermediate to low SI on T2WI relative to fat ← immature chondroid matrix, hypercellularity, calcifications, hemosiderin

√ extensive intramedullary signal abnormalities ← bone marrow edema

√ peripheral rim of very low signal intensity

√ hypointense changes on T1WI + hyperintense on T2WI in adjacent soft tissues (← muscle edema in 50%)

√ ± joint effusion

Prognosis: almost always benign; may become locally aggressive; rarely metastasizes

Dx: surgical biopsy

Rx: curettage + bone chip grafting (recurrence in 25%)

DDx: (1) Ischemic necrosis of femoral head (may be indistinguishable, more irregular configuration)

(2) Giant cell tumor (usually larger + less well demarcated, not calcified, older age group with closed growth plate)

(3) Chondromyxoid fibroma

(4) Enchondroma

(5) Osteomyelitis (less well-defined, variable margins)

(6) Aneurysmal bone cyst

(7) Intraosseous ganglion

(8) Langerhans cell histiocytosis (less well-defined, variable margins)

(9) Primary bone sarcoma

CHONDRODYSPLASIA PUNCTATA

= CONGENITAL STIPPLED EPIPHYSES = DYSPLASIA EPIPHYSEALIS PUNCTATA = CHONDRODYSTROPHIA CALCIFICANS CONGENITA

= group of syndromes characterized by abnormal calcific foci in areas of enchondral bone formation

Etiology: peroxisomal disorder characterized by fibroblast plasmalogen deficiency

Prevalence: 1÷110,000 births

Genetics: X-linked autosomal

› recessive = alterations in peroxisomal metabolism

› dominant = mutations in delta 8 sterol isomerase enzyme → abnormal cholesterol biosynthesis (cholesterol is essential to proper function of Sonic hedgehog class of embryonic signaling proteins)

Associated with: congenital ichthyosiform erythroderma = generalized erythema with characteristic feathery adherent hyperkeratotic scale

Radiograph:

√ calcific stippling of epiphyses (prior to normal epiphyseal ossification)

√ scoliosis, kyphosis

A. **Autosomal Recessive Chondrodysplasia Punctata**

= RHIZOMELIC TYPE

Associated with: CHD (common)

- craniofacial dysmorphism = flat face with small saddle nose
- congenital cataracts
- severe mental retardation, spastic tetraplegia
- thermoregulatory instability
- cleft palate

√ multiple small punctate calcifications of varying size in epiphyses (knee, hip, shoulder, wrist), base of skull, posterior elements of vertebrae, respiratory cartilage and soft tissues (neck, rib ends) before appearance of ossification centers

√ prominent symmetrical shortening of femur + humerus (rarely all limbs symmetrically affected)

√ congenital dislocation of hip

√ multiple flexion (joint) contractures of extremities

√ clubfeet

√ metaphyseal splaying of proximal tubular bones (in particular about knee)

√ thickening of diaphyses

√ prominent vertebral + paravertebral calcifications

√ coronal clefts in vertebral bodies

OB-US:

√ ascites, polyhydramnios

Prognosis: death usually < 1 year of age

DDx: Zellweger syndrome

B. **Conradi-Hünermann-Happle Syndrome**

= NONRHIZOMELIC TYPE

more common milder nonlethal variety

Genetics: mutation localized to Xp11.23 to EBP gene

- normal intelligence

√ more widespread but milder involvement as above

Prognosis: survival often into adulthood

Cx: respiratory failure (severe underdevelopment of ribs), tracheal stenosis, spinal cord compression

DDx: (1) Cretinism (may show epiphyseal fragmentation, much larger calcifications within epiphysis)

(2) Warfarin embryopathy

(3) Zellweger syndrome

CHONDROECTODERMAL DYSPLASIA

= ELLIS-VAN CREVELD SYNDROME = MESODERMAL DYSPLASIA

= autosomal recessive acromesomelic dwarfism

Prevalence: 120 cases; in inbred Amish communities

Associated with: congenital heart disease in 50% (single atrium, ASD, VSD)

- ectodermal dysplasia:
  - › scant / fine hair

› absent / hypoplastic brittle spoon-shaped nails
› irregular + pointed dysplastic teeth, partial anodontia, teeth may be present at birth
› congenital heart disease
• obliteration of maxillary mucobuccal space (thick frenula between alveolar mucosa + upper lip); strabismus
• genital malformations: epispadia, hypospadia, hypoplastic external genitalia, undescended testicles
√ hepatosplenomegaly
√ accelerated skeletal maturation
√ normal spine
@ Skull
√ wormian bones
√ cleft lip
@ Chest
√ elongated narrow thorax in AP + transverse dimensions exaggerating cardiac size
√ cardiomegaly ← frequently ASD / single atrium
√ short horizontal ribs + anterior osseous expansion → barrel-shaped chest
√ elevated clavicles
@ Pelvis
√ small flattened ilium
√ trident morphology of acetabular roof = indentation in roof + bony spur (almost PATHOGNOMONIC)
√ acetabular + tibial exostoses
@ Extremities
√ variety of micromelia (= thickening + mild shortening of all long bones):
√ acromelia = hypoplasia / absence of terminal phalanges
√ mesomelia = shortening of forearms + lower legs (radius + tibia > humerus + femur)
√ cone-shaped epiphyses
√ premature ossification of proximal humeral + femoral epiphyses
@ Upper extremity
√ "drumstick" forearm = swelling of proximal end of ulna + distal end of radius
√ anterior dislocation of radial head ← shortening of ulna
√ carpal / tarsal fusion = frequent fusion of two / more carpal (hamate + capitate) + tarsal bones (after complete ossification)
√ supernumerary carpal bones
√ postaxial polydactyly common (usually finger, rarely toe) ± syndactyly of hands + feet
@ Lower extremity
√ genu valgum:
√ slanting of proximal tibial metaphysis (← delayed development of tibial plateau)
√ excessive shortening of fibula
√ widening of proximal tibial shaft
√ medial tibial diaphyseal exostosis
OB-US:
√ proportional shortening of long bones
√ small thorax with decreased circumference

√ increased cardiothoracic ratio
√ ASD
√ polydactyly

Prognosis: death within first month of life in 33–50% ← respiratory / cardiac complications

DDx: asphyxiating thoracic dysplasia (difficult distinction); rhizomelic achondroplasia

CHONDROMALACIA PATELLAE

= pathologic softening of patellar cartilage leading to defects of surface (chondrosis) / osteoarthritis

Cause: trauma, tracking abnormality of patella

• anterior knee pain
• asymptomatic (incidental arthroscopic diagnosis)

MR (60% sensitive, 84% specific, 73% accurate):

√ focal areas of increased T2 / PD signal intensity of cartilage
√ partial / full-thickness cartilage loss
√ underlying marrow / bone reactive changes

CHONDROMYXOID FIBROMA

= rare benign cartilaginous tumor; initially arising in cortex

Frequency: < 1% of all bone tumors

Histo: chondroid + fibrous + myxoid tissue (related to chondroblastoma); may be mistaken for chondrosarcoma

Age: peak 2nd–3rd decade (range, 5–79 years); M÷F = 1÷1

• slowly progressive local pain, swelling, restriction of motion

Location: (a) long bones (60%): about knee (50%), proximal tibia (82% of tibial lesions), distal femur (71% of femoral lesions), fibula
(b) short tubular bones of hand + feet (20%)
(c) flat bones: pelvis, ribs (classic but uncommon)

Site: metaphyseal (47–53%), metadiaphyseal (20–43%), metaepiphyseal (26%), diaphyseal (1–10%), epiphyseal (3%); eccentric

Size: 1–10 cm in length; 4–7 cm in width

√ expansile ovoid lesion with radiolucent center + oval shape at each end of lesion
√ long axis parallel to long axis of host bone
√ geographic bone destruction (100%)
√ well-defined sclerotic margin (86%)
√ expanded shell = bulged + thinned overlying cortex (68%)
√ partial cortical erosion (68%)
√ scalloped margin (58%)
√ septations (57%) may mimic trabeculations
√ stippled calcifications within tumor in advanced lesions (7%)
√ NO periosteal reaction (unless fractured)

Prognosis: 25% recurrence rate following curettage

Cx: malignant degeneration distinctly unusual

DDx: (1) Aneurysmal bone cyst

(2) Simple bone cyst
(3) Nonossifying fibroma
(4) Fibrous dysplasia
(5) Enchondroma
(6) Chondroblastoma
(7) Eosinophilic granuloma
(8) Fibrous cortical defect
(9) Giant cell tumor

CHONDROSARCOMA

A. PRIMARY CHONDROSARCOMA
no preexisting bone lesion

B. SECONDARY CHONDROSARCOMA
= complication of a preexisting skeletal abnormality such as
1. Osteochondroma
2. Enchondroma
3. Parosteal chondroma

Spread: via marrow cavity / periosteum

Metastases (uncommon) to: lung, epidural space

May be associated with: Ollier disease, Maffucci syndrome, Paget disease

CT:
√ chondroid matrix mineralization of "rings and arcs" (CHARACTERISTIC) in 70%
√ nonmineralized portion of tumor hypodense to muscle (high water content of hyaline cartilage)
√ extension into soft-tissues

MR:
√ low to intermediate signal intensity on T1WI
√ high SI on T2WI + hypointense areas ← mineralization / fibrous septa
√ enhancement of fibrous septations

NUC:
√ bone scan uptake intensity compared to anterior iliac crest: greater (82%) + equal to (12%) + less than (6%)

DDx: enchondroma; osteochondroma (marrow + cortical contiguity with cartilage cap); chordoma (calcification at periphery of lesion); chondroblastoma (lytic lesion with thin sclerotic margin; malignant fibrous histiocytoma; metastasis (history of primary tumor)

Central Chondrosarcoma

= INTRAMEDULLARY CHONDROSARCOMA = ENDOSTEAL CHONDROSARCOMA

Frequency: 3rd most common primary bone tumor (after multiple myeloma and osteosarcoma); 20–27% of all primary malignant neoplasms; 8–17% of biopsied primary bone tumors

Path: lobular morphology with variable amounts of calcium; presence of fibrous bands at tumor-marrow interface suggests malignancy (DDx from atypical enchondroma)

Histo: arises from chondroblasts (tumor osteoid never forms)

Age: median 45 years; 50% > 40 years; 10% in children (rapidly fatal); M÷F = 2÷1
• hyperglycemia as paraneoplastic syndrome (85%)
Location: neck of femur, pubic rami, proximal humerus, ribs (19%), skull (sphenoid bone, cerebellopontine angle, mandible), sternum, spine (3–12%)
Site: central within medullary canal of meta- / diaphysis
√ expansile osteolytic lesion 1 to several cm in size
√ short transition zone ± sclerotic margin (well defined from host bone)
√ ± small irregular punctate / snowflake type of calcification; single / multiple
√ late: loss of definition + break through cortex:
  √ pathologic fracture (in 3–17% at initial presentation)
√ endosteal cortical thickening, sometimes at a distance from the tumor ← invasion of haversian system
√ presence of large soft-tissue mass
DDx: benign enchondroma, osteochondroma, osteosarcoma, fibrosarcoma

Peripheral Chondrosarcoma

= EXOSTOTIC CHONDROSARCOMA
= malignant degeneration of hereditary multiple osteochondromatosis and rarely of a solitary exostosis (beginning in cartilaginous cap of exostosis)
Frequency: 8% of all chondrosarcomas
Average age: 50–55 years for solitary exostosis; 25–30 years for hereditary multiple osteochondromatosis; M÷F = 1.5÷1
Histo: low histologic grade in 67–85%
• growth after skeletal maturity
• gradually increasing pain, often worse at night
• local swelling / palpable mass (45%)
Location: pelvis, hip, scapula, sternum, ribs, ends of humerus / femur, craniofacial bones
√ growth of a previously unchanged osteochondroma in a skeletally mature patient
√ unusually large soft-tissue mass (= hyaline cartilage cap) containing flocculent / streaky chondroid calcifications (CHARACTERISTIC):
  √ cartilage cap 1.5–12 cm (average, 5.5–6 cm) thick
    ◊ > 1.5 cm is suspect of malignant transformation
√ irregular / indistinct lesion surface:
  √ dense radiopaque center with streaks radiating to periphery + loss of smooth margin
√ focal regions of radiolucency in interior of lesion
√ erosion / destruction of adjacent bone
Metastases: in 3–7%, most commonly to lung
Rx: wide resection
Prognosis: 70–90% long-term survival
DDx: (1) Osteochondroma (densely calcified with multiple punctate calcifications)
(2) Parosteal osteosarcoma (more homogeneous density of calcified osteoid)

Clear Cell Chondrosarcoma

◊ Usually mistaken for chondroblastoma because of low grade malignancy (both tumors may be related)!

Histo: small lobules of tissue composed of cells with centrally filled vesicular nuclei surrounded by large clear cytoplasm
Age: 19–68 years, predominantly after epiphyseal fusion
Location: proximal femur, proximal humerus, proximal ulna, lamina vertebrae (5%); pubic ramus
Site: epiphysis
√ single lobulated oval / round sharply marginated lesion of 1–2 cm in size
√ surrounding increased bone density
√ aggressive rapid growth to over 3 cm
√ may contain calcifications
√ bone often enlarged
√ indistinguishable from conventional chondrosarcoma / chondroblastoma (slow growth over years)

Extraskeletal Chondrosarcoma

Extraskeletal Myxoid Chondrosarcoma (most common)
Mean age: 50 years (range 4–92 years); M > F
Histo: surrounded by fibrous capsule + divided into multiple lobules by fibrous septa; delicate strands of small elongated chondroblasts suspended in an abundant myxoid matrix; rare foci of mature hyaline cartilage
• slowly growing soft-tissue mass; pain + tenderness (33%)
◊ Metastatic in 40–45% at time of presentation!
Location: proximal extremities (thigh most common)
Site: deep soft tissues; subcutis (25%)
Size: usually between 4 and 7 cm in diameter
√ lobulated soft-tissue mass WITHOUT calcification / ossification / cartilaginous differentiation
√ usually ill-defined margins
√ usually heterogeneous tumor ← necrosis + hemorrhage
MR:
√ SI equal to muscle on T1WI + equal to fat on T2WI
√ may mimic a cyst / myxoma
√ rings + arcs on contrast-enhanced images ← lobulated growth pattern
Prognosis: 45% 10-year survival rate; 5–15 years survival after development of metastases

Extraskeletal Mesenchymal Chondrosarcoma
= MESENCHYMAL CHONDROSARCOMA
Frequency: 2–10% of all chondrosarcomas
◊ 50% of all mesenchymal chondrosarcomas arise in soft tissues
Histo: proliferation of small primitive mesenchymal cells with scattered islands of cartilage; hemangiopericytoma-like vascular pattern
Bimodal age distribution: M = F
(a) tumors of head + neck in 2nd–3rd decade (common): meninges, periorbital region

(b) tumors of thigh + trunk in 5th decade

• frequently metastasized to lungs + lymph nodes

√ matrix mineralization (50–100%) characterized as rings + arcs / flocculent + stippled calcification / dense mineralization

MR:

√ lobulated soft tissue mass with:

√ low signal intensity on T1WI

√ variable heterogeneous signal intensity on T2WI

√ curvilinear / stippled areas of low signal intensity ← chondroid matrix calcifications

√ complex heterogeneous enhancement

Prognosis: 25% 10-year survival rate

Synovial Chondrosarcoma

= extremely rare intraarticular malignant cartilaginous neoplasm

Etiology: ? de novo / metaplastic transformation of synovial osteochondromatosis

◊ Concurrent (and presumably preexistent) primary synovial chondromatosis in 50%

Age: 4th–7th decade

Histo: permeation of trabecular bone, spindle-shaped chondrocytes, myxoid change in cellular matrix, shift from normal cell clusters to sheets of tumor cells

• pain + muscle swelling / contracture in presence of a mass

Location: knee, hip, shoulder, smaller joints (rare)

Spread to: lung

√ lobulated intraarticular soft-tissue mass:

√ mass isointense on T1WI + hyperintense on T2WI

√ calcified bodies of low SI on all pulse sequences

√ classic juxtaarticular ring-and-arc pattern

√ multiple nodules with peripheral enhancement

√ features suggestive of malignancy:

√ cortical bone erosion / destruction with marrow invasion

√ widespread extraarticular extension of tumor beyond joint capsule

√ hematogenous (to lung) / regional lymphatic metastases

DDx: synovial osteochondromatosis (indistinguishable with the exception that evidence of metastatic disease allows a definitive diagnosis)

CLEIDOCRANIAL DYSOSTOSIS

= CLEIDOCRANIAL DYSPLASIA = MUTATIONAL DYSOSTOSIS

= autosomal dominant disease with delayed ossification of midline structures (particularly of membranous bone)

@ Skull

• large head

√ diminished / absent ossification of skull (in early infancy)

√ wormian bones

√ widened fontanels + sutures with delayed closure

√ persistent metopic suture

√ brachycephaly + prominent bossing
√ large mandible
√ high narrow palate (± cleft)
√ hypoplastic paranasal sinuses
√ delayed / defective dentition

@ Chest
√ hypoplasia / absence (10%) of clavicles: usually defective development of lateral (R > L) portion of clavicle (DDx: congenital pseudarthrosis of clavicle)
√ thorax may be narrowed + bell-shaped
√ supernumerary ribs
√ incompletely ossified sternum
√ hemivertebrae, spondylosis (frequent)

@ Pelvis
√ delayed ossification of bones forming symphysis pubis (DDx: bladder exstrophy)
√ hypoplastic iliac bones

@ Extremities
√ radius short / absent
√ elongated second metacarpals
√ pseudoepiphyses of metacarpal bases
√ short hypoplastic distal phalanges of hand
√ pointed terminal tufts
√ coned epiphyses
√ coxa vara = deformed / absent femoral necks
√ accessory epiphyses in hands + feet (common)

OB-US:
√ cephalopelvic disproportion → large fetal head + narrow birth canal of affected maternal pelvis necessitates cesarean section

COCCIDIOIDOMYCOSIS

Cause: inhalation of fungus Coccidioides immitis
Endemic to: Mexico, South America, southwestern USA
Histo: chronic granulomatous process in bones, joints, periarticular structures
Location: (a) bones: most frequently in metaphyses of long bones + medial end of clavicle, spine, ribs, pelvis / bony prominences of patella, tibial tuberosity, calcaneus, olecranon, acromion
(b) arthritis of weight-bearing joints (33%):
Location: ankle, knee, wrist, elbow
• "desert rheumatism" = immune-complex–mediated arthritis
(c) tenosynovitis of hand, bursitis

√ focal areas of destruction, formation of cavities (early) = bubbly bone lesion
√ bone sclerosis surrounding osteolysis (later, rare)
√ proliferation of overlying periosteum
√ destruction of vertebra with preservation of disk space
√ psoas abscess indistinguishable from tuberculosis, may calcify

√ joints rarely infected (usually monoarticular from direct extension of osteomyelitic focus): synovial effusion, juxtaarticular osteopenia, bone destruction, rice bodies, joint space narrowing late in disease, ankylosis
√ soft-tissue abscess (common)
DDx: tuberculosis

CONGENITAL INSENSITIVITY TO PAIN WITH ANHYDROSIS

= rare autosomal recessive disorder presumably on the basis of abnormal neural crest development
Age: presenting at birth
Prevalence: 15 reported cases
Path: absence of dorsal + sympathetic ganglia, deficiency of neural fibers < 6 μm in diameter + disproportionate number of fibers of 6–10 μm in diameter
• history of painless injuries + burns (DDx: familial dysautonomia, congenital sensory neuropathy, hereditary sensory radicular neuropathy, acquired sensory neuropathy, syringomyelia)
• abnormal pain + temperature perception
• burns, bruises, infections (common); absence of sweating
• biting injuries of fingers, lips, tongue; mental retardation
Criteria: (1) defect must be present at birth
(2) general insensitivity to pain
(3) general mental / physical retardation
√ epiphyseal separation in infancy → epiphyseal injuries → growth problems
√ metaphyseal fractures in early childhood
√ diaphyseal fractures in late childhood
√ Charcot joints = neurotrophic joints (usually weight-bearing joints) with effusions + synovial thickening
√ ligamentous laxity
√ bizarre deformities + gross displacement + considerable hemorrhage ← unnoticed fractures + dislocations
√ ± osteomyelitis + septic arthritis → may progress extensively
DDx: (1) Sensory neuropathies (eg, diabetes mellitus)
(2) Hysteria
(3) Syphilis
(4) Mental deficiency
(5) Syringomyelia
(6) Organic brain disease

CORNELIA DE LANGE SYNDROME

= AMSTERDAM DWARFISM
• mental retardation (IQ < 50); hirsutism; hypoplastic genitalia
• feeble growling cry; high forehead; short neck; arched palate
• bushy eyebrows meeting in midline + long curved eyelashes

• small nose with depressed bridge; upward tilted nostrils; excessive distance between nose + upper lip
√ small + brachycephalic skull
√ hypoplasia of long bones: upper extremity more involved
√ forearm bones may be absent
√ short radius + elbow dislocation
√ thumbs placed proximally (hypoplastic 1st metacarpal)
√ short phalanges + clinodactyly of 5th finger

CORTICAL DESMOID

= AVULSIVE CORTICAL IRREGULARITY = PERIOSTEAL / SUBPERIOSTEAL DESMOID = SUBPERIOSTEAL / CORTICAL ABRASION = SUBPERIOSTEAL CORTICAL DEFECT
= rare fibrous lesion of the periosteum
Peak age: 14–16 (range, 3–17) years; M÷F = 3÷1
Histo: shallow defect filled with proliferating fibroblasts, multiple small fragments of resorbing bone (microavulsions) at tendinous insertions
• no localizing signs / symptoms
Location: posteromedial aspect of medial femoral epicondyle along medial ridge of linea aspera at attachment of adductor magnus aponeurosis; ⅓ bilateral
√ area of cortical thickening
√ 1–2 cm irregular, shallow, concave saucerlike crater with sharp margin
√ lamellated periosteal reaction
√ localized cortical hyperostosis proximally (healing phase)
◊ May be confused with a malignant tumor (eg, osteosarcoma) / osteomyelitis!

CRI-DU-CHAT SYNDROME

= deletion of short arm of 5th chromosome (5 p)
• generalized dwarfism ← marked growth retardation
• failure to thrive
• peculiar high-pitched cat cry (hypoplastic larynx)
• antimongoloid palpebral fissures; strabismus
• profound mental retardation; round facies; low-set ears
Associated with: congenital heart disease (obtain CXR!)
√ agenesis of corpus callosum
√ microcephaly
√ hypertelorism
√ small mandible
√ faulty long-bone development
√ short 3rd, 4th, 5th metacarpals
√ long 2nd, 3rd, 4th, 5th proximal phalanges
√ horseshoe kidney
Dx: made clinically

CROUZON SYNDROME

= CRANIOFACIAL SYNOSTOSIS / DYSOSTOSIS
= Apert syndrome without syndactyly
= skull + cranial base deformities characterized by craniosynostosis, maxillary hypoplasia, shallow orbits, ocular proptosis, bifid uvula, cleft palate

Prevalence: 1÷25,000

Etiology: autosomal dominant inheritance (in 67%)

Associated intracranial anomalies:

anomalous venous drainage, hydrocephalus (often progressive), Chiari I malformation (71%)

- parrot-beak nose; strabismus; deafness; mental retardation
- dental abnormalities; bifid uvula
- acanthosis nigrans (= hyperpigmented hyperkeratotic lesions on neck + near joint flexures)

√ premature craniosynostosis: acro(oxy)cephaly / brachycephaly / scaphocephaly / trigonocephaly / "cloverleaf" skull
√ hypertelorism + exophthalmos ← shallow orbits
√ hypoplastic maxilla → relative prominence of mandible
√ cleft palate
√ calcification of stylohyoid ligament (in 50% of patients > 4 years of age)
√ C2–C5 spine abnormalities (in up to 40%)
√ elbow malformation (18%)
√ minor hand deformities (10%)
√ visceral anomalies (7%)
√ musculoskeletal deformities (7%) but no limb anomaly

OB-US:

√ cloverleaf appearance (coronal view) + bilateral frontal indentations (axial view) of skull
√ increased interorbital distance + ocular proptosis
√ mild ventriculomegaly

CRUCIATE LIGAMENT INJURY

A. COMPLETE TEAR
   √ failure to identify ligament
   √ amorphous area of high SI on T1WI + T2WI with inability to define ligamentous fibers
   √ focal discrete complete disruption of all visible fibers
B. PARTIAL / INTRASUBSTANCE TEAR
   √ abnormal SI within substance of ligament with some intact + some discontinuous fibers

Anterior Cruciate Ligament Injury (ACL Tear)

Frequency: in up to 69% of all patients undergoing arthroscopy; in up to 72% of acutely injured knees with hemarthrosis

Mechanism: twisting, valgus impaction + internal rotation, hyperextension of knee with foot planted (football) / lower leg forcibly externally rotated during knee flexion (fall backwards while skiing)

- pivot shift test (82–90% sensitive) = examiner applies valgus stress on internally rotated leg while flexing the knee; induced anterolateral rotary subluxation reduces spontaneously at 40° flexion with an audible "pop"
- "anterior drawer" sign (22–80% sensitive) = proximal tibia displaces anteriorly with the

knee flexed at 60°–90°

• Lachman test (77–99% sensitive) = same as "anterior drawer" sign with knee flexed at 10°–20°

Location: midsubstance of ligament / near femoral attachment (in adults) / avulsion of anterior intercondylar eminence or tibial spines (in children)

◊ If the ACL appears intact in one of the sagittal oblique sequences discordant findings in other sequences can be disregarded!

Site: intrasubstance tear near insertion of femoral condyle (frequently); bone avulsion (rarely)

√ loss of fiber continuity + abnormal fiber orientation on PD image

√ T2-hyperintense signal (= focal fluid collection / soft-tissue edema) replacing the tendon substance in acute tear

√ pseudomass (hematoma + torn fibers) in intercondylar notch near femoral attachment

√ concavity of anterior margin of ligament

√ nondisplaced avulsion fracture of tibial eminence in children (coronal T1WI)

Secondary signs (low sensitivity, high specificity):

√ anterior translation of tibia (= "anterior drawer" sign) by > 5 mm with respect to femur measured at midsagittal plane of lateral femoral condyle

√ "uncovering" of lateral meniscus = posterior displacement of posterior horn of lateral meniscus > 3.5 mm behind tibial plateau

√ bowed PCL ← increased laxity = angle between proximal + distal limbs of PCL < 105°

Associated signs:

› for anterolateral rotary instability (football, skiing):

√ bone bruise in lateral compartment (posterolateral tibia + terminal sulcus of lateral femoral condyle) in 40–90% on fat-suppressed T2WI

◊ ACL intact in 28% of adolescents with bone bruise

√ low-signal–intensity line surrounded by region of high-signal–intensity marrow edema in posterior aspect of lateral tibial plateau (= occult fracture) on STIR image

› for hyperextension injury:

√ bone contusion in anterior tibial plateau + femoral condyles

› varus stress with external rotation:

√ avulsion of joint capsule from lateral tibial rim (Segond fracture)

√ deepening of lateral femoral sulcus > 1.5 mm ← osteochondral impaction injury when femur strikes posterior tibial plateau

False-positive Dx:

(1) slice thickness / interslice gap too great

(2) adjacent fluid / synovial proliferation

(3) cruciate ganglion / synovial cyst

Associated injuries: meniscal tear (lateral > medial) in 65%

Rx: (1) conservative: strengthening of quadriceps muscle + brace for activities

(2) arthroscopic reconstruction with autograft (patellar tendon / combined semitendinosus and gracilis tendon) or allograft (cadaveric patellar / Achilles tendon)

Subacute ACL Tear

Definition: few weeks after injury

√ fibers better defined as hemorrhage + edema subside
√ change in fiber contour + angle of residual fragments

Chronic ACL Tear

Definition: months to years after injury

√ bridging fibrous scar within intercondylar notch (simulating an intact ligament with its low SI)
√ disorganized scar tissue instead of linear parallel fibers
√ major distal ACL fragment assumes a more horizontal orientation (= less steep than the roof of the intercondylar notch or Blumensaat line)
√ ACL may fuse to posterior cruciate ligament
√ complete absence of ligament

Partial ACL Tear *(15%)*

◊ Extremely difficult to diagnose! 40–50% of partial tears are missed on MR!
• positive Lachman test (in 12–30%)
√ MR primary signs positive for injury (in 33–43%)

Posterior Cruciate Ligament Injury (PCL)

Prevalence: 2–23% of all knee injuries

√ midsubstance of PCL most frequently involved (best seen on sagittal images)
√ bone avulsion from posterior tibial insertion (< 10%), best seen on lateral plain film

Mechanism:

(1) Direct blow to proximal anterior tibia with knee flexed (dashboard injury)
  √ midsubstance PCL tear
  √ injury to posterior joint capsule
  √ bone contusion at anterior tibial plateau + femoral condyles farther posteriorly
(2) Hyperextension of knee
  √ avulsion of tibial attachment of PCL (with preservation of PCL substance)
  √ ± ACL rupture
  √ bone contusion in anterior tibial plateau + anterior aspect of femoral condyles
(3) Severe ab- / adduction + rotational forces
  √ + injury to collateral ligaments

Associated with: coexistent ligamentous injury in 70%

joint effusion 64–65%
bone marrow injury 35–36%
medial meniscal tear 32–35%
lateral meniscal tear 28–30%
anterior cruciate ligament 27–38%
medial collateral ligament 20–23%
lateral collateral ligament 6–7%

◊ A PCL injury is isolated in only 30%!

• posterior tibial laxity
• difficult to evaluate arthroscopically unless ACL torn

DEEP MUSCULOAPONEUROTIC FIBROMATOSIS

= DESMOID TUMOR [desmos, *Greek* = band / tendon]
= AGGRESSIVE FIBROMATOSIS = DEEP FIBROMATOSIS
= MUSCULOAPONEUROTIC FIBROMATOSIS
= musculoaponeurotic mass characterized by fibrous soft-tissue proliferation disrupting adjacent muscle + soft-tissue planes

Frequency: 1.5–3.0% of all soft-tissue masses
Origin: connective tissue of muscle, fascia, aponeurosis
Genetics: trisomies on chromosomes 8 + 20 (in many cases)
Association: (a) sporadic
(b) familial polyposis, Gardner syndrome
Classification: according to location
Peak age: 3rd decade (range, puberty to 40 years)
Histo: elongated spindle-shaped cells of uniform appearance, separated by dense bands of collagen, infiltration of adjacent tissue (DDx: low-grade fibrosarcoma, reactive fibrosis)
Location: extraabdominal, abdominal wall, intraabdominal
• hormonally responsive + dependent on estrogen
Imaging appearance:
dependent on tissue composition (spindle cells, collagen, myxoid matrix) + vascularity; may change over time
CT:
√ well-circumscribed / ill-defined and infiltrating mass
√ isoattenuating to muscle (predominantly collagenous) / hypoattenuating (myxoid stroma)
√ striated / whorled appearance (alternating collagenous and myxoid stroma)
√ mild to moderate contrast enhancement during parenchymal phase ± delayed enhancement
MR:
(a) early-stage hypercellular and myxoid lesion
√ predominantly hyperintense lesion on T2WI
(b) mature collagenous lesion
√ decrease in signal intensity on T2WI
√ hypointense bands in 62% (= conglomeration of collagen bundles)
√ moderate to marked enhancement
Prognosis: rapid aggressive growth; 50% recurrence rate after local excision; spontaneous regression (rare); malignant transformation (rare)
DDx: (1) Malignant tumor: metastasis, soft-tissue sarcoma (fibro-, rhabdomyo-, synovio-, liposarcoma), malignant fibrous histiocytoma, lymphoma
(2) Benign tumor: neurofibroma, neuroma, leiomyoma, giant cell tumor of tendon sheath
(3) Acute hematoma

Abdominal Wall Fibromatosis

= Abdominal wall desmoid
= solitary slow-growing neoplasm characterized by its progressive, locally infiltrative, and

aggressive behavior

Frequency: similar to desmoid-type fibromatosis

◊ The most common abdominal wall soft-tissue neoplasm!

Cause: ? genetics; estrogenic hormones (← regression after menopause / oophorectomy); trauma + surgery (= **cicatricial fibromatosis** of cesarean section scar)

Associated with:

(1) Familial adenomatous polyposis

(2) Gardner syndrome

Peak age: 3rd decade; M÷F = 13÷87 esp. young woman of childbearing age

› during 1st year after childbirth

› during pregnancy

› with use of oral contraceptives

Path: solid firm mass with often infiltrative spiculated margin toward skeletal muscle and subcutis; positive for estrogen receptors (in 79%)

• palpable firm slowly growing deep-seated mass

Location: musculoaponeurosis of rectus abdominis / internal oblique muscle; occasionally external oblique m.

Average size: 3–7 cm in diameter

√ identical to desmoid-type fibromatosis

MR:

√ hypo- to isointense mass to muscle on T1WI

√ variable intensity on T2WI

√ infiltrative border

√ nonenhancing low-signal-intensity bands

√ "fascial tail" sign = linear extension along superficial fascia

CT:

√ ill-defined / well-circumscribed mass

√ iso- / hypoattenuating mass compared to muscle

√ ± enhancement

√ retraction, angulation, distortion of small / large bowel with mesenteric infiltration

US:

√ sharply defined + smoothly marginated mass of low / medium / high echogenicity

Prognosis: locally aggressive; 25–65% recurrence rate

Rx: local resection + radiotherapy, antiestrogen therapy

DDx: scar endometriosis

Intraabdominal Fibromatosis

Age: peak age in 3rd decade, 70% between 20 and 40 years of age; M÷F = 1÷3

Location: mesentery, retroperitoneum, pelvis

◊ Most common mesenteric primary tumor!

In 9–18% associated with: familial adenomatous polyposis (Gardner syndrome)

√ masslike with significant displacement of contiguous structures / infiltrative causing compressive encasement

Cx: compression / displacement of bowel / ureter; vascular occlusion and ischemia;

intestinal perforation

DDx: (1) Malignant neoplasm of the mesentery (lymphoma, metastasis, soft-tissue sarcoma, malignant fibrous histiocytoma)

(2) Inflammatory pseudotumor, extrapleural solitary fibrous tumor, GIST

Desmoid-type Fibromatosis

= AGGRESSIVE FIBROMATOSIS = MUSCULOAPONEUROTIC FIBROMATOSIS = EXTRAABDOMINAL DESMOID TUMOR

= common benign aggressively growing soft-tissue tumor arising from connective tissue of muscle, fascia, aponeurosis outside abdominal cavity of intermediate malignant potential

Frequency: 2–4÷1,000,000 per year

Peak age: 25–35 years (range, 2nd–4th decade); M÷F = 1÷1.8; more aggressive behavior in children than in adults

- painless soft-tissue mass with slow insidious growth
- decreased mobility, reduced joint motion
- neurologic complaints: numbness, tingling, sharp pain, motor weakness; history of trauma (30%)

Path: firm mass often with spiculated tumor margins infiltrating muscle + subcutaneous tissue

Histo: proliferation of uniform spindle-shaped fibroblasts → poorly defined fascicles within a collagenous stroma

Associated with: Gardner syndrome (1–2%)

Genetics: activation of b-catenin signaling pathway ← APC (adenomatous polyposis coli) gene mutation on long arm of chromosome 5q21-22 (in Gardner syndrome) or somatic b-catenin mutation

Location: shoulder + upper arm (28%), chest wall and paraspinal region (17%), thigh (12%), neck (8%), knee (7%), pelvis / buttock (6%), lower leg (5%), forearm / hand (5%), head (2%); synchronous multicentricity in same extremity (10–15%)

@ head & neck (7–27%): supraclavicular neck > face

Site: centered in an intermuscular location with rim of fat ("split-fat" sign)

Size: mostly 5–10 cm in diameter

◊ Imaging appearance depends on cellularity of lesion + amount of collagen and myxoid material within it

√ poorly circumscribed mass infiltrating surrounding soft tissues + fixation to underlying muscle / bone (often)

US:

√ poorly defined hypoechoic soft-tissue mass

√ ± posterior acoustic shadowing in large lesion

√ ± hypervascularity

CT:

√ homogeneous / heterogeneous attenuation

√ iso- / hyper- / hypodense compared to muscle

√ indistinct lesion margins (often)

√ variable degree of enhancement

MR:
√ poorly defined lesion with irregular margin (50%) ← invasion of fat / muscle
√ lobulated well-defined lesion (50%)
√ "fascial tail" sign = linear extension along fascial planes (83%)
√ slightly hyper- / iso- (90%) / hypointense relative to muscle on T1WI
√ hyperintense (hypercellular) / hyperintense with areas of low intensity (intermixed with fibrous components) / hypointense (hypocellular) on T2WI
√ heterogeneous texture ← linear + curvilinear strands of low SI on CEMR / T2WI (62–91%) ← collagen fibers
√ moderate to marked enhancement (90%)

@ Bone (6–37%)
√ extensive pressure erosion / cortical scalloping without extension into medullary canal
√ skeletal dysplasia of multicentric desmoid-type fibromatosis (19%):
√ Erlenmeyer flask deformity: polyostotic / on affected side only
√ cortical thickening, focal lucent lesions
√ bone islands, osseous excrescences
Bone scintigraphy:
√ increased uptake on blood flow + blood pool images
Angio:
√ marked vascular staining ← hypervascularity

@ Breast
• palpable firm / hard mass
• history of minor trauma / breast surgery
Location: pectoralis fascia
√ round / irregular noncalcified mass
√ indistinct / spiculated margins
√ retraction of pectoralis muscle, skin, nipple

Prognosis: 20–75% recurrence within 2 years after surgical excision depending on location + extent (up to 87% local recurrence in < 30 years of age; 20% recurrence rate in > 20 years of age)

Infantile Myofibromatosis / Myofibroma

= GENERALIZED HAMARTOMATOSIS = CONGENITAL MULTIPLE / GENERALIZED FIBROMATOSIS = MULTIPLE VASCULAR LEIOMYOMAS = DESMOFIBROMATOSIS = INFANTILE F / JUVENILE FIBROMATOSIS
= rare disorder characterized by proliferation of fibroblasts
Cause: unknown
Frequency: 22% of all myofibroblastic lesions in childhood
◊ Most common fibromatosis in childhood!
Path: well-marginated soft-tissue lesion with scarlike consistency ± infiltration of surrounding tissues
Size: 0.5–7.0 cm in diameter
Histo: spindle-shaped cells in short bundles and fascicles in periphery of lesion with features of both smooth muscle + fibroblasts; centrally hemangiopericytoma-like pattern with necrosis, hyalinization, calcification

Types: solitary÷multicentric form = 1÷2 to 4÷1

(1) Solitary lesion = **myofibroma**

Age: < 2 years of age; M > F

Histo: contractile myoid cells arranged around thin-walled blood vessels

Location (ordered in diminishing frequency):

› head & neck (⅓): scalp, forehead, orbit, oral cavity (tongue, mandible, maxilla, mastoid bone), parotid

› trunk > extremities

Site: skin muscle, SQ tissue (86%), bone (9%), GI tract (4%)

Prognosis: spontaneous regression in 100%; recurrence after surgical excision in 7–10%

(2) Multicentric disease (2–100 lesions) = **myofibromatosis**

Age: at birth (in 60%), < 2 years (in 89%); M < F

Location: lung (28%), heart (16%), GI tract (14%), pancreas (9%), liver (8%)

Site: skin (98%), subcutis (98%), muscle (98%), bone (57%), viscera (25–37%)

Prognosis: related to extent + location of visceral lesions with cardiopulmonary + GI involvement as harbingers of poor prognosis (death in 75–80%); spontaneous regression (33%)

• firm nontender painless nodules in skin, subcutis, muscle

• ± overlying scarring of skin with ulceration

@ Skeleton

Location: any bone may be involved; commonly in calvarium, femur, tibia, rib, pelvis, vertebral bodies; often symmetric

Site: metaphysis of long bones

Age: early infancy (usually not present at birth)

√ circumscribed eccentric lytic foci with smooth margins 0.5 –1.0 cm in size:

√ sparing of region immediately adjacent to epiphysis

√ well-defined with narrow zone of transition

√ osseous foci may increase in size and number

√ unusual osseous findings:

√ periosteal reaction, pathologic fracture

√ vertebra plana, kyphoscoliosis with posterior scalloping of vertebral bodies

√ with healing → little residual abnormality:

√ resolution of osteolysis

√ formation of sclerotic margin (initially no sclerosis)

√ ± mineralization of center

NUC (bone scan):

√ increased / little radiotracer uptake

DDx: (1) Langerhans cell histiocytosis (skin lesions)

(2) Neurofibromatosis (multiple masses)

(3) Osseous hemangiomas / lymphangiomatosis / lipomatosis

(4) Metastatic neuroblastoma

(5) Multiple nonossifying fibromas

(6) Enchondromatosis

(7) Hematogenous osteomyelitis (unusual organism)

(8) Fibrous dysplasia

@ Soft tissue

◊ Most common fibrous tumor in infants

√ round well- / ill-defined solid mass with central necrosis

√ central / peripheral solitary / multiple calcifications

√ prominent vascularity of skin lesions resembling hemangioma

US:

√ hypo- to isoechoic mass

√ thick peripheral wall / septa

√ anechoic / partially anechoic center

√ echogenic shadowing foci ← calcifications

CT:

√ attenuation similar to muscle / mildly increased

√ central area of low attenuation ± calcifications

√ peripheral enhancement

MR:

√ lesion isointense to muscle on T1WI:

√ mildly T1-hyperintense center of myofibroma

√ lesion hyperintense to muscle on T2WI

√ intense occasionally targetlike enhancement

DDx: (1) Neurofibromatosis

(2) Infantile fibrosarcoma, leiomyosarcoma

(3) Angiomatosis

@ Lung

√ interstitial fibrosis, reticulonodular infiltrates

√ discrete mass

√ generalized bronchopneumonia

@ GI tract

√ diffuse narrowing / multiple small filling defects

@ Orbit

Aggressive Infantile Fibromatosis

= childhood equivalent of deep fibromatosis

Age: first 2 years of life; rarely > 5 years of age; M > F

Histo: may mimic infantile fibrosarcoma

• firm nodular soft-tissue mass within skeletal muscle / fascia / periosteum

Location: head, neck (tongue, mandible, mastoid), shoulder, thigh, foot

DERMATOFIBROSARCOMA PROTUBERANS

= uncommon spindle cell tumor arising in dermis typically spreading into subcutaneous tissue + muscle

Frequency: 6% of all soft-tissue sarcomas

Age: mostly adolescence

Location: trunk (50%)

Site: classified as skin tumor (= cutaneous lesion)
CT:
√ well-defined nodular subcutaneous lesion without calcification
MR:
√ unmineralized small nodule / large mass
√ nonspecific signal intensity:
√ hypointense on T1WI
√ hyperintense relative to fat on T2WI
√ ± heterogeneous foci of hemorrhage, myxoid change, necrosis
√ linear extension along skin surface
√ moderate enhancement

DERMATOMYOSITIS

= most common inflammatory myopathy with diffuse nonsuppurative inflammation of striated muscle + skin
Cause: cell-mediated (type IV) autoimmune attack on striated muscle
Pathophysiology: damaged chondroitin sulfate no longer inhibits calcification
Path: atrophy of muscle bundles followed by edema and coagulation necrosis, fibrosis, calcification
Histo: mucoid degeneration with round cell infiltrates concentrated around blood vessels
Age: bimodal: 5–15 and 50–60 years; M÷F = 1÷2
• elevated muscle enzymes (creatinine kinase, aldolase)
• myositis-specific autoantibodies: anti-Jo-1
(a) anti-aminoacyl-tRNA synthetase
• arthritis, Raynaud phenomenon, fever, fatigue
• interstitial lung disease
Prognosis: requires prolonged treatment
(b) anti-Mi-2 antibodies:
• V-shaped chest rash (= shawl rash)
• cuticular overgrowth
Prognosis: good response to medication
(c) anti-signal recognition particle antibodies
• abrupt onset myositis ± heart involvement
@ Skeletal musculature
Location: thigh (vastus lateralis + intermedius m. with relative sparing of rectus + biceps femoris m.) > pelvic girdle > upper extremity > neck flexors > pharyngeal muscles
√ bilateral symmetric edema in pelvic + thigh muscles
√ fatty infiltration + muscle atrophy (over months to years)
√ sheetlike confluent calcifications in soft tissues of extremities (quadriceps, deltoid, calf muscles), elbows, knees, hands, abdominal wall, chest wall, axilla, inguinal region) in 75%
@ Skeleton
√ pointing + resorption of terminal tufts

√ rheumatoid-like arthritis (rare)
√ "floppy-thumb" sign
Cx: flexion contractures; soft-tissue ulceration

@ Chest
• aspiration pneumonia is the most common occurrence ← pharyngeal muscle weakness
• hypoventilation + respiratory failure ← respiratory muscle weakness
√ disseminated pulmonary infiltrates (reminiscent of scleroderma)
√ diaphragmatic elevation with reduced lung volumes + basilar atelectasis
√ interstitial fibrosis (5–30%), most severe at lung bases:
• may precede development of myositis
• associated with presence of anti-Jo-1 antibodies
Patterns: NSIP, cryptogenic organizing pneumonia, UIP, diffuse alveolar damage
√ fine reticular pattern progressing to coarse reticulonodular pattern + honeycombing
HRCT:
√ predominantly linear abnormalities + ground-glass attenuation
√ air-space consolidation in middle + lower lung zones with peribronchial + subpleural distribution

@ Myocardium
√ changes similar to those of skeletal muscle involvement

@ GI tract
• dysphagia ← progressive weakness of proximal striated m.
√ atony + dilatation of esophagus
√ atony of small intestines + colon

Clinical forms:
(1) ACUTE FORM = childhood-onset form
• fever, joint pain, lymphadenopathy, splenomegaly, subcutaneous edema
√ more severe dermatomyositis
Prognosis: death within a few months
(2) CHRONIC FORM = adult-onset form
= insidious onset with periods of spontaneous remission and relapse
• low-grade fever, muscular aches + pains, edema
• muscle weakness (1st symptom in 50%) ← active inflammation, necrosis, muscle atrophy with fatty replacement, steroid-induced myopathy
• skin erythema (1st symptom in 25%): **heliotrope rash** (= dusky blue-purple erythema of eyelids) with periorbital edema, **Gottron papules** (= raised scaly violaceous rash over knuckles, major joints and upper body)

Cx: increased prevalence of malignant neoplasms of lung, breast, prostate, ovary, GI tract, kidney
Dx: measurement of serum muscle enzyme concentration; electromyography; muscle biopsy (normal in up to 15%)

Polymyositis
= subacute myopathy with weakness of proximal muscles evolving over weeks / months without skin involvement
Age: 4th decade

DDx: dermatomyositis (involvement of skin)

DESMOPLASTIC FIBROMA

= INTRAOSSEOUS DESMOID TUMOR
= rare locally aggressive benign neoplasm of bone with borderline malignancy resembling soft-tissue desmoids / musculoaponeurotic fibromatosis
Prevalence: 107 cases in world literature
Histo: intracellular collagenous material in fibroblasts with small nuclei
Age: mean of 21 years (range, 15 months to 75 years); in 90% < 30 years; M÷F = 1÷1
• slowly progressive pain + local tenderness; palpable mass
Location: mandible (26%), ilium (14%), > 50% in long bones (femur [14%], humerus [11%], radius [9%], tibia [7%], clavicle), scapula, vertebra, calcaneus
Site: central meta- / diaphyseal (if growth plate open); may extend into epiphysis with subarticular location (if growth plate closed)
√ geographic (96%) / moth-eaten (4%) bone destruction without matrix mineralization
√ narrow (96%) / poorly defined (4%) zone of transition
√ no marginal sclerosis (94%)
√ residual columns of bone with "pseudotrabeculae" are CLASSIC (91%)
√ bone expansion (89%); may grow to massive size (simulating aneurysmal bone cyst / metastatic renal cell carcinoma)
√ breach of cortex + soft-tissue mass (29%)
Cx: pathologic fracture (9%)
Prognosis: 52% rate of local recurrence
Rx: wide excision
DDx: (1) Giant cell tumor (round rather than oval, may extend into epiphysis + subchondral bone plate)
(2) Fibrous dysplasia (occupies longer bone, contains mineralized matrix, often with sclerotic rim)
(3) Aneurysmal bone cyst (eccentric blowout appearance rather than fusiform)
(4) Chondromyxoid fibroma (eccentric with delicate marginal sclerosis + scalloped border)

DEVELOPMENTAL DYSPLASIA OF HIP (DDH)

= CONGENITAL DYSPLASIA OF HIP
= deformity of acetabulum ← disrupted relationship between femoral head and acetabulum
◊ Acetabular dysplasia (without femoral subluxation / dislocation) can be determined only by imaging!
Etiology:
A. Late intrauterine event (98%)
(a) mechanical:
– oligohydramnios (restricted space in utero)
– firstborn (tight maternal musculature)
◊ in 60% of patients with DDH
– breech position (hip hyperflexion results in shortening of iliopsoas muscle; L÷R =

4÷1)
◊ in 30–50% of patients with DDH
◊ only 2–4% of deliveries are breech

(b) physiologic (females are more sensitive to):
– maternal estrogen (not inactivated by immature fetal liver) blocks cross-linkage of collagen fibrils
– pregnancy hormone relaxin

B. Teratologic (2%) ← neuromuscular disorder (myelodysplasia, arthrogryposis) occurring during 12th–18th week GA

C. Postnatal onset (< 1%)

Prevalence: 0.15% of neonates (Australia 1%, Netherlands 3.7%, Poland 3.9%, Israel 5.9%, Austria 6.6%, Norway 16.9%)

Age: most dislocations probably occur after birth;
M÷F = 1÷4–1÷8; Caucasians > Blacks

Increased risk:

(1) infants born in frank breech position (25%; risk of breech÷vertex = 6–8÷1)
(2) congenital torticollis (10–20%)
(3) skull-molding deformities; scoliosis; generalized joint laxity (Larsen syndrome, Ehlers-Danlos syndrome, Down syndrome [5%]); neuromuscular disorders (eg, myelodysplasia, spina bifida, sacral agenesis, arthrogryposis multiplex)
(4) family history of DDH (6–20%): 6% risk for subsequent sibling of normal parents, 36% risk for subsequent sibling of one affected parent; 12% risk for patient's own children
(5) foot deformities [metatarsus adductus, clubfoot (2%)]
(6) neonatal hyperextension of hips: swaddling of infants in hip extension / strapping to cradle board

Anatomy: acetabulum has a small bony component + a large cartilaginous component at birth; acetabulum highly susceptible for modeling within first 6 weeks of age + less susceptible > 16 weeks of age

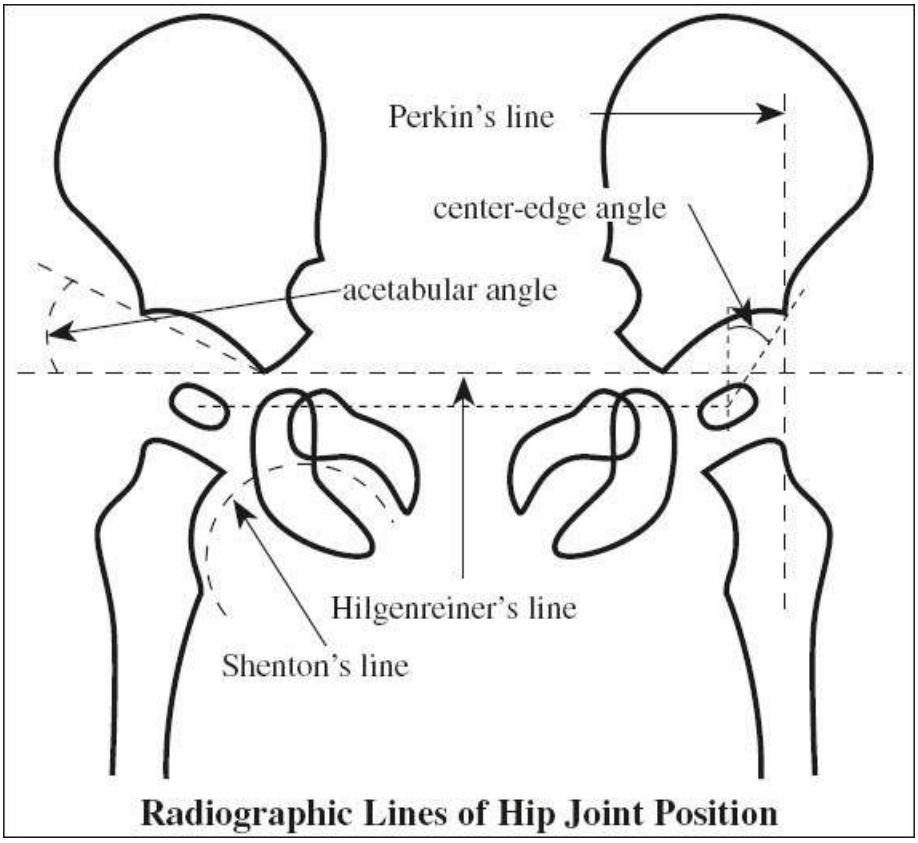
Classification:

1. Normal hip
2. Lax = subluxable hip
   ◊ Subluxability up to 6 mm is normal in newborns (still under influence of maternal hormones); decreasing to 3 mm by 2nd day of life
3. Concentric dislocatable unstable hip
   = joint laxity allowing nondisplaced femoral head to become subluxed / dislocated under stress
   Prevalence: 0.25–0.85% of all newborn infants (⅔ are firstborns)
   • Barlow positive
   √ slight increase in femoral anteversion
   √ mild marginal abnormalities in acetabular cartilage
   √ early labral eversion
   Prognosis: 60% will become stable after 1 week; 88% will become stable by age of 2 months
4. Decentered subluxed hip
   = femoral head shallow in location

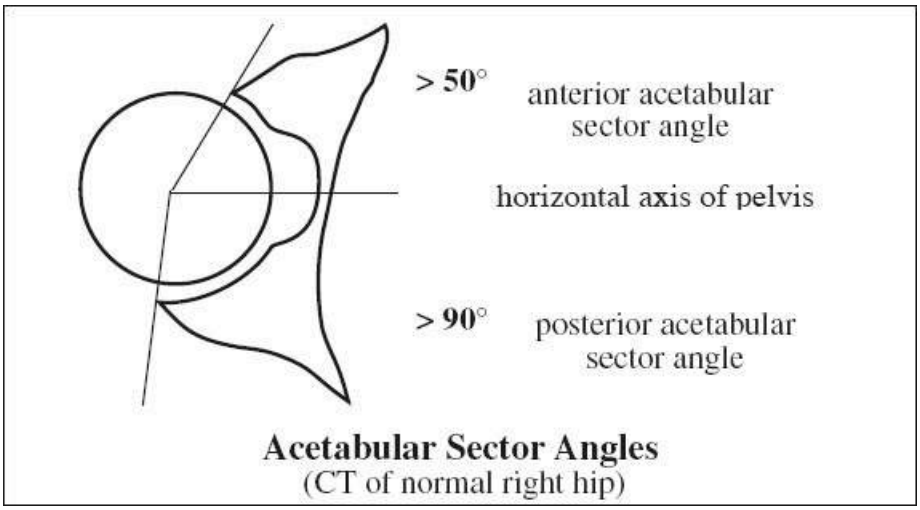
√ loss of femoral head sphericity
√ increased femoral anteversion
√ early labral inversion
√ shallow acetabulum

5. Eccentric dislocated hip
   = femoral head frankly displaced out of acetabulum
   (a) reducible = Ortolani positive
   (b) irreducible = Ortolani negative
   √ accentuated flattening of femoral head
   √ shallow acetabulum
   √ limbus formation (= inward growth + hypertrophy of labrum)

- "hip click" = usually result of joint capsule and tendon stretching + snapping (often confused with "hip clunk")
- positive examination result (up to 3 months of age):
  - positive Ortolani reduction test = reduction of dislocated femoral head into the acetabulum by lifting the flexed thigh + pushing the greater trochanter anteriorly; may be associated with audible "clunk"
  - positive Barlow dislocation test = posterior displacement of nondislocated proximal femur by progressive adduction with downward pressure (piston maneuver) on flexed hips and knees associated with audible "clunk"
- warning signs on physical examination:



Radiographic Lines of Hip Joint Position



Acetabular Sector Angles
(CT of normal right hip)

- limited hip abduction on affected side
- shortening of thigh on affected side:
  - asymmetric thigh / buttock creases
- Allis sign = Galeazzi sign = affected knee is lower with knees bent in supine position
- Trendelenburg test = visible drooping + shortening on dislocated side with child standing on both feet, then one foot

Location: left÷right÷bilateral = 11÷1÷4

Radiologic lines:

1. Line of Hilgenreiner
   = line connecting superolateral margins of triradiate cartilage
2. Acetabular angle / index
   = slope of acetabular roof = angle that lies between Hilgenreiner's line and a line drawn from most superolateral ossified edge of acetabulum to superolateral margin of triradiate cartilage
3. Perkin line
   = vertical line to Hilgenreiner's line through the lateral rim of acetabulum
4. Shenton curved line
   = arc formed by inferior surface of superior pubic ramus (= top of obturator foramen) + medial surface of proximal femoral metaphysis to level of lesser trochanter
   √ disruption of line (DDx: coxa valga)
5. Center-edge angle of Wiberg = angle subtended by one line drawn from the acetabular edge to center of femoral head + second line perpendicular to line connecting centers of femoral heads
   √ < 25° suggests femoral head instability

AP pelvic radiograph: > 4– 6 months of age (von Rosen view = legs abducted 45° + thighs internally rotated)

◊ Not reliable first 3 months of life!

√ proximal + lateral migration of femoral neck:

√ eccentric position of proximal femoral epiphysis (position estimated by a circle drawn with a diameter equivalent to width of femoral neck)

√ interrupted discontinuous arc of Shenton's line

√ line drawn along axis of femoral shaft will not pass through upper edge of acetabulum but intersect the anterior-superior iliac spine (during Barlow maneuver)
√ apex of metaphysis lateral to edge of acetabulum
√ femoral shaft above horizontal line drawn through the Y-synchondrosis
√ unilateral shortening of vertical distance from femoral ossific nucleus / femoral metaphysis to Hilgenreiner's line
√ femoral ossific nucleus / medial beak of femoral metaphysis outside inner lower quadrant of coordinates established by Hilgenreiner's + Perkin's lines

√ acetabular dysplasia = shallow incompletely developed acetabulum:
√ acetabular angle > 30° strongly suggests dysplasia
√ development of false acetabulum
√ delayed ossification of femoral epiphysis (usually evident by 4 months (range, 2nd–8th months) of life

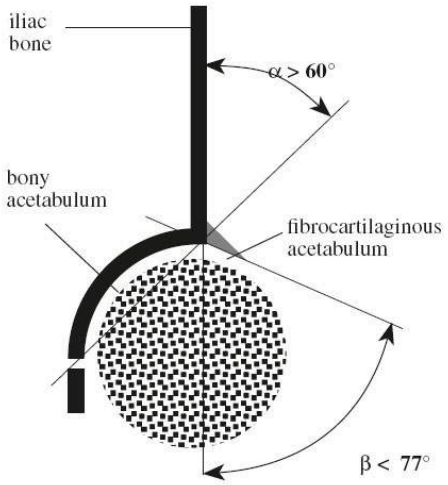
US (practical only):

Screening period: > 2 weeks and up to 4–6 months of age

◊ Instability often resolves spontaneously by 2 weeks of age!
◊ Examination impractical beyond 4–6 months of age

(1) static evaluation (popularized in Europe by Graf)
(2) dynamic evaluation (popularized in USA by Harcke)

@ Relationship of femoral head & acetabulum
√ femoral head position at rest in neutral position
√ hip instability under motion + stress maneuvers
√ dislocated (= eccentric) hip can be reduced (Ortolani positive):
√ hypoechoic femoral head not centered over triradiate cartilage between pubis + ischium (on transverse view)
√ increased amount of soft-tissue echoes ("pulvinar") between femoral head and acetabulum
√ cartilaginous acetabular labrum interposed between head and acetabulum (inverted labrum)



Coronal View of Left Hip

Sonographic Hip Types

Type	*Description*	*α Angle*	*β Angle*
1	mature hip	> 60°	
1A	narrow cartilaginous roof		< 55°
1B	wide cartilaginous roof		> 55°
2	deficient bony acetabulum		
2A	physiologic < 3 months	50–59°	
2B	delayed ossification > 3 months		
2C	concentric but unstable; critical range	43–49°	70–77°
2D	decentered = subluxed		> 77°
3	eccentric = dislocated	< 43°	
4	severe dysplasia with inverted labrum		

α angle = angle between straight lateral edge of ilium + bony acetabular margin (on coronal view); determines sonographic hip type

β angle = angle between straight lateral edge of ilium + fibrocartilaginous acetabulum; determines nuances of sonographic hip type

√ posterior + superior dislocation of head against ilium

√ "equator" sign = < 50% of femoral head lies medial to line drawn along iliac bone (on coronal view): > 58% coverage is normal; 58–33% coverage is indeterminate; < 33% coverage is abnormal

@ Femoral head

√ disparity in size of directly visualized unossified femoral head

√ disparity in presence + size of ossific nucleus

@ Acetabulum

√ delayed ossification of acetabular corner

√ wavy contour of bony acetabulum with only slight curvature

√ abnormally acute alpha angle (= angle between straight lateral edge of ilium + bony acetabular margin)

√ α > 60° in an infant is normal

√ α 55–60° can be normal < 4 weeks of age

√ α < 55° occurs in an immature acetabulum

◊ 4°–6° interobserver variation!

Prognosis: alpha-angle < 50° at birth / 50°–59° after 3 months indicates significant risk for dislocation without treatment; follow-up at 4-week intervals are recommended

CT (during cast treatment / attempted closed reduction):

√ sector angle = angle between line drawn from center of femoral head to acetabular rim + horizontal axis of pelvis (= reflects acetabular support)

√ anterior acetabular sector angle < 50°

√ posterior acetabular sector angle < 90°

Cx: (1) Degenerative joint disease

(2) Avascular necrosis of femoral head

Obstacles to reduction:

(1) Intraarticular obstacle to reduction

(a) pulvinar = fibrofatty tissue at apex of acetabulum
(b) hypertrophy of ligamentum teres
(c) labral hypertrophy / inversion

(2) Extraarticular obstacle to reduction (iliopsoas tendon impingement on anterior joint capsule with infolding of joint capsule)

Prognosis: 78% of hips become spontaneously normal by 4th week + 90% by 9th week; > 90% of abnormalities identified by ultrasound resolve spontaneously

Rx: (1) Flexion-abduction-external rotation brace (Pavlik harness) / splint / spica cast

(2) Femoral varus osteotomy

(3) Pelvic (Salter) / acetabular rotation

(4) Increase in acetabular depth (Pemberton)

(5) Medialization of femoral head (Chiari)

DIABETES MELLITUS

= multisystem disorder

Prevalence: 26 million (= 8.3% of population) in USA in 2010

Path: macro- and microvascular disease; neuropathy; increased susceptibility to infection

Sequelae: neuropathy, nephropathy, retinopathy

1. Genitourinary diabetes mellitus
2. Spinal disorders in diabetes
   (a) Dialysis-associated spondyloarthropathy
   (b) Pyogenic spondylodiskitis
   (c) Neuropathic spine
3. Musculoskeletal diabetes

Diabetic Foot

Diabetic neuropathy: 35% during lifetime

Neuropathic Joint of Diabetic Foot

= most common site of neuropathic joint in diabetes

Pathophysiology:

repetitive stress on insensitive foot → bone + joint disruption, valgus / varus deformity, joint instability → joint degeneration, subluxation, joint destruction

Prevalence: 5% of diabetic patients

Age: most commonly during 5th–7th decade

• grossly deformed usually painfree foot

Location: Lisfranc joint (60%), metatarsophalangeal joint (30%), tibiotalar joint (10%)

NUC:

√ labeled WBC accumulation in noninfected joint due to

(a) ↑ cytokine activity → conversion of yellow into red marrow (not due to infection)

(b) fracture → conversion of yellow into red marrow

Diabetic Foot Ulcer (mal perforans)

= focal skin interruption with elevated margins and associated soft-tissue defect

Cause: breakdown of callus / minor skin trauma (eg, toenail cutting)

Prevalence: 5% of US population

Lifetime risk among diabetics: 25%

Location:

@ typical sites: beneath heads of 1st + 5th metatarsal bones, tip of 1st toe, calcaneus, malleoli

@ additional sites due to neuropathic foot deformity: cuboid, midfoot (from arch collapse), dorsum of claw toe, heel

• poor healing ← vascular disease

• ESR > 70 mm/h (highly specific, 28% sensitive)

• bone contact during probing of ulcer (89% PPV, 56% NPV)

MR (in > 90% of diabetic osteomyelitis):

√ interruption of cutaneous signal (low PPV; higher PPV if ulcer > 2 cm^2 and > 3 mm

deep)= **ulcer**:
√ with low SI on T1WI + high SI on T2WI + intense peripheral enhancement (= **granulation tissue**)
√ reticulation of fat (of high T2 + intermediate T1 signal intensity) in area of soft-tissue swelling:
√ without enhancement = **edema**
√ with enhancement = **cellulitis**
√ focal ill-defined vaguely enhancing soft-tissue mass effect of low SI on T1WI + intermediate to high SI on T2WI replacing subcutaneous fat (= **phlegmon**)
√ focal fluid signal intensity with rimlike enhancement (= **abscess**)
√ sharply demarcated nonenhancing area of devitalized tissue ± peripheral enhancement = **dry gangrene**:
√ + multiple small foci of gas distributed along fascial planes displaying blooming artifact on T2 and GRE images = **wet gangrene**
√ thin linear soft-tissue signal with "tram-track" pattern of enhancing margins (high on T2WI) = **sinus tract**

Diabetic Osteomyelitis of Foot

Pathophysiology: pressure points → callus → ulceration → soft-tissue infection → osteomyelitis

X-ray (lags behind by 10–20 days):
◊ Repeat radiographs after 2–4 weeks!
√ bone destruction
√ periostitis
√ soft-tissue gas

NUC (80% accuracy for labeled leukocytes)

MR (modality of choice; 90% sensitive, 83% specific):
(a) primary osseous signs:
√ low marrow SI on T1WI + high marrow SI on T2WI (= bone marrow edema immediately adjacent to a soft-tissue infection / ulcer)
DDx: reactive osteitis (hyperintense on T2WI but not hypointense on T1WI) ← adjacent cortical (not medullary) / soft-tissue infection
√ marrow enhancement = infected viable tissue
◊ Estimated GFR should be > 30 mL/min before administering contrast medium!
√ ± cortical interruption / destruction
(b) secondary osseous signs:
√ periostitis = linear edema / enhancement along outer cortical margin
√ low-SI line (= calcified periosteum) separated from bone by high-SI layer (= fluid)
(c) secondary soft-tissue signs (in > 90%):
√ redistribution of fat away from planta of foot
√ **skin callus** = focal infiltration / mass within subcutaneous fat:
√ low SI on T1WI + enhancement
√ low to intermediate SI on T2WI
√ ± **adventitial bursitis** = thin flat fluid collection over osseous prominence with

preserved surrounding fat (DDx to abscess)

Location: same as for ulcers

√ tracking of ulcer / sinus track down to bone

Cx:

(1) Devitalized tissue without infection

√ focal often triangular sharply demarcated nonenhancing area of variable SI:

√ central tissue of usually high SI on T2WI + enhancing marginal zone = **dry gangrene**

√ multiple small foci of gas distributed along fascial planes displaying blooming artifact on T2WI + gradient-echo images = **wet gangrene**

(2) Bone infarct / necrosis

√ sharply demarcated nonenhancing marrow

(3) Spread of infection to foot compartments: tendon (tenosynovitis), joint (= septic arthritis), bone (= osteomyelitis)

Prognosis: 39–80% mortality rate at 5 years after diabetes-related amputation of lower extremity

DDx: Neuropathic osteoarthropathy (dislocation, disorganizaton, debris, destruction, density preserved, mildly symptomatic, joint effusion, multiple joints involved, marrow edema, periarticular enhancement; more common in ankle / Lisfranc / Chopart joints)

Diabetic Muscle Disorders

Diabetic Muscle Ischemia

= Diabetic muscle infarction / myonecrosis

Predisposed: long-standing poorly controlled diabetes

Path: fibrinous occlusion of arterioles + capillaries; muscle fiber necrosis + edema

Location: thigh, calf

Site: multiple noncontiguous foci of muscle involvement

- abrupt onset of severe pain + swelling
- palpable painful mass; NO leukocytosis / fever!

MRI:

√ muscle enlargement

√ edema of muscle + fascia

√ muscle enhancement + central nonenhancing region

Rx: glycemic control, analgesics, antiplatelet therapy

Prognosis: typically self-limited disorder responding to conservative therapy

DDx: infectious / inflammatory myositis, deep vein thrombosis, compartment syndrome

Diabetic Infectious Myositis

Cause: hematogenous spread of bacteria ← immune dysfunction in diabetic patients

- fever + leukocytosis with left shift, bacteremia

√ smooth-walled intramuscular abscess

√ rimlike enhancement

Rx: antibiotics, drainage

Diabetic Inflammatory Myositis

Cause: dermatomyositis, polymyositis, inclusion body myositis

• insidious gradually progressive proximal muscle weakness

Location: muscles in pelvis + thigh

√ bilateral symmetric edema

Dx: MRI-directed biopsy of affected muscle

Diabetic Muscle Denervation

Location: intrinsic muscles of foot (usually)

√ peripheral nerve distribution (!)

A. SUBACUTE

√ subacute T2 signal hyperintensity of affected muscle

√ maintained normal SI on T1WI

B. CHRONIC

√ reduced bulk + fatty infiltration of muscle on T1WI

DDx: diabetic muscle ischemia (fascial edema)

Diabetic Neuropathic (Charcot) Osteoarthropathy

Frequency: 1.4% of diabetics

Cause: repetitive trauma to insensate joint + autonomic dysfunction of blood flow

Pathophysiology: bone hyperemia → bone resorption → bone weakening; localized inflammation → bone destruction → joint subluxation → dislocation → foot deformity

Location: tarsometatarsal, subtalar, intertarsal, ankle joints

Eichenholtz classification:

stage 1: osteopenia, periarticular fragmentation, fracture, joint laxity with subluxation, capsular distension
• swollen erythematous foot

stage 2: absorption of bone debris, osseous fusion / osteosclerosis
• reduction in redness + warmth

stage 3: reconstruction + remodeling ± ankylosis of bone fragments, fixed rocker-bottom deformity
• absence of inflammation

NUC:

√ positive findings on blood-flow + blood-pool + delayed phase of 3-phase bone scan

√ combined leukocyte-bone marrow scintigraphy (procedure of choice) to separate from superimposed infection

MRI:

(a) acute

√ extensive soft-tissue edema

√ multiple foci of bone marrow + subchondral edema

√ enhancement far into medullary cavity

√ periarticular enhancement

√ subchondral cysts, articular erosions, joint effusion

(b) chronic

√ less inflammation + less enhancement
√ low marrow signal intensity (bone sclerosis)
√ bone debris, intraarticular bodies, ankylosis
√ joint subluxation + dislocation ← subchondral collapse

Cx: ulcers of midfoot → cuboid osteomyelitis

DIASTROPHIC DYSPLASIA

= DIASTROPHIC DWARFISM = EPIPHYSEAL DYSOSTOSIS

= severe rhizomelic dwarfism ← generalized disorder of cartilage followed by fibrous scars + ossifications

Genetics: autosomal recessive mutations in diastrophic dysplasia sulfate transporter gene located on chromosome 5q32–q33.1

Pathophysiology: disturbed sulfate transport → undersulfated proteoglycans in cartilage matrix

• diastrophic = "twisted" habitus; normal intellectual development
• "cauliflower ear" = ear deformity from inflammation of pinna
• laryngomalacia; lax + rigid joints with contractures

√ cleft palate (25%) + micrognathia

@ Axial skeleton
- √ cervical spina bifida occulta
- √ hypoplasia of odontoid
- √ severe progressive thoracolumbar kyphoscoliosis (not present at birth) + cervical kyphosis
- √ narrowed interpedicular space in lumbar spine
- √ short + broad bony pelvis
- √ posterior tilt of sacrum

@ Extremities
- √ shortening + metaphyseal widening of tubular bones
- √ severe micromelia (predominantly rhizomelic = humerus + femur shorter than distal long bones):
  - √ short and broad femoral neck
  - √ coxa vara (common)
- √ crescent-shaped flattened epiphysis (= retardation of epiphyseal ossification) with invagination of ossification centers into distal ends of femora
- √ multiple flexion contractures (notably of major joints)
- √ dislocation of one / more large joints (hip, elbow); lateral dislocation of patella
- √ clubfoot = severe talipes equinovarus:
  - √ medially bowed metatarsals + abduction of great toes
- √ deformity and shortening of metacarpals + phalanges:
  - √ ulnar deviation of hands
  - √ oval + hypoplastic 1st metacarpal bone + abducted proximally positioned thumb = "hitchhiker's thumb" (CHARACTERISTIC)
  - √ bizarre carpal bones with supernumerary centers
  - √ widely spaced fingers

OB-US:
√ proportionately shortened long bones
√ abducted / hitchhiker thumb
√ clubfeet
√ multiple joint flexion contractures
√ abnormal spinal curvature = scoliosis

Prognosis: death in infancy ← abnormal softening of tracheal cartilage

DIFFUSE IDIOPATHIC SKELETAL HYPEROSTOSIS

= DISH = FORESTIER DISEASE = ANKYLOSING HYPEROSTOSIS
= common ossifying diathesis characterized by bone proliferation at sites of tendinous + ligamentous attachment (enthesis)

Etiology:
(1) may be caused by altered vitamin A metabolism (elevated plasma levels of unbound retinol)
(2) long-term ingestion of retinoid derivatives for treatment of acne (eg, Accutane®); ? hypertrophic variant of spondylosis deformans

Age: > 50 years; M÷F = 3÷1

• pain, tenderness in extraspinal locations
• restricted motion of vertebral column
• hyperglycemia; positive HLA-B27 in 34%

√ increased incidence of hyperostosis frontalis interna

@ Spine
Location: middle + lower thoracic > lower cervical > entire lumbar spine
√ flowing ossification of at least 4 contiguous vertebral bodies:
√ osteophytes located anteriorly + laterally on right side (not on left because of aortic pulsations)
√ osteophytes largest at level of intervertebral disk
√ radiolucency beneath deposited bone
√ disk spaces well preserved, no apophyseal ankylosis, no sacroiliitis

@ Pelvis
√ bridge across superior aspect of symphysis pubis
√ ossification of iliolumbar + sacrotuberous + sacroiliac ligaments (high probability for presence of spinal DISH, DDx: fluorosis)
√ "whiskering" at iliac crest, ischial tuberosity, trochanters
√ broad osteophytes at lateral acetabular edge, inferior portions of sacroiliac joints

@ Extremities
√ big heel spurs (on plantar + posterior surface of calcaneus)
√ spur of olecranon process of ulna
√ spur on anterior surface of patella
√ ossification of coracoclavicular ligament, patellar ligament, tibial tuberosity, interosseous membranes

Cx: postoperative heterotopic bone formation (hip)

DDx: (1) Fluorosis (increased skeletal density)

(2) Acromegaly (posterior scalloping, skull features)

(3) Hypoparathyroidism

(4) X-linked hypophosphatemic vitamin D–resistant rickets

(5) Ankylosing spondylitis (squaring of vertebral bodies, coarser syndesmophytes, sacroiliitis, apophyseal alteration)

(6) Intervertebral osteochondrosis (vacuum phenomenon, vertebral body marginal sclerosis, decreased intervertebral disk height)

DISLOCATION

Hip Dislocation

Frequency: 5% of all dislocations

A. POSTERIOR HIP DISLOCATION (80–85%)

Mechanism: classical dashboard injury (= flexed knee strikes dashboard)

Associated with: fractures of posterior rim of acetabulum, femoral head

- adducted lower extremity flexed at hip

B. ANTERIOR HIP DISLOCATION (5–10%)

Mechanism: forced abduction + external rotation

Associated with: fractures of acetabular rim, greater trochanter, femoral neck, femoral head (characteristic depression on posterosuperior and lateral portion)

Subtypes: 1. anterior obturator dislocation
2. superoanterior / pubic hip dislocation

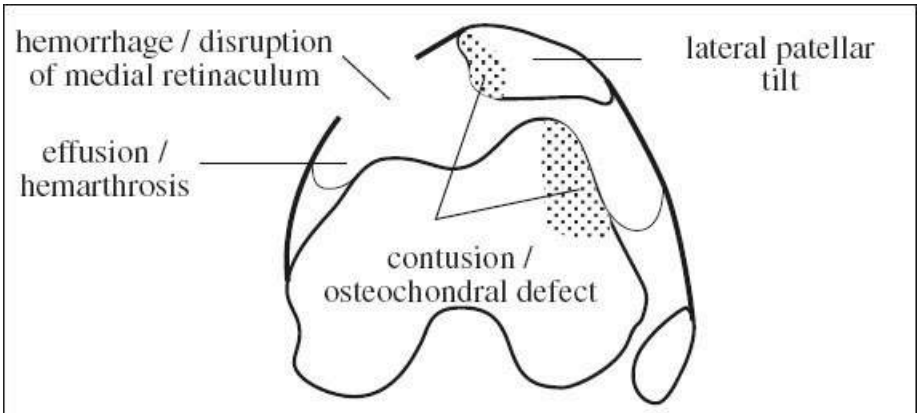
- lower extremity in external rotation

√ prominent lesser trochanter

√ obturator position of femoral head

C. CENTRAL ACETABULAR FRACTURE-DISLOCATION

Mechanism: force applied to lateral side of trochanter



MR Imaging Signs of Patellar Dislocation

Patellar Dislocation

= TRANSIENT LATERAL PATELLAR DISLOCATION

Frequency: 2–3% of all knee injuries

Mechanism: during attempt to slow forward motion while pivoting medially on a planted foot; internal rotation of femur on fixed tibia while knee is flexed + quadriceps contraction produces a net lateral force; direct blow (rare)

At risk: patellar dysplasia (with flattened articular surface); shallow trochlear groove of femur; passive lateral hypermobility of patella; dysplastic distal ⅓ of vastus medialis obliquus muscle; nail-patella syndrome

Associated with: medial meniscal tear / major ligamentous injury in 31%

Age: 13–20 years (young physically active person); M < F

• 50–75% not clinically diagnosed initially ← self-reduction!

√ lateral patellar tilt

√ hemarthrosis (most common cause of hemarthrosis in young conscripts)

√ concave impaction deformity of inferomedial patella (highly specific for prior patellar dislocation)

√ medial parapatellar ossification ← chronic instability with repetitive stress to medial patellofemoral ligament

MR:

√ "kissing" bone contusion / microfracture

√ osteochondral injury of anterolateral femoral condyle + medial patellar facet (90% sensitive):

√ intraarticular bodies (= avulsed osteochondral fragments of patella or lateral femoral condyle)

√ increased SI with sprain / disruption / avulsion of medial patellar retinaculum + medial patellofemoral ligament + medial patellotibial lig.

√ edema / hemorrhage within ± elevated vastus medialis obliquus muscle

√ knee joint effusion = fluid depth > 4 mm in suprapatellar recess (midline SAG image) or > 10 mm in lateral recess (on lateral SAG image):

√ hemarthros with fluid-fluid level (= sedimentation of blood components with low / intermediate T2 signal)

Rx: (1) Temporary immobilization + rehabilitation: successful in 75%

(2) Surgery: fixation of osteochondral fragments if > 1 cm^2, medial capsule repair, lateral retinacular release, vastus medialis et lateralis rearrangement, medial retinaculum reefing

Shoulder Dislocation

Sternoclavicular Dislocation *(3%)*

Posterior Sternoclavicular Dislocation

= posterior displacement of head of clavicle

Cause: blow to shoulder / medial clavicle

CECT confirms posterior sternoclavicular dislocation and may also disclose associated vascular injury.

Cx: injury to mediastinal blood vessels, trachea, esophagus

Anterior Sternoclavicular Dislocation

= anterior displacement of head of clavicle (more common but less serious type)

Cause: anterior blow to shoulder
• protruding clavicular head can be palpated
Cx: chronic pain, ankylosis, deformity
Rx: conservative therapy

Acromioclavicular Dislocation *(12%)*

Grade 1 (strain)
= stretching / partial tearing of acromioclavicular ligament fibers
√ soft-tissue swelling
√ stable AC joint without joint widening

Grade 2 (subluxation)
= disruption of acromioclavicular ligament + strain of coracoclavicular ligament
√ elevation of clavicle of < 100% of shaft width (weight-bearing!)
√ widening of AC joint

Grade 3 (superior dislocation)
= disruption of acromioclavicular + coracoclavicular ligg.
√ widening of AC joint
√ elevation of clavicle > 100% of shaft width

Grade 4 (posterior dislocation)
√ posterior position of clavicle with respect to acromion

Grade 5 (fascial injury)
√ penetration of clavicle through deltotrapezial fascia

Grade 6 (inferior dislocation)
√ inferior position of clavicle with respect to acromion

Glenohumeral Dislocation *(85%)*

◊ Glenohumeral joint dislocations make up > 50% of all dislocations!

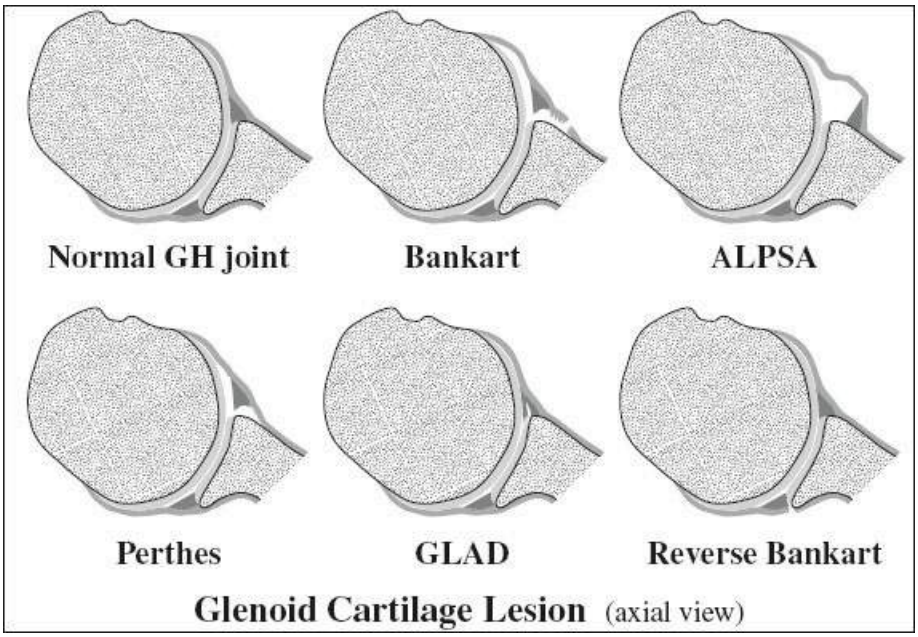
ANTERIOR / SUBCORACOID SHOULDER DISLOCATION

(85–95–98% of all shoulder dislocations)
Prevalence: up to 2% in general population
Types: subcoracoid, subglenoid, subclavicular, intrathoracic
Mechanism: external rotation + abduction (fall on outstretched arm); direct posterior blow in contact sport / forced ABER position)
Age: in younger individuals in their teens

(1) **Bankart lesion** = anterior capsulolabral avulsion
[Arthur Sydney Blundell Bankart (1879–1951), British orthopedic surgeon]
= detachment of glenoid labrum and joint capsule from anterior glenoid rim during anterior shoulder dislocation
√ detachment of anterior inferior glenohumeral labroligamentous complex (IGHLC = anterior-inferior glenoid labrum including labral insertion of inferior glenoid ligament) from glenoid at 3 to 6 o'clock position (= cartilaginous Bankart)
√ lifted disrupted scapular periosteum
√ labrum floats in anterior joint space

(a) Soft Bankart
√ no bony avulsion

(b) Osseous Bankart
√ fracture of anterior rim of glenoid



Shoulder instability increases with increasing size of the Bankart fragment. The redislocation rate is higher when the fragment involves > 20–25% of the glenoid surface area. A concomitant Hill-Sachs lesion reduces stability even further.

May be associated with:
√ fracture of greater tuberosity (15–35%)
√ fracture of coracoid process (3–13%)
√ **Hill-Sachs defect** / deformity (25–50–81%)
= depression / impacted fracture of posterolateral surface of humeral head at / above level of coracoid process ← impaction against anterior edge of glenoid rim in subglenoid type
[Harold Arthur Hill (1901–1973) and Maurice David Sachs (1909–1987), radiologists in San Francisco]

(2) **Perthes lesion** (variant of Bankart)
◊ easily overlooked on MR / arthroscopy → best detected in ABER position with traction on IGHL
√ labrum separated from articular cartilage
√ scapular periosteum stripped medially but with intact periosteal sleeve
√ nondisplaced avulsed labrum (DDx to ALPSA)

(3) **Glenoid Labrum Articular Disruption** (GLAD)
= combination of labral tear + cartilage defect
√ complete avulsion of anteroinferior glenoid labrum
√ small fragment of articular cartilage also detached
◊ chondral flaps best visualized on MR arthrogram

(4) **Humeral Avulsion of the Glenohumeral Ligament**

(HAGL) = failure at humeral attachment site
Prevalence: 52% in acute trauma; 2–9% of anterior glenohumeral instabilities
Age: 28 (range, 12–54) years; M÷F = 92÷8
√ "J / reversed J" sign (for RT / LT shoulder)
= detached end of anterior / posterior band of IGHL that falls inferiorly away from neck of humerus
√ extravasation of joint effusion / contrast material at the humeral insertion of disrupted capsule
Bony HAGL
√ avulsion of humeral cortex along with IGHL

(5) **Anterior Labroligamentous Periosteal Sleeve Avulsion** (ALPSA) = medialized Bankart
◊ best detected in ABER position
√ complete avulsion of anteroinferior glenoid labrum
√ avulsed scapular periosteum intact
√ labroligamentous complex rolls up + becomes displaced medially + inferiorly
• recurrent anterior humeral dislocations ← incompetent anterior band of IGHL
• can heal into a deformed labrum → difficult to diagnose

(6) **Reverse Bankart**
Prevalence: 2–4% of all shoulder instability
Mechanism: excessive force applied to adducted and internally rotated shoulder ← swimming, throwing, punching, convulsion
√ posterior labral tear

MRI (arthrography improves sensitivity to 89–99% and specificity to > 90%):
√ hemorrhagic effusion (in acute injury)
√ increased SI in anterior-inferior labrum + capsule (DDx: magic angle artifact)
√ discrete tear / fragmentation of labrum
√ ± tear of middle glenohumeral ligament
√ tear of degenerated supraspinatus tendon (in 33% of patients > 40 years of age)
√ tear of degenerated subscapularis tendon (in 33% of patients > 40 years of age)
√ myotendinous subscapularis strain / contusion
√ paralabral cysts are usually associated with labral tears; may cause denervation of suprascapular nerve simulating impingement syndrome (DDx: age-related degeneration)

Prognosis: significance of glenoid rim fracture is greater than of Hill-Sachs fracture
Cx: (1) Recurrent dislocations: inversely related to age (83% < 20 years; 16% > 40 years of age); M÷F = 3÷1
(2) Repeated dislocations ← incomplete / inadequate healing = chronic recurrent anterior shoulder instability
(3) Arthritis (with repeated subluxations)
Rx: (1) Conservative treatment for most
(2) Surgical fixation for young athletes

POSTERIOR SHOULDER DISLOCATION (2–5%)

Cause: (a) traumatic: convulsive disorders /electric shock therapy
(b) nontraumatic: voluntary, involuntary, congenital, developmental

Types: subacromial, subglenoid, subspinous

◊ In > 50% unrecognized initially + subsequently misdiagnosed as frozen shoulder!

◊ Average interval between injury and diagnosis is 1 year!

√ "rim" sign (66%) = distance between medial border of humeral head + anterior glenoid rim < 6 mm

May be associated with:

√ "trough" sign (75%) = "reverse Hill-Sachs"
= compression fracture of anteromedial humeral head (tangential Grashey view of glenoid!)

√ fracture of posterior glenoid rim

√ avulsion fracture of lesser tuberosity

MRI:

√ tear of subscapularis tendon

√ empty bicipital groove (= dislocated bicipital tendon)

Inferior Shoulder Dislocation (0.5%)

= LUXATIO ERECTA

= extremity held over head in fixed position with elbow flexed

Mechanism: severe hyperabduction of arm resulting in impingement of humeral head against acromion

√ humeral articular surface faces inferiorly

Cx: rotator cuff tear; fracture of acromion ± inferior glenoid fossa ± greater tuberosity; neurovascular injury

Superior Shoulder Dislocation (< 1%)

= humeral head driven upward through rotator cuff

May be associated with: fracture of humerus, clavicle, acromion

DDx: drooping shoulder (transient phenomenon after fracture of surgical neck of humerus ← hemarthrosis / muscle imbalance)

Gadolinium Shoulder Arthrography

» fluoroscopically guided needle insertion from an anterior approach

» confirmation of needle placement with iodinated contrast material

» injection of 12–20 mL of diluted gadolinium chelate solution:

- 0.1 mL of gadolinium DTPA (469 mg/mL) into
- 20 mL of bacteriostatic saline

» patient's arm and shoulder are moved through full range of motion

Biceps Tendon Dislocation

= total + permanent loss of contact between tendon and bicipital groove

Types:

(1) dislocation inside subscapularis tendon leaving anterior fascia intact

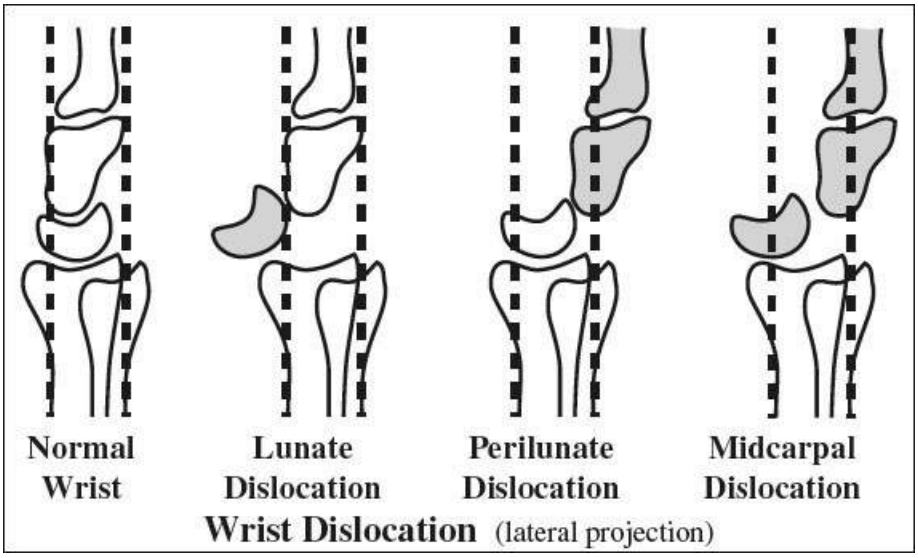
(2) intraarticular dislocation with complete tear of all insertions on lesser tuberosity but intact anterior fascia (lesion hidden in joint space)

(3) intraarticular dislocation with complete tear of all insertions on lesser tuberosity + anterior fascia
(4) dislocation over intact subscapularis tendon (= rupture of the supraspinatus tendon and CHL)

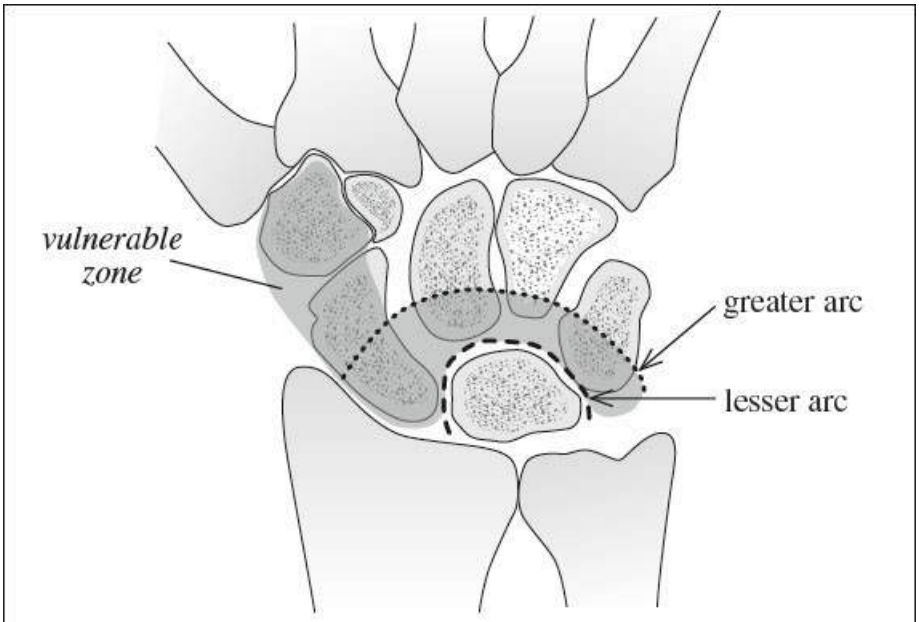
Associated with: tears of ligamentous pulley
Location: intraarticular extrasynovial (within reflection of synovial membrane)
MR:
√ dislocated biceps tendon medial to empty bicipital groove (axial image)
√ variably increased signal intensity
√ thickening, flattening, broadening of the tendon
√ fluid around displaced biceps tendon

Biceps Tendon Subluxation

= partial / transitional loss of contact between biceps tendon + bicipital groove
Direction:



Wrist Dislocation (lateral projection)



Fracture-Dislocation Zones of Wrist

(1) intraarticular
(2) between subscapularis tendon and CHL
(3) external to CHL
(4) intrasheath

Wrist / Carpal Dislocation

Mechanism: fall on outstretched hand
Frequency: 10% of all carpal injuries
◊ Up to 25% overlooked at initial examination!

Lunate Dislocation

= final stage of perilunate injury with highest degree of instablity
√ "spilled teacup" sign = lunate dislocated in volar direction (on LAT view)
√ rest of carpus assumes alignment with radius

Perilunate Dislocation

= dislocation of capitate head from concavity of distal lunate
Prevalence: 2–3 times more common than lunate dislocation
Mechanism: high-energy wrist hyperextension (MVC, fall from height, sports) with sequential injury of scapholunate → lunocapitate → lunotriquetral joints → complete dislocation
Average age: 30 years; M >> F
Associated with: fracture in 75%
√ disruption of carpal arcs (AP view)
√ Terry-Thomas sign = widening of space between scaphoid and lunate (AP view)
√ triangular lunate (AP view)
√ posterior dislocation of capitate head relative to lunate (LAT view)

GREATER ARC INJURY

= perilunate dislocation + fracture of scaphoid / trapezium / capitate / hamate / triquetrum
◊ Twice as common as lesser arc injury
◊ Most commonly transscaphoid perilunate dislocation
√ fracture of any carpal bone around lunate

LESSER ARC INJURY

= pure ligamentous disruption around lunate
√ most commonly dorsal dislocation
Rx: open reduction + internal fixation

Rotary Subluxation of Scaphoid

= Scapholunate dissociation
= tearing of interosseous ligaments of lunate, scaphoid, capitate
Mechanism: acute dorsiflexion of wrist; may be associated with rheumatoid arthritis
√ gap > 4 mm between scaphoid + lunate (PA view)
√ foreshortening of scaphoid
√ "ring" sign of distal pole of scaphoid

DOWN SYNDROME

= MONGOLISM = TRISOMY 21
Chromosomes: 95% nondisjunction, 5% translocation
Prevalence: 1÷870 live births, most common karyotype / chromosomal abnormality in USA
• mental retardation; hypotonia in infancy
• characteristic facies; Simian crease
@ Skull
√ hypotelorism
√ persistent metopic suture (40–79%) after age 10
√ hypoplasia of sinuses + facial bones
√ microcrania (brachycephaly)
√ delayed closure of sutures + fontanels
√ dental abnormalities (underdeveloped tooth No. 2)
√ flat-bridged nose
@ Axial skeleton
√ atlantoaxial subluxation (25%)
√ anterior scalloping of vertebral bodies
√ "squared vertebral bodies" = centra high and narrow
= positive lateral lumbar index (ratio of horizontal to vertical diameters of L2)
@ Chest
√ congenital heart disease (40%): endocardial cushion defect, VSD, tetralogy of Fallot
√ hypersegmentation of manubrium = 2–3 ossification centers (90%)
√ gracile ribs; 11 pairs of ribs (25%)
@ Pelvis (frontal view)
√ flaring of iliac wings (= rotation of iliac wings toward coronal plane at sacroiliac joints)

= "Mickey Mouse ears" / "elephant ears":
√ decreased iliac angle + index (in 70–80%)
√ flattening of acetabular roof (small acetabular angle)
√ elongated + tapered ischia
@ Extremities
√ metaphyseal flaring
√ clinodactyly (50%); widened space between first two digits of hands + feet
√ hypoplastic and triangular middle + distal phalanges of 5th finger = acromicria (DDx: normal individuals, cretins, achondroplastic dwarfs)
√ pseudoepiphyses of 1st + 2nd metacarpals
@ Gastrointestinal
√ umbilical hernia
√ "double bubble" sign (8–10%) = duodenal atresia / stenosis / annular pancreas
√ tracheoesophageal fistula
√ anorectal anomalies
√ Hirschsprüng disease

OB-US:

- advanced maternal age
  ◊ In 1÷385 live births for women > 35 years of age
  ◊ HOWEVER: 80% of fetuses with Down syndrome are born to mothers < 35 years of age
- quad test (2nd trimester maternal serum screening):
  (1) low (0.7 MoM) maternal alpha-fetoprotein (20–30%)
  (2) increased (2.04 MoM) hCG (DDx: decreased in trisomy 18)
  (3) decreased (0.79 MoM) unconjugated estriol (uE3)
  (4) decreased dimeric inhibin A levels
  ◊ Optimal time for test between 15 and 16 weeks GA
  ◊ Detects 75% of cases with Down syndrome with a 5% screen-positive rate
  Disadvantage: late performance in 2nd trimester, 25% of Down syndrome cases not detected, many amniocenteses unnecessarily recommended
- low pregnancy-associated plasma protein A (PAPP-A) at 10–14 weeks EGA

√ first-trimester ultrasound markers:
√ nuchal translucency
= measurement of space between spine and overlying skin on midsagittal view
Best time: 10w3d – 13w6d EGA
√ ≥ 5 mm during 14–18 weeks
√ ≥ 6 mm during 19–24 weeks
Cause: heart failure, abnormal extracellular matrix, abnormal lymphatic development
√ absent nasal bone
Best time: between 10 and 14 weeks EGA
√ absent / reversed Doppler flow in ductus venosus during atrial contraction
√ major structural malformations:
Best time: 18 weeks EGA
√ VSD / complete AV canal (50%)
√ cystic hygroma, resolved by 20th week MA (DDx: Turner syndrome, trisomy 18, trisomy 13, triploidy)

√ omphalocele
√ double bubble of duodenal atresia (8–10%), not apparent before 22 weeks GA
√ hydrothorax
√ mild cerebral ventricular dilatation
√ agenesis of corpus callosum
√ imperforate anus
√ minor markers:
√ elevated BPD / femur ratio ← short femur
√ ratio of measured-to-expected femur length ≤ 0.91 [expected femur length: –9.3105 + 0.9028 x BPD] (sensitivity 40%, specificity 95%, false-positive rate of 2–7%, 0.3% PPV for low-risk population [1÷700], 1% PPV for high-risk population [1÷250])
√ ratio of measured-to-expected humerus length ≤ 0.90 [expected humerus length: –7.9404 + 0.8492 x BPD] (1–2% PPV for low-risk population; 3% PPV for high-risk population)
√ flared iliac crest = iliac wings rotated toward coronal plane:
√ mean iliac angle at superiormost level of 95.6 ± 11.7° (compared to 76.4 ± 16.8° for euploid fetuses)
√ sandal-gap deformity = separation of great toe (45%)
√ hypoplasia of middle phalanx of 5th digit resulting in clinodactyly (= inward curve) in 60%
√ mild fetal pyelectasis (17–25%)
√ echogenic bowel at < 20 weeks GA (15%, in 0.6% of normals)
√ echogenic intracardiac focus, usually in left ventricle = thickening of papillary muscle (18%, in 5% of normals)
√ frontal lobe shortening (measured from the inner table of the frontal bone to the posterior margin of the thalamus)
√ brachycephaly
√ small cerebellum
√ IUGR (in 30%)
√ polyhydramnios

Cx: leukemia (increased frequency by 3–20 x)

DRUG-INDUCED MSK ANOMALIES

Aluminum

Source: dialysate containing a high concentration of aluminum, total parenteral nutrition, aluminum salts phosphate-binding antacids (to control hyperphosphatemia)

• aluminum serum level > 100 ng/mL
√ osteopenia → pathologic fractures
√ signs of osteomalacia (> 3 insufficiency fractures with predominant involvement of ribs)
√ widening of physis, fraying of metaphyses of long bones
√ avascular necrosis
√ lack of osteosclerosis
√ little evidence of subperiosteal resorption

Anticonvulsants

√ rickets, osteomalacia, osteoporosis
√ calvarial thickening + thickening of heel pad

Biphosphonates

= inorganic phosphates administered orally / IV

Use: decrease of bone pain + reduced complications in patients with metastatic lytic lesions, malignancy-induced hypercalcemia, multiple myeloma, Paget disease, osteoporosis

Pathophysiology: inhibition of endothelial proliferation → interruption of intraosseous circulation

@ Long bones
- √ bone-within-bone = bandlike metaphyseal sclerosis (in the maturing skeleton)
- √ atypical low-energy fractures:
  Location: proximal third of femur, distal to lesser trochanter, proximal to supracondylar flare
- √ transverse minimally comminuted fracture
- √ fracture fragment with medial spike / beak
- √ medial periosteal stress reaction + unicortical nipple (= focal thickening of lateral cortex)

@ Osteonecrosis of mandible
Location: mylohyoid ridge of mandible
Cause: spontaneous (increased risk with concurrent steroid therapy) / precipitated by trauma (tooth extraction)
May be associated with: infection by actinomyces
- painful / asymptomatic (occasionally)
- √ poorly marginated diffuse area of low attenuation with bilateral symmetric sclerosis

Corticosteroids

√ (most common cause of drug-induced) osteoporosis
√ insufficiency fractures
√ avascular necrosis + arthropathy

Deferoxamine

Use: removal of excess iron stores from multiple transfusions (treatment of severe β-thalassemia)

√ flattening of vertebrae → lower height percentile
√ irregular thickened cupped metaphyses (similar to rickets)

Fluorosis

Source of fluorides: high natural content in drinking water (parts of southeast Asia, South Africa); welding / manufacture of aluminum; medical drug therapy

√ sclerosis with granular pattern + thickened trabeculae
√ ossification of ligamentous insertions
√ osteophytic outgrowths around joints

√ increased bone fragility
√ diffuse periostitis

Lead

= Lead poisoning = **plumbism**

Source: paint, home-distilled liquors, folk remedies, cosmetics, industrial materials

Path: lead concentrates in metaphyses of growing bones (distal femur > both ends of tibia > distal radius) leading to failure of removal of calcified cartilaginous trabeculae in provisional zone

- loss of appetite, vomiting, constipation, abdominal cramps
- peripheral neuritis (adults), meningoencephalitis (children)
- anemia; lead line at gums (adults)

√ bands of increased density at metaphyses of tubular bones (only in growing bone):
  √ single transverse line of dense band
  √ bone-in-bone appearance
  - elevated serum levels (70–80 mg/dL)

√ lead lines may persist
√ clubbing if poisoning severe (anemia)

DDx: (1) Healed rickets
(2) Normal increased density in infants < 3 years old
(3) Hypervitaminosis D
(4) Healing leukemia
(5) Scurvy

Methotrexate

= dihydrofolate reductase inhibitor most often used in children for treatment of ALL / osteosarcoma / brain tumor

Methotrexate Osteopathy = syndrome that consists of
(1) bone pain (2) osteopenia (3) pathologic fractures

◊ Radiographic findings similar to scurvy:
  √ osteopenia:
    √ metaphyseal band of demineralization (simulating recurrent leukemia)
  √ broadening + increased density of the zone of provisional calcification
  √ sharply outlined epiphyses
  √ "corner" sign, ring epiphysis
  √ pathologic insufficiency fractures (most often metaphyseal)
  √ impaired healing of fractures
  √ NO massive subperiosteal hemorrhage

Prostaglandin E

Use: maintain patency of ductus arteriosus

√ periostitis = periosteal new bone growth

Location: symmetric involvement of long bones, ribs, clavicle, scapula, mandible

DDx: infantile cortical hyperostosis (Caffey disease); syphilis; effect of interleukin-11

therapy; scurvy; hypervitaminosis A

Retinoids
√ skeletal hyperostosis:
@ axial skeleton (esp. C-spine)
√ anterior vertebral osteophytes
√ ossification of anterior longitudinal ligament
√ osseous bridges between vertebrae
@ appendicular skeleton
√ calcification / ossification of coracohumeral ligament
√ enthesopathy
DDx: Diffuse idiopathic skeletal hyperostosis

Statins
√ muscle edema (= acute myositis)

Vitamin A
√ cortical thickening of tubular bones
√ cupping + fraying of metaphyses
√ irregularity of growth plates
√ premature fusion of ossification centers
DDx: Caffey disease (mandibular involvement, fever, > 4 months of age)

Vitamin D
√ generalized osteoporosis
√ metastatic calcifications in periarticular soft tissues

DYSCHONDROSTEOSIS
= LéRI-LAYANI-WEILL SYNDROME
= mesomelic long-bone shortening (forearm + leg); autosomal dominant; M÷F = 1÷4
• limited motion of elbow + wrist
√ bilateral Madelung deformity:
√ radial shortening in relation to ulna
√ bowing of radius laterally + dorsally
√ dorsal subluxation of distal end of ulna
√ carpal wedging between radius + ulna ← triangular shape of distal radial epiphysis + underdevelopment of ulna
DDx: pseudo-Madelung deformity (from trauma / infection)

DYSPLASIA EPIPHYSEALIS HEMIMELICA
= TREVOR DISEASE = TARSOEPIPHYSEAL ACLASIS
= uncommon skeletal developmental disorder representing an epiphyseal osteochondroma
Prevalence: 1÷1,000,000
Age: 2–4 years; M÷F = 3÷1
Cause: failure of normal progression of cellular cartilage breakdown (= aclasis); spontaneous

occurrence

Path: lobulated mass protruding from epiphysis with a cartilaginous cap

Histo: normal bone + hyaline cartilage with abundant enchondral ossification (= abnormal cellular activity at cartilaginous ossification center)

Types:

(1) Localized form = monostotic involvement: usually hindfoot and ankle

(2) Classic form (> 66%) = more than one area of involvement in a single extremity with characteristic hemimelic distribution: talus, distal femur, distal tibia

(3) Generalized / severe form = disease involving the whole lower extremity

√ pelvic involvement: femoral head, symphysis pubis, triradiate cartilage

√ hypertrophy of ipsilateral iliac bone

- antalgic (= pain-avoiding) gait; palpable mass
- varus / valgus deformity; limb length discrepancy
- limited joint mobility and function

Location: lower extremity (tarsus, knee, ankle); rare in upper extremity (humerus, ulna, scapula)

Site: restricted to medial OR lateral side of limb (= hemimelic), ie, medial÷lateral = 2÷1

@ Infant & toddler

√ premature appearance of an eccentric, lobulated, overgrown, asymmetric ossification center

√ stippled calcification of anomalous cartilage

@ Childhood

√ disorganized epiphyseal calcification accompanied by irregular ossification

√ osteochondroma-like growth from one side of epiphysis

√ premature closure of physis results in limb deformity and limb length discrepancy

√ irregular articular surface combined with angular deformity

√ undertubulation of bone as a consequence of secondary involvement of metaphysis

Cx: premature secondary osteoarthritis

DDx: osteochondroma

EHLERS-DANLOS SYNDROME

= group of autosomal dominant diseases of connective tissue characterized by abnormal collagen synthesis → excessive tissue fragility

Types: 10 types have been described that differ clinically, biochemically, and genetically

Age: present at birth; predominantly in males

- hyperelasticity of skin
- fragile brittle skin with gaping wounds and poor healing
- molluscoid pseudotumors over pressure points
- hyperextensibility of joints; joint contractures with advanced age
- bleeding tendency ← fragility of blood vessels
- blue sclera, microcornea, myopia, keratoconus, ectopia lentis

@ Soft tissues

√ multiple ovoid calcifications (2–10 mm) in subcutis / in fatty cysts (“spheroids”), most frequently in periarticular areas of legs

√ ectopic bone formation

@ Skeleton
- √ hemarthrosis (particularly in knee)
- √ malalignment / subluxation / dislocation of joints on stress radiographs
- √ recurrent dislocations: hip, patella, shoulder, radius, clavicle
- √ precocious osteoarthrosis (predominantly in knees)
- √ ulnar synostosis
- √ kyphoscoliosis
- √ spondylolisthesis
- √ spina bifida occulta

@ Chest
- √ diaphragmatic hernia
- √ panacinar emphysema + bulla formation
- √ tracheobronchomegaly + bronchiectasis

@ Arteries (= type IV of Ehlers-Danlos syndrome)
- √ aneurysm of great vessels, aortic dissection, aortic rupture, tortuosity of arch, ectasia of pulmonary arteries (in 60% by age 40)
- ◊ AORTOGRAPHY CONTRAINDICATED!
  (Cx following arteriography: aortic rupture, hematomas)

@ GI tract
- √ ectasia of gastrointestinal tract

ELASTOFIBROMA DORSI

= degenerative / reactive fibrous pseudotumor forming as a reaction to chronic mechanical friction

Frequency: in 24% of women + 11% of men > 55 years (autopsy study); in 2% of CT population

Average age: 60 (range, 41–80) years; M÷F = 1÷4

Histo: enlarged irregular serrated elastic hypereosinophilic fibers, collagen, scattered fibroblasts, occasional lobules of adipose tissue; lack of capsule

- slow growing, often asymptomatic + clinically inapparent
- stiffness (25%), moderate pain (10%) if > 5 cm in diameter
- clicking / snapping / clunking of scapula

Location: deep to serratus anterior + latissimus dorsi mm. at inferomedial border of scapula; R > L; bilateral in 10–66%
in < 1% at: greater trochanter, olecranon, thoracic wall

PET: incidental finding

CT:
- √ heterogeneous poorly defined lesion of soft-tissue attenuation similar to muscle

MR:
- √ well-defined heterogeneous intermediate-SI lesion similar to muscle on T1WI + T2WI
- √ interspersed streaks of fat intensity in fascicular pattern
- √ heterogeneous enhancement

Rx: local excision for symptomatic lesions

DDx: extraabdominal desmoid, neurofibroma, malignant fibrous histiocytoma

ENCHONDROMA

= benign cartilaginous growth in medullary cavity; bones preformed in cartilage are affected (NOT skull)

Frequency: 3–17% of biopsied primary bone tumors
◊ 2nd most common cartilage-containing tumor!

Etiology: continued growth of residual benign rests of cartilage displaced from the growth plate

Age: 10–30 years; M÷F = 1÷1

Histo: lobules of pure hyaline cartilage

• usually asymptomatic, painless swelling
• pain → suspect pathologic fracture

Location: (usually solitary; multiple = enchondromatosis)
(a) in 40% small tubular bones of hand (most frequent tumor here), distal + mid aspects of metacarpals, proximal / middle phalanges
◊ Most common benign tumor of the hand!
(b) proximal femur, proximal humerus, tibia, radius, ulna, foot, rib (3%)

Site: central within medullary canal + metaphyseal; epiphysis only affected after closure of growth plate

√ oval / round area of geographic destruction with lobulated contour + fine marginal line
√ chondroid matrix:
√ ground-glass appearance
√ dystrophic calcifications within small cartilage nodules / fragments of lamellar bone:
√ pinhead, flocculent, stippled "rings and arcs" pattern
√ bulbous expansion of bone with thinning of cortex in small tubular bones of phalanx, rib, fibula:
√ cortical endosteal scalloping
√ NO cortical breakthrough / periosteal reaction
√ Madelung deformity = bowing deformities of limb, discrepant length

MR:
√ low- to intermediate SI on T1WI
√ high SI on T2WI ← high water content of extracellular matrix
√ low-signal intensity matrix calcifications
√ normal fat marrow interspersed between cartilage nodules
√ peripheral enhancement pattern

CEMR:
√ peripheral nodular + septal enhancement ← avascular tumor

Cx: (1) Pathologic fracture → pain
√ may be better characterized on CT
(2) Malignant degeneration in long-bone enchondromas in 15–20% (severe new pain in an adult patient, interval growth at imaging, loss of marginal definition, cortical disruption, local periosteal reaction)

DDx: (1) Epidermoid inclusion cyst (phalangeal tuft, history of trauma, more lucent)
(2) Unicameral bone cyst (rare in hands, more radiolucent)

(3) Giant cell tumor of tendon sheath (commonly erodes bone, soft-tissue mass outside bone)

(4) Fibrous dysplasia (rare in hand, mostly polyostotic)

Enchondroma versus Chondrosarcoma in Appendicular Skeleton

	Enchondroma	*Intramedullary Chondrosarcoma*
Mean age and sex ratios	40 years; M÷F = 2÷3	50 years; M÷F = 11÷9
Palpable mass	28%	82%
Pain	40% (fracture associated)	95% (prolonged + increasing)
Lesion location	hands, feet	axial skeleton
Radiographic Features		
Site	diaphysis	metaphysis, epiphysis
Lesion size	< 5 cm	> 5–6 cm
Soft-tissue extension (MR)	3%	76%
Deep endosteal scalloping > ²/₃ of cortical thickness		90%
Periosteal reaction (X-ray)	3%	47%
Cortical destruction (CT)	8%	88%
Pathologic fracture (X-ray)	5%	27%
Endosteal scalloping > ²/₃ of length of lesion		79%
Cortical remodeling (X-ray)	15%	47%
Cortical thickening (X-ray)	17%	47%
Matrix mineralization (CT)	100%	94%
Small hyperintense T1 foci	65%	35%
Bone scintigraphy (↑ uptake c/w anterior iliac crest)	21%	82%

(5) Bone infarct

(6) Chondrosarcoma (exceedingly rare in phalanges, metacarpals, metatarsals)

ENCHONDROMATOSIS

= OLLIER DISEASE = DYSCHONDROPLASIA = MULTIPLE ENCHONDROMATOSIS

[Léopold Ollier (1830–1900), French orthopedic surgeon in Lyon]

= nonhereditary failure of cartilage ossification

Cause: derangement of cartilaginous growth resulting in migration of cartilaginous rests from epiphyseal plate into metaphysis where they proliferate

Prevalence: 1÷100,000 persons

Histo: persistent cartilage in bones formed by enchondral ossification

Mean age: 13 years

Association: juvenile granulosa cell tumor of ovary

• growth disparity with leg / arm shortening
• painless swelling, hand + foot deformity

Location: predominantly unilateral monomelic distribution (a) localized (b) regional (c) generalized

Site: metacarpals > phalanges

√ well-demarcated rounded radiolucencies / columnar streaks of decreased density from epiphyseal plate into diaphysis of long bones = cartilaginous rests

√ expansile remodeling of affected bone:
  √ clublike deformity / expansion of metaphyseal region
  √ predominant cortical thinning + endosteal scalloping
  √ bony spurs pointing toward the joint (DDx: exostosis points away from joint)

√ cartilaginous areas show punctate calcifications with age:
  √ matrix mineralization with TYPICAL arc-and-ring appearance of chondroid lesions

√ associated with dwarfing of the involved bone ← impairment of epiphyseal fusion

√ bowing deformities of limb bones → fracture

√ discrepancy in length = Madelung deformity (radius, ulna)

√ small bones of foot + hand: aggressive deforming tumors that may break through cortex ← tendency to continue to proliferate

√ fanlike radiation of cartilage from center to crest of ilium

Prognosis: skeletal findings often stabilize after puberty

Cx: sarcomatous transformation (in 5–50%): osteosarcoma (young adults); chondro- / fibrosarcoma (in older patients); mean age of 33 years
  ◊ ⇑ risk with tumor in long bones + axial skeleton
  ◊ ⇑ risk to develop multiple synchronous / metachronous chondrosarcomas

Maffucci Syndrome

[Angelo Maffucci (1847–1903), chief pathologist in Pisa, Italy]

= variant of Ollier disease

= rare nonhereditary early mesodermal dysplasia characterized by enchondromatosis + hemangiomatosis (= multiple low-flow vascular malformations [venous >> lymphatic])

Incidence: 180 cases confirmed

Histo of hemangioma:
spindle cell hemangioma > (originally described) cavernous hemangioma affecting SQ tissue of distal extremities

Age: 25% during 1st year of life; 45% prior to 6 years; 78% before puberty; M=F

Association: juvenile granulosa cell tumor of ovary

• multiple soft red-blue / skin-colored acral spongy subcutaneous nodules (= hemangiomas)
• swelling of dorsum of hand + foot (lymphatic form)
• normal intelligence

Location: unilateral involvement (50%) / marked asymmetry; distinct predilection for metaphyses of tubular bones of hand (88%) + foot (61%), lower leg (59%), femur (53%), humerus (42%), forearm (41%), pelvis (21%), vertebra (10%)

√ hemangioma + less commonly lymphangioma

√ phleboliths frequently present

√ striking tendency for enchondromas to be very large projecting into soft tissues

√ growth disturbance of long bones (common)

MR:

√ increased SI centrally on fluid-sensitive sequence ← myxoid change

Cx: (a) malignant transformation of

› enchondroma → chondrosarcoma / fibrosarcoma (15–20%)

› hemangioma → hemangiosarcoma / hemangio-endothelioma / lymphangiosarcoma (in 3–5%)

(b) ↑ prevalence of ovarian carcinoma, pancreatic ca., carcinoma, CNS glioma, gastrointestinal adenoca.

Prevalence of malignancy: 23–100% → lifelong follow-up

DDx: Ollier disease (without hemangiomas)

EPIDERMOID CYST

= INFUNDIBULAR CYST = SEBACEOUS CYST (misnomer)

= proliferation of surface epidermal cells within a circumscribed space in the dermis

Histo: production of keratin within closed space lined by surface epidermis

Associated with: nevoid basal cell syndrome (Gorlin syndrome) + high prevalence of epidermoid / dermoid cysts

• intradermal / subcutaneous mass

Location: anywhere; subungual (common)

√ small unilocular / (rarely) large multiloculated mass

US:

√ circumscribed circular / oval hypoechoic mass on US

√ often associated with hair follicle

MR:

√ isointense / slightly hypointense relative to muscle on T1WI

√ hyperintense with focal areas of decreased signal on T2WI

√ no appreciable enhancement

Epidermal Inclusion Cyst

= INTRAOSSEOUS KERATIN CYST = IMPLANTATION CYST

Age: 2nd–4th decade; M > F

Cause: trauma / migration of nail bed fragment → entrapment of epidermal fragments within other tissues

Path: encapsulated round / oval lesion lined by stratified squamous epithelium + filled with laminated keratin (soft white cheesy contents)

Histo: stratified squamous cells, keratin, cholesterol crystals

• history of trauma (implantation of epithelium under skin → secondary bone erosion); asymptomatic

• swelling of fingertip with redness, pain, sensation of heat

Location: superficially situated bones such as calvarium (typically in frontal / parietal bone), phalanx (usually terminal tuft of middle finger), L > R hand, occasionally in foot

√ well-defined round osteolysis with sclerotic margin

√ cortex frequently expanded + thinned
√ NO calcifications / periosteal reaction / soft-tissue swelling
√ ± wall calcification / ossification
√ pathologic fracture often without periosteal reaction

US:
√ round / oval an- or hypoechoic subungual mass with edge shadowing containing variably echogenic foci
√ no internal vascularity

MR:
√ well-defined round lesion of intermediate T1 + T2 SI
√ central debris + thin peripheral rim of enhancement
√ scalloping of distal phalanx underlying nail bed
√ extensive inflammation of surrounding soft tissue ← suggestive of lesion rupture

DDx: (a) in finger: glomus tumor, enchondroma (rare in terminal phalanx)
(b) in skull: infection, metastasis (poorly defined), eosinophilic granuloma (beveled margin)

EPIPHYSEOLYSIS OF FEMORAL HEAD

= SLIPPED CAPITAL FEMORAL EPIPHYSIS
= atraumatic fracture through hypertrophic zone of physeal plate

Frequency: 2÷100,000 people

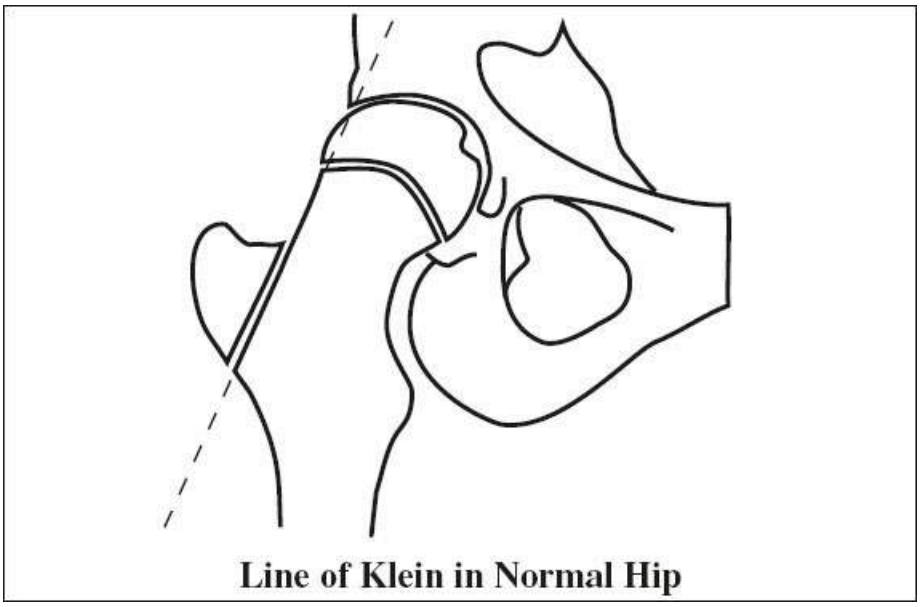
Etiology: growth spurt, renal osteodystrophy, rickets, childhood irradiation, growth hormone therapy, trauma (Salter-Harris type I epiphyseal injury)

Pathogenesis: widening of physeal plate during growth spurt + change in orientation of physis from horizontal to oblique increases shear forces

Mean age: 13 years for often overweight boys (range, 8–17 years), 11 years for girls; M÷F = 3÷1; Black > White

Associated with:
(a) malnutrition, endocrine abnormality, developmental dysplasia of hip (during adolescence)
(b) delayed skeletal maturation (after adolescence)

• hip pain (50%) / knee pain (25%) for 2–3 weeks



Line of Klein in Normal Hip

Location: usually unilateral; bilateral in 20–37% (at initial presentation in 9–18%)

√ widening of epiphyseal growth plate (preslip phase):
- √ irregularity + blurring of physeal physis
- √ demineralization of neck metaphysis

√ posteromedial displacement of head (acute slip):
- √ decrease in neck-shaft angle with alignment change of growth plate to a more vertical orientation
- √ line of Klein (= line drawn along superior edge of femoral neck) fails to intersect the femoral head
- √ epiphysis appears smaller ← posterior slippage: early slips are best seen on cross-table LAT view

CAVE: positioning into a frog leg view may cause further displacement

√ sclerosis + irregularity of widened physis (chronic slip):
- √ metaphyseal "blanch" sign = area of increased opacity in proximal part of metaphysis (healing response)

Grading (based on femoral head position):

mild = displaced by < ⅓ of metaphyseal diameter
moderate = displaced by ⅓–⅔ of diameter
severe = displaced by > ⅔ of metaphyseal diameter

Cx: (1) Chondrolysis = acute cartilage necrosis (7–10%)
= rapid loss of > 50% of thickness of cartilage
√ joint space < 3 mm

(2) Avascular necrosis of femoral head (10–15%): risk increases with advanced degree of slip, delayed surgery for acute slip, anterior pin placement, large number of fixation pins, subcapital osteotomy

(3) Pistol-grip deformity = broadening + shortening of femoral neck in varus deformity

(4) Degenerative osteoarthritis (90%)

(5) Limb-length discrepancy ← premature physeal closure

Rx: (1) limitation of activity
(2) prophylactic pinning
(3) osteotomy
◊ Attempted reductions increase risk of AVN!

EPITHELOID SARCOMA

Frequency: 1–2% of all soft-tissue sarcomas
Age: 10–35 years; M>> F
• firm solid nodule / multiple nodules
Location: forearm, hand, finger
◊ 21–29% of all malignant lesions of hand + wrist
√ soft-tissue mass ± speckled calcifications
√ cortical thinning / osseous erosion

ESSENTIAL OSTEOLYSIS

= progressive slow bone-resorptive disease
Histo: proliferation + hyperplasia of smooth muscle cells of synovial arterioles
√ progressive osteolysis of carpal + tarsal bones
√ thinned pointed proximal ends of metacarpals + metatarsals
√ elbows show same type of destruction
√ bathyrocephalic depression of base of skull
DDx: (1) Massive osteolysis = Gorham disease (local destruction of contiguous bones, usually not affecting hands / feet)
(2) Mutilating forms of rheumatoid arthritis
(3) Tabes dorsalis
(4) Leprosy
(5) Syringomyelia
(6) Scleroderma
(7) Raynaud disease
(8) Regional posttraumatic osteolysis
(9) Ulceromutilating acropathy
(10) Mutilating forms of rheumatoid arthritis
(11) Acrodynia mutilante (nonhereditary)

EWING SARCOMA / TUMOR

[James Stephen Ewing (1866–1943), American pathologist, first professor of pathology at Cornell University]
Frequency: 3% of all pediatric cancers; 2nd most common primary malignant bone tumor in children and adolescents after osteosarcoma; 4th most common bone tumor after multiple myeloma, osteosarcoma, chondrosarcoma
Incidence: 200 cases / year in USA; 1–3÷1,000,000 children

Histo: crowded sheets of small round cells (10–15 μm), uniformly sized + solidly packed invading medullary cavity and entering subperiosteum via Haversian canals producing osteolysis, periostitis, soft-tissue mass; glycogen granules present (DDx to reticulum cell sarcoma); absence of alkaline phosphatase (DDx to osteosarcoma)

DDx small round cells:

Ewing sarcoma, lymphoma, osteosarcoma, myeloma, neuroblastoma, embryonal rhabdomyosarcoma, eosinophilic granuloma

Immunohisto: positive for CD99 (MIC2, in 90%), vimentin, neuronspecific enolase, Leu7 (CD57), FL-1 protein

Peak age: 10–15 years (range, 5 months – 54 years); in 95% 4–25 years; in 30% < 10 years; in 39% 11–15 years; in 31% > 15 years; in 50% < 20 years; M÷F = 1.5÷1; Caucasians in 96%, Blacks in 0.5–2%

- severe localized pain (82–88%); soft-tissue mass / swelling (60%)
- fever (20–49%), leukocytosis; anemia (in early metastases)
- ↑ erythrocyte sedimentation rate (43%) simulating infection

Location:

femur (21%), ilium (13%), tibia (11%), humerus (10%), fibula (8%), hand or foot (5%), radius or ulna (4%), clavicle (2%)

(a) long bones in 60%: metadiaphysis (44–59%), middiaphysis (33%), metaphysis (15%), metaepiphyseal (6%), epiphysis (2%); extension into epiphysis (in up to 10%)

(b) flat bones in 40%:, ribs (in 7% > age 10; in 30% < age 10), vertebrae (in 3–10%, lumbar > thoracic > cervical spine), pelvis, sacrum (6%), scapula (5%), calvaria (1%), mandible or maxilla (1%), facial bones (0.5%), sternum (0.2%)

◊ > 20 years of age predominantly in flat bones

◊ < 20 years of age predominantly in cylindrical bones (tumor derived from red marrow)

√ 8–10 cm long aggressive lesion in shaft of long bone (62% lytic, 23% mixed density, 15% dense):

√ mottled "moth-eaten" to permeative destructive lesion (76–82%) with wide zone of transition in 96%

√ geographic bone destruction with wide zone of transition (= poor margination) in 15%

√ penetration into soft tissue (56–80%) with preservation of tissue planes (DDx: osteomyelitis with diffuse soft-tissue swelling)

√ early fusiform lamellated "onionskin" periosteal reaction (53–84%) / spiculated "sunburst" / "hair-on-end" (23%), Codman triangle

√ cortical thickening (21%) + saucerization (6%)

√ cortical destruction (19–42%) ± cortical sequestration

√ reactive sclerotic new bone (32–40%) of dense cloudlike osteoid appearance

√ pathologic fracture (15%)

√ expansile bone remodeling (13%)

CT:

√ density of soft-tissue component similar to muscle (98%):

√ commonly homogeneous

√ frequently asymmetrically circumferential

√ linear channels of low attenuation extending through dense cortex ← tumor extension along neurovascular + haversian channels (66%)

√ diffuse / peripheral nodular enhancement

MR (best modality):

√ homogeneous (73%) intermediate SI (95%) on T1WI

√ homogeneous (86%) low to intermediate (68%) SI on T2WI

√ heterogeneously high signal commonly in larger lesions ← hemorrhage + necrosis

√ marrow replacement (100%)

√ cortical destruction (92%)

√ associated asymmetrically circumferential soft-tissue mass (96%)

√ visible connection between medullary canal + soft-tissue component (74%)

√ diffuse / peripheral nodular enhancement

NUC:

√ ↑ uptake on bone scintigraphy (blood flow, blood pool, delayed imaging)

√ ↑ uptake on gallium scintigraphy

PET:

√ ↑ uptake of primary on PET with mean SUV of (a) 5.3 without metastases, (b) 11.3 with metastases

√ depiction of osseous metastasis (37–88% sensitive)

@ Ewing sarcoma of vertebra:

Prevalence: 3.5–15%

Mean age: 19 years; M÷F = 3÷2

Location: sacrum (55%), lumbar (25%), thoracic > cervical; > 1 segment involved (8%)

Site: (a) posterior elements (70%) with extension into vertebral body (86%)
(b) vertebral body (30%) with extension into posterior elements (83%)

√ large soft-tissue mass with invasion of spinal canal (91%)

√ disk spaces usually preserved

@ Ewing sarcoma of rib:

√ primarily lytic / sclerotic / mixture of lysis + sclerosis

√ disproportionately large inhomogeneous soft-tissue mass

√ large intrathoracic + minimal extrathoracic component

√ may spread into spinal canal via intervertebral foramen

Metastases to: lung, bones, regional lymph nodes in 11–30% at time of diagnosis, in 40–45% within 2 years of diagnosis

Cx: pathologic fracture (5–14%)

Prognosis: 60–75% 5-year survival

DDx: (1) Multiple myeloma (older age group)
(2) Osteomyelitis (duration of pain < 2 weeks)
(3) Eosinophilic granuloma (solid periosteal reaction)
(4) Osteosarcoma (ossification in soft tissue, near age 20, no lamellar periosteal reaction)
(5) Reticulum cell sarcoma (clinically healthy, between 30 and 50 years, no glycogen)
(6) Neuroblastoma (< age 5)
(7) Anaplastic metastatic carcinoma (> 30 years of age)
(8) Osteosarcoma

(9) Hodgkin disease

Extraskeletal Ewing Sarcoma

= aggressive tumor with high rate of recurrence
Origin: likely neuroectodermal
Prevalence: 15–20% of Ewing sarcoma of bone
Median age: 20 (range, 20 months–30 years)
• pain and tenderness (49%)
Location: paravertebral (32%), lower extremity (26%), chest wall (18%), retroperitoneum (11%), pelvis and hip (11%), upper extremity (3%), head & neck (nose, nasopharynx, parotid gland, cervical soft tissues)
Site: deep (92%), subcutaneous (8%)
Metastatic to: lung
√ 5–10 cm rapidly growing solitary soft-tissue tumor
√ well-defined pseudocapsule (35%), infiltrative growth (45%), neurovascular involvement (73%)
√ lesion calcification (25–30%)
√ extension to bone (25–42%): erosion of adjacent bone, cortical thickening, osseous invasion, aggressive periosteal reaction
√ no replacement of fatty bone marrow by tumor
√ hypervascular lesion by angiography, CT, MR
US:
√ hypoechoic lesion
CT:
√ mass of muscle density (87%)
√ hypoattenuating areas ← hemorrhage + cellular necrosis
MR:
√ heterogeneous mass of low to intermediate SI relative to muscle on T1WI
√ intermediate to high SI relative to muscle on T2WI
√ heterogeneous enhancement
√ serpentine hypointense high-flow vascular channels
PET:
√ ↑ uptake after injection with FDG

Ewing Sarcoma Family of Tumors

◊ Clinically, radiologically, and histologically very similar to PNET and Askin tumor!
Common karyotype abnormality = translocation between long arms of chromosomes 11 and 22 (t[11:22][q24;q12]) in 90%

EXTRAMEDULLARY HEMATOPOIESIS

= abnormal deposits of hematopoietic tissue outside bone marrow ← deficient bone marrow blood cell production
Etiology: prolonged erythrocyte deficiency due to
(1) destruction of RBCs:
congenital hemolytic anemia (sickle cell anemia, thalassemia, hereditary spherocytosis),

acquired hemolytic anemia, idiopathic severe anemia, erythroblastosis fetalis

(2) inability of normal blood-forming organs to produce RBCs: iron deficiency anemia, pernicious anemia, myelofibrosis, myelosclerosis, polycythemia vera, carcinomatous / leukemic / lymphomatous replacement depletion of bone marrow (chronic myelogenous leukemia, Hodgkin disease)

◊ NO hematologic disease in 25%

Histo: erythroid precursors in extramedullary sites

• absence of pain, bone erosion, calcification; chronic anemia

Sites: in areas of fetal erythropoiesis

@ Spleen

√ splenomegaly

√ focal isodense masses on enhanced CT

@ Liver, lymph nodes

@ Thorax: mediastinum, heart, thymus, pleura, lung

√ uni- / bilateral smooth lobulated paraspinal masses between T8 and T12

√ anterior rib ends expanded by masses

@ Spine

◊ Most commonly afflicted in thalassemia

• back pain, symptoms of spinal cord compression

√ coarsened trabeculation

√ extramedullary hematopoiesis in epidural space

@ Adrenal glands

@ Renal pelvis

@ Retroperitoneum (uncommon)

Site: perirenal (uncommon)

√ hyper- / isoattenuating masses in paravertebral region ± macroscopic fat on CT

√ hypointense mass on T1WI + T2WI ← red marrow / hemosiderin content

√ hyperintense on T1WI + T2WI ← fat tissue

√ variable mild enhancement

@ Gastrointestinal lymphatics

@ Dura mater (falx cerebri and over brain convexity)

√ expanded diploic space

@ Cartilage, broad ligaments

@ Thrombi, adipose tissue

@ Bone marrow reconversion = conversion of fatty to hematopoietic marrow

Sequence: vertebrae > flat bones of pelvis > long bones of extremities (proximal metaphysis > distal metaphysis > diaphysis)

√ lack of calcification / bone erosion

√ signs of hemochromatosis

FAMILIAL IDIOPATHIC ACROOSTEOLYSIS

= HAJDU-CHENEY SYNDROME

= rare bizarre entity of unknown etiology

Location: may be unilateral

• fingernails remain intact; sensory changes + plantar ulcers rare
√ pseudoclubbing of fingers + toes with osteolysis of terminal + more proximal phalanges
√ genu varum / valgum
√ hypoplasia of proximal end of radius
√ subluxation of radial head
√ scaphocephaly, basilar impression
√ wide sutures, persistent metopic suture, wormian bones, poorly developed sinuses
√ kyphoscoliosis
√ severe osteoporosis + fractures at multiple sites (esp. of spine)
√ protrusio acetabuli

FANCONI ANEMIA

= autosomal recessive disease with severe hypoplastic anemia + skin pigmentation + skeletal and urogenital anomalies
• skin pigmentation (melanin deposits) in 74% (trunk, axilla, groin, neck); microphthalmia (20%)
• anemia onset between 17 months and 22 years of age
• bleeding tendency (pancytopenia); hypogonadism (40%)
√ anomalies of radial component of upper extremity (strongly suggestive):
  √ absent / hypoplastic / supernumerary thumb
  √ hypoplastic / absent radius
  √ absent / hypoplastic navicular / greater multangular bone
√ slight / moderate dwarfism
√ minimal microcephaly
√ renal anomalies (30%): renal aplasia, ectopia, horseshoe kidney
Prognosis: fatal within 5 years after onset of anemia; patient's family shows high incidence of leukemia

FARBER DISEASE

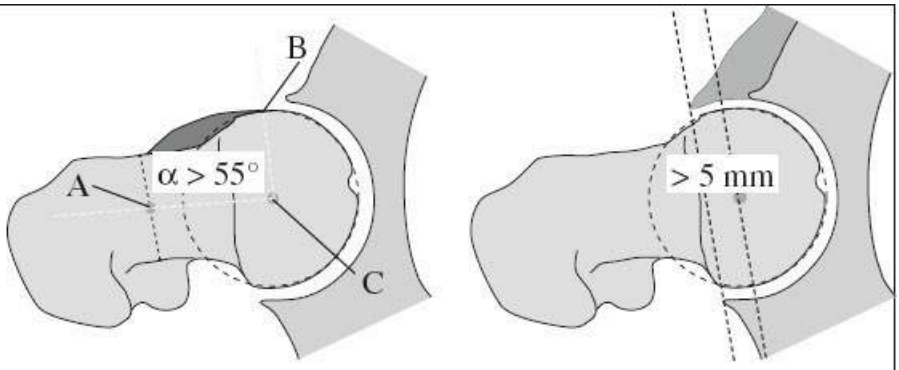
= DISSEMINATED LIPOGRANULOMATOSIS
Histo: foam cell granulomas; lipid storage of neuronal tissue (accumulation of ceramide + gangliosides)
• hoarse weak cry; subcutaneous + periarticular granulomas
• swelling of extremities; generalized joint swelling
• intermittent fever, dyspnea; lymphadenopathy
√ capsular distension of multiple joints (hand, elbow, knee)
√ juxtaarticular bone erosions from soft-tissue granulomas
√ subluxation / dislocation
√ disuse / steroid deossification
Prognosis: death from respiratory failure within 2 years

FEMOROACETABULAR IMPINGEMENT

= repetitive microtrauma due to an anatomic conflict between proximal femur + acetabular rim at extreme range of motion, especially hip flexion and internal rotation

Mean age: 20–45 yrs; in patients with increased physical activity; M÷F = 3÷2 to 9÷1
Prevalence: 10–15%
Cause: anatomic variations; developmental dysplasia of the hip; slipped capital femoral epiphysis; Legg-Calvé-Perthes; posttraumatic deformity
Pathophysiology:

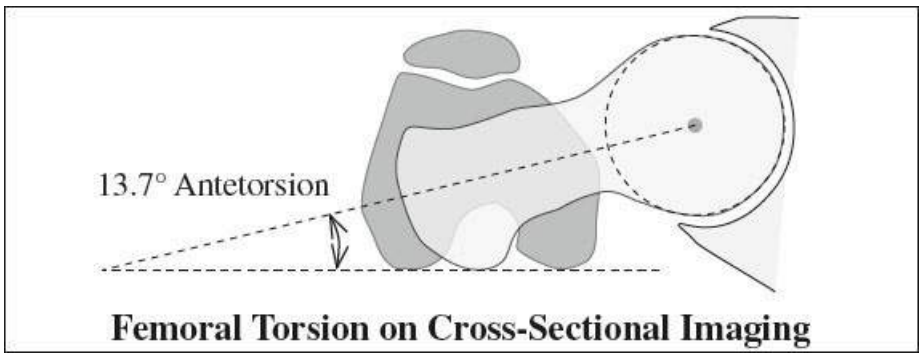
labrum caught between femoral head and acetabulum (impingement) → labral tear typically anterosuperiorly → chondral damage → secondary osteoarthritis (other causes of labral tears: trauma; capsular laxity; dysplasia; degeneration)



Femoroacetabular Impingement

A = center of the femoral neck at its narrowest point
B = point where the distance from the center of the femoral head to the peripheral contour of the femoral head exceeded the radius of the femoral head
C = center of femoral head
α = angle between line A–C and line B–C

Radial Sections perpendicular to Hip Joint Surface
for Imaging of Femoroacetabular Impingement



Femoral Torsion on Cross-Sectional Imaging

Types:

(1) Cam FAI (56% of all labral tears from sports injury)
= nonspherical shape of femoral head with reduced depth of femoral waist (= femoral waist deficiency) leads to abutment of femoral head-neck junction against acetabular rim

Age: athletic male 20–30 years

√ aspheric (= osseous bump) femoral head / head-neck junction (50%)
√ large areas of labral avulsion
√ broad areas of cartilage lesions often > 1 cm in width
√ carpet phenomenon = focal cartilage delamination
√ α-angle of > 55° (measured at the anterosuperior position on radial images rotated around center line of femoral neck)

N.B.: substantial overlap in α-angle measurements between volunteers and patients

(2) Pincer FAI (12% of all labral tears from sports injury)
= acetabular overcoverage limits range of motion

Cause: protrusio acetabuli, acetabular retroversion

Age: athletic woman 30–40 years

Associated with: increased femoral antetorsion

√ deep acetabulum (head center > 5 mm below rim)
√ acetabular retroversion = anterior acetabular rim overlaps posterior rim on AP
√ osseous bump deforming femoral head-neck junction (33%)
√ anterosuperior labral avulsion (pincer FAI)
√ thin rim of adjacent cartilage lesion often < 5 mm in width

(3) Mixed pattern (frequent)

- groin pain (83%) owing to initially activity overparticipation + later osteoarthritis; impaired ability to squat
- decreased range of motion (ROM)
- positive impingement test in supine position:

(a) anterior impingement (= groin pain during passive hip flexion + adduction + internal rotation)
(b) posterior impingement (= groin pain during hip extension + external rotation)

√ cystic / bony proliferative changes at femoral head-neck junction
√ ossicle along acetabular rim / os acetabuli

MR:
requires use of multiplanar capability to obtain radial sections perpendicular to surfaces of

hip joint → true cross section of cartilage + labrum without partial-volume effects

Cx: premature osteoarthritis initially with cartilage damage + labral tears

DDx: healthy young adult (common!), adult hip dysplasia, pseudoacetabular overcoverage in diffuse idiopathic skeletal hyperostosis (abnormal thoracolumbar spine) / ankylosing spondylitis (abnormal sacroiliac joints)

Rx: surgery in patients without osteoarthritis consisting of reshaping of femoral waist / trimming of acetabular rim / periacetabular osteotomy

FIBROCHONDROGENESIS

= autosomal recessive lethal short-limb skeletal dysplasia

Prevalence: 5 cases

√ severe micromelia + broad dumbbell-shaped metaphyses

√ flat + clefted pear-shaped vertebral bodies

√ short + cupped ribs

√ frontal bossing

√ low-set abnormally formed ears

Prognosis: stillbirth / death shortly after birth

DDx: (1) Thanatophoric dysplasia

(2) Metatropic dysplasia

(3) Spondyloepiphyseal dysplasia

FIBRODYSPLASIA OSSIFICANS PROGRESSIVA

= MYOSITIS OSSIFICANS PROGRESSIVA (misnomer since primarily connective tissues are affected)

= rare slowly progressive sporadic / autosomal dominant disease with variable penetrance characterized by remissions + exacerbations of fibroblastic proliferation, subsequent calcification + ossification of subcutaneous fat, skeletal muscle, tendons, aponeuroses, ligaments

Histo: edema with proliferating fibroblasts in a loose myxoid matrix; subsequent collagen deposition plus calcification + ossification of collagenized fibrous tissue in the center of nodules

Age: presenting by age 2 years (50%)

- initially subcutaneous painful masses on neck, shoulders, upper extremities
- progressive involvement of remaining musculature of back, chest, abdomen, lower extremities
- lesions may ulcerate and bleed
- muscles of back + proximal extremity become rigid followed by thoracic kyphosis
- inanition ← jaw trismus (masseter, temporal muscle)
- "wry neck" = torticollis ← restriction of sternocleidomastoid m.
- respiratory failure ← thoracic muscles affected
- conductive hearing loss ← fusion of middle ear ossicles

A. ECTOPIC OSSIFICATION

√ rounded / linear calcification in neck / shoulders, para-vertebral region, hips, proximal extremity, trunk, palmar and plantar fascia forming ossified bars + bony bridges

√ ossification of voluntary muscles, complete by 20–25 years (sparing of sphincters + head)

B. SKELETAL ANOMALIES
may appear before ectopic ossification
• clinodactyly
√ microdactyly of big toes (90%) and thumbs (50%)
= usually only one large phalanx present / synostosis of metacarpal + proximal phalanx (first sign)
√ phalangeal shortening of hand + foot (middle phalanx of 5th digit)
√ shortened 1st metatarsal + hallux valgus (75%)
√ shortened metacarpals + metatarsals
√ shallow acetabulum
√ short widened femoral neck
√ thickening of medial cortex of tibia
√ progressive fusion of posterior arches of cervical spine
√ narrowed AP diameter of cervical + lumbar vertebral bodies
√ ± bony ankylosis

CAVE: surgery is hazardous causing accelerated ossification at the surgical site

FIBROMA OF TENDON SHEATH

Histo: paucicellular tumor with scattered spindle-shaped myofibroblasts embedded in dense collagenous stroma + slitlike vascular channels and cleftlike spaces = crossover to giant cell tumor of tendon sheath

Mean age: 31 (range, 20–50) years; M÷F = 2÷1

Location: tendon sheath of upper extremity (fingers, hands, wrists) in 82%

Size: usually < 3 (range, 1–5) cm

• mostly painless soft-tissue mass

MR:
√ small hypointense nodule on all pulse sequences compared to muscle
√ areas of high signal intensity ← myxoid change
√ no / moderate / marked enhancement
√ attachment to tendon sheath

Rx: local excision (24% recurrence rate)

DDx: giant cell tumor of tendon sheath (blooming artifact ← hemosiderin deposition)

FIBROSARCOMA

Frequency: 4% of all primary bone neoplasm

Etiology:

A. PRIMARY FIBROSARCOMA (70%)
B. SECONDARY FIBROSARCOMA (30%)
1. following radiotherapy of giant cell tumor / lymphoma / breast cancer
2. underlying benign lesion: Paget disease (common); giant cell tumor, bone infarct, osteomyelitis, desmoplastic fibroma, enchondroma, fibrous dysplasia (rare)
3. dedifferentiation of low-grade chondrosarcoma

Histo: spectrum of well to poorly differentiated fibrous tissue proliferation; will not produce osteoid / chondroid / osseous matrix

Age: predominantly in 3rd–5th decade (range, 8–88 years); M÷F = 1÷1
Metastases to: lung, lymph nodes
• localized painful mass
Location: tubular bones in young, flat bones in older patients; femur (40%), tibia (16%) (about knee in 30–50%), jaw, pelvis (9%); rare in small bones of hand + feet or spinal column
Site: eccentric at diaphyseal-metaphyseal junction into metaphysis; intramedullary / periosteal

A. CENTRAL FIBROSARCOMA
= intramedullary
√ well-defined lucent bone lesion
√ thin expanded cortex
√ aggressive osteolysis with geographic / ragged / permeative bone destruction + wide zone of transition
√ occasionally large osteolytic lesion with cortical destruction, periosteal reaction + soft-tissue invasion
√ sequestration of bone may be present (DDx: eosinophilic granuloma, bacterial granuloma)
√ sparse periosteal proliferation (uncommon)
√ intramedullary discontinuous spread
√ no calcification
DDx: malignant fibrous histiocytoma, myeloma, telangiectatic osteosarcoma, lymphoma, desmoplastic fibroma, osteolytic metastasis

B. PERIOSTEAL FIBROSARCOMA
= rare tumor arising from periosteal connective tissue
Location: long bones of lower extremity, jaw
√ contour irregularity of cortical border
√ periosteal reaction with perpendicular bone formation may be present
√ rarely extension into medullary cavity

Cx: pathologic fracture (uncommon)
Prognosis: 20% 10-year survival
DDx: (1) Osteolytic osteosarcoma (2nd–3rd decade)
(2) Chondrosarcoma (usually contains characteristic calcifications)
(3) Aneurysmal bone cyst (eccentric blown-out appearance with rapid progression)
(4) Malignant giant cell tumor (begins in metaphysis extending toward joint)

FIBROUS CORTICAL DEFECT

= developmental abnormality classified as benign bone tumor
Prevalence: 30–35% of children; M÷F = 2÷1
Peak age: 7–8 (range, 2–20) years; mostly before epiphyseal closure
Histo: fibrous tissue from periosteum invading underlying cortex
• asymptomatic, usually incidental finding
In 5% associated with: neurofibromatosis
Location: metaphyseal cortex of long bone (near physis); multiple locations bilateral + symmetric in 50%

(a) femur (40%): posterior medial aspect of distal femur, proximal femur
(b) tibia (40%): proximal tibia
(c) fibula (10%)
(d) others: proximal humerus, ribs, ilium

Size: < 2 cm in largest diameter

Early stage:

√ circular / oval eccentrically located radiolucent area extending parallel to long axis of host bone
√ smooth lobulated / scalloped margins with well-defined thin rim of sclerosis
√ no periosteal reaction
√ high SI on T2WI (cystic component early stage) + low SI on T1WI
√ little / no uptake on bone scintigraphy

Late stage:

√ low SI on T2WI (progressive sclerosis + ossification) and on T1WI
√ sclerotic bone island (may be residue of incompletely involuted cortical defect in the adult)

Prognosis:

(a) involution over 2–4 years
(b) potential to grow and encroach on the medullary cavity leading to nonossifying fibroma (defined as > 2 cm in size)

DDx: Nonossifying fibroma

FIBROUS DYSPLASIA

= FIBROUS OSTEODYSTROPHY = OSTEODYSTROPHIA FIBROSA = OSTEITIS FIBROSA DISSEMINATA

= benign developmental anomaly of mesenchymal precursor of bone → slowly progressive replacement of normal bone marrow by immature fibroosseous tissue centered in medullary canal

Prevalence: 7% of benign bone tumors; 2.5% of all bone tumors; 1% of primary bone tumors at biopsy

Cause: probable gene mutation during embryogenesis manifested as defect in osteoblastic differentiation and maturation

Age: 1st–2nd decade (highest incidence between 3 and 15 years), 75% before age 30; progresses until growth ceases; M÷F = 1÷1 (range, 1÷1.2 to 2÷1)

Histo: spongiosa of medullary cavity replaced by

(a) abnormal fibrous tissue = variable degree of immature collagen and myxoid component, and
(b) osseous tissue containing poorly calcified + dysplastic + non–stress oriented + disorganized trabeculae of woven bone varying from solid round areas to curved / serpentine / curlicue shapes (= "Chinese characters" / alphabet soup); NO osteoblastic rimming of trabeculae (DDx from ossifying fibroma); cartilaginous islands present in 10% (DDx to chondrosarcoma)

Clinical Types:

1. Monostotic fibrous dysplasia (70–80%)
2. Polyostotic fibrous dysplasia (20–30%)

3. Craniofacial fibrous dysplasia = leontiasis ossea
   Variants: McCune-Albright syndrome (10%), Jaffé-Lichtenstein Disease (10%)
4. Cherubism (special variant)*1*

May be associated with:

(a) endocrine disorders:
- › precocious puberty in girls
- › hyperthyroidism
- › hyperparathyroidism: renal stones, calcinosis
- › acromegaly
- › diabetes mellitus
- › Cushing syndrome: osteoporosis, acne
- › growth retardation

(b) intramuscular soft-tissue myxoma (rare)
= **Mazabraud syndrome**:
[André Mazabraud (1921–2006), French rheumatologist and pathologist at Curie Institute, Paris]
- √ typically <u>multiple</u> intramuscular myxomas in vicinity of most severely affected bone
- √ polyostotic fibrous dysplasia (in 81%); M÷F = 1÷2
- • renal phosphate wasting

(c) aneurysmal bone cyst
- • swelling + tenderness; limp, pain (± pathologic fracture)
- • increased alkaline phosphatase
- • advanced skeletal + somatic maturation (early)

Common location: rib cage (30%), craniofacial bones [calvarium, mandible] (25%), femoral neck + tibia (25%), pelvis

Site: metaphysis is primary site with extension into diaphysis
= expands along longitudinal axis of bone (rarely over entire length)

Radiography:
- √ lesions in medullary cavity: characteristic "ground-glass" / radiolucent appearance / increased density:
  - √ expansile remodeling:
    - √ HALLMARK endosteal scalloping with thinned / lost cortex (rib, long bone) and intervening normal cortex
    - √ expansion of cortices (rib, skull, long bone) with "blown-out" appearance (DDx from ossifying fibroma which is focally more altered)
  - √ trabeculated appearance ← reinforced subperiosteal bone ridges in wall of lesion
  - √ ill-defined wide zone of transition (DDx to ossifying fibroma)
- √ well-defined thick sclerotic margin of reactive bone = rind
- √ lesion may undergo calcification + enchondral bone formation = fibrocartilaginous dysplasia
- √ no periosteal reaction unless fractured

CT (best technique for characterization):
- ◊ Most cases of monostotic fibrous dysplasia are incidental findings on (a cranial / other) CT examination!
- √ attenuation of typically 70–130 HU + intermixed areas of sclerosis with higher values:

√ **pagetoid** / ground glass appearance (53%) ← equal mixture of dense woven trabecular bone + radiolucent areas of fibrous tissue
√ homogeneously dense opaque **sclerotic** bone (23%) ← predominance of osseous elements
√ radiolucent **cystic** bone (21%) = spherical / ovoid density surrounded by dense bony shell ← abundance of fibrous elements
DDx: central ossifying fibroma, central giant cell granuloma, aneurysmal bone cyst, osteomyelitis, early fibro-osseous lesion
√ expansion of bone
√ fibrous dysplasia enhances ← inherent vascularity

MR:
◊ MRI should not be used to differentiate fibrous dysplasia from other entities due to extreme variability in appearance of bone lesions (depending on ratio of fibrous tissue to mineralized matrix)!
√ homogeneous / mildly heterogeneous marrow lesions:
√ low to intermediate SI on T1WI, typically hypointense to muscle
√ hyperintense to fat (63%) / low SI (18–38%) / intermediate SI (18%) on T2WI
√ intense heterogeneous enhancement:
(a) centrally (73%) ← numerous small vessels
(b) peripherally (27%) ← large sinusoids

NUC:
√ uptake on bone scan (lesions remain metabolically active into adulthood):
(a) intense activity on blood flow + blood pool images
(b) most intense activity on static delayed images

PET:
√ marked radiotracer avidity (SUV of 3–19)

@ Skull & facial bones
√ "blistering / bubbling" cystic calvarial lesions (CHARACTERISTIC), commonly crossing sutures:
√ widened diploic space displacing outer table + sparing inner table (DDx: Paget disease, inner table involved)
√ diffuse sclerosis of skull base obscuring ground-glass appearance:
√ sclerosis of orbital plate (DDx: Paget disease, meningioma en plaque)
√ occipital thickening
√ hypoplasia / obliteration of sphenoid + frontal sinuses ← encroachment by fibrous dysplastic bone
√ narrow neural foramina → visual + hearing loss
√ inferolateral displacement of small orbit
√ mandibular cystic lesion (very common) = osteocementoma, ossifying fibroma

@ Ribs
√ bubbly cystic multiseptated lesion (extremely common)
√ fusiform enlargement of rib + loss of normal trabecular pattern + thin preserved cortex (in up to 30%)

◊ Fibrous dysplasia is the most common cause of a benign expansile lesion of a rib!

◊ A rib is the most common site of monostotic (6–20%) + polyostotic (55%) fibrous dysplasia!

@ Pelvis

√ protrusio acetabuli

@ Extremities

• short stature as adult / dwarfism

√ premature fusion of ossification centers

√ epiphysis rarely affected before closure of growth plate

√ bowing deformities + discrepant limb length (tibia, femur) ← stress of normal weight bearing

√ "shepherd's crook" deformity of femoral neck = coxa vara

√ pseudarthrosis in infancy = osteofibrous dysplasia (DDx: neurofibromatosis)

√ premature onset of arthritis

@ Spine

• frequently asymptomatic / pain / fracture

√ mildly expansile lesion with "blown-out" cortical shell

√ lytic lesion with a sclerotic rim

√ common "ground-glass" matrix (characteristic)

Cx: (1) Dedifferentiation into osteo- / fibro- / (rarely) chondrosarcoma or malignant fibrous histiocytoma (0.4–1%; more often in polyostotic form)

• increasing pain

√ enlarging soft-tissue mass

√ previously mineralized lesion turns lytic

(2) Pathologic fractures: transformation of woven into lamellar bone may be seen, subperiosteal healing without endosteal healing

DDx: (1) Paget disease (older age group, mosaic pattern histologically, radiographically similar to monostotic cranial lesion, outer table involved, usually sparing of facial bones)

(2) Ossifying fibroma (narrow zone of transition, displacement of teeth)

(3) HPT (polyostotic, no bone expansion, chemical changes, generalized deossification, subperiosteal resorption)

(4) Osteofibrous dysplasia (almost exclusively in tibia of children < 10 years + anterior bowing, monostotic, lesion begins in cortex, spontaneous regression)

(5) Neurofibromatosis (rarely osseous lesions, vertebral column is primary target, ribbon ribs, cystic intraosseous neurofibroma rare, café-au-lait spots smooth, familial disease)

(6) Nonossifying fibroma = fibroxanthoma

(7) Simple bone cyst (more lucent than fibrous dysplasia, not affecting growth plate, straw-colored fluid on aspiration)

(8) Giant cell tumor (no well-defined sclerotic margin)

(9) Enchondroma (often calcified chondroid matrix)

(10) Eosinophilic granuloma = LCH

(11) Osteoblastoma

(12) Hemangioma

(13) Meningioma

(14) Low-grade osteosarcoma (invasion of surrounding soft tissues, osteolysis, cortical destruction)

Prognosis: bone lesions usually do not progress beyond puberty

Craniofacial Fibrous Dysplasia

= Leontiasis ossea [*leon*, Greek = lion]

Frequency: monostotic in 10–27%; polyostotic form in 50%

◊ Most common site of malignant degeneration!

• cranial asymmetry, facial deformity; nasal stuffiness

• hypertelorism, proptosis, exophthalmos, diplopia

• visual impairment, extraocular muscle palsy

Location: frontal > sphenoid > ethmoid maxilla > zygoma > parietal > occipital > temporal area; orbit (20–39%); hemicranial involvement (DDx: Paget disease is bilateral)

√ unilateral overgrowth of facial bones + calvarium:

√ NO extracranial lesions

√ outward expansion of outer table maintaining convexity

√ expanded diploic space + thin rim of cortical bone

DDx: Paget disease with destruction of inner + outer table

√ encroachment on orbits, sinuses, vascular + neural channels

√ prominence of external occipital protuberance

√ teeth nondisplaced (DDx from ossifying fibroma)

√ feline facial appearance ("leontiasis ossea"):

√ slowly progressive protrusion of malar surface

√ loss of the nasomaxillary angle

Cx: neurologic deficit of cranial nerves (eg, blindness) ← narrowed cranial foramina

DDx: juvenile ossifying fibroma, cherubism (limited to jaw), renal osteodystrophy

Familial / Hereditary Fibrous Dysplasia

= CHERUBISM [*kerubh*, Hebrew = winged angel]

= autosomal dominant disorder of variable penetrance; probably form of giant cell reparative granuloma rather than fibrous dysplasia

Age: childhood; more severe in males

• bilateral jaw fullness

• slight upward turning of eyes directed heavenward

Location: bilateral symmetric involvement of mandible + maxilla

√ bilateral mandibular swelling ← expansile multiloculated cystic masses

√ upward bulging of orbital floor ← maxillary expansion

Cx: problems with dentition after perforation of cortex

Prognosis: rapid progression until age of 7 years followed by regression after adolescence

McCune-Albright Syndrome (10%)

[Donovan James McCune (1902–1976), American pediatrician at Columbia University,

New York]
[Fuller Albright (1900–1969), American endocrinologist at Massachusetts General Hospital in Boston]
= nonhereditary phakomatosis
Genetics: gain-of-function mutation in GNAS1 gene → constitutive stimulation of cyclic AMP protein signaling pathway
Age: childhood
Sex: almost exclusively in girls
(1) Polyostotic fibrous dysplasia (mostly unilateral)
Location: skull + face (50%), pelvis, femur, tibia
√ medullary ground-glass lytic areas + thin cortices + endosteal scalloping
√ areas of sclerotic / cystic change
√ "shepherd's crook" deformity of femur ← multiple cortical microfractures
Cx: osteosarcoma (in 4%)
(2) Café-au-lait macules (35%)
= few large segmental yellowish to brownish dark tan patches of cutaneous pigmentation with jagged irregular / serrated border = **coast of Maine** patches (DDx: more numerous and lighter "coast of California" spots in neurofibromatosis)
Site: lumbosacral area (30–50%), buttocks, neck, shoulders without crossing the midline; often ipsilateral to bone lesions
(3) Endocrinopathy = increased endocrine function:
(a) peripheral sexual precocity (in females in 65–79%, in males in 15%)
• menarche in infancy (in 20%)
√ bilateral >> unilateral testicular enlargement
√ testicular microlithiasis
(b) hyperthyroidism ← hypothalamic dysfunction
• pituitary gigantism
• Cushing syndrome, galactorrhea
• hepatobiliary dysfunction
• renal phosphate wasting
√ adrenal + thyroid nodules

Jaffé-Lichtenstein Disease *(10%)*
[Henry Lewis Jaffe (1896–1979), American pathologist and director of laboratories at the Hospital for Joint Diseases, Langone Medical Center in New York]
[Louis Lichtenstein (1906–1977), American pathologist in New York, Los Angeles and San Francisco]
Location: craniofacial + noncraniofacial bones
• cutaneous café-au-lait spots
• rare endocrinopathies

Monostotic Fibrous Dysplasia (70–80%)
Age: 10–70 years
• usually asymptomatic until 2nd–3rd decade
• incidental discovery: obvious deformity / dull aching pain

• pain ← pathologic fracture

Location: ribs (6–28%), proximal femur (23%), tibia, craniofacial bones (10–25%)[frontal, sphenoid, maxillary, ethmoid], humerus

Rules: (1) No conversion to polyostotic form
(2) No increase in size over time
(3) Disease becomes inactive at puberty

Polyostotic Fibrous Dysplasia (20–30%)

Mean age: 8 years

• ⅔ symptomatic by age 10; coast of Maine café-au-lait spots
• leg pain, limp, pathologic fracture (75%)
• abnormal vaginal bleeding (25%)
• short stature ← bowing of extremities + premature fusion of growth plates + scoliosis

Associated with: endocrinopathy (in 2–3%)
◊ 2–3% of patients with polyostotic fibrous dysplasia have McCune-Albright syndrome

Location: usually unilateral + asymmetric; femur (91%), tibia (81%), pelvis (78%), foot (73%), ribs (55%), skull + facial bones (50%), upper extremities, lumbar spine (14%), clavicle (10%), cervical spine (7%)

Site: metadiaphysis

Rules: (1) Often unilateral + sometimes monomelic
(2) Tendency to involve larger segments of bone
(3) Frequently associated with severe deformities and fractures
(4) No spread / proliferation over time
(5) Disease becomes quiescent at puberty

√ leg length discrepancy (70%)
√ "shepherd's crook" deformity (35%) = coxa vara angulation of proximal femur
√ "saber shin" deformity = anterior bowing of tibia
√ facial asymmetry
√ tibial bowing
√ rib deformity
√ monomelic "ray" pattern = involvement of all phalanges and metacarpal bone in a single digit

FIBROUS HISTIOCYTOMA

Benign Fibrous Histiocytoma

Frequency: 0.1% of all bone tumors

Histo: interlacing bundles of fibrous tissue in storiform pattern (whorled / woven) interspersed with mono- / multinucleated cells resembling histiocytes, benign giant cells, and lipid-laden macrophages; resembles nonossifying fibroma / fibroxanthoma

Age: 23–60 years

• localized intermittently painful soft-tissue swelling

Location: long bone, pelvis, vertebra (rare)

Site: typically in epiphysis / epiphyseal equivalent
√ well-defined radiolucent lesion with septa / soap-bubble appearance / no definable matrix
√ may have reactive sclerotic rim
√ narrow transition zone (= nonaggressive lesion)
√ no periosteal reaction
Rx: curettage
DDx: nonossifying fibroma (childhood / adolescence, asymptomatic, eccentric metaphyseal location)

Atypical Benign Fibrous Histiocytoma

Histo: "atypical aggressive" features = mitotic figures present
√ lytic defect with irregular edges
Prognosis: may metastasize

Malignant Fibrous Histiocytoma

= MFH = UNDIFFERENTIATED PLEOMORPHIC SARCOMA
= MALIGNANT FIBROUS XANTHOMA
= XANTHOSARCOMA = MALIGNANT HISTIOCYTOMA
= FIBROSARCOMA VARIANT
Histo: spindle-cell neoplasm of a mixture of fibroblasts + giant cells resembling histiocytes with nuclear atypia and pleomorphism in pinwheel arrangement; closely resembles high-grade fibrosarcoma (= fibroblastic cells arranged in uniform pattern separated by collagen fibers)
(a) pleomorphic-storiform subtype (50–60%)
(b) myxoid subtype (25%)
(c) giant cell subtype (5–10%)
(d) inflammatory subtype (5–10%)
(e) angiomatoid subtype (< 5%)
Mean age: 50 (range, 10–90) years; peak prevalence in 5th decade; more frequent in Caucasians; M÷F = 3÷2
Location: potential to arise in any organ (ubiquitous mesenchymal tissue); soft tissues >> bone

Soft-tissue MFH

Frequency: 20–24–30% of all soft-tissue sarcomas; most common primary malignant soft-tissue tumor of late adult life
◊ Any deep-seated invasive intramuscular mass in a patient > 50 years of age is most likely MFH!
• large painless lobulated soft-tissue mass with progressive enlargement over several months
Location: extremities (75%), [lower extremity (50%), upper extremity (25%)], retroperitoneum (15%), head + neck (5%); subcutis (7–10%)
Site: within large muscle groups
Size: usually 5–10 cm → increasing over months / years
√ poorly defined curvilinear / punctate peripheral calcifications / ossifications (in 5–20%)

√ commonly cortical erosion of adjacent bone (HIGHLY SUGGESTIVE FEATURE)

CT:

√ well-defined large lobulated soft-tissue mass with attenuation similar to that of muscle

√ central hypodense area = myxoid MFH (DDx: hemorrhage, necrosis, leiomyosarcoma with necrosis, myxoid lipo- / chondrosarcoma)

√ enhancement of solid components

√ invasion of adjacent organs

MR:

√ inhomogeneous poorly defined lesion:

√ low to intermediate SI similar to muscle on T1WI

√ heterogeneously intermediate to high SI on T2WI

√ contrast enhancement more pronounced in periphery than at center ← central location of hemorrhage + necrosis + myxoid tumor component:

√ myxoid tumor component similar to fluid

√ nodular + peripheral enhancement of nonmyxomatous cellular region

Prognosis: larger + more deeply located tumors have a worse prognosis; 2-year survival rate of 60%; 5-year survival rate of 50%; local recurrence rate of 19–31%; metastatic rate of 31–35% (lung [90%], bone [8%], liver [1%], lymph nodes [4–17%])

DDx: (1) Liposarcoma (younger patient, presence of fat in > 40%, calcifications rare)

(2) Rhabdomyosarcoma

(3) Synovial sarcoma (cortical erosion)

Osseous MFH

Prevalence: 5% of all primary malignant bone tumors

- painful, tender, rapidly enlarging mass
- pathologic fracture (20%)

Associated with:

prior radiation therapy, bone infarcts, Paget disease, fibrous dysplasia, osteonecrosis, fibroxanthoma (= nonossifying fibroma), enchondroma, chronic osteomyelitis

◊ 20% of osseous MFH arise in areas of abnormal bone!

Location: femur (45%), tibia (20%), 50% about knee; humerus (10%); ilium (10%); spine; sternum; clavicle; rarely small bones of hand + feet

Site: central metaphysis of long bones (90%); eccentric in diaphysis of long bones (10%)

Size: 2.5–10 cm in diameter

√ radiolucent defect with ill-defined margins

√ extensive mineralization / small areas of focal metaplastic calcification

√ permeation + cortical destruction

√ expansion in smaller bones (ribs, sternum, fibula, clavicle)

√ occasionally lamellated periosteal reaction (especially in presence of pathologic fracture)

√ soft-tissue extension

Cx: pathologic fracture (30–50%)

DDx: (1) Metastasis
(2) Fibrosarcoma (often with sequestrum)
(3) Reticulum cell sarcoma
(4) Osteosarcoma
(5) Giant cell tumor
(6) Plasmacytoma

Pulmonary MFH (extremely rare)
√ solitary pulmonary nodule without calcification
√ diffuse infiltrate
NUC:
√ increased uptake of ^{99m}Tc-MDP (mechanism not understood)
√ increased uptake of ^{67}Ga-citrate
US:
√ well-defined mass with hyperechoic + hypoechoic (necrotic) areas
CT:
√ mass of muscle density with hypodense areas (necrosis)
√ invasion of abdominal musculature, but not IVC / renal veins (DDx to renal cell carcinoma)
Angio:
√ hypervascularity + early venous return

FLORID REACTIVE PERIOSTITIS

• progressive painful inflammatory swelling
Age: 20–30 years
Location: small bones of hands + feet with predilection for proximal phalanx
Site: index > middle > little > any other finger
√ calcified paraosseous mass (paraosseous = radiolucent band between mass and cortex of adjacent bone)
√ lamellar / compact periosteal reaction → maturing on follow-up without bone destruction

FOCAL FIBROCARTILAGINOUS DYSPLASIA OF TIBIA

Associated with: tibia vara
Age: 9–28 months
Histo: dense hypocellular fibrous tissue resembling tendon with lacuna formation
• slight shortening of affected leg
Location: insertion of pes anserinus (= tendinous insertion of gracilis, sartorius, semitendinosus muscles) distal to proximal tibial physis; unilateral involvement
√ unilateral tibia vara
√ well-defined elliptic obliquely oriented lucent defect in medial tibial metadiaphyseal cortex
√ sclerosis along lateral border of lesion
√ absence of bone margin superomedially
Prognosis: resolution in 1–4 years
DDx: (1) Unilateral Blount disease (typically bilateral in infants, varus angulation of upper

tibia, decreased height of medial tibial metaphysis, irregular physis)

(2) Chondromyxoid fibroma, eosinophilic granuloma, osteoid osteoma, osteoma, fibroma, chondroma (not associated with tibia vara, soft-tissue mass)

FRACTURE

= soft-tissue injury with break in continuity of bone or cartilage

General description:

(1) OPEN / CLOSED

open Fx = communication between fractured bone + skin

(2) COMPLETE / INCOMPLETE

complete Fx = all cortical surfaces disrupted

incomplete Fx = partial separation of bone

Incomplete pediatric fractures:

(a) longitudinal compressive force:
buckle / torus Fx

bowing Fx = plastic deformity of thin long bone (ulna > clavicle, fibula)

(b) force perpendicular to long axis of bone **greenstick Fx**

(c) combination fracture

lead-pipe Fx = combination of greenstick + torus Fx

(3) SIMPLE / COMMINUTED

simple Fx = noncomminuted

comminuted Fx = > 2 fragments

segmental Fx = isolated segment of shaft

butterfly fragment = V-shaped fragment not completely circumscribed by cortex

(4) DIRECTION OF FRACTURE LINE relative to long axis of bone:
transverse, oblique, oblique-transverse, spiral

Special terminology:

avulsion Fx = fragment pulled off by tendon / joint capsule / ligament from parent bone

transchondral Fx = cartilaginous surface involved

chondral Fx = cartilage alone involved

osteochondral Fx = cartilage + subjacent bone involved

Description of anatomic positional changes:

= change in position of distal fracture fragment in relation to proximal fracture fragment

LENGTH = longitudinal change of fragments

distraction = increase from original anatomic length

shortening = decrease from original anatomic length

› impacted = fragments driven into each other

› overriding = also includes latitudinal changes

› overlapping = bayonet apposition

DISPLACEMENT = latitudinal change of anatomic axis

› undisplaced

› anterior, posterior, medial / ulnar, lateral / radial

ANGULATION / TILT

= long axes of fragments intersect at the fracture apex:

› medial / lateral, ventral / dorsal
› varus = angular deviation of distal fragment toward midline on frontal projection
› valgus = angular deviation of distal fragment away from midline on frontal projection
eg, "ventral angulation of fracture apex"
eg, "in anatomic / near anatomic alignment"

ROTATION
◊ Difficult to detect radiographically!
√ differences in diameters of apposing fragments
√ mismatch of fracture line geometry
› internal / external rotation

NUC:

Typical time course:

1. Acute phase (3–4 weeks) abnormal in 80% < 24 hours, in 95% < 72 hours
   ◊ Elderly patients show delayed appearance of positive scan
   √ broad area of increased tracer uptake (wider than fracture line)
2. Subacute phase (2–3 months) = time of most intense tracer accumulation
   √ more focal increased tracer uptake corresponding to fracture line
3. Chronic phase (1–2 years)
   √ slow decline in tracer accumulation
   √ in 65% normal after 1 year; > 95% normal after 3 years

Return to normal:

◊ Non–weight-bearing bone returns to normal more quickly than weight-bearing bone
→ rib fractures return to normal most rapidly
◊ Complicated fractures with orthopedic fixation devices take longest to return to normal

1. Simple fractures: 90% normal by 2 years
2. Open reduction / fixation: < 50% normal by 3 years
3. Delayed union: slower than normal for type of fracture
4. Nonunion: persistent intense uptake in 80%
5. Complicated union (true pseudarthrosis, soft-tissue interposition, impaired blood supply, presence of infection)
   √ intense uptake at fracture ends
   √ decreased uptake at fracture site
6. Vertebral compression fractures: 60% normal by 1 year; 90% by 2 years; 97% by 3 years

Pathologic Fracture

= fracture at site of preexisting osseous abnormality

Cause: tumor, osteoporosis, infection, metabolic disorder

Stress Injury (Fracture)

= fracture produced as a result of repetitive prolonged muscular action on bone exceeding its capability for self-repair

Insufficiency Fracture

= normal physiologic stress applied to bone with abnormal elastic resistance / deficient

mineralization

Cause:

1. Osteoporosis
2. Renal osteodystrophy

Types of Fractures		
Type	*Bone Quality*	*Load*
Traumatic	normal	single large
Fatigue (stress)	normal	repetitive
Insufficiency (stress)	abnormal (metabolic)	minimal
Pathologic	abnormal (tumor)	minimal

3. Osteomalacia / rickets
4. Hyperparathyroidism
5. Radiation therapy
6. Rheumatoid arthritis
7. Paget disease
8. Fibrous dysplasia
9. Osteogenesis imperfecta
10. Osteopetrosis
11. Prolonged corticosteroid treatment
12. Tumor treatment with ifosfamide, methotrexate

Location: thoracic vertebra, sacrum, pubic bone, ilium, lower extremity (calcaneus, tibia, fibula)

Fracture orientation: perpendicular to long axis of bone

Plain film / CT (1–2 weeks after onset of fracture):

√ often normal in early stage of fracture
√ cortical linear lucency ← disruption (= fracture line)
√ localized cortical thickening
√ periosteal new bone formation
√ medullary sclerosis (endosteal callus formation)

MR:

√ zone of low SI on T1WI + variable intensity on T2WI (= discrete fracture line)
√ surrounded by diffuse marrow edema (hypointense on T1WI + hyperintense on T2WI) = stress reaction
√ circumferential periosteal reaction + early callus + surrounding edema adjacent to bone hyperintense on T2WI + enhancement after IV Gd-chelate (DDx: osteomyelitis with more eccentric involvement)

NUC (bone scan):

√ increased abnormal uptake

Pelvic Insufficiency Stress Fracture

- severe pain in lower back + sacroiliac joints; radiates to buttocks, hips, groin, legs; worsens with weight bearing
- walking ability impaired

Prevalence: 1.8–5% of women > 55 years
Predisposed: postmenopausal women
Location: sacral ala, parasymphyseal region of os pubis, pubic rami, supraacetabular region, iliac blades, superomedial portion of ilium
Types:
(a) occult fracture:
Site: sacrum > supraacetabulum, ilium
√ sclerotic band, cortical disruption, fracture line
◊ Often obscured by overlying bowel gas + osteopenia!
(b) aggressive fracture:
Site: parasymphysis, pubic rami
√ exuberant callus formation, osteolysis + fragments ← prolonged / delayed healing / chronic nonunion
CAVE: fracture may be misdiagnosed as neoplasm; interpretation also histologically difficult
NUC:
√ butterfly / H-shaped ("Honda" sign) / asymmetric incomplete H-shaped pattern of sacral uptake
√ pelvic outlet view for parasymphyseal fx
CT and MR (most accurate modalities):
√ sclerotic band, linear fracture line, cortical disruption, fragmentation, displacement
√ bone marrow edema
◊ Excludes bone destruction + soft-tissue masses!
Prognosis: healing in 12–30 months

FEMORAL INSUFFICIENCY FRACTURE

Site: subcapital
√ subtle femoral neck angulation
√ trabecular angulation
√ subcapital impaction line

Fatigue (Stress) Fracture

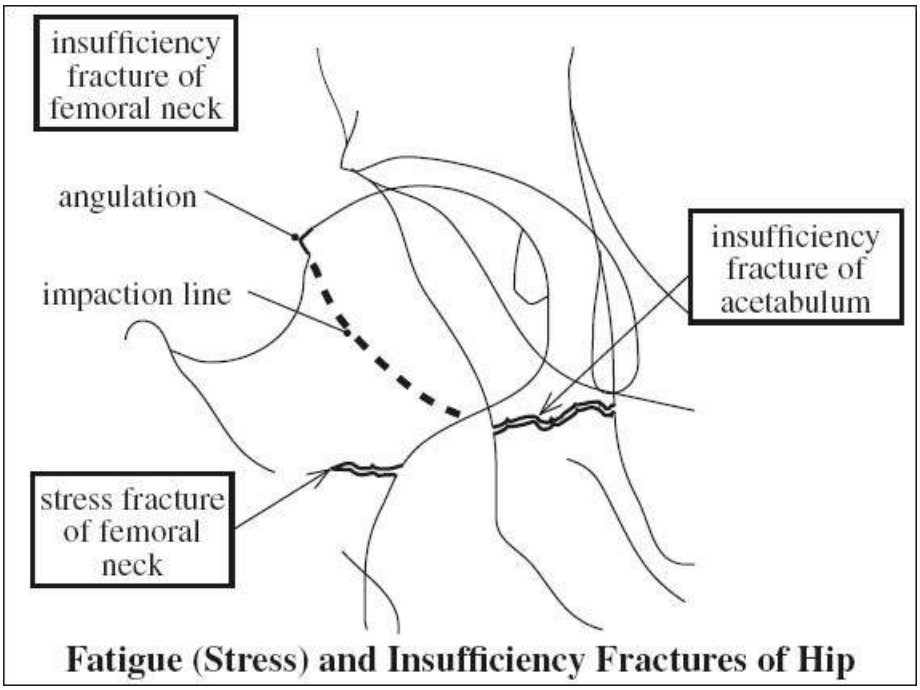
= normal bone subjected to repetitive stresses (none of which is singularly capable of producing a fracture) → leading to mechanical failure over time
Risk factors: new / different / rigorous repetitive activity; female sex; increased age; Caucasian race; low bone mineral density; low calcium intake; fluoride treatment for osteoporosis; condition resulting in altered gait
• activity-related pain abating with rest
• constant pain with continued activity
√ infraction in the center of an area of cortical thickening
√ extensive bidirectional cortical thickening from endosteum to periosteum
√ focal cortical ridge
NUC:
√ linear intense uptake of tracer
DDx: Osteoid osteoma (round nidus, no cortical ridge, "double-density" sign on bone

scan)

@ Spine
1. Clay shoveler's fracture: spinous process of lower cervical / upper thoracic spine
2. Spondylolysis = pars interarticularis of lumbar vertebra: ballet, gymnastics, diving
3. Ribs: carrying heavy pack, golf, coughing

@ Pelvis
1. Obturator ring of pelvis: stooping, bowling, gymnastics
   Site: superior / inferior pubic ramus
2. Sacrum (< 2%): long-distance runner, military recruits
   Site: unilateral ? ← leg length discrepancy

@ Upper extremity
1. Clavicle: postoperative (radical neck dissection)
2. Coracoid process of scapula: trap shooting



Fatigue (Stress) and Insufficiency Fractures of Hip

3. Coronoid process of ulna: pitching ball, throwing javelin, pitchfork work, propelling wheelchairs
4. Distal shaft of humerus: throwing ball (basketball, baseball, softball, javelin)
5. Hook of hamate: swinging golf club / tennis racquet / baseball bat
6. Other wrist bones: capitate > lunate > scaphoid

@ Lower extremity
1. Femur
   › neck: ballet, long-distance running
   Site: inferior surface of medial femoral neck
   √ subtle lucency / sclerosis (= acute fracture)
   √ lucent line surrounded by sclerosis (= subacute fracture)
   › shaft: ballet, marching, long-distance running, gymnastics

› distal metaphysis: endurance athlete (runner, soccer player, triathlete)

3. Patella: hurdling
4. Tibial shaft:
   › proximal diaphysis: running
   › middle + distal diaphysis: football, soccer, tennis, ballet, jogging
   ◊ Shin splint = early stress response
5. Fibula (distal diaphysis): long-distance running, jumping, parachuting

@ Foot (in order of frequency):

1. $2^{nd} > 3^{rd} + 4^{th}$ metatarsal: marching, stomping on ground, prolonged standing, ballet, long-distance running, postoperative bunionectomy
2. Calcaneus: jumping, parachuting, prolonged standing, long standing, recent immobilization
   √ vertical / oblique fracture orientation anterior to tuberosity
3. Tarsal navicular: stomping on ground, marching, long-distance running, prolonged standing, ballet
   √ vertically oriented fracture in midbody
   ◊ Midfoot fractures are difficult to diagnose by conventional radiography; CT + MRI are often helpful
4. Sesamoids of metatarsal: prolonged standing, gymnastics, long jumping

X-RAY (15% sensitive in acute fractures, increasing to 50% on follow-up):

› cancellous (trabecular) bone (notoriously difficult to detect)
  √ subtle blurring of trabecular margins
  √ faint sclerotic radiopaque area of peritrabecular callus (50% change in bone density needed)
  √ sclerotic band (← trabecular compression + callus formation) usually perpendicular to cortex
› compact (cortical) bone
  √ "gray cortex" sign = subtle ill definition of cortex
  √ intracortical radiolucent striations (early)
  √ solid thick lamellar periosteal new bone formation
  √ endosteal thickening (later)

◊ Follow-up radiography after 2–3 weeks of conservative therapy

NUC (no longer "gold standard" compared with MR):

◊ Highly sensitive with low specificity + ineffective in early cortical stress injuries
√ abnormal uptake within 6–72 hours of injury (prior to radiographic abnormality)
√ "stress reaction" = focus of subtly increased uptake
√ focal fusiform area of intense cortical uptake
√ abnormal uptake persists for months

MR (very sensitive modality; fat saturation technique most sensitive as it detects an increase in water content of medullary edema / hemorrhage):

√ increased marrow SI on T2WI + STIR (extensive micro- fractures cause edema + hemorrhage, which may obscure the fracture line); resolves within 6 months in 90%
√ low-intensity band contiguous with cortex on T2WI = fracture line of more advanced lesion
√ diminished marrow SI on T1WI of fracture line (less helpful)

√ periosteal edema = hyperintense line along periosteal surface on T2WI

CT (best modality for cortical abnormalities):

helpful in: longitudinal stress fracture of tibia; in confusing pediatric stress fracture (to detect endosteal bone formation)

√ cortical abnormalities:

√ osteopenia = increased hypoattenuation

√ resorption cavities = round / oval hypoattenuating intracortical defect

√ striations = subtle hypoattenuating intracortical lines

DDx: (1) Shin splints (activity not increased in angiographic / blood-pool phase)
√ long linear uptake on posteromedial (soleus muscle) / anterolateral (tibialis anterior muscle) tibial cortex on delayed images (from stress to periosteum at muscle insertion site)

(2) Osteoid osteoma (eccentric, nidus, solid periosteal reaction, night pain)

(3) Chronic sclerosing osteomyelitis (dense, sclerotic, involving entire circumference, little change on serial radiographs)

(4) Osteomalacia (bowed long bones, looser zones, gross fractures, demineralization)

(5) Osteogenic sarcoma (metaphyseal, aggressive periosteal reaction)

(6) Ewing tumor (lytic destructive appearance with soft-tissue component, little change on serial radiographs)

Apophyseal Injury = Avulsion Fracture

Mechanism: excessive avulsive force

◊ Physis under secondary ossification center is weakest part!

At risk: young athletes: hurdlers, sprinters, cheerleaders (repetitive to and fro adduction / abduction + flexion / extension)

Age: children > adults

◊ Avulsion injury of lesser trochanter in adults suggests underlying malignant disease

• pain, point tenderness, swelling

√ physeal widening

√ irregularity at site of avulsion

√ displaced pieces of bone of variable size:

√ crescentic ossific opacity if viewed on tangent

√ very subtle disk-shaped opacity if seen en face

√ abnormal foci of heterotopic ossification (later)

√ prominent bone formation in chronic avulsion injury from overuse with repeated microtraumas

DDx of healing acute injury: osteomyelitis, Ewing sarcoma

Overuse Injury to Physis

Little League Shoulder

= overuse injury to proximal humeral physis

Mechanism: excessive overhead throwing

Apophyseal Avulsion Injuries	
Location	*Muscle Origin / Insertion*
Iliac crest	abdominal musculature
Anterior superior iliac spine	sartorius muscle + tensor fasciae latae m.
Anterior inferior iliac spine	rectus femoris muscle
Symphysis pubis + inferior pubic ramus	long + short adductors, gracili
Ischial tuberosity	hamstrings
Lesser trochanter	iliopsoas muscle
Greater trochanter	gluteus medius + minimus, internal obturator, gemellus, piriformis
Inferior pole of patella	patellar tendon
Tibial tuberosity	patellar tendon

√ widening + irregularity of proximal humeral physis

Little League Elbow

= traction injury of medial humeral epicondyle

Mechanism: pitching → valgus stress of cocking and acceleration

√ localized bone marrow edema

√ widening of physis

Gymnast Wrist

Mechanism: repetitive weight bearing on wrist

√ physeal stress changes of distal radius ± ulna

√ positive ulnar variance ← abnormal distal radial growth

Cx: strain / tear of triangular fibrocartilage complex

Epiphyseal Plate Injury

Prevalence: 6–18–30% of bone injuries in children < 16 years

Peak age: 12 years

Location: distal radius (28%), phalanges of hand (26%), distal tibia (10%), distal phalanges of foot (7%), distal humerus (7%), distal ulna (4%), proximal radius (4%), metacarpals (4%), distal fibula (3%)

Mechanism: 80% shearing force; 20% compression

Resistance to trauma: ligament > bone > physis (hypertrophic zone most vulnerable)

MR:

√ focal dark linear area (= line of cleavage) within bright physis on gradient echo images (GRE)

Cx: (1) progressive angular deformity from segmental arrest of germinal zone growth with formation of a bone bridge across physis = "bone bar"

(2) limb length discrepancy from total cessation of growth

(3) articular incongruity from disruption of articular surface

(4) Bone infarction in metaphysis / epiphysis

Salter-Harris Classification:
(considering probability of growth disturbance)
[Robert Bruce Salter (1924–) and W. Robert Harris (1922–), orthopedic surgeons in Toronto, Canada]
◊ Prognosis is worse in lower extremities (ankle + knee) irrespective of Salter-Harris type!
mnemonic: SALTR

Slip of physis	=	type 1
Above physis	=	type 2 (distal)
Lower than physis	=	type 3 (proximal)
Through physis	=	type 4
Rammed physis	=	type 5

Salter Type 1 (6–8.5%)
= slip of epiphysis (← shearing force separates epiphysis from physis)
Line of cleavage: confined to physis
Location: most commonly in phalanges, distal radius (includes: apophyseal avulsion, slipped capital femoral epiphysis)
√ widening of growth plate
√ displacement of epiphyseal ossification center
Prognosis: favorable irrespective of location

Salter Type 2 (73–75%)
= shearing force splits growth plate
Line of fracture: through physis + extending through margin of metaphysis separating a triangular metaphyseal fragment (= "corner" sign)
Location: distal radius (33–50%), distal tibia + fibula, phalanges
Prognosis: good, may result in minimal shortening

Salter Type 3 (6.5–8%)
= intraarticular fracture, often occurring after partial closure of physis
Line of fracture: vertically / obliquely through epiphysis + extending horizontally to periphery of physis
Location: distal tibia, distal phalanx, rarely distal femur
√ epiphysis split vertically
Prognosis: fair (imprecise reduction leads to alteration in linearity of articular plane)

Salter Type 4 (10–12%)
Location: lateral condyle of humerus, distal tibia
√ fracture involves metaphysis + physis + epiphysis
Prognosis: guarded (may result in deformity + angulation)

TRIPLANE FRACTURE (6%)
Location: distal tibia, lateral condyle of distal humerus
√ vertical fracture of epiphysis + horizontal cleavage plane within physis + oblique

fracture of adjacent metaphysis

Salter Type 5 (< 1%)

= crush injury with injury to vascular supply
Location: distal femur, proximal tibia, distal tibia
Often associated with: fracture of adjacent shaft
√ no immediate radiographic finding
√ shortening of bone + cone epiphysis / angular deformity on follow-up
Prognosis: poor (impairment of growth in 100%)

Scapula Fracture

Most scapular fractures are minimally displaced extraarticular fractures of the scapular body, acromion, or coracoid process. Fractures of the glenoid neck or articular surface are more likely to require surgical repair.

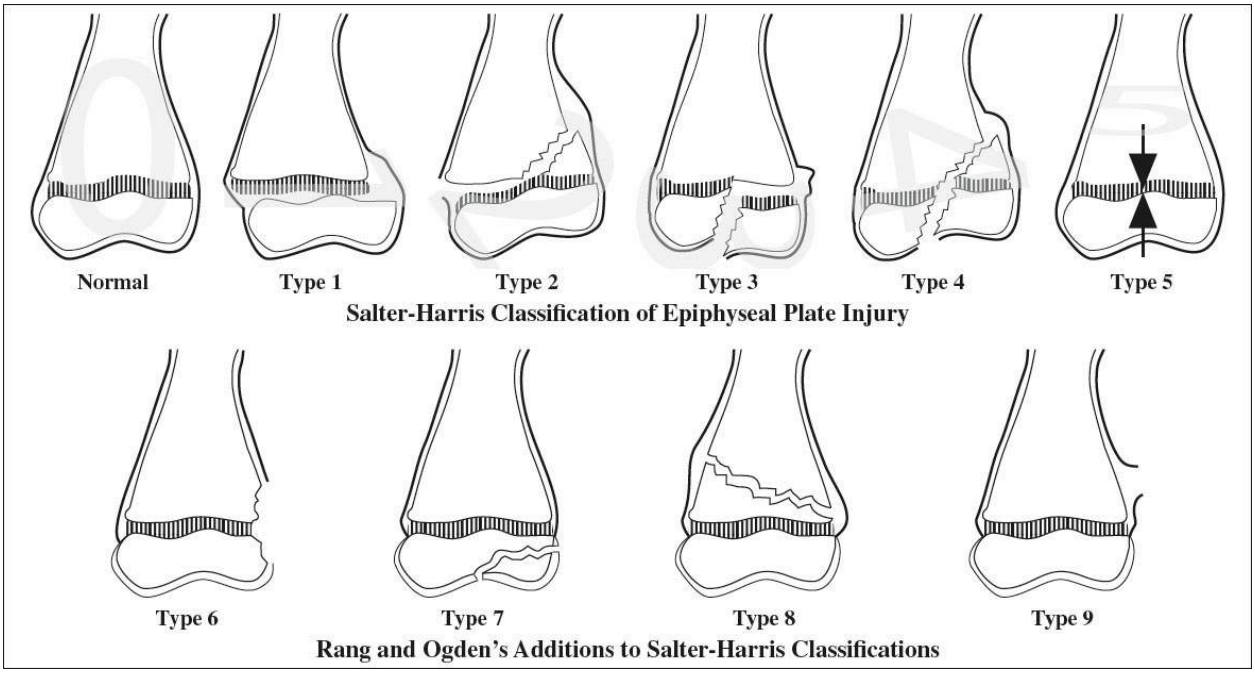
= rare < 1% of all extremity fractures
Mechanism: high-energy chest trauma
In 90% associated with: injury to chest, spine, pelvis, internal organs, brachial plexus, axillary vessels

Proximal Humerus Fracture

= may consist of up to 4 parts (fragment displaced by ≥ 1 cm / angled by ≥ 45°)
(1) anatomic head
(2) metaphyseal fragment with lesser tuberosity
(3) metaphyseal fragment with greater tuberosity
(4) humeral shaft

Prognosis: anatomic neck fractures are associated with an increased risk of avascular necrosis. The PPV is 97% if combined with a medial metaphyseal fragment < 8 mm short and > 2 mm displaced.

Neer classification (1970):
› 1-part fracture (85%) = no displacement / angulation
› 2- / 3- / 4-part fracture (15%)



Elbow Fracture

Pediatric Elbow Fracture

Age: common at 2–14 years

@ Soft-tissue

√ displacement of anterior + posterior fat pads (= elbow joint effusion with supracondylar / lateral condylar / proximal ulnar fractures)

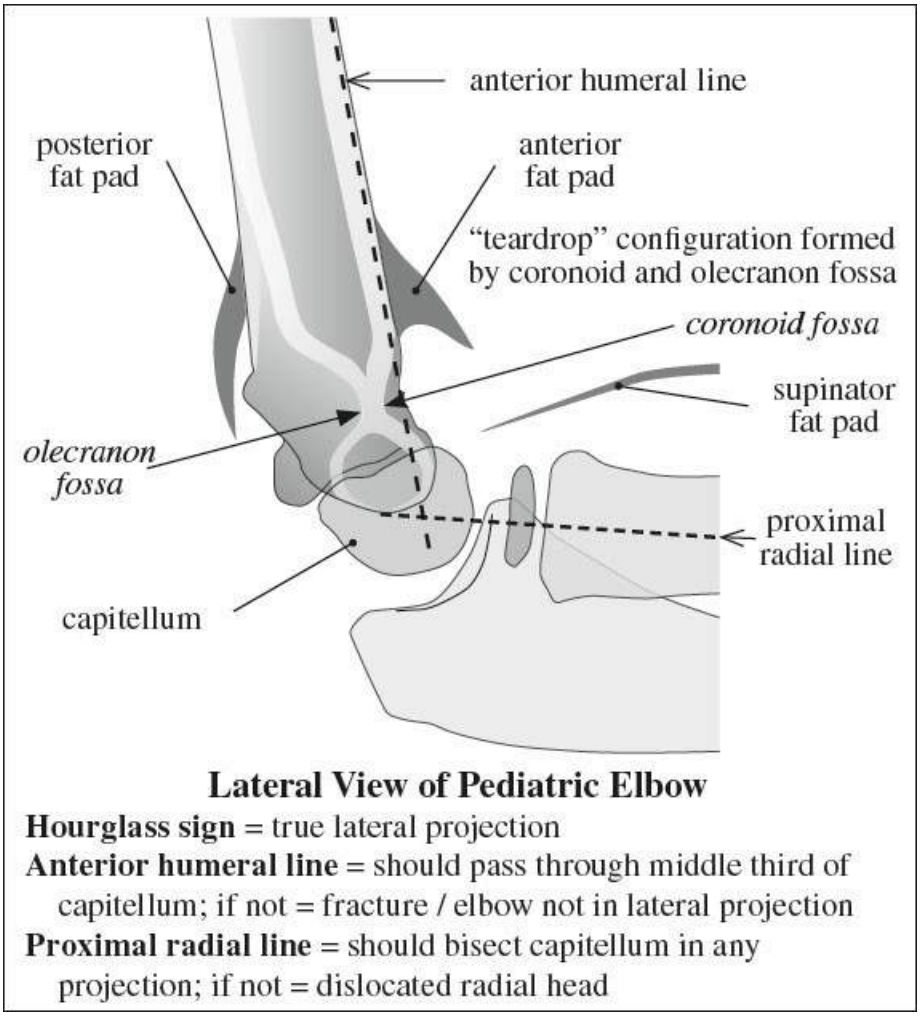
√ displaced supinator fat pad (= fracture of proximal radius)

√ focal edema medially (= medial epicondyle fx) / laterally (= lateral condyle fx)

@ Humerus (80%)

Supracondylar fracture (55%)

Mechanism: hyperextension with vertical stress



Lateral View of Pediatric Elbow

Hourglass sign = true lateral projection
Anterior humeral line = should pass through middle third of capitellum; if not = fracture / elbow not in lateral projection
Proximal radial line = should bisect capitellum in any projection; if not = dislocated radial head

√ transverse fracture line
√ distal fragment posteriorly displaced / tilted
√ anterior humeral line intersecting anterior to posterior third of capitellum (on lateral x-ray)

Lateral condylar fracture (20%)

Mechanism: hyperextension with varus stress

√ fracture line between lateral condyle + trochlea / through capitellum

Medial epicondylar fracture (5%)

Mechanism: hyperextension with valgus stress

√ avulsion of medial epicondyle (by flexor muscles of forearm)
√ may become trapped in joint space (after reduction of concomitant elbow dislocation)

@ Radius (10%)

Mechanism: hyperextension with valgus stress

√ Salter-Harris type II / IV fracture
√ transverse metaphyseal / radial neck fracture

Mechanism: hyperextension with varus stress

√ dislocation as part of Monteggia fracture (from rupture of annular ligament)

@ Ulna (10%)

√ longitudinal linear fracture through proximal shaft
Mechanism: hyperextension with vertical stress

√ transverse fracture through olecranon
Mechanism: hyperextension with valgus / varus stress; blow to posterior elbow in flexed position

√ coronoid process avulsion
Mechanism: hyperextension-rotation associated with forceful contraction of brachial m.

Elbow Dislocation

2nd most common joint dislocation in adult after shoulder

(a) Posterior elbow dislocation

(b) Anterior dislocation (rare): most often in child as a result of rebound following posterior dislocation

Associated soft-tissue injury (in sequence): lateral → medial

1. Lateral collateral ligament complex
2. Joint capsule + other lateral structures
3. MCL complex

Associated osseous injury:

Fracture of radial head + coronoid process (= terrible triad); medial epicondyle fracture; Essex-Lopresti fracture (rare)

Forearm Fracture

Pediatric Distal Forearm Fracture

BUCKLE / TORUS FRACTURE

= break in soft fibrous cortex with frequently intact periosteal sleeve

Cause: longitudinal compressive force

Location: distal radial + ulnar metaphyses

√ buckle in cortex on compression side of fracture

√ intact cortex on tension side

Prognosis: excellent stability; healing without complications after cast / splint immobilization

GREENSTICK FRACTURE

= break of bone cortex on tension side + intact periosteum

Cause: force perpendicular to long axis of bone

√ cortical disruption on tension (convex) side of fracture

√ intact cortex on compression side

Prognosis: unstable fracture → continued displacement for first 2 weeks

Barton Fracture

[John Rhea Barton (1794–1871), orthopedic surgeon at Pennsylvania Hospital,

Philadelphia]

Mechanism: fall on outstretched hand

√ intraarticular oblique fracture of ventral / dorsal lip of distal radius

√ carpus dislocates with distal fragment up + back on radius

Chauffeur Fracture

= HUTCHINSON FRACTURE = BACKFIRE FRACTURE = LORRY DRIVER FRACTURE

[Jonathan Hutchinson (1828–1913), British surgeon]

= name derived from direct trauma to radial side of wrist sustained from recoil of crank used in era of hand cranking to start automobiles

Mechanism: acute dorsiflexion + abduction of hand

√ triangular fracture of radial styloid process

Colles Fracture

[Abraham Colles (1773–1843), surgeon in Dublin, Ireland]

= POUTEAU FRACTURE (term used in France)

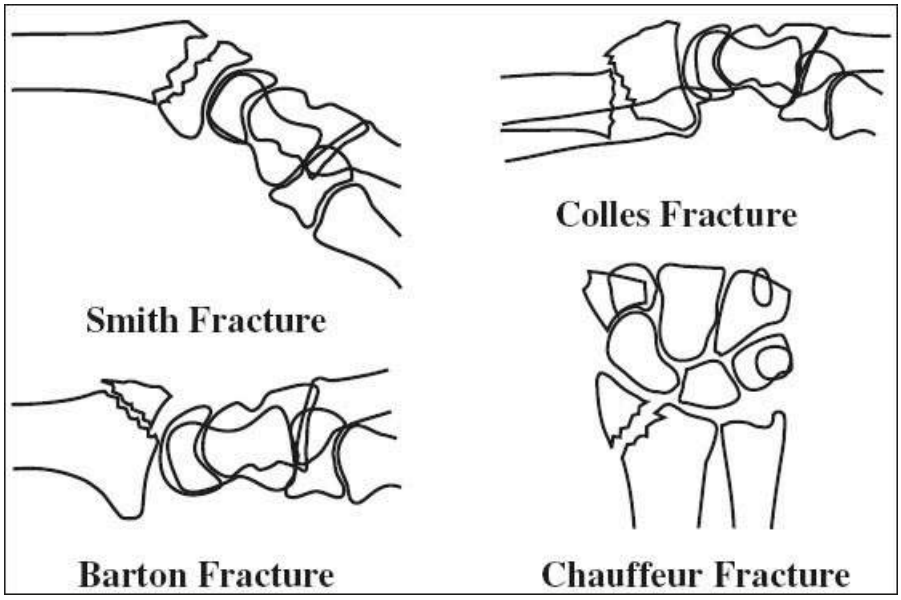
[Claude Pouteau (1725–1775), surgeon in Lyon, France]

◊ Most common fracture of forearm!

Mechanism: fall on outstretched hand

√ nonarticular radial fracture in distal 2 cm

√ dorsal displacement of distal fragment + volar angulation of fracture apex



√ ± ulnar styloid fracture

√ "silver-fork" deformity

Cx: posttraumatic arthritis

Rx: anatomic reduction important

Significant postreduction deformity:

1. Residual positive ulnar variance > 5 mm indicates unsatisfactory outcome in 40%

2. Dorsal angulation of palmar tilt > 15° decreases grip strength + endurance in > 50%

Essex-Lopresti Fracture

[Peter Gordon Essex-Lopresti (1918–1951), surgeon at Birmingham Accident Center, England]

Mechanism: FOOSH-type injury

• wrist pain / tenderness

√ "floating radius":

√ comminuted displaced radial head fracture

√ dislocation of distal radioulnar joint = discrepancy of radioulnar distance > 5 mm compared to contralateral uninjured wrist (on lateral radiograph)

√ disruption of interosseous membrane

Rx: nearly always surgical intervention

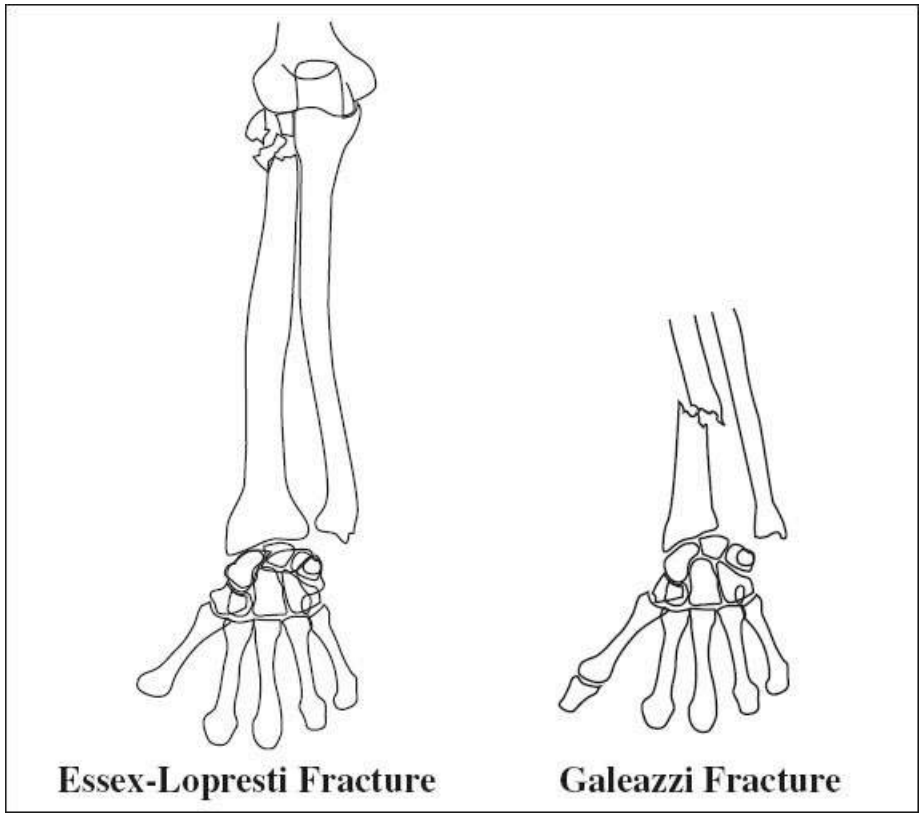
Galeazzi Fracture

[Ricardo Galeazzi (1866–1952), orthopedic surgeon in Italy]

= PIEDMONT FRACTURE

Mechanism: fall on outstretched hand with elbow flexed

√ radial shaft fracture (most commonly) at junction of distal to middle third with dorsal angulation



√ subluxation / dislocation of distal radioulnar joint

√ ulnar plus variance (= radial shortening) of > 10 mm implies complete disruption of

interosseous membrane = complete instability of radioulnar joint

Cx: (1) High incidence of nonunion, delayed union, malunion (unstable fracture)
(2) Limitation of pronation / supination

GALEAZZI-EQUIVALENT FRACTURE

= exclusively in skeletally immature children

Mechanism: hyperpronation / hypersupination

√ radial shaft fracture (4 primary types)

√ dislocation / epiphyseolysis of distal ulna

Monteggia-type Fracture

= ulnar shaft fracture + (often missed) radiocapitellar dislocation

Bado Classification:

[Jose Luis Bado (1903–1977), orthopedic surgeon in Uruguay]

Type I = classic fracture

[Giovanni Battista Monteggia (1762–1815), professor of anatomy and surgery at Istituzioni Chirurgiche at University of Pavia]

Mechanism: direct blow to the forearm

√ anteriorly angulated proximal ulnar fracture

√ anterior dislocation of radial head

√ may have associated wrist injury

Cx: nonunion, limitation of motion at elbow, nerve abnormalities

Type II = reverse Monteggia fracture

√ radial head displaced posteriorly / posterolaterally

√ dorsally angulated proximal ulnar fracture

Type III

√ lateral dislocation of radial head

√ ulnar metaphyseal fracture

Type IV

√ anterior displacement of radial head

√ fracture of proximal third of radius + ulna at the same level

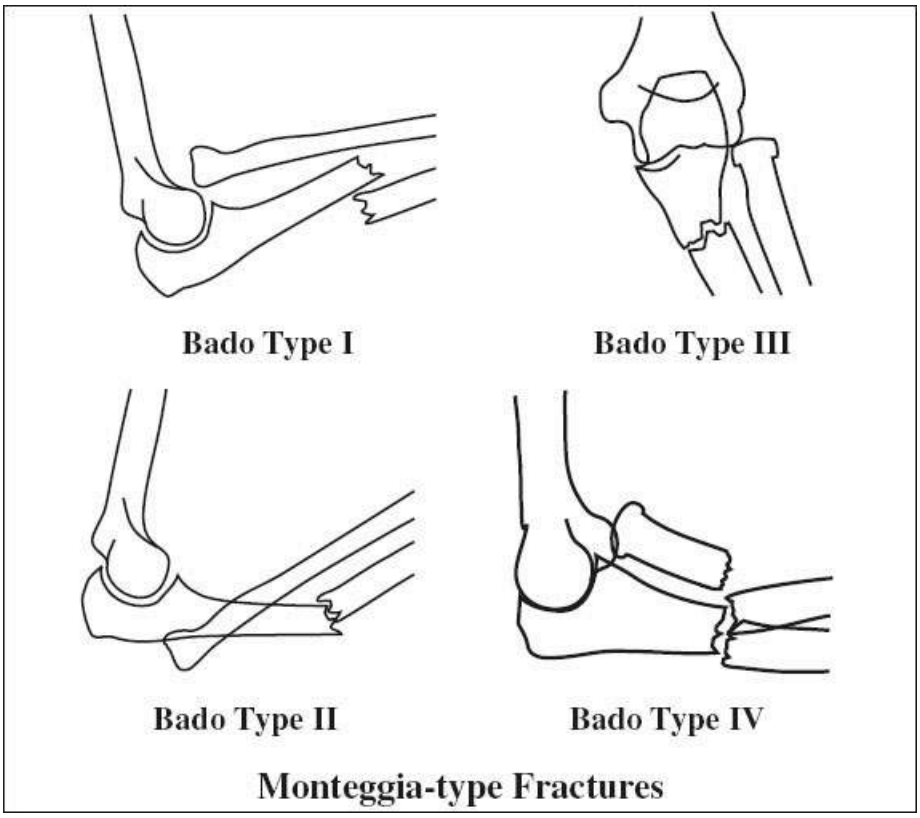
Smith Fracture

= REVERSE COLLES FRACTURE = REVERSE BARTON FRACTURE = GOYRAND FRACTURE (term used in France)

[Robert William Smith (1807–1873), succeeding Colles as professor of surgery at Trinity College in Dublin, Ireland]

Mechanism: hyperflexion with fall on back of hand

√ nonarticular distal radial fracture



Monteggia-type Fractures

√ ventral displacement of fragment
√ radial deviation of hand
√ "garden spade" deformity
Cx: altered function of carpus

Carpal Injury

Hamate Fracture

Prevalence: 1.7% of all carpal fractures
Mechanism: handle of racket / bat / club presses against protruding hook; axial loading force on body with clenched fist; fall on outstretched hand
May be associated with: perilunate dislocation
Location:
(a) hamate hook at palmar nonarticular surface
(b) body

• grip weakness; pain with resistance to flexion of 5th finger
√ hamulus not depicted on standard PA view
√ cortical density of hamulus lower than normal
Cx: 5th finger flexor tendon rupture; ulnar nerve palsy; hook nonunion
DDx: os hamuli proprium (ovoid / pyramidal bone with peripheral cortical bone)
Rx: open reduction with internal fixation for fractures displaced > 1 mm

Lunate Fracture

Prevalence: 4% of all carpal fractures
Mechanism: direct axial compression from head of capitate driven into lunate
Location: volar pole; dorsal pole; body
Fracture orientation: transverse, sagittal
Cx: nonunion → Kienböck disease

Pisiform Fracture

Prevalence: 1.3% of all carpal fractures (only 50% are diagnosed on PA radiograph)
Mechanism: fall on outstretched hand with direct impact on pisiform bone
May be associated with: carpal dislocation, distal radial fracture
Fracture type: linear, comminuted, chip
Cx: ulnar nerve injury
Rx: excision of pisiform bone

Scaphoid Fracture

= NAVICULAR FRACTURE
◊ Most frequent (90%) of all carpal bones fractures!
Age: active men during 2nd + 3rd decade
Mechanism: fall on dorsiflexed outstretched hand (hyperextension injury)
Location: waist (80%) > proximal pole
Fracture orientation: horizontal oblique, vertical oblique, transverse
• pain + tenderness at anatomic snuff box
Radiographic misses: 25–33–65%
N.B.: If initial radiograph negative, reexamine in 2 + 6 weeks after treatment with thumb-spica cast or proceed to CT / MRI!
CT: 89–97% sensitive; 85–100% specific; 97–99% NPV; 6–12 seconds examination time
MR: high sensitivity; 30–40 minutes examination time
Bone scan: up to 100% sensitive, 93% PPV after 2–3 days
Prognosis: dependent on following factors
√ fracture displacement with > 1 mm offset / angulation / rotation of fragments (less favorable)
√ location of blood supply:
› distal ⅓ (10%) = usually fragments reunite
› middle ⅓ (70%) = failure to reunite in 30%
› proximal ⅓ (20%) = failure to reunite in 90%
√ orientation of fracture
› transverse / horizontal oblique = relatively stable
› vertical oblique (less common) = unstable
◊ Good prognosis with distal fracture + no displacement + no ligamentous injury!
◊ Less favorable prognosis with displaced / comminuted fracture + proximal pole fracture!
Cx: (1) Malunion; delayed union; nonunion (5–15%)
(2) Progressive fragment displacement
(3) Avascular necrosis of proximal fragment (13–50%); higher prevalence if proximal pole fractured ← distal location of main nutrient a.

Trapezium Fracture

Prevalence: 3–5% of all carpal fractures
Mechanism: direct blow to volar surface / avulsion
Location: trapezial ridge (= vertical prominence on volar aspect); body
Associated with: carpometacarpal joint involvement; fracture through base of 1st metacarpal / scaphoid

Triquetral Fracture

Prevalence: 18% of all carpal fractures
Mechanism: wrist hyperextension with ulnar deviation → impingement of ulnar styloid process against dorsal surface of triquetrum
Location:
(a) dorsal ridge fracture
(b) triquetral body fracture (in combination with perilunate dislocation)
√ fragment along dorsal edge of triquetrum (LAT view in slight pronation)

Hand Fracture

Bennett Fracture

[Edward Halloran Bennett (1837–1907), surgeon in Dublin, Ireland]
Mechanism: forced abduction of thumb
√ intraarticular fracture-dislocation of base of 1st metacarpal
√ small fragment of 1st metacarpal continues to articulate with trapezium
√ lateral retraction of 1st metacarpal shaft by abductor pollicis longus
Rx: anatomic reduction important, difficult to keep in anatomic alignment
Cx: pseudarthrosis

Boxer's Fracture

Mechanism: direct blow with clenched fist
√ transverse fracture of distal metacarpal (usually 5th)

Gamekeeper's Thumb

= SKIER'S THUMB (originally described as chronic lesion in hunters strangling rabbits)
Frequency: 6% of all skiing injuries; 50% of skiing injuries to the hand
Mechanism: violent abduction of thumb with injury to ulnar collateral ligament (UCL) in 1st MCP (faulty handling of ski pole)
√ disruption of ulnar collateral ligament of 1st MCP joint, usually occurring distally near insertion on proximal phalanx
√ avulsed bone fragment (in 12% of lesions)
√ radial stress examination results in abduction angle > 35–45° or > 10° greater than on opposite side
◊ Controversial maneuver to document ligamentous disruption as it may complete incomplete tear
√ displacement of UCL superficial to aponeurosis of adductor pollicis (= **Stener lesion**) [torn end of UCL may be marked by avulsed bone fragment]

Rolando Fracture

[Silvio Rolando (?–1931?), surgeon in Genoa, Italy]

√ comminuted Y- / T-shaped intraarticular fracture-dislocation through base of thumb metacarpal

Prognosis: worse than Bennett fracture (difficult to reduce)

Chest Wall Fracture

Rib Fracture

◊ Most common skeletal injury in blunt chest trauma (in 50%)

Associated with: pneumothorax, hemothorax, lung contusion / laceration

CT is the most sensitive technique for imaging rib fractures by determining the site and number of fractures and providing information about any associated injuries.

@ 1st–3rd rib

◊ Indicates high-energy trauma ← protected location

Cause: acute trauma / fatigue fracture (from carrying a heavy back pack)

Associated with: aortic / great vessel + subclavian vascular injury; brachial plexus injury; thoracic vertebral fracture; scapular fracture

@ Lower ribs

Associated with: injury to liver, spleen, kidney, diaphragm

Cx: atelectasis + subsequent pneumonia ← limited respiratory movement

FLAIL CHEST

= segmental fracture of > 3 contiguous ribs in > 2 places

In > 50% associated with: significant intrathoracic injury that requires surgical Rx

- paradoxic motion of fractured chest wall with respiration on clinical examination
- respiratory failure

Rx: mechanical ventilation for prolonged periods

COUGH FRACTURE

Location: 4th–9th rib in anterior axillary line

Scapula Fracture

Prevalence: 3–5% of all shoulder girdle fractures

◊ In 3.7% of patients with multiple injuries

Cause: motor vehicle accident, fall from great height

Associated with: pneumothorax, hemothorax, lung injury, spinal injury (in 35–98%)

Prognosis: displaced glenoid intraarticular fracture + displaced juxtaarticular fracture require surgical management

Sternal Fracture

Cause: deceleration, direct blow

Associated with: anterior mediastinal hemorrhage

Sternal fractures are best demonstrated on multiplanar reformatted CT images, especially on sagittal views.

Pelvic Fracture

Unstable pelvic fractures:

(a) anterior compression
   1. Bilateral vertical pubic rami fractures
   2. Symphysis + sacroiliac joint diastasis

(b) lateral compression
   1. Malgaigne (ipsilateral anterior + posterior fx)
   2. Bucket-handle (contralateral anterior + posterior fx)

(c) vertical shear
   1. Superior displacement of pelvis

Acetabular Fracture

Anatomy & Function:

most important portion of acetabulum is roof / dome;
weight-bearing surface for entire lower limb is derived + supported by 2 columns which are oriented in an inverted "Y" and join above the acetabular roof at an angle of 60°:

(a) anterior iliopubic column of acetabulum
(b) posterior ilioischial column of acetabulum

Classification (Judet and Letournel):

A. Elementary 5 fractures
   Posterior wall* 27% Anterior column 5%
   Transverse* 9% Posterior column 4%
   Anterior wall 2%

B. Associated 5 fractures (= combinations / partial combinations of elementary fractures)
   Transverse + posterior wall* 27%
   Both columns* 19%
   T-shaped* 6%
   Anterior wall + posterior hemitransverse 5%
   Posterior column + posterior wall 3%

*= account for 80%of all acetabular fractures (3 most common types underlined)

POSTERIOR WALL (LIP / RIM) FRACTURE (27%)

Mechanism: indirect force transmitted through length of femur with flexed hip joint (knee strikes dashboard)

Associated with: posterior dislocation of femur

A posterior wall fracture involves only the posterior articular surface and is not seen on the medial acetabular surface.

TRANSVERSE FRACTURE (9%)

N.B.: most difficult to diagnose + comprehend

√ transects both the iliopubic + ilioischial columns with fracture line in an anteroposterior direction

On subsequent axial CT images, a transverse acetabular fracture is represented by a sagittal fracture line simulating anterior and posterior wall fractures, a pitfall easily avoided with 3-D

reconstructions.

ANTERIOR COLUMN FRACTURE (5%)

Mechanism: blow to greater trochanter with hip externally rotated

Associated with: posterior column / transverse fracture

√ fracture begins between anterior iliac spines + traverses the acetabular fossa + ends in the ischiopubic ramus

POSTERIOR COLUMN FRACTURE (4%)

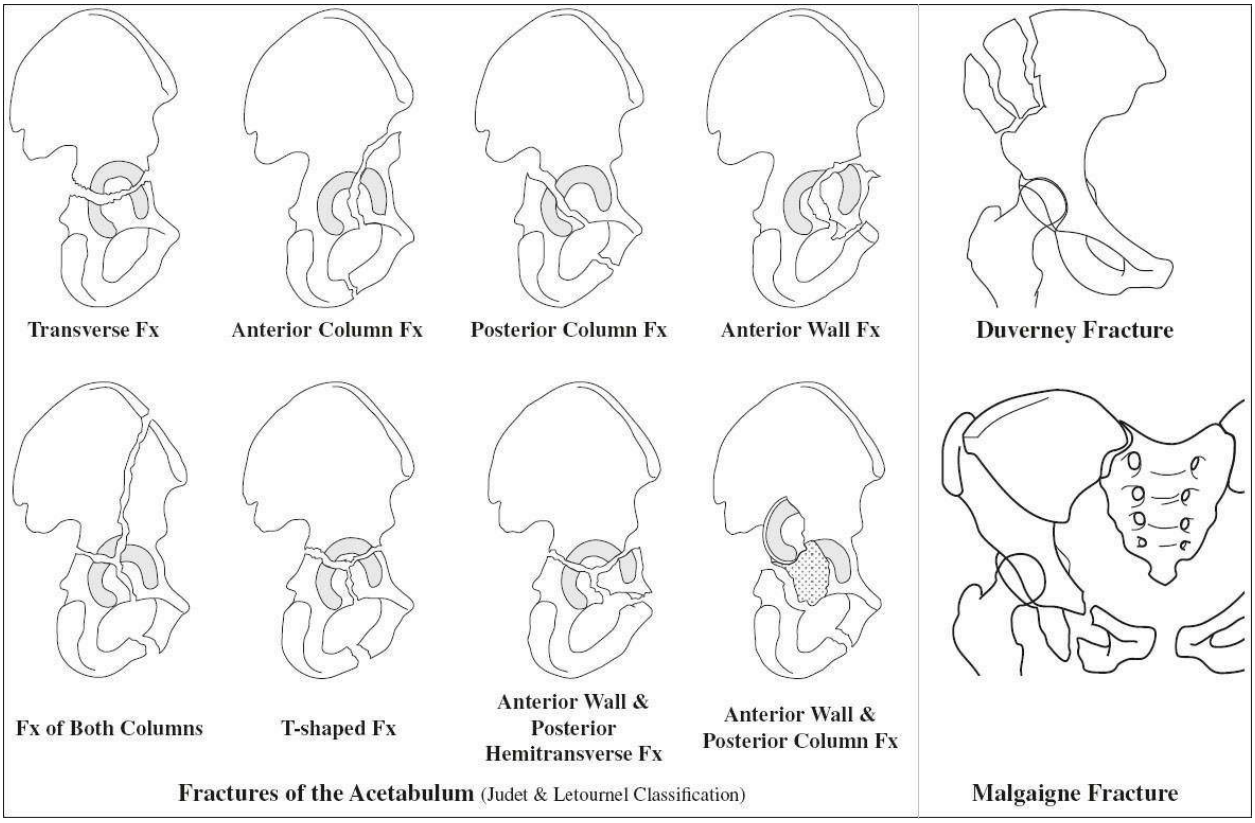
Mechanism: indirect force transmitted through length of femur with hip abducted

Associated with: posterior dislocation of femur + sciatic nerve injury

√ fracture begins at greater sciatic notch + traverses the posterior aspect of acetabular fossa + ends in the ischiopubic ramus

ANTERIOR WALL FRACTURE (2%)

Mechanism: force transmitted through greater trochanter



Fractures of the Acetabulum (Judet & Letournel Classification)

Associated with: posterior dislocation of femur + sciatic nerve injury

√ fracture begins on anterior rim of acetabulum + emerges on lateral aspect of superior pubic ramus

ASSOCIATED BOTH COLUMN FRACTURE (19%)

= separation of both columns from each other with 2 dominant fractures nearly perpendicular to each other

Associated with: additional fracture lines + medial displacement of femoral head
√ "spur sign" = shard of bone superior to femoral neck (on obturator view)

With both-column fractures the entire weight-bearing portion of the acetabulum is disconnected from the sciatic buttress.

Bucket Handle Fracture

√ double vertical fracture through superior and inferior pubic rami + sacroiliac joint dislocation on contralateral side

Duverney Fracture

[Joseph Guichard Duverney (1648–1730), French surgeon]
√ isolated fracture of iliac wing

Malgaigne Fracture

[Joseph François Malgaigne (1806–1865), French surgical historian, published first comprehensive book on fractures]
= fracture-dislocation of one side of the pelvis with anterior + posterior disruption of pelvic ring
Mechanism: direct trauma
• shortening of involved extremity
√ vertical fractures through one side of pelvic ring
(1) superior to acetabulum (ilium)
(2) inferior to acetabulum (pubic rami)
(3) ± sacroiliac dislocation / fracture
√ lateral unstable fragment contains acetabulum

Proximal Femur Fracture

Intracapsular Femur Fracture

A. Complete Femoral Head Fracture *(uncommon)*
Often associated with: posterior hip dislocation
Pipkin classification:

Type 1	below fovea centralis
Type 2	above fovea centralis with ligamentum teres often attached to fracture fragment
Type 3	type 1/2 + femoral neck fracture
Type 4	type 1/2 + acetabular fracture

The lateral margin of the femoral head-neck junction is crucial as it is the most common penetration point of the lateral epiphyseal vessels. Fractures involving this area create a high risk of critical vascular injury resulting in nonunion / AVN, with decreasing risk as fractures occur more distally along the femoral neck.

B. Osteochondral Impaction Fracture of Femoral Head

Often associated with: anterior hip dislocation
√ radiographically relatively occult:
√ subtle flattening / focal compression defect of head
√ subchondral fracture line + marrow edema at MRI

C. Femoral Neck Fracture
Location: subcapital, transcervical, basicervical
√ valgus-impacted / nondisplaced

N.B.: frequently missed on initial radiographs ← subtlety of cortical distortion at femoral head-neck junction + only mild fracture angulation

√ varus-impacted ("mushroom cap" = medially rotated head) / displaced → high risk for AVN

D. Femoral Neck Stress Fracture
√ often initially radiographically occult
@ Inferomedial cortex = fatigue fracture
Age: young athletic patient
√ cortical thickening + incomplete fracture line
√ extensive marrow edema
@ Superolateral cortex = insufficiency / fatigue fracture
Age: osteoporotic elderly
√ frequently displaced ← side of high tension

Extracapsular Fracture

A. Intertrochanteric Fracture
Cause: frequently osteoporosis in the elderly woman

N.B.: Isolated fractures of the lesser trochanter in adults should be considered pathognomonic for tumor infiltration.

B. Subtrochanteric Fracture
√ comminuted / spiral morphology

Knee Fracture

Anterior Cruciate Ligament Avulsion Fracture

Age: children > adults
Mechanism:
(a) children: forced flexion of knee + internal rotation
(b) adults: severe hyperextension
May be associated with: kissing bone contusion + tear of medial collateral lig. + PCL
• aching flexed knee; signs of anterior instability
√ avulsion of ACL from its distal insertion site just medial and anterior to tibial eminence

Arcuate Complex Avulsion Fracture

Mechanism: direct blow to anteromedial tibia with knee in extension / varus force to externally rotated tibia / sudden hyperextension
May be associated with:
disruption of ACL and PCL, lateral capsular lig., iliotibial band, popliteal muscle,

menisci, damage to peroneal nerve

- subtle physical finding
- mild swelling + tenderness

√ "arcuate" sign = avulsed elliptic bone fragment at fibular styloid process with its long axis horizontally oriented (AP view)

√ bone marrow edema in head of fibula + adjacent soft-tissue swelling

Biceps Femoris Tendon Avulsion Fracture

May be associated with:
disruption of lateral collateral lig., Segond fracture, damage to popliteal musculotendinous unit

√ irregular bone fragment off lateral fibular head in posterolateral aspect of knee joint (DDx: "arcuate sign" = horizontally oriented elliptic fragment off fibular styloid process)

√ avulsion + retraction of biceps femoris tendon

Iliotibial Band Avulsion Fracture

= primary stabilizing structure of anterolateral knee

Mechanism: pure varus force (rare)

May be associated with: ACL injury

√ avulsion + retraction of iliotibial band from its distal insertion on Gerdy tubercle

Posterior Cruciate Ligament Avulsion Fracture

Location: at tibial insertion site (40–55%)

Mechanism: direct blow to anterior tibia with flexed knee (dashboard injury); severe hyperextension

May be associated with:
disruption of medial / lateral collateral ligament complexes; medial / lateral meniscal tear; bone contusion of anterior tibia + lateral femoral condyle

√ focal discontinuity of posterior articular surface (LAT view)

Quadriceps Tendon Avulsion Fracture

Cause: strong deceleration in young athletes

Mechanism: sudden contraction of quadriceps muscle during jumping / kicking

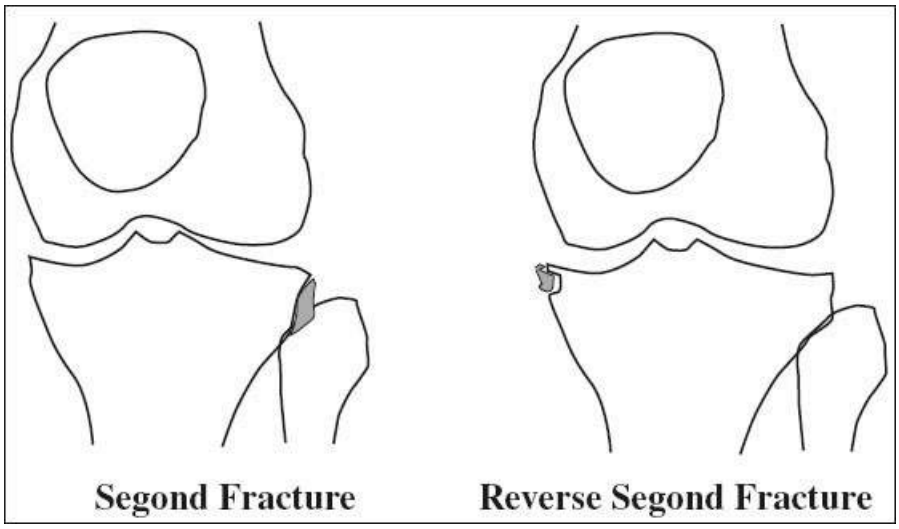
√ comminuted bone fragments off superior aspect of patella (LAT view)

√ patella baja deformity = abnormally low position of patella with respect to femur

√ marrow edema in upper pole of patella

√ suprapatellar joint effusion

DDx: rupture of quadriceps tendon (at musculotendinous junction; repetitive microtrauma / systemic diseases like HPT, diabetes, collagen vascular disease, gout)



Reverse Segond Fracture

= cortical avulsion of tibial insertion of deep capsular component of medial collateral ligament

Mechanism: external rotation + valgus stress

May be associated with:

midsubstance tear of posterior cruciate ligament; avulsion of PCL from posterior tibial plateau; tear of medial meniscus

√ elliptic bone fragment arising from medial aspect of proximal tibia

Segond Fracture

[Paul Ferdinand Segond (1851–1912), surgeon in chief at Salpêtrière in Paris, France]

= cortical avulsion of the tibial insertion of middle third of lateral capsular ligament ± avulsion of iliotibial tract ± anterior oblique band

Mechanism: internal rotation + varus stress

May be associated with:

lesion of anterior cruciate ligament (75–100%), meniscal tear (67%), avulsion of fibular attachment of long head of biceps femoris tendon + fibular collateral ligament

• pain at lateral joint line

• anterolateral rotational instability of the knee

√ "lateral capsular" sign = small elliptic fragment of proximal lateral tibial rim just distal to lateral plateau parallel to tibia (AP view)

√ marrow edema on MRI

Semimembranosus Tendon Avulsion Fracture

Mechanism: external rotation + abduction of flexed knee; varus force applied to flexed knee; valgus force applied to tibia

May be associated with:

ACL tear; tear of posterior horn of medial meniscus; posterior meniscocapsular separation

√ tiny avulsed bone fragment off tibia displaced posterosuperiorly (difficult to see on LAT view)

Tibial Plateau Fracture (Schatzker classification)

Type I = wedge-shaped pure cleavage fracture 6%
√ < 4 mm depression / displacement
√ ± distraction injury to MCL / ACL

Type II = combined cleavage + lateral plateau compression fracture 25%
√ distraction injury of MCL / medial meniscus in 20%

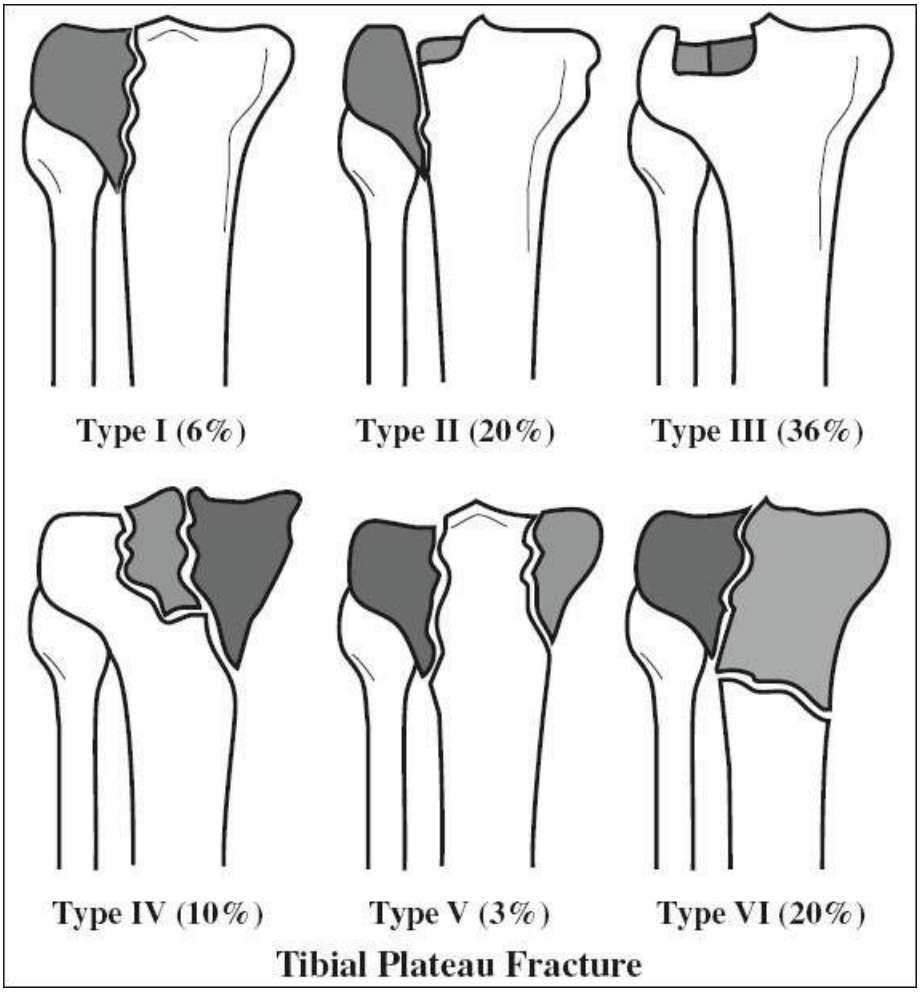
Type III = pure compression fracture of lateral tibial plateau 36%
√ depression of articular surface:
√ lateral depression (type IIIA)
√ central depression (type IIIB)

Type IV = medial plateau fracture with a split / depressed comminution 10%
√ ± distraction injury of lateral knee with LCL tear / posterolateral corner injury
√ ± fracture / dislocation of proximal fibula
Cx: injury to peroneal nerve / popliteal vessels

Type V = wedge fracture of medial + lateral plateau in 3%
√ often inverted Y appearance
√ articular depression typically of lateral tibial plateau
√ ± fracture of intercondylar eminence (= unstable 4-part fracture)
√ peripheral meniscal detachment (50%)
√ ACL avulsion injury (33%)

Type VI = transverse / oblique fracture with dissociation of metaphysis from diaphysis 20%
√ open fracture in (33%)

◊ Lateral plateau fractures (type I–III) are most common!



◊ Fractures of medial plateau are associated with greater violence and higher percentage of associated injuries!

Mechanism:

(a) for type I + II + III = valgus force combined with axial loading ("bumper / fender fracture" from lateral force of automobile against a pedestrian's fixed knee) / compression force often on extended knee

(b) for type IV = varus force combined with axial loading on hyperflexed knee

(c) type V + VI = combination of valgus + varus stresses combined with axial loading

Tibial Tubercle Fracture

Ogden classification:

Type 1: involvement of distal portion of tubercle
- 1A: without displacement
- 2A: with displacement

Type 2: involvement of entire ossification center
- 2A: separation of tubercle from proximal tibia
- 2B: comminuted fracture

Type 3: involvement of proximal tibial epiphysis into joint space

3A: without displacement
3B: with displacement

Toddler's Fracture

= CHILDHOOD ACCIDENTAL SPIRAL TIBIAL FRACTURE (CAST)
= lower extremity fracture associated with onset of ambulation
Cause: low-energy trauma ± rotational component
Age: toddler (9 months–3 years), young child (< 8 years)
• refusal to bear weight without recognized trauma
Location: distal third to distal half of tibia; fibula, tarsus (posterior calcaneus > base of cuboid > talus)
√ (typically) nondisplaced oblique spiral fracture of distal tibia
√ undisplaced spiral fracture

Foot Fracture

Ankle Fracture

Frequency: ankle injuries account for 10% of all emergency room visits; 85% of all ankle sprains involve lateral ligaments

LATERAL MALLEOLAR FRACTURES

Weber Type A

[Bernhard Georg Weber (1929–), orthopedic surgeon in St. Gall, Switzerland]
= SUPINATION-ADDUCTION INJURY = INVERSION-ADDUCTION INJURY
Mechanism:
(1) avulsive forces affect lateral ankle structures
(2) impactive forces ← talar shift stresses medial structures
√ sprain / rupture of lateral collateral ligament
◊ Anterior tibiofibular ligament ruptures alone in 66%
◊ Injury of all 3 lateral ligaments in 20%
Prognosis: chronic lateral ankle instability in 10–20%
√ transverse avulsion of malleolus sparing tibiofibular ligaments
√ ± oblique fracture of medial malleolus
√ ± posterior tibial lip fracture

Weber Type B

= SUPINATION-ABDUCTION INJURY = EVERSION-EXTERNAL ROTATION
Mechanism:
(1) avulsive forces on medial structures
(2) impacting forces on lateral structures (talar impact)
√ oblique / spiral fracture of lateral malleolus starting at level of joint space extending proximally
√ lateral subluxation of talus
√ partial disruption of tibiofibular ligament
√ ± sprain / rupture / avulsion of deltoid ligament

√ ± transverse fracture of medial malleolus

(a) **Dupuytren Fracture**

[Guillaume Dupuytren (1777–1835), French surgeon]

√ fracture of distal fibula above a disrupted tibiofibular ligament + disruption of deltoid lig.

(b) **Le Fort Fracture of Ankle**

[Léon Clément Le Fort (1829–1893), French surgeon]

√ vertical fracture of anterior medial portion of distal fibula

√ avulsion of anterior tibiofibular ligament

Weber Type C

= PRONATION-EXTERNAL ROTATION = EVERSION + EXTERNAL ROTATION

√ fibular fracture higher than ankle joint (Maisonneuve fracture if around knee)

√ ± deltoid ligament tear

√ ± medial malleolar fracture

√ tear of tibiofibular ligament / avulsion of anterior tubercle (Tillaux-Chaput) / avulsion of posterior tubercle (Volkmann)

√ tear of interosseous membrane = lateral instability

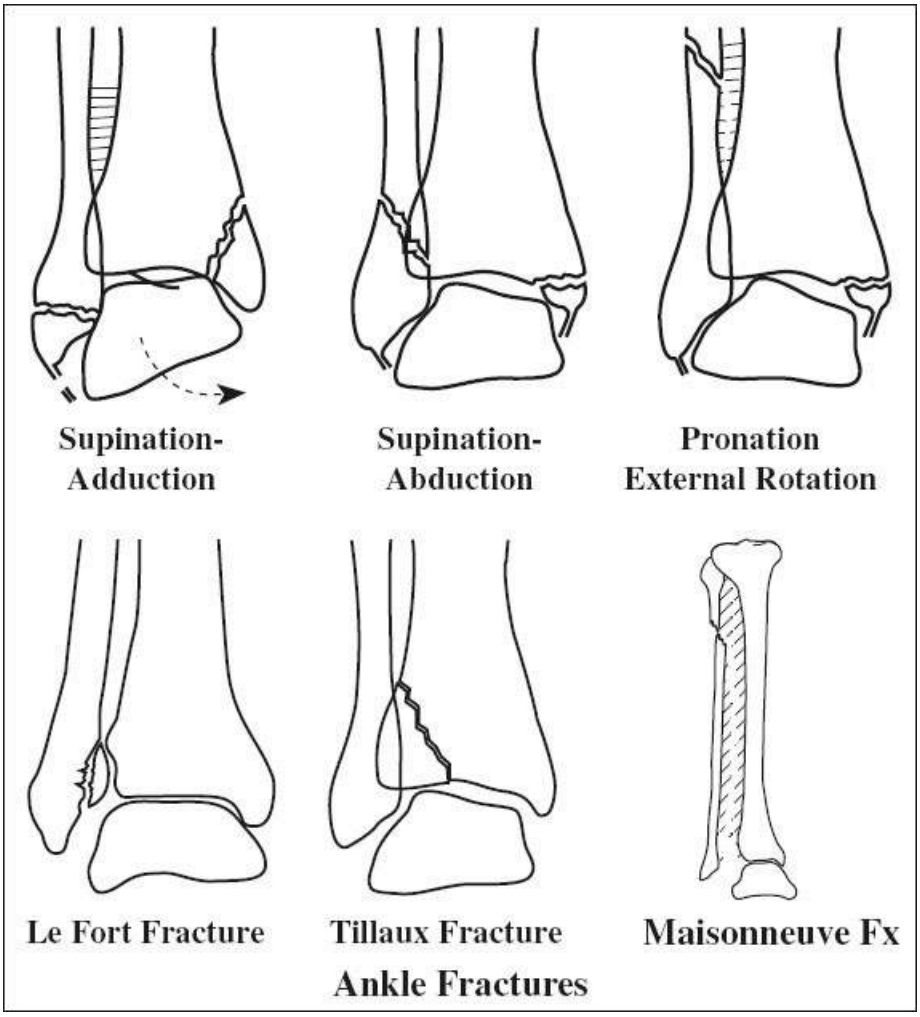
(a) **Tillaux Fracture**

[Paul Jules Tillaux (1834–1904), French surgeon and anatomist]

√ avulsion injury of anterior tibial tubercle at attachment of distal anterior tibiofibular ligament

√ type 3 epiphyseal plate injury in children

√ CT more sensitive in identification of fracture displacement > 2 mm (cutoff that requires reduction)



(b) **Maisonneuve Fracture**
[Jacques Gilles Maisonneuve (1809–1897), student of Dupuytren]
√ tear of distal tibiofibular syndesmosis + interosseous membrane
√ spiral fracture of upper third of fibula
√ associated fracture of medial malleolus / rupture of deep deltoid ligament

Calcaneal Fracture

Frequency: most commonly fractured tarsal bone; 60% of all tarsal fractures; 2% of all fractures in the body; commonly bilateral
Mechanism: fall from heights (axial overload)
In 10% associated with: thoracolumbar compression fracture
Age: 95% in adults, 5% in children
› adulthood: intraarticular (75%), extraarticular (25%)
› childhood: extraarticular (63–92%)
Classification:
(a) extraarticular fracture (25%) = no involvement of posterior talar facet:
› anterior process fracture
› fracture of mid calcaneus (body, sustentaculum tali, peroneal tubercle, lateral

calcaneal process)
› fracture of posterior calcaneus (tuberosity, medial calcaneal tubercle)

(b) intraarticular fracture (75%)
› subtalar joint involvement: undisplaced, displaced, comminuted
› calcaneocuboid joint involvement

Sanders Classification of intraarticular fractures (correlates with prognosis):

Technique: CT with image reformation parallel + per-pendicular to posterior facet of subtalar joint

Type I	nondisplaced (< 2 mm) fracture
Type II	2 articular fragments
Type IIA	laterally located fracture line
Type IIB	centrally located fracture line
Type IIC	medially located fracture line
Type III	3 articular fragments
Type IIIAB	lateral+ central fracture line
Type IIIAC	lateral + medial fracture line
Type IIIBC	central + medial fracture line
Type IV	> 3 intraarticular fracture lines

√ apex of lateral talar process does not point to "crucial angle" of Gissane
√ Böhler angle decreased below 28°–40°

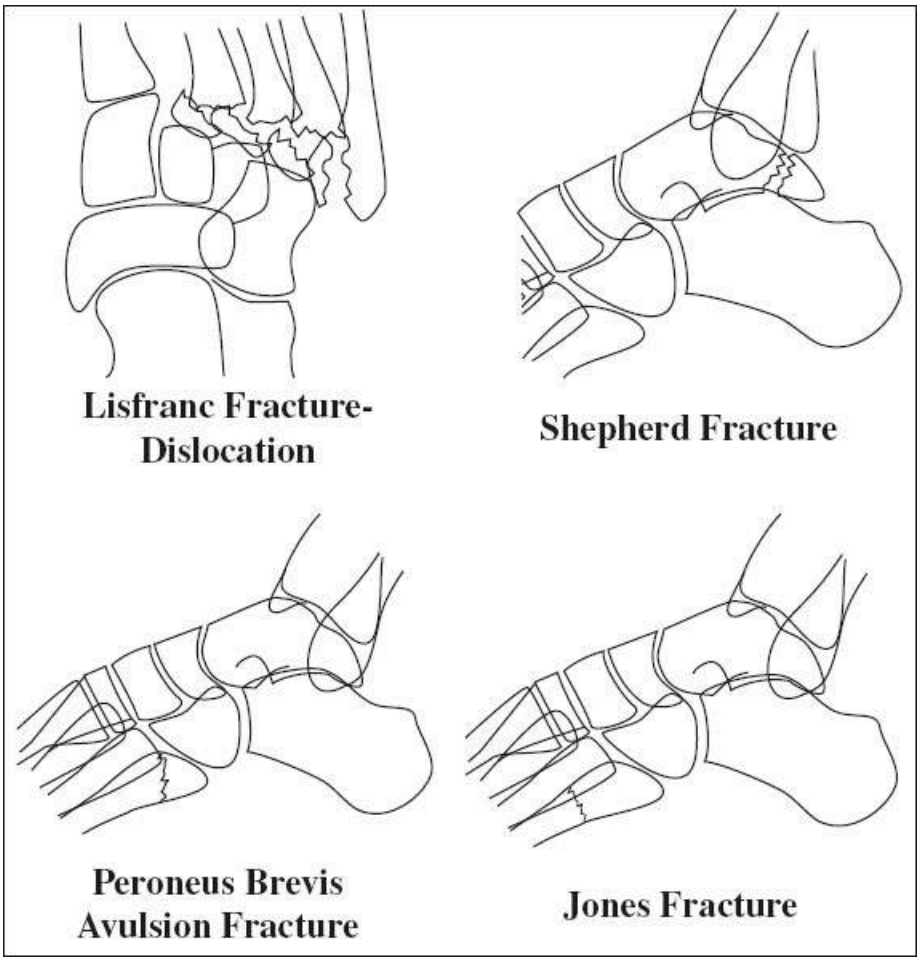
Chopart Fracture

[François Chopart (1743–1795), surgeon in Paris, France]
√ fracture-dislocation through midtarsal / Chopart (calcaneocuboid + talonavicular) joint
√ commonly associated with fractures of the bones abutting the joint

Jones Fracture

[Robert Jones (1857–1933), British orthopedic surgeon and pioneer in radiology described fracture in Ann Surg 1902]

Mechanism: adduction of forefoot with ankle in plantar flexion
√ transverse fracture at base of 5th metatarsal bone at junction of diaphysis and metaphysis (> 1.5 cm distal to proximal tip of metatarsal tuberosity)
Cx: delayed union / nonunion (poor blood supply)



Lisfranc Fracture

[Jacques Lisfranc de Saint Martin (1787–1847), field surgeon in Napoleon's army]

Mechanism: metatarsal heads fixed and hindfoot forced plantarward and into rotation

√ fracture-dislocation / fracture-subluxation of tarsometatarsal joints (typically 2 through 5)

√ lateral displacement of metatarsals

Peroneus Brevis Avulsion Fracture

= METATARSAL 5 TUBEROSITY FRACTURE

◊ Most common fracture of the proximal 5th metatarsal bone

Mechanism: plantar flexion + inversion (stepping off a curb)

√ transverse avulsion fracture of base of 5th metatarsal bone

Location: proximal to metatarsal tuberosity (insertion of peroneus brevis tendon); usually extraarticular

DDx: Jones fracture (slightly different location)

Shepherd Fracture

[Francis J. Shepherd (1851–1929), demonstrator in anatomy at McGill University in Montreal, Canada]

√ fracture of lateral tubercle of posterior process of talus

DDx: os trigonum

FROSTBITE

Cause: (1) cellular injury + necrosis from freezing process
(2) cessation of circulation ← cellular aggregates and thrombi forming as a result of exposure to low temperatures below –13° C (usually cold air)

• firm white numb areas in cutis (separation of epidermal-dermal interface)

Location: feet, hands (thumb commonly spared ← protection by clenched fist)

Early changes:

√ soft-tissue swelling + loss of tissue at tips of digits

CHILD

√ fragmentation / premature fusion / destruction of distal phalangeal epiphyses
√ secondary infection, articular cartilage injury, joint space narrowing, sclerosis, osteophytosis of DIP
√ shortening + deviation / deformity of fingers

ADULT

√ osteoporosis (4–10 weeks after injury)
√ periostitis
√ acromutilation ← osteomyelitis + surgical removal + tuftal resorption ← soft-tissue loss
√ small round punched-out areas near edge of joint
√ interphalangeal joint abnormalities (simulating osteoarthritis)
√ calcification / ossification of pinna

Angio:

√ vasospasm, stenosis, occlusion
√ proliferation of arterial + venous collaterals (in recovery phase)

Bone scintigraphy:

√ persistent absence of uptake (= lack of vascular perfusion) indicates nonviable tissue

Rx: selective angiography with intraarterial reserpine

GANGLION

Origin: coalescence of smaller cysts formed by myxomatous degeneration of periarticular connective tissue

Path: capsule of dense fibrous connective tissue

Histo: no synovial lining (frequent lack of communication with joint, infrequent association with joint / tendon sheath effusion)

Cause: repetitive stress

Location: joint capsule, tendon sheath, ligament, bursa, intraarticular, subchondral intraosseous, periosteal

Prognosis: symptomatic; bone erosion; spontaneous resolution frequent in pediatric cases

DDx: Synovial cyst (differentiation from ganglion cyst radiologically not possible)

Soft-tissue Ganglion

= cystic tumorlike lesion usually attached to a tendon sheath

Frequency: 50% of adult wrists

• asymptomatic / pain
• uni- / multilocular swelling
Location: periarticular hand, wrist, foot (over dorsum)
Site: arise from tendon, muscle, semilunar cartilage
√ soft-tissue mass with surface bone resorption
√ periosteal new-bone formation
√ arthrography may demonstrate communication with joint / tendon sheath
√ internal septations
√ lobulated configuration with peripheral fluid-filled pseudopodia ("bunch of grapes")
√ hypointense relative to muscle / hyperintense cyst content (high mucinous content, hemorrhage) on T1WI
√ hyperintense relative to fat on T2WI
√ no enhancement
Prognosis: may resolve spontaneously
Rx: steroid injection may improve symptomatology

Intraosseous Ganglion

= benign subchondral radiolucent lesion WITHOUT degenerative arthritis
• mild localized pain (in 4% of unexplained wrist pain)
Age: middle age
Origin: (1) mucoid degeneration of intraosseous connective tissue (perhaps due to trauma / ischemia)
(2) penetration of juxtaosseous soft-tissue ganglion (= synovial herniation) into underlying bone (occasionally)
Path: uni- / multilocular cyst surrounded by fibrous lining, containing gelatinous material
Location:
(a) epiphysis of long bone
1. proximal tibia (at attachment of cruciate ligaments)
2. medial malleolus
3. femoral head
4. carpal bones

(b) subarticular flat bone (acetabulum)
√ well-demarcated solitary 0.6–6 cm lytic lesion
√ sclerotic margin
√ NO communication with joint
√ increased radiotracer uptake on bone scintigraphy (in 10%)
DDx: posttraumatic / degenerative cyst

Periosteal Ganglion

= cystic structure with viscid / mucinous contents
Prevalence: 11 cases in literature
Age: 39–50 years; M > F
• swelling, mild tenderness
Location: long tubular bones of lower extremity
√ cortical erosion / scalloping / reactive bone formation

√ NO intraosseous component (endosteal surface intact)

CT:

√ well-defined soft-tissue mass adjacent to bone cortex with fluid contents

MR:

√ homogeneously isointense compared to muscle on T1WI

√ homogeneously hyperintense compared to fat on T2WI

√ NO internal septations (DDx to soft-tissue ganglion)

DDx: periosteal chondroma without matrix calcification, cortical desmoid, subperiosteal aneurysmal bone cyst, acute subperiosteal hematoma (history of trauma / blood dyscrasia), subperiosteal abscess (involvement of adjacent bone marrow)

Rx: surgical excision (local recurrence possible)

GAUCHER DISEASE

[Philippe Charles Ernest Gaucher (1854–1918), French dermatologist]

= rare autosomal recessive / dominant (in a few) lipid storage disorder; the most common lysosomal storage disorder;

Prevalence: 1÷50,000–100,000 (general population); 1÷500–1,000 (in Ashkenazi Jews); M = F

Etiology: deficiency of lysosomal hydrolase acid β-glycosidase (= b-glucocerebrosidase) → accumulation of glucosylceramide (glucocerebroside) within macrophages of RES (liver, spleen, bone marrow, lung, lymph nodes)

Histo: bone-marrow aspirate shows Gaucher cells (kerasin-laden histiocytes) of 20–100 μm in diameter with a foamy wrinkled-paper appearance

Clinical types:

(1) Adult / chronic nonneuropathic form = type 1 (most common form in USA)

Age of onset: 3rd–4th decade

• no clinical signs (most)

Prognosis: longest time of survival; pulmonary involve-ment / hepatic failure may lead to early death

(2) Rapidly fatal infantile / acute neuropathic form = type 2

Age of onset: 1–3–12 months

• early onset of significant hepatosplenomegaly

• severe progressive neurologic symptoms: seizures, mental retardation, strabismus, spasticity

√ skeletal manifestations are rare

Prognosis: fatal during first 2 years of life

(3) Juvenile / subacute neuropathic form = type 3 (rarest type)

Age of onset: 2–6 years

• variable hepatosplenomegaly

• mild neurologic involvement: seizures

√ delayed onset of skeletal manifestations

Prognosis: survival into adolescence

• hepatosplenomegaly, impairment of liver function, ascites

• elevated serum acid phosphatase

- pancytopenia, anemia (chronic fatigue), leukopenia, thrombocytopenia (easy bruising, hypersplenism)
- hemochromatosis (yellowish brown pigmentation of conjunctiva + skin)
- dull bone pain (bone involvement in 75%)

Location: predominantly long tubular bones (distal femur), axial skeleton, hip, shoulder, pelvis; bilateral

√ generalized osteopenia (decrease in trabecular bone density):
  √ striking cortical thinning + bone widening
  √ endosteal scalloping ← marrow packing
√ numerous sharply circumscribed lytic lesions resembling metastases / multiple myeloma (marrow replacement)
√ periosteal reaction = cloaking
√ Erlenmeyer flask deformity of distal femur + proximal tibia ← marrow infiltration (MOST CHARACTERISTIC)
√ weakening of subchondral bone:
  √ osteonecrosis (common, frequently of femoral head)
  √ degenerative arthritis
√ bone infarcts in long-bone metaphyses (most common in femoral + humeral heads):
  √ focal / serpentine areas of sclerosis
  √ bone-within-bone appearance
√ H-shaped / "step-off" / biconcave "fish-mouth" vertebrae (DDx: sickle cell disease)

MR:
  √ focal / diffuse replacement of adipocytes in bone marrow by Gaucher cells results in decreased marrow signal on T1WI + T2WI (marrow involvement follows the distribution of hematopoietic marrow in spine, pelvis, proximal femoral metaphysis; from proximal to distal in appendicular skeleton):
    √ epiphyses generally not involved
  √ myelofibrotic marrow of low SI on T1WI + T2WI (in long-standing disease)

@ Liver
  √ hepatomegaly
  √ nonspecific fatty + cirrhotic changes
  √ focal lesions hypointense on T1WI + hyper- to isointense on T2WI

@ Spleen
  √ splenomegaly + lymphadenopathy
  √ multiple nodular lesions (= clusters of RES cells laden with glucosylceramide):
    √ hypodense without enhancement on CT
    √ hypoechoic / hyperechoic on US
    √ slightly hypo- to isointense on T1WI
    √ hypointense (Gaucher cells / fibrosis) or hyperintense (dilated sinusoids filled with blood around Gaucher cell infiltrates) on T2WI
  √ splenic infarcts leading to fibrosis, especially in massively enlarged spleen

@ Lung
  √ normal
  √ nonspecific diffuse reticulonodular / miliary infiltrates at lung bases (= infiltration with Gaucher cells)

Dx: elevated serum activity of β-glucocerebrosidase; genotyping

Cx: ◊ > 90% have orthopedic complications at some time

(1) Pathologic fractures + compression fractures of vertebrae
(2) Avascular necrosis of femoral head, humeral head, wrist, ankle (common)
(3) Osteomyelitis (increased incidence)
(4) Myelosclerosis in long-standing disease
(5) Repeated pulmonary infections
(6) Cancer of hematopoietic origin (14.7-fold risk)

Prognosis: highly variable clinical course; strong relationship between splenic volume and disease severity

Rx: no cure; bone marrow transplantation; enzyme replacement therapy with Cerezyme®

DDx: metastatic disease, multiple myeloma, leukemia, sickle-cell disease, fibrous dysplasia

GIANT CELL REPARATIVE GRANULOMA

= GIANT CELL REACTION = GIANT CELL GRANULOMA

Cause: ? reactive inflammatory process to trauma / infection (not a true neoplasm)

Histo: numerous giant cells in exuberant fibrous matrix arranged in clusters around foci of hemorrhage + commonly exhibiting osteoid formation (unusual in giant cell tumor); indistinguishable from brown tumor of HPT; cystic degeneration + ABC components distinctly uncommon

Peak age: 2nd + 3rd decade (range, childhood to 76 years); 74% < 30 years of age; M÷F = 1÷1

May be associated with: enchondromatosis, Goltz syndrome, fibrous dysplasia, Paget disease

Location:

@ Gnathic (1–7% of all benign oral tumors): gingiva + alveolar mucosa of mandible, maxilla
(a) central type = in bone
(b) peripheral type = in gingival soft tissue
M÷F = 1÷2
• nonspecific pain + swelling (increasing during pregnancy)
√ expansile bone remodeling with multilocular appearance
√ thinned usually intact cortex
DDx: indistinguishable from odontogenic cyst, ABC, ameloblastoma, odontogenic myxoma, odontogenic fibroma

@ Small bones of hand + feet (less common): phalanges of hand > metacarpals > metatarsals > carpal bones > tarsal bones > phalanges of foot
M÷F = 1÷1
• nonspecific pain + swelling for months to years
Site: metaphysis ± extension into diaphysis; extension into epiphysis is UNCOMMON
√ expansile lytic defect of 2–2.5 cm in diameter with internal trabeculations
√ thinning of overlying cortex
√ matrix mineralization may be seen (DDx to GCT)
√ periosteal reaction is unusual (as in GCT)
√ extension beyond cortex is unusual

@ Other locations (rare):
ethmoid sinus, sphenoid sinus, temporal bone, skull, spine, clavicle, tibia, humerus, ribs,

femur

Cx: pathologic fracture

Prognosis: may recur; no malignant transformation

Rx: curettage (22–50% recurrence rate) / local excision

DDx: (1) Enchondroma (same location, matrix calcification)

(2) Aneurysmal bone cyst (rare in small bones of hand + feet, typically prior to epiphyseal closure)

(3) Giant cell tumor (more aggressive appearance)

(4) Infection (clinical)

(5) Brown tumor of HPT (periosteal bone resorption, abnormal Ca + P levels)

GIANT CELL TUMOR

= OSTEOCLASTOMA = OSTEOBLASTOCLASTOMA = TUMOR OF MYELOPLEXUS

= nonmineralized eccentric lytic meta-epiphyseal lesion involving a long bone with extension to subarticular bone in the skeletally mature patient (= with closed physis)

Origin: probably arises from zone of intense osteoclastic activity (of endochondral ossification) in skeletally immature patients

Frequency: 5% of all primary bone tumors; 20% of benign skeletal tumors; unusually high prevalence in China + southern India

Path: friable vascular stroma of numerous thin-walled capillaries with necrosis + hemorrhage + cyst formation (DDx: aneurysmal bone cyst without solid areas)

Histo: large number of multinucleated osteoclastic giant cells in a diffuse distribution in a background of ovoid mononuclear cells intermixed throughout a spindle cell stroma (DDx: giant cells characteristic of all reactive bone disease as in pigmented villonodular synovitis, benign chondroblastoma, nonosteogenic fibroma, chondromyxoid fibroma, fibrous dysplasia)

Peak age: 3rd (range, 2nd–4th) decade; < 3% below age 14; 80% between 20 and 50 years; 13% > age 50; M÷F = 1÷1.1 to 1÷1.5 (in spine 1÷2.5)

May be associated with: Paget disease located in skull + facial bones (50–60%), pelvis, spine

Hormonal stimulation: occasionally dramatic increase in size during pregnancy

Staging:

Stage 1 indolent radiographic + histologic appearance (10–15%)

Stage 2 more aggressive radiographic appearance with expansile remodeling (70–80%):

√ wide zone of transition
√ cortical thinning
√ expansile remodeling
√ cortical bone destruction

Stage 3 extension into adjacent soft tissues with histologically benign appearance (10–15%)

- pain at affected site (most common – in 10% pathologic fracture)
- local swelling + tenderness
- weakness + sensory deficits (if in spine)

Location:

@ long bones (75–90%)

› lower extremity:

(a) about knee (50%–65%):
» distal end of femur (23–30%)
» proximal end of tibia (20–25%)
(b) away from knee: proximal femur (4%) > distal tibia (2–5%) > proximal fibula (3–4%) > foot (1–2%)
rare: patella (the largest sesamoid bone), greater trochanter (epiphyseal equivalent)

› upper extremity (away from elbow): distal end of radius (10–12%) > proximal end of humerus (4–8%) > hand & wrist with predilection for metacarpal bones (1–5%)

@ flat bones (15%)
› pelvis: upper sacrum near SIJ (4%), iliac bone (3%) ← Paget disease
◊ 2nd most common primary sacral neoplasm after chordoma!
› rib (anterior / posterior end)
› skull (sphenoid bone) ← Paget disease
› scapula (< 1%)

@ spine (3–7%): lumbar > thoracic > cervical spine (2nd most frequent tumor after chordoma); vertebral body and pedicles (21%); frequent involvement of posterior arch

Site:
(a) eccentric metaepiphyseal (42–93%) = in metaphysis of long bones adjacent to ossified epiphyseal line
(b) extension to within 1 cm of subarticular bone (85–99%) after fusion of epiphyseal plate (MOST TYPICAL)
(c) intraarticular extension possible / transarticular spread (rare)

◊ The open epiphyseal plate acts as a barrier to tumor growth!

X-Ray:
√ well-circumscribed expansile solitary lytic bone lesion:
√ nonsclerotic margin ← aggressive rapid growth
√ narrow (80–90%) / (less well-defined) wide zone of transition
√ large lesions more centrally located
√ "soap bubble" appearance (47–60%) = expansile remodeling of multiloculated appearance:
√ NO internal mineralization of tumor matrix
√ prominent trabeculation (33–57%):
(a) reactive with appositional bone growth
(b) pseudotrabeculation of osseous ridges in endosteal scalloping
√ periosteal reaction (10–30%)
√ cortical penetration / disruption (33–50%):
√ cortical thinning
√ soft-tissue invasion (25%)
√ complete / incomplete pathologic fracture (11–12–37%)
√ may cross joint space in long bones (exceedingly rare)
@ Spine & sacrum (< 3%)
√ destruction of vertebral body with secondary invasion of posterior elements (DDx: ABC, osteoblastoma):

- √ purely osteolytic / with cortical expansion
- √ absence of mineralization
- √ lack of a sclerotic rim at tumor margins

√ frequently vertebral collapse
√ may involve adjacent vertebral disks + vertebrae
√ commonly involving both sides of the midline
√ joint transgression is unusual except for sacroiliac joint (38%) with sacral lesion
√ extraosseous involvement of soft tissues (79%)

NUC:
√ diffusely increased uptake on delayed bone scintigraphy
√ "doughnut" sign (57%) of central photopenia ← osteolysis / central necrosis
√ increased uptake across an articulation + in adjacent joints (62%) ← increased blood flow + disuse osteoporosis and NOT secondary to tumor extension

Angio:
√ hypervascular (60–65%) / hypovascular (20%) / avascular (10%) lesion

CT:
√ tumor of soft-tissue attenuation similar to muscle with foci of low attenuation (hemorrhage / necrosis):
- √ NO matrix mineralization

√ well-defined margins ± thin rim of sclerosis (in up to 20%)
√ soft-tissue extension (33–44%) usually at metaphyseal end of tumor
√ secondary ABC (aneurysmal bone cyst) components of low density with fluid-fluid levels (in up to 14%)
√ significant enhancement

MR: (nonspecific!)
√ low to intermediate SI on T1WI ± areas of hyperintensity ← recent hemorrhage
√ relatively well-defined heterogeneous lesion with low to intermediate SI on T2WI (63–96%) ← increased cellularity + high collagen content + hemosiderin
- ◊ HELPFUL feature to distinguish from other subarticular lesions (solitary subchondral cyst, intraosseous ganglion, Brodie abscess, clear cell chondrosarcoma with hyperintense matrix on T2WI)

√ focal aneurysmal bone cyst components with fluid-fluid level (in 14%) in tumor center with marked hyperintensity on T2WI
- ◊ Direct biopsy toward peripheral solid-tissue component to prevent misdiagnosis!

√ ± low-signal-intensity margin ← pseudocapsule
√ significant enhancement of solid-tissue component

Cx: in < 1% malignant transformation into high-grade sarcoma within first 9 years (M÷F = 3÷1) after radiation treatment / spontaneously after 19 years

Prognosis: ± locally aggressive; 10–20–90% recurrence rate within first 3 years after initial treatment

Dx: core needle / open bone biopsy

Rx: arterial embolization before surgery / for palliation; curettage + bone grafting (40–60% recurrence); curettage with filling of void with high-speed burr and polymethylmethacrylate (15–25% recurrence); wide resection (7% recurrence) + reconstruction with allografts / metal prosthesis; radiation therapy for inoperable GCT

(39–63% recurrence); denosumab

DDx: (1) Aneurysmal bone cyst (contains only cystic regions without enhancing soft-tissue component; in posterior elements of spine)

(2) Brown tumor of HPT (lab values, multicentric)

(3) Expansile lytic bone metastasis (primary renal / thyroid carcinoma)

(4) Plasmacytoma / multiple myeloma

(5) Chondroblastoma (extensive surrounding soft-tissue + marrow edema, sclerotic margin, central "rings-and-arcs" matrix)

(6) Clear cell chondrosarcoma

(7) Osteosarcoma subtypes: telangiectatic, giant cell-rich, fibroblastic

(8) Osteoblastoma

(9) Nonossifying fibroma

(10) Bone abscess

(11) Hemangioma

(12) Fibrous dysplasia

(13) Giant cell reparative granuloma

Benign Metastasizing Giant Cell Tumor (1–6%)

Cause: locally aggressive lesion / local recurrence / lesion of distal radius

√ lung metastasis

Multifocal Giant Cell Tumor

= additional GCTs (up to a maximum of 20) developing synchronously / metachronously for up to 20 years without increased risk of pulmonary metastases

Frequency: < 1% of all GCT cases

Age: 25 years (range, 11–62 years); M< F

May be associated with:

Paget disease, usually polyostotic (GCT develops at a mean age of 61 years + after an average time lapse of 12 years) with involvement of skull + facial bones

Location: increased prevalence for hands + feet

Malignant Giant Cell Tumor

= group of giant cell–containing lesions capable of malignant behavior + pulmonary metastases

Prevalence: 5–10% of all GCTs

Age: older than patients with benign GCTs

Types:

(1) Benign metastasizing GCT

Prevalence: 1–5%

√ pulmonary metastases may remain stable / regress spontaneously

√ pulmonary nodules may show peripheral ossification

Prognosis: death in 13%

(2) Primary malignant transformation of GCT

= malignant tumor of bone composed of sarcomatous growth juxtaposed to zones of typical benign GCT without a history of radiation therapy / repeated curettage / resection

Prognosis: median survival time of 4 years

(3) Secondary malignant GCT (86%)

= sarcomatous growth that occurs at a site of previously documented GCT usually after radiation therapy (80%) / repeated resections

Prognosis: median survival time of 1 year

(4) Osteoclastic (giant cell) sarcoma

= highly malignant tumor composed of anaplastic osteoclast-like giant cells without tumor osteoid / bone / cartilage

GOLTZ-GORLIN SYNDROME

= FOCAL DERMAL HYPOPLASIA

= X-linked dominant connective tissue genodermatosis

Genetics: defect in PORCN gene encoding a key protein involved in developmental Wnt signaling pathway

• soft red-yellow nodules in linear arrangement = fat herniating through hypoplastic dermis; short stature

Location: antecubital + popliteal fossa

• CHARACTERISTIC asymmetric erythematous / hyperpigmented / hypopigmented atrophic linear streaks:

• ± telangiectasia (often) ± superficially erosions + ulcers

Age: present at birth

√ scoliosis

√ generalized osteopenia

√ osteopathia striata = bilateral symmetric vertical metaphyseal striations of long bones with sparing of vertebrae and ilia

√ skeletal defects:

Location: hand, foot (60%)

√ "lobster claw" deformity = split hands and feet

√ clinodactyly, oligodactyly, polydactyly, syndactyly

√ regional asymmetric underdevelopment

√ spina bifida

√ rib and clavicular abnormalities

GLOMUS TUMOR

= rare small benign hamartoma of digits

Origin: cells derived from neuromyoarterial apparatus (responsible for thermoregulation in skin)

Glomus body = encapsulated oval organ of 300 µm length; located in reticular dermis (= deepest layer of skin); concentrated in tips of digits (93–501/cm²)

Components: afferent arteriole, tortuous arteriovenous anastomosis with an anastomotic vessel (= Sucquet-Hoyer canal lined by endothelium + surrounded by smooth

muscle fibers), system of collecting veins, intraglomerular neurovascular reticulum + capsule

Histo: endothelium-lined vascular spaces surrounded by masses of round epitheloid cells with tendency toward spindle form

Subtypes: (a) vascular (b) myxoid (c) solid form

Prevalence: 1–5% of soft-tissue tumors of hand

Age: mostly in 4th–5th decade; M÷F = 1÷1

Location: highly concentrated in digits (75% of glomus tumors)

◊ Account for 1.0–4.5% of all hand tumors

Site: subungual space (65%); multiple tumors in 2.3%

- intense joint tenderness + excruciating pain provoked by temperature sensitivity + mild trauma (on average 4–7 years duration prior to diagnosis); ± nail ridging + discoloration
- Love test = eliciting pain by applying precise pressure with a pencil tip
- Hildreth sign = disappearance of pain after application of a tourniquet proximally on arm (PATHOGNOMONIC)

@ SUBUNGUAL GLOMUS TUMOR

√ increased distance between dorsum of phalanx + underside of nail (25%)

√ extrinsic pressure erosion of adjacent bone (14–25–65%), often with sclerotic border

US:

√ small hypoechoic solid tumor (> 3 mm detectable)

√ ±erosion of underlying phalangeal bone

√ specific hypervascularity on color Doppler

MR:

√ lesion of intermediate / low SI on T1WI

√ homogeneously T2-hyperintense lesion (detectable if > 2 mm in diameter)

√ strong enhancement during arterial phase

√ tumor blush during delayed phase on CEMR images

@ GLOMUS TUMOR OF BONE occasionally within bone

√ resembles enchondroma

DDx: (1) Mucoid cyst (painless, in proximal nail fold, communicating with DIP joint, associated with osteoarthritis)

(2) Angioma (more superficially located)

GOUT

= metabolic disorder characterized by derangement of purine metabolism manifested by:

(1) Hyperuricemia ← ↑ production / ↓ excretion of uric acid exceeding physiologic saturation threshold of urate (around 380 μmol/L)

Kelley-Seegmiller syndrome = partial hypoxanthine-guanine phosphoribosyltransferase (HPRT) deficiency with onset of gout in late childhood

DDx: Lesch-Nyhan syndrome (complete HPRT deficiency)

(2) Deposition of positively birefringent monosodium urate monohydrate (MSU) crystals in synovial fluid

(3) Gross deposits of sodium urate in periarticular soft tissues (synovial membranes, articular cartilage, ligaments, bursae)

(4) Recurrent episodes of arthritis

Age: males > 40 years; gout may occur after menopause

Cause:

A. Primary Gout (90%)

Prevalence: 1–2% of population; M÷F = 20÷1; 5% in postmenopausal women

◊ Most prevalent form of metabolic arthritis in older men

Disturbance:

- overproduction of uric acid ← inborn error of metabolism
- inherited defect in renal urate excretion

(a) Idiopathic (99%)

- normal urinary excretion (80–90%)
- increased urinary excretion (10–20%)

(b) Specific enzyme / metabolic defect (1%)

(1) increased activity of PP-ribose-P synthetase

(2) partial deficiency of hypoxanthine-guanine phosphoribosyltransferase

B. Secondary Gout (10%)

◊ Rarely cause for radiographically apparent disease

(a) increased turnover of nucleic acids:

(1) Myeloproliferative disorders + sequelae of their treatment: polycythemia vera, leukemia, lymphoma, multiple myeloma

(2) Blood dyscrasias: chronic hemolysis

(b) increase in purine synthesis de novo ← enzyme defects:

(1) Glycogen storage disease Type I (von Gierke = glucose-6-phosphatase deficiency)

(2) Lesch-Nyhan syndrome (choreoathetosis, spasticity, mental retardation, self-mutilation of lips + fingertips) ← absence of hypo-xanthine-guanine phosphoribosyltransferase

(c) acquired defect in renal excretion of urates ← reduction in renal function:

(1) Chronic renal failure

(2) Drugs, toxins: lead poisoning

(3) Endocrinologic: myxedema, hypo- / hyperparathyroidism

(4) Vascular: myocardial infarction, hypertension

Histo: tophus (PATHOGNOMONIC LESION) composed of crystalline / amorphous urates surrounded by highly vascularized inflammatory tissue rich in histiocytes, lymphocytes, fibroblasts, foreign-body giant cells (similar to a foreign-body granuloma)

Clinical stages (phases) in chronologic order:

(1) Asymptomatic hyperuricemia: cumulative crystal deposition is frequently clinically silent

(2) **Acute gouty arthritis**

◊ 10% of hyperuricemic individuals develop clinical gout

◊ Gout accounts for 5% of all cases of arthritis

Precipitated by: trauma, surgery, alcohol, dietary indiscretion, systemic infection

Distribution:

(a) monoarticular (90%): lower limb joints 1st MTP joint (= podagra), tarsal joints, ankles, knees → progression to elbows + hands

(b) polyarticular (10%): any joint may be affected

• pain, swelling, erythema of affected joint

Prognosis:

(1) usually self-limited episodes (pain resolving within a few hours / days) without treatment

(2) recurrent longer attacks of acute arthritis → chronic arthropathy+ tophus deposition + renal disease

(3) **Chronic tophaceous gout** (30% within 5 years)

= multiple large aggregates of urate crystals + proteinaceous matrix surrounded by intense inflammatory reaction

Prevalence: < 50% of patients experience acute attacks

Histo: cartilage degeneration + destruction, synovial proliferation + pannus, destruction of subarticular bone + proliferation of marginal bone

Age: 5th–7th decades; M÷F = 20÷1

Distribution: symmetric polyarticular disease (resembling rheumatoid arthritis), asymmetric polyarticular disease, monoarticular disease

Site: intraarticular, extraarticular, intraosseous

Target areas: Achilles tendon, knee extensor mechanism, popliteal tendon

• more severe prolonged attacks

• may ulcerate expressing whitish chalky material

Cx: tendon rupture, nerve compression / paralysis

(4) **Gouty nephropathy** / nephrolithiasis

(a) Acute urate nephropathy

(b) Uric acid urolithiasis

◊ May precede arthritis in up to 20% of cases!

• renal hypertension

• isosthenuria (inability to concentrate urine)

• proteinuria

• pyelonephritis

Cx: increased incidence of calcium oxalate stones (urate crystals serve as a nidus)

Location:

(a) joints: hand + foot (1st MTP joint most commonly affected = **podagra**) > ankle > heel > wrist (carpometacarpal compartment especially common and severe) > finger > elbow; knee; shoulder; sacroiliac joint (15%, unilateral)

[pod = *Greek*, foot; agra = *Greek*, seizing]

◊ Involvement of hip + spine is rare

(b) bones, tendon, bursa

(c) external ear; pressure points over elbow, forearm, knee, foot

◊ Radiologic features present in 45% of afflicted patients but usually not seen until 6–12 years after initial attack!

@ Soft tissues

√ eccentric juxtaarticular lobulated soft-tissue masses (hand, foot, ankle, elbow, knee)

Site: tendency for extensor tendons, eg, quadriceps, triceps, Achilles tendon

√ calcific deposits in periphery of gouty tophi in 50%

(sodium urate crystals are not radiopaque, tophi radio-graphically visible only after

calcium deposition which requires an underlying abnormality of calcium metabolism)
√ bilateral effusion of bursae olecrani (PATHOGNOMONIC), prepatellar bursa
√ aural calcification

@ Joints
√ joint effusion (earliest sign)
√ periarticular soft-tissue nodules
√ preservation of joint space until late in disease
(IMPORTANT CLUE):
√ cartilage destruction (late in course of disease)
√ ABSENCE of periarticular demineralization ← short duration of attacks; important DDx for rheumatoid arthritis)
√ eccentric erosions with thin sclerotic margins:
√ scalloped erosion of bases of ulnar metacarpals
√ chondrocalcinosis (5%):
Location: menisci (fibrocartilage only)
◊ Patients with gout have a predisposition for calcium pyrophosphate dihydrate deposition disease (CPPD)
Cx: secondary osteoarthritis
√ round / oval well-marginated subarticular cysts (pseudotumor) up to 3 cm (containing tophus / urate crystal-rich fluid)
DDx: rheumatoid arthritis (marginal erosions without sclerotic rim, periarticular demineralization)

@ Bone
√ "punched-out" lytic bone lesion ± sclerosis of margin = "mouse / rat bite" erosion ← long-standing soft-tissue tophus
√ "overhanging margin" (40%) = elevated osseous spicule separating tophaceous nodule from adjacent erosion (in intra- and extraarticular locations) (HALLMARK)
√ proliferative bone changes:
√ club-shaped metatarsals, metacarpals, phalanges
√ enlargement of ulnar styloid process
√ diaphyseal thickening
√ ischemic necrosis of femoral / humeral heads
√ intraosseous calcification:
√ punctate / circular calcifications of subchondral / subligamentous regions (DDx: enchondroma)
√ bone infarction ← deposits at vascular basement membrane (DDx: bone island)

@ Kidney
√ renal stones (in up to 20%):
› pure uric acid stones (84%): radiolucent on radiographs, hyperdense on CT
› uric acid + calcium oxalate (4%)
› pure calcium oxalate / calcium phosphate (12%)

US:
√ distended joint capsule
√ intra-articular echogenic material with snowstorm appearance of multiple dotted bright foci ← urate acid crystals movable with transducer pressure

√ sharply defined erosion
√ positive color Doppler signals ← synovitis
√ lobulated echogenic mass(es) ← tophaceous gout

MR:
√ tophus (most frequently) isointense to muscle on T1WI
√ low to intermediate signal intensity on T2WI
√ homogeneous intense enhancement

Dx: needle-shaped negatively birefringent monosodium urate crystals in aspirated joint fluid / tophus

Rx: colchicine, allopurinol (effective treatment usually does not improve roentgenograms)

DDx:
(1) CPPD (pseudogout symptomatology, polyarticular chondrocalcinosis involving hyaline and fibrocartilage + degenerative arthropathy with joint space narrowing)
(2) Psoriasis (progressive joint space destruction, paravertebral ossification, sacroiliac joint involvement)
(3) Rheumatoid arthritis (nonproliferative marginal bone erosions, fusiform soft-tissue swelling, symmetric distribution, early joint-space narrowing, osteopenia)
(4) Septic arthritis (rapid destruction of joint space, loss of articular cortex over a continuous segment)
(5) Amyloidosis (bilateral symmetric involvement, periarticular osteopenia)
(6) Xanthomatosis (laboratory work-up)
(7) Osteoarthritis (symmetric distribution, elderly women)

GRANULOCYTIC SARCOMA

= CHLOROMA = MYELOID SARCOMA = MYELOBLASTOMA
= uncommon extramedullary solid tumor consisting of primitive precursors of the granulocytic series of WBCs (myeloblasts, promyelocytes, myelocytes)

Peak age: 7–8 years; child > adult; M=F

Myeloid sarcoma is a rare extramedullary proliferation of immature myeloid cells occurring in 3–5% of AML patients.

Clinical setting:
(1) patient with acute myelogenous leukemia (in 3–8%)
(2) harbinger of AML in nonleukemic patient: usually developing within 1 year (rare)
(3) indicator of impending blast crisis in CML (in 1%) / leukemic transformation in myelodysplastic syndromes (polycythemia rubra vera, myelofibrosis with myeloid metaplasia, hypereosinophilic syndrome)
(4) during remission of hematologic malignancy (up to 20%)
(5) isolated event

Associated with: chronic myeloid leukemia, myelodysplastic syndrome, essential thrombocythemia, polycythemia vera

• 60% are of green color (chloroma) ← high levels of **myeloperoxidase** (30% are white / gray / brown depending on preponderance of cell type + oxidative state of myeloperoxidase)

Location: often multifocal
(a) common: bone (skull, orbit, paranasal sinus, periosteum); lymph nodes; soft tissues; skin;

breast
(b) less common: GU tract, GI system, head & neck, chest

Site: propensity for bone marrow (arises from bone marrow traversing haversian canal + reaching the periosteum), perineural + epidural tissue

Radiography:
√ osteolysis with ill-defined margins

CT:
√ soft-tissue mass infrequently with bone erosion / demineralization / periosteal reaction
√ generally homogeneously isoattenuating to slightly hyperattenuating relative to muscle / brain
√ homogeneous enhancement on CT / MR (DDx to hematoma / abscess)

MR:
√ iso- to hypointense relative to gray matter / bone marrow / muscle on T1WI
√ heterogeneously iso- to slightly hyperintense on T2WI

Prognosis: poor outcome; resolution under chemotherapy ± radiation therapy; recurrence rate of 23%

DDx: osteomyelitis, histiocytosis X, neuroblastoma, lymphoma, multiple myeloma

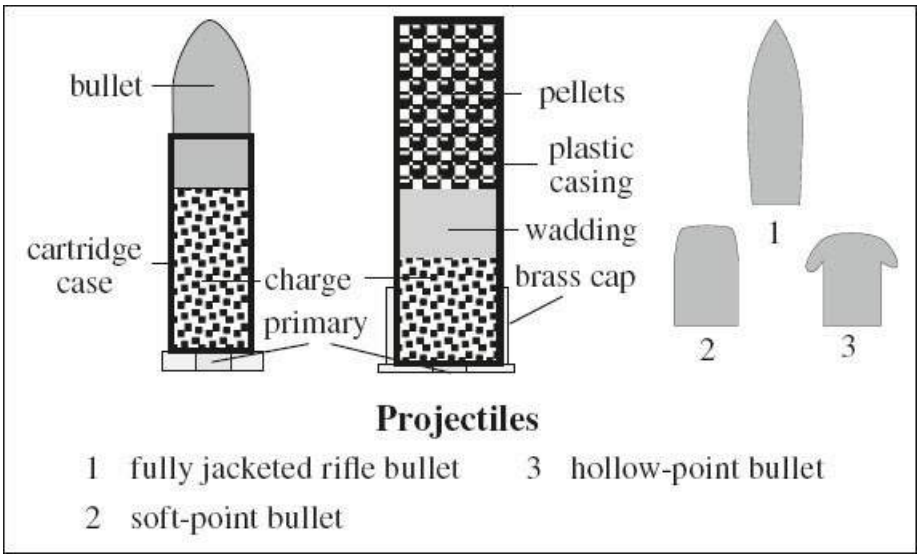
GUNSHOT INJURY

Prevalence: 200,000 gun-related injuries per year; 31,224 firearm-related deaths in USA (2007)

Firearms: handgun, rifle (great energy), shotgun

Projectiles:
(a) bullet:
› jacketed bullet with mantle of copper
› semi jacketed bullet = exposed lead at tip
› non jacketed bullet
(b) pellets of steel / lead:
› birdshot = small pellets
› buckshot =large pellets

Assessment of type of projectile:
√ fully jacketed bullets show no trail of lead fragments
√ semi- / non jacketed bullets distribute lead fragments along bullet track
√ hollow-point bullets transform into mushroom shape
√ "lead snowstorm" of high-velocity soft-point rifle bullets:
√ conical distribution with apex pointing toward entry site
√ steel pellets remain round, lead pellets become deformed + fragmented



Assessment of trajectory:
- √ bullet tips points to entry wound (after tumbling through 180°):
  - √ impact deformation of bullet modifies tumbling
- √ bullet + bone fragments deposited along track
- √ bone fracture beveled toward the direction of travel

Location: liver > small bowel > colon > spleen > kidney > pancreas

Pathophysiology of gunshot: complex interaction of mass, velocity, path, type of organ
- (a) projectile: bullet imparts kinetic energy to surrounding tissue → tissue displacement radially away from path of bullet → temporary cavity much larger than bullet diameter (depending on mass, material, design, velocity of projectile)
- (b) tissue: damage depends on specific gravity (density) and elasticity of type of soft tissue ↓ density + ↑ elasticity: skin, lung (less damage) ↑ density + ↓ elasticity: liver, spleen, muscle
- (c) fluid: pressure wave → bursting of fluid-filled organ
- (d) bone: bone fragments = numerous secondary missiles

Cx: pellet embolization, magnetization in MRI

HEMANGIOENDOTHELIAL SARCOMA

= HEMANGIOENDOTHELIOMA = HEMANGIOEPITHELIOMA

= neoplasm of vascular endothelial cells of intermediate aggressiveness with either benign or malignant behavior

Histo: irregular anastomosing vascular channels lined by one / several layers of atypical anaplastic endothelial cells

Age: 4th–5th decade; M÷F = 2÷1

- history of trauma / irradiation

Kaposiform Hemangioendothelioma

= locally aggressive vascular tumor of infancy

Path: infiltrative growth pattern with predominant Kaposi sarcoma–like content consisting of

fascicles of spindle cells (DDx: hemangioma of infancy)
Histo: fibrinogenic thrombi in capillaries, hemorrhage, foci resembling lymphangiomatosis (⅔)
Age: 1st year of life; present at birth (½)
√ cutaneous thickening, stranding of subcutaneous fat, hemorrhage
√ ill-defined margins ← involvement of multiple tissue planes
√ destructive changes and remodeling of adjacent bone
MR:
√ signal intensity similar to muscle on T1WI
√ heterogeneously hyperintense relative to muscle on T2WI
√ apparent infiltration of subcutaneous tissues
√ signal voids on GRE ← accumulation of blood products
√ diffuse heterogeneous enhancement

Soft-tissue Hemangioendothelioma (common)
Location: deep tissues of extremities
Site: in 50% closely related to a vessel (often a vein)

Osseous Hemangioendothelioma (rare)
= EPITHELIOID HEMANGIOENDOTHELIOMA OF BONE
= rare endothelial intermediate-grade malignant vascular neoplasm
Path: well-circumscribed tumor with irregular borders
Histo: solid nests + anastomosing cords of round polygonal / spindle-shaped cells with eosinophilic cytoplasm; intracytoplasmic vacuolization (= primitive vascular channels); few mitoses, only mild pleomorphism
Average age: 2nd–3rd decade; M÷F = 2÷1
Location: calvarium, spine, pelvis, tibia (23%), femur (18%), humerus (13%); visceral involvement of lung, liver, spleen
◊ Multifocal (> 50%) often with regional distribution (less aggressive)
N.B.: A thorough evaluation requires CT of chest and abdomen + bone scintigraphy + skeletal survey!
Site: metaphyseal / diaphyseal > epiphyseal
• pain + swelling of affected area
X-RAY:
√ eccentric lytic lesion without matrix mineralization
√ osteolytic aggressively destructive area with indistinct margins (high grade)
√ well-demarcated margins with scattered bony trabeculae (low grade)
√ osteoblastic area in vertebrae, contiguous through several vertebrae
√ ± osseous expansile remodeling
CT:
√ cortical disruption with extension into soft tissues
√ joint invasion (common)
√ homogeneous enhancement
MR:
√ low to intermediate signal intensity on T1WI

√ high signal intensity on T2WI
√ homogeneous enhancement
√ no serpentine vascular structures

Metastases to: lung (early)

Prognosis: variable course; poor prognosis with visceral involvement; local recurrence (18%); regional / distant metastasis (31%)

DDx: aneurysmal bone cyst, poorly differentiated fibrosarcoma, alveolar rhabdomyosarcoma, cystic angiomatosis, Langerhans cell histiocytosis, angiosarcoma, osteomyelitis, multiple myeloma, highly vascular metastasis, lymphoma

HEMANGIOMA

= benign nonreactive process involving an increase in number reminiscent of embryonic capillaries or veins

◊ Most common benign soft-tissue tumor of vascular origin!

Prevalence: 1–2% of population (higher in premature infants); in up to 10% of whites

Histo: increased number of thin-walled vessels containing RBCs / transudate lined by flat monolayered endothelial cells; frequently with variable amounts of nonvascular elements (fat, smooth muscle, fibrous tissue, bone, hemosiderin, thrombus)

◊ Fat overgrowth may be so extensive that some lesion may be misdiagnosed as a lipoma!

Age: most common tumor of infancy; present at birth in 30–40% M÷F = 1÷3

Location: lower extremity (common), head & neck (mid cheek, upper lip, upper eyelid)

Site: any soft tissue (eg, muscle), tendon, connective tissue, fatty tissue, synovium, bone

Distribution: focal + localized / diffuse + segmental

• painless mass; red (superficial); flesh colored / blue (deep)

√ multiple variable-sized phleboliths (frequent)

US:

√ partially defined hypoechoic hypervascular solid mass
√ mixed echogenicity ← reactive fat overgrowth
√ intratumoral bright foci of variable size + posterior acoustic shadowing = phleboliths
√ prominent vascular channels
√ abnormal arterial signal of low resistance with continuous forward flow during systole + diastole

MR:

√ mass of intermediate signal intensity on T1WI:
  √ serpentine / lattice-like enhancement
√ mass of extremely high signal intensity on T2WI:
  √ heterogeneous hyperintensity ← reactive fatty tissue around neoplastic vessels / vessels filled with blood
  √ serpentine pattern + flow voids (DDx to rhabdomyosarcoma)
√ well-defined / infiltrative margin
√ foci of low SI on T1WI + T2WI ← phleboliths / calcifications / fibrosis

Prognosis: cellular proliferation + enlargement during 1st year of life

A. CAPILLARY HEMANGIOMA (most common)

= small-caliber vessels lined by flattened epithelium
Site: skin, subcutaneous tissue; vertebral body
Classification:
(a) Juvenile capillary hemangioma
(b) Verrucous capillary hemangioma
(c) Senile capillary hemangioma
√ enlarged arteries + arteriovenous shunting
√ pooling of contrast material

B. CAVERNOUS HEMANGIOMA
= dilated blood-filled spaces lined by flattened endothelium
Site: deeper soft tissues, frequently intramuscular; calvarium
Age: childhood
√ phleboliths = dystrophic calcification in organizing thrombus (in nearly 50%)
√ large cystic spaces
√ enlarged arteries + arteriovenous shunting
√ pooling of contrast material
Prognosis: NO involution

C. ARTERIOVENOUS HEMANGIOMA
= persistence of fetal capillary bed with abnormal communications of an increased number of normal / abnormal arteries and veins
Etiology: (?) congenital arteriovenous malformation
Age: young patients
Site: soft tissues
(a) superficial lesion without arteriovenous shunting
(b) deep lesion with arteriovenous shunting
- limb enlargement, bruit
- distended veins, overlying skin warmth
- Branham sign = reflex bradycardia after compression

√ large tortuous serpentine feeding vessels
√ fast blood flow + dense staining
√ early draining veins

D. VENOUS HEMANGIOMA
= thick-walled vessels containing muscle
Site: deep soft tissues of retroperitoneum, mesentery, muscles of lower extremities
Age: adulthood
√ ± phleboliths
√ serpentine vessels with slow blood flow
√ vessels oriented along long axis of extremity (in 78%) + neurovascular bundle (in 64%)
√ multifocal involvement (in 37%)
√ muscle atrophy with increased subcutaneous fat
√ may be normal on arterial angiography

Osseous Hemangioma

Frequency: 10%
Histo: mostly cavernous; capillary type is rare

Age: 4th–5th decade; M÷F = 2÷1
• usually asymptomatic
@ Vertebra (28% of all skeletal hemangiomas)
Prevalence: in 5–11% of all autopsies; multiple in ⅓
Histo: capillary hemangioma interspersed in fatty matrix
◊ The larger the degree of fat overgrowth, the less likely the lesion will be symptomatic!
Age: any age; young adult; female
Location: in lower thoracic / upper lumbar spine
Site: vertebral body; may extend into posterior elements
• mostly asymptomatic
√ "accordion" / "corduroy" / "honeycomb" vertebra
= coarse vertical trabeculae with osseous reinforcement adjacent to bone rarefaction ← resorption caused by vascular channels (also in multiple myeloma, lymphoma, metastasis)
√ bulge of posterior cortex
√ extraosseous extension beyond bony lesion into spinal canal (with cord compression) / neural foramina
√ paravertebral soft-tissue extension
√ lesion enhancement ← hypervascularity
CT:
√ polka-dot appearance = small punctate areas of sclerosis (= thickened vertical trabeculae)
MR:
√ high signal intensity on T1WI + T2WI ← amount of adipocytes / vessels / interstitial edema (CHARACTERISTIC)
√ thick vertical struts of low SI
√ rarely low / intermediate SI on T1WI (= less fat indicating a more vascular / more aggressive lesion)
NUC:
√ photopenia / moderate increase in radiotracer uptake
Cx: vertebral collapse (unusual), spinal cord compression
@ Calvarium (20% of all hemangiomas)
Location: frontal / parietal region
Site: diploe
√ < 4 cm round osteolytic lesion with sunburst / weblike / spoke-wheel appearance of trabecular thickening
√ expansion of outer table to a greater extent than inner table producing a palpable lump
@ Flat bones & long bones (rare)
› ribs, clavicle, mandible, zygoma, nasal bones, metaphyseal ends of long bones (tibia, femur, humerus)
√ radiating trabecular thickening
√ bubbly bone lysis creating honeycomb / latticelike / "hole-within-hole" appearance
MR:
√ serpentine vascular channels with low SI on T1WI + high SI on T2WI (= slow blood flow) / low SI on all sequences (= high blood flow)

NUC (bone / RBC-labeled scintigraphy):
√ photopenia / moderate increased activity

Intracortical Hemangioma

Histo: expanded haversian canals containing dilated cavernous vessels
Location: tibia > femur, ulna, mandible
√ intracortical osteolytic lesion with vertically aligned intralesional calcifications
√ cortical thickening / periostitis
CT:
√ hypoattenuating intracortical lesion with spotty internal calcification = "wire-netting" appearance
MR:
√ hyperintense lesion with hypointense septa on T2WI
DDx: osteoid osteoma

Soft-tissue Hemangioma

Frequency: 7% of all benign soft-tissue tumors; most frequent tumor of infancy + childhood
Age: primarily in neonates
May be associated with: Maffucci syndrome (= multiple cavernous hemangiomas + enchondromas)
• intermittent change in size; painful
• bluish discoloration of overlying skin (rare)
• may dramatically increase in size during pregnancy
Location: usually intramuscular; synovium (< 1% of all hemangiomas)
√ nonspecific soft-tissue mass
√ infiltrating lesion of serpentine vessels interdigitating with fibroadipose tissue (in cavernous hemangioma)
√ may extend into bone creating subtle rounded / linear areas of hyperlucency (rare)
√ ± longitudinal / axial bone overgrowth ← chronic hyperemia
√ may contain phleboliths (30% of lesions, SPECIFIC)
√ nonspecific curvilinear / amorphous calcifications
√ may contain large amounts of fat → indistinguishable from lipoma
CT:
√ poorly defined mass with attenuation similar to muscle
√ areas of decreased attenuation approximating subcutaneous fat (= fat overgrowth) most prominent in periphery of lesion
MR:
√ poorly marginated mass hypo- / isointense to muscle on T1WI
√ interspersed areas of increased SI on T1WI in periphery of lesion ← fat extending into tumor septa
√ well-marginated markedly hyperintense ("cystic") mass on T2WI (← increased free water content in stagnant blood) with striated / septated configuration
√ tubular structures with blood flow characteristics (flow void / inflow enhancement; avid contrast enhancement)
√ foci of signal voids ← high-flow vascular channels / phleboliths / thrombi

√ high-signal-intensity areas on T1WI + T2WI (= hemorrhage + fat deposition)
√ internal fluid-fluid levels ← high proteinaceous / hemorrhagic content

US:
√ complex mass
√ low-resistance arterial signal (occasionally)

Juvenile Capillary Hemangioma

= STRAWBERRY NEVUS
Prevalence: 1÷200 births; in 20% multiple
Age: usually neonate within 1st week; apparent at birth in only 20%; M÷F = 1÷3 to 1÷5
Histo: neoplastic features of endothelial proliferation
Location: head and neck (60%) > trunk (25%) > extremity (15%)
• "strawberry marks" (= bright red protuberant compressible lesions) of face, scalp, back, anterior chest wall
Prognosis: rapid proliferation from 2–10 months; followed by variable period of stability; slow involution in 75–90% by age 7 years
Indication for imaging:
deep hemangioma, compromise of airway, impaired vision, heart failure, thrombocytopenic coagulopathy
√ flow voids (DDx to rhabdomyosarcoma)
√ T1 shortening during involuting phase ← fatty replacement of nidus
Cx: necrosis of overlying skin / Kasabach-Merritt syndrome (during proliferative phase)
Rx: expectant observation, assurance to parents, steroids, transcatheter embolization

Synovial Hemangioma

= rare benign vascular malformation
Age: child, young adult
• joint pain, swelling ← repetitive bleeding into joint
Location: knee (60%), elbow (30%)
√ phleboliths (not uncommon)
MR:
√ lobulated intraarticular mass
√ intermediate SI on T1WI
√ marked hyperintensity on T2WI ← pooling of blood within vascular spaces
√ linear hypointense structures on T2WI ← fibrous septa / vascular channels
DDx: hemophilic arthropathy (polyarticular)

Lobular Capillary Hemangioma

= PYOGENIC GRANULOMA
= relatively common acquired benign vascular neoplasm of skin + mucous membranes
Cause: presumed neoplastic process; not a reaction to trauma / infection
Path: well-circumscribed lesion with central vessel as branching point for capillary lobules
Histo: lobules of capillaries in an edematous fibromyxoid stroma containing elongated spindle cells with numerous mitotic figures
Average age: 38 (range, 15–60) years; M < F

Location: head, neck, upper extremity (esp. fingers)
- solitary rapidly growing bright red cutaneous mass
- commonly ulcerating + bleeding

US:
√ well-defined mildly to moderately echogenic mass containing small hypoechoic foci
√ prominent tumor vascularity with arterial waveform

MR:
√ lesion isointense on T1WI + hyperintense on T2WI
√ marked enhancement

DDx: true hemangioma, glomus tumor

HEMANGIOPERICYTOMA

= borderline tumor with benign / locally aggressive / malignant behavior (counterpart of glomus tumor)

◊ Clinical behavior + histopathologic features are similar to solitary fibrous tumor

Age: 4th–5th decade; M÷F = 1÷1

Path: large vessels predominantly in tumor periphery

Histo: cells packed around vascular channels containing cystic + necrotic areas closely resembling cellular areas of solitary fibrous tumor; arising from contractile cells that surround the walls of vessels (= Zimmermann pericytes)

May be associated with: hypoglycemia (← overproduction of insulinlike growth factor), arthralgia, osteoarthropathy, digital clubbing

- slow-growing mass ± local mass effect

MR:
√ well-circumscribed solid mass
√ low to intermediate SI on T1WI + T2WI
√ heterogeneously high SI on T2WI ← myxoid / cystic degeneration
√ low signal-intensity rim around lesion (= pseudocapsule) on T2WI

@ Soft tissue
= deep-seated well-circumscribed lesion arising in muscle
Location: lower extremity in 35% (thigh), pelvic cavity, retroperitoneum, head & neck (unlikely), meninges
- painless slowly growing mass up to 20 cm

√ large lobulated well-circumscribed hypervascular mass
√ foci of calcification + areas of necrosis
√ displacement of kidney

@ Breast (extremely rare)

@ Bone (rare)
Location: lower extremity, vertebrae, pelvis, skull (dura similar to meningioma)
√ osteolytic lesion in metaphysis of long / flat bone
√ subperiosteal large blowout lesion (similar to aneurysmal bone cyst)

Angio:
√ displacement of main artery
√ pedicle of tumor feeder arteries

√ spider-shaped arrangement of vessels encircling tumor
√ small corkscrew arteries
√ dense tumor stain

Prognosis: 47–86% 10-year survival rate

DDx: hemangioendothelioma, angiosarcoma

HEMOCHROMATOSIS

= excess iron deposition in tissues (hemosiderosis) resulting in tissue injury

Primary / Idiopathic Hemochromatosis

= autosomal recessive genetic disorder (abnormal iron-loading gene on short arm of chromosome 6) in thalassemia, sideroblastic anemia

Defect: increased absorption + parenchymal accumulation of dietary iron

Organs: liver, pancreas, heart (parenchymal iron overload)

Homozygous frequency: 1÷200; M÷F = 1÷1

Age: > 30 years (M), usually after menopause (F);
◊ Females protected by menstruation

- cirrhosis (frequently present at time of diagnosis)
- "bronzed diabetes" (50%) = insulin-dependent diabetes ← excess intracellular iron reduces function of beta islet cells while reserve capacity of exocrine function is not exceeded by toxic effects of iron; skin pigmentation
- congestive cardiomyopathy ← myocardial muscle accumulates toxic levels of intracellular iron
- hypogonadism + decreased libido ← pituitary dysfunction
- slowly progressive arthritic symptoms (30%)
- increased serum iron + ferritin level (nonspecific)
- transferrin saturation + serum ferritin assay (specific)

@ Skeleton

Distribution: most commonly in hands (metacarpal heads, particularly 2nd + 3rd MCP joints), carpal (30–50%) + proximal interphalangeal joints, knees, hips, elbows

√ generalized osteoporosis
√ small subchondral cystlike rarefactions with fine rim of sclerosis (metacarpal heads)
√ arthropathy in 50% (iron deposition in synovium)
√ uniform symmetric joint space narrowing (unusual for degenerative joint disease)
√ enlargement of metacarpal heads:
√ hook-like osteophytes on radial aspect of metacarpal heads (CHARACTERISTIC)
√ chondrocalcinosis in > 60%, knees most commonly affected
(a) calcium pyrophosphate deposition ← inhibition of pyrophosphatase enzyme within cartilage which hydrolyzes pyrophosphate to soluble orthophosphate
(b) calcification of triangular cartilage of wrist, menisci, annulus fibrosus, ligamentum flavum, symphysis pubis, Achilles tendon, plantar fascia

@ Brain

√ marked loss in SI of anterior lobe of pituitary gland ← iron deposition

@ Abdomen

√ decreased T2 signal intensity in liver, pancreas
√ normal SI of spleen on T2WI + T2*WI

Dx: liver biopsy with hepatic iron index > 2 (= iron concentration in μmol/g of dry weight divided by patient's age in years)

Cx: hepatoma in 14% (iron stimulates growth of neoplasms)

Prognosis: death from CHF (30%), death from hepatic failure (25%), death from HCC (in up to 33%)

Rx: (1) Phlebotomy (returns life expectancy to normal if instituted prior to complications)

(2) Screening of family members (gene can be located by human leukocyte antigen typing)

DDx: (1) Pseudogout (no arthropathy)

(2) Psoriatic arthritis (skin + nail changes)

(3) Osteoarthritis (predominantly distal joints in hands)

(4) Rheumatoid arthritis

(5) Gout (may also have chondrocalcinosis)

Secondary Hemochromatosis

= nongenetic iron overload

(1) ineffective erythropoiesis: thalassemia major increases demand for iron resulting in increased absorption + retention of dietary iron

Cx: increase in parenchymal iron

(2) Bantu siderosis = parenchymal + RES iron overload ← extensive use of iron pots for cooking

Transfusional Siderosis

[**siderosis** = exposure to excess iron]

= iron overload of RES (NOT a form of secondary hemochromatosis); iron less toxic

Pathophysiology: large number of damaged erythrocytes from blood transfusions are incorporated into RES cells + undergo lysis with liberation of iron from hemoglobin (extravascular hemolysis)

Organs of RES: Kupffer cells, spleen, bone marrow

√ decreased signal intensity of liver + spleen on T2WI

Iron storage capacity of RES: 10 g (equivalent to 40 units of packed RBCs)

HEMOLYTIC ANEMIA

Cause:

A. Anemia:
   1. Sickle cell disease
   2. Thalassemia
   3. Hereditary spherocytosis
   4. Paroxysmal nocturnal hemoglobulinuria
B. Chronic / severe blood loss
C. Marrow replacement by neoplastic cells

D. Treatment with GCSF (= granulocyte-macrophage colony-stimulating factor)

Reconversion = recruitment of yellow marrow for hematopoiesis once hematopoietic capacity of existing red marrow stores is exceeded

Order of reconversion: spine > flat bones > skull > long bones (proximal > distal metaphysis > diaphysis > epi- / apophyses)

MR:

√ SI of hyperplastic marrow similar to muscle on T1WI + T2WI + STIR

√ red marrow hypointense relative to fat on T2WI

√ low SI of renal cortex on T1WI + T2WI ← hemosiderin deposition (after intravascular hemolysis)

Cx:

(1) **Hemosiderosis** (histologic term of iron deposition in tissue) = excess iron in cells of RES ← repeated blood transfusions

√ magnetic susceptibility effects of hemosiderin produce hypointense marrow on T2WI (+ T1WI if hemosiderosis severe)

(2) Medullary infarction (common in sickle cell disease)

DDx: leukemia (hyperintense on STIR)

HEMOPHILIA

= X-linked deficiency / functional abnormality of coagulation factor VIII (= hemophilia A) in > 80% / factor IX (= hemophilia B = Christmas disease)

Prevalence: 1÷10,000 males

Hemophilic Arthropathy (most common)

Cause: repeated bleeding into synovial joint

Path: pannus formation erodes cartilage with loss of sub-chondral bone plate and formation of subarticular cysts

Histo: synovial hyperplasia, chronic inflammatory changes, fibrosis, siderosis of synovial membrane

Age: 1st and 2nd decade

• tense red warm joint with decreased range of motion ← muscle spasm; fever, elevated WBC (DDx: septic arthritis)

Location: knee > ankle > elbow > shoulder; commonly bilateral although bleeding episodes tend to recur within same joint

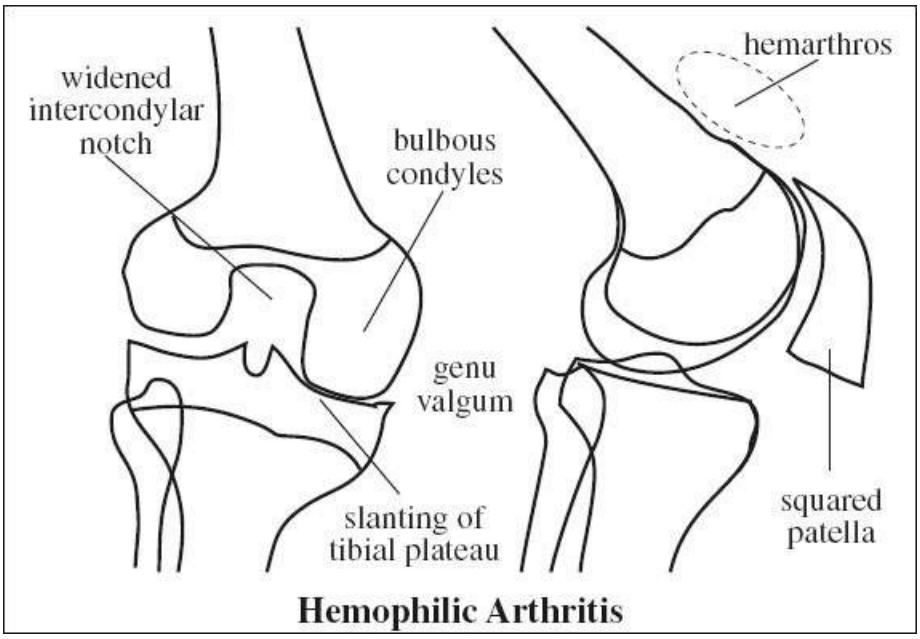
√ joint effusion (= hemarthrosis)

√ enlargement of epiphysis ← synovial inflammation with hyperemia)

√ juxtaarticular osteoporosis ← synovial inflammation with hyperemia

√ joint space narrowing (particularly patella) ← cartilaginous denudation

√ erosion of articular surface with multiple subchondral cysts



Hemophilic Arthritis

√ sclerosis + osteophytosis ← superimposed degenerative joint disease

@ Knee

√ "squared" patella

√ widening of intercondylar notch

√ flattening of condylar surface

√ medial "slanting" of tibiotalar joint

MR:

√ low SI of hypertrophied synovial membrane on all pulse sequences ← magnetic susceptibility effect of hemosiderin

√ varying intensity of subarticular defects (depending on substrate: fluid / soft tissue / hemosiderin)

Hemophilic Pseudotumor (1–2%)

= posthemorrhagic cystic swelling within muscle + bone characterized by pressure necrosis + destruction

(a) juvenile form = usually multiple intramedullary expansile lesions without soft-tissue mass in small bones of hand / feet (before epiphyseal closure)

(b) adult form = usually single intramedullary expansile lesion with large soft-tissue mass in ilium / femur

(c) soft-tissue involvement of retroperitoneum (psoas muscle), bowel wall, renal collecting system

√ mixed cystic expansile lesion

√ bone erosion + pathologic fracture

CT:

√ sometimes encapsulated mass containing areas of low attenuation + calcifications

MR:

√ hemorrhage of varying age

Cx: joint contracture (after repeated bleeding into muscle)
N.B.: Needle aspiration / biopsy / excision may cause fistulae / infection / uncontrolled bleeding!
Rx: palliative radiation therapy (destroys vessels prone to bleed) + transfusion of procoagulation factor concentrate

HEREDITARY HYPERPHOSPHATASIA

= "JUVENILE PAGET DISEASE"
= rare autosomal recessive disease with sustained elevation of serum alkaline phosphatase, especially in individuals of Puerto Rican descent
Histo: rapid turnover of lamellar bone without formation of cortical bone; immature woven bone is rapidly laid down, but simultaneous rapid destruction prevents normal maturation
Age: 1st–3rd year; usually stillborn
• rapid enlargement of calvarium + long bones; dwarfism
• cranial nerve deficit (blind, deaf); hypertension
• frequent respiratory infections; pseudoxanthoma elasticum
• elevated alkaline phosphatase
√ deossification = decreased density of long bones with coarse trabecular pattern
√ metaphyseal growth deficiency
√ wide irregular epiphyseal lines (resembling rickets in childhood), persistent metaphyseal defects (40% of adults)
√ bowing of long bones + fractures with irregular callus
√ widened medullary canal with cortical thinning (cortex modeled from trabecular bone)
√ skull greatly thickened with wide tables, cotton wool appearance
√ vertebra plana
OB-US:
√ diagnosis suspected in utero in 20%
Cx: pathologic fractures; vertebra plana universalis
DDx: (1) Osteogenesis imperfecta
(2) Polyostotic fibrous dysplasia
(3) Paget disease (> age 20, not generalized)
(4) Pyle disease (spares midshaft)
(5) van Buchem syndrome (only diaphyses > age 20, no long-bone bowing)
(6) Engelmann syndrome (lower limbs)

HEREDITARY MULTIPLE DIAPHYSEAL SCLEROSIS

= RIBBING DISEASE
= autosomal recessive disorder of intramembranous ossification similar to progressive diaphyseal dysplasia
Age: after puberty, typically in middle-aged adults
• mild neuromuscular symptoms
Location: typically tibia / femur

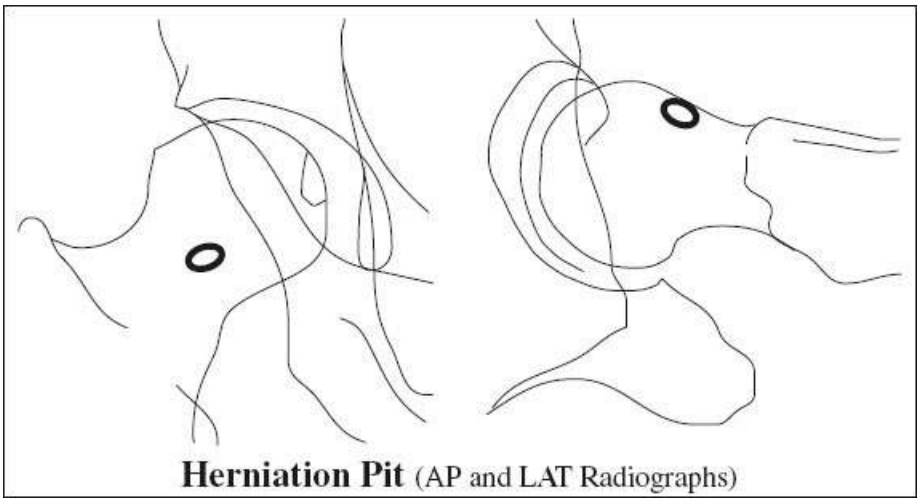
Site: diaphyseal portion of long bones only
Distribution: either unilateral / asymmetric + asynchronous bilateral involvement of long bones
√ cortical thickening of periosteal + endosteal surfaces
√ epiphyses characteristically spared
√ ± narrowing of medullary canal
√ disease may progress slowly and then stabilize
DDx: progressive diaphyseal dysplasia (begins in childhood, severe neuromuscular symptoms, symmetric bilateral sclerosis of long bones, skull involved)

HEREDITARY SPHEROCYTOSIS

= autosomal dominant congenital hemolytic anemia
Age: anemia begins in early infancy to late adulthood
• rarely severe anemia; jaundice; spherocytes in peripheral smear
√ bone changes rare (← mild anemia); long bones rarely affected
√ widening of diploe with displacement + thinning of outer table
√ hair-on-end appearance
Rx: splenectomy corrects anemia even though spherocytemia persists
√ improvement in skeletal changes following splenectomy

HERNIATION PIT

= SYNOVIAL HERNIATION PIT = CONVERSION DEFECT
= ingrowth of fibrous + cartilaginous elements from adjacent joint through perforation in cortex
Histo: fibroalveolar tissue
Age: usually in older individuals
• may be symptomatic; no clinical significance
Location: anterior superolateral aspect of proximal femoral neck; uni- or bilateral
Site: subcortical
Size: usually < 1 cm in diameter; may enlarge over time
√ well-circumscribed round lucency
√ reactive thin sclerotic border
√ hyperintense area on T2WI (= fluid signal intensity)
√ bone scan may be positive



Herniation Pit (AP and LAT Radiographs)

HIBERNOMA

[hibernus, *Latin* = winter]

= rare benign slow-growing soft-tissue tumor composed of brown fat arising in regions in which vestiges of fetal brown fat persist

Histo: admixture of multivacuolar adipocytes (containing multiple granular fine cytoplasmatic vacuoles) + brown fat cells interspersed with univacuolar adipocytes

Age: 20–40 years: M < F

Location: thigh, buttock, scapular region, trunk, neck, mediastinum, chest wall, perirenal, breast, scalp, periureteric region

• painless firm slow-growing mass

• warm overlying skin ← metabolic mitochondrial activity with relatively increased vascularity

Mean size: 9.4 (range, 1–24) cm

√ well-demarcated mass with attenuation and signal intensity between that of subcutaneous fat and muscle

√ varying degrees of internal contrast enhancement

√ no calcifications

US:

√ echogenic mass with well- / ill-defined border

√ increased flow in large surface vessels

CT:

√ well-defined hypoattenuating lesion with intratumoral septa

√ enhancement of septa ± entire mass

MR:

√ usually slightly hypointense relative to subcutaneous fat on T1WI

√ variable intensity on T2WI

√ hyperintense to subcutaneous fat on STIR

√ variable contrast enhancement of septations

√ rarely isointense to subcutaneous fat on all sequences (if multivacuolated adipocytes constitute < 70% of mass)

PET:

√ very high standardized uptake values (SUV): 1.9 – 26.7

HOLT-ORAM SYNDROME

Autosomal dominant; M < F

Associated with CHD: secundum type ASD (most common), VSD, persistent left SVC, tetralogy, CoA

- intermittent cardiac arrhythmia; bradycardia (50–60/min)

Location: upper extremity only involved; symmetry of lesions is the rule; left side may be more severely affected

√ aplasia / hypoplasia of radial structures: thumb, 1st metacarpal, carpal bones, radius
√ absent / "fingerized" hypoplastic / triphalangeal thumb
√ slender elongated hypoplastic carpals + metacarpals
√ hypoplastic radius; absent radial styloid
√ shallow glenoid fossa → voluntary dislocation of shoulder (common)
√ hypoplastic clavicula
√ high arched palate
√ cervical scoliosis
√ pectus excavatum

HOMOCYSTINURIA

Autosomal recessive disorder

Etiology: cystathionine B synthetase deficiency results in defective methionine metabolism with accumulation of homocystine + homocysteine in blood and urine; causes defect in collagen / elastin structure

- thromboembolic phenomena due to stickiness of platelets
- ligamentous laxity
- downward + inward dislocation of lens (DDx: upward + outward dislocation in Marfan syndrome)

Differences between Homocystinuria and Marfan

	Homocystinuria	*Marfan Syndrome*
Inheritance	autosomal recessive	autosomal dominant
Biochemical defect	cystathionine synthetase	not known
Osteoporosis	yes	no
Spine	biconcave vertebrae	scoliosis
Lens dislocation	downward	upward
Arachnodactyly	33%	100%

- mild / moderate mental retardation; malar flush
- crowding of maxillary teeth and protrusion of incisors

√ arachnodactyly in ⅓ (DDx: Marfan syndrome)
√ microcephaly
√ enlarged paranasal sinuses
√ osteoporosis of vertebrae (biconcave / flattened / widened vertebrae)
√ scoliosis

√ pectus excavatum / carinatum (75%)
√ osteoporosis of long bones (75%) with bowing + fracture
√ children: metaphyseal cupping (50%); enlargement of ossification centers in 50% (knee, carpal bones); epiphyseal calcifications (esp. in wrist, resembling phenylketonuria); delayed ossification
√ Harris lines = multiple growth lines
√ genu valgum, coxa valga, coxa magna, pes cavus
√ premature vascular calcifications

Prognosis: death from occlusive vascular disease / minor vascular trauma

HYPEROSTOSIS CORTICALIS GENERALISATA

= GENERALIZED CORTICAL HYPEROSTOSIS = ENDOSTEAL HYPEROSTOSIS
= extremely uncommon homozygous disorder of intramembranous ossification part of craniotubular hyperostoses; may be related to hyperphosphatasemia

Classification:

(1) **Van Buchem disease** (autosomal recessive)
[Franciscus Stephanus Petrus (Frans) van Buchem (1897–1979), Dutch internist]
• facial nerve palsy

(2) Truswell-Hansen disease = sclerosteosis (autosomal recessive)
• progressive facial nerve palsy
• syndactyly of 2nd + 3rd digits with nail dysplasia, tall stature

(3) Worth disease (autosomal dominant)
• flattened forehead
• elongated mandible, decreased gonial angle

(4) Nakamura disease (autosomal dominant)
• enlargement of mandible + maxilla with sparing of mandibular rami

Genetics: mutations in Wnt signaling pathway of osteoblasts on chromosome 17q12-q21 → inhibition of formation of a complex composed of 4 proteins (axin, adenomatous polyposis coli, glycogen synthase kinase 3, b-catenin) → proliferation and differentiation of osteoblasts → increased bone formation

• facial distortion; paralysis of facial nerve
• recurring headaches + dizziness ← reduced intracranial space + increased intracranial pressure
• auditory + ocular disturbances (in late teens ← foraminal encroachment)
• increased alkaline phosphatase (in 50%)

Location: skull, mandible, clavicles, ribs, long-bone diaphyses

@ Long bones
√ symmetrical dense homogeneous endosteal cortical thickening of diaphyses of long bones
√ narrowed medullary canals

@ Skull
√ thickening of skull, facial bones, mandible
√ obliteration of diploe

@ Spine
√ increased density of the axial skeleton

√ spinous processes thickened + sclerotic

MR:

√ herniation of cerebellar tonsils

√ subtotal depletion of subarachnoid space

√ distention of subarachnoid space along optic nerve sheaths

DDx: (1) Osteopetrosis (sclerosis of all bones, not confined to diaphyses)

(2) Generalized hyperostosis with pachydermia (involves entire long bones, considerable pain, skin changes)

(3) Hyperphosphatasia (infancy, widened bones but decreased cortical density)

(4) Camurati-Engelmann disease (rarely generalized, involves lower limbs)

(5) Pyle disease (does not involve middiaphyses)

(6) Polyostotic fibrous dysplasia (rarely symmetrically generalized, paranasal sinuses abnormal, skull involvement)

HYPERPARATHYROIDISM

= uncontrolled production of parathyroid hormone

Age: 3rd–5th decade; M÷F = 1÷3

Histo: decreased bone mass ← increased number of osteoclasts + increased osteoid volume (defect in mineralization) + slightly increased number of osteoblasts

- increase in parathyroid hormone (100%)
- increase in serum alkaline phosphatase (50%)
- elevation of serum calcium ← accelerated bone turnover and ↑ calcium absorption + ↓ in serum phosphate (30%)
- hypotonicity of muscles, weakness, constipation, difficulty in swallowing, duodenal / gastric peptic ulcer disease ← hypercalcemia
- polyuria, polydipsia (hypercalciuria + hyperphosphaturia)
- renal colic + renal insufficiency (nephrocalculosis + nephrocalcinosis)
- rheumatic bone pain + tenderness (particularly at site of brown tumor → pathologic fracture)

A. BONE RESORPTION

(a) subperiosteal (most constant + specific finding; virtually PATHOGNOMONIC of hyperparathyroidism):

√ lacelike irregularity of cortical margin; may progress to scalloping / spiculation (pseudoperiostitis)

Site: phalangeal tufts (earliest involvement), radial aspect of middle phalanx of 2nd + 3rd finger beginning in proximal metaphyseal region (early involvement), bandlike zone of resorption in middle / base of terminal tuft, distal end of clavicles, medial tibia plateau, medial humeral neck, medial femoral neck, distal ulna, superior + inferior margins of ribs in midclavicular line, lamina dura of skull and teeth

DDx: acroosteolysis

(b) subchondral:

√ pseudowidening of joint space

√ collapse of cortical bone + overlying cartilage with development of erosion, cyst, joint narrowing (similar to rheumatoid arthritis)

Site: DIP joint (most commonly 4th + 5th digit), MCP joint, PIP joint, distal clavicle, acromioclavicular joint (clavicular side), "pseudowidening" of sacroiliac joint (iliac side), sternoclavicular joint, temporomandibular joint, symphysis pubis, "scalloping" of posterior surface of patella, Schmorl nodes; typically polyarticular

(c) cortical (← osteoclastic activity within haversian canal):
- √ intracortical tunneling
- √ scalloping along inner cortical surface (= endosteal resorption)

(d) trabecular:
- √ spotty deossification with indistinct + coarse trabecular pattern
- √ granular salt and pepper skull
- √ loss of distinction between inner and outer table
- √ ground-glass appearance

(e) subligamentous / subtendinous:
- √ bone resorption with smooth scalloped / irregular ill-defined margins

Site: inferior surface of calcaneus (long plantar tendons + aponeurosis), Achilles tendon, inferior aspect of distal clavicle (coracoclavicular ligament), greater trochanter (hip abductors), lesser trochanter (iliopsoas), anterior inferior iliac spine (rectus femoris), humeral tuberosity (rotator cuff), ischial tuberosity (hamstrings), proximal extensor surface of ulna (anconeus), posterior olecranon (triceps)

B. BONE SOFTENING
- √ basilar impression of skull
- √ wedged vertebrae, kyphoscoliosis, biconcave vertebral deformities
- √ bowing of long bones
- √ slipped capital femoral epiphysis

C. BROWN TUMOR

= OSTEOCLASTOMA = CENTRAL GIANT CELL LESION

= focal osteolytic area with bone swelling

Cause: PTH-stimulated osteoclastic activity (more frequent in 1° HPT; in 1.5% of 2° HPT)

Path: localized replacement of bone by hypervascularized reactive fibrous stroma containing proliferating osteoclasts, osteoblasts and multinucleated giant cells; may become cystic following hemorrhage + necrosis + liquefaction (= osteitis fibrosa cystica)

Histo: differentiation from giant cell tumor not possible

- in patients with long-standing HPT
- hypercalcemia, hypophosphatemia
- elevated levels of parathyroid hormone

Location: rib, metaphysis of long bones (femur), facial bones, jaw, pelvis, axial skeleton

Site: often eccentric / cortical; frequently solitary

- √ expansile lytic cystlike lesion with variably defined margin (DDx: giant cell tumor)
- √ cortical expansion + endosteal scalloping
- √ generalized demineralization of medullary bones of jaw
- √ loss of lamina dura around roots of teeth
- √ no adjacent reactive bone formation

√ destruction of midportions of distal phalanges with telescoping
√ osteolytic vertebra + tumor growth within spinal canal
√ remineralization after parathyroidectomy

D. OSTEOSCLEROSIS

More frequent in 2° HPT

Cause: ? PTH-stimulated osteoblastic activity, ? role of calcitonin (poorly understood)

Site: strong predilection for axial skeleton, pelvis, ribs, clavicles, metaphysis + epiphysis of appendicular skeleton

√ "rugger jersey spine"

E. SOFT-TISSUE CALCIFICATION

More frequent in 2° HPT

• metastatic calcification when Ca x P product > 70 mg/dL

(a) cornea, viscera (lung, stomach, kidney)
(b) periarticular in hip, knee, shoulder, wrist
(c) arterial tunica media (resembling diabetes mellitus)
(d) chondrocalcinosis (15–18%) = calcification of hyaline / fibrous cartilage in menisci, wrist, shoulder, hip, elbow
(e) bilateral basal ganglia, dentate nuclei, peripheral subcortical white matter

Calciphylaxis = calcific uremic arteriolopathy
= systemic medial calcification of arterioles
• subcutaneous necrosis ← ischemia
• ± chronic hemodialysis / recent renal transplantation
√ calcium deposits in kidney, stomach, heart, lung

Prognosis: high mortality

F. EROSIVE ARTHROPATHY

• asymptomatic
√ simulates rheumatoid arthritis with preserved joint spaces

G. PERIOSTEAL NEW-BONE FORMATION

Cause: PTH-stimulation of osteoblasts

Site: pubic ramus along iliopectineal line (most frequent), humerus, femur, tibia, radius, ulna, metacarpals, metatarsals, phalanges

√ linear new bone paralleling cortical surface; may be laminated; often separated from cortex by radiolucent zone
√ increase in cortical thickness (if periosteal reaction becomes incorporated into adjacent bone)

Sequelae:

1. Renal stones / nephrocalcinosis (70%)
2. Increased osteoblastic activity (25%)
   • increased alkaline phosphatase
   (a) osteitis fibrosa cystica
      √ subperiosteal bone resorption + cortical tunneling
      √ brown tumors (primary HPT)
   (b) bone softening
      √ fractures
3. Peptic ulcer disease ← increased gastric secretion from gastrinoma

4. Calcific pancreatitis
5. Soft-tissue calcifications (2° HPT)
6. Marginal joint erosions + subarticular collapse (DIP, PIP, MCP)

Primary Hyperparathyroidism

= pHPT = 1° HPT = hypercalcemia due to autonomous hypersecretion of parathormone by one / more hyperfunctioning parathyroid glands featuring
(1) brown tumor
(2) chondrocalcinosis (20–30%)

◊ requires surgical Rx

Prevalence: 2–3 ÷ 1000 (female) and 1 ÷ 1000 (male)

Incidence: 25 ÷ 100,000 per year; 25–40% incidence of bone lesions in HPT

Etiology: sporadic / familial
(1) Parathyroid adenoma (94%): solitary (90%); double adenomas (4%)
(2) Parathyroid hyperplasia of multiple glands(6%): chief cell (4%); clear cell (2%)
◊ Hereditary disorders often involve multiple-gland hyperplasia
(3) Parathyroid carcinoma (< 1%)

Age: 3rd–5th decade; M÷F = 1÷3

Associated with:
(a) Familial hyperparathyroidism
(b) Multiple endocrine neoplasia syndrome
1. Wermer syndrome = MEA 1 (+ pituitary adenoma + pancreatic islet cell tumor)
2. Sipple syndrome = MEA 2A (+ medullary thyroid carcinoma + pheochromocytoma)

(c) Hyperparathyroidism–jaw tumor syndrome

- asymptomatic (75–80%): more common due to earlier detection ← widespread availability of laboratory screening for hypercalcemia
- symptomatic (20–25%):
  - weakness, easy fatigability, mild depression, anorexia
  - dementia, depression, constipation
  - peptic ulcer disease, pancreatitis, renal calculi
  - diffuse bone + joint pain ← osteitis fibrosa cystica

X-RAY (skeletal involvement in 10–20%):
√ generalized osteopenia
√ thin cortices with lacy cortical pattern ← subperiosteal bone resorption
√ brown tumor (particularly in jaw + long bones)
√ osteitis cystica fibrosa (= intertrabecular fibrous connective tissue)

NUC:
√ bone scan: normal in 80%
√ foci of abnormal uptake: calvarium (especially periphery), mandible, sternum, acromioclavicular joint, lateral humeral epicondyles, hands
√ increased uptake in brown tumors
√ extraskeletal uptake: cornea, cartilage, joint capsules, tendons, periarticular areas, lungs, stomach
√ normal renal excretion [except in stone disease / calcium nephropathy (10%)]
√ ^{99m}Tc-sestamibi parathyroid scintigraphy

Rx: pathologic glands identified by experienced surgeons in 90–95% on initial neck exploration (ectopic + supernumerary glands often overlooked at operation; recurrent hypercalcemia in 3–10%)

Indications for surgery:

(1) serum calcium level 1.0 mg/dL above upper limit of normal
(2) 24-hour urinary calcium level > 400 mg
(3) creatinine clearance reduced by 30%
(4) bone mineral density T-score of < −2.5 SD
(5) age < 50 years
(6) undesirability / impossibility of surveillance

Surgical risk for repeat surgery:

6.6% recurrent laryngeal nerve injury
20.0% permanent hypoparathyroidism
< 1.0% perioperative mortality

DDx of hypercalcemia:

(1) Malignancy (2nd most common cause): low / suppressed parathyroid hormone levels
(2) Benign familial hypocalciuric hypercalcemia:
= autosomal dominant disorder characterized by hypercalcemia + relative hypocalciuria distinguished by calcium-creatinine clearance ratio < 0.01

Secondary Hyperparathyroidism

= sHPT = 2° HPT = stimulation of all four parathyroid glands as a response to
(1) hypocalcemia → diffuse / adenomatous hyperplasia
(2) apparent insensitivity of parathyroid glands to ↑ serum calcium ← dysregulation of normal negative feedback loop (= pseudohyperparathyroidism)

◊ requires medical Rx

Etiology:

(a) endstage renal disease (most common cause) → decreased renal production of $1,25(OH)_2$-vitamin D
(b) calcium deprivation, hypovitaminosis D, maternal hypoparathyroidism, pregnancy
(c) rise in serum phosphate → decrease in calcium by feedback mechanism

- dementia, depression; peptic ulcer disease, constipation
- diffuse joint pain
- low (hypocalcemia) to normal calcium levels
- phosphate retention (hyperphosphatemia) = $Ca_3(PO_4)_2$ solubility product often exceeded
- vitamin D deficiency = ⇓ vitamin D serum levels → compensatory ⇑ in PTH production

√ soft-tissue calcifications
√ "rugger jersey" spine = striped osteosclerotic appearance
√ periostitis
√ brown tumor

NUC:

√ "superscan" in 2° HPT:
√ "absent kidney" sign
√ increased ratio of bone-to-soft tissue uptake

√ increased uptake in calvarium, mandible, acromioclavicular region, sternum, vertebrae, distal third of long bones, ribs

√ diffuse ^{99m}Tc-MDP uptake in lungs (60%)

Tertiary Hyperparathyroidism

= tHPT = 3° HPT = development of autonomously functioning parathyroid glands despite correction of initial cause → hypersecretion of PTH in spite of normal calcium levels in patients with chronically overstimulated hyperplastic parathyroid glands

Cause: secondary HPT ← renal insufficiency + renal dialysis with prolonged hypocalcemia and hyperphosphatemia

◊ requires surgical Rx

Clue: (a) intractable hypercalcemia

(b) inability to control osteomalacia by vitamin D administration

Ectopic Parathormone Production

= pseudohyperparathyroidism as paraneoplastic syndrome in bronchogenic carcinoma + renal cell carcinoma

HYPERTROPHIC OSTEOARTHROPATHY

= HYPERTROPHIC PULMONARY OSTEOARTHROPATHY (HPO) = MARIE-BAMBERGER DISEASE

= paraneoplastic syndrome

Etiology:

(1) Release of vasodilators which are not metabolized by lung
(2) Increased flow through AV shunts
(3) Reflex peripheral vasodilation (vagal impulses)
(4) Hormones: estrogen, growth hormone, prostaglandin

Histo: round cell infiltration of the outer fibrous layer of periosteum followed by new bone proliferation

A. THORACIC CAUSES

(a) malignant tumor (0.7–12%): bronchogenic carcinoma (88%), mesothelioma, lymphoma, pulmonary metastasis from osteogenic sarcoma, melanoma, renal cell carcinoma, breast cancer

◊ 4–17% of patients with bronchogenic carcinoma may develop HPO!

(b) benign tumor: benign pleural fibroma, tumor of ribs, thymoma, esophageal leiomyoma, pulmonary hemangioma, pulmonary congenital cyst

(c) chronic infection / inflammation: pulmonary abscess, bronchiectasis, blastomycosis, TB (very rare); cystic fibrosis, interstitial fibrosis

(d) cyanotic congenital heart disease with R-to-L shunt

B. EXTRATHORACIC CAUSES (less common)

(a) GI tract: ulcerative colitis, amebic + bacillary dysentery, intestinal TB, Whipple disease, Crohn disease, gastric ulcer, bowel lymphoma, gastric carcinoma

(b) liver disease: biliary + alcoholic cirrhosis, posthepatic cirrhosis, chronic active hepatitis, bile duct carcinoma, benign bile duct stricture, amyloidosis, liver abscess

(c) undifferentiated nasopharyngeal carcinoma, pancreatic carcinoma, chronic myelogenous leukemia

- burning pain, painful swelling of limbs, and stiffness of joints: ankles (88%), wrists (83%), knees (75%), elbows (17%), shoulders (10%), fingers (7%)
- peripheral neurovascular disorders: local cyanosis, areas of increased sweating, paresthesia, chronic erythema, flushing + blanching of skin
- hippocratic fingers + toes (clubbing)
- hypertrophy of extremities (soft-tissue swelling)

Location: tibia + fibula (75%), radius + ulna (80%), proximal phalanges (60%), femur (50%), metacarpus and metatarsus (40%), humerus + distal phalanges (25%), pelvis (5%); unilateral (rare)
◊ Spine, pelvis, ribs usually spared!

Site: in diametaphyseal regions

√ cortical thickening

√ lamellar periosteal proliferation of new bone, at first smooth then undulating + rough
Site: most conspicuous on concavity of long bones (dorsal + medial aspects)

√ soft-tissue swelling ("clubbing") of distal phalanges

Bone scan (reveals changes early with greater sensitivity + clarity):
√ "parallel track" / "double stripe" / "tramline" sign = patchy linear diffusely increased symmetric uptake along cortical margins of metaphysis + diaphysis of tubular bones ← periostitis
√ increased periarticular uptake ← synovitis
√ scapular involvement in $^{2}/_{3}$
√ mandible ± maxilla abnormal in 40%

Prognosis: treatment of underlying condition leads to remission of symptoms often within 24 hours + regression of radiographic findings in months

DDx: (1) Pachydermoperiostosis (self-limited, adolescence, autosomal dominant, M > F)
(2) Metastases (axial skeleton, focal asymmetric distribution)
(3) Chronic vascular insufficiency
(4) Thyroid acropachy
(5) Hypervitaminosis A

Differences between 1° and 2° HPT

Skeletal Findings	*1° HPT*	*2° HPT*
Osteopenia, diffuse	present	present
Osteosclerosis, regional / diffuse	rare	common
Bone resorption	common	common
Brown tumor	common	less common
Soft-tissue calcification	not infrequent	common
Chondrocalcinosis	not infrequent	rare

HYPERVITAMINOSIS A

Age: usually infants + children

Cause: overdosing vitamin A, 13-cis-retinoic acid (treatment for neuroblastoma)

- anorexia, irritability; jaundice, enlargement of liver
- loss of hair, dry skin, pruritus, fissures of lips

√ separation of cranial sutures (coronal > lambdoid) ← hydrocephalus in children < 10 years of age, may appear within a few days

√ symmetrical solid periosteal new-bone formation along shafts of long + short bones (ulna, clavicle)

√ premature epiphyseal closure + thinning of epiphyseal plates

√ accelerated growth

√ tendinous, ligamentous, pericapsular calcifications

√ changes usually disappear after cessation of vitamin A ingestion

DDx: infantile cortical hyperostosis (mandible involved)

HYPERVITAMINOSIS D

= excessive ingestion of vitamin D (large doses act like parathormone)

- loss of appetite, diarrhea, drowsiness, headaches
- polyuria, polydipsia, renal damage; convulsions
- excessive phosphaturia (parathormone decreases tubular absorption); hypercalcemia + hypercalciuria; anemia

√ deossification

√ widening of provisional zone of calcification

√ cortical + trabecular thickening

√ alternating bands of increased + decreased density near / in epiphysis (zone of provisional calcification)

√ vertebra outlined by dense band of bone + adjacent radiolucent line within

√ dense calvarium

√ metastatic calcinosis in

(a) arterial walls (between age 20 and 30 years)
(b) kidneys = nephrocalcinosis
(c) periarticular tissue (puttylike)
(d) premature calcification of falx cerebri (most consistent sign!)

HYPOPARATHYROIDISM

- tetany = hypocalcemic neuromuscular excitability (numbness, cramps, carpopedal spasm, laryngeal stridor, generalized convulsions)
- hypocalcemia + hyperphosphatemia
- normal / low serum alkaline phosphatase

√ premature closure of epiphyses

√ hypoplasia of tooth enamel + dentine; blunting of roots

√ generalized increase in bone density in 9%:

√ localized thickening of skull

√ sacroiliac sclerosis
√ bandlike density in metaphysis of long bones (25%), iliac crest, vertebral bodies
√ thickened lamina dura (inner table) + widened diploe
√ deformed hips with thickening + sclerosis of femoral head + acetabulum
@ Soft tissue
√ intracranial calcifications in basal ganglia, choroid plexus, occasionally in cerebellum
√ calcification of spinal and other ligaments
√ subcutaneous calcifications
√ ossification of muscle insertions
√ ectopic bone formation

Differences between Various Types of Hypoparathyroidism

	HypoPT	*Pseudo HypoPT*	*Pseudopseudo HypoPT*
Serum Ca	↓	↓	↔
Serum P	↑	↑	↔
AlkaPhos	↓ or ↔	↓ or ↔	↔
Response to PTH-Injection			
Urine cAMP	↑	↔	
Urine P	↑	↔	
Plasma AMP	↑	↔	

Differential Signs between PHypoPT and PPHypoPT

Radiographic Signs	*PHypoPT*	*PPHypoPT*
√ calcification of basal ganglia	44%	8%
√ soft-tissue calcifications	55%	40%
√ metacarpal shortening (4 + 5 always involved)	75%	90%
√ metatarsal shortening (3 + 4 involved)	70%	99%

Idiopathic Hypoparathyroidism

= rare condition of unknown cause
• round face, short dwarflike, obese; mental retardation
• cataracts; dry scaly skin, atrophy of nails
• dental hypoplasia (delayed tooth eruption, impaction of teeth, supernumerary teeth)

Secondary Hypoparathyroidism

= accidental removal / damage to parathyroid glands in thyroid surgery / radical neck dissection (5%); ^{131}I therapy (rare); external beam radiation; hemorrhage; infection; thyroid carcinoma; hemochromatosis (iron deposition)

Pseudohypoparathyroidism

= PHypoPT = congenital X-linked dominant abnormality with renal + skeletal resistance to

PTH due to
(1) Endorgan resistance
(2) Presence of antienzymes
(3) Defective hormone

May be associated with: hyperparathyroidism ← hypocalcemia; F > M

- short obese stature, round face, mental retardation
- abnormal dentition (hypoplasia, delayed eruption, excessive caries); corneal + lenticular opacity
- hypocalcemia + hyperphosphatemia (resistant to PTH injection); normal levels of PTH

√ brachydactyly in bones in which epiphysis appears latest: metacarpal, metatarsal bones I, IV, V (75%)
√ accelerated epiphyseal maturation resulting in dwarfism + coxa vara / valga
√ multiple diaphyseal exostoses (occasionally)
√ calcification of basal ganglia + dentate nucleus
√ calcification / ossification of skin + subcutaneous tissue

Pseudopseudohypoparathyroidism

= PPHypoPT = different expression of same familial disturbance with identical clinical + radiographic features as pseudohypoparathyroidism but normocalcemic

Cause: end-organ resistance to PTH

- short stature, round facies
- NO blood chemical changes = normal calcium + phosphorus
- normal response to injection of PTH

√ brachydactyly

HYPOPHOSPHATASIA

= autosomal recessive congenital disease with low activity of serum-, bone-, liver-alkaline phosphatase resulting in poor mineralization (= deficient generation of bone crystals)

Prevalence: 1÷100,000

Histo: indistinguishable from rickets

- phosphoethanolamine in urine as precursor of alkaline phosphatase; normal serum calcium + phosphorus

A. GROUP I = neonatal = congenital lethal form
√ marked demineralization of calvarium ("caput membranaceum" = soft skull)
√ lack of calcification of metaphyseal end of long bones
√ streaky irregular spotty margins of calcification
√ cupping of metaphysis
√ angulated shaft fractures with abundant callus formation
√ short poorly ossified ribs
√ poorly ossified vertebrae (especially neural arches)
√ small pelvic bones
OB-US:
√ high incidence of intrauterine fetal demise
√ increased echogenicity of falx (enhanced sound transmission ← poorly mineralized calvarium)

√ poorly mineralized short bowed tubular bones + multiple fractures
√ poorly mineralized spine
√ short poorly ossified ribs
√ polyhydramnios

Prognosis: death within 6 months

B. GROUP II = juvenile severe form
onset of symptoms within weeks to months
• moderate / severe dwarfism
• delayed weight bearing
√ resembles rickets
√ separated cranial sutures; craniostenosis in 2nd year

Prognosis: 50% mortality

C. GROUP III = adult mild form
recognized later in childhood / adolescence / adulthood
• dwarfism
√ clubfoot, genu valgum
√ demineralization of ossification centers (at birth / 3–4 months of age):
√ widened metaphyses
√ wormian bones

Prognosis: excellent; after 1 year no further progression

D. GROUP IV = latent form of heterozygous state
• normal / borderline levels of alkaline phosphatase
• patients are small for age
• disturbance of primary dentition
√ bone fragility + healed fractures
√ enlarged chondral ends of ribs
√ metaphyseal notching of long bones
√ Erlenmeyer flask deformity of femur

HYPOTHYROIDISM

Hypothyroidism during Childhood = Cretinism

Frequency: 1÷4,000 live births have congenital hypothyroidism

Cause: sporadic hypoplasia / ectopia of thyroid

√ delayed skeletal maturation (= delayed appearance + growth of ossification centers, delayed epiphyseal closure)
√ fragmented stippled epiphyses
√ wide sutures / fontanels with delayed closure
√ delayed dentition
√ delayed / decreased pneumatization of sinuses + mastoids
√ hypertelorism
√ dense vertebral margins
√ demineralization
√ hypoplastic phalanges of 5th finger

MR:

√ reduced myelination of brain (usually beginning during midgestation)

OB-US:

√ fetal goiter (especially in hyperthyroid mothers treated with methimazole / propylthiouracil / ^{131}I)

Hypothyroidism during Adulthood

√ calvarial thickening / sclerosis
√ wedging of dorsolumbar vertebral bodies
√ coxa vara with flattened femoral head
√ premature atherosclerosis
◊ No skeletal changes with adult onset!

INFANTILE CORTICAL HYPEROSTOSIS

= CAFFEY DISEASE
= uncommon self-limiting proliferative bone disease of infancy; remission + exacerbations are common

[John Patrick Caffey (1895–1978), pediatrician and professor of radiology at Columbia University, New York]

Cause: ? infectious; ? autosomal dominant with variable expression + incomplete penetrance / sporadic occurrence (rare)

Age: < 6 months, reported in utero; M÷F = 1÷1

Histo: inflammation of periosteal membrane, proliferation of osteoblasts + connective tissue cells, deposition of immature bony trabeculae

• sudden, hard, extremely tender soft-tissue swellings over bone
• irritability, fever; leukocytosis, anemia
• ± elevated ESR, increased alkaline phosphatase

Location: mandible (80%) > clavicle > ulna + others (except phalanges + vertebrae + round bones of wrists and ankles)

Site: hyperostosis affects diaphysis of tubular bones asymmetrically, epiphyses spared

√ massive periosteal new-bone formation + perifocal soft-tissue swelling
√ "double-exposed" ribs
√ narrowing of medullary space (= proliferation of endosteum)
√ bone expansion with remodeling of old cortex

Prognosis: usually complete recovery by 30 months

Rx: mild analgesics, steroids

Chronic Infantile Hyperostosis

• disease may persist or recur intermittently for years
• delayed muscular development, crippling deformities
√ bowing deformities, osseous bridging, diaphyseal expansion

DDx: (1) Hypervitaminosis A (rarely < 1 year of age)
(2) Periostitis of prematurity
(3) Healing rickets
(4) Scurvy (uncommon < 4 months of age)

(5) Syphilis (focal destruction)
(6) Child abuse
(7) Prostaglandin administration (usually following 4–6 weeks of therapy)
(8) Osteomyelitis
(9) Leukemia
(10) Neuroblastoma
(11) Kinky hair syndrome
(12) Hereditary hyperphosphatasia

INFECTIOUS MYOSITIS

= acute / subacute / chronic infection of skeletal muscle

Organism: viruses, bacteria (including mycobacteria), fungi, parasites; S. aureus (77%)

Pyomyositis / Bacterial Myositis

Risk factors: underlying HIV infection (17%), strenuous activity, rhabdomyolysis, muscle trauma (hematoma as nidus for infection)

Others: skin infection, infected insect bite, injection of illicit drug, underlying diabetes mellitus

Location: usually single muscle; multiple in 11–43%; quadriceps m. > gluteal m. > iliopsoas m. > upper extremity

Iliopsoas abscess: TB of spine (formerly), GI / GU infection (currently)

Stages:

(a) invasive: muscle edema → pain
(b) suppurative: fever → abscess
(c) late stage: toxicity → life-threatening sepsis

CT:

√ enlarged hypoattenuating muscle
√ effacement of surrounding fat planes
√ intramuscular fluid collection
√ nonenhancement of necrotic tissue
√ rim-enhancement of abscess

Cx: (1) Compartment syndrome
(2) Osteomyelitis
(3) Septic arthritis
(4) Muscle scarring, weakness, dysfunction

DDx: cellulitis (involvement of SQ tissue > muscle group)

INTRAMEDULLARY OSTEOSCLEROSIS

= rare condition increased bone formation within medullary cavity of long bones of lower extremity similar to progressive diaphyseal dysplasia / hereditary multiple diaphyseal sclerosis

Age: adulthood; F > M

• chronic leg pain that increases with physical activity

Location: uni- / bilateral in ≥ 1 long bone of lower extremity; most frequently in tibia
Site: middiaphyseal region
√ osteosclerosis limited to medullary cavity with minimal / no cortical thickening
Dx: after exclusion of other causes of osteosclerosis (eg, stress fractures, osteomyelitis, metabolic / endocrine disorders, malignancy)

IRON DEFICIENCY ANEMIA

Age: infant
Cause:
(1) inadequate iron stores at birth
(2) deficient iron in diet
(3) impaired gastrointestinal absorption of iron
(4) excessive iron demands from blood loss
(5) polycythemia vera
(6) cyanotic CHD
√ widening of diploe + thinning of tables with sparing of occiput (no red marrow)
√ hair-on-end appearance of skull
√ osteoporosis in long bones (most prominent in hands)
√ absence of facial bone involvement

JACCOUD ARTHROPATHY

[Sigismond Jaccoud (1830–1913), Swiss physician and professor of internal pathology at several hospitals in Paris]
= irreversible nonerosive deforming arthropathy after subsidence of frequent severe attacks of rheumatic fever / SLE
◊ Rheumatoid arthritis + SLE may occur simultaneously!
Path: pericapsular soft-tissue edema (= synovitis around small joints); periarticular fascial + tendon fibrosis
• rheumatic valve disease
Location: primarily involvement of hands; occasionally in great toe
√ periarticular swelling of small joints of hands + feet
√ ulnar deviation + flexion of MCP joints most marked in 4th + 5th finger
√ > 3 mm distance between scaphoid and lunate / other carpal bones = **carpal instability** (in 15% of SLE)
√ swan neck + boutonniere deformity
√ NO joint narrowing / erosion
√ juxtaarticular osteoporosis
√ muscular atrophy

JUVENILE XANTHOGRANULOMA

= relatively benign non-LCH dendritic cell disorder of early childhood
Age: < 1 year (majority)
@ Skin
• small yellow-reddish papule / plaque / nodule (early) with usually spontaneous

regression within a few years
Location: head, neck, upper trunk
@ Soft tissue
Location: subcutaneous to deep
√ heterogeneously hypoechoic hypovascular nodule
√ infiltrative nonenhancing mass of intermediate T1 signal
@ Bone
√ well-defined medullary lytic lesion with sclerotic margins
@ Liver, spleen, lung, bones, lymph nodes, GI tract
Dx: based on typical dermal findings

KELOID

= benign fibroblastic proliferation arising from dermis
Age: 15–45 years
Predisposed: persons of African / Chinese descent
Associated with: trauma, infection, connective tissue disease (at sites of increased skin tension)
Histo: hypocellular densely collagenous lesions
Location: face, shoulder, forearm, hand
• mass effect, pruritus, paresthesia, cosmetic deformity
MR:
√ short T2 relaxation
Rx: surgical excision combined with surgical injection of corticosteroids / postsurgical radiation therapy

KERATOACANTHOMA

[*acantha*, Greek =thorn, sharp spiny structure]
= rare benign neoplasm characterized by localized proliferation of squamous epithelium and central keratinized crater
Cause: exposure to sunlight, coal tar, other chemical carcinogens, trauma, immunocompromised state, vaccination, arterial puncture, burns
Path: keratin fills a central tumor crater; surrounding overhanging edges of normal epidermis
Histo: marked acanthosis (= diffuse thickening of stratum spinosum) + hyperkeratosis; proliferation of large squamous cells with glassy cytoplasm
Maybe associated with: eczema, psoriasis, atopic dermatitis, xeroderma pigmentosum
Peak age: 5th decade; M > F
• painful
√ crescent-shaped soft-tissue mass
√ osteolytic defect of underlying bone ← pressure erosion
√ no periosteal reaction / bone sclerosis
MR:
√ intermediate SI on T1WI + mixed SI on T2WI
√ thin peripheral rim enhancement
Prognosis: spontaneous involution within 12 months leaving a small pitted scar
Cx: malignant transformation to squamous cell carcinoma

Subungual Keratoacanthoma

= rare usually painful destructive variant of keratoacanthoma

• rapidly growing painful mass beneath nail

Location: nail bed

US:

√ well-circumscribed mass of mixed echogenicity

√ posterior acoustic enhancement + cortical erosion

Prognosis: spontaneous involution uncommon

DDx: squamous cell carcinoma (radiologically indistinguishable, older patient, slow growing, histologically aggressive, ulceration, numerous mitoses, marked pleomorphism, anaplasia)

KLINEFELTER SYNDROME

[Harry Fitch Klinefelter, Jr. (1912–1990), American rheumatologist and endocrinologist at Johns Hopkins Medical School]

47,XXY (rarely XXYY) chromosomal abnormality

Frequency: 1÷750 live births (probably commonest chromosomal aberration)

• testicular atrophy (hyalinization of seminiferous tubules) = small / absent testes, sterility (azoospermia)

• eunuchoid constitution: gynecomastia; paucity of hair on face + chest; female pubic escutcheon; mild mental retardation

• high level of urinary gonadotropins + low level of 17-ketosteroids after puberty

◊ NO distinctive radiological findings!

√ may have delayed bone maturation

√ failure of frontal sinus to develop

√ small bridged sella turcica

√ ± scoliosis, kyphosis

√ ± coxa valga

√ ± "metacarpal" sign (short 4th metacarpal)

√ accessory epiphyses of 2nd metacarpal bilaterally

Cx: breast cancer (3% risk + 20-fold increase in incidence due to elevated estrogen÷androgen ratio)

47,XXX = Superfemale Syndrome

• usually over 6 feet tall; subnormal intelligence; frequently antisocial behavior

KLIPPEL-TRÉNAUNAY SYNDROME

[Maurice Klippel (1858–1942), neurologist and psychiatrist, general medicine chief at Hôpital Tenon in Paris, France]

[Paul Trénaunay (1875–????), neurologist in Paris, France]

= rare sporadic (nonhereditary) combined capillary-venous malformation of trunk + extremities in association with limb overgrowth characterized by a triad of:

(1) Port-wine nevus = unilateral large flat infiltrative cutaneous capillary malformation often in dermatomal distribution of affected limb; may fade in 2nd–3rd decade

(2) Congenital varicose veins / venous malformation affecting superficial + deep venous system = megaveins on lateral aspect of affected limb; usually ipsilateral to capillary malformation
(a) superficial venous system: ectasia of small veins, persistent embryologic veins, large venous malformations
(b) deep venous system:" aneurysmal dilatation, aplasia, hypoplasia, duplications, venous incompetence
(3) Gigantism = overgrowth of distal digits / entire extremity (especially during adolescent growth spurt) involving soft-tissue + bone (most variable of the 3 classic features)

VARIANT: **Klippel-Trénaunay-Weber syndrome** = associated with (4) arteriovenous fistula

Incidence: > 1,000 cases reported

Pathogenesis:
failure of regression of large caliber superficial lateral venous channel at 6 weeks GA (= fetal lateral limb bud vein) → varicosity → impaired venous return → tissue overgrowth

Age: usually manifest at birth; M÷F = 1÷1

Associated with:
› polydactyly, syndactyly, clinodactyly, oligodactyly, ectrodactyly, congenital dislocation of hip
› vascular malformation of colon, rectum, bladder (1–10%)
› spinal hemangiomas + AVMs
› hemangiomas in liver / spleen
› lymphangiomas of limb

Location: one lower limb in 75–95% (10–15 x more common than upper extremity); bilateral in < 5%; lower limb ± upper limb; extension into trunk may occur

• pain in usually thicker + longer extremity
• spontaneous cutaneous hemorrhage
• chronic venous insufficiency
• cutaneous lymphatic vesicles, lymphorrhea

√ elongation of bones:
√ leg-length discrepancy
√ increased metatarsal / metacarpal + phalangeal size
√ cortical thickening
√ circumferential soft-tissue hypertrophy (at birth / later in life)
√ phleboliths in pelvis (bowel wall, anterior wall of urinary bladder) ← prior hemorrhage / thrombus
√ pulmonary vein varicosities
√ cystic lung lesions

CT / MR:
√ slow uptake of contrast material in visceral vascular malformations during delayed phase

Venogram:
√ extensive dilation of superficial veins
√ enlarged perforating veins
√ aplasia / hypoplasia of lower extremity veins (18–40%): ? selective flow of contrast material up the lateral venous channel may fail to opacify the deep venous system
√ incompetent valveless collateral venous channels (? persistent lateral limb bud vein =

Klippel-Trénaunay vein) arises near the ankle + extends a variable distance up the extremity and drains into deep femoral vein / iliac veins (in > 66%)

Color Doppler US:

√ deep venous malformations of femoral vein (common)

Lymphangiography:

√ hypoplasia of lymphatic system

Cx: stasis dermatitis, thrombophlebitis, cellulitis, deep venous thrombosis, pulmonary embolism, infected lymphangitis ± sepsis, bloody stool, hematuria, epistaxis, Kasabach-Merritt syndrome (= consumptive coagulopathy)

Rx: (1) conservative: application of graded compressive stockings, pneumatic compression devices, percutaneous sclerosis of localized venous malformations / superficial varicosities

(2) surgical: epiphysiodesis, excision of soft-tissue hypertrophy, vein stripping, life-threatening bleeding

DDx: (1) Parkes-Weber syndrome congenital persistence of multiple microscopic AV fistulas + spectrum of Klippel-Trénaunay-Weber syndrome (pulsatility, thrill, bruit)

(2) Neurofibromatosis (café-au-lait spots, axillary freckling, cutaneous neurofibromas, macrodactyly ← plexiform neurofibromas, wavy cortical reaction, early fusion of growth plate, limb hypertrophy not as extensive / bilateral)

(3) Beckwith-Wiedemann syndrome (aniridia, macroglossia, cryptorchidism, Wilms tumor, broad metaphyses, thickened long-bone cortex, advanced bone age, periosteal new-bone formation, hemihypertrophy)

(4) Macrodystrophia lipomatosis (hyperlucency of fat, distal phalanges most commonly affected, overgrowth ceases with puberty, usually limited to digits)

(5) Maffucci syndrome (cavernous hemangiomas, soft tissue hypertrophy, phleboliths, multiple enchondromas)

(6) Cutis marmorata telangiectatica congenita

(7) Servelle-Martorell syndrome

LABRAL TEARS OF SHOULDER

Anterior Labral Tear

Location: anteroinferior labrum > entire anterior labrum > isolated tear of anterosuperior labrum

Subtypes of anteroinferior labral tears:

(1) Bankart lesion

(2) Anterior labroligamentous periosteal sleeve avulsion

(3) Perthes lesion

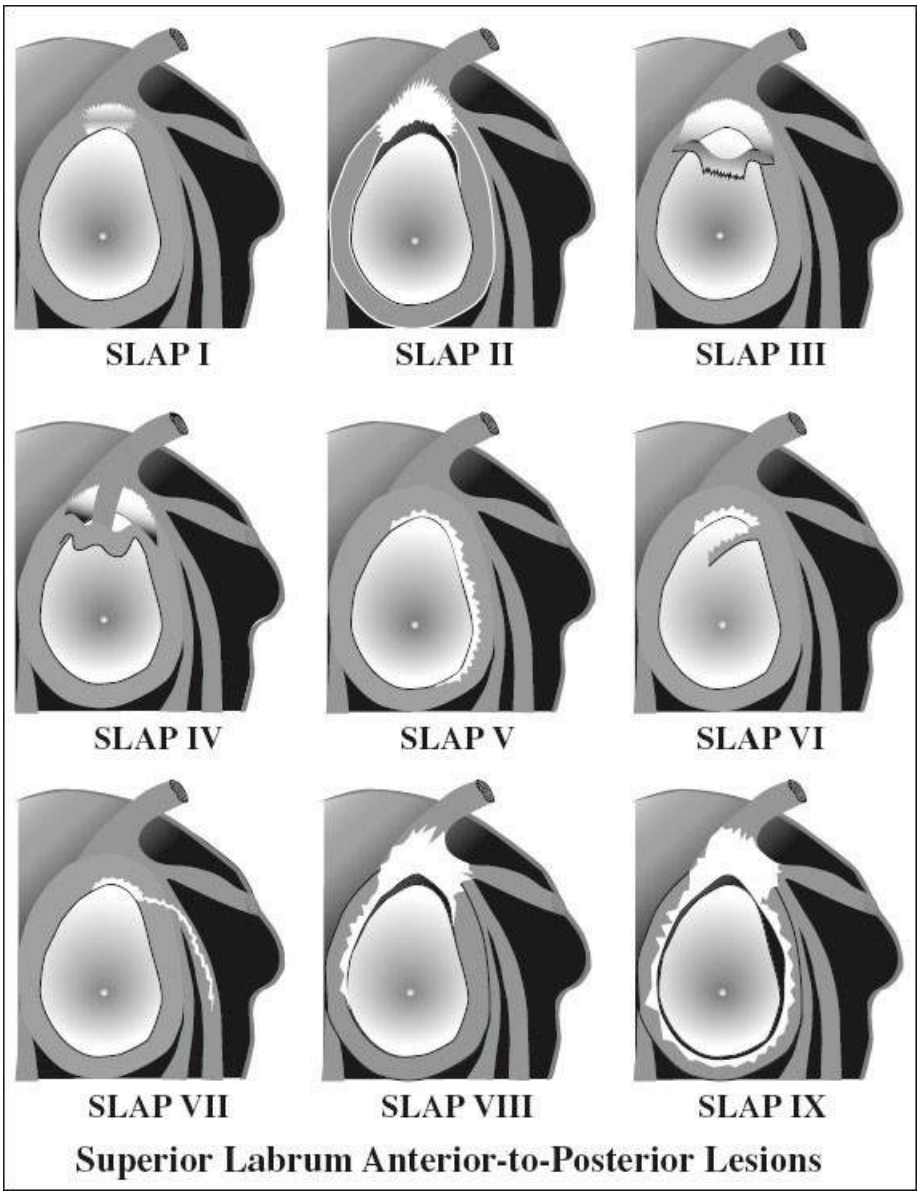
√ absence / detachment of labrum

√ frayed labrum with irregular margin

DDx: (1) Middle + inferior glenohumeral ligaments closely apposed to anterior labrum

(2) Recess between anterior labrum + glenoid rim

(3) Recess between middle + inferior ligaments



SLAP Lesion

= anterior-to-posterior lesion of the superior labrum centered at biceps tendon attachment

Mechanism: fall on an outstretched hand (most common), anterior shoulder dislocation, sports activity with overhead arm motion

- pain, clicking sensation
- after fall on outstretched hand (31%) patient usually presents with SLAP III, IV, V lesion

SLAP I = fraying of free edge of superior labrum; common in elderly as a degenerative tear

SLAP II = detachment of superior biceps-labral complex from glenoid rim

DDx: superior sublabral recess (less distance between labrum + glenoid, no irregular appearance, no lateral extension of defect)

SLAP III = bucket-handle tear of superior labrum leaving biceps tendon attached to

glenoid

SLAP IV = bucket-handle tear of superior labrum with tear extending into biceps tendon

SLAP V = Bankart lesion dissecting upward to involve the biceps tendon

SLAP VI = unstable radial / flap tear with separation of biceps anchor

SLAP VII = superior labral tear extending into middle glenohumeral ligament

SLAP VIII = SLAP II + entire posterior labral tear; anterior inferior labrum not involved

SLAP IX = circumferential labral tear

LANGERHANS CELL HISTIOCYTOSIS

= LCH = HISTIOCYTOSIS X (former name)

[Paul Langerhans (1847–1888), German pathologist, physiologist, and microscopist in Berlin, close friend of Virchow, discoverer of dendritic cells in the skin and islet cells of the pancreas]

= poorly understood group of disorders characterized by abnormal nonmalignant proliferation of monoclonal Langerhans cells within one / multiple organ systems

◊ Leading (most common) dendritic cell disorder apart from

(1) Erdheim-Chester disease
(2) Juvenile xanthogranuloma
(3) Rosai-Dorfman disease
(4) Hemophagocytic lymphohistiocytosis

Histo:

granuloma contains Langerhans cells (= large histiocyte of bone marrow origin), foamy histiocytes, lymphocytes, plasma cells, eosinophils

Langerhans cell:

› dendritic cell found in basal layer of skin + in liver (Kupffer cell), lymph nodes, spleen, bone marrow, lung (detects + phagocytizes pathogenic organisms and presents their surface antigens to T and B lymphocytes)

› contains unique mostly pentalaminar rods / "tennis racket"-shaped cytoplasmatic inclusion bodies known as **Birbeck granules** (identifiable by electron microscopy)

› stains positive for S100, CD1a, CD207

› proliferation triggers release of chemokines + proteases + enzymatic reactions → production of damaging free radicals → destruction of lung architecture → airway fibrosis + failed wound healing

Cause: uncertain (? primary proliferative disorder possibly due to defect in immunoregulation; neoplasm; virus)

Prevalence: 1÷2,000,000 children per year

Path: influx of eosinophilic leukocytes simulating inflammation; reticulum cells accumulate cholesterol + lipids (= foam cells); sheets or nodules of histiocytes may fuse to form giant cells, cytoplasm contains (? viral) Langerhans bodies

Age: any age, mostly presenting at 1–4 years; adults affected in < 30%; < 30 years in 80%; M÷F = 1÷1

Location: bone + bone marrow, lymph nodes, thymus, ear, liver and spleen, gallbladder, GI tract, endocrine system; multifocal (10–20%)

DDx: osteomyelitis, Ewing sarcoma, leukemia, lymphoma, metastatic neuroblastoma

Clinical manifestations:

A. Localized LCH (70%) = eosinophilic granuloma
B. Disseminated LCH (30%)
   1. Chronic disseminated LCH (20%) = Hand-Schüller-Christian disease
   2. Fulminant disseminated LCH (10%) = Letterer-Siwe disease

formerly: Histiocytosis X = eosinophilic granuloma / Letterer-Siwe disease / Hand-Schüller-Christian syndrome
- ◊ Names should be disregarded as they were thought of formerly as different diseases!

@ Bone (80%)

√ bone lesions: in 80% (most common radiographic manifestation)
Location: predilection for flat bones (skull > mandible > rib > pelvis > spine) especially in adults

› Skull:
- asymptomatic/ focal pain
- soft-tissue swelling in scalp

√ well-defined lytic "punched-out" lesion of skull
√ characteristic beveled edge = asymmetric destruction of inner + outer cortices
√ geographic skull = skull lesions may grow in size and coalesce

N.B.: calvarial disease lacks periosteal reaction

DDx for single lesion: epidermoid / dermoid cyst, osteomyelitis

DDx for multiple lesions: lymphoma, leukemia, multiple myeloma, metastases

» Mastoid bone
- swelling, dizziness, vertigo, otorrhea

√ soft-tissue component : T1-isointense + T2-hyperintense + enhancement; isoechoic on US

» Mandible
- gingival bleeding + facial swelling

√ "floating teeth" = destruction of alveolar ridge

› Vertebral body
- pain, substantial neurologic defects

√ lytic lesion in early disease
√ vertebra plana = symmetric uniform vertebral collapse + preservation of intervertebral disk spaces

DDx: leukemia, metastatic neuroblastoma, aneurysmal bone cyst, Ewing sarcoma

› Long bone: most commonly femur, humerus, tibia
- asymptomatic / focal pain + swelling

Site: intramedullary lesion of diaphysis / metaphysis

√ lytic expansile aggressive lesion (in early disease)
√ cortical thickening, smooth periosteal reaction
√ extramedullary soft-tissue component with decreased T1 + increased T2 signal intensity
√ increased radiotracer uptake on bone scan; may be falsely negative (not uncommon)
√ lesion resolution turning sclerotic ← periosteal new bone + sharply defined sclerotic

margin (in chronic mature lesion)

DDx: chondromyxoid fibroma, plasmacytoma, metastasis, unicameral cyst, aneurysmal bone cyst

@ Liver (15%)

- hepatic dysfunction

√ hepatomegaly + focal solid / cystlike lesions

√ hypoattenuating, hypoechoic, hypointense T1 and T2 signal along biliary tracts + portal triads= periportal fibrosis

Cx: progressive sclerosing cholangitis

◊ Involvement indicates a worse prognosis

@ Spleen (< 15%)

√ splenomegaly → hypersplenism → cytopenias

◊ Involvement indicates a worse prognosis

@ Lymph Nodes (20%)

Location: predominantly in neck

√ hard / soft matted groups of nodes → lymphedema

@ CNS (~16%)

- ataxia, cognitive dysfunction ← neurodegeneration (with T2-hyperintense lesions in cerebellum + basal ganglia)
- growth hormone deficiency (later in life)
- diabetes insipidus (most common) ← decreased secretion of antidiuretic hormone ← infiltration of posterior pituitary gland

√ loss of normal posterior pituitary bright spot

√ thickening of pituitary stalk (~70%) on CEMR

DDx: germinoma, craniopharyngioma, tuberculosis, sarcoidosis, lymphocytic hypophysitis

√ leukoencephalopathy-like white matter changes

√ lesions in meninges + choroid plexus

@ Lung (~10%)

Age: more common in adults + almost always associated with smoking

- shortness of breath, nonproductive cough
- fever / weight loss (sometimes)

√ centrilobular micronodules

Distribution: bilateral symmetric upper- to mid-lung with sparing of costophrenic angles

DDx: metastases, miliary tuberculosis, sarcoidosis, silicosis

√ usually < 1 cm cysts ± confluence to bulla formation → recurrent spontaneous pneumothorax

√ pleural effusion + enlarged hilar lymph nodes (rare)

DDx: lymphangioleiomyomatosis, lymphocytic interstitial pneumonia, bullous emphysema

Localized Langerhans Cell Histiocytosis (70%)

= EOSINOPHILIC GRANULOMA

= localized often solitary bone lesion as the most benign variety of LCH

Age: 5–10 years (highest frequency); range 2–30 years; < 20 years (in 75%); M÷F = 3÷2
Path: bone lesion arises within medullary canal (RES)
Histo: considerable number of eosinophils in addition to the dominant Langerhans cell constituent

- painful tender bone lesion + soft-tissue swelling (may be misdiagnosed as local trauma / seborrhoic skin lesion)
- fever, leukocytosis, elevated sedimentation rate
- eosinophilia in blood + CSF

Location: limited to single / few bones (in children); may involve lung (in adults)
Sites: monostotic involvement in 50–75%;
(a) flat bones: calvarium > mandible > ribs > pelvis > vertebrae (rarely posterior elements)
(b) long bones: diaphyseal (58%) + metaphyseal (28%) + metadiaphyseal (12%) + epiphyseal (2%) in humerus, femur, tibia

X-ray:
√ osteolytic bone lesions 1–15 cm in diameter:
√ geographic / permeative / moth-eaten configuration
√ well- / poorly defined borders
√ ± sclerosis
DDx: neuroblastoma metastasis, leukemia, lymphoma

CT:
√ moderately to markedly enhancing soft-tissue mass with bone erosion

MR:
√ low to intermediate SI on T1WI + hyperintense T2WI
√ diffuse avid contrast enhancement (fat suppression!)
√ depicts intracranial extension of LCH

@ Skull (40–50%)
Site: diploic space of parietal bone > temporal bone (petrous ridge, mastoid)
√ round / ovoid punched-out lytic lesion:
DDx: venous lake, arachnoid granulation, parietal foramen, epidermoid cyst, hemangioma
√ beveled edge / "hole-within-hole" appearance ← asymmetric destruction of inner + outer tables
√ sharply marginated without sclerotic rim (DDx: epidermoid with bone sclerosis)
√ sclerotic margin during healing phase (50%)
√ "button sequestrum" = remnants of bone as a central bone density within a lytic lesion ← erosive accumulation of histiocytes
√ soft-tissue mass overlying the lytic process in calvarium (often palpable)

@ CNS involvement (4%)
Site: predilection for hypothalamic pituitary axis
- diabetes insipidus (in 5 –50%)

√ thickening of the infundibular stalk > 3 mm
√ isodense markedly homogeneously enhancing mass in superior aspect of stalk / hypothalamus
√ absence of posterior pituitary "bright spot" on T1WI

√ partially / completely empty sella
√ threadlike narrowing of infundibulum (< 1 mm)

@ Orbit
• ptosis, palpebral and periocular erythema, enlargement of associated palpebral fissure
Site: superior / superolateral orbital region
√ osseous destruction + soft-tissue mass extending into orbit / temporal fossa / forehead / face / epidural space

@ Mastoid process
• intractable otitis media with chronically draining ear (in temporal bone involvement)
√ destructive lesion near mastoid antrum
DDx: otomastoiditis, cholesteatoma, metastasis
Cx: extension into middle ear may destroy ossicles leading to deafness

@ Jaw
• gingival + contiguous soft-tissue swelling
√ "floating" teeth = destruction of alveolar bone
√ mandibular fracture

@ Axial skeleton (8–25%)
• pain, rapidly subsiding after bed rest
• mild hyperpyrexia, mild ↑ ESR, slight eosinophilia, slight leukocytosis
• rarely mild neurologic complications
Site: vertebral body > posterior elements
√ "vertebra plana" = "coin on edge" = Calvé disease (6%) = collapse of vertebra (most commonly thoracic):

◊ Most common cause of vertebra plana in children!

√ pertinent negatives:
√ increased opacity in collapsed vertebral body
√ absence of osteolysis
√ preserved disk space + pedicles
√ rare involvement of posterior elements
√ no kyphosis
√ absence of adjacent paravertebral soft-tissue

√ lytic lesion in supraacetabular region
Prognosis: reconstitution of vertebral height is usual

@ Rib (9–15%)
√ rib lesions with fractures (common)
√ ± perilesional edema, especially in early phase

@ Proximal long bones (15–33%)
Site: mostly diaphyseal; epiphyseal lesions are uncommon
√ expansile lytic lesion with ill-defined / sclerotic edges
√ endosteal scalloping, widening of medullary cavity
√ cortical thinning, intracortical tunneling
√ erosion of cortex + soft-tissue mass
√ laminated periosteal reaction (frequent), may show interruptions
√ may appear rapidly within 3 weeks

√ lesions respect joint space + growth plate

@ Lung involvement (20%)

@ GI tract

Location: terminal ileum (most commonly)

• diarrhea, protein-losing enteropathy, malabsorption

√ diffuse concentric bowel wall thickening

@ Skin involvement (up 50%)

• erythematous papules + plaques → become eroded + develop serous / hemorrhagic crust

Frequently accompanied by: petechiae / purpura

Location: scalp, perinasal + preauricular areas of face, flexural areas

NUC:

√ negative bone scans in 35% (radiographs more sensitive)

√ bone lesions generally not ^{67}Ga avid

√ ^{67}Ga may be helpful for detecting nonosseous lesions

Prognosis: excellent with spontaneous resolution of bone lesions in 6–18 months

Chronic Disseminated LCH (20%)

= Hand-Schüller-Christian Disease

[Alfred Hand (1868–1949), American pediatrician at University of Pennsylvania, Philadelphia]

[Artur Schüller (1874–1957), neurologist, psychiatrist and neuroradiologist in Vienna, Austria and Melbourne, Australia]

[Henry Asbury Christian (1876–1951), American pathologist and first physician in chief at Peter Bent Brigham Hospital, Boston]

= chronic disseminated form of LCH characterized by CLASSIC triad (in 10–15%) of

(1) Exophthalmos (mass effect on orbital bone)

(2) Diabetes insipidus (basilar skull disease / direct infiltration of posterior pituitary gland)

(3) Destructive bone lesions (often of calvaria)

Path: proliferation of histiocytes, may simulate Ewing sarcoma

Age at onset: < 5 years (range from birth to 40 years); M÷F = 1÷1

• diabetes insipidus (30–50%) often with large lytic lesion in sphenoid bone / panhypopituitarism

• otitis media with mastoid + inner ear invasion

• exophthalmos (33%), sometimes with orbital wall destruction

• generalized eczematoid skin lesions (30%)

• ulcers of mucous membranes (gingiva, palate)

Sites: bone, liver, spleen, lymph nodes, skin

@ Bone

√ osteolytic skull lesions with overlying soft-tissue nodules

√ "geographic skull" = ovoid / serpiginous destruction of large area

√ "floating teeth" with mandibular involvement

√ destruction of petrous ridge + mastoids + sella turcica

@ Orbit

√ diffuse orbital disease with multiple osteolytic bone lesions

@ Liver
- √ hepatosplenomegaly (rare)
- √ scattered echogenic / hypoattenuating liver granuloma
- √ lymphadenopathy (may be massive)
- √ gallbladder wall thickening (from infiltration)

@ Lung
- √ cyst + bleb formation → spontaneous pneumothorax (25%)
- √ ill-defined diffuse nodular infiltration often progressing to fibrosis + honeycomb lung

@ Thymus
- √ enlarged thymus + punctate calcifications

Prognosis: spontaneous remissions + exacerbations; fatal in 15%

Fulminant Disseminated LCH (10%)

= LETTERER-SIWE DISEASE

= acute disseminated fulminant form of LCH characterized by wasting, pancytopenia (from bone marrow dysfunction), generalized lymphadenopathy, hepatosplenomegaly

Frequency: 1÷ 2,000,000

Age: several weeks after birth to 2 years

Path: generalized involvement of reticulum cells; may be confused with leukemia

- hemorrhage, purpura ← coagulopathy
- severe progressive anemia / pancytopenia
- intermittent fever
- failure to grow / malabsorption + hypoalbuminemia
- skin rash: scaly erythematous seborrhea-like brown to red papules

Location: especially pronounced behind ears, in axillary, inguinal, and perineal areas

Sites: liver, spleen, bone marrow, lymph nodes, skin

√ hepatosplenomegaly + lymphadenopathy (most often cervical)

√ obstructive jaundice

@ Bone involvement (50%):
- √ widespread multiple lytic lesions; "raindrop" pattern in calvarium

Prognosis: rapidly progressive with 70% mortality rate

LATERAL EPICONDYLITIS

= TENNIS ELBOW = TENDINITIS (epicondylitis is a misnomer)

= chronic overuse syndrome involving origin of extensor carpi radialis brevis tendon

Age: 35–50 years

Cause: tennis, throwing sports, swimming, carpentry, plumbing (repetitive forearm pronation + supination with wrist extension)

- pain + tenderness in region of lateral epicondyle radiating into forearm

Histo: tendon microtears followed by formation of angiofibrotic hyperplasia (= noninflammatory reactive tissue)

MR (oblique coronal images):

√ focally hyperintense signal compared with muscle + less intense than fluid on all sequences

Rx: (1) conservative management: avoidance of painful activity, application of ice, NSAID
(2) splints, steroid injection
(3) excision of abnormal tissue + decortication of epicondyle + reattachment of tendon

DDx of painful elbow: injury to radial collateral ligament / extensor carpi radialis longus tendon, cartilage defect

LAURENCE-MOON-BIEDL SYNDROME

• retardation; obesity; hypogonadism
√ craniosynostosis
√ polysyndactyly

LEPROSY

= HANSEN DISEASE

Organism: Mycobacterium leprae

Types:

(1) lepromatous: in cutis, mucous membranes, viscera
(2) neural: enlarged indurated nodular nerve trunks; anesthesia, muscular atrophy, neurotrophic changes
(3) mixed form

@ Osseous changes (in 15–54% of patients)
√ specific osseous signs of leprosy:
Location: center of distal end of phalanges / eccentric
√ ill-defined areas of decalcification, reticulated trabecular pattern, small rounded osteolytic lesions, cortical erosions
√ joint spaces preserved
√ healing phase: complete resolution / bone defect with sclerotic rim + endosteal thickening
√ nasal spine absorption + destruction of maxilla, nasal bone, alveolar ridge
√ enlarged nutrient foramina in clawlike hand
√ erosive changes of ungual tufts
√ nonspecific osseous signs of leprosy:
√ soft-tissue swelling; calcification of nerves
√ contractures / deep ulcerations
√ neurotrophic joints (distal phalanges in hands, MTP in feet, Charcot joints in tarsus)

LEUKEMIA OF BONE

A. CHILDHOOD

Most common malignancy of childhood:
⅓ of all pediatric malignancies

Histo:

1. Acute Lymphocytic Leukemia (ALL in 75%)
most often in children < 5 years of age
√ lymph node enlargement rare
2. Acute Myelogenous Leukemia (AML)

tends to affect older children + adolescents
√ lymph node enlargement common

- migratory paraarticular arthralgias (25–50%) ← adjacent metaphyseal lesions (may be confused with acute rheumatic fever / rheumatoid arthritis)
- low-grade fever, bruising, fatigue
- bone pain ← increased intraosseous pressure from proliferation of malignant cells
- elevated erythrocyte sedimentation rate, anemia
- hepatosplenomegaly, occasionally lymphadenopathy

◊ Peripheral blood smears may be negative in aleukemic form!

Skeletal manifestations in 50–90%:

Location: proximal + distal metaphyses of long bones, flat bones, spine

(a) Diffuse osteopenia (most common pattern)
√ diffuse demineralization of spine + long bones ← leukemic infiltration of bone marrow + catabolic protein / mineral metabolism
√ coarse trabeculation of spongiosa ← destruction of finer trabeculae
√ multiple biconcave / partially collapsed vertebrae (14%)

(b) "Leukemic lines" (40–53% in ALL):
√ transverse radiolucent metaphyseal bands, uniform + regular across the width of metaphysis (= leukemic infiltration of bone marrow / osteoporosis at sites of rapid growth)
Location: large joints (proximal tibia, distal femur, proximal humerus, distal radius + ulna)
√ horizontal / curvilinear bands in vertebral bodies + edges of iliac crest
√ dense metaphyseal lines after treatment

(c) Focal destruction of flat / tubular bones:
√ multiple small clearly defined ovoid / spheroid osteolytic lesions (destruction of spongiosa, later cortex) in 30–60%
√ moth-eaten appearance, sutural widening, prominent convolutional markings of skull

◊ Lytic lesions distal to knee / elbow in children are suggestive of leukemia (rather than metastases)!

(d) Isolated periostitis of long bones (infrequent):
√ smooth / lamellated / sunburst pattern of periosteal reaction (= cortical penetration by sheets of leukemic cells into subperiosteum) in 12–25%

(e) Metaphyseal osteosclerosis + focal osteoblastic lesion (very rare)
√ osteosclerotic lesions ← reactive osteoblastic proliferation (late in disease)
√ mixed (lytic + bone-forming) lesions in 18%

Dx: sternal marrow / peripheral blood smear

Cx: proliferation of leukemic cells in marrow leads to extraskeletal hematopoiesis

DDx: metastatic neuroblastoma, Langerhans cell histiocytosis

B. ADULTHOOD

◊ Death usually occurs before skeletal abnormalities manifest
√ osteoporosis
√ solitary radiolucent foci (vertebral collapse)

√ permeating radiolucent mottling (proximal humerus)

MR:

√ diffuse decrease in SI compared with normal marrow on T1WI

√ isointense / mildly hyperintense compared with normal marrow on T2WI ← high water content of leukemic cells + displacement of fat

√ abnormally hyperintense relative to normal marrow on STIR

LIPOBLASTOMA

= rare rapidly growing benign tumor in children < 3 years of age (= postnatal proliferation) composed of mesenchymal cells ranging from prelipoblasts (spindle cells) to mature adipocytes

Origin: derived from fetal adipose tissue

Frequency: 30% of adipocytic tumors in children

Path: encapsulated immature adipose tissue (embryonal fat) separated by septa into multiple lobules

Histo: uni- and multivacuolated lipoblasts interspersed between spindle / stellate mesenchymal cells + suspended in myxoid stroma

Molecular features: translocation involving 8q11–13 with rearrangement of Plag1 gene

Median age: 12–18 months of age (range, newborn to 16 years); < 3 years of age (in > 90%); M÷F = 2÷1

Types:

(a) lipoblastoma proper = circumscribed encapsulated form in superficial adipose tissue (⅔)

(b) lipoblastomatosis = diffuse nonencapsulated infiltrative form in deep adipose tissue (⅓)

Location: subcutaneous tissue of extremities (70%), head and neck, trunk, mediastinum, mesentery, perineum, retroperitoneum

Size: 3–5 cm

• gradually increasing painless soft-tissue mass

√ no enhancement for tumors composed purely of lipocytes

√ marked heterogeneous enhancement for tumors composed predominantly of lipoblasts

US:

√ homogeneous finely textured echogenic (relative to liver / adjacent muscle) mass

√ may contain occasionally cystic / focal hypoechoic ares

CT:

√ tumor of fat density separated by fibrous septa

√ intratumoral fat stranding

MR (preferred preoperative evaluation):

√ high (mature adipocytes) / intermediate SI (immature adipocytes) on T1WI + T2WI with a predominance of lipocytes

√ heterogeneous texture with T1-hypointense + T2-hyperintense areas ← excessive amount of immature fat (lipoblasts) / myxocollagenous stromal tissue / intratumoral infarction / extensive mucoid + cystic degeneration

√ CHARACTERISTIC areas of high signal intensity on fat-suppressed images ← predominance of myxocollagen (NEVER in lipoma!)

Prognosis: may evolve into mature lipoma; capable of invading surrounding tissue (=

lipoblastomatosis); NO metastatic potential

Rx: wide surgical resection; recurrence in 10–25% for lipoblastomatosis

DDx: (1) Teratoma (calcifications)
(2) Lipoma (very rare in children)
(3) Well-differentiated liposarcoma (no distinguishing imaging features, patient age < 3 years allows reliable differentiation)
(4) Dermoid cyst

LIPOFIBROMATOSIS

= INFANTILE FIBROMATOSIS OF NONDESMOID TYPE
= rare fibrofatty tumor of childhood

Histo: mass with abundant adipose tissue traversed by bundles of spindle-shaped fibroblasts

Location: hand + foot > head & neck, chest wall, abdominal wall, jaw

Median age: 1 year (range, 11 days to 12 years); present at birth in 18%; M÷F = 2÷1

• slow-growing painless subcutaneous mass

Median size: 2 (range, 1–10) cm

MR (modality of choice):
√ mass isointense to fat interspersed by low- to intermediate SI (= fibrous component) on all sequences:
√ infiltrative toward subcutaneous + deeper soft tissues
√ ± enhancement of fibrous component

LIPOMA OF BONE

= INTRAOSSEOUS LIPOMA

Frequency: < 0.1% of primary bone tumors

Age: any (4^{th}–5^{th} decade); M÷F = 1.6÷1

May be associated with: hyperlipoproteinemia

• asymptomatic / localized bone pain (in up to 66%)

Milgram classification:

Stage I viable large fat cells organized into lobules replacing bone marrow + encasing trabeculae
√ trabecular resorption + thin sclerotic rim
√ lucent lesion (–60 to 100 HU)
√ isointense to subcutaneous fat

Stage II areas of partial fat necrosis accompanied by foamy macrophages + fibrosis associated with calcifications + reactive bone formation
√ regions of increased density (calcifications)
√ variable SI on T1WI + hyperintense on T2WI for fat necrosis
√ thick rim of reactive sclerosis

Stage III almost complete involution of lipoma with cyst formation (= myxomatous degeneration) + thick radiodense border
√ expansile remodeling (DDx: osseous infarct)
√ regions of cyst formation (cystic degeneration)

Location in order of frequency:

extremities (proximal femur > proximal tibia, fibula, humerus, radius), calcaneus, ilium, ribs, skull, mandible, maxilla, sacrum, coccyx, vertebrae; multiple locations = **intraosseous lipomatosis**

Site: metaphysis > diaphysis of long bones; epiphysis unusual

√ expansile nonaggressive radiolucent lesion

√ loculated / septated appearance (trabeculae)

√ thin well-defined sclerotic border

√ ± thinned cortex (NO cortical destruction)

√ NO periosteal reaction

√ may contain clumps of calcification centrally (= dystrophic calcification from fat necrosis)

◊ VIRTUALLY DIAGNOSTIC in:

@ Proximal femur

Site: intertrochanteric / subtrochanteric

√ marked ossification of margins of lesion

@ Calcaneus

Site: in triangular region between major trabecular groups (on LAT projection)

√ calcified / ossified nidus

@ Ileum

Site: adjacent to sacroiliac joint

◊ Radiographic appearance similar to unicameral bone cyst (infarcted lipoma = unicameral bone cyst ?)

MR:

√ similar to fat on all sequences (T1-hyperintense lesion)

Cx: rarely malignant transformation

DDx: fibrous dysplasia, simple bone cyst, posttraumatic cyst, giant cell tumor, desmoplastic fibroma, chondromyxoid fibroma, osteoblastoma

LIPOMA OF SOFT TISSUE

Lipoma composed of mature adipose tissue is the most common mesenchymal tumor (16% of soft tissue tumors).

Histo: mature fat cells (adipocytes) of uniform size and shape with a small portion of surrounding / intervening connective tissue stroma; fat unavailable for systemic metabolism

Variants: fibrolipoma, osteolipoma, chondrolipoma, intramuscular lipoma, angiolipoma, chondroid lipoma, spindle cell lipoma, pleomorphic lipoma, sialolipoma

Molecular features: translocation of 12q13–15; absence of MDM2 + CDK4 amplification (= liposarcoma)

• stable size after initial period of discernible growth

Age: 5th–6th decade; M > F

Location:

(a) superficial = subcutaneous lipoma (more common) in posterior trunk, head & neck (25%), proximal extremities

(b) deep lipoma in retroperitoneum, mediastinum, chest wall, deep soft tissue of hands + feet;

multiple in 5–7% (up to several hundred tumors)

◊ The deeper + more centrally located a fatty mass resides the more likely it is malignant!

√ well-defined encapsulated mass of fat opacity / density / intensity identical to subcutaneous fat
√ no enhancement
√ cortical thickening (with adjacent parosteal lipoma)

CT:
√ well-defined + homogeneous tumor with low attenuation coefficient (–65 to –120 HU)
√ no enhancement following IV contrast material

MR:
√ well-defined + homogeneous, often with septations
√ SI characteristics similar to subcutaneous fat: hyperintense on T1WI + moderately intense on T2WI
√ thin septations of low SI (not uncommon) correspond to fibrous connective tissue
√ differentiation from other lesions by fat suppression technique

Atypical features:
√ septa > 2 mm thick + septal nodularity
√ soft tissue component with attenuation / SI of muscle / fibrous tissue / hemorrhage / calcification ± contrast enhancement

Rx: resection with < 5% recurrence rate

DDx: normal fatty deposit (no internal architecture, no mass effect on adjacent structures and their metabolic behavior)

Angiolipoma

= lesion composed of fat separated by small branching vessels

Age: 2nd + 3rd decade; 5% familial incidence

• tender

Location: upper extremity, trunk

√ signal characteristics of fat + mixed with varying numbers of large / small vessels
√ mostly encapsulated lesion, may infiltrate

Benign Mesenchymoma

= long-standing lipoma with chondroid + osseous metaplasia

Infiltrating Lipoma

= INTRAMUSCULAR LIPOMA
= relatively common benign lipomatous tumor extending between muscle fibers that become variably atrophic

Peak age: 5th–6th decade; M > F

Location: thigh (50%), shoulder, upper arm

Lipoma Arborescens

= DIFFUSE SYNOVIAL LIPOMA
= rare idiopathic intraarticular lesion characterized by replacement of subsynovial tissue by mature fat cells with villous synovial proliferation

Cause: nonspecific proliferative synovial reaction to chronic irritation from inflammation / trauma

Frequently associated with:
degenerative joint disease, chronic rheumatoid arthritis, prior trauma

Mean age: 59 years (range, 5th–7th decade); M÷F = 1÷1

Path: frondlike appearance resembling a tree in leaf [*arborescens*, Latin = treeforming / treelike]

Histo: fatty proliferation with hypertrophic synovial villi distended by fat + dense focally nodular lymphocytic and plasmacellular infiltrate

Location: knee >> other joints; monoarticular (94%)

Site: suprapatellar pouch of knee

- long-standing painless slowly progressive swelling
- recurrent joint effusions; joint pain + swelling (47%)

X-ray:
√ joint fullness with radiolucent areas
√ (frequently) osteoarthritic changes

US:
√ hyperechoic frondlike mass bending and waving in real time with joint manipulation

MR:
√ frondlike synovial mass isointense to fat on all sequences (PATHOGNOMONIC)
√ joint effusion
√ lack of magnetic susceptibility artifact

Rx: synovectomy

Neural Fibrolipoma

= FIBROLIPOMATOUS HAMARTOMA OF NERVE
= rare tumorlike condition characterized by sausage-shaped / fusiform enlargement of a nerve by fibrofatty tissue

Age: early adulthood < 30 years / at birth

Histo: infiltration of epineurium + perineurium by fibrofatty tissue with separation of nerve bundles

- soft slowly enlarging mass
- pain, tenderness, decreased sensation, paresthesia

Location: volar aspect of hand, wrist, forearm

Site: median n. (most frequently), ulnar n., radial n., brachial plexus

May be associated with:
macrodactyly (in 2/3) = macrodystrophia lipomatosa

√ may not be visible radiographically

MR:
√ longitudinally oriented, cylindrical, linear / serpiginous structures of signal void about 3 mm in diameter (= nerve fascicles with epi- and perineural fibrosis) separated by areas of fat SI (= mature fat infiltrating the interfascicular connective tissue)

US:
√ "cablelike appearance" = alternating hyper- and hypoechoic bands on US

DDx: cyst, ganglion, lipoma, traumatic neuroma, plexiform neurofibroma, vascular

malformation

LIPOSARCOMA

= malignant tumor of mesenchymal origin rarely arising from lipoma

Frequency: 10–16–35% of all soft-tissue sarcomas; 2nd most common soft-tissue sarcoma in adults (after malignant fibrous histiocytoma)

Prevalence: 4.1÷1,000,000 in USA (2001)

Age: 5th–6th decade; M÷F = 1÷1

Path: wide spectrum of pathologic appearances varying from circumscribed lesions consisting predominantly of adipose tissue to circumscribed / infiltrating masses without any macroscopically visible adipose elements

Histo: < 50% of liposarcomas contain lipid material; nonadipose components include fibrosis, inflammation, areas of myxoid change, fat necrosis ± calcification

Categories:

(1) well-differentiated = lipogenic subtype (50%)
(2) dedifferentiated round cell subtype (10%)
(3) myxoid subtype (20–50%)
(4) pleomorphic subtype (5–15%)
(5) mixed subtype (5–12%)

Molecular features: ring chromosome derived from chromosome 12; MDM2 + CDK4 amplification

Location: lower extremity (45%), abdominal cavity and retroperitoneum (14%), trunk (14%), upper extremity (7.6%), head & neck (4–6.5%), miscellaneous (13.5 %)

Spread: hematogenous to lung, visceral organs; myxoid liposarcoma shows tendency for serosal + pleural surfaces, subcutaneous tissue, bone; regional nodal metastases (in < 10%)

• typically painless, slow-growing (months – years) soft-tissue mass; pain + tenderness (10–15%)

√ unifying radiologic feature = adipose tissue (vast majority) of nodular / finely reticulated / amorphous appearance

√ associated nonlipomatous components and lesion location often allow specific diagnosis of subtype

Criteria favoring liposarcoma over lipoma:

• male patient age > 60 years
√ size of lesion > 10 cm
√ < 75% fat component
√ associated nonadipose mass
√ presence of thick septa > 2 mm of nodular / globular appearance with contrast enhancement
√ deep lesions in mediastinum / retroperitoneum

Rx: wide surgical excision ± radiation therapy ± adjunct chemotherapy

Well-differentiated Liposarcoma (50%)

= ATYPICAL LIPOMATOUS TUMOR

= locally aggressive tumor of intermediate malignant potential with < 25% of tissue volume consisting of fat

Peak age: 6th–7th decade; M÷F = 1÷1
Path: large multilobulated well-circumscribed mass
Histo: malignant lipoblasts with large amounts of lipid + scanty myxoid matrix; 5 variants (lipoma-like, sclerosing, inflammatory, spindle cell, liposarcoma with meningothelial whorls)
Location:
(a) deep soft tissues of extremities (65–75%): thigh
(b) retroperitoneum (20–33%): presenting quite large with > 20 cm in diameter
(c) upper extremity (14%)
(d) head & neck (5%)
Site: intramuscular > intermuscular / subcutaneous
√ round / lobulated mass of fat density displacing surrounding structures
X-Ray:
√ soft-tissue mass of >10 cm in diameter:
√ fat detectable in extremities, not in retroperitoneum
√ calcification / metaplastic ossification (10–32%)
US:
√ heterogeneous multi-lobulated well-defined mass
√ hyperechoic / variably echogenic fat
CT / MR:
√ adipose mass with low proportion of fat content (< 25% of tumor volume)
√ presence of nonadipose focal globular masslike areas and enhancing septa > 2 mm ± nodularity:
√ high attenuation on CT
√ hypo- / isointense relative to skeletal muscle on T1WI
√ hyperintense relative to skeletal muscle on T2WI
CEMR:
√ moderate (¼) / marked (¾) septal enhancement
Prognosis: no metastatic potential; risk of local recurrence (43% in extremity, 70% in groin, 91% in retroperitoneum)

Dedifferentiated Liposarcoma (10%)
Path: high-grade fibrosarcoma / malignant fibrous histiocytoma (90%) mixed with well-differentiated areas
Histo: supernumerary ring / giant chromosomes derived from 12q13–15 regions
Age: 7th decade; M÷F = 1÷1
Location: deep (retroperitoneum÷extremity = 3÷1); head & neck + trunk + spermatic cord (< 20%); subcutis (< 1%)
Development: 7–8 years from well-differentiated liposarcoma
√ large components identical to well-differentiated liposarcoma
√ additionally focal nodular nonlipomatous regions > 1 cm in size of low to intermediate SI on T1WI + high SI on T2WI:
√ fibrous collagenized tissue
√ metaplastic mineralization
√ fat necrosis

Prognosis: more aggressive than well-differentiated liposarcoma with local recurrence in 41% + distant metastasis (lung, liver, bone) in 21%

Myxoid Liposarcoma

= tumor of intermediate differentiation with varying degrees of mucin + fibrous tissue + relatively little lipid (< 10%)

Path: fat content often < 10–25% obscuring typical features of lipomatous tumors

Histo: plexiform vascular network + mixture of stellate spindle-shaped mesenchymal cells + lipoblasts in a basophilic myxoid ground substance

Genetics: reciprocal translocation of t(12;16)(q13;p11)

Peak age: 4th–5th decade (most common subtype to affect children); M÷F= 1÷1

Location: intermuscular fascial plane (70–80%) in deep-seated area

Site: (a) lower extremity (75–80%): medial thigh, popliteal region, groin, buttock, calf
(b) retroperitoneum (8%)
(c) upper extremity (5%)

√ well-defined multilobulated intermuscular mass:
- √ density between water + muscle on CT mimicking a cyst
- √ T1 prolongation with a cystic appearance (in 5–10%)
- √ very long relaxation times of large component of myxoid matrix (22%)
- √ pathognomonic lacy / linear amorphous foci of fat intensity (in 90–95%) of approx. 10% of entire lesion
- √ peripheral nodular (61%) / central nodular (44%) / diffuse (17%) enhancement

US:
- √ anechoic mass ± thin septa (disproving fluid content)

Dx: biopsy of adipose area

Prognosis: frequent recurrence; metastasis in unusual locations (opposite extremity, retroperitoneum, chest wall, pelvis); 5-year mortality of 47–77%

DDx: (1) Myxoma (intramuscular, only thin rind of perilesional fat on T1WI, surrounding muscle atrophy + edema)
(2) Synovial cyst / ganglion (typical location, thick wall and surrounding edema, clinical history of liquefied hematoma / abscess)

Pleomorphic Liposarcoma

Histo: marked cellular pleomorphism, paucity of lipid + mucin = highly undifferentiated

√ well-defined mass ± infiltrative margins:
- √ intensity of muscle (no distinguishing imaging features from other soft-tissue sarcomas) in 84%
- √ small lacy / linear / amorphous foci containing < 1% fat in 62–75% (fat suppression technique!)
- √ prominent heterogeneity with tumor necrosis in 81%

Dx: biopsy of adipose foci

Prognosis: aggressive high-grade sarcoma with marked propensity for tumor recurrence + metastases (lung); 5-year survival of 21–63%

LYME ARTHRITIS

= heterogeneous zoonosis with geographical variation in animal reservoir + tick species + spirochete subspecies

Agent: spirochete Borrelia burgdorferi transmitted by tick bite Ixodes dammini; in Europe Borrelia garinii

Histo: inflammatory synovial fluid, hypertrophic synovia with vascular proliferation + cellular infiltration

- endemic areas: Lyme and Old Lyme, Connecticut (first recognized location); now throughout USA, Europe, Australia
- recurrent attacks of arthralgias within days to 2 years after tick bite (80%); history of erythema chronicum migrans

Location: mono- / oligoarthritis of large joints (especially knee)

√ erosion of cartilage / bone (4%)

√ no neuroimaging manifestations (frequent)

√ painful meningoradiculitis (= Bannwarth syndrome)

√ abnormal smooth leptomeningeal enhancement with cranial or spinal nerve involvement

√ enhancing periventricular + callososeptal + infratentorial white matter lesions ← perivascular extension of lymphocytic inflammation (DDx: multiple sclerosis)

Rx: antibiotics

Posttreatment Lyme disease (10–20%) = syndrome due to autoimmune effects of molecular mimicry and antigen cross-reactivity

DDx: (1) Rheumatic fever
(2) Rheumatoid arthritis
(3) Gonococcal arthritis
(4) Reiter syndrome

LYMPHANGIOMA

= sequestered noncommunicating lymphoid tissue lined by lymphatic endothelium

Cause: congenital obstruction of lymphatic drainage

Subtypes:

(1) Capillary lymphangioma (rare)
Location: subcutaneous tissue

(2) Cavernous lymphangioma
Location: about the mouth + tongue

(3) Cystic lymphangioma (most common)
= cystic hygroma
Associated with: hydrops fetalis, Turner syndrome
Location: head, neck (75%), axilla (20%), extension into mediastinum (3–10%)
- soft fluctuant mass

◊ Lymphangiomas are frequently a mixture of subtypes!

Age: found at birth (50–65%); within first 2 years of life (90%)

Location: soft tissue; bone (rare)

√ multilocular cystic lesion with fibrous septations

√ occasionally serpentine vascular channels

√ opacification during lymphangiography / direct puncture
√ clear / milky fluid on aspiration
DDx: hemangioma (blood on aspiration)

LYMPHANGIOMATOSIS OF BONE

= MASSIVE OSTEOLYSIS = GORHAM-STOUT DISEASE
= VANISHING BONE DISEASE = PHANTOM BONE DISEASE
[Lemuel Whittington Gorham (1885–1968), internist, New York]
[Arthur Purdy Stout (1885–1967), surgeon and pathologist at College of Physicians & Surgeons of Columbia University, New York]
= infrequent disorder of bone + soft tissues characterized by aggressive nonneoplastic proliferation of lymphangiomatous tissue → massive local osteolysis
Cause: persistence of dilated lymphatics from 14th–20th week EGA
Prevalence: > 200 cases confirmed
Histo: proliferation of dilated lymph channels communicating with blood vessels in bone
Age: infant + child + adolescent, M=F
◊ Consider Gorham-Stout disease for any osteolytic lesion of unknown cause!
Associated with: cystic hygroma (neck, axilla, chest wall, mediastinum), splenic cysts, chylothorax, soft-tissue hemangiomas without calcifications
• frequently history of severe trauma (50%)
• little / no pain in affected body part
Location: any bone (frequently multiple locations); most commonly major long bones (humerus, shoulder, mandible), pelvis, spine, thorax, short tubular bones of hand + feet (unusual)
√ progressive relentless osteolytic resorption / destruction of bone with monocentric spread:
√ patchy osteopenia (early)
√ expanding intramedullary lytic lesion (later)
√ complete resorption of entire bone segments (late) of one bone / group of bones
√ no regard for joint boundaries
√ lack of reaction (no periosteal reaction, minimal sclerosis)
√ advancing edge of destruction not sharply delineated
√ tapering margins of bone ends at sites of osteolysis with conelike spicule of bone (early changes)
√ no soft-tissue calcifications / phleboliths
√ serous / chylous pleural effusions → significant mortality
MR:
√ varying SI depending on disease activity
√ hypointense soft tissue around osteolytic area on T1WI
√ hyperintense soft tissue around osteolytic area on T2WI
√ minimal contrast enhancement
Rx: no known validated treatment; interferon; steroids
DDx: Langerhans cell histiocytosis, fibrous dysplasia, brown tumor of hyperparathyroidism, infection, trauma, tumor, gout, scleroderma

LYMPHOMA OF BONE

Primary Lymphoma of Bone

= RETICULUM CELL SARCOMA = OSTEOLYMPHOMA

= singular bone lesion without evidence of distal nodal /disseminated disease for at least 6 months after diagnosis (= stage E in Ann Arbor classification)

N.B.: presence of locoregional lymphadenopathy is not a criterion of exclusion

Prevalence: < 5% of all primary bone tumors; < 1% of all NHL; 5% of extranodal lymphomas; 2–6% of all primary malignant bone tumors in children

Histo: (a) NHL (94%): mostly diffuse large B-cell (80%) / T-cell category; sheets of reticulum cells, larger than those in Ewing sarcoma (DDx: myeloma, inflammation, granulocytic osteosarcoma, eosinophilic granuloma)

(b) Hodgkin disease in 6%

Median age: 36–52 (range, 1.5–86) years; bimodal distribution with peaks in 2nd–3rd and 5th–7th decades; 50% < 40 years; 35% < 30 years; M÷F = 6÷1

- intermittent chronic dull pain; local swelling, palpable mass
- systemic symptoms such as weight loss and fever
- striking contrast between lesion size + patient's well-being

Location: lower femur (25%), upper tibia (40% about knee), humerus, pelvis, head & neck, vertebra (25%), scapula, ribs

Site: meta- / diaphysis

Radiography:

√ lytic process at end of a long bone with aggressive periosteal reaction (almost pathognomonic)

√ lytic-destructive pattern (70%):

√ "permeative" pattern = numerous small elongated rarefactions parallel to long bone axis

√ "moth-eaten" pattern = many medium to large areas of radiolucency in poorly marginated area of bone

√ lamellated / layered "onion-peel" / broken periosteal reaction (60%):

√ disrupted periosteal bone (poorer prognosis)

√ sunburst periosteal response (rare and less than in Ewing sarcoma)

√ blastic-sclerotic pattern (rare):

√ mixed lytic lesion with sclerotic areas

√ may develop after therapy

√ near absence of detectable abnormalities on plain X-ray

CT:

√ cortical destruction (late)

√ sequestrum within lytic lesion

MR:

√ bone marrow replacement:

√ areas of low signal intensity within marrow on T1WI

√ high SI on T2WI for tumor + peritumoral edema + reactive marrow changes

√ areas of enhancement within lesion

√ soft-tissue involvement ← spread of tumor cells from marrow through small vascular channels through cortex into surrounding soft tissue:
√ soft-tissue mass without calcification (70%)
N.B.: relatively minimal cortical destruction with extensive soft-tissue + marrow involvement
√ synovitis of knee joint common
√ cortical erosion (earliest detection by MR)

Cx: pathologic fracture (25% = most common among malignant bone tumors)

Rx: combination of radiation therapy + chemotherapy

Prognosis: 83% 5-year survival

DDx: (1) Osteosarcoma (less medullary extension, younger patient)
(2) Ewing tumor (systemic symptoms, debility, younger patient)
(3) Metastatic malignancy / secondary lymphoma (multiple bones involved, more destructive, recognized by whole-body surveillance)

Secondary Lymphoma of Bone

= disseminated malignant lymphoma (stage IV)

MACRODYSTROPHIA LIPOMATOSA

= rare nonhereditary congenital form of localized gigantism = neural fibrolipoma with macrodactyly

Path: striking increase in adipose tissue in a fine fibrous network involving periosteum, bone marrow, nerve sheath, muscle, subcutaneous tissue

May be associated with: syn-, clino-, polydactyly

• painless

Location: 2nd or 3rd digit of hand / foot; unilateral; one / few adjacent digits may be involved in the distribution of the median / plantar nerves

√ long + broad splayed phalanges with endosteal + periosteal bone deposition
√ overgrowth of soft tissue, greatest at volar + distal aspects
√ slanting of articular surfaces
√ lucent areas of fat (DIAGNOSTIC)

Prognosis: accelerated maturation possible; growth stops at puberty

DDx: fibrolipomatous hamartoma associated with macrodystrophia lipomatosa (indistinguishable), Klippel-Trénaunay-Weber syndrome, lymphangiomatosis, hemangiomatosis, neurofibromatosis, chronic vascular stimulation, Proteus syndrome

MARFAN SYNDROME

[Antoine Bernard-Jean Marfan (1858–1942), Chef de clinique medicale de l'Université de Paris and Hôpital des Enfants Malades]

= Arachnodactyly

= autosomal dominant (in 75%) multisystemic connective tissue disorder with high penetrance but extremely variable expression; new sporadic mutations in 25–30%

Genetics: > 135 mutations in fibrillin-1 gene (FBN1) on chromosome 15 which encodes a large glycoprotein (= component of extracellular microfibrils → connects elastic lamina to

adjacent endothelial cells + smooth muscle cells for structural integrity and coordination of contractile + elastic tension of vessel walls

Prevalence: 2–3÷10,000; M÷F = 1÷1

Path: disintegration and elastolysis of connective tissue with abnormal cross-linking of collagen fibers → aneurysm formation and dissection

Most common cause of death: aortic dissection, CHF, cardiac valvular disease

A. MUSCULOSKELETAL MANIFESTATIONS

- tall thin stature with long limbs, arm span greater than height (commonly basketball + volleyball players)
- muscular hypoplasia + hypotonicity
- scarcity of subcutaneous fat (= emaciated look)

√ generalized osteopenia

@ Skull

- elongated face

√ dolichocephaly

√ prominent jaw

√ high arched palate

@ Hand

√ **arachnodactyly** = elongation of phalanges + metacarpals:

- Steinberg sign = protrusion of thumb beyond confines of clenched fist (found in 1.1% of normal population)
- metacarpal index (averaging the 4 ratios of length of 2nd–5th metacarpals divided by their respective middiaphyseal width) > 8.8 (male) or 9.4 (female)

√ flexion deformity of 5th finger

@ Foot

√ pes planus (25%) / planovalgus ← increased ligamentous laxity

√ clubfoot

√ hallux valgus

√ hammer toes

√ disproportionate elongation of 1st digit of foot

@ Chest wall deformity (66%)

Cause: longitudinal overgrowth of ribs during periods of rapid growth (adolescence)

- reduction in lung capacity + forced vital capacity + forced expiratory volume in 1 second

√ **pectus excavatum** = retraction of lower sternum:

√ displacement of heart + lungs + diaphragm

Rx: surgery (Ravitch / Nuss procedure) for pectus index > 3.25 (dividing width of chest wall at its widest point by distance between posterior surface of sternum and anterior surface of spine) after maturation of skeleton

√ **pectus carinatum** = anterior protrusion of upper portion of sternum

Rx: surgery for cosmetic reasons

@ Spine

- ratio of measurements between symphysis and floor + crown and floor > 0.45

√ severe rigid progressive **scoliosis** (45–62%) / kyphosis (16%) / kyphoscoliosis

◊ Most frequent + potentially severe manifestation of Marfan syndrome → restriction

of lung volume
Age: young patient; M÷F = 1÷1
Rx: bracing for curvature < 25°; surgical correction for curvature > 40°
√ atlantoaxial translation (54%)
√ increased incidence of Schmorl nodes (Scheuermann disease) and spondylolisthesis
√ straight back syndrome
√ winged scapulae
√ **dural ectasia** (56–65%) of lumbosacral spine:
= ballooning / widening of dural sac ± nerve root sleeves
• usually asymptomatic
• occasionally back pain, headache, neurologic deficit
Location: lumbosacral spine
May be associated with: bone erosion, meningocele, arachnoid cyst
√ widening of interpediculate distance
√ posterior scalloping of vertebral body
√ dilatation of nerve root sleeve
√ expansion of sacral spinal canal
√ presacral + lateral sacral meningoceles
√ enlargement of sacral foramina

@ Joints
• ligamentous laxity + hypermobility + instability
√ premature osteoarthritis
√ patella alta
√ genu recurvatum
√ recurrent dislocations of patella, hip, clavicle, mandible
√ slipped capital femoral epiphysis
√ progressive protrusio acetabuli (16–27%) = invasion of acetabulum + femoral head into pelvic cavity
Location: bilateral > unilateral; F > M
• limited internal rotation + abduction of hip
√ increased center-edge angle of Wiberg > 40°
√ "teardrop" crossed by ilioischial line / obscured by femoral head

B. OCULAR MANIFESTATIONS
• bilateral ectopia lentis, usually upward + outward ← poor zonular attachments
• glaucoma, macrophthalmia
• hypoplasia of iris + ciliary body
• miosis (= contracted pupils) ← absence of dilatory effect of hypoplastic ciliary muscle
• myopia (= increased axial length of globe)
• retinal detachment
• strabismus, ptosis
• blue sclera
• megalocornea = flat thickened cornea

C. CARDIOVASCULAR MANIFESTATIONS (60–98%)
affecting mitral valve, ascending aorta, pulmonary artery, splenic + mesenteric arteries (occasionally)

◊ Dominant cause of death in 93%!
• chest pain, palpitations, shortness of breath, fatigue
• mid-to-late systolic murmur + one / more clicks
In ¹/³ associated with: congenital heart defect (ASD, incomplete coarctation)
@ Aorta (cause of death in 55%)
Histo: degeneration of elastic tissue in aortic media + cystic medial necrosis of smooth muscle cells

1. **Annuloaortic ectasia** (in 60–80% of adults
= uniform dilatation of all 3 sinuses of Valsalva with distal progression to sinotubular junction (= obliteration of normal sinotubular ridge) and aortic annulus
Histo: cystic medial necrosis
• leading cause of aortic valve insufficiency
√ "tulip bulb aorta" = symmetrical dilatation of aortic sinuses of Valsalva slightly extending into ascending aorta (58%)
√ triangular coaptation defect of valve cusps (during middiastolic closure at 70% of R-R interval of gated CT) = radiographic sign of aortic insufficiency
√ tethered valve cusps at midsystolic opening (= at 10% of R-R interval of a gated CT) ← dilatation of the sinus of Valsalva
Cx: aortic regurgitation (in 81% if root diameter > 5 cm; in 100% if root diameter > 6 cm), aortic root dissection, aortic root rupture
Prognosis: average age of death at 35 (75) years in untreated (treated) patients
Rx: prophylactic surgery at a sinus diameter of 55 mm in adulthood + 45–50 mm in childhood / aneurysm expansion of > 0.5–1 mm per year

The classic phenotypic appearance of the aorta in Marfan syndrome is annuloaortic ectasia with dilatation of aortic annulus and sinuses of Valsalva, and effacement of the sinotubular junction, resulting in a tulip-shaped configuration of the aortic root.

2. **Aortic aneurysm** (without annuloaortic ectasia)
√ fusiform dilatation of ascending aorta, rarely beyond innominate artery (rapid enlargement, young patient)
√ more rapid enlargement than atherosclerotic aneurysm
√ rarely intimal calcifications of the aortic wall
DDx: atherosclerotic aneurysm (older patient, less rapid enlargement, frequent thrombosis, intimal calcifications common)
3. **Aortic dissection**
CXR:
√ progressive aortic enlargement at serial imaging
√ enlarged aortic arch
√ double contour of aortic arch
√ displacement of intimal calcifications > 6 mm
√ new pericardial / pleural effusion
CT:
√ intimal flap + false lumen (in 70%) PATHOGNOMONIC
√ increased attenuation of thrombosed false lumen
√ internal displacement of intimal calcification

√ mediastinal / pericardial hematoma
√ infarction of organs supplied by branch vessels from the false lumen

Prognosis: recurrence common

Rx: composite graft to replace aortic root (Bentall procedure); antihypertensive medication

@ Mitral valve

Histo: myxomatous degeneration of valve leads to redundancy + laxness

• mid-to-late systolic murmur + one / more clicks

√ "floppy valve syndrome" (95%) = redundant chordae tendineae with mitral valve prolapse + regurgitation

Cx: (1) Mitral regurgitation

(2) Rupture of chordae tendineae (rare)

@ Coarctation (mostly not severe)

@ Pulmonary artery aneurysm and dilatation of pulmonary artery:
> 35 mm at root (in 43%) and > 28 mm at bifurcation

@ Cor pulmonale ← chest deformity

Criteria for Diagnosis of Marfan Syndrome (*Ghent Classification*)		
System Affected	*Major Criteria*	*Minor Criteria*
Cardio-vascular	√ dilatation of ascending aorta ± aortic regurgitation involving > 1 sinus of Valsalva √ dissection of descending aorta	√ dilatation / dissection of descending aorta < 50 years of age
Musculo-skeletal	√ scoliosis with curvature > 20° / spondylolisthesis √ pectus carinatum √ pectus excavatum requiring surgery √ acetabular protrusion √ reduced upper-to-lower segment ratio / arm span-to-height ratio > 1.05 √ wrist and thumb signs √ reduced extension of elbow < 170° √ medial displacement of medial malleolus causing pes planus	√ pectus excavatum of moderate severity √ joint hypermobility √ highly arched palate with crowding of teeth √ abnormal facial appearance (dolichocephaly, malar hypoplasia, enophthalmos, retrognathism, downslanting palpebral fissures)
CNS	√ lumbosacral dural ectasia	
Lung		√ spontaneous pneumothorax √ apical blebs
Eye	√ ectopia lentis	√ abnormal flat cornea √ increased axial length of globe √ hypoplastic iris / ciliary muscle causing decreased miosis
Skin		√ striae atrophicae √ recurrent / incisional hernia

D. PULMONARY MANIFESTATIONS (rare)

- √ lung cysts, bullae, blebs + diffuse apical bullous emphysema
- √ congenital malformation of bronchus + bronchiectasis
- √ recurrent spontaneous pneumothoraces (4–15%; 10 x times more common than in general population)
- √ interstitial parenchymal disease ± honeycombing

E. ABDOMINAL MANIFESTATION
√ recurrent biliary obstruction
F. INTEGUMENTUM
• striae atrophicae
√ recurrent incisional hernia

Prognosis: life expectancy close to normal; death (in 90% from aortic dissection, CHF, valvular disease)

DDx: (1) Homocystinuria (osteoporosis)
(2) Ehlers-Danlos syndrome
(3) Congenital contractural arachnodactyly (ear deformities, NO ocular / cardiac abnormalities)
(4) MEN 3 (medullary thyroid carcinoma, mucosal neuromas, pheochromocytoma, marfanoid habitus)

MELORHEOSTOSIS

= LÉRI DISEASE [melos, *Greek* = limb; rhein, *Greek* = flow]
[André Léri (1875–1930), pupil of Joseph Babinski and Pierre Marie, president of French Ophthalmological Society]
= rare sporadic mixed sclerosing bone dysplasia with disturbances in endochondral + intramembranous ossification characteristically appearing as flowing hyperostosis

Age: usually occult until adulthood; slow chronic progressive course in adults; rapid progression in children

Cause: developmental error of intramembranous bone formation related to mutation in LEMD3 on chromosome 12q, which codes for an inner nuclear membrane protein responsible for inhibition of transforming growth factor b + bone morphogenic protein

Path: overproduction of bone matrix + increased angiogenesis

Associated with: osteopoikilosis, osteopathia striata, tumors / malformations of blood vessels (hemangioma, vascular nevi, glomus tumor, AVM, aneurysm, lymphedema, lymphangiectasia)

• often asymptomatic incidental finding
• severe pain + limited joint motion (bone may encroach on nerves, blood vessels, or joints) → ± joint contracture
• thickening + fibrosis of overlying skin (resembling scleroderma); muscle atrophy (frequent)
• Dermatofibrosis lenticularis disseminata (**Buschke-Ollendorff syndrome)** = asymptomatic small flesh-colored to yellow dermal papules / coalescent plaques (in 25%) on buttocks, trunk, arms, skin folds
Age: usually in childhood; often during 1st year of life
Histo: connective tissue nevi with predominantly abnormal elastin / abnormal collagen

Location:
› common: in diaphysis of appendicular skeleton (lower > upper extremity); usually monomelic with at least two bones involved in dermatomal distribution (following spinal sensory nerve sclerotomes) / monostotic / polyostotic
› rare: in axial skeleton (skull, spine, ribs)

Site: entire cortex / limited to one side of cortex

Patterns: (1) osteoma-like, (2) myositis ossificans-like, (3) osteopathia striata-like, (4) classic dripping candle (5) mixed (overlap syndrome)

√ cortical + medullary hyperostosis of single / multiple adjacent bones:
  √ "dripping / flowing candle wax" sign = continuous / interrupted streaks / blotches of irregular cortical hyperostosis along tubular bone beginning at proximal end extending distally with slow progression
√ may cross joint with joint fusion
√ small opacities in scapula + hemipelvis (similar to osteopoikilosis)
√ discrepant limb length
√ flexion contractures of hip + knee
√ genu valgum / varus
√ dislocated patella
√ ossified soft-tissue masses (27%)

DDx: (1) Osteopoikilosis (generalized)
(2) Fibrous dysplasia (normal bone structure not lost, not as dense)
(3) Engelmann disease
(4) Hyperostosis of neurofibromatosis, tuberous sclerosis, hemangiomas
(5) Osteoarthropathy

MENISCAL TEAR

Cause: acute injury; degeneration related to aging; tear contributes to degenerative joint disease
Prevalence: increases with age
Type of cross-sectional tear pattern:
(a) vertical tear with longitudinal / radial / oblique surface pattern
(b) horizontal tear with longitudinal / oblique / cleavage surface pattern
(c) mixed pattern
Site of injury:
(a) medial meniscus (MM) in 45%:
  › no isolated tears of body
  › isolated tear of anterior horn in 2%
(b) lateral meniscus (LM) in 22%:
  › tear of posterior horn in 80% of all LM tears
  ◊ more common in acute injury of young individuals
  ◊ with ACL tear → increased prevalence of peripheral tears → decreased sensitivity for tear detection in LM
  › isolated tear of anterior horn in 16%
(c) both menisci involved in 33%
  › posterior horn of both menisci: constrained MM > LM
Associated with: ligamentous injury
• asymptomatic in up to 20% of older individuals
MR:
(a) DIRECT SIGNS (in the absence of prior surgery):
  √ increased signal extending to articular surface:
    √ "two-slice-touch" rule = ≥ 2 images with signals contacting the surface (94% PPV in

MM, 96% PPV in LM)
√ 1 image with signal contacting surface (43% PPV in MM, 18% PPV in LM) reported as **possible tear**

◊ Diagnosis of tear hinges on surface involvement!

◊ Truncation artifact + magic angle artifact may cause increased intrameniscal signal!

√ distortion of meniscal shape

(b) INDIRECT SIGNS

√ **meniscal cyst** (meniscal tear in 98–100%)
= synovial fluid accumulation in degenerated tissue
Location: intrameniscal, meniscocapsular margin, parameniscal
√ cyst in continuity with horizontal cleavage / complex meniscal tear

√ **meniscal extrusion**
= peripheral margin of meniscus extends ≥ 3 mm beyond edge of tibial plateau
N.B.: Exclude hypertrophic osteophyte for determination of outer margin!
Pathophysiology: disruption of circumferentially oriented collagen bundles → loss of meniscal hoop strength
Cause: root tear, complex tear, large radial tear, severe meniscal degeneration
◊ 76% of medial root tears have extrusion
◊ 39% of extrusions have medial root tears

√ **subchondral bone marrow edema**
= superficial edema adjacent to meniscal attachment site paralleling articular surface < 5 mm deep
@ medial meniscus (in 60%): 64–70% sensitive, 94–100% specific
√ posterior lip medial tibial plateau bone bruise (64% PPV for tear in posterior horn of MM)
@ lateral meniscus (in 90%): 88–89% sensitive, 98–100% specific

√ torn popliteomeniscal fascicle (79% PPV)

MR sensitivity, specificity, and accuracy:

Tear of	*Sensitivity*	*Specificity*	*Accuracy*
Medial meniscus	93%	88%	59–92%
Lateral meniscus	79%	96%	87–92%
Anterior cruciate lig.			91–96%
Posterior cruciate lig.			up to 99%

◊ MR has a high negative predictive value!
◊ 60–97% accuracy for arthrography
◊ 84–99% accuracy for arthroscopy (poor at posterior horn of medial meniscus)

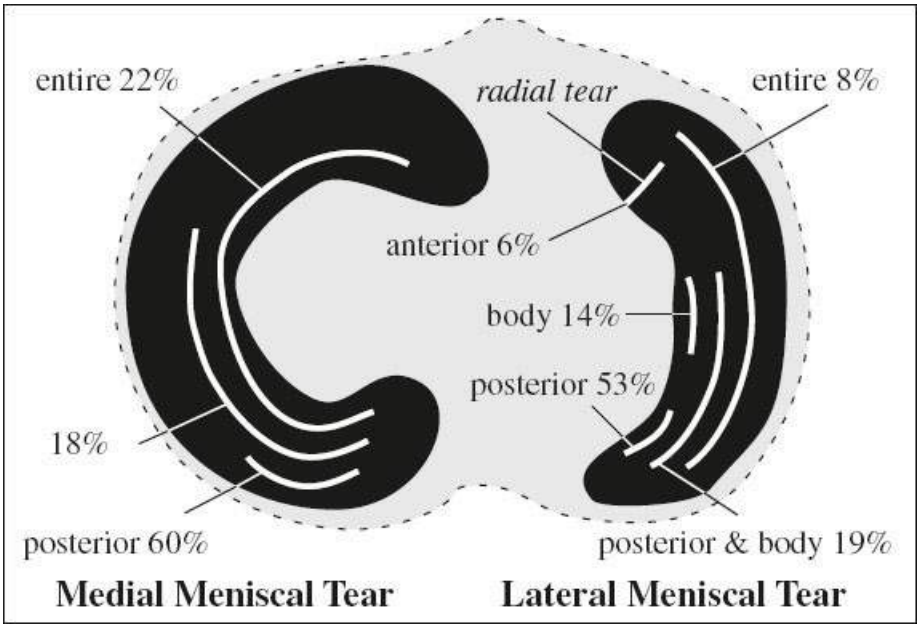
Interpretative / Diagnostic Error

(12% for experienced radiologist)
(a) anatomic error
FN: tear mistaken for normal anatomic structure
FP: normal anatomic structure mistaken for a tear
(b) technique-related error obscuring a tear

1. Arterial pulsation
2. Healed tear = retained abnormal increased SI
3. Magic-angle effect = collagen fibers oriented at 55° relative to magnetic field
   √ often seen in upslope medial segment of LM posterior horn

Lateral meniscus: 5.0% FN (middle + posterior horn)
1.5% FP (posterior horn)

Medial meniscus: 2.5% FN (posterior horn)
2.5% FP (posterior horn)



Pitfalls in Diagnosing Meniscal Tears

A. Normal variants simulating tears
   1. Superior recess on posterior horn of MM
   2. Popliteal hiatus
   3. Transverse ligament
   4. Meniscofemoral ligaments
   5. Oblique meniscomeniscal ligament (1–4%)
   6. Soft tissue between capsule + medial meniscus

B. Diskoid meniscus

C. Healed meniscus
   √ persistent grade 3 signal at least up to 6 months
   √ S/P meniscectomy (false-positive type IV finding)

D. Globular / linear increase in SI (grade 1 /2 signal)
   Cause:
   (a) internal mucinous degeneration in adults
   (b) normal vascularity in children + young adults
   (c) acute contusion in trauma

E. Tears difficult to detect on SAG images ← volume averaging
   (a) better depiction on COR images for

1. Small radial tear
2. Horizontal tear of body
3. Bucket-handle tear

(b) AXIAL images helpful for detection of
1. Small radial tear
2. Displaced tear
3. Peripheral tear of posterior horn of LM

Easily Missed Meniscal Injury
1. Radial tears
2. Displaced flap tears
3. Meniscocapsular separation

Horizontal Meniscal Tear
= CLEAVAGE TEAR
= tear oriented parallel to tibial plateau
› involving either articular surface / central free edge
› dividing meniscus into superior + inferior halves

Cause: degenerative in patients > 40 years

Associated with: parameniscal cyst formation ← direct communication with joint fluid

√ horizontally oriented line of high signal intensity contacting meniscal surface / free edge

Rx: débridement of smaller unstable meniscal leaf + decompression of associated parameniscal cyst

Longitudinal Meniscal Tear
= tear oriented parallel to long axis / outer margin of meniscus + perpendicular to tibial plateau dividing meniscus into central + peripheral halves

Cause: significant knee trauma in younger patient

MR Classification of Meniscal Signal Intensity vs. Injury

Grade	*Type*	*MR Finding*	*PPV for Tear*
0	0	normal meniscus	1%
1	I	globular / punctate intrameniscal signal	2%
2	II	linear signal not extending to surface	5%
	III	short tapered apex of meniscus	23%
	IV	truncated / blunted apex of meniscus	71%
3	V	signal extending to only one surface	85%
3	VI	signal extending to both surfaces	95%
3	VII	comminuted reticulated signal pattern	82%

Site: propensity to involve peripheral $^{1}/_{3}$ of meniscus + posterior horn (difficult diagnosis for LM because of complex attachment anatomy)

√ vertically oriented line of high SI contacting one / both articular surfaces (full / partial-thickness tear)

√ no involvement of free edge of meniscus
√ disruption of posterosuperior popliteomeniscal fascicle = high PPV for tear of LM posterior horn
Close association with: ACL tear (in 90% for MM, in 83% for LM)
Rx: may be amenable to repair if
(a) in vascularized (peripheral) outer 3–5 mm
(b) between 7 and 40 mm long

Radial Tear (6%)
= TRANSVERSE TEAR
= tear perpendicular to tibial plateau + long axis / free edge of meniscus → disruption of meniscal hoop strength → dramatic loss of function + possible meniscal extrusion
• tears < 3 mm may be asymptomatic
Site: posterior horn of medial meniscus, junction of anterior horn + body of lateral meniscus
√ cleft oriented perpendicular to free edge on AXIAL image:
√ "truncated triangle" sign / "ghost meniscus" sign" ← tear through horn on COR view
√ "cleft" sign ← tear through body on SAG view
√ "marching cleft" sign
√ blunting of the inner margin of meniscus (if image plane parallel to tear)
√ poorly defined meniscus with diffusely increased SI (if tear extends to outer margin)
√ usually seen on only 1 image = normal meniscus in adjacent sections
√ discrete vertical focus of increased SI (if image plane perpendicular to tear)
Cx: lack of resistance to hoop stresses
Rx: frequently not repaired because of its location within avascular "white zone" → low likelihood of healing / regaining significant function

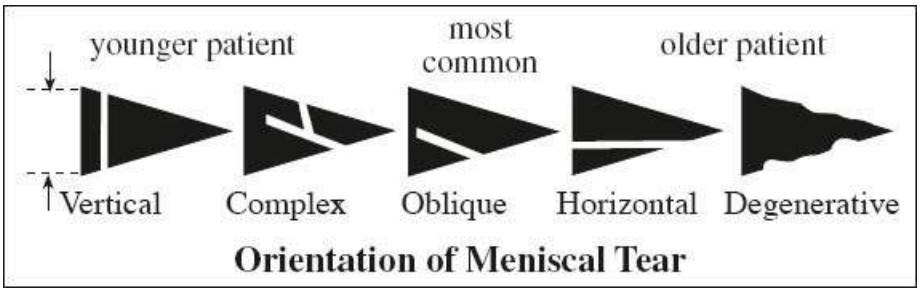
Meniscal Root Tear
= radial-type tear
High association with: meniscal extrusion, particularly in MM
Incidence: increased if ACL tear present
√ root should course over its respective tibial plateau on at least one COR image
√ posterior root of MM should be detected just medial to PCL on SAG image (otherwise suspect root tear)

Complex Meniscal Tear
= combination of radial, horizontal, longitudinal components → frequent fragmentation of meniscus

Parrot Beak Tear
= free edge tear with vertical + horizontal component

Truncation Sign & Ghost Sign *(on SAG Views)*

Marching Cleft Sign *(on SAG View)*
marching from free edge into substance



Orientation of Meniscal Tear

Cause: usually degenerative
Site: in body of lateral meniscus near the junction of body + posterior horn

Displaced Meniscal Tear

Free Meniscal Fragment

Flap Tear
= composite of radial tear that curves into longitudinal tear
Cause: traumatic, at times degenerative
Frequency: most common type of tear
N.B.: Search for displaced fragment in the absence of prior surgery / radial-type tear / severe underlying chondrosis if a foreshortened meniscus is present
Origin of flap: medial÷lateral meniscus = 7÷1
Site: common in midportion of medial meniscus
Location of displaced fragment:
@ Medial meniscus
› posteriorly near / posterior to PCL (²/³)
› intercondylar notch / superior recess (¹/³)
@ Lateral meniscus
› posterior joint line (½)
› lateral recess (½)
• persistent pain, potential knee locking
√ both horizontal and vertical components
√ commonly extending to inferior surface of meniscus

Rx: partial meniscectomy

Bucket-handle Tear

= longitudinal vertical tear with attached unstable central migration of inner "handle" fragment

MR sensitivity: 60–88%

Cause: traumatic

Age: frequently in young individuals

Prevalence: 9–19% of symptomatic patients; 10% of all meniscal tears

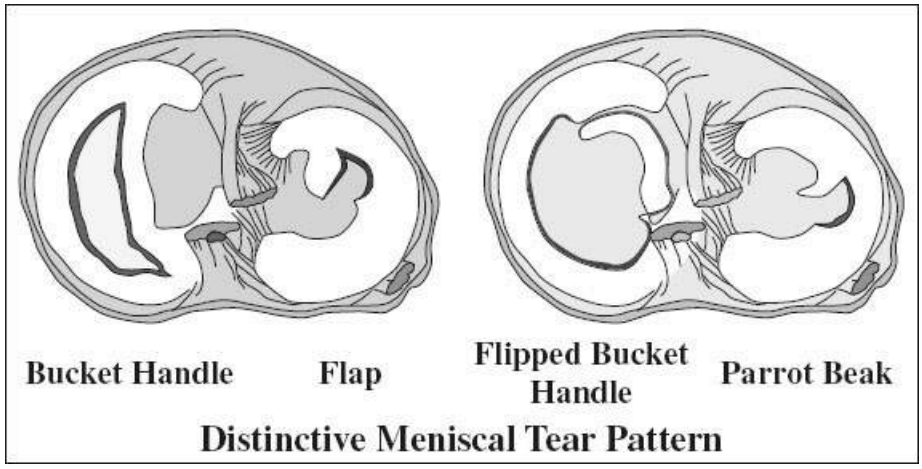
Origin of handle flap: medial÷lateral meniscus = 7÷1

• locked knee, lack of full knee extension

√ "absent bow-tie" sign (SAG image) = peripheral image fails to demonstrate normal bow-tie configuration on > 2 consecutive images (71–98% sensitive, 63% specific)

DDx: radial tear of body, macerated meniscus, prior partial meniscectomy (in small / pediatric patient)

√ "fragment-in-notch" sign (COR image) = displaced fragment in intercondylar notch



√ "double PCL" sign (SAG image) = medial meniscal fragment displaced into notch between PCL + medial tibial eminence oriented parallel to PCL (> 98% specific, 27–53% sensitive, 93% PPV) ← intact ACL acts as barrier against further lateral displacement

DDx: ligament of Humphry (smaller and thinner, very close to PCL); oblique meniscomeniscal ligament, intercondylar osseous bodies

√ double anterior horn

√ "flipped meniscus" sign

√ disproportionately small posterior horn = hypoplastic / truncated anterior + posterior horns on sagittal image

√ "double ACL" sign (LM) = fragment posterior to ACL

Rx: arthroscopic / surgical repair (reattachment / excision)

Meniscal Fraying

= surface irregularity along meniscal free edge without discrete tear

√ loss of sharp tapered central edge
√ subtle ill-defined horizontally oriented increased intrameniscal signal intensity contacting articular surface in posterior root
DDx: shallow partial-thickness tear / fraying / surrounding synovitis

Meniscocapsular Separation

= Peripheral Tear
= tearing of peripheral attachments of meniscus
√ linear region of fluid separating meniscus from capsule
√ uncovering of a portion of tibial plateau owing to inward movement of separated meniscus

MESOMELIC DWARFISM

= heritable bone dysplasia with shortening of intermediate segments (radius + ulna or tibia + fibula)

A. Langer type autosomal recessive
• mental impairment
√ mesomelic shortening of limbs
√ hypoplasia of ulna + fibula
√ hypoplasia of mandible with short condyles

B. Nievergelt type autosomal dominant
√ severe mesomelic shortening of lower limbs
√ marked thickening of tibia + fibula in central portion
√ clubfoot (frequent)

C. Reinhardt type: autosomal dominant

D. Robinow type: autosomal dominant

E. Werner type: autosomal dominant

F. Lamy-Bienenfeld type autosomal dominant
• ligamentous laxity
√ shortening of radius + ulna + tibia
√ absent fibula
√ normal femur + humerus

√ shortening of all long bones at birth, most marked in tibia + radius
√ modeling deformity with widening of diaphysis
√ mild to moderate bowing
√ hypoplasia of fibula with absent lateral malleolus
√ short + thick ulna with hypoplastic distal end
√ Madelung deformity of wrist
√ hypoplasia of a vertebral body may be present

METAPHYSEAL CHONDRODYSPLASIA

= severe short-limbed dwarfism
√ metaphyseal flaring (Erlenmeyer flask deformity) extending into diaphysis

A. Schmid type (most common)
autosomal dominant

- waddling gate

Distribution: more marked in lower limbs; mild involvement of hands + wrists

√ shortened bowed long bones
√ widened epiphyseal growth plates
√ irregular widened cupped metaphyses
√ coxa vara
√ genu varum

DDx: vitamin D–refractory rickets

B. McKusick type

autosomal recessive (eg, in Amish)

- sparse brittle hair, deficient pigmentation
- normal intelligence

√ shortening of long bones with normal width
√ cupped + widened metaphyses with lucent defects
√ short middle phalanges + narrow distal phalanges becoming triangular and bullet-shaped (more frequent in hands than feet)
√ widened costochondral junctions + cystic lucencies

C. Jansen type (less common)

sporadic occurrence with wide spectrum

- intelligence normal / retarded
- serum calcium levels often elevated

Distribution: symmetrical involvement of all long + short tubular bones

√ widened epiphyseal plates
√ expanded irregular + fragmented metaphyses (unossified cartilage extending into diaphyses)

DDx: rickets

D. Pyle disease = Metaphyseal dysplasia

- often tall
- often asymptomatic

Distribution: major long bones, tubular bones of hands, medial end of clavicle, sternal end of ribs, innominate bone

√ splaying of proximal + distal ends of long bones with thinned cortex
√ relative constriction of central portion of shafts
√ craniofacial hyperostosis
√ genu valgum

METASTASES TO BONE

◊ 15–100 times more common than primary skeletal neoplasms!

If primary known		If primary unknown	
Breast	35%	Prostate	25%
Prostate	30%	Lymphoma	15%
Lung	10%	Breast	10%
Kidney	5%	Lung	10%
Uterus	2%	Thyroid	2%
Stomach	2%	Colon	1%
Others	13%		

SOLITARY BONE LESION

◊ Of all causes only 7% are due to metastasis

◊ In patients with known malignancy solitary bone lesions are due to metastasis (55%), due to trauma (25%), due to infection (10%)

Location: axial skeleton (64–68%), ribs (45%), extremities (24%), skull (12%)

mnemonic: **S**everal **K**inds **O**f **H**orribly **N**asty **T**umors **L**eap **P**romptly **T**o **B**one
Sarcoma, **S**quamous cell carcinoma
Kidney tumor
Ovarian cancer
Hodgkin disease
Neuroblastoma
Testicular cancer
Lung cancer
Prostate cancer
Thyroid cancer
Breast cancer

Breast cancer: extensive osteolytic lesions; involvement of entire skeleton; pathologic fractures common

Thyroid / kidney: often solitary; rapid progression with bone expansion (bubbly); frequently associated with soft-tissue mass (distinctive)

Rectum / colon: may resemble osteosarcoma with sunburst pattern + osteoblastic reaction

Hodgkin tumor: upper lumbar + lower thoracic spine, pelvis, ribs; osteolytic / occasionally osteoblastic lesions

Osteosarcoma: 2% with distant metastases, adjuvant therapy has changed the natural history of the disease in that bone metastases occur in 10% of osteosarcomas without metastases to the lung

Ewing sarcoma: extensive osteolytic / osteoblastic reaction (13% with distant metastases)

Neuroblastoma: extensive destruction, resembles leukemia (metaphyseal band of rarefaction), mottled skull destruction + increased intracranial pressure, perpendicular spicules of bone

Mode of spread: through bloodstream / lymphatics / direct extension

Location: predilection for marrow-containing skeleton (skull, spine, ribs, pelvis, humeri, femora)

√ single / multiple lesions of variable size

√ usually nonexpansile

√ joint spaces + intervertebral spaces preserved (cartilage resistant to invasion)

Osteolytic Bone Metastases

Most common primary:

1. Lung
2. Breast
3. Thyroid
4. Kidney
5. Colon
6. Neuroblastoma (in childhood)

√ may begin in spongy bone (associated with soft tissue mass in ribs)
√ vertebral pedicles often involved (not in multiple myeloma)

Osteoblastic Bone Metastases

= evidence of slow-growing neoplasm

Most common primary:

1. Prostate carcinoma (elderly man)
2. Breast cancer (woman)
3. Lymphoma
4. Carcinoid tumor
5. Mucinous adenocarcinoma of GI tract
6. Pancreatic adenocarcinoma
7. Transitional cell (bladder) carcinoma
8. Neuroblastoma
9. Medulloblastoma (in childhood)

mnemonic: 6 **B**ees **L**ick **P**ollen

Brain (medulloblastoma)
Breast
Bronchus (especially carcinoid)
Bone (osteogenic carcinoma)
Bowel (mucinous)
Bladder
Lymphoma
Prostate

√ frequent in vertebrae + pelvis
√ may be indistinguishable from Paget disease

Mixed Bone Metastases

breast, prostate, lymphoma

Expansile / Bubbly Bone Metastases

kidney, thyroid

Permeative Bone Metastases

Burkitt lymphoma, mycosis fungoides

Bone Metastases with "Sunburst" Periosteal Reaction

= infrequent presentation in prostatic carcinoma, retinoblastoma, neuroblastoma (skull), GI tract cancer

Bone Metastases with Soft-tissue Mass

thyroid, kidney

Calcifying Bone Metastases

mnemonic: BOTTOM

Breast
Osteosarcoma
Testicular
Thyroid
Ovary
Mucinous adenocarcinoma of GI tract

Skeletal Metastases in Children

1. Neuroblastoma (most often): diffuse / focal
2. Lymphoma
3. Rhabdomyosarcoma
4. Ewing sarcoma
5. Retinoblastoma
6. Hepatoma

Skeletal Metastases in Adult

mnemonic: **C**ommon **B**one **L**esions **C**an **K**ill **T**he **P**atient

Colon
Breast
Lung
Carcinoid
Kidney
Thyroid
Prostate

Role of Bone Scintigraphy in Bone Metastases

Pathophysiology: accumulation of tracer at sites of reactive bone formation
False-negative scan: very aggressive metastases
False-positive scan: degeneration, healing fractures, metabolic disorders
Baseline bone scan:

(a) high sensitivity for many metastatic tumors to bone (particularly carcinoma of breast, lung, prostate); 5% of metastases have normal scan; 5–40% occur in appendicular skeleton
(b) substantially less sensitive than radiographs in infiltrative marrow lesions (multiple myeloma, neuroblastoma, histiocytosis)
(c) screening of asymptomatic patients
› useful in: prostate cancer, breast cancer

› not useful in: non–small-cell bronchogenic carcinoma, gynecologic malignancy, head and neck cancer

√ multiple asymmetric areas of increased uptake

√ axial > appendicular skeleton (dependent on distribution of bone marrow); vertebrae, ribs, pelvis involved in 80%

√ superscan in diffuse bony metastases

Follow-up bone scan:

√ stable scan = suggestive of relatively good prognosis

√ increased activity in:

(a) enlargement of bone lesions / appearance of new lesions indicate disease progression

(b) "healing flare" phenomenon (in 20–61%) = transient increase in lesion activity ← healing under antineoplastic treatment concomitant with increased sclerosis, detected at 3.2 ± 1.4 months after initiation of hormonal / chemotherapy, of no additional favorable prognostic value

(c) avascular necrosis particularly in hips, knees, shoulders caused by steroid therapy

(d) osteoradionecrosis / radiation-induced osteosarcoma

√ decreased activity in:

(a) predominately osteolytic destruction

(b) metastases under radiotherapy; as early as 2–4 months with minimum of 2000 rads

DDx: pulmonary metastasis (SPECT helpful in distinguishing nonosseous lung from overlying rib uptake)

Role of Bone Scintigraphy in Breast Cancer

Routine preoperative bone scan not justified:

Stage I : unsuspected metastases in 2%, mostly single lesion

Stage II : unsuspected metastases in 6%

Stage III : unsuspected metastases in 14%

Follow-up bone scan:

At 12 months no new cases; at 28 months in 5% new metastases; at 30 months in 29% new metastases

Conversion from normal:

Stage I : in 7%

Stage II : in 25%

Stage III : in 58%

◊ With axillary lymph node involvement conversion rate 2.5 x that of those without!

◊ Serial follow-up examinations are important to assess therapeutic efficacy + prognosis!

Role of Bone Scintigraphy in Prostate Cancer

Stage B: 5% with skeletal metastases

Stage C: 10% with skeletal metastases

Stage D: 20% with skeletal metastases

Test sensitivities for detection of osseous metastases:

(a) scintigraphy 1.00
(b) radiographic survey 0.68
(c) alkaline phosphatase 0.50
(d) acid phosphatase 0.50

Role of Magnetic Resonance in Bone Metastases

= ideal for bone marrow imaging ← high contrast between bone marrow fat + water-containing metastatic deposits

◊ Metastases are most often found in sites of dominant hematopoietic marrow because of its rich vascular supply!

in children: proximal + distal metaphyses of long bones, flat bones, spine

in adults: calvarium, spine, flat bones, proximal humeral + femoral metaphyses

(1) Focal lytic lesion (usual):
- √ hypointense on T1WI (more conspicuous when surroundings contain large number of fat cells)
- √ hyperintense on T2WI / STIR ← increased water content of hypercellular tumor tissue
- √ occasionally surrounded by mild edema

(2) Focal sclerotic lesion (eg, medulloblastoma, retinoblastoma):
- √ hypointense on T1WI + T2WI ← bone production

(3) Diffuse heterogeneous lesions (eg, neuroblastoma):
- √ inhomogeneously hypointense on T1WI + hyperintense on T2WI

(4) Diffuse homogeneous lesions:
- √ homogeneously hypointense on T1WI + hyperintense on T2WI

METATROPIC DYSPLASIA

= HYPERPLASTIC ACHONDROPLASIA = METATROPIC DWARFISM

metatropic = "changeable" (change in proportions of trunk to limbs over time ← developing kyphoscoliosis in childhood)

• longitudinal double skin fold overlying coccyx

√ long bones short with dumbbell-like / trumpet-shaped configuration (= exaggerated metaphyseal flaring)

√ "hourglass" phalanges (= short phalanges with widened ends)

√ wide separation of major joint spaces (thick articular cartilage)

√ delayed ossification of flat irregular epiphyses

@ Chest
- √ cylindrical narrowed elongated thorax
- √ short + wide ribs
- √ pectus carinatum

@ Vertebrae
- √ odontoid hypoplasia with atlantoaxial instability
- √ progressive kyphoscoliosis
- √ platyspondyly + very wide intervertebral spaces
- √ wedge- / keel-shaped vertebral bodies

@ Pelvis
- √ coccygeal appendage similar to a tail (rare but CHARACTERISTIC)

√ short squared iliac bones + irregular acetabula
√ narrowed greater sciatic notch

Prognosis: compatible with life; increasing disability from kyphoscoliosis

DDx: achondroplasia, mucopolysaccharidoses

MORTON NEUROMA

= INTERDIGITAL NEUROMA (neuroma is a misnomer)

= benign nonneoplastic lesion due to fibrosis + degeneration around a plantar digital nerve

Age: highest prevalence in 5th + 6th decade; M÷F = 1÷4

Path: perineural fibrosis entrapping a plantar digital nerve

Often associated with: intermetatarsal bursitis

Histo: dense collagenous + fibrous tissue

- numbness; burning / tingling electric forefoot pain increasing with activity + wearing of narrow shoes
- Mulder sign = painful palpable click when metatarsal heads are squeezed together with one hand + involved metatarsal space simultaneously compressed between thumb and index finger of the other hand

Location: plantar side of deep transverse intermetatarsal ligament beyond MTP joint

Site: typically 2nd / 3rd intermetatarsal space (rarely 1st / 4th)

√ splaying of metatarsal heads in large lesion

MR (87% sensitive, 100% specific):

◊ Best depicted prone (positional changes)

√ small well-demarcated teardrop-shaped mass isointense to muscle on T1WI + hypointense to fat on T2WI

√ variably hyperintense on gadolinium-enhanced fat-suppressed T1WI (easier to see)

√ ± fluid in intermetatarsal bursa (vertically oriented between metatarsal heads)

Rx: conservative treatment; surgical excision for neuromas > 5 mm in transverse diameter (more commonly symptomatic)

MUCOPOLYSACCHARIDOSES

= inherited lysosomal storage disorder from deficiency of specific lysosomal enzymes involved in degradation of mucopoly-saccharides (= inability to break down glycosaminoglycan)

Types:

Type I = Hurler
Type II = Hunter
Type III = Sanfilippo
Type IV = Morquio (most common)
Type V = Scheie
Type VI = Maroteaux-Lamy
Type VII = Sly

◊ All autosomal recessive except for Hunter (X-linked)!

Associated with: valvular heart disease

- corneal clouding; elevation of glycosaminoglycan in urine

• mental retardation (prominent in types I, II, III, VII)
• skeletal involvement dominates in types IV and VI
√ scaphocephaly, macrocephaly; thick calvarium; hypertelorism
√ platyspondyly with kyphosis + dwarfism
√ irregularity at anterior aspect of vertebral bodies
√ atlantoaxial subluxation + instability ← laxity of transverse ligament / hypoplasia or absence of odontoid
√ limb contractures
√ broad hands + brachydactyly
√ hepatosplenomegaly
@ Brain
√ brain atrophy
√ varying degrees of hydrocephalus
√ dilated Virchow-Robin spaces (from accumulation of glycosaminoglycan) resulting in cribriform appearance of white matter, corpus callosum and basal ganglia
√ increased SI of white matter surrounding Virchow-Robin spaces on T2WI + FLAIR ← edema, gliosis, de- / dysmyelination
√ ± arachnoid cyst ← meningeal glycosaminoglycan deposition
Cx: cord compression at atlantoaxial joint (types IV + VI)
Dx: combination of clinical features, radiographic abnormalities correlated with genetic + biochemical studies
Prenatal Dx: occasionally successful analysis of fibroblasts cultured from amniotic fluid
DDx: Gaucher disease, Niemann-Pick disease

Hurler Syndrome

[Gertrud Hurler (1889–1965), pediatrician in München-Neuhausen, Germany]
= GARGOYLISM = PFAUNDLER-HURLER DISEASE = MPS I-H
[Meinhard von Pfaundler (1872–1947), Austrian pediatrician and director of the university children's hospital in München]
= autosomal recessive disease
Cause: homozygous for MPS III gene with excess chondroitin sulfate B ← deficient X-L iduronidase (= Hurler corrective factor)
Prevalence: 1÷10,000 births
Age: usually appears > 1st year
• dwarfism; progressive mental deterioration after 1–3 years
• large head; sunken bridge of nose; hypertelorism
• early corneal clouding progressing to blindness
• "gargoyle" features = everted lips + protruding tongue
• teeth widely separated + poorly formed
• progressive narrowing of nasopharyngeal airway
• protuberant abdomen ← dorsolumbar kyphosis + hepatosplenomegaly
• urinary excretion of chondroitin sulfate B (dermatan sulfate) + heparan sulfate
• Reilly bodies (metachromic granules) in white blood cells or bone marrow cells
@ Skull (earliest changes > 6 months of age)
√ frontal bossing

- √ calvarial thickening
- √ premature fusion of sagittal + lambdoid sutures
- √ deepening of optic chiasm
- √ enlarged J-shaped sella (undermining of anterior clinoid process)
- √ small facial bones
- √ wide mandibular angle + underdevelopment of condyles
- √ communicating hydrocephalus

@ Extremities
- √ thick periosteal cloaking of long-bone diaphyses (early changes)
- √ swelling / enlargement of diaphyses + cortical thinning (← dilatation of medullary canal) + tapering of either end: distal humerus, radius, ulna, proximal ends of metacarpals
- √ deossification with heterogeneous bone density + course trabeculation ← deposition of accumulated precursor metabolites in bone marrow
- √ flexion deformities of knees + hips
- √ trident hands; clawing (occasionally)
- √ delayed maturation of irregular carpal bones

@ Spine
- √ thoracolumbar kyphosis with lumbar gibbus
- √ oval centra with normal / increased height + anterior beak at T12/L1/L2
- √ long slender pedicles
- √ proximally long slender ribs at level of neck and wide distally = spatulate rib configuration

@ Pelvis
- √ widely flared iliac wings with inferior tapering
- √ constriction of iliac bones
- √ coxa valga

Prognosis: death by age 10–15 years

Morquio Syndrome

= KERATOSULFATURIA = MPS IV (most common type)
= autosomal recessive; excess keratosulfate
Prevalence: 1÷40,000 births
Etiology: N-acetyl-galactosamine-6-sulfatase deficiency resulting in defective degradation of keratin sulfate (mainly in cartilage, nucleus pulposus, cornea)
Age: normal at birth; skeletal changes manifest within first 18 months; M÷F = 1÷1

- excessive urinary excretion of keratan sulfate
- normal intelligence; muscular weakness + hypotonia
- ligamentous laxity, but joint stiffness; progressive deafness
- short-trunk dwarfism (< 4 feet tall)
- semicrouching stance + knock knees ← flexion deformities of knees + hips
- head thrust forward + sunken between high shoulders
- corneal clouding evident around age 10
- coarse face with short nose, broad mouth, widely spaced teeth with thin enamel

@ Skull

√ mild dolichocephaly
√ hypertelorism
√ poor mastoid air cell development
√ short nose + depression of bridge of nose
√ prominent maxilla

@ Chest
√ increased AP diameter + marked pectus carinatum (horizontal protuberant sternum)
√ slight lordosis with wide short ribs
√ bulbous costochondral junctions
√ failure of fusion of sternal segments

@ Spine
√ hypoplasia / absence of odontoid process of C2
√ C1-C2 instability with anterior (life-threatening) atlanto-axial subluxation + progressive disabling myelopathy
√ thick C2-body with narrowing of vertebral canal
√ atlas close to occiput / posterior arch of C1 within foramen magnum
√ platyspondyly = universal vertebra plana esp. affecting lumbar spine by age 2–3 years (DDx: normal height in Hurler syndrome)
√ ovoid vertebral bodies with central anterior beak / tongue at lower thoracic / upper lumbar vertebrae
√ mild gibbus at thoracolumbar transition = low dorsal kyphosis
√ exaggerated lumbar lordosis
√ widened intervertebral disk spaces

Mucopolysaccharidoses

Type	*Eponym*	*Inheritance*	*Enzyme Deficiency*	*Urinary Glycosaminoglycan*	*Neurologic Signs*
I-H	Hurler	autosomal recessive	alpha-L-iduronidase	dermatan sulfate	marked
II	Hunter	X-linked recessive	iduronate sulfatase	dermatan / heparan sulfate	mild to moderate
III	Sanfilippo	autosomal recessive		heparan sulfate	mental deterioration
	A		heparan sulfate sulfatase		
	B		N-acetyl-alpha-D-glucosaminidase		
	C		alpha-glucosamine-N-acetyl-transferase		
	D		N-acetylglucosamine-6-sulfate sulfatase		
IV	Morquio	autosomal recessive	N-acetylgalactosamine-6-sulfate sulfatase	keratan sulfate	none
	A–D		beta-galactosidase		
I-S(V)	Scheie	autosomal recessive	alpha-L-iduronidase	heparan sulfate	none
VI	Maroteaux-Lamy	autosomal recessive	arylsulfatase B	dermatan sulfate	none
VII	Sly	autosomal recessive	beta-glucuronidase	dermatan / heparan sulfate	variable

@ Pelvis
√ “goblet-shaped” / “wineglass” pelvis = constricted iliac bodies + elongated pelvic inlet + broad flat “flared” iliac wings
√ oblique hypoplastic acetabular roofs

@ Femur
√ initially well-formed femoral head epiphysis, then involution + fragmentation by age 3–6 years
√ lateral subluxation of femoral heads; later hip dislocation

√ wide femoral neck + coxa valga deformity

@ Tibia

√ delayed ossification of lateral proximal tibial epiphysis

√ sloping of superior margin of tibial plateau laterally + severe genu valgum

@ Hand & foot

√ short bones of forearm with widening of proximal ends

√ delayed appearance + irregularity of carpal centers

√ small irregular carpal bones

√ proximally pointed short metacarpals 2–5

√ enlarged joints; hand + foot deformities (flat feet)

√ ulnar deviation of hand

Cx: cervical myelopathy (traumatic quadriplegia / leg pains / subtle neurologic abnormality) most common cause of death ← C2 abnormality; frequent respiratory infections (from respiratory paralysis)

Rx: early fusion of C1–C2

Prognosis: may live to adulthood (3rd–4th decade)

DDx: (1) Hurler syndrome (normal / increased vertebral height; vertebral beak inferior)

(2) Spondyloepiphyseal dysplasia (autosomal dominant, present at birth, absent flared ilia / deficient acetabular ossification, small acetabular angle, deficient ossification of pubic bones, varus deformity of femoral neck, minimal involvement of hand + foot, myopia)

MULTIPLE EPIPHYSEAL DYSPLASIA

= FAIRBANK DISEASE

[Harold Arthur Thomas Fairbank (1876–1961), English orthopedic surgeon at King's College Hospital, London]

= ? tarda form of chondrodystrophia calcificans congenita

√ mild limb shortening

√ irregular mottled calcifications of epiphyses (in childhood + adolescence)

√ epiphyseal irregularities + premature degenerative joint disease, especially of hips (in adulthood)

√ short phalanges

DDx: Legg-Perthes disease, hypothyroidism

MULTIPLE MYELOMA

= hematologic malignancy characterized by monoclonal proliferation of mature plasma cells

Precursor: premalignant asymptomatic monoclonal gammopathy of undetermined significance (MGUS) with cumulative risk for progression to multiple myeloma of 1% per year / Waldenström macroglobulinemia / lymphoma / primary amyloidosis / chronic lymphocytic leukemia

Frequency: 10% of all hematologic malignancies

◊ Most common primary malignant neoplasm in adults!

◊ Most frequent primary neoplasm of bone marrow!

◊ Most common primary osseous malignancy in elderly

◊ 2nd most common hematologic malignancy after NHL

Incidence: 22,350 new patients + 10,710 deaths in USA (2013)

Histo: normal / pleomorphic plasma cells (not PATHOGNOMONIC), may be mistaken for lymphocytes (lymphosarcoma, reticulum cell sarcoma, Ewing tumor, neuroblastoma)

(a) diffuse infiltration: myeloma cells intimately admixed with hematopoietic cells

(b) tumor nodules: displacement of hematopoietic cells by masses entirely composed of myeloma cells

Median age: 66 years (range, 5th–8th decade); 98% > 40 years; rare < 30 years; M÷F = 2÷1

Genetics: deletion of chromosome 13q14 (del13q14), amplification of chromosome 1q21 (amp1q21), deletion of chromosome 17p13 (del17p13)

Forms: (a) DISSEMINATED FORM: > 40 years of age (98%); M÷F = 3÷2

(b) SOLITARY FORM: mean age 50 years

Clinical manifestation:

(1) Plasma cell leukemia = aggressive form with a proportion of circulating plasma cells of > 20%

(2) Nonsecretory multiple myeloma (3%) = positive bone marrow biopsy without elevated level of M protein

- Symptomatic multiple myeloma:
  mnemonic: CRAB
  - **C**alcium elevation = hypercalcemia (30–50%)
  - **R**enal insufficiency (55%)
  - **A**nemia = normochromic normocytic anemia (62–73%)
  - **B**one abnormalities (lysis, osteopenia), bone pain (68%)
- fatigue, weight loss
- cutaneous / subcutaneous nodules (in < 5%)
- RBC rouleaux formation
- proteinuria (88%), Bence-Jones proteinuria (50%):
  - ↑ globulin production (= monoclonal gammopathy) of heavy chain (typically IgG or IgA) and light chain (typically κ)

Location:

A. DISSEMINATED FORM:
scattered; axial skeleton predominant site; vertebrae (50%) > ribs > skull > pelvis > long bones (distribution correlates with normal sites of red marrow)

B. SOLITARY PLASMACYTOMA OF BONE (< 5%):
vertebrae > pelvis > skull > sternum > ribs
→ progression to multiple myeloma within 3 years

C. SPINAL PLASMA CELL MYELOMA
√ sparing of posterior elements (no red marrow) (DDx: metastatic disease)
√ paraspinal soft-tissue mass with extradural extension
√ scalloping of anterior margin of vertebral bodies (osseous pressure from adjacent enlarged lymph nodes)

Extraosseous manifestations of multiple myeloma are radiologically detectable in 10–16%, most commonly involving lymph nodes, pleura, and liver.

Staging (Durie & Salmon Plus System):

◊ Detection of bone lesions at conventional radiography best correlates with measured myeloma cell mass

Stage	*Serum creatinine*	*End organ damage*	*Imaging*
IA	< 2.0 mg/dL	-	normal / limited disease / plasmacytoma
IB	> 2.0 mg/dL	+	mild diffuse disease < 5 focal lesions
IIA, B		+	moderate diffuse disease 5–20 focal lesions
IIIA, B		+	severe diffuse disease > 20 focal lesions
≥ 10% plasma cells for all stages; end organ damage = elevated blood calcium level / renal insufficiency / anemia / bone abnormalities			

Spread: to extramedullary sites (in 70%)

√ generalized osteopenia only (15%) with accentuation of trabecular pattern, especially in spine (early)
√ widespread punched-out osteolytic lesions (skull, long bones) with endosteal scalloping and of uniform size
√ diffuse osteolysis (pelvis, sacrum)
√ expansile osteolytic lesions (ballooning) in ribs, pelvis, long bones
√ soft-tissue mass adjacent to bone destruction (= extrapleural + paraspinal mass adjacent to ribs / vertebral column)
√ periosteal new-bone formation exceedingly rare
√ involvement of mandible (rarely affected by metastatic disease)
√ sclerosis may occur after chemotherapy, radiotherapy, fluoride administration
√ sclerotic form of multiple myeloma (1–3%)
(a) solitary sclerotic lesion: frequently in spine
(b) diffuse sclerosis

Associated with: **POEMS syndrome**

Polyneuropathy
- distal symmetric sensorimotor neuropathy (50%) affecting sensory + motor + autonomic neurons → severe disabling numbness, tingling, weakness in feet, legs, hands

Organomegaly
- hepatosplenomegaly, Castleman disease

Endocrine abnormalities
- amenorrhoea, gynecomastia, erectile dysfunction, testicular atrophy, type 2 diabetes, hypothyroidism, adrenal insufficiency

Monoclonal paraprotein (IgA / IgG in 75%)
√ osteosclerotic lesions mimicking metastatic prostate carcinoma

Skin lesions
- hypertrichosis, hirsutism, sclerodermatous thickening, hyperpigmentation, hemangiomas

- papilledema, pseudotumor cerebri (66%)

- edema: peripheral, pulmonary, pleural effusion, ascites, anasarca

MR (recognition dependent on knowledge of normal range of bone marrow appearance for age):

√ pattern of multiple myeloma infiltration:
- √ normal marrow
- √ micronodular pattern = variegated / salt-and-pepper
- √ focal pattern
- √ diffuse pattern
  - ◊ Diffuse infiltration apparent only if at least 20–30% of bone marrow infiltrated
  - ◊ Whole-body MRI detects additional lesions in 10%

√ hypointense multiple focal areas on T1WI (25%)
√ hyperintense multiple focal areas on T2WI (53%)
√ absence of fatty infiltration (nonspecific)

PET/CT (for staging, prognosis, monitoring treatment after suspension of corticosteroids for > 5 days):

√ metabolic activity of bone lesions
√ extraosseous manifestations of disease
√ quantification of marrow metabolic activity (SUV)

SENSITIVITY OF BONE SCANS VS. RADIOGRAPHS

Radiographs : in 90% of patients and 80% of sites
Bone scan : in 75% of patients and 24–54% of sites
Gallium scan : in 55% of patients and 40% of sites

◊ 30% of lesions only detected on radiographs
◊ 10% of lesions only detected on bone scans

Cx: (1) Renal involvement frequent
(2) Predilection for recurrent pneumonias ← leukopenia
(3) Secondary amyloidosis in 6–15%
(4) Pathologic fractures occur often

Prognosis: 43% 5-year survival; death from renal insufficiency, bacterial infection, thromboembolism

Rx: thalidomide, lenalidomide, bortezomib, autologous stem cell transplantation (ASCT), monoclonal antibodies

DDx:

› with osteopenia:
(1) Postmenopausal osteoporosis
(2) Hyperparathyroidism
(3) Steroid use

› with lytic lesion:
(1) Metastatic disease
(2) Amyloidosis
(3) Myeloid metaplasia

› with sclerotic lesion:
(1) Osteopoikilosis
(2) Lymphoma

(3) Osteoblastic metastasis
(4) Mastocytosis
(5) Myelosclerosis
(6) Fluorosis
(7) Renal osteodystrophy

10–20% of patients with multiple myeloma have normal findings at conventional radiography and differentiation of osteopenia from osteoporosis, steroid use, or excessive alcohol intake is difficult.

Myelomatosis

√ generalized deossification without discrete tumors
√ vertebral flattening

Solitary Plasmacytoma of Bone

= focal proliferation of malignant plasma cells without diffuse bone marrow involvement = early stage of multiple myeloma, precedes multiple myeloma by 1–20 years

Age: 5th–7th decade; > 60 years (in 70%)

• negative marrow aspiration; no IgG spike in serum / urine
• monoclonal immunoglobulin at low serum level (in 40%)

A. SOLITARY MYELOMA OF BONE (3–7%)

Site: thoracic / lumbar spine (most common) > pelvis > ribs > sternum, skull, femur, humerus

√ solitary "bubbly" osteolytic grossly expansile lesion replacing cancellous bone
√ poorly defined margins, Swiss-cheese pattern
√ hollow vertebral body / pedicle = partly preserved / sclerotic cortical bone
√ frequently pathologic fracture (collapse of vertebra)

MR:

√ low signal intensity on T1WI + high SI on T2WI
√ homogeneous marked enhancement

DDx: giant cell tumor, aneurysmal bone cyst, osteoblastoma, solitary metastasis from renal cell / thyroid carcinoma

B. EXTRAMEDULLARY PLASMACYTOMA

Location: majority in head + neck; 80% in nasal cavity, paranasal sinuses, upper airways of trachea, lung parenchyma

MUSCULOTENDINOUS INJURY

Muscle Contusion

Cause: direct trauma, usually by blunt object
Site: deep within muscle belly
• injury at point of impact
√ NO architectural changes
√ feathery appearance of diffuse muscle edema
√ increased muscle girth
√ deep intramuscular hematoma (with severe trauma resulting in disruption of muscle fibers):
  √ high SI on T1WI (= T1 shortening of methemoglobin)
  √ low SI on T2WI (= T2 shortening of hemosiderin)
  √ blooming with gradient-echo sequence

Myotendinous Strain

Cause: single traumatic event from excessive stretching
Susceptibility factors:
(1) muscle composed of (fast contracting) type II fibers
(2) fusiform shape of muscle
(3) extension across two joints
(4) superficial location of muscle
(5) eccentric muscle action
Site: myotendinous junction (= weakest point of musculotendinous unit)
Classification:
1° degree = stretch injury (some fiber disruptions)
• no loss of muscle function
Path: interstitial edema + hemorrhage at myotendinous junction with extension into adjacent muscle fibers
√ feathery appearance of muscle
2° degree = partial tear without retraction
• mild loss of muscle function
√ hematoma at myotendinous junction
√ perifascial fluid collection
3° degree = complete rupture
• complete loss of muscle function
√ retracted muscle tendon
√ hematoma at myotendinous junction

Acute Avulsion Injury

Cause: forceful unbalanced often eccentric muscle contraction
Path: periosteal stripping with hematoma at tendon attachment site
Site: at tendon insertion
• loss of function, severe tenderness
√ waviness + retraction of the torn end of tendon with fragment of bone / cartilage

MYELOFIBROSIS

= MYELOSCLEROSIS = AGNOGENIC MYELOID METAPLASIA = MYELO-PROLIFERATIVE SYNDROME = PSEUDOLEUKEMIA

= hematologic disorder of unknown etiology with gradual replacement of bone marrow elements by fibrotic tissue

Characterized by:

(1) extramedullary hematopoiesis
(2) progressive splenomegaly
(3) anemia
(4) variable changes in number of granulocytes + platelets; often predated by polycythemia vera

Cause:

(a) primary: rare in children
(b) secondary: radiation therapy / chemotherapy for leukemia or lymphoma or metastatic disease; Gaucher disease

Age: usually > 50 years

Path: fibrous / bony replacement of bone marrow; extramedullary hematopoiesis

Associated with: metastatic carcinoma, chemical poisoning, chronic infection (TB), acute myelogenous leukemia, polycythemia vera, McCune-Albright syndrome, histiocytosis

- dyspnea, weakness, fatigue, weight loss, hemorrhage
- normochromic normocytic anemia; polycythemia may precede myelosclerosis in 59%
- dry marrow aspirate

Location: red-marrow–containing bones in 40% (thoracic cage, pelvis, femora, humeral shafts, lumbar spine, skull, peripheral bones)

√ hepatosplenomegaly ← hematologic proliferation

√ widespread diffuse increase in bone density (ground-glass sclerosis) predominantly affecting medullary cavity:
  √ "jail-bar" ribs
  √ sandwich / rugger jersey spine

√ generalized increase in bone density in skull + obliteration of diploic space; scattered small rounded radiolucent lesions; or combination of both

MR:
  √ hypointense marrow on T1WI + T2WI
  √ signal intensity slightly higher than muscle on STIR

NUC:
  √ diffuse increased uptake of bone tracer in affected skeleton, possibly "superscan"
  √ increased uptake at ends of long bones

DDx: (1) With splenomegaly: chronic leukemia, lymphoma, mastocytosis
(2) Without splenomegaly: osteoblastic metastases, fluorine poisoning, osteopetrosis, chronic renal disease

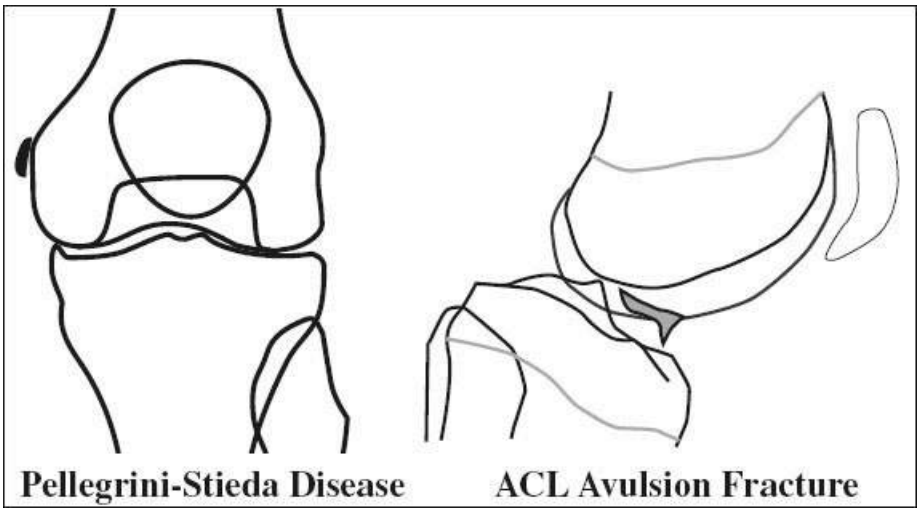
MYELOID DEPLETION

= APLASTIC ANEMIA

Cause: idiopathic; ? sequelae of viral infection, medication, toxin, chemo- / radiation therapy
Path: normal marrow replaced by fat cells
MR:
√ high signal intensity on T1WI
√ low signal intensity on fat-suppressed T2WI
◊ Best seen in areas with high percentage of hematopoietic marrow: proximal femoral metaphyses, spine

MYOSITIS OSSIFICANS

= PSEUDOMALIGNANT OSSEOUS TUMOR OF SOFT TISSUE = EXTRAOSSEOUS LOCALIZED NONNEOPLASTIC BONE AND CARTILAGE FORMATION = MYOSITIS OSSIFICANS CIRCUMSCRIPTA = HETEROTOPIC OSSIFICATION
= benign solitary self-limiting ossifying soft-tissue mass typically occurring within skeletal muscle as a mesenchymal response to soft tissue injury
◊ Myositis is a misnomer for lack of muscle inflammation!
Cause: direct trauma (75%), paralysis, burn, tetanus, intramuscular hematoma, spontaneous
Age: 2nd–3rd decades; M > F
Path: lesion rimmed by compressed fibrous connective tissue + surrounded by atrophic skeletal muscle
Histo: hypercellular fibrous tissue with mature bone formation usually within 6–8 weeks after onset of symptoms
(a) early stage: focal hemorrhage + degeneration + necrosis of damaged muscle → histiocytic invasion; central nonossified core of proliferating benign fibroblasts + myofibroblasts; mesenchymal cells enclosed in ground substance assume characteristics of osteoblasts → subsequent mineralization + peripheral bone formation
(b) intermediate stage (3–8 weeks): "zoning phenomenon":
› *central:* cellular osteoid with atypical mitotic figures (impossible to differentiate from soft-tissue sarcoma)
› *middle:* immature osteoid
› *outer:* well-formed lamellar mature trabeculated bone
(c) mature stage: shrinkage of mass → resolution in 30%
• pain, tenderness, soft-tissue mass
Location: large muscles of extremities (80%)



(a) within muscle: head & neck (temporalis, masseter, buccinator, sternocleidomastoid); anterolateral aspect of thigh + arm; small muscles of hands; gluteal muscle; "rider's bone" (adductor longus); "fencer's bone" (brachialis); "dancer's bone" (soleus); breast, elbow, knee

(b) periosteal at tendon insertion: **Pellegrini-Stieda disease** (in / near medial (tibial) collateral ligament of knee) as a result of Stieda fracture (= avulsion injury from medial femoral condyle at origin of tibial collateral ligament)
[Augusto Pellegrini (1877–1958), surgeon in Florence, Italy]
[Alfred Stieda (1869–1945), surgeon in Königsberg, Germany]

√ gradual ossification from periphery toward center (!) of mass:
- √ faint calcifications develop in 2–6 weeks after onset of symptoms
- √ well-defined partially ossified soft-tissue mass apparent by 6–8 weeks, becoming smaller + mature by 5–6 months
- √ radiolucent zone separating lesion from bone (DDx: periosteal sarcoma on stalk)
- √ ± periosteal reaction

CT:

Early phase:
- √ well-defined geometric hypodense mass with peripheral calcification after 4–6 weeks + less distinct lucent center

Mature phase:
- √ diffuse dense ossification in mature lesion

MR:
- √ initially heterogeneous muscle edema
- √ progression to masslike region of high SI on T2WI (during first days to weeks after injury simulating malignancy)

Early phase:
- √ mass with poorly defined margins + surrounding edema
- √ inhomogeneously hyperintense to fat on T2WI
- √ isointense to muscle on T1WI
- √ contrast enhancement

Intermediate phase:

√ isointense / slightly hyperintense core on T1WI, increasing in intensity on T2WI
√ diagnostic curvilinear hypointense rim surrounding the lesion (= peripheral mineralization / ossification)
√ increased peritumoral SI on T2WI (= edema of diffuse myositis)
√ focal signal abnormality within bone marrow (= marrow edema)

Mature phase: signal intensity characteristics of bone
√ well-defined hypointense rim and trabeculae, dense fibrosis and central adipose tissue
√ decreased SI inside and around lesion (dense ossification + fibrosis, hemosiderin from previous hemorrhage)

NUC:
√ intense tracer accumulation on bone scan (directly related to deposition of calcium in damaged muscle)
√ in phase of mature ossification activity becomes reduced + surgery may be performed with little risk of recurrence

Angio:
√ diffuse tumor blush + fine neovascularity in early active phase
√ avascular mass in mature healing phase

Prognosis: ? resorption in 1 year

DDx:
◊ In early stages difficult to differentiate histologically + radiologically from soft-tissue sarcomas!
(1) Osteosarcoma (densest calcification in center, least radiopaque bone at ill-defined periphery, no surrounding edema)
(2) Synovial sarcoma
(3) Fibrosarcoma
(4) Chondrosarcoma
(5) Rhabdomyosarcoma
(6) Parosteal sarcoma (usually metaphyseal with thick densely mineralized attachment to bone)
(7) Posttraumatic periostitis (ossification of subperiosteal hematoma with broad-based attachment to bone)
(8) Acute osteomyelitis (substantial soft-tissue edema + early periosteal reaction)
(9) Tumoral calcinosis (periarticular calcific masses of lobular pattern with interspersed lucent soft-tissue septa)
(10) Osteochondroma (stalk contiguous with normal adjacent cortex + medullary space)

Myositis Ossificans Variants

Panniculitis Ossificans

Location: subcutis of mostly upper extremities
√ less prominent zoning phenomenon

Fasciitis Ossificans

Location: fascia

Fibro-osseous Pseudotumor of Digits

= FLORID REACTIVE PERIOSTITIS
= nonneoplastic solitary self-limiting process of unknown pathogenesis, probably related to trauma
Mean age: 32 (range, 4–64) years; M÷F = 1÷2
• fusiform soft-tissue swelling / mass
Location: predominantly tubular bones of hand + foot: fingers ($2^{nd} > 3^{rd} > 5^{th}$)
Site: proximal > distal > middle phalanx
√ radiopaque soft-tissue mass with radiolucent band between mass + cortex
√ visible calcifications (50%)
√ focal periosteal thickening (50%)
√ cortical erosion (occasionally)
Rx: local excision
DDx: parosteal / periosteal osteogenic sarcoma, peripheral chondrosarcoma, periosteal chondroma, soft-tissue chondroma

MYXOMA

= true mesenchymal benign neoplasm
Histo: bland spindle shaped cells embedded in hypovascular abundantly myxoid stroma ± hypercellular areas with increased vascularity
Age: 4^{th}–6^{th} decade; M<F
Location: head & neck (scalene muscle, masticator space and posterior paraspinal muscles)
Site: intramuscular myxoma (82%), intermuscular, subfascial
Associated with: Mazabraud syndrome McCune-Albright syndrome
CT:
√ well-defined ovoid mass with attenuation similar to water
MR:
√ well-defined ovoid lesion with SI characteristic of fluid ← high mucin + low collagen content
√ thin peritumoral rim of perilesional fat on T1WI (70%):
√ T2 hyperintense ← fatty atrophy of muscle
√ fine inner linear stranding on T2WI ← fibrous septa
√ internal enhancement: (a) peripheral ← pseudocapsule (b) peripheral + internal linear stranding (c) peripheral + internal central focal patchy areas
Dx: core-needle / surgical biopsy
DDx: myxoid peripheral nerve sheath tumor, myxofibrosarcoma, myxoid liposarcoma, extraskeletal myxoid chondrosarcoma, undifferentiated pleiomorphic sarcoma

MYXOFIBROSARCOMA

= Myxoid malignant fibrous histiocytoma
= among the most common sarcomas in elderly
Histo: resembles myxoid liposarcoma with infiltrative growth along fascial planes
MR: similar to myxoma + myxoid liposarcoma
√ low to intermediate SI on T1WI + high SI on T2WI
√ septa of low SI

√ no fatty component
√ hyperintense cystlike myxoid component
√ heterogeneous nodular + peripheral enhancement of solid components

Prognosis: multiple recurrences ← infiltrative growth

DDx: other adult pleomorphic sarcomas (difficult DDx)

NAIL-PATELLA SYNDROME

= FONG DISEASE = ILIAC HORNS = FAMILIAL / HEREDITARY OSTEO-ONYCHODYSPLASIA = OSTEO-ONYCHODYSOSTOSIS = HOOD SYNDROME = ELBOW-PATELLA SYNDROME

= rare autosomal-dominant disorder characterized by symmetrical meso- and ectodermal anomalies

Etiology: ? enzymatic defect in collagen metabolism

Genetics: mutation of LMX1B gene encoding a transcription factor important to development of kidneys + limbs, particularly embryologically dorsal limb structures including nail + patella

Age: evident in 2nd + 3rd decades

◊ Diagnosed only late in life (if at all)!

- bilateral spooning / splitting / ridging of fingernails
- abnormal gait; abnormal pigmentation of iris
- renal dysfunction ← abnormal glomerular basement membrane: proteinuria, hematuria, failure later in life

√ 4 key features:

(1) Nail abnormality (98%):

Site: 1st–5th digit (in decreasing order of frequency)

- absent / hypoplastic / split nails
- hypoplasia of both thumbnails
- PATHOGNOMONIC triangular lunula
- lack of skin creases over dorsum of DIP joints

(2) Patella abnormality (74%):

√ fragmentation / hypoplasia / absence of patella
√ recurrent lateral dislocations (frequent)
- "squared" appearance of knees upon genuflection ← lateral subluxation

Cx: knee joint instability, restriction, pain, arthritis

(3) pathognomonic bilateral posterior iliac horns (= conical exostosis) in 68–80%

√ occasionally capped by an epiphysis

Site: at attachment of gluteus medius to posterior iliac wing

(4) Elbow abnormality (33%):

- pterygia = skin webs → restricted range of motion / dislocation

√ radial head / capitellum hypoplasia with subluxation / dislocation of radial head dorsally and increased carrying angle of elbow (DDx: congenital dislocation of radial head)

√ flared iliac crest with protuberant anterior iliac spines
√ flexion contractures of hip, knee, elbow, fingers, foot with inability of full extension

√ deltoid, triceps, quadriceps hypoplasia
√ mandibular cysts (occasionally)
√ scoliosis
@ Hand
√ clinodactyly of 5th finger
√ short 5th metacarpal
@ Knee
√ genu valgum ← asymmetrical development of femoral condyles
√ prominent tibial tubercles
@ Kidney
• accelerated age-related decline in renal function
• mild proteinuria (nephrotic-range in 5–10%)
√ renal osteodystrophy
Cx: renal failure and death
@ Eye
• open-angle glaucoma

DDx: (1) Seckel syndrome = bird-headed dwarfism
(2) Popliteal pterygium syndrome (absence of patella, toenail dysplasia)

NECROTIZING FASCIITIS

= progressive rapidly spreading infection of deep fascia → secondary necrosis of SQ tissue
N.B.: life-threatening surgical emergency!
Prevalence: 500 cases in literature
Age: 58 ± 14 years; M> F
Cause: deep internal infection / malignancy (perforated duodenal ulcer / retroperitoneal appendix, retroperitoneal / perirectal infection, infiltrating rectal / sigmoid carcinoma
Predisposed: immunocompromised patients (with diabetes, cancer, alcohol / drug abuse, vascular insufficiency, organ transplant), poor nutrition, foreign body in surgical wound
Organism: often gas-forming anaerobic bacteria in combination with aerobic gram-negative organisms: Staphylococcus, E. coli, Bacteroides, Streptococcus, Peptostreptococcus, Klebsiella, Proteus, C. perfringens (5–15%); multiple organisms in 75%
Histo: necrotic superficial fascia, leukocytic infiltration of deep fascial layers; fibrinoid thrombosis of arterioles + venules with vessel wall necrosis; microbial infiltration of destroyed fascia
• indolent: 1–21 days delay before diagnosis
• nonspecific symptoms: severe pain, fever, leukocytosis, shock, altered mental status
• crepitus (50%), overlying skin may be completely intact
Location: lower extremity, arm, neck, back, male perineum / scrotum (= Fournier gangrene)
√ image findings similar to cellulitis but more severe with involvement of deeper structures
√ asymmetric fascial thickening with fat stranding (80%) ← fluid
√ fluid collections along deep fascial sheaths
√ gas in soft-tissues dissecting along fascial planes ← gas-forming organisms (in 55%)
√ associated deep abscess (35%)

√ ± secondary muscle involvement:
  √ extension of edema into intermuscular septa and muscles
  √ no demonstrable enhancement of fascia ← necrosis

Prognosis: poor with delay in diagnosis ← progresses rapidly; morbidity and mortality rate of 70–80%

Rx: extensive surgical débridement + antibiotics

DDx: (1) Myonecrosis (= infection originating in muscle)
(2) Fasciitis-panniculitis syndromes (chronic swelling of skin + underlying soft tissues + fascial planes in arm + calf)
(3) Soft-tissue edema of CHF / cirrhosis (symmetrical diffuse fat stranding)
(4) cellulitis (less severe, without involvement of deeper structures)

NEUROPATHIC OSTEOARTHROPATHY

= NEUROTROPHIC JOINT = CHARCOT JOINT = "OSTEOARTHRITIS WITH A VENGEANCE"

[Jean-Martin Charcot (1825–1893), first professor of neurology at the Salpêtrière hospital in Paris]

= progressive degenerative + destructive joint disorder in patients with abnormal pain sensation + proprioception

Cause:

A. Congenital
  1. Myelomeningocele
  2. Congenital indifference to pain = asymbolia
  3. Familial dysautonomia (Riley-Day syndrome)
  4. Hereditary sensory and motor neuropathy (Charcot-Marie-Tooth disease)

B. Acquired
  (a) central neuropathy
    1. Injury to brain / spinal cord
    2. Syringomyelia (in ⅓ of patients): shoulder, elbow
    3. Neurosyphilis = tabes dorsalis (in 15–20% of patients): hip, knee, ankle, tarsals
    4. Spinal cord tumors / infection
    5. Extrinsic compression of spinal cord
    6. Multiple sclerosis
    7. Alcoholism
  (b) peripheral neuropathy
    1. Diabetes mellitus (most common cause, although incidence low): midfoot, tarsometatarsal joints (middle cuneiform + base of 2nd metatarsal bone first affected), intertarsal joints, subtalar joints, metatarsophalangeal joints, ankle
    2. Peripheral nerve injury
    3. Peripheral nerve tumor
    4. Leprosy (Hansen disease)
    5. Poliomyelitis
  (c) others
    1. Scleroderma, Raynaud disease, Ehlers-Danlos syndrome

2. Rheumatoid arthritis, psoriasis
3. Amyloid infiltration of nerves, adrenal hypercorticism
4. Uremia
5. Pernicious anemia

C. Iatrogenic
1. Prolonged use of pain-relieving drugs
2. Intraarticular / systemic steroid injections

mnemonic: DS6
Diabetes
Syphilis
Steroids
Spinal cord injury
Spina bifida
Syringomyelia
Scleroderma

Pathophysiology:
loss of proprioception with sensory deficits arising in the spinal cord / peripheral nerves
(1) Neurotraumatic theory
= repetitive trauma with absence of normal protective sensory feedback
(2) Neurovascular theory
= absence of neural stimuli → loss of sympathetic tone resulting in vasodilatation and hyperemia, which promotes bone resorption + weakening of subchondral bone

Pathology:
(a) atrophic pattern (most common):
joint destruction, resorption of fragments (osteoclasts + macrophages remove bone + cartilage debris), dissolution / "amputation" of periarticular bones, joint effusion
• notable absence of osteosclerosis + osteophyte formation
Associated with: syringomyelia, peripheral nerve lesion, also in diabetes
Location: non-weight-bearing joints of upper extremity
DDx: surgical amputation, septic arthritis
(b) hypertrophic pattern (only sensory nerves affected):
joint destruction, fragmentation of bone, periarticular bony debris
• osteosclerosis + osteophyte formation (early, attaining enormous size)
DDx: severe osteoarthritis
(c) mixed pattern
(d) common to both: joint disorganization, large persistent bloody joint effusion

• no history of trauma
• swollen + warm joint with normal WBC count + ESR (infection may coexist)
• usually painless joint; pain at presentation (in ⅓) with decreased response to deep pain + proprioception
• joint changes frequently precede neurologic deficit
• synovial fluid: frequently xanthochromic / bloody, lipid crystals (from bone marrow)
√ persistent joint effusion (first sign)
√ narrowing of joint space
√ speckled calcification in soft tissue (= calcification of synovial membrane)

√ fragmentation of eburnated subchondral bone
√ NO juxtaarticular osteoporosis (unless infected)
√ "bag-of-bones" appearance in late stage (= marked deformities around joint)
mnemonic: 6 Ds
√ **D**ense subchondral bone (= sclerosis)
√ **D**egeneration (= attempted repair by osteophytes)
√ **D**estruction of articular cortex (with sharp margins resembling those of surgical amputation)
√ **D**eformity ("pencil point" deformity of metatarsal heads)
√ **D**ebris (loose bodies)
√ **D**islocation (nontraumatic)
√ subluxation of joints (laxity of periarticular soft tissues)
√ progressive rapid bone resorption
√ joint distension (by fluid, hypertrophic synovitis, osteophytes, subluxation)
√ fracture: healing with exuberant bizarre callus formation
MR:
√ decreased SI in bone marrow on T1WI + T2WI ← osteosclerotic changes
@ Shoulder
Cause: syringomyelia, cord trauma with paraplegia
• shoulder mass (due to fluid distension)
√ amputated appearance of proximal humerus
√ dislocation
√ large joint effusion
√ fragmented osseous debris in joint capsule + subacromial-subdeltoid bursa
DDx: chondrosarcoma
@ **Neuropathic spine** = **Charcot spine** (involved in 6–21%)
Cause: diabetes mellitus > traumatic spinal cord injury, syringomyelia, inadequately treated syphilis, amyloidosis, congenital insensitivity to pain
Site: lower thoracic spine, lumbar spine > cervical spine, upper thoracic spine, sacrum
• mild pain and spinal deformity
√ intervertebral disk space narrowing
√ disk vacuum phenomenon
√ osteolysis / sclerosis of vertebrae:
√ extensive osseous fragmentation extending beyond confines of vertebral body margins into paraspinous musculature + into spinal canal
√ large hypertrophic beaking endplate osteophytes
√ paraspinous soft-tissue calcification:
√ mineralized paraspinal fluid collections containing osseous debris
√ facet joint erosion + subluxation (early findings) → spondylolisthesis
√ scoliosis + abrupt curvature
√ rimlike enhancement of disk + signal intensity changes of bone marrow
DDx: infectious spondylitis (NO involvement of facet joints, diffuse enhancement of disk + endplates), metastasis, granulomatous infection, severe degenerative disk disease
@ Hands + feet
Cause: leprosy (due to trauma + secondary bacterial infection)

√ claw hand / claw toes
√ "licked candy cane" appearance of metatarsal bone / tapered phalanx ← concentric bone atrophy with decrease in bone length + width
DDx: diabetes mellitus, frostbite, pernicious anemia, scleroderma, syringomyelia, tabes dorsalis, familial sensory neuropathy

@ Foot + ankle
Cause: long-term poorly controlled diabetes mellitus, syphilis
• soft-tissue swelling, warmth, erythema
Site: often begins in midfoot
√ vascular calcifications
√ subluxation (starting at 2nd tarsometatarsal joint)

NODULAR FASCIITIS

= mass-forming fibrous proliferation
Age: 2nd–4th decades (most common)
Pathogenesis: unknown: ? reactive / inflammatory process
Histo: immature fibroblasts + variable amount of mature birefringent collagen
Types:
(a) subcutaneous [3–10 x more common than (b) or (c)]
√ well-defined margins
(b) intramuscular
√ typically larger + deeper in location
√ ill-defined margins with extension along fascial planes
(c) intermuscular (fascial)
Location: head & neck (15–20%)
Size: 0.5–10 cm
CT:
√ homogeneous mass with attenuation similar to fluid
√ ± erosion of underlying bone
MR:
√ heterogeneous mass usually slightly hyperintense relative to muscle on T1WI
√ hyperintense relative to muscle on T2WI
√ ± marked enhancement

NONOSSIFYING FIBROMA

= FIBROXANTHOMA = NONOSTEOGENIC FIBROMA = XANTHOMA = XANTHOGRANULOMA OF BONE = FIBROUS METAPHYSEAL-DIAPHYSEAL DEFECT = FIBROUS MEDULLARY DEFECT
Frequency: up to 40% of all children > 2 years of age
Etiology: lesion resulting from proliferative activity of a fibrous cortical defect that has expanded into medullary cavity
Histo: interlacing whorled bundles of spindle-shaped fibroblasts + scattered multinucleated giant cells + foamy xanthomatous cells, variable degree of hemosiderin; usually cellular with only small amounts of collagen

Age: 8–20 years; 75% in 2nd decade of life
• usually asymptomatic; pain if large
Location: shaft of long bone; mostly in bones of lower extremity, esp. about knee (posteromedial surface of distal femur (55%) + proximal tibia); distal tibia; fibula
Site: eccentric / cortical to subcortical metaphyseal region, several cm shaftward from epiphysis, mostly intramedullary, rarely purely diaphyseal
√ well-circumscribed multiloculated bubbly oval osteolytic area
√ alignment along long axis of bone, > 2 cm in length
√ scalloped sclerotic margin toward medulla; V- or U-shaped at one end
√ mild expansile remodeling = endosteal scalloping + thinning ± overlying bulge
√ no periosteal reaction
√ migrates toward center of diaphysis
√ resolves with age
NUC:
√ minimal / mild uptake on bone scan
MR:
√ 80% hypointense on T1WI + T2WI ← extensive hypocellular fibrous tissue, hemosiderin pigment
√ 20% hypointense on T1WI + hyperintense on T2WI ← massive aggregation of foamy histiocytes
√ peripheral hypointense rim + internal septation ← marginal reactive sclerosis + trabeculation
√ adjacent marrow edema generally absent
√ intense contrast enhancement (in 80%) / marginal septal enhancement (in 20%) on T1WI
CAVE: lesions > 33 mm long involving > 50% of the transverse bone diameter need observation
Prognosis: spontaneous healing in most cases
Cx: (1) Pathologic fracture (not uncommon)
(2) Hypophosphatemic vitamin D–resistant rickets + osteomalacia (tumor may secrete substance that increases renal tubular resorption of phosphorus)
DDx: (1) Fibrous cortical defect (< 2 cm in greatest diameter)
(2) Adamantinoma (midshaft of tibia)
(3) Chondromyxoid fibroma (bulging of cortex more striking, hyperintense on T2WI)
(4) Fibrous dysplasia (internal septations rare)
(5) Aneurysmal bone cyst (heterogeneously hyperintense with fluid-fluid levels)
(6) Intraosseous ganglion (hyperintense on T2WI)

Multiple Fibroxanthomas (in 8–10%)
Associated with: neurofibromatosis, fibrous dysplasia, Jaffé-Campanacci syndrome

Jaffé-Campanacci Syndrome
= nonossifying fibroma with extraskeletal manifestations in children
• mental retardation; hypogonadism; ocular defect
• cardiovascular congenital defect; café-au-lait spots

NOONAN SYNDROME

= PSEUDO–TURNER = MALE TURNER SYNDROME
= phenotype similar to Turner syndrome but with normal karyotype (occurs in both males + females)
Genetics: striking familial incidence
• short / may have normal height
• webbed neck; agonadism / normal gonads
• delayed puberty; mental retardation
√ osteoporosis
√ retarded bone age
√ cubitus valgus
@ Skull
  √ mandibular hypoplasia with dental malocclusion
  √ hypertelorism
  √ biparietal foramina
  √ dolichocephaly, microcephaly / cranial enlargement
  √ webbed neck
@ Chest
  √ sternal deformity: pectus excavatum / carinatum
  √ right-sided CHD (valvar pulmonic stenosis, ASD, eccentric hypertrophy of left ventricle, PDA, VSD)
  √ coronal clefts of spine
  √ may have pulmonary lymphangiectasis
@ Gastrointestinal tract
  √ intestinal lymphangiectasia
  √ eventration of diaphragm
  √ renal malrotation, renal duplication, hydronephrosis, large redundant extrarenal pelvis
DDx: Turner syndrome (mental retardation rare, renal anomalies frequent)

OCHRONOSIS

= ALKAPTONURIA
[ochros, *Greek* = pale, light yellow brown color]
[alkapton from al-qaly, *Arabic* = potash + kapto, *Greek* = to suck up]
= rare inborn error of metabolism
Pathophysiology:
inherited absence of enzyme homogentisate 1,2-deoxygenase → inability to normally degrade aromatic amino acids tyrosine + phenylalanine → accumulation of their alternate degradation product homogentisic acid within bloodstream → excretion in urine + deposition in connective tissue (including cartilage, synovium, and bone)
Prevalence: 1÷250,00 to 1÷1,000,000 births; M÷F = 2÷1
Histo: black-pigmented cartilage subject to deterioration → calcification + denudation of cartilaginous tissue
• ochronosis =dark pigment in soft tissues (in 2nd decade): yellowish skin; gray pigmentation of sclera; bluish tinge of auricular + nasal cartilage

• alkaptonuria with black staining of diapers (homogentisic acid in urine is oxidized to benzoquinones which form melanin-like polymers responsible for discoloration)
• heart failure, renal failure (pigment deposition)

@ Spine

Age: 3rd–4th decade

Site: lumbar region with progressive ascension (cervical spine typically spared)

• progressive kyphosis with loss of height
• decreased lumbar flexion
√ CHARACTERISTIC laminated calcifications of multiple intervertebral disks (primarily of annulus fibrosus)
√ severe narrowing of intervertebral disk space + eventual obliteration
√ multiple "vacuum" phenomena (common)
√ osteopenia of adjoining vertebrae
√ loss of normal lumbar lordosis
√ massive vertebral osteophytosis (resembling syndesmophytes of ankylosing spondylitis) + ankylosis of spine (in older patient)
√ spotty calcifications in tissue anterior to vertebral bodies

@ Joints = **ochronotic arthropathy**

= manifestation of long-standing alkaptonuria in axial + peripheral skeleton similar to osteoarthritis
• long-standing joint pain + limited range of motion
√ hypertrophic changes in humeral head
√ severe progressive premature osteoarthritis (knee > shoulder > hip):
√ joint narrowing + subchondral sclerosis
√ prominence of intraarticular osteochondral fragments
√ relative lack of prominent osteophyte formation
√ small calcifications in paraarticular soft tissues + tendon insertions

DDx: ankylosing spondylitis (erosions and ankylosis of SI joints, severe facet joint involvement)

ORODIGITOFACIAL SYNDROME

= OROFACIODIGITAL SYNDROME
= heterogeneous group of defects, probably representing varying expressivity, involving face, oral cavity, and digits

Prevalence: 1÷50,000 live births
Etiology: autosomal trisomy of chromosome No. 1 with 47 chromosomes; X-linked dominant
Sex: nuclear chromatin pattern female (lethal in male)
Associated with: renal polycystic disease

• mental retardation; hypertelorism
• cleft lip + tongue, lingual hamartoma; bifid nasal tip
√ cleft in palate + jaw bone
√ hypoplasia of mandible (micrognathia) + occiput of skull
√ hypodontia
√ clinodactyly, syndactyly, brachydactyly (metacarpals may be elongated), polysyndactyly,

duplication of hallux

OSGOOD-SCHLATTER DISEASE

[Robert B. Osgood (1873–1956), orthopedic surgeon in Boston, USA]
[Carl Schlatter (1864–1934), surgeon in Zurich, Switzerland]
= chronic avulsion injury of the attachment of the patellar ligament to the tibial tuberosity (= traction osteochondritis, NOT osteonecrosis); bilateral in 25–50%
Age: 10–15 years; M > F
Anatomy: tibial tubercle develops as an anterior extension of proximal tibial physis; closes at 13–15 years (in girls) and 15–19 years (in boys)
Cause: repetitive microtrauma (common in sports that involve jumping, kicking, squatting)
• local pain + tenderness on pressure
• painful visible swelling of overlying soft tissue
√ soft-tissue swelling in front of tuberosity ← edema of skin + subcutaneous tissue
√ thickening + calcification of distal portion of patellar tendon
√ indistinct margin of patellar tendon
√ obliteration of inferior angle of infrapatellar fat pad
√ separation of several small ossicles from the developing ossification center of tibial tuberosity (= reactive secondary heterotopic bone formation)
√ single / multiple ossifications in avulsed fragment
√ comparison with other side (irregular development normal)
MR:
√ patellar tendon enlargement
√ increased SI at tibial insertion site of patellar tendon on T1WI + T2WI
√ distension of deep infrapatellar bursa
√ bone marrow edema adjacent to tibial tuberosity + tibial apophysis (rare)
√ thickened cartilage anterior to tibial tubercle
Cx: tibial tubercle fracture with nonunion of bone fragments, patellar subluxation, chondromalacia, avulsion of patellar tendon, genu recurvatum
Rx: immobilization / steroid injection
DDx: (1) Normal irregular ossification pattern of tibial tuberosity between ages 8–14 (asymptomatic)
(2) Osteitis: tuberculous / syphilitic
(3) Soft-tissue sarcoma with calcifications

OSSIFYING FIBROMA

= encapsulated circumscribed benign neoplasm closely related to fibrous dysplasia + adamantinoma
Incidence: peaks in 3rd–4th decade
Age: 2nd–4th decade; M < F
Histo: highly cellular fibrous connective tissue composed of spindle cells with osteoblastic activity producing varying amounts of osteoid in a pattern of uniform small round lamellated "psammoma-like" ossicles; irregular spicules / trabeculae of lamellar bone rimmed by osteoblasts (DDx from fibrous dysplasia)

Subtypes:
(a) cementifying fibroma
(b) cemento-ossifying fibroma
(c) juvenile ossifying fibroma: aggressive destructive, most common in boys < 15 years of age

Location: frequently in face / posterior mandible
• asymptomatic
• tooth displacement; facial asymmetry ← bone expansion
√ intense focal uptake on bone scan
@ Tibia
√ eccentric ground-glass lesion (resembling fibrous dysplasia)
√ initially lucent (= nonmineralized osteoid) + later often opaque lesion (depending on degree of calcification) similar to fibrous dysplasia
√ surrounded by thin line of lucency (= fibrous capsule) + thin outer rim of sclerotic (reactive) bone
√ ± soft-tissue enhancement
@ Mandible, maxilla
Site: premolar / molar region
• painless swelling of tooth-bearing portion of jaw
√ 1–5 cm well-circumscribed round / oval tumor
√ moderate unilocular expansion of intact cortex
√ homogeneous tumor matrix
√ dislodgment of teeth
√ NO halo of low attenuation; sclerotic border (occasionally)
Cx: significant potential for centrifugal growth perpendicular to long axis of bone; frequent recurrences
DDx: (1) Fibrous dysplasia (longitudinal growth pattern, nondisplaced teeth, crossing of sutures, osteoblastic rimming, no radiolucent boundary)
(2) Odontoma
(3) Sequestrum
(4) Vascular lesion

Juvenile Ossifying Fibroma
= PSAMMOMATOID OSSIFYING FIBROMA
= nonmetastasizing benign tumor that arises in sinonasal region of young patients often involving orbit with tendency for locally aggressive behavior
Age: children and adolescents; M÷F = 1÷1
Location: facial bones (85%), esp. paranasal sinuses; more than one sinus in ½
Site: ethmoid region / superior orbital plate of frontal bone
• proptosis, headache, sinusitis
• facial swelling, nasal obstruction
• visual / ocular motility disturbance
√ intracranial extension
Radiography:
√ monostotic round / ovoid well-demarcated expansile lesion of mixed lytic + sclerotic

density
√ ballooned / bowed appearance of sclerotic margin

CT:
√ predominantly soft-tissue attenuation with multiple foci of calcifications
√ ± multiloculated internal composition with sclerotic septa / enhancing septa of soft-tissue attenuation
√ lower-attenuation areas ← cystic changes
√ usually surrounded by a possibly partially disrupted sclerotic rim / shell
√ enhancement of shell + solid tumor portions

MR:
√ lesion isointense relative to muscle on T1WI
√ hypointense relative to muscle on T2WI
√ foci of high T2-signal intensity ← fluid-filled cystic spaces

DDx: fibrous dysplasia, cementifying fibroma (arises from periodontal ligament in molar teeth), aneurysmal bone cyst (infrequently in sinonasal region, fluid levels throughout its cystic component)

OSTEITIS CONDENSANS ILII

Prevalence: 2% of population
Cause: chronic stress ← instability of pubic symphysis
Age: young multiparous women
• associated with low back pain when instability of pubic symphysis present
√ triangular area of sclerosis along inferior anterior aspect of ileum adjacent to SI joint (joint space uninvolved)
√ similar triangle of reparative bone on sacral side
√ usually bilateral + symmetric; occasionally unilateral
√ sclerosis dissolves in 3–20 years following stabilization of pubic symphysis
DDx: (1) Ankylosing spondylitis (affects ilium + sacrum, joint space narrowing, involvement of other bones)
(2) Rheumatoid arthritis (asymmetric, joint destruction)
(3) Paget disease (thickened trabecular pattern)

OSTEOARTHRITIS

= DEGENERATIVE JOINT DISEASE = ARTHROSIS
= predominantly noninflammatory degeneration of cartilage in synovial joints
◊ Most common arthropathy ← repetitive articular cartilage damage
Age: prevalence increasing with age
Cause: (1) abnormal forces acting on a normal joint (eg, slipped capital femoral epiphysis)
(2) normal forces acting on abnormal joint due to
(a) cartilage abnormality
(b) subchondral bone abnormality
Path: ↓ chondroitin sulfate with age creates unsupported collagen fibrils → irreversible hyaline cartilage degeneration (= inability for regeneration)
√ joint space narrowing (stage III) = inaccurate indicator of cartilage integrity

√ subchondral sclerosis / eburnation in areas of stress
√ subchondral cyst formation (geodes)
√ increased joint fluid
√ synovial inflammation (in severe osteoarthritis)
√ osteophytosis at articular margin / nonstressed area

US:

√ step-up prominences of cortex = peripheral marginal osteophytes ← new bone formation
√ joint space narrowing, noted if marginal and severe
√ joint effusion ± hyperemia of synovitis (on color Doppler)

MR:

@ Cartilage

Stages of damage to cartilage:

I cartilage swelling + softening (from damage to collagen matrix → decreased proteoglycan content + increase in water content)
II increased cartilage thickness (from proliferation of chondrocytes)
III cartilage loss → fibrillation + erosion + cracking of articular cartilage ← decrease in cellular proliferation of chondrocytes

√ increased SI of abnormal cartilage on T2WI (= increased amount of free water)
√ morphologic defects on surface of cartilage (best seen on fat-suppressed spoiled gradient-echo MR)

Cartilage damage score on MR:

0 normal
1 increased T2 signal intensity
2 partial-thickness defect < 50%
3 partial-thickness defect > 50%
4 full-thickness defect

@ Bone

√ hyperintense subchondral bone marrow edema-like lesion on fat-suppressed T2WI / STIR ← increased fatty acid consumption
√ subchondral pseudocysts in weight-bearing areas (= contusional bone necrosis / intrusion of synovial fluid across damaged cartilage)
√ subchondral sclerosis (= stress-induced new bone deposition + trabecular microfractures + callus formation) hypointense on all sequences
√ osteophytes at joint margins ← stimulation of enchondral ossification in areas of low stress
√ flattening or depression of the articular cortex (= bone attrition)

@ Synovium

√ synovial thickening with positive correlation between pain and degree synovitis
√ joint effusion
√ popliteal bursal fluid (common)
√ joint bodies

Origin: chondral fragments, detached osteophytes, meniscal fragments, synovial osteochondromatosis

@ Hand + foot
Target area: 1st MCP; trapezioscaphoid; DIP > PIP; 1st MTP
√ loss of joint space, subchondral eburnation, marginal osteophytes, small ossicles in DIP + PIP:
√ Bouchard node = osteophytosis at PIP joint
√ Heberden node = osteophytosis at DIP joint: M÷F = 1÷10
√ radial subluxation of 1st metacarpal base
√ joint space narrowing + eburnation of trapezioscaphoid area
@ Shoulder
√ elevation of humeral head + lack of significant glenohumeral joint involvement (DDx to rheumatoid arthritis)
@ Hip
Predisposed: hip dysplasia, slipped capital femoral epiphysis, Legg-Calvé-Perthes disease, malunited femoral neck fracture, femoroacetabular impingement
√ femoral + acetabular osteophytes, sclerosis, subchondral cyst formation
√ thickening / buttressing of medial femoral cortex / calcar
√ migration of femoral head:
√ superolateral subluxation of femoral head
√ medial / axial subluxation ± protrusio acetabuli (in 20%)
√ primary hereditary protrusio = Otto pelvis (M < F)
@ Knee
Location: medial > lateral femorotibial > patellofemoral compartment
√ varus deformity (M>> F)
Associated with:
medial (66%), lateral (24%), bilateral (10%) meniscal tears (in 60% for asymptomatic + symptomatic patients alike), commonly associated with extrusion of meniscus from the joint line
@ Spine
√ sclerosis + narrowing of intervertebral apophyseal joints
√ osteophytosis usually associated with diskogenic disease
@ Sacroiliac joint
◊ Most common disorder of sacroiliac joints
Location: bi- / unilateral (contralateral SIJ with bad hip)
√ diffuse joint space loss
√ vacuum phenomenon
√ well-defined line of sclerosis, esp. on iliac side of articulation
√ prominent bridging osteophyte at superior + inferior limits of joint
DDx: osteoblastic metastasis

Erosive Osteoarthritis

= inflammatory form of osteoarthrosis
Predisposed: postmenopausal females
Site: distribution identical to noninflammatory osteoarthritis: DIP > PIP > MCP joints of hands; radial aspect of wrist; bilateral + symmetric
√ "bird-wing" / "sea-gull" joint configuration = central erosions + osteophytosis

√ may lead to bony ankylosis
DDx: Rheumatoid arthritis, Wilson disease, chronic liver disease, hemochromatosis

Early Osteoarthritis

mnemonic: **E**arly **O**steo**A**rthritis
Epiphyseal dysplasia, multiple
Ochronosis
Acromegaly

Milwaukee Shoulder

= association of
(1) Complete rotator cuff tear
(2) Osteoarthritic changes
(3) Noninflammatory joint effusion containing calcium hydroxyapatite and calcium pyrophosphate dihydrate (CPPD) crystals
(4) Hyperplasia of synovium
(5) Destruction of cartilage + subchondral bone
(6) Multiple osteochondral loose bodies
Age: older woman
• frequent history of trauma
• rapidly progressive arthritis of shoulder
Radiograph:
√ joint space narrowing
√ subchondral sclerosis + cyst formation
√ destruction of subchondral bone
√ soft-tissue swelling
√ capsular calcifications
√ intraarticular loose bodies
MR:
√ large effusion
√ complete rotator cuff tear
√ narrowing of glenohumeral joint

Rapidly Destructive Articular Disease

= unusual form of osteoarthritis typically involving the hip (almost always unilateral)
Age: elderly women
Associated with: conventional osteoarthritis in hands, wrists, knees, opposite hip
• hip pain
√ progressive loss of joint space
√ loss of subchondral bone in femoral head + acetabulum resulting in "hatchet" deformity of femoral head
√ superolateral subluxation of femoral head / intrusion deformity within ilium
√ no / small osteophytes
Prognosis: rapid destruction of hip within 14 months after onset of symptoms
Rx: total joint replacement

DDx: osteonecrosis, septic arthritis, neuroarthropathy, crystal-induced arthropathy

OSTEOBLASTOMA

= GIANT OSTEOID OSTEOMA = OSTEOGENIC FIBROMA OF BONE = OSSIFYING FIBROMA

= rare benign locally aggressive tumor with unlimited growth potential + capability of malignant transformation

Frequency: < 1% of all primary bone tumors; 3% of all benign bone tumors

Mean age: 6–19 years; 6–30 years (90%); 2nd decade (55%); 3rd decade (20%); M÷F = 2÷1

Size: lesion > 1.5 cm

N.B.: smaller lesions are classified as osteoid osteoma

Histo: numerous multinucleated giant cells (osteoclasts), irregularly arranged osteoid + bone; very vascular connective tissue stroma with interconnecting trabecular bone; trabeculae broader + longer than in osteoid osteoma

- dull localized pain of insidious onset (84%), worse at night in 7–13%; asymptomatic in < 2%
- response to salicylates in 7%
- localized swelling, tenderness, decreased range of motion (29%)
- painful scoliosis in 50% (with spinal / rib location) ← muscle spasm, may be convex toward side of tumor
- paresthesias, mild muscle weakness, paraparesis, paraplegia (← cord compression)
- occasional systemic toxicity (high WBC, fever)

Location: (rarely multifocal)

(a) spine (32–46%): 62–94% in neural arch, secondary extension into vertebral body (28–42%); cervical spine (31%), thoracic spine (34%), lumbar spine (31%), sacrum (3%)

(b) long bones (26–32%): femur (50%), tibia (19%), humerus (19%), radius (8%), fibula (4%); unusual in neck of femur

(c) small bones of hand + feet (15–26%): dorsal talus neck (62%), calcaneus (4%), scaphoid (8%), metacarpals (8%), metatarsals (8%)

(d) calvarium + mandible (= cementoblastoma)

Site: diaphyseal (58%), metaphyseal (42%); eccentric (46%), intracortical (42%), centric (12%), may be periosteal

√ similar to osteoid osteoma:
- √ radiolucent nidus > 2 (range, 2–12) cm in size
- √ well demarcated (83%)
- √ ± stippled / ringlike small flecks of matrix calcification
- √ reactive sclerosis (22–91%) / no sclerosis (9–56%)

√ progressive expansile lesion that may rapidly increase in size (25%):
- √ cortical expansion (75–94%) / destruction (20–22%)
- √ tumor matrix radiolucent (25–64%) / ossified (36–72%)
- √ sharply defined soft-tissue component
- √ thin shell of periosteal new bone (58–77%) / no periosteal reaction

√ scoliosis (35%)

√ talar osteoporosis ← disuse + hyperemia

√ rapid calcification after radiotherapy

√ marked enhancement
CT:
√ multifocal matrix mineralization + sclerosis
√ expansile bone remodeling, thin osseous shell
NUC:
√ intense focal accumulation of bone agent (100%)
Angio:
√ tumor blush in capillary phase (50%)
MR (of limited value in characterization & staging):
√ mainly lytic lesion by CT:
√ low to intermediate signal intensity on T1WI
√ mixed intermediate to high intensity on T2WI
√ lesion with some mineralization by CT:
√ mixed low and high signal intensity on T2WI
√ mainly of low signal intensity on T2WI
√ surrounding edema

Prognosis: 10–15% recurrence after excision; incomplete curettage can effect cure due to cartilage production + trapping of host lamellar bone

DDx: (1) Osteo- / chondrosarcoma (periosteal new bone)
(2) Osteoid osteoma (dense calcification + halo of bone sclerosis, stable lesion size < 2 cm due to limited growth potential)
(3) Cartilaginous tumors (lumpy matrix calcification
(4) Giant cell tumor (no calcification, epiphyseal involvement)
(5) Aneurysmal bone cyst
(6) Osteomyelitis
(7) Hemangioma
(8) Lipoma
(9) Epidermoid
(10) Fibrous dysplasia
(11) Metastasis
(12) Ewing sarcoma

OSTEOCHONDROMA

= OSTEOCARTILAGINOUS EXOSTOSIS
= developmental hyperplastic / dysplastic bone outgrowth composed of cortical + medullary bone with overlying cartilaginous cap; growth ends when nearest epiphyseal plate fuses
◊ Most common benign growth of the skeleton!
◊ Most common benign cartilage-containing tumor!

Prevalence: 20–50% of all benign bone tumors; 10% of all bone tumors

Etiology: separation of a fragment of physeal cartilage herniating through periosteal bone cuff that surrounds the growth plate (encoche of Ranvier); the fragment continues to grow and undergoes enchondral ossification

(a) developmental

(b) microtrauma / Salter-Harris injury with in vivo transplantation of physeal tissue
(c) radiation therapy (in 6–24%) with latency period of 3–17 years in patients between 8 months and 11 years of age receiving 1,500–5,500 cGy (frequently for treatment of neuroblastoma / Wilms tumor); at periphery of radiation field
◊ Most common benign radiation-induced tumor

Path: continuity of lesion with marrow + cortex of host bone (HALLMARK)

Histo: hyaline cartilage cap containing a basal surface with enchondral ossification (thin cortex + trabecular bone + marrow space) resembling growth plate

Location: 10% in small bones of the hands and feet; 1–4% in spine (50% in posterior elements of cervical spine)

• progressive painless deformity around a joint

Radiographic types:

√ sessile broad based exostosis
√ pedunculated with slender stalk / pedicle:
√ growth pointing away from nearest joint + toward center of shaft:
√ at right angle on diaphyseal side of stalk
√ slope on epiphyseal side
√ continuity of bone cortex with host bone cortex
√ <u>continuity (!) of medullary marrow space</u> with host bone
√ hyaline cartilaginous cap:
√ arcs / rings / flocculent calcifications on radiographs

CT:

√ optimal depiction of cortical + marrow continuity with host bone (PATHOGNOMONIC) by CT
√ nonmineralized cartilage cap hypodense to muscle (in 75–80%):
√ 6–8 mm thick in skeletally mature patients
√ up to 30 mm thick in skeletally immature patients

MR (best modality):

√ cortical + medullary continuity:
√ peripheral rim of low signal intensity = cortical bone
√ hyaline cartilage cap very hyperintense on T2WI + of low to intermediate intensity on T1WI ← high water content:
√ central area of fat signal intensity = cancellous bone
√ smooth continuous appearance with relatively thin cap
√ hypointense mineralized areas of cartilage
√ hypointense periphery = perichondrium
√ slight septal + peripheral enhancement
√ cartilage tends to thin and disappear at numerous points on surface of osteochondroma

US:

√ hypoechoic nonmineralized cartilaginous cap easily distinguished from muscle and fat
√ posterior acoustic shadowing for mineralized portion

NUC:

√ active lesion (predominantly in young patient)
√ quiescent lesion in older patient

Prognosis: exostosis begins in childhood; stops growing when nearest epiphyseal center fuses

after skeletal maturity

Rx: surgical excision (2% recurrence rate, 13% complication rate [neuropraxia, arterial laceration, compartment syndrome, fracture])

Cx:

(1) Osseous and cosmetic deformity (most frequent)
- mechanical limitation of joint movement
- snapping tendon / ligament
- hematuria (irritating pubic osteochondroma)

√ saucerization / scalloping of cortex of adjacent bone due to extrinsic pressure erosion (of paired tubular bones)

√ premature osteoarthritis

√ pleural effusion / spontaneous hemothorax ← irritating rib lesion

(2) Fracture through stalk of osteochondroma

(3) Vascular compromise

› venous / arterial stenosis

› arterial occlusion / venous thrombosis

› pseudoaneurysm formation:

Cause: repetitive trauma to vessel wall

Age: near end of normal skeletal growth

Location: popliteal a., brachial a., superficial femoral a., posterior tibial a.

(4) Neurologic compromise

› peripheral nerve compression with entrapment neuropathy: foot drop with peroneal nerve involvement (most frequent)

› central nerve compression: cranial nerve deficit, radiculopathy, cauda equina syndrome, cord compression with myelomalacia

√ often very narrow stalk of attachment

√ difficult imaging diagnosis owing to complex anatomy of skull base (21% TP)

√ spinal canal osteochondroma (15% FN)

(5) Reactive bursa formation (in 1.5%)
- enlarging mass overlying an osteochondroma simulating malignant transformation

Location: scapula (> 50%), lesser trochanter, shoulder

√ fluid-filled mass ± chondral filling defects:

√ mineralization of intrabursal chondral bodies may mimic a thick cartilage cap with growth

Cx: inflammation, infection, hemorrhage into bursa, secondary synovial chondromatosis

(6) Malignant transformation into secondary / peripheral chondrosarcoma / osteosarcoma

Frequency: 1% in solitary osteochondroma; 3–5% in hereditary multiple osteochondromatosis

Location: iliac bone commonest site

Of concern: interval growth, indistinct cortical margins, erosion of lesion + adjacent parent bone, large soft-tissue component

◊ Any cartilage cap > 1.0–1.5 cm thick / continued growth after skeletal maturation is suspect of malignant transformation!

mnemonic: GLAD PAST

Growth after physeal closure
Lucency (new radiolucency)
Additional scintigraphic activity
Destruction (cortical)
Pain after puberty
And
Soft-tissue mass
Thickened cartilaginous cap > 1.5 cm

DDx: parosteal osteosarcoma (no corticomedullary continuity)

Osteochondromatous Variants

1. Dysplasia epiphysealis hemimelica
2. Subungual exostosis
3. Turret exostosis
4. Traction exostosis (at tendinous attachments)
5. Bizarre parosteal osteochondromatous proliferation = Nora lesion
6. Florid reactive periostitis

Solitary Osteochondroma

Frequency: 1–2%; 20–50% of benign bone tumors; 10–15% of all bone tumors

Average age: 33 years (range, 1st–3rd decade); M÷F = 1.3÷1 to 4.1÷1

- incidental nontender painless mass near joints
- symptomatic (in 75% before the age of 20 years)

Site: metaphysis of long bones; rarely diaphysis

Location: in any bone that develops by enchondromal calcification; femur (30%), tibia (15–20%), about knee (40%), humerus (10–20%), hands and feet (10%), pelvis (5%), scapula (4%), rib (3%), spine (2%, cervical [esp. C2] > thoracic [T8 > T4] > lumbar)

Type: (a) pedunculated osteochondroma = narrow stalk
(b) sessile osteochondroma = broad base

Hereditary Multiple Exostoses

= DIAPHYSEAL ACLASIS (ACLASIA) = MULTIPLE OSTEOCHONDROMAS = FAMILIAL OSTEOCHONDROMATOSIS

= most common of osteochondrodysplasias characterized by formation of multiple exostoses

Prevalence: 1÷50,000 to 1÷100,000; 1÷1,000 on Guam / Mariana Islands

Genetics: autosomal dominant (incomplete penetrance in females); 3 distinct loci on chromosomes 8, 11, 19
◊ 2/3 of affected individuals have a positive family history

Age: forms shortly after birth; virtually all patients discovered by 12 years of age; M÷F = 1.9÷1.0

- short stature (40%) ← development of exostoses at the expense of longitudinal bone growth

Location: multiple + usually bilateral; knee (70–98%), humerus (50–98%), scapula + rib (40%), elbow (35–40%), hip (30–90%), wrist (30–60%), ankle (25–54%), hand (20–30%), foot (10–25%), pelvis (5–15%), vertebra (7–9%)

Site: metaphyses of long bones near epiphyseal plate (distance to epiphyseal line increases with growth)

√ disproportionate shortening of an extremity (50%)

@ Upper extremity

√ pseudo-Madelung deformity:

Classification of Acute Osteochondral Injury *(Outerbridge)*	
Type	*MRI Description*
1	thickening of articular cartilage with abnormal SI
2	superficial loss of cartilage thickness / fissuring
3	deep loss of cartilage thickness / fissuring
4	full-thickness injury + abnormal SI of subchondral bone
5	free osteochondral fragment

√ ulnar shortening + longer bowed radius

√ ulnar tilt of distal radial articular surface

√ ulnar deviation of hand

√ dislocation of radial head

√ radioulnar synostosis

√ shortening of 4th + 5th metacarpals

√ supernumerary fingers / toes

@ Lower extremity

√ coxa valga (25%)

√ genu valgus (20–40%)

√ valgus deformity of ankle = tibiotalar tilt (45–54%)

√ undertubulation with widened metadiaphyseal junction:

√ Erlenmeyer flask deformity of distal femur

CT:

√ "wavy pelvis" sign = small sessile lesion create undulating cortical contour

Cx: malignant degeneration in 3–5%

OSTEOCHONDROSIS DISSECANS

= OSTEOCHONDRITIS DISSECANS = OSTEOCHONDRAL FRACTURE

= fragmentation + possible separation of a portion of the articular surface

Etiology:

(1) subchondral fatigue fracture as a result of shearing, rotatory / tangentially aligned impaction forces / repetitive microtrauma

(2) ? autosomal dominant trait associated with short stature, endocrine dysfunction, Scheuermann disease, Osgood-Schlatter disease, tibia vara, carpal tunnel syndrome

Age: adolescence; M > F

- asymptomatic / vague complaints
- clicking, locking, limitation of motion
- swelling, pain aggravated by movement

Location:

(a) knee: medial (in 10% lateral) femoral condyle close to fossa intercondylaris; bilateral in

20–30%
(b) humeral head
(c) capitellum of elbow
(d) talus

√ purely cartilaginous fragment unrecognized on plain film
√ fracture line parallels joint surface
√ mouse = osteochondrotic fragment
Location: posterior region of knee joint, olecranon fossa, axillary / subscapular recess of glenohumeral joint
√ mouse bed = sclerosed pit in articular surface
√ soft-tissue swelling, joint effusion

MR:
√ focus of abnormal signal in subarticular marrow
√ defect in overlying cartilage
√ loose bodies of heterogeneous low-SI in coronoid and olecranon fossa outlined by hyperintense joint fluid on T2WI

DDx: spontaneous osteonecrosis, neuroarthropathy, degenerative joint disease, synovial osteochondromatosis

Juvenile Osteochondritis Dissecans of Knee

= disease manifestation before physeal closure
Etiology: repetitive trauma
Age: 10–15 years; M÷F= 3÷1 to 4÷1
• pain, clicking / catching of joint, loss of function ← intra-articular loose bodies
Site: (a) medial femoral condyle: posterolateral aspect (51%), weight-bearing portion (19%)
(b) lateral femoral condyle: medial aspect (7%)
√ signs of lesion instability (= high-grade lesion):
√ line of fluid signal intensity on T2WI between fragment + parent bone surrounded by low-intensity rim
√ multiple / > 5 mm cysts near lesion
√ fracture in articular cartilage
√ fluid-filled osteochondritis dissecans lesion

Osteochondritis Dissecans of Capitellum

Age: adolescent boys 13–16 years of age
Cause: overhead throwing activity / gymnastics
• dull poorly localized pain in elbow
• limited extension + locking of elbow
√ lucent defect within capitellum
√ flattening of anterior border of capitellum

OSTEOFIBROUS DYSPLASIA

= entity previously mistaken for fibrous dysplasia

Age: newborn up to 5 years
Histo: fibrous tissue surrounding trabeculae in a whorled storiform pattern
Location: normally confined to tibia (middiaphysis in 50%), lesion begins in anterior cortex; ipsilateral fibula affected in 20%
√ enlargement of tibia with anterior bowing
√ cortex thin / invisible
√ periosteal expansion
√ sclerotic margin (DDx: nonosteogenic fibroma, chondromyxoid fibroma)
√ spontaneous regression in ⅓
Cx: pathologic fracture in 25%, fractures will heal with immobilization; infrequently complicated by pseudarthrosis
DDx: fibrous dysplasia, Paget disease

OSTEOGENESIS IMPERFECTA

= PSATHYROSIS = FRAGILITAS OSSIUM = brittle bone disease = LOBSTEIN DISEASE
= heterogeneous group of a rare generalized connective tissue disorder leading to micromelic dwarfism characterized by bone fragility, blue sclerae, and dentinogenesis imperfecta
Incidence: 1÷15,000 live births per year; M÷F = 1÷1
Genetics: in 80% mutation of COL1A1 gene on chromosome 17 and COL1A2 gene on chromosome 7 that encode type I collagen
Pathophysiology: decreased / defective synthesis of type I collagen → immature collagen matrix → increased bone fragility
• hyperlaxity of joints; blue sclerae; otosclerosis; thin loose skin
@ Cranium
• soft skull (caput membranaceum)
• triangular shape of face + frontal bossing
• poor dentition
• malocclusion (← mandibular malformation)
√ multiple Wormian bones may persist into adulthood
√ retarded calvarial bone formation = abnormally thick / thin calvaria
√ brachycephaly = premature fusion of coronal suture → restricted anteroposterior skull growth → compensatory overgrowth of sagittal suture laterally + lambdoid sutures caudally
√ frontal fontanel is wider and remains open longer than normal
√ sinus + mastoid cell enlargement
√ mandibular prognathism ← vertical underdevelopment of dentoalveolar structures + condylar process
@ Ear
√ otosclerosis = otospongiosis (= thickened undermineralized otic capsule ← markedly delayed + deficient ossification of all 3 layers)
√ microfractures + deformities of middle ear ossicles (crus of stapes + handle of malleolus)
@ Brain
√ generalized cerebral atrophy ← ? impaired outflow of CSF
√ hydrocephalus
√ widened basilar cistern

Cx: intracranial hemorrhage ← moyamoya disease / vertebral artery damage / vascular fragility / spontaneous intracranial hypotension / friction between multiple bone fragments of skull

@ Craniocervical junction

√platybasia
√ basilar impression
√basilar invagination

@ Spine

√ diffuse osteopenia
√ defective cortical bone formation
√ sclerosis of vertebral endplates
√biconcave vertebral bodies + Schmorl nodes

√ collapsed vertebral bodies:
√ severe kyphoscoliosis
√ platyspondyly = loss of vertebral body height
√ biconvex / ellipsoid intervertebral disk spaces of increased height
√ spondylolisthesis (5%)

@ Thorax

√ rib thinning / notching / fractures

@ Tubular bones

√ generalized osteoporosis = diffuse demineralization, deficient trabecular structure, cortical thinning
√ defective cortical bone: increase in diameter of proximal ends of humeri + femora; slender fragile bone; multiple cystlike areas
√ multiple fractures + pseudarthrosis with bowing deformity
√ normal / exuberant callus formation
√ bowing deformities after child begins to walk

OB-US:

√ fetal movement may be reduced
√ weight of US probe may deform head quite easily

Rx: IV pamidronate administered once every 4–6 months for several years → reduced incidence of fractures and increased bone density, vertebral body height, and cortical bone thickness.

Cx: (1) Impaired hearing / deafness from otosclerosis (20–60%)
(2) Death from intracranial hemorrhage ← abnormal platelet function

Dx: chorionic villous sampling

Classification of Osteogenesis Imperfecta *(Sillence, 1979)* *based on overlapping clinical + radiologic manifestations*					
Type	*Severity*	*Sclerae*	*Fractures*	*Stature*	*Hearing*
I	mild	blue	childhood	slightly short	30%
II	lethal	dark blue	multiple in utero	death in utero / at birth	none
III	severe	white	at birth	markedly short	normal
IV	moderate	white	fragile bones	moderate growth failure	yes

Osteogenesis Imperfecta Type I

= OSTEOGENESIS IMPERFECTA TARDA
◊ Most common form of nondeforming mild disease
Transmission: autosomal dominant with varying expression; compatible with life
Prevalence: 3-4÷100,000 live births
Age at presentation: 2–6 years
• blue sclerae (50%); presenile hearing loss (50%)
• normal / abnormal dentinogenesis
√ infants of normal weight + length
√ osteoporosis; bone density may be normal in adults
√ fractures in neonate (occurring during delivery)
◊ Fractures rare after puberty as ossification is complete!

OB-US:
√ marked bowing of long bones
√ NO IUGR

Osteogenesis Imperfecta Type II

= Congenital lethal osteogenesis imperfecta
= least common perinatal (obstetrical) lethal form
Transmission: sporadic new dominant mutations / autosomal recessive
Prevalence: 1÷54,000 births
• disease manifest at birth (in utero); NO hearing loss
• blue sclerae; ligamentous laxity + loose skin
√ shortened broad crumpled long bones
√ bone angulations, bowing, demineralization
√ localized bone thickening from callus formation
√ thin beaded ribs ± fractures → bell-shaped / narrow chest
√ thin poorly ossified skull
√ wormian bones (present in most cases)
√ spinal osteopenia
√ platyspondyly

OB-US:
◊ A normal sonogram after 17 weeks MA excludes the diagnosis!
√ increased through-transmission of skull ← extremely poor mineralization:

√ unusually good visualization of brain surface + orbits
√ increased visualization of intracranial arterial pulsations
√ abnormal compressibility of skull vault with transducer
√ decreased visualization of skeleton
√ multiple fetal fractures + deformities of long bones + ribs:
√ wrinkled appearance of bone ← more than one fracture in single bone
√ beaded ribs ← callus formation around fractures
√ abnormally short limbs
√ small thorax ← collapse of chest cage
√ decreased fetal movement
√ infants small for gestational age (frequent)
√ polyhydramnios + nonimmune hydrops

Prognosis: stillborn / death shortly after birth ← pulmonary hypoplasia / cerebral hemorrhage

DDx: congenital hypophosphatasia; achondrogenesis type I; camptomelic dysplasia

Osteogenesis Imperfecta Type III

= SEVERE PROGRESSIVELY DEFORMING OI

Transmission: autosomal recessive; progressively deforming disorder compatible with life

Prevalence: 1-2÷100,000 live births

• bluish sclerae during infancy that turn pale with time
• joint hyperlaxity (50%); small nose, soft skull
• NO hearing loss
√ micrognathia
√ decreased ossification of skull
√ normal vertebrae + pelvis
√ shortened + bowed long bones
√ progressive deformities of limbs + spine into adulthood
√ ± rib fractures
√ multiple fractures present at birth in ²/₃ of cases
√ fractures heal well

OB-US:
√ short + bowed long bones
√ fractures
√ humerus almost normal in shape
√ normal thoracic circumference

Prognosis: progressive limb + spine deformities during childhood / adolescence

Osteogenesis Imperfecta Type IV

= less severely deforming than type III

Transmission: autosomal dominant

Prevalence: 3-4÷100,000 live births

• normal scleral color; hearing loss
√ tubular bones of normal length; mild femoral bowing may occur
√ osteoporosis

OB-US:
√ bowing of long bones

OSTEOID OSTEOMA

= benign osteoblastic neoplasm characterized by intracortical nidus of osteoid tissue / woven mineralized immature bone, often surrounded by dense sclerotic reactive bone

Size: < 1.5 cm in diameter (per definition);
N.B.: lesion > 1.5 cm = osteoblastoma

Frequency: 12% of benign bone tumors

Etiology: ? inflammatory response

Histo: small nidus of osteoid-laden interconnected trabeculae with background of highly vascularized fibrous connective tissue surrounded by zone of reactive bone sclerosis; osteoblastic rimming; indistinguishable from osteoblastoma [*nidus*, Latin = nest]

Mean age: 7–25 years (range, 19 months–56 years); 2nd + 3rd decade (73%); 5–25 years (90%); uncommon < 5 and > 40 years of age; uncommon in Blacks; M÷F = 2÷1 to 3÷1

- tender to touch + pressure
- local pain (95–98%), weeks to years in duration, worse at night, decreased by activity:
  - salicylates give relief in 20–30 minutes in 75–90%
- prostaglandin E2 elevated 100–1000 x normal within nidus (probable cause of pain and vasodilatation)

Location:

(a) meta- / diaphysis of long bones (73%): upper end of femur (43%), hands (8%), feet (4%); frequent in proximal tibia + femoral neck, fibula, humerus; no bone exempt

(b) spine (10–14%): predominantly in neural arch (50% in pedicle + lamina + spinous process); 20% in articular process) of lumbar (59%), cervical (27%), thoracic (12%), sacral (2%) segments
  - painful scoliosis, focal / radicular pain
  - gait disturbance, limb atrophy

(c) skull, scapula, rib, pelvis, mandible, patella

√ round / oval radiolucent nidus (75%) of < 1.5 cm in size
√ variable surrounding sclerosis ± central calcification
√ painful scoliosis concave toward lesion / kyphoscoliosis / hyperlordosis / torticollis with spinal location ← spasm
√ may show extensive synovitis + effusion + premature loss of cartilage with intraarticular site (lymphofollicular synovitis)
√ osteoarthritis (50%) with intraarticular site 1.5–22 years after onset of symptomatology
√ regional osteoporosis ← probably disuse
◊ Radiographically difficult areas: vertebral column, femoral neck, small bones of hand + feet

NUC (bone scintigraphy is the most sensitive method!):
√ intensely increased radiotracer uptake (increased blood flow + new-bone formation)
√ "double density" sign = small area of focal activity (nidus) superimposed on larger area of increased tracer uptake

CT (for characterization + precise localization of nidus):

√ small well-defined round / oval nidus of low attenuation:
√ surrounded by variable amount of sclerosis
√ nidus with variable amount of mineralization (50%): punctate / amorphous / ringlike / dense
√ nidus enhances on dynamic scan

MR (diminished conspicuity of lesion compared with CT):
√ heterogeneous nidus ← depending on tumor vascularity and presence of calcifications:
√ mostly hypo- to isointense to muscle on T1WI
√ variable signal intensity on T2WI; SI may increase to between that of muscle + fat / remains low on T2WI
√ perinidal edema / inflammation in adjacent bone marrow + soft tissues (47%)
√ synovitis + joint effusion with intraarticular site

Angio:
√ highly vascularized nidus with intense circumscribed blush appearing in early arterial phase + persisting late into venous phase

Prognosis: no growth progression, infrequently regression

Rx: (1) complete surgical excision of nidus (reactive bone regresses subsequently)
(2) percutaneous CT-guided removal
(3) percutaneous ablation with radio-frequency electrode / laser / alcohol

DDx: (1) Stress fracture (focal cortical ridge, decreasing size, linear intense uptake of bone tracer)
(2) Intracortical abscess (irregular inner margin, eccentric sequestrum, no central enhancement)
(3) Intracortical hemangioma (vertically aligned intralesional calcifications, hyperintense lesion with hypointense septa)
(4) Small chondroblastoma (epiphyseal intramedullary location, punctate calcification)
(5) Osteoblastoma (less painful, no response to salicylate, more expansile + larger than 2 cm, progressive growth)
(6) Compensatory hypertrophy of pedicle (contralateral spondylolysis, lack of nidus)

Intracortical Osteoid Osteoma (most common)

= nidus within cortex accompanied by cortical thickening + reactive sclerosis

Location: shaft of long bone

√ solid / laminated periosteal reaction
√ fusiform sclerotic cortical thickening
√ round / oval radiolucent area < 2 cm in diameter within center of osteosclerosis

DDx: Brodie abscess, sclerosing osteomyelitis, syphilis, bone island, stress fracture, osteosarcoma, Ewing sarcoma, osteoblastic metastasis, lymphoma, subperiosteal aneurysmal bone cyst, osteoblastoma

Cancellous Osteoid Osteoma (intermediate frequency)

= intramedullary

◊ Intraarticular lesion difficult to identify with delay in diagnosis of 4 months–5 years!

Site: juxta- / intraarticular at femoral neck, vertebral posterior elements, small bones of hands + feet

√ little osteosclerosis / sclerotic cortex distant to nidus ← functional difference of intraarticular periosteum

√ joint space widened ← effusion, synovitis

Subperiosteal Osteoid Osteoma (rare)

= round soft-tissue mass adjacent to bone

Site: juxta- / intraarticular at medial aspect of femoral neck, hands, feet (neck of talus)

√ juxtacortical mass excavating the cortex with almost no reactive sclerosis ← bony pressure atrophy

Intraarticular Osteoid Osteoma (rare)

= nidus within / near a joint

Location: hip

• joint tenderness, not necessarily worse at night

√ prominent joint effusion ± synovial hypertrophy

√ minimal / absent reactive cortical thickening ← lack of cambium (= inner layer of periosteum)

DDx: inflammatory / septic / tuberculous / rheumatoid arthritis, nonspecific synovitis / Legg-Calvé-Perthes disease

OSTEOMA

= benign tumor of membranous bone (= hamartoma)

Histo: mature compact / cancellous bone

Age: adult life

Associated with: Gardner syndrome (multiple osteomas + colonic polyposis)

Location: craniofacial bones

(1) inner / outer table of calvarium (usually from external table)

(2) paranasal sinuses (frontal / ethmoid sinuses)

(3) mandible (posterior body / condyle)

√ non–tooth-related circumscribed sclerotic mass

DDx: idiopathic osteosclerosis WITHOUT bone expansion cannot be differentiated from osteoma.

(4) nasal bones

√ well-circumscribed round extremely dense structureless lesion usually < 2 cm in size

√ ± bone expansion / exophytic growth

√ NO perilesional halo

Fibrous Osteoma

Probably a form of fibrous dysplasia

Age: childhood

√ less dense than osteoma / radiolucent

√ expanding external table without affecting internal table

DDx: endostoma, bone island, bone infarct (located in medulla)

OSTEOMYELITIS

= inflammation of bone and marrow caused by bacteria (most commonly pyogenic bacteria + mycobacteria), fungi, parasites, viruses

Predisposed: immunosuppression, diabetes mellitus, sickle cell disease, intravenous drug abuse, alcoholism

Source of infection:

(a) direct inoculation: open fracture / direct trauma (commonly in young adults)
- prominent local signs and symptoms

(b) hematogenous: bacteremia (commonly in elderly / child)
- slow insidious progression of symptoms
- positive blood culture (in 50%)

(c) extension from adjacent soft-tissue infection

Location: tibia, wrist, femur, rib, thoracolumbar spine

Dx: requires 2 out of 4 of the following criteria

(1) purulent material draining from site of osteomyelitis
(2) positive findings at bone tissue / blood culture
(3) localized classic physical findings of bone tenderness
(4) positive radiologic findings

Acute Pyogenic Osteomyelitis

Age: most commonly affects children

Organism:

(a) newborns: S. aureus, group B streptococcus, E. coli
(b) children: S. aureus (blood cultures in 50% positive)
(c) adults: S. aureus (60%), enteric species (29%), Streptococcus (8%)
(d) drug addicts: Pseudomonas (86%), Klebsiella, Enterobacteriae; (57 days average delay in diagnosis)
(e) sickle cell disease: S. aureus, Salmonella
(f) diabetics: often multiple organisms like S. aureus, Streptococcus, E. coli, Klebsiella, Clostridia, Pseudomonas (in soil + sole of shoes)
(g) HIV-infected patients: TB, atypical mycobacteria

Cause:

(1) genitourinary tract infection (72%)
(2) lung infection (14%)
(3) dermal infection (14%): direct contamination from a soft-tissue lesion in diabetic patient

Pathophysiology:

bacterial growth in bone → entrapped bone becomes necrotic within 48 hours → spread to shaft ± periosteum (large subperiosteal abscess in children) → lifted periosteum impedes blood supply → sequestrum (= dead bone) → rupture of periosteum → draining sinus + soft-tissue abscess; host response causes reactive sleeve of new bone deposition (= involucrum) [involucrum, *Latin* = covering / sheath]
[sequestrum, *Latin* = deposit], [cloaca, *Latin* = sewer, canal]

Location:

@ Lower extremity (75%) over pressure points in diabetic foot

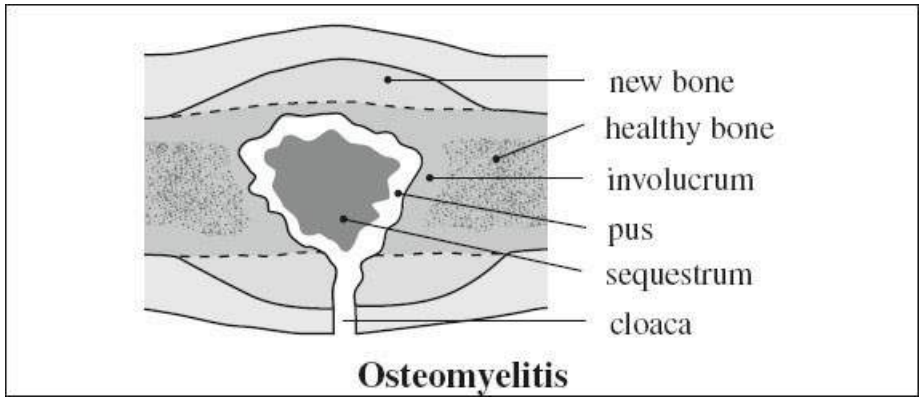
@ Vertebra (53%) = infectious spondylitis:
lumbar (75%) > thoracic > cervical
@ Radial styloid (24%)
@ Sacroiliac joint (18%)

• leukocytosis + fever (66%)

Conventional radiographs (insensitive):

√ radiographs normal in 95% at presentation (notoriously poor in early phase of infection for as long as 10–21 days)
DDx: infarction (similar radiographic findings)

√ some abnormality in 90% 28 days after onset of infection:
√ localized soft-tissue swelling adjacent to metaphysis with obliteration of usual fat planes (after 3–10 days)
√ permeative metaphyseal osteolysis (lags 7–14 days behind pathologic changes)
√ endosteal erosion
√ intracortical fissuring
√ involucrum = cloak of laminated / spiculated periosteal reaction (develops after 20 days)



Osteomyelitis

√ button sequestrum = detached necrotic cortical bone (develops after 30 days)
√ cloaca formation = space in which dead bone resides

US:

√ soft-tissue changes, fluid collection, periosteal reaction

CT:

√ overlying soft-tissue swelling
√ periosteal reaction
√ hypoattenuating marrow = density difference of > 20 HU compared to healthy side indicates marrow infection
√ trabecular coarsening
√ focal cortical erosion
√ extramedullary fat-fluid level ← cortical breach

MR (82% sensitive, 80% specific in diabetics):

◊ demonstrates extent of infection
◊ normal marrow / low SI on T2WI excludes osteomyelitis!
√ bone marrow hypointense on T1WI in geographic confluent pattern ← infiltration by

inflammatory cells + purulent material

√ hyperintense relative to normal fatty marrow on T2WI / STIR (= water-rich inflammatory tissue + edema fluid)

◊ Periarticular bone marrow edema can be seen adjacent to joints involved by noninfectious inflammatory arthropathy / osteoarthritis and does not reliably indicate osteomyelitis!

DDx: noninfectious inflammatory arthropathy (Charcot joint), osteoarthritis, cellulitis, normal hematopoietic marrow in children

√ variable enhancement after IV administration of Gd-chelate

√ focal / linear cortical involvement hyperintense on T2WI

√ subperiosteal infection = hyperintense halo surrounding cortex on T2WI

√ sinus tract (= communication of medullary fluid collection with soft-tissue fluid collection through cortical disruption) = hyperintense line on T2WI extending from bone to skin surface + enhancement of its borders

√ sequestrum = central hypointense area on T2WI

Abscess characteristics at MRI:

√ hyperintense enhancing rim (= hyperemic zone) around a central focus of low intensity (= necrotic / devitalized tissue) on contrast-enhanced T1WI

√ hyperintense fluid collection surrounded by hypointense pseudocapsule on T2WI + contrast enhancement of granulation tissue

√ adjacent hyperintense soft tissues on T2WI

√ fat-suppressed contrast-enhanced imaging (88% sensitive + 93% specific compared with 79% + 53% for nonenhanced MR imaging)

DDx: bone tumor ("no penumbra" sign = higher-SI layer of granulation tissue lining abscess cavity on T1WI)

NUC (~ 90% accurate):

Advantage: imaging of whole skeleton!

(1) ^{67}Ga scan: 100% sensitivity; increased uptake 1 day earlier than for ^{99m}Tc-MDP

◊ Gallium also helpful for chronic osteomyelitis!

(2) Static ^{99m}Tc-diphosphonate: 83% sensitive with 5–60% false-negative rate in neonates + children because of

(a) masking effect of epiphyseal plates

(b) early diminished blood flow with infection

(c) spectrum of uptake pattern from hot to cold

(3) **Triple-phase skeletal scintigraphy**:

92% sensitive + 87% specific

◊ Positive within 1–2 days after onset of symptoms!

Phase 1: Radionuclide angiography = increased perfusion phase of regional blood flow

Phase 2: "blood pool" images ← hyperemia = tissue phase

Phase 3: "bone uptake" ← increased osteoblastic activity = delayed phase

√ increased activity in all 3 phases (HALLMARK)

√ photopenia (rare) = "cold" osteomyelitis (due to vascular thrombosis + bone infarct) → may become "hot" at subsequent imaging (esp. TB)

◊ No uptake during delayed phase = no osteomyelitis!

◊ Obtain SPECT whenever possible!

Limitations: diagnostic difficulties in children (motion), in posttraumatic / postoperative state, diabetic neuropathy (poor blood supply), neoplasia, septic arthritis, Paget disease, healed osteomyelitis, noninfectious inflammatory process

(4) WBC-scan:

(a) ^{111}In-labeled leukocytes: best agent for acute infections

(b) ^{99m}Tc-hexamethylpropyleneamine oxime labeled leukocytes: preferred over ^{111}In-leukocyte imaging especially in extremities

◊ WBC scans have largely replaced gallium imaging for acute osteomyelitis ← faster imaging + greater resolution ← improved photon flux and improved dosimetry (higher dose allowed relative to ^{111}In)

(5) Bone marrow imaging (^{99m}Tc-sulfur colloid) in combination with WBC-scan

√ "cold" area in early osteomyelitis subsequently becoming "hot" if localized to long bones / pelvis (not seen in vertebral bodies)

√ local increase in radiopharmaceutical uptake (positive within 24–72 hours)

Scintigraphy is more useful than MR imaging in a child when the suspected site of osteomyelitis is not clinically evident (+ bacteremia / limping / refusing to bear weight)

Cx: (1) Abscess of soft-tissue / bone

(2) Fistula formation

(3) Pathologic fracture

(4) Septic arthritis (← extension into joint)

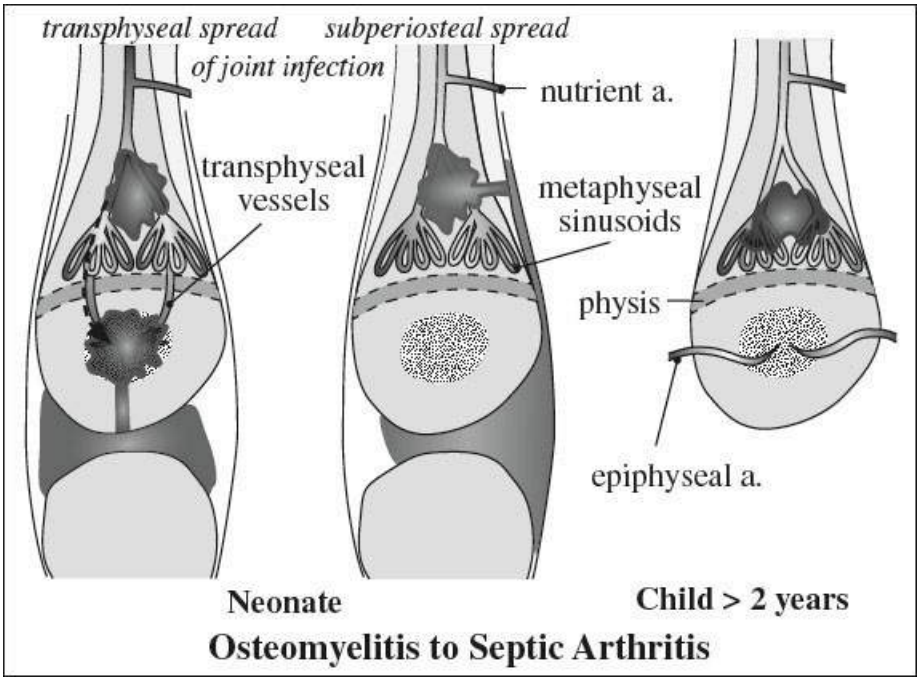
(5) Growth disturbance due to epiphyseal involvement

(6) Neoplasm

(7) Amyloidosis

(8) Severe deformity with delayed treatment

Acute Pyogenic Neonatal Osteomyelitis



Age: onset < 30 days of age
Prevalence: 1–3 ÷1000 admissions to nursery
Risk factors: prematurity, low birth weight, complicated delivery, antecedent illness, umbilical artery catheterization, invasive procedure
Anatomy: metaphyseal vessels penetrate growth plate (= physis) crossing into epiphysis
Site: metaphysis + epiphysis of long bones

• little / no systemic disturbance
√ multicentric involvement more common
√ often joint involvement (transphyseal / subperiosteal route)
√ bone scan falsely negative / equivocal in 70%

Acute Pyogenic Osteomyelitis in Infancy

Age: < 18 months of age
Anatomy: metaphyseal vessels penetrate growth plate (= physis) crossing into epiphysis
Pathomechanism: spread from metaphysis to epiphysis
√ striking soft-tissue component
√ subperiosteal abscess with extensive periosteal new bone
Cx: frequent infection of epiphysis + joint ← transphyseal blood flow

◊ osteomyelitis of proximal femur is usually associated with septic arthritis in children < 1 year of age.

Prognosis: rapid healing

Acute Pyogenic Osteomyelitis in Childhood

Cause: hematogenous spread ← bacteremia
Organism: Staphylococcus aureus, β-hemolytic Streptococcus, Streptococcus pneumoniae, Escherichia coli, Pseudomonas aeruginosa; increasing incidence

of methicillin-resistant S. aureus (MRSA) and Kingella kingae

Age: 2–16 years of age

Anatomy: transphyseal vessels closed; metaphyseal vessels adjacent to growth plate loop back toward metaphysis

Site: primary focus of infection located in metaphysis via nutrient artery; abscess formation in medulla with spread to cortex

Pathophysiology: metaphyseal capillaries lack phagocytic lining cells → uninhibited growth of microorganisms

Location: femur, tibia

√ sequestration frequent

√ periosteal elevation → disruption of periosteal blood supply

√ small single / multiple osteolytic areas in metaphysis

√ extensive periosteal reaction parallel to shaft (after 3–6 weeks); may be "lamellar nodular" (DDx: osteoblastoma, eosinophilic granuloma)

√ shortening of bone ← destruction of epiphyseal cartilage

√ growth stimulation ← hyperemia + premature maturation of adjacent epiphysis

√ midshaft osteomyelitis less frequent site

√ serpiginous tract with small sclerotic rim (PATHOGNOMONIC)

CAVE:

(1) Increased uptake in contralateral limb in patient with a limp

(2) Diffuse hyperemia in normal bones of an extremity involved with focal osteomyelitis should not be mistaken for multifocal osteomyelitis / septic arthritis.

Acute Pyogenic Osteomyelitis in Adulthood

Associated with: soft-tissue abscess, pathological fracture

Risk factors: IV drug use, previous trauma, immunosuppressed state, diabetes

Site: epiphysis + subchondral region (after growth plate closure)

√ delicate periosteal new bone

√ joint involvement common

Chronic Osteomyelitis

◊ ^{67}Ga citrate more useful than ^{111}In-labeled leukocytes ← lymphocytes are predominant cell type

◊ CT considered superior to MR for chronic osteomyelitis

√ cortical destruction and gas

√ thick irregular sclerotic bone with radiolucencies, elevated periosteum, chronic draining sinus

Sclerosing Osteomyelitis of Garré

= STERILE OSTEOMYELITIS

= low-grade nonnecrotic nonpurulent infection

Location: mandible (most commonly)

√ focal bulge of thickened cortex ← sclerosing periosteal reaction)

DDx: osteoid osteoma, stress fracture

Chronic Recurrent Multifocal Osteomyelitis

= benign self-limited disease of genetic etiology

◊ May be identical to chronic sclerosing osteomyelitis of Garré; childhood equivalent to SAPHO syndrome

Age: children + adolescents; M÷F = 1÷2

Histo: nonspecific subacute / chronic osteomyelitis

- pain, tenderness soft-tissue swelling
- limited range of motion
- elevated ESR + C-reactive protein; normal WBC

Associated with: psoriasis, palmoplantar pustulosis, inflammatory bowel disease

Location: tibia > femur > clavicle > fibula

◊ Whole-body imaging (^{99m}Tc bone scintigraphy, MRI) usually shows additional unsuspected locations

Site: metaphyses of long bones (75%); often symmetric

√ No abscess formation, fistula, sequestra

Early:

√ small areas of bone lysis, often confluent

√ progressive sclerosis surrounding osteolytic foci

MRI:

√ bone marrow edema, periostitis, soft-tissue inflammation, transphyseal disease

√ joint effusion (30%), synovial thickening, cartilage destruction, destruction of subchondral bone

Late:

√ sclerosis + hyperostosis

Prognosis: delayed spontaneous resolution

DDx: subacute + chronic infectious osteomyelitis; histiocytosis; hypophosphatasia; malignancy (leukemia, lymphoma, Ewing sarcoma)

Brodie Abscess

= small intraosseous abscess involving cortex surrounded by reactive bone (in smoldering indolent infection of subacute pyogenic osteomyelitis / inadequate treatment of acute osteomyelitis)

Organism: S. aureus (most common); cultures often negative

Histo: granulation tissue + eburnation

Age: more common in children; M > F

Location: predilection for ends of tubular bones (proximal / distal tibial metaphysis most common); carpal + tarsal bones

Site: metaphysis, rarely traversing the open growth plate; epiphysis (in children + infants)

√ lytic lesion often in an oval configuration that is oriented along the long axis of the bone

√ surrounded by thick dense rim of reactive sclerosis that fades imperceptibly into surrounding bone

√ lucent tortuous channel extending toward growth plate prior to physeal closure (PATHOGNOMONIC)

√ periosteal new-bone formation

√ ± adjacent soft-tissue swelling

√ may persist for many months
MR:
√ "double line" effect = high SI of granulation tissue surrounded by low SI of bone sclerosis on T2WI
√ well-defined lesion of low- to intermediate SI outlined by low-signal rim on T1WI
√ generally surrounded by marrow edema
√ no / rim enhancement after IV Gd-chelate
DDx: Osteoid osteoma

Epidermoid Carcinoma

Etiology: complication of chronic osteomyelitis (0.2–1.7%)
Histo: squamous cell carcinoma (90%); occasionally: basal cell carcinoma, adenocarcinoma, fibro-sarcoma, angiosarcoma, reticulum cell sarcoma, spindle cell sarcoma, rhabdomyosarcoma, parosteal osteosarcoma, plasmacytoma
Age: 30–80 (mean 55) years; M >> F
Latent period: 20–30 (range of 1.5–72) years
• history of childhood osteomyelitis
• exacerbation of symptoms with increasing pain, enlarging mass
• change in character / amount of sinus drainage
Location: at site of chronically / intermittently draining sinus; tibia (50%), femur (21%)
√ lytic lesion superimposed on changes of chronic osteomyelitis
√ soft-tissue mass
√ pathologic fracture
Prognosis:
(1) Early metastases in 14–20–40% (within 18 months)
(2) No recurrence in 80%

OSTEOPATHIA STRIATA

= VOORHOEVE DISEASE
= disorder of secondary spongiosa of X-linked dominant inheritance / sporadic occurrence
• usually asymptomatic (similar to osteopoikilosis)
• no known associated physical / laboratory abnormality → incidental radiographic discovery
Genetics: unknown
Location: all long bones symmetrically affected
Site: the only bone sclerosis primarily involving metaphysis (with extension into epi- and diaphysis)
√ dense linear longitudinal striations in diaphyses + metaphysis of long tubular bones: typically in areas of rapid growth
√ radiating fan-shaped densities of "sunburst" appearance from acetabulum into ileum

OSTEOPETROSIS

= rare hereditary disorder
Path: normal / increased number of osteoclasts → defective acidification function of osteoclast required to dissolve bone matrix → failure of proper reabsorption and

remodeling of primary spongiosa → bone sclerotic + thick but structurally weak + brittle

Cx: (1) Usually transverse fractures (common because of brittle bones) with abundant callus + normal healing
(2) Crowding of marrow (myelophthisic anemia + extramedullary hematopoiesis)
(3) Frequently terminates in acute leukemia

Rx: bone marrow transplant

DDx: (1) Heavy metal poisoning
(2) Melorheostosis (limited to one extremity)
(3) Hypervitaminosis D
(4) Pyknodysostosis
(5) Fibrous dysplasia of skull / face

Infantile Autosomal Recessive Osteopetrosis

= congenital more severe form / malignant subtype

Cause: defect on chromosome 11q13

Genetics:
(a) inactivation mutation of T-cell immune regulator 1 encoding α3 subunit of vacuolar proton pump ATP6i, responsible for proton transport in resorption lacunae
(b) homozygous mutations in chloride 7 channel
(c) defect in gray-lethal / osteopetrosis-associated transmembrane protein gene

- failure to thrive; lymphadenopathy
- premature senile appearance of facies; severe dental caries
- pancytopenia (= anemia, leukocytopenia, thrombocytopenia) ← severe marrow depression
- cranial nerve compression → optic atrophy, deafness
- hepatosplenomegaly ← extramedullary hematopoiesis
- subarachnoid hemorrhage ← thrombocytopenia

May be associated with: renal tubular acidosis + cerebral calcification

√ dense skeleton

√ splayed metaphyses + costochondral junctions

√ fractures from minor trauma ← brittle bones

Prognosis: stillbirth / early demise, survival beyond middle life uncommon (death due to recurrent infection, massive hemorrhage, terminal leukemia)

DDx: chronic renal failure, oxalosis, pyknodysostosis, physiologic sclerosis

Benign Adult Autosomal Dominant Osteopetrosis

= Osteopetrosis type 2 = = ALBERS-SCHÖNBERG DISEASE = MARBLE BONE DISEASE

[Heinrich Ernst Albers-Schönberg (1865–1921), radiologist, founder of the journal Fortschritte auf dem Gebiete der Röntgenstrahlen]

Cause: defect on chromosome 1p21

Genetics:
(a) deactivation of one allele of chloride 7 channel gene → some loss of function of the chloride 7 channel

(b) mutations in carbonic anhydrase II, T-cell immune regulator 1, osteopetrosis-associated transmembrane, and pleckstrin homology domain–containing family M member 1 (PLEKHM1)

Onset: in adolescence / adulthood with variable penetrance

- 50% asymptomatic; recurrent fractures
- mild anemia ← narrowed medullary canals
- occasionally cranial nerve palsy

√ increased density of medullary portion of bone with relative sparing of cortices (hallmark)

Phenotype I:

Distribution: long bones, skull, spine

√ diffuse osteosclerosis = generalized dense amorphous structureless bones with obliteration of normal trabecular pattern; mandible least commonly involved

√ Erlenmeyer flask deformity = clublike long bones with cortical thickening and medullary encroachment ← lack of tubulization + flaring of ends

Phenotype II:

Distribution: pelvis, spine

√ bone-within-bone appearance (= endobones)

√ "sandwich" vertebrae / rugger-jersey spine = dense endplate sclerosis with sharp margins

√ longitudinal metaphyseal striations:

√ alternating sclerotic + radiolucent transverse metaphyseal lines (phalanges, ilium) = indicators of fluctuating course of disease

√ sclerosis predominantly involving base of skull; calvaria often spared:

√ obliteration of mastoid cells, paranasal sinuses, basal foramina by osteosclerosis

Prognosis: normal life expectancy

OSTEOPOIKILOSIS

[*poikilos*, Greek = mottled]

= OSTEOPATHIA CONDENSANS DISSEMINATA

= rare autosomal dominant sclerosing bone dysplasia ← disorder of endochondral ossification involving the secondary spongiosa characterized by multiple bone islands / enostoses

Age: no age predilection (may not develop until after childhood); M = F

Histo: hamartomatous foci of lamellar cortical bone within dense trabeculae of spongy bone / inner bone cortex = compact bone islands

Genetics: inactivating mutation in LEM domain–containing protein 3 gene (LEMD = protein that antagonizes transforming growth factor (TGF)–b and bone morphogenic protein signaling focal deposits of compact lamellar bone in spongiosa

Associated with:

@ Dermatologic disorders:

1. Dermatofibrosis lenticularis disseminata (**Buschke-Ollendorff syndrome)** = asymptomatic small flesh-colored to yellow dermal papules / coalescent plaques (in 25%) on buttocks, trunk, arms, skin folds

Age: usually in childhood; often in 1st year of life

Histo: connective tissue nevi with predominantly abnormal elastin / abnormal

collagen
2. Scleroderma
3. Keloid formation

@ Bone abnormalities:
1. Melorheostosis
2. Osteopathia striata
3. Synovial chondromatosis
4. Rheumatoid arthritis

• commonly asymptomatic
• mild articular pain + joint effusion (15–20%)

Site: metaphyses + epiphyses (rarely extending into midshaft)

Location: long tubular bone epiphysis / metaphysis; hand (carpal + metacarpal), foot (tarsal + metatarsal), ankle, pelvis (glenoid + acetabulum), scapula; rare in skull, ribs, vertebral centra, mandible

√ multiple round / ovoid / lenticular bone islands (2–10 mm) in an often symmetric distribution:
√ long axis of lesions parallel to long axis of bone
√ may increase / decrease in size and number
√ may disappear

√ bone scintigraphic activity usually normal / mildly increased (similar to bone island / enostosis)

√ MR signal characteristics equal to cortical bone

Prognosis: not progressive, no change after cessation of growth

DDx: (1) Epiphyseal dysplasia (metaphyses normal)
(2) Melorheostosis (diaphyseal involvement)
(3) Mastocytosis
(4) Tuberous sclerosis
(5) Osteoblastic metastases

OSTEOSARCOMA

= malignant tumor of connective tissue producing osteoid matrix + variable amounts of cartilage matrix + fibrous tissue

Most common malignant primary bone tumor in adolescents + children; 2nd most common primary malignant bone tumor after multiple myeloma

Prevalence: 4–5÷1,000,000 annually; 15% of all primary bone tumors confirmed at biopsy; < 1% of all cancers in USA

Types & Frequency: *<u>underlined</u> are types recognized by WHO*

A. <u>Conventional</u> osteosarcoma:
› high-grade intramedullary 75%
› <u>telangiectatic</u> 4.5–11%
› <u>low-grade intraosseous</u> 4–5%
› <u>small cell</u> 1–4%
› osteosarcomatosis 3–4%
› gnathic 6–9%

B. Surface / juxtacortical osteosarcoma: 4–10%

associated with periosteum + variable medullary canal involvement
› parosteal 65%
› periosteal 25%
› high-grade surface 10%
› intracortical rare

C. Extraskeletal 4%

D. Secondary osteosarcoma 5–7%

Work-up: local staging by MR before biopsy; distant staging with bone scan + chest CT

Prognosis: dependent on age, sex, tumor size, site, classification; best predictor is degree of tissue necrosis in postresection specimen following chemotherapy (91% survival with tumor necrosis > 90%, 14% survival with < 90% tumor necrosis)

Extraskeletal Osteosarcoma

= extremely uncommon high-grade malignant tumor that occurs in older age group than osteosarcoma of bone

Frequency: 1.2% of soft-tissue sarcomas

Histo: variable amounts of neoplastic osteoid + bone + cartilage; frequently associated with fibrosarcoma, malignant fibrous histiocytoma, malignant peripheral nerve sheath tumor

Mean age: 50 years; 94% > 30 years of age; M > F

Location: lower extremity (thigh in 42–47%); upper extremity (12–23%); retroperitoneum (8–17%); buttock, back, orbit, submental, axilla, abdomen, neck, cheek, parotid gland, scalp, soft tissues adjacent to mandible, kidney, breast

Site: in soft tissue without attachment to bone / periosteum

- slowly growing firm soft-tissue mass; painful + tender (in 25–50%)
- history of trauma (12–31%): in preexisting myositis ossificans / site of intramuscular injection
- history of irradiation (5–10%)
- elevated levels of alkaline phosphatase (prognostic)

Size: average diameter of 9 cm

√ well circumscribed often deep-seated and fixed tumor

√ focal / massive area of characteristically amorphous mineralization (> 50%) most prominent at center of lesion

√ faint moderate inhomogeneous enhancement

√ increased radionuclide uptake on bone scan

Prognosis:

(1) multiple local recurrences (in 80–90%) after interval of 2 months to 10 years
(2) metastases after interval of 1 month to 4 years: lungs (81–100%), lymph nodes (25%), bone, subcutis, liver
(3) death within 2–3 years (> 50%) with tumor size as major predictor

DDx: myositis ossificans (calcifications most prominent at periphery of lesion)

High-grade Intramedullary Osteosarcoma

= CENTRAL / CONVENTIONAL OSTEOSARCOMA

Histo: arising from undifferentiated mesenchymal tissue; forming fibrous / cartilaginous / osseous matrix (mostly mixed) that produces osteoid / immature bone

(a) osteoblastic (50–80%)
(b) chondroblastic (5–25%)
(c) fibroblastic-fibrohistiocytic (7–25%)

Age: bimodal distribution 10–25 years and > 60 years; 21% < 10 years; 68% < 15 years; 70% between 10 and 30 years; M÷F = 3÷2 to 2÷1;
> 35 years: related to preexisting condition

- painful swelling (1–2 months' duration); fever (frequent)
- slight elevation of alkaline phosphatase
- diabetes mellitus (paraneoplastic syndrome) in 25%

Location: long bones (70–80%), femur (40–45%), tibia (16–20%); 50–55% about knee; proximal humerus (10–15%); facial bones (8%); cylindrical bone < 30 years; flat bone (ilium) > 50 years; spine (0.6–3.2%)

Site: origin in metaphysis (90–95%) / diaphysis (2–11%) /epiphysis (< 1%); growth through open physis with extension into epiphysis (75–88%)

Doubling time: 20–30 days

√ usually large bone lesion of > 5–6 cm when first detected
√ cloudlike density (90%) / almost normal density / osteolytic (fibroblastic type)
√ aggressive periosteal reaction: sunburst / hair-on-end / onion-peel = laminated / Codman triangle
√ moth-eaten bone destruction + cortical disruption
√ soft-tissue mass with tumor new bone (osseous / cartilaginous type)
√ transphyseal spread before plate closure (75–88%); physis does NOT act as a barrier to tumor spread
√ spontaneous pneumothorax ← subpleural metastases

NUC (bone scintigraphy):
√ intensely increased activity on blood flow, blood pool, delayed images (hypervascularity, new-bone formation)
√ soft-tissue extension demonstrated, especially with SPECT
√ bone scan establishes local extent (extent of involvement easily overestimated due to intensity of uptake), skip lesions, metastases to bone + soft tissues

CT:
√ very high attenuation (mineralized matrix) in 80%
√ soft-tissue attenuation (nonmineralized portion) replacing fatty bone marrow
√ low attenuation (higher water content of chondroblastic component / hemorrhage / necrosis)

MR (preferred modality):
√ tumor of intermediate SI on T1WI + high SI on T2WI
√ clearly defines marrow extent (best on T1WI), vascular involvement, soft-tissue component (best on T2WI)

Evaluate for:
(1) extent of marrow + soft-tissue involvement
(2) invasion of epiphysis
(3) joint (19–24%) + neurovascular involvement
(4) viable tumor + mineralized matrix for biopsy

Metastases (in 2% at presentation):

(a) hematogenous lung metastases (15%): calcifying; spontaneous pneumothorax ← subpleural cavitating nodules rupturing into pleural space
(b) lymph nodes, liver, brain (may be calcified)
(c) skeletal metastases uncommon (unlike Ewing sarcoma); skip lesions = discontinuous tumor foci in marrow cavity in 1–25%

Cx: (1) pathologic fracture (15–20%)
(2) radiation-induced osteosarcoma (30 years delay)

Rx: chemotherapy followed by wide surgical resection

Prognosis: 60–80% 5-year survival
(1) Amputation: 20% 5-year survival; 15% develop skeletal metastases; 75% dead within < 2 years
(2) Multidrug chemotherapy: 55% 4-year survival more proximal lesions carry higher mortality (0% 2-year survival for axial primary)

Predictors of poor outcome:
metastasis at presentation, soft-tissue mass > 20 cm, pathologic fracture, skip lesions in marrow

Predictors of poor response to chemotherapy:
no change / increase in size of soft-tissue mass, increase in bone destruction

DDx: Osteoid osteoma, sclerosing osteomyelitis, Charcot joint

High-grade Surface Osteosarcoma

Frequency: 0.4% of all osteosarcomas; least common of juxtacortical osteosarcomas
Histo: entirely high-grade mitotic activity
Origin: surface of bone
Age: 2nd + 3rd decades
Location: femur > humerus, fibula
Site: diaphysis + metaphysis of long bone
Size: usually 4.5–22 cm large tumor
√ dense ossification + periosteal reaction similar to periosteal osteosarcoma with bulk of lesion external to bone
√ cortical erosion + thickening (frequent)
√ often involves entire circumference of bone
√ invasion of medullary canal (in 8–48%)
Prognosis: 5-year survival rate of 46% (slightly better than conventional osteosarcoma)

DDx: (1) Parosteal osteosarcoma (ill-defined fluffy bone formation)
(2) Periosteal osteosarcoma (diaphysis, cortical destruction, periosteal reaction)
(3) Conventional osteosarcoma

Intracortical Osteosarcoma

Rarest form of osteosarcoma
Histo: sclerosing variant of osteosarcoma which may contain small foci of chondro- or fibrosarcoma
Location: femur, tibia
√ tumor < 4 cm in diameter

√ intracortical geographic bone lysis
√ tumor margin may be well defined with thickening of surrounding cortex
√ metastases in 29%

Low-grade Intraosseous Osteosarcoma

= LOW-GRADE CENTRAL OSTEOSARCOMA = WELL-DIFFERENTIATED / SCLEROSING OSTEOSARCOMA

Frequency: < 1% of all osteosarcomas

Path: penetration among bony trabeculae; fibrous stroma sometimes lacking nuclear atypia + pleomorphism; permeative extension of tumor cells between mature bone trabeculae

Histo: microtrabecular osseous matrix in bland stroma with highly variable amount of tumor osteoid production (similar to fibro-osseous lesions) = equivalent to low-grade parosteal osteosarcoma

Age: most frequently 3rd + 4th decade; M÷F = 1÷1

• protracted clinical course with nonspecific symptoms

Location: about the knee; femur involved in 50%

Site: medullary canal of metaphysis; often with extension into epiphysis

√ variable radiographic features:
  √ expansile lytic bone destruction with coarsely thick / thin trabeculations (61%)
  √ diffuse dense sclerosis (< 30%)
√ remodeling of bone
√ may have well-defined margins + sclerotic rim
√ subtle signs of aggressiveness: bone lysis, focally indistinct margin, cortical destruction, soft-tissue mass, variable periosteal reaction (22–50%)

N.B.: the relatively benign appearance has resulted in misdiagnosis as a benign entity!

Cx: transformation into high-grade osteosarcoma

Rx: surgical resection alone

Prognosis: 80–90% 5-year survival rate, similar to parosteal osteosarcoma; local recurrence in 10% (due to inadequate resection)

DDx: benign fibro-osseous lesions (fibrous dysplasia, nonossifying fibroma, desmoplastic fibroma, chondromyxoid fibroma); chondrosarcoma

Osteosarcoma of Jaw

= GNATHIC OSTEOSARCOMA

Average age: 34 years (10–15 years older than in conventional osteosarcoma)

Histo: chondroblastic predominance (~50%), osteoblastic predominance (~25%); better differentiated (grade 2 or 3) than conventional osteosarcoma (grade 3 or 4)

• simulating periodontal disease: rapidly enlarging mass, lump, swelling
• paresthesia (if inferior alveolar nerve involved)
• painful / loose teeth, bleeding gum

Location: body of mandible (lytic), alveolar ridge of maxilla (sclerotic), maxillary antrum

√ osteolytic / osteoblastic / mixed pattern
√ osteoid matrix (60–80%)
√ aggressive periosteal reaction for mandibular lesion
√ soft-tissue mass (100%)

√ opacification of maxillary sinus (frequent in maxillary lesions)
Prognosis: 40% 5-year survival rate (lower probability of metastases, lower grade)
DDx: metastatic disease (lung, breast, kidney), multiple myeloma, direct invasion by contiguous tumor from oral cavity, Ewing sarcoma, primary lymphoma of bone, chondrosarcoma, fibrosarcoma, acute osteomyelitis, ameloblastoma, Langerhans cell histiocytosis, giant cell reparative granuloma, "brown tumor" of HPT

Osteosarcomatosis

= MULTIFOCAL OSTEOSARCOMA = MULTIPLE SCLEROTIC OSTEOSARCOMA
Frequency: 2.7–4.2% of osteosarcomas
Etiology:
(a) multicentric type of osteosarcoma
(b) multiple metastatic bone lesions
Classification (Amstutz):

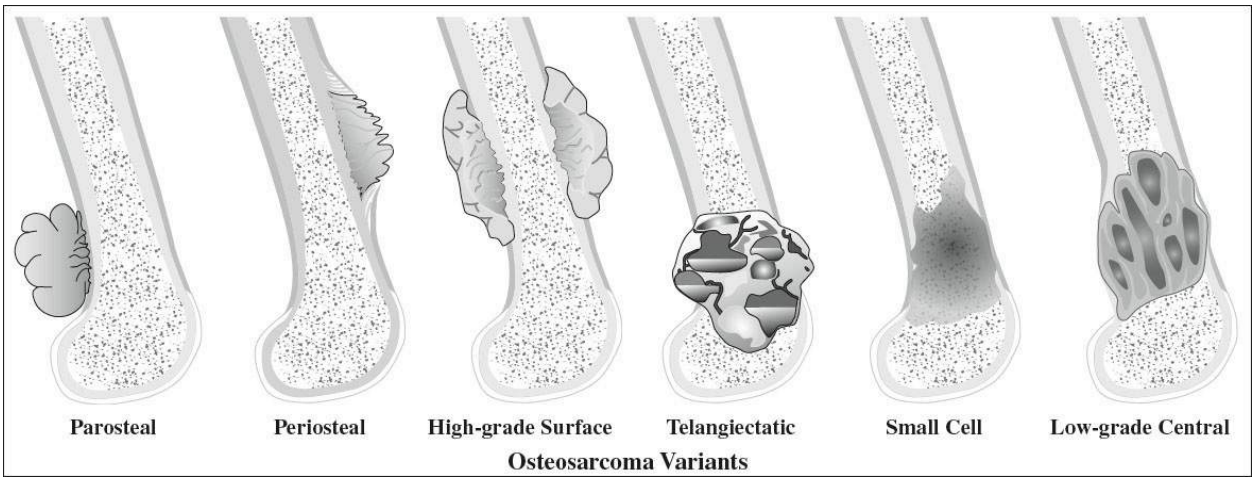
Type I	multiple synchronous bone lesions occurring within 5 months of diagnosis + patient ≤ 18 years of age
Type II	multiple synchronous bone lesions occurring within 5 months of presentation + patient > 18 years of age
Type IIIa	early metachronous metastatic osteosarcoma occurring 5 to 24 months after diagnosis
Type IIIb	late metachronous metastatic osteosarcoma occurring > 24 months after diagnosis

Mean age: Amstutz type I = 11 (range, 4–18) years
Amstutz type II = 30 (range, 19–63) years
Site: metaphysis of long bones; may extend into epiphyseal plate / begin in epiphysis
√ multicentric simultaneously appearing lesions with a radiologically dominant tumor (97%)
√ smaller lesions are densely opaque (osteoblastic)
√ lesions bilateral + symmetrical
√ early: bone islands
√ late: entire metaphysis fills with sclerotic lesions breaking through cortex
√ lesions are of same size
√ lung metastases (62%)
Prognosis: uniformly poor with mean survival of 12 (range, 6–37) months
DDx: heavy metal poisoning, sclerosing osteitis, progressive diaphyseal dysplasia, melorheostosis, osteopoikilosis, bone infarction, osteopetrosis

Parosteal Osteosarcoma

Frequency: 4–5% of all osteosarcomas; 65% of all juxtacortical osteosarcomas
Origin: outer fibrous layer of periosteum; slowly growing lesion with fulminating course if tumor reaches medullary canal
Histo: low-grade lesion with higher-grade regions (22–64%), invasion of medullary canal (8–59%); fibroblastic stroma + extensive osteoid with small foci of cartilage
Age: peak age 38 years (range of 12–58 years); 50% > age 30 (for central osteosarcoma 75% < age 30); M÷F = 2÷3

Location: posterior aspect of distal femur (50–65%), either end of tibia, proximal humerus, fibula, rare in other long bones



Site: metaphysis of long bones (80–90%)

• palpable mass

√ large lobulated "cauliflower-like" homogeneously ossified exophytic mass extending away from cortex

√ "string" sign = initially fine radiolucent cleavage plane separating tumor mass from cortex (30–40%)

√ tumor stalk (= attachment to cortex) grows with tumor obliterating the radiolucent cleavage plane

√ cortical thickening without aggressive periosteal reaction

√ tumor periphery less dense than center (DDx: myositis ossificans with periphery more dense than center + without attachment to cortex)

√ large soft-tissue component with osseous + cartilaginous elements

MR:

√ predominantly low SI on T1WI + T2WI = ossified tumor

√ unmineralized soft-tissue mass > 1 cm^3 / predominantly high T2-SI suggests high-grade tumor component

Prognosis: 86–91% 5-year survival rate (best prognosis of all osteosarcomas) compared to 53–61% for conventional osteosarcoma; dedifferentiation from low to high grade (in 16–43%)

DDx: (1) Osteochondroma (corticomedullary continuity)

(2) Myositis ossificans, periosteal chondroma, juxtacortical hematoma, fibrous malignancy, periosteal chondrosarcoma, other subtypes of juxtacortical osteosarcomas

Periosteal Osteosarcoma

Frequency: 1.5% of all osteosarcomas; 2nd most common of juxtacortical osteosarcomas

Origin: deep inner germinative layer of periosteum

Histo: intermediate-grade lesion; highly chondroblastic lesion with smaller areas of osteoid formation

Average age: 20 (range, 3–70) years); M÷F = 1.7÷1

Location: tibia (40%), femur (38%), ulna + humerus (5–10%)
Site: anteromedial diaphysis of proximal tibia + middle / distal femur; limited to periphery of cortex with normal endosteal margin + medullary canal (resembles parosteal sarcoma)
√ broad-based soft-tissue mass attached to cortex over entire extent of tumor (100%):
  √ tumor 7–12 cm in length, 2–4 cm in width
  √ involving 50–55% of osseous circumference
√ cortical thickening (82%): solid nonaggressive (51%)
√ cortical erosion
√ extrinsic scalloping of cortex (92%):
  √ affecting only thickened cortex (68%)
  √ involving native cortex (32%)
√ periosteal reaction (95%):
  √ short spicules of new bone perpendicular to shaft extending into soft-tissue mass (51%)
  √ aggressive periosteal reaction of laminated appearance / Codman triangle (11%)
  √ both patterns (38%)
√ cortical destruction / medullary cavity invasion (rare):
  √ marrow signal abnormality on MR usually due to reactive changes – unless continuous with surface component (2%)
√ additional areas of matrix calcification by CT (91%)
√ chondroblastic areas (80%) with inherent high water content of hyaline cartilage:
  √ hypodense on CT compared to muscle (91%)
  √ very high signal intensity on T2WI (83%)
  ◊ Biopsy may lead to erroneous diagnosis of chondrosarcoma!
NUC (bone scintigraphy):
  √ eccentric uptake (100%)
Prognosis: 83% 5-year survival rate (better than for conventional osteosarcoma but worse than for parosteal osteosarcoma)
DDx: (1) Juxtacortical chondrosarcoma (4^{th}–5^{th} decade, extensive osteoid + chondroid mineralization, no perpendicular periosteal reaction)
(2) Ewing sarcoma (rarely periosteal, no perpendicular periosteal reaction, soft-tissue component not mineralized + not low in attenuation + not of very high intensity)
(3) Parosteal osteosarcoma (densely ossified juxtacortical mass, 3^{rd} + 4^{th} decade, posterior distal metaphysis of femur, attached to bone by narrow stalk, no perpendicular periosteal reaction)
(4) High-grade surface osteosarcoma (surrounds > 50% of bone circumference, frequent invasion of medullary cavity, no high water content of soft-tissue mass)
(5) Periosteal chondroid tumor (well-defined border, typically metaphyseal location, curvilinear peripheral calcifications)

Secondary Osteosarcoma

= lesion arising from a preexisting abnormality
◊ Most osteosarcomas in patients > age 60 are secondary!

Cause: malignant transformation of benign process
(1) Paget disease (67–90%)
◊ 0.2–7.5% of patients with Paget disease develop osteosarcoma dependent on extent of disease
(2) Sequelae of irradiation (6–22%) 2–40 years ago (malignant fibrous histiocytoma most common; fibrosarcoma 3rd most common)
◊ 0.02–4% of patients with radiation therapy develop osteosarcoma related to exposure dose (usually > 1,000 cGy)
(3) Osteonecrosis, fibrous dysplasia, metallic implants, osteogenesis imperfecta, chronic osteomyelitis, retinoblastoma (familial bilateral type)
Path: high-grade anaplastic tissue with little / no mineralization
Age: middle-aged / late adulthood
Location: thoracic + lumbar spine > sacrum > cervical spine
Site: posterior elements (79%), 2 vertebral levels (17%)
√ aggressive bone destruction in area of preexisting condition associated with large soft-tissue mass
Prognosis: < 5% 5-year survival rate

Small-cell Osteosarcoma

Frequency: 1% of all osteosarcomas
Age: 2nd + 3rd decade; M÷F = 1÷1
Histo: small round blue cells (similar to Ewing sarcoma / primitive neuroectodermal tumor) lacking cellular uniformity and consistently producing fine reticular osteoid
Location: distal femur
Site: metaphysis with frequent extension into epiphysis; diaphysis (in 15%)
√ permeative lytic medullary lesion in all cases
√ cortical breakthrough
√ aggressive periosteal reaction (> 50%)
√ associated soft-tissue mass
Prognosis: 53–61% 5-year survival rate
DDx: (1) Ewing sarcoma (rare calcifications, cortical thickening + saucerization)
(2) Lymphoma (spread outside bone without osseous destruction, calcification uncommon)
(3) Conventional osteosarcoma

Telangiectatic Osteosarcoma

= MALIGNANT BONE ANEURYSM
Frequency: 1.2–12% of all osteosarcomas
Mean age: 20 (range, 3–67) years; M÷F = 3÷2
Path: malignant destructive osteoid-forming sarcoma of bone with > 90% of tumor volume consisting of large hemorrhagic + necrotic cavities mimicking an ABC
Histo: blood-filled cavernous vessels lined with osteoclastic giant cells; nuclear pleomorphism + high mitotic rate
Location: (a) about knee (62%): distal femur (48%), proximal tibia (14%)

(b) proximal humerus (16%), proximal femur, fibula, midfemur, midhumerus, mandible

Site: medullary cavity of metaphysis (90%); extension into epiphysis (87%)

√ radiolucent appearance of tumor ← scant bone matrix subtly visible radiographically in 58%

√ minimal peripheral sclerosis

√ geographic bone destruction with a wide zone of transition

√ marked aneurysmal expansion of bone (19%)

√ endosteal scalloping

√ extensive invasion of surrounding soft tissues

MR:

√ heterogeneous signal intensity with fluid levels (74%):

√ high T1 + variable T2 signal = hemorrhage (96%)

√ enhancing thickened nodular tumor periphery + septa

CT:

√ soft-tissue mass with attenuation lower than muscle

√ fluid levels (49%)

√ nodular calcific foci of osteoid matrix mineralization (85%) at periphery / within septa = SPECIFIC ← viable neoplastic tissue

√ thick peripheral + nodular septal enhancement ← viable high-grade sarcomatous tissue

NUC:

√ "doughnut" sign = peripherally increased uptake with central photopenia on bone scan = TYPICAL

Cx:

√ pathologic fracture (43–61%)

Prognosis: 67% 5-year survival rate

DDx: (1) Aneurysmal bone cyst (expansile remodeling with well-defined encapsulated margin, thin septa without nodularity, enhancing thin peripheral rim, no soft-tissue involvement)

(2) Giant cell tumor (epiphyseal location, solid mass, isointense to muscle on T1WI)

(3) Lytic metastasis(no fluid levels)

(4) Chondroblastic conventional osteosarcoma

(5) Ewing sarcoma, chondrosarcoma, lymphoma

OXALOSIS

Rare inborn error of metabolism

Etiology: excessive amounts of oxalic acid combine with calcium and deposit throughout body (kidneys, soft tissue, bone)

• hyperoxaluria = urinary excretion of oxalic acid > 50 mg/ day

• progressive renal failure

√ osteoporosis = cystic rarefaction + sclerotic margins in tubular bones on metaphyseal side, may extend throughout diaphysis

√ erosions on concave side of metaphysis near epiphysis (DDx: hyperparathyroidism)

√ bone-within-bone appearance of spine

√ nephrocalcinosis (2° HPT: subperiosteal resorption, rugger jersey spine, sclerotic metaphyseal bands)
Cx: pathologic fractures

PACHYDERMOPERIOSTOSIS

= OSTEODERMOPATHIA HYPERTROPHICANS (TOURAINE-SOLENTE-GOLE) = PRIMARY HYPERTROPHIC OSTEOARTHROPATHY
Autosomal dominant
Age: 3–38 years with progression into late 20s / 30s; M >> F
• large skin folds of face + scalp
Location: epiphyses + diametaphyseal region of tubular bones; distal third of bones of legs + forearms (early); distal phalanges rarely involved
√ enlargement of paranasal sinuses
√ irregular periosteal proliferation of phalanges + distal long bones (hand + feet) beginning in epiphyseal region at tendon / ligament insertions
√ thick cortex, BUT NO narrowing of medulla
√ clubbing
√ may have acroosteolysis
Prognosis: self-limiting = progression ceases after several years
DDx: hypertrophic pulmonary osteoarthropathy, thyroid acropachy

PAGET DISEASE

= OSTEITIS DEFORMANS
[Sir James Paget, 1st. Baronet (1814–1899), professor of anatomy & surgery at the Royal College of Surgeons at St. Bartholomew Hospital, London]
= multifocal chronic skeletal disease characterized by disordered and exaggerated bone remodeling
Etiology: ? chronic paramyxoviral infection
Prevalence: 3% of individuals > 40 years; 10% of persons > 80 years; higher prevalence in northern latitudes; 2nd most common disease (after osteoporosis) affecting older individuals
Age: Caucasian of Northern European descent > 55 years (in 3%); > 85 years (in 10%); unusual < 40 years; M÷F = 2÷1
Histo: increased resorption + increased bone formation; newly formed bone is abnormally soft with disorganized trabecular pattern ("mosaic pattern") causing deformity

A. ACTIVE PHASE = OSTEOLYTIC PHASE
= intense osteoclastic activity = aggressive bone resorption with lytic lesions
Path: replacement of hematopoietic bone marrow by fibrous connective tissue with numerous large vascular channels
√ osteoporosis circumscripta of skull
√ flame-shaped radiolucency extending from end of long bone into diaphysis

B. MIDDLE / MIXED / BLASTIC PHASE (common)
= decreased osteoclastic activity + increased osteoblastic activity
Location: polyostotic in axial skeleton: skull, pelvis, spine

√ coexistence of lytic + sclerotic phases
√ osseous sclerosis → coarse trabecular + cortical thickening + bone enlargement

C. INACTIVE / LATE PHASE = QUIESCENT PHASE
= diminished osteoblastic activity with decreased bone turnover
Path: loss of excessive vascularity
√ osteosclerosis + cortical accretion (eg, ivory vertebral body)

- asymptomatic (1/**5**–¾)
- fatigue; enlarged hat size; peripheral nerve compression
- neurologic disorders from compression of brainstem (basilar invagination)
- hearing loss, blindness, facial palsy ← narrowing of neural foramina (rare)
- pain from (a) primary disease process – rare
  (b) pathologic fracture
  (c) malignant transformation
  (d) degenerative joint disease / rheumatic disorder aggravated by skeletal deformity
- local hyperthermia of overlying skin
- high-output congestive heart failure from markedly increased perfusion (rare)
- increased alkaline phosphatase ← increased bone formation
- hydroxyproline increased ← increased bone resorption
- normal serum calcium + phosphorus

Sites: usually polyostotic + asymmetric; pelvis (75%) > lumbar spine > thoracic spine > proximal femur > calvarium > scapula > distal femur > proximal tibia > proximal humerus

Sensitivity: scintigraphy + radiography (60%) scintigraphy only (27–94%) radiography only (13–74%)

√ osseous expansion
√ trabecular coarsening
√ cortical thickening
√ cystlike areas (fat-filled marrow cavity / blood-filled sinusoids / liquefactive degeneration + necrosis of proliferating fibrous tissue)

@ Skull (involvement in 29–65%)
√ inner + outer table involved
√ diploic widening
√ osteoporosis circumscripta = well-defined lysis, most commonly in calvarium anteriorly, occasionally in long bones (destructive active stage)
√ "cotton wool" appearance = mixed lytic + blastic pattern of thickened calvarium (late stage)
√ basilar impression with encroachment on foramen magnum
√ deossification + sclerosis in maxilla
√ sclerosis of base of skull

@ Long bones (almost invariable at end of bone; rarely in diaphysis)
√ "candle flame" / "blade of grass" lysis = advancing tip of V-shaped lytic defect in diaphysis of long bone originating in subarticular site (CHARACTERISTIC)
√ lateral curvature of femur, anterior curvature of tibia (commonly resulting in fracture)

@ Ribs (involvement in 1–4%)

@ Small / flat bones
√ bubbly destruction + periosteal successive layering
@ Pelvis
√ thickened trabeculae in sacrum, ilium; rarefaction in central portion of ilium
√ thickening of iliopectineal line
√ acetabular protrusion (DDx: metastatic disease not deforming) + secondary degenerative joint disease
@ Spine (upper cervical, low dorsal, midlumbar)
√ expansion of vertebra
√ lytic / coarse trabeculations at periphery of bone
√ "picture-frame vertebra" = bone-within-bone appearance = enlarged square vertebral body with reinforced peripheral trabeculae + central osteopenia, typically in lumbar spine
√ "ivory vertebra" = blastic vertebra with increased density
√ isolated posterior arch involvement
√ ossification of spinal ligaments, paravertebral soft tissue, disk spaces

Bone scan (94% sensitive):
√ usually markedly increased uptake (symptomatic lesions strikingly positive ← increased blood flow + osteoblastic activity)
√ normal scan in some sclerotic burned-out lesions
√ marginal uptake in lytic lesions
√ enlargement + deformity of bones

Bone marrow scan:
√ sulfur colloid bone marrow uptake is decreased ← marrow replacement by cellular fibrovascular tissue

MR:
Indications: imaging of complications (spinal stenosis, basilar impression, sarcoma staging)
√ areas of decreased SI within marrow on T1WI + increased intensity on T2WI (= fibrovascular tissue resembling granulation tissue)
√ hypointense area / area of signal void on T1WI + T2WI (cortical thickening, coarse trabeculation)
√ reduction in size + SI of medullary cavity (= replacement of high-SI fatty marrow by ↑ medullary bone formation)
√ focal areas of higher SI than fatty marrow (= cystlike fat-filled marrow spaces)
√ widening of bone

Cx: (1) Associated neoplasia (0.7–1–20%)
(a) sarcomatous transformation into osteosarcoma (22–90%), fibrosarcoma / malignant fibrous histiocytoma (29–51%), chondrosarcoma (1–15%)
√ osteolysis in pelvis, femur, humerus
Prognosis: < 10% 5-year survival
(b) multicentric giant cell tumor (3–10%)
√ lytic expansile lesion in skull, facial bones
(c) lymphoma, plasma cell myeloma
(2) Insufficiency fracture

(a) "banana fracture" = tiny horizontal cortical infractions on convex surfaces of lower extremity long bones (lateral bowing of femur, anterior bowing of tibia)
(b) compression fracture of vertebra (soft bone despite increased density)

(3) Neurologic entrapment
(a) basilar impression with obstructive hydrocephalus + brainstem compression + syringomyelia
(b) spinal stenosis with extradural spinal block (osseous expansion / osteosarcoma / vertebral retropulsion ← compression fracture)

(4) Early-onset osteoarthritis
Pathogenesis: altered biomechanics across affected articulations

Cx: sarcomatous degeneration: most commonly osteo- / chondrosarcoma / malignant fibrous histiocytoma

Rx: calcitonin, biphosphonates, mithramycin

Detection of recurrence:
(a) in ⅓ detected by bone scan
(b) in ⅓ detected by biomarkers (alkaline phosphatase, urine hydroxyproline)
(c) in ⅓ by bone scan + biomarkers simultaneously
√ diffuse (most common) / focal increase in tracer uptake
√ extension of uptake beyond boundaries of initial lesion

DDx: osteosclerotic metastasis, osteolytic metastasis, Hodgkin disease, vertebral hemangioma

PARAOSTEOARTHROPATHY

= HETEROTOPIC BONE FORMATION = ECTOPIC OSSIFICATION = MYOSITIS OSSIFICANS

Common complication following surgical manipulation, total hip replacement (62%) and chronic immobilization (spinal cord injury / neuromuscular disorders)

Mechanism: pluripotent mesenchymal cell lays down matrix for formation of heterotopic bone similar to endosteal bone

Causes: para- / quadriplegia (40–50%), myelomeningocele, poliomyelitis, severe head injury, cerebrovascular disease, CNS infections (tetanus, rabies), surgery (commonly following total hip replacement)

Evolution: calcifications seen 4–10 weeks following insult; progression for 6–14 months; trabeculations by 2–3 months; stable lamellar bone ankylosis in 5% by 12–18 months

√ largest quantity of calcifications around joints, especially hip, along fascial planes
√ disuse osteoporosis of lower extremities
√ renal calculi (elevation of serum calcium levels)

Radiographic grading system (Brooker):

0 no soft-tissue ossification
I separate small foci of ossification
II > 1 cm gap between opposing bone surfaces of heterotopic ossifications
III < 1 cm gap between opposing bone surfaces
IV bridging ossification

Bone scan:
√ tracer accumulation in ectopic bone

√ assessment of maturity for optimal time of surgical resection (indicated by same amount of uptake as normal bone)

Cx: ankylosis in 5%

Rx: 1000–2000 rad within 4 days following surgical removal

PARKES WEBER SYNDROME

= KLIPPEL-TRÉNAUNAY-WEBER SYNDROME

[Frederick Parkes Weber (1863–1962), dermatologist, London]

= characterized by cutaneous capillary malformation and limb overgrowth in combination with high-flow malformations (small arteriovenous fistulas and shunts) and congenital varicose veins

• pseudo-Kaposi sarcoma = pseudo-capillary malformation = feeling of warmth over affected skin ← high oxygen partial pressure

• high-output cardiac failure (occasionally)

√ hemihypertrophy = outgrowth of soft tissues + overgrowth of bone in affected limb

√ arteriovenous fistula-like stains in periarticular region

DDx: Klippel-Trénaunay syndrome (low-flow vascular malformations)

PATELLAR TENDON RUPTURE

Cause: (a) acute trauma (b) repetitive microtrauma

Mechanism: eccentric contraction of quadriceps while foot planted + knee flexed

Predisposed: diabetes, systemic lupus erythematosus, chronic soft-tissue swelling

√ patella alta = high-riding patella

PFEIFFER SYNDROME

= ACROCEPHALOSYNDACTYLY TYPE 2

√ broad thumbs + toes

√ mild soft-tissue syndactyly

PHENYLKETONURIA

High incidence of x-ray changes in phenylalanine-restricted infants:

√ metaphyseal cupping of long bones (30–50%), especially wrist

√ calcific spicules extending vertically from metaphysis into epiphyseal cartilage (DDx to rickets)

√ sclerotic metaphyseal margins

√ osteoporosis

√ delayed skeletal maturation

DDx: homocystinuria

PHOSPHORUS POISONING

Etiology:

(1) ingestion of metallic phosphorus (yellow phosphorus)

(2) treatment of rachitis or TB with phosphorized cod liver oil

Location: long tubular bones, ilium

√ multiple transverse lines (intermittent treatment with phosphorus)
√ lines disappear after some years

PIERRE ROBIN SYNDROME

May be associated with: CHD, defects of eye and ear, hydrocephalus, microcephaly
• glossoptosis
√ micrognathia = hypoplastic receding mandible
√ arched ± cleft palate
√ rib pseudarthrosis
Cx: airway obstruction (relatively large tongue), aspiration

PIGMENTED VILLONODULAR SYNOVITIS

= PVNS
= benign hypertrophic neoplastic process characterized by villous + nodular + villonodular proliferation and pigmentation from hemosiderin
Classification:
(a) localized disease (77%)
› extraarticular: in bursa / tendon sheath (71%)
› intraarticular synovium (6%)
(b) diffuse intraarticular disease (23%)
Genetics: rearrangement in chromosome 1p11-13, a site for CSF-1 gene, commonly fusing to COL6a3 on chromosome 2q35; trisomy of chromosomes 5 and 7
Histo: mononuclear histiocytoid cells with reniform nuclei and plump eccentric eosinophilic cytoplasm, admixed with multinucleated giant cells + xanthoma cells; hemosiderin deposition

Diffuse Intraarticular PVNS 23%

= DIFFUSE-TYPE GIANT CELL TUMOR
= benign locally destructive proliferation of mononuclear cells that resemble those in the synovium, admixed with multinuclear giant cells and inflammatory cells
Incidence: 1.8÷1,000,000 population per year; 0.9% of all benign soft-tissue masses
Path: infiltrative mass involving synovium of entire joint with thickening + irregular papillary / villous projections + larger nodular / villonodular protrusions
Histo: diffuse villonodular infiltrative sheetlike growth of synovial membrane with hyperplasia of undifferentiated connective tissue + multinucleated large cells ingesting hemosiderin / lipoid (foam / giant cells) ± fibrosis
Age: mainly 3rd–4th decade (range, 12–68 years); 50% < 40 years; M÷F=1÷1
• history of antecedent trauma (44–53%)
• mean duration of symptoms: 15 (range 1–120) months
• hemorrhagic "chocolate" / serosanguinous / xanthochromic joint effusion without trauma
• insidious onset (93%) with intermittent fluctuating symptoms + slow progression:
  • pain (79–90%), swelling (72–79%)
  • soft-tissue mass (6–19%)
  • joint dysfunction (26–28%):

- stiffness with decreased range of motion, joint locking

Location: knee (66–80%), hip (4–16%) > ankle > shoulder > elbow > tarsal + carpal joints; predominantly monoarticular

Radiography:
- √ normal (in up to 21%)
- √ soft-tissue swelling ← effusion + synovial proliferation:
  - √ dense soft tissues ← hemosiderin deposits
- √ joint effusion in knee, but not relevant in other joints
- √ extrinsic pressure erosion with rim of sclerosis involving both sides of joint: hip (93%), shoulder (75%), elbow (63%), ankle (56%), knee (30%)
- √ multiple sites of irregular cystlike subchondral radiolucent defects ← invasion of bone by synovium
- √ normal bone mineralization, preservation of joint space, NO calcifications until late in the disease:
  - √ joint space narrowing (7%)
  - √ degenerative disease (4%)
  - √ intraarticular osteochondral bodies (7%)
  - √ osteopenia (7%)

US:
- √ joint effusion
- √ complex heterogeneous echogenic masses
- √ markedly thickened hypoechoic synovium ± nodular / villous projections with increased blood flow

CT:
- √ joint effusion of low-attenuation
- √ diffuse synovial thickening
- √ hyperattenuating to muscle (29%) ← hemosiderin
- √ small radiographically invisible extrinsic erosions
- √ subchondral cyst formation
- √ juxtaarticular soft-tissue mass ← involvement of synovium in joint recesses + bursae

MR (optimal modality):
- √ heterogeneous diffuse plaquelike synovial thickening ± nodularity of intermediate to low SI on T1WI + T2WI
- √ lobulated intraarticular masses of synovial tissue with joint effusion
- √ nearly pathognomonic “blooming” artifact of low SI on gradient-echo pulse sequences ← magnetic susceptibility artifact of hemosiderin
- √ high-SI areas ← fat, effusion, edema, inflammation
- √ bone erosion / subchondral cyst (62%), septations (67%)
- √ edema in adjacent bone / soft tissue (23%)
- √ articular cartilaginous defects (31%)
- √ scalloping / truncation of prefemoral fat pad

NUC:
- √ diffusely increased radionuclide activity on blood flow and blood pool > delayed images

PET:
- √ hypermetabolic activity with maximum SUV values of up to 11.3

Arthrography:
√ bloody (23%) / yellow (70%) / brownish (9%) effusion
√ extensive synovial thickening with villous / nodular projections extending into joint
Angiography:
√ prominent neovascularity with tumor blush
√ mild arteriovenous shunting
Rx: synovectomy (50% recurrence rate), arthrodesis, arthroplasty, radiation
DDx: (1) Degenerative / traumatic arthritis
(2) Synovial sarcoma (solitary calcified mass outside joint)
(3) Sclerosing hemangioma
(4) Benign xanthoma
(5) Xanthogranuloma

Intraarticular Localized Nodular Synovitis 6%

= synovial lining without hemosiderin
= 1.6%–3.9% of all benign soft-tissue masses
Location: knee
Site: infrapatellar (67%), suprapatellar (24%), posterior intercondylar (10%)
Size: mean lesion diameter of 2.7 cm
√ mostly normal x-rays
√ localized soft-tissue opacity replacing normal region of adipose tissue in Hoffa fat pad
MR:
√ joint effusion (38%)
√ extrinsic erosion of bone (20%)
√ moderate contrast enhancement (48%)
√ soft-tissue mass of low to intermediate SI on T2WI
√ focal circular areas of low SI on T2WI (76%) ← hemosiderin deposition
√ linear / cleftlike areas of high signal intensity within mass (33%) ← entrapped joint fluid

Tenosynovial Giant Cell Tumor 71%

= GIANT CELL TUMOR OF TENDON SHEATH
= localized extraarticular form of PVNS solely involving tendon sheath
Incidence: 9.2÷1,000,000 annually; M ÷F = 1 ÷1.5 to 1 ÷2.1
Path: circumscribed lobulated cauliflower-like nodular soft-tissue mass attached to tendon sheath / residing within known bursa
• mean duration of symptoms: 19 (range 1–120) months
• Chronic onset (88%) of:
  • soft-tissue mass (83–99%), pain (22–71%)
  • joint dysfunction / swelling (0–4%)
Size: 0.5–4.0 cm in greatest dimension
Location:
(a) tendon sheath:
› hand & wrist (65–89%) specifically index and long fingers; volar÷dorsal aspect = 2÷1

◊ 2nd most common soft-tissue mass of hand & wrist (after ganglia)

› foot & ankle (5–15%)
› rare: knee, hip, elbow, shoulder

(b) bursa: hip / knee

Radiography:
√ no abnormality (in up to 20%)
√ soft-tissue mass (50–70%)
√ extrinsic erosion of underlying bone with well-defined sclerotic margin (9–25%) simulating marrow invasion
√ periosteal reaction (8%), calcifications (6%)

US:
√ hypoechoic solid mass with well-defined margins intimately related to involved tendon
√ mean length of 5.7 cm and mean circumference of 136°
√ mass does not move with tendon during dynamic sonography

PILOMATRICOMA

= PILOMATRIXOMA (former name) = CALCIFYING EPITHELIOMA OF MALHERBE
= benign calcifying subcutaneous tumor arising from primitive cells of skin appendage that normally differentiate into hair matrix cells

Frequency: < 1% of all skin tumors;
◊ Most common solid cutaneous tumor in patients < 20 years

Histo: epithelial cells with basophilic cytoplasm arranged in arclike fashion at periphery (basaloid cells) → centrally transformed into shadow cells (= ghost cells); eosinophilic cells without nuclei + filled with keratin

Age: two peaks of < 20 years and 50–65 years

• slowly growing tumor confined to subcutis

Location: head & neck (68%), trunk (29%), extremities (17%)

√ typically centrally calcified (in 85%)

MR:
√ homogeneous intermediate signal intensity on T1WI
√ heterogeneous intermediate signal intensity on T2WI
√ peritumoral edema / inflammation
√ enhancement of connective tissue capsule but not center

DDx: calcified lymph node, ossifying hematoma, hemangioma with phlebolith, granuloma annulare, dermatofibrosarcoma protuberans

POLIOMYELITIS

√ osteoporosis
√ soft-tissue calcification / ossification
√ intervertebral disk calcification
√ rib erosion commonly on superior margin of 3rd + 4th rib ← pressure from scapula
√ "bamboo" spine (resembling ankylosing spondylitis)
√ sacroiliac joint narrowing

PROGERIA

= HUTCHINSON-GILFORD SYNDROME
= autosomal recessive inheritance; most commonly in populations with consanguineous marriages (Japanese, Jewish)
Age: shortly after adolescence; M÷F = 1÷1
• characteristic habitus + stature:
  • symmetric retardation of growth
  • absent adolescent growth spurt
  • dwarf with short stature + light body weight
  • spindly extremities with stocky trunk
  • beak-shaped nose + shallow orbits
• premature senescence:
  • birdlike appearance; graying of hair + premature baldness
  • hyperpigmentation; voice alteration; bilateral cataracts
  • diffuse arteriosclerosis; osteoporosis
• scleroderma-like skin changes:
  • atrophic skin + muscles; circumscribed hyperkeratosis
  • telangiectasia; tight skin; cutaneous ulcerations
  • localized soft-tissue calcifications
• endocrine abnormalities:
  • diabetes; hypogonadism
√ generalized osteoporosis
@ Skull
  √ thin cranial vault
  √ delayed sutural closure + wormian bones
  √ hypoplastic facial bones (maxilla + mandible)
@ Chest
  √ narrow thorax + slender ribs
  √ progressive resorption with fibrous replacement of outer portions of thinned clavicles (HALLMARK)
  √ coronary artery + heart valve calcifications with cardiac enlargement
@ Extremities & joints
  √ short + slender long bones
  √ coxa valga
  √ valgus of humeral head
  √ acroosteolysis of terminal phalanges (occasionally)
  √ flexion + extension deformities of toes (hallux valgus, pes planus)
  √ excessive degenerative joint disease of major + peripheral joints
  √ neurotrophic joint lesions (feet)
  √ widespread osteomyelitis + septic arthritis (hands, feet, limbs)
@ Soft tissue
  √ soft-tissue atrophy of extremities
  √ soft-tissue calcifications around bony prominences (ankle, wrist, elbow, knee)
  √ peripheral vascular calcifications = premature atherosclerosis

Prognosis: most patients die in their 30s / 40s from complications of arteriosclerosis (myocardial infarction, stroke) or neoplasm (sarcoma, meningioma, thyroid carcinoma)

DDx: Cockayne syndrome (mental retardation, retinal atrophy, deafness, family history)

PROGRESSIVE DIAPHYSEAL DYSPLASIA

= ENGELMANN-CAMURATI DISEASE = CAMURATI-ENGELMANN DISEASE

= autosomal dominant disorder of intramembranous ossification

Genetics: mutation in gene encoding transforming growth factor TGF-β1 (= latency-associated peptide causing premature activation of TGF-β1) on chromosome 19q13.1 → hyperostosis along periosteal + endosteal surfaces

Age: 5–25 years (primarily in childhood); M > F

- neuromuscular dystrophy = delayed walking (18–24 months) with broad-based waddling gait; often misdiagnosed as muscular dystrophy / poliomyelitis
- bone pain + tenderness usually in midshaft of long bones
- muscle pain + weakness with easy fatigability in legs:
  - underdevelopment of muscles ← malnutrition
- NORMAL laboratory values

Location: usually symmetric involvement of diaphyses of long bones, calvaria, mandible, facial bones, midsegment of clavicle; NO involvement of hands, feet, ribs, scapulae

@ Skull (initially affected)

√ amorphous sclerosis of skull base → cranial nerve palsy

√ encroachment of frontal + sphenoid sinus; sparing of maxillary sinus

√ mandible rarely affected

@ Long bones

Site: tibia > femur > fibula > humerus > ulna > radius

√ bilateral symmetric cortical thickening involving periosteal + endosteal surfaces of long bones:

√ fusiform enlargement of diaphysis

√ abrupt demarcation of lesions ← sparing of metaphyses + epiphyses ← formed by endochondral ossification

√ cortical thickening (= endosteal + periosteal accretion of mottled new bone) → progressive obliteration of medullary cavity

√ progression of lesions along long axis of bone toward either end

√ relative elongation of extremities

Rx: low-dose corticosteroids

DDx: (1) Chronic osteomyelitis (single bone)

(2) Hyperphosphatasemia (high alkaline phosphatase levels)

(3) Paget disease (age, new-bone formation, increased alkaline phosphatase)

(4) Infantile cortical hyperostosis (fever; mandible, rib, clavicles; regresses, < 1 year of age)

(5) Fibrous dysplasia (predominantly unilateral, subperiosteal new bone)

(6) Osteopetrosis (very little bony enlargement)

(7) Vitamin A poisoning

PROTEUS SYNDROME

[Proteus = Greek god who could change his shape, "Elephant Man"]

= cutaneous + visceral combined lymphatic-venous malformations with multiple subcutaneous hamartomas, pigmented nevi, hemihypertrophy, hand or foot overgrowth, bone exostoses, lipomatosis

Incidence: > 200 cases

Cause: mutation in Akt-1 kinase

• mild symptoms at birth with rapid aggravation at puberty

Diagnostic criteria:

group A › connective tissue nevi

group B
- › linear epithelial nevi
- › asymmetric overgrowth (limbs, spine, skull, internal organs)
- › bilateral ovarian cystadenomas / parotid monomorphic adenoma before 2nd decade of life

group C
- › lipomas / localized absence of fat
- › low-flow vascular malformations
- › lung cysts
- › facial malformations

Dx: A + 2 criteria of group B or 3 criteria of group C

√ asymmetric overgrowth of bones + soft tissues
√ hypertrophy of fat
√ skull enlargement
√ wall thickening of digestive tract
√ cystic emphysematous changes of lung

PSEUDOFRACTURES

= LOOSER LINES = LOOSER ZONES = OSTEOID SEAMS = MILKMAN SYNDROME

= insufficiency stress fractures + nonunion (incomplete healing ← mineral deficiency)

Path: area of unmineralized woven bone occurring at sites of mechanical stress / nutrient vessel entry

Associated with:

(1) Osteomalacia / rickets
(2) Paget disease ("banana fracture")
(3) Osteogenesis imperfecta tarda
(4) Fibrous dysplasia
(5) Organic renal disease in 1%
(6) Renal tubular dysfunction
(7) Congenital hypophosphatasia
(8) Congenital hyperphosphatasia ("juvenile Paget disease")

(9) Vitamin D malabsorption / deficiency
(10) Neurofibromatosis

mnemonic: "POOF"
Paget disease
Osteomalacia
Osteogenesis imperfecta
Fibrous dysplasia

Common locations:
scapulae (axillary margin, lateral + superior margin), medial femoral neck + shaft, pubic + ischial rami, ribs, lesser trochanter, ischial tuberosity, proximal ⅓ of ulna, distal ⅓ of radius, phalanges, metatarsals, metacarpals, clavicle

√ typically bilateral + symmetric at right angles to bone margin
√ paralleled by marginal sclerosis in later stages
√ healing fracture with little / no callus response
√ 2–3-mm stripe of lucency at right angle to cortex (= osteoid seam formed within stress-induced infractions (PATHOGNOMONIC) + nonunion (= incomplete healing due to mineral deficiency)

PSEUDOXANTHOMA ELASTICUM

= recessive hereditary systemic disorder characterized by degeneration of elastic tissue

@ Skin
- redundant skin folds, particularly in flexor regions
- yellowish xanthomatous papules

√ large amorphous calcific deposits in soft tissue about joints

@ Eyes
- diminished visual acuity due to alteration of chorioretinal structure
- angioid streaks = reddish brown serrated lines extending from optic disk in a spoke-wheel fashion

@ Arteries
- claudication + decreased pulses

Histo: tissue degeneration of internal elastic lamina + medial thickening
√ lobulated appearance of arteries (similar to fibromuscular hyperplasia)
√ aneurysm formation
√ vessel calcification at early age

Cx: GI tract hemorrhage

PSORIATIC ARTHRITIS

= uncommon autoimmune disease involving synovium + ligamentous attachments (= enthesopathy)with propensity for sacroiliitis / spondylitis classified as seronegative spondyloarthropathy 6/c

Frequency: 20% of patients with psoriasis (peripheral arthritis in 5%, sacroiliitis in 29%, peripheral arthritis + sacroiliitis in 10%)

Path: synovial inflammation (less prominent than in rheumatoid arthritis) with early fibrosis of proliferative synovium; bony proliferation at joint margins / tendon insertions /

subperiosteum

Age of onset: 30–50 years; rare under the age of 13 years; M = F

Types:

(1) true psoriatic arthritis (31%)
(2) psoriatic arthritis resembling rheumatoid arthritis (38%)
(3) concomitant rheumatoid + psoriatic arthritis (31%)

- plaque psoriasis = sharply demarcated erythematous plaques with thick white, laminated ("micaceous") scale
  - ◊ Skin rash precedes / develops simultaneously with onset of arthritis in 85%!
  - ◊ Arthritis may antedate dermatological changes by an interval of up to 20 years!
- pitting, discoloration, hyperkeratosis, subungual separation, ridging of nails (in 80%)
- positive HLA-B27 in 80%
- negative rheumatoid factor (= seronegative spondyloarthropathy)

Location: usually asymmetric + oligoarticular; upper > lower extremities, sacroiliac joints, spine

Distribution: widely variable terminal interphalangeal joints, ray distribution, unilateral polyarticular

√ NO / minimal juxtaarticular osteoporosis (early stage); frequent osteoporosis (later stages)
√ marginal erosions in joints
√ periarticular new bone formation (frequent)
√ intraarticular osseous excrescences
√ enthesitis (especially of calcaneus)

@ Hand + foot

Target area: DIP, PIP, MCP

√ CLASSIC "sausage digit" (40%) = nodular / irregular soft-tissue swelling of tendon sheath of entire digit ← dactylitis
Path: flexor tendon tenosynovitis

√ increased tenosynovial fluid
√ solid hyperemic nodules at color Doppler
√ destruction of interphalangeal joint of 1st toe with exuberant periosteal reaction + bony proliferation at distal phalangeal base (PATHOGNOMONIC)
√ destruction of distal interphalangeal joints (erosive polyarthritis) + osseous resorption
√ "pencil-in-cup" deformity = erosions with ill-defined margins + adjacent proliferation of periosteal new bone (CHARACTERISTIC)
√ **bony ankylosis** (10%)
√ **ivory phalanx** = sclerosis of terminal phalanx (28%)
√ poorly defined diffuse new bone formation at attachment of Achilles tendon + plantar aponeurosis
√ erosions at superior / posterior margin of calcaneus (20%)
√ acroosteolysis (occasionally)

@ Axial skeleton

√ "floating" osteophyte = large bulky vertically oriented paravertebral soft-tissue ossification (AP view):
√ ill-defined excrescence sweeping across the diskovertebral junction from midportion

of one vertebra to the next

Location: lower cervical, thoracic, upper lumbar spine; asymmetric / unilateral

√ squaring of vertebrae in lumbar region

√ sacroiliitis (40%) = (most commonly) bilateral + asymmetric sacroiliac joint widening, increased density, fusion

√ apophyseal joint narrowing + sclerosis

√ atlantoaxial subluxation + odontoid abnormalities

DDx: (1) Reiter syndrome (affects mostly lower extremity)

(2) Ankylosing spondylitis

(3) Rheumatoid arthritis (bilaterally symmetric well-defined erosions, juxtaarticular osteoporosis, no new bone formation)

PYKNODYSOSTOSIS

= MAROTEAUX-LAMY DISEASE

= autosomal recessive inherited disorder of primary spongiosa; probably variant of cleidocranial dysostosis

Genetics: mutation in cathepsin-K gene (= lysosomal cysteine proteinase expressed in osteoclasts and required for degradation of collagen)

Age: often diagnosed in infancy / early childhood; M÷F = 2÷1

• dwarfism; mental retardation (10%)

• no concurrent anemia ← preserved medullary cavities

√ generalized osteosclerosis of long bones with thickened cortices (resembling osteopetrosis but with preservation of medullary canal)

√ multiple spontaneous fractures ← brittle bones

@ Skull

• yellowish discoloration of teeth

• characteristic dysmorphic facies: beaked nose, receding jaw

√ brachycephaly + platybasia

√ wide cranial sutures, wormian bones

√ thick skull base

√ hypoplasia of mandible + obtuse mandibular angle

√ hypoplasia + nonpneumatization of paranasal sinuses

@ Hands

• widened hands + feet; dystrophic nails

√ hypoplastic tapered terminal tufts (= acroosteolysis)

@ Spine

√ nonsegmentation of C1/C2 and L5/S1

√ kyphoscoliosis with increased lumbar lordosis

√ dense vertebral bodies with characteristic sparing of transverse processes

@ Chest

√ pectus excavatum

√ clavicular dysplasia

DDx: (1) Osteopetrosis (no dwarfism, no mandibular / skull abnormality, no phalangeal hypoplasia, no transverse metaphyseal bands, anemia, Erlenmeyer flask deformity;

"bone-within-bone" appearance)

(2) Cleidocranial dysostosis (no dense bones / terminal phalangeal hypoplasia, short stature)

QUADRILATERAL SPACE SYNDROME

= neurovascular compression syndrome involving the posterior humeral circumflex artery ± axillary nerve

Quadrilateral space:

compartment formed by teres major m. (inferiorly) + long head of triceps m. (medially) + teres minor m. (posteriorly) + subscapularis m. (anteriorly) + surgical neck of humerus (laterally)

Cause: posttraumatic fibrotic bands, muscle hypertrophy in throwing athletes

Age: 20–35 years

- point tenderness over quadrilateral space aggravated by abduction + external rotation of arm
- burning pain over lateral aspect of shoulder and arm
- weakness of deltoid m. + teres minor m.

√ compression of posterior circumflex a.

√ atrophy of deltoid m. + teres minor m.

√ occlusion of posterior humeral circumflex a.

Rx: analgesics, physiotherapy

RADIATION INJURY TO BONE

Pathogenesis: vascular compromise with obliterative endarteritis + periarteritis → hypovascularity + hypoxia → damage to osteoblasts + osteoclasts → hypocellularity + fibrosis → decreased matrix production (growing bone + periosteal new bone most sensitive)

Dose effects:

depend on age of patient, absorbed dose, size of radiation field, beam energy, fractionation

> 300 rad:	microscopic changes
> 400 rad:	growth retardation
< 600–1200 rad:	histological recovery retained
> 1200 rad:	pronounced cellular damage to chondrocytes; bone marrow atrophy + cartilage degeneration after > 6 months; vascular fibrosis

A. FOCAL MARROW DEPLETION

Pathophysiology: marrow edema, vascular congestion, suppressed hematopoiesis; replacement of marrow elements by fibrosis + fat (complete by 3 months)

√ homogeneous high-intensity signal within radiation port on T1WI

√ occasionally bandlike appearance characterized by peripheral zone of low SI (red marrow) and a central zone of high SI (fatty marrow) on T1WI

B. BONE GROWTH DISTURBANCE

@ Appendicular skeleton

√ joint space widening ← cartilage hypertrophy (after 8–10 months)

√ growth plate widening in 1–2 months, often returning to normal by 6 months

√ permanent alteration in bone length / size ← premature fusion of physis
√ metaphyseal bowing
√ sclerotic metaphyseal bands
√ metaphyseal irregularity + fraying resembling rickets
√ longitudinal striations
√ overtubulation (= abnormal narrowing of the diaphyseal shaft)
Cx: slippage of femoral / humeral epiphysis ± ischemic necrosis (after doses of > 25 Gy)

@ Axial skeleton (dose of < 15 Gy)
√ "bone-within-bone" appearance after 9–12 months
√ irreversible scalloping + irregularity of vertebral endplate with decreased height of vertebra
(= failure of vertical growth)
√ scoliosis concave toward side of irradiation ← asymmetric vertebral growth + muscular fibrosis
√ hypoplasia of ilium + ribs
√ acetabular dysplasia, coxa vara / valga

C. RADIATION OSTEITIS = OSTEORADIONECROSIS
= RADIATION NECROSIS
= bone mottling due to osteopenia + coarse trabeculation and focally increased bone density ← attempts of osseous repair with deposition of new bone on ischemic trabeculae
Dose: > 6,000 cGy in adults; > 2,000 cGy in children
Time of onset: 1–3 years following radiation therapy
Location: mandible, ribs, clavicle, humerus, spine, pelvis, femur
√ focal lytic area with abnormal bone matrix:
√ radiolucency confined to radiation field with narrow zone of transition
√ periostitis
√ increased fragility with sclerosis (= pathologic insufficiency fracture)
√ ± cortical thinning from chronic infection
MR:
√ increased intensity of spinal bone marrow on T1WI + T2WI corresponding to radiation port (fatty infiltration)
NUC:
√ bone scan with decreased uptake in radiation field
Cx: increased susceptibility of irradiated bone to infection
DDx: recurrent malignancy, radiation-induced sarcoma (soft-tissue mass), infection

D. BENIGN NEOPLASM
Most likely in patients < 2 years of age at treatment; with doses of 1600–6425 rads
Latent period: 1.5–5–14 years
1. Osteochondroma = exostosis (exclusively in children under 2 years of age during treatment)
2. Osteoblastoma

E. MALIGNANT NEOPLASM
= RADIATION-INDUCED SARCOMA
Latency period: 3–55 (average of 11–14) years

Minimum dose: 1,660–3,000 rad

Criteria: (a) malignancy occurring within irradiated field
(b) latency period of > 5 years
(c) histologic proof of sarcoma
(d) microscopic evidence of altered histology of the original lesion

Histo: 1. Osteosarcoma (90%) = 4–11% of all osteogenic sarcomas
2. Fibrosarcoma > chondrosarcoma > malignant fibrous histiocytoma

• pain, soft-tissue mass, rapid progression of lesion

REACTIVE ARTHRITIS

= REITER SYNDROME
[Hans Conrad Julius Reiter (1881–1969), German bacteriologist and hygienist in institute of hygiene in Königsberg and Berlin-Dahlem convicted of war crimes at the Nürnberg trials for his medical experiments in the concentration camp at Buchenwald]

= noninfectious, asymmetric inflammatory oligoarthropathy characterized by the triad of
(1) Postinfectious peripheral arthritis
(2) Uveitis / conjunctivitis
(3) Urethritis / cervicitis
with characteristic skin lesions

M÷F = 98÷2

Types:
(1) endemic (venereal): Chlamydia + Ureaplasma (males)
(2) epidemic (postdysenteric): Shigella, Salmonella, Yersinia, Campylobacter (males + females)

Trigger: within a few weeks after infection of GU / GI tract; skeletal manifestations typically appear after urethral and ocular inflammation have subsided

• history of sexual exposure / diarrhea 3–11 days before onset of urethritis
• mucocutaneous lesions of coalescing pustules, vesicles, erosions (in up to 50%):
» **balanitis circinata sicca** (male)
» **ulcerative vulvitis** (females)
• **keratosis blennorrhagicum** = well-demarcated scaly hyperkeratotic + pustular papules coalescing to plaques
Location: palm, sole
• seronegative spondyloarthritis
• positive HLA-B27 in 76% → greater propensity for chronicity

Location: asymmetric mono- / pauciarticular with predilection for lower extremity (small joints of foot, calcaneus, ankle)

Spectrum: enthesitis, joint effusion, synovitis, bursitis, erosive + proliferative bone changes, diffuse soft-tissue edema with tenosynovitis of finger + toe

√ polyarthritis
√ articular soft-tissue swelling + joint space narrowing in 50% (particularly knee, ankle, foot)
√ widening + inflammation of Achilles + plantar fascial tendons → heel swelling + retrocalcaneal bursitis (frequent)
√ "fluffy" periosteal reaction (DISTINCTIVE) at metatarsal necks, proximal phalanges,

calcaneal spur, tibia + fibula at ankle and knee
√ juxtaarticular osteoporosis (rare in acute stage)
Chronic changes:
• recurrent joint attacks in a few cases
√ calcaneal spur at insertion of plantar fascia + Achilles tendon
√ periarticular deossification
√ marginal erosions, loss of joint space
√ bilateral sacroiliac changes indistinguishable from ankylosing / psoriatic spondylitis (in 10–40%)
√ paravertebral ossification = isolated "floating osteophyte" usually in thoracolumbar area
Cx: gastric ulcer + hemorrhage; aortic incompetence; heart block; amyloidosis
DDx: Psoriasis (radiographically indistinguishable; no predilection for lower extremities, asymmetric involvement, clinical findings)

REFLEX SYMPATHETIC DYSTROPHY

= CAUSALGIA = SHOULDER-HAND SYNDROME = POSTTRAUMATIC OSTEOPOROSIS = SUDECK DYSTROPHY
= serious + potentially disabling condition with poorly understood origin + cause
Etiology:
(1) Trauma in > 50% (fracture, frostbite; may be trivial)
◊ Affects 0.01% of all trauma patients
(2) Idiopathic in 27% (immobilization, infection)
(3) Myocardial ischemia in 6%
(4) CNS disorders in 6%
◊ Affects 12–21% of patients with hemiplegia
(5) Diskogenic disease in 5%
• burning pain, tenderness, allodynia, hyperpathia
• soft-tissue swelling ± pitting edema out of proportion to degree of injury; dystrophic skin + nail changes
• sudomotor changes: hyperhidrosis + hypertrichosis
• vasomotor instability (Raynaud phenomenon, local vasoconstriction / vasodilatation)
• end-stage (after 6–12 months): contractures, atrophy of skin + soft tissues
Location: hands and feet distal to injury
√ periarticular soft-tissue swelling
√ patchy osteopenia (50%) as early as 2–3 weeks after onset of symptoms (DDx: disuse osteopenia)
√ generalized osteopenia = ground-glass appearance with endosteal + intracortical excavation:
√ subperiosteal bone resorption
√ lysis of juxtaarticular + subchondral bone
√ preservation of joint space (DDx: rheumatoid / septic arthritis)
NUC (3-phase bone scan):
√ ↑ flow + ↑ blood pool + ↑ in periarticular uptake on delayed images in affected part (60%)
√ ↓ flow / delayed uptake (15–20%)

Rx: sympathetic block, α- / β-adrenergic blocking agents, nonsteroidal antiinflammatory drugs, radiation therapy, hypnosis, acupuncture, acupressure, transcutaneous nerve stimulation, physiotherapy, calcitonin, corticosteroids, early mobilization

RELAPSING POLYCHONDRITIS

= rare debilitating multisystem inflammatory + autoimmune disorder characterized by recurrent episodes of inflammation + destruction of cartilage in joints, ears, nose, larynx, airways

Etiology: acquired metabolic disorder (? abnormal acid mucopolysaccharide metabolism) / hypersensitivity / autoimmune process (antibodies directed against type II collagen)

Histo: loss of cytoplasm in chondrocytes; plasma cell and lymphocyte infiltration

Age: 40–60 years (no age predilection)

- nasal chondritis = saddle-nose deformity
- bilateral auricular chondritis = swollen + tender ears, cauliflower ears; ocular inflammation
- hearing loss ← obstruction of external auditory meatus / audiovestibular damage)
- cough, hoarseness, dyspnea ← collapse of trachea
- nonerosive seronegative inflammatory polyarthritis = arthralgia

@ Head
- √ calcification of pinna of ear

@ Chest
- √ manubriosternal / costochondral arthropathy (30%)

@ Respiratory tract (in up to 70%)
- √ ectasia + collapsibility (← cartilaginous destruction) of trachea and mainstem bronchi with focal thickening (← mucosal edema) + luminal narrowing (← fibrosis)
- √ bronchiectasis
- √ generalized + localized emphysema

@ Cardiovascular (in 15–46%)

Site: elastic elements of cardiac valves + aorta

Histo: cystic degeneration of collagen, destruction of elastic fibers, lymphocytic infiltration, decreased content of acid mucopolysaccharides

- √ aortic aneurysm (4–10%), mostly in ascending aorta, may be multiple / dissecting
- √ aortic / mitral valve insufficiency (8%)
- √ aortitis + systemic vasculitis (13%)
- √ obliterating vasculitis in medium-sized + large arteries

@ Bone
- √ periarticular osteoporosis
- √ erosive changes in carpal bones resembling rheumatoid arthritis
- √ soft-tissue swelling around joints + styloid process of ulna
- √ erosive irregularities in sacroiliac joints
- √ disk space erosion + increased density of articular plates

Rx: corticosteroids, immunosuppression

Prognosis: 74% 5-year survival rate; 55% 10-year survival rate; median survival time of 11 years; airway complications account for > 50% of deaths

RENAL OSTEODYSTROPHY

= constellation of musculoskeletal abnormalities that occur with chronic renal failure as a combination of

(a) osteomalacia (adults) / rickets (children)
(b) 2° HPT with osteitis cystica fibrosa + soft-tissue calcifications
(c) osteosclerosis
(d) soft-tissue + vascular calcifications

Classification:

A. Glomerular form = acquired renal disease: chronic glomerulonephritis (common)
B. Tubular form = congenital renal osteodystrophy:
   1. Vitamin D–resistant rickets = hypophosphatemic rickets
   2. Fanconi syndrome = impaired resorption of glucose, phosphate, amino acids, bicarbonate, uric acid, sodium, water
   3. Renal tubular acidosis

Pathogenesis:

(1) Renal insufficiency → decrease in vitamin D conversion into the active $1,25(OH)_2D_3$ (done by 25-OH D-1-α hydroxylase, which is exclusive to renal tissue mitochondria); <u>vitamin D deficiency</u> slows intestinal calcium absorption; <u>vitamin D resistance</u> predominates and calcium levels stay low (Ca x P product remains almost normal ← hyperphosphatemia); low calcium levels lead to OSTEOMALACIA; additional factors responsible for osteomalacia are (a) inhibitors to calcification produced in the uremic state, (b) aluminum toxicity, (c) dysfunction of hepatic enzyme system

(2) Renal insufficiency with diminished filtration → <u>phosphate retention</u>; maintenance of Ca x P product lowers serum calcium directly, which in turn increases PTH production (2° HPT); <u>2° HPT</u> predominates associated with mild vitamin D resistance → <u>increase in Ca x P product</u> with SOFT-TISSUE CALCIFICATION in kidney, lung, joints, bursae, blood vessels, heart as well as increase in osteoclastic activity = OSTEITIS FIBROSA

(3) Mixture of (a) and (b): increased serum phosphate inhibits vitamin D activation via feedback regulation

• phosphate retention; hypocalcemia

A. OSTEOPENIA (in 0–25–83%)

= diminution in number of trabeculae + thickening of stressed trabeculae = increased trabecular pattern

Cause: combined effect of

(1) Osteomalacia (= reduced bone mineralization ← acquired insensitivity to vitamin D / antivitamin D factor)
(2) Osteitis fibrosa cystica ← increase in bone resorption
(3) Osteoporosis ← decrease in bone quantity

Contributing factors:

chronic metabolic acidosis, poor nutritional status, pre- and posttransplantation azotemia, use of steroids, hyperparathyroidism, low vitamin D levels

Cx: fracture predisposition ← lessened structural strength with minor trauma / spontaneously; fracture prevalence increases with duration of hemodialysis + remains unchanged after renal transplantation

Site: vertebral body (3–25%), pubic ramus, rib (5–25%)

√ Milkman fracture / Looser zones (in 1%)
√ metaphyseal fractures
Prognosis: osteopenia may remain unchanged / worsen after renal transplantation + during hemodialysis

B. RICKETS (children)
Cause: in CRF normal vessels fail to develop in an orderly way along cartilage columns in zone of provisional calcification; this results in disorganized proliferation of the zone of maturing + hypertrophying cartilage and disturbed endochondral calcification
Location: most apparent in areas of rapid growth such as knee joints
√ diffuse bone demineralization
√ widening of growth plate
√ irregular zone of provisional calcification
√ metaphyseal cupping + fraying
√ bowing of long bones, scoliosis
√ diffuse concave impression at multiple vertebral end plates
√ basilar invagination
√ slipped epiphysis (10%): capital femoral, proximal humerus, distal femur, distal radius, heads of metacarpals + metatarsals
√ general delay in bone age

C. SECONDARY HPT (in 6–66%)
Cause: inability of kidneys to adequately excrete phosphate leads to hyperplasia of parathyroid chief cells (2° HPT); excess PTH affects the development of osteoclasts, osteoblasts, osteocytes
• hyperphosphatemia; hypocalcemia; ↑ PTH levels
√ subperiosteal, cortical, subchondral, trabecular, endosteal, subligamentous bone resorption:
√ replacement of trabeculation by ground-glass attenuation (early phase)
√ loss of definition of cortex, lamina dura, wall of inferior alveolar nerve canal
√ osteitis fibrosa (advanced pattern) = mixture of osteolysis + sclerosis + heterogeneous pattern of bone resorption with osteoid production and increased bone remodeling
√ osteoclastoma = brown tumor = osteitis fibrosa cystica in 1.5–1.7% ← PTH-stimulated osteoclastic activity (more common in 1° HPT)
√ periosteal new-bone formation (8–25%)
√ chondrocalcinosis (more common in 1° HPT)
@ Face
√ macrognathia + cortical thickening
√ protrusion + splaying of teeth

D. OSTEOSCLEROSIS (9–34%)
◊ One of the most common radiologic manifestations; most commonly with chronic glomerulonephritis; may be the sole manifestation of renal osteodystrophy
√ diffuse chalky density: thoracolumbar spine in 60% (rugger jersey spine); also in pelvis, ribs, long bones, facial bones, base of skull (children)
Prognosis: may increase / regress after renal transplantation

E. SOFT-TISSUE CALCIFICATIONS

= Uremic tumoral calcinosis = secondary tumoral calcinosis = pseudotumor calcinosis

◊ Most frequent cause of a periarticular calcified mass!

Cause: ?

(a) metastatic ← hyperphosphatemia (= solubility product for calcium + phosphate [Ca^{2+} • PO_4^{-2}] exceeds 60–75 mg/dL in extracellular fluid), hypercalcemia, alkalosis with precipitation of calcium salts

(b) dystrophic ← local tissue injury

Location:

› arterial (27–83%): in medial + intimal elastic tissue

Site: dorsalis pedis a., forearm, hand, wrist, leg

√ pipestem appearance without prominent luminal involvement

› periarticular (0.5–1.2%): multifocal, frequently symmetric, may extend into adjacent joint

• chalky fluid / pastelike material

• inflammatory response in surrounding tenosynovial tissue

√ discrete cloudlike dense areas

√ fluid-fluid level in tumoral calcinosis

Prognosis: often regresses with treatment

› visceral (79%): heart, lung, stomach, kidney

√ fluffy amorphous "tumoral" calcification

Rx: (1) Decrease of phosphorus absorption in bowel (in hyperphosphatemia)

(2) Vitamin D3 administration (if vitamin D resistance predominates)

(3) Parathyroidectomy for 3° HPT (= autonomous HPT)

Dialysis-associated Disorders

1. Osteomyelitis
2. Pyogenic spondylodiskitis
3. Osteonecrosis
4. Destructive spondyloarthropathy
5. Crystal deposition
6. Dialysis cysts
7. Amyloidosis

Congenital Renal Osteodystrophy

Vitamin D–Resistant Rickets

= PHOSPHATE DIABETES = PRIMARY HYPOPHOSPHATEMIA = FAMILIAL HYPOPHOSPHATEMIC RICKETS

= rare X-linked dominant disorder of renal tubular reabsorption characterized by

(a) impaired resorption of phosphate in proximal renal tubule ← defect in renal brush-border membrane

(b) inappropriately low synthesis of 1,25-dihydroxy-vitamin D3 [$1,25(OH)_2D_3$] in renal tubules → decreased intestinal resorption of calcium + phosphate

Age: < 1 year

- hypophosphatemia + hyperphosphaturia
- elevated serum alkaline phosphatase
- normal plasma + urine calcium
- normal / low serum $1,25(OH)_2D_3$

√ classic rachitic changes
√ skeletal deformity, particularly bowed legs
√ retarded bone age; dwarfism if untreated
√ osteosclerosis / bone thickening ← overabundance of incompletely calcified matrix

Rx: phosphate infusion + large doses of vitamin D

DDx: vitamin-D–deficient and –dependent rickets (absence of muscle weakness + seizures + tetany)

Fanconi Syndrome

Triad of
(1) Hyperphosphaturia
(2) Aminoaciduria
(3) Renal glucosuria (normal blood glucose)

Etiology: renal tubular defect

√ rickets, osteomalacia, osteitis fibrosa, osteosclerosis

Prognosis: functional renal impairment likely when bone changes occur

Rx: large doses of vitamin D + alkalinization

Renal Tubular Acidosis

- systemic acidosis, bone lesions

√ rickets, osteomalacia, pseudofractures, nephrocalcinosis, osteitis fibrosa (rare)

(a) **Lightwood syndrome** = salt-losing nephritis (transient self-limited form)
- NO nephrocalcinosis

(b) **Butler-Albright syndrome** (severe form)
- nephrocalcinosis

RHEUMATOID ARTHRITIS

= chronic systemic connective tissue disease
= type III (delayed) hypersensitivity
= immune complex disease (= formation of antigen-antibody complexes with complement fixation) with T-cell–mediated autoreactivity against synovium

Prevalence: 1–2% of world's population

Cause: genetic predisposition; ? reaction to antigen from Epstein-Barr virus / certain strains of E. coli

Peak age: 45–65 years; M÷F = 1÷3 if < 40 years; M÷F = 1÷1 if > 40 years

Pathogenesis:

injury to synovial endothelial cells → proliferative hyperplastic hypervascular synovitis (= pannus) mediated by TNF-α (tumor necrosis factor α) and IL-1 (interleukin 1) leads to invasion by local macrophages, fibroblasts, and activated lymphocytes; invasion of articular cartilage + bone ← secretion of degrading enzymes (metalloproteinases)

Diagnostic criteria of American Rheumatism Association (at least 4 criteria should be present):

(1) morning stiffness for ≥ 1 hour before improvement
(2) swelling of ≥ 3 joints, particularly of wrist / metacarpo-phalangeal / proximal interphalangeal joints for > 6 weeks
(3) symmetric swelling
(4) typical radiographic changes on PA views of hand & wrist
(5) subcutaneous rheumatoid nodules
(6) positive test for rheumatoid factor

- morning stiffness; fatigue, weight loss, anemia
- carpal tunnel syndrome
- rheumatoid factor (positive in 85–94%) = IgM-antibody
  = agglutination of sensitized sheep RBCs closely correlating with disease severity
  False positive: normal (5%), asbestos workers with fibrosing alveolitis (25%), viral / bacterial / parasitic infection, other inflammatory diseases
- human leukocyte antigen (HLA)–DR4 (positive in 70%)
- antinuclear antibodies (positive in many)
- LE cells (positive in some); positive latex flocculation test
- hormonal influence:
  (a) decrease in activity during pregnancy
  (b) men with RA have low testosterone levels

Location: bilateral symmetric involvement of > 3 diarthrodial joints (polyarthritis), commonly of hand, wrist, foot
◊ Symmetric arthritis of multiple small hand joints in > 60% of patients at initial presentation

Early signs:

MR and high-resolution US (methods of choice): ← greater sensitivity for detection of *synovitis* and articular erosions than either clinical examination / conventional radiography.

√ **synovitis** = abnormal hypo- / anechoic / (rarely) iso- / hyperechoic (relative to subdermal fat) <u>nondisplaceable poorly compressible</u> intra-articular material ± Doppler signals:
  √ positive Doppler signals = synovial hyperemia (in acute disease + exacerbation of chronic disease)
  √ synovial swelling (edema + cellular infiltrates)
  √ intermediate to low SI of **pannus** on T1WI + T2WI (= synovial hyperplasia = tumorlike focal proliferation of inflammatory tissue with destruction of cartilage and bone)

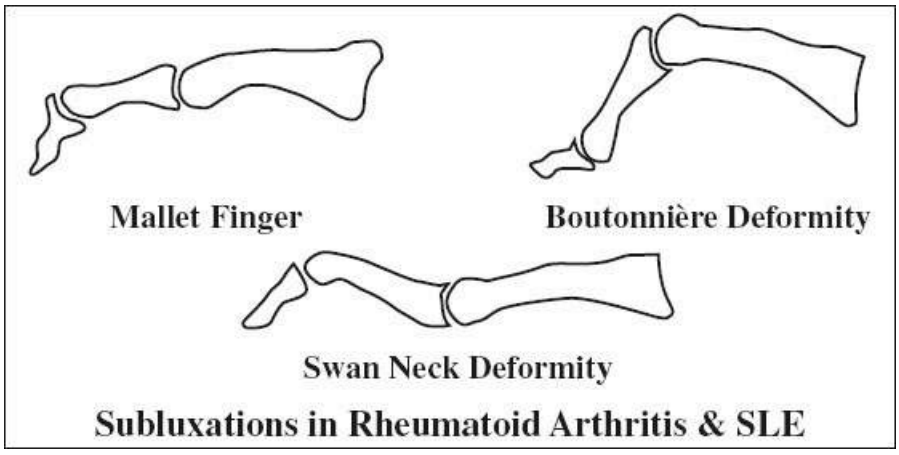
Synovitis occurs early in RA and is considered a strong predictor of developing bone erosion.

√ **tenosynovitis** = abnormal an- / hypoechoic (relative to tendon fibers) tendon sheath widening / distention ← abnormal tenosynovial fluid ± synovial hypertrophy
√ **joint effusion** = abnormal hypo- / anechoic / (rarely) iso- / hyperechoic (relative to subdermal fat) <u>displaceable compressible</u> intra-articular material without Doppler signals
√ **bursal effusion**
√ marginal **bone erosion** = intra-articular discontinuity of bone surface at *"bare area"* (= site of attachment of internal synovial layer of joint capsule to bone) ← lack of protective

cartilage layer:
√ pre-erosive subcortical cysts
√ bone marrow edema at site of erosion (by MRI only)
Time of onset: within first 6 symptomatic months
Prognosis: poor prognostic indicator in early disease

Radiography (indirect & nonspecific):
√ fusiform periarticular swelling ← joint effusion
√ periarticular osteoporosis ← inactivity due to pain + local inflammatory hyperthermia
√ translucent subchondral end plate
√ widened joint space ← synovial swelling + joint fluid
√ effacement of fat pads
√ subcortical synovial cyst
√ marginal erosion (up to 47% within 1st year after onset) initially at *"bare area"*
◊ Radiographically detectable 1–2 years after US / MR

Late signs:
√ concentric joint space narrowing ← destruction of cartilage, formation of scar tissue, fibrosis
√ subluxation ← laxity of capsule + ligaments ← inflammatory destruction + capsular shrinkage ← fibrosis + scar formation:
√ mallet finger = droopy distal phalanx due to disrupted extensor tendon insertion site
√ swan-neck deformity = hyperextension at PIP + flexion at DIP
√ boutonnière deformity = flexion at PIP + hyperextension at DIP
√ hitchhiker deformity = flexion at MCP + hyperextension at DIP
√ dislocation
√ marked destruction + fractures of bone ends:
√ intraarticular loose bodies
√ (polished) rice bodies = subset of loose bodies
√ soft-tissue rheumatoid nodule of heterogeneous echogenicity



@ Hand & wrist (typical)
Target areas:
all five MCP, PIP, interphalangeal joint of thumb, all wrist compartments (especially

radiocarpal, inferior radioulnar, pisiform-triquetral joints); earliest changes seen in MCP 2 + 3, PIP 3

√ marginal + central bone erosions (less common in large joints); site of first erosion is classically base of proximal phalanx of 4th finger

√ changes in ulnar styloid + distal radioulnar joint (early sign)

√ flexion + extension contractures with ulnar subluxation + dislocation

@ Cervical spine

√ erosions of odontoid process (1) between anterior arch of atlas + dens, (2) between transverse ligament of atlas + dens, (3) at tip of odontoid process

√ anterior atlantoaxial subluxation (in > 6%): > 2.5 mm in adults, > 4.5 mm in children during neck flexion

√ "cranial settling" = odontoid process projects into skull base ← significant disease of atlanto-occipital and atlantoaxial joints

√ lateral head tilt = lateral subluxation = asymmetry between odontoid process + lateral masses of atlas

√ "stepladder appearance" of cervical spine ← subaxial subluxations + absence of osteophytosis:

√ destruction + narrowing of disk spaces

√ irregular vertebral body outlines

√ erosion + destruction of zygapophyseal joints

√ resorption of spinous processes

√ osteoporosis

Cx: spinal cord compression

@ Cricoarytenoid arthritis (54–72%)

• hoarseness, sense of pharyngeal fullness in throat (26%)

• dyspnea, stridor, dysphagia, odynophagia

• pain radiating into ears, pain with speech

√ cricoarytenoid erosion, luxation, prominence / mass at CT

√ abnormal position of the true vocal cord

@ Ribs

√ erosion of superior margins of posterior portions of ribs 3–5

@ Shoulder

√ symmetric loss of glenohumeral joint space:

√ marginal erosions at superolateral aspect of humeral head

√ osteoporosis

√ elevation of humeral heads = narrowing of acromiohumeral distance ← tear / atrophy of rotator cuff

√ widened acromioclavicular joint:

√ erosions at acromial + clavicular end

√ tapered margins of distal clavicle

√ scalloped erosion on undersurface of distal clavicle opposite coracoid process (= attachment of coracoclavicular ligament)

@ Sacroiliac joint (rarely affected)

√ typically asymmetric unilateral distribution

√ shallow erosions + mild sclerosis

√ rare ankylosis

@ Hip (rarely affected)

√ often appears normal during early disease process

√ pannus formation (MR imaging)

√ symmetric loss of joint space with axial migration of femoral head

√ marginal + central erosions, cysts, localized sclerosis

√ decompression of joint effusion into iliopsoas bursa through weak anterior capsule displacing muscle + vasculature

√ rupture of gluteal tendon

√ protrusio acetabuli (from osteoporosis)

@ Knee

Location: medial + lateral femorotibial compartments; bilateral symmetric

√ diffuse loss of joint space

√ osteoporosis

√ superficial + deep marginal + central erosions

√ subchondral sclerosis (especially in tibia)

√ synovial herniation + cysts (eg, popliteal cyst)

√ varus / valgus angulation ← crumbling of osteoporotic bone of tibia + ligamentous abnormalities

@ Foot (typical)

Target areas:

medial aspect of MT heads (2,3,4), medial + lateral aspect of MT5 (earliest sign); interphalangeal joints of foot (esp. great toe); midfoot joints; talonavicular, subtalar, tarsometatarsal joints; bilateral + symmetric

• sinus tarsi syndrome = compression of tibial nerve

√ calcaneal plantar spur

√ retrocalcaneal bursitis

DDx: (1) Acute viral polyarthritis: Parvovirus B19, Rubella, Hepatitis B

(2) Seronegative spondyloarthropathies: psoriasis, reactive arthritis, inflammatory bowel disease, ankylosing spondylitis

(3) Connective tissue disease: SLE, primary Sjögren syndrome, mixed connective tissue disease, scleroderma, dermatomyositis-polymyositis

(4) Crystal disease: gout, CPPD, osteoarthritis

EXTRA-ARTICULAR MANIFESTATIONS (50–76%)

(a) **Felty syndrome** (< 1%)

= rheumatoid arthritis (present for > 10 years) + splenomegaly + neutropenia

Age: 40–70 years; F > M; rare in Blacks

• rapid weight loss; therapy refractory leg ulcers

• brown pigmentation over exposed surfaces of extremities

(b) Sjögren syndrome (15%)

= keratoconjunctivitis + xerostomia + rheumatoid arthritis

(c) Rheumatoid lung

(d) **Subcutaneous nodules**

(in 5–35% with active arthritis) over extensor surfaces of forearm + other pressure points

(eg, olecranon) without calcifications (DDx to gout)

(e) Cardiovascular involvement
1. Pericarditis (20–50%)
2. Myocarditis: arrhythmia, heart block
3. Aortitis (5%) of ascending aorta → aneurysm (2%)
4. Leaflet thickening of aortic valve → regurgitation

(f) **Rheumatoid vasculitis**
= leukocytoclastic lesion of small venules mimicking periarteritis nodosa
• polyneuropathy, cutaneous ulceration, gangrene, polymyopathy, myocardial / visceral infarction

(g) Neurologic sequelae
1. Distal neuropathy (related to vasculitis)
2. Nerve entrapment: atlantoaxial subluxation, carpal tunnel syndrome, Baker cyst

(h) Lymphadenopathy (up to 25%)
√ splenomegaly (1–5%)

Cystic Rheumatoid Arthritis

= intraosseous cystic lesions as dominant feature

Pathogenesis: increased pressure in synovial space from joint effusion → decompresses through microfractures of weakened marginal cortex into subarticular bone

◊ Increase in size + extent of cysts correlates with increased level of activity + absence of synovial cysts

Age: as above; M÷F = 1÷1

• seronegative in 50%

√ juxtaarticular subcortical lytic lesions with well-defined sclerotic margins

√ relative lack of cartilage loss, osteoporosis, joint disruption

DDx: gout (presence of urate crystals), pigmented villonodular synovitis (monoarticular)

Juvenile Rheumatoid Arthritis

= rheumatoid arthritis in patients < 16 years of age; M < F

• morning stiffness, arthralgia; subcutaneous nodules (10%)

• skin rash (50%); fever, lymphadenopathy

Location: early involvement of large joints (hips, knees, ankles, wrists, elbows); later of hands + feet

√ radiologic signs similar to rheumatoid arthritis (except for involvement of large joints first, late onset of bony changes, more ankylosis, wide metaphyses)

√ periarticular soft-tissue swelling

√ thinning of joint cartilage

√ large cystlike lesions removed from articular surface (invasion of bone by inflammatory pannus); rare in children

√ articular erosions at ligamentous + tendinous insertion sites

√ joint destruction may resemble neuropathic joints

√ juxtaarticular osteoporosis

√ "balloon epiphyses" + "gracile bones" (epiphyseal overgrowth + early fusion with bone shortening ← hyperemia

@ Hand / foot
√ "rectangular" phalanges (periostitis + cortical thickening)
√ ankylosis in carpal joints
@ Axial skeleton
Location: predominantly upper cervical spine
√ ankylosis of cervical spine (apophyseal joints), sacroiliac joints
√ decreased size of vertebral bodies + atrophic intervertebral disks
√ subluxation of atlantoaxial joint (66%)
√ thoracic spinal compression fractures
@ Chest
√ ribbon ribs
√ pleural + pericardial effusions
√ interstitial pulmonary lesions (simulating scleroderma, dermatomyositis)
√ solitary pulmonary nodules, may cavitate
Prognosis: complete recovery (30%); secondary amyloidosis
Clinical classification:
(1) Juvenile-onset adult type (10%)
• IgM RA factor positive; age 8–9; poor prognosis
√ erosive changes; profuse periosteal reaction; hip disease with protrusio
(2) Polyarthritis of the ankylosing spondylitic type
• iridocyclitis; boys age 9–11 years
√ peripheral arthritis; fusion of greater trochanter; complete fusion of both hips; heel spur
(3) **Still disease**
(a) systemic
(b) polyarticular
(c) pauciarticular + iridocyclitis (30%)
• fever, rash, lymphadenopathy, hepatosplenomegaly; pericarditis, dwarfism
• fatal kidney disease in 20%
Age: 2–4 and 8–11 years of age; M < F
Location: involvement of carpometacarpal joints ("squashed carpi" in adulthood), hind foot, hip (40–50%)
√ periosteal reaction of phalanges; broadening of bones; accelerated bone maturation + early fusion (stunting of growth)

RICKETS

= osteomalacia during enchondral bone growth
Age: 4–18 months
Histo: zone of maturation has an increase in the number of maturing cartilage cells with loss of normal columnar arrangement; zone of preparatory calcification does not form; failure of osteoid mineralization also in shafts so that osteoid production elevates periosteum
• irritability, bone pain, tenderness
• craniotabes; delayed dentition
• bowed legs; swelling of wrists + ankles; rachitic rosary

Location: metaphyses of long bones subjected to stress are particularly involved (wrists, ankles, knees); costochondral junction of ribs

√ poorly mineralized irregular epiphyseal centers with delayed appearance

√ axial widening of growth plate = ↑ distance between end of shaft and epiphyseal center ← ↑ osteoid production (earliest changes)

√ cupping + fraying of metaphysis with threadlike shadows into epiphyseal cartilage (weight-bearing bones)

√ cortical spurs projecting at right angles to metaphysis

√ coarse trabeculation (NO ground-glass pattern as in scurvy)

√ periosteal reaction may be present

√ deformities common (bowing of soft diaphysis, molding of epiphysis, fractures)

√ bowing of long bones

√ frontal bossing

mnemonic: "RICKETS"

Reaction of periosteum may occur
Indistinct cortex
Coarse trabeculation
Knees + wrists + ankles mainly affected
Epiphyseal plates widened + irregular
Tremendous metaphysis (fraying, splaying, cupping)
Spur (metaphyseal)

Cx: stress fracture, bowing deformity

Causes of Rickets

I. ABNORMALITY IN VITAMIN D METABOLISM associated with reactive hyperparathyroidism
   A. Vitamin D deficiency (most common cause)
      (a) dietary lack of vitamin D = famine osteomalacia = nutritional lack of vitamin precursors (vegetarian diet, prolonged total breast feeding without vitamin D supplementation)
      (b) lack of sunshine exposure eg, residence in high latitudes, clothing covering skin, sunshine avoidance for religious / cultural reasons, heavy skin pigmentation
      (c) malabsorption of vitamin D
         = gastroenterogenous rickets due to
         1. Pancreatitis + biliary tract disease
         2. Steatorrhea, celiac disease, postgastrectomy
         3. Inflammatory bowel disease
   B. Defective conversion of vitamin D to 25-OH-cholecalciferol (vitamin D3) in liver
      1. Liver disease
      2. Anticonvulsant drug therapy (= induction of hepatic enzymes that accelerate degradation of biologically active vitamin D metabolites)
   C. Defective conversion of prehormone calcifediol [$25(OH)D_3$] to cholecalciferol [$1,25(OH)_2D_3$] in kidney
      1. Chronic renal failure = renal osteodystrophy
      2. Vitamin D–dependent rickets = autosomal recessive enzyme defect of 25(OH)D-

1α-hydroxylase

II. ABNORMALITY IN PHOSPHATE METABOLISM not associated with hyperparathyroidism ← normal serum calcium
   A. Phosphate deficiency
      1. Intestinal malabsorption of phosphates
      2. Ingestion of aluminum salts [$Al(OH)_3$] forming insoluble complexes with phosphate
      3. Low phosphate feeding in prematurely born infants
      4. Severe malabsorption state
      5. Parenteral hyperalimentation
   B. Disorders of renal tubular reabsorption of phosphate
      1. Renal tubular acidosis (renal loss of alkali)
      2. **deToni-Debré-Fanconi** syndrome = hypophosphatemia, glucosuria, aminoaciduria
      3. Vitamin D–resistant rickets
      4. Cystinosis
      5. Tyrosinosis
      6. Lowe syndrome
      7. Ifosfamide nephrotoxicity (for the treatment of rhabdomyosarcoma, Wilms tumor)
   C. Hypophosphatemia with nonendocrine tumors
      = **Oncogenic rickets** = elaboration of humeral substance which inhibits tubular reabsorption of phosphates (paraneoplastic phenomenon)
      1. Nonossifying fibroma
      2. Sclerosing hemangioma
      3. Hemangiopericytoma
      4. Ossifying mesenchymal tumor
   D. Hypophosphatasia

III. CALCIUM DEFICIENCY
   1. Dietary rickets = milk-free diet (extremely rare)
   2. Malabsorption
   3. Consumption of substances forming chelates with calcium

Classification of Rickets

I. Primary vitamin D–deficiency rickets

II. Gastrointestinal malabsorption
   A. Partial gastrectomy
   B. Small intestinal disease: gluten-sensitive enteropathy / regional enteritis
   C. Hepatobiliary disease: biliary atresia / chronic biliary obstruction / biliary cirrhosis resulting in failure of the emulsifying action of bile salts (fat-soluble vitamin) or failure of conversion
   D. Pancreatic disease: chronic pancreatitis

III. Primary hypophosphatemia; vitamin D–deficiency rickets

IV. Renal disease
   A. Chronic renal failure

B. Renal tubular disorders: renal tubular acidosis

C. Multiple renal defects

V. Hypophosphatasia + pseudohypophosphatasia

VI. Fibrogenesis imperfecta osseum

VII. Axial osteomalacia

VIII. Miscellaneous:

Hypoparathyroidism, hyperparathyroidism, thyrotoxicosis, osteoporosis, Paget disease, fluoride ingestion, ureterosigmoidostomy, neurofibromatosis, osteopetrosis, macroglobulinemia, malignancy

ROSAI-DORFMAN DISEASE

= sinus histiocytosis with massive lymphadenopathy

= rare dendritic cell disorder characterized by macrophage proliferation

Age: children and young adults; M > F; predilection for individuals of African descent

Histo: ***emperipolesis*** (= phagocytosis of lymphocytes, plasma cells, erythrocytes, PMNs) by histiocytes that show S100 positivity; negative for CD1a + Birbeck granules [*em*, Greek= inside, *peri* = around, *polemai* = to wander about]

@ Lymphadenopathy

√ uptake of gallium and FDG by lymphadenopathy

• fever, elevated ESR, mild anemia

√ nonspecific imaging appearance of painless lymphadenopathy

Location: cervical > retroperitoneal, mediastinal, axillary, inguinal

@ Extranodal disease (50%) in nearly every organ system

› Head

√ intracranial lesions primarily in the epidural or subdural compartments

√ orbital extraconal soft-tissue mass

› Neck

√ enhancing polypoid masses / mucosal thickening of occasionally aggressive appearance

√ salivary gland lymphoid hyperplasia

› Bone: commonly in skull, tibia, femur

√ medullary multicentric lytic lesions ± sclerotic margin

› Lung mass

Prognosis: overall good with indolent clinical course ± spontaneous resolution

ROTATOR CUFF LESIONS

Pathogenesis: (controversial)

(1) Extrinsic theory (Neer):

(a) hypertrophic changes of acromion

(b) osteophytes from acromioclavicular joint

(c) Type 3 hooked acromion

→ impingement of subacromial-subdeltoid bursa and rotator cuff

(2) Intrinsic (intratendinous) theory: tendon degeneration → partial-thickness tear → superior

migration of humeral head → abrasion of rotator cuff against undersurface of acromion → full-thickness tear

Subacromial Pain Syndrome

(1) Impingement syndrome
(2) Rotator cuff tendinitis
(3) Degeneration without impingement
(4) Shoulder instability with secondary impingement
(5) Instability without impingement

Impingement Syndrome

= clinical NOT radiographic diagnosis consisting of lateral shoulder pain with abduction and forward flexion

Cause: inadequate space for the normal motion of rotator cuff

Age: lifelong process; 1st stage < 25 years; 2nd stage 25–40 years; complete rotator cuff tear > 40 years

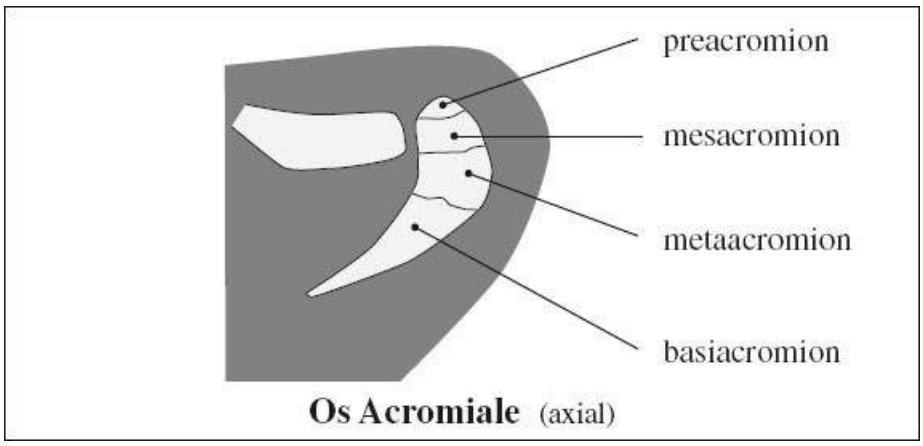
Pathophysiology:

movement of humerus impinges rotator cuff tendons against coracoacromial arch resulting in microtrauma, which causes inflammation of subacromial bursa (= fibrous thickening of subacromial bursa) / rotator cuff (*critical zone of rotator cuff* = supraspinatus tendon 2 cm from its attachment to humerus)

Impingement anatomy:

narrowing of subacromial space secondary to

(1) Acquired
  (a) degenerative subacromial enthesophyte / osteophyte
    › traction enthesophyte at coracoacromial ligament (= subacromial spur)
    › osteophytes ← acromioclavicular joint hypertrophy in osteoarthrosis
  (b) hypertrophy of coracoacromial ligament
  (c) primary bursitis in rheumatoid arthritis
  (d) swollen supraspinatus tendon ± calcific tendinosis impinging upon coracoacromial arch
(2) Congenital
  (a) curvature of acromion in anterior third (SAG)
    › flat (type 1)
    › curved downward (type 2)
    › hooked downward (type 3)
    › curved upward (type 4)
    ◊ Type 3 and possibly type 2 acromion processes have a higher prevalence of bursal-side rotator cuff tears!
  (b) lateral acromial angle (COR)



√ downsloping of acromion in lateral direction

(c) os acromiale = unfused acromial apophysis (8% of population)

◊ Impingement syndrome may exist without impingement anatomy and may be secondary to primary instability!

- night pain
- passive elevation of arm to 170° followed by passive internal + external rotation while arm adducted against ear → increased pain with rotation = test positive
- "arc of pain" sign = pain during active descent of abducted arm in abduction plane → minimal pain at full elevation with maximal pain between 70° and 120° = test positive

X-ray (AP view):

√ inferolateral tilt of acromion (on AP view)

X-ray (supraspinatus outlet [modified Y] view + caudal tilt view):

√ type III acromion = anterior aspect of acromion hooked inferiorly

√ anterior tilt / low position of acromion

√ anterior subacromial spur on undersurface of AC joint (= enthesophyte) at insertion site of coracoacromial lig.

MR (can identify the anatomy predisposing to impingement):

√ unstable os acriomale pulled downward by deltoid muscle during abduction

√ thickening of coracoacromial ligament

√ acromioclavicular joint osteoarthritis ± bone spurs

US:

√ bunching of subdeltoid bursa during abduction of arm

◊ US can direct steroid injection into bursa

Cx: (1) partial / complete tear (may be precipitated by acute traumatic event on preexisting degenerative changes; common cause of rotator cuff tears)

(2) cuff tendinitis / degenerative tendinosis

Dx: Lidocaine impingement test (= subacromial lidocaine injection relieves pain)

Rx: acromioplasty (= removal of a portion of the acromion), removal of subacromial osteophytes, removal / lysis / débridement of coracoacromial ligament, resection of distal clavicle, removal of acromioclavicular joint osteophytes

Internal Impingement

√ humeral head cysts / defects
√ undersurface degeneration + tearing of posterior supraspinatus and anterior infraspinatus tendons
√ posterosuperior labral tear
√ posterosuperior glenoid chondral lesion + cyst

Anterosuperior Impingement

= intraarticular impingement = pulley lesions (Habermeyer classification)
(1) Group 1 lesion
= isolated superior GHL lesions
(2) Group 2 lesion
= superior GHL lesion + partial articular-side supraspinatus tendon tear
(3) Group 3 lesion
= superior GHL lesion + partial articular-side subscapularis tendon tear
(4) Group 4 lesion
= superior GHL lesions + partial articular-side tears of supraspinatus and subscapularis tendons

Glenohumeral Instability

Glenohumeral stability is dependent on a functional anatomic unit (= anterior capsular mechanism) formed by: glenoid labrum, joint capsule, superior + middle + inferior (anterior + posterior parts) glenohumeral ligaments, coracohumeral ligament, subscapularis tendon, rotator cuff

Age: < 35 years
Frequency: acute, recurrent, fixed
Cause: traumatic, microtraumatic, atraumatic
Direction: anterior > multidirectional > inferior > posterior
Type of lesions: labral abnormalities (compression, avulsion, shearing), capsular / ligamentous tear / avulsion
Associated osseous lesions:
Hill-Sachs defect, glenoid rim fracture, trough line fracture
Associated soft-tissue lesions:
Bankart lesion, GLAD, Perthes, ALPSA, HAGL, labral cyst
◊ Normal clefts may exist within labrum!
False positive for labral separation:
(1) Articular cartilage deep to labrum
(2) Glenohumeral ligaments passing adjacent to labrum

Rotator Cuff Tear

Etiology:
(1) Attritional change ← repetitive microtrauma = overuse of shoulder from professional / athletic activities
(2) Subacromial impingement between humeral head + coracoacromial arch
(3) Tendon degeneration ← hypovascularity ← aging
(4) Acute trauma (rare)

Prevalence in asymptomatic patients:
in 40% of patients > 50 years (full-thickness tear); in > 60% of patients > 60 years (partial & full thickness)
Age: most commonly > 50 years; young athletic patient may have "rim-rent" tear (= avulsion of attachment at greater tuberosity
Location:
Supraspinatus tendon tear:
› "critical zone" of anterior supraspinatus tendon 1 cm medial to attachment (= area of relative hypovascularity)
Infraspinatus tendon tear (30–40%):
› precludes arthroscopic repair
› worst postoperative prognosis
› isolated tear more common in throwing sports
Teres minor tendon tear (rare):
› also affected by posterior instability
Subscapularis tendon tear:
› more common in superior articular surface
› associated with supraspinatus tendon tear + rotator interval lesion + biceps tendon pathology
› cysts of lesser tuberosity + edema (common)
• clinical assessment (during US):
› test of supraspinatus m.
(a) supraspinatus weakness
• straight hanging and 20° abducted arm pushed against applied force = assessment of strength
(b) impingement: 97% sensitive + 67% PPV
• "arc of pain": 98% sensitive + 67% PPV
(c) weakness of abduction: 64% sensitive + 78% PPV
• drop-arm test = active abduction of arm to 90° then slowly lowering arm: if arm drops abruptly test is positive (98% specific, 10% sensitive)
• combination of (a) + (b) + (c) = 98% chance of rotator cuff tear
› test of infraspinatus m. + teres minor m.
(d) weakness of external rotation: 76% sensitive + 79% PPV
• resist inward force with elbow flexed 90° + shoulder internally rotated
› test of subscapularis m.
• passive positioning of arm behind back with palm facing outward: failure to hold forearm + hand off the back = positive test
› patient age
• night pain: 88% sensitive + 70% PPV
Assessment:
(1) Depth of tear
(a) incomplete rupture = **partial-thickness tear** involves either bursal or synovial surface or remains intratendinous
◊ Articular-surface partial-thickness tear >> bursal-surface partial thickness tear
› PASTA = partial thickness articular supraspinatus tendon avulsion (at attachment

of tendon to greater tuberosity = footprint)
› PAINT = partial articular tear with intratendinous extension
√ fluid-filled defect not extending across the entire tendon width
√ disruption of superior / inferior tendon fibers only

(b) complete rupture = **full-thickness tear** from subacromial bursal surface to articular surface of glenohumeral joint
› pure transverse tear
› pure vertical / longitudinal tear
› tear with retraction of tendon edges
› global tear = massive tear / avulsion of cuff involving more than one of the tendons

(2) Size of tear

Depth of partial tear (normal thickness = 12 mm):

(a) small = grade 1 (< 25%) = < 3 mm
(b) medium = grade 2 (25–50%) = 3–6 mm
(c) large = grade 3 (> 50%) = > 6 mm

Greatest dimension of full-thickness tear:

(a) small = < 1 cm
(b) medium = 1–3 cm
(c) large = 3–5 cm
(d) massive = > 5 cm

(3) Geometry of tear (as viewed from tendon surface)
(a) crescentic = minimal retraction of tendon
(b) U-shaped = massive tear that may extend to level of glenoid fossa
(c) L-shaped = massive tear with longitudinal component

(4) Injury extension (to adjacent structures)
(a) in anterior direction: supraspinatus tendon → medial aspect of coracohumeral ligament (rotator interval) → superior subscapularis tendon fibers
(b) in posterior direction: supraspinatus tendon → infraspinatus tendon → teres minor tendon
(c) involvement of long head of biceps brachii tendon
◊ Injury / disruption of LHBB tendon in up to 77%
◊ Subluxation / dislocation in up to 44%

(5) Muscle atrophy (decreased bulk, fatty infiltration) as strongest prognosticator of surgical outcome
◊ Muscle cross-sectional area measurement correlates with muscle strength!
√ on SAG OBL plane at level of medial coracoid process:
√ "tangent" sign = supraspinatus muscle does not cross a line drawn through superior border of scapular spine + superior margin of coracoid process
√ scapular ratio of < 50% = occupation ratio of cross-sectional area of supraspinatus m. to area of supraspinatus fossa

(6) Impingement anatomy

X-ray (AP view):
√ usually normal in acute rotator cuff tear
√ acromiohumeral distance ≤ 2 mm (with active abduction to 90°) ← absence / retraction

of supraspinatus tendon
√ flattened / ill-defined superior soft-tissue contour with heterogeneous decreased density → fatty replacement (on supraspinatus outlet [modified Y] view)

X-ray (late findings):
√ superior migration of humeral head = acromiohumeral distance < 7 mm
√ cuff arthropathy = sclerosis, subchondral cysts, osteolysis, notching / pitting of greater tuberosity ← repetitive contact between humeral head + acromion
√ remodeling of acromial undersurface with matching sclerosis, faceting, concavity of inferolateral aspect of acromion

US (scans in hyperextended position, 75–100% sensitive, 43–97% specific, 65–95% NPV, 55–75% PPV):
Sequence of examination:
biceps, subscapularis, supraspinatus, infraspinatus, teres minor, posterior glenohumeral joint
√ direct primary signs of tendon tear
√ focal absence of rotator cuff= partial thickness:
√ well-defined hypo- / anechoic defect in tendon replaced by fluid → with extension either to bursal /or articular surface
√ abrupt + sharply demarcated focal thinning
√ small comma-shaped area of hyperechogenicity (= small tear filled with granulation tissue / hypertrophied synovium)
√ nonvisualization of retracted tendon in massive supraspinatus tear (most reliable sign):
√ discontinuity of rotator cuff filled with joint fluid
√ defect filled with hypoechoic thickened bursa + peribursal fat
√ "naked tuberosity" sign = retracted tendon leaves a bare area of bone
√ deltoid muscle directly on top of humeral head
√ hypervascularity of defect on color Doppler
√ <u>indirect primary signs of tendon tear</u>
√ "double cortex" / "cartilage interface" sign = 2 hyperechoic lines representing cartilage + cortex ← fluid-enhanced increase in through-transmission
√ compressibility = loss of normal convex contour of peribursal fat ← displacement of fluid with compression by transducer over hypoechoic defect
√ "sagging peribursal fat" sign = depression of hyperechoic peribursal fat into area of torn tendon
√ increased echogenicity + decreased bulk of muscle = muscle atrophy (in 77% of rotator cuff tears)
√ secondary signs of tendon tear:
√ cortical irregularity of greater tuberosity
√ shoulder joint effusion = anechoic fluid in axillary pouch, posterior recess, biceps tendon sheath
False negative: longitudinal tear, partial tear
False positive: intraarticular biceps tendon, soft-tissue calcification, small scar / fibrous tissue

Arthrography (71–100% sensitive, 71–100% specific for combined full + partial thickness

tears):
√ opacification of subacromial-subdeltoid bursa
√ contrast enters substance of rotator cuff tendons
MR (41–100% sensitive and 79–100% specific for combined full + partial thickness tears):
√ discontinuity of cuff with retraction of musculotendinous junction
√ focal / generalized intense / markedly increased SI on T2WI (= fluid within cuff defect) in < 50%
√ fluid within subacromial-subdeltoid bursa (most sensitive)
√ low / moderate SI on T2WI (= severely degenerated tendon, intact bursal / synovial surface, granulation / scar tissue filling the region of torn tendinous fibers)
√ cuff defect with contour irregularity
√ abrupt change in signal character at boundary of lesion
√ supraspinatus muscle atrophy (MOST SPECIFIC)
Pitfalls:
√ hyperintense focus in distal supraspinatus tendon
√ gray signal isointense to muscle on all pulse sequences:
(a) partial volume averaging with superior + lateral infraspinatus tendon
(b) vascular "watershed" area
(c) magic angle effect = orientation of collagen fibers at 55° relative to main magnetic field
√ hyperintense focus within rotator cuff on T2WI:
(a) partial volume averaging with fluid in biceps tendon sheath / subscapularis bursa
(b) partial volume averaging with fat of peribursal fat
(c) motion artifacts: respiration, vascular pulsation, patient movement
√ fatty atrophy of muscle
(a) impingement of axillary / suprascapular nn. = quadrilateral space syndrome

DDx: (1) Partial-thickness tear with diffuse less-than-fluid intensity on T2WI
(2) Tendon degeneration (tendinopathy)
(3) Tendinitis
(4) Full-thickness tear containing granulation tissue

Subacromial-Subdeltoid Bursitis

common finding in rotator cuff tears
√ peribursal fat totally / partially obliterated + replaced by low-signal-intensity tissue on all pulse sequences
√ fluid accumulation within bursa

Supraspinatus Tendinopathy / Tendinosis

= chronic tendon degeneration with disorganized repair
Cause: impingement, acute / chronic stress
Histo: mucinous + myxoid degeneration
√ increase in tendon SI on proton-density images without disruption of tendon
√ tendinous enlargement + inhomogeneous signal pattern

√ fibers on superior + inferior tendon surface remain visible and contiguous
Cx: main risk factor for subsequent rotator cuff tear (not impingement)
DDx: supraspinatus tear (tendon has fluid intensity)

RUBELLA

= CONGENITAL RUBELLA = GERMAN MEASLES
Prevalence: endemic rate of 0.1%
Age: infants (in utero transmission)
• neonatal dwarfism ← intrauterine growth retardation
• retinopathy, cataracts, glaucoma, microphthalmia
• deafness; mental deficiency with encephalitis + microcephaly
• thrombocytopenic purpura, petechiae, anemia; failure to thrive
√ "celery-stalk" sign (50%) = irregular metaphyseal margins + coarsened trabeculae extending longitudinally from epiphysis; distal end of femur > proximal end of tibia, humerus
√ no periosteal reaction
√ hepatosplenomegaly + adenopathy
√ pneumonitis
@ Cardiovascular:
√ congenital heart disease (PDA, VSD)
√ peripheral pulmonary artery stenosis
√ necrosis of myocardium
@ CNS
√ punctate / nodular calcifications
√ porencephalic cysts
√ occasionally microcephaly
Prognosis: osseous manifestations disappear in 1–3 months; severe congenital defects from infection during first trimester
DDx: (1) CMV
(2) Congenital syphilis (diaphysitis + epiphysitis)
(3) Toxoplasmosis

RUBINSTEIN-TAYBI SYNDROME

= BROAD THUMB SYNDROME
= rare sporadic syndrome without known chromosomal / biochemical markers; M÷F = 1÷1
• small stature; mental, motor, language retardation
@ Characteristic facies
• beaked / straight nose ± low nasal septum
• antimongoloid slant of palpebral fissures
• epicanthic folds; broad fleshy nasal bridge
• high-arched palate; dental abnormalities
@ Ophthalmologic findings
• strabismus, ptosis, refractive errors
@ Cutaneous findings
• keloids, hirsutism, simian crease

• flat capillary hemangioma on forehead / neck

@ Musculoskeletal findings
√ short broad "spatulate" terminal phalanges of thumb and great toe ± angulation deformity (MOST CONSISTENT + CHARACTERISTIC FINDING)
√ radial angulation of distal phalanx (50%) caused by trapezoid / delta shape of proximal phalanx
√ tufted "mushroom-shaped" fingers + webbing
√ thin tubular bones of hand + feet
√ club feet
√ retarded skeletal maturation
√ dysplastic ribs
√ spina bifida occulta
√ scoliosis
√ flat acetabular angle + flaring of ilia

@ Genitourinary tract anomalies
√ bilateral renal duplication
√ renal agenesis
√ bifid ureter
√ incomplete / delayed descent of testes

@ Cardiovascular abnormalities
√ atrial septal defect
√ patent ductus arteriosus
√ coarctation of aorta
√ valvular aortic stenosis
√ pulmonic stenosis

OB-US:
√ decreased head circumference
√ small for gestational age

Cx in infancy: obstipation, feeding problems, recurrent upper respiratory infection

SAPHO SYNDROME

= **S**ynovitis, **A**cne, **P**almoplantar pustulosis, **H**yperostosis, **O**steitis
= PUSTULOTIC ARTHROSTEITIS = STERNOCLAVICULAR HYPEROSTOSIS
= association of sterile osteoarticular inflammation with skin abnormalities (palmoplantar pustulosis + severe acne)
◊ Delay of several years can separate osseous from cutaneous lesions! Many patients have endured years of consultations and unnecessary invasive procedures before receiving the correct diagnosis!

Etiology: ? variant of psoriasis, exaggerated immune response in genetically susceptible individuals to Propionibacterium acnes

Age: young to middle-aged adults; M÷F = 1÷1

Histo: osteolytic portion of bone lesion contains plasma cells

• palmoplantar pustulosis (52%) = chronic eruption of yellowish intradermal sterile 2–4 mm monomorphic pustules limited to palms + soles

• acute severe acne (15%) = acne fulminans, acne conglobata, hidradenitis suppurativa → sudden eruption of highly inflammatory tender ulcerative nodules + plaques with hemorrhagic crust on face, back, chest
Organism: Propionibacterium acnes (= anaerobe typically found in acne lesions)
• blood + bone cultures usually negative
• chronic relapsing-remitting course with pain, soft-tissue swelling, limitation of motion at skeletal site of involvement (most often in anterior chest wall) ± fever
± elevated erythrocyte sedimentation rate + C-reactive protein
• rheumatoid factor negative + human leukocyte antigen (HLA)–B27 positive = seronegative spondyloarthropathy
√ bone sclerosis combined with variable degree of osteolysis and periostitis:
√ medullary trabecular changes = osteitis
√ cortical hyperostosis in long-standing disease
√ accompanied by adjacent inflammatory arthritis ± enthesitis + ankylosis
Bone scintigraphy:
√ often reveals asymptomatic skeletal lesions
@ Sternoclavicular joint (70–90%)
Age: adulthood + childhood
Site: manubrium sterni, insertion of costoclavicular ligament, clavicles with mediolateral progression
√ osteolysis at beginning of disease
√ hyperostosis + osteosclerosis later in disease
√ ankylosis of sternoclavicular joint
√ diagnostic costoclavicular enthesopathy + small hyperostotic foci at sternal end of 1st ribs
NUC (bone scintigraphy):
√ "bull's head" sign = increased radiotracer uptake in manubrium + both sternoclavicular joints (HIGHLY SPECIFIC)
@ Axial skeleton (33%)
Age: adulthood
√ homogeneous osteosclerosis / osteolysis of one / more vertebral bodies (usually monovertebral) → collapse
√ disk space narrowing + endplate erosion (mimicking infectious spondylodiskitis)
√ sclerosis + expansion (mimicking Paget disease)
√ asymmetric bulky paravertebral ossification + sacroiliitis (mimicking psoriatic arthritis):
√ paravertebral ossifications (mimicking marginal / nonmarginal syndesmophytes / massive bridging)
√ unilateral sacroiliitis + associated osteosclerosis of adjacent iliac bone
MR:
√ focal / diffuse marrow signal abnormality with enhancement (= edema / osteitis)
√ hyperintense paravertebral soft-tissue swelling
√ endplate irregularities + CHARACTERISTIC anterior vertebral body corner erosion at multiple levels
√ increased disk signal intensity on T2WI
√ disk enhancement after contrast administration
DDx: infectious spondylitis (abscess, epidural involvement, single level of involvement)

@ Appendicular skeleton (30%)
Age: childhood
• chronic recurrent multifocal osteomyelitis (misnomer)
Location: distal femur, proximal tibia, fibula, humerus, radius, ulna, rib
Site: metaphysis
√ osteosclerosis / osteolysis + periosteal new bone formation + bone expansion with aggressive appearance
@ Joints
Location: knee, hip, ankle, DIP of hand
√ synovial inflammation with juxtaarticular osteoporosis (early)
√ joint narrowing, marginal erosion, hyperostosis, enthesopathy (later)
Prognosis: chronic course with unpredictable exacerbations + remissions
Dx: sterile culture of osseous lesion
Rx: nonsteroidal antiinflammatory drugs, corticosteroids, methotrexate, tumor necrosis factor α inhibitor, analgesics, cyclosporine
DDx: infectious osteomyelitis / spondylitis, chronic recurrent multifocal osteomyelitis, osteosarcoma, Ewing sarcoma, metastasis, Paget disease, aseptic necrosis of clavicle

SCLEROSTEOSIS

= autosomal recessive inheritance
Cause: mutation in gene-encoding sclerostin on chromosome 17q12-q21 leading to osteoblast hyperactivity
Age: manifestation in infancy
• early cranial nerve paralysis
• increased intracranial pressure (in 80%)
√ massive square prognathic chin
√ frontal bossing
√ sclerosis of calvaria
@ Hand
√ radial deviation
√ syndactyly
Cx: sudden death ← increase in intracranial pressure ← impaction of brain stem in narrowed foramen
DDx: Van Buchem disease

SCURVY

= BARLOW DISEASE = HYPOVITAMINOSIS C
= vitamin C (= ascorbic acid) deficiency with defective osteogenesis from abnormal osteoblast function

Infantile Scurvy

Age: 6–9 months (maternal vitamin C protects for first 6 months)
Predisposed: feeding with pasteurized / boiled milk
Pathogenesis: abnormal collagen formation

- irritability
- tenderness + weakness of lower limbs
- scorbutic rosary of ribs
- bleeding of gums ← teething
- legs drawn up + widely spread = pseudoparalysis

Location: distal femur (esp. medial side), proximal and distal tibia + fibula, distal radius + ulna, proximal humerus, sternal end of ribs

√ "ground-glass" osteoporosis (CHARACTERISTIC)

√ cortical thinning

√ soft-tissue edema (rare)

@ Metaphysis

√ white line = metaphyseal zone of preparatory calcification (DDx: lead / phosphorus poisoning, bismuth treatment, healing rickets)

√ Trümmerfeld zone = radiolucent zone on shaft side of Fränkel white line (site of subepiphyseal infraction)

√ Pelkan spurs = metaphyseal spurs projecting at right angles to shaft axis
[Karl Francis Pel(i)kan (1890–????), University of California]

√ Park corner sign = subepiphyseal infraction / comminution resulting in mushrooming / cupping of epiphysis (DDx: syphilis, rickets)
[E. Park, 1935, pathologist]

@ Epiphysis

√ Wimberger ring = sclerotic ring around low-density epiphysis ← osteopenia of epiphysis

@ Diaphysis

√ subperiosteal hematoma with calcification of elevated periosteum (sure sign of healing)

@ Teeth

√ cyst formation + hemorrhage in enamel

DDx: TORCH infections, leukemia, neuroblastoma

Adult Scurvy

Frequency: rare

√ hemarthrosis + bleeding at synchondrosis

SEPTIC ARTHRITIS

N.B.: MEDICAL EMERGENCY = treatment necessary within 48 hours to prevent irreversible permanent joint damage!

Risk factors: advanced age, immunocompromised state, rheumatoid arthritis, intraarticular injection, prosthetic joint

Transmission: inoculation ← trauma / recent instrumentation; bacteremia → hematogenous seeding to large joints of shoulder, hip, knee

Organism:

› Staphylococcus aureus (with 31% most common)

› Gonorrhea (multifocal septic arthritis in young adults; indistinguishable from tuberculous

arthritis, but more rapid)
› Brucellar arthritis (indistinguishable from tuberculosis, slow infection)
› Salmonella (commonly associated with sickle cell disease / Gaucher disease)
(a) neonates, infants: group D streptococcus
(b) < 4 years of age: Haemophilus influenzae, Streptococcus pyogenes, S. aureus
(c) > 4 years of age: S. aureus
(d) > 10 years of age: S. aureus, Neisseria gonorrhoeae
(e) adults: S. aureus

Pathophysiology:
(1) lytic enzymes in purulent articular fluid → destruction of articular + epiphyseal cartilages
(2) pus in joint → increased intraarticular pressure → compromised blood flow → osteonecrosis

Age: most commonly encountered in neonates

Location: shoulder, hip, knee, elbow, ankle; multifocal involvement common in the very young

• painful joint, fever

Character of aspirated synovial fluid:
• frankly purulent / turbid fluid
• WBC > 20,000 / mm^3 with > 90% PMNs
• positive result on Gram stain; positive culture for bacteria

√ joint effusion

CT:
√ bone erosions around joint
√ fat-fluid level in the absence of trauma (specific)

MR:
√ intense enhancement of hypertrophied synovium
√ perisynovial edema of adjacent soft tissue
√ subtle bone marrow signal alterations adjacent to articular surface: decreased on T1WI + increased on T2WI + enhancement ← reactive marrow edema (DDx: osteomyelitis with more obvious SI alterations)

Cx: (1) Bone growth disturbance (lengthening, shortening, angulation)
(2) Osteonecrosis = avascular necrosis
(3) Chronic degenerative arthritis
(4) Ankylosis

DDx: (1) Transient synovitis (no MR-signal alterations in subarticular bone marrow)

SHIN SPLINTS

= SHIN SORENESS = MEDIAL TIBIAL STRESS SYNDROME = SOLEUS SYNDROME
= nonspecific term describing exertional lower leg pain

Frequency: 75% of exertional leg pain

Cause: ? atypical stress fracture, traction periostitis, compartment syndrome

• diffuse tenderness along posteromedial tibia in its middle to distal aspect

Location: posterior / posteromedial tibial cortex

Plain radiographs:
√ normal / longitudinal periosteal new bone

Bone scintigraphy:
√ normal radionuclide angiogram + blood-pool phase (DDx to stress fracture)
√ linear longitudinal uptake on delayed images
MR:
√ marrow edema / hemorrhage
√ periosteal fluid

SHORT-RIB POLYDACTYLY SYNDROME

= group of autosomal recessive disorders characterized by short limb dysplasia, constricted thorax, postaxial polydactyly (on ulnar / fibular side)

Type I = SALDINO-NOONAN SYNDROME
Type II = MAJEWSKI TYPE
Type III = NAUMOFF TYPE
Type IV = BEEMER

√ severe micromelia
√ pointed femurs at both ends (type I); widened metaphyses (type III)
√ narrow thorax
√ extremely short horizontally oriented ribs
√ distorted underossified vertebral bodies + incomplete coronal clefts
√ polydactyly
√ cleft lip / palate

Prognosis: uniformly lethal

SICKLE CELL DISEASE

= common inherited autosomal recessive hemoglobinopathy with 2 abnormal β-globin genes (homozygous / heterozygous in combination with other abnormal hemoglobins) characterized by sickle-shaped RBCs cleared by RES

Normal adult hemoglobin:

Hb A = 2 α globin chains on chromosome 16p13.3 (duplicated on each chromosome = 4 gene loci) + 2 β globin chains on chromosome 11p15.5 (one copy on each chromosome = 2 gene loci)
- makes up 96–98% of hemoglobin component

Genetics: mutation in both alleles of β-globulin gene

Hb S = DNA point mutation at the 6th codon in β-globin gene located on short arm of chromosome 11 → glutamic acid in position 6 on β-chain is substituted with valine (α2βS2)

Hb C = DNA point mutation substitutes glutamic acid in position 6 on β-chain with lysine (α2βC2)

Definition:

Sickle cell anemia = any formation of Hb S in combination with one other abnormal hemoglobin:

(a) <u>homozygous</u> (with another sickle cell chain Hb S)
1. Hb SS = sickle cell disease

(b) <u>heterozygous</u> (with other abnormal chain, not Hb S)

2. Hb SC disease
3. Hb S-thal

- lessens the severity of infection with falciparum malaria

Prevalence: 8–13% of African Americans carry sickling factor (gene for Hb S); 1÷600 African Americans in USA are homozygous (Hb SS) and have sickle cell disease; 1÷40 with sickling trait will manifest sickle cell disease; 1÷120 with sickling trait will manifest Hb SC disease; affects people from Middle East + eastern Mediterranean region

Pathogenesis:

low oxygen tension → deoxygenation of Hb S → aggregation of abnormal Hb molecules into long chains (= polymerization into twisted ropelike Hb molecule strands with binding between chains) →

(a) increase in blood viscosity with stasis in microvasculature ("log jam" occlusion of small blood vessels) → tissue ischemia → infarction, necrosis, superinfection

(b) altered plasticity + distortion of RBCs into sickle shape → intravascular hemolysis → endothelial injury → coagulopathy + vasomotor in stability + proliferative vasculopathy → pulmonary hypertension

Location: damage of intima occurs most frequently in vessels with high flow rates (terminal ICA); sickling occurs in areas of

(a) slow flow (spleen, liver, renal medulla)
(b) rapid metabolism (brain, muscle, placenta)

- Vaso-occlusion (earliest + most common manifestation):
  - stroke; retinal hemorrhages; sensorineural hearing loss
  - abdominal crisis; chronic leg ulcers (over bony prominences)
  - priapism; rheumatism-like joint pain
  - bone pain (vasoocclusive crisis÷osteomyelitis = 50÷1)
  - functional asplenia ← splenic autoinfarction
- Chronic normocytic hemolytic anemia (= intravascular hemolysis of sickled RBCs + reduction in sickled RBC life span to 1/10 its normal duration by sequestration in spleen)
  - increased cardiac output + high blood flow velocity
  - jaundice; splenomegaly (in children + infants)
- Infection (↑ susceptibility to encapsulated bacteria like Haemophilus influenzae type b, Streptococcus pneumoniae, Streptococcus group b, Neisseria meningitides, Klebsiella, Salmonella): osteomyelitis; cellulitis

Cx: high incidence of infections (lung, bone, brain)

Prognosis: death < 40 years (decrease of average life expectancy by 25–30 years)

Osseous Manifestation of Sickle Cell Disease

(1) DEOSSIFICATION DUE TO MARROW HYPERPLASIA

Cause: chronic anemia → constant marrow stimulation and medullary expansion → trabecular thickening + cortical thinning → bone softening → pathologic fractures

Pathogenesis: arrested conversion of red to yellow marrow → persistence of appendicular red marrow in ankles + wrists + shafts of long bones

√ granular appearance of skull ← porous decrease in bone density of skull (25%)
√ widening of diploe with thinning of inner and outer tables (22%)

√ vertical hair-on-end striations projecting from outer skull vault (5%) ← prominent trabeculae + new bone
√ coarse trabeculae of mandible
√ osteopenia with thinning of trabeculae
√ biconcave "fish-mouth" vertebrae = compression fracture of vertebral endplates ← invagination of intervertebral disks ← bone softening (in 70%)
Cx: kyphosis from vertebral collapse
√ widening of medullary space + thinning of cortices
Cx: pathologic fracture
√ coarsening of trabecular pattern in long + flat bones
√ rib notching

(2) EXTRAMEDULLARY HEMATOPOIESIS more common in other hemolytic anemias
Location: liver, spleen, paravertebral region, kidney, adrenal gland, skin, paranasal sinus
√ intermediate signal intensities on T1WI + T2WI
√ uptake by ^{99m}Tc-sulfur colloid

(3) THROMBOSIS AND INFARCTION OF BONE
Cause: abnormal RBCs → vaso-occlusive disease
(a) bone infarcts + avascular necrosis within epiphyses and medullary cavities
(b) infarcts of muscles + soft tissue → myonecrosis and ulcers
Location: in diaphysis of small tubular bones (children); in metaphysis + subchondrium of long bones (adults)
√ sickle cell dactylitis = hand-foot syndrome (in 50%):
Age: 6 months – 2 years; rare > 6 years ← regression of red marrow
Cause: cold-induced vasoconstriction
• tender swollen hand / foot with reduction in movement; fever
√ patchy areas of lucency + periosteal reaction
√ ± bone destruction → deformity
√ osteolysis (in ACUTE infarction)
√ bone sclerosis (= dystrophic medullary calcification) in pelvis, ribs, spine
√ bone-within-bone appearance = periosteal reaction / layered new bone deposits along inner surface of infarcted cortex
√ juxtacortical sclerosis
√ Lincoln log = Reynold sign = H-vertebrae = steplike endplate depression
√ articular disintegration
√ epiphyseal infarction (in 50% by age 35 years)
= avascular necrosis = frequently bilateral collapse of femoral head (DDx: Legg-Calvé-Perthes disease)
• joint pain + limited movement

NUC (bone agent):
√ decreased / normal radiotracer uptake (first few days)
√ increased uptake (with revascularization)
√ return to normal (after a few months in old infarcts with adequate blood supply)
√ photopenic foci (in avascular bone of old infarcts)

MR:
√ high signal intensity of bone marrow edema on STIR

√ "serpiginous double line" sign on T2WI = hyperintense inner border (← inflammatory response with granulation tissue) + hypointense periphery (← reactive bone interface)
√ heterogeneous rimlike enhancement
√ ± subperiosteal hemorrhage + fluid collection

(4) SECONDARY OSTEOMYELITIS (18%)

Pathogenesis: hyposplenism → impaired phagocytosis, complement dysfunction → increased susceptibility to osteomyelitis + septic arthritis

Organism: Salmonella in unusual frequency (S. typhimurium, S. enteritidis, S. choleraesuis, S. paratyphi B) > Staphylococcus aureus (10%) > gram-negative enteric bacilli

Location: long bones (mostly), vertebrae

• positive blood culture (50%)

(5) GROWTH EFFECTS ← diminished blood supply

Location: particularly in metacarpus / phalanx

√ bone shortening = premature fusion of infarcted physis
√ epiphyseal deformity with cupped metaphysis
√ tibiotalar slant
√ protrusio acetabuli (20%)
√ cup / peg-in-hole defect of distal femur
√ diminution in vertebral height (shortening of stature + kyphoscoliosis)
√ H-shaped vertebra with central growth plate infarction
√ tower vertebrae = compensatory lengthening of vertebrae adjacent to H-shaped vertebra

Bone marrow scintigraphy:

√ usually symmetric marked expansion of hematopoietic marrow beyond age 20 involving entire femur, calvarium, small bones of hand + feet (normally only in axial skeleton + proximal femur and humerus)
√ bone marrow defects indicative of acute / old infarction

^{99m}Tc-diphosphonate scan:

√ increased overall skeletal uptake (high bone-to-soft tissue ratio)
√ prominent activities at knees, ankles, proximal humerus (delayed epiphyseal closure / increased blood flow to bone marrow)
√ bone marrow expansion (calvarial thickening with relative decrease in activity along falx insertion)
√ decreased / normal uptake on bone scan within 24 hr in acute infarction / posthealing phase following infarction (cyst formation)
√ increased uptake on bone scan after 2–10 days persistent for several weeks in healing infarction
√ increased uptake on bone scan within 24–48 hours in osteomyelitis
√ increased blood-pool activity + normal delayed image on bone scan in cellulitis
√ renal enlargement with marked retention of tracer in renal parenchyma (medullary ischemia + failure of countercurrent system) in 50%
√ persistent splenic uptake ← degeneration, atrophy, fibrosis, calcifications

CNS Manifestations of Sickle Cell Disease

Pathophysiology:

chronic anemia produces cerebral hyperemia, hypervolemia, impaired autoregulation

(a) cerebral blood flow cannot be increased leading to infarction in time of crisis

(b) increased cerebral blood flow → produces epithelial hyperplasia of large intracranial vessels (terminal ICA / proximal MCA) resulting in thrombus formation

• stroke (5–17%): ischemic infarction (70%), ischemia of deep white matter (25%), hemorrhage (20%), embolic infarct

√ arterial tortuosity (= adaptive response to chronic anemia):

√ ectasia of arterial segment

√ abnormal increase in length of an arterial segment → obvious bowing of an arterial segment

Angio (in 87% abnormal):

√ arterial stenosis / occlusion of supraclinoid portion of ICA + proximal segments of ACA and MCA

√ moyamoya syndrome (35%)

√ distal branch occlusion ← thrombosis / embolism

√ aneurysm (rare)

CT:

√ cerebral infarction (mean age of 7.7 years)

√ subarachnoid hemorrhage (mean age of 27 years)

Splenic Manifestations of Sickle Cell Disease

√ splenomegaly < age 10 (in patients with heterozygous sickle cell disease)

Cx: splenic rupture

√ splenic infarction

√ hemosiderosis

Functional Asplenia

= anatomically present nonfunctional spleen

• Howell-Jolly bodies, siderocytes, anisocytosis, irreversibly sickled cells

√ normal-sized / enlarged spleen on CT

√ absence of tracer uptake on sulfur colloid scan

Autosplenectomy

= autoinfarction of spleen in homozygous sickle cell disease (function lost by age 5)

Histo: extensive perivascular fibrosis with deposition of hemosiderin + calcium

√ small (as small as 5–10 mm) densely calcified spleen

Acute Splenic Sequestration Crisis

= sudden trapping of large amount of blood in spleen

Cause: obstruction of small intrasplenic veins / sinusoids; unknown trigger event

Age: (a) homozygous: infancy / childhood

(b) heterozygous: any age

• LUQ pain ← sudden massive splenic enlargement

• rapid drop in hemoglobin, hematocrit, platelets ← spleen traps large volumes of blood
• rise in reticulocytes
√ enlarged spleen
√ multiple lesions at periphery of spleen: hypoechoic by US, of low attenuation by CT
√ hyperdense areas ← acute hemorrhage
√ hyperintense areas on T1WI + T2WI ← subacute hemorrhage
√ main splenic vessels patent by Doppler US
Prognosis: in 50% death < 2 years of age ← hypovolemic shock

Other Manifestations of Sickle Cell Disease

@ Chest
√ cardiomegaly + CHF
@ Gallbladder
√ cholelithiasis
@ Kidney
• hematuria ← multiple infarctions
• hyposthenuria
• nephrotic syndrome
• renal tubular acidosis (distal)
• hyperuricemia ← increased cell turnover
• progressive renal insufficiency
√ normal urogram (70%)
√ papillary necrosis (20%)
√ focal renal scarring (20%)
√ smooth large kidney (4%)
US:
√ increased cortical echogenicity ← glomerular hypertrophy + interstitial fibrosis
√ increased medullary echogenicity ← vascular congestion (in older child)
MR:
√ decreased cortical signal on T2-weighted images ← renal cortical iron deposition
@ **Fat embolism syndrome**
= rare potentially lethal complication of sickle cell disease with diagnosis based on clinical manifestations
Cause: bone marrow infarcts + necrosis → embolization of fat to multiple organs
Pathomechanism:
bone marrow necrosis → fat globules enter venous channels + circulation → R-to-L shunt / traversing pulmonary capillary bed → systemic fat emboli
(a) occlusion of end-organ capillaries → local ischemia + inflammation → release of vasoactive amines
(b) hydrolysis of free fatty acids → toxic intermediates → damage of capillary endothelium
Primary criteria:
• cutaneous petechiae (= microscopic hemorrhagic infarcts) ← vessel wall rupture from embolus / extravasation of blood surrounding area of necrosis
• progressive respiratory distress: dyspnea, severe hypoxemia, ARDS

- cerebral involvement: altered level of consciousness, seizures, focal neurologic deficits, coma

Secondary criteria:

- tachycardia
- fever
- anemia + thrombocytopenia

CT: typically negative

MR:

Location: diffuse widespread + unusual sites (splenium, internal capsule)

√ starfield pattern = innumerable bright punctate foci on DWI

√ numerous "blooming" black dots of susceptibility artifacts on T2* (= microhemorrhages)

√ diffuse hyperintense foci on FLAIR + T2WI ← edema

Sickle Cell Trait= Sickling Trait

= mild disease with few episodes of crisis + infection; sickling provoked only under extreme stress (unpressurized aircraft, anoxia with CHD, prolonged anesthesia, marathon running)

Prevalence: 8–10% of American Blacks

Composition: Hb AS formation (55% Hb A + 45% Hb S)

- asymptomatic; recurrent gross hematuria
- may have normal laboratory tests = NO anemia

√ splenic infarction

SC Disease

Prevalence: 3% of American Blacks (more common but less severe form than sickle cell disease)

- less frequent + less severe symptoms of sickle cell disease
- occasionally normal Hb levels
- retinal hemorrhages
- gross hematuria ← multiple infarctions

√ aseptic necrosis of femoral head

Rx: similar to sickle cell disease

Sickle-Thal Disease = β-Thalassemia (rare)

[*thalassa*, Greek = sea]

= underproduction of the β chain ← mutations in the HBB gene on chromosome 11

Composition: Hb SA (65–90% Hb S + 5–25% Hb A + elevated Hb A_2 and Hb F)

- clinically resembling Hb SS patients
- anemia (no normal adult hemoglobin)

√ persistent splenomegaly

SINDING-LARSEN-JOHANSSON DISEASE

[Christian Magnus Falsen Sinding-Larsen (1866–1930), director of Rikshospitalet in Kristiania (now Oslo), Norway]

[Sven Christian Johansson (1880–1959), surgeon and head physician in Gothenburg, Sweden]

= osteochondrosis of inferior pole of patella, often bilateral (NOT osteonecrosis / epiphysitis / osteochondritis)
Cause: traction tendinitis / traumatic avulsion of bone; repeated subluxation ± dislocation of patella
Mechanism: forceful contraction of quadriceps against resistence
Age: adolescents (often 10–14 years)
Predisposed: cerebrospastic children
• tenderness + soft-tissue swelling over lower pole of patella
√ peripatellar soft-tissue swelling
√ calcification / ossification of patellar tendon
√ patella alta deformity = abnormally elevated position of patella with respect to femur (LAT view)
√ small bone fragments at lower pole of patella (LAT view)
MR:
√ hypointense area on T1WI + hyperintense on T2WI in inferior pole of patella + proximal portion of patellar tendon + surrounding soft tissues
DDx:
1. Jumper's knee
= pain syndrome involving proximal / distal insertion of patellar tendon, commonly seen in young athletes
Cause: chronic stress + inflammation
√ thickening of patellar tendon without tear / avulsion
2. Patellar sleeve avulsion
= cartilage of inferior patellar pole pulled off patella often in combination with small avulsed bone fragment (= cartilaginous injury)
Mechanism: vigorous contraction of quadriceps applied to flexed knee
Age: 8–12 years (unique to pediatric population)
√ small bone fragment inferior to lower pole of patella
√ patella alta
√ joint effusion
√ bone marrow edema of patella (MRI!)

SMALLPOX

5% of infants
Location: elbow bilateral; metaphysis of long bones
√ rapid bone destruction spreading along shaft
√ periosteal reaction
√ endosteal + cortical sclerosis frequent
√ premature epiphyseal fusion with severe deformity
√ ankylosis is frequent

SOFT-TISSUE CHONDROMA

= EXTRASKELETAL CHONDROMA = CHONDROMA OF SOFT PARTS
= rare benign cartilage-forming tumor in extraarticular soft tissue consisting of small nodule of

cartilage without connection to underlying bone

Origin: ? embryonal remnants in areas of preexistent fetal cartilage / pluripotential mesenchyme; not from mature cartilaginous / osseous tissue

Frequency: 1.5% of all benign soft-tissue tumors

Age: 30–60 (range, 1–85) years; M÷F = 1.2÷1

Histo: lobules of adult-type hyaline cartilage with areas of calcification + ossification; myxoid change; regions of increased cellularity + cytologic atypia

- asymptomatic (usually), slow-growing soft-tissue mass
- occasionally pain + tenderness

Location: hand (54–80%) + foot (20–28%); head & neck (rare): tongue, auricle, cheek, parotid gland, parapharyngeal space, masticator space

√ lobulated well-defined extraskeletal mass < 2 cm in size

√ may contain calcifications (33–70%) with ringlike appearance / ossifications

√ scalloping of adjacent bone with sclerotic reaction

CT:

√ circumscribed heterogeneously enhancing mass

√ typically punctate / curvilinear / ringlike chondroid calcifications (in 33–70%)

US:

√ well-defined heterogeneously hypoechoic mass

√ salient vascularity in subungual area

MR:

√ multilobulated mass of high signal intensity on T2WI

√ low to intermediate SI relative to muscle on T1WI

√ conspicuous peripheral / septal contrast enhancement

Rx: local excision

Prognosis: 15–25% recurrence rate

DDx: (1) Extraskeletal myxoid chondrosarcoma (deep-seated in large muscles of upper + lower extremities, pelvic + shoulder girdles)

(2) Periosteal chondroma

Periosteal (Juxtacortical) Chondroma

= benign hyaline cartilage tumor akin to enchondroma

Origin: deep layer of periosteum

Location: metaphyseal surface of long bones

√ radiolucent lesion with variable degrees of chondroid matrix calcifications

√ cortical excavation of tissue forming shallow shelving depression = **saucerization** ← local periosteal destruction by tumor + surrounding periosteal reaction

√ well-formed periosteal reaction

MR:

√ round mass with hyperintense T2 signal ← high water content of chondroid matrix

√ adjacent marrow edema (uncommon)

DDx: periosteal chondrosarcoma (size usually > 4 cm); periosteal osteosarcoma

SOFT-TISSUE OSTEOMA

= OSTEOMA OF SOFT PARTS (extremely rare)

Histo: mature lamellar bone with well-defined haversian system; bone marrow, myxoid, vascular, fibrous connective tissue between bone trabeculae; collagenous capsule blending into benign hyaline cartilage

Location: head (usually posterior part of tongue), thigh

√ ossified mass

NUC:

√ intense tracer accumulation, greater than adjacent bone

SOLITARY BONE CYST

= UNICAMERAL / SIMPLE BONE CYST

Frequency: up to 5% of primary bone lesions

Etiology: ? trauma (synovial entrapment at capsular reflection), ? vascular anomaly (blockage of interstitial drainage)

Histo: cyst filled with clear yellowish fluid often under pressure, wall lined with fibrous tissue + hemosiderin, giant cells may be present

Age: 3–19 years (80%); occurs during active phase of bone growth; M÷F = 3÷1

• asymptomatic, unless fractured

Location: proximal femur + proximal humerus (60–75%); fibula; at base of calcaneal neck (4%, > 12 years of age); talus; rare in ribs, ilium, small bones of hand + feet; NOT in spine / calvarium; solitary lesion

Site: intramedullary centric metaphyseal, adjacent to epiphyseal cartilage (during active phase) / migrating into diaphysis with growth (during latent phase), does not cross epiphyseal plate

√ 2–3 cm oval radiolucency with long axis parallel to long axis of host bone

√ fine sclerotic boundary

√ scalloping + erosion of internal aspect of underlying cortex

√ photopenic area on bone scan (if not fractured)

√ "fallen fragment" sign if fractured (20%) = centrally dislodged fragment falls into a dependent position

Prognosis: mostly spontaneous regression

Cx: pathologic fracture (65%)

DDx: (1) Enchondroma (calcific stipplings)
(2) Fibrous dysplasia (more irregular lucency)
(3) Eosinophilic granuloma
(4) Chondroblastoma (epiphyseal)
(5) Chondromyxoid fibroma (more eccentric + expansile)
(6) Giant cell tumor
(7) Aneurysmal bone cyst (eccentric)
(8) Hemorrhagic cyst
(9) Brown tumor

SOLITARY FIBROUS TUMOR

= mesenchymal tumor of fibroblastic / myofibroblastic origin and intermediate malignant potential
◊ Clinical behavior + histopathologic features are similar to hemangiopericytoma
◊ Most solitary fibrous tumors are benign!
Histo: patternless architecture characterized by alternating hypo- and hypercellular areas separated by thick bands of hyalinized collagen and branching vessels
Age: middle-aged adults
Location: anywhere; extrapleural > pleural site
@ head & neck: nasal cavity, paranasal sinus, nasopharynx, parapharyngeal space, larynx
@ meninges
May be associated with: hypoglycemia (← overproduction of insulinlike growth factor), arthralgia, osteoarthropathy, digital clubbing
• slow-growing mass ± local mass effect
CT:
√ solitary well-circumscribed lobulated mass
√ soft-tissue attenuation
√ intense contrast enhancement
√ heterogeneous texture if large ← hemorrhage, necrosis, cysts
MR:
√ well-circumscribed solid mass
√ low to intermediate SI on T1WI + T2WI
√ heterogeneously high SI on T2WI ← myxoid / cystic degeneration
√ low signal-intensity rim around lesion (= pseudocapsule) on T2WI
√ hypervascularity with prominent enhancement + flow voids
DDx: hemangiopericytoma (overlapping histology)

SPONDYLOEPIPHYSEAL DYSPLASIA

Spondyloepiphyseal Dysplasia Congenita

Autosomal dominant / sporadic (most)
• disproportionate dwarfism with spine + hips more involved than extremities
• waddling gait + muscular weakness
• flat facies; short neck; deafness
√ cleft palate
@ Axial skeleton
√ ovoid vertebral bodies + severe platyspondyly (incomplete fusion of ossification centers + flattening of vertebral bodies)
√ hypoplasia of odontoid process (Cx: cervical myelopathy)
√ progressive kyphoscoliosis (short trunk) involving thoracic + lumbar spine
√ narrowing of disk spaces → short trunk
√ broad iliac bases + deficient ossification of pubis
√ flat acetabular roof
@ Chest
√ bell-shaped thorax

√ pectus carinatum

@ Extremities

√ normal / slightly shortened limbs

√ severe coxa vara + genu valgum

√ multiple accessory epiphyses in hands + feet

√ talipes equinovarus

Cx: (1) Retinal detachment, myopia (50%)

(2) Secondary arthritis in weight-bearing joints

Spondyloepiphyseal Dysplasia Tarda

= sex-linked recessive form with milder manifestation + later clinical onset

Age: apparent by 10 years; exclusive to males

√ hyperostotic new bone along posterior ²/₃ of vertebral end plate (PATHOGNOMONIC)

√ platyspondyly with depression of anterior ⅓ of vertebral body

√ narrowing with calcification of disk spaces + spondylitic bridging

√ short trunk

√ dysplastic joints (eg, flattened femoral heads)

√ premature osteoarthritis

DDx: Ochronosis

SPRENGEL DEFORMITY

[Otto Gerhard Karl Sprengel (1852–1915), president of the Surgical Society of Germany and medical privy counsellor of Braunschweig]

= failure of descent of scapula ← fibrous / osseous omovertebral connection

Associated with: Klippel-Feil syndrome, renal anomalies

• webbed neck; shoulder immobility

√ elevation + medial rotation of scapula

SUBUNGUAL EXOSTOSIS

= DUPUYTREN EXOSTOSIS

= uncommon solitary benign bone lesion arising from distal phalanx beneath the nail producing a bony stalk under a fibrocartilaginous cap

Cause: repetitive trauma (14–25%); ? infection

Age: 2nd–3rd decade (range, 7–58 years); M÷F = 1÷2

Histo: inflammatory growth of proliferating fibroblasts and cartilage undergoing enchondral ossification at the base

Location: toes (86–90%, big toe in 77–80%), thumb + index finger (10–14%, dominant hand in 75%)

Site: dorsal / dorsomedial aspect of distal phalanx under / adjacent to nail bed

• rapidly growing mass ± pain + overlying skin ulceration

√ radiographic appearance similar to osteochondroma:

√ broad sessile / narrow pedunculated base of bone spur

√ indistinct / well-demarcated cartilage cap larger than base

√ NO continuity to cortex / medulla of host bone (DDx to osteochondroma)

√ ossific mass with trabecular bony overgrowth distal to physeal scar: ± defined cortex
US:
√ heterogeneously hyperechoic lesion
√ well-defined margins + calcifications
√ hypoechoic fibrocartilaginous cap of < 20 mm in diameter
√ no / mild vascularity
MR:
√ subungual exostosis hypointense on all sequences
Rx: complete surgical excision
Prognosis: 11–53% recurrence rate
DDx: osteochondroma (exostosis continuous with cortex and medulla of host bone, hyaline cartilage of high SI on T2WI)

SUPERFICIAL FIBROMATOSES

= benign disease with somewhat aggressive biologic behavior between that of fibrous proliferation and fibrosarcoma arising from fascia or aponeurosis
Histo: spindle-shaped myofibroplastic cells in dense deposits of intercellular collagen fibers with variable amounts of extracellular myxoid matrix + compressed elongated vessels

Infantile Digital Fibromatosis

= INCLUSION BODY FIBROMATOSIS = REYE TUMOR = INFANTILE DIGITAL FIBROMA / MYOFIBROMATOSIS / MYOFIBROBLASTOMA / FIBROMATOSIS = INFANTILE DERMAL FIBROMATOSIS /FIBROMA = DIGITAL FIBROUS TUMOR OF INFANCY AND CHILDHOOD
= single / multiple nodular dermal protrusion of fibrous tissue on extensor surface of digits
Age: 1st year of life (80%); 33% congenital; M < F
Histo: intracytoplasmic perinuclear inclusion bodies
Location: fingers (60%), toes (40%)
Site: lateral aspect of distal / middle phalanx
√ nonspecific soft-tissue mass involving a digit
√ infrequently bone involvement
Prognosis: spontaneous regression (in 8%); 60% recurrence rate after excision

Juvenile Aponeurotic Fibroma

= CALCIFYING APONEUROTIC FIBROMA
= rare locally aggressive benign fibrous tumor in childhood
Prevalence: 0.4% of all benign soft-tissue tumors
Histo: cellular dense fibrous tissue with focal often calcified chondral elements infiltrating adjacent structures (= cartilaginous tumor)
Peak age: 8–14 years; M÷F = 2÷1
• slow-growing asymptomatic soft-tissue mass
Location: palm of hand (67–75%); sole of foot; neck, thigh, forearm, popliteal fossa, lumbosacral region
Site: deep volar (palmar) fascia + tendon + aponeurosis
√ nonspecific soft-tissue mass overlying inflamed bursa (often mistaken for calcified bursitis)

√ stippled calcifications (frequent)
√ interosseous soft-tissue mass of forearm + wrist
√ erosion / scalloping of bone may occur
Prognosis: recurrence rate of > 50% after resection
Dx: biopsy (to differentiate from synovial sarcoma)
DDx: synovial sarcoma (commonly calcifies, bone erosion), chondroma, fibrosarcoma, osteosarcoma, myositis ossificans

Palmar Fibromatosis

= DUPUYTREN DISEASE / CONTRACTURE
◊ Most common type of superficial fibromatosis
Prevalence: 1–2%
Ethnicity: Caucasians esp. of Northern European ancestry; northern Scotland, Iceland, Norway, Australia
Age: > 65 years(in 20%); M÷F = 4÷1
Path: < 1 cm small often coalescent nodules attached to palmar aponeurosis and adherent to overlying skin; 2–10 mm in diameter, 10–55 mm in length; terminate in branching configuration at level of distal metacarpals
Histo: uniform fibromyoblastic proliferation of spindle-shaped cells with variably prominent vascularity
Associated with: plantar fibromatosis (5–20%), Peyronie disease, knuckle pads; diabetes (20%), epilepsy, alcoholism, keloids
• painless subcutaneous nodules on palmar surface of distal crease of hand progressing to cords and bands causing skin puckering / dimpling
• flexion contractures of digits ← fibrous attachment to flexor tendons
Location: 4th + 5th (most commonly) > 2nd + 3rd digit; bilateral in 40–60%
Site: volar aponeurosis = flexor tendons
√ hypervascular hypoechoic nodules
√ nodular thickening iso- to hyperattenuating to muscle
(a) early stage hypercellular mitotically active lesion → higher rate of recurrence after local excision
√ high to intermediate signal intensity on T2WI
(b) mature lesion with high collagen content
√ low signal intensity on T2WI
Rx: surgical excision (of mature lesion)
Prognosis: 70% recurrence rate for early stage disease

Plantar Fibromatosis

= PLANTAR FASCIITIS = LEDDERHOSE DISEASE
Prevalence: 0.23%
Cause: trauma; likely multifactorial
Age: 30–50 years; < 30 years (44%); M÷F = 2÷1
Path: abnormal fibrous tissue replacing the plantar aponeurosis and infiltrating subcutaneous tissue + skin
Histo: nonencapsulated proliferation of fibroblasts separated by variable amounts of

collagen

At risk: runners, obese patients

Associated with: Dupuytren contracture (10–65%), knuckle pads (42%), Peyronie disease; diabetes, epilepsy, keloids, alcoholism

- heel pain (one of the most common causes)
- one / multiple firm fixed subcutaneous nodules

Location: proximal / central portion of plantar aponeurosis; bilateral in 20–50%, typically metachronous with a 2–7-year interval

Site: middle to medial aspect of plantar arch; may involve skin + deep structures of the foot

√ hypervascular (92%) hypoechoic / mixed echogenic nodules in subcutaneous tissues superficial to often thickened plantar aponeurosis, medially (60%) / centrally (40%)

√ calcaneal spur

MR:

√ single or multiple nodules / poorly defined infiltrative heterogeneous (92%) mass iso- / hypointense compared to plantar muscles on T1WI + T2WI

√ marked contrast enhancement in 64%

√ ± subcutaneous edema

Rx: local excision with wide margins (for painful or disabling lesion); intralesional steroid injection; postoperative radiation therapy

SYNOVIAL CYST

◊ Often used interchangeably with ganglion (lined by flat spindle cells)

Histo: lined by synovial cells

Cause: herniation of synovial membrane through joint capsule

DDx: fluid distention of paraarticular bursa, synovial cyst (differentiation from ganglion cyst radiologically not possible)

Popliteal Cyst

= BAKER CYST

[William Morrant Baker (1839–1896), surgeon and governor at St. Bartholomew's Hospital, London]

= synovial cyst in the posterior aspect of knee joint communicating with posterior joint capsule

Prevalence: 19% in general orthopedic patients; 61% in patients with rheumatoid arthritis

Pathophysiology:

formed by escape of synovial effusion into one of the bursae; fluid trapped by one-way valvular mechanism

(a) Bunsen-type valve = expanding cyst compresses the communicating channel

(b) ball-type valve = ball composed of fibrin + cellular debris plugs the communication channel

Etiology:

(1) Arthritis: degenerative, rheumatoid, pyogenic

(2) Internal derangement: meniscal / anterior cruciate ligament tears

(3) Pigmented villonodular synovitis

- pseudothrombophlebitis syndrome (= pain + swelling in calf)
- cellulitis (after leakage / rupture)

Location:

(a) gastrocnemius-semimembranosus bursa = posterior to gastrocnemius muscle at level of medial condyle

(b) supralateral bursa = between lateral head of gastrocnemius muscle + distal end of biceps muscle superior to lateral condyle (uncommon)

(c) popliteal bursa = beneath lateral meniscus + anterior to popliteal muscle (uncommon)

√ communication with bursa (documented on arthrogram)

√ well-outlined hypointense collection on T1WI + hyperintense on T2WI

√ septa in 50%

Types:

1. Intact cyst
   - √ smooth contour
2. Dissected cyst
   - √ smooth contour extending along fascial planes (usually between gastrocnemius + soleus)
3. Ruptured cyst
   - √ leakage into calf tissues

DDx of other synovial cysts about the knee:

(1) Meniscal cyst (at lateral / medial side of joint line; associated with horizontal cleavage tears)

(2) Tibiofibular cyst (at proximal tibiofibular joint, which communicates with knee joint in 10%)

(3) Cruciate cyst (surrounding anterior / posterior cruciate ligaments following ligamentous injury)

SYNOVIAL OSTEOCHONDROMATOSIS

= SYNOVIAL CHONDROMATOSIS = JOINT CHONDROMA

Primary Synovial Osteochondromatosis

= benign self-limiting monoarticular disorder characterized by proliferation + metaplastic transformation of synovium with formation of multiple intrasynovial cartilaginous / osteocartilaginous nodules with tendency for detachment and migration within joint space

Cause: hyperplastic synovium with cartilage metaplasia (foci < 2–3 cm); loose body may remain free floating / form conglomerate with other loose bodies into large mass / reattach to synovium with either reabsorption or continued growth

Histo: foci of hyaline cartilage with mineralized chondroid matrix beneath synovial surface + within subsynovial connective tissue; hypercellularity + nuclear atypia may be confused with malignancy

Composition of cartilaginous bodies:

cartilage alone / cartilage + bone / mature bone + fatty bone marrow

Age: 3rd–5th decade; M÷F = 2÷1 – 4÷1

Phase:

(a) early phase = synovial proliferation → formation of intrasynovial cartilaginous

nodules
(b) late phase = inactive synovial disease with persistent nodules that may break off into joint cavity

- slow-growing soft-tissue mass within joint
- progressive joint pain for several years
- limitation of motion / locking ± hemorrhagic joint effusion

Location: knee (most common in > 50%, in 10% bilateral) elbow > hip > shoulder > ankle > wrist; usually monoarticular, occasionally bilateral

Sites: joint / tendon sheath / ganglion / bursa / periarticular

√ pathognomonic multiple calcified / ossified loose bodies in a single joint (bony shell of remodeled lamellar bone is rare) in a rings-and-arcs morphology

√ varying degrees of bone mineralization (25–30% of chondromas show no radiopacity)

√ characteristically uniform size of nodules that may vary between a few mm and several cm

√ marginal pressure erosion of adjacent bone in joints with tight capsule (eg, hip)

√ widening of joint space (from accumulation of loose bodies)

√ joint effusion uncommon

√ NO osteoporosis

CT:

√ multiple calcified / ossified intraarticular bodies

√ intraarticular soft-tissue mass of near-water attenuation containing multiple small calcifications

MR:

√ homogeneous lobulated intraarticular mass isointense to muscle on T1WI + hyperintense to muscle on T2WI ± osteochondral bodies

DDx: large effusion, soft-tissue tumor

√ osteochondral bodies:

√ multiple foci of low signal intensity ← calcifications

√ peripheral contrast enhancement of chondral lesions

√ intraarticular bodies with central area of high SI on T1WI = with fatty marrow

Cx: (1) Long-standing disease → secondary degenerative arthritis ← chronic mechanical irritation + destruction of articular cartilage by loose bodies

(2) Malignant dedifferentiation to synovial chondrosarcoma (in < 5%)

Rx: surgical synovectomy with removal of loose bodies (recurrence is common)

DDx: (1) Synovial sarcoma, chondrosarcoma

(2) Osteochondral fracture (history of trauma), osteochondritis dissecans, osteonecrosis

(3) Secondary osteochondromatosis

(4) Pigmented villonodular synovitis, synovial hemangioma, lipoma arborescens

Secondary Synovial Osteochondromatosis

= joint surface disintegration

Cause: trauma, osteonecrosis, rheumatoid arthritis, neuropathic arthropathy, tuberculous arthritis, degenerative joint disease

√ intraarticular bodies tend to be larger, less numerous, more varied in size compared to

primary synovial osteochondromatosis
√ prominent osteoarthritis

SYNOVIAL SARCOMA

= (MALIGNANT) SYNOVIOMA = TENDOSYNOVIAL SARCOMA = SYNOVIOBLASTIC SARCOMA = SYNOVIAL ENDOTHELIOMA
= [misnomer related to appearance of cells not their origin] slow-growing expansile malignant tumor originating from mesenchymal tissue (not synovium, named for its histologic resemblance of synovium) with extensive metastatic potential
Origin: pluripotential mesenchymal cell of variable epithelial differentiation; it has been proposed to rename tumor carcinosarcoma / spindle cell sarcoma of soft tissue
Frequency: 4th most common soft-tissue sarcoma (after malignant fibrous histiocytoma, liposarcoma, rhabdomyosarcoma); 7–10% of all primary soft-tissue sarcomas
Histo: in 90% positive staining for keratin (epithelial marker) pankeratin, EMA, CK7 (absent in malignant peripheral nerve sheath tumor + Ewing sarcoma)
(a) biphasic (20–30%): mesenchymal spindle cell + epithelial component usually forming glands
(b) monophasic (50–60%): spindle cell component with fascicular interlacing growth pattern predominates
(c) poorly differentiated (15–25%): generally epitheloid with high mitotic activity + geographic necrosis
Cytogenetics: t(X;18) translocation + SYT-SSX gene fusion products (identified by FISH / RT-PCR studies)
Median age: 30–38 (84% between 15 and 50) years; M÷F = 1.2÷1.0
• slow-growing occasionally painful palpable soft-tissue mass (2–4 years average duration of symptoms) often mistaken for benign indolent process
Site: in synovial lining / bursa / tendon sheath adjacent to joint (40–50%) / within 5 cm of joint (60–75%); uncommonly intraarticular (in 5–10%)
Location: 80–95% in extremities; pelvis (8%); trunk (7%); head & neck (5%, pharynx); retroperitoneum (0.3%); rare in: chest wall, mediastinum, heart, lung, pleura; usually solitary
(a) lower extremity (2/3): thigh, popliteal fossa (most common), hip, foot & ankle (18%)
(b) upper extremity (1/3): elbow, wrist, hands, feet
√ large spheroid well-defined soft-tissue mass:
√ homogeneous / heterogeneous dependent on degree of hemorrhage / necrosis
√ amorphous punctate calcifications / ossification (30–40%), often eccentric or at periphery of tumor
◊ Calcifications in other soft-tissue connective tissue sarcomas are uncommon!
√ lesion about 1 cm removed from joint cartilage
√ often indolent nonaggressive appearance of involvement of adjacent bone (11–20%):
√ periosteal reaction
√ bone remodeling (pressure from tumor)
√ invasion of cortex with wide zone of transition

√ infiltration of adjacent soft tissue (infrequent)
√ juxtaarticular osteoporosis

CT:
√ heterogeneous deep-seated multinodular soft-tissue mass with attenuation slightly less than muscle ← necrosis / hemorrhage (in 50%)
√ multinodular morphology with well-defined (53%) / irregular (47%) margins
√ areas of lower attenuation represent necrosis / hemorrhage
√ predominantly areas of low attenuation mimicking hematoma / cystic mass (in 6%)
√ calcifications (in 27–41%)
√ bone erosion / marrow invasion (25%)
√ heterogeneous enhancement (89–100%)

MR:
√ predominantly well-defined mass of homogeneous texture for lesions < 5 cm (rare) mimicking a benign process
√ prominently heterogeneous soft-tissue mass with SI similar to / slightly higher than muscle on T1WI
√ heterogeneously increased SI on T2
√ "triple signal intensity" sign on T2WI (in 35–57%) = marked heterogeneity with a mixture of areas of
(1) hypointensity ← calcified / fibrotic collagenized tissue,
(2) isointensity ← solid cellular elements, and
(3) hyperintensity ← hemorrhage / necrosis (in 40%)
√ "bowl of grapes" sign = large multilocular multilobulated cystic spaces + prominent hemorrhagic foci separated by septa (67–75%) on T2WI
√ fluid-fluid levels (10–25%) ← previous hemorrhage
√ bone marrow invasion / cortical erosion (in up to 21%)
√ neurovascular encasement (17–24%)

CEMR:
√ prominent heterogeneous (83%) / homogeneous (17%) enhancement
√ peripheral / nodular enhancement for necrotic tumor
√ serpentine vascular channels (1/3)
√ initially rapid progressive linear increase in SI followed by washout (60%) / late sustained increase (40%)

US:
√ focal nodular round / lobulated hypoechoic solid soft-tissue mass (66%)
√ heterogeneous texture with irregular margins

Angio:
√ hypervascular tumor displacing native vessels
√ arteriovenous shunting (in 24%)

NUC:
√ prominently increased uptake on blood flow + blood pool images of bone scan ← increased tumor vascularity
√ heterogeneous mild uptake (← mixture of viable + necrotic tissue) perhaps associated with calcifications

PET:

√ markedly increased activity with high SUV

Spread: distant metastases develop in 41% within 2–5 years; lung (94%) > lymph nodes (4–18%) > bone (8–11%)

◊ Metastasis present in 16–25% at presentation

Rx: local excision / amputation + radiation + chemotherapy

Prognosis: local recurrence in 30–50% within 2 years after Rx; 36–76% 5-year survival rate; 20–63% 10-year survival rate

Poor prognosticators: tumor size > 5 cm, trunk > peripheral location, poorly differentiated areas

SYPHILIS OF BONE

[*syphlos*, Greek = crippled]

= "The Great Imitator" of neoplastic / autoimmune conditions

Organism: spirochete Treponema pallidum = spiral-shaped extracellular microorganisms with internal flagella resulting in twisting locomotion; evades immune system through antigenic variation

Transmission: sexually / placentally

• local mucocutaneous infection → gradual progression to chronic systemic disease

Congenital Syphilis

◊ Transplacental transmission cannot occur < 16 weeks gestational age

• positive rapid plasma reagin (measures quantity of antibodies to assess new infection / efficacy of Rx)

• positive microhemagglutination test for Treponema pallidum (remains reactive for life)

√ pneumonia alba

√ hepatomegaly

Location: symmetrical bilateral osteomyelitis involving multiple bones (HALLMARK)

A. Early phase

◊ Skeletal radiography abnormal in 19% of infected newborns without overt disease!

1. Metaphysitis
   - √ lucent metaphyseal band adjacent to thin / widened zone of provisional calcification ← disturbance in enchondral bone growth
   - √ frayed edge of metaphyseal-physeal junction (osteochondritis) = erosions + lytic defects
2. Diaphyseal periostitis = "luetic diaphysitis"
   - √ solid / lamellated periosteal new-bone growth = bone-within-bone appearance
3. Spontaneous epiphyseal fractures causing Parrot pseudopalsy (DDx: battered child syndrome)
4. Bone destruction
   - √ marginal destruction of spongiosa + cortex along side of shaft with widening of medullary canal (in short tubular bones)
   - √ patchy rarefaction in diaphysis
5. Wimberger sign
   - √ symmetrical focal bone destruction of medial portion of proximal tibial metaphysis (ALMOST PATHOGNOMONIC)

B. Late phase
- Hutchinson triad = dental abnormality, interstitial keratitis, 8th nerve deafness
  √ frontal bossing of Parrot = diffuse thickening of outer table
  √ saddle nose + high palate (syphilitic chondritis + rhinitis)
  √ short maxilla (maxillary osteitis)
  √ thickening at sternal end of clavicle
  √ "saber-shin" deformity = anteriorly convex bowing in upper ²/₃ of tibia with bone thickening

Acquired Syphilis

= TERTIARY SYPHILIS resembles chronic osteomyelitis
√ dense bone sclerosis of long bones
√ irregular periosteal proliferation + endosteal thickening with narrow medulla
√ extensive calvarial bone proliferation with mottled pattern (anterior half + lateral skull) in outer table (DDx: fibrous dysplasia, Paget disease)
√ ill-defined lytic destruction in skull, spine, long bones (= gumma formation)
√ enlargement of clavicle ← cortical + endosteal new bone
√ Charcot arthropathy of lower extremities + spine

Primary Syphilis
- HALLMARK painless cutaneous ulcer (chancre)

Meningovascular Neurosyphilis
Cause: direct spirochete invasion of vascular endothelial cells → vasculitis
- stroke in young adult (MCA > basilar artery territory)

TARSAL COALITION

= abnormal fibrous / cartilaginous / osseous fusion of two or more tarsal ossification bones
◊ Clinically most important congenital problem of calcaneus
Prevalence: 1–2% of population
Cause: abnormal segmentation of primitive mesenchyme with lack of joint formation
Age: fibrous coalition at birth, ossification during 2nd decade of life with onset of symptoms; M÷F = 1÷1
- asymptomatic: often first noted after antecedent trauma / weight gain / increase in athletic activity
- peroneal spastic / rigid pes planus (= flatfoot) in adjustment for calcaneus valgus (= heel valgus)
- hindfoot / tarsal pain or stiffness

√ both feet affected in 20–50%
√ osseous bars between bones of hindfoot / bones in close proximity with irregular surfaces
MR (of joint space):
√ bone marrow contiguity (osseous coalition)
√ fluid- / cartilage-intensity (cartilaginous coalition)
√ intermediate- to low-signal intensity (fibrous coalition)
√ reactive periarticular bone changes

√ bone marrow edema along fused joint (STIR images)

Types:

(1) CALCANEONAVICULAR COALITION (45%)

Age: 8–12 years ← earlier ossification

• rigid flat foot ± pain in 2nd decade of life

Radiographs:

√ narrowed calcaneonavicular joint with indistinct articular margins (bones that usually do not articulate)

√ widening / flattening of anteromedial calcaneus

√ "anteater's nose" = elongation of anterior dorsal calcaneus on lateral radiograph

√ hypoplastic talar head

CT (axial scan):

√ broadening of medial aspect of anterodorsal calcaneus in apposition to navicular

√ narrowing of space between calcaneus and navicular + minimal marginal reactive sclerosis

Dx: mostly diagnosed on 45° internal oblique films

(2) Talocalcaneal coalition (45%)

Age: 12–16 years

• painful peroneal spastic flat foot, relieved by rest

Site: middle facet at level of sustentaculum tali (most frequently)

Secondary radiographic signs ← alteration in hindfoot biomechanics:

√ prominent talar beak (66%) arising from dorsal aspect of head / neck of talus ← impaired subtalar joint motion

√ rounding of the lateral talar process

√ narrowing of posterior subtalar joint

√ lack of depiction of middle facets

√ asymmetric anterior talocalcaneal joint

√ "ball-in-socket" ankle mortise in severe cases

√ "C" sign = C-shaped outline of the medial talar dome + posteroinferior sustentaculum on lateral radiograph (from bone bridge between talar dome + sustentaculum)

CT (coronal scan):

√ bony bar bridging the middle facet of subtalar joint

√ narrowed middle facet with reactive cystic + hypertrophic changes

√ downward or horizontal slope of sustentaculum, instead of upward

Dx: requires cross-sectional imaging for diagnosis

(3) TALONAVICULAR COALITION

(4) CALCANEOCUBOID COALITION

(5) CUBONAVICULAR COALITION

Rx: orthotics, casting, NSAID, steroid injections, physical therapy, resection, arthrodesis

DDx: acquired intertarsal ankylosis (infection, trauma, arthritis, surgery)

TARSAL TUNNEL SYNDROME

= entrapment / compression neuropathy (analogous to carpal tunnel syndrome) of

(a) posterior tibial nerve (most common)
(b) its terminal branches (= medial and lateral plantar nn., medial calcaneal n.)

Tarsal tunnel = fibro-osseous passageway from level of medial malleolus to navicular bone distally

Medial floor: tibia, talus, sustentaculum tali, medial wall of calcaneus

Lateral roof: deep fascia of leg, flexor retinaculum = lacinate lig., abductor hallucis

Contents: medial ankle tendons (tibialis posterior, flexor hallucis longus, flexor digitorum longus) + posterior tibial nerve and artery and veins

Cause:

(a) intrinsic (mass effect): ganglion cyst, neural sheath tumor, lipoma, tenosynovitis of flexor hallucis longus, marked varicosities, accessory muscle, fracture, fibrosis of chronic ankle sprain, rheumatoid arthritis, diabetes
(b) extrinsic (tension): tarsal coalition, excessive pronation, valgus / varus heel, repetitive stress (jogger's foot)

- burning pain, tingling, numbness, nocturnal paresthesia along plantar surface of heel, foot and toes
- radiation of paresthesia to medial aspect of calf (Valleix phenomenon)
- positive Tinel sign = percussion of posterior tibial n. posteroinferiorly from medial malleolus causes paresthesia

√ mass in tarsal tunnel (ganglion, neurilemmoma, lipoma, thickened flexor retinaculum, muscle)
√ muscle edema from denervation in abductor hallucis (supplied by medial plantar nerve) / abductor digiti minimi (supplied by lateral plantar nerve)
√ fracture of sustentaculum tali / medial tubercle of posterior talar process
√ serpiginous varicosities

Rx: orthotics, release

THALASSEMIA SYNDROMES

= inherited disorders of hemoglobin synthesis typically seen in individuals of Mediterranean descent

Physiologic hemoglobins:

(a) in adulthood:
Hb A (98% = 2 α- and 2 β-chains);
Hb A_2 (2% = 2 α- and 2 δ-chains)
(b) in fetal life:
Hb F (= 2 α- and 2 γ-chains)
rapidly decreasing up to 3 months of newborn period

A. ALPHA-THALASSEMIA
= decreased synthesis of α-chains → excess of β-chains and γ-chains (Hb H = 4 β-chains; Hb Bart = 4 γ-chains)
- disease begins in intrauterine life as no fetal hemoglobin is produced
- homozygosity is lethal (lack of oxygen transport)

B. BETA-THALASSEMIA
= decreased synthesis of β-chains leading to excess of α-chains + γ-chains (= fetal hemoglobin)

• disease manifest in early infancy
(a) homozygous defect = thalassemia major = Cooley anemia
(b) heterozygous defect = thalassemia minor

Thalassemia Major

= COOLEY ANEMIA = MEDITERRANEAN ANEMIA
= HEREDITARY LEPTOCYTOSIS = β-THALASSEMIA
= most severe form with trait inherited from both parents (= homozygous form)
Prevalence: 1% for American Blacks; 7.4% for Greek population; 10% for certain Italian populations
Age: develops after newborn period within first 2 years of life
• retarded growth
• elevated serum bilirubin
• hyperpigmentation of skin
• hyperuricemia
• secondary sexual characteristics retarded, normal menstruation rare ← primary gonadotropin insufficiency ← iron overload in pituitary gland
• hypochromic microcytic anemia (Hb 2–3 g/dL), nucleated RBC, target cells, reticulocytosis, decrease in RBC survival, leukocytosis
• susceptible to infection ← leukopenia ← splenomegaly
• bleeding diathesis ← thrombocytopenia
@ Skull:
• mongoloid facies
√ marrow expansion of diploe:
√ widening of diploic space with coarsened trabeculations and displacement ← marrow hyperplasia (= extramedullary hematopoiesis)
√ thinning of outer table
√ frontal bossing
√ severe hair-on-end appearance (frontal bone, NOT inferior to internal occipital protuberance)
√ marrow expansion in paranasal sinuses:
√ impaired pneumatization of maxillary antra + mastoid sinuses
√ narrowing of nasal cavity
√ rodent facies = ventral displacement of incisors ← marrow overgrowth in maxillary bone with dental malocclusion
√ lateral displacement of orbits
@ Peripheral skeleton:
• earliest changes in small bones of hands + feet (> 6 months of age)
√ diffuse osteopenia:
√ atrophy + coarsening of trabeculae ← marrow hyperplasia
√ prominence of nutrient foramina
√ widened medullary spaces with thinning of cortices
√ Erlenmeyer flask deformity = bulging of normally concave outline of metaphyses
√ premature fusion of epiphyses (10%), usually at proximal humerus + distal femur
√ arthropathy ← hemochromatosis + CPPD + acute gouty arthritis

√ regression of peripheral skeletal changes (as red marrow becomes yellow)

@ Chest:

√ cardiac enlargement + congestive heart failure ← anemia

√ paravertebral masses (= extramedullary hematopoiesis)

@ Ribs

√ costal osteomas = bulbous widening of posterior aspect of ribs with thinned cortices

√ undertubulated broad ribs

√ heterogeneous rib ossification:

√ localized lucencies

√ cortical erosion

√ rib-within-rib appearance

@ Abdomen:

√ hepatosplenomegaly

√ gallstones

Cx: (1) Pathologic fractures

(2) Iron overload + hemosiderosis ← frequent blood transfusion therapy (absent puberty, diabetes mellitus, adrenal insufficiency, myocardial insufficiency)

Prognosis: usually death within 1st decade

Rx: systematic transfusion has lessened the severity of skeletal abnormalities

DDx: chronic anemia, storage diseases, fibrous dysplasia

Thalassemia Intermedia

= subgroup of homozygous form

• milder clinical presentation

• not requiring hypertransfusion to maintain an adequate hematocrit

Prognosis: longer life expectancy

Thalassemia Minor

= beta-thalassemia trait inherited from one parent (heterozygous)

• usually asymptomatic except for periods of stress (pregnancy, infection)

• microcytic hypochromic anemia (Hb 9–11 g/dL)

• occasionally jaundice + splenomegaly

THANATOPHORIC DYSPLASIA

[*thanatos*, Greek = death; *phoric*, Greek = bearing]

= sporadic lethal skeletal dysplasia characterized by severe rhizomelia (micromelic dwarfism)

Prevalence: 6.9÷100,000 births; 1÷6,400–16,700 births;

◊ Most common lethal bone dysplasia after osteogenesis imperfecta type II

Genetics: autosomal dominant mutation of gene-encoding fibroblast growth factor receptor 3 (FGFR3)

• severe respiratory distress (early in life)

• hypotonic infants; protuberant abdomen

• extended arms + abducted externally rotated thighs

@ Head

√ disproportionately large head with short base of skull + prominent forehead
√ occasionally trilobed cloverleaf skull = "Kleeblattschädel"
√ depressed nasal bridge + protruding eyes

@ Chest radiograph (PATHOGNOMONIC)
√ narrow chest with normal trunk length
√ short horizontal ribs:
  √ not extending beyond anterior axillary line
  √ cupped anterior ends
√ short curved "telephone handle" humeri
√ H- / U-shaped vertebra plana
√ small scapula + normal clavicles

@ Spine
√ normal length of trunk
√ reduction of interpediculate space of last few lumbar vertebrae
√ extreme generalized platyspondyly = severe H- / U-shaped vertebra plana
√ excessive intervertebral space height

@ Pelvis (hypoplastic iliac bones)
√ iliac wings small + square (vertical shortening but wide horizontally)
√ flat acetabulum
√ narrow sacrosciatic notch
√ short pubic bones

@ Extremities
√ severe micromelia:
  √ bowing of extremities (type 1) / straight (type 2)
√ metaphyseal flaring = "telephone handle" appearance of long bones
√ thornlike projections in metaphyseal area
√ polydactyly

OB-US (findings may be seen very early in pregnancy):
√ polyhydramnios (50–71%)
√ short-limbed dwarfism with extremely short + bowed "telephone receiver"-like femurs
√ extremely small hypoplastic thorax with short ribs + narrowed in anteroposterior dimension
√ protuberant abdomen
√ macrocrania with frontal bossing ± hydrocephalus (increased HC÷AC ratio)
√ "cloverleaf skull" (in 14%) (DDx: encephalocele)
√ diffuse platyspondyly
√ redundant soft tissues

Prognosis: often stillborn; uniformly fatal within a few hours / days after birth ← respiratory failure

DDx: (1) Ellis-van Creveld syndrome (extra digit, acromesomelic short limbs)
(2) Asphyxiating thoracic dysplasia (less marked bone shortening, vertebrae spared)
(3) Short-rib polydactyly syndrome
(4) Homozygous achondroplasia
(5) Achondrogenesis

THROMBOCYTOPENIA-ABSENT RADIUS SYNDROME

= TAR SYNDROME
= rare autosomal recessive disorder
May be associated with: CHD (33%): ASD, tetralogy
• platelet count < 100,000/mm^3 (decreased production by bone marrow)
√ usually bilateral radial aplasia / hypoplasia
√ uni- / bilaterally hypoplastic / absent ulna / humerus
√ defects of hands, feet, legs
Prognosis: death in 50% in early infancy ← hemorrhage

THYROID ACROPACHY

Onset: after > 18 months following surgical / radioactive ablation of thyroid gland for hyperthyroidism (does not occur with antithyroid medication)
Frequency: 0.5–1% of patients with thyrotoxicosis
• clubbing, soft-tissue swelling, NO pain
• eu- / hypo- / hyperthyroid state
Location: metacarpals + phalanges of hand; less commonly feet, lower legs, forearms
√ thick spiculated lacy "feathery" periosteal reaction in an asymmetric distribution; mostly on radial aspect of bone
DDx: (1) Pulmonary osteoarthropathy (painful)
(2) Pachydermoperiostosis
(3) Fluorosis (ligamentous calcifications)

TRANSIENT REGIONAL OSTEOPOROSIS

= TRANSIENT BONE MARROW EDEMA
Cause: unknown; ? overactivity of sympathetic nervous system + local hyperemia similar to reflex sympathetic dystrophy syndrome, trauma, synovitis, transient ischemia

Regional Migratory Osteoporosis

= rapid onset of self-limiting episodes of severe localized osteoporosis and pain but repetitive occurrence of same symptoms in other regions of same / opposite lower extremity
• rapid onset of local pain
• diffuse erythema, swelling, increased heat
• significant disability ← severe pain on weight bearing
Age: middle-aged males
Location: usually lower extremity (ie, ankle, knee, hip, foot)
√ rapid localized osteoporosis within 4–8 weeks after onset migrating from one joint to another; may affect trabecular / cortical bone
√ linear / wavy periosteal reaction
√ preservation of subchondral cortical bone
√ no joint space narrowing / bone erosion
MR:
√ affected area has low SI on T1WI, high SI on T2WI (= bone marrow edema)

NUC:
√ increased activity
Prognosis: persists for 6–9 months in one area; cycle of symptoms may last for several years
Rx: variable response to analgesics / corticosteroids

Partial Transient Osteoporosis
= variant of regional migratory osteoporosis with more focal pattern of osteoporosis, which may eventually become more generalized
(a) zonal form = portion of bone involved, ie, one femoral condyle / one quadrant of femoral head
(b) radial form = only one / two rays of hand / foot involved

Transient Osteoporosis of Hip

= self-limiting disease of unknown etiology
Age: typically in middle-aged males / in 3rd trimester of pregnancy in females involving left hip; M > F
• spontaneous onset of hip and groin pain, usually progressive over several weeks
• painful swelling of joint followed by progressive demineralization
• rapid development of disability, limp, ↓ range of motion
Site: hip most commonly affected; generally only one joint at a time
√ progressive marked osteoporosis of femoral head, neck, acetabulum (3–8 weeks after onset of illness)
√ virtually PATHOGNOMONIC striking loss of subchondral cortex of femoral head + neck region
√ NO joint space narrowing / subchondral bone collapse
NUC:
√ markedly increased uptake on bone scan without cold spots / inhomogeneities (positive before radiograph)
MR:
√ diffuse bone marrow edema involving femoral head + neck + sometimes intertrochanteric region
√ small joint effusion
Cx: pathologic fracture common
Prognosis: spontaneous recovery within 2–6 months; recurrence in another joint within 2 years possible
DDx: (1) AVN (cystic + sclerotic changes, early subchondral undermining)
(2) Septic / tuberculous arthritis (joint aspiration!)
(3) Monoarticular rheumatoid arthritis
(4) Metastasis
(5) Reflex sympathetic dystrophy
(6) Disuse atrophy
(7) Synovial chondromatosis
(8) Villonodular synovitis

TRANSIENT SYNOVITIS OF HIP

= OBSERVATION HIP = TRANSITORY SYNOVITIS = TOXIC SYNOVITIS = COXITIS FUGAX
= nonspecific inflammatory reaction

◊ Most common nontraumatic cause of acute limp in a child!

Etiology: unknown; no organism on joint aspiration
Average age: 6 (range, 5–10) years; M÷F = 2÷1
• history of recent viral illness (65%)
• mild fever (25%), mildly elevated ESR (50%)
• developing limp over 1–2 days; pain in hip, thigh, knee
• serosanguinous joint fluid
√ radiographs usually normal
√ joint effusion:
  √ displacement of femur from acetabulum
  √ displacement of psoas line
  √ lateral displacement of gluteal line (least sensitive + least reliable)
√ regional osteoporosis (? hyperemia, disuse)
US:
  √ fluid in anterior recess between capsule + femoral neck
MR:
  √ joint effusion
  √ intense enhancement of hypertrophied synovium (DDx: septic arthritis)
NUC:
  √ normal / slight increase in activity → excluding osteomyelitis + avascular necrosis
Prognosis: complete recovery within a few weeks
Dx: per exclusion
Rx: non–weight-bearing treatment
DDx: (1) Septic arthritis
(2) Trauma
(3) Legg-Perthes disease
(4) Acute rheumatoid arthritis
(5) Acute rheumatic fever
(6) Tuberculosis
(7) Malignancy

TREACHER-COLLINS SYNDROME

[Edward Treacher Collins (1862–1932), English surgeon and ophthalmologist at Moorfields Eye Hospital, London]
= MANDIBULOFACIAL DYSOSTOSIS
= autosomal dominant disease (with new mutations in 60%) characterized by bilateral malformations of eyes, malar bones, mandible, and ears resulting in birdlike face
Prevalence: 1÷50,000 births
Cause: defect in growth of 1st + 3rd branchial arches before the 7th–8th week of gestation

◊ NO limb anomalies (important DDx!)
• extension of scalp hair growth onto cheek; microstomia
√ craniosynostosis
√ narrowing of retropharyngeal space (apnea, speech difficulties)
@ Eyes
• antimongoloid eye slant (drooping lateral lower eyelids ← hypoplasia of lateral canthal tendon of orbicular muscle
• sparse / absent eye lashes / coloboma in lower lids
√ egg-shaped orbits = drooping of outer inferior orbital rim
√ hypoplasia of lateral wall of orbits + shallow / incomplete orbital floor
@ Nose
• broad / protruded nose
√ choanal shortening
@ Malar bone
√ sunken cheek ← marked hypoplasia / agenesis of zygomatic arches (= malar hypoplasia)
@ Maxilla
√ hypoplasia of maxilla + maxillary sinus
√ narrow / overprojected maxilla
√ high-arched / narrow palate
@ Mandible
• retruded chin, retrognathism; dental malocclusion
√ pronounced micrognathia = mandibular hypoplasia with broad concave curve on lower border of body
@ Ear
• dysplastic low-set auricles; preauricular skin tags / fistulas
• conductive hearing loss (common)
√ microtia with small middle ear cavity
√ deformed / fused / absent auditory ossicles
√ atresia / stenosis of external auditory canal
OB-US:
√ polyhydramnios ← swallowing difficulty
Prognosis: early respiratory problems (tongue relatively too large for hypoplastic mandible)
Rx: surgical correction
DDx: (1) Goldenhar-Gorlin syndrome (unilateral microtia + midface anomalies, hemivertebrae, block vertebrae, vertebral hypoplasia, microphthalmia, coloboma of upper lid)
(2) Acrofacial dysplasia (limb malformations)
(3) Crouzon disease (maxillary hypoplasia with protrusion of mandible, hypertelorism, exophthalmos, craniosynostosis)

TRISOMY D SYNDROME

= TRISOMY 13–15 GROUP SYNDROME
Etiology: additional chromosome in D group; high maternal age
• severe mental retardation

• hypertonic infant
• cleft lip + palate

Associated with: capillary hemangioma of face + upper trunk
• hypotelorism; coloboma, cataract, microphthalmia
• malformed ear with hypoplastic external auditory canal
• hyperconvex nails

√ postaxial polydactyly

@ Skull
- √ deficient ossification of skull
- √ cleft / absent midline structures of facial bones
- √ poorly formed orbits
- √ slanting of frontal bones
- √ microcephaly
- √ arrhinencephaly
- √ holoprosencephaly

@ Chest
- √ thin malformed ribs
- √ diaphragmatic hernia (frequent)
- √ congenital heart disease

Prognosis: death within 6 months of age

TRISOMY E SYNDROME

= TRISOMY 16–18 GROUP SYNDROME

Etiology: additional chromosome at 18 or E group location

Sex: usually female

◊ Marked phenotypic variability!

- hypertonic spastic infant; mental + psychomotor retardation
- typical facies: micrognathia, high narrow palate with small buccal cavity, low-set deformed ears
- flexed ulnar-deviated fingers + short adducted thumb
- 2nd finger overlapping 3rd (CHARACTERISTIC)

Associated with: congenital heart disease in 100% (PDA, VSD); hernias; renal anomalies; eventration of diaphragm

√ stippled epiphyses

@ Skull
- √ thin calvarium
- √ persistent metopic suture
- √ dolichocephaly with prominent occiput
- √ micrognathia ← hypoplastic mandible (most constant feature) + maxilla

@ Chest
- √ increase in AP diameter of thorax
- √ "shield deformity" ← hypoplastic short sternum
- √ hypoplastic clavicles (DDx: cleidocranial dysostosis)
- √ 11 rib pairs with slender hypoplastic + tapered ribs
- √ diaphragmatic eventration (common)

@ Pelvis
- √ small pelvis with forward rotation of iliac wings
- √ increased obliquity of acetabulum
- √ acute iliac angle (DIAGNOSTIC)

@ Hand & foot
- √ adducted thumb = short 1st metacarpal + phalanges (DIAGNOSTIC)
- √ 2nd finger overlapping 3rd (DIAGNOSTIC)
- √ flexed ulnar-deviated fingers
- √ short 1st toe
- √ varus deformities of forefoot + dorsiflexion of toes
- √ rocker bottom foot / extreme pes planus (frequent)

OB-US:
- √ hydrocephalus
- √ cystic hygroma
- √ diaphragmatic hernia
- √ clubfoot
- √ overlapping index finger
- √ choroid plexus cyst (30%)

Prognosis: child rarely survives beyond 6 months of age

DDx: osteogenesis imperfecta, trisomy 13 syndrome, Cockayne syndrome, Werdnig-Hoffmann disease

TUBERCULOSIS OF BONE

Frequency: 1–3–5% of tuberculous patients
Age: any; rare in 1st year of life; M÷F = 1÷1
- negative skin test excludes diagnosis; 14% FN rate
- history of active pulmonary disease (in 30–50%)

Location: spinal column, pelvis, hip, knee, wrist, elbow
Pathogenesis:
1. Hematogenous spread from
   (a) primary infection of lung (particularly in children)
   (b) quiescent primary pulmonary site / extraosseous focus
   (c) lymphatic focus in synovium
2. Direct spread from adjacent focus of osteomyelitis (rare)
3. Reactivation: especially in hip

Average delay in Dx: 16–19 months

Tuberculous Arthritis

= joint involvement usually ← direct spread from adjacent osteomyelitis / hematogenous dissemination
Prevalence: 84% of skeletal tuberculosis (about 50% as tuberculous spondylitis)
Pathophysiology: synovitis with pannus formation leads to chondronecrosis
Age: middle-aged / elderly
- chronic pain, weakness, muscle wasting
- soft-tissue swelling, draining sinus
- joint fluid: high WBC count, low glucose level, poor mucin clot formation (similar to rheumatoid arthritis)

Location: hip, knee (large weight-bearing joints) >> elbow, wrist, sacroiliac joint, glenohumeral, articulation of hand + foot
◊ TYPICALLY monoarticular!

Nonspecific imaging findings similar to other arthritides:
√ osteopenia
√ synovitis + other soft-tissue swelling
√ marginal erosions
√ varying degrees of cartilage destruction

√ Phemister triad:
1. Gradual narrowing of joint space ← slow cartilage destruction (DDx: much quicker cartilage destruction in pyogenic arthritis)
   Associated with: hyperemia + epiphyseal overgrowth in young patients
2. Peripherally located (= marginal) bone erosions
3. Juxtaarticular osteoporosis

(DDx: fungal disease, rheumatoid arthritis)

Imaging findings favoring tuberculous arthritis:

√ insidious onset
√ minimal sclerosis
√ relative absence of periosteal reaction + bone proliferation
√ relative preservation of joint space in early stages

Early radiographs:
√ joint effusion (hip in 0%, knee in 60%, ankle in 80%)
√ extensive periarticular osteopenia (deossification) adjacent to primarily weight-bearing joints
√ soft tissues usually normal

Late radiographs:
√ small cystlike marginal erosions in non–weight-bearing line opposing one another
DDx: pyogenic arthritis (erodes articular cartilage)
√ no joint space narrowing for months (CLASSIC!) ← preservation of articular cartilage until late in disease
√ articular cortical bone destruction earlier in joints with little unopposed surfaces (hip, shoulder)
√ "kissing sequestra" = wedge-shaped areas of necrosis on both sides of the joint ← infection of subchondral bone
√ increased density with extensive soft-tissue calcifications in healing phase
√ rice bodies
√ sinus formation

Cx: fibrous (rarely osseous) ankylosis; leg shortening
Dx: joint aspiration (microscopic analysis), synovial biopsy (in 90% positive), culture of synovial fluid (in 80% positive)
DDx: pyogenic / fungal arthritis (central erosion of articular cartilage, early joint space narrowing, bony ankylosis)

Tuberculous Osteomyelitis

◊ Isolated tuberculous osteomyelitis in the absence of tuberculous arthritis is RARE !

Frequency: 16% of skeletal tuberculosis
Age: children < 5 years (0.5–14%); rare in adults
Predisposed: HIV-infected individuals
• painless swelling of hand / foot
Location: femur, tibia, small bones of hand + foot (most common); any bone may be involved
Site:
(a) metaphysis (TYPICALLY) with transphyseal spread (in child) (DDx: pyogenic infections usually do not extend across physis)
(b) epiphysis with spread to joint / spread from adjacent affected joint
(c) diaphysis (< 1%)

√ initially round / oval poorly defined lytic lesion with minimal / no surrounding sclerosis
√ varying amounts of eburnation + periostitis:
√ no periosteal reaction (in adult)
√ advanced epiphyseal maturity / overgrowth ← hyperemia

√ ± limb shortening from premature physeal fusion
√ **cystic tuberculosis** = well-marginated round / oval radiolucent lesions with variable amount of sclerosis
(a) in children (frequent): in peripheral skeleton, ± symmetric distribution, no sclerosis
(b) in adults (rare): in skull / shoulder / pelvis / spine, with sclerosis
(*DDx:* eosinophilic granuloma, sarcoidosis, cystic angiomatosis, plasma cell myeloma, chordoma, fungal infection, metastasis)
√ **tuberculous dactylitis** = digit with exuberant lamellated / solid periosteal new-bone formation and fusiform soft-tissue swelling (children >> adults):
√ spina ventosa ("wind-filled sail") = ballooning dactylitis forming an enlarging cystlike cavity with erosion of endosteal cortex (end-stage disease)
√ formation of sinus tracts

DDx: (1) Pyogenic osteomyelitis (no transphyseal spread)
(2) Syphilitic dactylitis (bilateral symmetric involvement, less soft-tissue swelling and sequestration)
(3) Sarcoidosis, hemoglobinopathies, hyperparathyroidism, leukemia

TUMORAL CALCINOSIS

= LIPOCALCINOGRANULOMATOSIS = TEUTSCHLäNDER DISEASE
= rare familial metabolic disorder characterized by solitary or multiple painless, periarticular masses
= disease with progressive large nodular juxtaarticular calcified soft-tissue masses in patients with normal serum calcium and phosphorus + no evidence of renal, metabolic, or collagen-vascular disease

Etiology: autosomal dominant ($^{1}/_{3}$) with variable clinical expressivity; unknown biochemical defect of phosphorus metabolism → abnormal phosphate reabsorption + 1,25-dihydroxy-vitamin D formation

Path: multilocular cystic lesions with creamy white fluid (calcium hydroxyapatite crystals with amorphous calcium carbonate and calcium phosphate) + many giant cells (granulomatous foreign body reaction) surrounded by fibrous capsule

Associated with: hyperostosis, diaphysitis, pseudoxanthoma elasticum

Age: onset mostly within 1st / 2nd decade (range of 1–79 years); M÷F = 1÷1; predominantly in Blacks

- progressive painful / painless soft-tissue mass with overlying skin ulceration + sinus tract draining chalky milklike fluid
- prominent dental abnormalities
- swelling; limitation of motion
- <u>hyperphosphatemia</u> + ↓ fractional phosphate excretion
- hypervitaminosis D (↑ 1,25-dihydroxy–vitamin D formation)
- <u>normal</u> serum calcium, alkaline phosphatase, renal function, parathyroid hormone

@ Soft tissue

Location: hip (greater trochanteric bursa) > elbow > shoulder > foot, rib, ischial spine, wrist; single / multiple joints; ALMOST NEVER knees

Distribution: periarticular; usually along <u>extensor surface</u> of joints (? initially a calcific

bursitis)

X-ray:

√ amorphous cystic multilobulated homogeneously calcified soft-tissue mass of 1–20 cm in size

√ underlying bones NORMAL without erosion / osseous destruction

√ periosteal reaction ← bone marrow involvement

CT:

√ patchy areas of increased attenuation

√ cystic appearance with radiolucent septa (= connective tissue)

√ "sedimentation" sign = fluid-fluid levels with milk-of-calcium consistency

NUC:

√ ↑ tracer uptake of soft-tissue mass on bone scan

MR:

√ inhomogeneous high SI on T2WI (in spite of large amount of calcium) of 2 distinctive patterns:

√ diffuse lower-signal-intensity pattern

√ bright nodular pattern with alternating areas of high signal intensity and signal void

√ inhomogeneous lesion with low SI on T1WI

@ Bone

√ diaphyseal periosteal reaction (diaphysitis)

√ patchy areas of calcification in medullary cavity (= calcific myelitis)

√ increased uptake on bone scintigraphy

@ Teeth

√ bulbous root enlargement

√ pulp stones = intrapulp calcifications

@ Pseudoxanthoma elasticum-like features

√ calcinosis cutis = skin calcifications

√ vascular calcifications

√ angioid streaks of retina

@ Eye

• angioid streaks / corneal calcification deposits

Prognosis: tendency for recurrence after incomplete excision

Rx: phosphate depletion

DDx: Chronic renal failure on hemodialysis, calcinosis universalis, calcinosis circumscripta, calcific tendonitis, CPPD, paraosteoarthropathy, hyperparathyroidism

TURNER SYNDROME

[Henry Hubert Turner (1892–1970), chair of medicine at the University of Oklahoma, secretary and president of the Endocrine Society]

= nondisjunction of sex chromosomes as

(1) Complete monosomy (45,XO)

(2) Partial monosomy (structurally altered 2nd X chromosome)

(3) Mosaicism (XO + another sex karyotype)

Prevalence: 1÷3,000–5,000 livebirths

Associated with: coarctation (20–36% affected), aortic stenosis, horseshoe kidney (most common)

- sexual infantilism (spontaneous puberty in 5–15%):
  - primary amenorrhea
  - absent secondary sex characteristics
- short stature; absence of prepubertal growth spurt
- webbed neck; low irregular nuchal hair line
- shield-shaped chest + widely spaced nipples
- mental deficiency (occasionally); high palate; thyromegaly
- multiple pigmented nevi; keloid formation
- idiopathic hypertension; elevated urinary gonadotropins

@ Cardiovascular
- √ dilatation of ascending aorta (40%)
- √ juxtaductal coarctation / pseudocoarctation of aortic arch (10%); aortic stenosis; bicuspid aortic valve; elongation of aortic arch; partial anomalous pulmonary venous return

@ General
- √ normal skeletal maturation with growth arrest at skeletal age of 15 years
- √ delayed fusion of epiphyses > age 20 years
- √ osteoporosis during / after 2nd decade ← gonadal hormone deficiency
- √ coarctation of aorta (10%); aortic stenosis
- √ renal ectopia / horseshoe kidney
- √ lymphedema

@ Skull
- √ basilar impression; basal angle > 140°
- √ parietal thinning
- √ small bridged sella
- √ hypertelorism

@ Axial skeleton
- √ hypoplasia of odontoid process + C1
- √ osteochondrosis of vertebral plates
- √ squared lumbar vertebrae; kyphoscoliosis
- √ deossification of vertebrae
- √ small iliac wings; late fusion of iliac crests
- √ android pelvic inlet with narrowed pubic arch + small sacrosciatic notches

@ Chest
- √ thinning of lateral aspects of clavicles
- √ thinned + narrowed ribs with pseudonotching

@ Hand + arm
- √ "positive metacarpal" sign = relative shortening of 3rd and 4th metacarpal
- √ "positive carpal" sign = narrowing of scaphoid-lunate-triquetrum angle < 117°
- √ phalangeal preponderance = length of proximal + distal phalanx exceeds length of 4th metacarpal by > 3 mm
- √ shortening of 2nd + 5th middle phalanx (also in Down syndrome)
- √ "drumstick" distal phalanges = slender shaft + large distal head
- √ "insetting" of epiphyses into bases of adjacent metaphyses (phalanges + metacarpals)

√ Madelung deformity = shortening of ulna / absence of ulnar styloid process
√ cubitus valgus = bilateral radial tilt of articular surface of trochlea
√ deossification of carpal bones

@ Knee
√ tibia vara = enlarged medial femoral condyle + depression of medial tibial plateau (DDx: Blount disease)
√ small exostosis-like projection from medial border of proximal tibial metaphysis

@ Foot
√ deossification of tarsal bones
√ shortening of 1st, 4th, and 5th metatarsals
√ pes cavus

US:
√ prepubertal uterus
√ nonvisualized / streaky ovaries (in complete monosomy); normal ovaries (in mosaic karyotype)

OB-US:
√ large nuchal cystic hygroma
√ lymphangiectasia with generalized hydrops
√ symmetrical edema of dorsum of feet
√ CHD (20%): coarctation of aorta (70%), left heart lesions
√ horseshoe kidney

Bonnevie-Ullrich Syndrome

= infantile form of Turner syndrome
(1) Congenital webbed neck
(2) Widely separated nipples
(3) Lymphedema of hands + feet

TURRET EXOSTOSIS

Cause: trauma with formation of subperiosteal hematoma
• immobile, occasionally painful lump on dorsum of finger
• reduced ability to flex finger (= ossified hematoma diminishes excursion of extensor tendon)
Location: dorsum of proximal / middle phalanx of hand
√ smooth dome-shaped extracortical mass

ULNAR COLLATERAL LIGAMENT TEAR

Cause: chronic overuse in throwing / other overhead motion (eg, tennis serving) generating increased valgus stress
• acute onset of sharp / gradual onset of increasing pain in medial elbow
• ulnar nerve dysfunction (40%): pain, paresthesia of forearm + in 4th and 5th digits
√ ossification within ulnar collateral ligament (UCL)
√ loose bodies
√ osteoarthritis of ulnohumeral articulation
√ osteochondritis dissecans of capitellum

√ excessive medial joint opening on stress radiographs
MR (coronal plane):
√ laxity / discontinuity of UCL
√ increased signal intensity of UCL + surrounding tissues
√ poor definition of ligament margins
Rx: rest, application of ice, NSAID, exercise, steroid injections; reconstruction of ligament

ULNAR NEUROPATHY

= GUYON CANAL SYNDROME
= ulnar nerve entrapment / injury at wrist (2nd most common site after elbow)
Cause:
(1) Repetitive continuous pressure on ulnar nerve in sports: cycling (esp. mountain biking), martial arts, racket sport
(2) Exposure to frequent vibration: work in foundry / with pneumatic drills
(3) Adjacent mass: ganglion cyst, lipoma, ulnar artery aneurysm, dislocation of pisiform bone, fracture of hamulus, os hamuli proprium, osteoarthritis of pisotriquetral joint, anomalous muscle (abductor digit minimi, flexor digiti minimi brevis), abnormal tendon (flexor carpi ulnaris)
- tenderness over Guyon canal
- Tinel sign = tingling radiating to 4th + 5th fingers
- reduced strength of grip
- loss of motor function (= zone 2 injury): handlebar palsy
- sensory loss (= zone 3 injury) to hypothenar eminence + 4th finger + part of 5th finger
- combination of motor + sensory function (zone 1 injury): injury proximal to bifurcation of ulnar n.

WILLIAMS SYNDROME

[J. C. P. Williams (1900–????), New Zealand cardiologist]
= IDIOPATHIC HYPERCALCEMIA OF INFANCY
- peculiar elfinlike facies, dysplastic dentition
- neonatal hypercalcemia (not in all patients)
- mental + physical retardation

@ Skeletal manifestations
√ osteosclerosis ← trabecular thickening
√ dense broad zone of provisional calcification
√ radiolucent metaphyseal bands
√ dense vertebral end plates + acetabular roofs
√ bone islands in spongiosa
√ metastatic calcification
√ craniostenosis

@ Cardiovascular manifestations
√ supravalvular aortic stenosis (33%), aortic hypoplasia
√ valvular + peripheral pulmonary artery stenosis
√ ASD, VSD

√ stenoses of major vessels (innominate, carotids, renal aa.)

@ GI and GU tract:

√ colonic diverticula

√ bladder diverticula

Prognosis: spontaneous resolution after 1 year in most

Rx: withhold vitamin D + calcium

DDx: Hypervitaminosis D

CENTRAL NERVOUS SYSTEM

DIFFERENTIAL DIAGNOSIS OF SKULL AND SPINE DISORDERS

BIRTH TRAUMA

1. **Caput succedaneum**
   = localized edema in presenting portion of scalp
   Frequently associated with: microscopic hemorrhage and subcutaneous hyperemia
   Cause: trauma of vaginal delivery
   Location: commonly at vertex
   • soft superficial pitting edema
   √ crosses suture lines
2. **Subgaleal hemorrhage**
   = hemorrhage between *galea aponeurotica* (= central fascia formed by occipitofrontal + temporoparietal muscles) and periosteum of outer table
   • may become symptomatic ← significant blood loss in children
   • firm fluctuant mass increasing in size after birth
   • may dissect into subcutaneous tissue of neck
   • usually resolves over 2–3 weeks
   ◊ Occasionally due to spontaneous decompression of intracranial (epidural) hematoma
3. **Cephalohematoma**
   = traumatic hematoma beneath outer layer of periosteum confined by cranial sutures
   Cause: incorrect application of obstetric forceps / skull fracture during birth
   Prevalence: 1–2% in spontaneous vaginal deliveries; 3–4% in forceps- / vacuum-assisted deliveries
   Location: most commonly parietal
   • firm tense mass; usually increase in size after birth
   • resolution in few weeks to months
   √ crescent-shaped lesion adjacent to outer table of skull
   √ will not cross cranial suture line
   √ usually resolved by a few weeks to 3–4 months
   √ may calcify / ossify causing thickening of diploe ← prolonged resorption (= chronic cephalohematoma)
   MR:
   √ T1- and T2-hyperintense lesion ← subacute hemorrhage
   Cx: infection
4. Skull fracture
   Frequency: 1% of all deliveries
   √ CT shows associated intracranial hemorrhage
5. Subdural hemorrhage
   (a) convexity hematoma

(b) interhemispheric hematoma
(c) posterior fossa hematoma

6. **Benign subdural effusion**
= benign condition that resolves spontaneously
• clear / xanthochromic fluid with elevated protein level
√ extracerebral fluid collection accompanied by ventricular dilatation (= communicating hydrocephalus caused by impaired CSF absorption of these subdural fluid collections)

LOW BACK PAIN

Low Back Pain in Adults

◊ 80% of population experiences lower back pain at some time in their lives
◊ A specific cause is accurately determined in 5–10% of patients with acute symptoms + in 50% with chronic symptoms

Cause: viscerogenic, vascular, psychogenic, neurogenic

(a) spondylogenic / degenerative disease (most prevalent)
Age: 50% at 40 years; > 85% at 80 years
1. Disk herniation
2. Facet disease
3. Acquired stenosis
4. Spondylolisthesis

(b) infectious
1. Diskitis
2. Osteomyelitis

(c) inflammatory
1. Rheumatoid arthritis
2. Ankylosing spondylitis
3. Sacroiliitis

(d) trauma, iatrogenic
(e) congenital: congenital stenosis
(f) metabolic: osteoporosis
(g) neoplastic: primary, metastatic

Low Back Pain in Childhood

Frequency: in 40% of pediatric + adolescent population; structural causes in 12–26%

^{99m}Tc methylene diphosphonate (MDP) SPECT bone scintigraphy with coregistered CT is an important tool in imaging workup of pediatric low back pain, because of its utility in assessment of spondylolysis.

1. Spondylolysis (60–83%)
2. Spondylolisthesis
3. Osteomyelitis, diskitis
4. Leukemia
5. Histiocytosis X
6. Osteoid osteoma, osteoblastoma

7. Facet arthropathy / fracture

Abnormalities of Posterior Elements

1. Spondylolysis
2. Lumbar interspinous bursitis = Baastrup disease
3. Spinous process avulsion / transverse process fracture
4. Facet hypertrophy
5. Osteochondroma

Endplate and Disk Abnormalities

(a) endplate-apophyseal injury
   1. Schmorl node = central disk herniation
   2. Limbus vertebrae

(b) degenerative disk disease

(c) endplate compression fractures

Sacroiliac Abnormalities

1. Bertolotti syndrome
2. Sacroiliac joint syndrome
3. Sacral stress fracture

Lumbosacral Postsurgical Syndrome

= FAILED BACK SURGERY SYNDROME

= signs of dysfunction and disability + pain and paresthesia following surgery

◊ Interpretation in immediate postoperative period difficult, stabilization of findings occurs in 2–6 months

Frequency: failure of improvement in 5–15%

A. OSSEOUS CAUSE

(a) mechanical instability
   1. Spondylolisthesis
   2. Pseudarthrosis

(b) osseous stenosis
   1. Central stenosis
   2. Foraminal stenosis

B. SOFT-TISSUE CAUSES

1. Perioperative intraspinal hemorrhage (onset < 1 week)
2. Residual disk herniation (onset < 1 week)
3. Recurrent disk herniation (onset 1 week – 1 month)
   √ no enhancement on early T1WI (appears enhanced ≥ 30 min post injection)
4. Spinal / meningeal / neural inflammation / infection (onset 1 week – 1 month) = **Postoperative diskitis**
   • elevated ESR + frequently normal WBC count
   √ deceased marrow signal intensity on T1WI
   √ contrast enhancement of disk + adjacent vertebral bodies
5. Intraspinal scar formation (onset > 1 month)
   (a) **Epidural fibrosis** (scarring)

√ enhancing epidural plaque / mass
√ heterogeneous enhancement on early T1WI (maximum at about 5 min post injection) most pronounced within 9 months of surgery

(b) **Fibrosing arachnoiditis** = adhesive arachnoiditis
√ thickened irregular clumped nerve roots
√ adhesion of roots to wall of thecal sac
√ abnormal enhancement of thickened meninges + matted nerve roots

C. SURGICAL ERRORS
1. Wrong level / side of surgery
2. Direct nerve injury

D. Remote phenomena unrelated to spine

mnemonic: ABCDEF
Arachnoiditis
Bleeding
Contamination (infection)
Disk (residual / recurrent / new level)
Error (wrong disk excised)
Fibrosis (scar)

Cauda Equina Syndrome

= constellation of signs + symptoms resulting from compressive lesion in lower lumbar spinal canal

Cause:
(1) Displaced disk fragment
(2) Intra- / extramedullary tumor
(3) Osseous: Paget disease, osteomyelitis, osteoarthrosis of facet joints, complication of ankylosing spondylitis

- diminished sensation in lower lumbar + sacral dermatomes
- wasting + weakness of muscles; decreased ankle reflexes
- impotence; decreased sphincter tone
- disturbed sphincter function + overflow incontinence

SKULL

Lumps & Bumps of Pediatric Skull

A. Congenital Lesions
1. Encephalocele
2. Nasal glioma
3. Dermoid
4. Epidermoid cyst
5. Hemangioma
6. Vascular malformation: venous, lymphatic, sinus pericranii
7. PHACE syndrome

B. Acquired Lesions
1. Rhabdomyosarcoma

2. Fibrosarcoma
2. Langerhans cell histiocytosis
3. Metastatic neuroblastoma
4. Infection: Pott puffy tumor
5. Trauma: cephalohematoma

Sutural Abnormalities

Wide Sutures

= > 10 mm at birth, > 3 mm at 2 years, > 2 mm at 3 years of age; (sutures are splittable up to age 12–15; complete closure by age 30)

A. NORMAL VARIANT
in neonate + prematurity; growth spurts occur at 2–3 years and 5–7 years

B. CONGENITAL UNDEROSSIFICATION
osteogenesis imperfecta, hypophosphatasia, rickets, hypothyroidism, pyknodysostosis, cleidocranial dysplasia

C. METABOLIC DISEASE
hypoparathyroidism; lead intoxication; hypo- / hypervitaminosis A

D. RAISED INTRACRANIAL PRESSURE
Cause:
(1) Intracerebral tumor
(2) Subdural hematoma
(3) Hydrocephalus
Age: seen only if < 10 years of age
Location: coronal > sagittal > lambdoid > squamosal suture

E. INFILTRATION OF SUTURES
Cause: metastases to meninges from
(1) Neuroblastoma
(2) Leukemia
(3) Lymphoma
√ poorly defined margins

F. RECOVERY from
(1) Deprivational dwarfism
(2) Chronic illness
(3) Prematurity
(4) Hypothyroidism

Craniosynostosis

= CRANIOSTENOSIS = premature closure of sutures (closing normally at about 30 years of age)

Age: often present at birth; M÷F = 4÷1

Etiology:

A. PRIMARY CRANIOSYNOSTOSIS

B. SECONDARY CRANIOSYNOSTOSIS
(a) hematologic: sickle cell anemia, thalassemia

(b) metabolic: rickets, hypercalcemia, hyperthyroidism, hypervitaminosis D
(c) bone dysplasia: hypophosphatasia, achondroplasia, metaphyseal dysplasia, mongolism, Hurler disease, skull hyperostosis, Rubinstein-Taybi syndrome
(d) syndromes: Crouzon, Apert, Carpenter, Treacher-Collins, cloverleaf skull, craniotelencephalic dysplasia, arrhinencephaly
(e) microcephaly: brain atrophy / dysgenesis
(f) after shunting procedures

Types:

Sagittal suture most commonly affected followed by coronal suture

1. **Scaphocephaly** = Dolichocephaly (55%): premature closure of sagittal suture (long skull)
2. **Brachycephaly** = Turricephaly (10%): premature closure of coronal / lambdoid sutures (short tall skull)
3. **Plagiocephaly** (7%): unilateral early fusion of coronal + lambdoidal suture (lopsided skull)
4. **Trigonocephaly**: premature closure of metopic suture (forward pointing skull)
5. **Oxycephaly= Acrocephaly**: premature closure of coronal, sagittal, lambdoid sutures (conical skull); most severe form of craniosynostosis
6. **Cloverleaf skull** = Kleeblattschädel: intrauterine premature closure of sagittal, coronal, lambdoid sutures (3-fold bulging skull)

May be associated with: thanatophoric dysplasia

√ sharply defined thickened sclerotic suture margins
√ delayed growth of BPD in early pregnancy

Wormian Bones

[Ole Worm (1558–1654), Professor of Anatomy, Copenhagen]
= intrasutural ossicles in posterior sutures (lambdoid, posterior sagittal, temporosquamosal), normal up to 6 months of age (most frequently)

With > 10 wormian bones an underlying pathologic process should be considered.

mnemonic: PORK CHOPS I

Pyknodysostosis
Osteogenesis imperfecta
Rickets in healing phase
Kinky hair syndrome
Cleidocranial dysostosis
Hypothyroidism / Hypophosphatasia
Otopalatodigital syndrome
Primary acroosteolysis (Hajdu-Cheney) / **P**achydermoperiostosis / **P**rogeria
Syndrome of Down
Idiopathic (normal variant)

Increased Skull Thickness

A. GENERALIZED
1. Chronic severe anemia (eg, thalassemia, sickle cell dz)

2. Cerebral atrophy following shunting of hydrocephalus
3. Engelmann disease: mainly skull base
4. Hyperparathyroidism
5. Acromegaly
6. Osteopetrosis

B. FOCAL
1. Meningioma
2. Fibrous dysplasia
3. Paget disease
4. Dyke-Davidoff-Mason syndrome
5. **Hyperostosis frontalis interna** = dense hyperostosis of inner table of frontal bone; M < F

mnemonic: HIPFAM
Hyperostosis frontalis interna
Idiopathic
Paget disease
Fibrous dysplasia
Anemia (sickle cell disease, iron deficiency, thalassemia, spherocytosis)
Metastases

Hair-on-end Skull

mnemonic: HI NEST
Hereditary spherocytosis
Iron deficiency anemia
Neuroblastoma
Enzyme deficiency: glucose-6-phosphate dehydrogenase deficiency → hemolytic anemia
Sickle cell disease
Thalassemia major

Leontiasis Ossea

= overgrowth of facial bones causing leonine (lionlike) facies
1. Fibrous dysplasia
2. Paget disease
3. Craniometaphyseal dysplasia
4. Hyperphosphatasia

Abnormally Thin Skull

A. GENERALIZED
1. Obstructive hydrocephalus
2. Cleidocranial dysostosis
3. Progeria
4. Rickets
5. Osteogenesis imperfecta
6. Craniolacunia

B. FOCAL
   1. Neurofibromatosis
   2. Chronic subdural hematoma
   3. Arachnoid cyst

Inadequate Calvarial Calcification

1. Achondroplasia
2. Osteogenesis imperfecta
3. Hypophosphatasia

Osteolytic Lesion of Skull

A. NORMAL VARIANT
   1. **Emissary vein**
      connecting venous systems inside + outside of skull
      √ bony channel < 2 mm in width
   2. **Venous lake**
      = outpouching of diploic vein
      √ extremely variable in size, shape, and number
      √ irregular well-demarcated contour
   3. **Fossae lacunae** = pacchionian granulations
      = agglomeration of hypertrophic arachnoid villi communicating with dural sinus
      Age: > 18 months; usually adulthood
      √ usually multiple "punched-out" lesions with irregular contour in parasagittal location
      Location: within 3 cm of superior sagittal sinus, anterior > posterior frontal bone
      Site: inner table > diploe > outer table
   4. **Parietal foramina**
      nonossification of embryonal rests in parietal fissure; bilateral at superior posterior angles of parietal bone; hereditary transmission

B. TRAUMA
   1. Surgical burr hole
   2. Leptomeningeal cyst

C. INFECTION
   1. Osteomyelitis
   2. Hydatid disease
   3. Syphilis
   4. Tuberculosis

D. CONGENITAL
   1. Epidermoid / dermoid
   2. Neurofibromatosis (asterion defect)
   3. Meningoencephalocele
   4. Fibrous dysplasia
   5. Osteoporosis circumscripta of Paget disease

E. BENIGN TUMOR
   1. Hemangioma

2. Enchondroma
3. Brown tumor
4. Eosinophilic granuloma

F. MALIGNANT TUMOR
1. Solitary / multiple metastases
2. Multiple myeloma
3. Leukemia
4. Neuroblastoma

Solitary Lytic Lesion in Skull

mnemonic: HELP MFT HOLE

Hemangioma
Epidermoid / dermoid
Leptomeningeal cyst
Postop, **P**aget disease
Metastasis, **M**yeloma
Fibrous dysplasia
Tuberculosis
Hyperparathyroidism
Osteomyelitis
Lambdoid defect (neurofibromatosis)
Eosinophilic granuloma

Multiple Lytic Lesions in Skull

mnemonic: BAMMAH

Brown tumor
AVM
Myeloma
Metastases
Amyloidosis
Histiocytosis

Lytic Area in Bone Flap

mnemonic: "RATI"

Radiation necrosis
Avascular necrosis
Tumor
Infection

Button Sequestrum

mnemonic: TORE ME

Tuberculosis
Osteomyelitis
Radiation
Eosinophilic granuloma
Metastasis

Epidermoid

Absent Greater Sphenoid Wing

mnemonic: M FOR MARINE

Meningioma
Fibrous dysplasia
Optic glioma
Relapsing hematoma
Metastasis
Aneurysm
Retinoblastoma
Idiopathic
Neurofibromatosis
Eosinophilic granuloma

Absence of Innominate Line

= OBLIQUE CAROTID LINE
= vertical line projecting into orbit (on PA skull film) produced by orbital process of sphenoid

A. CONGENITAL
   1. Fibrous dysplasia
   2. Neurofibromatosis
B. INFECTION
C. TUMOR

Widened Superior Orbital Fissure

mnemonic: A FAN

Aneurysm (internal carotid artery)
Fistula (cavernous sinus)
Adenoma (pituitary)
Neurofibroma

Tumors of Central Skull Base

A. DEVELOPMENTAL
   1. Encephalocele
B. INFECTION / INFLAMMATION
   1. Extension from paranasal sinus / mastoid infection
   2. Complication of trauma
   3. Fungal disease: mucormycosis in diabetic, aspergillosis in immunosuppressed patient
   4. Sinus + nasopharyngeal sarcoidosis
   5. Radiation necrosis
C. BENIGN
   1. Juvenile angiofibroma
   2. Meningioma
   3. Chordoma

4. Pituitary tumor
5. Paget disease
6. Fibrous dysplasia

D. MALIGNANT
1. Metastasis: prostate, lung, breast
2. Chondrosarcoma
3. Nasopharyngeal carcinoma
4. Rhabdomyosarcoma
5. Perineural tumor spread: head + neck neoplasm

Craniofacial Syndromes

= developmental malformations of the face + skull associated with CNS malformations

1. Midfacial clefts
2. Goldenhar syndrome
3. Apert syndrome
4. Crouzon syndrome
5. Treacher-Collins syndrome

MAXILLA AND MANDIBLE

Attenuation (lytic / sclerotic / mixed / ground-glass attenuation), margination (narrow / wide transition zone), and relationship to adjacent teeth determine the radiologic diagnosis of jaw lesions.

Maxillary Hypoplasia

1. Down syndrome
2. Drugs (alcohol, dilantin, valproate)
3. Apert / Crouzon syndrome
4. Achondroplasia
5. Cleft lip / palate

Mandibular Hypoplasia = Micrognathia

A. WITH ABNORMAL EARS
1. Treacher-Collins syndrome
2. Goldenhar syndrome (hemifacial microsomia) = facioauriculovertebral spectrum (x-rays of vertebrae!)
3. Langer-Giedion syndrome (IUGR, protruding ears)

B. ABNORMALITIES OF EARS + OTHER ORGANS
1. Miller syndrome (severe postaxial hand anomalies)
2. Velocardiofacial syndrome (hand + cardiac lesions)
3. Otopalatodigital syndrome - type II (hand abnormalities)
4. Stickler syndrome (ear anomalies not severe)
5. Pierre-Robin syndrome (large fleshy ears)

C. NO EAR ANOMALIES
1. Pyknodysostosis

D. OTHERS

1. Seckel syndrome (bird-headed dwarfism)
2. Multiple pterygium syndrome
3. Pena-Shokeir syndrome
4. Beckwith-Wiedemann syndrome
5. Arthrogryposis
6. Skeletal dysplasias
7. Trisomy 13, 18, 9 (abnormal karyotype in 25%)

Destruction of Temporomandibular Joint

mnemonic: HIRT

Hyperparathyroidism
Infection
Rheumatoid arthritis
Trauma

Mandibular Lesion by Location

A. Anterior mandible
   1. Adenomatoid odontogenic tumor
   2. Periapical cemental dysplasia
   3. Florid cemento-osseous dysplasia
   4. Central giant cell granuloma
   5. Odontoma
B. Posterior mandible
   1. Follicular (dentigerous) cyst
   2. Odontogenic keratocyst
   3. Solitary bone cyst
   4. Ameloblastoma
   5. Cementoblastoma
   6. Ossifying fibroma
   7. Ameloblastic carcinoma
   8. Stafne cyst
   9. Metastasis
C. Nonspecific location
   1. Periapical (radicular) cyst

Odontogenic Lesion Of Impacted 3rd Molar Tooth

1. Dentigerous cyst (93%)
2. Odontogenic keratocyst (7%)
3. Ameloblastoma (0.41%)

Solid Benign Lesion of Jaw

Primary Odontogenic Tumor of Jaw

1. Odontoma
2. Ameloblastoma = Adamantinoma of Jaw
3. Odontogenic Myxoma

4. Calcifying Epithelial Odontogenic Tumor
5. Cementoblastoma
6. Ameloblastic fibroma
7. Adenomatoid odontogenic tumor

Primary Nonodontogenic Tumor of Jaw

1. Ossifying fibroma
2. Cemento-osseous dysplasia

Prevalence of Solid Benign Mandibular Lesions

A. Most common
   1. Odontoma
B. Fairly common
   1. Ameloblastoma
   2. Periapical cemento-osseous dysplasia
   3. Florid cemento-osseous dysplasia
   4. Ossifying fibroma
C. Less common
   1. Calcifying epithelial odontogenic (Pindborg) tumor
   2. Ameloblastic fibroma
   3. Odontogenic myxoma
   4. Cementoblastoma
D. Rare
   1. Adenomatoid odontogenic tumor
   2. Juvenile ossifying fibroma
   3. Clear cell odontogenic tumor
   4. Squamous odontogenic tumor
   5. Calcifying odontogenic cyst

Vascular Lesion of Jaw

1. Central giant cell granuloma
2. Brown tumor of hyperparathyroidism
3. Arteriovenous Malformation of jaw

Solid Malignant Lesion of Jaw

1. Odontogenic Carcinoma
   = rare aggressive intraosseous lesion
   Histo: poorly differentiated epithelial + clear cells
   √ diffuse honeycomb-like radiolucent lesion
   √ surrounding cortical destruction
   Prognosis: high rate of recurrence
2. Ameloblastic Carcinoma
   = malignant ameloblastoma
   √ aggressive features of cortical destruction, extraosseous extension, extensive solid components
3. Sarcoma

Histo: osteo~, chondro~, fibro~, leiomyosarcoma
√ symmetrically widened periodontal membrane in a single tooth (earliest sign of osteogenic sarcoma of mandible)

4. Mucoepidermoid Carcinoma
   ◊ typically originate from minor salivary glands of buccal mucosa
5. Lymphoma / leukemia
6. Multiple Myeloma
   • may present with chin numbness ← involvement of inferior alveolar nerve

Prevalence of Solid Malignant Mandibular Lesions

A. Most common
   1. Squamous cell carcinoma arising from adjacent mucosa
B. Fairly common
   1. Multiple myeloma, plasmacytoma
   2. Lymphoma, leukemia
   3. Metastasis
   4. Mucoepidermoid carcinoma arising from adjacent mucosa
   5. Adenoid cystic carcinoma arising from adjacent mucosa
C. Rare
   1. Nonodontogenic sarcoma
   2. Odontogenic carcinoma
   3. Odontogenic sarcoma
   4. Odontogenic carcinosarcoma

Sclerotic Lesion of Jaw

Sclerotic Tooth-Related Jaw Lesion

1. Cementoblastoma
2. Cemento-osseous dysplasia
3. Condensing osteitis
4. Odontoma
5. Idiopathic osteosclerosis
6. **Hypercementosis**
   = bulbous enlargement of a root
   (a) idiopathic
   (b) associated with Paget disease

Sclerotic Non–Tooth-Related Jaw lesion

1. Osteoma
2. Torus = exostosis
3. Benign fibro-osseous lesions
   (a) Ossifying fibroma: young adult; mandible > maxilla
   (b) Monostotic fibrous dysplasia: M < F; younger patient
   √ near apex of nonvital tooth
4. Paget disease
   involvement of jaw in 20%; maxilla > mandible

Location: bilateral, symmetric involvement
√ widened alveolar ridges
√ flat palate
√ loosening of teeth
√ hypercementosis
√ may cause destruction of lamina dura

5. Sclerosing metastasis / multiple myeloma

Jaw Lesion with Ground-glass Attenuation

(a) diffuse
1. Renal osteodystrophy
2. Fibrous dysplasia

(b) multifocal
1. Florid cemento-osseous dysplasia
2. Multiple ossifying fibromas
3. Brown tumor of HPT

(c) unifocal jaw lesion with ground-glass attenuation
(1) Ossifying fibroma
Path: osteoblastic rim
√ narrow zone of transition
(2) Monostotic fibrous dysplasia
√ wide zone of transition
√ longitudinal growth pattern
√ nondisplaced teeth

PERIAPICAL SCLEROTIC LESION WITH PERIAPICAL HALO

1. Cementoblastoma
2. Cemento-osseous dysplasia

Mixed Lytic and Sclerotic Jaw Lesion

1. Osteoradionecrosis
Vulnerability: mandible > maxilla buccal > lingual cortex
◊ Chin + angle of mandible spared ← muscle insertions
√ area of marked osteosclerosis
√ loss of trabeculation in spongiosa
√ cortical interruptions + fragmentation
√ poorly marginated areas of soft-tissue attenuation + fluid collections + gas attenuation
√ sequestration
2. Biphosphonate-related osteonecrosis of jaw (BRONJ)
3. Mandibular osteomyelitis
Cause: caries, extractions, fracture, osteoradionecrosis
√ cortical interruption
√ sclerotic sequestra in low-attenuation zones
√ periosteal new bone formation
√ areas of gas attenuation
4. Primary chronic osteomyelitis

Age peak: childhood and > 50 years
- insidious jaw swelling, normal mucosa, vital teeth
- absence of fever + leukocytosis

√ poorly marginated lesion with progressive sclerosis
√ scattered osteolysis + bone expansion
√ "onion skin" periosteal reaction

Radiolucent Lesion of Mandible

Sharply Marginated Radiolucent Lesion of Mandible

A. around apex of tooth
   1. Radicular cyst
   2. Cementoma

B. around unerupted tooth
   1. Dentigerous cyst
   2. Ameloblastoma

C. unrelated to tooth
   1. Simple bone cyst
   2. Fong disease
   3. Basal cell nevus syndrome

DDx: (1) Early cemento-osseous dysplasia
(2) Early ossifying fibroma

Poorly Marginated Radiolucent Lesion of Mandible

√ "floating teeth": suggestive of primary / secondary malignancy
√ resorption of tooth root: hallmark of benign process

A. INFECTION

Cause: mostly dental caries → irreversible pulpitis → periapical cyst → granuloma → abscess

1. Apical periodontitis
   √ thickened periodontal ligament space (earliest sign of the cystic form)
   √ contrast-enhancing rim around abscess
2. Osteomyelitis
   = infection of bone and marrow
   √ focal / diffuse radiolucent / radiopaque lesion

B. RADIOTHERAPY

1. Osteoradionecrosis
   √ scattered sclerotic + lytic lesion
   √ enlarged trabecular spaces
   √ sequestered bone

C. MALIGNANT NEOPLASM

1. Osteosarcoma (⅓ lytic, ⅓ sclerotic, ⅓ mixed)
2. Local invasion from gingival / buccal neoplasms (more common)
3. Metastasis from breast, lung, kidney in 1% (in 70% adenocarcinoma)
   Location: posterior body and angle ← increased marrow vascularity

D. OTHER
1. Eosinophilic granuloma: "floating tooth"
2. Fibrous dysplasia
3. Osteocementoma
4. Ossifying fibroma (very common)

Cystic Lesion of Jaw

1. **Periapical cyst = Radicular cyst**

◊ Most common cyst of the jaw

Cause: periapical inflammatory lesion ← pulpal necrosis in deep carious lesion / deep filling / trauma

Age: 30–50 years

Pathogenesis: secondary apical periodontitis → granuloma → abscess → cyst

Site: intimately associated with apex of nonvital tooth

√ round / pear-shaped unilocular well-defined periapical lucent lesion, usually < 1 cm in diameter

√ bordered by thin sclerotic rim of cortical bone

√ ± displacement of adjacent teeth

√ ± mild root resorption

Cx: root canal therapy, tooth extraction, surgery (creation of mucoperiosteal flap over tooth apex)

DDx: periapical granuloma, periapical abscess

2. **Dentigerous cyst = follicular cyst**

◊ Most common type of noninflammatory developmental odontogenic cyst

Path: epithelial-lined cyst from odontogenic epithelium developing around crown of an unerupted tooth

Histo: fluid collection between follicular epithelium and crown of tooth

Age: 30–40 years

• typically painfree

Location: mandible, maxilla (may expand into maxillary sinus)

Site: around crown of unerupted tooth (usually 3rd molar)

√ expansile cystic pericoronal lesion containing the crown of an impacted tooth projecting into cystic cavity (PATHOGNOMONIC)

√ roots of tooth often outside lesion

√ well-defined round / ovoid corticated lucent lesion ± mandibular remodeling rather than expansion

Cx: may degenerate into mural ameloblastoma (rare)

DDx: unilocular odontogenic keratocyst

3. **Odontogenic keratocyst** (OKC)

Origin: dental lamina + other sources of odontogenic epithelium

Prevalence: 5–15% of all jaw cysts

Age: 2nd–4th decade

Associated with: basal cell nevus (Gorlin-Goltz) syndrome if OKC multiple

Path: daughter cysts + nests of cystic epithelia in vicinity (high rate of recurrence)

Histo: parakeratinized lining epithelium + "cheesy" material in lumen of lesion

Location: body + ramus of mandible (most often); may be anywhere in mandible / maxilla
√ unilocular lucent lesion with smooth corticated border
√ often associated with impacted tooth
√ ± undulating borders / multilocular appearance (daughter cysts)
√ ± cortical thinning / erosion, tooth displacement, root resorption
Prognosis: high recurrence rate after resection
DDx: indistinguishable from dentigerous cyst (no cortical erosion or expansion) / ameloblastoma

4. **Primordial cyst**
arising from follicle of tooth that never developed
Cause: dental follicle undergoes cystic degeneration
√ well-defined radiolucent nonexpansile lesion

5. **Stafne Cyst**
= Static bone cavity = LINGUAL SALIVARY GLAND INCLUSION DEFECT
= well-defined depression in lingual surface of mandible
Path: cavity filled with fat ± aberrant submandibular gland tissue
• asymptomatic
Location: posterior mandible, usually near mandibular angle
Site: just above inferior border of mandible, anterior to angle of jaw, inferior to mandibular canal, posterior to 3rd molar
√ oval / round / rectangular well-defined radiolucent lesion within cortical defect
√ typically < 2 cm
√ border surrounded by an opaque line
√ may extend to buccal cortex
DDx: arteriovenous malformation

6. **Solitary bone cyst**
= TRAUMATIC BONE CYST = SIMPLE BONE CYST = HEMORRHAGIC BONE CYST
= not a true cyst for lack of epithelial lining
Pathogenesis: trauma → intramedullary hemorrhage → resorption
Age: 2nd decade
• asymptomatic
Location: marrow space of posterior mandible
√ unilocular sharply marginated lucent defect
√ CHARACTERISTIC scalloped superior margin with fingerlike projections extending between roots of adjacent teeth
√ ± thinning of mandibular cortex ± osseous expansion
DDx: vascular lesion, central giant cell granuloma, ossifying fibroma

7. Residual cyst
= any cyst that remains after surgical intervention

Periapical Lucency

1. Periapical cyst
2. Periapical cemento-osseous dysplasia
3. Hyperparathyroidism

4. Langerhans cell histiocytosis
5. Odontogenic keratocyst
6. Leukemia / lymphoma

Prevalence of Cystic Mandibular Lesion of Jaw

A. Most common
   1. Periapical (radicular) cyst
   2. Follicular (dentigerous) cyst)
B. Fairly Common
   1. Odontogenic keratocyst
   2. Stafne cyst
   3. Solitary bone cyst
C. Rare
   1. Aneurysmal bone cyst
   2. Calcifying odontogenic cyst
D. Lesions radiolucent ONLY early in their development

> Periapical inflammatory lesions are entirely radiolucent. So are early ossifying fibromas or early cemento-osseous dysplasia (the latter associated with a vital tooth + intact lamina dura ± central calcifications)

   1. Cemento-osseous dysplasia
   2. Ossifying fibroma (= pure osteoid matrix)

UNILOCULAR CYSTIC LESION OF JAW

1. Radicular cyst: surrounding apex of infected tooth
2. Dentigerous cyst: adjacent to unerupted tooth

CRANIOVERTEBRAL JUNCTION

Craniovertebral Junction Anomaly

mnemonic: PF ROACH

Paget disease
Fibrous dysplasia
Rheumatoid arthritis, **R**ickets
Osteogenesis imperfecta, **O**steomalacia
Achondroplasia
Cleidocranial dysostosis, **C**hiari malformation
Hyperparathyroidism

Cx: compression of brainstem
(a) → aqueductal stenosis → hydrocephalus
(b) → cord edema, syrinx

Rx: surgical decompression of posterior cranial fossa / foramen magnum (posterior approach); resection of odontoid (anterior approach)

Basilar Invagination

= congenital primary developmental anomaly with abnormally high position of vertebral

column prolapsing into skull base ← bone softening

Associated with: Chiari malformation, syringohydromyelia in 25–35%

Cause: mnemonic: MACKO

Mucopolysaccharidosis
Achondroplasia
Cleidocranial dysostosis
Klippel-Feil syndrome
Osteogenesis imperfecta

• limitation in range of motion of CVJ

√ abnormal craniometry:

1. Condylus tertius = ossicle at distal end of clivus
   √ pseudojoint with odontoid process / anterior arch of C1
2. Condylar hypoplasia
   √ lateral masses of atlas may be fused to condyles
   √ violation of Chamberlain line
   √ widening of atlanto-occipital joint axis angle
   √ tip of odontoid > 10 mm above bimastoid line
3. Basiocciput hypoplasia
   √ shortening of clivus
   √ violation of Chamberlain line
   √ clivus-canal angle typically decreased
4. Atlanto-occipital assimilation
   = complete / partial failure of segmentation between skull + 1st cervical vertebra
   √ violation of Chamberlain line
   √ clivus-canal angle decreased
   May be associated with: fusion of C2 + C3
   Cx: atlantoaxial subluxation (50%); sudden death

√ C-spine + foramen magnum bulge into cranial cavity

√ elevation of posterior arch of C1

Basilar Impression

= acquired form of basilar invagination with bulging of C-spine and foramen magnum into cranial cavity with normal bone

√ tip of odontoid process protrudes upward through foramen magnum into cranium = projects > 5 mm above Chamberlain line (= line between hard palate + opisthion)

Cause: mnemonic: HORRIFic P

Hyperparathyroidism
Osteomalacia
Rickets
Rheumatoid arthritis
Infection of skull base
Fibrous dysplasia
Paget disease

Platybasia

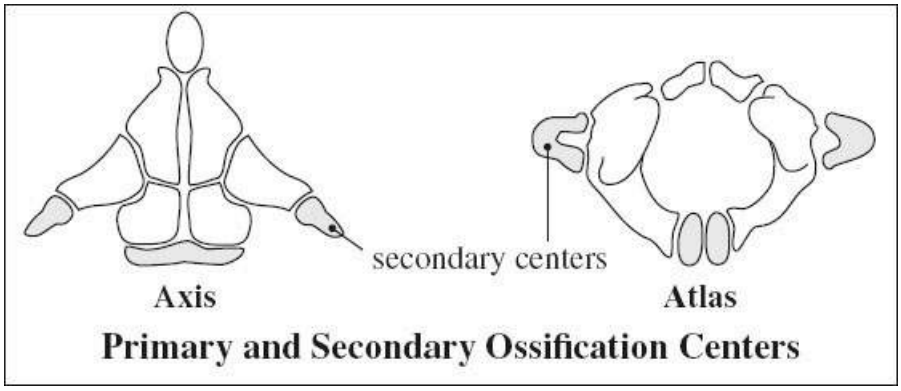
= anthropometric term referring to flattening of skull base
May be associated with: basilar invagination
• cord symptoms
√ craniovertebral = clivus-canal angle becomes acute (< 150°)
√ Welcher basal angle = sphenoid angle > 140–145°
√ bowstring deformity of cervicomedullary junction

ATLAS AND AXIS

Atlas Anomalies

A. POSTERIOR ARCH ANOMALIES
1. Posterior atlas arch rachischisis (4%)
Location: midline (97%); lateral through sulcus of vertebral artery (3%)
√ absence of arch-canal line (LAT view)
√ superimposed on odontoid process / axis body simulating a fracture (open-mouth odontoid view)
2. Total aplasia of posterior atlas arch
3. Keller-type aplasia with persistence of posterior tubercle
4. Aplasia with uni- / bilateral remnant + midline rachischisis
5. Partial / total hemiaplasia of posterior arch

B. ANTERIOR ARCH ANOMALIES
1. Isolated anterior arch rachischisis (0.1%)
2. Split atlas = anterior + posterior arch rachischisis
√ plump rounded anterior arch overlapping the odontoid process making identification of predental space impossible (LAT view)
√ duplicated anterior margins (LAT view)



Primary and Secondary Ossification Centers

Axis Anomalies

1. Persistent ossiculum terminale = Bergman ossicle
√ unfused odontoid process > 12 years of age
DDx: type 1 odontoid fracture
2. Odontoid aplasia (extremely rare)
3. Os odontoideum
= independent os cephalad to axis body in location of odontoid process

√ absence of odontoid process
√ anterior arch of atlas hypertrophic + situated too far posterior in relation to axis body
Cx: atlantoaxial instability
DDx: type 2 odontoid fracture (uncorticated margin)

Odontoid Erosion

mnemonic: P LARD
Psoriasis
Lupus erythematosus
Ankylosing spondylitis
Rheumatoid arthritis
Down syndrome

Atlantoaxial Subluxation

= displacement of atlas with respect to axis
(1) Posterior atlantoaxial subluxation (rare)
(2) Anterior atlantoaxial subluxation (common)
= distance between dens + anterior arch of C1 (measurement along midplane of atlas on lateral view):
(a) predental space: > 2.5 mm > 4.5 mm (in children)
(b) retrodental space: < 18 mm

Causes of subluxation:

A. Congenital
1. Occipitalization of atlas
0.75% of population; fusion of basion + anterior arch of atlas
2. Congenital insufficiency of transverse ligament
3. Os odontoideum / aplasia of dens
4. Down syndrome (20%)
5. Morquio syndrome
6. Bone dysplasia

B. Arthritis
due to laxity of transverse ligament or erosion of dens
1. Rheumatoid arthritis
2. Psoriatic arthritis
3. Reiter syndrome
4. Ankylosing spondylitis
5. SLE
rare: in gout + CPPD

C. Inflammatory process
pharyngeal infection in childhood, retropharyngeal abscess, coryza, otitis media, mastoiditis, cervical adenitis, parotitis, alveolar abscess
√ dislocation 8–10 days after onset of symptoms

D. Trauma (very rare without odontoid fracture)

E. Marfan disease

mnemonic: JAP LARD

Juvenile rheumatoid arthritis
Ankylosing spondylitis
Psoriatic arthritis
Lupus erythematosus
Accident (trauma)
Retropharyngeal abscess, **R**heumatoid arthritis
Down syndrome

Pseudosubluxation of Cervical Spine

= ligamentous laxity in infants allows for movement of the vertebral bodies on each other, esp. C2 on C3

SPINAL DYSRAPHISM

= abnormal / incomplete fusion of midline embryologic mesenchymal, neurologic, bony structures

External signs (in 50%):

- subcutaneous lipoma
- hypertrichosis
- pigmented nevi
- pathologic plantar response
- bladder + bowel dysfunction
- spastic gait disturbance
- foot deformities
- absent tendon reflexes
- sinus tract
- skin dimple

Spina Bifida

= incomplete closure of bony elements of the spine (lamina + spinous processes) posteriorly

Spina Bifida Occulta

= OCCULT SPINAL DYSRAPHISM

= cleft / tethered cord WITH skin cover

Frequency: 15% of spinal dysraphism

- rarely leads to neurologic deficit in itself

Associated with:

(a) vertebral defect (85 – 90%)

(b) lumbosacral dermal lesion (80%):

- hairy tuft (= hypertrichosis), dimple, sinus tract, nevus, hyperpigmentation, hemangioma, subcutaneous mass

1. Diastematomyelia
2. Lipomeningocele
3. Tethered cord syndrome
4. Filum terminale lipoma
5. Intraspinal dermoid

6. Epidermoid cyst
7. Myelocystocele
8. Split notochord syndrome
9. Meningocele
10. Dorsal dermal sinus
11. Tight filum terminale syndrome

Spina Bifida Aperta

= SPINA BIFIDA CYSTICA

= posterior protrusion of all / parts of the contents of the spinal canal through a bony spinal defect

Frequency: 85% of spinal dysraphism

Associated with: hydrocephalus, Arnold-Chiari II malformation

◊ Most severe form of midline fusion defect

• neural placode WITHOUT skin cover

Associated with: neurologic deficit in > 90%

1. Simple meningocele
   = herniation of CSF-filled sac without neural elements
2. Myelocele
   = midline plaque of neural tissue lying exposed at the skin surface
3. Myelomeningocele
   = a myelocele elevated above skin surface by expansion of subarachnoid space ventral to neural plaque
4. Myeloschisis
   = surface presentation of neural elements completely uncovered by meninges

Caudal Spinal Anomalies

= malformation of distal spine and cord

Associated with: hindgut, renal, genitourinary anomalies

1. Terminal myelocystocele
2. Lateral meningocele
3. Caudal regression

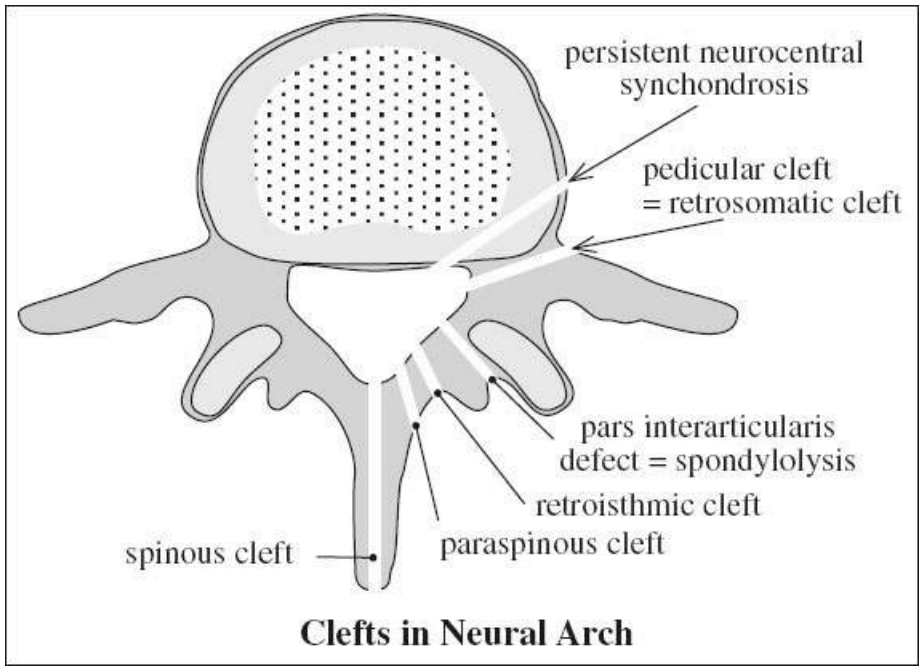
Segmentation Anomalies of Vertebral Bodies

during 9th–12th week of gestation two ossification centers form for the ventral + dorsal half of vertebral body

1. **Asomia** = agenesis of vertebral body
   √ complete absence of vertebral body
   √ hypoplastic posterior elements may be present
2. **Hemivertebra**
   (a) Unilateral wedge vertebra
   √ right / left hemivertebra
   √ scoliosis at birth
   (b) Dorsal hemivertebra
   √ rapidly progressive kyphoscoliosis

(c) Ventral hemivertebra (extremely rare)

3. **Coronal cleft**
   = failure of fusion of anterior + posterior ossification centers
   May be associated with: premature male infant, Chondrodystrophia calcificans congenita
   Location: usually in lower thoracic + lumbar spine
   √ vertical radiolucent band just behind midportion of vertebral body; disappears mostly by 6 months of life
4. **Butterfly vertebra**
   = failure of fusion of lateral halves ← persistence of notochordal tissue
   May be associated with: anterior spina bifida ± anterior meningocele
   √ widened vertebral body with butterfly configuration (AP view)
   √ adaptation of vertebral endplates of adjacent vertebral bodies
5. **Block vertebra**



Clefts in Neural Arch

   = congenital vertebral fusion
   Location: lumbar / cervical
   √ height of fused vertebral bodies equals the sum of heights of involved bodies + intervertebral disk
   √ "waist" at level of intervertebral disk space
6. Hypoplastic vertebra
7. Klippel-Feil syndrome

VERTEBRAL BODY

Increased T1 Signal Intensity of Spinal Bone Marrow

= mostly benign

A. FOCAL

1. Hemangioma (11%)
2. Modic type 2 endplate changes
3. Lipoma
4. Paget disease (later stage)
5. Hemorrhage (with fracture)
6. Melanoma

B. DIFFUSE / multifocal
1. Normal variant
2. S/P radiation treatment
3. Osteoporosis
4. Multiple hemangiomas
5. Spondyloarthritis
6. Anorexia nervosa

Decreased T1 Signal Intensity of Spinal Bone Marrow

= equal to / lower than SI of muscle

A. CENTERED ON ENDPLATE
1. Modic type 1 + 3 endplate changes
2. Osteomyelitis
3. Amyloid

B. CENTERED IN VERTEBRAL BODY
1. Malignancy (metastasis, lymphoma, plasma cell dyscrasia, solitary plasmacytoma, multiple myeloma)
2. Fracture
3. Hemangioma (rare presentation)
4. Fibrous dysplasia

C. CENTERED IN POSTERIOR ELEMENTS METASTASES, MYELOMA, LYMPHOMA, FRACTURE, PRIMARY BONE TUMOR

D. DIFFUSE / MULTIFOCAL
1. Hematopoietic hyperplasia
   (a) chronic anemia: sickle cell disease, thalassemia, hereditary spherocytosis
   (b) chronic illness: HIV
   (c) heavy smoking
   (d) obesity
   (e) drugs: granulocyte-colony-stimulating factor, erythropoietin
2. Neoplasm
   √ avid enhancement
3. Renal osteodystrophy
4. Systemic inflammation: sarcoidosis, gout, spondyloarthropathy
4. Hematologic malignancy: myelofibrosis. mastocytosis

Destruction of Vertebral Body

A. NEOPLASM
1. Metastasis
2. Primary neoplasm: chordoma, chondrosarcoma, lymphoma, multiple myeloma

B. INFECTION
1. Pyogenic vertebral osteomyelitis
2. Tuberculous spondylitis
3. Brucellosis
4. Fungal disease
5. Echinococcosis
6. Sarcoidosis

Granulomatous Spondylitis
1. TB
2. Brucellosis
3. Sarcoidosis

Gas in Vertebral Body
1. Osteonecrosis = Kümmell disease
   √ linear collection
2. Osteomyelitis
   √ small gas bubbles ± extension into adjacent soft-tissues
3. Intraosseous displacement of cartilaginous / Schmorl node
   √ branching gas pattern
4. Malignancy

Small Vertebral Body
1. Radiation therapy
   during early childhood in excess of 1,000 rad
2. Juvenile rheumatoid arthritis
   Location: cervical spine
   √ atlantoaxial subluxation may be present
   √ vertebral fusion may occur
3. Eosinophilic granuloma
   Location: lumbar / lower thoracic spine
   √ compression deformity / vertebra plana
4. Gaucher disease
   = deposits of glucocerebrosides within RES
   √ compression deformity
5. **Platyspondyly generalisata**
   = flattened vertebral bodies associated with many hereditary systemic disorders: achondroplasia, spondyloepiphyseal dysplasia tarda, mucopolysaccharidosis, osteopetrosis, neurofibromatosis, osteogenesis imperfecta, thanatophoric dwarfism
   √ disk spaces of normal height

Vertebra Plana
mnemonic: FETISH
Fracture (trauma, osteogenesis imperfecta)
Eosinophilic granuloma (Langerhans cell histiocytosis)
Tumor (metastatic neuroblastoma, myeloma, leukemia, aneurysmal bone cyst, Ewing

sarcoma)
Infection
Steroids (avascular necrosis)
Hemangioma

mnemonic: MELT
Metastasis / **M**yeloma
Eosinophilic granuloma
Lymphoma
Trauma / **T**B

SIGNS OF ACUTE VERTEBRAL COLLAPSE ON MR

1. Osteoporosis
   √ retropulsion of posterior bone fragment
2. Malignancy
   √ epidural soft-tissue mass
   √ no residual normal marrow signal intensity
   √ abnormal enhancement

Enlarged Vertebral Body

1. Paget disease
   √ "picture framing"; bone sclerosis
2. Gigantism
   √ increase in height of body + disk
3. Myositis ossificans progressiva
   √ bodies greater in height than width
   √ osteoporosis
   √ ossification of ligamentum nuchae

Enlarged Intervertebral Foramen

= NEUROFORAMINAL WIDENING = DUMBBELL-SHAPED / HOURGLASS LESION

A. SOLID BENIGN
   1. Benign peripheral nerve sheath tumor (PNST):
      › Neurofibroma
      › Neurilemmoma = schwannoma
   2. Meningioma
   3. Extradural cavernous hemangioma
   4. Congenital absence / hypoplasia of pedicle

B. SOLID MALIGNANT
   1. Metastatic destruction of pedicle: neuroblastoma
   2. Malignant PNST
   3. Ewing sarcoma / primitive neuroectodermal tumor
   4. Solitary bone plasmacytoma
   5. Chondrosarcoma

C. CYSTIC
   1. Dural ectasia (Marfan syndrome, Ehlers-Danlos syndrome)

2. Synovial cyst
3. Traumatic pseudomeningocele
4. Arachnoid cyst
5. Hydatid cyst

Cervical Spine Fusion

mnemonic: SPAR BIT

Senile hypertrophic ankylosis (DISH)
Psoriasis, **P**rogressive myositis ossificans
Ankylosing spondylitis
Reiter disease, **R**heumatoid arthritis (juvenile)
Block vertebra (Klippel-Feil)
Infection (TB)
Trauma

Vertebral Border Abnormality

Straightening of Anterior Border

1. Ankylosing spondylitis
2. Paget disease
3. Psoriatic arthritis
4. Reiter disease
5. Rheumatoid arthritis
6. Normal variant

Anterior Scalloping of Vertebrae

1. Aortic aneurysm
2. Lymphadenopathy
3. Tuberculosis
4. Multiple myeloma (paravertebral soft-tissue mass)

Posterior Scalloping of Vertebrae

in conditions associated with dural ectasia

A. INCREASED INTRASPINAL PRESSURE
    1. Communicating hydrocephalus
    2. Ependymoma
B. MESENCHYMAL TISSUE LAXITY (**dural ectasia**)
    1. Neurofibromatosis
    2. Marfan syndrome
    3. Ehlers-Danlos syndrome
    4. Posterior meningocele
C. BONE SOFTENING
    1. Mucopolysaccharidoses: Hurler, Morquio, Sanfilippo
    2. Achondroplasia
    3. Acromegaly (lumbar vertebrae)
    4. Ankylosing spondylitis (lax dura acting on osteoporotic vertebrae)

mnemonic: SALMON
Spinal cord tumor
Achondro**P**lasia
Mucopolysaccharidosis
Osteogenesis imperfecta
Neurofibromatosis

mnemonic: DAMN MALE SHAME
Dermoid
Ankylosing spondylitis
Meningioma
Neurofibromatosis
Marfan syndrome
Acromegaly
Lipoma
Ependymoma
Syringohydromyelia
Hydrocephalus
Achondroplasia
Mucopolysaccharidoses
Ehlers-Danlos syndrome

Bony Outgrowths from Vertebra

A. CHILDHOOD
1. Hurler syndrome = gargoylism
   √ rounded appearance of vertebral bodies
   √ mild kyphotic curve with smaller vertebral body at apex of kyphosis displaying tonguelike beak at anterior half (usually at T12 / L1)
   √ "step-off" deformities along anterior margins
2. Hunter syndrome
   less severe changes than in Hurler syndrome
3. Morquio disease
   √ flattened + widened vertebral bodies
   √ anterior "tonguelike" elongation of central portion of vertebral bodies
4. Hypothyroidism = cretinism
   √ small flat vertebral bodies
   √ anterior "tonguelike" deformity (in children only)
   √ widened disk spaces + irregular endplates

B. ADULTS
1. Spondylosis deformans
   √ osteophytosis along anterior + lateral aspects of endplates with horizontal + vertical course ← shearing of outer annular fibers (Sharpey fibers connecting annulus fibrosus to adjacent vertebral body)
2. Diffuse idiopathic skeletal hyperostosis (DISH)
   √ flowing calcifications + ossifications along anterolateral aspect of > 4 contiguous thoracic vertebral bodies ± osteophytosis

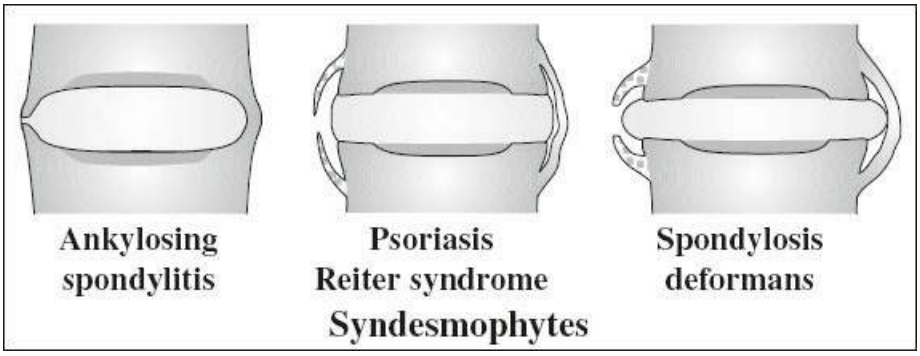
3. Ankylosing spondylitis
   √ bilateral symmetric syndesmophytes (= ossification of annulus fibrosus)
   √ "bamboo spine"
   √ "diskal ballooning" = biconvex intervertebral disks ← osteoporotic deformity of endplates
   √ straightening of anterior margins of vertebral bodies ← erosions
   √ ossification of paraspinal ligaments
4. Fluorosis
   √ vertebral osteophytosis + hyperostosis
   √ sclerotic vertebral bodies + kyphoscoliosis
   √ calcification of paraspinal ligaments
5. Acromegaly
   √ increase in anteroposterior diameter of vertebrae + concavity on posterior portion
   √ enlargement of intervertebral disk
6. Hypoparathyroidism
7. Neuropathic arthropathy
8. Sternoclavicular hyperostosis

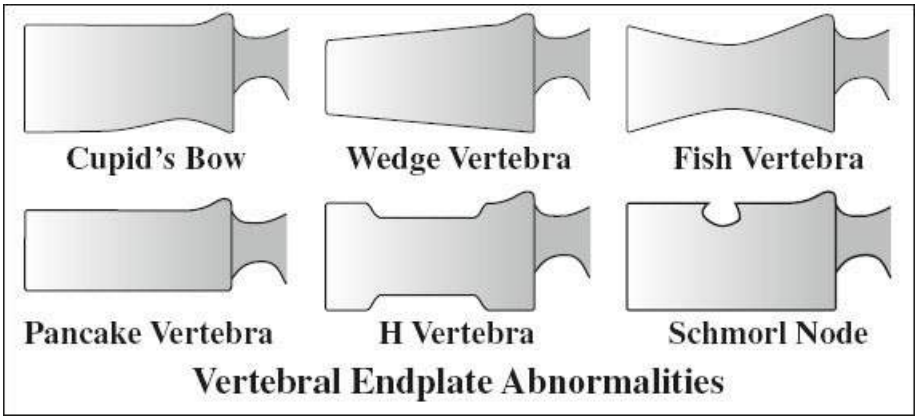
Spine Ossification

1. Syndesmophyte = ossification of annulus fibrosus
   √ thin slender vertical outgrowth extending from margin of one vertebral body to next
   Associated with: ankylosing spondylitis, ochronosis
2. Osteophyte
   = ossification of anterior longitudinal ligament
   √ initially triangular outgrowth several millimeters from edge of vertebral body
   Associated with: osteoarthritis
3. Flowing anterior ossification
   = ossification of disk, anterior longitudinal ligament, paravertebral soft tissues
   Associated with: DISH
4. Paravertebral ossification
   √ initially irregular / poorly defined paravertebral ossification eventually merging with vertebral body
   Associated with: psoriatic arthritis, Reiter syndrome

Vertebral Endplate Abnormality

1. Cupid's bow vertebra
   Cause: ? (normal variant)
   Location: 3rd–5th lumbar vertebra
   √ two parasagittal posterior concavities on inferior aspect of vertebral body (best viewed on AP)
2. Osteoporosis (senile / steroid-induced)
   (a) "fish vertebra / fish-mouth vertebra"





Cause: osteoporosis, osteomalacia, Paget disease, osteogenesis imperfecta, multiple myeloma, hyperparathyroidism, Gaucher disease

√ biconcave vertebra

√ bone sclerosis along endplates

(b) wedge-shaped vertebra

√ anterior border height reduced by > 4 mm compared to posterior border height

(c) "pancake" vertebra

√ overall flattening of vertebra

3. "H-vertebra"
   = compression of central portions ← subchondral infarcts
   Cause: sickle cell + other anemias, Gaucher disease
4. Schmorl / cartilaginous node
   = intraosseous herniation of nucleus pulposus at center of weakened endplate
   Cause: Scheuermann disease, trauma, hyperparathyroidism, osteochondrosis
5. Butterfly vertebra
   Cause: congenital defect
6. Limbus vertebrae
   = intraosseous herniation of disk material at junction of vertebral bony rim of centra + endplate (anterosuperior corner)
7. "Rugger-jersey spine"
   Cause: hyperparathyroidism, myelofibrosis
   √ horizontal sclerosis subjacent to vertebral endplates with intervening normal osseous density (resembling the stripes on rugby jerseys)

8. "Sandwich" / "Hamburger" vertebra
   Cause: osteopetrosis, myelofibrosis
   √ sclerotic endplates alternate with radiolucent midportions of vertebral bodies
9. "Ring" epiphysis

Ring Epiphysis

= normal small steplike recess at corner of anterior edge of developing vertebral body that calcifies ~ 6 years of age, ossifies ~ 13 years of age, and fuses with vertebral body ~ 17 years of age

1. Severe osteoporosis
2. Healing rickets
3. Scurvy

Bullet-shaped Vertebral Body

mnemonic: HAM

Hypothyroidism
Achondroplasia
Morquio syndrome

Bone-within-bone Vertebra

= "ghost vertebra" following stressful event during vertebral growth phase in childhood

1. Stress line of unknown cause
2. Leukemia
3. Heavy metal poisoning
4. Thorotrast injection, TB
5. Rickets
6. Scurvy
7. Hypothyroidism
8. Hypoparathyroidism

Ivory Vertebra

= increase in opacity of vertebral body retaining its size and contours

Cause: stimulation of osteoblasts, coarsening of trabeculae, reactive bone formation

(a) in adults:	metastasis (prostate, breast), lymphoma (Hodgkin disease), Paget disease, osteosarcoma, carcinoid
(b) in children:	Hodgkin disease >> osteosarcoma, metastatic neuroblastoma, medulloblastoma, osteoblastoma

mnemonic: LOST FROM CHOMP

Lymphoma
Osteopetrosis
Sickle cell disease
Trauma, **T**uberculous spondylitis
Fluorosis
Renal osteodystrophy
Osteoblastic metastasis

Myelosclerosis
Chronic sclerosing osteomyelitis, **C**hordoma
Hemangioma
Osteosarcoma
Myeloma
Paget disease

Sclerotic Pedicle

1. Osteoid osteoma
2. Unilateral spondylolysis
3. Contralateral congenitally absent pedicle

TUMOR OF VERTEBRA

Expansile Lesion of Vertebra

A. INVOLVEMENT OF MULTIPLE VERTEBRAE
Metastases, multiple myeloma / plasmacytoma, lymphoma, hemangioma, Paget disease, angiosarcoma, eosinophilic granuloma

B. INVOLVEMENT OF ≥ 2 CONTIGUOUS VERTEBRAE
Osteochondroma, chordoma, aneurysmal bone cyst, myeloma

C. BENIGN LESION

1. Osteochondroma (1–5% of solitary osteochondromas, 7–9% in hereditary multiple exostoses) commonly arising from posterior elements, esp. C2
2. Osteoblastoma (30–40% in spine)
M÷F = 2÷1; equal distribution in spine; posterior elements (lamina, pedicle), may involve body if large; expansile lesion with sclerotic / shell-like rim, foci of calcified tumor matrix in 50%; younger patient
3. Giant cell tumor (5–7% in spine)
commonly sacrum, expansile lytic lesion of vertebral body with well-defined borders; secondary invasion of posterior elements; malignant degeneration in 5–20% after radiation therapy
4. Osteoid osteoma (10–25% in spine)
commonly lower thoracic / upper lumbar spine, posterior elements (pedicle, lamina, spinous process)
   - younger patient
   - painful scoliosis with concavity toward lesion

   √ involvement of pedicle + lamina (in 63%)
   √ extending anteriorly affecting ⅓ to ⅔ of posterolateral vertebral body
   √ sparing of intervertebral disk space
   √ edema in neural arch at adjacent level possible
5. Aneurysmal bone cyst (12–30% in spine)
thoracic > lumbar > cervical spine, posterior elements with frequent extension into vertebral bodies, well-defined margins, may arise from primary bone lesion (giant cell tumor, fibrous dysplasia) in 50%, may involve two contiguous vertebrae
6. Hemangioma (30% in spine)

10% incidence in general population; commonly lower thoracic / upper lumbar spine, vertebral body, "accordion" / "corduroy" appearance

7. Hydatid cyst (1% in spine)
   slow-growing destructive lesion, well-defined sclerotic borders, endemic areas
8. Paget disease
   vertebral body ± posterior elements, enlargement of bone, "picture framing"; bone sclerosis
9. Eosinophilic granuloma (6% in spine)
   most often cervical / lumbar spine; multiple involvement common
   √ vertebra plana / incomplete collapse of vertebra
   √ absence of osteolytic area
   √ preservation of posterior elements + pedicles
10. Fibrous dysplasia (1% in spine)
    vertebral body, nonhomogeneous trabecular "ground-glass" appearance
11. Enostosis (1–14% in spine)
    Location: T1–T7 > L2–L3

D. MALIGNANT LESION

1. Chordoma (15% in spine)
   ◊ Most common nonlymphoproliferative primary malignant tumor of the spine in adults
   Location: particularly C2, within vertebral body; violates disk space
2. Chondrosarcoma (3–12% in spine)
   ◊ 2nd most common nonlymphoproliferative primary malignant tumor of the spine in adults
   Mean age: 45 years; M > F
   Location: thoracic spine (mostly)
   Site: vertebral body (15%), posterior elements (40%), both (45%)
   • pain (95%); palpable mass (28–82%)
   • neurologic symptoms (45%)
   √ large calcified mass with bone destruction
   √ involvement of adjacent vertebra by extension through disk (35%)
3. Metastasis: osteolytic, osteoblastic
4. Multiple myeloma / plasmacytoma

   Clue: vertebral pedicles usually spared

   √ single vertebral collapse as usual manifestation
   √ "minibrain" appearance on axial CT = hollow vertebral body / pedicle + cortical thickening

   Characteristics suggestive of multiple myeloma:
   √ sharply demarcated scalloped lytic lesions
   √ marked osteoporosis
   √ "cold" lesions on bone scans
   √ lack of a primary neoplasm
5. Angiosarcoma
   10% involve spine, most commonly lumbar

6. Ewing sarcoma and PNET
   ◊ Most common nonlymphoproliferative primary malignant tumor of the spine in children; metastases more common than primary
   Site: vertebral body with extension to posterior elements
   √ diffuse sclerosis + osteonecrosis (69%)
7. Osteosarcoma (4% in spine)
   Average age: 4th decade; M > F
   Histo: mostly osteoblastic
   Location: thoracic + lumbar segments
   Site: vertebral body, posterior elements (79%)
   • neurologic symptoms
   √ may present as "ivory vertebra"
8. Lymphoma
   Peak age: 5th–7th decade; M÷F = 8÷1
   Location: paraspinal, vertebral, epidural
   Site: tumor spread from medullary cavity along small vascular channels
   √ lytic in NHL
   √ sclerotic "ivory vertebra" or mixed pattern in HD
   √ ↑ radionuclide uptake on bone scintigraphy

Bone Tumors Favoring Vertebral Bodies

(a) benign
   1. Hemangioma
   2. Eosinophilic granuloma
   3. Giant cell tumor

(b) malignant
   1. Metastasis
   2. Myeloma
   3. Plasmacytoma
   4. Lymphoma
   5. Chordoma

mnemonic: CALL HOME

Classification of Primary Spinal Tumors by Tissue Origin		
Tissue Origin	*Benign*	*Malignant*
Osteogenic	Enostosis (bone island) Osteoid osteoma Osteoblastoma	Osteosarcoma
Chondrogenic	Osteochondroma Chondroblastoma	Chondrosarcoma
Fibrogenic	Fibrous dysplasia Benign fibrous histiocytoma	Malignant fibrous histiocytoma
Vascular	Hemangioma Hemangiopericytoma	Epithelioid hemangio-endothelioma
Hematopoietic, reticulo-endothelial, lymphatic	Eosinophilic granuloma	Schüller-Christian syndrome, Letterer-Siwe disease Lymphoma / leukemia Plasmacytoma / multiple myeloma Ewing sarcoma
Notochordal		Chordoma
Unknown	Aneurysmal bone cyst Giant cell tumor	

Chordoma
Aneurysmal bone cyst
Leukemia
Lymphoma
Hemangioma
Osteoid osteoma, **O**steoblastoma
Myeloma, **M**etastasis
Eosinophilic granuloma

Primary Vertebral Tumors in Children

[in order of frequency:]

1. Osteoid osteoma
2. Benign osteoblastoma
3. Aneurysmal bone cyst
4. Ewing sarcoma

Primary Tumor of Posterior Elements

A. BENIGN

1. Osteoid osteoma
2. Osteoblastoma
3. Osteochondroma
4. Aneurysmal bone cyst

B. MALIGNANT
1. Chondrosarcoma
2. Osteosarcoma
3. Ewing sarcoma

mnemonic: A HOG
Aneurysmal bone cyst
Hydatid cyst, **H**emangioma
Osteoblastoma, **O**steoid osteoma
Giant cell tumor

Blowout Lesion of Posterior Elements

mnemonic: GO APE
Giant cell tumor
Osteoblastoma
Aneurysmal bone cyst
Plasmacytoma
Eosinophilic granuloma

Multiple Bone Lesions of Spine

A. BENIGN
1. Enostosis
2. Hemangioma

B. MALIGNANT
1. Metastasis
2. Myeloma
3. Lymphoma
4. Eosinophilic granuloma

Spine Lesions Involving Adjacent Levels

A. BENIGN
1. Chordoma
2. Aneurysmal bone cyst
3. Giant cell tumor

B. MALIGNANT
1. Osteosarcoma
2. Chondrosarcoma
3. Myeloma / plasmacytoma
4. Lymphoma
5. Ewing sarcoma

Osteoblastic Tumor of Spine

A. BENIGN
   1. Bone island
   2. Reactive bone sclerosis adjacent to osteoid osteoma and osteoblastoma
B. malignant
   1. Metastasis
   2. Lymphoma
   3. Osteosarcoma

Tumor of Spine with Fluid-fluid Level

1. Aneurysmal bone cyst
2. Telangiectatic osteosarcoma

Fat-containing Tumor of Spine

1. Vertebral hemangioma
2. Fibrous dysplasia
3. Paget disease
4. Schmorl node

Benign Tumor of Spine with Soft-tissue Extension

1. Aneurysmal bone cyst
2. Aggressive hemangioma
3. Eosinophilic granuloma

PARAVERTEBRAL MASSES

A. NONTUMOROUS
   1. Extramedullary hematopoiesis
      • hemolytic anemia / myelofibrosis
   2. Pott abscess
      √ calcification in a large paraspinal abscess WITHOUT new bone formation / sclerosis favors tuberculosis
   3. Castleman disease
      √ intense homogeneous enhancement
      √ frequent calcifications
B. TUMOROUS
   1. Lymphoma
      √ faint homogeneous enhancement
   2. Neurogenic tumor: neurofibroma, schwannoma, ganglion tumor
      √ commonly erosions / scalloping of vertebrae ± ribs
      √ moderate homogeneous enhancement
   3. Pleuropulmonary synovial sarcoma
   4. Extraadrenal neuroblastoma
   5. Extraskeletal Ewing sarcoma

Neurogenic Tumor

A. Nerve sheath

1. Schwannoma
2. Neurofibroma
3. Malignant nerve sheath tumor

B. Ganglionic cell
1. Ganglioneuroma
2. Ganglioneuroblastoma
3. Neuroblastoma

C. Paraganglionic cell
1. Paraganglioma
2. Pheochromocytoma

SACRUM

Pediatric Presacral Mass

A. Congenital & developmental mass
1. Sacrococcygeal teratoma
2. Anterior sacral meningocele
3. Dermoid cyst
4. Enteric cyst
5. Cystic lymphatic malformation

B. Neurogenic mass
1. Neuroblastoma
2. Ganglioneuroma
3. Schwannoma
4. Neurofibroma

C. Mesenchymal mass
1. Rhabdomyosarcoma
2. Undifferentiated sarcoma
3. Lymphoma
4. Vascular malformation

D. Sacral mass with presacral extension
(a) benign primary sacral tumor
1. Giant cell tumor
2. Aneurysmal bone cyst

(b) malignant primary sacral tumor
1. Chordoma
2. Ewing sarcoma

E. Inflammatory mass
1. Pelvic abscess
2. Pelvic hematoma

Sacroiliitis

√ findings predominate on the iliac side (thinner cartilage)

A. BILATERAL SYMMETRIC
1. Ankylosing spondylitis

√ small regular erosion = loss of definition of white cortical line on iliac side (initially)
√ subchondral sclerosis + subsequent ankylosis
√ ossification of interosseous ligaments

2. Enteropathic arthropathy
   √ same signs as in ankylosing spondylitis
3. Rheumatoid arthritis (in late stages)
   √ joint space narrowing without reparation
   √ osteoporosis
   √ ankylosis may occur
4. Deposition arthropathy: gout, CPPD, ochronosis, acromegaly
   √ slow loss of cartilage
   √ subchondral reparative bone + osteophytes
5. Osteitis condensans ilii

DDx: Hyperparathyroidism (subchondral bone resorption on iliac side resembling erosion + widening of joint)

B. BILATERAL ASYMMETRIC
1. Psoriatic arthritis
   √ large extensive erosion
   √ subchondral sclerosis + occasional ankylosis
2. Reiter syndrome
3. Juvenile rheumatoid arthritis

C. UNILATERAL
1. Infection
2. Osteoarthritis from abnormal mechanical stress

Differential Diagnosis of Sacroiliac Joint Disease

	Osteoarthritis	*Ankylosing spondylitis ilii*	*Osteitis condensans*
Age	older	younger	younger
Sex	M, F	M > F	F > M
Distribution	bi- / unilateral symmetric	bilateral symmetric	bilateral
Sclerosis	iliac mild focal	iliac ± extensive	iliac triangular
Erosions	absent	common	absent
Intraarticular ankylosis	rare	common	absent
Ligamentous ossification	less common	common	absent

√ no erosions
√ irregular narrowing of joint space with subchondral sclerosis
√ osteophytes at anterosuperior / -inferior aspect of joint (may resemble ankylosis)

DDx: psoriatic arthritis, Reiter syndrome, trauma, gout, pigmented villonodular synovitis, osteitis condensans ilii

Sacroiliac Joint Widening

mnemonic: CRAP TRAP

Colitis
Rheumatoid arthritis
Abscess (infection)
Parathyroid disease
Trauma
Reiter syndrome
Ankylosing spondylitis
Psoriasis

Sacroiliac Joint Fusion

mnemonic: CARPI

Colitic spondylitis
Ankylosing spondylitis
Reiter syndrome
Psoriatic arthritis
Infection (TB)

Widened Symphysis Pubis

mnemonic: EPOCH

Exstrophy of the bladder
Prune belly syndrome
Osteogenesis imperfecta
Cleidocranial dysostosis
Hypothyroidism

Destructive Sacral Lesion

mnemonic: SPACEMONG

Sarcoma: chondrosarcoma
Plasmacytoma
Aneurysmal bone cyst
Chordoma
Ependymoma, myxopapillary
Metastasis
Osteomyelitis
Neuroblastoma
Giant cell tumor

Sacral Tumor

Sacral Bone Tumor

A. BENIGN
   1. Giant cell tumor (2nd most common primary)
   2. Aneurysmal bone cyst (rare)
   3. Cavernous hemangioma (very rare)

4. Osteoid osteoma / osteoblastoma (very rare)

B. MALIGNANT
   1. Metastases (most common sacral neoplasm):
      › hematogenous: lung, breast, kidney, prostate
      › contiguous: rectum, uterus, bladder
   2. Plasmacytoma, multiple myeloma
   3. Lymphoma, leukemia
   4. Chordoma (most common primary)
   5. Sacrococcygeal teratoma
   6. Ewing sarcoma (rare)

Sacral Canal Tumor *(less common)*

A. BENIGN
   1. Neurofibroma: multiple suggestive of NF
   2. Schwannoma (rare)
   3. Meningioma (very rare)

B. MALIGNANT
   1. Ependymoma
   2. Drop metastases
   3. Carcinoid tumor

INTERVERTEBRAL DISK

Loss of Disk Space

1. Degenerative disk disease
2. Neuropathic osteoarthropathy
3. Dialysis spondyloarthropathy with amyloidosis
4. Ochronosis
5. Ankylosing spondylitis with pseudarthrosis
6. Sarcoidosis

Spinal Vacuum Phenomena

Pathophysiology:

= gaslike density due to

(a) <u>acute</u> / true vacuum phenomenon ← rapid increase in volume of joint space
   √ acute protraction of shoulder in children

(b) subacute / <u>chronic</u> vacuum phenomenon
   √ common in degenerative disk of spine

Cause: reduction of barometric pressure up to 1/20th of atmosphere

Location: joint under traction, spine

(a) nucleus pulposus	Osteochondrosis
(b) annulus fibrosus	Spondylosis deformans
(c) disk within vertebral body	Cartilaginous node
(d) disk within spinal canal	Intraspinal disk herniation

(e) apophyseal facet joint — Osteoarthritis ± ~listhesis
(f) vertebral body — Ischemic necrosis

Vacuum Phenomenon in Intervertebral Disk Space

= liberation of nitrogen gas from surrounding tissues into clefts with an abnormal nucleus or annulus attachment

Composition: N_2 (90-92%) + O_2 + CO_2 + traces of other gases

Prevalence: in 1–3% of all spinal radiographs; in up to 20% of plain radiographs; in up to 50% of spinal CT in patients > age 40

Cause:

1. Primary / secondary degeneration of nucleus pulposus
2. Intraosseous herniation of disk (= Schmorl node)
3. Spondylosis deformans (gas in annulus fibrosus)
4. Adjacent vertebral metastatic disease with vertebral collapse
5. Infection (extremely rare)

√ accentuated on supine X-ray during spine extension
√ obscured on upright radiograph during spine flexion

Site:

(a) marginal = traumatic / degenerative crack in peripheral fibers of annulus fibrosus
  √ spondylosis deformans = associated with marginal single anterior osteophyte
(b) central = intradiskal cleft due to
  › primary disk degeneration
  › secondary ← injury, interference with nutrition (CPPD, alkaptonuria, trauma, Scheuermann disease, osteoporotic vertebral collapse)

Intravertebral Gas

Cause:

1. Schmorl node = accumulation of gas from fissuring intravertebral disk
   √ rounded intravertebral gas with sclerotic rim
2. Limbus vertebrae
   √ intradiskal gas extends into vertebral cleft beneath superior / inferior ring apophysis
3. Pneumatocyst
   Incidence: 9% (on CT)
   Location: iliac bone, sacrum, humeral head, clavicle
   • asymptomatic
   √ cystlike lesion of gas attenuation ± sclerotic rim ± communication with adjacent joint
   √ erosive defect in osteocartilaginous endplates → direct extension of gas into vertebra
4. Intravertebral vacuum cleft
5. Intraspinal gaseous cyst
   (a) gas-containing intraspinal disk herniation
   (b) gas expulsion through rent in annulus fibrosus

Intervertebral Disk Calcification

mnemonic: A DISC SO WHITE

Amyloidosis, **A**cromegaly
Degenerative disk disease
Infection
Spinal fusion
CPPD
Spondylitis ankylosing
Ochronosis
Wilson disease
Hemochromatosis, **H**yperparathyroidism, **H**omocystinuria
Idiopathic skeletal hyperostosis
Traumatic
Etceteras: Gout and other causes of chondrocalcinosis

Intervertebral Disk Ossification

Associated with: fusion of vertebral bodies

1. Ankylosing spondylitis
2. Ochronosis
3. Sequelae of trauma
4. Sequelae of disk-space infection
5. Degenerative disk disease

SPINAL CORD

◊ Most spinal cord neoplasms are malignant!
◊ 90–95% are classified as gliomas

Intramedullary Lesion

Prevalence: 4–10% of all CNS tumors; 20% of all intraspinal tumors in adults (35% in children)

A. TUMOR
√ expansion of cord
√ heterogeneous signal on T2WI
√ cysts + necrosis
√ variable degrees of enhancement (vast majority with some enhancement)
(a) primary:
1. Ependymoma 60%
◊ Most common glial tumor in adults
2. Astrocytoma 25%
◊ Most common intramedullary tumor in children
3. Hemangioblastoma 5%
4. Oligodendroglioma 3%
5. Epidermoid, dermoid, teratoma 1–2%
6. Ganglioglioma 1%
7. Lipoma 1%

Location:

- › cervical region: astrocytoma
- › thoracic region: teratoma-dermoid, astrocytoma
- › lumbar region: ependymoma, dermoid

(b) metastatic: eg, malignant melanoma, breast, lung

B. CYSTIC LESION

√ fluid isointense to CSF
√ smooth well-defined internal margins
√ thinned adjacent parenchyma
√ cord atrophy
√ no contrast enhancement

(a) peritumoral cyst = syringomyelia

1. Syringomyelia
2. Hydromyelia
3. Reactive cyst

(b) tumoral cyst

√ shows peripheral enhancement

1. Ganglioglioma (in 46%)
2. Astrocytoma (in 20%)
3. Ependymoma (in 3%)
4. Hemangioblastoma (2–4%)

C. VASCULAR

1. Cord concussion = reversible local edema
2. Hemorrhagic contusion
3. Cord transection
4. AVM

D. chronic inflammation

1. Sarcoid
2. Transverse myelitis
3. Multiple sclerosis

mnemonic: I'M ASHAMED

Inflammation (multiple sclerosis, sarcoidosis, myelitis)
Medulloblastoma
Astrocytoma
Syringomyelia / hydromyelia
Hematoma, Hemangioblastoma
Arteriovenous malformation
Metastasis
Ependymoma
Dermoid

Intramedullary Neoplastic Lesion

A. GLIAL NEOPLASM (90–95%)

1. Ependymoma 60%
2. Astrocytoma 33%
3. Ganglioglioma 1%

B. NONGLIAL NEOPLASM
   (a) highly vascular lesions
      1. Hemangioblastoma
      2. Paraganglioma
   (b) rare lesions
      3. Metastasis
      4. Lymphoma
      5. Primitive neuroectodermal tumor

C. USUALLY EXTRAMEDULLARY NEOPLASM
   1. Intramedullary meningioma
   2. Intramedullary schwannoma

Intramedullary Nonneoplastic Mass

1. Epidermoid
2. Congenital lipoma
3. Posttraumatic pseudocyst
4. Wegener granuloma
5. Cavernous malformation
6. Abscess

Intramedullary Nonneoplastic Lesion

Prevalence: 4%

√ no cord expansion

1. Demyelinating disease
2. Sarcoidosis
3. Amyloid angiopathy
4. Pseudotumor
5. Dural arteriovenous fistula
6. Cord infarction
7. Chronic arachnoiditis
8. Cystic myelomalacia

Cord Lesions

A. INFLAMMATION
   1. Multiple sclerosis
   2. Acute disseminated encephalomyelitis
   3. Acute transverse myelitis
      √ involves half the cross-sectional area of cord
   4. Lyme disease
   5. Devic syndrome

B. INFECTION
   1. Cytomegalovirus
   2. Progressive multifocal leukoencephalopathy

3. HIV

C. VASCULAR
   1. Anterior spinal artery infarct
      √ affects central gray matter first
      √ extends to anterior two-thirds of cord
   2. Venous infarct / ischemia
      √ starts centrally progressing centripetally

D. NEOPLASM

Intradural Extramedullary Mass

1. Nerve sheath tumor (35%)
2. Meningioma (25%)
3. Lipoma
4. Dermoid
   commonly conus / cauda equina; associated with spinal dysraphism (⅓)
5. Ependymoma commonly filum terminale; NO spinal dysraphism
6. Metastasis
   (a) "Drop metastases" from CNS tumors
   (b) Metastases from outside CNS
8. Arachnoid cyst
9. Neurenteric cyst
10. Hemangioblastoma
11. Paraganglioma

mnemonic: MAMA N
Metastasis
Arachnoiditis
Meningioma
AVM, **A**rachnoid cyst
Neurofibroma

CSF-isointense Focal Spinal Cord Displacement

= space-occupying CSF-isointense intradural / intraspinal extramedullary lesion with widened CSF space

• nonspecific symptoms: back pain, weakness, numbness, Brown-Séquard syndrome

1. Epidermoid cyst
2. Intradural arachnoid cyst
3. Synovial cyst
4. Cystic schwannoma
5. Teratoma
6. Meningocele
7. Epidural abscess of spine
8. Epidural hematoma
9. Idiopathic spinal cord herniation

Epidural Extramedullary Lesion

= EXTRADURAL LESIONS OF SPINE
arise from bone, fat, vessels, lymph nodes, extramedullary neural elements
Prevalence: 30% of all spinal tumors

A. TUMOR
   (a) benign
      1. Dermoid, epidermoid
      2. Lipoma: over several segments
      3. Fibroma
      4. Neurinoma (with intradural component)
      5. Meningioma (with intradural component)
      6. Ganglioneuroblastoma, ganglioneuroma
   (b) malignant
      1. Hodgkin disease
      2. Lymphoma: most commonly in dorsal space
      3. Metastasis: breast, lung – most commonly from involved vertebrae without extension through dura
      4. Paravertebral neuroblastoma

B. DISK DISEASE
   1. Bulging disk
   2. Herniated nucleus pulposus
   3. Sequestered nucleus pulposus

C. BONE
   1. Tumor of vertebra
   2. Spinal stenosis
   3. Spondylosis

D. INFECTION: epidural abscess / phlegmon

E. BLOOD: hematoma

F. OTHERS: synovial cyst, arachnoid cyst, extradural lipomatosis, extramedullary hematopoiesis

mnemonic: MANDELIN
Metastasis (drop mets from CNS tumor), Meningioma
Arachnoiditis, Arachnoid cyst
Neurofibroma
Dermoid / epidermoid
Ependymoma
Lipoma
Infection (TB, cysticercosis)

Normal but tortuous roots

Anterior Epidural Space Abnormality

A. Neoplasm
   Histo: metastases spread from marrow via venous foramina into spinal canal preserving cortex
   √ solid enhancement

√ may have central necrosis
√ commonly uni- / bilobed appearance (= preservation of tethered appearance of posterior longitudinal ligament [PLL])

B. Infection
√ frequently central convex appearance (= disruption of posterior vertebral cortex by osteomyelitis)
1. Epidural abscess
√ peripheral enhancement
2. Epidural phlegmon
√ solid enhancement

C. Hemorrhage
√ frequently central convex appearance (= disruption of posterior vertebral cortex by fracture)
√ no enhancement

D. Disk herniation
√ sequestered / extruded disk rarely crosses midline

Cord Atrophy

1. Multiple sclerosis
2. Amyotrophic lateral sclerosis
3. Cervical spondylosis
4. Sequelae of trauma
5. Ischemia
6. Radiation therapy
7. AVM of cord

Delayed Uptake of Water-Soluble Contrast in Cord Lesion

1. Syringohydromyelia
2. Cystic tumor of cord
3. Osteomalacia

exceedingly rare:

4. Demyelinating disease
5. Infection
6. Infarction

Extraarachnoid Myelography

A. SUBDURAL INJECTION
√ spinal cord, nerve roots, blood vessels not outlined
√ irregular filling defects
√ slow flow of contrast material
√ CSF pulsations diminished
√ contrast material pools at injection site within anterior / posterior compartments

B. EPIDURAL INJECTION
√ contrast extravasation along nerve roots
√ contrast material lies near periphery of spinal canal

√ intraspinal structures are not well outlined

MUSCULOSKELETAL NEUROGENIC TUMORS

A. BENIGN NEUROGENIC TUMOR
   1. Traumatic neuroma
   2. Morton neuroma
   3. Neural fibrolipoma
   4. Nerve sheath ganglion
   5. Benign peripheral nerve sheath tumor (PNST)
      (a) Schwannoma = Neurilemmoma
      (b) Neurofibroma: localized, diffuse
      (c) Plexiform neurofibroma

B. MALIGNANT NEUROGENIC NEOPLASM
   = malignant peripheral nerve sheath tumor (MPNST)

SURGICAL LUMBAR PROCEDURES

Posterior Lumbar Surgical Procedures

= posterior decompression + fusion

1. Posterior lumbar interbody fusion
   › bilateral caudad + cephalad partial laminectomies
   › diskectomy
   › bone graft into disk space + interbody spacer
   › posterior stabilization (until bone fusion occurs)
2. Transforaminal lumbar interbody fusion
   = lateral approach leaving midline bone structures intact
   › total facetectomy for access to lateral disk space
   › transforaminal interbody spacers
3. Posterolateral fusion
   = alternative to posterior lumbar interbody fusion ← severe loss of disk space height
   › bone graft material placed laterally between transverse processes
   › supplemented by posterior instrumentation

Anterior Lumbar Surgical Procedures

= anterior fusion for predominantly diskogenic pain without need for posterior decompression

1. Anterior lumbar interbody fusion
   › lower abdominal incision / retroperitoneal flank approach
   › removal of degenerate disk
   › spacers for anterior osseous fusion replacing disk height
2. Stand-alone lumbar interbody fusion
   › cage fixed to the adjacent vertebral bodies by screws

SPINAL FIXATION DEVICES

Function:

(1) to restore anatomic alignment in fractures (fracture reduction)
(2) to stabilize degenerative disease
(3) to correct congenital deformities (scoliosis)
(4) to replace diseased / abnormal vertebrae (infection, tumor)

Posterior Fixation Devices

using paired / unpaired rods attached with

1. Sublaminar wiring
   = passing a wire around lamina + rod
2. Interspinous wiring
   = passing a wire through a hole in the spinous process; a Drummond button prevents the wire from pulling through the bone
3. Subpars wiring
   = passing a wire around the pars interarticularis
4. Laminar / sublaminar hooks
   used on rods for compression / distraction forces to be applied to pedicles / laminae
   (a) upgoing hook curves under lamina
   (b) downgoing hook curves over lamina
5. Pedicle / transpedical screws
   √ connected by plates / rods spanning single / multiple segments
   √ crossbars (for additional strength)
6. Rods
   (a) Luque rod = straight / L-shaped smooth rod 6–8 mm in diameter
   (b) O-ring fixator, rhomboid-shaped bar, Luque rectangle, segmental rectangle = preshaped loop to form a flat rectangle
   (c) Harrington distraction rod
   (d) Harrington compression rod
   (e) Knodt rod = threaded distraction rod with a central fixed nut (turnbuckle) and opposing thread pattern
   (f) Cotrel-Dubousset rods = a pair of rods with a serrated surface connected by a cross-link with ≥ 4 laminar hooks / pedicle screws
7. Plates
   (a) Roy-Camille plate
   = simple straight plates with round holes
   (b) Luque plate
   = long oval holes with clips encircling the plate
   (c) Steffee plate = straight plates with long slots
8. Translaminar / facet screw
   = cancellous screws for single level fusion when posterior elements are left intact
9. Percutaneous pinning
   = (hollow) interference screws placed across disk level

Anterior Fixation Devices

1. Dwyer device

= screws threaded into vertebral body over staples embedded into vertebral body connected by braided titanium wire; placed on convex side of spine

2. Zielke device
   = modified Dwyer system replacing cable with solid rod
3. Kaneda device
   = 2 curved vertebral plates with staples attached to vertebral bodies with screws, plates connected by 2 threaded rods attached to screw heads
4. Dunn device
   (similar to Kaneda device, discontinued)

Reconstruction after Diskectomy / Corpectomy

1. Auto- / allograft bone block
2. Allograft strut (eg, fibula, humerus)
3. Interbody spacers: titanium / radiolucent material (eg, polyetheretherketone)
   (a) ramp
   (b) bone graft cage: open structure filled with bone graft material
   √ 2 radiopaque markers for assessment of spacer position: posterior marker should be ≥ 2 mm anterior to posterior vertebral body margin
4. Vertebral body replacement device
   (a) expandable hollow cylinder packed with bone graft / cement (Synex cage)
   (b) mesh (Moss cage)
   (c) stackable carbon-fiber-reinforced polymer cages held together by metallic rods
5. Disk replacement device
   Indication: pain from disk degeneration only
   Contraindication: facet joint degeneration, < 4 mm residual disk height, significant endplate degeneration

Complications of Spinal Instrumentation

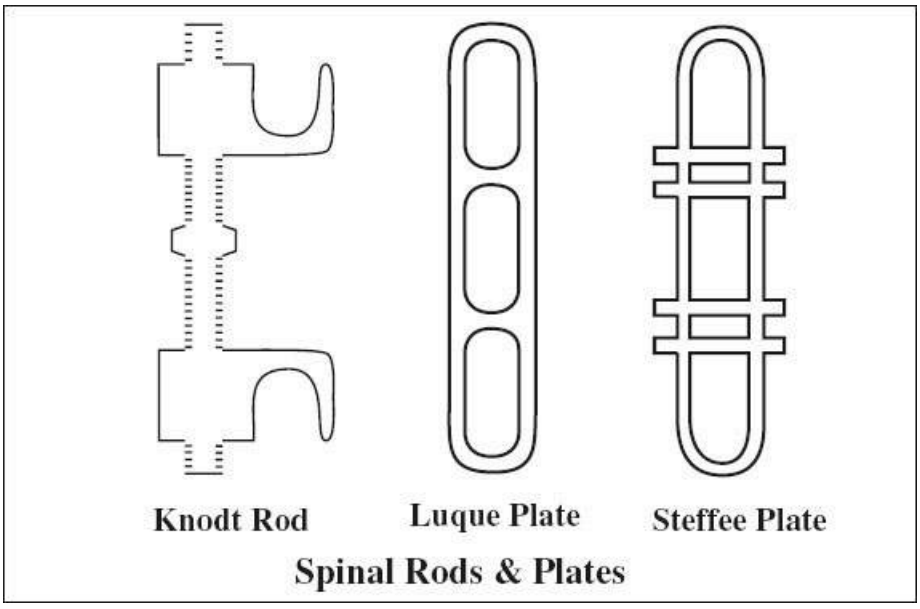
1. Pseudarthrosis
   √ corticated linear lucency across graft material
   √ focally increased signal on T2WI
   √ increased tracer activity on bone scintigraphy
2. Malpositioned pedicle screws (2.4% complication rate)
   • nerve root irritation (medial angulation of screw)
   √ disruption of cortical bone
   (a) medial deviation
   (b) lateral deviation
   (c) penetration of anterior cortex (exception are sacral screws which may be anchored in anterior cortex of the sacrum for additional stability)
   √ lucent rim around screw threads ← loosening
3. Malpositioned anterior cervical plate
   √ penetration into adjacent disk space / foramen transversarium / spinal cord / nerve roots
4. Herniation of graft material
   √ anteriorly / posteriorly displaced graft

5. Postoperative hematoma
6. Surgery at wrong level
7. Accelerated degenerative changes / ligamentous instability / fracture at adjacent levels
8. Superficial / deep infection (diskitis, osteomyelitis)
9. Arachnoiditis

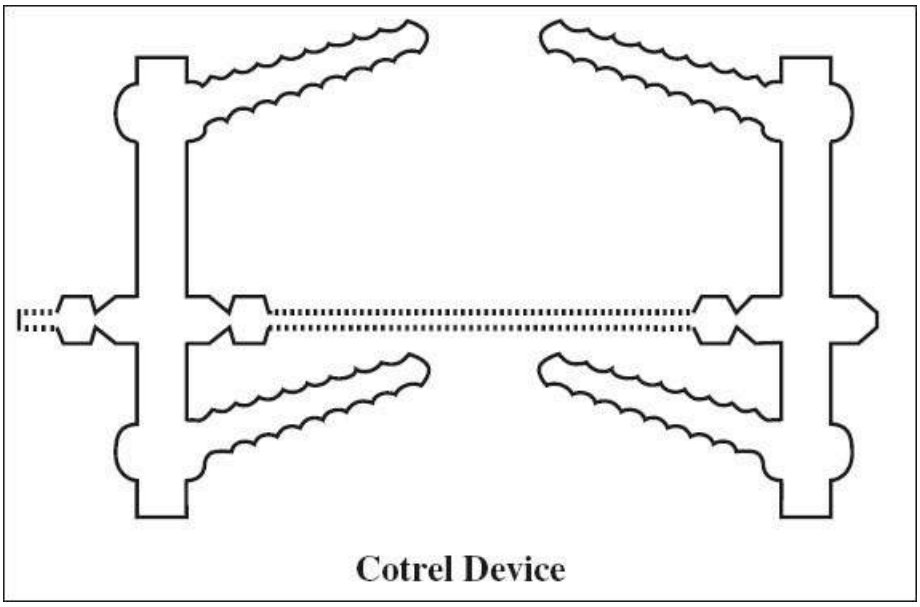
Assessment of Bridging Spinal Fusion

Time from surgery: 6–9 months

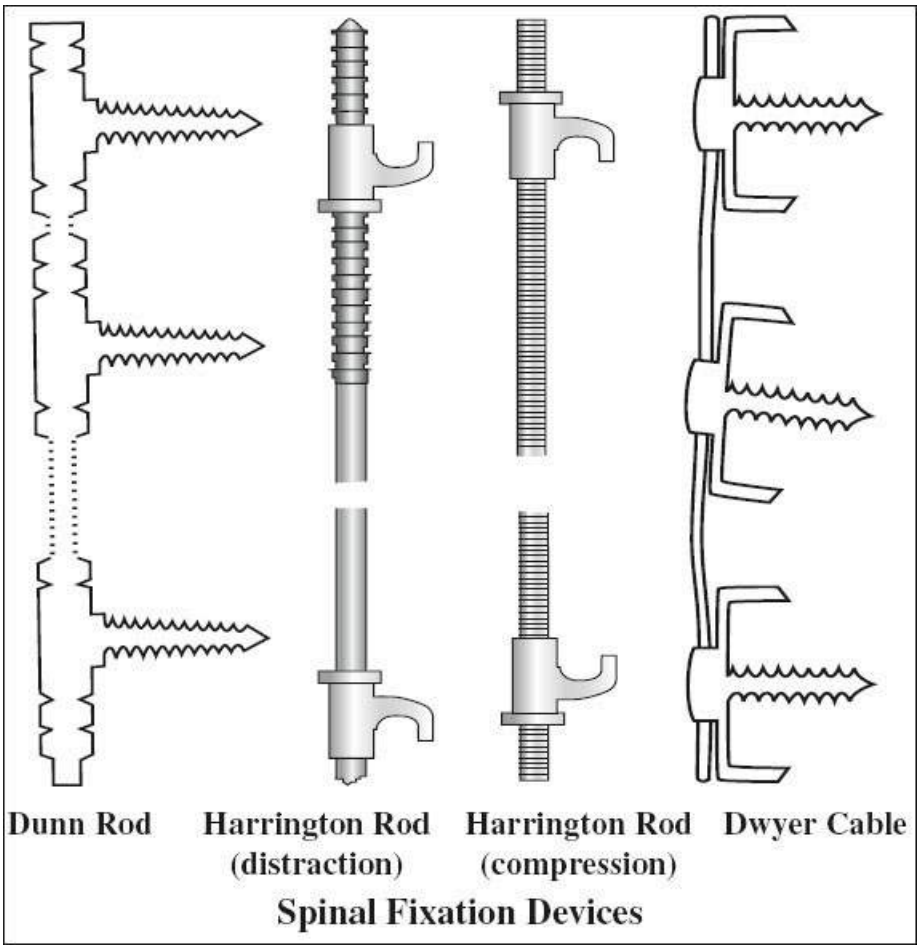
√ < 3° of intersegmental positional change on lateral flexion + extension views
√ visible bone formation in / about graft material
√ minimal loss of disk height
√ absence of lucency around implant
√ absence of fracture of device / graft / vertebra



Spinal Rods & Plates



Cotrel Device



Spinal Fixation Devices

ANATOMY OF SKULL AND SPINE

SCALP

◊ Outer 3 layers are often torn off as a unit in accidents; wounds do not gape if epicranius (occipitofrontal) m. not involved

Area: from supraorbital ridge to superior nuchal line, laterally to zygomatic arch and external auditory meatus 3 primary muscle groups: frontalis, occipitalis, temporalis

1. SKIN
   √ linear hyperattenuating structure
2. SUBCUTIS
   = fibroadipose tissue closely adherent to skin and underlying epicranius
   √ thick layer of fat attenuation
3. GALEA APONEUROTICA
   = layer of thick fibrous tissue continuous with epicranius (occipitofrontal) muscle consisting of
   (a) frontal muscle belly + auricularis m. anteriorly
   (b) occipital muscle belly posteriorly
   forming centrally the large epicranial aponeurosis
   √ thin line of increased attenuation ← temporalis fascia
4. SUBGALEAL SPACE
   = subaponeurotic areolar tissue between periosteum of outer table and galea aponeurotica
   Histo: analogous to loose areolar tissue containing fat
   • allows the 3 superficial layers of scalp to move as a unit on the cranium → enabling the scalp to wrinkle
   √ allows fluid to accumulate and spread across the cranium analogous to intracranial subdural fluid collections
5. PERICRANIUM = periosteum of outer table
   • firmly adheres to margins of underlying skull bones at suture lines
   √ usually not visible by CT without subperiosteal hematoma
6. SUBPERIOSTEAL SPACE
   = potential space created when periosteum of outer table becomes detached from calvaria (= cephalohematoma); analogous to intracranial extradural hematoma

SKULL VAULT / CALVARIA

[*calvaria*, Latin = top part of skull, from *calvus* = bald]

1. OUTER TABLE = outer layer of cortical bone
   √ well defined and of very high attenuation
   √ very low signal intensity
2. DIPLOË = layer of cancellous bone
   [*diploë* from *diploos*, Latin = double]
   √ slightly lower attenuation than outer table

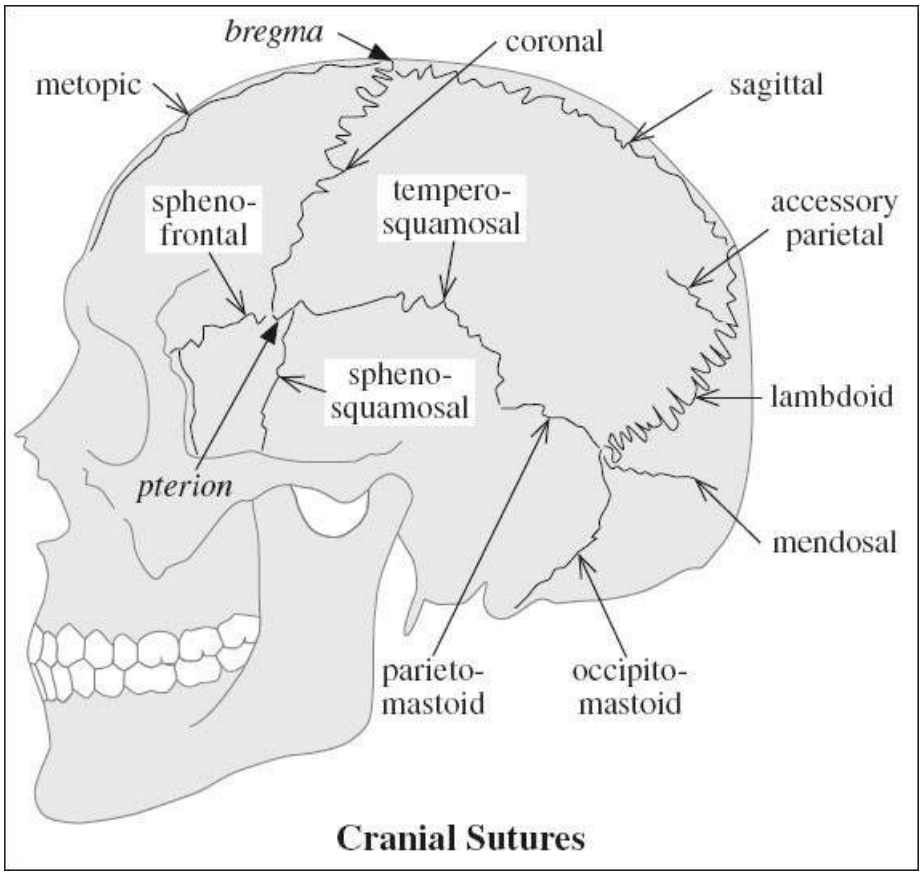
√ low signal intensity on T1WI during first 2 decades
√ high signal intensity later ← fatty marrow conversion

3. INNER TABLE = inner layer of cortical bone
   √ well defined and of very high attenuation
   √ very low signal intensity
4. DURA MATER = double-layered membrane composed of
   (a) outer layer = periosteum of inner table
   (b) inner layer = dura mater proper

   The usually continuous double-layered membrane separates to form:
   › dural venous sinuses
   › tentorium cerebelli, falx cerebri, falx cerebelli
   › diaphragm sellae
   √ short low-signal-intensity segments with enhancement (no blood-brain barrier) most prominent over convexities

SUTURES

A. METOPIC / FRONTAL SUTURE



Cranial Sutures

= from nasion to anterior angle of bregma
[*bregma*, Greek = top of head]

Closure: by 3 months – 6 years of age; in up to 10% open until adulthood

Sutura frontalis persistens = metopism
= no closure of incomplete / complete metopic suture
DDx: anterior vertical fracture

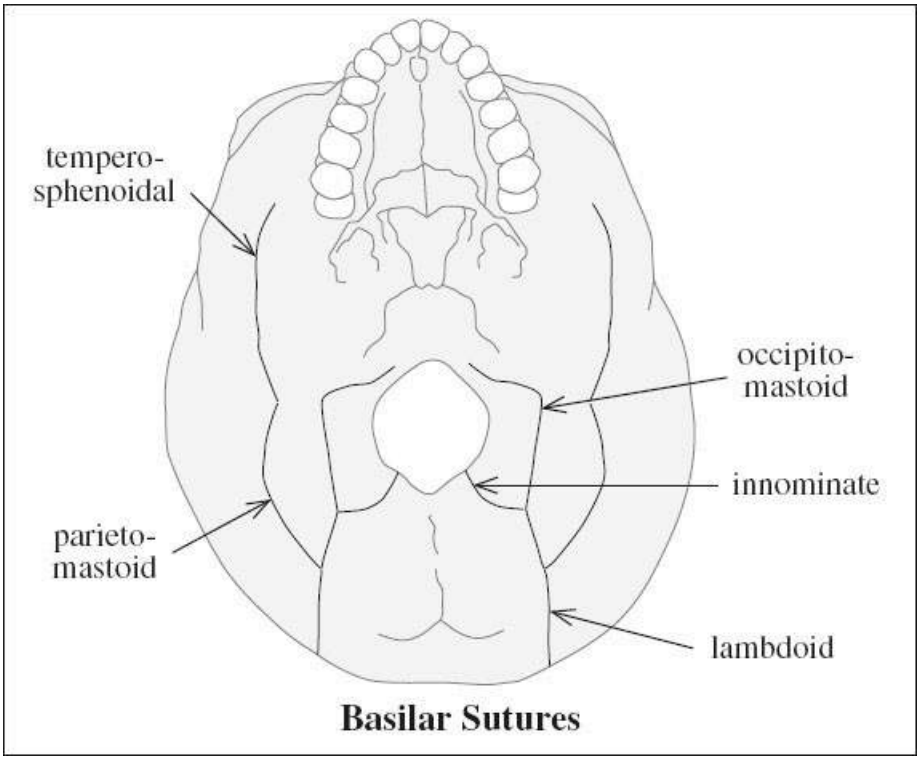
B. SAGITTAL SUTURE
[*sagitta*, Latin = arrow]
= fibrous connective tissue joint between two parietal bones
Average width: 5.0 ± 0.2 mm (at birth), 2.4 ± 0.1 mm (1 month of age); narrowing further over time
Closure: 21–30 years of age; fusing anteriorly beginning at intersection with lambdoid suture

C. CORONAL SUTURE
= separates frontal from parietal bones
Average width: 2.5 ± 0.1 mm (at birth), 1.3 ± 0.1 mm (1 month of age)
Closure: 24 years of age

D. SQUAMOSAL SUTURE
(a) temporosquamosal suture
= connects temporal bone squama with lower border of parietal bone; arches posteriorly from pterion (= contact point between frontal, parietal, temporal, sphenoid)
[*pteron*, Greek = wing]
√ often visualized at two points at CT with lambdoid suture acting as a useful posterior reference point
= continuous posteriorly with parietomastoid suture uniting mastoid process of temporal bone with region of mastoid angle of parietal bone
(b) sphenosquamosal suture
= courses inferiorly from pterion separating sphenoid bone from squama of temporal bone
N.B.: often mistaken for skull base fracture

E. LAMBDOID SUTURE
[upper case *Greek* letter lambda = L]
= connects parietal with occipital bone
Closure: 26 years of age
N.B.: the most common site of wormian bones

F. OCCIPITOMASTOID SUTURE



Basilar Sutures

= inferior continuation of lambdoid suture at the point where lambdoid suture intersects with temporosquamosal suture

G. PARIETOMASTOID SUTURE

= links temporosquamosal and lambdoid sutures

√ often not seen on axial CT images

H. OCCIPITOMASTOID SUTURE

= between occipital bone + mastoid process of temporal bone as a continuation of the lambdoid suture toward skull base

N.B.: not infrequently mistaken for a skull base fracture

I. SPHENOFRONTAL SUTURE

= transverse suture between anterior margin of lesser sphenoid wing + posterior margin of horizontal orbital plate

√ lesser sphenoid wing (posterior to suture) is a useful landmark for suture localization

J. ACCESSORY PARIETAL SUTURE (RARE)

= the most common of all usually bilateral and symmetric accessory sutures

Location: parietal and occipital bone → multiple ossification centers

K MENDOSAL / ACCESSORY OCCIPITAL SUTURE

Frequency: 3% in an Indian subcontinent population

Closure: in utero / first few days of life; may persist up to 6 years of age

Os incae = large single centrally located intrasutural bone at junction of lambdoid and sagittal sutures; often forms in a persistent mendosal suture

K SKULL BASE SUTURES

Ossification: 50% (84%) of anterior base by 6 (24) months

(a) innominate / intraoccipital

Closure: 4 years of age

(b) lambdoid
(c) occipitomastoid
(d) parietomastoid
(e) temporosphenoidal

Symmetry and knowledge of the anatomic appearances of basal sutures are important for avoiding misdiagnosis.
A persistent hypoattenuating area of any length extending from foramen magnum beyond 4 years of age indicates a fracture.

FORAMINA OF BASE OF SKULL

on inner aspect of middle cranial fossa 3 foramina are oriented along an oblique line in the greater sphenoidal wing from anteromedial behind the superior orbital fissure to posterolateral

mnemonic: "rotos"
foramen **rot**undum
foramen **o**vale
foramen **s**pinosum

Foramen Rotundum

= canal within greater sphenoid wing connecting middle cranial fossa + pterygopalatine fossa

Location: inferior and lateral to superior orbital fissure

Course: extends obliquely forward + slightly inferiorly in a sagittal direction parallel to superior orbital fissure

Contents: (a) nerves: V_2 (maxillary nerve)
(b) vessels: (1) artery of foramen rotundum
(2) emissary vv.

√ best visualized by coronal CT

Foramen Ovale

= canal connecting middle cranial fossa + infratemporal fossa

Location: medial aspect of sphenoid body, situated posterolateral to foramen rotundum (endocranial aspect) + at base of lateral pterygoid plate (exocranial aspect)

Contents: (a) nerves: (1) V_3 (mandibular nerve)
(2) lesser petrosal nerve (occasionally)
(b) vessels: (1) accessory meningeal artery
(2) emissary veins

Foramen Spinosum

Location: on greater sphenoid wing posterolateral to foramen ovale (endocranial aspect) + lateral to eustachian tube (exocranial aspect)

Contents: (a) nerves: (1) recurrent meningeal branch of mandibular nerve
(2) lesser superficial petrosal nerve
(b) vessels: (1) middle meningeal artery

(2) middle meningeal vein

Foramen Lacerum

covered (occasionally) by fibrocartilage, carotid artery rests on endocranial aspect of fibrocartilage

Location: at base of medial pterygoid plate

Contents: (inconstant)

(a) nerve: pterygoid canal n. (actually pierces cartilage)

(b) vessel: meningeal branch of ascending pharyngeal a.

Foramen Magnum

basion = anterior lip of foramen

opisthion = posterior lip of foramen

Contents: (a) nerves: (1) medulla oblongata
(2) CN XI (spinal accessory nerve)

(b) vessels: (1) vertebral artery
(2) anterior spinal artery
(3) posterior spinal artery

Pterygoid Canal

= VIDIAN CANAL

= within sphenoid body connecting pterygopalatine fossa anteriorly to foramen lacerum posteriorly

Location: at base of pterygoid plate below foramen rotundum

Contents: (a) nerves: vidian nerve = nerve of pterygoid canal = continuation of greater superficial petrosal nerve (from cranial nerve VII) after its union with deep petrosal nerve

(b) vessel: vidian artery = artery of pterygoid canal = branch of terminal portion of internal maxillary a. arising in pterygopalatine fossa → passing through foramen lacerum posterior to vidian n.

Hypoglossal Canal

= ANTERIOR CONDYLAR CANAL

Location: in posterior cranial fossa anteriorly above condyle starting above anterolateral part of foramen magnum, continuing in an anterolateral direction + exiting medial to jugular foramen

Contents: (a) nerves: cranial nerve XII (hypoglossal n.

(b) vessels: (1) pharyngeal artery
(2) branches of meningeal artery

Jugular Foramen

Location: at posterior end of petrooccipital suture directly posterior to carotid orifice

(a) anterior part:

(1) inferior petrosal sinus

(2) meningeal branches of pharyngeal artery + occipital a.

(b) intermediate part:

(1) cranial nerve IX (glossopharyngeal nerve)

(2) cranial nerve X (vagus nerve)

(3) cranial nerve XI (spinal accessory nerve)

(c) posterior part: internal jugular vein

CRANIOVERTEBRAL JUNCTION (CVJ)

CRANIOCERVICAL JUNCTION: C1 (atlas) + C2 (axis) + occiput

Variants of CVJ: precondylar tubercles, third occipital condyle, ossification of ligament of odontoid process

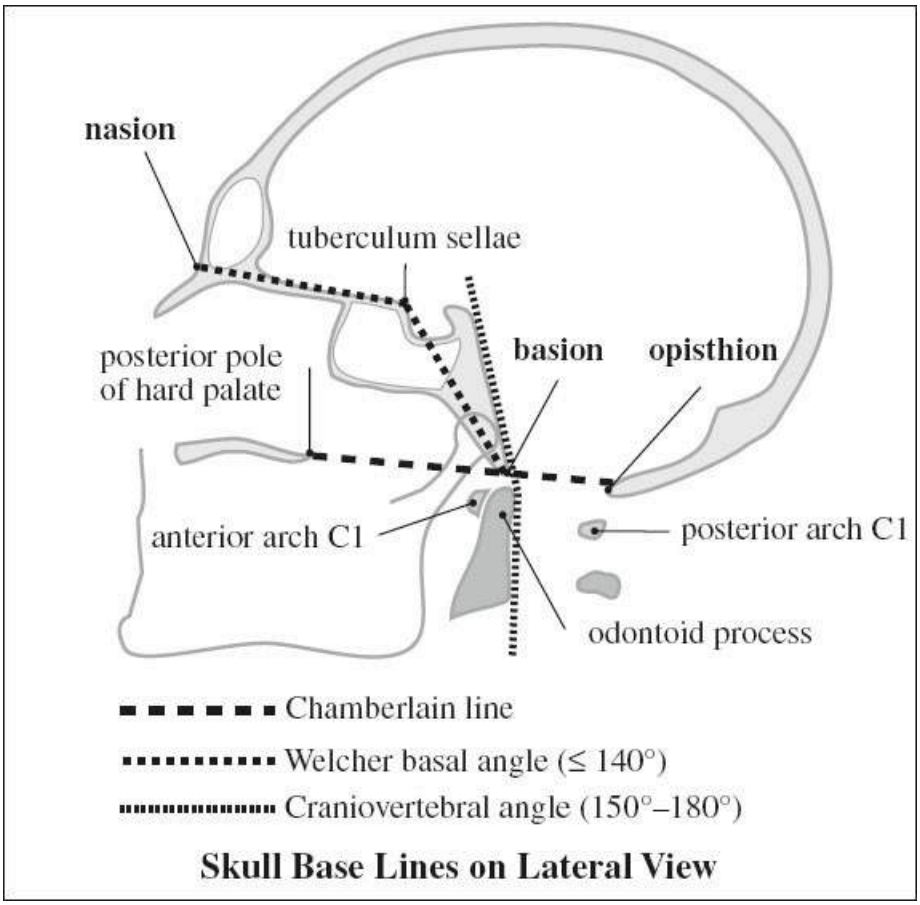
Craniometry:

› LATERAL VIEW

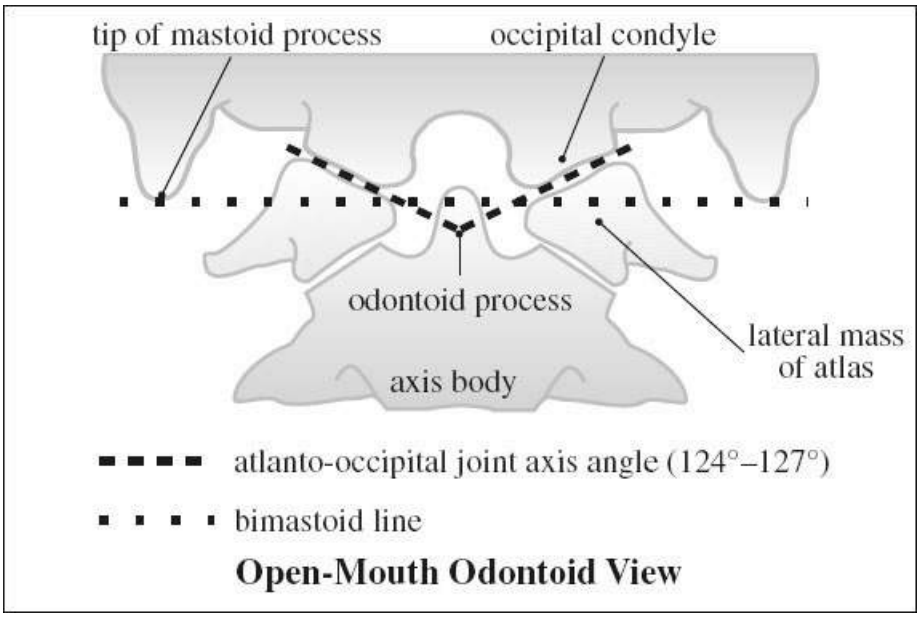
1. **Chamberlain line**
   = line between posterior edge of hard palate + posterior margin of foramen magnum (= opisthion)
   √ tip of odontoid process usually lies below / tangent to Chamberlain line by > 3 mm
   √ tip of odontoid process may lie up to 1 ± 6.6 mm above the Chamberlain line
2. **McGregor line**
   = line between posterior edge of hard palate + most caudal portion of occipital squamosal surface
   ◊ Substitute to Chamberlain line if opisthion not visible
   √ tip of odontoid < 4.5–5.0 mm above this line
3. **Wackenheim clivus baseline**
   = BASILAR LINE = CLIVAL LINE = line along clivus
   √ usually falls tangent to posterior aspect of tip of odontoid process
4. **Craniovertebral angle** = clivus-canal angle
   = angle formed by line along posterior surface of axis body and odontoid process + basilar line
   √ ranges from 150° in flexion to 180° in extension
   √ ventral spinal cord compression may occur at < 150°
5. **Welcher basal angle**
   = intersection of nasion-tuberculum line and of tuberculum-basion line (along clivus)
   √ angle averages 132° (should be < 140–145°)
6. **McRae line**
   = line between anterior lip (= basion) to posterior lip (= opisthion) of foramen magnum
   √ tip of odontoid below this line = NO basilar invagination; if poorly seen → Chamberlain line

› ANTEROPOSTERIOR VIEW (= "open-mouth" / odontoid view)

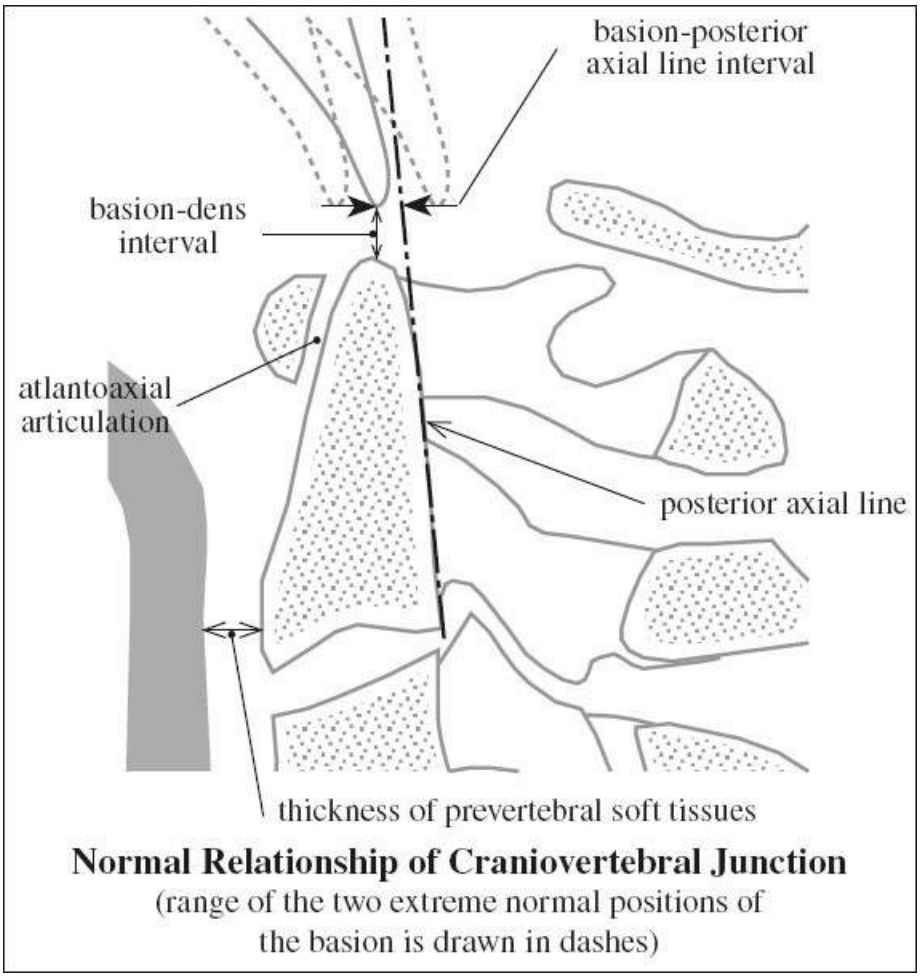
7. **Atlanto-occipital joint axis angle**
   = formed by lines drawn parallel to atlantooccipital joints
   √ lines intersect at center of odontoid process
   √ average angle of 125° (range, 124° to 127°)



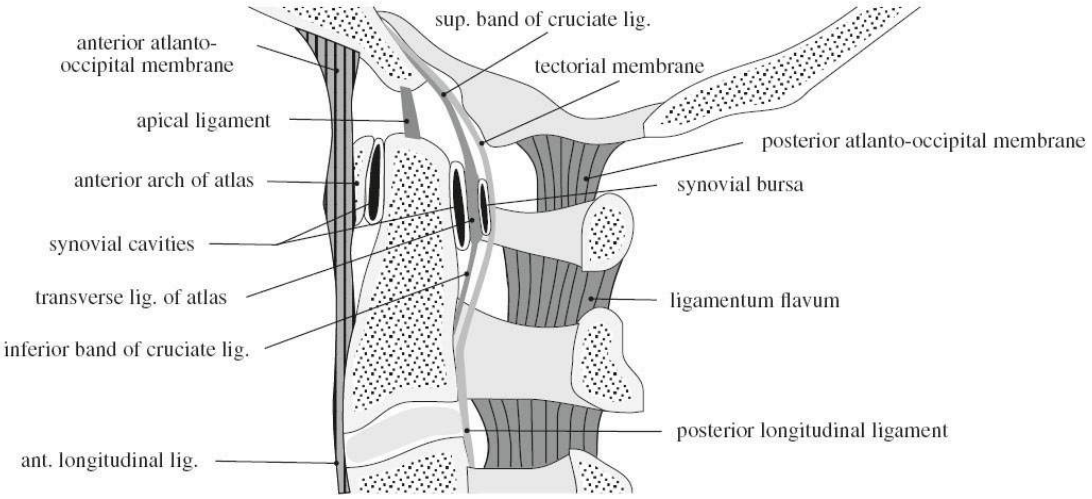
Skull Base Lines on Lateral View



Open-Mouth Odontoid View



Normal Relationship of Craniovertebral Junction
(range of the two extreme normal positions of the basion is drawn in dashes)



Joints and Ligaments of Occipitoatlantoaxial Region

8. **Digastric line**
   = line between incisurae mastoideae (origin of digastric muscles)
   √ tip of odontoid below this line

9. **Bimastoid line**
   = line connecting the tips of both mastoid processes
   √ tip of odontoid < 10 mm above this line

Normal dimensions for adults:

[posterior axial line = vertical line drawn along posterior aspect of the subdental body of C2]

Basion-dens interval (in 95%) < 12 mm

Basion-posterior axial line interval (in 98%)
  posterior to dens < 12 mm
  anterior to dens < 4 mm

Prevertebral soft tissues at C2 < 6 mm

Anterior atlanto-dens interval < 2 mm

Lateral atlanto-dens interval (side-to-side) < 3 mm

Atlanto-occipital articulation < 2 mm

Atlantoaxial articulation < 3 mm
  (for children < 5 mm)

Atlas (C1)

= ring-shaped vertebra

Composition:

(1) bilateral paired lateral masses
  › superior articulation with occipital condyles = **atlanto-occipital joints**
  › inferior articulation with C2 = **atlantoaxial joints**
  › groove for vertebral artery on superior aspect

(2) anterior arch
  › articular surface for odontoid process on dorsal aspect = **atlantoaxial joint**

(3) posterior arch
  › attachment of posterior atlanto-occipital membrane

◊ The only vertebra without a body / intervertebral disc!

Axis (C2)

Composition:

(1) Paired superior articular processes
(2) Paired inferior articular processes
(3) Superior projection = odontoid process / dens

ATLANTOAXIAL (C1-C2) JOINT

Motion mechanics: flexion, extension, minimal rotation

Physiologic range of rotation: 25°–53°

Major joint stabilizers (thickest + strongest ligaments):

› transverse lig. → allowing axial rotation
› alar ligg. → restrictors of lateral flexion, limiting excessive rotation
› joint capsules

A. INTRINSIC LIGAMENTS (= 3 layers anterior to dura mater)

(1) **Odontoid ligament**

(a) ***Apical ligament***
Function: secondary stabilizer preventing anterior shift
Course: from middle aspect of tip of odontoid process → anterior margin of foramen magnum

(b) ***Alar ligaments*** (paired)
Function: secondary stabilizer preventing anterior shift
Course: from lateral aspect of tip of dens → medial aspect of occipital condyles

(2) **Cruciate (cross-shaped) ligament**

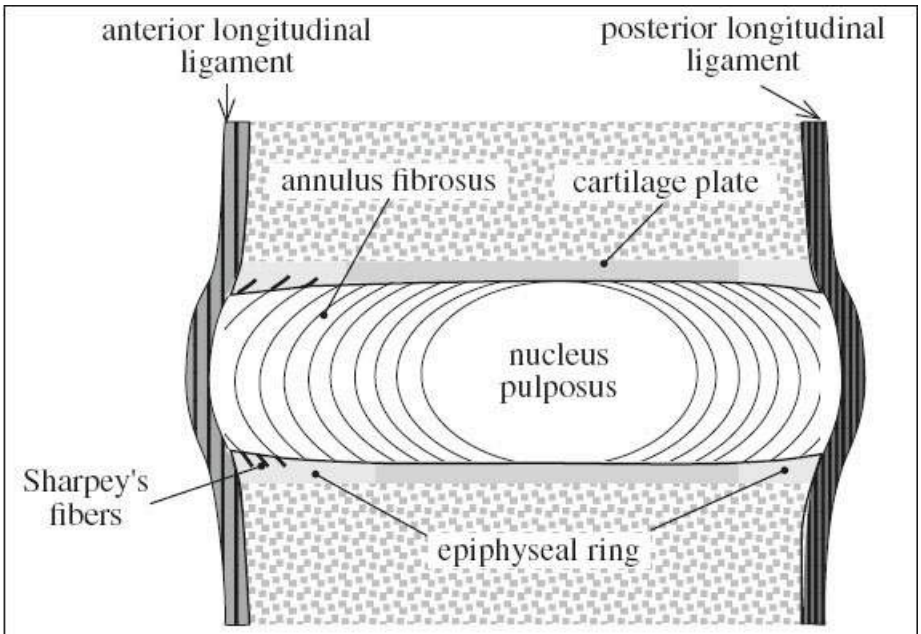
(a) ***Transverse ligament*** of atlas
Function: primary stabilizer of joint preventing excessive anterior motion of atlas on axis
Course: between medial portions of lateral masses: horizontal course behind dens

(b) ***Crus superioris***
Location: superior extension from transverse lig.
Attachment: lower margin of occipital bone

(c) ***Crus inferioris***
Location: inferior extension from transverse lig.
Attachment: posterior surface of body of axis

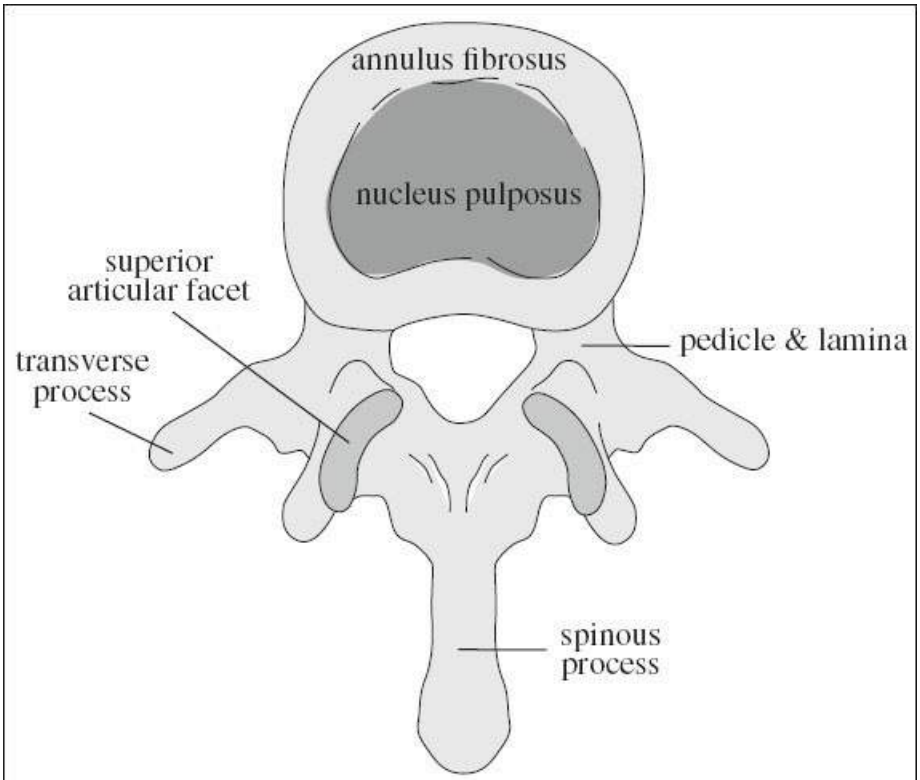
(3) **Tectorial membrane**
= rostral continuation of posterior longitudinal lig.
Course: from body of C2 → anterior margin of foramen magnum
Function: restricts extension

B. EXTRINSIC LIGAMENTS
= fibroelastic membranes as rostral continuations of
(1) Anterior longitudinal lig.
(2) Ligamentum flavum
(3) Nuchal ligament
= continuation of inter- and supraspinous ligaments

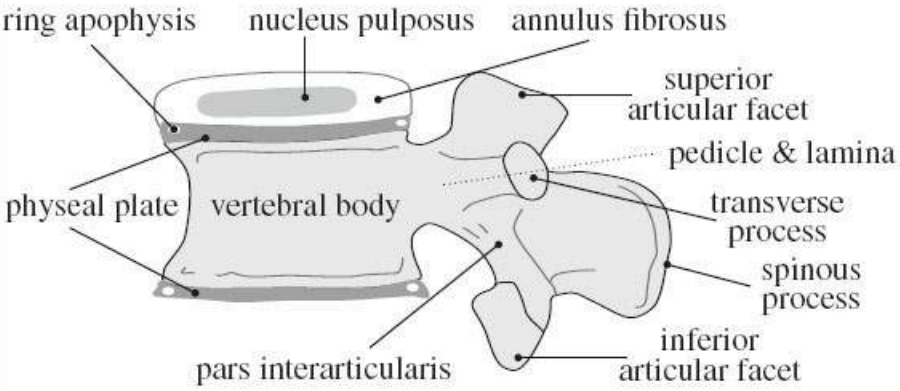


Anatomy of Diskovertebral Junction

anterior longitudinal ligament attaches to anterior surface of vertebral body; it is less adherent to intervertebral disk; posterior longitudinal ligament is applied to back of intervertebral disk and vertebral bodies

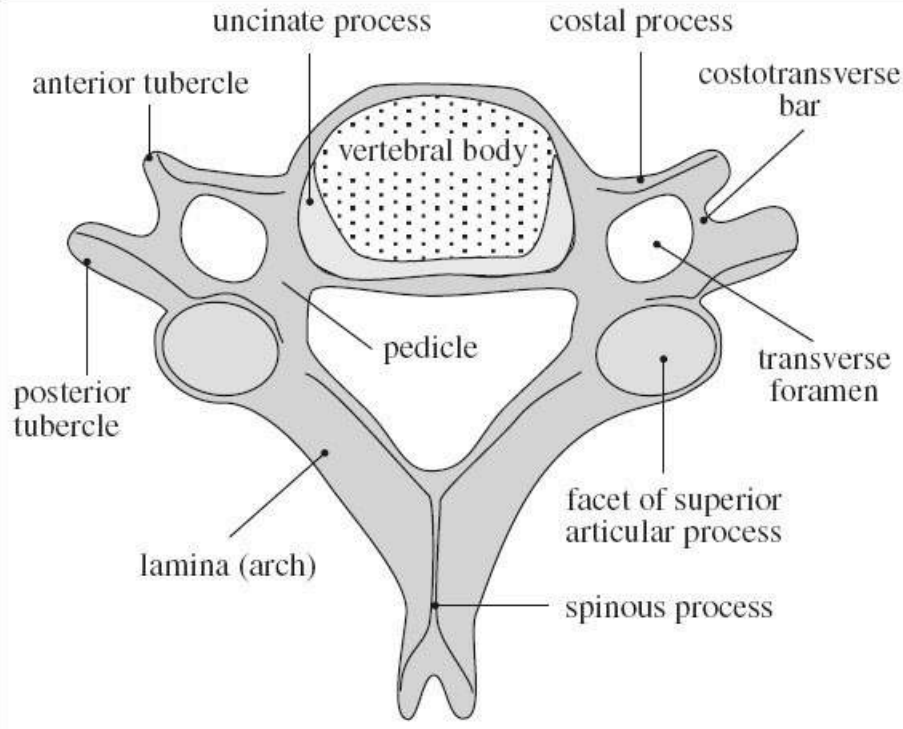


Normal Axial Lumbar Pediatric Vertebral Anatomy

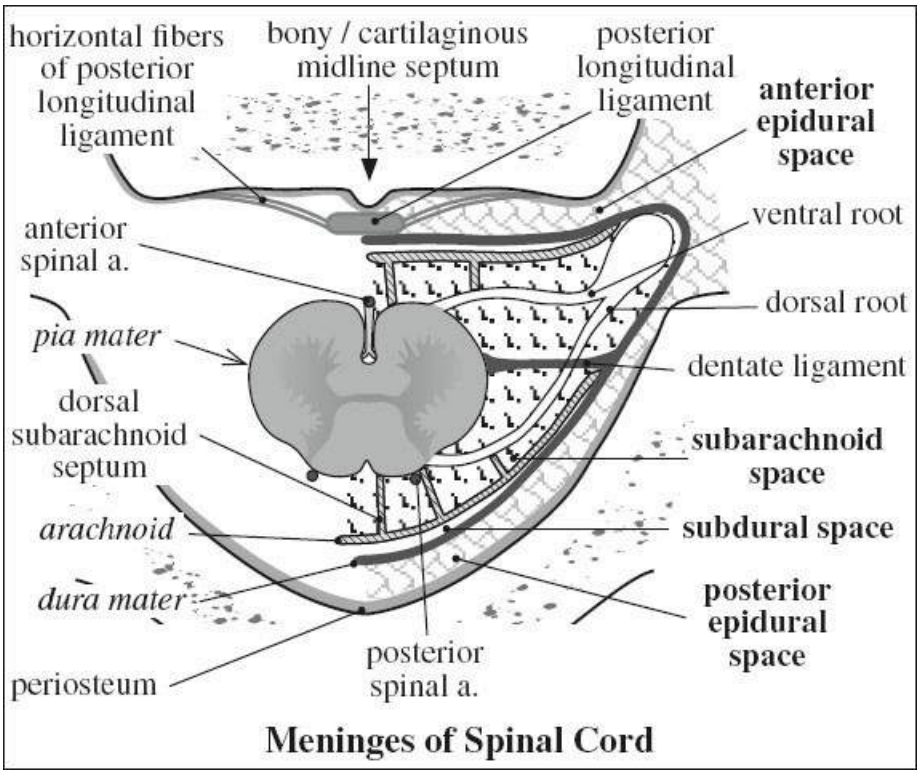


Normal Sagittal Lumbar Pediatric Vertebral Anatomy

3 ossification centers: fusion of 1 vertebral body + 2 posterior elements usually complete by 6 years of age;
physeal plates provide longitudinal growth through enchondral ossification;
ring apophysis calcifies around 6 years of age, ossifies around 13 years of age, and fuses with vertebral body around 17 years of age



Typical Cervical Vertebra (cranial aspect)



Course: 7th cervical vertebra → external occipital protuberance
Function: restriction of hyperflexion

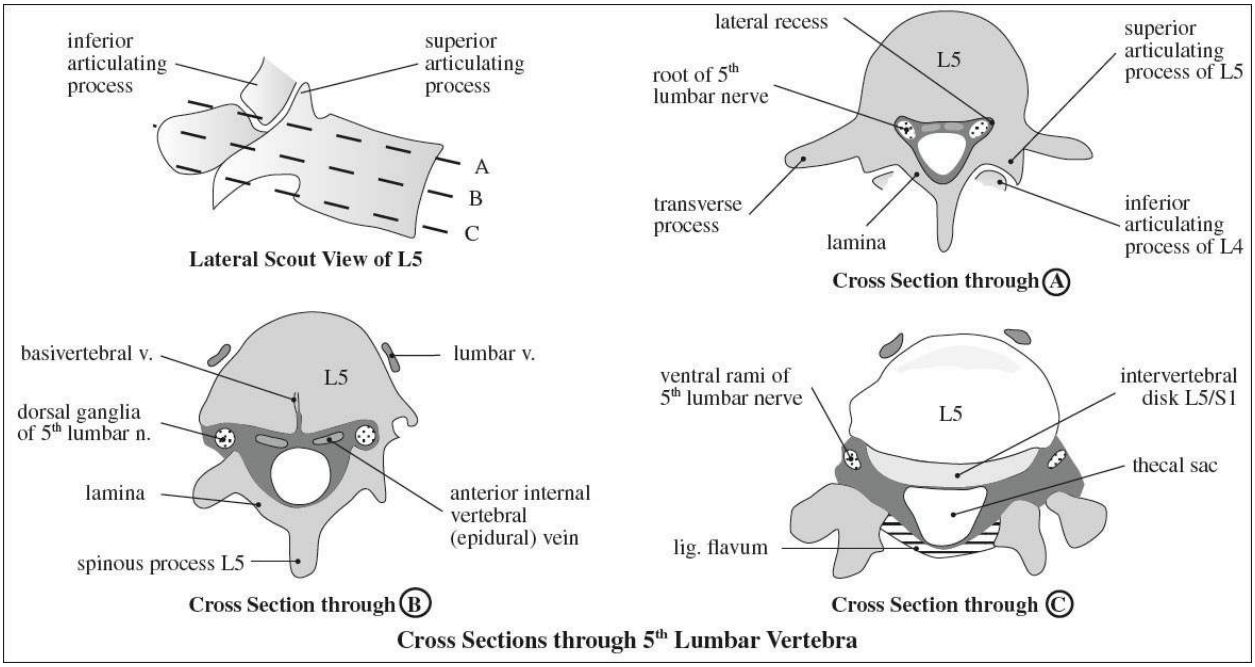
(4) Posterior atlanto-occipital membrane
= cephalic projection of ligamentum flavum
Course: posterior arch of atlas → posterior margin of foramen magnum

MENINGES OF SPINAL CORD

A. PERIOSTEUM
= continuation of outer layer of cerebral dura mater

B. EPIDURAL SPACE
= space between dura mater + bone containing rich plexus of epidural veins, lymphatic channels, connective tissue, fat
(a) cervical + thoracic spine: spacious posteriorly, potential space anteriorly
√ normal thickness of epidural fat 3–6 mm at T7
(b) lower lumbar + sacral spine: may occupy more than half of cross-sectional area

C. DURA
= continuation of meningeal / inner layer of cerebral dura mater; ends at 2nd sacral vertebra + forms coccygeal ligament around filum terminale; sends tubular extensions around spinal nerves; continuous with epineurium of peripheral nerves



Attachment: at circumference of foramen magnum, bodies of 2nd + 3rd cervical vertebrae, posterior longitudinal ligament (by connective tissue strands)

D. SUBARACHNOID SPACE

= space between arachnoid and pia mater containing CSF, reaching as far lateral as spinal ganglia

dentate ligament partially divides CSF space into an anterior + posterior compartment extending from foramen magnum to 1st lumbar vertebra, is continuous with pia mater of cord medially + dura mater laterally (between exiting nerves)

dorsal subarachnoid septum connects the arachnoid to the pia mater (cribriform septum)

E. PIA MATER

= firm vascular membrane intimately adherent to spinal cord, blends with dura mater in intervertebral foramina around spinal ganglia, forms filum terminale, fuses with periosteum of 1st coccygeal segment

Artery of Adamkiewicz

[Albert Wojciech Adamkiewicz (1850–1921) Polish physician and chair of General and Experimental Pathology of Jagiellonian University in Kraków, Poland]

= GREAT ANTERIOR RADICULOMEDULLARY ARTERY

= most important feeder artery of thoracolumbar spinal cord

Diameter: 0.8–1.3 mm

Supply: lower ⅓ of spinal cord

Origin: left intercostal / lumbar artery (68–73%)

Level: 9–12th intercostal artery (62–75%)

Anatomy:

descending aorta →

<u>intercostal / lumbar</u> artery → division into

(a) anterior branch

(b) posterior branch → subdivision into
› muscular branch
› dorsal somatic branch
› radiculomedullary artery → subdivision into
» posterior radiculomedullary artery
» anterior radiculomedullary artery

Hairpin turn: at junction of artery of Adamkiewicz and anterior spinal artery ← increasing disparity between spinal segmental and vertebral levels during growth of spine

Visualization of hairpin: by MR angiography in 93%
by CT angiography in 83%
by selective angiography in 86%

Rx: paraplegia ← conventional selective angiography

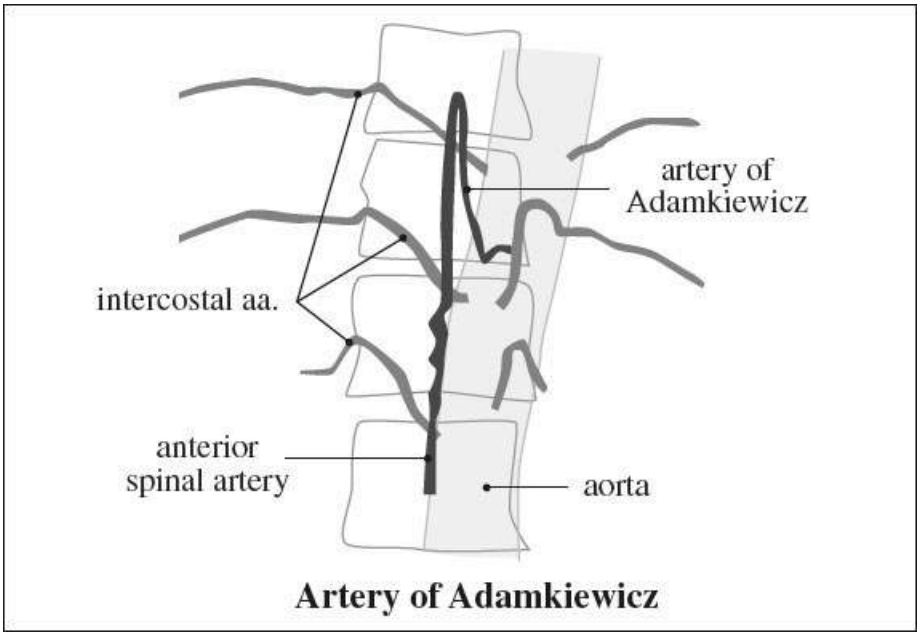
DDx: anterior radiculomedullary vein (very similar shape and course as artery of Adamkiewicz)

BIOMECHANICS OF SPINAL COLUMN

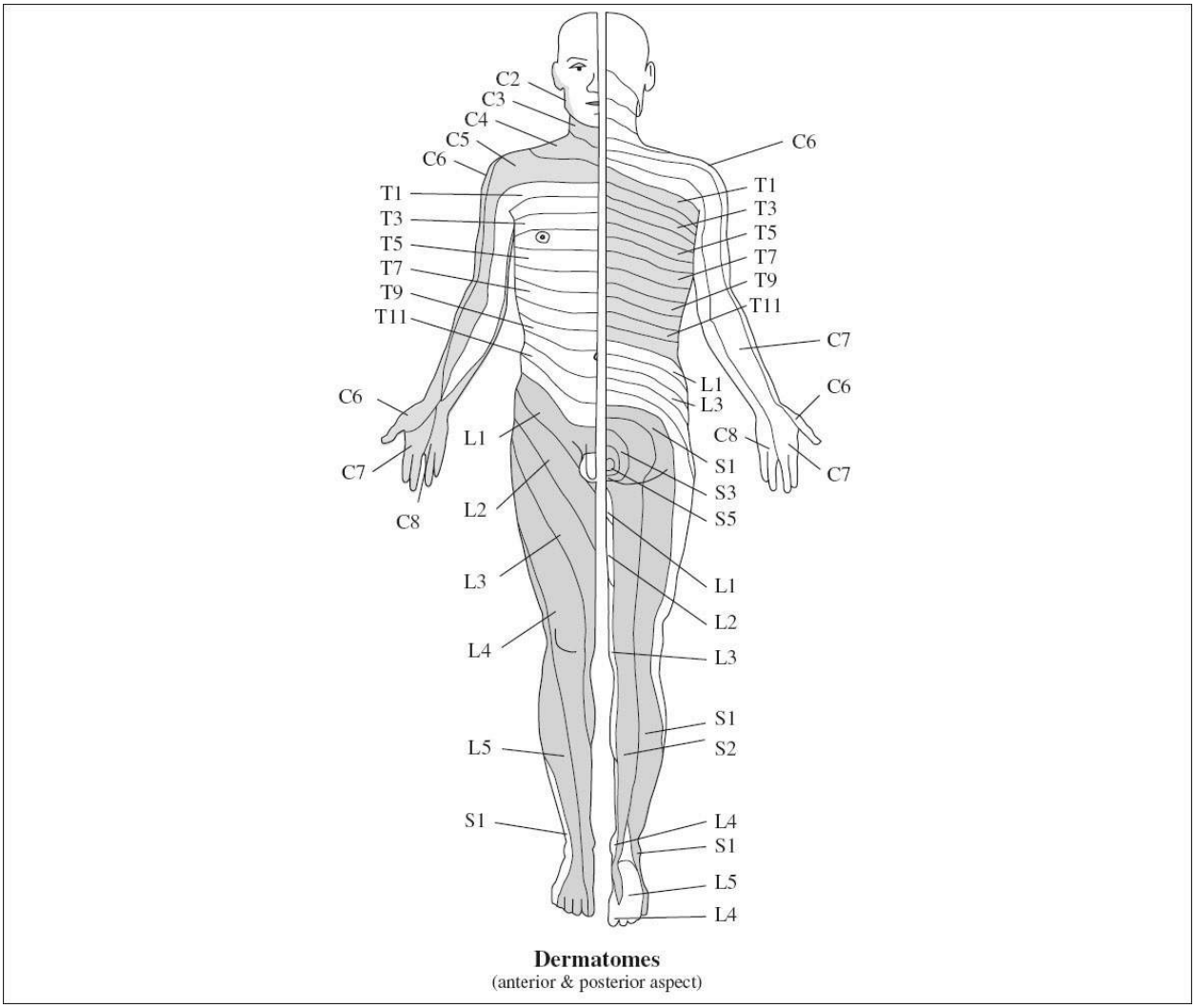
= primary structural support of human body (Francis Denis, 1983)
(a) transmitting axial load of most of the body's weight
(b) restraining motion during flexion, extension, rotation, lateral bending

A. **Anterior column**
= anterior longitudinal ligament, anterior annulus fibrosus, anterior ⅔ of vertebral body
Function: bearing axial load, resisting extension

B. **Middle column**
= posterior ⅓ of vertebral body, nucleus pulposus, posterior annulus fibrosus, posterior longitudinal ligament



Artery of Adamkiewicz



Dermatomes
(anterior & posterior aspect)

Function: bearing some axial load, resisting flexion

◊ Integrity of the middle column is synonymous with stability!

C. **Posterior column**

= posterior elements (pedicles, facets, laminae) + ligaments (lig. flavum, interspinous ligament, supraspinous ligament)

Function: resisting flexion, stabilizing rotation + lateral bending

Posterior Ligamentous Complex (PLC)

Function: "tension band" of spinal column resisting compressive forces on vertebral bodies

1. Supraspinous ligament
   = strong cordlike ligament connecting tips of spinous processes from C7 to sacrum
2. Interspinous ligament
3. Articular facet capsules
4. Ligamentum flavum
   = thick broad structure connecting laminae of adjacent vertebrae

Posterior Longitudinal Ligament

Function: contributes to stability of spinal column

Attachment: tethered to vertebral body via a central septum creating a left + right anterior epidural space

(a) superficial dorsal layer: 8–10 mm wide at disk space level separable from dura at dissection

(b) deep layer: 2–3 mm wide at disk space level

Thoracic Spine

› 12 load-bearing vertebrae

› posterior arch (= pedicles, laminae, facets, transverse processes) handles tensional forces

› vertebral bodies:

(a) height of vertebrae anteriorly 2–3 mm less than posteriorly → mild kyphotic curvature

(b) AP diameter: gradual increase from T1 to T12

(c) transverse diameter: gradual increase from T3 to T12

Thoracolumbar Spine (T12–L1)

Functional unit: 2 vertebrae + interconnecting soft tissues

(a) anterior portion = 2 aligned vertebral bodies + intervertebral disk + anterior and posterior longitudinal ligaments

(b) posterior portion = vertebral arches + facet joints + posterior ligamentous complex

Transitional Vertebra

= vertebra retaining partial features of segments below and above; total number of vertebrae in 92% unchanged with 24 (= 7 + 12 + 5) segments

Incidence: 3–21% of population

- **Bertolotti syndrome** = back pain from transitional 5th lumbar vertebra resulting in partial sacralization
- incidental finding

Location: thoracolumbar (4%) + lumbosacral (15%) junction

Variability of distribution (see table):

(a) variation from 12 thoracic + 5 lumbar segments maintaining together 17 presacral segments, eg, 11 thoracic + 6 lumbar OR 13 thoracic + 4 lumbar

(b) anomalous number of vertebrae (= 23 / 25 presacral segments)

(c) thoracolumbar / lumbosacral transitional vertebra

Thoracolumbar Transitional Vertebra

√ one side with a rib (= laterally downsloping osseous structure with articulation to vertebra)

√ other side with a transverse process (= horizontal osseous structure without central articulation to vertebra)

Lumbosacral Transitional Vertebra

◊ The first non–rib-bearing vertebra = L1

√ "sacralized L5" = L5 incorporated into sacrum

√ "lumbarized S1" = S1 incorporated into lumbar spine

√ uni- / bilateral dysplastic / enlarged transverse processes of lumbosacral transitional vertebra ± uni- / bilateral contact / pseudarthrosis / fusion to adjacent sacral ala
√ "squared" morphology of transitional vertebra
√ decreased height of intervertebral lumbosacral disk
√ none / small residual / well-formed S1-2 disk
√ alteration of lumbosacral intervertebral disk angle

Cx: confusion over labeling / assignment of vertebral levels during treatment planning
◊ Counting cephalad from presumed lumbosacral angle can lead to errors!

Numbering Vertebral Levels at Lumbar MR

Nota bene:

(1) The **iliolumbar ligament** (= low SI structure extending from transverse process to posteromedial iliac crest) identifies the lumbosacral junction (99%), but does NOT ALWAYS denote level of L5
(2) The magnitude of the **lumbosacral intervertebral disk angle** is not useful
(3) A **thoracolumbar transitional vertebra** is NOT associated with an anomalous number of presacral segments

Distribution of Presacral Segments			
Segments			*thoracic + lumbar seg.*
23	5%	3.5%	*11 + 5
		1.5%	*12 + 4
24	92%	89.0%	*12 + 5
		2.2%	*13 + 4
		0.8%	*11 + 6
25	3%	2.4%	*12 + 6
		0.6%	*13 + 5
*The cervical spine is morphologically stable with 7 vertebrae			

(4) A **lumbosacral transitional vertebra** is associated with an anomalous number of presacral segments:
◊ Avoid wrong-level spine surgery and obtain whole-spine localizer image!

MR Report:

"This report assumes that there are five lumbar-type vertebrae, with the lowest lumbar vertebra identified by the iliolumbar ligament."
"A lumbosacral transitional vertebra is present characterized by …. The lowest well-formed intervertebral disk is at …."

NORMAL POSITION OF CONUS MEDULLARIS

◊ Vertebral bodies grow more quickly than spinal cord during fetal period of < 19 weeks MA!
◊ No significant difference regardless of age!

Inferior-most aspect of conus:

L1–L2 level: normal (range T12 to L3)
L2–L3 or higher: in 97.8%

L3 level: indeterminate (in 1.8%)
L3–L4 / lower: abnormal
by 3 month: above inferior endplate of L2 (in 98%)

N.B.: If conus is at / below L3 level, a search should be made for tethering mass, bony spur, thick filum!

SACROILIAC JOINT

A. Upper dorsal part = syndesmosis
   = bone surfaces united by interosseous sacral ligaments
   Location: superior ⅔ to ½ of joint
   √ irregular syndesmotic margins
B. Lower ventral part = synovial joint
   = anatomic characteristics of cartilaginous articulation (hyaline cartilage firmly attached to adjacent bone by fibrous tissue with inner capsule of synovial cells)
   Location: inferior ⅓ to ½ of joint
   √ smooth parallel joint margins
   √ normal joint space width of 2.49 ± 0.66 mm in people < 40 years of age
   (a) 3–5 mm thick cartilage on sacral side
   (b) 1 mm thick cartilage on iliac side
   √ loss of joint space width in people > 40 years of age to 1.47 ± 0.21 mm ± asymmetry of joint width
   √ focal joint space narrowing + nonuniform ill-defined subchondral iliac sclerosis frequent > 30 years of age
C. Ligamentous stabilizers of SI joint
   1. Interosseous ligament
   2. Ventral + dorsal sacroiliac ligaments
   3. Sacrospinous ligament
   4. Sacrotuberous ligament
   5. Iliolumbar ligament

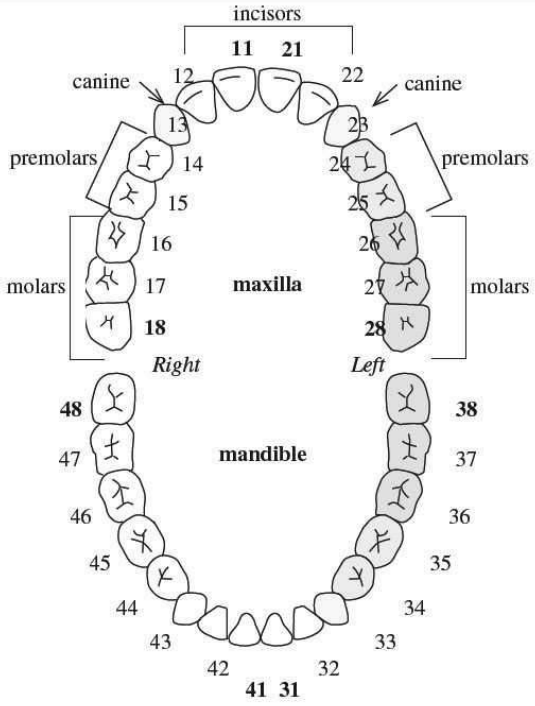
Positioning: oblique view + modified Ferguson view = AP projection with 23° cephalad angulation

Anatomic Variants of SI Joint

1. Accessory sacroiliac joint (most common)
   Site: posterosuperior portion
2. Iliosacral complex
   = iliac projection inserted into a complementary sacral recess
   Site: transition between ligamentous + synovial portion
3. Bipartite iliac bone plate
   Site: posteroinferior portion

Int	A	
11	8	Central incisor
12	7	Lateral incisor
13	6	Cuspid (canine / eye tooth)
14	5	1st Bicuspid (1st premolar)
15	4	2nd Bicuspid (2nd premolar)
16	3	1st Molar (6-year molar)
17	2	2nd Molar (12-year molar)
18	1	3rd Molar (wisdom tooth)

Int	A	
48	32	3rd Molar (wisdom tooth)
47	31	2nd Molar (12-year molar)
46	30	1st Molar (6-year molar)
45	29	2nd Bicuspid (2nd premolar)
44	28	1st Bicuspid (1st premolar)
43	27	Cuspid (canine / eye tooth)
42	26	Lateral incisor
41	25	Central incisor



Int	A	
21	9	Central incisor
22	10	Lateral incisor
23	11	Cuspid (canine / eye tooth)
24	12	1st Bicuspid (1st premolar)
25	13	2nd Bicuspid (2nd premolar)
26	14	1st Molar (6-year molar)
27	15	2nd Molar (12-year molar)
28	16	3rd Molar (wisdom tooth)

Int	A	
38	17	3rd Molar (wisdom tooth)
37	18	2nd Molar (12-year molar)
36	19	1st Molar (6-year molar)
35	20	2nd Bicuspid (2nd premolar)
34	21	1st Bicuspid (1st premolar)
33	22	Cuspid (canine / eye tooth)
32	23	Lateral incisor
31	24	Central incisor

Tooth Numbering System for Permanent Arch
(according to American Dental Association [A] & Fédération Dentaire Internationale [Int])
Tooth surfaces: (a) anterior / *buccal* (vestibular) for maxilla + mandible (b) posterior / *palatine* for maxilla (c) *lingual* for mandible
Relationship of dental structures to mental foramen: *mesial* = anterior to mental foramen; *distal* = posterior to mental foramen

TEETH

Primary (deciduous) Dentition (20 teeth)

= 5 teeth in each quadrant: NO premolars + only 2 molars

Permanent Dentition (32 teeth)

= 8 teeth in each quadrant

Development:

from occlusal surface toward root apex within maxilla and mandible; resorption of root of primary tooth during migration toward oral cavity; eruption continues until tooth occludes with tooth from opposite jaw

Anomalous Tooth Development

Hypodontia = < 32 teeth

Hyperdontia = > 32 teeth

Frequency: molar (44%), premolar (33%), incisor (23%)

May be associated with: Gardner syndrome, cleidocranial dysplasia

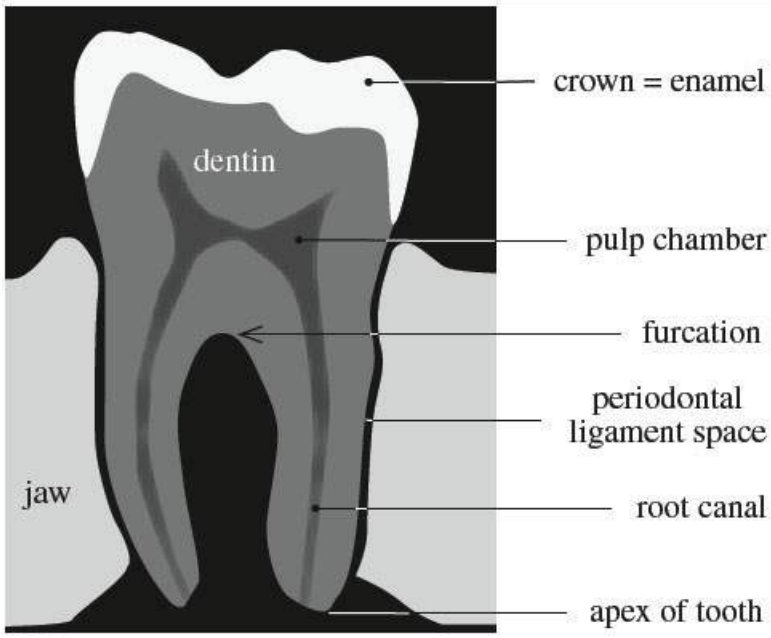
mesiodens: in maxillary midline adjacent to incisors

distodens: posterior to 3rd molar, often impacted causing dental inflammation / infection

Cx of supernumerary teeth:

crowding / abnormal eruption / noneruption / damage of normal teeth

DDx: odontoma, hamartoma of odontogenic origin



Drawing of CT Image of Mandibular Molar
(sagittal oblique view)

lamina dura = lining of tooth socket;
periodontal ligament = thin radiolucent layer between surface of root + lamina dura

Tooth surface: outward = **facial** (**buccal / labial**); inward = **lingual** (for mandible) / **palatal** (for maxilla);
anterior = **mesial**; posterior = **distal**;
premolar / molar biting surface = **occlusal**

ADENOMATOID ODONTOGENIC TUMOR

= rare tumor
Age: 2nd decade; M << F
Location: 70% in maxilla
√ well-demarcated radiolucent lesion + punctate calcifications
DDx: dentigerous cyst (less apical in location)

AMELOBLASTIC FIBROMA

Histo: epithelium representing enamel + embryonic connective tissue
Associated with: impacted tooth
Location: posterior mandible
√ well-defined pericoronal radiolucent lesion
√ mostly multiloculated

AMELOBLASTOMA OF JAW

= ADAMANTINOMA OF JAW
= benign locally aggressive infiltrative epithelial neoplasm
Prevalence: most common (10%) of odontogenic tumors
Origin: enamel-forming odontogenic epithelium of dental follicle that failed to regress during embryonic development; 30–50% arise from epithelium of dentigerous cyst (= mural ameloblastoma)
Classification (WHO 2006):
(a) intraosseous: arises in jaw as unicystic / desmoplastic / mixed cystic + solid (most aggressive) lesion
(b) extraosseous (peripheral): sessile / pedunculated mass confined to gingiva / alveolar mucosa
Age: 20–40 years; M÷F = 1÷1
• slow-growing painless mass
Location: ramus + posterior body of mandible (75%), maxilla (25%)
Site: in region of bicuspids + molars, typically 3rd molar (angle of mandible commonly affected)
√ well-defined well-corticated unilocular lucent lesion (DDx: odontogenic keratocyst, dentigerous cyst)
√ uni- / multilocular lesion with internal septations (honeycomb / soap bubble appearance)
√ typically expansile with scalloped margin
√ may perforate lingual cortex + infiltrate adjacent soft tissues
√ erosion of roots of adjacent teeth (UNIQUE)
√ often associated with crown of an impacted / unerupted tooth
CT:

√ cystic areas of low attenuation + isoattenuating enhancing solid component
√ ± resorption of roots of adjacent teeth

Prognosis: frequently local recurrence even more aggressive after excision; rarely metastasize to lung

Cx: may undergo carcinomatous change

Rx: wide surgical resection ± radiation therapy

ANKYLOSING SPONDYLITIS

= autoimmune disease of unknown etiology characterized by inflammation of multiple articular + paraarticular structures frequently resulting in bone ankylosis primarily affecting axial skeleton

Prevalence: 0.1–0.2% of general population

Peak age: 15–35 years; M÷F = 3÷1 to 10÷1; Caucasian÷Blacks = 3÷1

Associated with: (1) Ulcerative colitis, regional enteritis
(2) Iritis in 25%
(3) Aortic insufficiency + atrioventricular conduction defect

• HLA-B27 antigen positive in 96%
• insidious onset of low back pain + stiffness

Path: involves synovial + cartilaginous joints and sites of ligamentous attachment

Location:
(a) axial skeleton: sacroiliac joints, thoracolumbar + lumbosacral junctions
◊ HALLMARK is sacroiliac joint involvement!
(b) peripheral skeleton (10–20%): sternal joint, symphysis pubis, hip, glenohumeral joint
(c) tendinous insertions in pelvis + proximal femur

Temporal course: initial abnormalities of sacroiliac joints + thoracolumbar + lumbosacral junctions with gradual involvement of remaining spine

@ Skull
√ temporomandibular joint space narrowing, erosions, osteophytosis

@ Hand (30%)
√ exuberant osseous proliferation
√ osteoporosis, joint space narrowing, osseous erosions (deformities less striking than in rheumatoid arthritis)

@ Sacroiliac joint / symphysis pubis
√ initially sclerosis of joint margins primarily on iliac side (bilateral + symmetric late in disease, may be unilateral + asymmetric early in disease)
√ later irregularities + widening of joint (= cartilage destruction)
√ bony fusion

@ Pelvis
√ periostitic "whiskering": ischial tuberosity, iliac crest, ischiopubic rami, greater femoral trochanter, external occipital protuberance, calcaneus

@ Spine
√ squaring = straightened / convex anterior vertebral margins = erosive osteitis of anterior corners
√ "shiny corners" = reactive sclerosis of corners of vertebral body

√ diskitis = erosive abnormalities of diskovertebral junction
√ "diskal ballooning" = biconvex shape of intervertebral disk related to osteoporotic deformity + diskal calcification
√ marginal syndesmophyte formation (in 15%) = thin vertical radiodense spicules bridging the vertebral bodies = ossification of outer fibers of annulus fibrosus (NOT anterior longitudinal ligament):
  √ "bamboo spine" on AP view = undulating contour due to syndesmophytosis
    Cx: prone to insufficiency fracture → pseudarthrosis
√ ankylosis of vertebral edges / center (with bony extension through disk)
√ asymmetric erosions of laminar + spinous processes of lumbar spine
√ ossification of supraspinous + interspinous ligaments:
  √ "dagger" sign = single radiodense line on AP view
  √ "trolley-track" sign on AP view = central line of ossification with two lateral lines of ossification (= apophyseal joint capsules)
√ apophyseal + costovertebral joint ankylosis (on oblique views)
√ dorsal arachnoid diverticula in lumbar spine with erosion of posterior elements (Cx: cauda equina syndrome)
√ atlantoaxial subluxation

MR:
  √ anterior / posterior / marginal spondylitis
  √ spondylodiskitis
  √ transdiskal / transvertebral insufficiency fracture
  √ arthritis of zygapophyseal (facet), costovertebral, costotransverse joints (best seen on axial images)
  √ bone marrow edema
  √ joint effusion, synovitis, erosions
  √ ankylosis in late stage → impairing chest excursion
  √ enthesitis of interspinous ligaments ± osteitis of subjacent spinous processes
  √ syndesmophytes + ankylosis of diskovertebral unit

@ Chest

Frequency: 1% of patients with ankylosing spondylitis, usually at an advanced stage of disease

Histo: interstitial + pleural fibrosis with foci of dense collagen deposition, NO granulomas

• bone manifestation obvious + severe

Location: apices / upper lung fields

√ sternomanubrial joint irregularities + sclerosis
√ uni- / bilateral coarse upper lobe pulmonary fibrosis with upward retraction of hila (DDx: tuberculosis)
√ reticulonodular progressively confluent opacities in lung apices
√ apical bullae, cysts + cavitation (mimicking TB)

HRCT:
  √ peripheral interstitial lung disease
  √ bronchiectasis
  √ paraseptal emphysema
  √ tracheobronchomegaly

√ apical fibrosis

Cx: superinfection, especially with aspergillus (mycetoma formation) in 19–60% / atypical mycobacteria
- hemoptysis

DDx: other causes of pulmonary apical fibrosis (primary infection by fungi / mycobacteria; cancer)

@ Cardiovascular (up to 80% paralleling duration of disease)

Location: ascending aorta, aortic valve

√ aortic wall thickening (60%)

√ aortic valve thickening + nodularity → aortic valve insufficiency

Prognosis: 20% progress to significant disability; occasionally death from cervical spine fracture / aortitis

Rx: regular lifelong exercises + NSAID; tumor-necrosis factor (TNF)–α inhibitors

DDx: (1) Reiter syndrome (unilateral asymmetric SI joint involvement, paravertebral ossifications)

(2) Psoriatic arthritis (unilateral asymmetric SI joint involvement, paravertebral ossification)

(3) Inflammatory bowel disease

(4) Sternoclavicular hyperostosis (pustulosis palmaris et plantaris)

ARACHNOIDITIS

Etiology: idiopathic; trauma, back surgery (spinal fusion, laminectomy), meningitis, subarachnoid hemorrhage (spinal tap, epidural steroid injections, difficult epidural blood patch); Pantopaque® myelography (pre 1986) ← inflammatory effect potentiated by presence of blood

M > F ← spinal / epidural anesthesia for delivery

Associated with: syrinx
- chronic low back pain ± radicular symptoms
- par- and hypesthesia, gait disturbance, incontinence, myelopathic symptoms

Location: most easily seen in lumbar region (= cauda equina)

√ residual oil-soluble contrast media in dural sac

√ intrathecal calcification

Myelo:

√ blunting of nerve root sleeves

√ blocked nerve roots without cord displacement (⅔)

√ streaking + clumping of contrast

CT:

√ fusion / clumping (= abnormal distribution) of nerve roots

√ intradural pseudomass

√ intradural cysts

√ "empty thecal sac" = featureless empty-looking sac with individual nerve roots adherent to wall (final stage)

MR:

√ conglomeration of adherent roots centrally within thecal sac:

√ thickened nerve roots
√ pseudotethering
√ "empty-sac" sign = roots adherent to wall of dural sac:
√ deformed / narrowed dural sac ← extra- / intradural scarring
√ intrathecal pseudocysts
√ soft-tissue mass replacing subarachnoid space
√ enhancement of nerve roots (= edema during first 3 months)
Cx: syringomyelia

ARACHNOID CYST OF SPINE

= subset of meningeal cysts
Cause: posttraumatic, postinfectious, congenital diverticulum, idiopathic (arachnoid herniation through dural defect /abnormal distribution of arachnoid trabeculations)
Histo: lined with fibrous tissue + scattered meningothelial cells
Age: 15–45 years (in 77%); range of several months to 80 years; M=F
Relationship to CSF:
(a) encapsulated completely separate from CSF
(b) communication with subarachnoid space via a neck ± one-way valve
• pain (waxing + waning), sensory changes, urinary dysfunction, weakness
• progressive spastic / flaccid paresis improving in supine position + worsening during Valsalva maneuver
• symptomatic with compression of spinal cord / nerve root ← arachnoid cyst expansion (osmotic gradient, ball-valve mechanism, active secretions from cyst lining)
√ oval sharply demarcated extramedullary mass
√ filling with intrathecal contrast material depending upon size of opening between cyst + subarachnoid space:
initially in 50%, nearly 100% with delayed imaging
DDx: epidermoid cyst (asymmetric filling defect)
√ local displacement + compression of spinal cord
√ higher SI than CSF (from relative lack of CSF pulsations)
√ NO enhancement
MR:
√ iso- to hyperintense to CSF on T1WI + T2WI
√ variability in signal intensity ← pulsatility of CSF / higher protein content
√ isointense to CSF on FLAIR MR images
√ NO restricted diffusion at DWI
Types:

I	extradural arachnoid cyst without nerve root fibers
	Ia extradural arachnoid cyst
	Ib sacral meningocele
II	extradural meningeal cyst containing neural tissue (= Tarlov cyst)
III	intradural arachnoid cyst

Pitfalls of CT myelography / MRI:

(1) Nonopacification of noncommunicating arachnoid cyst → misidentification as a different type of lesion
(2) Absence of mass effect on cord → failure to detect additional cysts / small CSF-isointense arachnoid cyst

DDx: traumatic / lateral thoracic meningoceles
Cx: spinal cord myelopathy, nerve root radiculopathy

Extradural Arachnoid Cyst

Cause: congenital / acquired dural defect
Age: 2nd decade of life; M>F
Location: thoracic (80%) > cervical (15%) > lumbar (5%)spine; extending over 3.7 vertebral bodies
Site: posteriorly / posterolaterally to cord
√ scalloping of vertebral body
√ thinning / erosion of pedicles
√ widening of interpeduncular distance

Intradural Arachnoid Cyst

Cause: congenital deficiency within arachnoid (= true arachnoid cyst) / adhesion from prior infection or trauma (= arachnoid loculation)
√ focal displacement and compression of spinal cord
√ widened dorsal subarachnoid space with diminished CSF flow artifact

ARACHNOID DIVERTICULUM

= widening of root sheath with arachnoid space occupying > 50% of total transverse diameter of root + sheath together
Cause: ? congenital / traumatic, arachnoiditis, infection
Pathogenesis: hydrostatic pressure of CSF
√ scalloping of posterior margins of vertebral bodies
√ myelographic contrast material fills diverticula

ARTERIOVENOUS MALFORMATION OF SPINAL CORD

Classification:
1. True intramedullary AVM
   = nidus of abnormal intermediary arteriovenous structure with multiple shunts
   Age: 2nd–3rd decade
   Cx: subarachnoid hemorrhage, paraplegia
   Prognosis: poor (especially in midthoracic location)
2. Intradural arteriovenous fistula
   = single shunt between one / several medullary arteries + single perimedullary vein
3. Dural arteriovenous fistula
   = single shunt between meningeal arteries + intradural vein
4. Metameric angiomatosis

ARTERIOVENOUS MALFORMATION OF JAW

• occasionally pulsatile soft-tissue swelling

Location: ramus + posterior body of mandible

√ cystlike due to bone resorption ± calcifications

√ ± multilocular ± bone expansion

√ ± erosive margins

√ angiogram confirms diagnosis

Cx: Tooth extraction can result in lethal exsanguination!

DDx: traumatic bone cyst, central giant cell granuloma, ossifying fibroma

ATLANTOAXIAL ROTARY FIXATION

= AARF = ATLANTOAXIAL ROTATORY SUBLUXATION (AARS)
= ATLANTOAXIAL ROTATORY FIXATION (AARF)
= SPONTANEOUS HYPEREMIC DISLOCATION
= ATLANTOAXIAL ROTATORY / ROTARY DISLOCATION
= DISTENTION LUXATION = NASOPHARYNGEAL TORTICOLLIS

= nontraumatic subluxation / rotational disorder of atlantoaxial joint leading to limited rotation / fixation of neck comprising many different entities

Cause: idiopathic spontaneous

(a) increased ligamentous laxity: rheumatoid arthritis, Marfan syndrome, Down syndrome, Morquio syndrome

(b) congenital abnormality: incomplete odontoid process, incomplete transverse ligament

(c) infection: sinusitis, otomastoiditis, otitis media, pharyngitis, adenotonsillitis, cervical / retropharyngeal / tonsillar abscess = **Grisel syndrome**
(= not associated with trauma or bone disease primarily in children) ← hyperemia + pathologic ligamentous relaxation

Predisposed: cervical dystonia, post surgery

May be associated with: ipsilateral contracted SCMM

• history of insignificant cervical spine trauma / upper respiratory tract infection

• limited painful neck motion = painful torticollis

• head held in "cock-robin" position = rotation + flexion + tilt of head contralateral to direction of rotation with inability to turn head that does not resolve within 5–7 days after injury

X-ray (Dx difficult to make):

√ atlanto-odontoid asymmetry (open mouth odontoid view):

√ decrease in atlanto-odontoid space + widening of lateral mass on side ipsilateral to rotation

√ increase in atlanto-odontoid space + narrowing of lateral mass on side contralateral to rotation

√ atlantoaxial asymmetry remains constant with head turned into neutral position

√ posterior arch of C1 not identified in true lateral projection

√ obscuration of craniovertebral junction in true lateral view

CT (dynamic with 3D reconstruction [a] with head in resting position [b] with maximal contralateral rotation):

√ facet displacement in neutral head position

√ asymmetrically fixed C1-C2 rotation

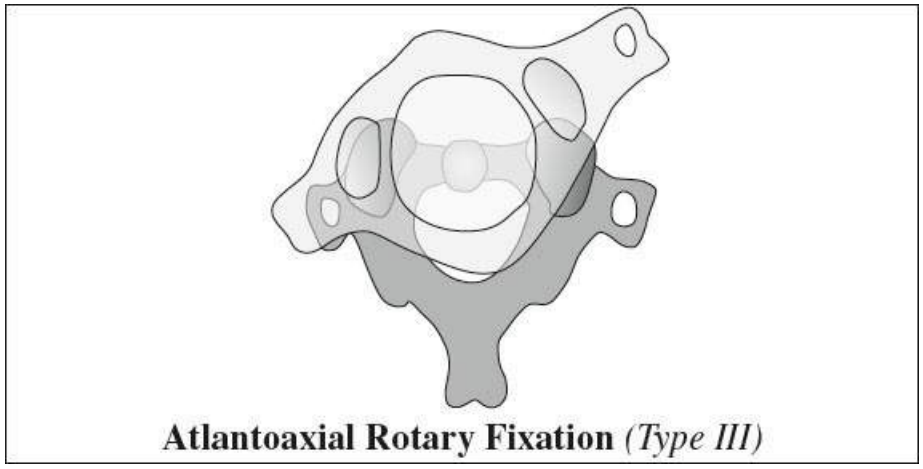
Rotation up to an average of 79° in adult volunteers, loss of contact of articular facets of C1 and C2 during rotation as high as 74–85% in physiologic conditions. Therefore, a diagnosis of subluxation of the atlanto-occipital joint should not be made based solely on the CT appearance of this joint.

MR:
√ disruption of alar + transverse ligg.
√ spinal cord compression (rare)

Types:

I < 3 mm anterior displacement of atlas on axis = rotatory fixation within normal range of movement (most common)
Injury: intact alar + transverse ligaments
√ pivot around dens, NO anterior displacement of atlas

II 3–5 mm anterior displacement of atlas + unilateral displacement of lateral mass of atlas ← restraint by alar lig.
Injury: transverse ligament



Atlantoaxial Rotary Fixation *(Type III)*

√ center of rotation shifted to one of lateral masses

III > 5 mm anterior displacement of atlas + anterior displacement of both lateral masses
Injury: deficiency of both (alar + transverse) ligaments

IV posterior displacement of atlas on axis (rare)
Injury: deficiency of both (alar + transverse) ligaments

DDx: torticollis (atlantoaxial symmetry reverts to normal with head turned into neutral position)

Traumatic Rotatory Subluxation

Cause: injury of alar ligaments ← flexion + rotation forces
Age: more prevalent in children than in adults ← mostly flat articular facets allow ample movement in multiple directions

BRACHIAL PLEXUS INJURY

= most severe nerve injury of extremities
Cause: severe traction force on upper limb at birth / in traffic accident (motorcycle)

1. **Erb-Duchenne palsy**: adduction injury affecting C5-6 ← downward displacement of shoulder
   - paralysis of shoulder muscles + biceps
2. **Klumpke palsy**: abduction injury at C7, C8, T1 ← arm stretched over head
   - paralysis of forearm flexors + intrinsic hand muscles

CT myelography (preferred method):

◊ Shoulder artifacts may be problematic at C8–T1 level

√ displacement of spinal cord to contralateral side ← absence of normal nerve root traction on cord

√ pouchlike nerve root sleeve at site of avulsion

√ asymmetric slightly deformed root sleeve + nerve roots

√ obliteration of tip of root sleeve

√ traumatic meningocele

√ contrast extravasation collecting in axilla

√ metrizamide in neural foramina

MR:

◊ Conventional MR only in 50% accurate!

Pitfalls: partial root avulsion, intradural fibrosis, traumatic meningocele, movement artifacts (respiration, swallowing, blood flow)

√ focal T2-hyperintense cord changes ← edema of acute phase / myelomalacia in chronic phase

√ focal T2-hypointense cord changes ← hemosiderin

√ enhancement of morphologically normal intradural nerve root / root stump ← functional impairment (mostly preganglionic)

√ abnormal enhancement of paraspinal (multifidus) muscle ← muscle denervation = indirect sign of root avulsion

√ thickening of postganglionic brachial plexus ← edema + fibrosis

CAUDAL REGRESSION SYNDROME

= SACRAL AGENESIS = CAUDAL DYSPLASIA SEQUENCE

= midline closure defect of neural tube with a spectrum of anomalies including complete / partial agenesis of sacrum + lumbar vertebrae and pelvic deformity

Etiology: disturbance of caudal mesoderm < 4th week of gestation from toxic / infectious / ischemic insult

Prevalence: 1÷60,000 births; 0.005–0.01% of population; in 0.1–1% of pregnancies in diabetic women; M÷F = 2.7÷1

Predisposed: infants of diabetic mothers; risk increases 200–400 times in women dependent on insulin

◊ 16–22% of children with sacral agenesis have mothers with diabetes mellitus

◊ NOT associated with VATER syndrome!

A. Musculoskeletal anomalies

@ Lower extremity

- symptoms from minor muscle weakness to complete sensorimotor paralysis of both lower extremities

√ hip dislocation
√ hypoplasia of lower extremities
√ flexion contractures of lower extremities
√ foot deformities

@ Lumbosacral spine = SACRAL AGENESIS

Spectrum:

Type 1 = unilateral partial agenesis localized to sacrum / coccyx
Type 2 = bilateral partial symmetric defects of sacrum + iliosacral articulation
Type 3 = total sacral agenesis + iliolumbar articulation
Type 4 = total sacral agenesis + ilioilial fusion posteriorly

√ nonossification of lower spine
√ fusion of caudal-most 2 or 3 vertebrae
√ spina bifida (lipomyelomeningocele often not in combination with Arnold-Chiari malformation)
√ narrowing of spinal canal rostral to last intact vertebra
√ hypoplastic iliac wings

B. Spinal cord anomalies
√ characteristic club- / wedge-shaped configuration of conus medullaris (= hypoplasia of distal spinal cord)
√ ± tethered spinal cord
√ ± dural sac stenosis with high termination
√ ± spinal cord lipoma, teratoma, cauda equina cyst
√ ± syrinx

C. Genitourinary anomalies
• neurogenic bladder (if > 2 segments are missing)
• malformed external genitalia
√ ± bilateral renal aplasia with pulmonary hypoplasia and Potter facies

D. Hindgut anomalies
• lack of bowel control
√ anal atresia

OB-US:
• normal / imperforate anus
√ short CRL in 1st trimester ← diabetic embryopathy
√ normal / mildly dilated urinary system
√ normal / increased amniotic fluid
√ 2 umbilical arteries
√ 2 hypoplastic nonfused lower extremities in a CHARACTERISTIC froglike position
√ fusion of pelvic bones
√ sacral agenesis, absent vertebrae from lower thoracic / upper lumbar spine caudally

N.B.: brain, proximal spine, and spinal cord are notably spared!

Sirenomelia

= fused lower extremities resembling a mermaid (siren)

Cause: aberrant vessel that shunts blood from the high abdominal aorta to the umbilical cord (steal phenomenon) → severe ischemia of caudal portion of fetus

◊ NOT associated with maternal diabetes mellitus!

• pulmonary hypoplasia + Potter facies

• absence of anus; absent genitalia

√ bilateral renal agenesis / dysgenesis (lethal)

√ marked oligohydramnios

√ single aberrant umbilical artery

√ two-vessel umbilical cord

√ single / fused lower extremity often with fewer leg bones than normal

√ sacral agenesis, absent pelvis, lumbosacral "tail", lumbar rachischisis

Prognosis: incompatible with life

CEMENTOBLASTOMA

= rare benign periapical lesion

Origin: true neoplasm of cementum

Prevalence: <1% of all odontogenic tumors

Age: < 20 years (50%); < 30 years (75%)

Associated with: erupted permanent tooth (common); near impacted / unerupted tooth (rare)

Location: mandible (>75%): 90% molar / premolar region

Site: fusion with root of tooth(s); invasion of root canal / pulp chamber (occasionally)

√ periapical sclerotic sharply marginated round opaque sunburst lesion

√ surrounded by thin halo of low attenuation

Rx: complete removal of tooth to avoid recurrence

DDx: condensing osteitis (periodontal ligament space not obscured)

CEMENTO-OSSEOUS DYSPLASIA

= CEMENTOMA = FIBROOSTEOMA

= nonneoplastic benign hamartoma associated with tooth apex

Histo: proliferation of connective tissue within periodontal membrane

Age: 4th–5th decade; in woman: black / Asian descent

• asymptomatic / dull ache

Associated with: vital nonrestored tooth + intact lamina dura

Location: mandible >> maxilla

Site: usually apex of vital tooth

√ one / more, closely apposed / confluent, round / ovoid lucent lesion with varying amounts of opacity:

√ initially lytic lesion

√ later mixed lysis + sclerosis with varying amounts of opacity; little expansion

√ calcifies centrally with time

√ periapical sclerotic sharply marginated area NOT fused to tooth

√ ± low-attenuation halo

√ adjacent lesions may coalesce

Cementoblastoma and cemento-osseous dysplasia are both periapical sclerotic sharply marginated

lesions with low-attenuation halo.
DDx: (1) Cementoblastoma (in child + young adult, fuses directly to tooth root)
(2) Cemento-osseous dysplasia (common in black woman + woman of Asian descent during 4th / 5th decade of life, does not fuse to tooth root)

Periapical Cemento-osseous Dysplasia

Site: anterior mandible between mandibular canine teeth involving one / a few teeth
√ often multicentric
DDx: ossifying fibroma, fibrous dysplasia, Paget disease

Focal Cemento-osseous Dysplasia

Site: posterior mandible involving molar teeth
√ no extension into adjacent bone
√ no cortical expansion
DDx: periapical periodontitis, ossifying fibroma

Florid Cemento-osseous Dysplasia

= diffuse form of periapical cemento-osseous dysplasia
Location: involving ≥ 2 jaw quadrants / entire mandible
May be complicated by: osteomyelitis with drainage of necrotic bone debris into oral cavity

CENTRAL GIANT CELL GRANULOMA (COMMON)

= single lesion of altered vascular + reactive response within bone
Age: < 30 years (75%); in girls + young women
• painless swelling, tenderness on palpation
Location: mandible÷maxilla = 2÷1
Site: anterior to 1st molar (= deciduous teeth); propensity for crossing midline (especially in maxilla)
√ small unilocular area of lucency (early)
√ multilocular honeycomb with wispy internal septa (later)
√ expansion of bone + erosion / remodeling of cortex
√ displacement of teeth + root resorption
√ usually well-defined border
DDx: brown tumor of HPT (histologically similar)

CHONDROSARCOMA OF SPINE

= 2nd most common nonlymphoproliferative primary malignant tumor of spine in adults
Peak age: 30 and 70 years; M÷F = 2÷1 to 4÷1
Location: thoracic + lumbar spine > sacrum
Site: posterior element (40%), vertebral body (15%), both (45%)
√ large calcified mass with bone destruction
√ ± true ossification ← residual osteochondroma
CT:
√ low attenuation of nonmineralized portion of tumor

√ chondroid matrix mineralization

MR:

√ nonmineralized portion of tumor = high water content:

√ low to intermediate SI on T1WI

√ very high signal intensity on T2WI

√ rings and arcs enhancement pattern ← lobulated growth

√ extension through intervertebral disk (in 35%)

Rx: en bloc resection

CHORDOMA

Prevalence: 1÷2,000,000; 2–4% of all primary malignant bone tumors; 1% of all CNS tumors

◊ 2nd most common primary malignant tumor of spine in adults after lymphoproliferative neoplasms! Highly malignant in children.

Etiology: originates from embryonic remnants of notochord / ectopic cordal foci between Rathke pouch + coccyx (notochord appears between 4th and 7th week of embryonic life and forms nucleus pulposus)

Mean age: 50 (range, 30–70) years; peak in 5th decade; M÷F = 2÷1

Path: lobulated tumor with fluid, gelatinous mucoid substance, recent + old hemorrhage, necrotic areas, occasionally calcifications + sequestered bone fragments contained within pseudocapsule

Histo: [*physallis*, Greek = bladder, bubble; *phoros* = bearing]

(1) typical chordoma: cords + clusters of **physaliferous cells** (PAS-positive stain) in a lobular arrangement with a large bubblelike multivacuolated cytoplasm containing intracytoplasmic mucous droplets; abundant extracellular mucus deposition + areas of hemorrhage

(2) chondroid chordoma: cartilage instead of mucinous differentiation of extracellular matrix

Location: (a) 50–60% in sacrum (sacrococcygeal chordoma)

(b) 30–35% in clivus (sphenooccipital chordoma)

(c) 15% in vertebrae (vertebral chordoma): cervical > thoracic / lumbar spine; vertebral body with sparing of posterior elements

(d) other sites (5%) in mandible, maxilla, scapula

Site: midline / paramedian

√ amorphous calcification (50–75%)

√ heterogeneous enhancement

CT:

√ low-attenuation within soft-tissue mass ← myxoid-type tissue

√ higher attenuation fibrous pseudocapsule

MR (modality of choice):

√ low to intermediate intensity on T1WI, occasionally hyperintense ← high protein content:

√ heterogeneous internal texture ← calcification, necrosis, gelatinous mucoid collections

√ very high SI on T2WI ← physaliferous cells similar to nucleus pulposus with high water content

Angio:

√ prominent vascular stain

NUC:
√ cold lesion on bone scan
√ no uptake on gallium scan
Metastases (in 5–43%) to: liver, lung, regional lymph nodes, peritoneum, skin (late), heart
Prognosis: poor in spite of low grade + slow growth; almost 100% recurrence rate despite radical surgery
DDx: giant notochordal rest (nonprogressive indistinct lesion, normal bone / variable degree of sclerosis, no soft-tissue involvement)

Intracranial Chordoma (35%)
= locally invasive + destructive lesion of clivus
Location: infrasellar midline
√ mass of usually T1 hypointensity + T2 signal hyperintensity
√ hypointense intratumoral septations
√ foci of T1 signal hyperintensity within tumor / periphery ← residual ossified fragments / tumor calcifications, / small collections of proteinaceous fluid / hemorrhage
√ posterior extension indenting pons
DDx: cartilaginous tumor (more lateral location, at petrooccipital synchondrosis, curvilinear calcifications)

Sacrococcygeal Chordoma (50–70%)
= large destructive sacral mass with 2ndary soft-tissue extension
◊ Most common primary sacral tumor after giant cell tumor!
Peak age: 40–60 years; M÷F = 2–3÷1
Path: slow-growing tumor → large size at presentation
• clinically indolent and subtle; rectal bleeding (42%)
• low back pain (70%); sciatica + weakness in hip / lower limbs ← sacral root compression
• constipation, frequency, urgency, straining on micturition ← compression by tumor
• autonomic dysfunction → urinary / fecal incontinence
• palpable sacral mass on digital examination (17%)
Location: predominantly in 4th + 5th sacral segment
√ presacral mass with average size of 10 cm extending superiorly + inferiorly; rarely posterior location
√ displacement of rectum + bladder
√ solid tumor with cystic areas (in 50%)
√ amorphous peripheral calcifications (15–89%)
√ secondary bone sclerosis in tumor periphery (50%)
√ honeycomb pattern with trabeculations (10–15%)
√ may cross sacroiliac joint
X-ray:
√ osteolytic midline mass in sacrum + coccyx associated with soft-tissue mass and calcifications
CT (useful for defining extent of bone involvement):
√ bone destruction associated with lobulated midline soft-tissue mass
√ areas of low attenuation within mass ← high water content of myxoid properties

MR:
√ hypo- / isointense mass relative to muscle on T1WI:
√ intrinsic hyperintense areas on T1WI ← hemorrhage or myxoid / mucinous collections
√ hyperintense mass similar to nucleus pulposus on T2WI ← high water content:
√ dividing septa + hemosiderin of low signal intensity
√ heterogeneous often moderate enhancement

The combination of high T2 signal intensity in a lobulated sacral mass that contains areas of hemorrhage and calcification is strongly suggestive of a chordoma!

Prognosis: 7–10 years average survival; 50–74% 5-year survival rate (in adulthood); 52–64% 10-year survival; 52% 20-year survival
Dx: fine-needle aspiration biopsy
Rx: radical surgical excision (most critical); radiation therapy; 70% rate of local recurrence after excision

DDx:
› Primary neural tumor: schwannoma, neurofibroma, meningioma, myxopapillary ependymoma (from within spinal canal, more intense enhancement)
› Primary bone tumor:
(1) Giant cell tumor (2nd most common primary, upper sacrum, may be eccentric, ± extension across SI joint, low-to-intermediate T2 intensity ± fluid-fluid levels)
(2) Chondrosarcoma (off midline from sacroiliac joint space cartilage, heterogeneous T2 SI, no hemorrhage)
(3) Aneurysmal bone cyst
(4) Osteoblastoma
(5) Lymphoma
› Metastasis, plasmacytoma
› Soft-tissue neoplasm: atypical hemangioma, prostatic carcinoma, osteosarcoma, osteomyelitis

Sphenooccipital Chordoma (15–35%)

Age: younger patient (peak age of 20–40 years); M÷F - 1÷1
• orbitofrontal headache
• visual disturbances, ptosis
• 6th nerve palsy / paraplegia
Location: clivus, sphenooccipital synchondrosis
√ bone destruction (in 90%): clivus > sella > petrous bone > orbit > floor of middle cranial fossa > jugular fossa > atlas > foramen magnum
√ reactive bone sclerosis (rare)
√ calcifications / residual bone trabeculae (20–70%)
√ soft-tissue extension into nasopharynx (common), into sphenoid + ethmoid sinuses (occasionally), may reach nasal cavity + maxillary antrum
√ variable degree of enhancement
MR:
√ large intraosseous mass extending into prepontine cistern, sphenoid sinus, middle cranial

fossa, nasopharynx
√ posterior displacement of brainstem
√ usually hypo- / isointense to brain / occasionally inhomogeneously hyperintense on T1WI
√ hyperintense on T2WI
√ ± CHARACTERISTIC honeycomb enhancement pattern
Prognosis: 4–5 years average survival
DDx: meningioma, metastasis, plasmacytoma, giant cell tumor, sphenoid sinus cyst, nasopharyngeal carcinoma, chondrosarcoma

Vertebral / Spinal Chordoma (15–20%)
◊ More aggressive than sacral / cranial chordomas
Age: younger patient; M÷F = 2÷1
• low back pain + radiculopathy + retention of urine
Location: cervical (8% – particularly C2), thoracic spine (4%), lumbar spine (3%)
Site: midline centra sparing posterior elements; arising in perivertebral musculature (uncommon)
√ destructive expansile lesion of vertebral body:
√ + epidural soft-tissue mass of collar button / mushroom / dumbbell shape over several segments
√ often incomplete sparing of disk spaces to involve adjacent bodies (10–14%) simulating infection
√ exophytic anterior soft-tissue mass
√ expansion into neural foramen mimicking nerve sheath tumor
√ solitary midline spinal mass
√ sclerosis / "ivory vertebra" in 43–62%
√ total destruction of vertebra, initially without collapse
√ amorphous peripheral calcifications in 40%
Cx: complete spinal block
Prognosis: 4–5 years average survival
DDx: metastasis, primary bone tumor, primary soft-tissue tumor, neuroma, meningioma

CONDENSING OSTEITIS OF JAW
= reactive osteitis surrounding apex of tooth with pulpitis / pulpal necrosis
Associated with: carious tooth
√ periapical inflammatory lesion: granuloma / cyst / abscess
√ periapical poorly marginated nonexpansile sclerosis

CSF FISTULA
= characterized by egress of CSF from intracranial cavity through abnormal communication between subarachnoid space and pneumatized structure within skull base (= osteodural defect)
Cause:
A. CONGENITAL: ENCEPHALOCELE
B. ACQUIRED

(a) traumatic (80–90% of all cases)
◊ 2% of all head injuries develop CSF fistula
(b) nontraumatic:
› infection
› tumor (esp. those arising from pituitary gland)
(c) spontaneous: idiopathic intracranial hypertension

• rhinorrhea / otorrhea (may be exacerbated by Valsalva maneuver)
• "serous otitis media" with conductive / sensory hearing loss
• presence of β-2 transferrin (= polypeptide specific for CSF) / β-trace protein

Technique:

(a) invasive techniques (time-consuming, poorly tolerated)
1. Radionuclide cisternography
2. CT cisternography
◊ Contraindicated in active meningitis / elevated intracranial pressure!

Disadvantage:
› requires poorly tolerated lumbar puncture
› time-consuming
› slight risk of complications (low-tension headache, infection, bleeding at puncture site)
› hypersensitivity reaction to contrast
› high dose of radiation
› requires active CSF leak

(b) noninvasive techniques (best used in combination)
1. Multidetector CT (92% sensitive, 100% specific)
√ bone defect / dehiscence at skull base
√ adjacent prominent arachnoid granulations
√ air-fluid level / opacification of contiguous sinus / middle ear / mastoid
√ pneumocephalus
√ lobular / nondependent area of soft-tissue opacification (meningocele, meningoencephalocele)
DDx: mucosal reaction, cholesteatoma, granulation tissue, cholesterin granuloma
2. MR cisternography (87–100% sensitive, 57–100% specific, 78–89% accurate)
√ hyperintense CSF fistulous tract
√ CSF collection = meningocele
DDx: inflammatory paranasal secretions
√ extradural brain = meningoencephalocele
√ secondary gliosis of herniated brain
√ dural enhancement in stalk of meningoencephalocele

Spontaneous CSF Fistula

Location: cribriform plate along course of anterior ethmoid artery (most common), lateral lamella, perisellar region (sphenoid roof > floor of sella > posterior wall), lateral recess of sphenoid, tegmen tympani, tegmen mastoideum, skull base foramina

Traumatic CSF Fistula

- traumatic leak: usually unilateral; onset within 48 hours after trauma, usually scanty; resolves in 1 week
- nontraumatic leak: profuse flow; may persist for years
- anosmia (in 78% of trauma cases)

Location: fractures through frontoethmoidal complex + middle cranial fossa (most commonly)

Cx: (1) meningitis / encephalitis / brain abscess (in 25–50% of untreated cases)
(2) pneumocephalus

CURRARINO TRIAD

= triad of **a**norectal malformation + **s**acrococcygeal osseous defect + **p**resacral mass (= ASP triad)

= rare syndrome characterized by autosomal dominant genetic inheritance (in > 50%)

Path: presacral mass consists of teratoma, anterior sacral meningocele > dermoid cyst, hamartoma, enteric duplication cyst

Age: < 16 years at diagnosis (in 80%)

- constipation

DEGENERATIVE DISK DISEASE

◊ Therapeutic decision-making should be based on clinical assessment alone!

◊ There are no prognostic indicators on images in patients with acute lumbar radiculopathy!

◊ 35% of individuals without back trouble have abnormal findings (HNP, disk bulging, facet degeneration, spinal stenosis)

◊ Imaging is only justified in patients for whom surgery is considered!

Pathophysiology:

loss of disk height leads to stress on facet joints + uncovertebral joints (= uncinate process), exaggerated joint motion with misalignment (= rostrocaudal subluxation) of facet joints, spine instability with arthritis, capsular hypertrophy, hypertrophy of posterior ligaments, facet fracture

Plain film:

√ **intervertebral osteochondrosis** = disease of nucleus pulposus (= desiccation = loss of disk water):
- √ narrowing of disk space
- √ vacuum disk phenomenon
- √ disk calcification
- √ bone sclerosis of adjacent vertebral bodies

√ **spondylosis deformans** = degeneration of the outer fibers of the annulus fibrosus:
- √ endplate osteophytosis growing initially horizontally and then vertically several millimeters from diskovertebral junction ← displacement of nucleus pulposus in anterior + anterolateral direction producing traction on osseous attachment of annulus fibrosus [= fibers of Sharpey])
- √ enlargement of uncinate processes

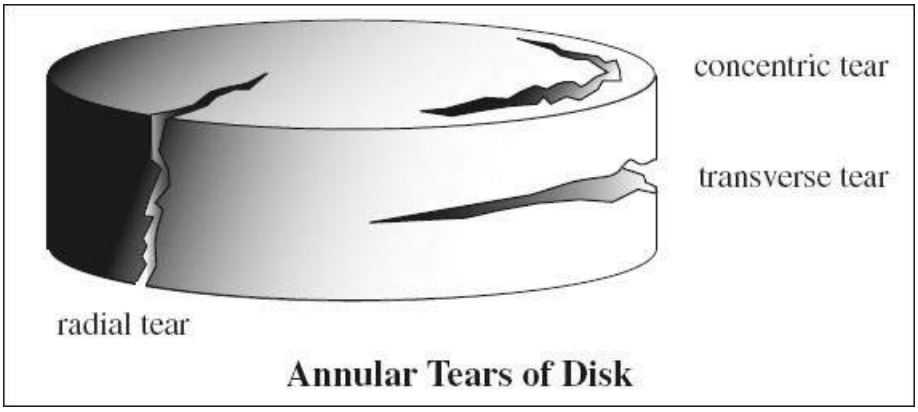
√ **osteoarthritis** = degenerative disease of synovium-lined apophyseal / costovertebral joints:

√ degenerative spondylolisthesis
√ cartilaginous node = intraosseous disk herniation

Myelography:
√ delineation of thecal sac, spinal cord, exiting nerve roots

CT (accuracy > 90%):
√ facet joint disease (marginal sclerosis, joint narrowing, cyst formation, bony overgrowth)
√ uncovertebral joint disease of cervical spine (osteophytes project into lateral spinal canal + neuroforamen)

MR:
√ **scalloping of cord** (T2WI FSE / GRE images):
√ anterior encroachment by disk / spondylosis
√ posterior encroachment by ligamentum flavum hypertrophy
√ **loss of disk signal** ← desiccation ←decrease in water-binding proteoglycans + increase in collagen within nucleus pulposus) on T2WI
√ **annular tear:**
(1) concentric tear - separation of annular lamellae
(2) transverse tear
(3) radial tear - crossing multiple annular lamellae with greater vertical dimension + more limited horizontal extent
• diskogenic pain
◊ does NOT imply disk herniation
√ gap near middle of annulus



Annular Tears of Disk

Modified Dallas Diskogram Classification	
Grade	*Description*
0	contrast confined within nucleus pulposus
1	contrast extends to inner third of annulus
2	contrast extends to middle third of annulus
3	outer third of annulus + < 30° of circumference
4	outer third of annulus + > 30° of circumference
5	extension of contrast beyond annulus

√ cleft of high SI in a normally hypointense outer annulus on T2WI

√ contrast enhancement ← granulation tissue / hyperemia / inflammation

√ **reduction in disk height** (late):

√ Schmorl's node

√ moderate linear uniform enhancement on T1WI

√ vacuum phenomenon with low signal on T1WI

√ **endplate + marrow changes** (Modic & DeRoos):

= linear signal alterations paralleling adjacent endplates

(a) Type 1 (4%) = *edema pattern*

Cause: replacement of bone marrow with hyperemic fibrovascular tissue + edema ← acute disk degeneration

√ hypointense on T1WI + hyperintense on T2WI

√ contrast-enhancement of marrow

(b) Type 2 (16%) = *fatty marrow pattern*

Cause: replacement of bone marrow with fat ← chronic disk degeneration

√ hyperintense marrow signal on T1WI

√ iso- to mildly hyperintense on T2WI

√ hypointense on STIR

(c) Type 3 = *bony sclerosis pattern*

Cause: replacement of bone marrow with sclerotic bone ← chronic disk degeneration after a few years

√ hypointense marrow signal on T1WI + T2WI

√ juxtaarticular **synovial cyst** in posterolateral spinal canal (most frequently at L4-5):

√ smooth well-defined extradural mass adjacent to facet joint

√ variable signal pattern ← serous, mucinous, gelatinous fluid components, air, hemorrhage

√ contrast-enhancing hypointense perimeter ← fibrous capsule with calcium + hemosiderin

NUC:

SPECT imaging of vertebrae can aid in localizing increased uptake to vertebral bodies, posterior elements, etc.

√ eccentrically placed increased uptake on either side of an intervertebral space (osteophytes, diskogenic sclerosis)

Sequelae:

(1) Disk bulging

(2) Disk herniation

(3) Spinal stenosis

(4) Facet joint disease

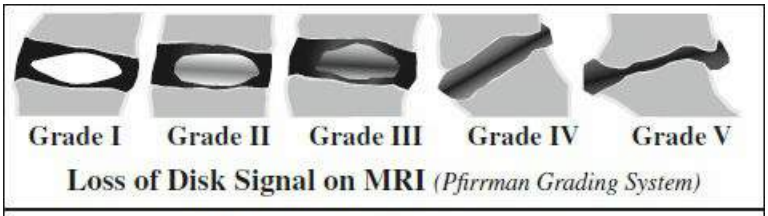
(5) Instability

√ dynamic slip > 3 mm on flexion-extension

√ static slip > 4.5 mm

√ traction spurs

√ vacuum phenomenon



Loss of Disk Signal on MRI *(Pfirrman Grading System)*

MRI Grades of Disk Degeneration

Grade	*T2 signal*	*Structure of Nucleus*	*Distinction to Annulus*	*Height*
I	⇑	white, homogeneous	clear	normal
II	↑	heterogeneous, horizontal bands	clear	normal
III	↔	gray, heterogeneous	unclear	↓
IV	↔/↓	gray to black, hetero	none	⇓
V	⇓	black, heterogeneous	none	collapsed

DDx: **Idiopathic segmental sclerosis of vertebral body** (middle-aged / young patient, hemispherical sclerosis in anteroinferior aspect of lower lumbar vertebrae with small osteolytic focus, only slight narrowing of intervertebral disk; unknown cause)

Bulging Disk = Disk Bulge

= concentric smooth expansion of softened disk material beyond the confines of endplates with disk extension outward involving > 50% of disk circumference

Cause: weakened and lengthened but intact annulus fibrosus + posterior longitudinal ligament

Age: common finding in individuals > 40 years of age

Location: L4-5, L5-S1, C5-6, C6-7

√ rounded symmetric defect localized to disk space level

√ smooth concave indentation of anterior thecal sac

√ encroachment on inferior portion of neuroforamen

√ accentuated by upright myelography

MR:

√ nucleus pulposus hypointense on T1WI + hyperintense on T2WI ← desiccation (= water loss through degeneration + fibrosis)

Herniation of Nucleus Pulposus

= HNP = protrusion of disk material > 3 mm beyond margins of adjacent vertebral endplates involving < 50% of disk circumference

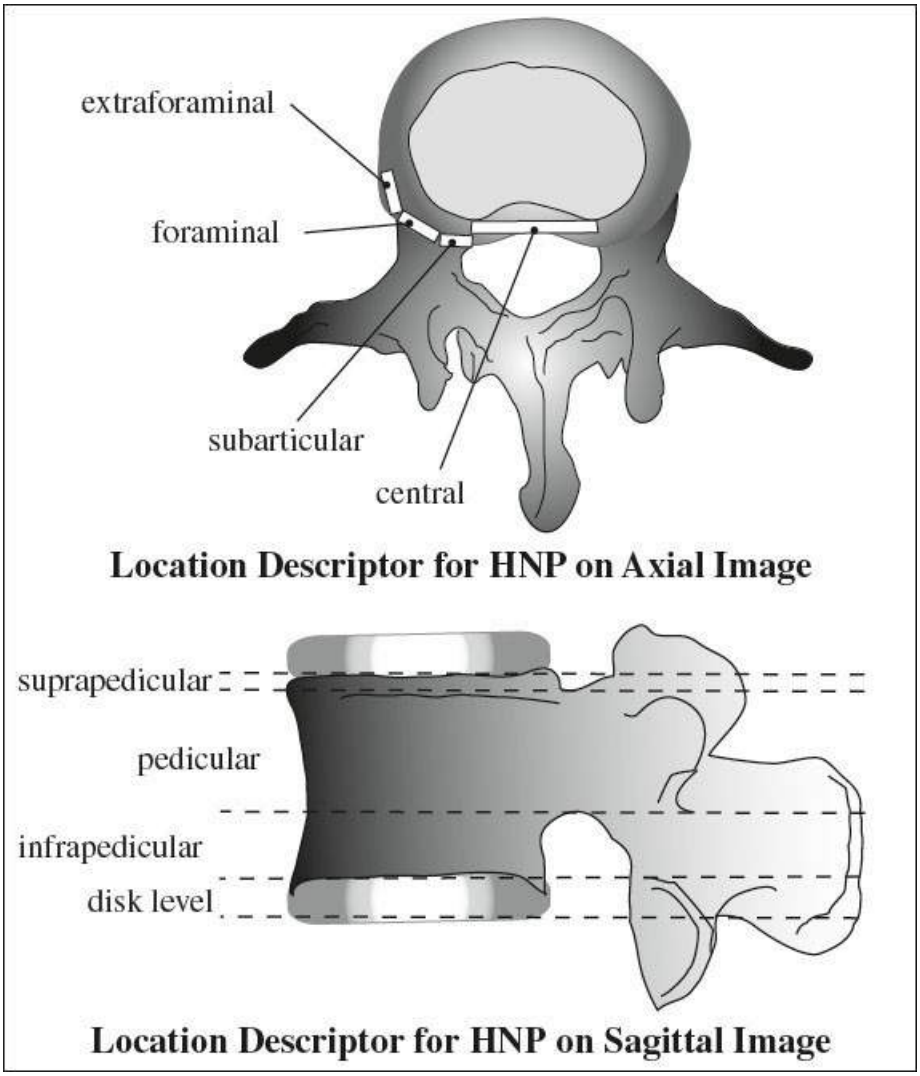
Cause: rupture of annulus fibrosus with disk material confined within posterior longitudinal ligament

◊ 21% of an asymptomatic population has a herniated disk!

- local somatic spinal pain = sharp / aching, deep, localized
- centrifugal radiating pain = sharp, well-circumscribed, superficial, "electric," confined to dermatome
- centrifugal referred pain = dull, ill-defined, deep or superficial, aching or boring, confined to somatome (= dermatome + myotome + sclerotome)

Site:

(a) posterolateral (49%) = weakest point along posterolateral margin of disk at lateral recess of spinal canal



◊ The posterior longitudinal ligament is tightly adherent to posterior central margins of disk!

(b) posterocentral (8%)
(c) bilateral (to both sides of posterior ligament)
(d) lateral / foraminal (< 10%)
(e) extraforaminal = anterior (commonly overlooked) (29%)
(f) intraosseous / vertical = Schmorl node (14%)

Myelography:

√ sharply angular indentation on lateral aspect of thecal sac with extension above / below level of disk space (ipsilateral oblique projection best view)
√ asymmetry of posterior disk margin
√ double contour ← superimposed normal + abnormal side (horizontal beam lateral view)

√ narrowing of intervertebral disk space (most commonly a sign of disk degeneration)
√ deviation of nerve root / root sleeve
√ enlargement of nerve root ("trumpet" sign) ← edema
√ amputated / truncated nerve root (= nonfilling of root sleeve)

MR:

√ herniated disk material of low SI displaces the posterior longitudinal ligament and epidural fat of relative high SI on T1WI
√ "squeezed toothpaste" effect = hourglass appearance of herniated disk at posterior disk margin on sagittal image
√ asymmetry of posterior disk margin on axial image

Cx: (1) spinal stenosis mild = < ⅓
moderate = ⅓ to ⅔
severe = > ⅔
(2) neuroforaminal stenosis

Prognosis:

conservative therapy reduces size of herniation by
0–50% in 11% of patients,
50–75% in 36% of patients,
75–100% in 46% of patients
(secondary to growth of granulation tissue)

Broad-based Disk Protrusion

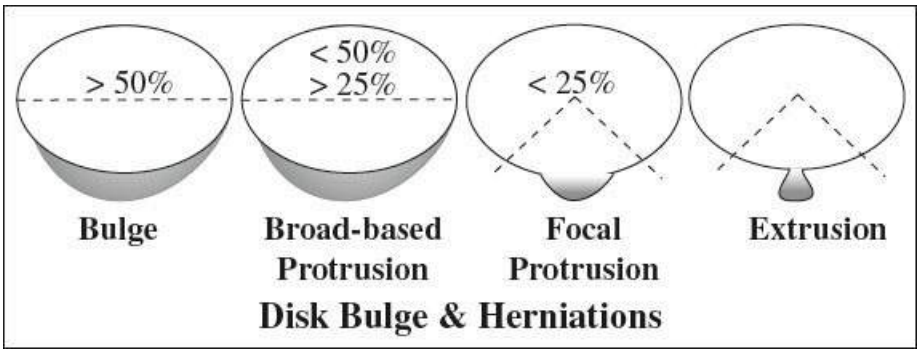
√ triangular shape of herniation with a base wider than the radius of its depth
√ 25–50% of disk circumference

Focal Disk Protrusion

√ triangular shape of herniation with a base wider than the radius of its depth
√ < 25% of disk circumference

Disk Extrusion

= prominent focal extension of disk material through the annulus with only an isthmus of connection to parent disk through intact / ruptured posterior longitudinal ligament
√ mushroom-shaped herniation with base narrower than the radius of its depth
√ "toothpaste" sign



Disk Sequestration

= FREE FRAGMENT HERNIATION
= complete separation of disk material from parent disk with rupture through posterior longitudinal ligament into epidural space
◊ Missed free fragments are a common cause of failed back surgery!
√ migration superiorly / inferiorly away from disk space with compression of nerve root above / below level of disk herniation
√ disk material > 9 mm away from intervertebral disk space = NO continuity
√ soft-tissue density with higher value than thecal sac
DDx: (1) Postoperative scarring (retraction of thecal sac to side of surgery)
(2) Epidural tumor
(3) Tarlov cyst (dilated nerve root sleeve)
(4) **Conjoined nerve root** (2 nerve roots arising from thecal sac simultaneously representing mass in ventrolateral aspect of spinal canal; normal variant in 1–3% of population)

Free Fragment Migration

= separated disk material travels above / below intervertebral disk space
√ ± continuity

Cervical Disk Herniation

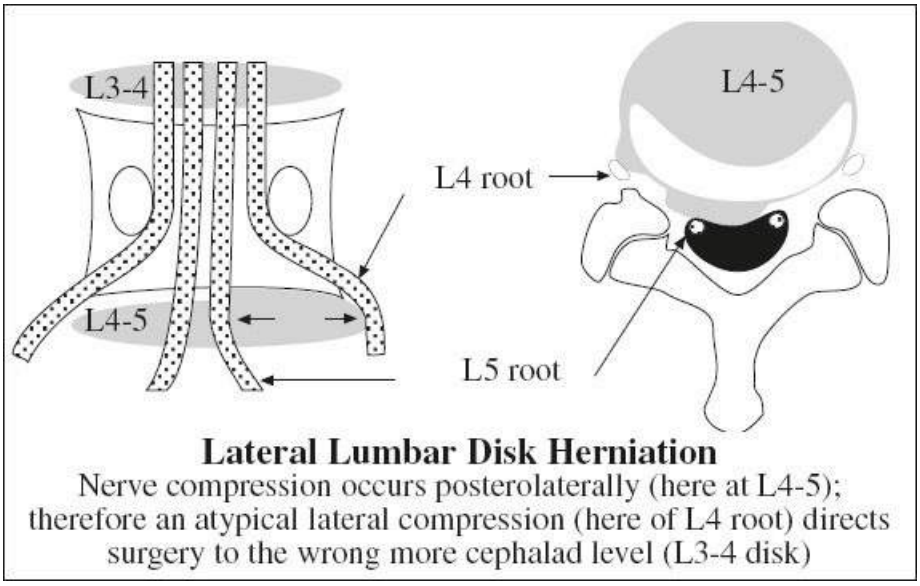
Peak age: 3rd–4th decade
• neck stiffness, muscle splinting; dermatomic sensory loss
• weakness + muscle atrophy; reflex loss
Sites: C6-7 (69%); C5-6 (19%); C7-T1 (10%); C4-5 (2%)
Sequelae:
(1) compression of exiting nerve roots with pain radiating to shoulder, arm, hand
(2) cord compression (spinal stenosis + massive disk rupture)

Thoracic Disk Herniation

Prevalence: 1% of all disk herniations
Sites: T11-12
√ calcification of disk fragments + parent disk (frequent)

Lumbar Disk Herniation

• **sciatica** =
(1) Stiffness in back
(2) Pain radiating down to thigh / calf / foot
(3) Paresthesia / weakness / reflex changes
• pain exaggerated by coughing, sneezing, physical activity + worse while sitting / straightening of leg
Sites: L4-5 (35%) > L5/S1 (27%) > L3-4 (19%) > L2-3 (14%) > L1-2 (5%)



Lateral Lumbar Disk Herniation
Nerve compression occurs posterolaterally (here at L4-5); therefore an atypical lateral compression (here of L4 root) directs surgery to the wrong more cephalad level (L3-4 disk)

DIASTEMATOMYELIA

= SPLIT CORD = MYELOSCHISIS [*diastema*, Greek = slit, cleft]
= sagittal division of spinal cord into two hemicords, each containing a central canal, one dorsal horn + one ventral horn

Etiology: congenital malformation as a result of adhesions between ectoderm and endoderm; M÷F = 1÷3

Path:

(a) 2 hemicords each covered by layer of pia within single subarachnoid space + dural sac (60%); not accompanied by bony spur / fibrous band
(b) 2 hemicords each with its own pial, subarachnoidal + dural sheath (40%); accompanied by fibrous band (in 25%), cartilaginous / bony spurs (in 75%)

Associated with: myelomeningocele

- hypertrichosis, nevus, lipoma, dimple, hemangioma overlying the spine (26–81%)
- muscle wasting, ankle weakness in one leg; clubfoot (50%)

Location: lower thoracic / upper lumbar > upper thoracic > cervical spine

√ sagittal cleft in spinal cord resulting in 2 asymmetric hemicords which usually reunite caudal to cleft
√ occasionally 2 coni medullaris
√ eccentric central canal within both hemicords
√ bony spur through center of spinal canal arising from posterior aspect of centra (< 50%)
√ thickened filum terminale > 2 mm (> 50%)
√ tethered cord (> 50%)
√ low conus medullaris below L2 level (> 75%)
√ defect in thecal sac on myelogram
@ Vertebrae
  √ congenital scoliosis (50–75%)
    ◊ 5% of patients with congenital scoliosis have diastematomyelia
  √ spina bifida over multiple levels

√ anteroposterior narrowing of vertebral bodies
√ widening of interpediculate distance
√ narrowed disk space with hemivertebra, butterfly vertebra, block vertebra
√ fusion + thickening of adjacent laminae (90%)
(a) fusion to ipsilateral lamina at adjacent levels
(b) diagonal fusion to contralateral adjacent lamina = intersegmental laminar fusion

Cx: progressive spinal cord dysfunction

DISKITIS

◊ Most common pediatric spine problem!

Etiology:

(1) Bloodborne bacterial invasion of vertebrae infecting disk via communicating vessels through endplate
◊ Vertebral osteomyelitis + diskitis may be the same entity!
(2) Invasive procedure / trauma: surgery, diskography, myelography, chemonucleolysis
(3) Extension of adjacent infection

Organism:

(a) pyogenic: Staphylococcus aureus (> 50%), gram-negative rods (in IV drug abusers / immunocompromised patients)
(b) nonpyogenic: tuberculosis, coccidioidomycosis
◊ TB has a propensity to extend beneath longitudinal ligaments with involvement of multiple vertebral levels

Pathogenesis: infection starts in disk (still vascularized in children) / in anterior inferior corner of vertebral body (in adults) with spread across disk to adjacent vertebral endplate

Age peaks: 6 months to 4 years; 10–14 years; 6th–7th decade

- over 2–4 weeks gradually progressing irritability, malaise, low-grade fever; refusal to bear weight; myelopathy
- neck / back / referred hip pain, limp, focal tenderness
- elevated sedimentation rate, WBC count often normal
- positive blood culture (in 58%)

Location: L3-4, L4-5, unusual above T9

Distribution: 2 adjacent vertebrae + intervening disk

Plain film (positive 2–4 weeks after onset of symptoms):

√ decrease in disk space height (earliest sign) = intraosseous herniation of nucleus pulposus into vertebral body through weakened endplate
√ indistinctness of adjacent endplates with destruction
√ endplate sclerosis (during healing phase beginning anywhere from 8 weeks to 8 months after onset)
√ bone fusion (after 6 months to 2 years)

CT (SAG / COR reformatted images more sensitive!):

√ early loss of disk height
√ endplate irregularities ← destruction
√ vertebral body collapse

√ paravertebral inflammatory mass / abscess
√ epidural soft-tissue extension with deformity of thecal sac

MR (preferred modality; 93% sensitive, 97% specific, 95% accurate):
◊ Very sensitive modality early on in disease process!
√ ↓ marrow intensity on T1WI in 2 contiguous vertebrae
√ signal intensity of disk decreased on T1WI + increased on T2WI compared to skeletal muscle
◊ Fluid-sensitive sequence with fat suppression!
√ progressive destruction of vertebral body
√ in early stage preserved disk height with variable intensity on T2WI (often increased)
√ in later stages loss of disk height with increased intensity on T2WI (= intradiskal fluid)

CEMR:
√ focal enhancement of involved disk + adjacent vertebral endplates ± bone marrow

NUC (41% sensitive, 93% specific, 68% accurate on ^{99m}Tc-MDP + ^{99m}Tc WBC scans):
√ positive before radiographs
√ increased uptake in vertebral endplate adjacent to disk
√ bone scan usually positive in adjacent vertebrae (until age 20) ← vascular supply via endplates; may be negative after age 20

Dx: needle biopsy (77% positive) before IV antibiotics
Cx: (1) epidural / paravertebral abscess ← extension of infection
(2) kyphosis
Rx: immobilization in body cast for ~ 4 weeks
DDx: neoplastic disease (no breach of endplate, disk space often intact)

Postoperative Diskitis

Frequency: 0.75–2.8%
Organism: Staphylococcus aureus; many times no organism recovered
- severe recurrent back pain 7–28 days after surgery accompanied by decreased back motion, muscle spasm, positive straight leg raising test
- fever (33%), wound infection (8%)
- persistently elevated / increasing ESR

MR:
√ decreased SI within disk + adjacent vertebral body marrow on T1WI
√ increased SI in disk + adjacent marrow on T2WI often with obliteration of intranuclear cleft
√ contrast-enhancement of vertebral bone marrow ± disk space

DDx: degenerative disk disease type I (no gadolinium-enhancement of disk)

Pyogenic Spondylodiskitis

= INFECTIOUS SPONDYLODISKITIS
Pathophysiology: infection of anterior vertebral body (2° to rich blood supply) → extension into disk → extension into neighboring vertebra
Predisposed: diabetes mellitus, immunocompromised, IV drug abuse
Location: lumbar > thoracic > cervical spine
- insidious back pain, fever, chills, night sweats

• elevated ESR, elevated C-reactive protein, ±leukocytosis

DDx: (1) Dialysis-associated spondyloarthropathy (intradiskal fluid + enhancement uncommon, NO epidural / paraspinal abscess)

(2) Degenerative disk disease (hypointense T1 and hyperintense T2 endplate changes flanking a degenerated disk ± enhancement, NO fluidlike disk signal intensity, disk vacuum phenomenon)

DISLOCATION OF CERVICAL SPINE

= CRANIOCERVICAL DISSOCIATION

Atlantooccipital Dislocation

= ATLANTOOCCIPITAL DISTRACTION INJURY = ATLANTO-OCCIPITAL DISSOCIATION (AOD)

= disruption of tectorial membrane + paired alar ligaments resulting in grossly unstable injury

◊ Diagnosis difficult to make and easy to overlook at whole-body CT!

Cause: rapid deceleration with either hyperextension or hyperflexion → in up to ⅓ of high-velocity injuries

Age: in adults much less common than in children ← larger size of head relative to body, increased laxity of ligaments, shallow horizontally oriented occipitoatlantoaxial joint, hypoplastic occipital condyles

May be associated with: occipital condyle fracture

• neurologic symptoms: range from respiratory arrest with quadriplegia to normal neurologic exam

• discomfort, stiffness

Direction of dislocation / subluxation: anteriorly, posteriorly, superiorly (vertical = life-threatening)

Lateral radiograph:

√ **Powers ratio** (assessment for anterior subluxation) = BC÷OA ratio > 1 = ratio of distance between basion + spinolaminar line of C1 and distance between posterior cortex of anterior tubercle of C1 + opisthion (74% sensitive)

√ **basion-dens interval** (BD) > 12 mm on X-ray / 9.5 mm on CT without traction placed on head / neck

√ **basion-axial interval** > 12 mm anterior / > 4 mm posterior to posterior axial line (PAL)

√ **atlanto-dental interval** > 3 mm (man) / > 2.5 mm (woman):

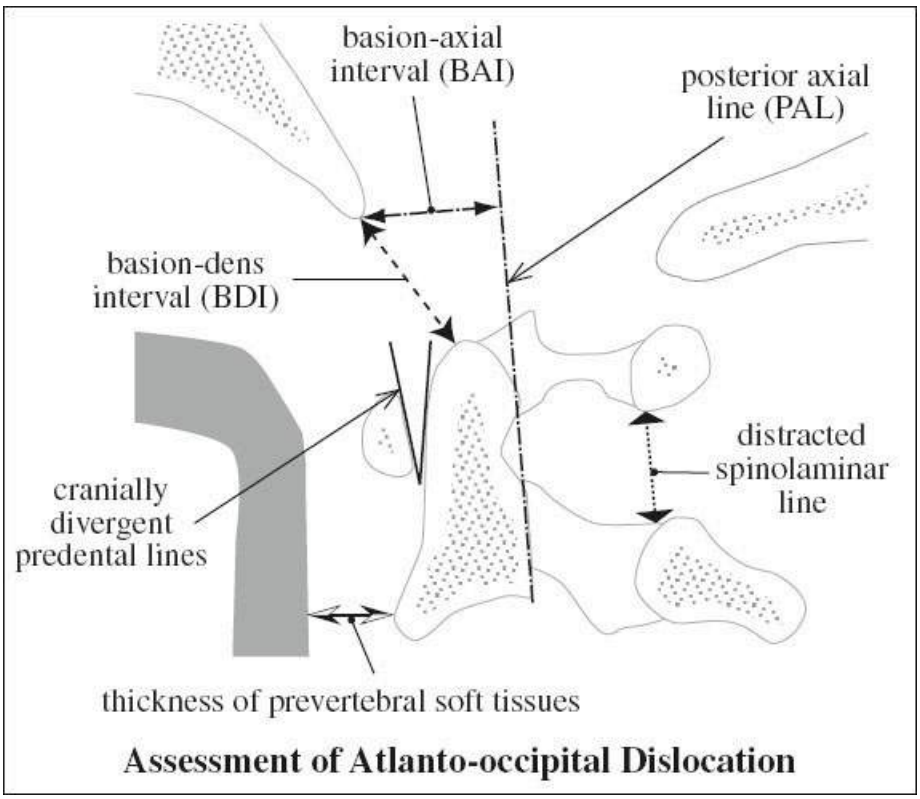
√ "V sign" = cranially divergent predental lines ← transverse ligament injury

√ atlanto-occipital interval > 4 mm

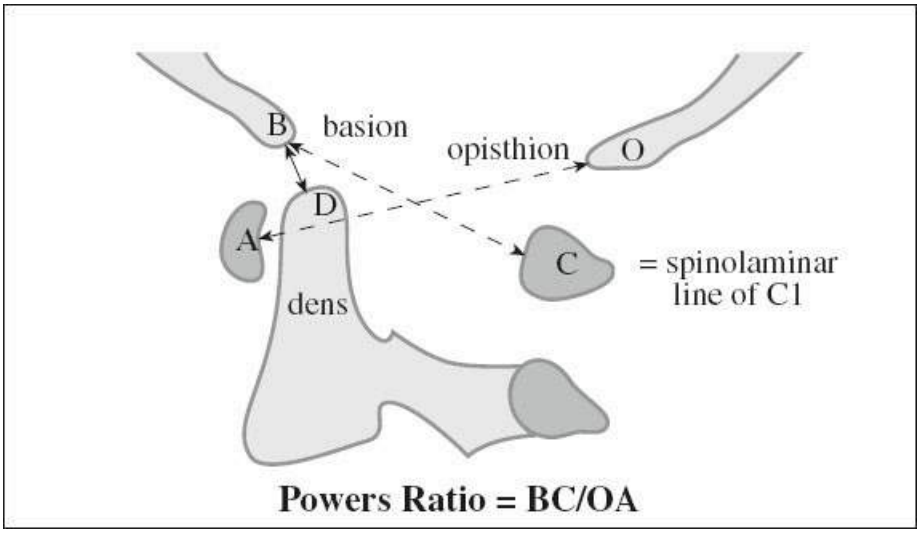
√ atlanto-axial interval > 2.6–4 mm

√ > 10 mm soft-tissue swelling anterior to C2 + pathologic convexity of soft tissues (80%)

CT (≤ 1.25 mm thick sections, superior to radiographs):



Assessment of Atlanto-occipital Dislocation



Powers Ratio = BC/OA

A basion-dens distance > 10 mm is highly suggestive of dissociation. The alar ligaments + tectorial membrane are the most important stabilizing ligaments given the little inherent osseous stability.

√ blood in region of tectorial membrane + alar ligaments
√ condylar fracture ± fracture extension through hypoglossal canal (for cranial nerve XII)
√ widening / incongruity of articulation between occipital condyles + lateral masses of C1

MR:

Indications for MRI:

(1) Detection of soft-tissue injury + spinal cord injury

(2) Treatment planning of unstable cervical spine
(3) Patients with neurologic deficits
(4) Suspected ligamentous injury
(5) Patients who cannot be clinically evaluated for > 48 hours ← altered level of consciousness

√ fluid in articular capsules, nuchal ligament, interspinous ligament

Cx: (1) Injury to caudal cranial nn. + upper 3 cervical nerves
(2) Epidural hematoma with brainstem compression + upper spinal cord injury
(3) Vasospasm / dissection of internal carotid and vertebral arteries

Prognosis: usually fatal; more survivable in skeletally immature pediatric trauma patients

Atlantoaxial Distraction

= traumatic widening of atlantoaxial interval

Cause: injury to transverse atlantal ligament, alar ligaments, tectorial membrane between C1 and C2, disruption of articular capsules

May be associated with: type 1 dens fracture

√ prevertebral soft-tissue swelling

√ subluxation with enlargement of predental space to
> 5 mm in children < 9 years of age
> 3 mm in adults

√ widening of C1-C2 facets

MR:
√ prevertebral, interspinous, nuchal ligament edema
√ facet widening / fluid
√ increased signal intensity of spinal cord
√ ± epidural hematoma

DORSAL DERMAL SINUS

= epithelium-lined dural tube extending from skin surface to intracanalicular space + frequently communicating with CNS / its coverings

Cause: focal point of incomplete separation of cutaneous ectoderm from neural ectoderm during neurulation

Age: early childhood to 3rd decade; M÷F = 1÷1

• small midline dimple / pinpoint ostium
• hyperpigmented patch / hairy nevus / capillary angioma

Location: lumbosacral (60%), occipital (25%), thoracic (10%), cervical (2%), sacrococcygeal (1%), ventral (8%)

Course: in a craniad direction from skin level toward cord ← ascension of cord relative to spinal canal during embryogenesis

Associated with: epidermoid / dermoid tumors in up to 20%
◊ 50% of dorsal dermal sinuses end in dermoid / epidermoid cysts!
◊ 20–30% of dermoid cysts / dermoid tumors are associated with dermal sinus tracts!

CT myelography (best modality to define intraspinal anatomy):
√ groove in upper surface of spinous process + lamina of vertebra
√ hypoplastic spinous process
√ single bifid spinous process

√ focal multilevel spina bifida
√ laminar defect
√ dorsal tenting of dura + arachnoid
√ sinus may terminate in conus medullaris / filum terminale / nerve root / fibrous nodule on dorsal aspect of cord / dermoid / epidermoid
√ nerve roots bound down to capsule of dermoid / epidermoid cyst
√ displacement / compression of cord by extramedullary dermoids / epidermoids
√ expansion of cord by intramedullary dermoids / epidermoids
√ clumping of nerve roots from adhesive arachnoiditis

Cx: (1) Meningitis (bacterial / chemical)
(2) Subcutaneous / epidural / subdural / subarachnoid / subpial abscess (bacterial ascent)
◊ Dermal sinus accounts for up to 3% of spinal cord abscesses!
(3) Compression of neural structures

DDx: pilonidal sinus / simple sacral dimple (no extension to neural structures)

EPIDURAL ABSCESS OF SPINE

Incidence: ~ 1.8÷100,000 annually; 0.2–2.8÷10,000 hospital admissions annually

Organism: Staphylococcus aureus including methicillin-resistant S aureus (²/₃ of cases); rarely fungus / parasite / mycobacterium

Cause:
(a) hematogenous (50%):
› urinary tract infection (Escherichia coli)
› pneumonia (Streptococcus pneumoniae)
› prior soft-tissue / skin infection (S epidermidis)
› IV drug abuse (Pseudomonas aeruginosa)
(b) contiguous infection from adjacent structures (33%):
› vertebral osteomyelitis, diskitis
› psoas abscess
(c) iatrogenic / penetrating trauma to spine:
» invasive procedure on spine + nearby structures (Staphylococcus epidermidis)

At risk: acquired immunosuppressive / immunodeficiency disorder, drug addiction, cancer, alcoholism, systemic inflammation / infection, liver disease, diabetes, trauma, surgical procedure involving spine / surrounding structures

Age: > 20 years (range, 10 days to 87 years); M÷F = 1.7÷1

• classic triad:
  • localized severe back pain (70%) → radicular pain
  • fever, leukocytosis (60%)
  • neurologic disease (30%): fecal / urinary incontinence with motor / sensory deficit → eventual rapid irreversible neurologic deterioration

Location: thoracic spine (50%)

Site: dorsolateral spanning multiple vertebral levels

Category: (a) focal ≤ 5 vertebrae (b) diffuse > 5 vertebrae

May be associated with: (1) Osteomyelitis

(2) Diskitis
(3) Paravertebral abscess

N.B.: NO myelography! → may seed infection into subarachnoid space

MR:
- √ ± effacement of epidural fat + subarachnoid space
- √ thickening of epidural tissues (early stage):
  - √ isointense on T1WI
  - √ moderately hyperintense on T2WI
- √ liquefied abscess cavity oval-shaped on axial images:
  - √ hypointense on T1WI + hyperintense on T2WI

DDx: CSF

- √ hyperintense at DWI + reduced apparent diffusion coefficient (ADC) ← restricted diffusion

CEMR:
- √ diffuse heterogeneous / homogeneous enhancement (= phlegmonous infection with microabscesses)
- √ peripheral enhancement of varying thickness around a central pus collection

- √ cellulitis surrounding abscess ← inflamed hypervascular tissue (best seen on fat-suppressed CEMR)
- √ linear enhancement along compressed dura mater (in only 75% of diffuse spinal epidural abscess)
- √ engorgement of epidural / basivertebral veins (best seen on sagittal images)

EPIDURAL HEMATOMA OF SPINE

Cause: (1) Trauma (71%)
(a) vertebral fracture / dislocation
(b) traumatic lumbar puncture
(c) spine surgery (0.1–3%)
(2) Hypertension
(3) Pregnancy
(4) AVM
(5) Vertebral hemangioma
(6) Bleeding diathesis / anticoagulation / hemophilia
(7) Idiopathic (45%)

Pathophysiology: tearing of epidural veins

Mean age: 41–52 years

• acute radicular pain; rapid onset of paraplegia

Location: cervical > thoracic > lumbar spine

Site: anterior / posterior to cord

√ spinal cord compression

√ high attenuation lesion on CT

MR:
- √ iso- / hyperintense on T1WI + hyperintense on T2WI compared to spinal cord (intensities quite variable)

√ strikingly low SI on gradient-echo sequences ← deoxyhemoglobin

Rx: conservative management

FRACTURES OF SKULL

1. Linear fracture (most common type)
   √ deeply black sharply defined line
   DDx:
   (1) Vascular groove, esp. temporal artery (gray line, slightly sclerotic margin, branching like a tree, typical location (temporal artery projects behind dorsum sellae)
   (2) Suture
2. Depressed fracture
   • often palpable
   √ bone-on-bone density
   Rx: surgery indicated if depression > 3–5 mm ← arachnoid tear / brain injury
   N.B.: CT / MR mandatory to assess extent of underlying brain injury
3. Skull-base fracture = **basilar skull fracture**
   • rhinorrhea (CSF); otorrhea (CSF / hemotympanum)
   • raccoon eyes = periorbital ecchymosis
   √ basic rules for skull fractures:
   √ overlying soft-tissue injury / hematoma
   √ sharp nonsclerotic border, often crossing sutures
   √ may bifurcate
   √ increase in diameter as fracture approaches suture
   √ diastasis of suture
   √ pneumocephalus
   √ air in sulci
   √ air-fluid level in sinuses
   Cx: infection, acute / delayed cranial nerve deficit, vascular laceration / dissection / occlusion / infarction
   DDx: suture (same diameter, interdigitating "zigzag" pattern)
4. **Healing skull fracture**
   @ infants: in 3–6 months without a trace
   @ children (5–12 years): in 12 months
   @ adults: in 2–3 years
   √ persistent lucency mimicking vascular groove
   Cx: leptomeningeal cyst (= growing fracture)

Le Fort Fracture

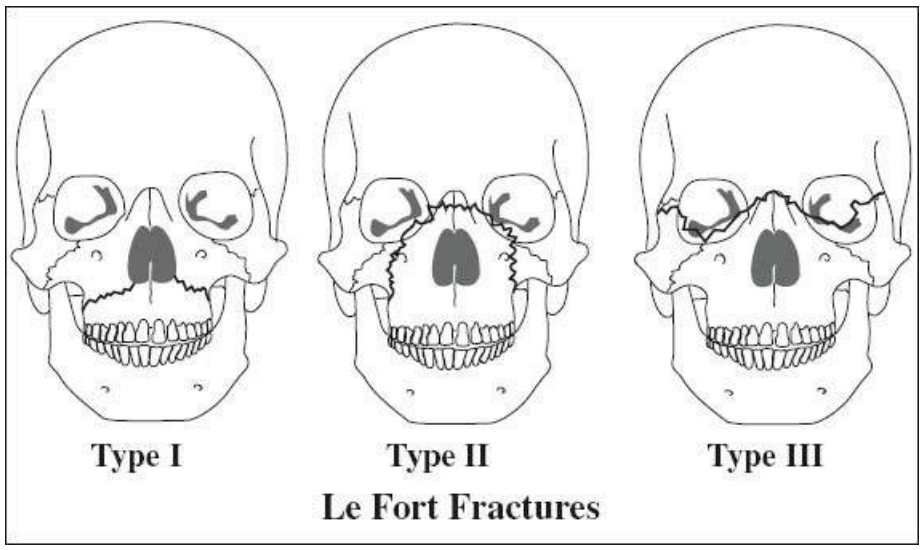
[René Le Fort (1869–1951), French surgeon]

◊ All Le Fort fractures involve the pterygoid process!

A. Le Fort I = transverse (horizontal) maxillary fracture caused by blow to premaxilla
   Fracture line: (a) alveolar ridge
   (b) lateral aperture of nose
   (c) inferior wall of maxillary sinus

√ detachment of alveolar process of maxilla
√ teeth contained in detached fragment

B. Le Fort II = "pyramidal fracture"
◊ May be unilateral



Le Fort Fractures

Fracture line: arch through
(a) posterior alveolar ridge
(b) medial orbital rim
(c) across nasal bones

√ separation of midportion of face
√ floor of orbit + hard palate + nasal cavity involved

C. Le Fort III = **"craniofacial disjunction"**

Fracture line: horizontal course through
(a) nasofrontal suture
(b) maxillofrontal suture
(c) orbital wall
(d) zygomatic arch

√ separation of entire face from base of skull

Sphenoid Bone Fracture

Prevalence: involved in 15% of skull-base fractures

- CSF rhinorrhea / otorrhea; hemotympanum
- "battle" sign = mastoid region ecchymosis
- raccoon eyes = periorbital ecchymosis; 7th / 8th nerve palsy
- muscular dysfunction: problems with ocular motility, mastication, speech, swallowing, eustachian tube function

√ air-fluid level in sinuses + mastoid
√ axial thin-slice high-resolution CT for best delineation of fractures
√ water-soluble intrathecal contrast material for CSF fistula

Temporal Bone Fracture

Frequency: 14–22% of skull fractures

Mechanism: motor vehicle crash (45–47%), fall (31–33%), assault (11–12%)

Cause of conductive hearing loss of temporal bone fracture:

(1) Hemotympanum
(2) Disruption of tympanic membrane
(3) Disruption of the ossicular chain:
  › commonly incus injury:
    (a) incudostapedial joint subluxation
    (b) malleoincudal subluxation
    (c) incus dislocation
    (d) dislocation of the malleoincudal complex
  › less commonly: stapedial and mallear fracture

A common complication of temporal bone fractures is hearing loss, either sensorineural, conductive, or mixed.

Longitudinal Fracture of Temporal Bone *(75%)*

= fracture parallel to long axis of petrous pyramid typically traversing middle ear cavity with frequent disruption of ossicles → conductive hearing loss

Line of force:

usually extralabyrinthine from lateral to medial terminating in foramen lacerum; commonly involving EAC (external auditory canal), tegmen tympani, squamosa of temporal bone

Subtypes:

(a) anterior to labyrinthine structures toward eustachian tube + middle cranial fossa (common)
  Cx: epidural hematoma in middle cranial fossa ← vascular injury to middle meningeal artery
(b) posterior to labyrinth, toward jugular foramen and posterior cranial fossa (less common)

Commonly associated with: fracture of temporal squamosa + parietal bone

- bleeding from EAC ← disruption of tympanic membrane
- otorrhea ← CSF leak with ruptured tympanic membrane (rare)
- conductive hearing loss ← dislocation of auditory ossicles (most commonly incus as the least anchored ossicle)
  - NO neurosensory hearing loss
- facial nerve palsy (7–20%) ← edema / fracture of facial canal near first genu / anterior tympanic segment of facial nerve; frequent spontaneous recovery

√ pneumocephalus
√ herniation of temporal lobe
√ incudostapedial joint dislocation (weakest joint):
  √ "ice cream" (malleus) has fallen off the "cone" (incus) on direct coronal CT scan
  √ fracture of "molar tooth" on direct sagittal CT scan
√ mastoid air cells opaque / with air-fluid level

Plain film views: Stenvers / Owens projection

Cx: ossicular injury, tympanic membrane rupture, hemotympanum → conductive hearing loss, (rarely) facial n. injury

Transverse Fracture of Temporal Bone *(25%)*

= fracture perpendicular to long axis of petrous pyramid

Line of force:

anterior to posterior originating in occipital bone (near jugular foramen / foramen magnum) extending anteriorly across the base of skull + across the petrous pyramid into middle cranial fossa; commonly passing through / near vestibular aqueduct with variable involvement of otic capsule

Subtypes:

(a) medial relative to arcuate eminence

Course: traversing fundus of IAC

- ± complete SNHL ← transection of cochlear n.

(b) lateral relative to arcuate eminence

Course: traversing bony labyrinth

Associated with: ± perilymphatic fistula ← injury of stapes footplate

- ± complete SNHL

- irreversible sensorineural hearing loss ← fracture line across apex of IAC / labyrinthine capsule with injury to both parts of cranial nerve VIII)
- persistent vertigo (benign paroxysmal positional vertigo resolves in 6–12 months, perilymphatic fistula, cupulolithiasis = otolith detachment, trauma to semicircular canals)
- facial (cranial nerve VII) nerve palsy in 50% (injury in IAC); less frequent spontaneous recovery because of disruption of nerve fibers

Site: labyrinthine segment, geniculate ganglion

- rhinorrhea ← CSF leak with intact tympanic membrane
- bleeding into middle ear

Plain film views: posteroanterior (transorbital) + Towne projection

Mixed Temporal Bone Fracture

Temporal bone fractures may be complex with mixed features of both longitudinal + transverse fractures.

= combination of longitudinal + transverse fractures

- sensorineural hearing loss ← disruption of otic capsule
- conductive hearing loss ← ossicular injury

◊ Quite common!

Ossicular Injury

- persistent conductive hearing deficit after healing of tympanic membrane / resorption of middle ear debris

A. Ossicular dislocation: incudostapedial separation > complete separation of incus including incudomalleolar separation > dislocation of malleoincudal complex > stapediovestibular dislocation

A. Ossicular fracture: long process of incus > crura of stapes > neck of malleus

Zygomaticomaxillary Fracture

= "TRIPOD" FRACTURE = MALAR / ZYGOMATIC COMPLEX FRACTURE

Cause: direct blow to malar eminence

- loss of sensibility of face below orbit
- deficient mastication
- double vision / ophthalmoplegia
- facial deformity

Fracture line:
(a) lateral wall of maxillary sinus
(b) orbital rim close to infraorbital foramen
(c) floor of orbit
(d) zygomaticofrontal suture / zygomatic arch

Blowout Fracture

= isolated fracture of orbital floor

Cause: sudden direct blow to globe (ball or fist) with increase in intraorbital pressure transmitted to weak orbital floor

- diplopia on upward gaze (entrapment of inferior rectus + inferior oblique muscles)
- enophthalmos
- facial anesthesia

Associated with: fracture of the thin lamina papyracea (= medial orbital wall) in 20–50%

√ soft-tissue mass extending into maxillary sinus ← herniation of orbital fat
√ complete opacification of maxillary sinus ← edema + hemorrhage
√ depression of orbital floor (= orbital process of maxilla)
√ posttraumatic atrophy of orbital fat → enophthalmos
√ opacification of adjacent ethmoid air cells
√ disruption of lacrimal duct

Occipital Condyle Fracture

Anderson & Montesano Types (I–III):

I = stable <u>comminution-impaction</u> with minimal / no fracture displacement ← axial loading injury

II = linear <u>skull base fracture</u> extending into occipital condyle ← direct blow to head

III = unstable <u>avulsion fracture</u> (75%) of occipital condyle ← avulsion injury of alar ligaments ← forced rotation + lateral bending

Tuli Types (1, 2A, 2B)

1 = nondisplaced fracture

2A = displaced fracture WITHOUT ligamentous instability
Rx: rigid collar

2B = displaced fractures WITH ligamentous instability
Rx: surgical intervention

FRACTURES OF CERVICAL SPINE

◊ Clearing of the cervical spine on clinical grounds has become the standard of care in alert adult patients.

Factors associated with higher risk of fracture:

(1) Glasgow Coma Score < 14
(2) Neck tenderness
(3) Loss of consciousness
(4) Neurologic deficit
(5) Drug ingestion
(6) Specific mechanism of injury: motor vehicle accident, fall from a height > 3 m

Indications for screening CT of cervical spine:

high-risk adult patients (= > 5% pretest probability of injury) defined by:

(1) High-speed (> 35 mph) motor vehicle accident
(2) Crash resulting in death at scene of accident
(3) Fall from height > 3 m (10 feet)
(4) Significant closed head injury (intracranial hemorrhage seen on CT)
(5) Neurologic signs / symptoms referred to C-spine
(6) Pelvic / multiple extremity fractures

Frequency: 1–3% of all trauma cases;
C2, C6 > C5, C7 > C3, C4 > C1
◊ Cervical spine trauma accounts for ⅔ of all spinal cord injuries!

• neurologic / spinal cord damage (39–50%)

Location:

(a) upper cervical spine = C1/2 (19–25%): atlas (4%), odontoid (6%)
(b) lower cervical spine = C3–7 (75–81%)
(c) cervicothoracic junction (9–18%)
(d) multiple noncontiguous spine fractures (15–20%)

Site: vertebral arch (50%), vertebral body (30%), intervertebral disk (25%), posterior ligaments (16%), dens (14%), locked facets (12%), anterior ligament (2%)

Associated with injury to:

head (70%), thoracic spine (15%), lumbar spine (10%), thorax (35%), pelvis (15%), upper extremity (10%), lower extremity (30%)

N.B.: 5–8% of patients with fractures may have normal radiographs!
◊ Most missed fractures involve C2 (34%), C6-7 (14%), C4 (12%), C1 (8%), occipital condyles
◊ C7–T1 space not visualized in at least 26% of all trauma patients

Normal range of motion: 10–20° during flexion and extension; 4–12° of lateral tilting

Cx: neurologic deterioration with delay in diagnosis

A. HYPERFLEXION INJURY (46–79%)

1. Odontoid fracture
2. Simple wedge fracture (stable)
3. **Flexion teardrop fracture** = avulsion of anteroinferior corner by anterior ligament (unstable)
◊ Most severe + unstable injury of C-spine
Location: C5, C6, C7

√ triangular fragment in soft tissues anterior to vertebral body
√ retrolisthesis
√ widening of facets
√ narrowing of spinal canal
√ mild kyphosis
Associated with: ligamentous tears, spinal cord compression

Subaxial Injury Classification and Scoring
*(CT Severity Score for Entire Spine, 2007)**

Injury Category	*Point Value*
Injury Morphology	
Compression	1
Burst	2
Distraction	3
Translation / rotation	4
Discoligamentous complex	
Intact	0
Indeterminate	2
Disrupted	3
Neurologic status	
Intact	0
Root injury	1
Spinal cord injury	
incomplete	2
complete	3
Cord injury + ongoing compression	4
Total Score: ≤ 3 manageable without surgery	
4 indeterminate;	
≥ 5 need for surgical intervention	

* a separate score is given to each injured level

◊ Triangular teardrop fracture without posterior element distraction / vertebral body translation should be characterized as (1) compression or (2) burst injury.

4. Anterior subluxation
5. **Bilateral facet lock** = interlocking of articular surfaces (unstable)
   √ anterolisthesis of affected vertebra by ½ vertebral body width
   √ mild focal kyphosis
   √ soft-tissue swelling
   √ no rotation
6. Anterior disk space narrowing
7. Spinous process fracture = **clay shoveler's fracture**
   = sudden load on flexed spine with avulsion fracture of C6 / C7 / T1 (stable)
8. **Flexion instability** = isolated rupture of posterior ligaments
   ◊ Dx may be missed without delayed flexion views
   √ no fracture

√ interspinous widening
√ loss of facet parallelism
√ widening of posterior portion of disk
√ anterolisthesis > 3 mm
√ focal kyphosis

B. HYPEREXTENSION INJURY (20–38%)

Mechanism: impact on forehead / face, whiplash

◊ High risk for neurologic deficit!
◊ Radiographs may be completely normal!

1. Hyperextension dislocation
   followed by immediate realignment
   • upper extremity paresthesia to complete quadriplegia
   √ disruption of anterior longitudinal ligament, annulus, intervertebral disk, lig. flavum
   √ prevertebral swelling ← hemorrhage + edema
   √ stripping of posterior longitudinal ligament
   √ tears of paraspinal muscles
   √ widening of disk space anteriorly
   √ avulsion of anteroinferior endplate
   √ transverse dimension of anteroinferior avulsion fragment greater than vertical dimension
2. **Extension teardrop fracture**
   = avulsion of intact fibers of anterior longitudinal ligament off anteroinferior endplate
   Location: C2, C3
   • acute central cord syndrome (in up to 80%)
   √ vertical dimension of triangular fragment greater than transverse dimension
3. Neural arch fracture of C1 (stable fracture = anterior ring + transverse ligament intact)
   √ vertically oriented fracture of posterior arch (stable if isolated / part of Jefferson burst fracture)
4. Anterior arch fracture of C1
   • biomechanically stable
   √ transverse fracture through inferior pole / midportion at attachment of atlantodental lig. / longus colli m.
5. Uni- / bilateral laminar fracture commonly part of a burst fracture / pedicolaminar fracture-separation / flexion teardrop fracture
   √ extension into adjacent spinous process (frequent)
6. Subluxation (anterior / posterior)
7. Hangman's fracture

C. FLEXION-ROTATION INJURY (12%)

1. **Unilateral facet lock** (oblique views!, stable fracture)
   √ anterolisthesis < ¼ vertebral body width
   √ "bow-tie" sign = the 4 rotated facets on LAT view
   √ decrease in spinolaminar space
   √ rotation of spinous process (on AP view)
   √ "naked facet" (on CT)

D. VERTICAL COMPRESSION (4%)

= axial loading

1. Jefferson fracture
2. **Burst fracture** = intervertebral disk driven into vertebral body below (fracture may be stable / unstable)
   √ loss of posterior vertebral body height with several fragments:
   √ sagittal fracture component extending to inferior endplate
   √ retropulsed fragment from posterior superior margin in spinal canal
   √ interpedicular widening
   √ posterior element fracture
   Associated with: widening of apophyseal joints, fracture of posterior vertebral arches

E. LATERAL FLEXION / SHEARING (4–6%)

1. Uncinate fracture
2. Isolated pillar fracture
3. Transverse process fracture
4. Lateral vertebral compression

Normal Variants as Pitfalls in Cervical Trauma

1. Congenital absence of posterior arch(es)
2. Congenital cleft (smooth well-corticated)
3. Os odontoideum
4. Os terminale
5. Partial ossification of atlanto-occipital membrane
6. Ponticulus posticus = bone excrescence partially covering horizontally oriented vertebral artery
7. Arcuate foramen = bone excrescence completely surrounding vertebral artery

Signs of Significant Cervical Vertebral Trauma

(a) most reliable + specific:
   √ widening of interspinous space (43%)
   √ widening of facet joint (39%)
   √ displacement of prevertebral fat stripe (18%)

(b) reliable but nonspecific:
   √ wide retropharyngeal space > 7 mm (31%)
   DDx: mediastinal hemorrhage of other cause, crying in children, S/P difficult intubation)

(c) nonspecific:
   √ loss of lordosis (63%)
   √ anterolisthesis / retrolisthesis (36%)
   √ kyphotic angulation (21%)
   √ tracheal deviation (13%)
   √ disk space: narrow (24%), wide (8%)

Atlas Fracture

Prevalence: 4% of cervical spine injuries, 25% of craniocervical injuries
Associated with: axis fracture (44%), fractures of C7 (25%), C2 pedicle (15%), extraspinal fractures (58%)

N.B.: A ring tends to fracture in more than one place!

Types:

I Isolated fracture of posterior arch ← hyperextension

II Isolated fracture of anterior arch (rare)

III Bilateral posterior arch fractures + uni- / bilateral anterior arch fracture ← axial loading

1. **Jefferson fracture**

   [Sir Geoffrey Jefferson (1886–1961), neurosurgeon in Manchester, England]

   √ comminuted burst fracture of ring of C1 (unstable) with 4 uni- / bilateral ipsilateral anterior + posterior fractures

   √ lateral displacement of lateral masses (self-decompressing) on AP view

   DDx: **Pseudo-Jefferson fracture** = lateral offset of lateral masses of atlas without fracture = fusion anomaly of anterior / posterior arches of C1 (in children as lateral masses of atlas ossify earlier than C2)

IV fracture of lateral mass ← excessive lateral flexion

V Transversely oriented anterior arch fracture ← avulsion of longus colli / atlantoaxial ligament

Burst and lateral mass fractures are unstable and can be associated with tears of the transverse ligament, which may compromise the atlantodental relationship → dorsal displace-ment of dens → compression of thecal sac and its contents.

Axis Fracture

Prevalence: 17–20% of cervical spine fractures

Associated with: fractures of C1 in 8%

Odontoid / Dens Fracture *(59%)*

Prevalence: 59% of C2 fractures

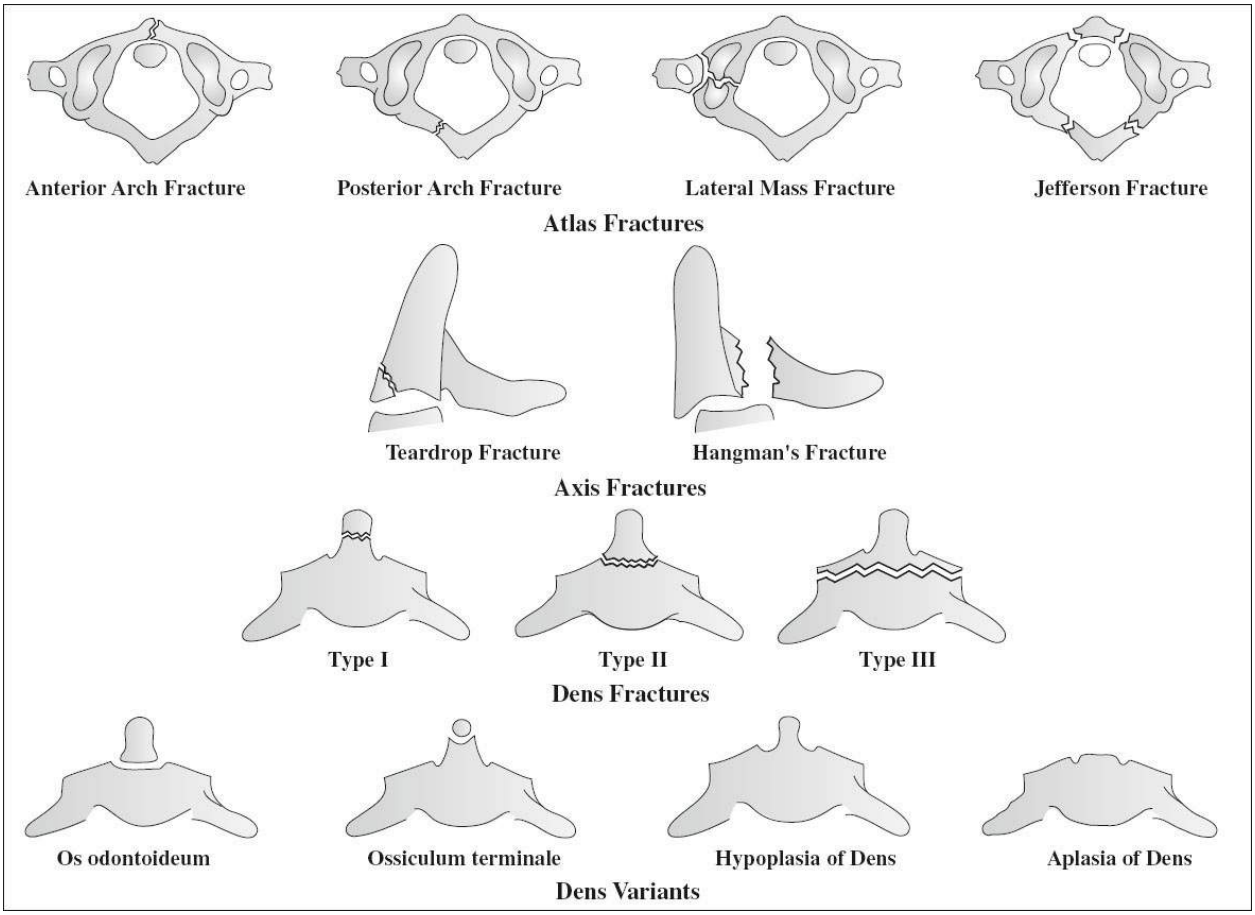
Type I avulsion fracture through odontoid tip (1–8%) at attachment of alar ligaments

√ obliquely oriented fracture through tip of odontoid that is difficult to detect

Prognosis: bone fusion in almost 100% with collar / halo immobilization

Type II fracture through base of dens (54–60%)

Cx: nonunion (in 26% of nonsurgical treatment, with fracture gap ≥ 6-mm increased to 67%)



◊ Axial CT alone misses > 50%!

Type III horizontal subdental fracture (39–42%) through cancellous portion of body

Prognosis: heals in 88% with immobilization

DDx: os odontoideum, ossiculum terminale, hypoplasia of dens, aplasia of dens

Hangman's Fracture *(23%)*

= TRAUMATIC SPONDYLOLISTHESIS

Prevalence: 23% of C2 fractures, 4% of cervical fractures

◊ 2nd most common C2 fracture; unstable

Mechanism: direct impact to face ← compressive hyperextension / distractive hyperflexion

Associated with: neurologic sequelae in only 26%, atlas fracture in 6–26%, other cervical fractures in 8–32%

Types:

I minimally displaced with < 2-mm translation, no angulation / posterior intervertebral disk space widening (stable)

II anterior angulation >11° + anterior translation ← distractive flexion / compressive hyperextension

III (7–10% of hangman fractures) ← severe distractive flexion + bilateral facet dislocation / fracture-dislocation

√ bilateral vertical pars interarticularis fracture of C2 → separation of body from posterior arch → decompression of spinal canal
√ fracture through posterior body of C2
√ prevertebral soft-tissue swelling > 5 mm at anterior-inferior margin of C2
√ ± widening of C2-C3 disk space
√ ± bilateral interfacetal dislocation
√ anterior subluxation of C2 on C3:
  √ disruption of C1–C2 spinolaminar line
  √ disruption of C2–C3 posterior vertebral body line
√ avulsion of anteroinferior corner of C2 (= rupture of anterior longitudinal ligament) = **teardrop fracture**

FRACTURES OF THORACOLUMBAR SPINE

◊ 40% of all vertebral fractures that cause neurologic deficit; mostly complex (body + posterior elements involved)

Location: ⅔ at thoracolumbar junction

Morphology:

1. Compression
   = loss of vertebral body height / disruption of vertebral endplate
   √ vertebral height loss (approximate percentage!)
   √ degree of kyphosis
2. Burst
   = compression of posterior vertebral body + varying degrees of retropulsion
   √ "burst" fragments at superior surface of body
   √ retropulsion of body fragments into spinal canal:
     = distance of line drawn between posterior margins of adjacent vertebral bodies + most posterior margin of bone fragment
   √ narrowing of spinal canal (approximate percentage!)
3. Translation / rotation
   = horizontal displacement or rotation of one vertebral body with respect to another
   √ rotation of spinous processes
   √ uni- / bilateral facet fracture-dislocation
   √ vertebral subluxation
4. Distraction
   = dissociation along vertical axis ← disruption of anterior and posterior ligaments + osseous elements
   √ diastasis of apophyseal joints:
   √ widening of facet joints
   √ empty "naked" facet joints
   √ perched / dislocated facet joints
   √ widening of interspinous space
   √ avulsion fracture of superior / inferior aspects of contiguous spinous processes
   √ vertebral body translation / rotation
   Cx: kyphotic progression → subsequent vertebral collapse

Injury of Posterior Ligament Complex

MRI (only modality for direct assessment!):

- √ disruption of hypointense black stripe on sagittal T1WI / T2WI = tear of supraspinous ligament / ligamentum flavum / interspinous ligament
- √ fluid in facet capsules
- √ interruption of disk
- √ tear of anterior / posterior longitudinal ligaments
- √ edema in interspinous region = capsular / interspinous ligament injury

CT:

- √ widening of facet joints
- √ widening of interspinous distance
- √ spinous process avulsion fracture
- √ significant vertebral body subluxation / dislocation /translation
- √ UNRELIABLE: loss of vertebral body height, kyphosis

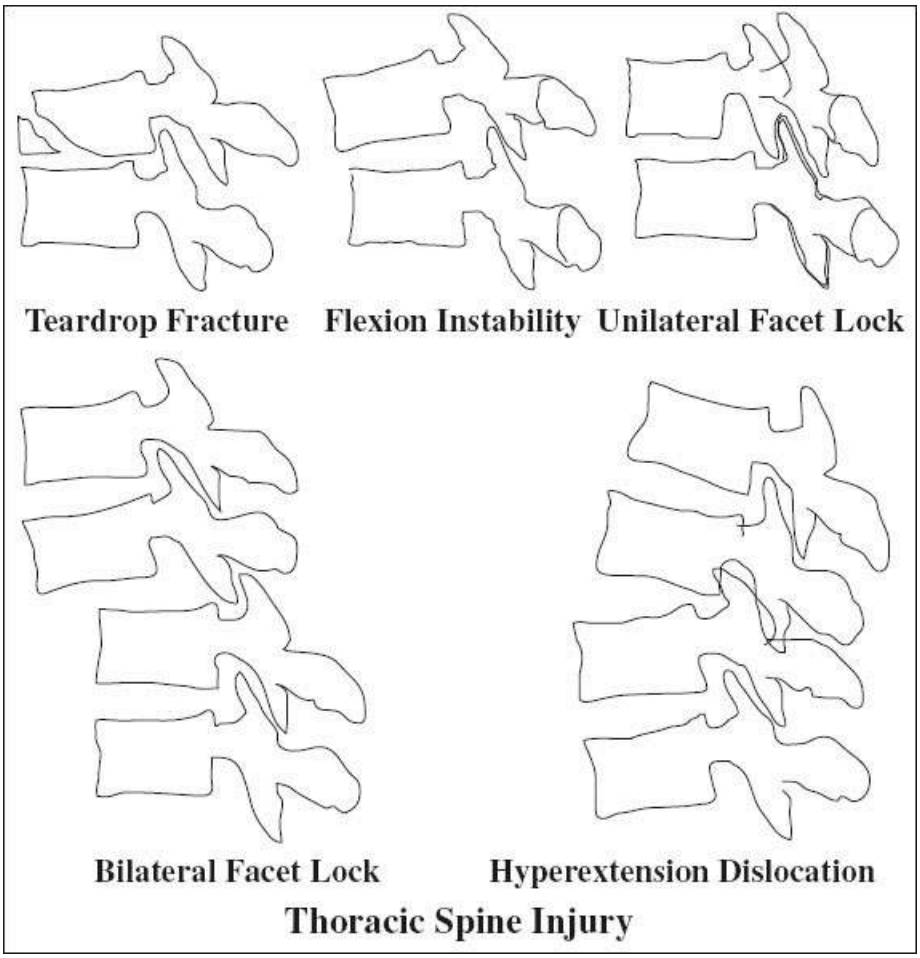
N.B.: inverse relationship between osseous destruction and ligamentous injury!

Fracture of Upper Thoracic Spine (T1 to T10)

Frequency: in 3% of all blunt chest trauma

Types:

1. Compression / axial loading fracture (most common)
   - √ wedging of vertebral body
   - √ retropulsion of bone fragments
   - √ posttraumatic disk herniation



2. Burst fracture (more severe compression fracture)
   √ associated fracture of posterior neural arch
   √ comminuted retropulsed bone fragments
3. Sagittal slice fracture
   √ vertebra above telescopes into vertebra below, displacing it laterally
4. Anterior / posterior dislocation
   √ torn anterior / posterior longitudinal ligament
   √ facet dislocation

◊ Relatively stable fractures due to rib cage + strong costovertebral ligaments + more horizontal orientation of facet joints!

◊ Only 51% detected on initial CXR!

Often associated with: fracture of sternum

√ widening of paraspinal lines
√ mediastinal widening
√ loss of height of vertebral body
√ obscuration of pedicle
√ left apical cap
√ deviation of nasogastric tube

Signs of Spinal Instability:

= inability to maintain normal associations between vertebral segments while under physiologic load

√ displaced vertebra

√ widening of interspinous / interlaminar distance

√ facet dislocation

√ disruption of posterior vertebral body line

Fracture of Thoracolumbar Junction (T11 to L2)

= area of transition between a stiff + mobile segment of spine

• neurologic deficit (in up to 40%)

Classification based on injury to the middle column:

(1) **Hyperflexion injury** (most common)

= compression of anterior column + distraction of posterior spinal elements

(a) hyperflexion-compression fracture

√ loss of height of vertebral body anteriorly + laterally

√ focal kyphosis / scoliosis

√ fracture of anterosuperior endplate

(b) flexion-rotation injury (unusual)

◊ Very unstable!

• catastrophic neurologic sequelae: paraplegia

√ subluxation / dislocation

√ widening of interspinous distance

√ fractures of lamina, transverse process, facets, adjacent ribs

(c) shearing fracture-dislocation

= damage of all 3 columns ← horizontally impacting force

(d) flexion-distraction injury: Chance fracture

2. **Hyperextension injury** (extremely uncommon)

√ widened disk space anteriorly

√ posterior subluxation

√ vertebral anterior superior corner avulsion

√ posterior arch fracture

3. **Axial compression fracture**

◊ Unstable!

√ burst fracture with herniation of intervertebral disk through endplates + comminution of vertebral body

√ marked anterior vertebral body wedging

√ retropulsed bone fragment

√ increase in interpediculate distance

√ ± vertical fracture through vertebral body, pedicle, lamina

Chance Fracture

= SEATBELT FRACTURE

[George Quentin Chance, British radiologist in Manchester, England]

Mechanism: shearing flexion-distraction injury (lap-type seatbelt injury in back-seat

passengers)

• neurologic deficit infrequent (20%)

Location: L2 or L3

√ horizontal splitting of spinous process, pedicles, laminae + superior portion of vertebral body

√ disruption of ligaments

√ distraction of intervertebral disk + facet joints

◊ Fracture often unstable!

Often associated with:

(1) other bone injury
rib fractures along the course of diagonal strap; sternal fractures; clavicular fractures

(2) soft-tissue injury
transverse tear of rectus abdominis muscle; anterior peritoneal tear; diaphragmatic rupture

(3) vascular injury
mesenteric vascular tear; transection of common carotid artery; injury to internal carotid artery, subclavian artery, superior vena cava; thoracic aortic tear; abdominal aortic transection

(4) visceral injury
perforation of jejunum + ileum > large intestine > duodenum (free intraperitoneal fluid in 100%, mesenteric infiltration in 88%, thickened bowel wall in 75%, extraluminal air in 56%); laceration / rupture of liver, spleen, kidneys, pancreas, distended urinary bladder; uterine injury

Chance Equivalent

= purely ligamentous disruption leading to lumbar subluxation / dislocation

√ mild widening of posterior aspect of affected disk space

√ widened facet joints

√ splaying of spinous processes = "empty hole" sign on AP view

Holdsworth Fracture

[Sir Frank Wild Holdsworth (1904–1969), British pioneering orthopedist in rehabilitation of spinal injuries]

Location: thoracolumbar junction

√ unstable spinal column fracture-dislocation with fracture through vertebral body + articular processes

√ rupture of posterior spinal ligaments

Seatbelt Injury

= injury caused by three-point restraint type (combined lap and shoulder belt device)

• bruise in subcutaneous tissue + fat of anterior chest wall

• skin abrasions are associated with significant internal injuries (in 30%)

@ Skeleton
sternum, ribs (along diagonal course of shoulder harness), clavicle, transverse processes of C7 or T1

@ Cardiovascular
aortic transection, cardiac contusion, ventricular rupture, subclavian artery, SVC
@ Airways
tracheal / laryngeal tear, diaphragmatic rupture

Transverse Process Fracture of Lumbar Spine

Cause: direct trauma, violent lateral flexion-extension forces, avulsion of psoas muscle, Malgaigne fracture
Frequency: 7%
In 21–51% associated injury:
genitourinary injury, hepatic + splenic laceration
Location: L3 > L2 > L1 > L4 > L5; L÷R = 2÷1; multiple÷single = 2÷1; unilateral÷bilateral = 20÷1
√ vertical÷horizontal (94%÷6%) fractures
√ associated lumbar burst / compression fracture
◊ Detection by conventional radiography in 40% only!
Prognosis: minor and stable injury; 10% mortality

Sacral Fracture

Zone 1 = fracture lateral to sacral foramina
• significant neurologic deficit (uncommon)
Zone 2 = fracture through ≥ 1 foramina
• unilateral lumbar / sacral radiculopathy (rare)
Zone 3 = fracture through central canal
• significant bilateral neurologic damage (frequent): bowel / bladder incontinence
Cx: chronic disability (in up to 50%)

Acute Atraumatic Compression Fractures of Spine

Osteoporotic Compression Fracture of Vertebra

√ low-signal-intensity band on T1WI and T2WI (93% sensitive)
√ spared normal bone marrow SI of the vertebral body (85% sensitive)
√ retropulsion of a posterior bone fragment into spinal canal (60% sensitive)
√ "fluid" sign = circumscribed fluidlike SI on T2WI + STIR subjacent to fractured end plate
√ multiple compression fractures
√ rimlike enhancement around low-signal-intensity bands
√ "wafer-like" distribution of radionuclide activity along endplate

Metastatic Compression Fracture of Vertebra

√ convex posterior border of vertebral body (74% sensitive)
√ abnormal SI of the pedicle or posterior element on enhanced fat-suppressed T1WI
√ epidural mass
√ encasing epidural mass
√ focal paraspinal soft-tissue mass (41% sensitive)
√ other sites of spinal metastases without compression fractures (63% sensitive)

√ enhancement of metastatic foci
√ completely replaced bone marrow of vertebral body (by tumor cells before trabeculae critically weakened)
Cx: spinal cord compression

GLIOMA OF SPINAL CORD

Astrocytoma of Spinal Cord

◊ Most common intramedullary neoplasm in children!
◊ 2nd most common intramedullary neoplasm in adults
Frequency: 30% of spinal cord tumors; 2nd in prevalence to ependymoma in adults
Mean age: 29 years; M÷F = 58÷42
Path: ill-defined fusiform cord enlargement without cleavage plane / capsule
Histo: hypercellularity with infiltrative growth along scaffold of normal astrocytes, oligodendrocytes and axons

Grade I	pilocytic astrocytoma (75%), usually most common in cerebellum
Grade II	low-grade fibrillary type
Grade III	anaplastic astrocytoma with necrosis (up to 25%)
Grade IV	glioblastoma multiforme with endothelial proliferation (0.2–1.5%)

Location: thoracic cord (67%), cervical cord (49%), conus medullaris (3%); on average over 4–7 vertebral segments involved; holocord presentation (in up to 60% in children); often extending into lower brainstem
Site: eccentric within spinal cord (57%)
• pain + sensory deficit (54%); torticollis (27%)
• motor dysfunction (41%), gait abnormalities (27%)
√ eccentric irregular tumor cysts + polar cysts + syrinx (common):
√ water-soluble myelographic contrast enters cystic space on delayed CT images
Radiographs:
√ scoliosis (24%)
√ widened interpedicular distance
√ bone erosion
MR:
√ usually extensive ill-defined homogeneous cord tumor with expansion of spinal cord:
√ iso- to hypointense to cord on T1WI
√ hyperintense on T2WI
√ poorly defined margins
√ dilated veins on surface of cord
√ patchy irregular enhancement
√ leptomeningeal spread (in 60% of glioblastoma multiforme)
Rx: tumor debulking + radiation therapy
Prognosis: 95% 5-year survival in low-grade tumors; higher mortality rate than for ependymoma
DDx: ependymoma ("cap" sign, central location, well defined, hemorrhage common, focal

intense enhancement, predilection for conus)

Ependymoma of Spinal Cord

◊ Most common intramedullary spinal neoplasm in adults!

Frequency: 40–60% of primary spinal cord tumors; 90% of primary tumors in filum terminale

Mean age: 39 years; M÷F = 57÷43

Origin: ependymal cells lining the central canal (62–76%)

Path: symmetric cord expansion with displacement of neural tissue yielding a cleavage plane

Histo: perivascular pseudorosettes; cystic degeneration (50%); hemorrhage at superior + inferior tumor margins

Subtypes: cellular (most common, cervical cord), myxopapillary (along filum terminale), papillary, clear cell, tanycytic, melanotic

Location: cervical cord alone (44%) / with extension into thoracic cord (23%); thoracic cord alone (26%); conus medullaris (7%); extends over several vertebral segments (on average 3.6 segments involved)

ectopic: sacrococcygeal region, broad ligament of ovary (associated with spina bifida occulta [33%])

Site: central within spinal cord

- long antecedent history (mean duration of 37 months) ← slow tumor growth:
  - back / neck pain (67%) = compression / interruption of central spinothalamic tracts first
  - sensory deficits (52%), motor weakness (46%)
  - bowel / bladder dysfunction (15%)

Metastases to: lung, retroperitoneum, lymph nodes

√ well-demarcated / diffusely infiltrating cord tumor

√ associated with at least one cyst (in 78–84%):

- √ polar cyst (62%) at cranial and caudal aspect of tumor, which do not contain malignant cells
- √ tumoral cyst (4–50%), which may contain tumor
- √ syringohydromyelia (9–50%)

Radiographs:

- √ scoliosis (16%)
- √ widening of spinal canal (11%):
  - √ scalloping of vertebral body
  - √ pedicle erosion, laminar thinning

Myelography:

- √ enlarged cord with complete / partial block to flow of contrast material

CT:

- √ iso- / slightly hyperattenuating cord mass
- √ intense enhancement

MR:

- √ iso- / hypointense (rarely hyperintense from hemorrhage) mass relative to spinal cord on T1WI
- √ hyper- / isointense on T2WI

√ **"cap" sign** = extremely hypointense rim at the tumor poles on T2WI (in 20–33%) due to hemosiderin deposits from prior hemorrhage
√ cord edema (60%)
√ mostly intense homogeneous enhancement (84%) with well-defined margins (89%)
Prognosis: 82% 5-year survival rate
DDx: astrocytoma (pediatric tumor, eccentric location, ill defined, hemorrhage uncommon, patchy irregular enhancement)

Myxopapillary Ependymoma of Spinal Cord
= special variant of ependymoma of lower spinal cord
Prevalence: 13% of all spinal ependymomas; most common neoplasm of conus medullaris (83%)
Mean age: 35 years; M> F
Origin: ependymal glia of filum terminale
Path: heterogeneous tumor with generous mucin production
• lower back / leg / sacral pain
• weakness / sphincter dysfunction
Location: conus medullaris, filum terminale; occasionally multiple (14–43%)
√ isointense on T1WI + hyperintense on T2WI
√ occasionally hyperintense on T1WI + T2WI ← mucin content / hemorrhage
√ almost always contrast enhancing
√ occasionally large lytic area of bone destruction

Subependymoma of Spinal Cord
= variant of CNS ependymoma
Origin: tanycytes that bridge pial + ependymal layers [*tanyos*, Greek = stretch]
Mean age: 42 years; M÷F = 74÷26
Histo: sparsely dispersed ependymal cells among predominant fibrillar astrocytes
• 52 months mean duration of symptoms:
  • pain, sensory + motor dysfunction
  • atrophy of one / both distal upper extremities (83%)
Location: ventricular system of brain, some in cervical cord
√ fusiform dilatation of spinal cord:
  √ enhancing lesion with well-defined borders (50%)
  √ nonenhancing lesion with diffuse symmetric cord enlargement
√ eccentrically located mass
√ ± edema

Ganglioglioma of Spinal Cord
= GANGLIOGLIONEUROMA = GANGLIONIC NEUROMA = NEUROASTROCYTOMA = NEUROGANGLIOMA = GANGLIONIC GLIOMA = = NEUROGLIOMA = NEUROMA GANGLIOCELLULARE
Prevalence: 0.4–6.2% of all CNS tumors; 1.1% of all spinal neoplasms
Mean age: 12 years; children > adults; M÷F = 1÷1
Histo: mixture of irregularly oriented neoplastic mature neuronal elements (neurons /

ganglion cells) + glial elements (neoplastic astrocytes), arranged in clusters = grade I or II lesions

Location: cervical cord (48%), thoracic cord (22%), conus, holocord (average length of 8 vertebral segments); usually supratentorial (temporal lobe)

• duration of symptoms between 1 month and 5 years

√ scoliosis (44%), spinal remodeling (93%) ← relatively slow growth (rare in astrocytoma / ependymoma)

√ eccentric

√ small tumoral cysts (in 46%)

√ calcifications (rare compared with intracranial tumor)

MR:

√ mixed tumor signal intensities on T1WI (in 84%)

√ tumor homogeneously hyperintense on T2WI

√ surrounding edema (less common than in ependymoma / astrocytoma)

√ patchy (65%) / no (15%) tumor enhancement

√ enhancement of pial surface (58%)

Cx: malignant transformation (10%)

Prognosis: slow growth; 89% 5-year and 83% 10-year survival rate; 27% recurrence rate

HEMANGIOBLASTOMA OF SPINE

= ANGIOBLASTOMA = ANGIORETICULOMA

Prevalence: 1–7.2% of all spinal cord tumors; mostly sporadic

Associated with: Von Hippel-Lindau disease (in ⅓)

Recommendation: screening MR imaging of brain + spine in patients with Von Hippel-Lindau syndrome

Age: middle age; M÷F = 1÷1

Path: nonglial highly vascular discrete nodular masses abutting leptomeninges with prominent dilated + tortuous vessels on posterior cord surface

Histo: large pale stromal cells of unknown origin packed between blood vessels of varying sizes

Location: intramedullary (75%), radicular (20%), intradural extramedullary (5%); thoracic cord (50%), cervical cord (40%); solitary in > 80%, multiple lesions indicate Von Hippel-Lindau syndrome + require screening of entire spine

Site: subpial aspect of dorsal spine; may extend exophytically into subarachnoid / extradural space

• mean duration of symptoms is 38 months:

• sensory changes (39%): impaired proprioception

• motor dysfunction (31%), pain (31%)

√ increased interpediculate distance (mass effect)

Angio:

√ highly vascular mass with dense prolonged blush

√ large draining veins form sinuous mass along posterior aspect of cord

MR:

√ iso- (50%) / hyperintense (25%) diffuse cord expansion on T1WI

√ hyperintense lesion with intermixed focal flow voids on T2WI:
  √ curvilinear areas of signal voids
√ cyst formation / syringohydromyelia (in up to 100%):
  √ intratumoral cystic component (50–60%)
  √ occasionally cystic mass with enhancing mural nodule (CLASSIC for cerebellar hemangioblastoma)
  √ densely staining tumor nodule
√ ± surrounding edema and "cap" sign
√ well-demarcated Gd-enhancing mass
Cx: intramedullary hemorrhage, hematomyelia, subarachnoid hemorrhage (rare)
DDx: arteriovenous fistula (not well circumscribed, heterogeneous signal intensity)

IDIOPATHIC OSTEOSCLEROSIS OF JAW

Age: late 1st / early 2nd decade
• asymptomatic
Location: mandible (90%)
Site: periapical near 1st molar / 2nd molar / premolar
√ small focal round / oval solitary sclerotic lesion
√ sharply marginated ± peripheral spiculations
√ nonexpansile WITHOUT rim of low attenuation

IDIOPATHIC SPINAL CORD HERNIATION

= spinal cord displacement through anterior / lateral dura mater defect → uncommon cause of thoracic myelopathy
Cause: ? occult minor trauma / remote traumatic event (herniated / calcified disk may cause thinning / erosion / rupture of dura)
Mean age: 51 (range, 21–78) years; M÷F = 2÷3
• symptomatic for 1–20 years: Brown-Séquard syndrome (66%), chronic progressive paraparesis (30%), isolated sensory deficit (3%), ataxia, pain, spastic monoparesis

Idiopathic spinal cord herniation often present with symptoms of Brown-Séquard syndrome, including ipsilateral upper motor neuron paralysis, loss of proprioception and contralateral loss of pain and temperature sensation

Location: T3–T7 ← anterior position of spinal cord with physiologic kyphosis; usually solitary lesion
Site: level of intervertebral disk >> vertebral body; spanning (usually) 1–2 / multiple vertebrae (rare)
√ variable degree of cord deformity / kinking:
Type K: obvious **k**inking toward the ventral region
Type D: **d**isappearance of spinal cord completely
Type P: **p**rotrusion of ventral aspect of spinal cord with full effacement of anterior subarachnoid space + little posterior cord kinking
Type C: **c**entral hiatus
Type L: **l**ateral hiatus
Myelography:

√ acute anterior kink of thoracic spinal cord with enlargement of dorsal subarachnoid space
√ free flow of contrast material (cannot completely exclude space-occupying lesion as in wide-necked communicating arachnoid cyst)

N.B.: arachnoid cyst must be excluded!

CT myelography:

√ "nuclear trail" sign = linear high-attenuation lesion in inferior endplate of adjacent vertebra ← posterior interosseous disk herniation
√ soft tissue extending from apex of cord displacement through dural defect into epidural space
√ ± concomitant scalloping of vertebral body

MR:

√ obliteration of CSF space ventral to cord
√ widened dorsal CSF space
√ absence of solid / cystic mass posterior to cord
√ small amount of extradural soft tissue extending from ventral apex of displaced cord into epidural space (occasionally)
√ NO enhancement
√ ± cord atrophy and high T2 signal intensity

Errors in diagnosis (common):

intradural arachnoid cyst, extradural mass with cord compression, disk herniation with cord tethering

Rx: postoperatively improved neurologic symptoms (88%)

DDx: traumatic / iatrogenic cord herniation; CSF flow artifact

INCLUSION CYST OF SPINE

Cause:

(a) congenital dermal rest / focal expansion of dermal sinus ← inclusion / aberrant implantation of ectodermal cells at time of neural groove closure (3rd–5th week of GA)
(b) acquired from implantation of viable epidermal / dermal tissue (lumbar puncture by spinal needle without trocar)

Similarities: both composed of

(a) outer wall formed by collagenous tissue
(b) inner lining formed by ectodermal tissue only (= stratified squamous epithelium)

Histologic differentiation:

1. Epidermoid cyst
   › thin squamous lining
   • cyst content = waxy white **"pearly tumor"** composed of desquamated epithelial cells (= keratin, triglycerides, fatty acids, cholesterol crystals)
2. Dermoid cyst (may arise earlier in embryonic process)
   › thicker lining including calcifications, sebaceous secretions, sweat glands, hair follicles, hair
   › forming fat-fluid levels
   • cyst content = composed of (1) desquamated epithelium and (2) secretions of sebaceous glands

- nonspecific symptoms: weakness, back pain
- slowly progressive myelopathy ← space-occupying lesion causing irritation / compression of adjacent structures:
  - motor + sensory disturbance (paresthesia)
  - urinary / fecal incontinence
- acute onset of chemical / aseptic meningitis / arachnoiditis ← spread of cholesterol crystals via CSF ← cyst rupture:
  - headache, nausea, vomiting, vertigo, visual problems
  - meningism, mental change, hemiplegia, coma

Dermoid Cyst of Spine

= uni- / multilocular benign cystic tumor lined by stratified squamous epithelium containing skin (dermal) appendages

Path: (a) wall ± calcifications (in 31%) and papillary projections along inner surface
(b) cystic contents of fluid-like mucoid (in virtually 100%) and lipid fatty (67–75%) components
- thick foul-smelling yellow material ← secretion of sebaceous glands + desquamated epithelium

Prevalence: 1–2% of intraspinal tumors; 0.7–1.8% of all CNS tumors

Age at presentation: 2nd–3rd decade; M÷F = 1÷1

May be associated with:
myelomeningocele, dermal sinus tract (in 20%), hypertrichosis; **Currarino triad** (= anorectal malformation + sacral dysplasia + presacral mass → severe constipation since birth)

Location: lumbosacral (60%), cauda equina (20%)

Site: extramedullary (60%), intramedullary (40%)

CT:
√ almost always complete spinal block on myelography
√ CT myelography facilitates detection
√ well-demarcated isoattenuating mass ± hypoattenuating fat
√ ± wall calcifications + papillary projections

MR:
√ uni- / multilocular cystic lesion with variable SI:
  √ hyperintense on T1WI + hypointense on Gd-enhanced fat-suppressed T1WI (fatty component)
  √ occasionally hypointense on T1WI + hyperintense on T2WI (fluid secretions from sweat glands within tumor)
  √ ± fat-fluid level
√ NO contrast enhancement (except for small soft-tissue component)
√ dissemination of lipid droplets scattered throughout CSF and intra-axially throughout spinal cord

Cx: spontaneous / intraoperative / traumatic dermoid cyst rupture → lipid droplets transported along CSF pathway

Prognosis: high risk of morbidity + mortality (with rupture)

Rx: dependent on symptoms

DDx: (1) Epidermoid cyst (without dermal appendages, T1 hypointense + T2 hyperintense)
(2) Lipoma (homogeneous midline T1-hyperintense lesion with smooth well-defined border)
(3) Teratoma (heterogeneous enhancement)
(4) Intraaxial tumor: ependymoma, astrocytoma, hemangioblastoma

Epidermoid of Spine

= cystic tumor lined by a membrane composed of epidermal elements of skin
Prevalence: 0.2%–1% of intracranial tumors; < 1% of spinal cord tumors
Mean age: 34 (range, 3–71) years; M÷F = 1.35÷1.00
May be associated with:
(a) skin lesion: hairy nevus, dyschromia, angioma, scar
(b) spinal dysraphism: dermal sinus, spina bifida, hemivertebra, syringomyelia, tethered cord syndrome, dorsal meningocele, diastematomyelia
Mean delay in Dx: 6 years (range, 2 days to 53 years)
Location: upper thoracic (17%), lower thoracic (26%), lumbosacral (22%), cauda equina (35%)
Site: intradural extramedullary (60%), intramedullary (40%)
Growth rate: similar to that of normal skin
√ displacement of spinal cord / nerve roots
√ NO internal enhancement + faint to NO rim enhancement
Myelography (CT facilitates detection):
√ asymmetric filling defect / complete spinal block
DDx: communicating arachnoid cyst typically opacifies
MR:
√ circumscribed mass WITHOUT peripheral edema
√ variable signal intensity ← differing concentrations of cyst content of keratin + water + cholesterol:
√ T1 isointense (especially when tumor small) to slightly hyperintense relative to CSF
√ iso- to slightly hyperintense relative to CSF on T2WI
√ T1 hyperintense + T2 hypointense "**white epidermoid**" (rare) ← high protein concentration
√ hyperintense to CSF on FLAIR and D WI ← restricted diffusion (DD x: arachnoid cyst (isointense to CSF on FLAIR and D WI)
Cx: malignant transformation (extremely rare)

KLIPPEL-FEIL SYNDROME

= BREVICOLLIS
= synostosis of two / more cervical segments
[André Feil (1884–?), neurologist in Paris]
May be associated with:
platybasia, syringomyelia, encephalocele, facial + cranial asymmetry, Sprengel deformity (25–40%), syndactyly, clubbed foot, hypoplastic lumbar vertebrae; renal anomalies in 50% (agenesis, dysgenesis, malrotation, duplication, renal ectopia); congenital heart disease in 5%

(atrial septal defect, coarctation)
- clinical triad of
  (1) short neck
  (2) restriction of cervical motion
  (3) low posterior hairline
- deafness (30%)
- torticollis; webbed neck

Location: cervical spine
√ wide and flat vertebral bodies
√ ± cervicothoracic / cervical / occipitoatlantal fusion:
  √ fusion of vertebral bodies and posterior elements
√ ± hemivertebrae
√ scoliosis
√ rib fusion
√ Sprengel deformity (25–40%)
√ ear anomalies: absent auditory canal, microtia, deformed ossicles, underdevelopment of bony labyrinth

KüMMELL DISEASE

[Hermann Kümmell (1852–1937), professor of surgery at the University of Hamburg, published Chirurgische Operationslehre]
= INTRAVERTEBRAL VACUUM PHENOMENON
= delayed posttraumatic collapse of vertebral body
Incidence: < 1% (on X-ray), 12% (on CT); in 15–30% of osteoporotic fractures
Cause: ischemic necrosis weeks to months following acute fracture
Pathophysiology: compression fracture → subsequent partial distraction by paraspinal muscles in supine position → vertebral cavity / cleft → low pressure within cleft allows accumulation of gas (principally nitrogen) in the absence of bleeding = "ischemic vertebral collapse"
Age: > 50 years
Location: thoracolumbar junction: T12 & L1
√ collapsed vertebral body
√ transverse linear / semilunar radiolucency located centrally within / adjacent to endplate
√ gas collection increases with extension + traction, decreases with flexion
√ contiguous intradiskal vacuum phenomenon (in 83%)
√ gas may become replaced by fluid
N.B.: presence of gas virtually excludes tumoral + infectious etiology (rare exceptions: myeloma, E. coli, clostridia, TB, brucellosis, peptococcus, streptococcus, staphylococcus)

LEPTOMENINGEAL CYST

= **"Growing" fracture** = loculation of CSF into / through skull
Prevalence: 1% of all pediatric skull fractures
Pathogenesis: skull fracture with dural tear leads to arachnoid herniation into dural defect;

CSF pulsations produce fracture diastasis + erosion of bone margins (apparent 2–3 months after injury)

√ skull defect with indistinct scalloped margins

√ CSF-density cyst adjacent to / in skull, may contain cerebral tissue

MR:

√ cyst isointense with CSF + communicating with subarachnoid space

√ area of encephalomalacia underlying fracture (frequent)

√ intracranial tissue extending between edges of bone

LIPOMA OF SPINE

= partially encapsulated mass of fat + connective tissue in continuity with leptomeninges / spinal cord

• skin-coated subcutaneous back mass, occasionally associated with hemangiomatous / hairy lesion

• sensory deficiency, paresis, neurogenic bladder

Types:

(a) lipomyelomeningocele (84%)

(b) fibrolipoma of filum terminale (12%)

(c) intradural lipoma (4%)

Location: lumbosacral region

◊ Intradural lipomas + lipomyelomeningoceles represent 35% of skin-covered lumbosacral masses + 20–50% of occult spinal dysraphism!

Intradural Lipoma

= subpial juxtamedullary mass totally enclosed in intact dural sac

Prevalence: < 1% of primary intraspinal tumors

Etiology: abnormal embryonic neurulation

Age peaks: first 5 years of life (24%), 2nd + 3rd decade (55%), 5th decade (16%)

• slow ascending mono- / paraparesis, spasticity, cutaneous sensory loss, defective deep sensation (with cervical + thoracic intradural lipoma)

• flaccid paralysis of legs, sphincter dysfunction (with lumbosacral intradural lipoma)

• overlying skin most often normal

• elevation of protein in CSF (30%)

Location: thoracic (30%) / cervicothoracic (24%) / cervical (12%)

Site: dorsal aspect of cord (75%), lateral / anterolateral (25%)

√ spinal cord open in midline dorsally

√ lipoma in opening between lips of placode

√ exophytic component at upper / lower pole of lipoma

√ syringohydromyelia (2%)

√ focal enlargement of spinal canal ± adjacent neural foramina

√ narrow localized spina bifida

Lipomyelomeningocele

= lipoma tightly attached to exposed dorsal surface of neural placode blending with subcutaneous fat

Prevalence: 20% of skin-covered lumbosacral masses; in up to 50% of occult spinal dysraphism
Age: typically < 6 months of age; M < F
• semifluctuant lumbosacral mass with overlying skin intact
• sensory loss in sacral dermatomes, motor loss, bladder dysfunction; foot deformities, leg pain
Location: lumbosacral; longitudinal extension over entire length of spinal canal (in 7%)
Site:
› lipoma dorsally continuous with subcutaneous fat
› lipoma may extend upward within spinal canal external to dura (= "epidural lipoma")
› lipoma may enter central canal and extend rostrally (= "intradural intramedullary lipoma")
√ deformed undulating spinal cord with dorsal cleft
√ tethered cord
√ ventral + dorsal nerve roots leave neural placode ventrally
√ dilated subarachnoid space
US:
√ echogenic intraspinal mass adjacent to deformed spinal cord + continuous with slightly hypoechoic subcutaneous fat
@ Vertebral changes
√ large spinal canal
√ erosion of vertebral body + pedicles
√ posterior scalloping of vertebral bodies (50%)
√ focal spina bifida
√ segmental anomalies / butterfly vertebra (up to 43%)
√ confluent sacral foramina / partial sacral agenesis (up to 50%)

Fibrolipoma of Filum Terminale

Prevalence: 6% of autopsies
• asymptomatic
Location: intradural filum, extradural filum, involvement of both portions
√ thin linear fat-containing mass of filum terminale
Prognosis: potential for development of symptoms of tethered cord

LÜCKENSCHÄDEL

= CRANIOLACUNIA = LACUNAR SKULL
= mesenchymal dysplasia of calvarial ossification (developmental disturbance)
Age: present at birth
Associated with:
(1) Meningocele / myelomeningocele / encephalocele
(2) Spina bifida
(3) Cleft palate
(4) Arnold-Chiari II malformation
• normal intracranial pressure
Location: particularly upper parietal area

√ honeycombed appearance about 2 cm in diameter (thinning of diploic space)
√ premature closure of sutures (turricephaly / scaphocephaly)
Prognosis: spontaneous regression within first 6 months of life
DDx: (1) Convolutional impressions = "digital" markings (visible at 2 years, maximally apparent at 4 years, disappear by 8 years of age)
(2) "Hammered silver" appearance of increased intracranial pressure

LYMPHOMA OF SPINAL CORD

Prevalence: 3.3% of CNS lymphoma, 1% of all lymphomas
Mean age: 47 years; M< F
Histo: monotonous collection of lymphocytes packed tightly into perivascular space; predominantly B-cell lymphocyte population; no necrosis
• weakness, numbness, progressive difficulty in ambulation
Location: cervical > thoracic > lumbar cord
Site: in extradural compartment (most commonly)
MR:
√ mostly solitary, rarely multicentric
√ isointense relative to cord on T1WI
√ hypointense with cord on T2WI (related to high nuclear-to-cytoplasmic ratio)
√ extensive cord edema
√ hetero- / robust homogeneous enhancement
√ restricted diffusion ← high cellularity + reduced extracellular matrix
Cx: compression of cord due to narrowing of spinal canal
Rx: initial response to steroids; radiation therapy results in rapid reduction in size + compressive effects

MENINGEAL CYST

= abnormal dilatation of meninges within sacral canal / foramina ± presacral component
Prevalence: 5%
Cause: diverticulum of spinal meningeal sac / nerve root sheath / arachnoid
√ unilocular / multilocular cyst
√ remodeling erosion of sacral canal / foramen ← CSF pulsations
√ thinned cortical margins
DDx of presacral cyst: cystic sacrococcygeal teratoma; anal duct cyst; degenerative neurogenic tumor; adnexal cyst

Perineural Sacral Cyst / Tarlov Cyst

[Isadore Max Tarlov (1905–1977), professor of neurology and neurosurgery at New York Medical College]
= dilated nerve-root sleeve as normal variant
Cause: ? congenital, traumatic
Location: posterior rootlets (S2 + S3 most common)
• neurologic symptoms if large (in 22%)
√ cyst communicates freely with subarachnoid space

√ cyst wall continuous with arachnoid + dura
√ cyst cavity occupies space between peri- and endoneurium
√ bone remodeling + enlargement of neural foramen
Rx: surgical decompression, sacral laminectomy, percutaneous drainage

Sacral Meningeal / Arachnoid Cyst (less common)
= OCCULT INTRASACRAL MENINGOCELE
• usually asymptomatic
√ cyst does not communicate with subarachnoid space

MENINGIOMA OF SPINE

Prevalence: 25–45% of all spine tumors; 2–3% of pediatric spinal tumors; 12% of all meningiomas
Age: > 40 years + female (80%)
Location: thoracic region (82%); cervical spine on anterior cord surface near foramen magnum (2nd most common location); 90% on lateral aspect
Site: intradural extramedullary (50%); entirely epidural; intradural + epidural
• spinal cord / nerve root compression
√ bone erosion in < 10%
√ scalloping of posterior aspect of vertebral body
√ widening of interpedicular distance
√ enlargement of intervertebral foramen
√ may calcify (not as readily as intracranial meningioma)
CT:
√ solid smoothly marginated mass isodense with skeletal muscle
√ marked enhancement
MR:
√ isointense with spinal cord on T1WI + T2WI
√ ± dural tail reflecting tumor spread / reactive changes
√ rapid + intense enhancement after Gd-DTPA
DDx: nerve sheath tumor

METASTASIS TO VERTEBRA

◊ Most common vertebral tumor!
Prevalence: 5–10% of cancer patients
Age: usually > 50 years of age
Source:
(a) Metastatic tumor: lung, breast, prostate (15–20%) > kidney, lymphoma, malignant melanoma
(b) Primary tumor: multiple myeloma
Spread:
(a) hematogenous spread to vertebral body (bones with greatest vascularity) + epidural space
(b) contiguous spread from paraspinal region: lymphoma, sarcoma, lung carcinoma
• back pain; motor deficits; sensory abnormality

• autonomic dysfunction (bladder, bowel)

Location: thoracic > lumbosacral > cervical spine

Clues: √ multiple lesions of variable size
√ pedicles often destroyed
√ vertebral compression fracture
√ associated epidural tumor
√ cortical disruption (= osteolysis)

Radiograph:
√ osteolytic >> osteoblastic > mixed metastases

MR (93% sensitive, 97% specific, 97% accurate):
√ patchy multifocal relatively well-defined lesions
√ diminished signal on T1WI on background of high-signal appearance of marrow fat
√ increased signal on T2WI (except for blastic metastases with diminished T1 + T2 signals)
√ contrast enhancement on T1WI (majority)
√ pathologic compression fracture:
√ fracture only after all vertebral body fat replaced
√ hyperintense on diffusion-weighted images (DDx: hypointense benign osteoporotic fracture)
◊ Whole-spine MRI to search for multifocal involvement!

Risk: malignant **spinal cord compression** (5–10%)

◊ Metastatic extension into spinal canal can result in neurologic symptoms and paralysis.

DDx: (1) Infection (centered around disk space)
(2) Primary vertebral tumor (rare in older patients, almost always benign in patients < 21 years of age)

METASTASIS TO SPINAL CORD

Frequency: 90% of all spinal cord + vertebral neoplasms

Intramedullary Metastasis

Prevalence: 0.9–2.1% of CNS metastases (autoptic)

Origin: lung (40–85%), breast (11%), melanoma (5%), renal cell (4%), colorectal (3%), lymphoma (3%), cerebellar medulloblastoma; 5% of unknown origin

Spread:
(a) common: hematogenous (via arterial supply) / direct extension from leptomeninges
(b) rare: dissemination along central canal / extension along Batson venous plexus from retroperitoneal primary tumor / extension along perineural lymphatic ducts

• symptomatic for < 1 month (in 75%):
• motor weakness, bowel / bladder dysfunction (60%)
• pain (70%), paresthesia (50%)

Location: cervical (45%), thoracic (35%), lumbar cord (8%)

Myelography (up to 40% undetected)

MR:
√ mild cord expansion over several segments (average length of 2–3 vertebral segments)

√ central area of low SI (mimicking syrinx) on T1WI
√ high SI on T2WI ← edema / tumor infiltration
√ intense homogeneous enhancement
√ disproportionately large amount of surrounding edema
Prognosis: 66% die within 6 months
Rx: radiation therapy, corticosteroids

Extradural / Epidural Metastasis

Origin: breast (22%), lung (15%), lymphoma (10%), prostate (10%), kidney (7%), gastrointestinal (5%), melanoma (4%)
DDx: schwannoma, neurofibroma, cysts

Intradural Metastasis

= MENINGEAL CARCINOMATOSIS OF SPINE
√ round multifocal masses varying substantially in size from a few mm to > 10 mm
√ enlarged cord (from diffuse tumor coating of spinal cord) simulating an intramedullary lesion
√ thickening of meninges (especially in lymphoma, breast cancer, prostate cancer)
√ thickened + nodular matted nerve roots
√ nodular + irregularly narrowed thecal sac
√ Gd-DTPA enhancement (difficult to detect due to adjacent fat + enhancing epidural venous plexus)
Dx: CSF analysis (more sensitive than imaging)
DDx: moderate to severe meningitis, benign postoperative arachnoiditis, neurofibromatosis

Metastases from Outside CNS

(a) with subarachnoid hemorrhage:
bronchogenic carcinoma, malignant melanoma, choriocarcinoma, hypernephroma
(b) others: breast (most common), lymphoma
√ predominantly dorsal location

Drop Metastases

= CSF SEEDING OF INTRACRANIAL NEOPLASMS
Age: occurs more frequently in pediatric age group than in adults
Location: lumbosacral + dorsal thoracic spine ← CSF flow / gravitation)
Site: on spinal arachnoid / pia mater
CNS tumors causing drop metastases:

1. Primitive neuroectodermal tumor
2. Medulloblastoma: up to 33%
3. Anaplastic glioma
4. Ependymoma: after local recurrence, more common in infra- than supratentorial ependymomas
5. Germinoma
6. Pineoblastoma, pineocytoma

Less common: choroid plexus carcinoma, teratoma, angioblastic meningioma
mnemonic: MEGO TP

Medulloblastoma
Ependymoma
Glioblastoma multiforme
Oligodendroglioma
Teratoma
Pineoblastoma, **P**NET

MYELOCYSTOCELE

= SYRINGOCELE
= hydromyelic spinal cord + arachnoid herniated through posterior spina bifida; least common form of spinal dysraphism
May be associated with: GI tract anomalies, GU tract anomalies
• cystic skin-covered mass over spine
• cloacal exstrophy (frequent)
Location: lower spine > cervical > thoracic spine
√ direct continuity of meningocele with subarachnoid space
√ cyst communicating with widened central canal of spinal cord typically posteriorly + inferiorly to meningocele
√ lordosis, scoliosis, partial sacral agenesis (common)

MYELOMENINGOCELE

= sac covered by leptomeninges containing CSF + variable amount of neural tissue; herniated through a defect in the posterior / anterior elements of spine
Prevalence: 1÷1,000–2,000 births (in Great Britain 1÷200 births); twice as common in infants of mothers > 35 years of age; Caucasians > Blacks > Orientals; most common congenital anomaly of CNS
Etiology: localized defect of closure of caudal neuropore (usually closed by 28 days); persistence of neural placode causes derangement in the development of mesenchymal + ectodermal structures
• positive family history in 10%
• neural placode = reddish neural tissue in the middle of back made up of open spinal cord
• normal skin / cutaneous abnormality: pigmented nevus, abnormal distribution of hair, skin dimple, angioma, lipoma
• MS-AFP (≥ 2.5 S.D. over mean) permits detection in 80% (2–5% PPV) if defect not covered by full skin thickness
Recurrence rate: 3–7% chance of NTD with previously affected sibling / in fetus of affected parent
Associated with:
(1) Hydrocephalus (70–90%): requiring ventriculoperitoneal shunt in 90%
◊ 25% of patients with hydrocephalus have spina bifida!
(2) Chiari II malformation (99%)
(3) Congenital / acquired kyphoscoliosis (90%)
(4) Vertebral anomalies: vertebral body fusion, hemivertebrae, cleft vertebrae, butterfly vertebrae

(5) Diastematomyelia (20–46%): spinal cord split above (31%), below (25%), at the same level (22%) as the myelomeningocele
(6) Duplication of central canal (5%) cephalic to + at level of placode
(7) **Hemimyelocele** (10%) = two hemicords in separate dural tubes separated by fibrous / bony spur: one hemicord with myelomeningocele on one side of midline, one hemicord normal / with smaller myelomeningocele at a lower level
• impaired neurological function on side of hemimyelocele
(8) Hydromyelia (29–77%) cranial to placode ← disturbed CSF circulation
(9) Chromosomal anomalies (10–17%): trisomy 18, trisomy 13, triploidy, unbalanced translocation
◊ In 20% no detectable associated anomalies!
(10) Tethering of spinal cord (70–90%)
(11) Arachnoid cyst (2%) ← developmental deficiency during formation of arachnoid / dura mater with a subdural location

Distribution: thoracic (2%), thoracolumbar (32%), lumbar (22%), lumbosacral (44%)

Location:
(a) cranial meningocele = encephalocele
(b) dorsal / posterior meningocele
(c) anterior sacral meningocele
(d) lateral thoracic / lumbar meningocele

OB-US:
detection rate of 85–90%; sensitivity dependent on GA (fetal spine may be adequately visualized after 16–20 weeks GA); false-negative rate of 24%
√ spinal level estimated by counting up from last sacral ossification center = S4 in 2nd trimester + S5 in 3rd trimester (79% accuracy for ± spinal level)
√ may have clubfoot / rocker-bottom foot
√ polyhydramnios
@ Spine:
√ loss of dorsal epidermal integrity
√ soft-tissue mass protruding posteriorly + visualization of sac
√ widening of lumbar spine with fusiform enlargement of spinal canal:
√ splaying (= divergent position) of ossification centers of laminae with cup- / wedge-shaped pattern (in transverse plane = most important section for Dx)
√ absence of posterior line = posterior vertebral elements (in sagittal plane)
√ gross irregularity in parallelism of lines representing laminae of vertebrae (in coronal plane)
√ anomalies of segmentation / hemivertebrae (33%) with short-radius kyphoscoliosis
√ tethered cord + lumbar / lumbosacral myelomeningocele
@ Head:
√ "lemon" sign = concave / linear frontal contour abnormality located at coronal suture strongly associated with spina bifida
√ "banana" sign
Prevalence: in 96% of fetuses ≤ 24 weeks; in 91% of fetuses > 24 weeks
√ "nonvisualization" of cerebellum
√ effaced cisterna magna (100% sensitivity)

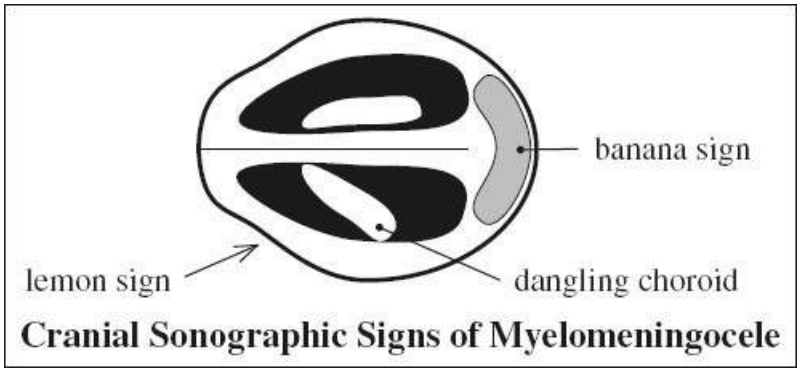
◊ A normal cisterna magna is 3–10 mm deep and usually visualized in 97% at 15–25 weeks GA

√ BPD < 5th percentile during 2nd trimester (70% sensitive)

√ HC < 5th percentile (35% sensitivity)

√ ventriculomegaly (40–90%) with choroid plexus incompletely filling the ventricles (54–63% sensitivity) = "dangling" choroid on dependent side

Prevalence: in 44% of myelomeningoceles < 24 weeks GA; in 94% of myelomeningoceles during 3rd trimester



Cranial Sonographic Signs of Myelomeningocele

Plain films:

√ bony defect in neural arch

√ deformity + failure of fusion of lamina

√ absent spinous process

√ widened interpedicular distance

√ widened spinal canal

Rx: (1) Possibly elective cesarean section at 36–38 weeks GA (may decrease risk of contaminating / rupturing the meningomyelocele sac)

(2) Repair within 48 hr

Postoperative complications:

(1) Postoperative tethering of spinal cord by placode / scar

(2) Constricting dural ring

(3) Cord compression by lipoma / dermoid / epidermoid cyst

(4) Ischemia from vascular compromise

(5) Syringohydromyelia

Prognosis:

(1) Mortality 15% by age 10 years

(2) Intelligence: IQ < 80 (27%); IQ > 100 (27%); learning disability (50%)

(3) Urinary incontinence: 85% achieve social continence (scheduled intermittent catheterization)

(4) Motor function: some deficit (100%); improvement after repair (37%)

(5) Hindbrain dysfunction associated with Chiari II malformation (32%)

(6) ventriculitis: 7% in initial repair within 48 hours, more common in delayed repair > 48 hours

Dorsal / Posterior Meningocele

› lumbosacral (70% below L2): may be associated with tethered cord, partial sacral agenesis
› suboccipital

Anterior Sacral Meningocele

= prolapse through sacral foramen / anterior bony defect
May be associated with:
neurofibromatosis type 1, Marfan syndrome, partial sacral agenesis, imperforate anus, anal stenosis, tethered spinal cord, GU tract / colonic anomalies; Currarino triad
Prevalence: 1÷40,000
Age: 1st decade of life (in 80%); M÷F = 1÷4
• usually asymptomatic in older children
• constipation, dysmenorrhea, urinary incontinence ← mass effect
• back pain, numbness in lower limbs, headache ← neurologic compromise / meningitis / rupture
√ vertebral body scalloping, hypoplasia, aplasia
√ scimitar sacrum = sickle-shaped sacrum

Lateral Thoracic Meningocele

= outpouching of leptomeninges through enlarged intervertebral foramen into extrapleural aspect of thorax
Location: right > left side, in 10% bilateral
Often associated with: neurofibromatosis (75–85%) with sharply angled scoliosis convex to meningocele
√ expanded spinal canal
√ erosion of posterior surface of vertebral body
√ thinning of neural arch
√ enlarged neural foramen
√ spinal abnormalities: kyphoscoliosis, scalloping of dorsal vertebrae, enlargement of intervertebral foramen, pedicle erosion, thinning of ribs

Lateral Lumbar Meningocele

Site: through enlarged neural foramina into subcutaneous tissue / retroperitoneum
Often associated with: Marfan / Ehlers-Danlos syndrome / neurofibromatosis
√ expanded spinal canal
√ erosion of posterior surface of vertebral body
√ thinning of neural arch
√ enlarged neural foramen

Traumatic Meningocele

= avulsion of spinal nerve roots ← tear in meningeal root sheath
Location: (most commonly) in C-spine after brachial plexus injury
√ small irregular arachnoid diverticulum with extension outside the spinal canal

NEURENTERIC CYST

= incomplete separation of foregut and notochord with persistence of canal of Kovalevski between yolk sac and notochord; cyst connected to meninges through midline defect

Frequency: rarest of bronchopulmonary foregut malformations (like pulmonary sequestration, bronchogenic cyst, enteric cyst)

Associated with: neurofibromatosis; meningocele; spinal malformation (stalk connects cyst and neural canal; usually no stalk between cyst and esophagus)

Location: anterior to spinal canal on mesenteric side of gut

√ posterior mediastinal mass

√ air-fluid level (if communicating with GI tract through diaphragmatic defect)

√ spinal dysraphism at the same level:

- √ midline cleft in centra (accommodates stalk)
- √ anterior / posterior spina bifida
- √ vertebral body anomalies: absent vertebra, butterfly vertebra, hemivertebra, scoliosis
- √ diastematomyelia
- √ thoracic myelomeningocele

Tailgut Cyst

= RETRORECTAL CYSTIC HAMARTOMA = RECTAL DUPLICATION CYST = MUCIN-SECRETING CYST = TAILGUT VESTIGES = MYOEPITHELIAL HAMARTOMA OF RECTUM

= rare congenital abnormality in presacral space ← persistent remnant of embryonic gut

Age: manifested in childhood / adulthood

Histo: NO smooth muscle layer

√ uni- / multilocular cyst

√ high signal intensity on T1WI ← mucoid content

ODONTOGENIC MYXOMA

= clinically + radiographically indistinguishable from ameloblastoma

Prevalence: 3–6% of odontogenic tumors

Origin: mesenchymal odontogenic tissue

Age: 10–30 years; M < F

• usually painless

Location: maxilla > mandible

√ well-demarcated / ill-defined lytic lesion of varying size

√ often multilocular + honeycomb-like internal osseous trabeculae

√ foci of irregular calcifications (frequent)

Cx: can be locally aggressive causing considerable destruction of adjacent bone + soft-tissue infiltration

DDx: malignancy, traumatic bone cyst, central giant cell granuloma, calcifying epithelial odontogenic tumor

ODONTOMA

= odontogenic developmental hamartomatous malformation → obstruction of tooth eruption
Prevalence: most common odontogenic tumor (67%)
Age: 2nd decade; before or after tooth eruption
Histo: various tooth components including dentin + enamel
Associated with: impacted tooth (in 50%); dentigerous / calcifying odontogenic cyst (occasionally)
Location: between roots of teeth
Site: pericoronal
√ sharply marginated lesion
√ initially purely radiolucent ± small calcifications
√ later radiopaque mass with a lucent halo
√ 1–3 cm in diameter
√ may be surrounded by lucent follicle
Types:
(a) simple
√ supernumerary tooth
(b) compound odontoma (more common)
√ multiple small toothlike structures (abortive teeth = denticles)
Site: anterior maxilla
(b) complex odontoma
= conglomerate mass of enamel + dentin
Site: molar region (most common)
√ well-defined lesion with amorphous calcifications
√ low-attenuation halo surrounds odontoma
DDx: osteoma (NO halo)
Cx: impaction, malpositioning, resorption of adjacent teeth
DDx: focal cemento-osseous dysplasia, osteoma, ameloblastic fibroodontoma, adenomatoid odontogenic tumor

OSSIFYING FIBROMA

Peak incidence: first 2 decades of life
Histo: areas of osseous tissue intermixed with highly cellular fibrous tissue
Site: maxilla > frontal > ethmoid bone > mandible; rarely seen elsewhere
√ areas of increased + decreased attenuation
√ intact inner + outer table
√ slow-growing expansile lesion
√ usually unilateral + monostotic
DDx: may be impossible to differentiate from fibrous dysplasia

OSTEOMYELITIS OF VERTEBRA

Prevalence: 2–10% of all cases of osteomyelitis
Cause:
(1) Direct penetrating trauma (most common) following surgical removal of nucleus pulposus
(2) Hematogenous: associated with urinary tract infections / following genitourinary surgery /

instrumentation; diabetes mellitus; drug abuse

Pathophysiology: infection begins in low-flow end-vascular arcades adjacent to subchondral plate

Organism: Staphylococcus aureus, Salmonella

Peak age: 5th–7th decade

- pain in back, neck, chest, abdomen, flank, hip
- neurologic deficit; positive blood / urine culture
- fever (most common presenting symptom), leukocytosis
- increased erythrocyte sedimentation rate

Location: vertebral body, intervertebral disk, posterior elements (20%)

√ disk space narrowing (earliest radiographic sign)

√ demineralization of adjacent vertebral endplates

√ bulging of paraspinal lines

MR (90% accuracy = method of choice):

√ hypointense decreased marrow signal on T1WI

√ iso- / hyperintense marrow signal on T2WI

√ hyperintense signal on STIR sequence

CEMR:

√ enhancing foci in bone marrow + disk space

NUC (time-intensive combined bone-gallium scan):

√ tracer uptake in adjacent portions of two vertebral bodies

√ PET-CT (comparable to gallium imaging)

Cx: secondary infection of intervertebral disk (frequent)

Rx: > 4 weeks course of IV antibiotics

DDx: diskitis

PARAGANGLIOMA OF SPINAL CORD

Mean age: 46 years; M > F

Path: soft encapsulated (75%) slightly hemorrhagic mass supplied by numerous feeding arteries

Histo: chief cells + sustentacular cells surrounded by fibrovascular stroma; nests of chief cells in classic "Zellballen" configuration

- lower back pain, sciatica (mean duration for 4 years)

Location: cauda equina, filum terminale

Site: intradural extramedullary compartment

Mean size: 3.3 (range, 1.5–10.0) cm

CT:

√ bone erosion of spine

MR:

√ well-circumscribed mass isointense to cord on T1WI

√ iso- to hyperintense on T2WI:

√ "cap" sign = low-signal–intensity rim on T2WI from hemorrhage

√ ± "salt-and-pepper" appearance

√ intense enhancement

√ serpentine flow voids along surface + within tumor nodule
√ ± syringohydromyelia

Angio:
√ intense early blush persisting well into late arterial + early venous phase

PERIPHERAL NERVE SHEATH TUMOR (PNST)

Dx: distinctive features suggesting peripheral nerve sheath tumor:
(1) Location in region of a major nerve
(2) Depiction of nerve entering / exiting mass
(3) Presence of split fat sign, fascicular sign, target sign

MR:
√ "split-fat" sign = lesion surrounded by a rim of fat ← displacement of fat surrounding neurovascular bundle suggesting a tumor origin in intermuscular space
√ "fascicular" sign = multiple small ringlike structures with peripherally higher SI on T2WI ← fascicular bundles within nerves
√ "target" sign= fibrocollagenous tissue centrally and myxomatous tissue peripherally:
√ tumor periphery of high SI ← myxoid degeneration
√ center of tumor of low SI ← fibrocollagenous tissue of condensed Schwann cells

Angio:
√ displacement of major vascular structures
√ corkscrew-type vessels at upper / lower pole of tumor (= hypertrophy of nutrient nerve vasculature)

Benign Peripheral Nerve Sheath Tumor

= (BENIGN PNST) = BENIGN TUMOR OF NERVE SHEATH = NEURINOMA
Frequency: 10% of benign soft-tissue tumors

Schwannoma = Neurilemmoma

[neuron, *Greek* = nerve, sinew; eilema, *Greek* = covering, coil]
= usually solitary well-encapsulated slow-growing benign proliferation of Schwann cells in a collagenous matrix → eccentric displacement of nerve fibers
Schwann cell = cell that surrounds cranial, spinal, and peripheral nerves producing myelin sheath around axons thus providing mechanical protection and serving as a tract for nerve regeneration
◊ NOTE that myelin sheaths within brain substance are made by oligodendrocytes!
[Theodor Schwann (1810–1882), German physiologist at Belgian Universities Löwen/Leuven/Louvain and Lüttich/Liège]
◊ Nerve root NOT incorporated
Prevalence: 5% of all benign soft-tissue tumors
Age: 40–60 years; M=F
Uncommonly associated with: neurofibromatosis type 1
Path: › fusiform mass entering + exiting the nerve
› mass exophytic / eccentric to nerve of origin
› surrounded by a true capsule of epineurium
› nerve flattened against periphery of tumor

Histo: positive for S-100 protein + vimentin + CD56

(a) cellular component (**Antoni type A** tissue):
more organized area composed of densely packed cellular spindle cells with carrot-shaped or wavy nuclei arranged in short cordlike bundles / interlacing fascicles forming Verocay bodies (= palisading arrangements of elongated cells)
[Nils RE Antoni (1887-1968), professor of neurology at Karolinska Institutet in Stockholm, Sweden]
Location: posterior mediastinum, retroperitoneum, 25% of extremity lesions
√ hypointense on T2WI
√ smaller lesion with uptake of contrast material

(b) myxoid component (**Antoni type B** tissue):
less organized loosely arranged stellate cells in a mucoid stroma (= hypocellular myxoid tissue with high water content)
√ larger lesion hyperintense on T2WI

(c) ancient / cystic schwannoma (see below)

◊ Antoni type A & B often coexist in a single tumor!

- painless, fairly mobile mass
- ± motor and sensory nerve disturbance

Location: in typical peripheral nerve distribution (94%)

(a) intracranial: mostly from sensory nerves
@ Vestibulocochlear (CN VIII) nerve (most common) > trigeminal (V) cranial nerve (2nd most common) > VII
◊ Usually sporadic tumor, but 5–20% of patients with solitary intracranial schwannomas have NF2!

(b) extracranial:
@ Orbit (rare): branches of trigeminal (V) nerve (most common) > oculomotor > trochlear > abducens > parasympathetic > sympathetic fibers > ciliary ganglia
@ Neck, flexor surfaces of upper + lower extremities
Site: ulnar n., peroneal n.
◊ Usually solitary, but in 5% associated with neurofibromatosis type 1 (= > 2 schwannomas / one plexiform neurofibroma)
@ Spine
Location: spinal and sympathetic nerve roots; most common in lower thoracic and lumbar spine > presacral
Site: intradural (70–75%), extradural (15%), both intra- and extradural (15%), intramedullary (< 1%)
@ Posterior mediastinum + retroperitoneum (commonly paravertebral, adjacent to kidneys)
Frequency: 6% of retroperitoneal neoplasms
@ Abdominal wall

Size: 0.1–2.5 cm at time of surgery

Plain film:
√ fusiform mass delineated by surrounding fat
√ soft-tissue and osseous overgrowth
√ bone involvement + mineralization (osteoid / chondroid / amorphous) only in larger

lesions

US:

√ hypoechoic well-circumscribed mass ± cystic spaces

CT:

√ solitary fusiform well-encapsulated round tumor:

√ entering + exiting nerve (intradural / extradural)

√ dumbbell shape with extension into enlarged neural foramen (intra- and extradural)

√ low attenuation (as low as 5–25 HU) due to

(a) high lipid content of myelin from Schwann cells

(b) entrapped fat

(c) endoneural myxoid tissue with high water content (Antoni B areas)

√ well-defined hyperdense margins

√ marked uniform enhancement (most helpful for intradural lesions)

√ slow growth

√ homo- / heterogeneous (33%) enhancement: homogeneous (heterogeneous) if small (large)

√ muscle atrophy with striated increased fat content (in 23%)

√ punctate / mottled / curvilinear calcifications

MR:

√ well-delineated mass of hypo– to isointense signal relative to skeletal muscle on T1WI

√ moderate to markedly increased slightly heterogeneous signal intensity on T2WI:

√ T2 hypointense foci centrally ← dense cellularity / collagen / hemorrhage

√ markedly T2 hyperintense focal areas ← zones of fluid signal = cystic degeneration

√ frequently low-signal-intensity rim ← capsule

√ peritumoral edema in 33%

Cx: malignant transformation (rare)

Rx: excision (affected nerve usually separable from neoplasm after incision of epineurium)

DDx: may appear similar to meningioma

ANCIENT / CYSTIC SCHWANNOMA

= rare variant of schwannoma characterized by marked degenerative changes (old hemorrhage, calcification, cystic change) + decreased cellularity

Age: elderly

Histo: significantly decreased Antoni type A (hypercellular) area with Antoni type B areas occupying majority of tumor

Location: head & neck (orbit, intraventricular, olfactory groove, cavernous sinus), mediastinum, retroperitoneum, pelvis

√ heterogeneously enhancing mass with cystic areas ← myxoid + hemorrhagic change

√ fluid-fluid levels ← hemorrhage

√ ± calcifications / ossification

DDx: serous / mucinous cystadenocarcinoma, abscess, necrotic metastatic lymphadenopathy, arachnoid cyst, dermoid cyst

Ganglioneuroma

Origin: ganglion cell

Mean age: 7 years; M<F

Histo: mature gangliocytes and stroma

◊ Neuroblastoma + ganglioneuroblastoma may mature into ganglioneuroma!

Location: sympathetic ganglia (commonly in mediastinum and retroperitoneum)

• rarely symptoms of catecholamine excess (= vanillylmandelic acid / homovanillic acid)

Average size: 8 cm

Histo: stroma composed of Schwann cells + variable amounts of mature ganglion cells; stains with neuron-specific enolase, neurofilament protein, synaptophysin

US:

√ well-defined homogeneously hypoechoic mass

√ ± punctate echogenic foci ← calcifications

CT:

√ speckled / coarse calcifications within solid homogeneously hypoattenuating mass

√ mild to moderate homogeneous / heterogeneous enhancement

MR:

√ low T1 SI + heterogeneous high T2 signal intensity

√ heterogeneous progressive enhancement

NUC:

√ ± metaiodobenzylguanidine (MIBG) uptake

Rx: complete surgical resection

Neurofibroma

= benign slow-growing peripheral nerve sheath tumor → fusiform enlargement of nerve by separating nerve fibers

Prevalence: 5% of all benign soft-tissue tumors

Path: › round / ovoid mass arising from nerve fascicle

› centrally located mass intrinsic to host nerve

› often infiltrative + rarely encapsulated

› inseparable from parent nerve with tendency to insinuate between tissue planes

Histo: swirls of neuronal elements containing fibroblasts, Schwann cells, nerve fibers; spindle-shaped cells arranged in ribbons and cords among a background of loose myxoid stroma; tumor expresses S100

Typical Demographic and Radiologic Features of Nerve Sheath Tumors			
Feature	*Schwannoma*	*Neurofibroma*	*Malignant Nerve Sheath Tumor*
Demographics			
Prevalence	5% of all benign soft-tissue tumors	5% of all benign soft-tissue tumors	6% of all sarcomas
Age [years]	25–65	20–55	20–65
M÷F ratio	1.3÷1	1.2÷1	1÷1
Multiplicity	rarely multiple	typically solitary	solitary
Associated with NF1	in 18% (with multiple lesions)	in 63% (with multiple lesions)	~ 50%
Malignant change	extremely rare	extremely rare (except for NF1)	in < 5% of NF1
Location	lower extremity > torso > upper extremity > retroperitoneum	head & neck, lower extremity, torso > upper extremity	major nerve trunk of proximal extremity, torso
Radiology			
Mass vs. nerve	eccentric to but inseparable from nerve	central to nerve, intimately intertwined	central to nerve + infiltrating
Capsule	in 70%	in 30%	rare
Target sign	in 0–50%	in 50–70%	absent
Fascicular sign	25%	63%	occasional
Intratumoral cyst	common	rare	N/A
Margin	well-circumscribed	well-circumscribed	more often well-circumscribed than irregular
Central enhancement	3%	63%	

Types: localized (90%), diffuse, plexiform

Age: 20–30 years; M÷F = 1÷1

In 10% associated with: neurofibromatosis type 1 (HALLMARK lesion of NF1)

◊ Neurofibroma is the hallmark lesion of NF1!

◊ Schwannoma is more characteristic of NF2!

Location: skin, soft tissues, viscera; any level, but particularly cervical

(a) peripheral nerves

√ nonencapsulated well-circumscribed fusiform mass of peripheral nerves

(b) intradural extramedullary mass

◊ The spinal neurofibroma is rarely sporadic and usually a sign of type 1 neurofibromatosis!

√ well-defined mass of dumbbell configuration (= intradural + extradural component extending through neural foramen)

√ widening of intervertebral foramen + erosion of pedicles

√ scalloping of vertebral bodies

US:

√ nonspecific solid round / oval mass

√ well-defined homogeneously hypoechoic lesion

√ may demonstrate posterior acoustic enhancement

√ "target" appearance = more hypoechoic periphery (= homogeneous myxoid material) and hyperechoic central zone (= fibrocollagenous core)

CT:

√ well-defined round / oval homogeneously hypodense (CHARACTERISTIC) mass of 20–25 HU (= mucinous matrix + lipid-rich Schwann cells + adipocytes + entrapment of adjacent fat + cystic degeneration)

√ fusiform shape ← entering + exiting nerve = best imaging feature

CECT:
√ typically homogeneous enhancement (30–50 HU)
√ occasionally targetlike enhancement
MR:
√ homogeneous mass hypo- to isointense to cord / muscle on T1WI
√ T2 hyperintense with some heterogeneity
√ "target sign" = central T2-hypointense area (← central core of collagenous + fibrillary tissue) surrounded by high peripheral T2 signal (← fat and myxoid matrix / cystic degeneration, hemorrhage, calcifications)
√ "whorled" appearance with T2 hypointense curvilinear areas ←bundles of collagen and Schwann cells
CEMR:
√ ringlike enhancement of areas of low T2 signal (= myxoid stroma / complex fascicular arrangement)
√ ± muscular atrophy
Cx: malignant transformation (7–13% lifetime risk) → rapid growth, necrosis, hemorrhage, calcification, loss of "target sign", invasion of adjacent structures associated with edema
Rx: surgical resection with sacrifice of nerve (tumor not separable from normal nerve)
DDx: conjoined nerve root sleeve

AMPUTATION NEUROMA *(extremely rare)*
= TRAUMATIC NEUROMA
= nonneoplastic proliferation of the proximal end of a severed / partially transected injured nerve
Histo: nonencapsulated tangled multidirectional regenerating axonal masses + Schwann cells + endo- and perineural cells in dense collagenous matrix with surrounding fibroblasts
Types:
(a) spindle neuroma = internal focal fusiform swelling
Cause: chronic friction / irritation of nondisrupted injured but intact nerve trunk
(b) lateral / terminal neuroma
Cause: severe trauma with partial avulsion / disruption / total transection of nerve
Time of onset: 1–12 months after injury
• history of prior surgery
• Tinel sign = palpation / tapping on lesion reproduces pain
Location: lower extremity (after amputation), head and neck (after tooth extraction), radial nerve, brachial plexus
√ fusiform mass / focal enlargement with entering and exiting nerve (spindle type)
√ bulbous mass in continuity with normal nerve proximally (lateral / terminal type)
MR:
√ isointense to muscle on T1WI
√ heterogeneous intermediate to high SI on T2WI
√ "fascicular" sign = heterogeneous ringlike T2 pattern

Rx: acupuncture, cortisone injection, transcutaneous / direct nerve stimulation, physical therapy, surgical resection

LOCALIZED SOLITARY NEUROFIBROMA *(90%)*

Prevalence: 90% of all neurofibromas
Path: fusiform tumor, often remaining within epineurium as a true capsule
Histo: interlacing fascicles of wavy elongated cells containing abundant amounts of collagen
• painless fusiform mass
Location: affecting primarily superficial cutaneous nerves, occasionally deep-seated larger nerves
√ mostly solitary slow-growing lesion < 5 cm in size
◊ Solitary lesion associated with NF1 in ~ 12%!
US:
√ homo- or heterogeneous hypoechoic mass
MR:
√ "string" sign = visualization of entering + exiting nerve roots at both ends of vertically oriented fusiform mass
√ characteristically low signal intensity on T1WI
√ heterogeneously high on T2WI:
√ high SI on T2WI ← areas of cystic degeneration / myxoid matrix
√ areas of low T2 signal show enhancement ← collagen + fibrous tissue
DDx: schwannoma (encapsulated, difficult DDx)
@ Orbit
Location: superior extraconal orbit
• hypoglobus = downward displacement of globe

DIFFUSE NEUROFIBROMA

Age: children + young adults
Path: poorly defined lesion within subcutaneous fat, infiltrating along connective tissue septa, inseparable from normal nerve tissue
Histo: very uniform prominent fibrillary collagen
Location: most frequently in subcutaneous tissues of head + neck
• plaquelike elevation of skin with thickening of entire subcutis
◊ Isolated lesion (in 90%) unassociated with NF1!
√ always indistinct infiltrative margins ← subcutaneous spread along connective tissue septa
√ hypointense on T2WI

PLEXIFORM NEUROFIBROMA

= involvement of a long segment of nerve + branches extending into adjacent muscle, fat, subcutaneous tissue
Histo: heterogeneous mixture of Schwann cells, perineural cells and fibroblasts
Age: earlier age than other neurofibromas
Location: nerve plexus / multiple fascicles in a medium- to large-sized nerve like lumbosacral plexus; usually bilateral + symmetric

◊ In combination with multiple localized neurofibromas PATHOGNOMONIC of neurofibromatosis type 1

• reticulated linear branching pattern within subcutaneous tissue; often large disfiguring mass

√ serpentine "bag of worms" appearance = tortuous tangles / fusiform enlargement of a branching peripheral nerve

√ ropelike mass involving nonbranching nerve

√ infiltrative mass without respect for fascial boundaries (= transspatial involvement)

√ heterogeneous uptake of contrast material

US:

√ homo- or heterogeneously hypoechoic well-defined masses

CT:

√ iso- or hypoattenuating infiltrative mass ← lipid-rich Schwann cells + adipocytes + myxoid change

√ "targetlike" with benign neurogenic tumor (in 52%)

√ hypovascular / intensely enhancing soft-tissue mass

MR:

√ innumerable ringlike structures corresponding to cross sectioning of ropelike masses

√ T1 + T2 prolongation:

√ heterogeneous intensity on T1WI

√ marked T2-hyperintensity with multiple linear hypointense areas

√ diffuse intense contrast enhancement

√ typically "targetlike" pattern on T2WI:

√ peripheral high SI (← myxoid stroma)

√ central low SI (← fibrous-collagenous tissue)

@ Orbit (1st division of CN V in orbital apex):

Path: tumor may cross tissue planes + involve large portions of face

√ enlargement of affected orbit + neural foramina and erosion of orbital walls + skull base (esp. sphenoid)

Cx: potential for malignant transformation to malignant peripheral nerve sheath tumor (5%)

DDx: lymphatic malformation (fluid-fluid levels)

Malignant Peripheral Nerve Sheath Tumor

= (MPNST) MALIGNANT TUMOR OF NERVE SHEATH = NEUROFIBROSARCOMA = MALIGNANT SCHWANNOMA = NEUROGENIC (SPINDLE CELL) SARCOMA

Prevalence: 5–6–10% of all soft-tissue sarcomas

Lifetime risk in NF1: 4–5%

Age: 20–50 years (mean, 26 years); M÷F = 1÷1

Associated with: neurofibromatosis type 1 (in 10–50–70%), radiation therapy (in 11% of all malignant PNSTs after a latent period of 10–20 years)

Path: fusiform mass with areas of necrosis (in 60%)

Histo: tumor cells arranged in fascicles in a herring-bone pattern resembling fibrosarcoma;

additional heterotopic foci with mature cartilage and bone, rhabdomyosarcoma elements, glandular and epithelial components (in 10–15%)

- progressive enlargement
- pain, motor weakness, sensory deficits in extremity
- clinically silent tumors in abdomen + retroperitoneum

Location: major nerve trunks (commonly in proximal extremities + paraspinal region of torso (sciatic n., sacral plexus, brachial plexus); head & neck

Size: frequently > 5 cm in diameter

Metastases: lung, bone, pleura, retroperitoneum (60%); regional lymph nodes (9%)

√ fusiform mass with entering + exiting nerve typically larger than benign PNST

√ frequently indistinct irregular + infiltrative margins = aggressive biology

√ sudden increase in size of a previously stable neurofibroma

√ heterogeneous tumor with heterogeneous enhancement ← areas of hemorrhage + necrosis

√ invasion of adjacent organs → destruction of adjacent vertebrae / pelvic bones (NO difference to benign PNST)

NUC:

√ ^{67}Ga-citrate uptake in majority of MPNST (DDx: benign tumors show no uptake)

N.B.: only helpful in ^{67}Ga-positive tumors (← false negative rate unknown for MPNST)

Rx: resection + adjuvant chemo- and radiation therapy with local recurrence in 40%

Prognosis: highly aggressive tumor with a 44% 5-year survival rate

PRIMITIVE NEUROECTODERMAL TUMOR OF SPINAL CORD

Prevalence: 20 cases reported in literature

Location: spinal cord, intradural-extramedullary compartment, extradural compartment

Age: more common in adults than children; M÷F = 6÷4

Histo: small round blue cells with hyperchromatic nuclei + scanty cytoplasm, frequent mitoses

- weakness, paresthesia, gait disturbance, pain

Spread: throughout CSF space into cranium, lung, bone, lymph node

√ T1 and T2 prolongation

Prognosis: in > 50% death within 2 years

SACROCOCCYGEAL TERATOMA

Prevalence: 1÷40,000 live births

◊ Most common presacral germ cell tumor in children!

◊ Most common congenital solid tumor in newborn!

Pathogenesis:

(1) growth of residual primitive pluripotential cells derived from the primitive streak + knot (Hensen node) of very early embryonic development

(2) attempt at twinning

- increased prevalence of twins in family

Histo:

(1) **Mature teratoma** (55–75%) with elements from glia, bowel, pancreas, bronchial mucosa, skin appendages, striated + smooth muscle, bowel loops, bone components (metacarpal bones + digits), well-formed teeth, choroid plexus structures (→ production

of CSF)

◊ MATURE TERATOMA = benign tumor composed of tissues foreign to anatomic site in which they arise, usually contains tissue from at least 2 germ cell layers

(2) **Immature teratoma** (11–28%): admixed with primitive neuroepithelial / renal tissue

◊ IMMATURE TERATOMA = benign teratoma with embryonic elements

(3) **Malignant germ cell tumor**

(a) mixed malignant teratoma (7–17%): elements of endodermal sinus tumor (= yolk sac tumor) + either form of teratoma

(b) pure endodermal sinus tumor (rare)

(c) seminoma (dysgerminoma), embryonal carcinoma, choriocarcinoma (extremely rare)

Metastases to: lung, bone, lymph nodes (inguinal, retroperitoneal), liver, brain

Age: 50–70% during first few days of life; 80% by 6 months of age; < 10% > 2 years of age; rare in adulthood (only 100 cases reported); M÷F = 1÷4

◊ Older age means increased prevalence of malignancy (in 50–90% > 2–4 months of age)!

Classification (Altman):

Type I predominantly external lesion covered by skin with only minimal presacral component (47%)

Type II predominantly external tumor with significant presacral component (35%)

Type III predominantly sacral / abdominal component + external extension (8%)

Type IV presacral tumor with no external component (10%)

◊ Internal component suggests malignant transformation!

Associated with: other congenital anomalies (in 18%):

(1) Musculoskeletal (5–16%): spinal dysraphism, sacral agenesis, hip dislocation, clubbed feet

(2) Renal anomalies: hydronephrosis, renal cystic dysplasia, Potter syndrome, urethral atresia, urinary ascites

(3) GI tract: imperforate anus, rectal atresia / stenosis, gastroschisis

(4) Hydrocolpos, undescended testes

(5) Fetal hydrops ← high-output cardiac failure

(6) Placentomegaly ← fetal hydrops

(7) Curvilinear sacrococcygeal defect (rare autosomal dominant inheritance with equal sex incidence, low malignant potential, absence of calcifications) + anorectal stenosis / atresia, vesicoureteral reflux

- ↑ AFP elevated with mixed malignant teratoma + endodermal sinus tumor (CAVE: fetal + newborn serum contains AFP, which does not reach adult levels until about 8 months of age)
- premature labor ← polyhydramnios + large mass
- uterus large for dates
- radicular pain, constipation, urinary frequency / incontinence
- asymptomatic / mass + pressure symptoms like constipation
- recurrent pilonidal infections

Average size: 8 (range, 1–30) cm in diameter

Plain film:

√ amorphous, punctate, spiculated calcifications, possibly resembling bone (36–50%); suggestive of benign tumor

√ soft-tissue mass in pelvis protruding anteriorly + inferiorly

BE:

√ anterosuperior displacement of rectum

√ luminal constriction

IVP:

√ displacement of bladder anterosuperiorly

√ development of bladder neck obstruction

Myelography:

√ intraspinal component may be present

Angio:

√ neovascularity (arterial supply by middle + lateral sacral + gluteal branches of internal iliac artery, branches of profunda femoris artery)

√ enlargement of feeding vessels

√ arterial encasement

√ arteriovenous shunting

√ early venous filling with serpiginous dilated tumor veins

US / CT:

√ solid (25%) / mixed (60%) / cystic (15%) sacral mass

√ polyhydramnios (⅔)

√ poor prognostic factors : oligohydramnios, fetal hydrops with ascites, fetal hydronephrosis, pleural effusions, skin edema, placentomegaly

OB-US:

Age: as early as 14 weeks GA

√ increased size of uterus ← mass / polyhydramnios

√ rapid growth reaching enormous volumes:

√ assessment of tumor volume, amniotic fluid index, placental thickness, diameter of IVC, cardiothoracic ratio, pulmonary hypoplasia

√ oligohydramnios ← obstruction of urinary tract

√ arteriovenous shunting (Doppler US)

Cx (in 18%): preterm labor, preeclampsia, HELLP syndrome, premature delivery, dystocia, intratumoral hemorrhage, tumor avulsion → fetal exsanguination

Rx: US-guided drainage of cystic component, fetal surgery + Cesarean section for solid tumor

MR (preferred modality for initial Dx + surveillance):

√ lobulated + sharply demarcated tumor extremely heterogeneous on T1WI ← high signal from fat, intermediate signal from soft tissue, signal void from Ca2+

√ best modality to detect spinal canal invasion

Prognosis: likely benign: predominantly fatty / cystic tumor

likely malignant: hemorrhagic / necrotic tumor, sacral destruction, patient > 2 months of age

Mortality: 5% for infant; 50% for fetus (worse < 30 weeks GA)

Cx: (1) Dystocia in 6–13%

(2) Massive intratumoral hemorrhage

(3) Fetal death in utero / stillbirth

Rx: 1. Complete tumor resection + coccygectomy + reconstruction of pelvic floor: up to 37% recurrence rate, esp. without coccygectomy
2. Multiagent chemotherapy (in malignancy) with long-term survival rate of 50%

DDx: (1) Myelomeningocele (superior to sacrococcygeal region, not septated, axial bone changes)
(2) Rectal duplication, anterior meningocele (purely cystic)
(3) Hemangioma, lymphangioma, lipomeningocele, lipoma, epidermal cyst, chordoma, sarcoma, ependymoma, neuroblastoma

SACROILIITIS

Radiography:

◊ Conventional radiographic diagnosis insensitive
(= delay in diagnosis by 8–11 years)

Benefit: helpful if positive

Disadvantage: low intra- and interobserver agreement

√ uniform narrowing of joint space
√ erosions
√ intraarticular ankylosis
√ osteophytes
√ pneumocysts
√ articular "vacuum" sign

Grading: 0 normal
1 incipient sclerosis + ↓ focal joint width
2 minimally abnormal with loss of definition of articular margins, subchondral osteoporosis, areas of reactive sclerosis
3 unequivocally abnormal with subchondral sclerosis of sacral + iliac articular margins, erosions, reduced width, widening of joint space, incipient ankylosis
4 complete ankylosis + residual sclerosis

CT: (more sensitive than conventional radiography)

Grading: IA SI joint space > 4 mm
IB SI joint space < 2 mm
IIA joint contour irregularities
IIB erosions on iliac > sacral side
IIIA significant subchondral sclerosis
IIIB spur formation
IVA transarticular bone bridge
IVB total ankylosis

MR: (cardinal tool + biomarker for disease activity)

√ bone marrow edema (first to appear)
√ subchondral sclerosis = low SI bands extending > 5 mm from joint space (DDx: physiologic sclerosis)
√ erosions = T1-hypointense + T2-hyperintense bone defect at margins of cartilaginous

compartment
√ periarticular fat deposits (= previous inflammation)
√ ankylosis (= fusion of bone buds)

CEMR:
√ vasoactive bone marrow edema
√ synovitis = enhancement of synovium
√ capsulitis = enhancing anterior + posterior joint capsule
√ enthesitis = enhancing ligamentous attachments

DDx: (1) Osteoarthritis (anterior osteophytes)
(2) Septic sacroiliitis (joint effusion, bone marrow edema, intramuscular abscess)
(3) Sacral insufficiency fracture
(4) Osteitis condensans ilii (middle-aged woman, mainly iliac bone sclerosis, normal joint space)
(5) Bone tumor

SCHEUERMANN DISEASE

= SPINAL OSTEOCHONDROSIS = KYPHOSIS DORSALIS JUVENILIS = VERTEBRAL EPIPHYSITIS

[Holger Werfel Scheuermann(1877–1960), Danish orthopedic surgeon and radiologist, head physician to the navy]

= disorder consisting of vertebral wedging + endplate irregularity + narrowing of intervertebral disk space

Prevalence: in 31% (21%) of males (females) with back pain

Age: onset at puberty

Location: lower thoracic / upper lumbar vertebrae; in mild cases limited to 3–4 vertebral bodies

√ anterior wedging of vertebral body of > 5°
√ increased anteroposterior diameter of vertebral body
√ slight narrowing of disk space
√ kyphosis of > 40°/ loss of lordosis; scoliosis
√ Schmorl nodes = intravertebral herniation of nucleus pulposus = depression in contour of endplate in posterior half of vertebral body; found in up to 30% of adolescents + young adults
√ flattened area in superior surface of epiphyseal ring anteriorly = avulsion fracture of ring apophysis due to migration of nucleus pulposus through weak point between ring apophysis + vertebral endplate (fusion of ring apophysis usually occurs at about 18 years of age)
√ detached epiphyseal ring anteriorly

DDx: (1) Developmental notching of anterior vertebrae (NO wedging or Schmorl nodes)
(2) Osteochondrodystrophy (earlier in life, extremities show same changes)

SCHMORL NODE

= CARTILAGINOUS NODE

= superior / inferior intravertebral herniation / prolapse of disk material through weakened area of vertebral endplate

[Christian Georg Schmorl (1861–1932), pathologist at city hospital in Dresden, Germany]

Pathogenesis: disruption of cartilaginous plate of vertebral body left during regression of chorda dorsalis, ossification gaps, previous vascular channels

Cause:

(a) osseous: osteoporosis, osteomalacia, Paget disease, hyperparathyroidism, infection, neoplasm

(b) cartilaginous: intervertebral osteochondrosis, disk infection, juvenile kyphosis

Location: predominantly in thoracolumbar spine

• acute Schmorl nodes may be painful

√ concave defects at upper and lower vertebral endplates with sharp margins

MR:

√ node of similar signal intensity as disk

√ low signal intensity of rim

√ associated with narrowed disk space

DDx: inflammatory disease

mnemonic of DDx: SHOOT

Scheuermann disease

Hyperparathyroidism

Osteoporosis

Osteomalacia

Trauma

SCOLIOSIS

= presence of ≥ 1 lateral curves of the vertebral column in the coronal plane with a Cobb angle of ≥ 10°

◊ A curve of < 10° represents *spinal asymmetry* and NOT scoliosis, is asymptomatic and nonprogressive!

Mechanism: rotation of vertebrae in axial plane → discrepant axial loading between ventral + dorsal portions

Etiology:

A. Primary = idiopathic (80%)

1. Infantile (0–3 yrs.): M÷F=3.5÷1; levoscoliosis; self-limited
2. Juvenile (4–10 yrs.): progression in 70–95%
3. Adolescent (11–18 yrs.): M÷F=1÷4; dextroscoliosis; progression in 5%

B. Secondary

(a) congenital (10%) with progression in 75%

1. Osteogenic: wedge-shaped vertebra, hemivertebra, fused vertebra, unilateral bar
2. Neuropathic: tethered cord, syringomyelia, Chiari malformation, (myelo)meningocele, diastematomyelia

(b) developmental

1. Skeletal dysplasia: achondroplasia
2. Skeletal dysostosis: neurofibromatosis, osteogenesis imperfecta
3. Degenerative scoliosis
4. Traumatic scoliosis

(c) neuromuscular

1. Neuropathic (acquired): cerebral palsy, spinocerebellar degeneration, poliomyelitis
2. Myopathic: muscular dystrophy

(d) tumor-associated

1. Osseous: osteoid osteoma, osteoblastoma
2. Extraosseous: extramedullary (eg, neurofibroma) / intramedullary (eg, astrocytoma) tumor

A focal short-segment scoliosis or painful scoliosis should raise suspicion for an underlying lesion.

Nomenclature:

apex = vertebra / disk with the greatest rotation / farthest deviation from center of vertebral column

end vertebra = vertebra with maximum tilt toward apex of curvature; used to measure Cobb angle

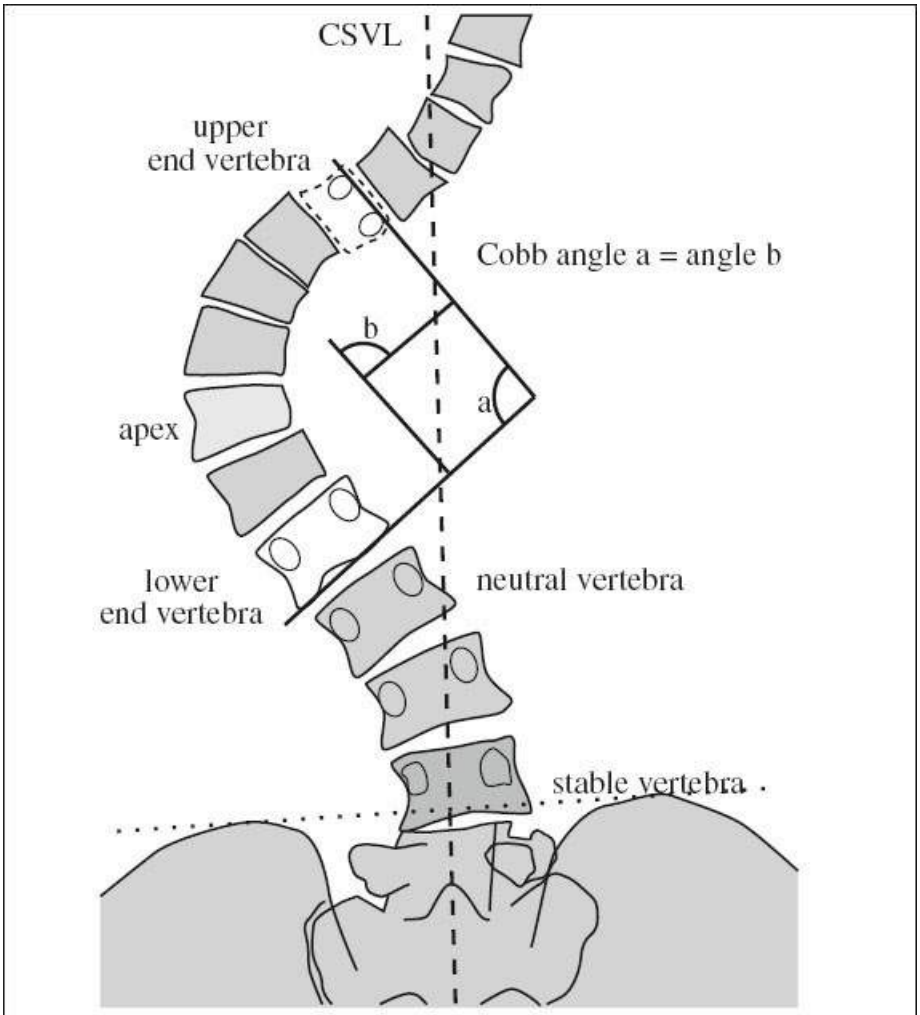
neutral vertebra = vertebra without rotation (= symmetric pedicles) on standing frontal radiograph

stable vertebra = vertebra farthest cephalad roughly bisected by CSVL below end vertebra of distal curve

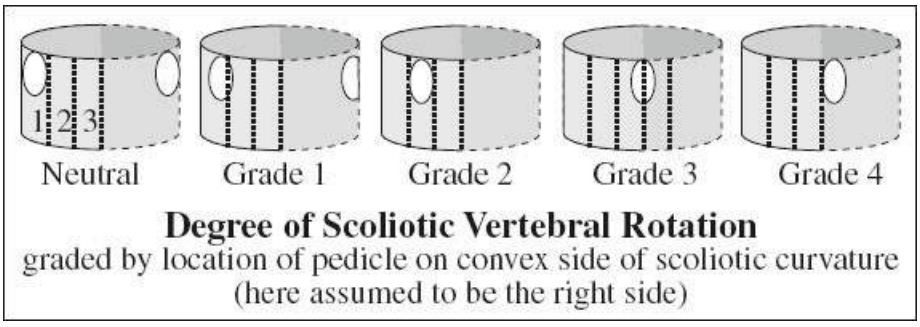
CSVL = central sacral vertical line = line drawn perpendicular to tangential line across iliac crests bisecting sacrum

Primary and Secondary Curves

Major curve = primary structural curve with a Cobb angle of > 25° on ipsilateral bending; largest abnormal curve that develops first; not correctable with ipsilateral bending



Significant Vertebrae in Scoliosis with Cobb Angle
if endplates are not reliably visualized
the borders of the pedicles are used to draw the Cobb angle a



Degree of Scoliotic Vertebral Rotation
graded by location of pedicle on convex side of scoliotic curvature
(here assumed to be the right side)

Minor curve = secondary nonstructural compensatory smaller curve that develops later by repositioning the head and trunk over pelvis to maintain balance; correctable with ipsilateral bending

Vertebral Balance

Plumb line = vertical line drawn downward from center of C7 parallel to lateral edge of radiograph

Coronal imbalance = distance between CSVL + plumb line > 2 cm on frontal x-ray; plumb line to right (left) of CSVL = positive (negative) imbalance

Sagittal imbalance = distance between posterosuperior aspect of S1 + plumb line > 2 cm on lateral x-ray; plumb line anterior (posterior) to S1 = positive (negative) imbalance

Vertebral Rotation (Nash-Moe method)

Cobb angle: angle formed by intersection of 2 lines parallel to endplates of superior + inferior end vertebrae or intersection of the 2 lines drawn perpendicular to the endplate lines

Accuracy: ± 5°

Progressive curve: angle increase of ≥ 5°

Limitation: 2-D radiograph describing a 3D deformity with vertebral rotation

Pitfalls: diurnal variation of 5° (worse in afternoon); 2–7° measurement error; 5–10° interobserver error; actual angle may be 20% greater than plotted depending on accuracy + reproducibility of patient positioning on frontal x-ray

Progression: parallels spinal growth; after skeletal maturity at < 30° no progression, at 30–50° increase by 10–15° per year, at 50–75° increase by 1° per year

Prognosis: with Cobb angle > 50° higher rate of back pain + mortality associated with cardiopulmonary Cx

SERONEGATIVE SPONDYLOARTHRITIS

= SPONDYLOARTHROPATHY

= group of chronic inflammatory rheumatic diseases not associated with rheumatoid factor / rheumatoid nodules

Prevalence: 0.5–1.9%

Subgroups:

1. Ankylosing spondylitis 0.86%
2. Undifferentiated spondyloarthritis 0.67%
   √ NO definite signs of sacroiliitis
3. Psoriatic arthritis 0.29%
   √ parasyndesmophytes
   • psoriatic skin lesions
4. Reactive arthritis (eg, Reiter disease)
   • urogenital tract infection
5. Arthritis associated with inflammatory bowel disease (eg, Crohn disease, ulcerative colitis)

• pain and stiffness; seronegative for rheumatoid factor
• often associated with human lymphocyte antigen (HLA)–B27

Stage of Spondyloarthropathy by MR characteristics			
Stage	*Vertebra*	*Disk*	*Interpretation*
0	↔ T1 + ↓ T2	↓ T1+ ↑ T2	normal
1	↓ T1 + ↑ T2	↓ T1+ ↑ T2	florid inflammation
2	↑ T1 + ↓ T2	↓ T1 + ↑ T2	fatty marrow degeneration
3	↔ T1 + ↓ T2	↔ T1 + ↓ T2	ankylosis

◊ 20-fold greater risk to develop spondyloarthritis in patients with positive HLA–B27 antigen

Location: predominantly axial skeleton (sacroiliac joints frequently first involved)

Site: vertebra, intervertebral disk, synovial joints of spine, tendon, ligamentous attachment (enthesis)

√ sacroiliitis

Extraaxial involvement:

• uveitis

√ calcaneal enthesitis

√ peripheral arthritis

Prognosis: syndesmophytes + ankylosing spondylitis with longstanding disease

Rx: NSAID, TNF (tumor necrosis factor)–α inhibitors, intensive physical therapy

DDx: rheumatoid arthritis, degenerative disk disease, diffuse idiopathic skeletal hyperostosis, pyogenic spondylodiskitis, vertebral fracture, Paget disease

Spondylitis

= ROMANUS LESION (ENTHESITIS)

= inflammation of attachment of annulus fibrosus to vertebral endplate (rim of endplate)

Site: edge of endplates

› **anterior spondylitis** @ anterior endplate

› **posterior spondylitis** @ posterior endplate

› **marginal spondylitis** = both

√ irregularities / erosions involving edges of vertebral endplates (epiphyseal ring)

√ "shiny corners" = sclerotic changes of edges of vertebral endplates during chronic phase

MR:

√ hypointense on T1WI + hyperintense on STIR (← bone marrow edema / osteitis during acute phase)

√ hyperintense on T1WI (← postinflammatory fatty bone marrow degeneration during chronic phase)

Spondylodiskitis

= ANDERSON LESION = RHEUMATIC SPONDYLODISKITIS

= noninfectious inflammation of intervertebral disk by spondyloarthritis

Prevalence: 8% of radiographs in ankylosing spondylitis

Site: diskovertebral unit (= intervertebral disk and adjacent halves of superior and inferior vertebrae)

√ irregularities / erosions of central portion of vertebral endplates (during late phase)

MR:

√ T1-hypointense + STIR-hyperintense disk signals involving one / both halves of adjacent vertebral bodies (in acute edematous phase)

Dialysis-associated Spondyloarthropathy

= spondyloarthropathy in patients on long-term hemodialysis of > 3 years duration
Frequency: 20% of patients on long-term hemodialysis
Cause: amyloid (β2-microglobulin) deposition in synovium and intervertebral disks
Location: lower cervical spine > craniocervical junction > thoracolumbar spine
Associated with: amyloid arthropathy of hands + wrists
Site: usually multiple levels of involvement
• frequently asymptomatic / mild pain + stiffness
• radiculopathy + myelopathy are unusual
• normal ESR, normal WBC count
• elevated levels of β2-microglobulin
√ intervertebral disk space loss ± disc vacuum phenomenon
√ extensive marginated erosions of vertebral endplates and facet joints + cyst formation
√ NO / minimal osteophytosis
√ frequently subluxation + spondylolisthesis
MR:
√ mostly hypointense disk space on T2WI
DDx: (1) Infectious spondylodiskitis (T2-hyperintense disk space, fever)
(2) Ankylosing spondylitis
(3) Degenerative disk disease (no endplate erosions, marked osteophytosis)

SINUS PERICRANII

= venous anomaly (? subperiosteal venous angioma)
= collection of abnormal nonmuscular scalp veins adherent to skull (= dilated subperiosteal epicranial venous structure) connected to intracranial venous system (sinus / cortical vein) by anomalous diploic veins through a well-defined calvarial defect
Etiology: congenital; ? traumatic
Age: childhood; M = F
• focal soft painless scalp mass that reduces under compression
• headache, scalp pressure, pain (rare)
Location: frontal + parietal bone
√ calvarial thinning + defect
√ mild ↓ / mild ↑ / no change in size over time
CT:
√ sessile sharply marginated homogeneous densely enhancing mass adjacent to outer table of skull
√ transcalvarial perforating channels
√ connection to adjacent dural venous sinus
√ possible drainage into extracranial scalp veins
Angio:
√ extracalvarial sinus may not opacify ← slow flow
Rx: ligation of communicating veins + removal of sinus; endovascular embolization

DDx: cephalocele, hemangioma, dermoid cyst, calvarial metastasis

SPINAL STENOSIS

= encroachment on central spinal canal, lateral recess, or neuroforamen by bone / soft tissue

Cause:

A. Congenitally short pedicles
   (a) idiopathic
   (b) developmental: Down syndrome, achondroplasia, hypochondroplasia, Morquio disease

B. Acquired:
   1. Hypertrophy of ligamentum flavum = buckling of ligament ← joint slippage in facet joint osteoarthritis (most common)
   2. Facet joint hypertrophy
   3. Degenerated bulging / herniated disk
   4. Spondylosis, spondylolisthesis
   5. Surgical fusion
   6. Fracture
   7. Ossification of posterior longitudinal ligament
   8. Paget disease
   9. Epidural lipomatosis

Age: middle-aged for congenital cause / elderly during 6th–8th decade for acquired cause; M > F

Location: generally involves lumbar spinal canal; cervical spinal canal may be similarly affected

√ obliteration of epidural fat
√ interpedicular distance < 25 mm
◊ Measurements are NOT a valid indicator of disease!

Cervical Spinal Stenosis

Location: multiple levels in mid- and lower cervical spine
√ sagittal diameter of cervical spinal canal < 13 mm
√ hourglass narrowing of thecal sac with scalloping of the dorsal + ventral margins of the cord
√ greater degree of stenosis in hyperextended position ← buckling of ligamenta flava:
  √ ± spinal block in hyperextended neck on AP views

Lumbar Spinal Stenosis

Cause:

1. Achondroplasia:
   √ narrowed interpediculate distance progressive toward lumbar spine
2. Paget disease: bony overgrowth
3. Spondylolisthesis
4. Operative posterior spinal fusion
5. Herniated disk
6. Metastasis to vertebrae

7. Developmental / congenital

Age: presentation between 30 and 50 years of age

- often asymptomatic until middle age (until development of secondary degenerative changes); low back pain
- "neurogenic / spinal claudication" = bilateral lower extremity pain, numbness, weakness worse during walking / standing + relieved in supine position and flexion
- cauda equina syndrome: paraparesis, incontinence, sensory findings in saddlelike pattern, areflexia

√ sagittal diameter of spinal canal < 16 mm (normal range in adults: 15–23 mm)
√ diminished amount of CSF + crowding of nerve roots
√ unusual small quantity of contrast material to fill thecal sac
√ constricted anteroposterior + interpediculate diameter of spinal canal
√ dural sac area < 100 mm^2
√ hourglass configuration of thecal sac (SAG view)
√ triangular / trefoil shape of thecal sac (AXIAL view)
√ redundant serpiginous nerve roots above + below stenosis
√ thickened articular process, pedicles, laminae, ligaments
√ bulging disks

SPLIT NOTOCHORD SYNDROME

= spectrum of anomalies with persistent connection between gut + dorsal ectoderm

Etiology: failure of complete separation of ectoderm from endoderm with subsequent splitting of notochord and mesoderm around the adhesion about 3rd week of EGA

√ fistula / isolated diverticula / duplication / cyst / fibrous cord / sinus along the tract

Types:

1. **Dorsal enteric fistula**
   = fistula between intestinal cavity + dorsal midline skin traversing prevertebral soft tissue, vertebral body, spinal canal, posterior elements of spine
   - bowel ostium / exposed pad of mucous membrane in dorsal midline in newborn
   - opening passes meconium + feces

   √ dorsal bowel hernia into a skin- / membrane-covered dorsal sac after passing through a combined anterior + posterior spina bifida
2. **Dorsal enteric sinus**
   = blind remnant of posterior part of tract with midline opening to dorsal external skin surface
3. **Dorsal enteric enterogenous cyst**
   = prevertebral / postvertebral / intraspinal enteric-lined cyst derived from intermediate part of tract

   Intraspinal enteric cyst

   Age at presentation: 20–40 years
   - intermittent local / radicular pain worsened by elevation of intraspinal pressure

   Location: intraspinal in lower cervical / upper thoracic region

   √ enlarged spinal canal at site of cyst
   √ hemivertebrae, segmentation defect, partial fusion, scoliosis in region of cyst

4. **Dorsal enteric diverticulum**
   = tubular / spherical diverticulum arising from dorsal mesenteric border of bowel as a persistent portion of tract between gut + vertebral column
5. **Dorsal enteric cyst**
   = involution of portion of diverticulum near gut
   • mass in abdomen / mediastinum ← bowel rotation

SPONDYLOLISTHESIS

= anterior displacement of one vertebra over another

Direction: anterolisthesis, retrolisthesis, lateral translation

Prevalence: 4% of general population

Causes (Newman classification):

I congenital / dysplastic
II isthmic / spondylytic
III degenerative (disk disease)
IV traumatic (fracture)
V pathologic (bone tumor)
VI postsurgical (removal of > 50% of facet joint)

Grades I–IV (Meyerding method): each grade equals ¼ anterior subluxation of upper on lower vertebral body

Isthmic Spondylolisthesis = open-arch type

= pars interarticularis defect between superior + inferior articulating processes as weakest portion of spinal unit → separation of anterior part (vertebral body, pedicles, transverse processes, superior articular facet) slipping forward from posterior part (inferior facet, laminae, dorsal spinous process)

Cause: usually bilateral spondylolysis

Age: often < 45 years

Location: L5-S1 (most common) or L4-5

• symptomatic if intervertebral disk + posterosuperior aspect of vertebral body encroaches on superior portion of neuroforamen causing nerve root compression:
  • backache ± leg pain; sciatica ± backache

√ elongation of spinal canal in anteroposterior diameter
√ bilobed configuration of neuroforamen
√ ratio of maximum anteroposterior diameter of spinal canal at any level divided by diameter at L1 > 1.25
√ inverted "Napoleon's hat" sign (on AP view) = severely subluxed L5 body (= dome of hat) that projects end-on overlapping the sacrum with transverse processes forming the hat's tapered brim

Napoleon's Hat Sign

Degenerative Spondylolisthesis = closed-arch type

= PSEUDOSPONDYLOLISTHESIS

Cause: degenerative / inflammatory joint disease (eg, rheumatoid arthritis)

Pathophysiology: excess motion of facet joints allowing forward / posterior movement

Age: usually > 60 years; M < F (at L4-5)

• commonly symptomatic ← spinal stenosis + narrowing of neuroforamen

√ narrowing of spinal canal

√ hypertrophy of facet joints

√ ratio of maximum anteroposterior diameter of spinal canal at any level divided by diameter at L1 < 1.25

SPONDYLOLYSIS

= break in the interarticular portion of a vertebra

pars interarticularis = junction of vertebral pedicle, lamina, superior + inferior articular facets

> Pars interarticularis abnormalities are a spectrum of nonunion, spondylolysis and stress without spondylolysis.

Prevalence: 3–7% of population; in 30–70% other family members afflicted

Age: early childhood; M÷F = 3÷1; Whites÷Blacks = 3÷1

Cause:

A. Chronic low-grade trauma: stress (fatigue) fracture of pars interarticularis from repetitive minor trauma (in most); during teenage growth spurt; common in gymnastics (30%), ballet, scrubbing floors, lifting heavy objects, diving, contact sports (college football player (20%), wrestler (28%), soccer, hockey, lacrosse)

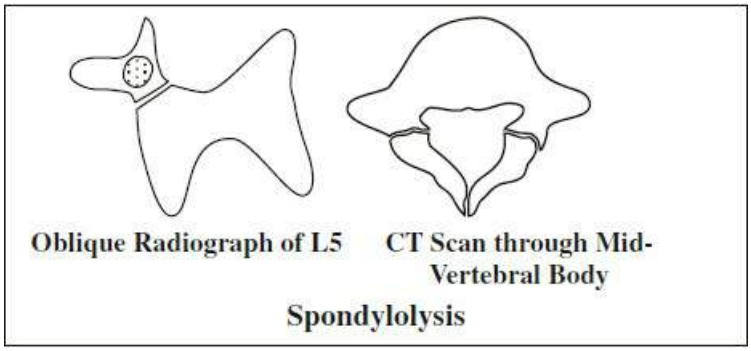
B. Developmental deficiency:
   (a) hereditary hypoplasia of pars → insufficiency fracture; eg, pars defect in 34% of Eskimos
   (b) congenital malformation: frequently associated with spina bifida occulta of S1, dorsally wedge-shaped body of L5, hypoplasia of L5; HOWEVER: no pars defects have been identified in fetal cadavers

C. Secondary spondylolysis: neoplasm, osteomyelitis, Paget disease, osteomalacia, osteogenesis imperfecta

• activity-related low back pain + hamstring tightness in 50% (if associated with degenerative

disk disease / spondylolisthesis)

Location: L5 (67–95%); L4 (15–30%); L3 (1–2%); in 75% bilateral



Plain film (57% PPV):

√ radiolucent band ± sclerotic margin resembling the collar of a "Scottish dog" (on oblique view)

√ may be associated with spondylolisthesis

√ subluxation of involved vertebra (if pars defect bilateral)

√ **Wilkinson syndrome** = reactive sclerosis + bony hypertrophy of contralateral pedicle + lamina ← stress changes related to weakening of neural arch in unilateral pars defect

CT:

√ pars defect located 10–15 mm above disk space

√ inner contour of spinal canal interrupted

NUC bone scintigraphy:

Sensitivity: SPECT/CT > SPECT > planar imaging

Spectrum: uni- / bilateral stress or break

√ stress (50%) = uni- / bilateral focal radiotracer uptake of pars interarticularis WITHOUT break BUT osteosclerosis

√ active spondylysis = uni- / bilateral focal radiotracer uptake + osteolysis (CLASSIC)

√ nonunion (pseudarthrosis) = NO radiotracer uptake + break in pars interarticularis and sclerosis along margins of defect

Cx: (1) Spondylolisthesis (uncommon; most likely before 16 years of age)

(2) Vertebral pedicle fracture (rare; typically unilateral fracture with contralateral spondylolysis; best seen on SAG reformatted CT)

Spondylolysis of Cervical Spine

= progressive degeneration of intervertebral disks leading to proliferative changes of bone + meninges; more common than disk herniation as a cause for cervical radiculopathy

Prevalence: 5–10% at age 20–30; > 50% at age 45; > 90% by age 60

- spastic gait disorder
- neck pain

Location: C4-5, C5-6, C6-7 (greater normal cervical motion at these levels)

Sequelae:

(a) direct compression of spinal cord

(b) neural foraminal stenosis

(c) ischemia due to vascular compromise
(d) repeated trauma from normal flexion / extension

DDx of myelopathy:
rheumatoid arthritis, congenital anomalies of craniocervical junction, intradural extramedullary tumor, spine metastases, cervical spinal cord tumor, arteriovenous malformation, amyotrophic lateral sclerosis, multiple sclerosis, neurosyphilis

SYRINGOHYDROMYELIA

= SYRINGOMYELIA = SYRINX (used in a general manner reflecting difficulty in classification)
= longitudinally oriented CSF-filled cavities + gliosis within spinal cord frequently involving both parenchyma + central canal
Age: primarily childhood / early adult life
Cause: Chiari I malformation (41%), trauma (28%), neoplasm (15%), idiopathic (15%)
• loss of sensation to pain + temperature ← interruption of spinothalamic tracts
• trophic changes = (skin lesions; Charcot joints in 25% affecting shoulder, elbow, wrist)
• muscle weakness ← anterior horn cell involvement
• spasticity, hyperreflexia ← upper motor neuron involvement
• abnormal plantar reflexes ← pyramidal tract involvement
Location: predominantly lower end of cervical cord; extension into brainstem (= syringobulbia)

CT:
√ distinct area of decreased attenuation in spinal cord (100%)
√ swollen / normal-sized / atrophic cord
√ NO contrast enhancement
√ change in shape + size of cord with change in position (rare)
√ flattened vertebral border (rare) with increased transverse diameter of cord
√ filling of syringohydromyelia with intrathecal contrast
(a) <u>early</u> filling ← direct communication with subarachnoid space
(b) <u>late</u> filling after 4–8 hours (80–90%) ← permeation of contrast material

Myelography:
√ enlarged cord (DDx: intramedullary tumor)
√ "collapsing cord" sign = collapsing of cord with gas myelography as fluid content moves caudad in the erect position (rare)

MR:
√ cord enlargement
√ cystic area → low SI on T1WI + increased SI on T2WI
√ presence of CSF flow-void (= low SI on T2WI) within cavity ← pulsations
√ beaded cavity ← multiple incomplete septations
DDx: **pseudosyrinx** = truncation artifact consisting of linear abnormal signal within cord on sagittal images in phase-encoding direction ← limited number of frequencies for fast Fourier transform

Hydromyelia

= PRIMARY / CONGENITAL SYRINGOHYDROMYELIA

= dilatation of persistent central canal of spinal cord (normally obliterated in 70–80%) which communicates with 4th ventricle (= **communicating syringomyelia**)

Histo: lined by ependymal tissue

Associated with:

(1) Chiari malformation in 20–70%
  √ metameric haustrations within syrinx on sagittal T1WI
(2) Spinal dysraphism
(3) Myelocele
(4) Dandy-Walker syndrome
(5) Diastematomyelia
(6) Scoliosis in 48–87%
(7) Klippel-Feil syndrome
(8) Spinal segmentation defects
(9) Tethered cord (in up to 25%)

DDx: transient dilatation of the central canal (transient finding in newborns during the first weeks in life)

Syringomyelia

= ACQUIRED / SECONDARY SYRINGOHYDROMYELIA

= any cavity within substance of spinal cord that may communicate with the central canal, usually extending over several vertebral segments

Histo: not lined by ependymal tissue

Pathophysiology: interrupted flow of CSF through the perivascular spaces of cord between subarachnoid space + central canal

Cause:

1. **Posttraumatic syringomyelia**
   Prevalence: in 3.2% after spinal cord injury
   Location: 68% in thoracic cord
   Average length: 6.0 (range, 0.5–40.0) cm
   √ syrinx may be septated (parallel areas of cavitation) on transverse T1WI
   √ loss of sharp cord-CSF interface (obliteration of arachnoid space by adhesions)
   √ in 44% associated with arachnoid loculations (extra-medullary arachnoid cysts) at upper aspect of syrinx
2. **Postinflammatory syringomyelia**
   subarachnoid hemorrhage, arachnoid adhesions, S/P surgery, infection (tuberculosis, syphilis)
3. **Tumor-associated syringomyelia** = peritumoral cyst of spinal cord tumor / herniated disk ← circulatory disturbance + thoracic spinal cord atrophy
   Prevalence: in 60% of all intramedullary tumors
   √ polar / satellite cysts = rostral / caudal cysts ← reactive dilatation of central canal
   ◊ A higher location within spinal canal raises the likelihood of syrinx development
4. Vascular insufficiency

Reactive Cyst

= POSTTRAUMATIC SPINAL CORD CYST

= CSF-filled cyst adjacent to level of trauma; usually single (75%)
• late deterioration in patients with spinal cord injury (NOT related to severity of original injury)
Rx: shunting leads to clinical improvement

TERATOMA OF SPINE

= neoplasm containing tissue belonging to all 3 germinal layers at sites where these tissues do not normally occur
Prevalence: 0.15% (excluding sacrococcygeal teratoma)
Age: all ages; M÷F = 1÷1
Path: solid thin- / thick-walled partially / wholly cystic space with clear / milky / dark cyst fluid; uni- / multilocular; presence of bone / cartilage
Location: intra- / extramedullary
√ complete block at myelography
√ syringomyelia above level of teratoma
√ spinal canal may be focally widened

TERMINAL MYELOCYSTOCELE

= combination of posterior spina bifida + meningocele + tethered cord + hydromyelia + cystic dilatation of distal central canal
Cause: disturbed CSF circulation resulting in dilatation of ventriculus terminalis + disruption of dorsal mesenchyme
Associated with: anorectal + genitourinary + vertebral anomalies: anal atresia, cloacal exstrophy, scoliosis, sacral agenesis
• skin-covered mass in lumbosacral region
√ spinal cord surrounded dorsally + ventrally by dilated subarachnoid space of the meningocele
√ nerve root exit ventrally
√ bifid spinal cord
√ hydromyelia

TETHERED CORD

= TIGHT FILUM TERMINALE SYNDROME = LOW CONUS MEDULLARIS
= abnormally short + thickened filum terminale with position of conus medullaris below L2-3
Normal location of tip of conus medullaris: L4/5 at 16 weeks of gestation, L2/3 at birth, L1-2 > 3 months of age
◊ RULE OF THREES: above L3 by age 3 months!
Etiology: incomplete involution of distal spinal cord with failure of ascent of conus
Pathophysiology: stretching of cord → vascular insufficiency at level of conus
Age at presentation: 5–15 years (in years of growth spurt); M÷F = 2÷3
Associated with: filar lipoma in 29–78%, filar cyst, diastematomyelia, imperforate anus
• dorsal nevus, dermal sinus tract, hair patch (50%)
• bowel + bladder dysfunction in childhood
• spastic gait with muscle stiffness; radiculopathy (adults)
• lower extremity weakness + muscle atrophy

- asymmetric hyporeflexia + fasciculations
- orthopedic anomalies: scoliosis, pes cavus, tight Achilles tendon
- hypalgesia, dysesthesia; paraplegia, paraparesis
- hyperactive deep tendon reflexes; extensor plantar responses
- anal / perineal pain (in adults)
- back pain (particularly with exertion)

@ Tight filum
- √ diameter of filum terminale > 2 mm (normal range, 0.5–2.0 mm) at L5/S1 level (55%)
- √ small fibrolipoma within thickened filum (23%)
- √ small filar cyst (3%)
- √ spinal cord ending in a small lipoma (13%)

@ Tethered cord (100%)
- √ conus medullaris below level of L3 at birth + below L2 by age 12 (86%)
- √ abnormal dorsal fixation of cord adjacent to vertebral arches (in prone position)
- √ reduced / absent pulsatile movement of the cord + nerve roots (on M-mode scanning)
- √ widened triangular thecal sac tented posteriorly (thecal sac pulled posteriorly by filum)
- √ abnormal lateral course of nerve roots (> 15° angle relative to spinal cord)

@ Vertebrae
- √ lumbar spina bifida occulta with interpedicular widening
- √ scoliosis (20%)

MR:
- √ prolonged T1 relaxation in center of spinal cord on T1WI in 25% (? myelomalacia / mild hydromyelia)

Rx: decompressive laminectomy / partial removal of lipoma ± freeing of cord

Dx: tip of conus medullaris below L2-3

TORUS

= oral exostosis

Age: adulthood (most commonly)

Types and location:
(1) Torus mandibularis: above mylohyoid line along lingual surface of mandible in region of bicuspids
(2) Torus palatinus: at midline of hard palate
(3) Torus maxillaris: lingual surface of posterior maxilla / buccal cortex of maxilla

√ exophytic lesion ± small amount of marrow

√ slowly growing with spontaneous growth arrest

TUBERCULOSIS OF SPINE

Tuberculous Meningitis

- √ CSF loculation
- √ obliteration of subarachnoid space
- √ loss of outline of spinal cord (cervicothoracic spine)
- √ matting of nerve roots (lumbar spine)

√ nodular thick linear intradural enhancement
Cx: syringomyelia

Tuberculous Spondylitis

= POTT DISEASE
[Percivall Pott (1714–1788), full surgeon at St. Bartholomew's Hospital, London, author of the Chirurgical works and discoverer of coal tar-induced cancer of the scrotum in chimney sweeps]
= destruction of vertebral body + intervertebral disk by tuberculous mycobacterium
Frequency: 5% of patients with tuberculosis; 25–50–60% of all skeletal tuberculosis
Associated with: pulmonary TB in 10%
Age: children / adults of 50 years; M > F
• insidious onset of back pain, stiffness
• local tenderness
• NO pulmonary lesions in 50%
Location: upper lumbar + lower thoracic spine (L1 most common); TYPICALLY more than one (up to 5–10) vertebrae + intervening disks affected
Site: vertebral body (82%) with predilection for anterior part adjacent to superior / inferior subchondral bone plate >> posterior elements (18%)
◊ RARELY affects posterior elements + pedicles!
Spread:
(a) contiguous into adjacent disk by penetrating subchondral endplate + cartilaginous endplate
(b) subligamentous spread beneath anterior / posterior longitudinal ligaments to adjacent vertebral bodies → sparing of adjacent disks
(c) hematogenous spread via paravertebral venous plexus of **Batson:** separate foci in 1–4%
(d) skip lesions = SPECIFIC but rare sign of TB
√ TYPICALLY little / NO reactive sclerosis / local periosteal reaction (DDx: pyogenic infection)
√ demineralization = vertebral osteopenia (= resorption of dense margin) of vertebral endplates (earliest change):
√ "gouge defect" = mild contour irregularity of anterior and lateral aspect of vertebral body (= erosion from subligamentous extension of tuberculous abscess)
√ collapse of vertebral body:
√ vertebra plana in children
√ angular kyphotic deformity (= gibbus deformity) ← preferential anterior involvement in adults
√ vertebra within a vertebra (= growth recovery lines)
√ ivory vertebra (= reossification as healing response to osteonecrosis)
√ slight narrowing + collapse of intervertebral disk space
N.B.: vertebral disk space maintained longer than in pyogenic arthritis (disk preserved, but fragmented)
√ <u>paraspinal infection</u>:
√ lateral bowing of psoas shadow (on abdominal film)

√ anterior scalloping of vertebral bodies (DDx: lymphoma, abdominal aortic aneurysm)
√ large cold fusiform abscess in paravertebral gutters / psoas (= Pott abscess), commonly bilateral ± anterolateral scalloping of vertebral bodies
√ nearly PATHOGNOMONIC amorphous / teardrop-shaped calcification in paraspinal area between L1 + L5 (DDx: nontuberculous abscess rarely calcifies)
√ abscess may extend into groin / thigh / internal viscus

MR:
√ centrosomatic rounded well-limited abscess
√ surrounded by bone marrow edema
√ normal disk spaces

NUC: 35% (up to 70%) FN rate for bone (gallium) scan

Cx: (1) Kyphoscoliosis
(2) Ankylosis of vertebrae with obliteration of intervening disk space ← with healing
(3) Osteonecrosis
(4) Paralysis ← spinal cord compression from abscess, granulation tissue, bone fragments, arachnoiditis)

Prognosis: 26–30% mortality rate

Imaging features favoring tuberculous spondylitis:
√ involvement of > 1 segment
√ delay in destruction of intervertebral disks
√ large calcified paravertebral mass
√ absence of sclerosis

DDx: (1) Pyogenic spondylitis (rapid destruction, multiple abscess cavities, no thickening / calcification of abscess rim, little new-bone formation, posterior elements not involved)
(2) Brucellosis (gas within disk, minimal paraspinal mass, no kyphosis, predilection for lower lumbar spine)
(3) Sarcoidosis
(4) Fungal spondylitis
(5) Neoplasia / metastasis (multiple noncontiguous lesions, no disk destruction, little soft-tissue involvement, posterior elements involved)

Tuberculous Spondylitis without Diskitis

increasingly more common type of TB
Predilection: foreign-born (sub-Saharan Africa)
Age: 40 years (10 years younger)
√ absence of disk destruction
√ initial multifocal vertebral involvement in 42%
√ extraspinal skeletal involvement (frequent)

VENTRICULUS TERMINALIS

= small ependyma-lined oval cyst at the transition from tip of conus medullaris to origin of filum terminale

Origin: result of canalization and regressive differentiation of the caudal end of the developing spinal cord during embryogenesis

Size: 8–10 mm long, 2–4 mm in diameter
◊ Regresses during the first weeks after birth

DIFFERENTIAL DIAGNOSIS OF NERVOUS SYSTEM DISORDERS

INCREASED INTRACRANIAL PRESSURE

1. Intracranial mass
2. Hydrocephalus
3. Malignant hypertension
4. Diffuse cerebral edema
5. Increased venous pressure
6. Elevated CSF protein
7. Pseudotumor cerebri

• papilledema

√ enlargement of perioptic nerve subarachnoid space

PROLACTIN ELEVATION

Normal level: up to 25 ng/mL

Cause:

1. Interference with hypothalamic-pituitary axis:
   (a) hypothalamic tumor
   (b) parasellar tumor
   (c) pituitary adenoma
   (d) sarcoidosis
   (e) histiocytosis
   (f) traumatic infundibular transection
2. Pharmacologic agents
   alpha-methyldopa, reserpine, phenothiazine, butyrophenone, tricyclic antidepressants, oral contraceptives
3. Hypothyroidism (TRH also stimulates prolactin)
4. Renal failure
5. Cirrhosis
6. Stress / recent surgery
7. Breast examination
8. Pregnancy
9. Lactation

STROKE

= sudden intracranial insult that leaves a permanent neurological residual

Incidence:

3rd leading cause of death in USA (after heart disease + cancer);
2nd leading cause of death due to cardiovascular disease in USA;
2nd leading cause of death in patients > 75 years of age;
~ 800,000 new cases per year (USA 2006);

leading cause of death in Orient

Age: > 55 years (12% occur in young adults); M÷F = 2÷1

Risk factors: heredity, hypertension (50%), smoking, diabetes (15%), obesity, familial hypercholesterolemia, myocardial infarction, atrial fibrillation, congestive heart failure, alcoholic excess, substance abuse, oral contraceptives, pregnancy, high anxiety + stress

Etiology:

A. NONVASCULAR (5%): eg, tumor, hypoxia
B. VASCULAR (95%)
   1. Brain infarction = ischemic stroke (80%)
      (a) Occlusive atheromatous disease of extracranial (35%) / intracranial (10%) arteries = large vessel disease between aorta + penetrating arterioles
         › critical stenosis, thrombosis,
         › plaque hemorrhage / ulceration / embolism
      (b) Small vessel disease of penetrating arteries (25%) = lacunar infarct
      (c) Cardiogenic emboli (6–15–23%)
         › Ischemic heart disease with mural thrombus
         » acute myocardial infarction (3% risk/year)
         » cardiac arrhythmia
         › Valvular heart disease
         » postinflammatory (rheumatic) valvulitis
         » infective endocarditis (20% risk/year)
         » nonbacterial thrombotic endocarditis (30% risk/year)
         » mitral valve prolapse (low risk)
         » mitral stenosis (20% risk/year)
         » prosthetic valves (1–4% risk/year)
         › Nonvalvular atrial fibrillation (6% risk/year)
         › Left atrial myxoma (27–55% risk/year)
      (d) Nonatheromatous disease (5%)
         › arterial elongation, coil, kinks (up to 20%)
         › fibromuscular dysplasia (typically spares origin + proximal segment of ICA)
         › aneurysm (rare) may occur in cervical / petrous portion / intracranially
         › dissection: traumatic / spontaneous (2%); up to 15% of strokes in young adults
         › cerebral arteritis (Takayasu, collagen disease, lymphoid granulomatosis, temporal arteritis, Behçet disease, chronic meningitis, syphilis)
         › postendarterectomy thrombosis / embolism / restenosis
      (e) Overactive coagulation (5%)
   2. Hemorrhagic stroke (20%)
      (a) Primary intracerebral hemorrhage (15%)
         › Hypertensive hemorrhage 45%
         › Amyloid angiopathy 7–17%
         › Anticoagulants 10%
         › Tumor 5–10%
         › Drug use 6%
         › Vascular malformation, aneurysm 5%

› Bleeding diathesis (eg, hemophilia) < 1%
› Severe migraine
› Surgery (carotid endarterectomy, heart)

(b) Vasospasm due to nontraumatic SAH (4%)
› Ruptured aneurysm 75–80%
› Vascular malformation 10–15%
› "Nonaneurysmal" SAH 5–15%

(c) Venoocclusive disease (1%): sinus thrombosis

- May be preceded by TIA:

◊ 10–14% of all strokes are preceded by TIA!
◊ 60% of all strokes ascribed to carotid disease are preceded by TIA!

Prognosis:

(1) Death during hospitalization (25%): alteration in consciousness, gaze preference, dense hemiplegia have a 40% mortality rate
◊ Hypodensity involving > 50% of MCA territory has a fatal outcome in 85%!
(2) Survival with varying degrees of neurologic deficit (75%)
(3) Good functional recovery (40%)

Role of imaging:

1. Confirm clinical diagnosis
◊ Clinical diagnosis is inaccurate in 13%!
2. Identify primary intracerebral hemorrhage
3. Detect structural lesions mimicking stroke:
tumor, vascular malformation, subdural hematoma
4. Detect early complications of stroke:
cerebral herniation, hemorrhagic transformation

Indications for cerebrovascular testing:

1. **TIA** = transient ischemic attack
2. Progression of carotid disease to 95–98% stenosis
3. Cardiogenic cerebral emboli

Temporal classification:

1. **TIA** = transient ischemic attack
• lasts 5 to 30 minutes + clears within 24 hours
2. **RIND** = reversible ischemic neurologic deficit
= fully reversible prolonged ischemic event resulting in minor neurologic dysfunction
• > 24 hours and < 8 weeks with eventual total recovery
Incidence: 16÷100,000 population / year
3. **Progressing stroke / intermittent progressive stroke**
= stepwise / gradually progressing accumulative neurologic deficit evolving over hours / days
4. **Slow stroke**
= rare clinical syndrome presenting as developing neuronal fatigue with weakness in lower / proximal upper extremity after exercise; occurs in patients with occluded ICA
5. **Completed stroke**
= severe + persistent stable neurologic deficit = cerebral infarction (death of neuronal

tissue) as end stage of prolonged ischemia > 21 days
- level of consciousness correlates well with size of infarct

Prognosis: 6–11% recurrent stroke rate

TRANSIENT ISCHEMIC ATTACK

= brief episode of transient focal neurological deficit ← ischemia of < 24 hours duration with return to pre-attack status

Incidence: 31÷100,000 population per year; increasing with age; 105,000 new cases per year in USA; M > F

Cause:

(a) embolic: usually from ulcerated plaque at carotid bifurcation
(b) hemodynamic: fall in perfusion pressure distal to a high-grade stenosis / occlusion

Risk factors:

(1) Hypertension → linear increase in probability of stroke with increase in diastolic blood pressure
(2) Cardiac disorders: prior myocardial infarction, angina pectoris, valvular heart disease, dysrhythmia, CHF
(3) Diabetes mellitus
(4) Cigarette smoking (weak risk factor)

Prognosis: 5.3% stroke rate per year for 5 years after first TIA; per year 12% increase of stroke / myocardial infarction / death; completed stroke in 5% (33%) within (1 month) 5 years

Rx:
1. Carotid endarterectomy (1% mortality, 5% stroke)
   › prophylactic carotid endarterectomy + chronic low-dose aspirin therapy in patients with recently symptomatic TIA / minor stroke + > 70% carotid artery stenosis
2. Anticoagulation
3. Antiplatelet agent: aspirin, ticlopidine (Ticlid®)

Carotid Transitory Ischemic Attack *(~ 66%)*

- carotid attacks < 6 hours in 90%
- transient weakness / sensory dysfunction CLASSICALLY in
  (a) hand / face with embolic event
  (b) proximal arm + lower extremity with hemodynamic event (located to watershed area)
  › motor dysfunction = weakness, paralysis, clumsiness of one / both limbs on same side
  › sensory alteration = numbness, loss of sensation, paresthesia of one / both limbs on same side
  › speech / language disturbance = difficulty in speaking (dys- / aphasia) / writing, in comprehension of language / reading / performing calculations
  › visual disturbance = loss of vision in one eye, homonymous hemianopia, amaurosis fugax
- paresis (mono-, hemiparesis) in 61%
- paresthesia (mono-, hemiparesthesia) in 57%
- amaurosis fugax (= transient premonitory attack of impaired vision due to retinal ischemia) in 12% ← transient hypotension or emboli of platelets / cholesterol crystals, (which may be

revealed by funduscopy)
- facial paresthesia in 30%

Vertebrobasilar Transient Ischemic Attack *(~ 33%)*

- vertebrobasilar events < 2 hours in 90%
  - › motor dysfunction = as with carotid TIA but sometimes changing from side to side including quadriplegia, diplopia, dysarthria, dysphagia
  - › sensory alteration = as with carotid TIA usually involving one / both sides of face / mouth / tongue
  - › visual loss = as with carotid TIA including uni- / bilateral homonymous hemianopia
  - › disequilibrium of gait / postural disturbance, ataxia, imbalance / unsteadiness
  - › drop attack = sudden fall to the ground without loss of consciousness
- binocular visual disturbance in 57%; vertigo in 50%
- paresthesia in 40%; diplopia in 38%; ataxia in 33%
- paresis in 33%; headaches in 25%; seizures in 1.5%

Accelerating / Crescendo TIA

= repeated periodic events of neurologic dysfunction with complete recovery to normal in interphase

DEMENTIA

= acquired progressive global impairment of intellectual functioning

Prevalence: 35 million worldwide; rising due to increase in life expectancy; in USA 14% of population > 65 years of age and > 50% of individuals > 85 years

Dx: multiple cognitive deficits representing a decrease from baseline + interfering with social / professional function including impairment of (1) memory (2) motor activity (3) recognition (4) executive function

Etiology: may be caused by more than 80 diseases

A. CORTICAL
   1. Alzheimer disease
   2. Pick disease = frontotemporal dementia
   3. Mild cognitive impairment
   4. Creutzfeldt-Jakob disease

B. SUBCORTICAL
   1. Vascular dementia: multi-infarct, Binswanger, CADASIL = cerebral autosomal dominant arteriopathy with subcortical infarcts and leukoencephalopathy)
   2. Dementia with Lewy bodies
   3. Huntington disease
   4. Parkinson disease
   5. Wernicke-Korsakoff syndrome
   6. Wilson disease
   7. Multiple sclerosis
   8. Infectious etiology (HIV, Lyme disease, syphilis
   9. Dementia syndrome of depression

C. OTHERS

1. MELAS
2. Cortical venous thrombosis
3. Normal pressure hydrocephalus
4. Subdural hematoma
5. Brain mass (CNS lymphoma + other neoplasms)

In order of frequency:

1. Alzheimer disease 60–70%
2. Dementia with Lewy bodies 25%
3. Frontotemporal dementia 5–10%
4. Vascular dementia ?% (declining)
5. Mixed etiology 6%
6. Normal pressure hydrocephalus 1%
7. Depression 1%
8. Tumor 1%

PET in Dementia

◊ PET is replacing SPECT ← (1) better spatial resolution, (2) greater sensitivity for hypometabolism compared to perfusion and (3) ability to quantify changes!

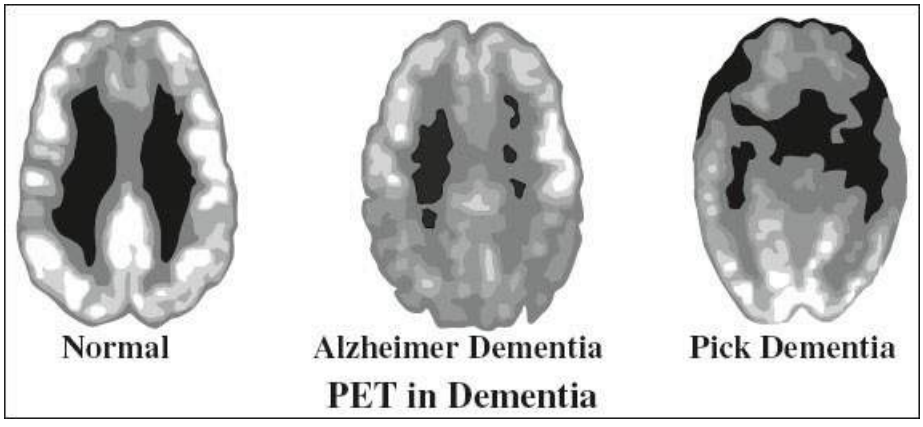
Rationale: dementia diminishes the usually high metabolic rate of active neurons in a typical pattern of distribution

Indication: distinguish between Alzheimer disease and frontotemporal (Pick) dementia

Requirements for PET imaging:

(1) > 6 months of progressive dementia
(2) Comprehensive neurological exam
(3) Diagnostic criteria for dementia have been met

√ sparing of sensorimotor cortex



TRIGEMINAL NEUROPATHY

- facial pain, numbness, weakness of masticatory muscles, trismus
- diminished / absent corneal reflex
- abnormal jaw reflex; atrophy of masticatory muscles
- decreased pain / touch / temperature sensation
- **tic douloureux** = paroxysmal facial pain (usually confined to V_2 and V_3) mainly ←

neurovascular compression (tortuous elongated superior cerebellar artery / anterior inferior cerebellar artery / vertebrobasilar dolichoectasia / venous compression)

A. BRAINSTEM LESION
   1. Vascular: infarct, AVM
   2. Neoplastic: glioma, metastasis
   3. Inflammatory: multiple sclerosis (1–8%), herpes rhombencephalitis
   4. Other: syringobulbia

B. CISTERNAL CAUSES
   1. Vascular: aneurysm, AVM, vascular compression
   2. Neoplastic: acoustic schwannoma, meningioma, trigeminal schwannoma, epidermoid cyst, lipoma, metastasis
   3. Inflammatory: neuritis

C. MECKEL CAVE + CAVERNOUS SINUS
   1. Vascular: carotid aneurysm
   2. Neoplastic: meningioma, trigeminal schwannoma, epidermoid cyst, lipoma, pituitary adenoma, base of skull neoplasm, metastasis, perineural tumor spread
   3. Inflammatory: Tolosa-Hunt syndrome

D. EXTRACRANIAL
   1. Neoplastic: neurogenic tumor, squamous cell carcinoma, adenocarcinoma, lymphoma, adenoid cystic carcinoma, mucoepidermoid carcinoma, melanoma, metastasis, perineural tumor spread
   2. Inflammatory: sinusitis
   3. Other: masticator space abscess, trauma

HORNER SYNDROME

= syndrome ← interruption of oculosympathetic pathway:
- ipsilateral blepharoptosis; pupillary miosis; facial anhidrosis

Oculosympathetic pathway:

(a) 1st order neuron: posterolateral hypothalamus → brainstem → intermediolateral column of spinal cord → exit at C8, T1, T2

(b) 2nd order preganglionic neuron: ventral spinal root → arch over apex of lung → cervical sympathetic chain → superior cervical ganglion

(c) 3rd order postganglionic neuron: with carotid artery → cavernous sinus → ophthalmic branch of cranial nerve V

A. CENTRAL HORNER (uncommon)

Location: hypothalamus, thalamus, brainstem, cervical cord

Cause: infarction of PICA / distal vertebral artery
- hypothalamic / brainstem / spinal cord signs

B. PREGANGLIONIC HORNER

Location: cervicothoracic cord, brachial plexus, anterior neck, mediastinum

Cause: trauma, lung (Pancoast) / mediastinal tumor, lesion in cervical spinal cord / brachial plexus

C. POSTGANGLIONIC HORNER

Location: superior cervical ganglion, internal carotid artery, cavernous sinus, orbital apex

Cause: ICA dissection / aneurysm, carotid-cavernous fistula / thrombophlebitis, inflammation (Tolosa-Hunt syndrome), skull base tumor

CLASSIFICATION OF CNS ANOMALIES

A. DORSAL INDUCTION ANOMALY
   = defects of neural tube closure
   1. Anencephaly
   2. Cephalocele at 4 weeks
   3. Chiari malformation at 4 weeks
   4. Spinal dysraphism
   5. Hydromyelia

B. VENTRAL INDUCTION ANOMALY
   = defects in formation of brain vesicles + face
   1. Holoprosencephaly: 5–6 weeks
   2. Septo-optic dysplasia: 6–7 weeks
   3. Dandy-Walker malformation: 7–10 weeks
   4. Agenesis of septum pellucidum

C. NEURONAL PROLIFERATION & HISTOGENESIS
   1. Neurofibromatosis: 5 weeks–6 months
   2. Tuberous sclerosis: 5 weeks–6 months
   3. Primary hydranencephaly: > 3 months
   4. Neoplasia
   5. Vascular malformation (vein of Galen, AVM, hemangioma)

D. NEURONAL MIGRATION ANOMALY
   due to infection, ischemia, metabolic disorders
   1. Schizencephaly: 2 months
   2. Agyria + pachygyria: 3 months
   3. Gray matter heterotopia: 5 months
   4. Dysgenesis of corpus callosum: 2–5 months
   5. Lissencephaly
   6. Polymicrogyria
   7. Unilateral megalencephaly

E. DESTRUCTIVE LESION
   1. Hydranencephaly
   2. Porencephaly
   3. Hypoxia: periventricular leukomalacia, germinal matrix hemorrhage
   4. Toxicosis
   5. Infections (TORCH)
      (a) **T**oxoplasmosis
      (b) **O**ther: syphilis, hepatitis, zoster
      (c) **R**ubella
         √ punctate / nodular calcifications
         √ porencephalic cysts
         √ occasionally microcephaly

(d) **C**ytomegalovirus inclusion disease
√ typically punctate / stippled / curvilinear periventricular calcifications
√ often hydrocephalus
(e) **H**erpes simplex

Absence of Septum Pellucidum

1. Holoprosencephaly
2. Callosal agenesis
3. Septo-optic dysplasia
4. Schizencephaly
5. Severe chronic hydrocephalus
6. Destructive porencephaly

Phakomatoses

[*phako* , Greek = lens / lentil-shaped object]
= NEUROCUTANEOUS SYNDROMES = NEUROECTODERMAL DYSPLASIAS
= development of benign tumors / malformations in organs of ectodermal origin (CNS, eye, skin)

(a) autosomal dominant:
1. Neurofibromatosis (von Recklinghausen)
2. Tuberous sclerosis (Bourneville)
3. Retinocerebellar hemangioblastoma (Von Hippel-Lindau)
4. Neurocutaneous melanosis

(b) not autosomal dominant:
5. Encephalotrigeminal angiomatosis (Sturge-Weber-Dimitri)
6. Ataxia-telangiectasia

DEGENERATIVE DISEASES OF HEMISPHERES

= progressive fatal disease characterized by destruction / alteration of gray and white matter

Etiology: genetic; viral infection; nutritional disorders (eg, anorexia nervosa, Cushing syndrome); immune system disorders (eg, AIDS); exposure to toxins (eg, CO); exposure to drugs (eg, alcohol, methotrexate + radiation)

Myelinoclastic / Demyelinating Disease

= disease that destroys normally formed myelin
◊ Usually affects older children / adults

(a) infectious
1. Progressive multifocal leukoencephalopathy
2. Subacute sclerosing panencephalitis (SSPE)
3. Acute disseminated encephalomyelitis (ADEM)

(b) noninfectious
1. Radiation
2. Anoxia
3. Hypertensive encephalopathy
4. Disseminated necrotizing leukoencephalopathy (from methotrexate therapy)

(c) others
1. Multiple sclerosis (most frequent of primary demyelinating disease)
2. Alzheimer disease (most common of diffuse gray matter degenerative diseases)
3. Parkinson disease (most common of subcortical degenerative disease)
4. Creutzfeldt-Jakob disease
5. Menkes disease (sex-linked recessive disorder of copper metabolism)
6. Globoid cell leukodystrophy
7. Spongiform degeneration
8. Cockayne syndrome
9. Spongiform leukoencephalopathy
10. Myelinoclastic diffuse sclerosis (= Schilder disease)

Dysmyelinating Disease

= metabolic disorder (= enzyme deficiency) resulting in deficient / absent myelin sheaths
◊ Usually presents in first 2 years / 1st decade of life!
◊ Associated with white matter atrophy

(a) macrencephalic:
1. Alexander disease (frontal areas affected first)
2. Canavan disease (white matter diffusely affected)

(b) hyperdense thalami, caudate nuclei, corona radiata
1. Krabbe disease

(c) family history (X-linked recessive)
1. X-linked adrenoleukodystrophy
2. Pelizaeus-Merzbacher disease

(d) others
1. Metachromatic leukodystrophy (most common hereditary leukodystrophy)
2. Binswanger disease (SAE)
3. Multi-infarct dementia (MID)
4. Pick disease
5. Huntington disease
6. Wilson disease
7. Reye syndrome
8. Mineralizing microangiopathy
9. Diffuse sclerosis

VASCULAR DISEASE OF BRAIN

Classification of Vascular CNS Anomalies

A. VASCULAR MALFORMATION

(a) arterial = arteriovenous malformation (AVM)
1. Classic brain AVM
2. Cerebral proliferative angiopathy
3. Cerebrofacial arteriovenous metameric syndrome
2. Vein of Galen malformation

(b) capillary = capillary telangiectasia

1. Capillary telangiectasia
2. Facial port-wine stain

(c) venous = venous malformation
1. Developmental venous anomaly
2. Sinus pericranii

(d) lymphatic
1. Cystic hygroma

(e) combinations
1. Sturge-Weber disease
2. Rendu-Osler-Weber disease

B. VASCULAR TUMOR
1. Hemangioma
(a) capillary hemangioma: seen in children, involution by 7 years of age in 95%
(b) cavernous hemangioma: seen in adults, no involution
2. Hemangiopericytoma
3. Hemangioendothelioma
4. Angiosarcoma

Blunt Cerebrovascular Injury

= carotid (CA) + vertebral artery (VA) injuries during generalized multitrauma / direct craniocervical trauma

Prevalence: 1.1–1.6% of all blunt trauma

Mechanism: partial / complete failure of arterial mural integrity ← longitudinal stretching of artery, direct blow to artery, piercing by bone fragment

Prognosis: 25–38% mortality if injury untreated

Cx: (1) Infarction ← intimal disruption / flap / hematoma
→ thromboembolism of platelet aggregates
→ critical luminal stenosis + occlusion
(2) Brain ischemia ← steal phenomenon by AV fistula
(3) Fatal exsanguination

Type of Arterial Injury

1. Minimal intimal injury
√ nonstenotic luminal irregularity
DDx: arterial spasm
2. Raised intimal flap
√ linear intraluminal filling defect emanating from arterial wall
3. Dissection with intramural hematoma
√ eccentric / circumferential mural thickening:
√ narrowed arterial lumen
√ increased arterial diameter
4. Arterial occlusion
√ lack of intraluminal enhancement
5. Pseudoaneurysm
√ eccentric outpouching from native arterial lumen:

√ minimal contour abnormality
√ large irregular saccular outpouching
√ focal ballooning of arterial lumen

6. Transection with active hemorrhage
   √ irregular collection of extravascular contrast material surrounding parent vessel
7. Arteriovenous fistula
   √ early venous enhancement during the arterial phase
   √ enlargement of draining vein

DDx: (1) Atherosclerosis (presence of calcification, characteristic location, increasing age)
Location: vessel origin, carotid bulb, cavernous carotid segment
(2) Coiled / looped cervical ICA segment (5–15%)
(3) Congenitally absent / small ICA (small / absent carotid canal)

Shunt Lesions of Cerebral Vasculature

1. AV malformation
2. AV fistula: pia, dura, carotid-cavernous sinus
3. Vein of Galen malformation

Congenital Venous Lesions

1. Developmental venous anomaly
2. Cerebral cavernous malformation
3. Sinus pericranii

Occlusive Vascular Disease

(a) Embolic state:
√ single vascular territory
(b) Hypoperfusive state:
√ multiple vascular territories

Cause:

1. Vasospasm from subarachnoid hemorrhage
2. **Embolic infarction** (50%)
   (a) thrombus (atrial fibrillation, valvular disease, atheromatous plaques of extracerebral arteries, fibromuscular dysplasia, intracranial aneurysm, surgery, paradoxic emboli, sickle cell disease, atherosclerosis, thrombotic thrombocytopenic purpura)
   • fluctuating blood pressures; hypercoagulability
   √ cerebral petechial hemorrhage within cortical / basal gray matter during 2nd week (from fragments of embolus) in up to 40%; initial ischemia is followed by reperfusion (= HALLMARK of embolic infarction)
   √ "supernormal artery" on NECT = high-density material lodged in cerebral vessel near major bifurcations
   √ atheromatous narrowing of vessels
   (b) fat
   (c) nitrogen

3. Watershed / border zone infarct (10%)
4. Hypertension
   (a) Hypertensive encephalopathy
   √ diffuse white matter hypodensity (edema ← arterial spasm)
   (b) Hypertensive hemorrhage
   Location: basal ganglia (putamen, external capsule), thalamus, pons, cerebellum
   (c) Lacunar infarction
   (d) Subcortical arteriosclerotic encephalopathy
5. Amyloidosis involvement of small- + medium-sized arteries of meninges + cortex
   • normotensive patient > 65 years of age
   √ multiple simultaneous / recurrent cortical hemorrhages
6. Vasculitis
   (a) Bacterial meningitis, TB, syphilis, fungus, virus, rickettsia
   (b) Collagen-vascular disease: Wegener granulomatosis, polyarteritis nodosa, SLE, scleroderma, dermatomyositis
   (c) Granulomatous angiitis: giant cell arteritis, sarcoidosis, Takayasu disease, temporal arteritis
   (d) Inflammatory arteritis: rheumatoid arteritis, hypersensitivity arteritis, Behçet disease, lymphomatoid granulomatosis
   (e) Drug-induced: IV amphetamine, ergot preparations, oral contraceptives
   (f) Radiation arteritis = mineralizing microangiopathy
   (g) Moyamoya disease
7. Anoxic encephalopathy cardiorespiratory arrest, near-drowning, drug overdose, CO poisoning
8. Venous thrombosis

Multiple Infarctions

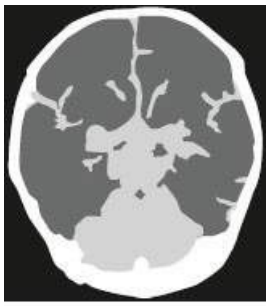
◊ Typical in extracranial occlusive disease, cardiac output problems, small vessel disease; in 6% from a shower of emboli

Location: usually bilateral + supratentorial (¾); supra- and infratentorial (¼)

Reversal Sign

= inversion of the normal attenuation relationship between gray and white matter (gray matter of lower attenuation than adjacent white matter of thalami, brainstem, cerebellum) on NECT of brain

Pathogenesis: not fully understood



Reversal Sign

Cause: global cerebral injury with anoxic insult ← head trauma, nonaccidental trauma, hypoxia, drowning, status epilepticus, hypothermia, bacterial meningitis, strangulation

Prognosis: poor ← irreversible brain damage; survivors with profound neurologic deficits + severe developmental delay

Diffusion Weighted Imaging (DWI)

Hyperintense Lesion on DWI

1. Cerebral infarction
2. Epidermoid inclusion cyst
3. Abscess with pus
4. Encephalitis of cortex
5. Creutzfeldt-Jakob disease
6. Trauma: axonal shearing injury
7. Neoplasm: medulloblastoma

INNUMERABLE PUNCTATE HYPERINTENSE LESIONS ON DWI

= Starfield pattern

1. Diffuse axonal injury (trauma)
2. Emboli: cardiogenic, septic, fat
3. Vasculitis
4. Minute hemorrhagic metastases

Hypointense Lesion on DWI

1. CSF
2. Tumor cyst: pilocytic, hemangioblastoma
3. Tumor nodules: hemangioblastoma

False Penumbra on Perfusion CT

True penumbra: successfully treatable with thrombolysis

√ mean transit time (MTT) ↑
√ cerebral blood flow (CBF) ↓
√ cerebral blood volume (CBV) ↔

False penumbra: area of abnormal perfusion as in ischemic penumbra NOT treatable with thrombolysis

A. Atherosclerosis at carotid bifurcation
   = upstream flow limitation WITHOUT significant intracranial collateral blood supply
   √ carotid bulb disease by CT angiography
B. Evolving ischemic condition / chronic infarct
   = delayed reperfusion + vascular collateralization of incomplete acute / chronic infarct
   √ hypoattenuation in the same region
   √ restricted diffusion on DWI + ADC map
C. Vascular dysregulation
   = hyperemia on symptomatic side with apparent perfusion abnormality on contralateral normal side
   • clinical history!
   Cause:
      1. Hypertensive encephalopathy (PRES)
         √ perfusion abnormality ← vasospasm
         √ hyperintensity on STIR sequence
         √ no restricted diffusion
      2. Seizure, subarachnoid hemorrhage, hemiplegic migraine
         • seizure activity
         √ no restricted diffusion
D. Head tilt / angulation
E. Variations in cerebrovascular anatomy
   = physiologic perfusion delay in circle of Willis variants, unequal blood supply between anterior + posterior circulation, congenitally absent ICA, etc.

CNS Vasculitis

A. LARGE-VESSEL VASCULITIS
   1. Takayasu arteritis
   2. Giant cell arteritis = Temporal arteritis
B. MEDIUM-SIZED–VESSEL VASCULITIS
   1. Polyarteritis nodosa
      √ aneurysm / stenosis / occlusion of intracranial carotid arteries
   2. Kawasaki disease
      √ nonspecific subdural effusion, cerebral infarction
      √ reversible hyperintense lesion in splenium
C. SMALL-VESSEL VASCULITIS
   1. IgA vasculitis = Henoch-Schönlein purpura
      √ hypertensive encephalopathy
      √ focal ischemic / hemorrhagic lesions
   2. Microscopic polyangiitis
      √ cerebral hemorrhage + infarction, pachymeningitis
      √ variable degree of small-vessel disease
   3. Granulomatosis with polyangiitis = Wegener granulomatosis
      √ leptomeningeal enhancement
   4. Eosinophilic granulomatosis with polyangiitis = Churg-Strauss syndrome
      √ macro- / microinfarctions + macro- / microhemorrhages

√ optic neuropathy

D. VARIABLE-SIZED VESSEL VASCULITIS
1. Behçet disease
2. Cogan syndrome
   √ nonspecific ischemic changes
   √ obliteration / narrowing of vestibular labyrinth

E. SINGLE-ORGAN VASCULITIS
1. Primary angiitis of CNS (PACNS)
   √ discrete / diffuse supra- and infratentorial lesions
   √ ± areas of infarction and hemorrhage

F. VASCULITIS OF SYSTEMIC DISEASE
1. Systemic lupus erythematosus (SLE)
   √ subcortical + periventricular white matter hyperintensity (60%)
   √ cerebral atrophy (30%), intracranial hemorrhage (3%)
2. Sjögren syndrome
   √ extensive white + gray matter lesions + microbleeds
3. Rheumatoid arthritis
   √ pachymeningitis with leptomeningeal enhancement
   √ cerebral vasculitis (rare)
4. APLA (antiphospholipid antibody) syndrome
   √ arterial / venous thrombosis, thrombocytopenia
5. Scleroderma
   √ nonspecific infarction, macro- and microhemorrhages

G. VASCULITIS WITH PROBABLE ETIOLOGY
1. Infection-induced vasculitis
2. Acute septic meningitis
   √ cerebral infarcts (5–15% in adults, 30% in neonates)
3. Mycobacterium tuberculosis
   √ vasculitis of smaller cerebral arteries → small infarcts in basal ganglia
4. Neurosyphilis
   √ predominantly MCA stroke in young adult
5. Viral (in childhood):
   › HIV-related vasculitis
     √ aneurysm, vessel occlusion, embolic disease, venous thrombosis
   › Varicella-zoster vasculopathy
     √ uni- / bilateral basal ganglia infarcts
6. Fungal: mucormycosis aspergillosis
7. Parasitic: cysticercosis
8. Malignancy-induced vasculitis
9. Drug-induced vasculitis
   › cocaine
     √ vasculitis, vasospasm, infarction, moyamoya-like
   › heroin
     √ spongiform leukoencephalopathy
10. Radiation-induced vasculitis

√ wall thickening + prominent wall enhancement in affected large arteries

11. **Reversible cerebral vasoconstriction syndrome**: Call-Fleming syndrome, postpartum angiopathy, migrainous vasospasm, benign angiopathy of CNS, vasoactive substances (cannabis, selective serotonin recapture inhibitors, nasal decongestants)

Imaging signs of cerebral vasculitis:

(a) direct
- √ vessel wall thickening
- √ vessel wall enhancement with contrast material

(b) indirect
- √ cerebral perfusion deficit
- √ ischemic brain lesion
- √ intracerebral / subarachnoid hemorrhage
- √ vascular stenosis

BRAIN ATROPHY

Cerebral Atrophy

= irreversible loss of brain substance + subsequent enlargement of intra- and extracerebral CSF-containing spaces (hydrocephalus ex vacuo = ventriculomegaly)

A. DIFFUSE BRAIN ATROPHY

Cause:

(a) Trauma, radiation therapy
(b) Drugs: dilantin, steroids, methotrexate, marijuana, hard drugs, chemotherapy, alcohol, hypoxia
(c) Demyelinating disease: multiple sclerosis, encephalitis
(d) Degenerative disease: eg, Alzheimer disease, Pick disease, Jakob-Creutzfeldt disease
(e) Cerebrovascular disease + multiple infarcts
(f) Advancing age, anorexia, renal failure

√ enlarged ventricles + sulci

B. FOCAL BRAIN ATROPHY

Cause: vascular / chemical / metabolic / traumatic / idiopathic (Dyke-Davidoff-Mason syndrome)

C. REVERSIBLE PROCESS SIMULATING ATROPHY (in younger people)

Cause: anorexia nervosa, alcoholism, catabolic steroid treatment, pediatric malignancy

√ prominent sulci
√ ipsilateral dilatation of basal cisterns + ventricles
√ ex vacuo dilatation of ventricles
√ thinning of gyri
√ focal areas of periventricular high signal intensity
√ increased iron deposition in putamen approaching the concentration in globus pallidus
√ dilatation of Virchow-Robin perivascular space

Cerebellar Atrophy

A. WITH CEREBRAL ATROPHY
   = generalized senile brain atrophy
B. WITHOUT CEREBRAL ATROPHY
   1. Olivopontocerebellar degeneration / Marie ataxia / Friedreich ataxia
      • onset of ataxia in young adulthood
   2. Ataxia-telangiectasia
   3. Ethanol toxicity: predominantly affecting midline (vermis)
   4. Phenytoin toxicity: predominantly affecting cerebellar hemispheres
   5. Idiopathic degeneration 2° to carcinoma (= paraneoplastic), usually oat cell carcinoma of lung
   6. Radiotherapy
   7. Focal cerebellar atrophy: (a) infarction
      (b) traumatic injury

Hippocampal Atrophy
1. Alzheimer Disease
2. Mesial temporal sclerosis
   • complex partial seizures
3. Normal in octogenarians

BRAIN HERNIATION

= shift of normal brain from high to low pressure through rigid structures of skull ← ⇑ intracranial pressure

Cause: mass effect by primary / metastatic tumor, trauma, infection (abscess) / inflammation, intracranial hemorrhage, subdural hematoma, ischemia / infarction, acute hydrocephalus, iatrogenic (after lumbar puncture / pneumocephalus following craniotomy)

Classification:

A. SUPRATENTORIAL HERNIATION
   1. Uncal (transtentorial)
   2. Central
   3. Cingulate (subfalcine)
   4. Transcalvarial
   5. Tectal (posterior)
B. INFRATENTORIAL HERNIATION
   1. Upward (upward cerebellar / upward transtentorial)
   2. Tonsillar (downward cerebellar)

Subfalcine / Cingulate Herniation (most common)

= contralateral shift of midline structures under falx cerebri
= herniation of cingulate gyrus across falx cerebri

Risk: compression of one of anterior cerebral arteries

May be associated with: transtentorial herniation

• weakness / paresis of contralateral leg ← compression of parafalcine cortex
• weakness ± sensory changes of contralateral leg ← infarction of paracentral lobule /

superior frontal gyrus ← compression of ACA / pericallosal artery
• somnolence ← raised intracranial pressure
√ <u>early signs:</u>
@ falx
√ shift of ipsilateral cingulate gyrus beneath falx
√ deviation of anterior falx with widened CSF space at contralateral side
N.B.: posterior falx remains relatively undisplaced due to greater height + rigidity
@ cingulate gyrus
√ compression of contralateral cingulate gyrus
@ corpus callosum
√ depression of ipsilateral corpus callosum
√ depression / elevation of contralateral corpus callosum
@ ventricle
√ compression / effacement of ipsilateral ventricle with amputation of ipsilateral frontal horn
√ <u>late signs:</u>
√ displacement of lateral ventricle to opposite side
√ obstruction of foramen of Monro → contralateral dilatation of the lateral ventricle + subependymal edema
√ infarction of cingulate gyrus
√ compression of anterior cerebral artery → infarction of ACA territory
Assessment: degree of greatest displacement of septum pellucidum / falx measured in mm relative to a straight line drawn through anterior and posterior falcine attachments on axial image
Prognosis: good with shift of < 5 mm; poor with shift > 15 mm
Cx: traumatic aneurysm of ACA / pericallosal artery

Transtentorial (Central) Herniation

= herniation of brain up / down across tentorium cerebelli
Tentorium cerebelli = inelastic reflection of dura
Connected to: occipital bone posteriorly, petrous temporal bone laterally, clinoid processes anteriorly
Content: transverse sinus, straight sinus
Tentorial hiatus / incisura
Content: cerebral peduncles + brainstem

Alert: NO lumbar puncture with effacement of basal cisterns + displacement of 4th ventricle!

Descending Transtentorial Herniation

= downward herniation of brain toward posterior fossa
• oculomotor nerve (cranial n. III) palsy:
• ipsilateral dilated pupil (= mydriasis) due to uncal herniation → compression of parasympathetic fibers traveling on outside of CN III → <u>unopposed sympathetic activity</u> to iris sphincter m.
• abnormal extraocular muscle function (except for superior oblique m., lateral rectus

m., levator palpebrae superioris m.)

- ipsilateral hemiparesis (on side of expanding lesion) (*false localizing sign* = **Kernohan notch** syndrome) due to severe lateral translation of midbrain against opposite tentorial edge → compression of opposite corticospinal tracts <u>above</u> decussation
- permanent anterograde amnesia ← infarction of uncal / parahippocampal gyrus ← arterial compression
- permanent visual field defect ← temporal / occipital lobe infarction ← compression of calcarine branch of PCA against tentorium

Location and degree of herniation:

(a) anterior / uncal herniation (see below)
(b) posterior: herniation of parahippocampal gyrus
(c) total: herniation of entire hippocampus

√ compression of ipsilateral cerebral peduncle
√ compression of contralateral cerebral peduncle → notching of midbrain (= Kernohan notch)
√ compression of aqueduct of Sylvius → early dilatation of temporal horn → obstructive hydrocephalus
√ widening of contralateral temporal horn
√ widening (obliteration) of ipsilateral (contralateral) basilar (ambient + quadrigeminal) cisterns

Cx:

(1) Occipital infarction ← compression of ipsilateral posterior cerebral artery against cerebral peduncle by uncus + parahippocampal gyrus
√ effacement / displacement of ipsilateral PCA
(2) **Duret hemorrhage** = hemorrhage in median / paramedian mesencephalon / tectum ← stretching of pontine perforators ← downward displacement of pons
(3) Respiratory arrest

UNCAL / ANTERIOR TRANSTENTORIAL HERNIATION

= herniation of uncus (most medial part of temporal lobe) across tentorium cerebelli into suprasellar cistern
◊ Most common subtype of transtentorial herniation caused by lesions in anterior half of brain
√ uncus displaced into suprasellar cistern → pressure on midbrain + brainstem
√ truncation of six-pointed star appearance of suprasellar cistern

Risk: (1) compression of midbrain (brainstem)
(3) Kernohan notch syndrome

Ascending Transtentorial / Cerebellar Herniation

= displacement of cerebellum through tentorial incisura superiorly = upward (superior vermian) displacement

Cause: slowly growing cerebellar / brainstem process, infarction

- nausea & vomiting → obtundation → coma

√ compression + anterior displacement of 4th ventricle
√ occlusion of aqueduct → obstructive hydrocephalus

√ narrowing / effacement of ambient + quadrigeminal cistern
√ compression of pons against clivus
√ upward displacement of cerebellar vermis
√ superior displacement of tectum
√ "spinning top" appearance of midbrain due to bilateral compression on posterolateral aspect of midbrain
√ downward displacement of cerebellar tonsils
Cx: (1) basilar artery compression ← displacement of midbrain / pons against clivus
(2) compression of vein of Galen / basal vein of Rosenthal → parenchymal congestion
(3) compression of posterior cerebral + superior cerebellar arteries ← superior displacement of cerebellum

Alar / Transalar / Retroalar / Sphenoid Herniation

= herniation of frontal lobe posteriorly across edge of sphenoid ridge
Associated with: transtentorial + subfalcine herniation
• paucity of clinical symptomatology, clinically occult
› posterior / descending: frontal lobe mass
√ frontal lobe displaced posteriorly
√ posterior displacement of sylvian fissure, temporal lobe + horizontal segment of MCA
› anterior / ascending: temporal lobe / insula lesion
√ temporal lobe displaced anteriorly

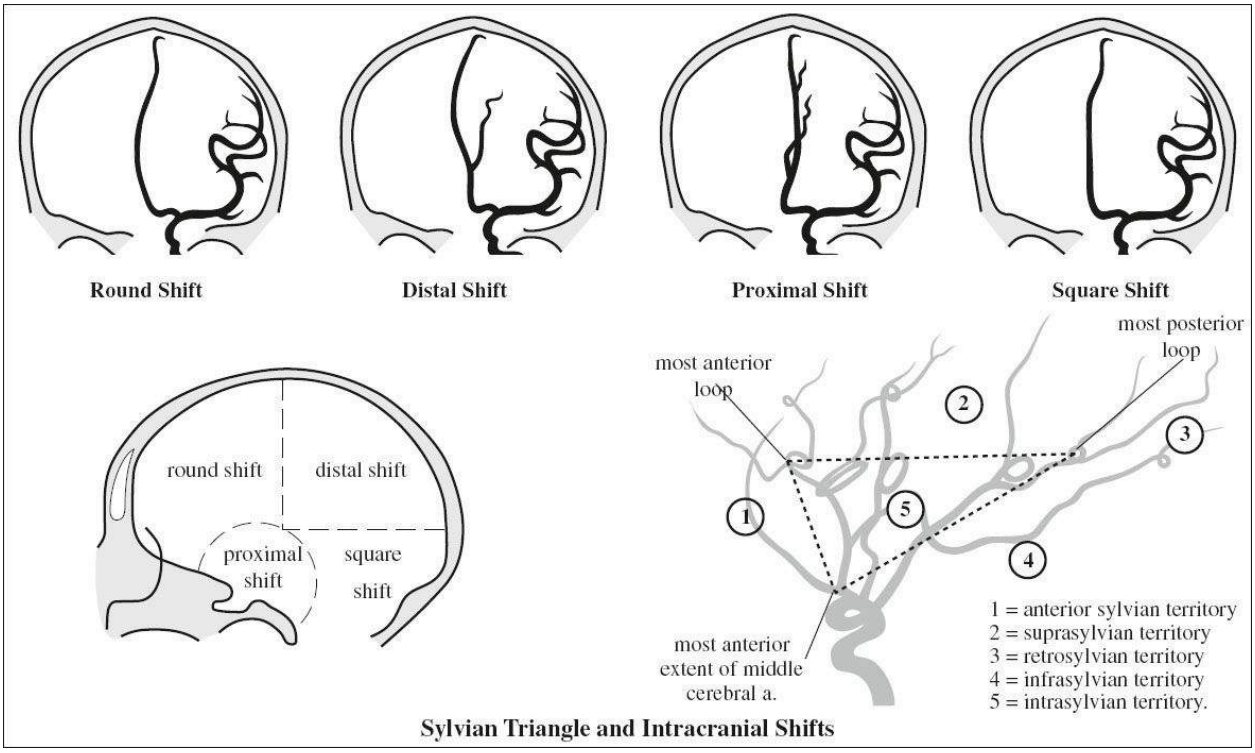
Transforaminal / Tonsillar Herniation

= herniation of inferior mesial portions of cerebellum (= inferior tonsils) downward through foramen magnum
Commonly associated with: ascending (⅔) or descending (⅓) transtentorial herniation
• neck pain, nystagmus, vomiting (in conscious patient)
• Cushing response (= irregular respiration, bradycardia, hypertension) as warning sign in unconscious patient
• decerebrate posturing
Risk: compression of medulla → respiratory arrest → cardiovascular collapse → coma → death
√ cerebellar tonsils at level of dens on axial images
√ cerebellar tonsils ≥ 5 mm below foramen magnum (= line connecting basion with opisthion) in adults; ≥ 7 mm in children on sagittal / coronal images
√ effacement of 4th ventricle / aqueduct → hydrocephalus of 3rd + lateral ventricles with transependymal CSF flow
√ ± concurrent upward displacement of vermis
Cx: compression of vulnerable PICA → cerebellar infarction

Alert: Known complication of lumbar puncture performed in context of elevated intracranial pressure!

Transcalvarial / External Herniation

= brain protrusion through fracture / surgical site of skull



Sylvian Triangle and Intracranial Shifts

Displacement of Vessels

A. ARTERIAL SHIFT

(a) Pericallosal arteries

1. Round shift = frontal lesion anterior to coronal suture
2. Square shift = lesion behind foramen of Monro in lower half of hemisphere
3. Distal shift = posterior to coronal suture in upper half of hemisphere
4. Proximal shift = basifrontal lesion / anterior middle cranial fossa including anterior temporal lobe

(b) Sylvian triangle

= branches of MCA within sylvian fissure on outer surface of insula form a loop upon reaching the upper margin of the insula; serves as angiographic landmark for localizing supratentorial masses

Location of lesion:

- anterior sylvian — frontal region
- suprasylvian — posterior frontal + parietal
- retrosylvian — occipital, parietooccipital
- infrasylvian — temporal lobe + extracerebral region
- intrasylvian — usually due to meningioma
- lateral sylvian — frontal, frontotemporal, parietotemporal
- central sylvian — deep posterior frontal, basal ganglia

B. CEREBRAL VEINS

= indicate the midline of the posterior part of the forebrain showing the exact location of the roof of the 3rd ventricle

BRAIN MASSES

Classification of Primary CNS Tumors

Incidence: 9% of all primary neoplasms (5th most common primary neoplasm); 5–10÷100,000 population per year; account for 1.2% of autopsied deaths

A. TUMORS OF BRAIN AND MENINGES
   (a) Gliomas
      ASTROCYTOMA (50%)
         1. Astrocytoma (astrocytoma grades I–II)
         2. Glioblastoma (astrocytoma grades III–IV)
      OLIGODENDROGLIOMA
      PARAGLIOMA
         1. Ependymoma
         2. Choroid plexus papilloma
      GANGLIOGLIOMA
      MEDULLOBLASTOMA
   (b) Pineal tumor
      1. Germinoma
      2. Teratoma
      3. Pineocytoma
      4. Pineoblastoma
   (c) Pituitary tumor
      1. Pituitary adenoma
      2. Pituitary carcinoma
   (d) Meningioma
   (e) Nerve sheath tumor
      1. Schwannoma
      2. Neurofibroma
   (f) Miscellaneous
      1. Sarcoma
      2. Lipoma
      3. Hemangioblastoma
B. TUMORS OF EMBRYONAL REMNANTS
   (a) Craniopharyngioma
   (b) Colloid cyst
   (c) Teratoid tumor
      1. Epidermoid (0.2–1.8%)
      2. Dermoid
      3. Teratoma

CNS Tumors Presenting at Birth

1. Hypothalamic astrocytoma
2. Choroid plexus papilloma / carcinoma
3. Teratoma

4. Primitive neuroectodermal tumor
5. Medulloblastoma
6. Ependymoma
7. Craniopharyngioma

CNS Tumors in Pediatric Age Group

Prevalence:

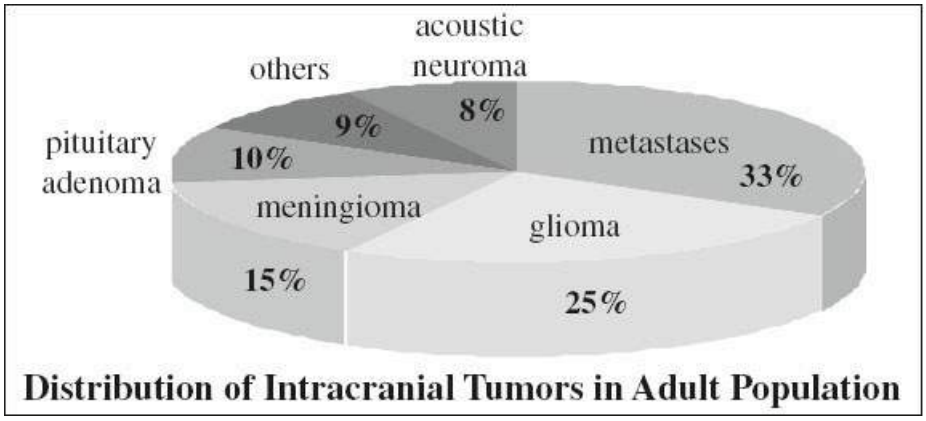
2.4÷100,000 (< 15 years of age); 2nd most common pediatric tumor (after leukemia); 15% of all pediatric neoplasms; 15–20% of all primary brain tumors; M > F

- increased intracranial pressure
- increasing head size

A. SUPRATENTORIAL (50%)

Age: first 2–3 years of life

Covering of brain	:	dural sarcoma, schwannoma, meningioma (3%)
Cerebral hemisphere	:	astrocytoma (37%), oligodendroglioma
Corpus callosum	:	astrocytoma
3rd ventricle	:	colloid cyst, ependymoma
Lateral ventricle	:	ependymoma (5%), choroid plexus papilloma (12%)
Optic chiasm	:	craniopharyngioma (12%), optic nerve glioma (13%), teratoma, pituitary adenoma
Hypothalamus	:	glioma (8%), hamartoma
Pineal region	:	germinoma, pinealoma, teratoma (8%)



Distribution of Intracranial Tumors in Adult Population

Incidence of Brain Tumors			
All Age Groups		*Pediatric Age Group*	
Glioma	34%	Astrocytoma	50%
Meningioma	17%	Medulloblastoma	15%
Metastasis	12%	Ependymoma	10%
Pituitary adenoma	6%	Craniopharyngioma	6%
Neurinoma	4%	Choroid plexus papilloma	2%
Sarcoma	3%		
Granuloma	3%		

Craniopharyngioma	2%	
Hemangioblastoma	2%	

Differences of Some Pediatric CNS Tumors			
	PNET	*Ependymoma*	*Astrocytoma*
CT	hyper	iso	hypo
T2WI	intermed.	intermed.	increased
Enhancement	moderate	minimal	nodule
Calcification	10–15%	40–50%	< 10%
Cyst formation	rare	common	typical
CSF seeding	15–40%	rare	rare
Foraminal spread	no	yes	no

B. INFRATENTORIAL (50%)

Age: 4–11 years

Cerebellum : astrocytoma (31–33%), PNET / medulloblastoma (26–31%)

Brainstem : glioma (16–21%)

4th ventricle : ependymoma (6–14%), choroid plexus papilloma

mnemonic: "BE MACHO"

Brainstem glioma
Ependymoma
Medulloblastoma
AVM
Cystic astrocytoma
Hemangioblastoma
Other

Supratentorial Tumor with Mural Nodule

1. Extraventricular ependymoma
2. Pleomorphic xanthoastrocytoma
3. Hemispheric pilocytic astrocytoma
4. Ganglioglioma
5. Dysembryoplastic neuroepithelial tumor (DNET)

Supratentorial Midline Tumors

1. Optic + hypothalamic glioma (39%)
2. Craniopharyngioma (20%)
3. Astrocytoma (9%)
4. Pineoblastoma (9%)
5. Germinoma (6%)
6. Lipoma (6%)
7. Teratoma (3.5%)
8. Pituitary adenoma (3.5%)
9. Meningioma (2%)

10. Choroid plexus papilloma (2%)

Classification by Histology

1. Astrocytic tumors (33.5%)
2. "Primitive" neuroectodermal tumor = PNET (21%)
   - › Medulloblastoma (16%)
   - › Ependymoblastoma (2.5%)
   - › PNET of cerebral hemisphere (2.5%)
3. Mixed gliomas (16%)
4. Malformative tumors (11.5%)
   - › Craniopharyngioma (5.5%)
   - › Lipoma (4.5%)
   - › Dermoid cyst (1%)
   - › Epidermal cyst (0.5%)
5. Choroid plexus tumors (4%)
6. Ependymal tumors (4%)
7. Tumors of meningeal tissues (3.5%)
   - › Meningioma (3%)
   - › Meningeal sarcoma (0.5%)
8. Germ cell tumors (2.5%)
   - › Germinoma (1.5%)
   - › Teratomatous tumor (1%)
9. Neuronal tumors
   - › Gangliocytoma (1.5%)
10. Tumors of neuroendocrine origin
    - › Pituitary adenoma (1%)
11. Oligodendroglial tumors (0.5%)
12. Tumors of blood vessel
    - › Hemangioma (1%)

Superficial Gliomas

= peripherally located cortical neoplasms serving as a seizure focus

1. Ganglioglioma
2. Desmoplastic infantile ganglioglioma
3. Gangliocytoma
4. Dysplastic cerebellar gangliocytoma
5. Pleomorphic xanthoastrocytoma
6. Dysembryoplastic neuroepithelial tumor

Multifocal CNS Tumors

A. METASTASES FROM PRIMARY CNS TUMOR
   (a) via commissural pathways: corpus callosum, internal capsule, massa intermedia
   (b) via CSF: ventricles / subarachnoid cisterns
   (c) satellite metastases
B. MULTICENTRIC CNS TUMOR

(a) true multicentric gliomas (4%)
(b) concurrent tumors of different histology (coincidental)

C. MULTICENTRIC MENINGIOMAS (3%) without neurofibromatosis
D. MULTICENTRIC PRIMARY CNS LYMPHOMA
E. PHAKOMATOSES
1. Generalized neurofibromatosis:
meningiomatosis, bilateral acoustic neuromas, bilateral optic nerve gliomas, cerebral gliomas, choroid plexus papillomas, multiple spine tumors, AVMs
2. Tuberous sclerosis:
subependymal tubers, intraventricular gliomas (giant cell astrocytoma), ependymomas
3. Von Hippel-Lindau disease:
retinal angiomatosis, hemangioblastomas, congenital cysts of pancreas + liver, benign renal tumors, cardiac rhabdomyomas

Multifocal Deep Hemispheric Masses

1. Primary CNS Lymphoma
2. Gliomatosis cerebri
√ nonenhancing tumor extension (common)

CNS Tumors Metastasizing Outside CNS

mnemonic: MEGO
Medulloblastoma
Ependymoma
Glioblastoma multiforme
Oligodendroglioma

Large Heterogeneous Intracerebral Mass

1. High-grade glioma
√ increased relative cerebral blood volume (rCBV) in zone of edema on perfusion-weighted images
2. Metastasis
√ reduced relative cerebral blood volume (rCBV) in zone of edema on perfusion-weighted images

Mass with Large Tumor Vessels and Edema

1. Glioblastoma multiforme
2. Meningioma

Avascular Mass of Brain

mnemonic: TEACH
Tumor: astrocytoma, metastasis, oligodendroglioma
Edema
Abscess
Cyst, **C**ontusion
Hematoma, **H**erpes

Calcified Intracranial Mass

1. Oligodendroglioma (frequent, although rare tumor)
2. Low-grade astrocytoma (in 10–20%)

mnemonic: Ca2+ COME

Craniopharyngioma
Astrocytoma, **A**neurysm
Choroid plexus papilloma
Oligodendroglioma
Meningioma
Ependymoma

HYPODENSE BRAIN LESIONS

Diffusely Swollen Hemispheres

A. METABOLIC
   1. Metabolic encephalopathy: eg, uremia, Reye syndrome, ketoacidosis
   2. Anoxia: cardiopulmonary arrest, near-drowning, smoke inhalation, ARDS

B. NEUROVASCULAR
   1. Hypertensive encephalopathy
   2. Superior sagittal sinus thrombosis
   3. Head trauma
   4. Pseudotumor cerebri

C. INFLAMMATION / INFECTION
   eg, herpes encephalitis, CMV, toxoplasmosis

Brain Edema

= increase in brain volume ← increased tissue-water content (80% for gray matter + 68% for white matter is normal)

Etiology:

(a) **Cytotoxic edema**
reversible increase in <u>intracellular</u> water content 2° to ischemia / anoxia (axonal pallor) → depletion of ATP → ion pump dysfunction across glial cell membrane → increase in intracellular Na+ and K+
- characteristically seen in cerebral infarction
- 30–60 min after onset of symptoms

√ decreased ADC value (dark)

(b) **Vasogenic edema** (most common form)
fluid leakage of water out of capillaries into extracellular interstitial space ← damage of capillary endothelium; increase in pinocytotic activity with passage of protein across vessel wall into intercellular space
- associated with primary brain neoplasm, metastases, hemorrhage, inflammation, infarction
- takes > 3–6 hours; requires residual / reestablished blood flow

√ lack of contrast enhancement means breakdown of blood-brain barrier is NOT the cause

√ increased ADC value (bright)
DDx: blood-brain barrier break-down after 8–10 days

Types:

1. Hydrostatic edema
   rapid increase / decrease in intracranial pressure
2. Interstitial edema
   increase in periventricular interstitial spaces ← transependymal flow of CSF with elevated intraventricular pressure
3. Hypo-osmotic edema
   produced by overhydration from IV fluid / inappropriate secretion of antidiuretic hormone
4. Congestive brain swelling
   rapid accumulation of extravascular water as a result of head trauma; may become irreversible (brain death) if intracranial pressure equals systolic blood pressure

√ decreased distinction between gray + white matter
√ compressed slitlike lateral ventricles
√ compression of cerebral sulci + perimesencephalic cisterns

CT:
√ areas of hypodensity
◊ Edema is always greatest in white matter!
√ mass effect: flattening of gyri, displacement + deformation of ventricles, midline shift
√ return to normal: from nonhemorrhagic edema / brain atrophy, from white matter shearing injury

MR:
√ decreased intensity on T1WI
√ increased intensity on T2WI
√ enhancement with gadolinium

US:
√ generalized / focal increase of parenchymal echogenicity with featureless appearance
√ decreased resistive indices

Midline Cyst

1. Cavum septi pellucidi
2. Cavum vergae
3. Cavum veli interpositi
4. Colloid cyst anterior + superior to cavum septi pellucidi
5. Arachnoid cyst in region of quadrigeminal plate cistern
   √ curvilinear margins

Intracranial Nonneoplastic Cyst

Characteristics:
√ no detectable wall / associated soft-tissue mass
√ homogeneous signal intensity identical to CSF
√ absence of surrounding edema / gliosis
√ NO contrast enhancement

1. Choroid plexus cyst (most common, abnormal DWI in ⅔)
2. Ependymal cyst
3. Neuroglial cyst
4. Enlarged perivascular spaces (typically multiple, clustered around basal ganglia)
5. Arachnoid cyst (typically extraaxial)
6. Porencephalic cyst (communication with lateral ventricle, surrounding gliosis)
7. Infectious cyst of neurocysticercosis (< 1 cm, partially enhancing)
8. Epidermoid cyst

Cyst with Mural Nodule

1. Ependymoma
2. Pilocytic astrocytoma (childhood)
3. Pleomorphic xanthoastrocytoma
4. Ganglioglioma
5. Glioblastoma multiforme
6. Hemangioblastoma (posterior fossa, spinal cord)

Multiple Tiny CNS Cysts

A. DIFFUSE DEGENERATIVE DISEASE
B. DIFFUSE INFLAMMATORY PROCESS
C. LOW-GRADE CYSTIC NEOPLASM
   1. Ganglioglioma
   2. Pyelocytic astrocytoma
   3. Pleomorphic xanthoastrocytoma

Anterior Temporal Cysts with Leukoencephalopathy

1. Congenital CMV infection
2. Leukoencephalopathy with subcortical temporal cysts and megalencephaly
3. Vanishing white matter disease

Cystic Lesions on Head Ultrasound

A. NORMAL VARIANTS
   1. Cavum septi pellucidi
   2. Cavum vergae
   3. Cavum veli interpositi
B. CYSTIC LESIONS OF POSTERIOR FOSSA
   Evaluate
   - size of 4th ventricle + communication with 4th ventricle
   - size of vermis + cerebellar hemispheres
   - mass effect on cerebellum

   1. Megacisterna magna
   2. Dandy-Walker continuum disorder
   3. Blake pouch cyst
   4. Arachnoid cyst
   5. Vein of Galen malformation

B. SUPRATENTORIAL PERIVENTRICULAR CYSTS
   1. **Connatal cyst**
      = coarctation of lateral ventricles + frontal horn cysts
      Location: at / just below superolateral angles of frontal horns / body of lateral ventricles anterior to foramen of Monro
      Cause: normal variant ← approximation of walls of frontal horns; NOT sequelae of ischemia
   2. Subependymal cyst
   3. Choroid plexus cyst
   4. Periventricular leukomalacia
   4. Pseudoporencephaly
C. SUPRATENTORIAL INTRA- / EXTRAAXIAL CYSTS
   1. Schizencephaly
   2. Ventriculomegaly: hydrocephalus, brain atrophy
   3. Holoprosencephaly
   4. Supratentorial arachnoid cyst
   5. Spontaneous intracranial hematoma
   6. Brain abscess (uncommon)

Cholesterol-containing CNS Lesions

1. Epidermoid inclusion cyst
2. Cholesterol granuloma
3. Acquired epidermoid of middle ear
4. Congenital cholesteatoma of middle ear
5. Craniopharyngioma

Mesencephalic Low-density Lesion

1. Normal: decussation of superior cerebellar peduncles at level of inferior colliculi
2. Syringobulbia found in conjunction with syringomyelia, Arnold-Chiari malformation, trauma
   √ CSF density centrally
   √ intrathecal contrast enters central cavity
3. Brainstem infarction
   √ abnormal contrast enhancement after 1 week
   √ well-defined low-attenuation region without enhancement after 2–4 weeks
4. Central pontine myelinolysis
5. Brainstem glioma
6. Metastasis
   √ well-defined contrast enhancement
7. Granuloma in TB / sarcoidosis (rare)

Intracranial Pneumocephalus

A. TRAUMA (74%):
   (a) blunt trauma
   in 3% of all skull fractures; in 8% of fractures involving paranasal sinuses (frontal >

ethmoid > sphenoid > mastoid) or base of skull
(b) penetrating injury

B. NEOPLASM INVADING SINUS (13%):
1. Osteoma of frontal / ethmoid sinus
2. Pituitary adenoma
3. Mucocele, epidermoid
4. Malignancy of paranasal sinuses

C. INFECTION WITH GAS-FORMING ORGANISM (9%) in mastoiditis, sinusitis

D. SURGERY (4%)
hypophysectomy, paranasal sinus surgery

E. SUPRATENTORIAL CRANIOTOMY
Location: in any compartment; most often in subdural space over frontal lobe
Duration after surgery: 2 days (100%), 7 days (75%), 2nd week (60%), 3rd week (26%), > 3 weeks (0%)

Mechanism of dural laceration:
(1) ball-valve mechanism during straining, coughing, sneezing
(2) vacuum phenomenon ← loss of CSF

Time of onset: on initial presentation (25%), usually seen within 4–5 days, delay up to 6 months (33%)

Mortality: 15%

Cx: (1) CSF rhinorrhea (50%)
(2) Meningitis / epidural / brain abscess (25%)
(3) Extracranial pneumocephalus = air collection in subaponeurotic space

HYPERDENSE INTRACRANIAL LESIONS

Intracranial Calcifications

mnemonic: PINEEAL
Physiologic
Infection
Neoplasm
Endocrine
Embryologic
Arteriovenous
Leftover Ls

A. PHYSIOLOGIC INTRACRANIAL CALCIFICATIONS

B. INFECTION
TORCH (toxoplasmosis, others [syphilis, hepatitis, zoster], CMV, rubella, herpes), healed abscess, hydatid cyst, granuloma (tuberculoma, actinomycosis, coccidioidomycosis, cryptococcosis, mucormycosis), cysticercosis, trichinosis, paragonimiasis
mnemonic:
CM**V** calcifications are circumventricular
Toxo**p**lasma calcifications are in**t**ra**p**arenchymal

C. NEOPLASM
Craniopharyngioma (40–80%), oligodendroglioma (50–70%), chordoma (25–40%),

choroid plexus papilloma (10%), meningioma (20%), pituitary adenoma (3–5%), pinealoma (10–20%), dermoid (20%), lipoma of corpus callosum, ependymoma (50%), astrocytoma (15%), after radiotherapy, metastases (1–2%, lung > breast > GI tract)
N.B.: Astrocytomas calcify less frequently but are the most common tumor!

D. ENDOCRINE Hyperparathyroidism, hypervitaminosis D, hypoparathyroidism, pseudohypoparathyroidism, CO poisoning, lead poisoning
E. EMBRYOLOGIC Neurocutaneous syndromes (tuberous sclerosis, Sturge-Weber, neurofibromatosis), Fahr disease, Cockayne syndrome, basal cell nevus syndrome
F. ARTERIOVENOUS Atherosclerosis, aneurysm, AVM, occult vascular malformation, hemangioma, subdural + epidural hematomas, intracerebral hemorrhage
G. LEFTOVER Ls
Lipoma, lipoid proteinosis, lissencephaly

Physiologic Intracranial Calcification

1. **Pineal calcification**
   Age: no calcification < 5 years of age, in 8–10% at 8–14 years of age, in 40% by 20 years of age; in ⅔ of adult population
   √ amorphous / ringlike calcification < 3 mm from midline usually < 10 mm in diameter
   √ ~ 30 mm above highest posterior elevation of pyramids

CAVE: pineal calcification > 14 mm suggests pineal neoplasm (teratoma / pinealoma)

2. **Habenula**
   Frequency: ~ in ⅓ of population
   Age: > 10 years of age
   √ posteriorly open C-shaped calcification 4–6 mm anterior to pineal gland
3. **Choroid plexus** may calcify in all ventricles: most commonly in glomus within atrium of lateral ventricles, near foramen of Monro, tela choroidea of 3rd ventricle, roof of 4th ventricle, along foramina of Luschka
   Age: > 3 years of age
   √ 20–30 mm behind + slightly below pineal on lateral projection, symmetrical on AP projection
   DDx: neurofibromatosis
4. **Dura, falx cerebri, falx cerebelli, tentorium**
   Frequency: 10% of population
   Age: > 3 years of age
   DDx: basal cell nevus syndrome (Gorlin syndrome), pseudoxanthoma elasticum, congenital myotonic dystrophy
5. **Petroclinoid ligament** (= reflection of tentorium between tip of dorsum sellae and apex of petrous bone)
   Age: > 5 years of age
6. **Interclinoid ligament** = interclinoid bridging
7. **Arteriosclerosis**: particularly intracavernous segment of ICA, basilar a., vertebral a.
8. **Basal ganglia**

Increased Density of Falx

1. Subarachnoid hemorrhage
2. Interhemispheric subdural hematoma
3. Diffuse cerebral edema (= increased density relative to low-density brain)
4. Dural calcifications (hypercalcemia from chronic renal failure, basal cell nevus syndrome, hyperparathyroidism)
5. Normal falx (can be normal in pediatric population)

Intraparenchymal Hemorrhage

mnemonic: "ITHACANS"

Infarction (hemorrhagic)
Trauma
Hypertensive hemorrhage
Arteriovenous malformation
Coagulopathy
Aneurysm, **A**myloid angiopathy
Neoplasm: metastasis / primary neoplasm
Sinus thrombosis

Dense Cerebral Mass

Substrate: calcification / hemorrhage / dense protein

A. VESSEL
   1. Aneurysm
   2. Arteriovenous malformation
   3. Hematoma (acute / subacute)

B. TUMOR
   1. Lymphoma
   2. Medulloblastoma
   3. Meningioma
   4. Metastasis
      (a) from mucinous-producing adenocarcinoma
      (b) hemorrhagic metastases: melanoma, choriocarcinoma, hypernephroma, bronchogenic carcinoma, breast carcinoma (rarely)

T1-HYPERINTENSE INTRACRANIAL LESIONS

A few naturally occurring substances reduce T1 relaxation times depending on the degree of substance concentration: methemoglobin, melanin, lipid, protein, and minerals.

A. METHEMOGLOBIN

Source: intracellular (early subacute phase = 3–7 days) + extracellular (late subacute phase = 8–31 days) methemoglobin

1. Hemorrhagic infarct
2. Intraparenchymal hematoma (eg, amyloid angiopathy)
3. Diffuse axonal injury
4. Subarachnoid hemorrhage
5. Epidural hematoma

6. Intraventricular hemorrhage
7. Thrombus: arterial / venous
8. Vascular malformation (eg, cavernous malformation)
9. Hemorrhagic neoplasm

B. MELANIN

Source: paramagnetic effect of stable free radicals + metal scavenging effect of melanin binding to chelated metal (= metallomelanin)

1. Metastatic melanoma
2. Primary diffuse meningeal melanomatosis
3. Melanocytoma
4. Neurocutaneous melanosis

C. LIPID

Source: short T1 relaxation time of H+ nuclei within lipid molecules

1. Intracranial lipoma
2. Teratoma
3. Dermoid cyst
4. Lipomatous ependymoma
5. Chemical meningitis from ruptured dermoid

D. PROTEIN

Source: high SI of protein + hydration layer effect

1. Colloid cyst
2. Rathke cleft cyst
3. Ectopic posterior pituitary gland

E. MINERAL DEPOSITION

1. Calcium concentration < 30%
2. Manganese, copper, iron
3. Cockayne syndrome
4. Neurodegeneration with iron accumulation (eg, Hallervorden-Spatz disease)
5. Hepatic encephalopathy
6. Wilson disease

F. OTHER

1. Type I neurofibromatosis
2. Cholesterol granuloma
3. Craniopharyngioma
4. Cortical laminar necrosis

Increased T1 Signal Intensity of Sellar Region

A. NORMAL CONDITION

1. Vasopressin storage

   Source: vasopressin–neurophysin II–copeptin macroprotein complex

   Site: posterior aspect of sella turcica immediately anterior to dorsum sellae

2. Anterior pituitary lobe hyperactivity

   Source: ↑ in intracellular protein concentration

   Cause: hypersecretion during first few weeks of life in newborn, pregnancy, postpartum period, lactation

T1-Hyperintense Intracranial Lesions by Location	
Location	*Lesion*
Deep gray matter nuclei	Cockayne syndrome: lentiform, dentate nuclei
	Pantothenate-kinase-associated neurodegeneration: bilateral globus pallidus + substantia nigra
	Hypertensive hemorrhage: putamen, external capsule, thalamus
	Hepatic encephalopathy: bilateral globus pallidus + substantia nigra
	Hypoxic-ischemic injury: lateral thalamus, posterior putamen + hippocampus
	Fabry disease: pulvinar
	Fahr disease: basal ganglia, thalamus, dentate, centrum semiovale
	Hypoparathyroidism, pseudo~, pseudopseudo~: similar to Fahr disease
	Lead, cyanide, methanol: bilateral putamen
	NF2: bilateral globus pallidus + internal capsule
	Wilson disease: basal ganglia + thalami
	Nonketotic hyperglycemia: bilateral caudate nucleus + globus pallidus
	HIV infection: caudate nucleus + putamen
	Neurodegenerative Langerhans cell histiocytosis: putamen
Cerebral hemi-sphere	Amyloid angiopathy, hemorrhagic metastasis / tumor, lipomatous ependymoma, vascular malformation, hemorrhagic contusion, hemorrhagic infarct, cortical laminar necrosis
Midline	Dermoid cyst, teratoma, lipoma, osteolipoma, hypothalamic hamartoma, pituitary microhemorrhage + apoplexy, deep cerebral vein thrombosis
Sellar / suprasellar	all above + craniopharyngioma, Rathke cleft cyst, ectopic posterior pituitary, thrombosed COW aneurysm, Langerhans cell histiocytosis
Ventricles	Intraventricular hemorrhage, 3rd ventricular colloid cyst, ruptured dermoid cyst
Dura mater	Lipomatous meningioma, hemorrhagic metastasis, melanoma, venous sinus thrombosis

3. Bone
   Source: marrow fat in elderly
   Site: nonpneumatized posterior sphenoid body, dorsum sellae, posterior clinoid process
4. Magnetic susceptibility artifact
   Source: abrupt transition between air-filled bone + dense cortical bone

Site: just above sellar floor

5. Flow artifact

B. LESION IN / NEAR SELLA TURCICA

(a) blood clot / hemorrhage

1. Pituitary apoplexy
2. Aneurysm

(b) lesion with high protein content

1. Rathke cleft cyst
2. Craniopharyngioma
3. Mucocele
4. Cholesterol granuloma

(c) lesion with high fat content

1. Lipoma of floor of 3rd ventricle, infundibulum, adjacent cranial nn.
2. Dermoid cyst
3. Lipoblastic meningioma

(c) intratumoral calcifications depending on degree of mineralization

1. Chordoma
2. Cartilaginous tumor (chondroma, chondrosarcoma)

(c) others

1. Pituitary abscess (very rare)
2. Excess manganese
   - parenteral nutrition / chronic liver deficiency

√ bilateral hyperintense T1 signal in adenohypophysis + globus pallidus

3. Melanoma

C. POSTTHERAPEUTIC CONDITION

(a) postoperative

1. Blood products
2. Surgical packing: fat, gelatin sponge
3. Metallic artifact
4. Mucocele

(b) medical therapy

1. Hemorrhage: bromocriptine
2. Hyperactive residual adenophysis

ENHANCING BRAIN LESIONS

Pachymeningeal Enhancement

= DURA-ARACHNOID ENHANCEMENT

Site: periosteum of inner table + meningeal layer

Location: dural reflections of falx cerebri + tentorium cerebelli + cavernous sinus; subcortical

√ inconspicuous enhancement against inner table on CT

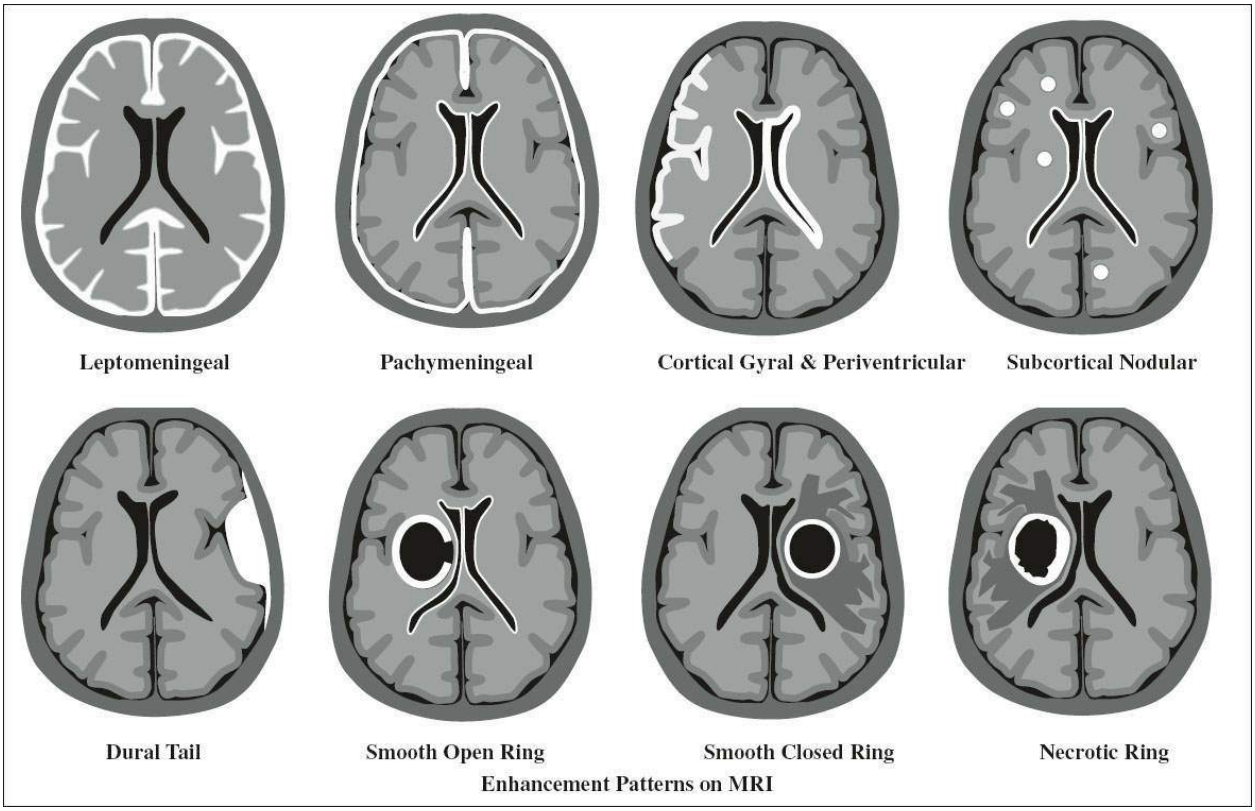
√ thin linear discontinuous enhancement on T1WI

Cause:

A. BENIGN

1. Transient postoperative enhancement
2. Intracranial hypotension
3. Granulomatous disease of basilar meninges (sarcoidosis, tuberculosis, Wegener granulomatosis, luetic gumma, rheumatoid nodules, fungal disease)
4. Uncomplicated lumbar puncture (in < 5%)

B. MALIGNANT
1. Meningioma
3. Secondary CNS lymphoma
2. Metastases: breast, prostate, melanoma, RCC



Enhancement Patterns on MRI

Leptomeningeal Enhancement

= PIA-ARACHNOID ENHANCEMENT

Site: pial surface of brain

Location: subarachnoid spaces of sulci + cisterns

√ gyriform / serpentine enhancement

Cause:

1. Infectious meningitis (bacterial, viral, fungal)
2. Carcinomatous meningitis
   (a) primary CNS tumor: medulloblastoma, ependymoma, glioblastoma, oligodendroglioma)
   (b) secondary tumor: lymphoma, breast cancer

Gyral Enhancement

√ serpentine enhancement

A. VASCULAR
- abrupt onset of symptoms

√ often in territory of single artery (MCA in 60%)

1. Reperfusion of ischemic brain
2. Vasodilative phase of migraine headaches
3. Posterior reversible encephalopathy syndrome
4. Vasodilation with seizures
5. Subarachnoid hemorrhage
   (enhancing fibroblastic proliferation)
6. Subacute / acute brain infarct: luxury perfusion
7. Dural sinus thrombosis: venous congestion

B. INFLAMMATORY
- nonspecific headache / lethargy

√ multiple territories

1. Herpes simplex encephalitis

C. NEOPLASTIC

(a) Meningeal carcinomatosis from systemic tumor, eg, breast carcinoma, small cell carcinoma of lung, malignant melanoma, lymphoma / leukemia

(b) Seeding primary CNS tumor:
1. Medulloblastoma
2. Pineoblastoma
3. Ependymoma

mnemonic: CAL MICE

Cerebritis
Arteriovenous malformation
Lymphoma
Meningitis
Infarct
Carcinomatosis
Encephalitis

Nodular Cortical / Subcortical Enhancement

Cause: hematogenous dissemination
1. Metastasis
2. Clot embolus

√ small < 2 cm circumscribed lesions near gray–white matter junction

Small Spherical Ring-enhancing Lesion at Corticomedullary Margin with Substantial Amount of Vasogenic Edema

1. Primary / secondary neoplasm
2. Abscess of brain

(a) bacterial / granulomatous: Streptococcus, Staphylococcus, Bacteroides, Mycobacteria, Nocardia, Actinomyces, Listeria

(b) fungal: Zygomycetes, Histoplasma, Coccidioides, Aspergillus, Cryptococcus

(b) parasitic: Toxoplasma, Taenia (cysticercosis), Entamoeba, Echinococcus

3. Subacute infarction
4. Resolving hematoma

Deep Ring-enhancing Lesion

Cause:

1. Glioma (40%): single lesion in 77%
2. Metastasis (30%): single lesion in 45%
3. Abscess (8%): multiple lesions in 75%
4. Demyelinating disease (6%): multiple lesions in 85%
5. Necrotic high-grade primary neoplasm (GBM)
   √ wavy undulating rim of > 10 mm in thickness
6. Fluid-secreting low-grade primary neoplasm (pilocytic astrocytoma, hemangioblastoma)
   √ enhancing mural nodule within cyst

Pathogenesis:

(1) hypervascular margin of lesion = granulation tissue / peripheral vascular channels / hypervascular tumor capsule

(2) breakdown of blood-brain barrier = leakage of contrast out of abnormally permeable vessels into extracellular fluid space

(3) hypodense center = avascular / hypovascular (requires time to fill) / cystic degeneration

Incidence of ring blush:

abscess (in 73%); glioblastoma (in 48%); metastasis (in 33%); grade II astrocytoma (in 26%) [NOT in grade I astrocytoma]

Multiple Ring-enhancing Lesions in Immunocompromised Patient

1. Lymphoma (necrotic)
   √ thick nodular ring enhancement
2. Metastatic disease
3. Multiple abscesses
   √ restricted diffusion (ADC values lower than lymphoma / metastatic disease / toxoplasmosis)

Solitary Ring-enhancing Lesion of Brain

A. NEOPLASM

1. Primary neoplasm: high-grade glioma, meningioma, lymphoma, leukemia, pituitary macroadenoma, acoustic neuroma, craniopharyngioma
2. Metastatic carcinoma + sarcoma

√ thick irregular peripheral enhancement

√ more nodular + irregular appearance compared with abscess

B. INFECTION / INFLAMMATION

Abscess / granuloma: bacterial, fungal, parasitic

√ thin ring iso- to hypointense relative to white matter using long repetition time

√ thin medial margin → propensity for intraventricular rupture

√ restricted diffusion of necrotic center

C. HEMORRHAGIC-ISCHEMIC LESION
1. Resolving infarction
2. Aging hematoma
3. Operative bed following resection
4. Thrombosed aneurysm

D. DEMYELINATING DISORDER
1. Radiation necrosis
2. Tumefactive demyelinating lesion ("singular sclerosis")
3. Necrotizing leukoencephalopathy after methotrexate
√ often incomplete ring enhancement with open portion of ring abutting gray matter
√ arc pattern with ongoing plaque activity at one margin = more classic asymmetric comma-shaped peripheral-enhancement pattern compared with abscess

mnemonic: MAGICAL DR
Metastasis
Abscess / cerebritis
Glioblastoma multiforme, **G**lioma
Infarct (resolving), **I**mpact
Contusion
AIDS toxoplasmosis
Lymphoma (often AIDS-related)
Demyelinating disease
Radiation necrosis, **R**esolving hematoma

Isolated Ring-enhancing Lesion of Brainstem

A. NEOPLASM
(a) primary
(b) secondary

B. INFECTION / INFLAMMATION
1. Abscess
2. Acute disseminated encephalomyelitis (ADEM)
3. Multiple sclerosis (1st episode)

Periventricular Enhancement

1. Primary CNS lymphoma
2. Primary glial tumor
3. Infectious ependymitis

Well-defined Superficial Enhancing Mass

A. EXTRAAXIAL DURA-BASED TUMOR
√ displacement of underlying cortex
√ adjacent dural thickening
√ reactive bone changes
√ supply by dural arteries
1. Meningioma

2. Metastasis (prostate, breast, melanoma, RCC)
3. Lymphoma

B. INTRAAXIAL
1. Glioblastoma multiforme

Dense & Enhancing Lesion

1. Aneurysm
2. Meningioma
3. CNS lymphoma
4. Medulloblastoma
5. Metastasis

Multifocal Enhancing Lesions

1. Multiple infarctions
2. Arteriovenous malformations
3. Multifocal primary / secondary neoplasms
4. Multifocal infectious processes
5. Demyelinating disease: eg, multiple sclerosis

Innumerable Small Enhancing Cerebral Nodules

A. METASTASES
B. PRIMARY CNS LYMPHOMA
C. DISSEMINATED INFECTION
1. Cysticercosis
2. Histoplasmosis
3. Tuberculosis

D. INFLAMMATION
1. Sarcoidosis
2. Multiple sclerosis

E. SUBACUTE MULTIFOCAL INFARCTION
from hypoperfusion, multiple emboli, cerebral vasculitis (SLE), meningitis, cortical vein thrombosis

BRAIN VENTRICLES

Ventriculomegaly

A. MACROCEPHALY
• increased intraventricular pressure
(a) Obstruction to CSF flow
1. Communicating hydrocephalus
2. Noncommunicating hydrocephalus

(b) Overproduction of CSF
= nonobstructive hydrocephalus

(c) Neoplasm

B. MICROCEPHALY

- normal intraventricular pressure

(a) Primary failure of brain growth
- › dysgenesis
  1. Holoprosencephaly
  2. Aneuploidy syndromes (trisomies)
  3. Migrational (< 6 layers)
- › environment: alcohol, drugs, toxins
- › infection: TORCH

(b) Loss of brain mantle
- › infection: TORCH
- › vascular accident
  1. Hydranencephaly
  2. Schizencephaly
  3. Porencephaly
- › hemorrhage
  1. Porencephaly
  2. Leukomalacia

C. NORMOCEPHALY

Colpocephaly

= dilatation of trigones + occipital horns + posterior temporal horns of lateral ventricles

1. Agenesis of corpus callosum
2. Arnold-Chiari malformation
3. Holoprosencephaly

Enhancing Ventricular Margins

(a) Subependymal spread of metastatic tumor
1. Bronchogenic carcinoma (esp. small cell carcinoma)
2. Melanoma
3. Breast carcinoma

(b) Subependymal seeding of CNS primary
1. Glioma
2. Ependymoma
3. Giant cell astrocytoma

(c) Ependymal seeding of CNS primary
1. Medulloblastoma
2. Germinoma

(d) Primary CNS lymphoma / systemic lymphoma

(e) Inflammatory ventriculitis

Intraventricular Tumor

Many intraventricular tumors have similar patterns of signal intensity + contrast enhancement. Lesion location + patient's age, gender, and underlying conditions help narrow the DDx.

Prevalence: 10% of all intracranial neoplasms

1. Ependymoma 20%
2. Astrocytoma 18%
3. Colloid cyst 12%
4. Meningioma 11%
5. Choroid plexus neoplasm 7%
6. Epidermoid / dermoid 6%
7. Craniopharyngioma 6%
8. Medulloblastoma 5%
9. Cysticercosis 5%
10. Arachnoid cyst 4%
11. Subependymoma 2%
12. AVM 2%
13. Teratoma 1%
14. Central neurocytoma 0.5%
15. Metastasis
16. Central neurocytoma
17. Oligodendroglioma

Supratentorial Intraventricular Tumors

(a) Lateral ventricle (¾)
   1. Choroid plexus neoplasm (44%)
   2. Giant cell astrocytoma (19%)
   3. Hemangioma in Sturge-Weber syndrome (12%)

(b) Third ventricle (¼)
   1. Astrocytoma (13%)
   2. Choroid plexus neoplasm (6%)
   3. Meningioma (6%)

UNIFORMLY ENHANCING TUMOR IN TRIGONE OF LATERAL VENTRICLE

1. Choroid plexus neoplasm
2. Ependymoma
3. Vascular malformation
4. Meningioma

DENSE LESION NEAR FORAMEN OF MONRO

A. INTRAVENTRICULAR LESION
   1. Colloid cyst
   2. Meningioma
   3. Choroid plexus neoplasm / granuloma
   4. AVM of septal, thalamostriate, internal cerebral v.

B. PERIVENTRICULAR MASS
   1. Primary CNS lymphoma
   2. Tuberous sclerosis
      (a) subependymal tuber
      (b) giant cell astrocytoma
   3. Metastasis from mucin-producing adenocarcinoma / hemorrhagic metastasis

(melanoma, choriocarcinoma, hypernephroma, bronchogenic carcinoma, breast carcinoma)

4. Glioblastoma of septum pellucidum

C. MASSES PROJECTING SUPERIORLY FROM SKULL BASE

1. Pituitary adenoma
2. Craniopharyngioma
3. Aneurysm
4. Dolichoectatic basilar artery

Mass in 3rd Ventricle

Purely intraventricular 3rd ventricle masses are rare:

(a) primary choroid plexus lesion: choroid plexus papilloma / carcinoma
(b) vascular malformation of choroid plexus
(c) lesion seeding to choroid plexus:
  › metastatic neoplasm
  › infection (eg, TB)

1. Colloid cyst
2. Glioma
3. Aneurysm
4. Craniopharyngioma
5. Ependymoma
6. Meningioma
7. Choroid plexus neoplasm
8. Central neurocytoma

CONGENITAL MALFORMATION OF THIRD VENTRICLE

1. Aqueductal stenosis
2. Persistent embryonic infundibular recess
3. Cavum veli interpositi cyst
4. **Congenital intraventricular cyst**

Origin: arachnoidal / endodermal / neuroepithelial
√ nonenhancing cyst of CSF density
√ hydrocephalus ← (possibly intermittent) obstruction of aqueduct / foramen of Monro
DDx: dilatation of 3rd ventricle

ACQUIRED MASS OF THIRD VENTRICLE

A. ANTERIOR MASS

Masses that distort / invade the 3rd ventricle most frequently arise in its anterior aspect and can be broadly grouped into

(a) sellar-suprasellar mass
(b) hypothalamic-chiasmatic mass

B. POSTERIOR MASS

(a) pineal mass: pineal germinoma, pineal cyst, pineocytoma, pineoblastoma, teratoma

(b) tectal mass
(c) inferior thalamic mass

C. INFERIOR / FLOOR MASS (uncommon)
1. Hypothalamic hamartoma
2. Basilar artery ectasia / aneurysm
3. Arachnoid cyst

D. MASS AT FORAMEN OF MONRO
1. Colloid cyst
2. Subependymal giant cell tumor (in TS complex)
3. Subependymoma

E. INTRAVENTRICULAR MASS

Mass in Anterior Portion of Third Ventricle

(a) pediatric patient
1. Germinoma
2. Pilocytic astrocytoma
3. Craniopharyngioma
4. Langerhans cell histiocytosis

(b) adult patient
1. Lymphoma
2. Pituitary macroadenoma
3. Craniopharyngioma
4. Metastasis
5. Granulomatous disease: eg, sarcoidosis
6. Sellar meningioma

Mass in 4th Ventricle

1. Choroid plexus papilloma
2. Ependymoma / glioma
3. Hemangioblastoma
4. Vermian metastasis
5. AVM
6. Epidermoid tumor (rare)
7. Inflammatory mass
8. Cyst

PERIVENTRICULAR REGION

Periventricular Calcifications in Childhood

1. Tuberous sclerosis
2. Congenital infection: CMV, toxoplasmosis

Periventricular Hypodensity

1. Encephalomalacia
   √ slightly denser than CSF

2. Porencephaly
   = cavity communicating with ventricle / cistern from intracerebral hemorrhage
   Associated with: dilated ventricle, sulci, fissures
   √ CSF density
3. Resolving hematoma
   • history of previously demonstrated hematoma
   √ may show ring enhancement + compression of adjacent structures
4. Cystic tumor
   √ mass effect + contrast enhancement

Periventricular T2-hyperintense Lesions

Leukoencephalopathy = disease of white matter
Leukodystrophy = degenerative diffuse sclerosis with symmetrical bilateral white matter lesions
Histo: reduced myelin, axonal loss, astrocytic gliosis
Associated with: dementia, gait abnormalities, late-onset depression

A. NORMAL (increasing with age)
   Frequency: 22% between 0 and 20 years; 22% between 21 and 40 years; 51% between 41 and 60 years; 92% over 60 years
   1. Enlarged perivascular spaces
   2. Ependymitis granularis
   3. Neuroepithelial cyst
B. DEMYELINATING DISEASE
   1. Multiple sclerosis
   2. Acute disseminated encephalomyelitis (ADEM) = postviral leukoencephalopathy
   3. Progressive multifocal leukoencephalopathy
   4. Lymphomatoid granulomatosis
C. VASCULAR DISEASE
   1. Arteriolosclerosis
   2. Lacunar infarcts
   3. **Migraine**: in 41% with classic migraine, in 57% with complicated migraine; presumed to represent vasculitis-induced small infarcts
   4. Vasculitis: Primary angiitis of CNS (PACNS), polyarteritis nodosa, Wegener granulomatosis, SLE, Behçet disease, syphilis, Sjögren syndrome, sickle cell disease
   5. Sarcoidosis
   6. Antiphospholipid antibodies (non-SLE)
   7. Susac syndrome
   8. Periventricular leukoencephalopathy / leukomalacia (= white matter injury of prematurity)
   9. Posterior reversible leukoencephalopathy syndrome (PRES) = hypertensive encephalopathy
D. INFECTION / INFLAMMATION
   1. HIV encephalitis:
      √ well-defined "patchy" / ill-defined "dirty white matter"
      √ central atrophy

2. Lyme encephalopathy
3. Neurocysticercosis
4. Fungal disease: cryptococcosis
5. Congenital CMV infection of CNS

E. TUMOR
1. Subependymal tumor
2. Multiple parenchymal metastases
3. Intravascular (angiocentric) lymphoma

F. TRAUMA
1. Diffuse axonal / shearing injury
2. Diffuse white matter injury = radiation-induced (mineralizing microangiopathy)
3. Diffuse necrotizing leukoencephalopathy = intrathecal methotrexate ± whole brain irradiation

G. METABOLIC
1. Vitamin B12 deficiency
2. Hydrocephalus = transependymal CSF flow
   √ smooth halo of even thickness
3. Pseudotumor cerebri
4. Mucopolysaccharidosis

H. GENETIC
1. Neurofibromatosis 1
2. CADASIL (= cerebral autosomal dominant arteriopathy with subcortical infarcts and leukoencephalopathy)
3. Fabry disease
4. Globoid cell leukodystrophy = Krabbe disease
5. Metachromatic leukodystrophy
6. Spongiform leukoencephalopathy
7. Adrenoleukodystrophy
8. Fibrinoid leukodystrophy = Alexander disease

Multifocal Black Dots on T2 + T2* GRE

= "blooming" susceptibility artifacts on T2* GRE

1. Cerebral amyloid disease
2. Hypertensive microhemorrhages
3. Hemorrhagic lacunar infarcts
4. Multiple vascular malformations (capillary telangiectasia, cavernous malformation)
5. Traumatic diffuse axonal injury
6. Embolic microhemorrhages:
   (a) Hemorrhagic micrometastases
   (b) Metallic microemboli from artificial heart valves
   (c) Microhemorrhages from fat emboli
7. CADASIL (= cerebral autosomal dominant arteriopathy with subcortical infarcts and leukoencephalopathy)

Corpus Callosum Lesion

A. TUMOR
   1. GBM
   2. Lymphoma
   3. Metastasis
B. TRAUMA
   1. Shearing injury
C. WHITE MATTER DISEASE
   1. Multiple sclerosis
   2. Progressive multifocal leukoencephalopathy
   3. Adrenoleukodystrophy
   4. Marchiafava-Bignami disease (often related to chronic alcoholism)
C. INFECTION
   1. Toxoplasmosis

Ring-enhancing Lesion Crossing Corpus Callosum

mnemonic: GAL

Glioblastoma multiforme (butterfly glioma)
Astrocytoma
Lymphoma

BASAL GANGLIA

Bilateral Basal Ganglia Lesions in Childhood

◊ Basal ganglia are susceptible to damage during childhood because of high energy requirements (ATP) mandating a rich blood supply + high concentration of trace metals (iron, copper, manganese)
• increased irritability, lethargy, dystonia
• seizure, behavioral changes
√ bilateral necrosis of basal ganglia

Acute Basal Ganglia Lesions

A. Compromise of vascular supply
   1. Hemolytic-uremic syndrome
      → microthrombosis of basal ganglia, thalami, hippocampi, cortex
   2. Arterial occlusion
   3. Deep cerebral venous thrombosis
B. Infection
   1. Encephalitis: Japanese encephalitis (Asia), West Nile fever (Middle East, North America), Murray Valley fever (Australia) by flavivirus infection
   2. Neurologic Behçet disease
   3. Toxoplasmosis
C. Compromise of nutrient supply
   1. Hypoxic ischemic encephalopathy
   2. Osmotic myelinolysis
   3. Hypoglycemia

√ hemorrhage rarely seen

In unexplained coma obtain blood sugar levels to differentiate this perhaps reversible condition from other causes!

D. Acute toxic poisoning
= impairment of mitochondrial cellular respiratory enzymes
• acute cognitive impairment, coma

1. **Carbon monoxide poisoning**
Action: inhibition of electron transport
Site: preferentially affects globus pallidus
(a) acute phase

√ foci of T2-hyperintensity
√ restricted diffusion
(b) delayed
√ delayed leukoencephalopathy in deep white matter
√ T1 shortening in globus pallidus

rare in children:

2. Hydrogen sulfide
3. **Cyanide poisoning**
Action: blockage of trivalent iron in respiratory chain
√ hemorrhagic necrosis in putamen
4. **Methanol poisoning**
• optic neuritis (initial symptom)
√ hemorrhagic necrosis in putamen
√ ± white matter edema
√ hypoattenuating areas in lentiform nuclei + corpus callosum + subcortical deep white matter in frontal and parietooccipital regions

Chronic Basal Ganglia Lesions

A. INBORN ERRORS OF METABOLISM
1. Leigh disease
2. Wilson disease

Basal Ganglia Lesion	
Thalamus involved	*Thalamus NOT involved*
Hypoxia	Toxic poisoning
Osmotic myelinolysis	Hypoglycemia
Wilson disease	Hyperglycemia
Leigh disease	Liver disease
Fahr disease	Huntington disease
Creutzfeldt-Jacob disease	Neurofibromatosis 1
Deep cerebral vein thrombosis	Neurodegeneration with Brain Iron Accumulation
Infection	
Primary CNS lymphoma	

3. **Mitochondrial encephalomyelopathies**
   = subset of lactic acidemias with structurally abnormal mitochondria
   • "ragged red" fibers in muscle biopsy
4. **Maple syrup urine disease**
   = inability to catabolize branched-chain amino acids (leucine, isoleucine, valine)
   • urine smells of maple syrup
5. **Methylmalonic acidemia**
   = group of genetically distinct autosomal recessive disorders of organic acid metabolism affecting conversion of methylmalonyl-CoA to succinyl-CoA
   • accumulation of methylmalonic acid in blood + urine

Symmetric diffuse abnormalities of the entire lentiform and caudate nuclei suggest systemic / metabolic causes!

B. DEGENERATIVE DISEASE
1. Huntington disease
2. Creutzfeldt-Jakob disease
3. Fahr disease
4. Neurodegeneration with brain iron accumulation (NBIA)

C. DYSMYELINATING DISEASE
N.B.: basal ganglia are a mixture of gray + white matter
1. Canavan disease
2. Metachromatic leukodystrophy

D. MALIGNANCY
1. Primary CNS lymphoma
2. Primary bilateral thalamic glioma

Asymmetric focal discrete lesions affecting only part of basal ganglia suggest involvement by infection / neoplasm

E. OTHERS
1. Neurofibromatosis type 1
   √ bilateral bright objects in globus pallidus, brainstem, cerebellum on T2WI (? hamartomas)
2. Hepatic cirrhosis
   √ bilateral T1-hyperintense areas in globus pallidus + substantia nigra ← deposition of manganese
3. Acute hyperammonemia
   √ bilateral symmetric swelling + T2 prolongation + restricted diffusion in basal ganglia + insular cortex + cingulate gyrus
4. Wernicke encephalopathy

Low-attenuation Lesion in Basal Ganglia

1. Poisoning: carbon monoxide, cyanide poisoning, methanol intoxication, barbiturate intoxication, hydrogen sulfide poisoning
2. Hypoxic ischemic encephalopathy
3. Hypoglycemia

4. Hypotension (lacunar infarcts)
5. Wilson disease

Hemorrhagic Basal Ganglia Lesions

1. Poisoning
2. CNS toxoplasmosis
3. Venous infarction
4. Flavivirus infection

Basal Ganglia Calcification

Prevalence in children: 1.1–1.6%

A. PHYSIOLOGIC WITH AGING
B. ENDOCRINE
   1. Hypoparathyroidism, pseudo-, pseudopseudo- (60%)
   2. Hyperparathyroidism
   3. Hypothyroidism
C. METABOLIC
   1. Leigh disease
   2. Mitochondrial cytopathy
      (a) **Kearns-Sayre syndrome** = ophthalmoplegia, retinal pigmentary degeneration, complete heart block, short stature, mental deterioration
      (b) **MELAS** = **M**itochondrial myopathy, **E**ncephalopathy, **L**actic acidosis, **A**nd **S**trokelike episodes
      (c) **MERRF** = **M**yoclonic **E**pilepsy with **R**agged **R**ed **F**ibers
   3. Fahr disease
D. CONGENITAL / DEVELOPMENTAL
   1. Familial idiopathic symmetric basal ganglia calcification
   2. Hastings-James syndrome
   3. Cockayne syndrome
   4. Lipoid proteinosis = hyalinosis cutis
   5. Neurofibromatosis
   6. Tuberous sclerosis
   7. Oculocraniosomatic disease
   8. Methemoglobinopathy
   9. Down syndrome
E. INFLAMMATION / INFECTION
   1. Toxoplasmosis, congenital rubella, CMV
   2. Measles, chicken pox
   3. Pertussis, Coxsackie B virus
   4. Cysticercosis
   5. Systemic lupus erythematosus
   6. AIDS
F. TRAUMA
   1. Childhood leukemia following methotrexate therapy
   2. S/P radiation therapy

3. Birth anoxia, hypoxia
4. Cardiovascular event

G. TOXIC
1. Carbon monoxide poisoning
2. Lead intoxication
3. Nephrotic syndrome

mnemonic: "BIRTH"
Birth anoxia
Idiopathic (most common), Infarct
Radiation therapy
Toxoplasmosis / CMV
Hypoparathyroidism / pseudoHPT

Multiple Small Enhancing Lesions in Deep Nuclei

1. Metastases
2. Primary CNS lymphoma
3. Disseminated infection
4. Noninfectious inflammatory process
5. Subacute multifocal infarction
6. Vasculitis

Linear Echogenic Foci in Thalamus + Basal Ganglia

A. IN UTERO INFECTION
= **mineralizing vasculopathy = lenticulostriate vasculopathy** = destruction of wall of lenticulostriate arteries + replacement by deposits of amorphous granular basophilic material
1. STORCH agents: **S**yphilis, **T**oxoplasma, **O**thers (hepatitis, zoster), **R**ubella virus, **C**ytomegalovirus, **H**erpes virus
2. Human immunodeficiency virus

B. CHROMOSOMAL ABNORMALITY
1. Down syndrome
2. Trisomy 13

C. OTHERS (anoxic injury?)
1. Perinatal asphyxia, respiratory distress syndrome, cyanotic congenital heart disease, necrotizing enterocolitis
2. Fetal alcohol syndrome
3. Nonimmune hydrops

Bithalamic T2-hyperintense Lesions

Only a few naturally occurring substances (methemoglobin, melanin, lipid, protein, minerals) are known to reduce T1 relaxation times, and the extent of that reduction depends on their occurrence in substantial concentrations.

1. Artery of Percheron infarction
2. Encephalitis

3. Acute disseminated encephalomyelitis (ADEM)
4. Creutzfeldt-Jakob disease
5. Wernicke encephalitis

Hypothalamic Lesions

- hormonal disorders; diencephalic syndrome (failure to thrive, vomiting, emaciation), precocious puberty, stunted growth, diabetes insipidus
- neurologic disorders: epilepsy (laughing fits)

A. DEVELOPMENTAL CYSTS
   1. Epidermoid cyst /dermoid
   2. Rathke cleft cyst
   3. Colloid cyst

B. DEVELOPMENTAL TUMORS
   1. Craniopharyngioma
   2. Germinoma
   3. Hamartoma
   4. Lipoma

C. INFLAMMATORY
   1. Langerhans cell histiocytosis
   2. Lymphocytic infundibuloneurohypophysitis
   3. Sarcoidosis

D. VASCULAR TUMORS
   1. Hemangioblastoma
   2. Cavernoma

E. PRIMARY CNS TUMORS
   1. Hypothalamic-chismatic glioma
   2. Ganglioglioma
   3. Choristoma

MENINGES

Diffuse Dural Thickening

1. Metastasis: prostate, melanoma, breast, rectum, lymphoma
2. Meningioma
3. Granuloma: TB, sarcoid, syphilis
4. Wegener granulomatosis
5. Granulomatous angiitis
6. Erdheim-Chester disease (lipid granulomatosis)
7. Rheumatoid arthritis
8. Neuroblastoma
9. Idiopathic hypertrophic pachymeningitis
10. Pachymeningitis interna hemorrhagica (breast mets)

Dural Calcifications

1. Normal variant (esp. if small)

2. Chronic renal failure
3. Tertiary hyperparathyroidism
4. Ankylosing spondylitis
5. **Arachnoiditis ossificans**
   Frequently associated with:
   significant often progressive neurologic deficit, trauma, surgery, subarachnoid hemorrhage, myelography (with oil-based contrast agents)

Mass Lesion of Dura

1. Meningioma
2. Hemangiopericytoma
3. Primary dural lymphoma
4. Metastasis: breast. lung, prostate
5. Rosai-Dorfman disease
6. Solitary fibrous tumor
7. EBV-associated leiomyoma and leiomyosarcoma
8. Melanocytic lesion: primary / metastatic
9. Melanocytoma
10. Erdheim-Chester disease
11. Sarcoid

Leiomyoma and leiomyosarcoma should be included in the DDx of dural-based masses in AIDS patients.

Dural Tail Sign

= curvilinear area of enhancement tapering off from the margin of the lesion along dural surface ← dural tumor infiltration / reactive inflammatory hypervascularity

1. Meningioma
2. Acoustic schwannoma

Other superficial masses

3. Chloroma
4. Primary CNS lymphoma
5. Sarcoidosis
6. Syphilitic gumma
7. Metastasis

Leptomeningeal Disease

A. INFLAMMATION
   1. Langerhans cell histiocytosis
   2. Sarcoidosis
   3. Wegener granulomatosis
   4. Chemical meningitis: rupture of epidermoid
B. INFECTION
   1. Bacterial meningitis
   2. Tuberculous meningitis
   3. Fungal meningitis

4. Neurosyphilis

C. TUMOR
   (a) Primary meningeal tumor
      1. Meningioma
      2. Glioma: primary leptomeningeal glioblastomatosis / gliosarcomatosis
      3. Melanoma / melanocytoma
      4. Sarcoma
      5. Lymphoma
   (b) CSF-spread from primary CNS tumor
      1. Medulloblastoma
      2. Germinoma
      3. Pineoblastoma
   (c) Metastasis
      1. Breast carcinoma
      2. Lymphoma / leukemia
      3. Lung carcinoma
      4. Malignant melanoma
      5. Gastrointestinal carcinoma
      6. Genitourinary carcinoma

D. TRAUMA
   1. Old subarachnoid hemorrhage
   2. Surgical scarring from craniotomy
   3. Lumbar puncture

EXTRAAXIAL LESIONS

Extraaxial Tumor

mnemonic: MABEL

Meningioma
Arachnoid cyst
Bony lesion
Epidermoid
Leukemic / lymphomatous infiltration

Low-attenuation Extraaxial Lesion

1. Acoustic schwannoma (occasionally low-density mass)
2. Epidermoid tumor
3. Arachnoid cyst

Pericerebral Fluid Collection in Childhood

A. ENLARGED SUBARACHNOID SPACE
   (a) due to macrocephaly
      1. Benign macrocephaly of infancy
   (b) due to brain atrophy

√ superficial cortical veins cross subarachnoid space to reach superior sagittal sinus

√ wide sulci, normal configuration of gyri
√ normal / prominent size of ventricles

B. SUBDURAL FLUID COLLECTION
(1) Subdural hygroma
(2) Subdural empyema / abscess ← meningitis
(3) Subdural hematoma
√ superficial cortical veins are prevented from crossing the subarachnoid space by the presence of arachnoid / neomembrane
√ wide interhemispheric fissure

Subdural Fluid Collection

A. Hyperdense = acute subdural hematoma
B. Isodense = subacute subdural hematoma
C. Hypodense
1. Chronic subdural hematoma
2. Subdural hygroma
3. Effusion from meningoencephalitis

Jugular Foramen Mass

A. NONNEOPLASTIC ENTITIES
1. Asymmetrically enlarged jugular foramen
2. High-riding jugular bulb
√ dome of bulb reaches above internal acoustic canal
√ thin osseous plate separates jugular bulb from middle ear cavity (thin-section CT!)
3. **Dehiscent jugular bulb**
• pulsatile tinnitus
• vascular tympanic membrane
√ middle ear soft-tissue mass contiguous with jugular foramen (= jugular bulb bulges into middle ear cavity)

Intra- versus Extraaxial Mass

	Intraaxial	*Extraaxial*
Relationship to dura	no attachment until advanced	contiguous
Local bony changes	uncommon	common
Cortex displaced	toward bone	away from bone, buckling of gray + white matter, displacement of vessels
Subarachnoid cistern	effaced	widened, CSF cleft
Feeding arteries	pial	dural

√ absence of bony plate separating jugular bulb from posteroinferior middle ear cavity

DDx: Jugular megabulb (rises above floor of EAC but with preservation of bony

plate)
4. Jugular vein thrombosis

B. NEOPLASM
1. Paraganglioma = glomus tumor
2. Nerve sheath tumor = neuroma
3. Meningioma
4. Vascular metastasis (renal / thyroid cancer)

C. PRIMARY BONE LESION
1. Multiple myeloma
2. Lymphoma
3. Langerhans cell histiocytosis

Cerebellopontine Angle Tumor

= extraaxial tumor arising in CSF-filled space bound by pons + cerebellar hemisphere + petrous bone

Frequency: 5–10% of all intracranial tumors

- cranial neuropathy: high frequency hearing loss (CN VIII), tinnitus, facial motor dysfunction (CN VII), facial sensory dysfunction (CN V), taste disturbance (chorda tympani)
- signs of posterior fossa mass effect: headache, nausea, vomiting, disequilibrium, ataxia
- hemifacial spasm, trigeminal neuralgia (tic douloureux)

√ may widen CSF space (cistern) in 25%
√ bone erosion / hyperostosis
√ sharp margination with brain

Types:

(a) benign condition
1. Vestibular schwannoma (60–90%)
2. Meningioma (10–18%)
3. Epidermoid cyst (5–9%)
4. Nonvestibular schwannoma:
   › trigeminal schwannoma
   › facial schwannoma
   › glossopharyngeal schwannoma
5. Arachnoid cyst(< 1%)
6. Lipoma (< 1%)
7. Dermoid
8. Choroid plexus papilloma
9. Ependymoma
10. Glomus jugulare tumor
11. Chordoma
12. Aneurysm of basilar / vertebral / posterior inferior cerebellar artery
13. Atherosclerotic dolichoectasia

(b) malignancy
1. Lymphoma
2. Melanoma
3. Metastasis (0.2–2%)

4. Chondrosarcoma
5. Exophytic brainstem glioma

mnemonic: **E**ver **G**rave **C**erebelloPontine **A**ngle **M**asses
Epidermoid
Glomus jugulare tumor
Chondroma, **C**hordoma, **C**holesteatoma
Pituitary tumor, **P**ontine glioma (exophytic)
Acoustic + trigeminal schwannoma, **A**neurysm of basilar / vertebral artery, **A**rachnoid cyst
Meningioma, **M**etastasis

POSTERIOR FOSSA

Congenital Anomalies of Posterior Fossa

Cerebellar vermis ± hemispheres may be hypo- / dysplastic.
Predominant involvement of cerebellar hemispheres is characteristic of pontocerebellar hypoplasia + disruptive cerebellar development in very premature newborns.
Posterior fossa malformations typically involve both cerebellar hemispheres equally.
Hypoplasia ± dysplasia of one cerebellar hemisphere is likely due to prenatal hemorrhage.

A. PREDOMINANTLY CEREBELLUM
   (a) predominantly vermian involvement
      1. Dandy-Walker malformation
      2. Blake pouch cyst
      3. Megacisterna magna
      4. Arachnoid cyst
      5. Isolated vermian hypoplasia
      6. Rhombencephalosynapsis
   (b) global cerebellar cortical maldevelopment
      1. Lissencephaly
      2. Polymicrogyria
      3. Periventricular nodular heterotopia
      4. Primary microcephaly
      5. Congenital CMV infection
   (c) unilateral cerebellar involvement
      1. PHACES syndrome
      2. Cerebellar cleft
B. CEREBELLUM + BRAINSTEM
   1. Pontocerebellar hypoplasia
   2. Joubert syndrome
C. PREDOMINANTLY BRAINSTEM
   1. Pontine tegmental cap dysplasia
D. PREDOMINANTLY MIDBRAIN
   1. Dysplasia of diencephalomesencephalic junction

Posterior Fossa Cystic Malformation

1. Dandy-Walker malformation
2. Dandy-Walker variant
3. Megacisterna magna
4. Arachnoid pouch

Cystic Mass in Cerebellar Hemisphere

1. Hemangioblastoma
2. Cerebellar astrocytoma
3. Metastasis
4. Lateral medulloblastoma (= "cerebellar sarcoma")
5. Choroid plexus papilloma with lateral extension

Differential Diagnosis of Predominantly Vermian Posterior Fossa Malformations

Entity	*Vermis*	*4th ventricle*	*Posterior fossa*	*Hydrocephalus*	*Scalloped occipital bone*
Dandy-Walker malformation	hypoplastic	⇑	⇑	(mostly) yes	no
Isolated vermian hypoplasia	inferior hypoplasia	⇑	↔	no	no
Blake pouch cyst	normal	⇑	normal	yes	no
Megacisterna magna	normal	normal	⇑ / ↔	no	±
Posterior fossa arachnoid cyst	10–15%	40–50%	< 10%	±	yes

Posterior Fossa Tumor In Adult

Extraaxial	*Intraaxial*
1. Acoustic neuroma	1. Metastasis (lung, breast)
2. Meningioma	2. Hemangioblastoma
3. Chordoma	3. Lymphoma
4. Choroid plexus papilloma	4. Lipoma
5. Epidermoid	5. Glioma

SELLA

Destruction of Sella

1. Pituitary adenoma
2. Suprasellar tumor
3. Carcinoma of sphenoid + posterior ethmoid sinus
   √ opacification of sinus + destruction of walls
   √ associated with nasopharyngeal mass (common)
4. Nasopharyngeal carcinoma
   (a) squamous cell carcinoma
   (b) lymphoepithelioma = Schmincke tumor = nonkeratinizing form of squamous cell carcinoma
   √ sclerosis of adjacent bone
5. Metastasis to sphenoid: from breast, kidney, thyroid, colon, prostate, lung, esophagus
6. Primary tumor of sphenoid bone (rare): osteogenic sarcoma, giant cell tumor, plasmacytoma
7. Chordoma
8. Mucocele of sphenoid sinus (uncommon)

9. Enlarged 3rd ventricle aqueductal stenosis ← infratentorial mass, maldevelopment

J-shaped Sella

mnemonic: "CONMAN"

Chronic hydrocephalus
Optic glioma, **O**steogenesis imperfecta
Neurofibromatosis
Mucopolysaccharidosis
Achondroplasia
Normal variant

Enlarged Sella

A. PRIMARY TUMOR
   1. Pituitary adenoma
   2. Craniopharyngioma
   3. Meningioma: hyperostosis
   4. Optic glioma: J-shaped sella
B. PITUITARY HYPERPLASIA
   1. Hypothyroidism
   2. Hypogonadism
   3. **Nelson syndrome**
      = rapid enlargement of pre-existing ACTH-secreting pituitary adenoma
      Frequency: in 7% of patients after removal of both adrenal glands
      Cause: absence of negative feedback of cortisol on production of ACTH
C. CSF SPACE
   1. Enlarged 3rd ventricle
   2. Hydrocephalus
   3. Empty sella
D. VESSEL
   1. Arterial aneurysm
   2. Ectatic internal carotid artery

mnemonic: CHAMPS

Craniopharyngioma
Hydrocephalus (empty sella)
AVM, **A**neurysm
Meningioma
Pituitary adenoma
Sarcoidosis, TB

Pituitary Gland Enlargement

1. Neoplasm: eg, pituitary gland adenoma
2. Hypertrophy: primary precocious puberty, primary hypothyroidism
3. Lymphocytic hypophysitis
4. Infection
5. Severe dural AV fistula

Complex Sellar / Parasellar Cyst

1. Cystic craniopharyngioma
2. Hemorrhagic pituitary adenoma
3. Hemorrhagic / proteinaceous Rathke cleft cyst

Intrasellar Mass

1. Pituitary adenoma / carcinoma (most common cause)
2. Craniopharyngioma (2nd most common cause)
3. Meningioma: from surface of diaphragm / tuberculum sellae
4. Chordoma
5. Metastasis: lung, breast, prostate, kidney, GI tract, spread from nasopharynx
6. Intracavernous ICA aneurysm: bilateral in 25%
7. Pituitary abscess: rapidly expanding mass associated with meningitis
8. Empty sella
9. Rathke cleft cyst: commonly at junction of anterior + posterior pituitary gland
10. Choristoma: benign neoplasm of posterior pituitary gland
11. Granuloma: sarcoidosis, giant cell granuloma, TB, syphilis, eosinophilic granuloma
12. Lymphoid adenohypophysitis
13. Pituitary hyperplasia, eg, in Nelson syndrome

Calcified Sellar Lesion

1. Aneurysm
2. Craniopharyngioma
3. Chordoma
4. Cartilaginous tumor

Decreased T2 Signal Intensity of Pituitary Gland

1. Hemochromatosis
2. Malignant melanoma
3. Pituitary hemorrhage
4. Flow void (aneurysm)
5. Rathke cleft cyst
6. Calcification (craniopharyngioma, chordoma)

Hypointense Lesion of Sella

1. Empty sella
2. Pituitary stone (= pituilith)
   = sequelae of autonecrosis of pituitary adenoma
3. Intrasellar aneurysm
4. Persistent trigeminal artery
5. Calcified meningioma
6. Pituitary hemochromatosis (anterior pituitary lobe only)

Thickened Pituitary Stalk

1. Langerhans cell histiocytosis
2. Germinoma

3. Craniopharyngioma
4. Tuberculosis
5. Sarcoidosis
6. Lymphocytic hypophysitis

Parasellar Mass

1. Meningioma: tentorium cerebelli
2. Neurinoma (III, IV, V_1, V_2, VI)
3. Metastasis: lung, breast, kidney, GI tract, spread from nasopharynx
4. Epidermoid
5. Aneurysm
6. Carotid-cavernous fistula

Suprasellar Mass

1. Meningioma
2. Craniopharyngioma: in 80% suprasellar
3. Chiasmal + optic nerve glioma in 38% of neurofibromatosis; adolescent girls
   DDx: chiasmal neuritis
4. Hypothalamic glioma
5. Hamartoma of tuber cinereum
6. Infundibular tumor: metastasis (esp. breast); glioma; lymphoma / leukemia; histiocytosis X; sarcoidosis; tuberculosis
   √ diameter of infundibulum > 4.5 mm immediately above level of dorsum; cone-shaped (on coronal scan)
7. Germinoma
   = malignant tumor similar to seminoma (= "ectopic pinealoma")
   √ frequently calcified (teratoma)
   √ CSF spread (germinoma + teratocarcinoma)
   √ enhancement on CECT (common)
8. Epidermoid / dermoid
   √ cystic lesion containing calcifications + fat
   √ minimal / no contrast enhancement
9. Arachnoid cyst
   • hydrocephalus (common), visual impairment
   • endocrine dysfunction
   Age: most common in infancy
10. Enlarged 3rd ventricle extending into pituitary fossa
11. Suprasellar aneurysm
    √ rim calcification + eccentric position

Suprasellar Mass in Adulthood

mnemonic: SATCHMO

Sarcoidosis, **S**ella neoplasm with superior extension
Aneurysm (ectatic carotid, carotid-cavernous sinus fistula), **A**rachnoid cyst, **A**denoma (pituitary)

Tuberculosis, **T**eratoma: dysgerminoma (usually), dermoid, epidermoid
Craniopharyngioma, **C**hordoma
Hypothalamic glioma, **H**istiocytoma, **H**amartoma
Meningioma, **M**etastatic disease, **M**ucocele
Optic nerve glioma, neuroma

Suprasellar Mass with Low Attenuation

1. Craniopharyngioma
2. Dermoid / epidermoid
3. Arachnoid cyst
4. Lipoma
5. Simple pituitary cyst
6. Glioma of hypothalamus

Suprasellar Low-density Lesion with Hydrocephalus

A. CYST
   1. Arachnoid cyst
   2. Ependymal cyst of 3rd ventricle
   3. Parasitic cyst of 3rd ventricle (cysticercosis)
   4. Dilated 3rd ventricle (in aqueductal stenosis)

B. CYSTIC MASS
   1. Epidermoid
   2. Hypothalamic pilocytic astrocytoma
   3. Cystic craniopharyngioma

N.B.: Cystic lesion may be inapparent within surrounding CSF; metrizamide cisternography is helpful in detection + to exclude aqueduct stenosis

Suprasellar Mass with Mixed Attenuation

A. IN CHILDREN
   1. Hypothalamic-chiasmatic glioma
   2. Craniopharyngioma
   3. Hamartoma of tuber cinereum
   4. Histiocytosis

B. IN ADULTS
   1. Suprasellar extension of pituitary adenoma
   2. Craniopharyngioma
   3. Epidermoid cyst
   4. Thrombosed aneurysm
   5. Low-grade hypothalamic / optic glioma
   6. Inflammatory lesion: sarcoidosis, TB, sphenoid mucocele

Suprasellar Mass with Calcification

A. CURVILINEAR
   1. Giant carotid aneurysm
   2. Craniopharyngioma

B. GRANULAR

1. Craniopharyngioma
2. Meningioma
3. Granuloma
4. Dermoid cyst / teratoma
5. Optic / hypothalamic glioma (rare)

Hyperintense Suprasellar Mass on T1WI

1. Craniopharyngioma
   √ viscous material in cystic region (protein concentration of 10-30%)
   √ intrasellar component in 70%
2. Germinoma
   √ hemorrhagic mass → methemoglobin
   • most common in adolescent girls
   • diabetes insipidus
3. Thrombosed aneurysm
   √ laminated internal architecture ← thrombus of differing age (best appreciated on T2WI)
4. Rathke cleft cyst
   √ containing thickly mucinous material
   √ no contrast enhancement
   √ intra- / suprasellar in location
5. Dermoid cyst
   √ with predominantly sebaceous material
   √ suppressed by fat saturation scan
6. Lipoma at floor of 3rd ventricle
   √ round + homogeneous
   √ suppressed by fat saturation scan
7. Ectopic neurohypophysis
   √ along floor of 3rd ventricle
   √ quite small
8. Cavernous angioma
   = collection of sinusoidal spaces
   • occasionally familial
   √ multinodular "popcorn" aggregate with central zones of T1 shortening surrounded by rind of T2 shortening
   √ frequently multiple
   √ angiographically occult /cryptic
9. Hemorrhagic metastasis

Suprasellar Mass with Uniform Enhancement

1. Pituitary adenoma
2. Pituitary Hyperplasia
   √ symmetrical masslike contour
   • appropriate clinical setting (hypothyroidism, pregnancy)
3. Meningioma

√ midline suprasellar lesion

4. Lymphocytic adenohypophysitis
   - usually in women during postpartum period
   - diabetes insipidus common

   √ suprasellar extension common
5. Chiasmatic / hypothalamic glioma
6. Unusual craniopharyngioma
7. Langerhans histiocytosis
8. Germinoma

Enhancing Supra- and Intrasellar Mass

1. Pituitary adenoma
2. Meningioma
3. Germinoma
4. Hypothalamic glioma
5. Craniopharyngioma

Perisellar Vascular Lesion

1. ICA aneurysm

   ◊ Giant aneurysms are those > 2.5 cm in diameter

   √ destruction of bony sella / superior orbital fissure

   √ calcified wall / thrombus

   √ CECT enhancement, nonuniform with thrombosis
2. Ectatic carotid artery

   √ curvilinear calcifications

   √ encroachment upon sella turcica
3. Carotid-cavernous sinus fistula

Lesion Expanding Cavernous Sinus

A. TUMOR
   1. Trigeminal schwannoma
   2. Pituitary adenoma
   3. Parasellar meningioma
   4. Parasellar metastasis
   5. Invasion by tumor of skull base

B. VESSEL
   1. Internal carotid artery aneurysm
   2. Carotid-cavernous fistula
   3. Cavernous sinus thrombosis

C. Tolosa-Hunt syndrome (← cavernous sinus inflammation)

PINEAL GLAND

Classification of Pineal Gland Tumors

Incidence of pineal mass:

< 1% of all intracranial tumors in adults; 3–8% of all intracranial masses in childhood; 9% of all intracranial masses in Asia

Symptoms of pineal region mass:

Cause: invasion / compression of tectal plate

- **Parinaud syndrome**:
  1. Failure of conjugate vertical eye movement (= paralysis of upward gaze)
  2. Failure of ocular convergence
  3. Mydriasis
  4. Blepharospasm (= eyelid contraction or twitch)
- precocious puberty = secretion of hCG by tumor (more common with germ cell tumor)
- pineal apoplexy = hemorrhage into pineal tumor / cyst:
  - sudden decrease in consciousness, headache

√ hydrocephalus ← obstruction of aqueduct of Sylvius:

- headache, nausea, vomiting

A. PRIMARY TUMOR

(a) Germ cell tumors (⅔)

Frequency: 0.4–3.4% of pediatric brain tumors in Western countries; up to 11% of those in Japan / other Asian countries

Age: 10–30 years; M÷F = 3÷1

› forming embryonic tissue

1. Germinoma (40–50%)
2. Teratoma (15%)
3. Embryonal carcinoma

› forming extraembryonic tissue

4. Choriocarcinoma (< 5%)
5. Endodermal sinus tumor = yolk sac tumor
6. Mixed germ cell tumor

(b) Pineal parenchymal cell origin (< 15%)

1. Pineocytoma
2. Pineoblastoma

Pineal parenchymal cell tumors expand and obliterate the pineal architecture → "exploding" normal pineal calcifications toward the periphery

(c) Other cell origin

1. Trilateral retinoblastoma
2. Astrocytoma (pineal + tectal glioma)
3. Meningioma
4. Lipoma
5. Ependymoma
6. Hemangiopericytoma
7. Cavernous hemangioma

(d) Cysts

1. Pineal cyst
2. Malignant teratoma
3. AVM, vein of Galen aneurysm

4. Arachnoid cyst
5. Congenital inclusion cysts (dermoid, epidermoid)

B. SECONDARY TUMOR

Metastasis: 0.4–3.8% in patients with solid tumors; lung > breast > kidney > esophagus > stomach > colon

DDx considerations:

female:	likely NOT germ cell tumor
hypodense matrix:	likely NOT pineal cell tumor
distinct tumor margins:	probably pineocytoma / teratoma / germinoma
calcification:	likely NOT teratocarcinoma, metastasis, germinoma
engulfed calcifications:	germinoma
CSF seeding:	NOT teratoma
intense enhancement:	likely NOT teratoma

Serum (oncoprotein) markers:

choriocarcinoma	β-hCG
embryonal cell carcinoma	α-FP and β-hCG
endodermal sinus tumor	α-FP
teratoma	β-hCG and α-FP
germinoma	placental alkaline phosphatase

Presence of oncoproteins / engulfment of pineal calcifications help narrow the differential diagnosis.

Intensely Enhancing Mass in Pineal Region

1. Germinoma
2. Pineocytoma / pineoblastoma
3. Pineal teratocarcinoma
4. Glioma of brainstem / thalamus
5. Subsplenial meningioma
6. Vein of Galen aneurysm

COMPLICATIONS OF BRAIN SURGERY

A. INFECTION (< 1%)

1. Bone flap infection (44% of all infections)
   At risk: postoperative CSF leakage, breach of paranasal sinuses, septic surgery performed for active infection, source of intracerebral contamination (compound skull fracture / penetrating injury)
2. Meningitis
3. Extradural abscess (0.43% of all craniotomies)
4. Subdural empyema (0.11% of all craniotomies)
5. Brain abscess

B. PERTAINING TO CRANIOTOMY / CRANIECTOMY

1. **Extracranial herniation** after decompressive craniectomy
   Cause: created craniectomy defect too small

Cx: compression of cortical veins → venous infarction; contusion of brain at craniectomy margins

2. **Subdural / subgaleal hygroma** (21–50%)
   Cause: disturbance of CSF circulation after craniectomy
   Location: fluid collection ipsilateral to craniectomy / contralateral / interhemispheric space
   Timing: appearance within days of surgery, resorption over weeks to months
3. **External brain tamponade**
   Cause: subgaleal fluid accumulates under pressure and pushes on the brain across craniectomy defect
   √ bulging skin flap + subgaleal fluid collection
4. **Trephine syndrome** (13%)
   = sinking skin flap syndrome = syndrome of the trephined
   Cause: atmospheric pressure + gravity overwhelm intracranial pressures → brain appears sunken
   Time after surgery: 28–188 days
   • headaches, seizures, dizziness, undue fatigability
   √ depressed skin flap at craniectomy site
   √ concave deformity of adjacent brain
5. Postsurgical brain herniation (see below)

C. HEMORRHAGE

1. "**Plunging**" = inadvertent breach of dura during drilling
   Cx: intracerebral hematoma (71%), cortical laceration (16%), extradural hematoma (5%), subdural hematoma (5%), intraventricular hemorrhage (3%)
2. Postoperative hemorrhage (6–7%)
   Location: intraparenchymal (43%), extradural (33%), subdural (5%), mixed (8%)
3. Extradural hematoma
   Location: regional (63%) = beneath bone flap; adjacent (31%) = at craniotomy margins: remote (6%) = distant to craniotomy site
4. Intraparenchymal hemorrhage (11%)
5. **Remote cerebellar hemorrhage**
   = CSF volume depletion → sagging of cerebellum → occlusion of superior bridging veins → hemorrhagic infarction
   √ "zebra" sign = streaky curvilinear areas of increased attenuation in cerebellar sulci + folia

Postsurgical Brain Herniation

Fungus Cerebri

= EXTRACRANIAL HERNIATION
= herniation of brain tissue through skull defect after trauma / therapeutic craniectomy
Cx: brain infarction

Paradoxical Brain Herniation

= SYNDROME OF THE TREPHINED

◊ Neurosurgical emergency!

• mesodiencephalic herniation syndrome: depressed level of consciousness, autonomic instability, signs of brainstem release, focal neurologic deficits

At risk: large craniectomy defect followed by CSF drainage procedure (lumbar puncture, external ventricular drainage, ventriculoperitoneal shunting)

Pathophysiology:

decrease in CSF pressure → reduction in intracranial pressure to below atmospheric pressure

√ sunken skin flap

√ subfalcine / transtentorial herniation of brain away from craniectomy defect:

- √ midline shift
- √ compression of midbrain
- √ effacement of basal cisterns

Rx: Trendelenburg position, clamping of ventricular shunt / drain, intravenous fluid, lumbar epidural blood patch, performing early cranioplasty to restore continuity of calvaria

Tension Pneumocephalus

◊ Rare life-threatening neurosurgical emergency!

= commonly following neurosurgical decompression of subdural hematoma / posterior fossa craniotomy

Cause: air enters via subdural defect → check-valve mechanism prevents escape of air → increasing intracranial pressure

• falling Glasgow coma scale

√ "peaking" sign = subdural air collections compress both frontal lobes

√ "Mount Fuji" sign = compression and separation of frontal lobes by air → widening of interhemispheric space

√ transtentorial ± tonsillar herniation

ANATOMY OF THE NERVOUS SYSTEM

EMBRYOLOGY

Neurulation

neural plate	=	CNS originates as a plate of thickened ectoderm on the dorsal aspect of the embryo
neural crest	=	elevation of the lateral margins of the neural plate; forms the peripheral nervous system
neural tube	=	invagination between the 2 neural crests; its wall forms the brain + spinal cord; its lumen forms the ventricles + spinal canal
4.6 weeks MA:		formation of neural tube
5.6 weeks MA:		rostral neuropore closes
5.9 weeks MA:		caudal neuropore closes
6.0 weeks MA:		3 primary brain vesicles develop (prosencephalon, mesencephalon, rhombencephalon) + development of cervical flexure
6.5 weeks MA:		prosencephalon cleaves into telencephalon anteriorly + diencephalon posteriorly
7.0 weeks MA:		2 additional primary brain vesicles form out of rhombencephalon (pontine flexure divides into myelencephalon, metencephalon)
15 weeks MA:		dorsal portion of alar plates bulging into 4th ventricle have fused in midline to form cerebellar vermis

Brain Growth

= increase in thickness of brain mantle with relative constant ventricular width

◊ Most rapid brain growth from 12 to 24 weeks MA!

Sulcal Development

10 weeks MA:	interhemispheric fissure ← longitudinal cleavage
14–19 weeks	sylvian fissure
16–22 weeks	calcarine, parieto-occipital, cingulate sulci
20–25 weeks	rolandic sulcus
23–26 weeks	superior temporal + intraparietal sulci
26–28 weeks	superior frontal, pre- and postcentral, middle temporal sulci
34 weeks	all primary + most secondary sulci present

Neuronal Migration

7th week	subependymal neuronal proliferation = germinal matrix depicted as low SI band along ventricular wall on T2WI

Germinal Matrix

= highly vascular gelatinous subependymal tissue adjacent to lateral ventricles in which the cells that compose the brain are generated; has its largest volume around 26 weeks GA; decreases in size with increasing fetal maturity; usually involutes by 32–34 weeks of gestation

Location: greatest portion of germinal matrix above caudate nucleus in floor of lateral ventricle, tapering as it sweeps from frontal horn posteriorly into temporal horn, roof of 3rd + 4th ventricle

Arterial supply: via Heubner artery from ACA, striate branches of MCA, anterior choroidal a., perforating branches from meningeal a.

Capillary network: persisting immature vascular rete = large irregular endothelial-lined channels devoid of connective tissue support (collagen and muscle)

Venous drainage: terminal vv., choroidal v., thalamostriate v. course anteriorly + feed into internal cerebral v. which has a posterior course

Myelination

Progression: caudal to rostral; posterior to anterior; center to periphery

MR: T1WI if < 7 months of age; T2WI if > 7 months of age

Milestones:

term birth: brainstem, cerebellum, posterior limb of internal capsule

2 months: anterior limb of internal capsule

3 months: splenium of corpus callosum

6 months: genu of corpus callosum

Occipital white matter:

√ central at 5 months (T1WI), 14 months (T2WI)

√ peripheral at 7 months (T1WI), 15 months (T2WI)

Frontal white matter:

√ central at 6 months (T1WI), 16 months (T2WI)

√ peripheral at 11 months (T1WI), 18 months (T2WI)

MENINGES OF BRAIN

A. CALVARIA = upper part of cranium enclosing the brain
   (a) outer table of resilient compact bone
   (b) diploë = trabecular bone containing red bone marrow
   (c) inner table of thin and brittle compact bone

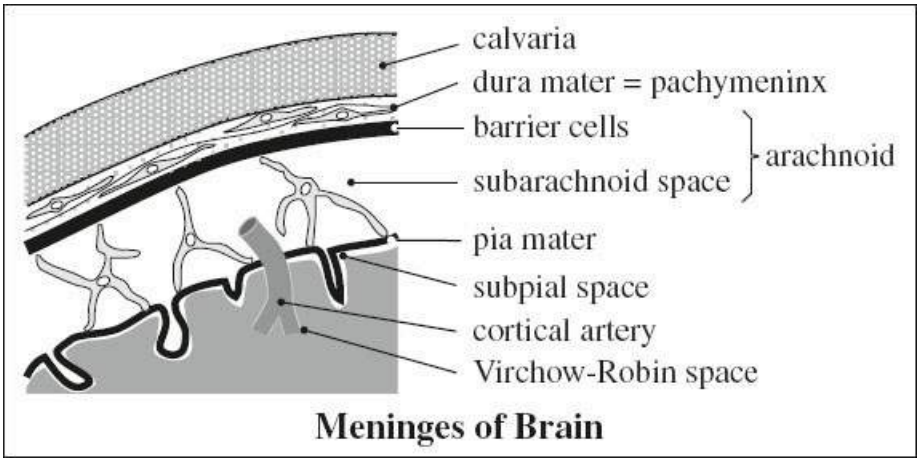
B. EPIDURAL SPACE
   = created when outer layer of dura (periosteum of inner table) becomes detached from calvaria

C. PACHYMENINGES = DURA MATER
   = thick inelastic membrane composed of 2 layers of fibrous + elastic connective tissue that are fused except for a separation allowing the passage of dural venous sinuses
   (a) outer endosteal dural layer
      = highly vascularized periosteum of inner table containing blood vessels that supply the bone

(b) space for venous sinuses
(c) inner meningeal dural layer
= protective meningeal layer lined on its inner brain surface by layer of mesothelium derived from meninx
→ extensions are reduplications of the meningeal layer projecting into skull cavity to form falx cerebri, tentorium cerebelli, falx cerebelli, diaphragma sellae

D. SUBDURAL SPACE
= cleft formed in pathologic states within inner layer of dura

E. LEPTOMENINGES
1. Arachnoid mater [*arakhnoeides*, Greek = like a cobweb]
= closely applied to inner surface of dura
2. Subarachnoid space



Meninges of Brain

Histo: fine connective tissue + cellular septa link pia and arachnoid
› contains CSF that drains through the valves of arachnoid granulations into venous sinuses
› forms basal cisterns

3. Pia mater [*pia* , Latin = tender]
= delicate innermost layer of meninges
Histo: thin fibrous tissue impermeable to fluid with perforations for blood vessels to pass through

F. SUBPIAL SPACE
= perivascular space = VR (Virchow-Robin) space
[Rudolf Virchow (1821–1902), pathologist in Berlin, Germany]
[Charles P. Robin (1821–1885), anatomist in Paris, France]
Histo: no communication with subarachnoid space; VR space around intracortical artery continues within subarachnoid space; VR space around cerebral vein is continuous with subpial space
Function: lymphatic drainage system of the brain
Sites: Type I = lenticulostriate arteries
Type II = medullary arteries over high convexities
Type III = collicular arteries in midbrain

√ smoothly demarcated typically < 5 mm fluid-filled cyst; often in clusters
√ SI visually similar to CSF (actually lower when measured as VR spaces are entrapments of interstitial fluid)
√ no restricted diffusion + no enhancement
√ inflow effects on flow-sensitive T1WI

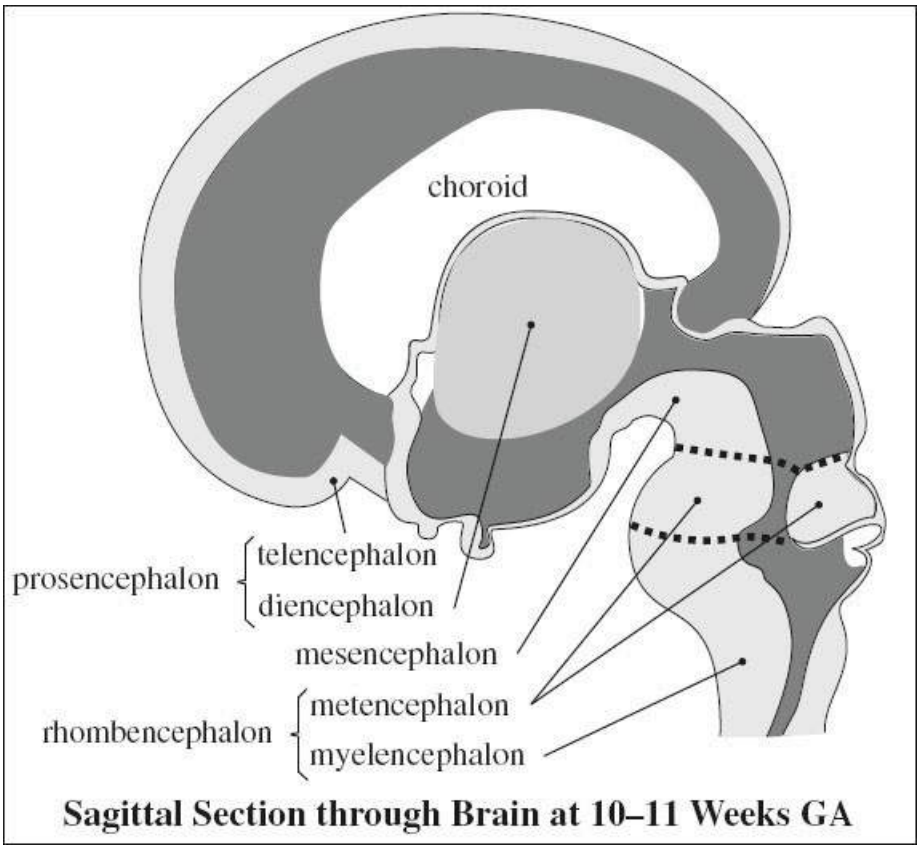
G. EPENDYMA
= thin epithelial-like lining of ventricular system + central canal of spinal cord composed of ciliated simple columnar ependymocytes
Origin: one of four types of neuroglia in CNS
Function: (1) Production + regulation of CSF, (2) Reservoir for neuroregeneration

Falx Cerebri [*falx*, Latin = curved blade or scythe]
= large crescent-shaped inelastic reflection of meningeal layer of dura mater that descends vertically in longitudinal fissure between cerebral hemispheres
Connected to:
(a) anteriorly: crista galli anteriorly in proximity to cribriform plate + frontal and ethmoid sinuses
(b) posteriorly: upper surface of the tentorium cerebelli
Margins:
(a) superior margin attached at midline to internal surface of skull as far back as internal occipital protuberance
› contains superior sagittal sinus overlying longitudinal cerebral fissure
(b) inferiorly adjacent to corpus callosum + cingulate gyrus + pericallosal arteries
› contains inferior sagittal sinus arching over corpus callosum deep in longitudinal cerebral fissure

Falx Cerebelli
= small sickle-shaped fold of dura mater projecting forward into posterior cerebellar notch + into cerebellar vallecula between cerebellar hemispheres
Base: attached to inferoposterior part of tentorium cerebelli
Posterior margin: attached to vertical crest of inner skull surface below internal occipital protuberance

CLASSIFICATION OF BRAIN ANATOMY

A. PROSENCEPHALON = forebrain
forms from process of ventral induction (ie, 3 closely interconnected sequential events of formation + cleavage + midline development)



√ cerebrum, lateral ventricles, choroid, thalami, cerebellum sonographically visible at 12 weeks MA

1. Telencephalon = cerebrum
   = cerebral hemispheres, putamen, caudate nucleus
2. Diencephalon
   = thalamus, hypothalamus, epithalamus (= pineal gland + habenula), globus pallidus, optic vesicles

B. MESENCEPHALON = midbrain
   = short segment of brainstem above pons; traverses the hiatus in tentorium cerebelli; contains cerebral peduncles, tectum, colliculi (corpora quadrigemina)

C. RHOMBENCEPHALON = hindbrain
   √ posterior cystic space of 4th ventricle sonographically detectable between 8 and 10 weeks MA
   1. Metencephalon = cerebellar hemispheres, vermis
   2. Myelencephalon = medulla oblongata, pons

D. BRAINSTEM = midbrain + pons + medulla contains
   (a) cranial nerve nuclei
   (b) sensory and motor tracts between thalamus, cerebral cortex, and spinal cord
   (c) reticular formation controlling respiration, blood pressure, gastrointestinal function, centers for arousal and wakefulness

THALAMUS

= midline structure situated between cerebral hemispheres + midbrain with paired symmetric portions

Location: on either side of 3rd ventricle

Function: relay of sensory + motor signals; regulation of consciousness, sleep, alertness

Blood supply: PCA + pCom

Hypothalamus [*hypo*, Greek = below; *thalamus*, Greek = bed]

= part of diencephalon below the thalamus

Origin: neuroectoderm

Boundaries:

(a) anterior = lamina terminalis extending from anterior commissure to optic chiasm
(b) posterior = line extending from mamillary bodies to posterior commissure
(c) lateral = medial thalamus
(d) inferior = tuber cinereum (posteriorly) + median eminence (middle) + infundibular stalk (anteriorly)

Function: homeostasis for blood pressure, body temperature, fluid + electrolyte balance, body weight

Regulatory mechanism:

(a) endocrine secretion:
› neuronal stimulation of posterior pituitary gland via infundibulum
› hypothalamic releasing factors to anterior pituitary gland via portal plexus as a vascular conduit
(b) autonomic function
(c) emotions

BASAL NUCLEI

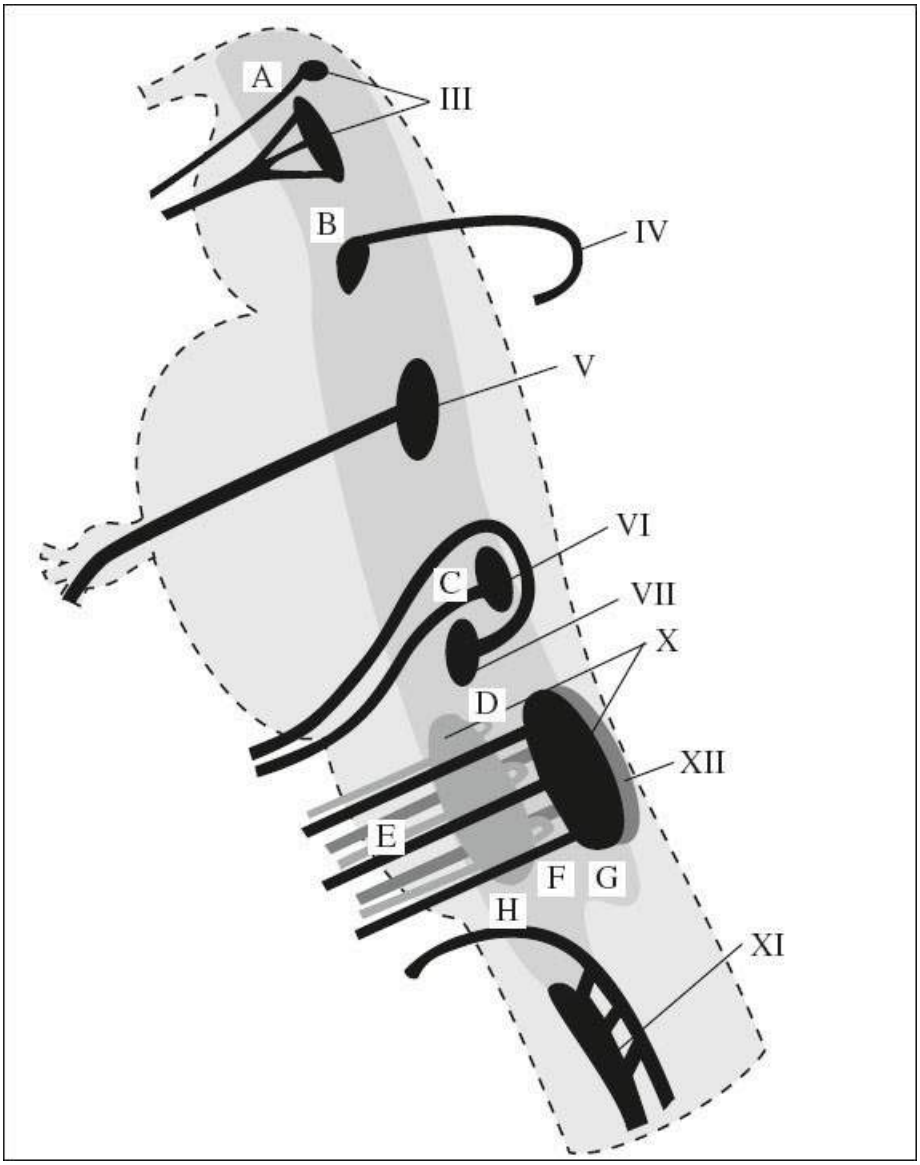
= BASAL GANGLIA (earlier incorrect designation)

Function: part of extrapyramidal motor system; involvement in memory, emotion, other cognitive function

Blood supply: ACA and MCA → medial + lateral lenticulostriate aa.

A. Amygdaloid body
B. Claustrum
C. Corpus striatum

Location: between lateral ventricle + insular cortex



Cranial Nuclei of Brainstem and Reticular Formation		
A	=	sleep, wakefulness, consciousness
B	=	visual spatial orientation, higher autonomic coordination of food intake
C	=	pneumotaxic center, coordination of breathing and circulation
D	=	swallowing
E	=	blood pressure, cardiac activity, vascular tone
F	=	expiration
G	=	area postrema = trigger zone for vomiting
H	=	inspiration

(1) Caudate nucleus
√ isointense to cortical gray matter on all pulse sequences
√ no enhancement
(2) Lentiform nucleus

√ may exhibit dilated Virchow-Robin perivascular spaces
√ may contain bilateral symmetric age-related calcifications
(a) pallidum = globus pallidus
√ slightly hypointense relative to putamen ← progressive iron deposition with age
(b) putamen
√ isointense to cortical gray matter on all pulse sequences
√ no enhancement

PITUITARY GLAND

= hypophysis cerebri within hypophyseal fossa of sphenoid, covered superiorly by sellar diaphragm (= dura mater) which has an aperture for the infundibulum centrally

Size: (adult size is achieved at puberty)
Height in adult females: 7 (range 4–10) mm
Height in adult males: 5 (range 3–7) mm
(normal height in men aged 40–49 = 4.89 ± 0.87 mm)

Shape:
√ flat / downwardly convex superior border
√ upwardly convex during puberty, pregnancy, in hypothyroidism (due to hyperplasia)

Anterior Lobe of Pituitary Gland

= larger anterior portion of adenohypophysis comprising 80% of pituitary gland volume

Origin: ectodermal derivative of stomadeum

Function:
(a) chromophil cells
1. acidophil cells = α cells
› growth hormone = somatotropin (STH)
› prolactin = lactogenic hormone (LTH)
2. basophil cells = β cells
› adrenocorticotropic hormone (ACTH)
› thyrotropin = thyroid-stimulating hormone (TSH)
› follicle-stimulating hormone (FSH)
› interstitial-cell-stimulating hormone (ICSH)
› luteinizing hormone (LH)
› melanocyte-stimulating hormone (MSH)

(b) chromophobe cells
50% of epithelial cell population, of unknown significance

MR:
√ larger homogeneous component isointense to white matter on T1WI + T2WI
√ prominent contrast enhancement (during first 3 minutes) ← lack of blood-brain barrier
√ hyperintense in newborn fading to normal adult signal by 2nd month of life

Pars Intermedia of Pituitary Gland

= posterior portion of adenohypophysis, separated from anterior lobe by hypophyseal cleft in fetal life

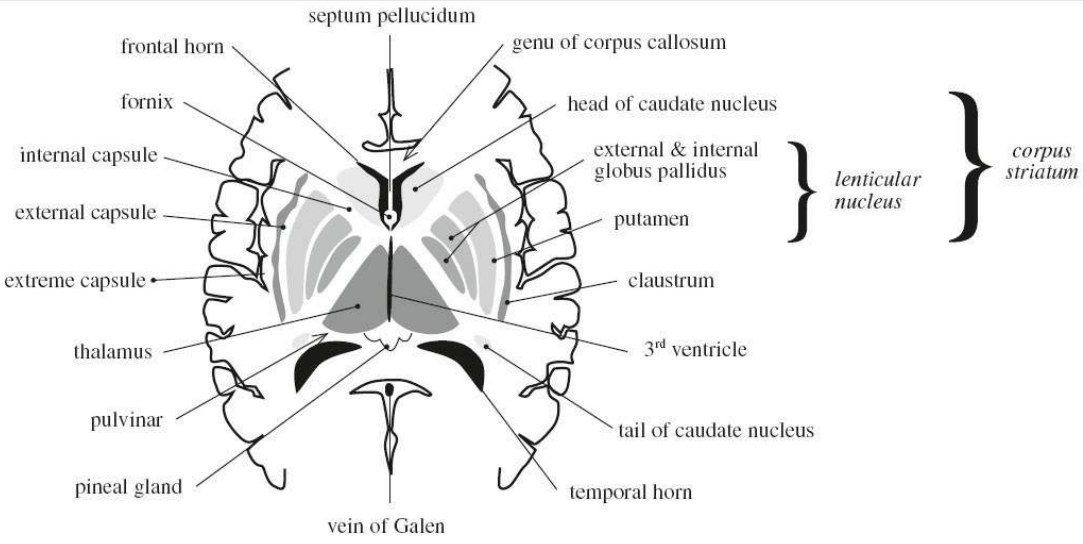
Origin: Rathke cleft / Rathke pouch within intermediate lobe of pituitary gland

Function: termination point of short hypothalamic axons elaborating tropic hormones (= releasing factors + prolactin inhibiting factor), which are carried to anterior lobe via the portal system

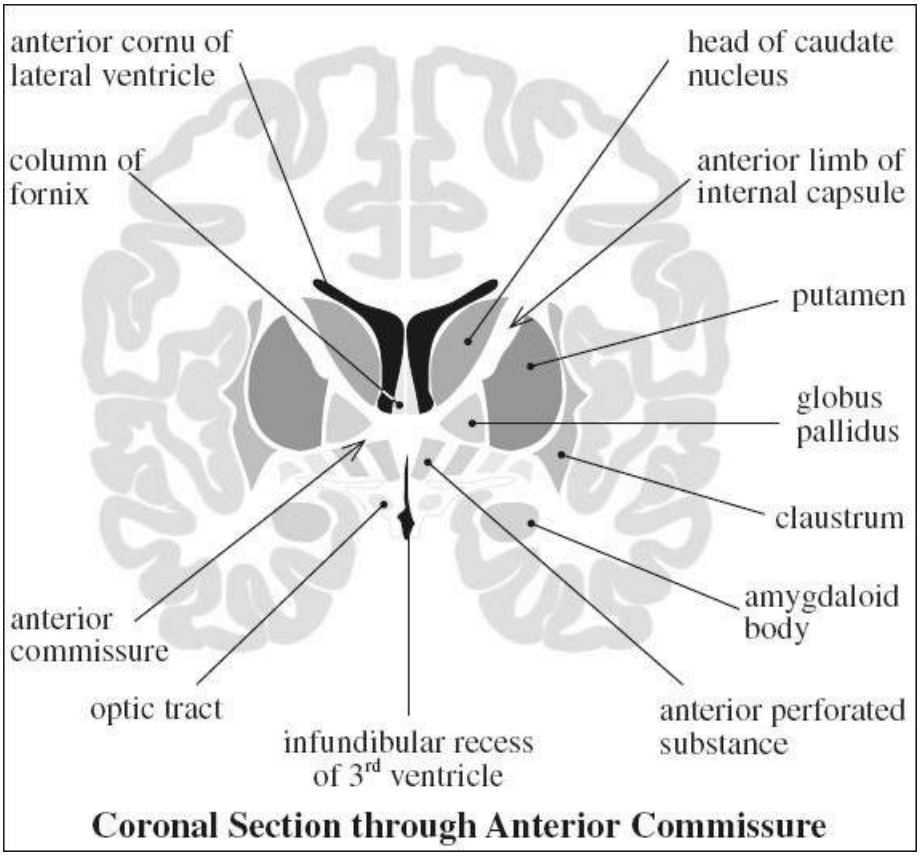
√ not visible with imaging techniques

Posterior Lobe of Pituitary Gland

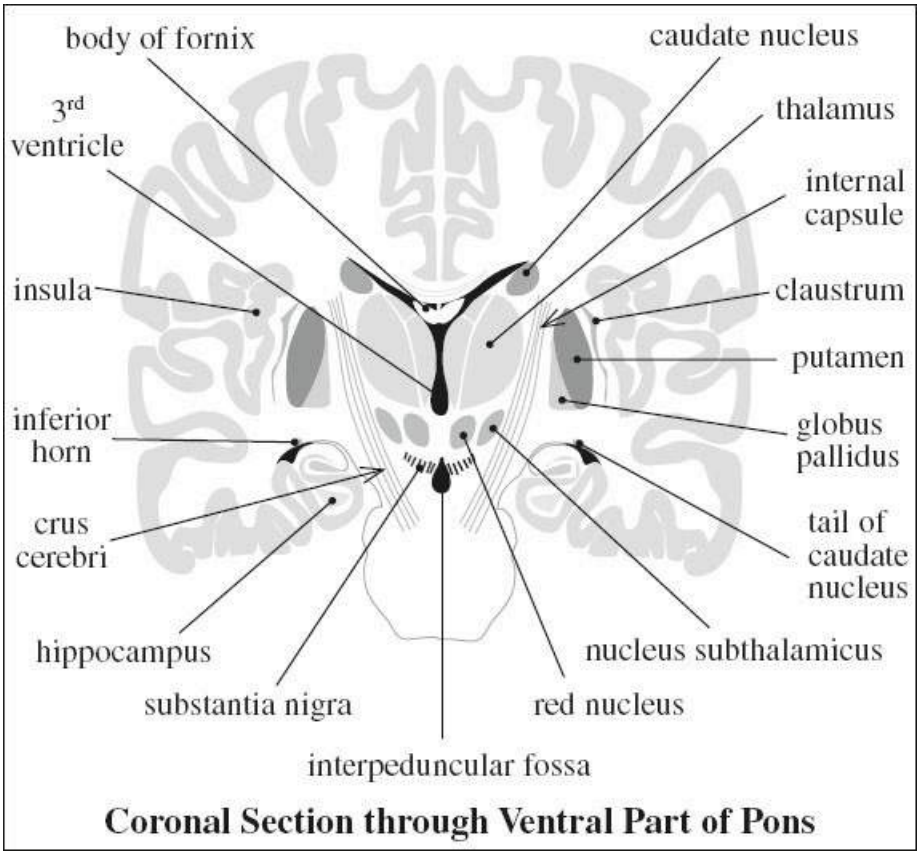
= major portion of neurohypophysis



Axial Section through Level of Third Ventricle



Coronal Section through Anterior Commissure



Coronal Section through Ventral Part of Pons

= termination point of neurosecretory axons from supraoptic and paraventricular nuclei of hypothalamus (= hypothalamohypophyseal tract)

Origin: diencephalic outgrowth

Function: storage site for transported
› vasopressin (= antidiuretic hormone [ADH])
› oxytocin

MR:
√ crescent of T1-hyperintensity + T2-isointensity compared with anterior pituitary lobe ← lipid in glial cell pituicytes + phospholipids of vasopressin
√ isointense in 10% of normal individuals

Pituitary Stalk / Infundibulum

Origin: arises from anterior aspect of floor of 3rd ventricle (infundibular recess)

Histo: formed from axons of cells lying in supraoptic + paraventricular nuclei of hypothalamus
√ joins posterior lobe at junction of anterior + posterior lobes
√ up to 3 mm thick superiorly, up to 2 mm thick inferiorly
√ usually in midline, may be slightly tilted to one side

MR:
√ prominent contrast enhancement

SEPTUM PELLUCIDUM

= 1.5–3.0 mm thin vertical membrane of triangular shape (when viewed from side)
› connecting corpus callosum to columns of fornix
› forming the medial wall of the lateral ventricles
› separating both anterior horns

Base of triangle: located anteriorly

Apex of triangle: located posteriorly

Five layers (leaves / laminae) of septum:
› CSF in anterior horn of RT lateral ventricle
› ependymal lining (gray matter) of RT lamina
› pial layer (white matter) of RT lamina
» potential space / slitlike cavity / cavum
› pial layer (white matter) of LT lamina
› ependymal lining (gray matter) of LT lamina
› CSF in anterior horn of LT lateral ventricle

Borders:
below: column + body of fornix
above: corpus callosum
ventral: continuous with precommissural septum + subcallosal gyrus
lateral: wall of lateral ventricles

Function: ?, part of limbic system moderating rage + arousal

Cavum Septi Pellucidi

= persistence / failure of fusion of potential space (= slitlike cavity = 5th ventricle) between the 2 laminae forming septum pellucidum

Frequency: in 80% of term infants; in 15% of adults
Location: posterior to genu of corpus callosum, inferior to body of corpus callosum, anterosuperior to anterior pillar of fornix
Marker for: cerebral dysfunction
√ extends to foramen of Monro
√ may dilate + cause obstructive hydrocephalus (rare)
Regression: from back to front as fetus approaches term / in first few weeks after birth

Cavum Vergae

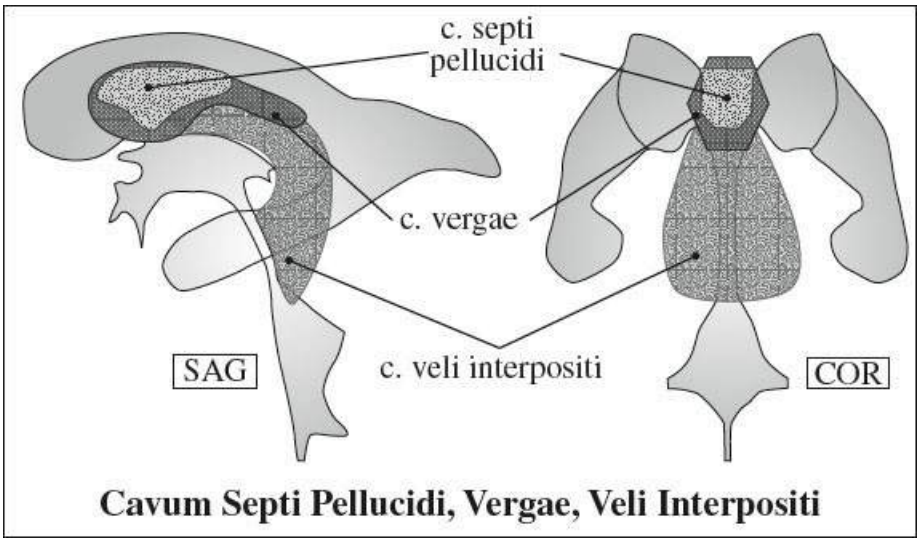
= "6th ventricle"
[Andrea Verga (1811–1895), clinical professor of psychiatry at Ospedale Maggiore in Milan, Italy]
= fluid-filled cavity located posterior to a vertical plane formed by columns of fornix
Frequency: in 30% of term infants; in 15% of adults
Location: posterior to fornix; anterior to splenium of corpus callosum inferior to body of corpus callosum superior to transverse fornix
√ posterior midline continuation of cavum septi pellucidi beyond foramen of Monro (= communicates with cavum septi pellucidi)
Regression: cavum vergae (1st) > cavum septi pellucidi (2nd); contracts after about 6th gestational month

VELUM INTERPOSITUM [*velum*, Latin = veil]

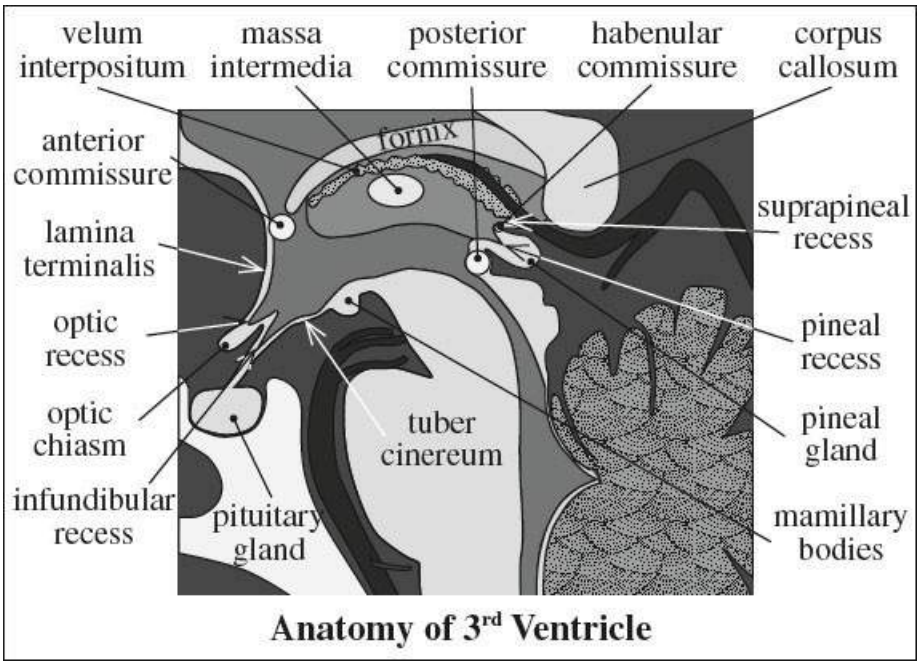
= small triangular (on axial view) membrane containing a closed space between the 2 layers of tela choroidea in the roof of the 3rd ventricle
Borders:
above: columns of fornices + hippocampal commissure
below: tela choroidea of 3rd ventricle, internal cerebral veins
lateral: thalamus
posterior: splenium of corpus callosum

Cavum Veli Interpositi

= anatomic variant characterized by dilated CSF space of the cistern of the velum interpositum / extension of quadrigeminal plate cistern above 3rd ventricle
Cause: abnormal separation of crura of fornices



Cavum Septi Pellucidi, Vergae, Veli Interpositi



Anatomy of 3rd Ventricle

√ triangular-shaped CSF space / cyst in pineal region
  › above tela choroidea of 3rd ventricle
  › below columns of fornices
√ separated from cavum vergae by crura of fornices

VENTRICLES

Third Ventricle

Position: in midline of diencephalon

Walls:

› inferiorly: curving floor of 3rd ventricle formed
  » anteriorly by median eminence and tuber cinereum

» posteriorly by mammillary bodies + midbrain posterior to tuber cinereum

› superiorly: curving roof with 5 layers:

(1) body of fornix

(2) superior layer of tela choroidea

(3) vascular layer = velum interpositum containing bathed in CSF:

(a) internal cerebral veins

(b) medial posterior choroidal arteries

(4) inferior layer of tela choroidea

(5) choroid plexus of 3rd ventricle

› superior lateral wall: formed by medial aspects of thalami

› inferior lateral wall: formed by hypothalamus anteriorly + subthalamus posteriorly

› massa intermedia = band of gray matter as a communication between 2 thalami across midline

› anteriorly: lamina terminalis

» anterosuperior border: anterior commissure

» anteroinferior border: optic chiasm

› posteriorly: pineal gland

Recesses: 2 anterior + 2 posterior recesses

(1) optic recess superiorly

(2) infundibular recess inferiorly = pars cava infundibuli formed by funnel-shaped proximal hypothalamic infundibulum (pituitary stalk)

» median eminence at base of infundibulum = raised portion of hypothalamic gray matter

(3) pineal recess in deep aspect of pineal gland

» posterior commissure in inferior wall of pineal recess

» habenular commissure in superior wall of pineal recess

(4) suprapineal recess above habenular commissure and below splenium of corpus callosum

Tela choroidea ventriculi tertii

= ependymal + glial layers forming choroid plexus (= richly vascularized tela) that projects into 3rd ventricle

(a) upper layer attached to lower surface of fornix

(b) lower layer attached anteriorly to stria medullaris thalami + posteriorly to superior surface of the pineal body

[*tela*, Latin = web], [*khorion*, Greek = membrane enclosing fetus, afterbirth] [chorioeides, Greek = membrane-like] [*plexus*, Latin = braid, network]

Interventricular Foramen of Monro

= Y-shaped communication between 2 lateral ventricles and 3rd ventricle

Location: posterior to anterior columns of fornix

Aqueduct of Sylvius

= opening at posterior aspect of 3rd ventricle below posterior commissure

MEGACISTERNA MAGNA

= GIANT CISTERNA MAGNA = ENLARGED CISTERNA MAGNA
= large retrocerebellar CSF space with normal vermis + cerebellar hemispheres
Prevalence: 1% of all brains
May be associated with: infarction, inflammation, infection (esp. CMV), chromosomal abnormalities (esp. trisomy 18)
Size of normal cisterna magna:
3–8 mm measured in midsagittal plane from posterior lip of foramen magnum to caudal margin of inferior vermis
√ intact vermis + normal 4th ventricle
√ paired linear echoes that join + descend toward base of posterior fossa = dural folds = inferior attachment of tentorium
√ NO enlarged posterior fossa, NO mass effect on cerebellum
DDx: arachnoid cyst

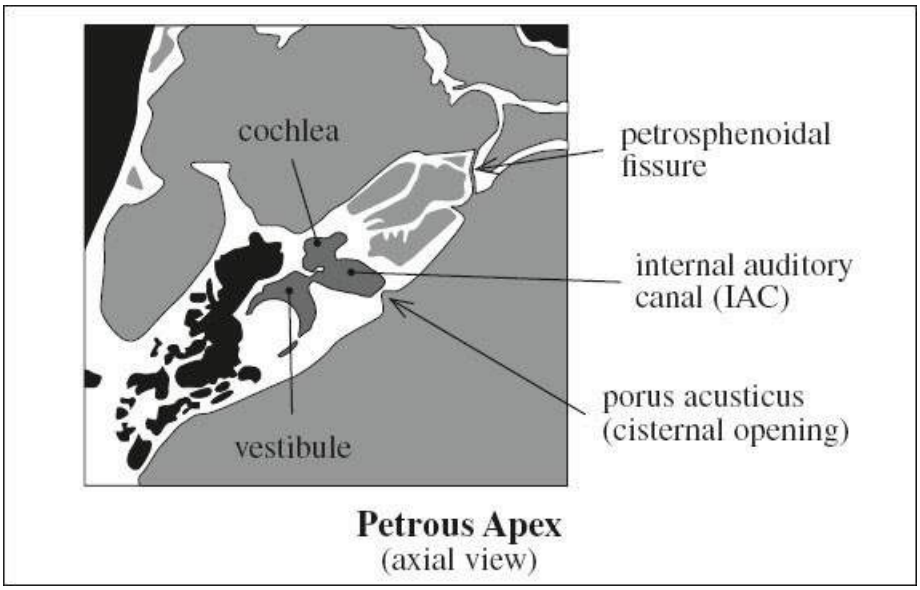
PINEAL GLAND

[*pinea* , Latin = pine cone]
= PINEAL BODY = EPIPHYSIS CEREBRI = "Third eye"
Development: diverticulum lined by ependyma at the most caudal portion of diencephalic roof of 3rd ventricle → area of ependymal thickening → evaginates into pinecone-shaped mass during 7th week GA
Function: secretion of melanin
1. Regulation of long-term biologic rhythm (eg, onset of puberty)
2. Regulation of short-term biologic rhythm (eg, diurnal / circadian) due to photoperiodic clues via accessory optic pathway

Histo:
(a) lobules of pineocytes with dendritic processes (= specialized neuronal cells related to retinal rods and cones) make up 95% of population
(b) astrocytes as neuroglial supporting cells = 5% of population
(c) fibrovascular stroma
(d) corpora arenacea = concentric calcifications appear in adolescence (in 40% of patients 17–29 years old)
[arenacea, *Latin* = sandy]

Location: midline
suspended from pineal stalk that is attached to upper aspect of posterior border of 3rd ventricle
(a) inferior to splenium + vein of Galen
(b) superior to tentorium + superior colliculi
(c) posterior to cistern of velum interpositum (= cistern of transverse fissure)
(d) surrounded by CSF of quadrigeminal cistern

Size: 10–14 mm
√ enhancement with contrast ← absence of blood-brain barrier



PETROUS APEX

= pyramid-shaped structure formed by medial portion of temporal bone

Borders:

lateral: inner ear
medial: petro-occipital fissure
anterior: petrosphenoidal fissure + internal auditory canal
posterior: posterior cranial fossa

Surfaces: superiorly: middle cranial fossa + Meckel cave + ICA
inferiorly: jugular bulb + inferior petrosal sinus

Division:

(a) large anterior portion (bone marrow):
- › filled with marrow (60%)
- › pneumatized (33%) with communication to mastoid and middle ear cavity; asymmetric (5–10%)

N.B.: with asymmetry high signal intensity fatty marrow may be mistaken for a cholesterol granuloma!

- › sclerotic (7%)

(b) small posterior portion (otic capsule)

N.B.: with asymmetry high–signal-intensity marrow in nonsclerotic apex can mimic a lesion!

Vascular & neural channels:

(1) **Petrous carotid canal** in anterior portion of petrous apex (= horizontal portion of petrous segment of ICA), passes over foramen lacerum
(2) **Internal auditory canal** (IAC) in midportion of petrous apex for vestibulocochlear + facial nn., anterolateral from cerebellopontine angle cistern
(3) **Dorello canal** extends through posteromedial portion of petrous apex, contains abducens n. (CN VI)

(4) **Subarcuate canal** = petromastoid canal between crura of superior semicircular canal, contains subarcuate a. (blood supply to bony labyrinth + facial canal + mastoid antrum)
(5) **Singular canal** extends from posterior margin of IAC to junction of ampulla of posterior semicircular canal and vestibule, contains singular n. (= division of inferior vestibular n. that innervates ampulla of posterior semicircular canal)
(6) **Meckel cave** = dura-lined diverticulum creating smooth depression along anterior aspect of petrous apex, contains trigeminal (gasserian / semilunar) ganglion + rootlets of trigeminal n. (CN V)

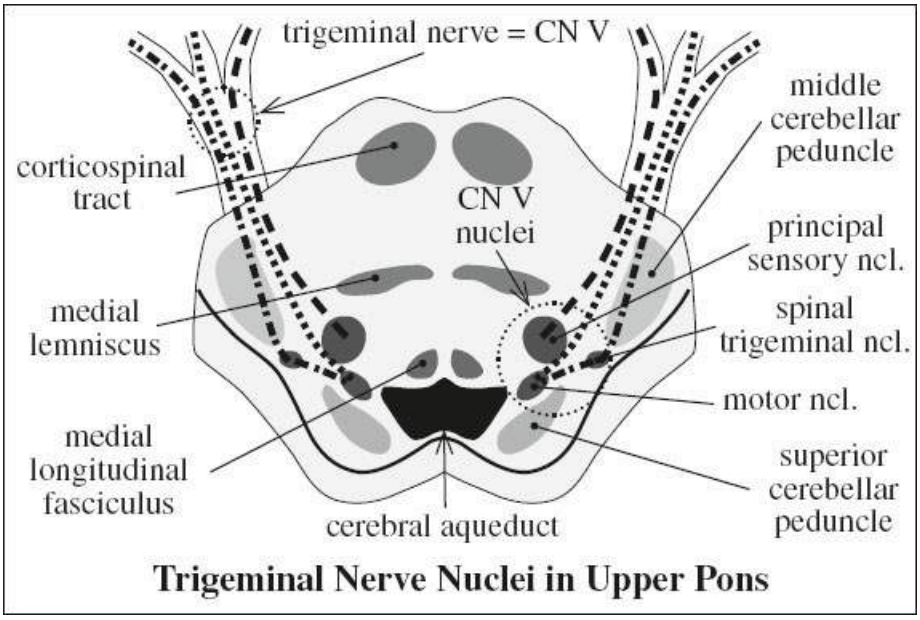
TRIGEMINAL NERVE (CN V)

Function: (1) sensation to face
(2) motor innervation to muscles of mastication

Nuclei: (3 sensory + 1 motor nucleus)
(1) mesencephalic nucleus: <u>proprioception</u> extends to level of inferior colliculus

Cranial Nerves

#	*Name*	*Nuclei*	*Function*
I	Olfactory	Anterior olfactory nucleus	Transmits sense of smell; Located in olfactory foramina of ethmoid
II	Optic	Lateral geniculate nucleus	Transmits visual information to brain; Located in optic canal
III	Oculomotor	Oculomotor nucleus, Edinger-Westphal nucleus	Innervates levator palpebrae superioris, superior rectus, medial rectus, inferior rectus, and inferior oblique; Located in superior orbital fissure
IV	Trochlear	Trochlear nucleus	Innervates superior oblique muscle; Located in superior orbital fissure
V	Trigeminal	Principal sensory trigeminal nucl., Spinal trigeminal nucleus, Mesencephalic trigeminal nucl., Trigeminal motor nucleus	Receives sensation from face and innervates muscles of mastication; Located in superior orbital fissure (ophthalmic branch), foramen rotundum (maxillary branch), and foramen ovale (mandibular branch)
VI	Abducens	Abducens nucleus	Innervates lateral rectus; Located in superior orbital fissure
VII	Facial	Facial nucleus, Solitary nucleus, Superior salivary nucleus	Provides motor innervation to muscles of facial expression and stapedius, receives special sense of taste from anterior ⅔ of tongue, and provides secretomotor innervation to salivary glands (except parotid) and lacrimal gland; Located and runs through internal acoustic canal to facial canal and exits at stylomastoid foramen
VIII	Vestibulocochlear (vestibular + statoacustic n .)	Vestibular nucleus, Cochlear nucleus.	Senses sound, rotation and gravity; Located in internal acoustic canal
IX	Glossopharyngeal	Nucleus ambiguus, Inferior salivary nucleus, Solitary nucleus	Receives taste from posterior ⅓ of tongue, provides secretomotor innervation to parotid gland, and provides motor innervation to stylopharyngeus (essential for tactile, pain, and thermal sensation). Sensation is relayed to opposite thalamus and some hypothalamic nuclei. Located in jugular foramen
X	Vagus	Nucleus ambiguus, Dorsal motor vagal nucleus, Solitary nucleus	Supplies branchiomotor innervation to most laryngeal and pharyngeal muscles; provides parasympathetic fibers to nearly all thoracic and abdominal viscera down to the splenic flexure; and receives special sense of taste from epiglottis. Major function: controls muscles for voice and resonance and soft palate. Located in jugular foramen
XI	Accessory	Nucleus ambiguus, Spinal accessory nucleus	Controls muscles of neck and overlaps with functions of vagus; Located in jugular foramen
XII	Hypoglossal	Hypoglossal nucleus	Provides motor innervation to muscles of tongue and other glossal muscles. Important for swallowing (bolus formation) and speech articulation. Located in hypoglossal canal
	mnemonic:	On Old Olympus Towering Tops A Finn And German Viewed Some Hops	



Trigeminal Nerve Nuclei in Upper Pons

(2) main sensory nucleus: tactile sensation
(3) motor nucleus: motor innervation
(4) spinal nucleus: pain + temperature sensation extends to level of 2nd cervical vertebra

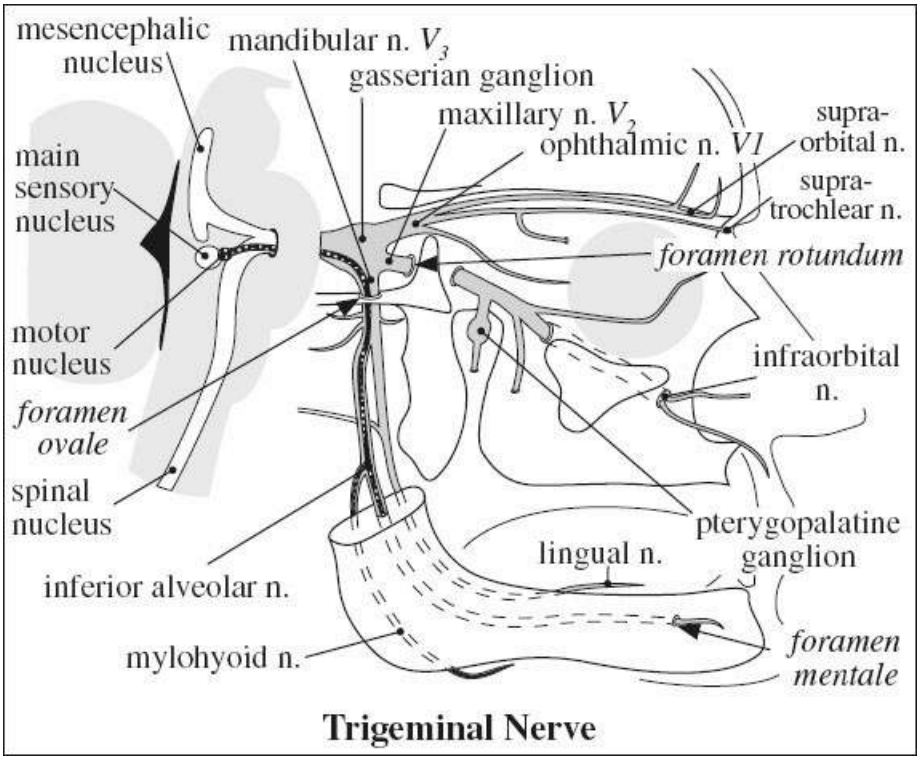
Location: tegmentum of lateral pons, along anterolateral aspect of 4th ventricle

Segments:

(1) cisternal portion exits lateral pons traversing prepontine cistern before passing underneath the tentorium to enter the middle cranial fossa at the petrous apex
(2) preganglionic portion passes through porus trigeminus (= opening in dura) into the Meckel cave (trigeminal cistern), where it synapses with trigeminal (= gasserian / semilunar) ganglion
Meckel cave: CSF-filled subarachnoid space formed by dura mater + leptomeninges at the most anteromedial portion of petrous pyramid
Gasserian ganglion: contains cell bodies of sensory fibers except those for proprioception
(3) postganglionic portion → trifurcation

Trifurcation into 3 principal branches:

(1) **Ophthalmic nerve** (V_1)
Course: travels within lateral cavernous sinus inferior to cranial nerve IV and superior to V_2
Exit: superior orbital fissure
Supply: sensory innervation of scalp, forehead, nose, globe
Division: lacrimal, frontal, nasociliary nn.
• mediates afferent aspect of corneal reflex



(2) **Maxillary nerve** (V_2)

Course: travels within lateral cavernous sinus inferior to V_1

Exit: through foramen rotundum into pterygopalatine fossa

Supply: sensory innervation of middle third of face, upper teeth

Main trunk: infraorbital nerve

(3) **Mandibular nerve** (V_3)

Course: NOT through cavernous sinus

Exit: from Meckel cave through foramen ovale into masticator space

Supply:

(a) sensory innervation of lower third of face, tongue, floor of mouth, jaw

(b) motor innervation of muscles of mastication (masseter, temporalis, medial + lateral pterygoid), mylohyoid m., anterior belly of digastric m., tensor tympani m., tensor veli palatini m.

Exits from Meckel cave:

mnemonic: **S**tanding **R**oom **O**nly

V_1 = **S**uperior orbital fissure

V_2 = Foramen **R**otundum

V_3 = Foramen **O**vale

FACIAL NERVE (CN VII)

Function: mixed nerve responsible for motor innervation of muscles of facial expression + taste of anterior ⅔ of tongue + parasympathetic innervation of lacrimal and submandibular glands

1. Lacrimation (via greater superficial petrosal nerve)
2. Stapedius reflex: sound damping
3. Taste of anterior ⅔ of tongue (via chorda tympani nerve to lingual nerve)
4. Facial expression (platysma + orbicularis oculi)
5. Secretion of lacrimal + submandibular + sublingual glands (via **nervus intermedius**)

Nuclei: one motor nucleus + two sensory nuclei located within ventrolateral pons

(1) Motor nucleus: ventrolateral deep in reticular formation of the caudal part of the pons
Innervation to: stapedius m., stylohyoid m., posterior belly of digastric m., occipitalis m., buccinator, muscles of facial expression, platysma

(2) Nucleus solitarius (sensory nucleus)
› **nervus intermedius**: sensation from anterior ⅔ of tongue, skin on + adjacent to ear

(3) Superior salivatory nucleus (parasympathetic secretomotor innervation)
› greater petrosal n.: secretion of lacrimal glands, nasal cavity, paranasal sinuses
› chorda tympani: submandibular + sublingual glands

Exit from brainstem: 2 separate nerve roots traversing cerebellopontine angle cistern
(1) motor root anteriorly
(2) sensory root posteriorly

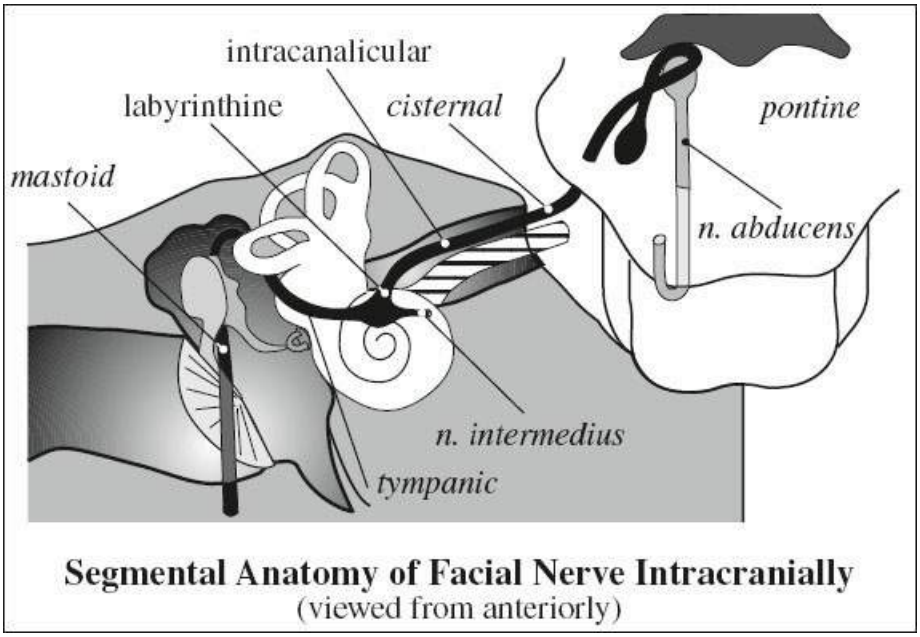
Segments: circuitous course

(a) intracranial segment from brainstem to porus acusticus internus:
› pontine segment:
» motor root fibers of facial n. run dorsomedially towards 4th ventricle
» curve anterolaterally to hook around upper pole of abducens nucleus (= **geniculum**)
» form **facial colliculus** (= elevation in floor of 4th ventricle)
» nerve descends anterolaterally through reticular formation + continues lateral from corticospinal tract
› cisternal segment:
» facial n. exits from lateral aspect of brainstem at pontomedullary junction
» courses anterolaterally in **cerebellopontine angle cistern** to internal auditory canal (IAC) above crista falciformis

(b) intracanalicular (IAC) segment

(c) labyrinthine segment emerges from anterosuperior aspect of IAC
› 3–4 mm short segment of facial n. traveling anterolaterally within its own bony canal (= **fallopian canal**) and curving anteromedially over top of cochlea
› terminates in anteromedial genu (**geniculate ganglion**) where greater superficial petrosal n. branches pass anteromedially to carry parasympathetic fibers to lacrimal gland

(d) tympanic segment
= 12 mm long segment from geniculate ganglion to posterior genu underneath lateral semicircular canal
› horizontal segment: facial n. at **first (anterior) genu** makes a 130° turn posteriorly + horizontally along medial wall of mesotympanum lateral to vestibule between lateral semicircular canal (above) and oval window (below) to reach sinus tympani
√ "snake eyes" on COR CT at level of cochlea corresponding to proximal portion of tympanic + distal portion of labyrinthine segments



Segmental Anatomy of Facial Nerve Intracranially
(viewed from anteriorly)

√ inferior to lateral semicircular canal + superolateral to oval window on COR CT at level of oval window

√ anterior genu superomedial to cochlear promontory

› pyramidal segment: at sinus tympani facial n. turns gently posteroinferiorly to form **second / posterior genu** in pyramidal eminence; gives off the nerve for the stapedius muscle

(e) mastoid segment (longest segment with 15–20 mm)

facial n. assumes a more vertical position + descends just behind the posterior wall of the tympanic cavity from posterior genu through anterior mastoid (= medial wall of aditus ad antrum) + gives off chorda tympani just prior to exit from skull base through **stylomastoid foramen**

(f) parotid / extracranial segment

facial n. travels forward between superficial + deep lobes of parotid gland lateral to styloid process + external carotid a. + retromandibular v.

Branches:

(1) **Greater superficial petrosal nerve** (parasympathetic + motor fibers) arises from geniculate ganglion, runs anteromedially, and exits at the facial hiatus on the anterior surface of the temporal bone + passes under Meckel cave near foramen lacerum

› forms **vidian nerve** after receiving sympathetic fibers from deep petrosal nerve, which surrounds the internal carotid artery

(2) **Stapedial nerve** (motor fibers) arises from proximal descending facial n.

(3) **Chorda tympani** (sensory + parasympathetic fibers) leaves facial n. about 5–6 mm above stylomastoid foramen from the lateral aspect of the mastoid segment of the facial nerve

› ascends in subtle curvature superoanteriorly in a bony canal (= canaliculus chorda tympani)

› perforates posterior wall of tympanic cavity

› proceeds anteriorly within tympanic cavity and crosses medial to handle of malleolus

underneath mucosa of tympanic cavity

› exits temporal bone through a minute canal (= anterior canaliculus) near petrotympanic fissure

› joins lingual nerve (= branch of V_2) containing sensory taste fibers from anterior ⅔ of tongue + secretomotor fibers for submandibular + sublingual glands

VESTIBULOCOCHLEAR NERVE (CN VIII)

Function: sensory nerve unified only within cisternal segment

Two main components:

(1) **Vestibular nerve** for balance

Course: arises from the Scarpa ganglion in IAC fundus

Division:

› central fibers coalesce to form **superior & inferior vestibular nerves**

Location: posterior aspect of IAC; components separated from each other by crista falciformis

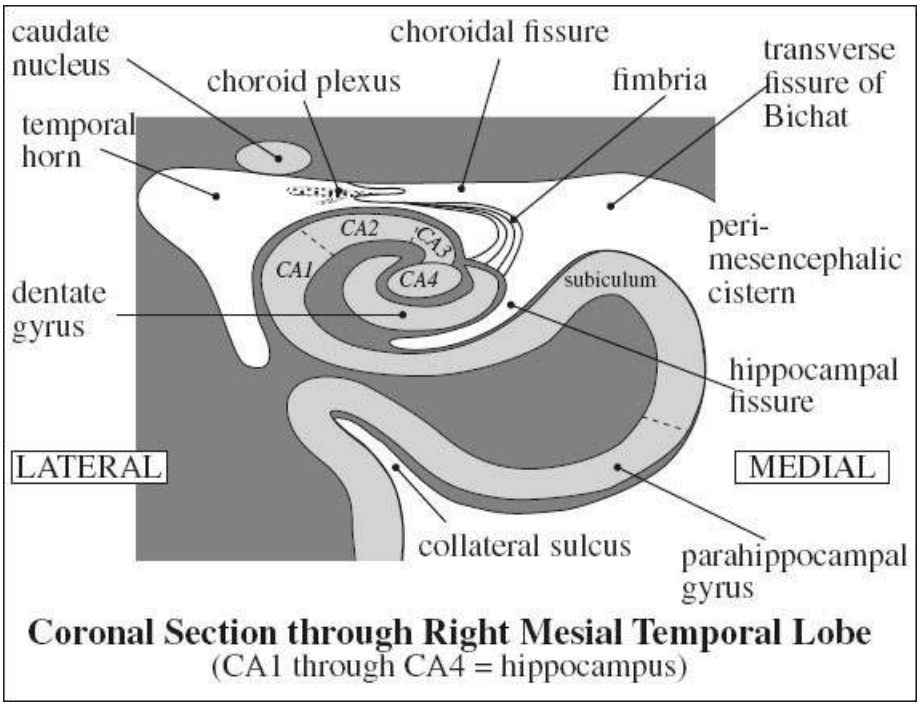
› peripheral fibers innervate sensory epithelium of utricle, saccule, and semicircular canals

(2) **Cochlear nerve** for hearing

Dysfunction:

damage from ***superficial siderosis*** ← hemosiderin ← slow / repeated episodes of subarachnoid hemorrhage exposing its long cisternal segment

√ deposition of hemosiderin within cerebellar folia + surrounding brainstem + along cisternal segment of CN VIII visible on gradient-echo T2*-weighted MR images



Coronal Section through Right Mesial Temporal Lobe
(CA1 through CA4 = hippocampus)

PERIHIPPOCAMPAL FISSURES

1. Transverse fissure of Bichat
   = lateral extension of perimesencephalic cistern separating thalamus superiorly from parahippocampal gyrus inferiorly
2. Choroidal fissure
   = superior lateral extension of transverse fissure extending superior to hippocampus
3. Hippocampal fissure
   = inferior lateral extension of transverse fissure extending between hippocampus and parahippocampal gyrus
4. Temporal horn of lateral ventricle
   = lateral margin of hippocampus; separated from transverse fissure by fimbria + choroid plexus
   ◊ Does not communicate with transverse fissure

Uncus [*uncus*, Latin = hook]
= medial protrusion near ventral surface of parahippocampal gyrus (= innermost gyrus) of temporal lobe
Function: part of primary olfactory area

CEREBROSPINAL FLUID

Total volume: 50 mL in newborn, 150 mL in adult
Composition: inorganic salts like those in plasma, traces of protein + glucose
Production: 0.3–0.4 mL/min resulting in 500 mL/day; secreted into ventricles by choroid plexuses (80–90%), 10–20% from parenchyma of cerebrum and spinal cord
Circulation:
from ventricles through foramina of Magendie + Luschka of 4th ventricle into cisterna magna + basilar cisterns; 80% of CSF flows initially into suprasellar cistern + cistern of lamina terminalis, ambient / superior cerebellar cisterns → eventually ascending over superolateral aspects of each hemisphere; 20% initially enters spinal subarachnoid space + eventually recirculates into cerebral subarachnoid space
Absorption: into venous system by
(a) arachnoid villi of superior sagittal sinus (villi behave as one-way valves with an opening pressure between 20–50 mm of CSF)
(b) cranial + spinal nerves with eventual absorption by lymphatics (50%)
(c) prelymphatic channels of capillaries within brain parenchyma
(d) vertebral venous plexuses, intervertebral veins, posterior intercostal + upper lumbar veins into azygos + hemiazygos veins
Opening pressure: 80–180 mm H_2O

Cerebral Aqueduct

pulsatile flow (← brain motion during cardiac cycle) + net outflow into 4th ventricle; diameter of 2.6–4.2 mm; peak outflow velocity of 6–51 mm/sec; inflow velocity of 3–28 mm/sec

CEREBRAL VESSELS

Common Carotid Artery

- 70% of blood flow is delivered to ICA

√ shares waveform characteristics of both internal + external carotid arteries

√ velocity increases toward the aorta (9 cm/sec for each cm of distance from the carotid bifurcation)

Carotid Bifurcation

= physiologic stenosis ← inertial forces of blood flow diverting main-flow stream from midvessel to a path along vessel margin at flow divider

Location: lateral to upper border of thyroid cartilage; at level of C3-4 intervertebral disk

Branches: ECA arises anterior + medial to ICA (95%)

External Carotid Artery Branches

mnemonic: **A**ll **S**ummer **L**ong **E**mily **O**gled **P**eter's **S**porty **I**suzu

Ascending pharyngeal artery
Superior thyroid artery
Lingual artery
External maxillary = facial artery
Occipital artery
Posterior auricular artery
Superficial temporal artery
Internal maxillary artery

Internal Carotid Artery

A. CERVICAL SEGMENT

ascends posterior and medial to ECA; enters carotid canal of petrous bone; NO branches

Carotid bulb = carotid sinus:

= dilated proximal part of ICA with thinner media + thicker adventitia containing many receptor endings of glossopharyngeal nerve

Function: baroreceptor responsive to changes in arterial blood pressure

- hypersensitive carotid sinus

= slight touch / head movement initiates

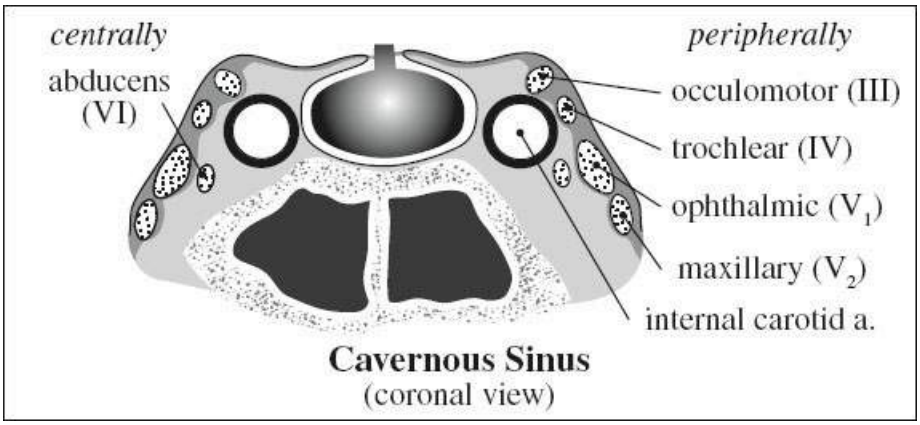
(a) vasodilatation with drop in blood pressure

(b) vagal stimulation with sinoatrial / atrioventricular cardiac block

√ stagnant eddy that rotates at outer vessel margin

B. PETROUS SEGMENT

ascends briefly in carotid canal → bends anteromedially in a horizontal course (anterior to tympanic cavity and cochlea); exits near petrous apex through posterior portion of foramen lacerum; ascends to juxtasellar location where it pierces dural layer of cavernous sinus



Branches:

1. **Caroticotympanic a.**: to tympanic cavity, anastomoses with anterior tympanic branch of maxillary a. + stylomastoid a.
2. **Pterygoid (vidian) a.**: through pterygoid canal; anastomoses with recurrent branch of greater palatine a.

C. CAVERNOUS SEGMENT

ascends to posterior clinoid process → then turns anteriorly + superomedially through cavernous sinus; exits medial to anterior clinoid process piercing dura

Branches:

1. **Meningohypophyseal trunk**
   (a) tentorial branch
   (b) dorsal meningeal branch
   (c) inferior hypophyseal branch
2. **Anterior meningeal a.**: supplies dura of anterior fossa; anastomoses with meningeal branch of posterior ethmoidal a.
3. Cavernous rami supply trigeminal ganglion, walls of cavernous + inferior petrosal sinuses

D. SUPRACLINOID SEGMENT

ascends posterior + lateral between oculomotor + optic nerve

Branches:

mnemonic: OPA

Ophthalmic a.
Posterior communicating a.
Anterior choroidal a.

1. **Ophthalmic a.** exits from ICA medial to anterior clinoid process, travels through optic canal inferolateral to optic nerve
   (a) recurrent meningeal branch: dura of anterior middle cranial fossa
   (b) posterior ethmoidal a.: supplies dura of planum sphenoidale
   (c) anterior ethmoidal a.
2. **Superior hypophyseal a.**: optic chiasm, anterior lobe of pituitary
3. **Posterior communicating a.** (pCom)
4. **Anterior choroidal a.**
5. **Middle + anterior cerebral arteries** (MCA, ACA)

Carotid Siphon

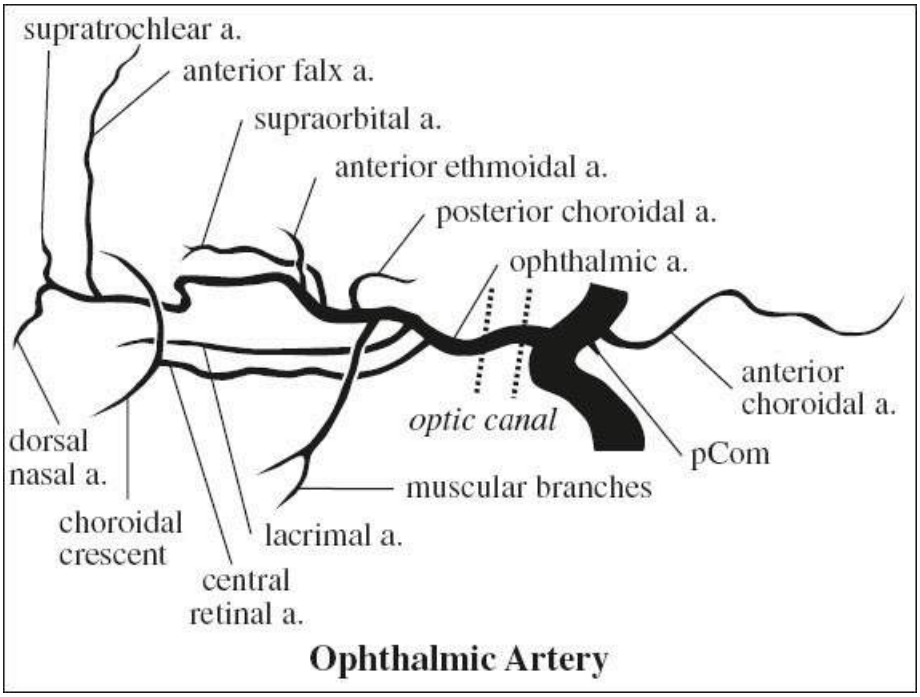
Flow direction: C4–C1

(a) C4 segment = before origin of ophthalmic a.

(b) C3 segment = genu of ICA

(c) C2 segment = supraclinoid segment after origin of ophthalmic a.

(d) C1 segment = terminal segment of ICA between pCom + ACA



Ophthalmic Artery

Duplex Identification of Carotid Arteries		
Criteria	*External Carotid Artery*	*Internal Carotid Artery*
Size	usually smaller than ICA	usually larger than ECA
Location	oriented medially + anteriorly toward face	oriented laterally + posteriorly toward mastoid process (*mnemonic:* IAC vis-à-vis ECA positioned like helix vis-à-vis tragus of your ear)
Branches	gives off arterial branches (superior thyroid artery as 1st branch)	NO arterial branches
Waveform	high-resistance flow pattern supplying capillary beds in skin + muscle: √ forward systolic component √ early diastolic flow reversal, occasionally followed by another component √ little / no flow in late diastole	low-resistance waveform pattern supplying capillary bed in brain: √ high-velocity forward systolic component √ sustained strong forward flow in diastole √ stagnant eddy with flow reversal opposite to flow divider in carotid bulb
Maneuver	oscillations on temporal tap maneuver	

Anterior Cerebral Artery (ACA)

A1 (horizontal) segment between origin and anterior communicating a. (aCom)

(a) inferior branches
supply superior surface of optic nerve + chiasm

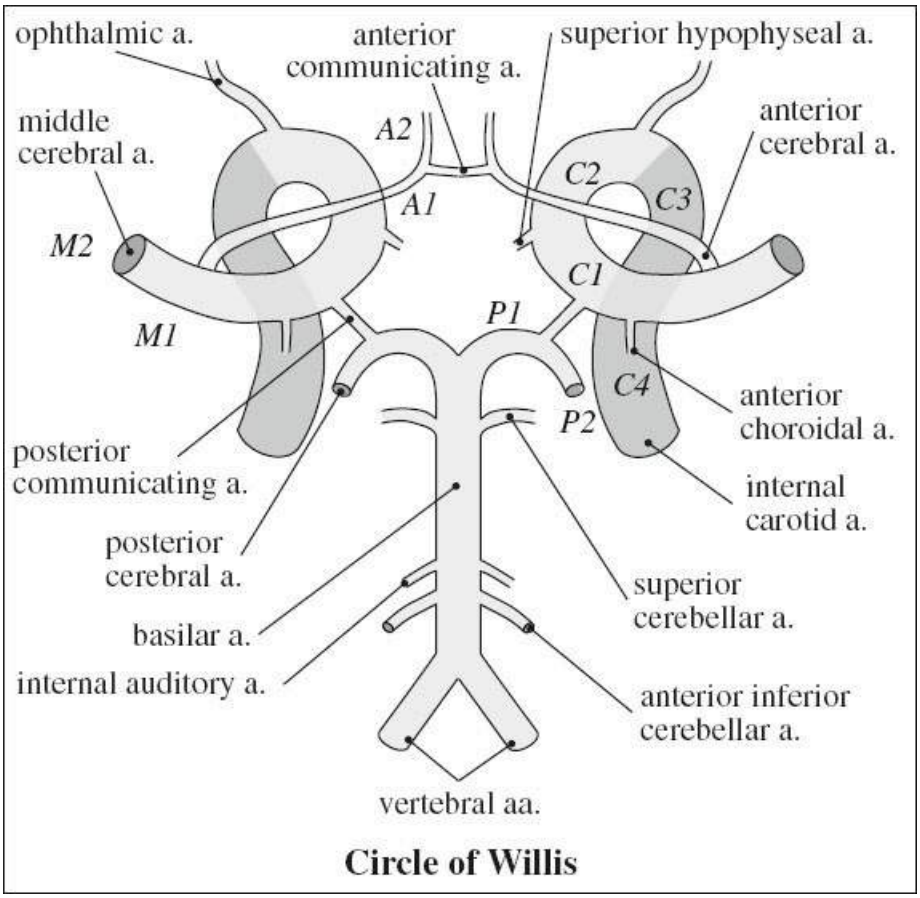
(b) superior branches penetrate brain to supply anterior hypothalamus, septum pellucidum, anterior commissure, fornix columns, anterior inferior portion of corpus

striatum

(c) medial lenticulostriate artery (largest striatal artery) = **recurrent artery of Heubner** for anteroinferior portion of head of caudate, putamen, anterior limb of internal capsule

A2 (interhemispheric) segment after origin of anterior communicating a. (aCom); ascends in cistern of lamina terminalis

Branches:



Circle of Willis

1. **Medial orbitofrontal a.:** along gyrus rectus
2. **Frontopolar a.**
3. **Callosomarginal a.**: within cingulus gyrus
4. **Pericallosal a.**: over corpus callosum within callosal cistern
   (a) Superior internal parietal a.: anterior portion of precuneus + convexity of superior parietal lobule
   (b) Inferior internal parietal a.
   (c) Posterior pericallosal a.

   from callosomarginal / pericallosal artery:
   - anterior + middle + posterior internal frontal aa.
   - paracentral a.: supplies pre- + postcentral gyri

Supply: anterior ⅔ of medial cerebral surface + 1 cm of superomedial brain over convexity

Middle Cerebral Artery

= largest branch of ICA arising lateral to optic chiasm

M1 (horizontal) segment = courses in lateral direction

Branches: lateral lenticulostriate aa.

Supply: part of head and body of caudate, globus pallidus, putamen, and posterior limb of internal capsule

M2 (sylvian) segment = enters sylvian fissure just ventral to anterior perforated substance; divides into superior and inferior divisions with 2 / 3 / 4 branches

Branches: temporal lobe and insular cortex (sensory language area of Wernicke), parietal lobe (sensory cortical areas), inferolateral frontal lobe

M3 (cortical) segment = distal branches lateral to insular cortex = candelabra [*candelabrum*, Latin = decorative candlestick / lamp with several arms or branches]

Branches:

1. **Anterior temporal artery**
2. **Ascending frontal artery** / prefrontal a.
3. **Precentral artery** = pre-Rolandic a.
4. **Central artery** = Rolandic a.
5. **Anterior parietal artery** = post-Rolandic a.
6. **Posterior parietal artery**
7. **Angular artery**
8. **Middle temporal artery**
9. **Posterior temporal artery**
10. **Temporooccipital artery**

Supply: lateral cerebrum, insula, anterior + lateral temporal lobe

Posterior Cerebral Artery

originates from bifurcation of basilar artery within interpeduncular cistern (in 15% as a direct continuation of posterior communicating artery); lies above oculomotor nerve and circles midbrain above the tentorium cerebelli

Branches:

1. Mesencephalic perforating branches: tectum + cerebral peduncles
2. Posterior thalamoperforating aa.: midline of thalamus + hypothalamus
3. Thalamogeniculate aa.: geniculate bodies + pulvinar
4. Posterior medial choroidal a.: circles midbrain parallel to PCA; enters lateral aspect of quadrigeminal cistern; passes laterally and above pineal gland and enters roof of 3rd ventricle; supplies quadrigeminal plate + pineal gland
5. Posterior lateral choroidal a.: courses laterally and enters choroidal fissure; anterior branch to temporal horn + posterior branch to choroid plexus of trigone and lateral ventricle + lateral geniculate body
6. Cortical branches:
   (a) Anterior inferior temporal artery
   (b) Posterior inferior temporal artery
   (c) Parietooccipital artery
   (d) Calcarine artery
   (e) Posterior pericallosal artery

Supply: medial + posterior temporal lobe, medial parietal lobe, occipital lobe

Thalamic Blood Supply

by multiple small vessels originating from Pcom + P1 and P2 segments of the PCAs

Territories:

(1) anterior: polar / thalamotuberal arteries ← Pcom
(2) paramedian: paramedian / thalamoperforating arteries ← P1 segment of PCA
(3) inferolateral: thalamogeniculate arteries ← P2 segment of PCA
(4) posterior: posterior choroidal arteries ← P2 segment

Anatomic variant (uncommon):

Artery of Percheron = single dominant thalamoperforating artery supplying both medial thalami (with variable contribution to rostral midbrain)

Occlusion:

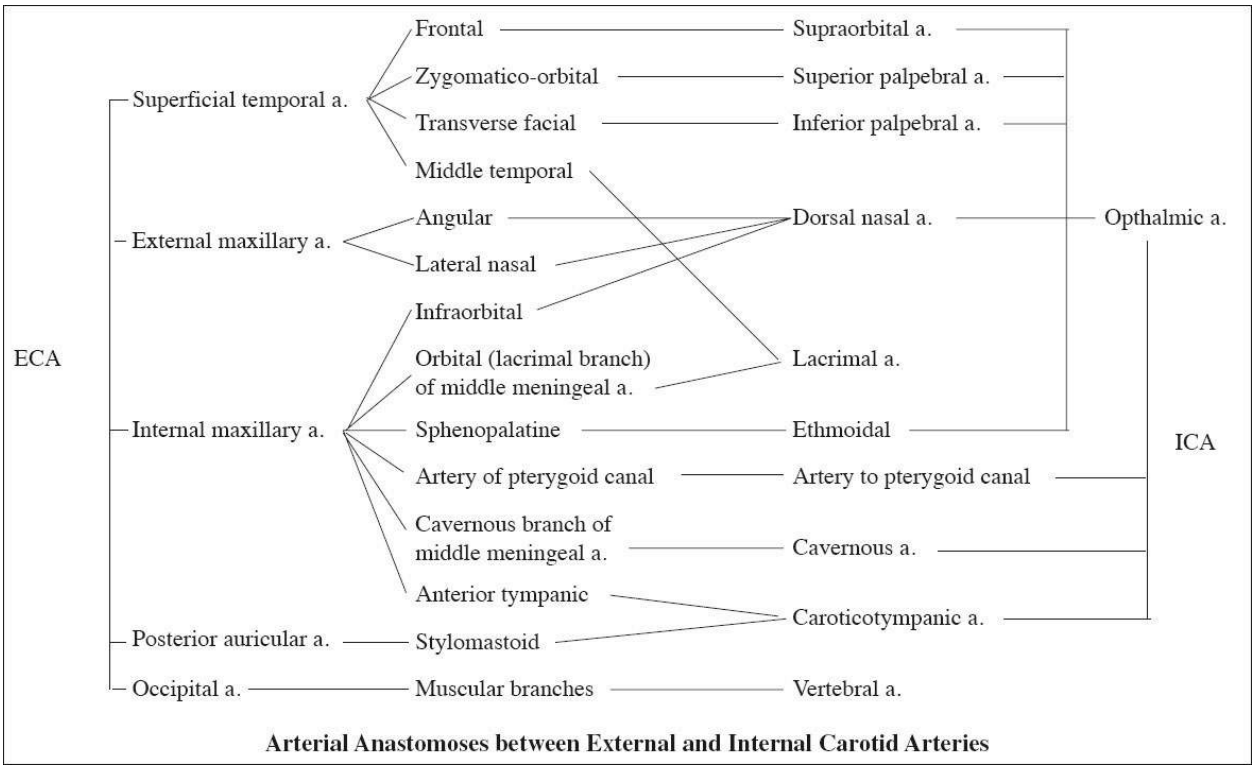
√ CHARACTERISTIC bilateral paramedian thalamic infarcts ± midbrain involvement

Arterial Anastomoses of the Brain

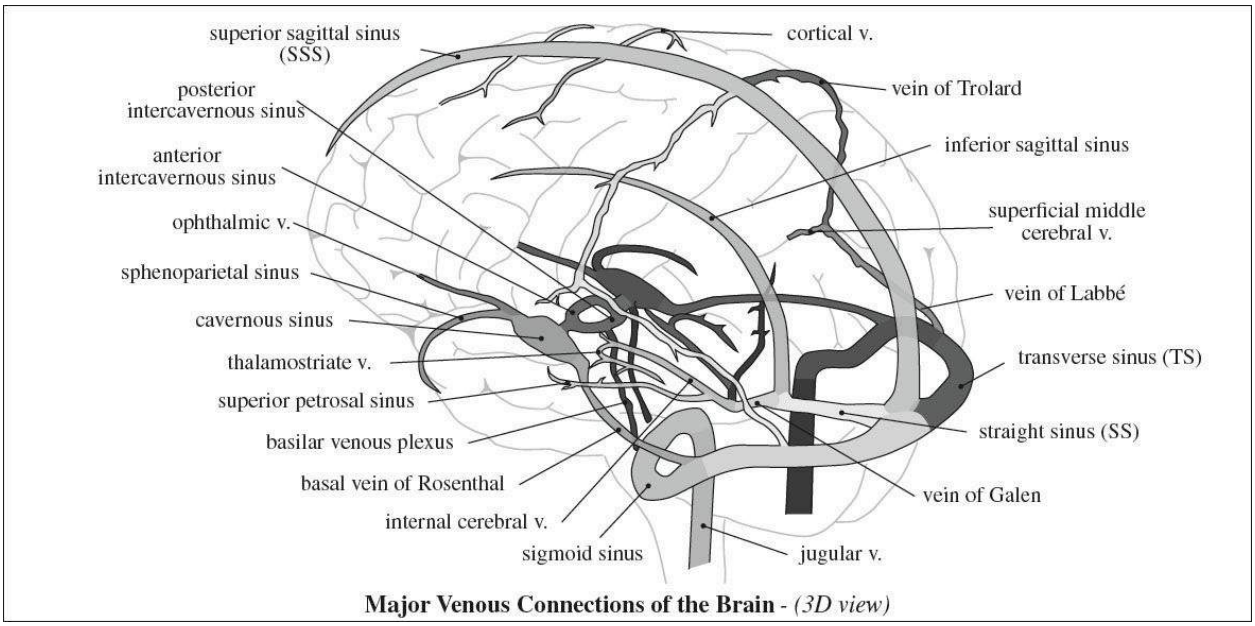
Anastomoses via Arteries at the Base of the Brain

A. Circle of Willis
   1. Right ICA ↔ right ACA ↔ aCom ↔ left ACA ↔ left ICA
   2. ICA ↔ pCom ↔ basilar a.
   3. ICA ↔ anterior choroidal a. ↔ posterior choroidal a. ↔ PCA ↔ basilar a.

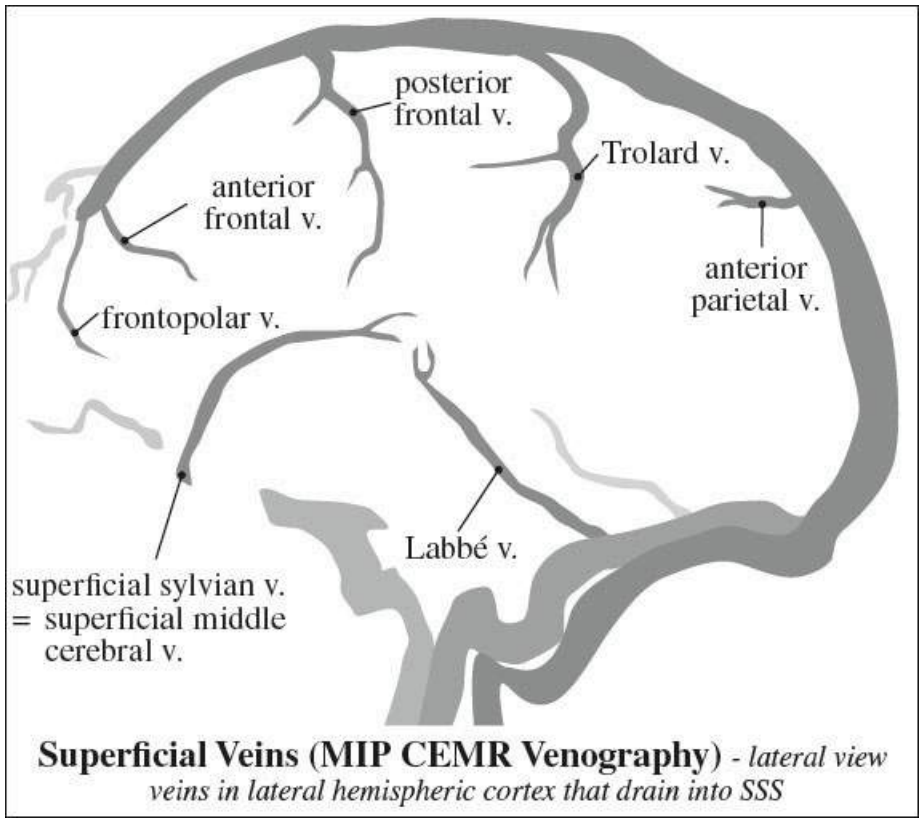
B. Developmental anomaly four transient embryonal carotid-basilar anastomoses named according to their corresponding cranial nerves that regress in the following sequence:
   1. **Primitive acoustic (otic) artery**
      = arterial connection between petrous portion of ICA within carotid canal + proximal basilar artery / posterior inferior cerebellar a.
      √ traverses internal auditory canal (with CN VIII)
   2. **Primitive hypoglossal artery**
      = arterial connection between the C1–C3 portion of ICA and proximal portion of basilar a.
      √ traverses hypoglossal canal (with CN XII)
   3. **Persistent primitive trigeminal artery**
      Frequency: ~ 1%
      √ short wide connection between the cavernous portion of ICA + basilar artery (between anterior inferior cerebellar a. and superior cerebellar a.)
      √ penetrates sella turcica (in 50%)



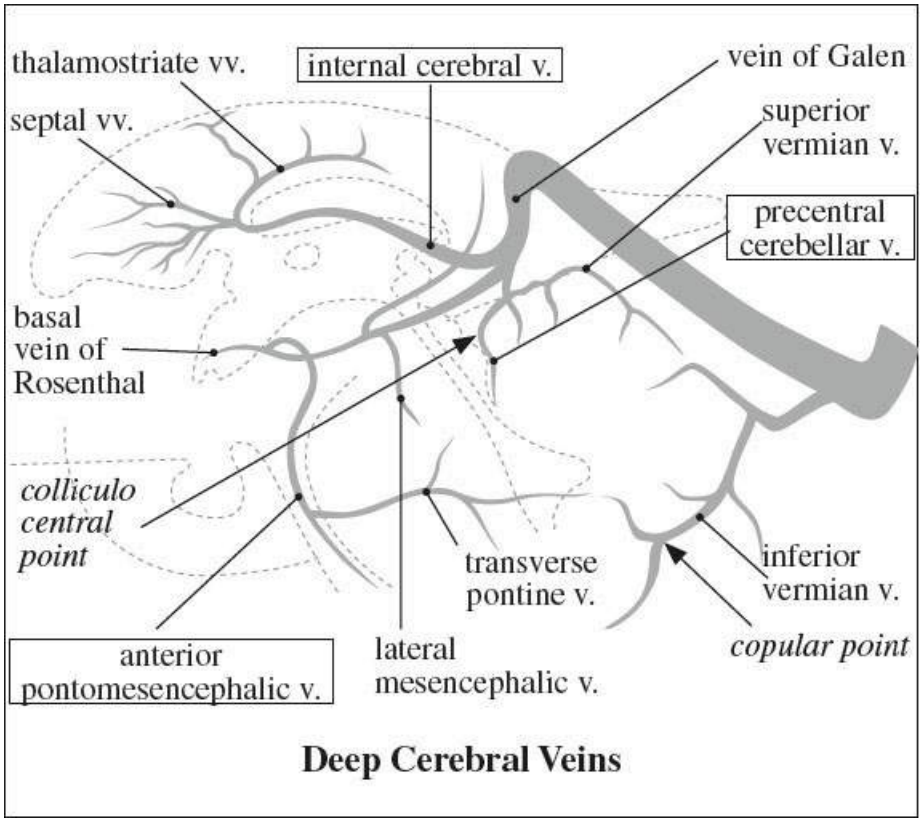
Arterial Anastomoses between External and Internal Carotid Arteries



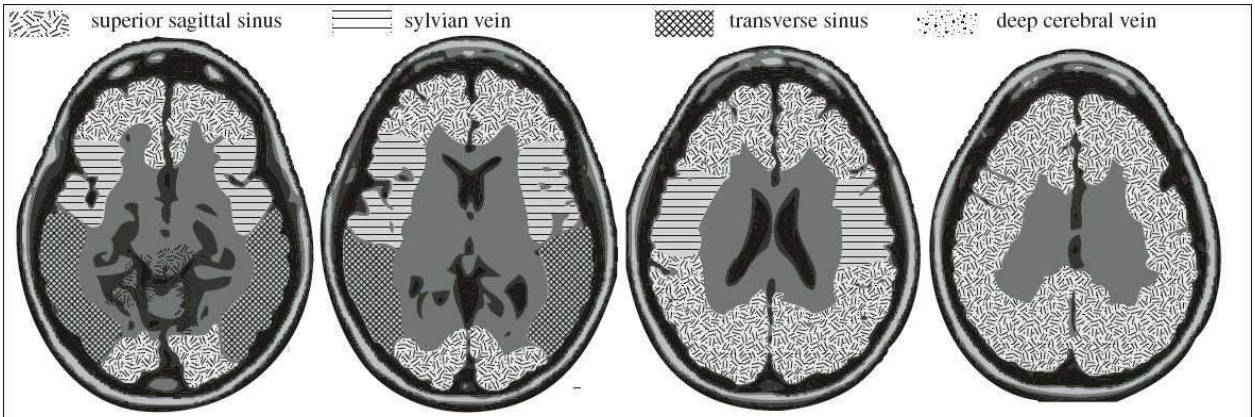
Major Venous Connections of the Brain - *(3D view)*



Superficial Veins (MIP CEMR Venography) - *lateral view*
veins in lateral hemispheric cortex that drain into SSS



Deep Cerebral Veins



Major Superficial Cortical Venous Drainage Territories of the Brain
(axial views from lower to higher levels)

√ enlargement of ipsilateral ICA
√ ectopic vessel crossing the pontine cistern to anastomose with basilar artery

4. **Proatlantal intersegmental artery**
   = arterial connection between CCA bifurcation / ECA (57%) / ICA at C2–C4 level (38%) and vertebral a. in suboccipital region
   √ traverses foramen magnum

Anastomoses via Surface Vessels

A. Leptomeningeal anastomoses of the cerebrum: ACA ↔ MCA ↔ PCA
B. Leptomeningeal anastomoses of the cerebellum: Superior cerebellar a. ↔ AICA ↔ PICA

Rete Mirabile

ECA ↔ middle meningeal a. / superficial temporal a. ↔ leptomeningeal aa. ↔ ACA / MCA

Cerebral Venous System

Histo: NO smooth muscle / venous valves → bidirectional flow

Dural Venous Sinuses

= major drainage pathway from cerebral veins into internal jugular veins; enclosed by leaves of dura

(a) Superior group draining majority of brain + skull

1. Superior sagittal sinus (SSS) collects superficial cerebral veins that drain cerebral convexities
   √ luminal surface of triangular shape
   √ traversed by septa → maintaining laminar flow + preventing venous reflux into cortical veins
2. Inferior sagittal sinus
3. Straight sinus (SS)
4. Occipital sinus small midline vein draining toward foramen magnum / into jugular fossa / suboccipital veins

Location: at attachment of falx cerebelli
√ may replace an aplastic transverse sinus

5. Transverse sinus (TS)
receives blood from the temporal, parietal, and occipital lobes
√ commonly asymmetric with right dominance
6. Sigmoid sinus
7. Confluence of sinuses (t**orcular herophili**) formed by union of the SSS +SS + TS
√ often asymmetric in appearance (see below)

(b) inferior group drains superficial cerebral veins + basal and medial parts of undersurface of the brain + orbits + sphenoparietal sinus + cavernous sinus

1. Cavernous sinus complex
2. Superior petrosal sinus
› arising from junction of transverse with sigmoid sinus
› extends along petrous ridge
3. Inferior petrosal sinus
› arising from distal portion of sigmoid sinus / jugular bulb
› extends along clivus

VARIANTS OF TORCULAR HEROPHILI

A. Codominant transverse sinuses (TS)
B. Dominant right TS
C. Dominant left TS
D. Segmental hypo- / aplasia of proximal left TS + inflow to distal segment of TS from vein of Labbé and tentorial tributaries
E. SSS drains into right TS + SS into left TS
F. high split of SSS + SS drains into both TS

Superficial Venous System

= SUPERFICIAL CORTICAL VEINS
= great variability in drainage territories
(a) ascending (= superiorly draining) veins named for cortical area that is drained
(b) descending (inferiorly draining) veins

1. Labbé vein
2. Sylvian (superficial middle cerebral) vein drains blood from peri-insular region into basal dural sinuses

◊ Relative luminal diameters of Trolard vein + Labbé vein + superficial sylvian vein are reciprocal

Location: subarachnoid space; traverse arachnoid mater + meningeal layer of dura mater to drain into dural venous sinus

Deep Venous System

= DEEP CEREBRAL VEINS
= centripetal drainage of hemispheric white matter and basal ganglia
(a) internal cerebral veins:

1. Internal cerebral vein ← thalamostriate v. ← corpus callosum drainage (from anterior to posterior)

(a) septal vein
(b) anterior caudate vein
(c) terminal vein

2. Basal vein of Rosenthal
3. Vein of Galen
4. Medullary + subependymal veins

(b) transcerebral veins:
draining cerebral white matter
√ typically not visualized due to small caliber

Infratentorial Venous System

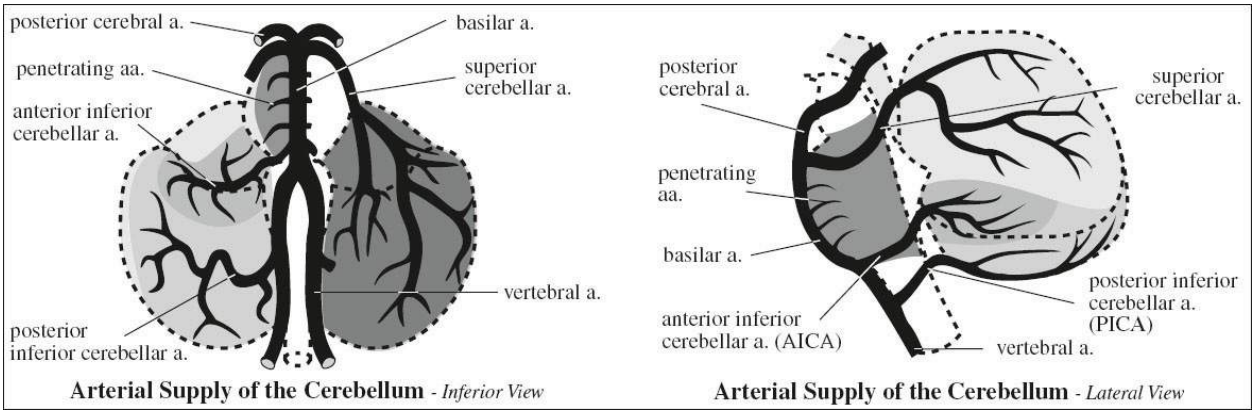
(a) superiorly into vein of Galen
(b) anteriorly into petrosal sinuses
(c) posteriorly into dural sinuses

Important vascular markers:

1. Pontomesencephalic v. = anterior border of brainstem
2. Precentral cerebellar v. = position of tectum
   ◊ Colliculocentral point = midpoint of Twining's line at knee of precentral cerebellar vein
3. Venous angle = acute angle at junction of thalamostriate with internal cerebral v. = posterior aspect of foramen of Monro
4. Internal cerebral vv. = demarcate caudad border of splenium of corpus callosum superiorly + pineal gland inferiorly
5. Copular point = junction of inferior + superior retrotonsillar tributaries draining cerebellar tonsils in region of copular pyramids of vermis

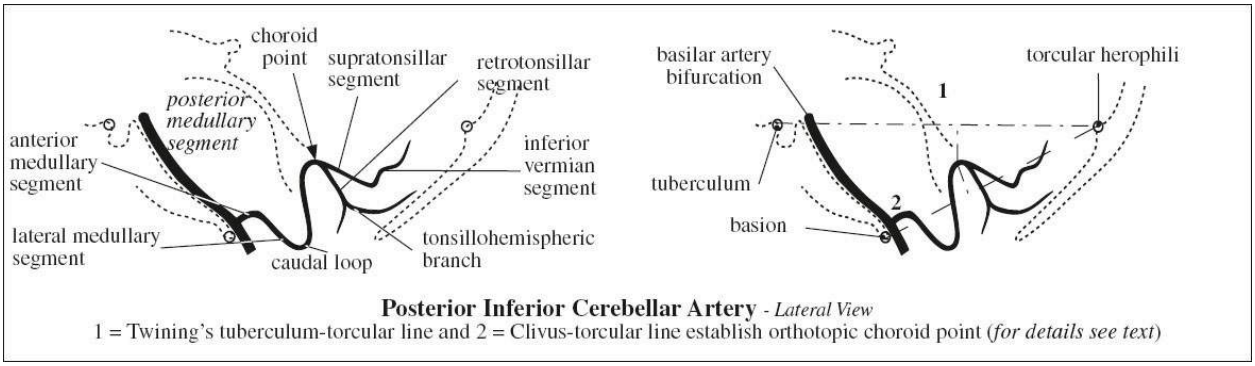
Arachnoid Granulations of Pacchioni

Prevalence: 66% (↑ in number + conspicuity with age)
Function: resorption of CSF
Location: within lacunae laterales of SSS
√ well-defined 2–9 mm focal filling defects within dural sinus
√ produce 13–15 mm calvarial impressions lateral to midline
√ iso- (⅓) / hypoattenuating (⅔) relative to parenchyma

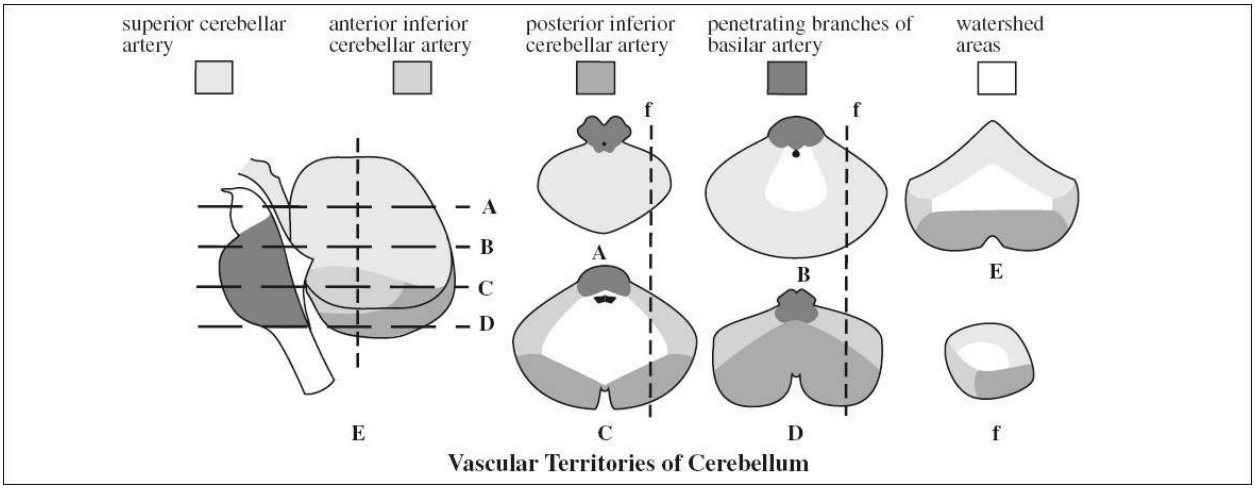


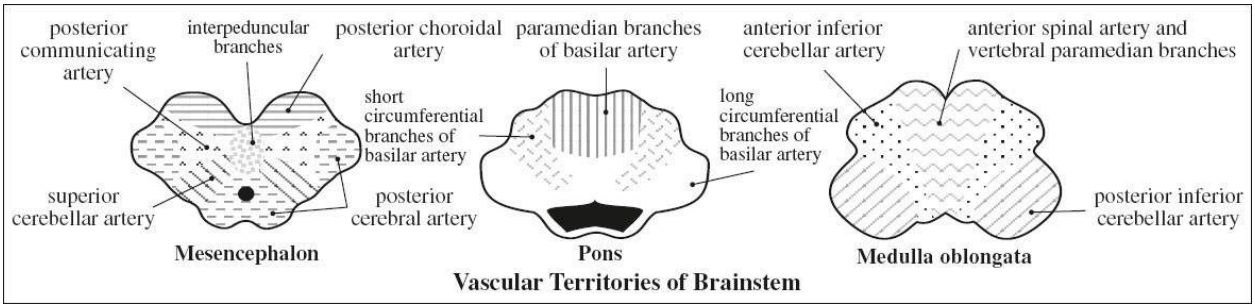
Arterial Supply of the Cerebellum - *Inferior View*

Arterial Supply of the Cerebellum - *Lateral View*



Posterior Inferior Cerebellar Artery - *Lateral View*
1 = Twining's tuberculum-torcular line and 2 = Clivus-torcular line establish orthotopic choroid point (*for details see text*)





CEREBELLAR VESSELS

Vertebral Artery

originates from subclavian a. proximal to thyrocervical trunk; left vertebral a. usually greater than right cerebral a.; left vertebral a. may originate directly from aorta (5%)

A. PREVERTEBRAL SEGMENT (V1)
ascends posterosuperiorly between longus colli + anterior scalene muscle; enters transverse foramen at C6
Branches: muscular branches

B. MIDCERVICAL SEGMENT (V2)
ascends through transverse foramina of C6 to C2 in close proximity to uncinate processes
Branches:

1. **Anterior meningeal a.**

C. ATLANTIC SEGMENT = Atlas loop (V3)
exits transverse foramen of atlas; passes posteriorly in a groove on superior surface of posterior arch of atlas; pierces atlanto-occipital membrane + dura mater to enter cranial cavity

Branches:

1. **Posterior meningeal branch** to posterior falx + tentorium

D. INTRACRANIAL SEGMENT (V4)
ascends anteriorly + laterally around medulla to reach midline at pontomedullary junction; anastomoses with contralateral side to form basilar artery at clivus

Branches:

1. Anterior + posterior spinal a.
2. Posterior inferior cerebellar a. (PICA)
3. Anterior inferior cerebellar a. (AICA)
4. Internal auditory a.
5. Superior cerebellar a.
6. Posterior cerebral a. (PCA)
7. Medullary + pontine perforating branches

◊ May terminate in common AICA-PICA trunk

Anterior Inferior Cerebellar Artery

= AICA = first branch of basilar artery

Supply: lateroinferior part of pons, middle cerebellar peduncle, floccular region, anterior petrosal surface of cerebellar hemisphere

◊ Quite variable course + vascular supply with reciprocal relation between vascular territories of AICA + PICA!

Posterior Inferior Cerebellar Artery

= PICA = last and largest branch of vertebral artery

Supply: inferoposterior surface of cerebellar hemisphere adjacent to occipital bone, ipsilateral part of inferior vermis, inferior portion of deep white matter only

Parts:

1. Premedullar segment = caudal loop around medulla, may descend below level of foramen magnum
2. Retromedullar segment = ascending portion up to the level of 4th ventricle and tonsils
3. Supratonsillar segment = the most cranial point is the choroidal point

P1 segment = horizontal segment between origin of PICA + pCom

P2 segment = segment downstream from pCom take-off

Variations: commonly asymmetric; hypoplastic / absent in 20% [vascular supply then provided by anterior inferior cerebellar artery (AICA)]

*Orthotopic **choroid point** established by:*

1. perpendicular line from choroid point onto Twining's line = TTT-line (Twining's Tuberculum-Torcular line) bisects TTT-line (length of anterior portion 52–60%)
2. perpendicular line from choroid point cuts CT-line (Clivus-Torcular line) < 1 mm

anterior / < 3 mm posterior to junction of anterior and middle thirds of CT-line

Superior Cerebellar Artery

= SCA = last but one branch of basilar artery

Supply: superior aspect of cerebellar hemisphere (tentorial surface), ipsilateral superior vermis, largest part of deep white matter including dentate nucleus, pons

ABSCESS OF BRAIN

Pyogenic Brain Abscess

= focal area of necrosis beginning in area of cerebritis with formation of surrounding membrane

Prevalence: 0.4–0.9÷100,000

Cause:

1. Extension from paranasal sinus infection (41%) / mastoiditis / otitis media (5%) / facial soft-tissue infection / dental abscess
2. Generalized septicemia (32%):
   (a) lung (most common): bronchiectasis, empyema, lung abscess, bronchopleural fistula, pneumonia
   (b) heart (less common): CHD with R-L shunt (in children > 60%), AVM, bacterial endocarditis
   (c) osteomyelitis
3. Penetrating trauma or surgery
4. Cryptogenic (25%)

Predisposed: diabetes mellitus, patients on steroids / immunosuppressive drugs, congenital / acquired immunologic deficiency

Organism: anaerobic streptococcus (most common), bacteroides, staphylococcus; in 20% multiple organisms; in 25% sterile contents

Pathophysiologic stages:

1 ***Early cerebritis*** = vascular congestion, petechial hemorrhage, edema ← neutrophilic response to invasive organism
√ ill-defined hypoattenuation on NECT
√ absent / variable enhancement on CECT

2 ***Late cerebritis*** = cerebral softening + necrosis ← marginal fibroblast accumulation (but NO collagen deposition) ← breakdown of blood-brain barrier
√ ringlike enhancement diffusing centrally on delayed images
√ suppressed enhancement after corticosteroid Rx

Capsule develops over 2–4 weeks = SIGNATURE imaging feature of an abscess!

3 ***Early capsule*** = fibroblasts create reticulin matrix ← blockage of necrotic material

4 ***Late capsule*** = matrix transitions to mature collagen

Histo: liquefaction + cavitation + capsule + pericapsular (progressively decreasing) edema

Capsule:
(a) inner layer of granulation tissue
(b) middle layer of collagen
(c) outer layer of astroglia

√ well-vascularized capsule tends not to persist on delayed scan
√ NO suppressed enhancement after corticosteroid Rx
√ capsule often thinner medially ← relatively poor vascularity + reduced fibroblast migration

Cx: (1) daughter abscesses
(2) intraventricular rupture

- headache, drowsiness, confusion, seizure
- focal neurologic deficit
- fever, leukocytosis (resolves with encapsulation)

Location: typically at corticomedullary junction; frontal and temporal lobes; supratentorial÷infratentorial = 2÷1

NECT:
√ well-defined hyperattenuated ring compared with central necrosis + peripheral edema:
√ zone of low density with mass effect (92%)
√ slightly increased rim density (4%) ← development of collagen layer takes 10–14 days
√ gas within lesion (4%) is diagnostic of gas-forming organism

CECT:
√ ring enhancement (90%) with peripheral zone of edema
√ continuous regular smooth 2–7-mm ring, nonspecific but HIGHLY CHARACTERISTIC of a pyogenic abscess!
√ homogeneous enhancement in lesions < 0.5 cm
√ edema + contrast enhancement suppressed by steroids
√ multiloculation + subjacent daughter abscess in white matter

MR: (most sensitive modality)
√ abscess centrally increased / variable intensity on T2WI
√ T1-hyperintense + T2-hypointense rim (= abscess capsule) ← paramagnetic effect of bactericidal free radicals generated by active macrophages
√ outside border of increased SI on T2WI (edema)
√ restricted diffusion in abscess core ← high cellularity and viscosity of pus impedes water mobility
√ (CHARACTERISTIC) hyperintensity on DWI
√ corresponding hypointensity on ADC maps

DWI is the best sequence for differentiation of ringenhancing pyogenic abscess from necrotic tumor.

MR spectroscopy:
√ ↑ amino acid level (0.9 ppm) = marker of proteolytic enzymes from neutrophils (in 80%)

Cx: (1) Development of daughter abscesses toward white matter
(2) Rupture into ventricular system / subarachnoid space (thinner capsule formation on medial wall of abscess related to relative hypovascularity) → ventriculitis ± meningitis

Dx helpful features:
› multiple lesions at gray-white matter border
› clinical history of altered immune status

› R-to-L shunt: eg, pulmonary AV fistula
› foreign travel
› high-risk behavior: eg, IV drug abuse

Rx: IV antibiotics (penetrate brain abscess to therapeutic levels) + needle aspiration for best clinical outcome

DDx: (1) Primary / metastatic neoplasm (restricted diffusion typically in tumor periphery ← high cellular density
(2) Subacute infarction
(3) Resolving hematoma

Granulomatous Brain Abscess

1. Tuberculoma
2. Sarcoid abscess
3. Fungal abscess: coccidioidomycosis, mucormycosis (in diabetics), aspergillosis, cryptococcus

Predisposed: immunocompromised host (candida, aspergillus)
√ enhancement of leptomeningeal surface
√ nodular / ring-enhancing parenchymal lesion
Cx: Communicating hydrocephalus ← thick exudate blocks basal cisterns

ACRANIA

= EXENCEPHALY
= developmental anomaly characterized by partial / complete absence of membranous neurocranium + complete but abnormal development of brain tissue
Incidence: 25 cases reported
Cause: impaired migration of mesenchyme to its normal location under calvarial ectoderm → failed development of dura mater + skull + musculature
Time: develops after closure of anterior neuropore during 4th week
May be associated with:
cleft lip, bilateral absence of orbital floors, metatarsus varus, talipes, cervicothoracic spina bifida
• ± elevation of maternal serum AFP
√ absence of calvarium
√ normal ossification of chondrocranium (face, skull base)
√ hemispheres surrounded by thin membrane
Prognosis: uniformly lethal; progression to anencephaly (brain destruction ← exposure to amniotic fluid and mechanical trauma)
DDx: encephalocele, anencephaly, osteogenesis imperfecta, hypophosphatasia

ADRENOLEUKODYSTROPHY

= BRONZED SCLEROSING ENCEPHALOMYELITIS
= inherited metabolic disorder characterized by progressive demyelination of cerebral white matter + adrenal insufficiency
Etiology: defective peroxisomal fatty acid oxidation ← impaired function of lignoceryl-

coenzyme A ligase with accumulation of saturated very long chain fatty acids (cholesterol esters) in white matter + adrenal cortex + testes

Dx: assay of plasma, red cells, cultured skin fibroblasts for the presence of increased amounts of very long chain fatty acids

Mode of inheritance:

(a) X-linked recessive in boys (common)

(b) autosomal recessive in neonates (uncommon)

Histo: PAS cytoplasmic inclusions in brain, adrenals, other tissues

Age: 3–10 years (X-linked recessive)

- loss of hearing (50%), ataxia
- deteriorating vision (27%), optic disk pallor
- adrenal gland insufficiency → abnormal increased pigmentation, elevated ACTH level
- altered behavior, attention disorder, mental deterioration, death

Location: disease process usually starts in central occipital white matter → advances anteriorly through internal and external capsules + centrum semiovale → centripetal progression to involve subcortical white matter → interhemispheric spread via corpus callosum particularly splenium → involvement of optic radiation ± auditory system ± pyramidal tract

CT:

√ large symmetric low-density lesions in occipitoparieto-temporal white matter (80%) advancing toward frontal lobes + cerebellum

√ thin curvilinear / serrated enhancing rims near edges of lesion

√ initial frontal lobe involvement (12%)

√ calcifications within hypodense areas (7%)

√ cerebral atrophy in late stage (progressive loss of cortical neurons)

MR:

√ hypointensity on T1WI in affected areas (= hypointense atrophic splenium of corpus callosum)

√ bilateral confluent hyperintense areas on T2WI

Prognosis: usually fatal within several years after onset of symptoms

Adrenomyeloneuropathy

= clinically milder form with later age of onset

- symptoms of spinal cord demyelination + peripheral neuropathy

AGENESIS OF CORPUS CALLOSUM

= COMPLETE DYSGENESIS OF CORPUS CALLOSUM

= failure of formation of corpus callosum originating at lamina terminalis at 7–13 weeks from where a phalanx of callosal tissue extends backward arching over the diencephalon; usually developed by 20 weeks EGA

Incidence: 0.7–5.3%

Cause: congenital / acquired (← infarction of ACA)

Histo: axons from cerebral hemispheres that would normally cross continue along medial walls of lateral ventricles as longitudinal callosal bundles of Probst that terminate randomly in occipital + temporal lobes

Associated with:

(a) CNS anomalies (85%):

1. Dandy-Walker cyst (11%)
2. Interhemispheric arachnoid cyst may be continuous with 3rd and lateral ventricles
3. Hydrocephalus (30%)
4. Midline intracerebral lipoma of corpus callosum often surrounded with ring of calcium (10%)
5. Arnold-Chiari II malformation (7%)
6. Midline encephalocele
7. Porencephaly
8. Holoprosencephaly
9. Hypertelorism median cleft syndrome
10. Polymicrogyria, gray-matter heterotopia

(b) Cardiovascular, gastrointestinal, genitourinary anomalies (62%)

(c) Abnormal karyotype (trisomy 13, 15, 18)

• normal brain function in isolated agenesis

• intellectual impairment; seizures

√ absence of septum pellucidum + corpus callosum + cavum septi pellucidi

√ longitudinal bundles of Probst create crescentic lateral ventricles:

- √ colpocephaly (= dilatation of trigones + occipital horns + posterior temporal horns in the absence of splenium
- √ "bat-wing" appearance of lateral ventricles (= wide separation of lateral ventricles with straight parallel parasagittal orientation with absent callosal body)
- √ laterally convex frontal horns in case of absent genu of corpus callosum

√ "high-riding third ventricle" = upward displacement of widened 3rd ventricle often to level of bodies of lateral ventricle

√ anterior interhemispheric fissure adjoins elevated 3rd ventricle ± communication (PATHOGNOMONIC)

√ "interhemispheric cyst" = interhemispheric CSF collection as an upward extension of 3rd ventricle

√ enlarged foramina of Monro

√ "sunburst gyral pattern" = dysgenesis of cingulate gyrus with characteristic radial orientation of cerebral sulci from the roof of the 3rd ventricle (on sagittal images)

√ failure of normal convergence of calcarine + parietooccipital sulci

√ persistent eversion of cingulate gyrus (rotated inferiorly + laterally) with absence on midsagittal images

√ incomplete formation of Ammon's horn in the hippocampus

OB-US (> 22 weeks GA):

- √ absence of septum pellucidum
- √ "teardrop" ventriculomegaly = disproportionate enlargement of occipital horns = colpocephaly
- √ dilated + elevated 3rd ventricle
- √ radial array pattern of medial cerebral sulci

Angio:

- √ wandering straight posterior course of pericallosal arteries (lateral view)

√ wide separation of pericallosal arteries ← intervening 3rd ventricle (anterior view)
√ separation of internal cerebral veins
√ loss of U-shape in vein of Galen

DDx: (1) Prominent cavum septi pellucidi + cavum vergae (should not be mistaken for 3rd ventricle)
(2) Arachnoid cyst in midline (suprasellar, collicular plate) raising and deforming the 3rd ventricle and causing hydrocephalus

Partial Agenesis of Corpus Callosum

= milder form of callosal dysgenesis (best seen on MR) depending on time of arrested growth (anteroposterior development of genu + body + splenium, however, rostrum forming last)

(a) genu only
(b) genu + part of the body
(c) genu + entire body
(d) genu + body + splenium (without rostrum)

AIDS

= late symptoms of DNA retrovirus infection attacking monocytes + macrophages → deficient cell-mediated immunity

Incidence: 1,200,000 HIV-seropositive persons (0.3% of population) in USA IN 2011; 14% undiagnosed; 50,000 new HIV infections per year

Histo: formation of microglial nodules instead of granulomas in 75–80% of autopsied brains

• neurologic symptoms as initial complaint in 7–10%, ultimately afflict up to 40–60%: personality + mental status changes, headache, memory loss, difficulty to concentrate, depression, confusion, dementia, new onset of seizures, focal deficit from mass lesion

◊ Any male with neurologic symptoms between age 20 and 50 has AIDS until proven otherwise

◊ Unusual presentations are clues to HIV infection: pansinusitis, mastoiditis, parotid cysts, cervical adenopathy, hypointense spine

Rx: azidothymidine (AZT)

A. ATROPHY:
(1) Malnutrition, dehydration, steroid therapy, chronic dialysis, normal aging
(2) **AIDS dementia complex** (ADC)
= SUBACUTE ENCEPHALITIS = HIV ENCEPHALITIS
= cognitive disturbances → progressing to dementia
Etiology: HIV-1 infection of CNS macrophages generating neurotoxic factors
Prevalence: 7–27% of AIDS patients
Histo: predominantly perivascular HIV encephalitis; HIV leukoencephalopathy characterized by diffuse myelin loss + infiltration by macrophages
√ cerebral atrophy
√ subtly increased signal intensities on T2 and FLAIR sequences without mass effect ← leaky capillaries with egress of water:
√ focal / diffuse
√ symmetric / asymmetric
√ reversible / nonreversible

B. INTRAAXIAL LESION WITHOUT MASS EFFECT

(1) Progressive multifocal leukoencephalopathy

C. MASS LESION
  (1) Toxoplasmosis
  (2) Primary CNS lymphoma (PCNSL)
  (3) Fungal, granulomatous, viral, bacterial infection
    (a) Cryptococcosis
    (b) Other opportunistic CNS infections:
      › tuberculosis
      › neurosyphilis

◊ With multiple CNS lesions toxoplasmic encephalitis is the more likely diagnosis!
◊ With a single CNS lesion the probability of lymphoma is at least equal to toxoplasmosis!

ALEXANDER DISEASE

= FIBRINOID LEUKODYSTROPHY
= rare autosomal dominant / sporadic CNS disease (< 500 cases)
Cause: mutation in gene for glial fibrillary acidic protein (GFAP) of chromosome 17q21
Age: as early as first few weeks of life to 2 years
• macrocephaly; failure to attain developmental milestones
• progressive spastic quadriparesis; intellectual failure
Location: frontal white matter gradually extending posteriorly into parietal region + internal capsule
CT:
  √ low-density white matter lesion
  √ contrast enhancement near tip of frontal horn
MR:
  √ prolonged T1 + T2 relaxation times
Prognosis: death in infancy / childhood usually within 10 years

ALZHEIMER DISEASE

= diffuse gray matter disease with large loss of cells from cerebral cortex + other areas
◊ Most common of dementing disorders in elderly!
Incidence: 10% of people > 65 years of age; 50% of people > 85 years of age
Histo: intraneuronal deposits of abnormally phosphorylated τ protein (neurofibrillary tangles) and extracellular β-amyloid (senile plaques)
• slowly progressive cognitive decline, memory impairment, adverse impact on activities of daily living (large overlap with other dementias of elderly)
Location: early neuronal loss + gliosis in mesiotemporal cortex
√ "cracked walnut" appearance of brain atrophy = symmetrically enlarged sulci in high-convexity area
√ focal atrophic change in medial temporal lobe (82% sensitive, 75% specific, 80% accurate):
  √ volume loss of hippocampus + parahippocampal gyrus
  √ enlargement of perihippocampal fissures
√ smooth periventricular halo of hyperintensity (50%)
PET (axial images with 3D stereotactic surface projection):

√ classic pattern of altered cortical metabolism:
√ hypometabolism in posterior cingulate gyrus, precuneus, posterior temporal + parietal lobes (earliest changes)
√ hypometabolism of prefrontal association cortices ± frontal lobe involvement
√ sparing of sensorimotor cortex, visual cortex, anterior cingulate cortex, basal ganglia, thalamus, posterior fossa

Prognosis: 4th leading cause of death in individuals > 65 years

AMYOTROPHIC LATERAL SCLEROSIS

= Lou Gehrig's disease (famous baseball player for NY Yankees)
= most common form of motor neuron disease (without autonomic / sensory / cognitive involvement)

Cause: free radical damage to neurons / autoimmune process / heavy metal toxicity
Age: middle – late adulthood; M > F
Path: atrophy of precentral gyrus
Histo: loss of pyramidal + Betz cells in motor cortex; loss of anterior horn cells in spinal cord; swelling of proximal axons of neuronal cells

• progressive neurodegenerative disorder
  • upper neuronal symptoms: hyperreflexia, spasticity
  • lower neuronal symptoms: fasciculation, atrophy

MR:
√ hyperintense corticospinal tracts (corona radiata, corpus callosum, posterior limb of internal capsule, ventral aspect of brain stem, anterolateral column of spinal cord) on T2WI
√ low SI in motor cortex on T2WI ← iron deposition

DDx: Friedreich ataxia, vitamin B12 deficiency (abnormal signal limited to internal capsule)

ANENCEPHALY

= lethal anomaly with failure of closure of the rostral end of the neural tube by 5.6 weeks MA
◊ Associated with highest AF-AFP and MS-AFP values; > 90% will be detected with MS-AFP ≥ 2.5 MoM

Incidence: 1÷1,000 births in USA (3.5÷1,000 in South Wales); M÷F = 1÷4; most common congenital defect of CNS; 50% of all neural tube defects
Recurrence rate: 3–4%
Etiology: multifactorial (genetic + environmental)
Path: absence of cerebral hemispheres + cranial vault; partial / complete absence of diencephalic + mesencephalic structures; hypophysis + rhombencephalic structures usually preserved
Risk factors: family history of neural tube defect; twin pregnancy
Associated anomalies:
spinal dysraphism (17–50%), cleft lip / palate (2%), clubfoot (2%), umbilical hernia, amniotic band syndrome
√ absence of bony calvarium cephalad to orbits
√ ± cranial soft-tissue mass (= angiomatous stroma)
√ bulging froglike eyes

√ short neck
√ polyhydramnios (40–50%) after 26 weeks GA (← failure of normal fetal swallowing) / oligohydramnios
Dx: in 100% > 14 weeks GA
Prognosis: uniformly fatal within hours to days of life; in 53% premature birth; in 68% stillbirth
DDx: acrania, encephalocele, amniotic band syndrome

ANEURYSM OF CNS

Etiology:
(a) congenital (97%) = "berry aneurysm" in 2% of population (in 20% multiple); associated with aortic coarctation and adult polycystic kidney disease
(b) infectious (3%) = mycotic aneurysm
(c) arteriosclerotic: fusiform shape
(d) traumatic
(e) neoplastic
(f) fibromuscular disease

Risk factors:
(1) Family history for aneurysms in 1st- / 2nd-degree relatives
(2) Female gender
(3) Oral contraceptives / pregnancy
(4) Advanced age > 50 years
(5) Hypertension
(6) Cigarette smoking
(7) Cerebral arteriovenous malformation
(8) Vasculitis
(9) Connective tissue disorder: Marfan syndrome, Ehlers-Danlos syndrome type IV, autosomal dominant polycystic renal disease, pseudoxanthoma elasticum, neurofibromatosis type 1
(10) Asymmetry of circle of Willis

Pathogenesis: arterial wall deficient in tunica media + external elastic lamina (natural occurrence with advancing age)

Aneurysm by shape:
A. Saccular
= berry- / bleb-like outpouching
Cause: hemodynamic stress + repeated endothelial damage ← turbulent blood flow
Site: circle of Willis (COW) in 90–95%, arterial bifurcation in 5–10%
Location: anterior circulation (90%), posterior circulation (10%), distal to COW (5%)
Size: 2–3 mm small to giant >2.5 cm
B. Fusiform
= circumferential involvement of wall
Cause: predominantly atherosclerotic degeneration
Location: posterior circulation
(a) Serpentine

= partly thrombosed containing tortuous vascular channels

Cause: recurrent cycles of thrombosis + recanalization within fusiform aneurysm

Location of aneurysm:

A. by autopsy:
   (a) circle of Willis (85%): aCom (25%), pCom (18%), MCA bifurcation (25%), distal ACA (5%), ICA at bifurcation (4%), ophthalmic a. (4%), anterior choroidal a. (4%)
   (b) posterior fossa (15%): basilar bifurcation (7%), basilar trunk (3%), vertebral-PICA (3%), PCA (2%)
B. by CT: detection rate of aneurysms at pCom (40%), aCom / MCA, basilar artery (80%)
C. by angiography (= symptomatic aneurysms): pCom (38%) > aCom (36%) > MCA bifurcation (21%) > ICA bifurcation > tip of basilar artery (2.8%)
D. by risk of bleeding: 1–2% per year aCom (70% bleed), pCom (2nd highest risk)

◊ Aneurysms at bifurcations / branching points are at greatest risk for rupture!

NECT:
- √ well-delineated round / lobulated slightly hyperdense extra-axial mass
- √ calcium deposit common in atherosclerotic fusiform aneurysm

CECT:
- √ enhancing lumen of partially thrombosed aneurysm
- √ rim-enhancement in completely thrombosed aneurysm

CTA: 95% positive detection rate

MR:
- √ mass:
  - √ iso- / hyperintense on T1WI
  - √ hypointense on T2WI (DDx to primary brain tumor)
- √ patent aneurysm with internal signal / flow void ← rapid internal blood flow:
  - √ flow void on T2WI = CLASSIC feature
  - √ flow void on T1WI in 50% (DDx: aerated anterior clinoid / supraorbital cell)
- √ partially / completely thrombosed aneurysm:
  - √ well-demarcated round para- / intrasellar lesion
  - √ internal T1-hyperintensity + CHARACTERISTIC heterogeneous T2-hypointensity ← blood clot
  - √ laminated layers of variable SI if thrombosed
- √ hypointense rim of hemosiderin
- √ high SI in sulci + cisterns on FLAIR = sign of rupture

CEMR (T1WI):
- √ enhancing slow flow in patent lumen
- √ increased phase artifact in patent aneurysm

MRA (3D TOF): detects aneurysm > 3 mm in diameter

Angio (all 4 cerebral vessels):
- √ contrast outpouching
- √ < 2 mm infundibuli typically occur at pCom / anterior choroidal a. origin
- √ mass effect in thrombosed aneurysm
- ◊ 2nd arteriogram within 1–2 weeks detects aneurysm in 10–20% following negative 1st

angiogram!

Purpose: confirm aneurysm and host vessel, detect multiple aneurysms, define neck, identify perforating arteries, assess potential for collateral circulation

Prognosis:

(1) Death in 10% within 24 hours from concomitant intracerebral hemorrhage, extensive brain herniation, massive infarcts + hemorrhage within brainstem
Mortality: 45% within 30 days (25% prior to admission)

(2) Complete recovery in 58% of survivors

(3) Cerebral ischemia + infarction

(4) Rebleeding rate: 12–20% within 2 weeks, 11–22% within 30 days, up to 50% within 6 months (increased mortality); thereafter 1–2–4% risk/year

Cx: subdural hematoma

Rx: clipping; endovascular coiling

Surgical mortality rate: 50% (1–3%) for ruptured (unruptured) aneurysm

Cavernous Sinus Aneurysm

Age: 20–70 years, peak 5th–6th decade; F >> M

Cause: sinus thrombophlebitis

- progressive visual impairment
- **cavernous sinus syndrome**: trigeminal nerve pain, oculomotor nerve paralysis

Site: extradural portion of cavernous sinus ICA

√ undercutting of anterior clinoid process
√ erosion of lateral half of sella
√ erosion of posterior clinoid process
√ invasion of middle cranial fossa
√ enlargement of superior orbital fissure
√ erosion of tip of petrous pyramid
√ rimlike calcification (33%)
√ displacement of thin bony margins without sclerosis

Rx: often inoperable; balloon embolization ± parent artery occlusion

Giant Aneurysm

= aneurysm > 25 mm in diameter, usually presenting with intracranial mass effect
◊ Risk of rupture increases proportionally with size!

Incidence: 5% of all intracranial aneurysms

Age: 5th–7th decade; M< F

- visual disturbance; cranial nerve palsy; seizure
- TIA / infarct ← thromboemboli from aneurysm

Type: saccular >> fusiform

Location: (arise from arteries at the base of the brain)

(a) middle fossa: cavernous segment of ICA (43%), supraclinoid segment of ICA, terminal bifurcation of ICA, middle cerebral artery

(b) posterior fossa: at tip of basilar artery, AICA, vertebral a.

Skull film:

√ predominantly peripheral curvilinear calcification (22%)

√ mass effect:
√ bone erosion (44%)
√ pressure changes on sella turcica (18%)

CT:
√ well-delineated, round / lobulated, slightly hyperattenuating extraaxial mass
√ often peripheral intramural / luminal calcified thrombus

CECT:
√ "target" sign = centrally opacified vessel lumen + ring of thrombus + enhancing fibrous outer wall
√ simple ring-blush (75%) of fibrous outer wall with total thrombosis
√ little / no surrounding edema

MR:
√ mixed heterogeneous signal intensity of laminated appearance (= combination of subacute + chronic hemorrhage, calcification)

Cx: 6% annual risk of rupture; subarachnoid hemorrhage in > 50%

Mortality for untreated giant aneurysm:
68% at 2 years, 80% at 5 years

DDx: partially thrombosed giant aneurysm may mimic slowly growing solid destructive tumor → MR / conventional angiography prior to biopsy!

Ruptured Berry Aneurysm

Incidence: 28,000 cases/year = 10 cases/10,000 persons/year

Age: 50–60 years of age; M÷F = 1÷2

Rupture size: 5–15 mm

- "worst headache of one's life" ± meningismus
- neck stiffness, nausea, vomiting
- history of warning leak / sentinel hemorrhage hours to days earlier; sudden loss of consciousness (in up to 45%)

Clues for which aneurysm is bleeding:
(a) the largest aneurysm (87%)
(b) anterior communicating artery (70%)
(c) contralateral side of all visualized aneurysms (60%), nonvisualization due to spasm

mnemonic: BISH
Biggest
Irregular contour
Spasm (adjacent)
Hematoma location

Location of blood suggesting accurately in 70% the site of the ruptured aneurysm:
(a) according to location of <u>subarachnoid hemorrhage</u>:

1. Anterior chiasmatic cistern:	aCom
2. Septum pellucidum:	aCom
3. Interhemispheric fissure:	aCom
4. Intraventricular:	aCom, ICA, MCA
5. Sylvian fissure:	MCA, ICA, pCom

6. Anterior pericallosal cistern: ACA, aCom
7. Prepontine cistern: basilar a.
8. Foramen magnum: PICA
9. Symmetric distribution in subarachnoid space: ACA + basilar a.

(b) according to location of cerebral hematoma:

1. Inferomedial frontal lobe: aCom
2. Temporal lobe: MCA
3. Corpus callosum: pericallosal a.

(c) intraventricular hemorrhage:
from aneurysms at aCom, MCA, pericallosal artery
CAVE: blood may have entered in retrograde manner from subarachnoid location

Multiple CNS Aneurysms

Cause: congenital in 20–30%, mycotic in 22%
mnemonic: FECAL P
Fibromuscular dysplasia
Ehlers-Danlos syndrome
Coarctation
Arteriovenous malformation
Lupus erythematosus
Polycystic kidney disease (adult)

◊ 35% of patients with one MCA aneurysm have one on the contralateral side (= mirror image aneurysms)!

◊ Simultaneous aneurysm + AVM in 4–15%

Mycotic Aneurysm

= 3% of all intracranial aneurysms; multiple in 20%
Source: subacute bacterial endocarditis (65%), acute bacterial endocarditis (9%), meningitis (9%), septic thrombophlebitis (9%), myxoma
Location: distal to first bifurcation of major vessel (64%); often located near surface of brain, especially over convexities
(a) suprasellar cistern = circle of Willis
(b) inferolateral sylvian fissure = MCA trifurcation
(c) genu of corpus callosum = origin of callosomarginal artery
(d) bottom of 3rd ventricle = pericallosal a.

NECT:
√ aneurysm rarely visualized; indirect evidence from focal hematoma after rupture
√ zone of increased density / calcification
√ increased density in subarachnoid, intraventricular, intracerebral spaces ← extravasated blood
√ focal / diffuse lucency of brain ← edema / infarction / vasospasm

CECT:
√ intense homogeneous enhancement within round / oval mass contiguous with vessel

√ incomplete opacification with mural thrombus

Cx: recurrent bleeding (more frequent than with congenital aneurysm)

Supraclinoid Carotid Aneurysm

= 38% of intracranial aneurysms

Site: (a) at origin of pCom (65%)
(b) at bifurcation of internal carotid artery (23%)
(c) at origin of ophthalmic artery (12%) medial to anterior clinoid process → most likely to become giant aneurysm

Presentation: bitemporal hemianopia ← extrinsic compression on chiasm

√ calcifications rare (DDx: frequent in atherosclerotic cavernous sinus aneurysm)

AQUEDUCTAL STENOSIS

= focal reduction in size of aqueduct at level of superior colliculi / intercollicular sulcus (normal range, 0.2–1.8 mm2)

Embryology:
aqueduct develops at 6th week GA + decreases in size until birth ← growth pressure from adjacent mesencephalic structures

Incidence: 0.5–1÷1,000 births; most frequent cause of congenital hydrocephalus (20–43%); 1–4.5% recurrence rate in siblings; M÷F = 2÷1

Manifestation: any time from fetal age to adulthood; age at presentation depends on severity of stenosis and hydrocephalus

Etiology:
(a) postinflammatory (50%): perinatal infection (toxoplasmosis, CMV, syphilis, mumps, influenza virus) OR intracranial hemorrhage → destruction of ependymal lining of aqueduct → marked adjacent fibrillary gliosis
(b) developmental: aqueductal forking (= marked branching of aqueduct into channels) / narrowing / transverse septum (X-linked recessive inheritance in 25% of males)
(c) neoplastic (extremely rare): pinealoma, meningioma, tectal astrocytoma (may be missed on routine CT scans, easily visualized by MR)

May be associated with: other congenital anomalies (16%): thumb deformities

Location: most often proximal aqueduct as congenital / acquired (= postinflammatory aqueductal gliosis) stenosis

√ enlargement of lateral + 3rd ventricles + normal-sized sulci and 4th ventricle (4th ventricle may be normal with communicating hydrocephalus)

◊ Adult hydrocephalus is in 10% due to aqueductal stenosis!

√ rounded anterior recesses extending into suprasellar cistern

√ 3rd ventricular floor displaced inferiorly into prepontine cistern

Prognosis: 11–30% mortality

Rx: 3rd ventriculostomy = creating a perforation in tuber cinereum → communication with prepontine cistern

N.B.: Alert surgeon prior to ventriculostomy of an anomalous floor contour of 3rd ventricle (long-standing hydrocephalus displaces floor downward)

ARACHNOID CYST

= CSF-containing intraarachnoid cyst without ventricular communication / brain maldevelopment

Incidence: 1% of all intracranial space-occupying lesions

Origin:

(1) congenital: arising from clefts / duplication / "splitting" of arachnoid membrane with expansion by CSF due to secretory activity of arachnoid cells = **true arachnoid cyst**

(2) acquired: following surgery / trauma / subarachnoid hemorrhage / infection in neonatal period / associated with extraaxial neoplasm = loculation of CSF surrounded by arachnoidal scarring with expansion by osmotic filtration / ball-valve mechanism = **leptomeningeal cyst** = **secondary arachnoid cyst** = **acquired arachnoid cyst**

Histo: cyst filled with clear fluid; thin wall composed of cleaved arachnoid membrane; lined by ependymal / meningothelial cells

Age: presentation at any time during life

- often asymptomatic
- symptomatic ← mass effect, hydrocephalus, seizures, headaches, hemiparesis, intracranial hypertension, craniomegaly, developmental delay, visual loss, precocious puberty, bobble-head doll syndrome

Location: in CSF cisterns between brain + dura

(a) floor of middle fossa near tip of temporal lobe (50%): common in sylvian fissure
- usually asymptomatic

(b) suprasellar / chiasmatic cistern (10%)
- propensity to become symptomatic in early childhood:
  - hydrocephalus (most common manifestation)
  - visual impairment
  - endocrinopathy: eg, precocious puberty

(c) posterior fossa (⅓–¼): cerebellopontine angle (11%), quadrigeminal plate cistern (10%), in relationship to vermis (9%), prepontine / interpeduncular cistern (3%)

Associated with: Aicardi syndrome, glutaric aciduria type I, unbalanced X,9 translocation

(d) interhemispheric fissure, cerebral convexity, anterior infratentorial midline

√ forward bowing of anterior wall of cranial fossa + elevation of sphenoid ridge
√ extraaxial unilocular thin-walled CSF-density cyst with well-defined smooth angular margins
√ compression of subarachnoid space + subjacent brain (minimal mass effect)
√ may erode inner table of calvarium
√ NO enhancement (intrathecal contrast penetrates into cyst on delayed scans)
√ NO calcifications

MR (best modality):

√ well-circumscribed extraaxial fluid collection / cyst isointense to CSF
√ lack of complete signal suppression (on fluid-attenuated inversion-recovery sequence) ← proteinaceous content
√ free water motion / facilitated diffusion similar to CSF on DWI
√ thin cyst wall not visualized on MR

Cx: (1) hydrocephalus (30–60%) + remodeling / thinning of overlying occipital bone ←

secondary obstruction of ventricular system ← mass effect on cerebellum + vermis ← enlargement during infancy

(2) concurrent subdural / intracystic hemorrhage

Prognosis: favorable if removed before onset of irreversible brain damage

Rx: resection, fenestration, endoscopic ventriculocystostomy, cystoperitoneal shunting

CT-DDx:

epidermoid cyst, dermoid, subdural hygroma, infarction, porencephaly

US-DDx:

choroid plexus cyst, porencephalic cyst (communicates with ventricle), cystic tumor (solid components), midline cyst associated with agenesis of corpus callosum, dorsal cyst associated with holoprosencephaly, Dandy-Walker cyst (extension of 4th ventricle, developmental delay), vein of Galen aneurysm

Posterior Fossa Arachnoid Cyst

Incidence: 10% of arachnoid cysts in children

- may be asymptomatic + discovered incidentally
- obstructed CSF flow possible → macrocephaly, signs of increased intracranial pressure, developmental delay

Location:

(a) retrocerebellar = inferior / posterior to vermis (in midsagittal location)

(b) supravermian = cranial to vermis in tentorial hiatus

(c) anterior / lateral to cerebellar hemispheres

(d) anterior to brainstem

√ NO communication with 4th ventricle / subarachnoid space

Differences between Epidermoid and Arachnoid Cyst

	Epidermoid	*Arachnoid Cyst*
CT density	± hyperdense to CSF	CSF-like
Margins	scalloped	smooth
Vessels	encased	displaced
Proton density	deviates from CSF	CSF-like
Diffusion	restricted	CSF-like

ARTERIOVENOUS FISTULA

= AVF

= abnormal communication between artery + vein resulting in tremendous amount of flow due to high pressure gradient → enlargement + elongation of draining veins; NO nidus

Cause:

(1) Vessel laceration (delay between trauma + clinical manifestation ← delayed lysis of hematoma surrounding arterial laceration)

(2) Angiodysplasia: fibromuscular disease, neurofibromatosis, Ehlers-Danlos syndrome

(3) Congenital arteriovenous fistula

Location:

(a) carotid-cavernous sinus fistula (most common)

(b) vertebral artery fistula
(c) external carotid artery fistula (rare)

Carotid-Cavernous Sinus Fistula

= abnormal communication between veins of cavernous sinus and ≥ 1 branches of internal / external carotid artery

(1) **Direct shunt** = direct communication between cavernous segment of ICA + cavernous sinus

Etiology:

(1) Trauma: laceration of ICA within cavernous sinus
  (a) usually due to basal skull fracture (cavernous ICA + small cavernous branches fixed to dura)
  (b) penetrating trauma
  (c) surgery
(2) Spontaneous: rupture of an intracavernous ICA aneurysm (in atherosclerosis, Ehlers-Danlos syndrome, osteogenesis imperfecta, pseudoxanthoma elasticum)
(3) Dural sinus thrombosis

Age: any

- classic triad:
  - pulsatile exophthalmos, conjunctival chemosis / edema
  - persistent auscultatory orbital bruit
- restricted extraocular movement
- decrease in vision ← increase in intraocular pressure (50%) / cranial nerve deficits = indication for EMERGENT TREATMENT

(2) **Indirect shunt** = communication between dural branch of ICA / ECA + cavernous sinus

Age: 40–60 years; M < F

Etiology: atherosclerosis

- proptosis, loss of vision

√ ± visualization of feeding dural branches of ECA / ICA

Route of drainage:

(a) superior ophthalmic vein (common)
(b) contralateral cavernous sinus
(c) petrosal sinus
(d) cortical veins (rare)

√ dilatation + tortuosity of ipsilateral superior ophthalmic vein, facial veins, internal jugular vein
√ enlargement of dural venous sinuses ← increased venous flow + pressure
√ enlarged edematous extraocular muscles
√ focal asymmetric / diffuse enlargement of cavernous sinus
√ occasionally sellar erosion / enlargement
√ enlargement of superior orbital fissure (in chronic phase)
√ stretching of optic nerve
√ proptosis
√ subchoroidal effusion

US:

√ arterial flow in cavernous sinus + superior ophthalmic vein

CECT:

√ early opacification of cavernous sinus

MR:

√ flow voids in cavernous sinus

Angio:

√ ipsilateral ICA contrast injection shows wall of ICA to be incomplete

√ contralateral ICA contrast injection + compression of involved ICA

√ early opacification of veins of cavernous sinus

√ retrograde flow through dilated superior ophthalmic vein

Rx: transvenous / transarterial coil ablation ± stent placement; latex / silicone balloon detached inside cavernous sinus to plug laceration (→ ocular signs resolve within 7–10 days with successful treatment)

DDx: cavernous sinus thrombosis, enhancing cavernous sinus mass (meningioma, metastasis)

Dural AV Fistula

Arterial supply: artery normally feeding meninges (meningeal artery) / bone / muscles

Draining vein: venules within wall of dural sinus / cortical vein

Cause: dural sinus thrombosis → collateral revascularization

Prevalence: 10–15% of intracranial AV shunts

Peak age: 20–40 years; M=F

- pulsatile tinnitus

Borden classification:

- benign fistula (Borden type 1) → no cortical venous reflux → no neurologic deficits
- malignant fistula (Borden type 2 & 3) → with cortical venous reflux
  - intracranial hemorrhage, seizure, dementia
  - focal neurologic symptoms due to venous congestion / rupture of venous pouches; altered consciousness

Location: cavernous sinus (20–40%), transverse / sigmoid sinus (20–60%), tentorium (12–14%), superior sagittal sinus (8%), anterior fossa (2–3%)

CECT:

√ multiple small vessels within wall of thrombosed / partially recanalized stenotic dural venous sinus

√ prominent feeding meningeal artery:

(a) ECA → dural / transosseous branch

(b) ICA / vertebral artery → tentorial / dural branch

√ enlarged draining veins

√ dilated transcalvarial channels ← transosseous feeding artery

MR:

√ dilated cortical veins (= pseudophlebitic pattern):

√ abnormal enhancing tubular structures

√ flow voids within cortical sulci

√NO true nidus within brain parenchyma

Rx: observation, embolization, surgical resection

DDx: dural venous sinus thrombosis with prominent collaterals, pial AV malformation, pial AV fistula

Pial AV Fistula

= often high-flow lesions with direct fistulous communication between a pial artery + a vein WITHOUT intervening nidus

Arterial supply: enlarged pial artery
Draining vein: enlarged draining vein / capillary bed
Prevalence: 5% of all brain AVMs
Associated with: hereditary hemorrhagic telangiectasia (frequent)
Location: brain surface
Cause: trauma, genetically dysregulated angiogenesis
√ dilated vessels of brain surface (from MCA, ACA, PCA)
√ asymmetric dilatation of pial feeder artery
√ dilated often (serpentine) varicose draining vein
√ ± dilated venous pouches outside brain parenchyma
√ NO nidus / classic intraparenchymal tangle of vessels
√ ± spontaneous intracranial hemorrhage
Rx: embolization of draining vein at fistula
DDx: AV malformation, dural AV fistula, vein of Galen malformation

ARTERIOVENOUS MALFORMATION

= congenital abnormality consisting of abnormal dilated closely packed pathologic vessels → shunting of blood from arterial to venous side without intermediary capillary bed

Risk of future hemorrhage:
(a) evidence of old hemorrhage (gradient-echo T2 sequence)
(b) angioarchitectural weak points:
› aneurysm: (1) intranidal (2) posterior fossa location
› venous caliber: (3) ectasia + (4) stenosis
› venous drainage: (5) deep + (6) single
◊ Imaging report should mention these risk factors!

Risk of nonhemorrhagic neurologic deficit:
high-flow shunt, venous congestion / outflow obstruction, long pial course of draining vein, perifocal / perinidal gliosis, mass effect / hydrocephalus, arterial steal

Classic Brain (Pial) AVM

◊ Most common type of symptomatic vascular malformation!

Diagnostic criteria:
(a) presence of a nidus = racemose tangle of abnormal dilated tortuous arteries + veins embedded within parenchyma
› glomerular / compact nidus = abnormal vessels without any interspersed normal brain tissue
› diffuse / proliferative nidus = interspersed normal brain parenchyma (2–4%)
(b) early venous drainage

Histo: affected arteries have thin walls (no elastica, small amount of muscularis)
Prevalence: 0.02–0.15% for sporadic AVM; 2% for syndromic AVM (hereditary hemorrhagic telangiectasia, cerebrofacial AV metameric syndrome)
Peak age: 20–40 years; 80% by end of 4th decade; 20% < 20 years of age; M=F
Associated with: aneurysm in feeding artery in 10%

- headaches, seizures (nonfocal in 40%), mental deterioration
- progressive hemispheric neurologic deficit (50%)
- ictus from acute intracranial hemorrhage (50%): multicompartmental in 31%, subarachnoid in 30%, parenchymal in 23%, intraventricular in 16%

Location: usually solitary; in 2% multiple
(a) supratentorial (90%): parietal > frontal > temporal lobe > paraventricular > intraventricular region > occipital lobe
(b) infratentorial (10%)

Site: (a) superficial / cortical:
› supply via pial arteries = branches of ACA, MCA, PCA;
› drainage via cortical veins
(b) deep / ventricular:
› supply via lenticulostriate, thalamoperforator branches, anterior / medial / lateral / posterior choroidal arteries
› drainage via deep venous system

Vascular supply:
(a) pial branches of ICA in 73% of supratentorial location, in 50% of posterior fossa location
(b) dural branches of ECA in 27% with infratentorial lesions
(c) mixed

√ NO mass effect (due to replacement of normal brain tissue) unless complicated by hemorrhage + edema:
√ intraparenchymal / intraventricular / subarachnoid hemorrhage
√ adjacent parenchymal atrophy ← vascular steal + ischemia

Skull film:
√ speckled / ringlike calcifications (15–30%)
√ thinning / thickening of skull at contact area with AVM
√ prominent vascular grooves on inner table of skull (= dilated feeding arteries + draining veins) in 27%

NECT:
√ irregular lesion with large feeding arteries + draining veins
√ mixed density (60%): dense large vessels + hemorrhage + calcifications
√ isodense lesion (15%): recognizable by mass effect
√ low density (15%): brain atrophy due to ischemia
√ not visualized (10%)

CECT:
√ tangle of intensely enhancing tubular structures = nidus ← tortuous dilated vessels (in 80%):
√ No avascular spaces within AVM
√ rapid shunting with veins seen during "arterial" phase

√ ± interspersed internal focal isoattenuating areas ← normal brain parenchyma (in diffuse subtype)

√ lack of mass effect / edema (unless thrombosed / bleeding)

√ No enhancement if thrombosed

√ thickened arachnoid covering

MR:

√ flow void ← rapid arteriovenous shunting (imaging with GRASS gradient echo + long TR sequences)

√ 3-D TOF demonstrates feeding arteries + nidus + draining veins

Pitfalls: (1) signal void in tortuous vessels

(2) nonvisualization of draining veins resulting from spin saturation

(3) difficulty differentiating blood flow from blood clot

Angio:

√ grossly dilated efferent + afferent vessels with a racemose tangle ("bag of worms")

√ arteriovenous shunting into at least one early draining vein

√ negative angiogram ← compression by hematoma / thrombosis

Cx: (1) Hemorrhage (common): bleeding on venous side ← increased pressure / ruptured aneurysm (5%)

(2) Infarction

Rx: embolization, stereotactic radiosurgery, microsurgery

Prognosis: 10% mortality; 30% morbidity

Risk of hemorrhage: lifelong; increasing yearly by 2–4%; increasing to 6% in year following 1st bleed + 25% in year following 2nd bleed

DDx: glioblastoma with AV shunting, dural AV fistula, cerebral proliferative angiopathy

Cerebral Proliferative Angiopathy

= diffuse nidus type AVM

Prevalence: 2–4%

Mean age: 20 years; M÷F = 1÷2

- progressive neurologic deficit
- transient ischemic attack, seizure, headaches

Histo: proliferative "nidus" composed of multiple arteries with intervening gliotic brain parenchyma between vessels

Pathophysiology: cortical ischemia → endothelial proliferation + angiogenesis

Location: often entire lobe / brain hemisphere

Vascular supply:

(a) arterial feeders of normal size / only moderately enlarged + associated stenoses

(b) extensive transdural supply through branches of ECA

(c) lack of clear early venous drainage

MR:

√ multiple flow voids

√ contrast-enhanced tubular structures

√ normal brain parenchyma interspersed between abnormal vessels

Angio:

√ relatively normal-sized arterial branches
√ lack of early venous drainage
√ extensive transdural supply via middle meningeal artery

Cerebrofacial Arteriovenous Metameric Syndrome

= CAMS = WYBURN-MASON SYNDROME = BONNET-DECHAUME-BLANC DISEASE

Cause: somatic mutation occurring in region of neural crest / adjacent cephalic mesoderm before migration of precursor cells to their final location = segmental neurovascular syndrome

Classification:

CAMS type 1: involves medial prosencephalon → AVMs in corpus callosum, hypothalamus (hypophysis), nose

CAMS type 2: involves lateral prosencephalon → AVMs in occipital lobe, optic tract including thalamus, retina, maxilla

CAMS type 3: involves rhombencephalon, → AVMs in cerebellum, pons, mandible

Clue: multiple AVMs in brain parenchyma + facial region in a segmental distribution

Age: childhood

- rarely manifest with hemorrhage
- symptoms related to facial AVMs:
  - progressive vision loss resulting in blindness
  - severe bleeding from teeth and gums
  - cosmetic problems like facial asymmetry

ASTROCYTOMA

Incidence: 70–75% of all primary intracranial tumors; most common brain tumor in children (40–50% of all primary pediatric intracranial neoplasms)

Distribution: proportional to amount of white matter

Location:

cerebral hemisphere (lobar), thalamus, pons, midbrain, may spread across corpus callosum; no particular lobar distribution

(a) in adults: central white matter of cerebrum (15–30% of all gliomas)
(b) in children: cerebellum (40%), brainstem (20%), supratentorial (30%)

Well-differentiated = Low-grade Astrocytoma

Incidence: 9% of all primary intracranial tumors; 10–15% of gliomas

Age: 20–40 years; M > F

Path: benign nonmetastasizing; poorly defined borders with infiltration of white matter + basal ganglia + cortex; NO significant tumor vascularity / necrosis / hemorrhage; blood-brain barrier may remain intact

WHO Classification of Astrocytomas		
Grade I	Circumscribed astrocytoma	generally benign well-circumscribed tumor, specific unique histologic features for each tumor, pilocytic astrocytoma (most common), subependymal giant cell astrocytoma; no tendency to progress to higher grade; low rate of recurrence
Grade II	Astrocytoma	diffusely infiltrating; well-differentiated; minimal pleomorphism or nuclear atypia; no vascular proliferation / necrosis
Grade III	Anaplastic astrocytoma	pleomorphism and nuclear atypia; increased cellularity; mitotic activity; vascular proliferation + necrosis absent
Grade IV	Glioblastoma multiforme	marked vascular proliferation and necrosis; increased cellularity; anaplasia + pleomorphism; variable mitotic activity; cell type may be poorly differentiated, fusiform, round or multinucleated

Histo: homogeneous relatively uniform appearance with proliferation of well-differentiated multipolar fibrillary / protoplasmic astrocytes; mild nuclear pleomorphism + mild hypercellularity; rare mitoses

Location: posterior fossa in children, supratentorial in adults (typically lobar)

√ may develop a cyst with high-protein content (rare)

CT:

√ usually hypodense lesion with minimal mass effect + minimal / NO peritumoral edema

√ well-defined tumor margins

√ central calcifications (15–20%)

√ minimal / no contrast enhancement (normal capillary endothelial cells)

MR:

√ well-defined hypointense lesion with little mass effect / vasogenic edema / heterogeneity on T1WI

√ hyperintense on T2WI

√ little / no enhancement on Gd-DTPA

√ cyst with content hyperintense to CSF ← protein

√ hyperintense area within tumor mass ← paramagnetic effect of methemoglobin

√ inhomogeneous gadolinium-DTPA enhancement of tumor nodule

Angio:

√ majority avascular

Prognosis: 3–10 years postoperative survival; may convert into more malignant form several years later

Anaplastic Astrocytoma

Incidence: 11% of all primary intracranial neoplasms; 25% of gliomas

Path: frequently vasogenic edema; NO necrosis / hemorrhage

Histo: less well differentiated with greater degree of hypercellularity + pleomorphism, multipolar fibrillary / protoplasmic astrocytes; mitoses + vascular endothelial proliferation common

Location: typically frontal + temporal lobes

MR:

√ moderate mass effect

√ well-defined slightly heterogeneous hypointense lesion on T1WI with prevalent vasogenic edema

√ hyperintense on T2WI

√ ± enhancement on Gd-DTPA

Prognosis: postoperative survival of 2 years

Cerebellar Astrocytoma

= CEREBELLAR PILOCYTIC ASTROCYTOMA

2nd most frequent tumor of posterior fossa in children

Incidence: 10–20% of pediatric brain tumors

Histo: mostly grade I

Age: children > adults; no specific age peak; M÷F = 1÷1

Path:

(1) cystic lesion with tumor nodule ("mural nodule") in cyst wall (50%); (midline astrocytomas cystic in 50%, hemispheric astrocytomas cystic in 80%)
(2) solid mass with cystic (= necrotic) center (40–45%)
(3) solid tumor without necrosis (< 10%)

- hydrocephalus, headache, vomiting, neck pain, 6th nerve palsy
- blurred vision, diplopia, papilledema, nystagmus
- cerebellar signs: truncal ataxia, dysdiadochokinesia appendicular dysmetria, gait disturbance

Location: originating in midline with extension into cerebellar hemisphere (29–53%), vermis (16–71%) > tonsils > brainstem (34%)

√ calcifications (20%): dense / faint / reticular / punctate / globular; mostly in solid variety

√ may develop extreme hydrocephalus (quite large when finally symptomatic)

CT:

√ round / oval cyst with density of cyst fluid > CSF
√ round / oval / plaquelike mural nodule with intense homogeneous enhancement
√ cyst wall slightly hyperdense + nonenhancing (= compressed cerebellar tissue)
√ uni- / multilocular cyst (= necrosis) with irregular enhancement of solid tumor portions
√ round / oval lobulated fairly well-defined iso- / hypodense solid tumor with hetero- / homogeneous enhancement

MR:

√ hypointense on T1WI + hyperintense on T2WI
√ enhancement of solid tumor portion

Angio:

√ avascular

Prognosis:

malignant transformation exceedingly rare
– 40% 25-year survival rate for solid cerebellar astrocytoma
– 90% 25-year survival rate for cystic juvenile pilocytic astrocytoma

DDx of solid astrocytoma:

(1) Medulloblastoma (hyperdense mass, noncalcified)
(2) Ependymoma (4th ventricle, 50% calcify)

DDx of cystic astrocytoma:

(1) Hemangioblastoma (lesion < 5 cm)
(2) Arachnoid cyst
(3) Trapped 4th ventricle

(4) Megacisterna magna
(5) Dandy-Walker cyst

Pilocytic Astrocytoma

= JUVENILE PILOCYTIC ASTROCYTOMA
= most benign histologic subtype of astrocytoma without progression to high-grade glioma
Incidence: 0.6–5.1% of all intracranial neoplasms
◊ Most common pediatric CNS glioma; 85% of all cerebellar + 10% of all cerebral astrocytomas in children
Age: predominantly in children + young adults; 75% in first 2 decades of life; peak age between birth and 9 years of age; M÷F = 1÷1
Histo: biphasic pattern of compact bipolar pilocytic (hairlike) astrocytes arranged mostly around vessels + loosely aggregated protoplasmic astrocytes undergoing microcystic degeneration
Associated with: neurofibromatosis type 1
Location: in / near midline
common: cerebellum, optic nerve / chiasm, hypothalamus (around 3rd ventricle)
less common: cerebral hemispheres (adults), cerebral ventricles, velum interpositum, spinal cord
Site: near ventricles (82%)
Imaging patterns:
(1) Cyst with intensely enhancing mural nodule (67%)
(a) nonenhancing cyst wall (21%)
(b) enhancing cyst wall (46%)
(2) Solid mass (33%)
(a) central nonenhancing necrotic zone (16%)
(b) minimal / no cystic component (17%)
CT:
√ well-demarcated smoothly marginated round / oval mass with cystic features
√ occasional calcifications
√ intense enhancement (94%)
√ multilobulated / dumbbell appearance along optic pathway
√ mural tumor nodule located in wall of cerebellar cyst
MR:
√ T1-isointense + T2-hyperintense to normal brain
√ small rim of vasogenic edema (low biologic activity)
√ increased heterogeneous signal intensity on early Gd-DTPA-enhanced T1WI; homogeneous enhancement on delayed images
Prognosis: relatively benign clinical course, almost never recurs after surgical excision; 94% (79%) postsurgical 10-year (20-year) survival; NO malignant transformation to anaplastic form
DDx: metastasis, hemangioblastoma, atypical medulloblastoma

Brainstem Pilocytic Astrocytoma

- nausea, vomiting, ataxia, torticollis

• papilledema, nystagmus, 6th & 7th nerve palsy
√ exophytic extension from dorsal surface of brainstem
√ obliteration of 4th ventricle
DDx: fibrillary astrocytoma (dismal prognosis)

Hypothalamic Pilocytic Astrocytoma
= HYPOTHALAMIC GLIOMA
• obesity, diabetes insipidus ← hypothalamic-pituitary dysfunction
• diencephalic syndrome (= emaciation despite normal / slightly decreased caloric intake, alert appearance, hyperkinesis, irritability, normal / accelerated growth)
• hemiparesis ← compression of corticospinal tracts
√ hydrocephalus
Prognosis: may regress spontaneously

Cerebral Pilocytic Astrocytoma
• headache, seizure activity, hemiparesis
• ataxia, nausea, vomiting
Location: temporal lobe

Optic Pathway Pilocytic Astrocytoma
= OPTIC NERVE GLIOMA
Location: optic nerve / chiasm
◊ Most common tumor in NF1 population (15–21%); NF1 diagnosed in ⅓ of all optic pathway gliomas; NF1 diagnosed in 40–70% of all tumors in this region; 1.5–3.5% of all orbital neoplasms; ²/₃ of all neoplasms of the optic nerve
Age: < 6 years; M÷F = 2÷1
• visual loss / visual-field deficit, optic disk pallor, optic nerve atrophy ← axonal damage + ischemia
• precocious puberty (39%) in NF1 patients

Pleomorphic Xanthoastrocytoma
= superficially located supratentorial tumor that involves leptomeninges
Prevalence: 1% of all brain neoplasms
Age: average age of 26 years (range, 5–82 years)
Path: circumscribed tumor attached to meninges with infiltration into surrounding brain
Histo: pleomorphic spindled tumor cells (reactive to glial fibrillary acidic protein) with intracytoplasmic lipid (xanthomatous) deposits in a dense intercellular reticulin network; giant cells; eosinophilic granular bodies; WHO grade II tumor
• long history of seizures (71%)
Location: supratentorial (98%): temporal (49%) / parietal (17%) / frontal (10%) / occipital (7%) lobe; thalamus; cerebellum; spinal cord
◊ Its PERIPHERAL LOCATION is the single most consistent imaging feature
√ cystic (48%) supratentorial mass with mural nodule
√ intense enhancement of solid portions
√ CHARACTERISTIC involvement of leptomeninges (71%)
√ peritumoral vasogenic edema / calcification / skull erosion are uncommon

CT:
√ hypo- / isoattenuating mass
MR:
√ hypo- to isointense mass relative to gray matter on T1WI
√ hyper- to isointense mass on T2WI
Rx: surgical resection (unresponsive to chemotherapy + radiation therapy)
Prognosis: 81% (70%) 5-year (10-year) survival rate; high rate of recurrence; malignant transformation in 20%
DDx: meningioma, glioblastoma multiforme, oligodendroglioma, metastatic disease, infection

ATAXIA-TELANGIECTASIA

= autosomal recessive disorder characterized by telangiectasias of skin + eye, cerebellar ataxia, sinus + pulmonary infections, immunodeficiencies, propensity to develop malignancies
Incidence: 1÷40,000 livebirths
Path: neuronal degradation + atrophy of cerebellar cortex (? from vascular anomalies)
• cerebellar ataxia at beginning of walking age
• progressive neurologic deterioration
• oculomotor abnormalities, dysarthric speech, choreoathetosis, myoclonic jerks
• mucocutaneous telangiectasias: bulbar conjunctiva, ears, face, neck, palate, dorsum of hands, antecubital + popliteal fossa
• recurrent bacterial + viral sinopulmonary infections
√ cerebellar cortical atrophy: diminished cerebellar size, dilatation of 4th ventricle, increased cerebellar sulcal prominence
√ cerebral hemorrhage ← rupture of telangiectatic vessels
√ cerebral infarct ← emboli shunted through vascular malformations in lung
Cx: (1) Bronchiectasis + pulmonary failure (most common cause of death)
(2) Malignancies (10–15%): lymphoma, leukemia, epithelial malignancies

BENIGN MACROCEPHALY OF INFANCY

= BENIGN ENLARGEMENT OF SUBARACHNOID SPACES = BENIGN EXTRAAXIAL COLLECTIONS OF INFANCY = EXTERNAL HYDROCEPHALUS
Cause: defective reabsorption of CSF at arachnoid villi; commonly familial with autosomal dominant inheritance
Age: presentation between 3 and 12 months
• infant with macrocephaly (head circumference > 90th percentile)
• delayed motor development, hypotonia (in up to 30%)
Location: bilateral frontoparietal area + interhemispheric fissure + sylvian fissure + basal cisterns
√ enlarged subarachnoid spaces
√ "floating" cortical veins
√ NO / mild ventricular enlargement
Cx: subdural hematoma in response to minor impacts
Prognosis: self-limiting transient development that usually resolves by 2–3 years

DDx: (1) Cerebral atrophy (diffuse sulcal prominence not localized to frontoparietal area)
(2) Spontaneous subdural hematoma (12%)

BINSWANGER DISEASE

= ENCEPHALOPATHIA SUBCORTICALIS PROGRESSIVA = LEUKOARIAOSIS = SUBCORTICAL ARTERIOSCLEROTIC ENCEPHALOPATHY (SAE)

Cause: arteriosclerosis affecting the poorly collateralized distal penetrating arteries (perforating medullary arteries, thalamoperforators, lenticulostriates, pontine perforators); positive correlation with hypertension + aging

Path: ischemic demyelination / infarction

Age: > 60 years

- psychiatric changes, intellectual impairment, slowly progressive dementia, transient neurologic deficits
- seizures, spasticity, syncope

Location: periventricular white matter, centrum semiovale, basal ganglia; sparing of subcortical white matter "U" fibers + corpus callosum

√ multifocal hypodense lesions (periventricular, centrum semiovale) with sparing of U fibers

√ lacunar infarcts in basal ganglia

√ sulcal enlargement + dilated lateral ventricles (brain atrophy)

MR:

√ focal areas of increased signal intensity on T2WI (= "unidentified bright objects")

DDx: leukodystrophy, progressive multifocal leukoencephalopathy, multiple sclerosis

BLAKE POUCH CYST

= embryonic midline outpouching of superior medullary velum extending inferior + posterior to vermis into cisterna magna

Blake pouch = rudimentary 4th ventricular tela choroidea membrane as a normal transient structure that regresses by 12 weeks GA to form the foramen of Magendie (communication between 4th ventricle + subarachnoid space)

Cause: failure of fenestration of foramen of Magendie

Age: neonate

√ retrocerebellar / infraretrocerebellar cyst = diverticulum of enlarged 4th ventricle

√ enhancing structure along anterosuperior aspect of cyst inferior to vermis = displaced choroid plexus (on SAG contrast-enhanced T1WI)

√ mild indentation of inferior vermis / caudomedial aspects of cerebellar hemispheres ← mass effect of cyst

√ tetraventricular hydrocephalus

Pertinent negatives:

√ NO supratentorial morphologic abnormalities aside from hydrocephalus

√ posterior fossa + cerebellum of normal size + shape

Prognosis: favorable (shunt-related complications possible)

DDx: megacisterna magna

BRAIN / CEREBRAL DEATH

Confirmatory tests of absent blood flow function:

1. Four-vessel contrast angiography (carotid and vertebral aa.)
2. Radionuclide cerebral blood flow angiography
3. CECT
4. Ultrasonic echoencephalography
5. Doppler ultrasound
6. Digital subtraction angiography (DSA)
7. MRI

◊ Administration of contrast may damage brain / kidney OR compromise tissue function

DDx by EEG:

Severe barbiturate intoxication (may produce a flat EEG response in the absence of brain death)

Radionuclide Angiography

= 1st-line test for cerebral perfusion; can be performed at the ICU bed site

Indication:

(1) Prior to organ harvest
(2) Hypothermia / drug intoxication interfering with clinical + EEG assessment of brain activity
(3) Brain death as a possible result of criminal activity

Pathophysiology: increased intracranial pressure above systemic arterial pressure results in markedly decreased cerebral perfusion → thrombosis → total cerebral infarction

Path: severe brain edema, diffuse liquefactive necrosis

Agent:

› nondiffusable hydrophilic ^{99m}Tc pentetic acid (^{99m}Tc-DTPA)
◊ Absence of effective cerebral perfusion at planar scintigraphy does NOT equate with brain death as blood flow to brainstem cannot be adequately assessed with ^{99m}Tc pentetic acid!
› diffusible brain imaging agents that cross the normal blood brain barrier
» lipophilic ^{99m}Tc bicisate (^{99m}Tc-ECD)
» lipophilic ^{99m}Tc exametazime (^{99m}Tc-HMPAO)

√ activity stops abruptly at the skull base = lack of activity in distribution of anterior and middle cerebral arteries + superior sagittal sinus (SSS) during 1st pass (= angiographic phase):
√ NO / faint activity in SSS on static image with ^{99m}Tc pentetic acid
√ absence of activity in cerebrum on delayed images with ^{99m}Tc bicisate / ^{99m}Tc exametazime
√ sagittal sinus not visualized

N.B.:

√ common carotid arteries must be clearly visualized on 1st pass which confirms a good technically adequate bolus
√ activity in face (“hot nose” sign) / scalp must not be mistaken as focal brain activity

False negative:

decrease in intracranial pressure may allow continuous flow through intracranial arteries

and has been observed in
(a) extensive liquefactive brain necrosis
(b) incompletely ossified skull in child
(c) open head injury in adults

CANAVAN DISEASE

= SPONGIFORM LEUKODYSTROPHY
= rare form of leukodystrophy as an autosomal recessive disorder, most common in Ashkenazi Jews
Incidence: < 100 reported cases
Cause: deficiency of aspartoacyclase leading to accumulation of N-acetylaspartic acid in brain, plasma, urine, CSF
Histo: spongy degeneration of white matter with astrocytic swelling + mitochondrial elongation
Age: 3–6 months
• marked hypotonia, spasticity, seizures
• progressive megalencephaly
• failure to attain motor milestones, intellectual failure
• optic atrophy with blindness, swallowing impairment
√ diffuse symmetric white matter abnormality
√ may involve basal ganglia
√ cortical atrophy
CT:
√ low-density white matter
MR:
√ white matter hypointense on T1WI + hyperintense on T2WI
Prognosis: death in 2nd–5th year of life
Dx: (1) elevation of N-acetylaspartic acid in urine
(2) deficiency of aspartoacyclase in cultured skin fibroblasts

CAPILLARY TELANGIECTASIA

= CAPILLARY ANGIOMA
= nest of dilated capillaries separated by normal neural tissue; commonly "cryptic"
May be associated with:
hereditary Rendu-Osler-Weber syndrome, ataxia-telangiectasia syndrome, irradiation (latency period of 5 months to 22 years)
Age: typically in elderly
• usually asymptomatic (incidental finding at necropsy)
Location: mostly in pons / midbrain > cerebral cortex > spinal cord; usually multiple / may be solitary
√ poorly defined area of dilated vessels (resembling petechiae)
√ best delineated with MR (due to hemorrhage) with focus of increased signal intensity on contrast-enhanced studies
Cx: punctate hemorrhage (uncommon); gliosis + calcifications (rare)

Prognosis: bleeding in pons (usually fatal)
DDx: cavernous angioma (identical image signature)

CAVUM VELI INTERPOSITI CYST

= cyst of ventricular roof in between two-layered tela choroidea
√ distortion of posterior superior contour of 3rd ventricle mimicking an obstructed 3rd ventricle
√ cyst of triangular contour on axial images
√ superior displacement of fornix
√ inferolateral displacement of internal cerebral veins

CENTRAL NEUROCYTOMA

= name reserved for neurocytoma that occurs in ventricles
Incidence: 0.25–0.5% of intracranial tumors
Origin: ? bipotential progenitor cells capable of both neuronal + glial differentiation
Histo: solid sheets / large lobules of small round to ovoid neoplastic cells with delicate vascular network + intervening irregular patches of fibrillary neuropils; pineocytomatous rosettes (not in oligodendroglioma)
Immunohisto: synaptophysin, neuron-specific enolase
Mean age: 29 years (range, 8 days to 67 years); M=F
• symptoms of increased intracranial pressure
Location: (a) lateral ventricle ± extension into 3rd ventricle
Site: septum pellucidum, ventricular wall
(b) extraventricular: parenchyma, cerebellum, spinal cord
√ well-circumscribed lobulated mass
√ frequently "bubbly" appearance ← presence of multiple cysts
√ calcifications (50%)
√ moderate to strong enhancement
CT:
√ hyperattenuating lesion
MR:
√ lesion T1-isointense + T2-hyperintense to gray matter
√ ± prominent flow voids
√ increased T2 signal intensity in adjacent periventricular white matter

MR spectroscopy:
√ presence of glycine (3.55 ppm)

Rx: usually curative resection
Cx: recurrence after resection, CSF dissemination

CEPHALOCELE

= mesodermal defect of calvarial suture + dura with extracranial extension (= herniation) of intracranial structures and persistent connection to subarachnoid space

Cranial meningocele: = herniation of meninges + CSF only

Encephalocele = herniation of meninges
(Meningoencephalocele) + CSF + neural tissue

Nomenclature: based on origin of their roof + floor
eg, frontonasal: frontal bone = roof, nasal bone = floor

Prevalence:
1–4÷10,000 live births; 5–6–20% of all craniospinal malformations; predominant neural axis anomaly in fetuses spontaneously aborted < 20 weeks GA; 3% of fetal anomalies detected with MS-AFP screening; 6% of all detected neural tube defects in fetuses

Cause:
failure of surface ectoderm to separate from neuroectoderm early in embryonic development (3rd week GA)

@ Skull base
(1) faulty closure of neural tube (without mesenchyme membranous cranial bone cannot develop)
(2) failure of basilar ossification centers to unite

@ Calvarium
(1) defective induction of bone
(2) pressure erosion of bone by intracranial mass / cyst

In 60% associated with:
1. Spina bifida (7–30%)
2. Corpus callosum dys- / agenesis
3. Chiari malformation
4. Dandy-Walker malformation
5. Cerebellar hypoplasia
6. Amniotic band syndrome: multiple irregular asymmetric off-midline encephaloceles
7. Migrational abnormalities
8. Chromosomal anomalies in 44% (trisomy 18)

• MS-AFP elevated in 3% (skin-covered in 60%)
• CSF rhinorrhea; meningitis

Prognosis: dependent on associated malformations + size and content of lesion; 21% liveborn; 50% survival of liveborns, 74% retarded
◊ The larger the brain volume the poorer the outcome

Risk of recurrence: 3% (25% with Meckel syndrome)

DDx: teratoma, cystic hygroma, iniencephaly, scalp edema, hemangioma, branchial cleft cyst, cloverleaf skull

Occipital Encephalocele (75%)
Most common encephalocele in Western Hemisphere

Associated with:
(1) Meckel-Gruber syndrome
= occipital encephalocele + microcephaly + cystic dysplastic kidneys + polydactyly
(2) Dandy-Walker malformation
(3) Chiari malformation
(4) Callosal + migrational anomalies

• external occipital mass

Location: supra- and infratentorial structures involved with equal frequency
√ skull defect (visualized in 80%)
√ flattening of basiocciput
√ ventriculomegaly
√ "lemon" sign = inward depression of frontal bones (33%)
√ cyst-within-a-cyst (ventriculocele = herniation of 4th ventricle into cephalocele)
√ acute angle between mass + skin line of neck and occiput
DDx: cystic hygroma

Sincipital Encephalocele (13–15%)
= FRONTOETHMOIDAL ENCEPHALOCELE
Most common variety in Southeast Asian population
Location: midface about dorsum of nose, orbits, and forehead
Cause: failure of anterior neuropore located near optic recess to close normally at 4th week GA
Types:
1. **Nasofrontal** (40–60%)
   = herniation of dura mater through foramen cecum + fonticulus frontalis
   Site: along nasal bridge between nasofrontal sutures into glabella
2. **Nasoethmoidal** (30%)
   = persistent herniation of dural diverticulum through foramen cecum into prenasal space
   Site: between nasal bone + nasal cartilage (beneath nasal bone + above nasal septum)
3. **Naso-orbital**
   Site: between maxilla + lacrimal bone (= along medial orbit at level of frontal process of maxilla and ethmoid-lacrimal bone junction)

Common root: foramen cecum (= small ostium anterior to crista galli formed by closure of frontal + ethmoid bones)
Associated with: midline craniofacial dysraphism (dysgenesis of corpus callosum, interhemispheric lipoma, anomalies of neural migration, facial cleft, schizencephaly)
• obvious nonprogressive pulsatile mass
• broad nasal root, hypertelorism, nasal stuffiness, rhinorrhea
• change in size during crying / Valsalva maneuver
• positive Fürstenberg test = change in size during jugular compression
√ soft-tissue mass extending to glabella / nasal cavity
√ pedunculated intranasal mass extending from superomedial nasal cavity downward
√ enlarged foramen cecum
OB-US:
√ widened interorbital distance
CT:
√ bifid / absent crista galli
√ absent cribriform plate / frontal bone
MR:
√ isointense relative to gray matter

√ may be hyperintense on T2WI (due to gliosis)

N.B.: biopsy is CONTRAINDICATED (→ potential for CSF leaks, seizures, meningitis)

Risk of recurrence: 6% of congenital CNS abnormalities for younger siblings

Rx: complete surgical resection with repair of dura mater (NO neurologic deficit due to abnormal function of herniated brain)

DDx: (1) Dacryocystocele / nasolacrimal mucocele
(2) Nasal glioma (no subarachnoid connection on cisternography)

Sphenoidal Encephalocele (10%)

= BASAL ENCEPHALOCELE

Age: present at end of 1st decade of life

- clinically occult ← internal protrusion
- mass in nasal cavity, nasopharynx, mouth, posterior portion of orbit increasing with Valsalva
- mouth breathing due to nasopharyngeal obstruction
- diminished visual acuity with hypoplasia of optic disks
- hypothalamic-pituitary dysfunction

Associated with: agenesis of corpus callosum (80%)

Types:

(a) transethmoidal = through midline cribriform plate
(b) sphenoethmoidal = through sphenoid + ethmoid
(c) trans-sphenoidal = through floor of sella may be associated with: cleft palate
√ displacement of cavernous sinus (laterally), pituitary gland, hypothalamus, optic nerves, chiasm
(d) frontosphenoidal
(e) sphenopharyngeal = through sphenoid body
(f) sphenoorbital = through superior orbital fissure
(g) sphenomaxillary = through maxillary sinus

Parietal Encephalocele (10–12%)

Associated with: dysgenesis of corpus callosum, large interhemispheric cyst

√ hole in sphenoid bone (seen on submentovertex film)
√ cranium bifidum = cranioschisis = "split cranium" (= skull defect) = smooth opening with well-defined sclerotic rim of cortical bone
√ hydrocephalus in 15–80% (from associated aqueductal stenosis, Arnold-Chiari malformation, Dandy-Walker cyst)
√ nonenhancing expansile homogeneous paracranial mass
√ mantle of cerebral tissue often difficult to image in encephalocele (except with MR)
√ intracranial communication often not visualized
√ metrizamide / radionuclide ventriculography DIAGNOSTIC
√ microcephaly (20%)
√ polyhydramnios

DDx: (1) sonographic refraction artifact at skull edge
(2) clover leaf skull (± temporal bone partially absent)

CEREBRAL AMYLOID ANGIOPATHY

= deposition of β-amyloid protein in media + adventitia of small + medium-sized vessels of cerebral cortex, subcortex and leptomeninges

Age: increasing with age: 33% in 60–70 years, 75% in > 90 years

Path: fibrinoid necrosis, focal vessel wall fragmentation, microaneurysm → vessel leakage + frank hemorrhage; luminal narrowing → ischemic change

Histo: yellow-green birefringent (under polarized light) deposits along vessel wall with Congo red stain

Types: sporadic form (common), hereditary form (rare)

- asymptomatic (in many): underrecognized with petechial microhemorrhages ≤ 5 mm
- headaches, emesis, focal neurologic deficit, seizure, coma with macrohemorrhage > 5 mm
- transient ischemic attack, dementia
- normotensive elderly without trauma

√ acute / chronic intracerebral hemorrhage (ICH)

◊ Cerebral amyloid angiopathy represents 2% of all ICH

Location: cortical / subcortical in any lobe; sparing of deep white matter + basal ganglia + brainstem

√ may be associated with subarachnoid / subdural hemorrhage

√ leukoencephalopathy ± involvement of U-fibers

√ cerebral atrophy

MR:

√ multiple foci of marked signal loss at GRE imaging (most sensitive sequence for hemosiderin)

DDx: hypertensive hemorrhage (basal ganglia, thalami, brainstem)

CEREBRAL CAVERNOUS MALFORMATION

= CAVERNOUS ANGIOMA OF BRAIN = CAVERNOUS HEMANGIOMA = CAVERNOMA

= benign vascular hamartoma of immature blood vessels + intralesional hemorrhage

Cause: sporadic + solitary (⅔); hereditary + multiple (⅓)

Prevalence: 0.2–0.4% of general population

Associated with: ? developmental venous anomaly

Path: well-circumscribed nodule of honeycomblike dilated endothelial lined spaces separated by fibrous collagenous bands WITHOUT intervening neural tissue

Age: any; 3rd–6th decade (most common); M = F

- asymptomatic (most)

◊ Most common asymptomatic vascular malformation!

- headache, seizures (commonly presenting symptom), neurologic deficit (15%)

Location: cerebrum (mainly superficial subcortical in close contact with subarachnoid space / ventricles) > pons > cerebellum; solitary > multiple

√ NO obvious mass effect / edema

√ usually contain blood degradation products of different stages

√ slow blood flow in vascular channels

NECT:

√ small round / lobulated hyperdense region (CLUE)

√ minimal surrounding edema
√ extensive calcifications = hemangioma calcificans (20%)

CECT:
√ none / minimal / intense enhancement
√ low-attenuation areas due to thrombosed portions

MR (DIAGNOSTIC):
√ typically popcorn appearance with bright lobulated center on T1WI + T2WI
√ well-defined area of mixed signal intensity centrally (= "mulberry"-shaped lesion) with a mixture of:
√ increased signal intensity (= extracellular methemoglobin / slow blood flow / thrombosis)
√ decreased intensity (= deoxyhemoglobin / intracellular methemoglobin / hemosiderin / calcification)
√ surrounded by hypointense rim (= hemosiderin) on T2WI

Angio:
√ negative = "cryptic / occult vascular malformation"

Cx: hemorrhage of varying age
Risk of hemorrhage: 0.4–3.1% (4.3–6.5%) per year for sporadic (familial) cases

Rx: none; microsurgery (if symptomatic)

DDx: (1) Hemorrhagic neoplasm (edema, mass effect)
(2) Hypertensive hemorrhage
(3) Small AVM (thrombosed / small feeding vessels, associated hemorrhage)
(4) Capillary telangiectasia / angioma (no difference)

CEREBRAL VENOUS THROMBOSIS

= DURAL SINUS THROMBOSIS = VENOUS SINUS / SUPERIOR SAGITTAL SINUS THROMBOSIS

◊ The radiologist may be the first to suggest the diagnosis!

Annual Incidence: 2–7÷1,000,000

Cause: > 100 causes suggested

A. IDIOPATHIC = spontaneous (10–30%)
B. LOCAL CAUSE (= intrinsic / mechanical conditions of veins / dural sinuses)
› Septic causes (esp. in childhood): sinusitis, otitis, mastoiditis, sub- / epidural empyema, meningitis, encephalitis, brain abscess, face + scalp cellulitis
› Aseptic causes:
(a) Tumor compressing sinus: meningioma
(b) Trauma: fracture through sinus wall, brain damage, cranial surgery, jugular vein catheterization
C. SYSTEMIC CAUSE (= conditions that promote thrombosis)
› Septic causes: septicemia
› Aseptic causes:
(a) Low-flow state: CHF, CHD, dehydration, shock, surgery, immobilization
(b) Hypercoagulability: antithrombin III deficiency, antiphospholipid syndrome, protein S + C deficiency, pregnancy, peripartum state, oral contraceptives,

malignancy, polycythemia vera, idiopathic thrombocytosis, thrombocytopenia, sickle cell disease, cryofibrinogenemia, disseminated intravascular coagulopathy

(c) Chemotherapy: eg, ARA-C, L-asparaginase

› Unusual causes: Behçet disease, AIDS, ulcerative colitis, SLE, nephrotic syndrome, sarcoidosis

Pathophysiology:

dural sinus thrombosis → thrombus propagation into cortical veins → venous congestion → cerebral venous infarction (in 50%) → vasogenic / cytotoxic edema → intracranial hemorrhage; occasionally hydrocephalus (→ decreased CSF absorption ← impaired function of arachnoid granulations)

Onset: acute = < 2 days (in 30%), subacute = 2–30 days (in 50%), chronic = > 30 days (20%)

- symptoms of intracranial hypertension (20–40%): headaches (75–95%), nausea, vomiting, visual blurring, papilledema
  often confused with: tension headaches, migraine
- drowsiness, confusion, coma, decreased mentation, lethargy, obtundation, seizures, fever
- focal neurologic deficits = stroke symptomatology (dysphasia, cranial nerve palsy, cerebellar incoordination) ← frequently parenchymal changes

Location: superior sagittal sinus (62%) > L transverse sinus (45%) > R transverse sinus (41%) > sigmoid sinus (15%) > straight sinus (18%) > cortical veins (17%) > deep venous system (11%) > jugular bulb (8%) > vein of Galen (7%) > cavernous sinus (1%) > cerebellar veins (0.3%)

√ bilateral parasagittal hemispheric lesions ← superior sagittal sinus thrombosis

√ ipsilateral temporo-occipital + cerebellar lobe lesions ← transverse sinus thrombosis

√ bilateral thalamic lesions ← deep cerebral venous thrombosis

NECT (usually subtle findings):

√ hyperattenuating intravascular material (← acute blood clot) in sagittal sinus = "**dense triangle" sign** / straight sinus / cerebral cortical vein = "**cord**" sign lasting for 1–2 weeks (seen in only 20% ← variability in degree of thrombus attenuation)

DDx to hyperattenuated thrombus:

dehydrated patient, elevated hematocrit level, polycythemia, nonmyelinated brain in neonates, subjacent subarachnoid / subdural hemorrhage

√ subdural collection

√ stroke (often hemorrhagic)

◊ Thrombosis of intracranial dural sinuses, cortical / deep cerebral veins, cavernous sinus is an easily recognizable condition that accounts for 1% of acute cerebral infarcts.

√ dense transcortical medullary vein ← collateral drainage

CECT venography (30–40 sec delay):

(a) direct

√ **"empty delta" sign** / "empty triangle" = filling defect in straight sinus / superior sagittal sinus surrounded by a triangular area of enhancing collateral dural venous channels + cavernous spaces (in 25–35–75%)

False positive: subdural hematoma / empyema, arachnoid granulations

False negative: partial volume averaging, small / recanalized organized thrombus

√ enlargement of thrombosed vein near obstruction

√ shaggy irregular contour of veins (= small collateral veins enhance near the obstructed vein)

(b) indirect (subtle early changes)

√ brain edema + swelling of gyri

√ low attenuation lesion of venous infarction

√ ± subcortical hemorrhage in venous distribution

Mimics of cerebral venous thrombosis on CECT:
1. Hypo- / aplastic transverse sinus
2. Variable bolus transit time with delayed filling
3. Arachnoid granulation
4. Sinus compression by adjacent mass
5. Extradural abscess

Advantage over MR: shorter exam time, NO contraindication to pacemaker, fewer equivocal findings, NO flow-related artifacts

Disadvantage over MR: difficult MIP reconstruction (due to adjacent bone), adverse reaction to contrast material, ionizing radiation

NEMR:

√ replacement of flow void by abnormal signal intensity

(a) acute thrombosis (first 5 days)

√ clot isointense to gray matter on T1WI (and therefore easily missed) + hypointense on T2WI (← deoxyhemoglobin in RBCs trapped in thrombus)

√ low SI rather than normal flow void on T1WI

√ blooming artifacts on GRE in thrombosed segment

√ hyperintense thrombosed sinus on DWI with diminished mean ADC value (in 41%)

(b) subacute thrombosis (6–15 days = in 55% of patients)

◊ most frequent stage at clinical presentation (55%) + easiest stage for thrombus detection

√ hyperintense thrombus within sinus on T1WI (← intra- and extracellular methemoglobin)

√ iso- / hyperintense thrombus on T2WI (← extracellular methemoglobin)

N.B.: hypointense thrombus on T2WI ← intracellular methemoglobin may mimic flow void of a patent dural sinus

(b) chronic thrombosis (> 15 days = 15% of patients) with incomplete recanalization

◊ Most difficult stage to diagnose!

√ isointense on T1WI + iso- / hyperintense T2WI

MR venography (TOF, CEMR):

√ excellent sensitivity to slow flow perpendicular to plane of acquisition for 2D-TOF

Pitfalls: nulling of venous signal in plane of acquisition; hyperintense thrombus on T1WI time-of-flight venography can simulate flow-related enhancement

√ filling defect in sinus on CEMR

Pitfall: marked contrast enhancement of organized revascularized thrombus in chronic thrombosis

◊ Sinus contrast enhancement does NOT DEFINITELY indicate patency!

√ wall-enhancement of thrombosed dural sinus

Angio (DSA):
√ nonfilling of thrombosed sinus
√ filling of collateral cortical veins, deep venous system, cavernous sinus

Prognosis: high mortality

Bad outcome: hemorrhage on admission CT, thrombosis of deep cerebral veins, CNS infection

Rx: heparin (full recovery in 70%), local thrombolysis (worsening in spite of adequate anticoagulation), reduction of intracranial pressure

Parenchymal Changes in Cerebral Venous Thrombosis
√ focal edema WITHOUT hemorrhage (CT in 8%, MR in 25%):
√ increased ADC value = vasogenic edema
√ decreased ADC value = cytotoxic edema (in 50%)
◊ The term "venous infarct" is discouraged as parenchymal abnormalities due to venous occlusion are reversible!
√ parenchymal swelling without SI abnormalities (in 42%):
√ sulcal effacement
√ diminished visibility of cisterns
√ reduction in ventricular size
√ parenchymal enhancement (in 1–29%):
√ gyral enhancement in periphery of infarction ± extension into white matter
√ increased tentorial enhancement ← dural venous collaterals (rare)
√ leptomeningeal enhancement
√ cortical venous enhancement ← venous congestion
√ parenchymal hemorrhage (in 33%):
√ flame-shaped irregular zones of hemorrhage in parasagittal frontal + parietal lobes (in superior sagittal sinus thrombosis)
√ temporal / occipital hemorrhage (in transverse sinus thrombosis)
√ cortical / subcortical hemorrhage ← retrograde extension of thrombus (in superficial venous thrombosis)
√ perfusion changes:
√ prolongation of mean transit time
√ normal / abnormal relative cerebral blood volume

Cavernous Sinus Thrombosis / Thrombophlebitis

Cause: vascular spread of infection from
(a) common: facial cellulitis, paranasal sinusitis, dental infection
(b) less frequent: orbit, middle ear, tonsils

Organism: Staphylococcus aureus, Streptococcus, gram-negative bacteria, anaerobes, mucormycosis

Spread: to contralateral side

- acute headache, periorbital pain + edema
- photophobia, ptosis, chemosis

• cranial nerve deficits III–VI: abducens nerve palsy (most common)
√ enlarged convex-shaped cavernous sinus + filling defect
√ enlarged superior ophthalmic vein
√ proptosis
Prognosis: visual impairment, permanent CN deficit, meningitis, sepsis, death
Rx: IV antibiotics, anticoagulation
DDx: neoplasm (meningioma, metastasis, lymphoma), sarcoidosis, cavernous-carotid fistula, Wegener granulomatosis, Tolosa-Hunt syndrome

Deep Cerebral Venous Thrombosis

Site: thrombus in straight sinus, vein of Galen, internal cerebral veins, vein of Rosenthal
√ T2 prolongation in thalamus, internal capsule, basal ganglia, deep white matter
√ hemorrhagic conversion (common)
√ thrombosed veins on MRV

With simultaneous involvement of both thalami and basal ganglia search for subtle signs of venous thrombosis!

CEREBRITIS

= focal area of inflammation within brain substance
CT:
√ area of decreased density ± mass effect
√ no contrast enhancement (initially) / central or patchy enhancement (later)
MR:
√ focal area of increased intensity on T2WI
Cx: brain abscess

CHIARI MALFORMATION

Chiari I Malformation (adulthood)

= CEREBELLAR TONSILLAR ECTOPIA
= herniation of cerebellar tonsils below a line connecting basion with opisthion (= level of foramen magnum)
◊ Frequently isolated hindbrain abnormality of little consequence without supratentorial anomalies!
Proposed causes:
(a) small posterior fossa
(b) disproportionate CSF absorption from subarachnoid spinal space
(c) cerebellar overgrowth
Associated with:
(1) syringohydromyelia (20–30%)
(2) hydrocephalus (25–44%)
(3) malformation of skull base and cervical spine:
(a) basilar impression (25%)
(b) craniovertebral fusion: eg, occipitalization of C1 (10%), incomplete ossification of

C1-ring (5%)
(c) Klippel-Feil anomaly (10%)
(d) platybasia
◊ NOT associated with myelomeningocele!
• benign cerebellar ectopia: < 3 mm of no clinical consequence; 3–5 mm of uncertain significance; > 5 mm clinical symptoms likely
• no symptoms in childhood (unless associated with hydrocephalus / syringomyelia)
• ± cranial nerve dysfunction / dissociated anesthesia of lower extremities in adulthood
√ downward displacement of cerebellar tonsils + medial part of inferior lobes of cerebellum > 5 mm below level of foramen magnum
√ inferior pointing peglike / triangular tonsils
√ obliteration of cisterna magna
√ elongation of 4th ventricle, which remains in normal position
√ slight anterior angulation of lower brainstem

Chiari II Malformation (childhood)
= ARNOLD-CHIARI MALFORMATION
= most common + serious complex of anomalies involving hindbrain, spine, mesoderm ← posterior fossa too small
HALLMARK is dysgenesis of hindbrain with
(a) caudally displaced 4th ventricle
(b) caudally displaced brainstem
(c) tonsillar + vermian herniation through foramen magnum
No association with: basilar impression / C1-assimilation / Klippel-Feil deformity
• newborn: respiratory distress, apneic spells, bradycardia, impaired swallowing, poor gag reflex, retrocollis, spasticity of upper extremities
• teenager: gradual loss of function + spasticity of lower extremities
Skull film:
√ Lückenschädel (most prominent near torcular herophili / vertex) in 85% = dysplasia of membranous skull disappearing by 6 months of age
√ scalloping of clivus + posterior aspect of petrous pyramids (from pressure of cerebellum) in 70–90% leading to shortening of IAC
√ small posterior fossa
√ enlarged foramen magnum + enlarged upper spinal canal secondary to molding (in 75%)
√ absent / hypoplastic posterior arch of C1 (in 70%)
@ Supratentorial
√ obstructive hydrocephalus (duct of Sylvius dysfunctional but probe patent); may not become evident until after repair of myelomeningocele (in 50–98%)
√ nonvisualization of aqueduct (in up to 70%)
√ colpocephaly (= enlargement of occipital horns + atria) ← maldeveloped occipital lobes
√ dysgenesis of corpus callosum (in 80–90%): hypoplasia / absence of splenium + rostrum
√ absence of septum pellucidum (40%)
√ interdigitation of medial cortical gyri ← hypoplasia + fenestration of falx (in up to

100%)

√ **"bat-wing"** configuration of frontal horns (on COR views) = frontal horns point inferiorly with blunt superolateral angle ← prominent impressions by enlarged caudate nucleus

√ "hourglass ventricle" = small biconcave 3rd ventricle ← large massa intermedia

√ wide prepontine + supracerebellar cisterns

√ **stenogyria** = multiple small closely spaced gyri separated by shallow sulci within cortex of normal thickness ← dysplasia (in up to 50%)
Location: medial occipital lobe (on SAG image)

@ Cerebellum

√ "cerebellar peg" = protrusion of vermis + hemispheres through foramen magnum (90%) → craniocaudal elongation of cerebellum

√ hypoplastic poorly differentiated cerebellum (poorly visualized folia on sagittal images) ← severe degeneration

√ elongated / obliterated vertically oriented thin-tubed 4th ventricle with narrowed AP diameter exiting below foramen magnum (40%)

√ obliteration of CPA cistern + cisterna magna by cerebellum growing around brainstem

√ dysplastic tentorium with wide U-shaped incisura inserting close to foramen magnum (95%)

√ "tectal beaking" = fusion of midbrain colliculi into a single beak pointing posteriorly and invaginating into cerebellum

√ V-shaped widened quadrigeminal plate cistern ← hypoplasia of cingulate gyri

√ "towering cerebellum" = "pseudomass" = cerebellar extension above incisura of tentorium

√ triple peak configuration = corners of cerebellum wrapped around brainstem pointing anteriorly+ laterally (on axial images)

√ flattened superior portion of cerebellum ← temporoparietal herniation

√ vertical orientation of shortened straight sinus

@ Spinal cord

√ medulla + pons displaced into cervical canal

√ "cervicomedullary kink" = herniation of medulla posterior to spinal cord (up to 70%) at level of dentate ligaments

√ widened anterior subarachnoid space at level of brainstem + upper cervical spine (40%)

√ AP diameter of pons narrowed

√ upper cervical nerve roots ascend toward their exit foramina

√ syringohydromyelia

√ lumbar myelomeningocele (> 95%)

√ low-lying often tethered conus medullaris below L2

OB-US:

√ hydrocephalus

√ "banana" sign = cerebellum wrapped around posterior brainstem + obliteration of cisterna magna ← small posterior fossa + downward traction of spinal cord

Chiari III Malformation

most severe rare abnormality; probably unrelated to type I and II Chiari malformation
√ low occipital / high cervical meningomyeloencephalocele
Prognosis: survival usually not beyond infancy

Chiari IV Malformation

extremely rare anomaly probably erroneously included as type of Chiari malformation
√ agenesis of cerebellum
√ hypoplasia of pons
√ small + funnel-shaped posterior fossa

CHORISTOMA

= INFUNDIBULOMA = GRANULAR CELL TUMOR
= benign slow-growing low-grade glioma = maldeveloped tissue in an abnormal site [*choristos* , Greek = separated, apart]
Incidence: rare tumor (70 cases reported in literature)
Origin: pituicyte (= modified astrocyte)
Age: 4th–5th decade; M÷F = 1÷2
Location: along neurohypophysis (sella, suprasellar cistern)
• visual field deficit, panhypopituitarism, diabetes insipidus (rare)
MR:
√ solid component iso- to mildly hypointense to brain on T1WI + T2WI
√ ± cystic component
√ heterogeneous enhancement
Prognosis: no invasion, no recurrence

CHOROID PLEXUS CYST

= cyst arising from folding of neuroepithelium with trapping of secretory products + desquamated choroid epithelium
Incidence: 0.9–3.6% in sonographic population; in up to 50% of autopsied brains
Histo: epithelial-lined cyst, filled with clear fluid ± debris
May be associated with: aneuploidy (76% in trisomy 18, 17% in trisomy 21, 7% in triploidy / Klinefelter syndrome)
◊ In the absence of other anomalies 1% of fetuses with choroid plexus cysts will have trisomy 18!
◊ In the presence of other anomalies 4% of fetuses with choroid plexus cysts will have trisomy 18!
◊ 40–71% of autopsied fetuses with trisomy 18 have choroid plexus cysts bilaterally > 10 mm in diameter
◊ The risk of chromosomal abnormalities is not linked to size, bilaterality, gestational age at appearance / disappearance of choroid plexus cysts!
• usually asymptomatic
Location: frequently at level of atrium; bi- / unilateral; 3rd ventricle (rare)
Site: body of plexus ± protrusion into ventricular cavity
Average size: 4.5 (range, 2–25) mm

US:
√ single / multiple round anechoic cysts
CT:
√ iso- to slightly hyperattenuating compared with CSF
MR:
√ iso- to hyperintense on T1WI compared with CSF
√ hyperintense on T2WI compared with CSF
√ incompletely hypointense (suppressed) on FLAIR
√ restricted diffusion = hyperintense on DWI (66%)
√ nodular / rim enhancement
Cx: hydrocephalus (if cyst large)
Prognosis: 90% disappear by 26th–28th week; may persist; in 95% of no significance
OB-management:
a choroid plexus cyst should stimulate a thorough sonographic examination at > 19 weeks; if no other sonographic abnormalities are identified, the yield of abnormal karyotype is low so that the risk of trisomy 18 (1÷450–500) is lower than risk of fetal loss due to amniocentesis (~ 1÷200–300)
Risk of karyotype abnormality:
increased by 10 times with 1 additional defect
increased by 600 times with ≥ 2 additional defects
DDx: (1) Choroid plexus pseudocyst in the inferolateral aspect of atrium (? corpus striatum) on oblique coronal plane, which elongates by turning transducer
(2) Ependymal cyst (no enhancement)
(3) Villous hyperplasia (very rare, uniform strong enhancement)

CHOROID PLEXUS NEOPLASM

Incidence: 0.5–0.6% of all primary intracranial tumors; 2–5% of pediatric brain tumors; 5% of all supratentorial tumors in children; 60–70% of all choroidal tumors
Age: up to 20% < 1 year of age; in 75% < 2 years of age; in 86% < 5 years of age; M >> F
Path: large aggregation of choroidal fronds producing great quantities of CSF; occasionally found incidentally on postmortem examination
Pathophysiology: abnormal rate of CSF production of 1.0 mL/min (normal rate = 0.2 mL/min)
Subdivision:
1. Choroid plexus **papilloma** (CPP) (WHO grade I)
2. **Atypical** choroid plexus papilloma (WHO grade II) ≥ 2 mitoses per 10 randomly selected high-power fields
3. Choroid plexus **carcinoma** (CPC) (WHO grade III) > 5 mitoses per high-power field

CPP÷CPC = 5÷1

Imaging does not allow distinction between subdivisions.
All subtypes may demonstrate CSF dissemination → imaging of the entire neuroaxis is recommended!

May be associated with: von Hippel-Lindau syndrome (papillomas in unusual locations), Aicardi syndrome, Li-Fraumeni syndrome
• signs of increased intracranial pressure
Location: anywhere within choroid plexus epithelium

(a) glomus of choroid plexus in atrium (trigone) of lateral ventricles (in 50% of adults, in 80% of children), L > R (in children); M=F
(b) 4th ventricle (40%) + cerebellopontine angle (in adults); M÷F = 3÷2
(c) 3rd ventricle (10%)
(d) multiple in 5–7%

√ large mass with papillary / smooth lobulated border (DDx from other intraventricular neoplasms)
√ small foci of calcifications (common)
√ ± cystic areas within tumor
√ engulfment of glomus of choroid plexus (DISTINCTIVE feature)
√ asymmetric diffuse ventricular dilatation = communicating hydrocephalus
Cause: (a) CSF overproduction by neoplasm
(b) obstruction of CSF absorption ← proteinaceous exudate / repeated occult hemorrhage
(c) direct obstruction of CSF pathway)
√ dilatation of temporal horn in atrial location (obstruction)
√ occasionally growth into surrounding white matter (more commonly a feature of choroid plexus carcinoma)
√ septa / cysts within ventricular system ← inflammatory reaction to tumor / tumoral hemorrhage

CT:
√ iso- / mildly hyperattenuating homogeneous mass
√ ± calcifications and foci of hemorrhage

CECT:
√ intense homogeneous enhancement ← very vascular lesion

MR:
√ iso- to slightly hypointense lesion on T1WI + iso- to hyperintense on T2WI relative to white matter
√ flow voids (common)
√ surrounded by hypointense signal on T1WI + hyperintense signal on T2WI (CSF)
√ intraventricular enhancing island of tumor on Gd-DTPA + retention of contrast within tumor interstitium

MR spectroscopy:
√ marked choline peak WITHOUT N-acetylaspartate / creatine peak; elevated lactate level for carcinomas

US:
√ echogenic mass adjacent to normal choroid plexus

Angio:
√ enlarged choroidal artery if neoplasm located in atrium ← supplied by anterior + posterior choroidal arteries

Cx: (1) Transformation into malignant choroid plexus papilloma = choroid plexus carcinoma (in 5%)
(2) Hydrocephalus (in children) ← increased intracranial pressure from CSF-overproduction
(3) Tumor infarction ← twist of pedicle

Rx: surgical removal (24% operative mortality) cures hydrocephalus
Prognosis: 97% 5-year survival rate for papilloma; 26–43% 5-year survival rate for carcinoma
DDx: intraventricular meningioma, ependymoma, metastasis, cavernous angioma, xanthogranuloma, astrocytoma

COCKAYNE SYNDROME

[Edward Alfred Cockayne (1880–1956), English pediatrician who published "Inherited Abnormalities of the Skin and its Appendages" in 1933, the first book on inherited skin disorders]
= autosomal recessive diffuse demyelinating disease
Age: beginning at age 1
• dwarfism; retinal atrophy + deafness
• progressive physical + mental deterioration
√ brain atrophy / microcephaly
√ calcifications in basal ganglia + cerebellum
√ skeletal changes superficially similar to progeria
DDx: Progeria

COLLOID CYST

Incidence: 2% of glial tumors of ependymal origin; 0.5–1% of CNS tumors
Origin: neuroepithelial / endodermal
Histo: single layer of ciliated + columnar mucin-secreting epithelium; squamous cells of ependymal origin; tough fibrous capsule; filled with thick viscous mucus consisting of blood products, macrophages, cholesterol crystals, numerous metallic ions
Age: 5th–6th decade; M > F
• positional headaches (← transient obstruction secondary to ball-valve mechanism at foramen of Monro)
• hypogonadism, galactorrhea (for intra- / suprasellar location)
• change in mental status ± dementia (related to increased intracranial pressure); gait apraxia
• papilledema (may become medical emergency with acute herniation)
Location: inferior aspect of septum pellucidum protruding into anterior superior portion of 3rd ventricle between columns of fornix; suprasellar cistern (rare)
Size: several mm to 3 cm
√ ± sellar erosion
√ 3rd ventricular enlargement (to accommodate cyst anteriorly)
√ asymmetric lateral ventricular enlargement (invariably)
√ occasionally widens septum pellucidum
√ may show enhancement of border ← draped choroid plexus / capsule
NECT:
√ spherical iso- / (often) hyperattenuating lesion with smooth surface contour without enhancement
√ fluid contents:
(a) in 20% similar to CSF (= isodense)

(b) in 80% mucinous fluid, proteinaceous debris, hemosiderin, desquamated cells (= hyperdense)

MR:

√ variable SI lesion (dependent on mucus composition):

√ hyperintense on T1WI + FLAIR ← large protein molecules / paramagnetic effect of magnesium, copper, iron in cyst

√ iso- to hypointense on T2WI (most common)

Prognosis: asymptomatic and stable in 90%; 10% enlarge / cause hydrocephalus; with rapid enlargement → coma and death

DDx: meningioma, ependymoma of 3rd ventricle (rare) with enhancement

CONGENITAL INCLUSION CYSTS OF CNS

Origin: defect in cleavage of neural tissue from cutaneous ectoderm during closure of neural tube in 5th week of fetal life (early inclusion results in midline lesion, later inclusion results in more lateral location)

Frequency: dermoid÷epidermoid = 1÷3 to 1÷10

Location: most commonly in midline (anterior fontanelle, glabella, nasion, vertex, subocciput) > frontotemporal > parietal location

Affected sutures: frontozygomatic, sphenofrontal, sphenosquamosal, squamosal, coronal, lambdoid, parietomastoid

• ± external skin ostia and deep sinus tracts

√ angiographically avascular

√ NO contrast enhancement internally (DDx to teratoma)

√ rare peripheral rim enhancement ← perilesional inflammation / infection

Cx: (1) Chemical / aseptic meningitis (rare)

(2) Squamous cell carcinoma (rare)

Dermoid Cyst of CNS

Path: ectoderm + skin elements = pilosebaceous mass of squamous epithelial cells + mesodermal cells (hair follicles, sweat glands and sebaceous glands)

Growth: desquamation of epithelial cells + glandular secretion → faster growth than epidermoids

Incidence: 1% of all intracranial tumors

Age: < 30 years (appears in adulthood due to slow growth); M < F

Location:

(a) spinal canal (most common): extra- / intramedullary in lumbosacral region

(b) posterior fossa within vermis / 4th ventricle (predilection for midline)

(c) posterior to superior orbital fissure, may be associated with bone defect

(d) sellar + parasellar region

(e) nasion ± sinus tract up to foramen cecum

Risk: CNS infection

• bouts of chemical / bacterial meningitis possible

√ thick-walled inhomogeneous mass with focal areas of fat

√ mural / central calcifications / bone (possible)

√ may have sinus tract to skin surface (dermal sinus) if located in midline at occipital / nasofrontal region
√ fat-fluid level if cyst ruptures into ventricles, fat droplets in subarachnoid space

CT:

√ variable appearance ± areas of low attenuation due to lipid component

MR:

Dermoid Cyst versus Teratoma	
Dermoid Cyst	*Teratoma*
Inclusion cyst	Germ cell neoplasm
√ unilocular	√ multilocular
√ rim enhancement	√ internal enhancement
√ rim calcification	√ internal calcification

√ variointense on T1WI (hyperintense with contents of liquefied cholesterol products)
√ curvilinear regions of low SI on T1WI + T2WI (= hair)
√ shortened T1 + T2 relaxation times (= fat)
√ suppressed fat signal on fat-suppressed images

Epidermoid Cyst of CNS

Path: ectoderm WITHOUT skin elements = "pearly tumor" = well-defined solid lesion with glistening irregular nodular surface; lamellar cyst contents consists of soft flaky desquamated keratinaceous debris rich in cholesterol + triglycerides = **primary / congenital cholesteatoma**

Incidence: 0.2–1.8% of all primary intracranial neoplasms; most common congenital intracranial tumor

Histo: tumor lined by simple stratified cuboidal squamous epithelium; surrounded by thin band of collagenous connective tissue

Growth: extremely slow linear growth resulting from desquamation of epithelial cells

Age: 10–60 years, peak age in 4th–5th decade (slow tumor expansion over decades thus becoming symptomatic in adulthood); M÷F = 1÷1

- facial pain
- cranial nerve palsies with CP angle epidermoid (50%)
- visual abnormality + endocrinologic disturbance (eg, diabetes insipidus) with suprasellar epidermoid
- hydrocephalus with suprasellar epidermoids
- chemical meningitis (← leakage of tumor contents into subarachnoid space) with middle cranial fossa epidermoids

Location:

(a) cerebellopontine angle (40%, account for 5% of CP angle tumors)
(b) suprasellar region, perimesencephalic cisterns (14%)
(c) in ventricles, brainstem, brain parenchyma
(d) pineal region (3–4%): peak age in 3rd decade
(e) skull vault

Site: midline / paramidline; intradural (90%) / extradural; transspatial growth (= extension

from one into another intracranial space)
√ soft lesion insinuating into adjacent brain parenchyma:
√ conforming to + molding itself around brain surfaces
√ intimately surrounding vessels + cranial nerves rather than displacing them (limited resectability)
√ little mass effect, no edema / hydrocephalus
√ may be associated with dermal sinus tract at occipital / nasofrontal region if midline in location
CT:
√ typically lobulated round homogeneous mass with density similar to CSF (between water and –20 HU)
√ occasionally hyperdense due to high protein content, saponification of keratinaceous debris, prior hemorrhage into cyst, ferrocalcium / iron-containing pigment, abundance of PMNs
√ bony erosion with sharply defined well-corticated margins
√ peripheral calcifications (in 25%)
MR:
√ lamellated onionskin appearance with septations (layer-on-layer accretion of desquamated material)
√ "**black epidermoid**" (majority) = SI similar to CSF:
√ heterogeneously hypointense lesion on T1WI
√ hyperintense on T2WI
Cause: cholesterol in solid crystalline state + keratin within tumor + CSF within tumor interstices
√ "**white epidermoid**" (rare) = SI similar to fat:
√ hyperintense on T1WI
√ iso- to hyperintense on T2WI
Cause: triglycerides + polyunsaturated fatty acids
√ SI similar to calcium = hypointense on T2WI (very rare) ← peripheral calcifications, low hydration, viscous secretion, paramagnetic iron-containing pigment
√ incomplete saturation on FLAIR = hyperintense relative to CSF (DDx: arachnoid cyst)
√ lesion very hyperintense on DWI
√ signal intensity suppression on fat-suppressed sequence (DDx: lipoma exhibits more suppression)
Cisternography:
√ papillary / frondlike surface with contrast material extending into tumor interstices
Rx: surgical resection (complicated by adherence to surrounding brain + cranial nerves, spillage of cyst contents with chemical meningitis, CSF seeding + implantation)
DDx: arachnoid cyst (smooth surface, earlier diffusion, equal to CSF), lipoma, cystic schwannoma, adenomatoid tumor, atypical meningioma, chondroma, chondrosarcoma, chordoma, calcified neurogenic tumor, teratoma, calcified astrocytoma, ganglioglioma

CORTICAL CONTUSION

= CEREBRAL CONTUSION = BRAIN CONTUSION

= traumatic injury to cortical surface of brain

Incidence: most common type of primary intraaxial lesion; in 21% of head trauma patients; children÷adults = 2÷1

Pathogenesis: capillary disruption leads to extravasation of whole blood, plasma (edema) and RBCs

Path: petechial hemorrhage (= admixture of blood with native tissue) followed by liquefaction + edema after 4–7 days, tissue necrosis

Mechanism: linear acceleration-deceleration forces / penetrating trauma

1. **Coup** (same side as impact)
   = small area of direct impact on stationary brain
   Associated with: skull fracture
2. **Contrecoup** (180° opposite to side of impact)
   = broad area of impact as a result of moving brain against stationary calvarium
   Associated with: fall

Location: multiple bilateral lesions;

– common: along anterior + lateral + inferior surfaces of <u>frontal lobe</u> (in orbitofrontal, inferior frontal, and rectal gyri above cribriform plate, planum sphenoidale, lesser sphenoid wing) and <u>temporal lobe</u> (just above petrous bone / posterior to greater sphenoid wing)
– less frequent: in parietal + occipital lobes, cerebellar hemispheres, vermis, cerebellar tonsils
– often bilateral / beneath an acute subdural hematoma

• confusion (mild initial impairment), focal cerebral dysfunction
• seizures, personality changes
• focal neurologic deficits (late changes)

CT (sensitive only to hemorrhage in acute phase):

◊ Look for scalp swelling to focus your attention on the location of the coup!
√ "salt and pepper lesion" = mottled / speckled densities as focal / multiple (29%) poorly defined areas of low attenuation with irregular contour (edema) intermixed with a few tiny areas of increased density (petechial hemorrhage)
√ diffuse cerebral hypodensity + swelling without hemorrhage in immediate posttraumatic period (common in children) ← hyperemia / ischemic edema
√ some degree of contrast enhancement ← leaking new capillaries
√ hemorrhage isodense after 2–3 weeks
√ true extent of lesions becomes more evident with progression of edema + cell necrosis + mass effect over ensuing weeks

MR (best modality for initial detection of contusional edema with accurate portrayal of extent of lesion):

√ hemorrhagic lesion (detected in 50% of all contusions):
  √ initially decreased intensity (← deoxyhemoglobin of acute hemorrhage) surrounded by hyperintense edema on T2WI
  √ hyperintense on T1WI + T2WI in subacute phase ← Met-Hb
  √ hyperintense gliosis + hypointense hemosiderin on T2WI in chronic phase
√ nonhemorrhagic lesion hypointense on T1WI + hyperintense on T2WI

Cx: (1) Progression to cerebral hematoma

(2) Encephalomalacia (= scarred brain)
(3) Porencephaly (= formation of cystic cavity lined with gliotic brain and communicating with ventricles / subarachnoid space)
(4) Hydrocephalus ← adhesions ← subarachnoid blood

CRANIOPHARYNGIOMA

Incidence: 3–4% of all intracranial neoplasms; 15% of supratentorial + 50% of suprasellar tumors in children; most common suprasellar mass
Origin: from epithelial rests along vestigial craniopharyngeal duct + primitive buccal epithelium (Rathke cleft cells within intermediate lobe of pituitary gland)
Path: cystic (rich in liquid cholesterol) / complex / solid
Age: from birth–7th decade; M > F; bimodal age distribution with age peaks in 1st–2nd decade (75%) and in 4th–6th decade (25%)
• diabetes insipidus ← compression of pituitary gland
• growth retardation ← compression of hypothalamus
• bitemporal hemianopia ← compression of optic nerve chiasm
• headaches from hydrocephalus ← compression of foramen of Monro / aqueduct of Sylvius
Location: anywhere along infundibular stalk from floor of 3rd ventricle to pituitary gland
(a) suprasellar (20%)
(b) intrasellar (10%)
(c) intra- and suprasellar (70%)
Ectopic craniopharyngioma:
(e) floor of anterior 3rd ventricle (more common in adults)
(f) sphenoid bone

Skull films:
√ normal sella (25%)
√ enlarged J-shaped sella with truncated dorsum
√ thickening + increased density of lamina dura in floor of sella (10%)
√ extensive sellar destruction (75%)
√ curvilinear / flocculent / stippled calcifications / lamellar ossification; calcifications seen in youth in 70–90%, in adults in 30–40%

CT:
√ multilobulated inhomogeneous suprasellar mass
√ solid (15%) / mixed (30%) / cystic lesion (54–75%) [cystic appearance ← cholesterol, keratin, necrotic debris with higher density than CSF]
√ enhancement of solid lesion, peripheral enhancement of cystic lesion
√ marginal hyperdense lesion (calcification / ossification) in 70–90% in childhood tumors + 30–50% of adult tumors
√ ± obstructive hydrocephalus
√ extension into middle > anterior > posterior cranial fossa (25%)

MR (relatively ineffective in demonstrating calcifications):
√ hyperintense (mostly), but also iso- / hypointense on T1WI (variability ← hemorrhage / cholesterol-containing proteinaceous fluid)
√ markedly hyperintense on T2WI

√ heterogeneous enhancement of solid components + cyst wall

Angio:

√ usually avascular

√ lateral displacement, elevation, narrowing of supraclinoid segment of ICA

√ posterior displacement of basilar artery

DDx: (1) Epidermoid (no contrast enhancement)

(2) Rathke cleft cyst (small intrasellar lesion)

(3) Hemorrhagic pituitary macroadenoma (fluid-fluid level)

CREUTZFELDT-JACOB DISEASE

[Hans Gerhard Creutzfeldt (1885–1964), German neuropathologist and director of the university psychiatric and neurological division in Kiel]

[Alfons Maria Jakob (1884–1931), German neurologist and head of the laboratory of anatomical pathology at the psychiatric State Hospital Hamburg-Friedrichsberg]

= rare subacutely progressive neurological disorder due to transmissible infectious disease developing over weeks

Cause: "**prion**" (self-replicating proteinaceous infectious particles) = protein devoid of functional nucleic acid converted to proteinaceous infectious scrapie particles that accumulate in + around neurons leading to cell death; kuru among aboriginal Fore people of New Guinea (ritualistic oral ingestion of body parts)

[scrapie = affected animals compulsively scrape off their fleece against rocks, trees or fences]

Iatrogenic causes: corneal transplantation, ingestion of prion-contaminated human growth hormone, transplantation of cadaveric dura mater

Age: older adults (57–73 years)

Histo: classified as spongiform encephalopathy "mad cow disease"

• rapidly progressive dementia, ataxia, generalized myoclonus

• synchronous discharges on EEG as generalized periodic sharp wave complexes (in 60%)

• CSF protein 14-3-3 (96% specific + 96% sensitive)

Subtypes: sporadic, familial, iatrogenic, variant

Location: cerebral cortex, basal ganglia (caudate nucleus), thalamus

CT:

√ usually normal

√ rapidly progressive atrophic changes

MR:

√ hyperintense T2 lesions in basal ganglia (head of caudate nucleus + putamen), occipital cortex, bilaterally (79% sensitive)

√ high-SI lesions on DWI (← vacuolization of neutrophil leading to gliosis + astrocytosis and restriction of water diffusion) + decreased ADC (94% sensitive, 92% specific):

Location: cerebral cortex, basal ganglia

√ restricted diffusion is more sensitive than T2-FLAIR, especially for cortical lesions ← spongiform neuronal degeneration

√ "pulvinar" sign / "hockey stick" sign = T2 prolongation + restricted diffusion in medial thalamus

√ NO gadolinium enhancement of lesions
√ NO white matter involvement
Dx: brain biopsy
Prognosis: usually fatal within 2 year of onset of symptoms (mean, 8.8 months)

CRYPTOCOCCOSIS OF BRAIN

= ubiquitous soil fungus Cryptococcus neoformans infects lungs followed by hematogenous spread
Organism: unicellular yeast
Transmission: inhalation of reproductive spores found in bird feces (eg, pigeon droppings)
◊ Most common cause of opportunistic fungal infection in immunocompromised + AIDS patients
◊ Most common fungal disease of CNS
Path: choroid plexitis, meningitis, encephalitis (lack of anticryptococcal factors in CSF)
Incidence: 5% of all patients with AIDS
• headache, malaise, fever, nausea, vomiting
Location: from base of brain extension along Virchow-Robin spaces
√ hydrocephalus + cortical / central atrophy (with inadequate immune response)
√ abnormal nodular leptomeningeal enhancement (with sufficient immune response), most pronounced at base of brain
√ enlargement of Virchow-Robin spaces = distension of perivascular spaces ← budding yeast + mucoid material from organism's capsule
√ gelatinous pseudocysts frequently in basal ganglia, thalami and midbrain
√ miliary (< 3 mm) / larger parenchymal cryptococcoma
CT:
√ frequently normal: edema + enhancement may be attenuated in immunodeficiency / corticosteroid therapy
√ pseudocystic perivascular lesions in region of basal ganglia
MR:
√ low T1 + high T2 signal intensities without enhancement in lenticulostriate region (= gelatinous pseudocyst = budding yeast + mucoid material from organism's capsule)
√ hyperintense lesions on FLAIR
√ restricted diffusion if contents of high viscosity
√ leptomeningeal enhancement
Dx: detection of cryptococcal antigen in CSF
Cx: hydrocephalus ← acute meningeal exudate / meningeal adhesions
Prognosis: mean survival of 2–3 months
DDx: enlarged Virchow-Robin spaces (hypointense on FLAIR)

CYSTICERCOSIS OF BRAIN

= NEUROCYSTICERCOSIS
Organism: Taenia solium = larva of pork tapeworm; frequently involving CNS, eyes, muscle, heart, fat tissue, skin
Incidence: most common parasitic infection involving CNS in developing countries (in up to 90%)

Endemic to: Mexico, South America, Africa, eastern Europe, Asia, Indonesia
Associated with: poverty
Route of infection:
(1) **Cysticercosis** = ingestion of ova by fecal-oral route via contaminated food / water or autoinfection; embryophore is dissolved by gastric acid and enzymes + oncosphere is liberated
(2) **Taeniasis** following ingestion of cysticercus by definitive host a tapeworm develops within intestinal tract

Life cycle:
embryos invade intestinal wall → cross mucosa and move into capillary system → enter circulation disseminating in brain, muscles, and various other parts of body; embryo develops into a cysticercus (= complex wall surrounding a cavity containing vesicular fluid + scolex) usually within < 3 months

Location: meninges (39%) esp. in basal cisterns, parenchyma (20%), intraventricular (17%), mixed (23%), intraspinal (1%)
Seeding: through subarachnoid space + ventricles

Site in brain: gray-white matter junction, basal ganglia, cerebellum, brainstem

A. STAGE OF LARVAL TISSUE INVASION
- asymptomatic
√ localized focus of edema on T2WI
√ nodular tissue enhancement

B. VESICULAR STAGE
= antigenetically inert, therefore without inflammatory reaction / circumferential edema; parasite protected by cyst wall rich in glycoproteins as an effective barrier toward surrounding tissue
- asymptomatic
√ single / multiple thin-walled nonenhancing 4–20 mm spherical cysts:
  √ center with clear fluid of CSF intensity
  √ "target" or "dot in a hole" appearance = 2–3 mm mural nodule (= scolex) of soft-tissue attenuation and signal intensity similar to brain parenchyma
√ NO surrounding edema

C. COLLOIDAL VESICULAR STAGE
= death of scolex from natural processes / from effects of therapy associated with disruption of cyst wall; unprotected decaying parasite and its metabolic breakdown (colloidal suspension) causes an intense inflammatory reaction → focal meningoencephalitis with breakdown of blood-brain barrier
- focal seizures (50–70%; in endemic countries most common cause of adult-onset epilepsy
√ markedly hyperintense lesion on FLAIR ← proteinaceous cyst fluid with gelatinous debris
√ center hypointense to white matter and hyperintense to CSF on T1WI
√ hypointense mural nodule on T2WI with strong homogeneous enhancement
√ surrounded by typically extensive white matter edema (DDx: metastasis without edema)
√ avidly ring-enhancing capsule on postcontrast T1WI

D. NODULAR-GRANULAR STAGE
= degeneration of cysticercus = cyst retraction + formation of granulomatous nodule →

surrounding gliosis and mineralization
√ gradually subsiding perilesional edema
√ shrinkage of cyst with thick retracted cyst wall becoming isointense with brain on T1WI + hypointense on T2WI
√ hypointense on all pulse sequences ← completely calcified
√ isoattenuating lesion with enhancement of thick nodular ring on CT

E. CALCIFIED (nonactive) STAGE
= complete involution of lesion with continued mineralization
• asymptomatic / posttreatment seizures
√ small focal calcifications; may appear within 8 months to 10 years after acute infection
√ "ricelike" muscle calcifications rarely visible
√ calcified scolex on GRE sequence

Radiographic types:

1. Parenchymal type
   √ multiple / solitary cystic lesions up to 6 cm in size:
   √ large cysts are usually multiloculated
   √ calcified granulomata (larvae not dead unless completely calcified)
   √ diffuse encephalitic form more common in young females, children, patients receiving antihelmintic therapy
   √ **progressive midbrain syndrome** = multiple areas of ischemic injury
   Cause: occlusion of vessels traversing cisterns
   Location: midbrain, thalamus
   Cx: arachnoiditis, meningitis, cranial nerve palsies, lacunar infarctions
2. **Subarachnoid / racemose neurocysticercosis**
   = infiltration of basal cisterns + sylvian fissures associated with local meningeal inflammation / fibrosis
   √ lucent cystic lesions up to several cm in basal cisterns (= racemose cysts) with variable enhancement, usually located in cerebellopontine angle / suprasellar cistern
   Cx: hydrocephalus; scattered infarctions ← vasculitis of basal perforating vessels
3. **Intraventricular neurocysticercosis**
   • symptoms related to hydrocephalus (30%)
   • papilledema, loss of consciousness (Bruns syndrome)
   √ obstructive hydrocephalus ← blockage within various portions of ventricular system from solitary / multiple cysts (OCCULT on CT!)
4. Mixed type (frequently different stages in same patient)

Rx: antihelmintic therapy (usually albendazole, praziquantel)

Taeniasis

= ingestion of raw / undercooked contaminated pork containing cysticerci (= T solium larvae); tapeworm develops in and is confined to intestinal lumen → release of eggs
• altered appetite, weight loss, abdominal pain, constipation
• vomiting, diarrhea, fever, eosinophilia, dyspnea
√ pleural effusion, ascites
√ rice grain–shaped calcifications in muscles ← calcified granulomas
Dx: stool analysis, serologic testing

CYTOMEGALOVIRUS INFECTION

= double-stranded DNA virus with replication inside cell nucleus causing a lytic productive / latent infection; member of Herpes viridae family (with varicella-zoster virus, Epstein-Barr virus, herpes simplex virus types 1 and 2)

◊ Most common intrauterine infection in USA!

Incidence: 0.4–2.4% of liveborn infants; 40,000 babies born each year with CMV infection in USA

Transmission:

(a) horizontally by contact with saliva / urine or sexually

(b) vertically from mother to fetus transplacentally; spreads hematogenously throughout fetus

◊ Outcome poorer if infected during first half of pregnancy at a younger gestational age!

Histo: necrotizing inflammatory process

Predilection: CMV has special affinity for metabolically active neuroblasts of germinal matrix

Prenatal screening:

antibodies in 30–60% of pregnant women;
primary CMV infection in 2.5% of pregnant women

Postnatal screening:

10% of neonates excrete virus;
1.6% of newborns shed CMV in urine / saliva

- asymptomatic + subclinical (90%)
- symptomatic at birth (10–15%):
  - sensorineural deafness, mental retardation, neurologic deficits, seizures
  - ocular abnormalities (15–50%): chorioretinitis, optic neuritis, optic atrophy, hypoplasia + coloboma of optic nerve, anterior uveitis, anophthalmia, microphthalmia, cataracts, cyclopia
  - jaundice, hemolytic anemia, thrombocytopenic purpura

  ◊ Leading cause of brain disease + hearing loss in children!
- symptomatic in adults (in up to 15%):
  - fever, pharyngitis, lymphadenopathy, polyarthritis

√ intrauterine growth retardation
√ hepatosplenomegaly (nontender)
√ ascites
√ hydrops
√ pneumonitis

Dx: polymerase chain reaction analysis of CSF / urine / saliva / blood to detect CMV DNA; positive viral culture within first 2 weeks of life

Rx: no effective treatment for maternal infection

DDx: toxoplasmosis, teratoma, tuberous sclerosis, Sturge-Weber syndrome, venous sinus thrombosis, microcephaly intracranial calcification syndrome

Acquired CMV Infection of CNS

Cause: HIV infection; immunosuppression; solid organ / bone marrow transplantation

- mental status change

Role of CT: rule out mass lesion / substantial cerebral edema before planned lumbar puncture

√ meningoencephalitis (most frequently):
  √ cortical + subcortical areas of hypointensity on T1WI + hyperintensity on T2WI
    Location: especially frontal + parietal lobes
  √ diffuse leptomeningeal enhancement
√ ventriculoencephalitis (with advanced HIV infection):
  √ cerebral volume loss
  √ ventriculomegaly
  √ periventricular enhancement
√ enhancing mass lesions (only with advanced AIDS)
  DDx: lymphoma / other neoplasm, pyogenic abscess
√ polyradiculopathy (in adults)

Congenital CMV Infection of CNS

√ intracranial calcifications (34–70%):
  ◊ Most common finding of congenital CMV infection!
  √ thick and chunky postinflammatory periventricular Ca2+
  √ faint punctate Ca2+ in basal ganglia + thalami + parenchyma
  Associated with: developmental delays
√ cerebral atrophy
  √ ventriculomegaly (in up to 45%)
    ◊ 2nd most common finding of congenital CMV infection!
    Cause: ventriculitis; obstruction by inflammatory exudate; brain atrophy
  √ microcephaly (in up to 27%)
    Cause: encephaloclastic effect of virus / disturbance of cell proliferation
  √ cerebral volume loss
  √ cerebellar volume loss (in up to 67%):
    √ widening of cerebellar folia
    √ expansion of CSF spaces in posterior fossa
    √ severe diffuse hypoplasia / dysplasia of cerebellum
√ neuronal migrational disorders (in up to 10%)
  √ lissencephaly = smooth surface with absence of sulcation of a thin / thickened cortical mantle

Congenital CMV Imaging Findings versus Time of Infection

Estimated Gestational Age:	*< 18 wks*	*18–24 wks*	*> 26 wks*
√ periventricular Ca^{2+}	+	+	++
√ ventriculomegaly	++	+	
√ lissencephaly + thin cortex	+		
√ cerebellar hypoplasia	+	+	
√ delayed myelination	+		+
√ polymicrogyria		+	
√ schizencephaly (rare)		+	
√ dysmyelination			+
√ leukoencephalopathy			+

√ pachygyria = broad gyri + partial sulcation
√ diffuse / focal polymicrogyria = nodular cortical surface + irregular scalloped gray-white matter junction + thickened cerebral cortex
rare: schizencephaly, cortical dysplasia, heterotopia

√ white matter disease (in up to 22%) = leukoencephalopathy = static nonprogressive focal patchy / confluent areas of hyperintensity on T2WI and FLAIR images in parietal / posterior regions

√ periventricular cysts = subependymal cysts (= focal areas of necrosis + glial reaction) commonly in anterior temporal lobes (initially vacuolization → cyst formation)
Location: anterior temporal lobe > occipital pole of lateral ventricles > frontoparietal white matter

√ ventricular adhesions = intraventricular septa = thin strands of tissue crossing the ventricle ← ventriculitis

√ lenticulostriate vasculopathy (in up to 27%) = uni- / bilateral curvilinear highly echogenic streaks within basal ganglia + thalami
Cause: mineralizing vasculopathy with deposition of amorphous basophilic material in arterial walls

Prognosis: poor neurologic outcome with microcephaly + calcifications

DANDY-WALKER MALFORMATION

= characterized CLASSICALLY by
(1) Vermian hypoplasia with cephalad rotation of remnant
(2) Cystlike dilatation of 4th ventricle → enlarged posterior fossa with abnormally high position of tentorium and torcular (lambdoid-torcular inversion)

Incidence: 12% of all congenital hydrocephaly
◊ Most common posterior fossa malformation

Genetics: sporadic occurrence; 1–5% risk of recurrence

Path: defect in vermis connecting an ependyma-lined retrocerebellar cyst with 4th ventricle (PATHOGNOMONIC)

Cause: dysmorphogenesis of roof of 4th ventricle with failure to incorporate the area membranacea into developing choroid plexus

Time of origin: high insertion of tentorium suggests development before end of embryonic period! Originally proposed as congenital atresia of foramina of **L**uschka (**l**ateral) + **M**agendie (**m**edian) – but proposal NOT likely since foramina are not patent until 4th month of GA

Associated anomalies:
› midline CNS anomalies (in > 60%)
(1) Dysgenesis of corpus callosum (20–25%), lipoma of corpus callosum
(2) Holoprosencephaly (25%)
(3) Malformation of cerebral gyri (dysplasia of cingulate gyrus) (25%)
(4) Cerebellar heterotopia + malformation of cerebellar folia (25%)
(5) Malformation of inferior olivary nucleus
(6) Hamartoma of tuber cinereum
(7) Syringomyelia

(8) Cleft palate
(9) Occipital encephalocele (< 5%)

› other CNS anomalies:
(1) Polymicrogyria / gray matter heterotopia (5–10%)
(2) Schizencephaly
(3) Lumbosacral meningocele

› non-CNS anomalies (25%)
(1) Polydactyly, syndactyly
(2) Klippel-Feil syndrome
(3) Cornelia de Lange syndrome
(4) Cleft palate
(5) Facial angioma
(6) Cardiac anomalies

Age: majority < 1 year

• macrocephaly (90%)

Skull film:

√ large skull ← hydrocephalus + dolichocephaly
√ diastatic lambdoid suture
√ disproportionately large expanded posterior fossa
√ torcular-lambdoid inversion = upward displacement of tentorium + torcular herophili + transverse and lateral dural sinuses high above lambdoid angle

CT / US / MR:

√ absence / <u>hypoplasia of cerebellar vermis</u>: total (25%), partial (75%)
√ superiorly displaced superior vermis cerebelli
√ small widely separated ± hypoplastic cerebellar hemispheres ← anterolateral displacement by cystic 4th ventricle
√ <u>large posterior fossa</u> cyst with extension through foramen magnum = diverticulum of roofless 4th ventricle
√ <u>elevated insertion of tentorium cerebelli</u>
√ cerebellar hemispheres in apposition without intervening vermis following shunt procedure
√ absence of falx cerebelli
√ scalloping of petrous pyramids
√ <u>ventriculomegaly</u> (in 72% open communication with 3rd ventricle; in 39% patent 4th ventricle; in 28% aqueductal stenosis; in 11% incisural obstruction); present prenatally in 30%, by 3 months of age in 75%
√ anterior displacement of pons

Angio:

√ high position of transverse sinus
√ elevated great vein of Galen
√ elevated posterior cerebral vessels
√ anterosuperiorly displaced superior cerebellar arteries above the posterior cerebral arteries
√ small / absent PICA with high tonsillar loop

Cx: trapping of cyst above tentorium = "keyhole configuration"

Prognosis: fetal demise in 66%; 22–50% mortality during 1st year of life
DDx: (1) Posterior fossa extra-axial cyst
(2) Arachnoid cyst (normal 4th ventricle, patent foramina, intact vermis)
(3) Isolated 4th ventricle
(4) Megacisterna magna
(5) Porencephaly

It is not recommended to use terms like Dandy-Walker variant, Dandy-Walker complex, Dandy-Walker spectrum because they lack specificity and add confusion.

Dandy-Walker Variant

characterized by
(1) Variable hypoplasia of posteroinferior portion of vermis → communication between 4th ventricle + cisterna magna
(2) NO / only mild enlargement of posterior fossa
(3) Cystic dilatation of 4th ventricle

◊ More common than Dandy-Walker malformation; accounts for ⅓ of all posterior fossa malformations
◊ Demarcation of classic from variant Dandy-Walker is vague!

Cause: focal insult to developing cerebellum
Associated CNS anomalies:
agenesis of corpus callosum (21%), cerebral gyral malformation (21%), heterotopia, holoprosencephaly (10%), diencephalic cyst (10%), posterior fossa meningoencephalocele (10%)
Other associated anomalies:
polydactyly; cardiac, renal, facial anomalies; abnormal karyotype (29%)

√ 4th ventricle smaller + better formed
√ retrocerebellar cyst smaller
√ communication between retrocerebellar cyst and subarachnoid space through a patent foramen of Magendie may be present
√ posterior fossa smaller than in usual Dandy-Walker syndrome

OB-US:
√ incomplete closure of vermis is normal until 18 weeks GA!

Dandy-Walker Continuum / Complex

= continuum of anomalies, including Dandy-Walker malformation + Dandy-Walker variant + megacisterna magna + Blake pouch cyst, characterized by partial / complete dysgenesis of vermis cerebelli

Cause: broad insult to alar plate from various abnormalities
Associated with:
A. Inherited genetic syndromes
› autosomal recessive:
1. Meckel-Gruber syndrome
2. Ellis-van Creveld syndrome
3. Walker-Warburg syndrome

› autosomal dominant:
1. X-linked cerebellar hypoplasia
2. Aicardi syndrome

B. Abnormal karyotype (33%)
1. Duplications of chromosomes 5p, 8p, 8q
2. Trisomies 9, 13, 18

C. Infection
1. Virus: CMV, rubella
2. Protozoan: toxoplasmosis

D. Teratogen: alcohol, sodium warfarin

E. Multifactorial

Pseudo-Dandy-Walker Malformation

= developing normal rhombencephalon during 1st trimester

√ fluid-filled space in posterior aspect of fetal head

DEMENTIA WITH LEWY BODIES

= 2nd most common neurodegenerative disorder in patients > 65 years

Histo: loss of dopaminergic neurons in substantia nigra

• classic clinical triad:
(1) Fluctuating levels of cognitive arousal
(2) Visual hallucinations
(3) Spontaneous parkinsonism

• clinical condition may worsen under neuroleptic medications

PET:

√ hypometabolism in both parietal + posterior temporal lobes and posterior cingulate gyrus (similar to Alzheimer's)

√ ± involvement of occipital lobes (spared in Alzheimer's)

DEVELOPMENTAL VENOUS ANOMALY

= VENOUS ANGIOMA

= intraparenchymal tangle / cluster of dilated medullary veins converging on a single enlarged draining vein; bleed rarely

◊ Most common cerebral vascular malformation (~ 60%)!

◊ Can be considered a normal variant!

Cause: (?) accidents during embryogenesis → occlusion / maldevelopment of superficial / deep veins → creation of compensatory pathway by recruiting and dilating preexisting transmedullary veins

Age: any; M = F

Histo: venous channels without internal elastic lamina, separated by gliotic neural tissue that may calcify; probably representing persistent fetal venous system; normal intervening brain parenchyma

Associated with: blue rubber bleb nevus syndrome with multiple angiomas; increased coexistence of cavernous angiomas which can bleed!

- asymptomatic (common)
- headache, seizure, hemorrhage (unusual)

Risk of hemorrhage: 0.15% (increased with thrombosed draining vein / coexistent cavernous malformation)

A DVA rarely bleeds and is unlikely the cause of an intraparenchymal hemorrhage → search for a cavernoma, which is best be seen with gradient-echo / blood oxygen level-dependent (BOLD) sequences (= heavily T2* weighted).

- soft + compressible without thrills / pulsations
- distension with Valsalva maneuver

Location: deep cerebral / cerebellar white matter; most commonly adjacent to frontal horn

√ "umbrella / spoked-wheel / medusa head" configuration = multiple small radially oriented transmedullary veins at periphery of lesion converging on venous collector

√ interspersed normal brain parenchyma

√ dense capillary stain in larger lesion

√ linear / curvilinear enhancing structure = venous collector draining into superficial dural sinus / deep venous system (ependymal vein)

√ NO enlarged arterial vessels

Cx (uncommon): hemorrhage, ischemia

DDx: vascular neoplasm, cavernous vascular malformation, venous varix, Sturge-Weber disease (diffuse pial angiomatosis with venous-type capillaries)

DIFFUSE AXONAL INJURY

= WHITE MATTER SHEARING INJURY

Incidence: most common type of primary traumatic injury in patients with severe head trauma (48%)

Cause: high-velocity trauma (MVA) resulting in indirect injury due to <u>rotational</u> / angular (especially coronal) acceleration / deceleration forces (direct impact to head or fracture not required)

Pathogenesis:

cortex and deep structures move at different speed causing shearing stress of

(a) axons resulting in axonal tears followed by wallerian degeneration

(b) small white-matter vessels resulting in small petechial hemorrhages

Path: much of the injury is microscopic

Histo: multiple axonal retraction balls (HALLMARK), numerous perivascular hemorrhages

- immediate severe impairment of consciousness at time of impact
- persistent vegetative state

Location (according to severity of trauma):

(a) lobar white matter at corticomedullary junction (67%): parasagittal region of frontal lobe + periventricular region of temporal lobe; occasionally in parietal + occipital lobes

(b) internal + external capsule / basal ganglia, corona radiata, cerebellar peduncles

(c) corpus callosum (21%):

¾ of lesions at undersurface of posterior body + splenium

√ often associated with intraventricular hemorrhage

(d) brainstem: posterolateral quadrants of midbrain + upper pons; superior cerebellar

peduncles especially vulnerable
√ sparing of cortex
√ 20% of lesions with small central areas of petechial hemorrhage
CT (negative in 30% of positive MR cases):
√ foci of decreased density (usually seen when > 1.5 cm in size)
MR (most sensitive modality):
√ multiple small oval / round foci of decreased signal intensity on T1WI + increased signal on T2WI
Prognosis:
(1) Poor due to sequelae (may go on to die without signs of high intracranial pressure)
(2) Brain atrophy with enlargement of sulci + ventricles

DIFFUSE (MYELINOCLASTIC) SCLEROSIS

= MYELINOCLASTIC DIFFUSE SCLEROSIS = SCHILDER DISEASE
= rare demyelinating disorder with episodic recurrence + remission
Age: children (5–14 years) > adults; M÷F = 1÷1
Histo: selective confluent demyelination with relative axonal sparing, perivascular inflammatory infiltrate, reactive astrocytosis (indistinguishable from multiple sclerosis)
• hemiplegia, aphasia, ataxia, blindness
• swallowing difficulties, progressive dementia
• increased intracranial pressure: headache, vomiting
• vision and speech impairment, deafness
• aphasia, seizures, personality changes, tremors, balance instability, incontinence, muscle weakness
Location: centrum semiovale in both hemispheres
√ large well defined bilateral low-attenuation white matter lesions with mass effect
√ enhancement with IV contrast material
Rx: usually responsive to corticosteroids
DDx: (1) Acute disseminated encephalomyelitis (history of recent viral illness, monophasic course, lesions less confluent, no mass effect / enhancement)
(2) Adrenoleukodystrophy (bilaterally symmetric, confluent lesions, parietal location)
(3) Tumor, abscess, infarct

DYKE-DAVIDOFF-MASON SYNDROME

= CEREBRAL HEMIATROPHY = INFANTILE / CONGENITAL HEMIPLEGIA = SYNDROME OF HEMICONVULSIONS, HEMIPLEGIA, AND EPILEPSY
= unilateral cerebral atrophy with ipsilateral small skull
Cause: insult to immature brain resulting in neuronal loss + impaired brain growth:
(a) prenatal: congenital malformation, infection, vascular insult
(b) perinatal: birth trauma, anoxia, hypoxia, intracranial hemorrhage
(c) postnatal: trauma, tumor, infection, prolonged febrile seizures
Age: presents in adolescence
• seizures, mental retardation
• hemiparesis (typically spastic hemiplegia)

√ unilateral thickening of skull
√ unilateral decrease in size of cranial fossa
√ unilateral overdevelopment of sinuses
√ contraction of a hemisphere / lobe
√ compensatory enlargement of adjacent ventricle + sulci with midline shift

DYSEMBRYOPLASTIC NEUROEPITHELIAL TUMOR

= benign tumor of neuroepithelial origin arising from cortical / deep gray matter
Origin: derived from secondary germinal layers; originally diagnosed as low-grade astrocytoma
Histo: specific glioneuronal element in a columnar pattern oriented perpendicular to cortical surface; admixture of astrocytes + oligodendroglial elements in association with "floating neurons" and mucinous degeneration; ± multinodular architecture
Age: usually < 20 years; M > F
• medically refractory partial seizures; neurologic deficits (rare)
Location: temporal (62%) / frontal (31%) lobe; caudate nucleus; cerebellum; pons
CT:
√ hypoattenuating mass ± calcifications
√ remodeling of inner table of skull
MR:
√ cortical mass without surrounding vasogenic edema:
√ hypointense on T1WI + hyperintense on T2WI
√ "soap bubble" / megagyrus appearance at cortical margin = enlargement of cortical surface
√ contrast enhancement (in 33%)
Prognosis: partial resection stops seizure activity; rarely recurs
DDx: diffuse astrocytoma, ganglioglioma, oligodendroglioma

EMPTY SELLA SYNDROME

= extension of subarachnoid space into sella turcica, which becomes exposed to CSF pulsations ← defect in diaphragma sellae; characterized by normal / molded pituitary gland + normal or enlarged sella (empty sella = misnomer)
Incidence: 24% in autopsy study
√ slowly progressive symmetrical / asymmetrical (double floor) enlargement of sella
√ remodeled lamina dura remains mineralized
√ small rim of pituitary tissue displaced posteriorly + inferiorly
√ "infundibulum" sign = infundibulum extends to floor of sella
DDx: cystic tumor, large herniated 3rd ventricle (displaced infundibulum)

Primary Empty Sella

Incidence: 10% of adult population; M÷F = 1÷4
Probable causes:
(1) pituitary enlargement followed by regression during pregnancy
(2) involution of a pituitary tumor

(3) congenital weakness of diaphragma sellae

◊ Occurs more frequently in patients with increased intracranial pressure

- usually asymptomatic
- increased risk for CSF rhinorrhea
- NO endocrine abnormalities

Secondary Empty Sella

= postsurgical after disruption of diaphragma sellae

- visual disturbance, headaches

EMPYEMA OF BRAIN

Cause: paranasal sinusitis, otitis media, calvarial osteomyelitis, infection after craniotomy or ventricular shunt placement, penetrating wound, contamination of meningitis-induced subdural effusion

√ rim-enhancing purulent collection

√ restricted diffusion on DWI (DDx: simple effusion of acute bacterial meningitis is WITHOUT diffusion restriction)

Subdural Empyema

20% of all intracranial bacterial infections

Location: frontal + inferior cranial space in close proximity to paranasal sinuses; 80% over convexity extending into interhemispheric fissure or posterior fossa

√ hypo- / isodense crescentic / lentiform zone adjacent to inner table

√ may show mass effect (sulcal effacement, ventricular compression, shift)

√ thin curvilinear rim of enhancement (7–10 days later) adjacent to brain

√ severe sinusitis / mastoiditis (may be most significant indicator)

Mortality: 30% (neurosurgical emergency)

Cx: venous thrombosis (= thrombophlebitis), infarction, seizures, hemiparesis, hemianopia, aphasia, cerebritis, brain abscess

◊ Subdural >> epidural empyema more likely to cause complications requiring urgent neurosurgery!

DDx: subacute / chronic subdural hematoma

Epidural Empyema

• NO neurologic deficits (dura minimizes pressure exerted on brain)

√ thick enhancing rim

ENCEPHALITIS

= term generally reserved for diffuse inflammatory process of viral etiology, most commonly arthropod-borne arboviruses (Eastern + Western equine encephalitis, California virus encephalitis, St. Louis encephalitis)

√ diffuse mild cerebral edema

√ small infarctions / hemorrhage (less frequent)

√ hyperintensity on T2WI in areas of cortical involvement

Granulomatous Amebic Encephalitis

= usually in immunocompromised patients

Organism: Acanthamoeba histolytica, Balamuthia species

Endemic: southern California, Texas, Georgia, Florida

Transmission:

(a) hematogenous: skin / lower respiratory tract for Acanthamoeba

(b) inhalation: airborne cysts in soil

(c) direct contamination: from skin lesion, organ transplantation, stagnant water

• headache, altered mental status, focal neurologic deficits

√ hypoattenuated / T1 hypointense lesions
√ heterogeneous hyperintensity on T2WI
√ variably restricted diffusion + enhancement
Dx: identification of trophozoites with "spiky" pseudopodia on wet mount / Giemsa stains of CSF; positive polymerase chain reaction test
Prognosis: death within 7–10 days after onset of illness
DDx: neoplasm; acute disseminated encephalomyelitis; neurocysticercosis; toxoplasmosis

Primary Amebic Meningoencephalitis
= extremely aggressive amebic infection
Organism: free-living thermophilic ameba Naegleria fowleri = "brain-eating ameba" with predilection for warm fresh water bodies and soil
Transmission: through nasal cavity during swimming / diving activity in nature or poorly chlorinated swimming pool water
◊ NOT by drinking contaminated water!
Path: amebic collections in olfactory grooves + extensive destruction of olfactory tracts
√ leptomeningeal enhancement, brain edema
√ cerebral infarction

Herpes Simplex Encephalitis (HSE)
= most common cause of nonepidemic necrotizing meningo-encephalitis in immunocompetent individuals in USA
◊ Neurologic emergency due to high morbidity + mortality
Organism: HSV type I (in adults); HSV type II (in neonates from transplacental infection)
• preceding viral syndrome, low-grade fever, headache, seizures
• mental status changes: confusion, disorientation, hallucination, personality change, aphasia
Location: inferomedial temporal > frontal > parietal lobes; propensity for limbic system (olfactory tract, temporal lobes, cingulate gyrus, insular cortex); initially predominantly unilateral
√ mild patchy peripheral / gyral / cisternal enhancement (50%), may persist for several months
CT:
√ may be negative in first 3 days
√ poorly defined bilateral areas of mildly decreased attenuation in one / both temporal lobes + insulae
√ spared putamen forms sharply defined concave / straight border (DDx: infarction, glioma)
√ mild mass effect with compression of lateral ventricles + loss of sylvian fissure (brain edema)
√ tendency for hemorrhage + rapid dissemination in brain
MR (study of choice, positive within 2 days):
√ increased signal intensity on T2WI + mild to moderate hypointensity on T1WI
√ increased signal on DWI ← cytotoxic edema
√ small foci of hemorrhage (common)
NUC:

Agents: standard brain imaging (eg, ^{99m}Tc-DTPA); newer brain agents (eg, ^{123}I-iodoamphetamine / ^{99m}Tc-HMPAO)
◊ SPECT imaging improves sensitivity
√ characteristic focal increase in activity in temporal lobes on brain scintigraphy ← breakdown of blood-brain barrier
Dx: (1) identification of virus within CSF (using polymerase chain reaction technique)
(2) fluorescein antibody staining / viral culture from brain biopsy
Mortality: 30–70%
Rx: adenine arabinoside
DDx: (1) Infarction (involves either medial or lateral temporal lobe, almost exclusively unilateral)
(2) Low-grade glioma
(3) Abscess

Human Immunodeficiency Virus Encephalitis (HIV)

often in combination with CMV encephalitis
Histo: microglial nodules + perivascular multinucleated giant cells accompanying gliosis of deep white + gray matter
√ predominantly central CNS atrophy
√ symmetric periventricular / diffuse white matter disease without mass effect:
√ hypodense on CT, hyperintense on T2WI

Postinfectious Encephalitis

following exanthematous viral illness (measles, mumps, rubella, smallpox, chickenpox, Epstein-Barr virus, varicella, pertussis) / vaccination

Acute Disseminated Encephalomyelitis (ADEM)

= POSTVIRAL LEUKOENCEPHALOPATHY
= autoimmune reaction against patient's white matter
• 7–14 days / several weeks following an exanthematous viral infection / vaccination
• confusion, headaches, fever
• seizures, focal neurologic deficits
Histo: diffuse perivenous inflammatory process resulting in areas of demyelination
Location: subcortical white matter of both hemispheres asymmetrically; may involve brainstem / posterior fossa
√ lesions may demonstrate contrast enhancement
CT:
√ multifocal hypodense white matter abnormalities
√ sparing of cortical gray matter, occasionally deep gray matter involvement
√ no additional lesions on follow-up exam
MR:
√ multifocal punctate / large confluent areas of hyperintensity on FLAIR / T2WI
Rx: corticosteroids result in dramatic improvement
Prognosis: complete resolution of neurologic deficits within 1 month (80–90%) / some permanent neurologic damage (10–20%)

DDx: multiple sclerosis (rarely recurrent episodes as in multiple sclerosis); autoimmune vasculitis; aging brain

Acute Hemorrhagic Leukoencephalitis

= fulminant myelinoclastic disease of CNS
= hyperacute form of acute disseminated encephalomyelitis
Cause: immunoreactive disease following prodromal illness (minor upper respiratory viral infection, ulcerative colitis)
Path: marked edema, brain softening
Histo: necrotizing angiitis of venules + capillaries within white matter with extravasation of PMNs and lymphocytes; fibrinoid necrosis of affected capillaries + surrounding tissues; confluent hemorrhages with ball-and-ring configuration due to diapedesis of RBCs

- progressive coma, motor disturbance, speech difficulty, seizures, pyrexia, leukocytosis
- pleocytosis (= ↑ WBC in spinal / other bodily fluid)
- elevated protein in spinal fluid

Location: unilateral disease; parietal + posterior frontal white matter at level of centrum semiovale (sparing subcortical U-fibers + cortex) > basal ganglia, cerebellum, brainstem, spinal cord
√ rapid development of profound mass effect resembling infarction
√ multiple punctate white matter hemorrhages
√ extensive hypoattenuation virtually confined to hemispheric white matter
Prognosis: usually results in death
DDx: (1) Herpes simplex encephalitis (cortical lesions in temporal + inferior frontal lobes + insular region, no imaging findings until 3–5 days after onset of significant symptoms)
(2) Tumefactive multiple sclerosis
(3) Osmotic demyelination
(4) Toxic encephalopathy: lipophilic solvent, methanol
(5) Hypertensive encephalopathy: eclampsia, thrombotic thrombocytopenic purpura

ENLARGED PERIVASCULAR SPACES

= ENLARGED / ATYPICAL VIRCHOW-ROBIN SPACES
= small invaginations of subarachnoid space following pia mater along perforating nutrient end vessels into brain substance
Location: inferior basal ganglia (lenticulostriate arteries); inferior third of putamen = état criblé (cribriform / sievelike); midbrain + deep white matter (perforating medullary arteries); subinsular cortex; thalamus, dentate nucleus; corpus callosum; cingulate gyrus; usually bilateral
√ no restricted diffusion
√ no enhancement
√ normal signal intensity of surrounding parenchyma
√ occasionally central high SI on T1WI ← inflow effect
√ small 1–2-mm round lesions isointense to CSF
√ moderate 2-5 mm round lesions isointense to CSF

√ clusters of variably sized bizarre cystic spaces bordering ventricles / subarachnoid space
Cx: hydrocephalus
DDx: multiple lacunar infarcts (adjacent parenchymal hyperintensity), cystic neoplasm (SI not like CSF), infectious / parasitic cysts (enhancing cyst wall); neuroepithelial cyst; mucopolysaccharidosis

État Criblé
= giant sievelike Virchow-Robin spaces
= clusters of variable sized cysts with bizarre cystic configuration and mass effect
√ ± hydrocephalus
√ ± surrounding reactive gliosis

EPENDYMAL CYST
= rare benign thin-walled cyst
Cause: sequestration of developing neuroectoderm during embryogenesis
Histo: thin-walled ependyma-lined cyst containing clear serous fluid
Location: lateral ventricle, juxtaventricular in temporoparietal region + frontal lobe; rare in subarachnoid space, brainstem, cerebellum
Site: along choroid fissure
√ thin-walled CSF-containing cyst
DDx: choroid plexus cyst (NOT of CSF signal intensity on all sequences, typically bilateral), arachnoid cyst (in arachnoid spaces), neurocysticercosis (hyperintense rim on FLAIR), asymmetric ventricles

EPENDYMOMA
= in majority benign slow-growing neoplasm of mature well-differentiated ependymal cells lining the ventricles
Incidence: most common in children; 5–9% of all primary CNS neoplasms; 15% of posterior fossa tumors in children; 63% of spinal intramedullary gliomas
Histo: benign aggregates of ependymocytes in form of perivascular pseudorosettes; may have papillary pattern (difficult DDx to choroid plexus papilloma)
Age: (a) supratentorial: at any age (atrium / foramen of Monro)
(b) posterior fossa: age peaks at 5 + 34 years; M÷F = 0.8÷1
Associated with: neurofibromatosis
• increased intracranial pressure (90%)
Location:
(a) infratentorial: floor of 4th ventricle (70% of all intracranial ependymomas)
(b) conus medullaris: 40–65% of all spinal intramedullary gliomas
(c) supratentorial: in frontal > parietal > temporoparietal juxtaventricular region (uncommonly intraventricular), lateral ventricle, 3rd ventricle
in children: infratentorial÷supratentorial = 7÷3
√ small cystic areas in 15–50% (central necrosis)
√ fine punctate multifocal calcifications (25–50%)
√ intratumoral hemorrhage (10%)

√ frequently grows into brain parenchyma with extension to cortical surface (particularly in frontal + parietal lobes)
√ may invaginate into ventricles
√ expansion frequently through foramen of Luschka into cerebellopontine angle (15%) or through foramen of Magendie into cisterna magna (up to 60%) (CHARACTERISTIC)
√ direct invasion of brainstem / cerebellum (30–40%)
√ insinuation around blood vessels + cranial nerves
√ communicating hydrocephalus (100%) ← protein exudate elaborated by tumor clogging resorption pathways

CT:
√ sharply marginated multilobulated iso- / slightly hyperdense 4th ventricular mass
√ thin well-defined low-attenuation halo (= distended effaced 4th ventricle)
√ heterogeneous / moderately uniform enhancement of solid portions (80%)

MR:
√ low to intermediate heterogeneous SI on T1WI
√ hypointense tumor margins on T1WI + T2WI in 64% (= hemosiderin deposits)
√ foci of high-signal intensity on T2WI (= necrotic areas / cysts) + low signal intensity (= calcification / hemorrhage)
√ fluid-fluid level within cysts
√ homogeneous Gd-DTPA enhancement of tumor

Cx: subarachnoid dissemination via CSF (rare) (DDx: malignant ependymoma, ependymoblastoma)

Rx: surgery (difficult to resect due to adherence to surrounding brain) + radiation (partially radiosensitive) + chemotherapy

DDx of cerebellar ependymoma:
(1) Astrocytoma (hypodense, displaces 4th ventricle from midline, cystic lucency, intramedullary)
(2) Medulloblastoma (hyperdense, calcifications in only 10%)
(3) Trapped 4th ventricle (no contrast enhancement)

EPIDURAL HEMATOMA OF BRAIN

= EXTRADURAL HEMATOMA
= hematoma within potential space between naked inner table of skull + calvarial periosteum (inner dura layer), which is bound down firmly to cranium at sutural margins (= subperiosteal hematoma of inner table)

Incidence: 2% of all serious head injuries; in < 1% of all children with cranial trauma; uncommon in infants

Cause: impact on skull causes linear fracture + laceration of periosteal layer of outer table; temporary inward displacement of fragments lacerates meningeal vessels and strips both dural layers from inner table while the inner layer (meningeal dura) remains intact; blood accumulates between naked inner table and dura

Age: more common in younger patients 20–40 years ← dura more easily stripped away from skull

Associated with:

(1) Skull fracture in 75–85–95%
√ best demonstrated on skull radiographs
◊ Skull fractures frequently not visible in children ("ping-pong fracture")!
(2) Subdural hemorrhage
(3) Contusion

Source of bleeding:

(a) laceration of (middle) meningeal artery (high pressure) / meningeal vein (low pressure) adjacent to inner table from calvarial fracture (91%)
(b) disruption of dural venous sinuses (transverse / superior sagittal sinus) with low pressure + high flow ← diastatic fracture of lambdoid / coronal suture (major cause in younger children)
(c) avulsion of diploic veins / marrow sinusoids at points of calvarial perforations

Time of presentation: within first few days of injury (80%), 4–21 days (20%)

- transient loss of consciousness(= brief period of unconsciousness from concussion of brainstem)
- "lucid interval" (in < 33%)
- delayed somnolence (24–96 hours after accident) due to accumulation of epidural hematoma:
  ◊ DANGEROUS because of focal mass effect + rapid onset (NEUROSURGICAL EMERGENCY unless small)!
- progressive deterioration of consciousness → coma
- focal neurologic signs: 3rd nerve palsy (as a sign of cerebral herniation), hemiparesis

◊ Only a minority of skull fractures across the middle meningeal artery groove result in an epidural hematoma!

Types:

I	acute epidural hematoma	(58%) from arterial bleeding
II	subacute hematoma	(31%)
III	chronic hematoma	(11%) from venous bleeding

Factors determining the rate of epidural expansion:

injury to artery or vein, spasm of artery, containment of bleed through pseudoaneurysm or tamponade, decompression of hematoma into meningeal + diploic veins or through fracture into scalp

Location:

◊ Most commonly clinically significant if located in temporoparietal region!
(a) in 66% temporoparietal (most often from laceration of middle meningeal artery)
(b) in 29% at frontal pole, parietooccipital region, between occipital lobes, posterior fossa (most often from laceration of dural sinuses by fracture)
◊ NO crossing of sutures unless diastatic fracture of suture present!

CT:

√ fracture line in area of epidural hematoma
√ expanding biconvex (lenticular = elliptical) extra-axial fluid collection (most frequent) = under high pressure:
√ usually does not cross suture lines
√ separation of venous sinuses / falx from inner table

◊ The ONLY intracranial hemorrhage displacing falx / venous sinuses away from inner table!

√ hematoma usually homogeneous:
√ fresh extravasated blood (30–50 HU) / coagulated blood (50–80 HU) in acute stage
√ rarely with hypoattenuated "swirl" ← admixture of fresh blood into clotted blood during active bleeding
√ mass effect ("compression cone effect") with effacement of gyri + sulci from:
› epidural hematoma (57%)
› hemorrhagic contusion (29%)
› cerebral edematous swelling (14%)
√ marked stretching of vessels
√ signs of arterial injury (rare): contrast extravasation, arteriovenous fistula, middle meningeal artery occlusion, formation of pseudoaneurysm

MR:
√ low intensity of fibrous dura mater allows differentiation of epidural from subdural blood in the late subacute phase (= extracellular methemoglobin) with hyperintensity on T1WI + T2WI

Angio:
√ meningeal arteries displaced away from inner table of skull
√ pseudoaneurysm = extravasation of contrast material
√ arteriovenous fistula at fracture line

Cx: herniation, coma, death (15–30%)

Rx: after surgical evacuation return of ventricular system to midline

◊ Epidural hematoma at another site may be unmasked following surgical decompression!

DDx: Chronic subdural hematoma (may have similar biconvex shape, crosses suture lines, stops at falx, no associated skull fracture, no displaced dura on MR)

FAHR DISEASE

= BILATERAL STRIOPALLIDODENTATE CALCINOSIS = FAMILIAL CEREBROVASCULAR FERROCALCINOSIS

= rare neurodegenerative disease characterized by bilateral symmetric deposition of calcium + other minerals in basal ganglia, thalamus, dentate nucleus, centrum semiovale

- slow onset of headaches, vertigo, movement disorder, syncope, seizures, paresis, spasticity, gait disturbance, speech disorder
- coma, dementia, Parkinsonism, chorea, tremor
- dystonia, myoclonia, orthostatic hypotension
- NO hypoparathyroidism

Affected area: basal ganglia, dentate nucleus, thalamus, cerebral subcortical white matter

√ bilaterally symmetric hyperdense + T1-hyperintense calcifications

DDx: hypoparathyroidism, pseudohypoparathyroidism, pseudopseudohypoparathyroidism

GANGLION CELL TUMOR

Gangliocytoma

= rare benign tumor composed of mature ganglion cells

Prevalence: 0.1–0.5% of all brain tumors

Age: children + young adults
Associated with: dysplastic + malformed brain
Cause: ? dysplastic brain
Histo: purely neuronal tumor composed of abnormal mature ganglion cells without neoplastic glial cells (= no immunoreactivity for glial fibrillary acidic protein)
Location: floor of 3rd ventricle > temporal lobe > cerebellum > parietooccipital region > frontal lobe > spinal cord
CT:
√ hyperattenuating mass with little mass effect
MR:
√ iso- to hypointense on T1WI + T2WI
√ bright on proton density images

Dysplastic Cerebellar Gangliocytoma
= LHERMITTE-DUCLOS DISEASE
= rare hamartomatous disorder
Average age: 34 years; occasionally pediatric patients
Associated with: polydactyly, partial gigantism, multiple hemangiomas, leontiasis ossea
Strong association with: Cowden syndrome
Path: disruption of normal cerebellar laminar structure
Histo: dysplastic hypertrophic ganglion cells expanding granule layer; increased myelination of molecular layer of cerebellar cortex; loss of Purkinje cells and white matter; marked reduction in myelination of central white matter of cerebellar folia
- asymptomatic / symptoms of increased intracranial pressure (headaches, blurred vision, vomiting)
- slowly progressive cerebellar syndrome (40%)
- megalencephaly (50%); mental retardation

X-ray:
√ thinning of skull in occipital region
CT:
√ hypo- / isoattenuating cerebellar mass
√ hydrocephalus ← compression of 4th ventricle + effacement of cerebellopontine angle cistern
√ calcification uncommon
√ NO enhancement
MR:
√ cerebellar mass with "striated cerebellum" sign = tiger-striped / corduroy laminated folial pattern of alternating intensity bands on T1WI + T2WI:
√ hyper- and isointense relative to gray matter on T2WI
√ iso- and hypointense relative to gray matter on T1WI
√ enhancement extremely uncommon
√ ± syringohydromyelia
Rx: decompression of ventricles + resection of mass
DDx: medulloblastoma

Ganglioglioma

= uncommon slow-growing relatively benign tumor composed of glial + nerve cells

Prevalence: 0.4–1.3% of all intracranial neoplasms; 1–4% of all pediatric CNS neoplasms

Peak age: 10–20 years; in 80% < 30 years of age; M > F

Histo: containS ganglion + glial elements: ganglion cells (neurons) arise from primitive neuroblasts and mature during growth; usually astrocytic glial cells predominate in various stages of neoplastic differentiation

• headaches; medically refractory seizures:

◊ Most common cause of chronic temporal lobe epilepsy!

Location: frequently above tentorium: in periphery of cerebral hemisphere [temporal (38%) / parietal (30%) / frontal (18%) lobes]; brainstem; cerebellum; pineal region; spinal cord; optic nerve; optic chiasm; ventricles; local involvement of subarachnoid space

√ circumscribed slow-growing mass:

√ solid (43%) / purely cystic (5%) / solid-cystic combination (52%)

√ calcifications (30%)

√ little associated mass effect / vasogenic edema

CT:

√ hypoattenuating (38%) / mixed attenuation (32%) / isoattenuating (15%) / hyperattenuating (15%) mass

√ ± remodeling of skull

√ contrast enhancement (16–80%)

◊ Occasionally completely undetectable by CT

MR:

√ variable (hypo- / isointense) nonspecific MR appearance on T1WI

√ commonly at least one hyperintense region on T2WI

√ cystic component may have higher signal intensity than CSF ← gelatinous material

√ nonenhancing / ringlike / homogeneously intense enhancement

Prognosis: favorable; malignant degeneration (6%)

Rx: gross total resection (with resolution of seizure activity in majority of patients)

Desmoplastic Infantile Ganglioglioma

= DESMOPLASTIC INFANTILE ASTROCYTOMA = SUPERFICIAL CEREBRAL ASTROCYTOMA ATTACHED TO DURA

= uncommon variety of ganglioglioma exclusively in infants

Age: < 18 months (vast majority); M÷F = 2÷1

Histo: spindle cell neoplasm with oval / elongated moderately pleomorphic nuclei + clusters of larger cells with large prominent eccentric nuclei and cytoplasm containing Nissl bodies

• rapidly increasing head circumference; seizure (uncommon)

Location: frontal + parietal > temporal > occipital lobes

√ exceptionally large heterogeneously mass:

√ slightly hyperattenuating solid portion typically located along cortical margin

√ cystic components

√ intense enhancement of solid component
√ CHARACTERISTIC extension of enhancement to leptomeningeal margin ← firm dural attachment
√ rare vasogenic edema
√ NO calcification
Prognosis: good
Rx: surgical resection

GERMINOMA

= malignant primitive germ cell neoplasm
Incidence: 1–2% of all cranial neoplasms
Age: < 20 years in 90%
Histo: lymphocytes + large polygonal primitive germ cells; absence of capsule facilitates invasion
◊ Identical to testicular seminoma + ovarian dysgerminoma with the same radiosensitivity.
Location: (a) pineal region (50–65%)
(b) suprasellar hypothalamic region (25–35%): infundibular stalk, floor of 3rd ventricle
(c) others: basal ganglia, thalamus
(d) synchronous locations in 10% of all intracranial germ cell tumors
√ hyperattenuated mass on CT + reduced perfusion on DWI ← to abundance of lymphocytes
Cx: frequent CSF seeding (CSF cytology more sensitive than imaging like contrast MR of entire neuroaxis)
Rx: combination of irradiation (very radiosensitive) and chemotherapy (doxorubicin, cisplatin, cyclophosphamide)
Prognosis: 90% 5-year survival

Suprasellar / Hypothalamic Germinoma

Age: childhood + young adulthood; M = F
• hypothalamic symptoms:
• diabetes insipidus, emaciation
• precocious puberty frequent in children < 10 years of age (tumor may be small / radiologically invisible)
√ homogeneous well-marginated round solid mass
√ prompt homogeneous contrast enhancement
MR:
√ iso- to hypointense to gray matter on T1WI
√ iso- to slightly hyperintense on T2WI ← diminished free water content
√ absence of hyperintense posterior pituitary lobe ← blockage of infundibulum by mass

Pineal Germinoma

= DYSGERMINOMA = ATYPICAL TERATOMA = PINEALOMA (former inaccurate names)
◊"pinealoma" = misnomer as it refers to any pineal mass

Incidence: 1–2% of all cranial neoplasms; most common pineal tumor (> 50% of all pineal tumors, 66% of pineal germ cell tumors)
Age: 10–25 years (90% < 20 years old); M÷F = 10÷1
May be associated with: ectopic pinealoma = secondary focus in inferior portion of 3rd ventricle

• Parinaud syndrome
√ ± hydrocephalus ← compression of aqueduct of Sylvius
√ well-defined lesion restricted to pineal gland
√ may infiltrate quadrigeminal plate / thalamus
CT:
√ sharply circumscribed hyperattenuating mass ← highly cellular lymphocyte component
√ mass engulfs pineal calcifications
√ moderate / marked uniform contrast enhancement
MR:
√ round / lobular well-circumscribed relatively homogeneous mass iso- to hyperintense to gray matter on T1WI and T2WI ± cystic components
√ reduced perfusion on DWI ← highly cellular lymphocyte component
√ avid homogeneous Gd-DTPA enhancement

Cx: common invasion of adjacent brain + dissemination by CSF requires imaging of the entire neuroaxis!
Prognosis: good ← lesions highly responsive to radiation therapy with ≥ 90% 5-year survival

DDx: primary pineal neoplasm

GLIOBLASTOMA MULTIFORME

= GBM
Most malignant form of all gliomas / astrocytomas; end stage of progressive severe anaplasia of preexisting Grade I / II astrocytoma (not from embryologic glioblasts)
Incidence: most common primary brain tumor; 50% of all intracranial tumors; 1–2% of all malignancies; 20,000 cases per year
Age: all ages; peak incidence at 65–75 years; M÷F = 3÷2; more frequently in whites
Genetics: Turcot syndrome, neurofibromatosis type 1, Li-Fraumeni syndrome (familial neoplasms in various organs based on abnormal p53 tumor-suppressor gene)
Path: multilobulated appearance; quite extensive vasogenic edema (transudation through structurally abnormal vascular tumor channels); deeply infiltrating neoplasm; hemorrhage; necrosis is essential for pathologic diagnosis (HALLMARK)
Histo: highly cellular, often bizarrely pleomorphic / undifferentiated multipolar astrocytes; common mitoses + prominent vascular endothelial proliferation; no capsule; pseudopalisading (= viable neoplastic cells form an irregular border around necrotic debris as the tumor outgrows its blood supply)
Subtypes:
(a) giant cell GBM = monstrocellular sarcoma
(b) small cell GBM = gliosarcoma = Feigin tumor
Location:
(a) hemispheric: white matter of centrum semiovale: frontal > temporal lobes; common in

pons, thalamus, quadrigeminal region; relative sparing of basal ganglia + gray matter
DDx: solitary metastasis, tumefactive demyelinating lesion ("singular sclerosis"), atypical abscess

(b) callosal: "butterfly glioma" may grow exophytically into ventricle
(c) posterior fossa: pilocytic astrocytoma, brainstem astrocytoma
(d) extraaxial: primary leptomeningeal glioblastomatosis
(e) multifocal: in 2–5%

Spread:

(a) direct extension along white matter tracts:
corpus callosum (36%), corona radiata, cerebral peduncles, anterior commissure, arcuate fibers
√ readily crosses midline = "*butterfly*" glioma (clue: invasion of septum pellucidum)
√ frontal + temporal gliomas tend to invade basal ganglia
√ may invade pia, arachnoid and dura (mimicking meningioma)
(b) subependymal carpet after reaching surface of ventricles
(c) via CSF (< 2%)
(d) hematogenous (extremely rare):
√ osteoblastic bone lesion

NECT:

√ inhomogeneous low-density mass with irregular shape + poorly defined margins (hypodense solid tumor / cavitary necrosis / tumor cyst / peritumoral "fingers of edema")
√ considerable mass effect → compression + displacement of ventricles, cisterns, brain parenchyma
√ iso- / hyperdense portions (= hemorrhage) in 5%
√ rarely calcifies (if coexistent with lower-grade glioma / after radio- or chemotherapy)

CECT:

Enhancement pattern: contrast enhancement ← breakdown of blood-brain barrier / neovascularity / areas of necrosis
(a) diffuse homogeneous enhancement
(b) heterogeneous enhancement
(c) ring pattern (occasionally enhancing mass within the ring)
(d) low-density lesion with contrast-fluid level ← leakage of contrast

√ almost always ring blush of variable thickness: multiscalloped ("garland"), round / ovoid; may be seen surrounding ventricles (= subependymal spread); tumor usually extends beyond margins of enhancement
√ sedimentation level ← cellular debris / hemorrhage / accumulated contrast material in tumoral cyst

MR:

√ poorly defined lesion with some mass effect / vasogenic edema / heterogeneity
√ hemosiderin deposits (gradient echo images)
√ hemorrhage (= hypointensity on T2WI and T2*WI)
√ T1WI + gadolinium-DTPA enhancement separates tumor nodules from surrounding edema, central necrosis and cyst formation

Angio:

√ wildly irregular neovascularity + early draining veins

√ avascular lesion

PET:

√ increase in glucose utilization rate

Rx: surgery + radiation therapy + chemotherapy

Prognosis: 16–18 months postoperative survival (frequent tumor recurrence ← during surgery uncertainty about tumor margins)

Multifocal GBM

(1) Spread of primary GBM
(2) Multiple areas of malignant degeneration in diffuse low-grade astrocytoma ("gliomatosis cerebri")
(3) Inherited / acquired genetic abnormality

GLIOMA

= malignant tumors of glial cells growing along white matter tracts with tendency to increase in grade with time; may be multifocal

Incidence: 30–40% of all primary intracranial tumors; 50% of solitary supratentorial masses

√ contrast enhancement:
→ increases in proportion to degree of anaplasia
→ intensity of enhancement diminishes with steroid therapy

CELL OF ORIGIN

1.	Astrocyte	Astrocytoma
2.	Oligodendrocyte	Oligodendroglioma
3.	Ependyma	Ependymoma
4.	Medulloblast	Medulloblastoma; (PNET = primitive neuroectodermal tumor)
5.	Choroid plexus	Choroid plexus papilloma

FREQUENCY OF INTRACRANIAL GLIOMAS

Glioblastoma multiforme	51%
Astrocytoma	25%
Ependymoma	6%
Oligodendroglioma	6%
Spongioblastoma polare	3%
Mixed gliomas	3%
Astroblastoma	2%

Age peak: middle adult life

Location: cerebral hemispheres; spinal cord; brainstem + cerebellum (in children)

Brainstem Glioma

Incidence: 1%; 12–15% of all pediatric brain tumors; 20–30% of infratentorial brain tumors in children

Histo: usually anaplastic astrocytoma / glioblastoma multiforme with infiltration along fiber tracts

Age: in children + young adults; peak age 3–13 years; M÷F = 1÷1

- become clinically apparent early before ventricular obstruction occurs
- ipsilateral progressive multiple cranial nerve palsies
- cerebellar dysfunction: ataxia, nystagmus
- contralateral hemiparesis, eventually respiratory insufficiency

Location: pons > midbrain > medulla; often unilateral at medullopontine junction
◊ Medullary + mesencephalic gliomas are more benign than pontine gliomas!

Growth pattern:
(a) diffuse infiltration of brainstem with symmetric expansion + rostrocaudal spread into medulla / thalamus + spread to cerebellum
(b) focally exophytic growth into adjacent cisterns (cerebellopontine, prepontine, cisterna magna)

√ asymmetrically expanded brainstem
√ flattening + posterior displacement of 4th ventricle + aqueduct of Sylvius
√ compression of prepontine + interpeduncular cistern (in upward transtentorial herniation)
√ paradoxical widening of CP angle cistern with tumor extension into CP angle
√ paradoxical anterior displacement of 4th ventricle with tumor extension into cisterna magna

CT:
√ isodense / hypodense mass with indistinct margins
√ hyperdense foci (= hemorrhage) uncommon
√ absent / vague (minimal / patchy) contrast enhancement (50%)
√ ring enhancement in necrotic / cystic tumors (= most aggressive tumors)
√ prominent enhancement in exophytic lesion
√ hydrocephalus uncommon (because of early symptomatology)

MR: (best evaluation in subtle cases)
√ hypointense on T1WI + hyperintense on T2WI
√ often only subtle enhancement
√ ± engulfment of basilar artery

Angio:
√ anterior displacement of basilar artery + anterior pontomesencephalic vein
√ posterior displacement of precentral cerebellar vein
√ posterior displacement of posterior medullary + supratonsillar segments of PICA
√ lateral displacement of lateral medullary segment of PICA

Prognosis: 10–30% 5-year survival rate
Rx: radiation therapy
DDx: focal encephalitis, resolving hematoma, vascular malformation, tuberculoma, infarct, multiple sclerosis, metastasis, lymphoma

Hypothalamic-Chiasmatic Glioma

Origin: often undeterminable: hypothalamic gliomas invade chiasm, chiasmatic gliomas invade hypothalamus
Incidence: 10–15% of supratentorial tumors in children
Age: 2–4 years; M÷F = 1÷1
Associated with: von Recklinghausen disease (20–50%)

- diminished visual acuity (50%) ← optic atrophy
- diencephalic syndrome (in up to 20%): marked emaciation, pallor, unusual alertness,

hyperactivity, euphoria
• short stature (in 20%) ← reduction in growth hormone
• obese child, sexual precocity, diabetes insipidus
√ suprasellar hypodense lobulated mass with dense inhomogeneous enhancement
√ heterogeneous lesion ← cyst formation, necrosis, calcifications
√ hypointense on T1WI + hyperintense on T2WI + FLAIR
√ obstructive hydrocephalus
DDx: hypothalamic hamartoma, ganglioglioma, choristoma

GLOBOID CELL LEUKODYSTROPHY

= KRABBE DISEASE
= autosomal recessive neurodegenerative disorder characterized by severe myelin loss + globoid cells in white matter
Cause: deficiency of galactosylceramide β-galactosidase → cerebroside accumulation + destruction of oligodendrocytes
Age: 3–6 months
• fever, hyperactive reflex, flaccidity, irritability, restlessness
• optic atrophy, hyperacusis
Lesion location: thalami, posterior limb of internal capsules, caudate nuclei, brainstem, cerebellar dentate nuclei, centrum semiovale
√ symmetric hyperintensity / hyperdensity in periventricular white matter, thalami, basal ganglia, dentate + caudate nuclei, corona radiata
√ decreased attenuation of white matter
√ brain atrophy with enlargement of ventricles
MR spectroscopy:
√ elevated choline + creatine + myo-inositol associated with moderate N-acetylaspartate
Dx: biochemical assay from white blood cells / skin fibroblasts
Prognosis: death within first few years of life

HALLERVORDEN-SPATZ DISEASE

= PANTOTHENATE KINASE-ASSOCIATED NEURODEGENERATION
= rare familial neurodegenerative metabolic disorder with abnormal iron retention in basal ganglia
Cause: mutation of PANK2 gene encoding pantothenate kinase → neurodegeneration with iron accumulation
Age: 2nd decade of life
Histo: hyperpigmentation and symmetrical destruction of globus pallidus + substantia nigra
Types:
(a) classic early-onset rapidly progressive disease
(b) atypical late-onset slowly progressive disease
• progressive gait impairment + rigidity of limbs
• slowing of voluntary movements, dysarthria
• choreoathetotic movement disorder, progressive dementia
CT:

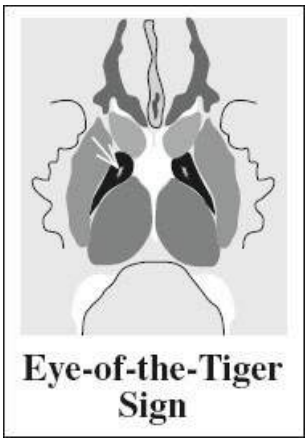
√ low- (= tissue destruction) / high-density (= dystrophic calcification) foci in globus pallidus

MR:

√ "eye-of-the-tiger" sign = high-signal-intensity center surrounded by the more typical hypointensity in globus pallidus:

√ initially bilateral hypointense globus pallidus on T2WI (= iron accumulation)

√ later central hyperintense foci on T2WI (= tissue destruction + gliosis)



HAMARTOMA OF CNS

rare tumor

(a) sporadic

(b) associated with tuberous sclerosis; may degenerate into giant cell astrocytoma

Age: 0–30 years

Location: temporal lobe, hamartoma of tuber cinereum, subependymal in tuberous sclerosis

√ cyst with little mass effect, possibly with focal calcifications

√ usually NO enhancement

Hypothalamic hamartoma

= HAMARTOMA OF TUBER CINEREUM

= rare developmental congenital malformation composed of normal neuronal tissue arising from posterior hypothalamus in region of tuber cinereum

Age: 1st–2nd decade; M > F

Histo: heterotopic collection of neurons, astrocytes, oligodendroglial cells (closely resembling histologic pattern of tuber cinereum)

• neurodevelopmental delay

• central precocious puberty, gelastic seizures

Location: mamillary bodies / tuber cinereum, hypothalamus

(a) **parahypothalamic** hamartoma (common)

• isosexual precocious puberty ← LHRH secretion

√ pedunculated mass attached to tuber cinereum / mamillary bodies by thin stalk

(b) **intrahypothalamic** hamartoma (rare)

• gelastic seizures, hyperactivity

√ sessile mass with broad attachment to hypothalamus
√ distortion of 3rd ventricle

Size: up to 4 cm in diameter

√ well-defined round / oval mass projecting from base of brain into suprasellar / interpeduncular cistern

√ stable in size over time

CT:

√ round homogeneous mass isodense with brain tissue

√ NO enhancement

MR:

√ well-defined round pedunculated mass suspended from tuber cinereum / mamillary bodies

√ imaging characteristics of gray matter:

√ iso- to mildly hypointense on T1WI

√ iso- to slightly hyperintense on T2WI

√ NO gadolinium enhancement

HEAD TRAUMA

= CNS TRAUMA

Incidence: 0.2–0.3% significant CNS trauma annually in USA; 550÷100,000 persons with peak age of 15–24 years; second peak > 50 years of age

Cause: motor vehicle accidents (51%), fall (21%), assault and violence (12%), sports and recreation (10%)

Classification:

A. Primary traumatic lesion

(a) primary neuronal injury

1. Cortical contusion
2. Diffuse axonal injury
3. Subcortical gray matter injury
   = injury to thalamus ± basal ganglia
4. Primary brainstem injury

(b) primary hemorrhages (from injury to a cerebral artery / vein / capillary)

1. Subdural hematoma
2. Epidural hematoma
3. Intracerebral hematoma
4. Diffuse hemorrhage (intraventricular, subarachnoid)

(c) primary vascular injuries

1. Carotid-cavernous fistula
2. Arterial pseudoaneurysm
   Location: branches of ACA + MCA, intracavernous portion of ICA, pCom
3. Arterial dissection / laceration / occlusion
4. Dural sinus laceration / occlusion

(d) traumatic pia-arachnoid injury

1. Posttraumatic arachnoid cyst

2. Subdural hygroma

(e) cranial nerve injury

B. Secondary traumatic lesion

• deterioration of consciousness / new neurologic signs some time after initial injury

1. Major territorial arterial infarction

Cause: prolonged transtentorial / subfalcine herniation pinching the artery against a rigid dural margin

Location: PCA, ACA territory

2. Boundary + terminal zone infarction
3. Diffuse hypoxic injury
4. Diffuse brain swelling / edema
5. Pressure necrosis from brain herniation

Cause: increased intracranial pressure

Location: cingulate, uncal, parahippocampal gyri, cerebellar tonsils

6. Secondary "delayed" hemorrhage
7. Secondary brainstem injury (mechanical compression, secondary (Duret) hemorrhage in tegmentum of rostral pons + midbrain, infarction of median / paramedian perforating arteries, necrosis)
8. Other (eg, fatty embolism, infection)

• **Duret hemorrhage**

= delayed 2ndary hemorrhage in ventral + paramedian aspects of upper brainstem (mesencephalon + pons) due to massive temporal lobe herniation causing stretching + laceration of pontine perforating branches of basilar artery

• **Kernohan phenomenon**

= contusion of contralateral brainstem caused by pressure of free edge of tentorium

Pathophysiology:

expanding supratentorial mass forces medial aspect of temporal lobe downward over tentorium compressing the neighboring oculomotor nerve (III); lateral pressure on midbrain compresses opposite crus cerebri against free edge of tentorium forming indentation in crus (*Kernohan notch*)

- ipsilateral pupillary dilatation
- ipsilateral oculomotor nerve palsy
- ipsilateral hemiparesis (false localizing sign)

Pathomechanism:

A. Direct impact on brain ← fracture / skull distortion

√ scalp / skull abnormal

√ superficial neural damage localized to immediate vicinity of calvarial injury

1. Cortical laceration ← depressed fracture fragment
2. Epidural hematoma

B. Indirect injury irrespective of skull deformation

√ scalp / skull normal

(a) compression-rarefaction strain = change in cell volume without change in shape (rare)

(b) shear strain = change in shape without change in volume

› rotational acceleration forces (more common)

√ bilateral multiple superficial / deep lesions possibly remote from the site of

impact

1. Cortical contusion (brain surface)
2. Diffuse axonal injury (white matter)
3. Brainstem + deep gray matter nuclei

› linear acceleration forces (less common)

1. Subdural hematoma

Glasgow Coma Scale			
Response	*Score*	*Response*	*Score*
Eye opening		**Verbal response**	
spontaneous	4	oriented	5
to voice	3	confused	4
to pain	2	inappropriate words	3
none	1	incomprehensible	2
		none	1
Motor response			
obeys commands	6	localizes pain	5
withdraws (pain)	4	flexion (pain)	3
extension (pain)	2	none	1

2. Small superficial contusion

Prognosis: 10% fatal, 5–10% with residual deficits

Centripetal approach in search of injury:

A. Scalp
   1. Scalp abrasion: not visible
   2. Scalp laceration: air inclusion
   3. Scalp contusion: salt-and-pepper densities
B. Subgaleal hematoma
   Location: between periosteum of outer table and galea (= underneath scalp fat)
C. Skull fracture:
   linear ~, stellate ~, depressed ~, basilar ~, eggshell fracture
D. Epidural hematoma
E. Subdural hematoma
F. Subarachnoid hemorrhage
G. Brain injury
   1. Contusion/ edema
   2. Brain hematoma
H. Ventricular hemorrhage

Indications for radiographic skull series:

Only in conjunction with positive CT scan findings!

1. Evaluation of difficult depressed skull fracture / fracture of base of skull

Indications for CT:

1. Loss of consciousness (more than transient)
2. Altered mental status during observation

3. Focal neurologic signs
4. Clinically suspected basilar fracture
5. Depressed skull fracture (= outer table of fragment below level of inner table of calvarium)
6. Penetrating wound (eg, bullet)
7. Suspected acute subarachnoid hemorrhage, epidural / subdural / parenchymal hematoma

CT report in CNS trauma must address:

√ midline shift
√ localized mass effect
√ distortion / effacement of basal, perimesencephalic, suprasellar, quadrigeminal cisterns
√ pressure on brainstem, brainstem abnormality
√ hemorrhage / contusion: extraaxial, intraaxial, subarachnoid, intraventricular
√ edema: generalized / localized
√ hydrocephalus
√ presence of foreign bodies, bullet, bone fragments, air
√ base of skull, face, orbit
√ scalp swelling

Indications for MR:

1. Postconcussive symptomatology
2. Diagnosis of small sub- / epidural hematoma
3. Suspected diffuse axonal (shearing) injury, cortical contusion, primary brainstem injury
4. Vascular damage (eg, pseudoaneurysm formation due to basilar skull fracture)

Sequelae of head injury:

1. Posttraumatic hydrocephalus (⅓)
   = obstruction of CSF pathways ← intracranial hemorrhage; develops within 3 months
2. Generalized cerebral atrophy (⅓)
   = result of ischemia + hypoxia
3. Encephalomalacia
   √ focal areas of decreased density, but usually higher density than CSF
4. Pseudoporencephaly
   = CSF-filled space communicating with ventricle / subarachnoid space from cystic degeneration
5. Subdural hygroma
6. Leptomeningeal cyst
   = progressive protrusion of leptomeninges through traumatic calvarial defect
7. Cerebrospinal fluid leak
   • rhinorrhea, otorrhea (indicating basilar fracture with meningeal tear)
8. Posttraumatic abscess
   due to (a) penetrating injury, (b) basilar skull fracture, (c) infection of traumatic hematoma
9. Parenchymal injury
   brain atrophy, residual hemoglobin degradation products, wallerian-type axonal degeneration, demyelination, cavitation, microglial scarring

Prognosis: up to 10% fatal;
5–10% with some degree of neurologic deficit

Mortality: 25÷100,000 per year (traffic-related in 20–50%, gunshot 20–40%; falls)

Extracerebral Hemorrhage

1. Subdural hematoma
   in adults: dura inseparable from skull
2. Epidural hematoma
   in children: dura easily stripped away from skull
3. Subarachnoid hemorrhage
   common accompaniment to severe cerebral trauma

Intracerebral Hemorrhage

1. Diffuse axonal injury
2. **Hematoma**
   = blood separating relatively normal neurons
   (a) shear-strain injury (most common)
   (b) blunt / penetrating trauma (bullet, ice pick, skull fracture fragment)
   Incidence: 2–16% of trauma victims
   Location: low frontal + anterior temporal white matter / basal ganglia (80–90%)
   • frequently no loss of consciousness
   • development may be delayed in 8% of head injuries
   √ well-defined homogeneously increased density
3. **Cortical contusion**
   = blood mixed with edematous brain
   √ poorly defined area of mixed high and low densities, may increase with time
4. **Intraventricular hemorrhage**
   = potential complication of any intracranial hemorrhage
   ◊ For earliest detection focus on occipital horns!

Other Posttraumatic Lesions

1. Pneumocephalus
2. Penetrating foreign body

HEMANGIOPERICYTOMA

= HPC = ANGIOBLASTIC MENINGIOMA
= rare neoplasm thought to arise from Zimmermann pericytes surrounding capillaries + postcapillary venules
Incidence: < 0.4% of all CNS tumors
Age: 38–42 years (younger age group than for meningiomas); M÷F = 1.4÷1
Path: part of spectrum with solitary fibrous tumor; WHO grade II / grade III lesion
Histo: closely packed randomly oriented cells with scant cytoplasm + interrupted by gaping capillary-caliber vessels with a branching "staghorn" pattern; CD34 positive; EMA negative
Location: supratentorial; almost always solitary
• headache, seizure, visual dysfunction, motor weakness
√ similar to meningioma
√ narrow base of attachment to dura

√ significant edema in subjacent brain parenchyma (frequent)

Angio:

√ hypervascular lesion with dual blood supply from ECA + ICA / vertebral artery

√ NO early draining veins

√ fluffy" stain (rather than "sunburst" stain of meningioma)

MR:

√ typically isointense to gray matter on both T1WI + T2WI

√ ± prominent flow voids

√ avid enhancement, sometimes heterogeneously

√ "mushrooming" into adjacent brain

√ lobulated / irregular borders

√ high myo-inositol peak at 3.56 ppm + lack of alanine

DDx: meningioma (broad base of dural attachment, sunburst" stain of tumor blush, low myo-inositol + positive alanine peak)

Hemangiopericytoma	*Meningioma*
√ erosion of adjacent bone	√ hyperostosis
√ NO intratumoral calcification	√ ± calcifications

Hemangioblastoma of CNS

= benign autosomal dominant tumor of vascular origin

Incidence: 1–2.5% of all intracranial neoplasms; most common primary infratentorial neoplasm in adults (10% of posterior fossa tumors)

Age: (a) adulthood (> 80%): 20–50 years, average age of 33 years; M > F
(b) childhood (< 20%): in von Hippel-Lindau disease (10–20%); girls

Associated with:

(a) von Hippel-Lindau disease (in 20%), may have multiple hemangioblastomas (only 20% of patients show other stigmata)

(b) pheochromocytoma (often familial)

(c) syringomyelia

(d) spinal cord hemangioblastomas

• headaches, ataxia, nausea, vomiting

• erythrocythemia in 20% (tumor elaborates stimulant)

Location: paravermian cerebellar hemisphere (85%) > spinal cord > cerebral hemisphere / brainstem; multiple lesions in 10%

√ solid (⅓) / cystic / cystic with mural nodule

√ solid portion often intensely hemorrhagic

√ almost never calcifies

CT:

√ cystic sharply marginated mass of CSF-density (⅔)

√ peripheral mural nodule with homogeneous enhancement (50%)

√ occasionally solid with intense homogeneous enhancement

MR:

√ well-demarcated tumor mass moderately hypointense on T1WI + T2WI

√ hyperintense areas on T1WI (= hemorrhage)

√ hypointense areas on T1WI + hyperintense areas on T2WI (= cyst formation)
√ intralesional vermiform areas of signal dropout (= high-velocity blood flow)
√ heterogeneous enhancement on Gd-DTPA with nonenhancing foci of cyst formation + calcification + rapidly flowing blood
√ perilesional Gd-DTPA enhancing areas of slow-flowing blood vessels feeding and draining the tumor
√ peripheral hyperintense rim on T2WI (= edema)

Angio:
√ densely stained tumor nidus within cyst ("contrast loading")
√ staining of entire rim of cyst
√ draining vein

Prognosis: > 85% postsurgical 5-year survival rate

DDx: (1) Cystic astrocytoma (> 5 cm in size, calcifications, larger nodule, thick-walled lesion, no angiographic contrast blush of mural nodule, no erythrocythemia)
(2) Arachnoid cyst (if mural nodule not visualized)
(3) Metastasis (more surrounding edema)

HEMATOMA OF BRAIN

= INTRACEREBRAL HEMATOMA

Etiology:

A. Very common
1. Chronic hypertension (50%)
Age: > 60 years
Location: external capsule and basal ganglia (putamen in 65%) / thalamus (25%), pons (5%), brainstem (10%), cerebellum (5%), cerebral hemisphere (5%)
2. Trauma
3. Aneurysm
4. Vascular malformation: AVM, cavernous hemangioma, venous angioma, capillary telangiectasia

B. Common
1. Hemorrhagic infarction = hemorrhagic transformation of stroke
2. Amyloid angiopathy (20%): elderly patients
3. Coagulopathy (5%): DIC, hemophilia, idiopathic thrombocytopenic purpura; aspirin, heparin, coumadin
4. Drug abuse (5%): amphetamines, cocaine, heroine
5. Bleeding into tumor
(a) primary: GBM, ependymoma, oligodendroglioma, pituitary adenoma
(b) metastatic: melanoma, choriocarcinoma, renal cancer, thyroid cancer, adenocarcinoma

C. Uncommon
1. Venous infarction
2. Eclampsia
3. Septic emboli
4. Vasculitis (especially fungal)

5. Encephalitis

Stages of Cerebral Hematomas

Progression: hematoma gradually "snowballs" in size, dissects along white matter tracts; may decompress into ventricular system / subarachnoid space

Resolution: resorption from outside toward the center; rate depends on size of hematoma (usually 1–6 weeks)

FALSE-NEGATIVE CT:

1. Impaired clotting
2. Anemia

√ iso- / hypodense stage

Hyperacute Cerebral Hemorrhage

Time period: 4–6 hr

Substrate: fresh oxygenated arterial blood contains 95% diamagnetic (= NO unpaired electrons) intracellular oxyhemoglobin (Fe2+) with higher water contents than white matter; oxyhemoglobin persists for 6–12 hr)

NECT:

√ homogeneous consolidated high-density lesion (50–70 HU) with irregular well-defined margins increasing in density during day 1–3 (hematoma attenuation dependent on hemoglobin concentration + rate of clot retraction)

√ usually surrounded by low attenuation appearing within 24–48 hours ← edema, contusion

(a) irregular shape in trauma

(b) spherical + solitary in spontaneous hemorrhage

√ less mass effect compared with neoplasms

MR (less sensitive than CT during first hours):

√ little difference to normal brain parenchyma = center of hematoma iso- to hypointense on T1WI + minimally hyperintense on T2WI

√ peripheral rim of hypointensity (= degraded blood products as clue for presence of hemorrhage)

Acute Cerebral Hematoma

Time period: 12–48 hours

Substrate: paramagnetic (= 4 unpaired electrons) intracellular deoxyhemoglobin (Fe2+); deoxyhemoglobin persists for 3 days

MR:

√ slightly hypo- / isointense on T1WI (= paramagnetic deoxyhemoglobin in intact hypoxic RBCs within blood clot does not cause T1 shortening)

√ very hypointense on T2WI ← progressive concentration of RBCs, blood clot retraction, and fibrin production shorten T2

√ surrounding tissue isointense on T1WI / hyperintense on T2WI ← edema

Early Subacute Cerebral Hematoma

Time period: 3–7 days

Substrate: intracellular strongly paramagnetic (= 5 unpaired electrons) methemoglobin

(Fe3+) inhomogeneously distributed within cells

NECT:

√ increase in size of hemorrhagic area over days / weeks

√ high-density lesion within 1st week; often with layering

MR:

√ very hyperintense on T1WI (= oxidation of deoxyhemo-globin to methemoglobin → marked shortening of T1)

(a) beginning peripherally in parenchymal hematomas

(b) beginning centrally in partially thrombosed aneurysm (oxygen tension higher in lumen)

DDx: melanin, high-protein concentration, flow-related enhancement, gadolinium-based contrast agent

√ very hypointense on T2WI (= intracellular methemoglobin causes T2 shortening)

Late Subacute Cerebral Hematoma

Time period: > 1 week

Substrate: extracellular strongly paramagnetic methemoglobin (homogeneously distributed)

NECT:

√ gradual decrease in density from periphery inward (1–2 HU per day) during 2nd + 3rd week

CECT:

√ peripheral rim enhancement at inner border of perilesional lucency (1–6 weeks after injury) in 80% ← blood-brain barrier breakdown / luxury perfusion / formation of hypervascular granulation tissue

√ ring blush may be diminished by administration of corticosteroids

MR:

√ hyperintense on T1WI (= RBC lysis allows free passage of water molecules across cell membrane)

√ hyperintense on T2WI (= compartmentalization of methemoglobin is lost ← RBC lysis)

√ surrounding edema isointense on T1WI + hyperintense on T2WI

Chronic Cerebral Hematoma

Time period: > 1 months

Substrate: superparamagnetic **ferritin** (= soluble and stored in intracellular compartment) and hemosiderin (= insoluble and stored in lysosomes) cause marked field inhomogeneities

NECT:

√ isodense hematoma from 3rd–10th week with perilesional ring of lucency

CT:

√ hypodense phase (4–6 weeks) ← fluid uptake by osmosis

√ decreased density (3–6 months) / invisible

√ after 10 weeks lucent hematoma (= encephalomalacia ← proteolysis and phagocytosis + surrounding atrophy) with ring blush (DDx: tumor)

MR:

√ rim slightly hypointense on T1WI and very hypointense on T2WI (= superparamagnetic hemosiderin + ferritin within macrophages); rim gradually increases over weeks in thickness, eventually fills in entire hematoma = HALLMARK

√ center hyperintense on T1WI + T2WI (= extracellular methemoglobin of lysed RBCs just inside the darker hemosiderin ring); present for months to 1 year

√ surrounding hyperintensity on T2WI (= edema + serum extruded from clot) with associated mass effect; should resorb within 4–6 weeks (DDx: malignant hemorrhage)

Prognosis:

(1) Herniation (if hematoma 3–4 cm in size)

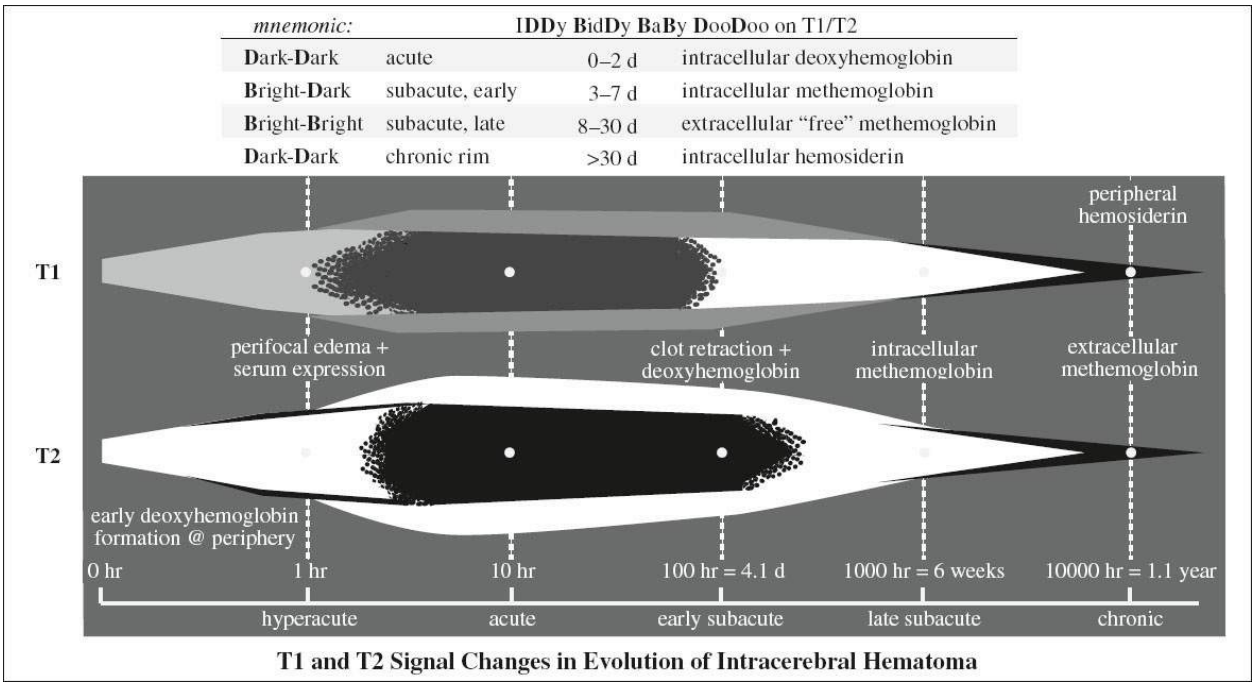
(2) Death (if hematoma > 5 cm in size)

Basal Ganglia Hematoma

= rupture of small distal microaneurysms in lenticulostriate arteries in patients with poorly controlled systemic arterial hypertension

MR Appearance of Intracerebral Hematoma

Phase	*Age*	*Compartment*	*Hemoglobin*	*T1*	*T2*	*Comments*
Hyperacute	<24 hr	intracellular	oxyhemoglobin	iso	~hyper	hyperacute bleed in <1 hr
						deoxygenation
Acute	1–3 d	intracellular	deoxyhemoglobin	~hypo	hypo	within clotted intact hypoxic RBCs
		extracellular	deoxyhemoglobin	iso	iso	after lysis of RBCs
Subacute						oxidation
early	>3 d	intracellular	methemoglobin	↑↑hyper	hypo	within intact RBCs inside retracting clot
late	>7 d	extracellular	methemoglobin	↑↑hyper	↑↑hyper	after lysis of RBCs
Chronic	>1 min					
center		extracellular	hemachromes	iso	~hyper	non–iron-containing heme pigments
rim		extracellular	hemosiderin	~hypo	↓↓hypo	within macrophages, present for years
		fibrous tissue		hypo	hypo	
		edema		iso	hyper	



T1 and T2 Signal Changes in Evolution of Intracerebral Hematoma

Cx: (1) Dissection into adjacent ventricles (⅔)
(2) Porencephaly
(3) Atrophy with ipsilateral ventricular dilatation

HEMOPHAGOCYTIC LYMPHOHISTIOCYTOSIS

= macrophage-related disorder characterized by excess lymphocytes + activated macrophages, typically with hemophagocytosis

Histo: absence of CD1a

Location: bone marrow, spleen, liver, lymph nodes

Classification:

(1) primary / familial autosomal recessive form (~ 25%) in infants
(2) secondary form in older children + adults
Associated with: infection, prolonged immunosuppression

- serum ferritin levels > 10,000 μg/L (90% sensitive, 96% specific)
- seizures, altered consciousness, hemiparesis, ataxia
- nuchal rigidity

Chest X-ray:

√ interstitial opacities ± pleural effusion

MR:

√ subcortical white matter foci with ↑ T2 signal intensity
Location: frontal + parietal lobes, basal ganglia
√ leptomeningeal enhancement
√ cerebral volume loss → dilated ventricles + prominent extra-axial fluid

CT:

√ calcifications favoring gray-white matter junction
√ hepatosplenomegaly

US:
√ gallbladder wall thickening, ↑ periportal echogenicity
√ ascites, lymphadenopathy
√ nephromegaly, ↑ renal cortical echogenicity

Dx: at least 5 of 8 criteria: (1) fever (2) splenomegaly (3) cytopenia of at least two cell lineages (4) hypertriglyceridemia ± hyperfibrinogenemia (5) tissue hemophagocytosis (6) low and/or absent natural killer cell activity (7) hyperferritinemia (8) high-soluble interleukin-2 receptor levels

Prognosis: variably relapsing + remitting / rapidly progressive; fatal if untreated

HETEROTOPIC GRAY MATTER

= collection of cortical neurons in an abnormal location ← arrest of migrating neuroblasts from ventricular walls to brain surface between 7–24 weeks of GA

Frequency: 3% of healthy population

May be associated with: agenesis of corpus callosum, aqueductal stenosis, microcephaly, schizencephaly

• seizures

Location:
(1) nodular form: usually symmetric bilaterally in subependymal region / periventricular white matter with predilection for posterior + anterior horns
(2) laminar form: deep / subcortical regions within white matter (less common)

√ single / multiple bilateral subependymal nodules along lateral ventricles
√ isointense with gray matter on all sequences, NO surrounding edema, NO contrast enhancement

DDx: subependymal spread of neoplasm, subependymal hemorrhage, vascular malformation, tuberous sclerosis, intraventricular meningioma, neurofibromatosis

HOLOPROSENCEPHALY

= HPE = spectrum of congenital structural forebrain + midface anomalies characterized by failure of prosencephalon to divide (= cleavage disorder) → varying degrees of frontal lobe "fusion" (= noncleavage of cerebral hemispheres)

Etiology: multifactorial with environmental factors (maternal diabetes, ethyl alcohol, cigarette smoking, retinoic acid); chromosomal and genetic abnormalities; teratogen exposure; syndromic associations

Classic holoprosencephaly is a primary defect of ventral induction and patterning → total / partial failure of separation of prosencephalon into 2 separate hemispheres.

Pathogenesis:
arrested lateral ventricular growth in 6-week embryo → lack of cleavage / diverticulation of forebrain (= prosencephalon), laterally (cerebral hemispheres), transversely (telencephalon, diencephalon), horizontally (optic + olfactory structures) → cortical brain tissue develops to cover monoventricle and fuses in midline → posterior part of the monoventricle becomes enlarged and saclike

Associated with: agenesis of corpus callosum, septo-optic dysplasia, absence of cavum septi pellucidi

◊ Septum pellucidum ALWAYS absent!

Sequence of disorders in prosencephalic ventral induction:
aprosencephaly → atelencephaly → alobar HPE → semilobar HPE → syntelencephaly → lobar HPE

Prevalence: 1÷10,000 in live and stillbirths; M÷F = 1÷1
◊ High rate of spontaneous abortions (50÷10,000)!
◊ Most common malformation of brain + face in humans

Classification (DeMyer):
(a) alobar = no hemispheric development
(b) semilobar = some hemispheric development
(c) lobar = frontal and temporal lobation + small monoventricle

Associated with:
polyhydramnios (60%), genital defects (24%), postaxial polydactyly (8%), vertebral defects (5%), limb reduction defects (4%), transposition of great arteries (4%), renal and cardiac anomalies; chromosomal anomalies (predominantly trisomy 13 + 18 in 24–45%)

Associated borderline syndromes ← diencephalic malformation:
1. Anophthalmia
2. Microphthalmia
3. Aplasia of pituitary gland
4. Olfactogenital dysplasia
5. Septooptic dysplasia

Prognosis: not uniformly lethal depending on severity of brain and facial malformations, presence of chromosomal abnormalities, involvement of other organs, and presence of multiple anomaly syndrome

DDx:
(1) Severe hydrocephalus (roughly symmetrically thinned cortex)
(2) Dandy-Walker cyst (normal supratentorial ventricular system)
(3) Hydranencephaly (frontal + parietal cortex most severely affected)
(4) Agenesis of corpus callosum with midline cyst (lateral ventricles widely separated with pointed superolateral margin)

Alobar Holoprosencephaly

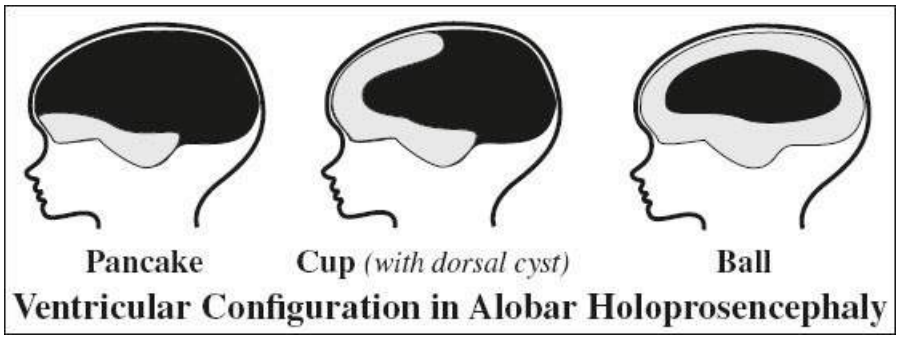
= extreme form in which the prosencephalon does not divide
- minimal motor activity, little sensory response (ineffective brain function); seizures
- severe facial anomalies ("the face predicts the brain"):
  1. Normal face in 17%
  2. **Cyclopia** (= midline single orbit); may have proboscis (= fleshy supraorbital prominence) + absent nose [*pro*, Greek = forward; *boscos*, Greek = feed; *proboskis*, latinized = forward feeder, eg, elephant trunk]
     Embryology: developmental interruption of single midline eye field into L + R eyes under signaling influence of prechordal plate
  3. **Ethmocephaly** = 2 hypoteloric orbits + proboscis between eyes and absence of nasal structures
  4. **Cebocephaly** = 2 hypoteloric orbits + single nostril with small flattened nose + absent

nasal septum
[*kebos*, Greek = monkey; *kephale*, Greek = head]

5. Median cleft lip + cleft palate + hypotelorism
   - absent philtrum
6. Others: micrognathia, trigonocephaly (early closure of metopic suture), microphthalmia, microcephaly

In alobar holoprosencephaly prosencephalic cleavage fails → single midline forebrain with primitive monoventricle often associated with a large dorsal cyst.

√ <u>crescent-shaped holoventricle</u> = single large ventricle without occipital or temporal horns:
  √ "horseshoe" / "boomerang" configuration of brain
    = peripheral rim of cerebral cortex displaced rostrally (coronal plane)
    (a) ball configuration (most common) = complete covering of monoventricle without dorsal cyst
    (b) cup configuration = more cortex visible posteriorly
    (c) pancake configuration = cortex covers monoventricle to edge of dorsal cyst



Ventricular Configuration in Alobar Holoprosencephaly

  √ cerebral mantle pachygyric
√ <u>absence of</u>: <u>anterior commissure</u>, <u>cavum septi pellucidi</u>, <u>falx cerebri</u>, <u>interhemispheric fissure</u>, <u>corpus callosum</u>, fornix, optic tracts, olfactory bulb (= arrhinencephaly), internal cerebral veins, superior + inferior straight sagittal sinus, vein of Galen, tentorium, sylvian fissure, opercular cortex
√ normal / fused / absent optic nerves
√ <u>fused thalami</u>:
  √ protrusion of anteriorly placed fused hypothalamic and thalamic nuclei + basal ganglia into monoventricle resulting in absence of 3rd ventricle
√ <u>large dorsal cyst</u> (in 92%) occupying most of calvarium widely communicating with single ventricle
  Cause: fused thalami obstruct CSF flow → posterior ballooning of 3rd ventricle through suprapineal recess (= point of least resistance)
√ <u>pancakelike cerebrum</u> in posterior cranium
√ ± single / azygos anterior cerebral artery:
  √ ± absence of middle + anterior cerebral arteries replaced by network of vessels arising from ICA + basilar vessels
√ midbrain, brainstem, cerebellum structurally normal
√ midline clefts in maxilla + palate

Prognosis: death within 1st year of life / stillborn
DDx: severe hydrocephalus, hydranencephaly (normal thalamic cleavage, partially visualized falx cerebri)

Semilobar Holoprosencephaly

= intermediate form with incomplete cleavage of prosencephalon (more midline differentiation + beginning of sagittal separation) with > 50%fusion of frontal lobes
• absent / mild facial anomalies: midline cleft lip + palate
• hypotelorism
• mental retardation
√ single ventricular chamber with partially formed occipital horns + rudimentary temporal horns
√ peripheral rim of brain tissue is several cm thick
√ partially fused thalami anteriorly situated + abnormally rotated resulting in small 3rd ventricle:
  √ dorsal cyst (in 28%) → macrocephaly (if cyst large)
√ absence of septum pellucidum + corpus callosum + olfactory bulb:
  √ part of corpus callosum may be present between posteriorly separated hemispheres
√ rudimentary falx cerebri + interhemispheric fissure form posteriorly + caudally with partial separation of occipital lobes
√ incomplete hippocampal formation
Prognosis: infants survive frequently into adulthood

Lobar Holoprosencephaly

= mildest form with formation of 3rd ventricle + some frontal horn + splenium and posterior body of corpus callosum
◊ May be part of septooptic dysplasia!
• usually not associated with facial anomalies except for hypotelorism, mild to severe mental retardation
• spasticity, athetoid movements
√ interhemispheric fissure present along nearly entire midline
√ separation into 2 cerebral hemispheres + 2 lateral ventricles
√ closely apposed bodies of mildly dilated lateral ventricles
√ distinct occipital + frontal horns
√ colpocephaly
√ dorsal cyst (in 9%)
√ rudimentary unseparated frontal horns of angular squared shape + flat roof (on coronal images) ← dysplastic frontal lobes
√ dysplastic anterior falx + interhemispheric fissure
√ absence of septum pellucidum + sylvian fissures
√ corpus callosum usually normal / incomplete
√ hippocampal formation nearly normal
√ basal ganglia + thalami completely / almost completely separated
√ pachygyria (= abnormally wide + plump gyri), lissencephaly (= smooth gyri)
Prognosis: survival into adulthood

HYDRANENCEPHALY

= liquefaction necrosis of cerebral hemispheres replaced by a thin membranous sac of leptomeninges in outer layer and remnants of cortex and white matter in inner layer, filled with CSF + necrotic debris

Incidence: 0.2% of infant autopsies

Etiology: absence of supraclinoid ICA system (? vascular occlusion / infection with toxoplasmosis or CMV) with intact posterior circulation
= extreme form of porencephaly

- seizures; respiratory failure; generalized flaccidity
- decerebrate state with vegetative existence

√ normal skull size / macrocrania / microcrania
√ complete filling of hemicranium with membranous sac
√ absence of cortical mantle (inferomedial aspect of temporal lobe, inferior aspect of frontal lobe, occipital lobe may be identified in some patients)
√ brainstem usually atrophic
√ cerebellum almost always intact
√ thalamic, hypothalamic, mesencephalic structures usually preserved projecting into cystic cavity
√ central brain tissue can be asymmetric
√ choroid plexus present
√ falx cerebri + tentorium cerebelli usually intact, may be deviated in asymmetric involvement, may be incomplete / absent

Prognosis: NOT compatible with prolonged extrauterine life (NO intellectual improvement from shunting!)

DDx: (1) Severe hydrocephalus (some identifiable cortex present)
(2) Alobar holoprosencephaly (facial midline anomalies)
(3) Schizencephaly (some spared cortical mantle)

HYDROCEPHALUS

= excess of CSF ← increased intraventricular pressure ← imbalance of CSF formation and absorption

Pathophysiology:

A. Overproduction (rare)
B. Impaired absorption
   1. Blockage of CSF flow within ventricular system, cisterna magna, basilar cisterns, cerebral convexities
   2. Blockage of arachnoid villi / lymphatic channels of cranial nerves, spinal nerves, adventitia of cerebral vessels

<u>Signs of raised intracranial pressure (skull film):</u>

(a) young infant / newborn
√ increase in craniofacial ratio
√ bulging of anterior fontanel
√ sutural diastasis
√ macrocephaly + frontal bossing

√ "beaten brass" = "hammered silver" appearance = prominent digital impressions (wide range of normals in 4–10 years of age)

(b) adolescent / adult → changes in sella turcica:
- √ atrophy of anterior wall of dorsum sellae
- √ shortening of the dorsum sellae producing pointed appearance
- √ erosion / thinning / discontinuity of floor of sella
- √ depression of floor of sella with bulging into sphenoid sinus
- √ enlargement of sella turcica

DDx: osteoporotic sella (aging, excessive steroid hormone)

Signs favoring hydrocephalus over white matter atrophy:
- √ commensurate dilatation of temporal horns of lateral ventricles (most reliable sign)
- √ narrowing of ventricular angle (= angle between anterior / superior margins of frontal horns at level of foramen of Monro) ← concentric enlargement:
  - √ Mickey Mouse ears on axial scan
- √ enlargement of frontal horn radius (= widest diameter of frontal horns taken at 90° angle to long axis of frontal horn):
  - √ rounding of frontal horn shape
- √ enlargement of ventricular system disproportionate to enlargement of cortical sulci (← compression of brain tissue against skull + consequent sulcal narrowing)
- √ interstitial edema from transependymal flow of CSF:
  - √ periventricular hypodensity
  - √ rim of prolonged T1 + T2 relaxation times surrounding lateral ventricles
- √ hydrocephalic distortion of ventricles + brain:
  - √ atrial diverticulum = herniation of ventricular wall through choroidal fissure of ventricular trigone into supracerebellar and quadrigeminal cisterns
  - √ dilatation of suprapineal recess expanding into posterior incisural space resulting in inferior displacement of pineal gland / shortening of tectum in rostral-caudal direction / elevation of vein of Galen
  - √ enlargement of anterior recess of 3rd ventricle extending into suprasellar cistern

Compensated Hydrocephalus

= new equilibrium established at higher intracranial pressure ← opening of alternate pathways (arachnoid membrane / stroma of choroid plexus / extracellular space of cortical mantle = transependymal flow of CSF)

Obstructive Hydrocephalus

= obstruction to normal CSF flow ← impaired absorption

NUC: radioisotope cisternography
- √ delay (up to 48 hours) for tracer to surround convexities + reach arachnoid villi
- √ positive "w" sign

Communicating Hydrocephalus

= EXTRAVENTRICULAR HYDROCEPHALUS

= elevated intraventricular pressure ← blockade beyond outlet of 4th ventricle within subarachnoid pathways

Incidence: 38% of congenital hydrocephaly

Pathophysiology: unimpeded CSF flow through ventricles; impeded CSF flow over convexities by adhesions / impeded reabsorption by arachnoid villi

Cause:

repetitive subarachnoid microhemorrhage (most common cause), immaturity of arachnoid villi, meningeal carcinomatosis (medulloblastoma, germinoma, leukemia, lymphoma, adenocarcinoma), purulent / tuberculous meningitis, subdural hematoma, craniosynostosis, achondroplasia, Hurler syndrome, venous obstruction (obliteration of superior sagittal sinus), absence of Pacchioni granulations

√ symmetric enlargement of lateral, 3rd + often 4th ventricles

√ dilatation of subarachnoid cisterns

√ normal / effaced cerebral sulci

√ symmetric low attenuation of periventricular white matter (transependymal CSF flow)

√ delayed ascent of radionuclide tracer over convexities

√ persistence of radionuclide tracer in lateral ventricles for up to 48 hours

Changes after successful shunting:

√ diminished size of ventricles + increased prominence of sulci

√ cranial vault may thicken

Cx: subdural hematoma ← precipitous decompression

Noncommunicating Hydrocephalus

= INTRAVENTRICULAR HYDROCEPHALUS

= <u>blockade</u> of CNS flow <u>within ventricular system</u> with dilatation of ventricles proximal to obstruction

Pathogenesis: increased CSF pressure causes ependymal flattening with breakdown of CSF-brain barrier → myelin destruction + compression of cerebral mantle (brain damage)

Location:

(a) Lateral ventricular obstruction

Cause: ependymoma, intraventricular glioma, meningioma

(b) Foramen of Monro obstruction

Cause: 3rd ventricular colloid cyst, tuber, papilloma, meningioma, septum pellucidum cyst / glioma, fibrous membrane (post infection), giant cell astrocytoma

(c) Third ventricular obstruction

Cause: large pituitary adenoma, teratoma, craniopharyngioma, glioma of 3rd ventricle, hypothalamic glioma

(d) Aqueductal obstruction

Cause: Congenital web / atresia (often associated with Chiari malformation), fenestrated aqueduct, tumor of mesencephalon / pineal gland, tentorial meningioma, S/P intraventricular hemorrhage or infection

(e) Fourth ventricular obstruction

Cause: Congenital obstruction, Chiari malformation, Dandy-Walker syndrome, inflammation (TB), tumor within 4th ventricle (ependymoma), extrinsic compression of 4th ventricle (astrocytoma, medulloblastoma, large CPA

tumor, posterior fossa mass), isolated / trapped 4th ventricle

√ enlarged lateral ventricles (enlargement of occipital horns precedes enlargement of frontal horns)
√ effaced cerebral sulci
√ periventricular edema with indistinct margins (especially frontal horns)
√ change in RI indicates increased intracranial pressure (ΔRI 47–132% versus 3–29% in normals)
√ radioisotope cisternography: no obstruction if tracer reaches ventricle

Nonobstructive Hydrocephalus

= rapid CSF production

Cause: Choroid plexus papilloma

√ ventricle near papilloma enlarges
√ intense radionuclide uptake in papilloma
√ enlarged anterior / posterior choroidal artery and blush

Congenital Hydrocephalus

= multifactorial CNS malformation during the 3rd / 4th week after conception

Etiology:

(1) Aqueductal stenosis (43%)
(2) Communicating hydrocephalus (38%)
(3) Dandy-Walker syndrome (13%)
(4) Other anatomic lesions (6%):
  (a) Genetic factors: spina bifida, aqueductal stenosis (X-linked recessive trait with a 50% recurrence rate for male fetuses), congenital atresia of foramina of Luschka and Magendie (Dandy-Walker syndrome; autosomal recessive trait with 25% recurrence rate), cerebellar agenesis, cloverleaf skull, trisomy 13–18
  (b) Nongenetic etiology: tumor compressing 3rd / 4th ventricle, obliteration of subarachnoid pathway due to infection (syphilis, CMV, rubella, toxoplasmosis), proliferation of fibrous tissue (Hurler syndrome), Chiari malformations, vein of Galen aneurysm, choroid plexus papilloma, vitamin A intoxication

Incidence: 0.3–1.8÷1,000 pregnancies

Associated with:

(a) intracranial anomalies (37%): hypoplasia of corpus callosum, encephalocele, arachnoid cyst, arteriovenous malformation
(b) extracranial anomalies (63%): spina bifida in 25–30% (with spina bifida hydrocephalus present in 80%), renal agenesis, multicystic dysplastic kidney, VSD, tetralogy of Fallot, anal agenesis, malrotation of bowel, cleft lip / palate, Meckel syndrome, gonadal dysgenesis, arthrogryposis, sirenomelia
(c) chromosomal anomalies (11%): trisomy 18 + 21, mosaicism, balanced translocation

• elevated amniotic α-fetoprotein level

OB-US (assessment difficult prior to 20 weeks GA as ventricles ordinarily constitute a large portion of cranial vault):

√ "dangling choroid plexus" sign:
  √ choroid plexus not touching medial + lateral walls of lateral ventricles

√ downside choroid plexus falling away from medial wall + hanging from tela choroidea
√ upside choroid falling away from lateral wall
√ lateral width of ventricular atrium ≥ 10 mm (size usually constant between 16 weeks MA and term)
◊ 88% of fetuses with sonographically detected neural axis anomalies have an atrial width > 10 mm
√ BPD > 95th percentile (usually not before 3rd trimester)
√ polyhydramnios (in 30%)

Recurrence rate: < 4%

Mortality: (1) Fetal death in 24%
(2) Neonatal death in 17%

Prognosis: poor with
(1) Associated anomalies
(2) Shift of midline (porencephaly)
(3) Head circumference > 50 cm
(4) Absence of cortex (hydranencephaly)
(5) Cortical thickness < 10 mm

Infantile Hydrocephalus

- ocular disturbances: paralysis of upward gaze, abducens nerve paresis, nystagmus, ptosis, diminished pupillary light response
- spasticity of lower extremities (from disproportionate stretching of paracentral corticospinal fibers)

Etiology:

mnemonic: **A VP-S**hunt **C**an **D**ecompress **T**he **H**ydrocephalic **C**hild

Aqueductal stenosis
Vein of Galen aneurysm
Postinfectious
Superior vena cava obstruction
Chiari II malformation
Dandy-Walker syndrome
Tumor
Hemorrhage
Choroid plexus papilloma

Doppler:
√ RI > 0.8 (sign of increased ICP) in neonate:
√ RI of 0.84 ± 13% decreasing to 0.72 ± 11% after shunting
√ RI > 0.65 (sign of increased ICP) in older children

Normal Pressure Hydrocephalus

= NPH = ADAM SYNDROME
= pressure gradient between ventricle + brain parenchyma in spite of normal CSF pressure

◊ Potentially treatable cause of dementia in elderly!

Cause: communicating hydrocephalus with incomplete arachnoidal obstruction from neonatal intraventricular hemorrhage, spontaneous subarachnoid hemorrhage, intracranial trauma, infection, surgery, carcinomatosis

mnemonic: PAM the HAM

Paget disease
Aneurysm
Meningitis
Hemorrhage (from trauma)
Achondroplasia
Mucopolysaccharidosis

Pathophysiology of CSF:

(?) brain pushed toward cranium from ventricular enlargement; brain unable to expand during systole thus compressing lateral + 3rd ventricles + expressing large CSF volume through aqueduct; reverse dynamic during diastole; "water-hammer" force of recurrent ventricular expansion damages periventricular tissues

Age: 50–70 years

- normal opening pressure at lumbar puncture
- dementia, gait apraxia, urinary incontinence

mnemonic: wacky, wobbly and wet

√ communicating hydrocephalus with prominent temporal horns
√ ventricles dilated out of proportion to any sulcal enlargement
√ upward bowing of corpus callosum
√ flattening of cortical gyri against inner table of calvarium (DDx: rounded gyri in generalized atrophy)

MR:

√ pronounced aqueductal flow void ← diminished compliance of normal pressure hydrocephalus
√ periventricular hyperintensity ← transependymal CSF flow

NUC: radioisotope cisternography

√ reversal of normal CSF flow dynamic = tracer moves from basal cisterns into 4th, 3rd and lateral ventricles
√ loss of "w" sign

Rx: CSF shunting (only in 50% improvement)

HYPOXIC-ISCHEMIC ENCEPHALOPATHY

= HIE = HYPOPERFUSION INJURY

Frequency: 2–9÷1,000 live births

Cause:

(a) <u>in utero</u> ← interruption of placental blood flow + gas exchange:

› fetal factors: fetomaternal hemorrhage, thrombosis, bradycardia, disrupted umbilical circulation (tight nuchal cord, cord prolapse)
› inadequate placental perfusion: maternal hypotension, preeclampsia, placental abruption, chronic vascular disease
› impaired maternal oxygenation: asthma, pulmonary embolism, pneumonia, CO

poisoning, severe anemia

(b) postnatally: severe hyaline membrane disease, pneumonia, meconium aspiration, CHD

(c) older child: cardiac arrest, near drowning, asphyxiation (strangling), barbiturate intoxication → circulatory / respiratory failure

Pathophysiology:

⇓ cerebral blood flow (= ischemia) and ⇓ blood oxygenation (= hypoxemia) → shift in metabolism from oxidative phosphorylation to inefficient anaerobic oxidation → rapid energy depletion, acidosis, release of inflammatory mediators and excitatory neurotransmitters (particularly glutamate), free radical formation, calcium accumulation, lipid peroxidation → necrosis → cell death

- low Apgar score (0–3) at birth, multiorgan dysfunction
- profound metabolic acidosis in cord blood
- seizures, coma, hypotonia, abnormal EEG

Prognosis: (a) full recovery

(b) neonatal death (20%)

(c) significant neurologic sequelae (25%): one of the most common causes of cerebral palsy (spastic quadriplegia, diplegia)

DDx: metabolic encephalopathy from inborn errors of metabolism (congenital lactic acidosis, urea cycle disorder, amino aciduria), congenital + neonatal CNS infections, congenital malformations, severe birth trauma

Temporal evolution and optimal imaging modality:

US:

√ increased parenchymal echogenicity in days 2–10

CT:

√ parenchyma of low attenuation in days 1–7

MR:

√ immediate ⇑ lactate (spectroscopy most useful within hours) → pseudonormalization ~ 24 hours after birth

√ restricted diffusion (DWI in days 1–5 most sensitive test) → pseudonormalization 5 days after birth

√ T1WI and T2WI (most useful after day 2):

√ T2 prolongation ← edema

√ T2 shortening ← mineral deposition

Hypoperfusion Injury in Older Child

Location:

(a) mild HIE: watershed zones

(b) severe HIE: gray matter of cerebral cortex, basal ganglia, hippocampi + sparing of brainstem and cerebral white matter

CT:

√ decreased attenuation of cortical gray matter (diffuse edema)

√ loss of normal gray matter–white matter differentiation

√ bilateral decreased attenuation of basal ganglia and thalami

√ "reversal" sign = higher attenuation of white matter

√ "white cerebellum" sign = lower attenuation of supratentorial brain with relative sparing of cerebellum + brainstem

MR:

√ increased signal intensity on DWI (after 2 hours)

√ subtle increased intensity + swelling of affected areas (after > 24 hours)

√ diffuse T2 prolongation in subcortical white matter (= delayed postanoxic leukoencephalopathy)

Hypoperfusion Injury in Preterm Infant

Gestational age: < 36 weeks

Frequency: 5% of infants born < 32 weeks EGA

Location:

› periventricular white matter (mild hypotension)

› thalami, brainstem, cerebellum = metabolically most active tissue (severe hypotension)

Consequence:

(1) Germinal matrix hemorrhage

(2) Periventricular leukomalacia

US:

√ globular hyperechoic change = PVL (early)

√ localized anechoic / hypoechoic lesions = cystic PVL (2–6 weeks later)

√ progressive periventricular necrosis + ventricular enlargement = end-stage PVL

MR:

√ hyperintense areas on T1WI within larger hyperintense area on T2WI (early)

√ ventricular enlargement with irregular margins of body + trigone of lateral ventricles (later):

√ loss of periventricular white matter with ↑ T2 signal

√ thinning of corpus callosum

Prognosis: germinal matrix hemorrhage upon reperfusion to ischemic tissues

Cx: cerebral palsy in up to 19% of infants < 28 weeks EGA

◊ 50% of cerebral palsy cases occur in infants born prematurely

Hypoperfusion Injury in Term Infant

Gestational age: ≥ 36 weeks

Location:

Mild to moderate hypoxic-ischemic injury causes lesions in watershed areas, parasagittal cortex, and subcortical white matter, while sparing brainstem, cerebellum, deep gray matter structures.

Severe hypoxic-ischemic injury involves the lateral + ventral thalamus, posterior putamen, perirolandic sensorimotor cortex, and corticospinal tracts.

Injury pattern:

(a) peripheral pattern (= parasagittal, watershed / borderzone) - more common

MR:

√ restricted diffusion in parasagittal cortex and underlying subcortical white matter

√ cortical thinning + diminution of underlying white matter

√ ex vacuo dilatation of adjacent lateral ventricles in trigones and occipital horns

(b) basal ganglia–thalamus pattern

MR:

√ bilateral abnormal T1 hyperintensity (days 3–7) in posterolateral putamen, ventrolateral thalamus, corticospinal tract

√ absent posterior limb sign = loss of normal mildly hyperintense T1 focus in posterior limb of internal capsule

√ indistinct / abnormally iso- or hyperintense T2 foci relative to adjacent gray matter instead of normal hypointense foci in posterolateral putamen, posterior limb of internal capsule, ventrolateral thalamus

Prognosis: 15–20% of neonatal mortality; significant developmental deficits in 25%

IDIOPATHIC INTRACRANIAL HYPERTENSION

= PSEUDOTUMOR CEREBRI = BENIGN INTRACRANIAL HYPERTENSION (BIH)

Pathophysiology:

(a) elevation in blood volume (85%)

(b) decrease in regional cerebral blood flow with delayed CSF absorption (10%)

Etiology:

1. Sinovenous occlusive disease, SVC occlusion, obstruction of dural sinus, obstruction of both internal jugular veins
2. Dural AVM
3. S/P brain biopsy with edema
4. Endocrinopathies
5. Hypervitaminosis A
6. Hypocalcemia
7. Menstrual dysfunction, pregnancy, menarche, birth control pills
8. Drug therapy

Predilection for: obese young to middle-aged women

- headache
- papilledema
- elevated opening pressures on lumbar puncture (normal range of 80–180 mm H_2O in horizontal lateral decubitus position)

√ normal ventricular size / pinched ventricles

√ increased volume of subarachnoid space

INFARCTION OF BRAIN

= brain cell death leading to coagulation necrosis

Cause: large vessel occlusion of ICA / MCA / PCA (50%) ← emboli from atherosclerotic stenosis, small-vessel lacunes (25%), cardiac cause (15%), blood disorder (5%), non-arteriosclerotic (5%), venous thrombosis (1%)

◊ 33% of TIAs will lead to infarction!

Pathophysiology:

distal microstasis occurs within 2 minutes after occlusion of cerebral artery; regional cerebral blood flow is acutely decreased in area of infarction + remains depressed for several days at center of infarct; arterial circulation time may be prolonged in entire

hemisphere; rapid development of vasodilatation due to hypoxia, hypercapnia, tissue acidosis; delayed filling + emptying of arterial channels in area of infarction (= arteriolar-capillary block) well into venous phase; by end of 1st week regional blood flow commonly increases to rates even above those required for metabolic needs (= hyperemic phase = luxury perfusion)

• stroke

Mimics: intracerebral hemorrhage, subdural hematoma, cerebritis, hemiplegic / hemisensory migraine, tumor, arteriovenous malformation

Detection rate by CT:

80% for cortex + mantle, 55% for basal ganglia, 54% for posterior fossa

◊ Positive correlation between degree of clinical deficit and CT sensitivity

CT sensitivity: on day of ictus 48%
1–2 days later 59%
7–10 days later 66%
10–11 days later 74%

Location: cerebrum÷cerebellum = 19÷1

(a) supratentorial
- cerebral mantle (70%) in territory of MCA (50%), PCA (10%), watershed between MCA + ACA (7%), ACA (4%)
- basal ganglia + internal capsule (20%)

(b) infratentorial (10%) upper cerebellum (5%), lower cerebellum (3%), pons + medulla (2%)

Hyperacute Ischemic Infarction

Time period: < 12 hr

NECT (100% specific):

Sensitivity: 57% (with standard 40/20 HU window width & level; increased to 71% with 8/32 HU)

√ normal (in 10–60%)

√ identifies hemorrhage

◊ Hemorrhage contraindicates thrombolytic therapy!

√ subtle <u>decrease in attenuation</u> within affected brain area due to cytotoxic edema:

√ "disappearing basal ganglia" sign = obscuration and loss of gray-white matter differentiation in basal ganglia:

√ lentiform nucleus becomes isodense to internal and external capsule within 2 hours after onset of stroke

√ "insular ribbon" sign = loss of gray-white matter differentiation of insular cortex (in 50–80% of MCA occlusions)

√ "<u>hyperdense vessel</u>" sign (HIGHLY SPECIFIC):

√ "hyperdense middle cerebral artery" sign = acute intraluminal thrombus of 80 HU (← extrusion of serum from thrombus) versus 40 HU of flowing blood in M1 segment; transient phenomenon

Incidence: 17–35–50% of acute MCA occlusions

Associated with: poor clinical outcome

DDx: high hematocrit, polycythemia, calcification of vessel wall (usually bilateral), arterial dolichoectasia

√ "MCA dot" sign = punctate focus of hyperattenuation in sylvian fissure (in M2/M3 segment of MCA) ← thromboembolus (38% sensitive, 100% specific)

√ calcified intraluminal embolus (rare)

√ hypoattenuating fat embolus (rare)

√ mass effect from brain swelling:

√ hemispheric cortical sulcal effacement / compression

√ narrowing of sylvian fissure (in MCA infarct)

CECT:

√ visualization of thrombus within intracranial arteries

√ assessment of carotid + vertebral arteries

Perfusion CT:

= monitoring first pass of a small iodinated contrast agent bolus through cerebral circulation with continuous cine imaging for 45 seconds of same slab of tissue

◊ Motion artifacts in ROI invalidate the study!

(1) *Time-attenuation curves* for arterial ROI in unaffected ACA / MCA + venous ROI in superior sagittal sinus / torcular Herophili and in each parenchymal pixel

(2) *Color-coded perfusion maps* for

(a) **mean transit time** (MTT)

= mathematical deconvolution on time-attenuation curve of each pixel with respect to arterial curve

◊ Most sensitive to disruption of cerebral perfusion

◊ MTT correlates directly with perfusion pressure

Increase in: ischemia (infarct core and penumbra), asymptomatic vessel stenosis, vasospasm

(b) **cerebral blood volume** (CBV)

= dividing areas under curve in parenchymal pixel by area under curve in arterial pixel

√ CBV higher in highly vascularized basal ganglia and cortical surface than in white matter

√ increased CBV in penumbra → functioning autoregulation → dilatation of vessels

√ decreased CBV in infarct core → loss of autoregulation → blood vessels no longer dilate

(c) **cerebral blood flow** (CBF = CBV÷MTT)

◊ Most important parameter!

Normal: > 50 mL / 100 g brain tissue

Ischemia threshold: 10–15 mL / 100 g

(3) *Summary map* of percentage *of mismatch*

= CBV area ÷ CBF area

√ ischemic area (= prolonged MTT) divided into:

(a) irreversibly infarcted nonsalvageable tissue ("**infarct core**")

√ markedly decreased CBF + markedly decreased CBV

(b) surrounded by stunned (nonfunctioning potentially salvageable) cells that

receive collateral blood supply ("**penumbra**")
√ decreased CBF + normal / mildly increased CBV ← autoregulatory mechanisms

Perfusion CT Analysis of Hyperacute Ischemic Stroke			
Entity	*Mean Transit Time*	*Cerebral Blood Flow*	*Cerebral Blood Volume*
Penumbra	↑ (> 145%)	↓ (> 34%)	↔ / ↑
Infarct core	↑	⇓	⇓ (< 2 mL/100 g)

MR (routinely positive by 4–6 hours post ictus):
√ parenchymal changes:
√ bright signal (← less signal loss) on DWI with ↓ ADC
Pathophysiology of homeostasis of tissue water:
excess intracellular water (= cytotoxic edema) + ↓ rate of water molecular diffusion (= restriction of normal brownian motion of water molecules)
Sensitivity & specificity: 88–100% & 86–100%

Rule of thumb: low signal intensity on ADC map means the stroke is < 1 week old!

√ hyperintense signal on T2WI + FLAIR involving cortical gray matter

In most ischemic strokes FLAIR images are positive 6–12 hours after onset of symptoms!

√ loss of gray-white matter differentiation on T2WI
√ subtle parenchymal swelling with sulcal effacement ← cytotoxic edema can be seen by 2 hours post ictus (best on T1WI)
√ abnormal blooming on T2*WI identifies hemorrhage

The diagnosis of ischemic stroke is unlikely if parenchymal enhancement persists > 8–12 weeks.

√ vessel signs:
√ loss of normal intravascular flow voids on T2WI
√ intravascular low SI on T2* + high SI on FLAIR (similar to "hyperdense MCA" sign)
√ stasis of contrast material within affected arteries ← stasis of flow distal to thrombus
√ ischemic penumbra = combination of perfusion + diffusion-weighted images allows identification of areas at risk for infarction

DWI & ADC Map in Acute Stroke		
Time Course	*DWI signal*	*ADC*
30 min – 5 days	bright (← restricted diffusion)	reduced
1 – 4 weeks	mildly bright (← T2 shine-through from infarcted tissue)	pseudonormal
weeks to months	variable	increased

NUC:
◊ Newer imaging agents (eg, ^{99m}Tc-HMPAO) may be positive within minutes of the event, while CT and MR are normal

√ hemispheric hypoperfusion throughout all phases
√ defect corresponding to nonperfused vascular territory
√ "flip-flop" sign in radionuclide angiogram (15%)
= decreased uptake during arterial + capillary phase followed by increased uptake during venous phase
√ "luxury perfusion syndrome" (14%) = increased perfusion

Rx: recombinant tissue plasminogen activator (tPA) if symptom onset < 6 hours ago
One-third rule: early ischemic changes on NECT in > ⅓ of MCA territory (in acute ischemic stroke within 6 hours of symptom onset) excludes patient for IV and intraarterial thrombolytic therapy → NO benefit with higher risk of symptomatic hemorrhage

Acute Ischemic Infarction

Histo: cortical cytotoxic edema (= accumulation of intracellular water due to cell membrane damage) followed by extracellular white matter vasogenic edema

√ bright lesion on DWI very conspicuous within 0–6 hours after onset of symptoms + up to 14 days after ictus (diffusion coefficient is a measure of proton mobility in tissue)
◊ false positive DWI:
diffusion coefficient of infarcts is influenced by T2 properties + b-value of gradient strength (T2 shine-through)
◊ 5% false negative DWI

√ hypointense signal on ADC map (negates T2 shine-through effect) within 24 hours (ADC map shows pure diffusion characteristics without T2 effect, but has low lesion conspicuity)
→ a low coefficient (acute infarct) gives a hyperintense signal
→ a high coefficient (CSF) gives a hypointense signal

Early Acute Ischemic Infarction

Time period: 12–24 hours

NECT:
√ low-density lesion (30–60% invisible)
√ loss of differentiation between cortical gray matter and subjacent white matter:
√ blurring of the clarity of internal capsule
√ "insular ribbon" sign = hypodense extreme capsule no longer distinguishable from insular cortex
√ subtle sulcal effacement (8%)

CECT:
√ no iodine accumulation in affected cortical region
√ meningeal gyriform enhancement

MR:
√ subtle narrowing of sulci
√ blurring of gray-white matter junction on T2- and proton-density images
√ increase in thickness of cortex (= gyral swelling)
√ subtle low signal intensity on T1WI, high signal intensity on T2WI (masking of gyral infarcts on heavily T2WI ← sulcal CSF intensity)

◊ 20–30% false negative T2WI during first 24 hours

MRA:

√ absence of flow for infarcts > 2 cm in diameter

Late Acute Ischemic Infarction

Time period: 1–3–7 days

NECT:

√ hypodense wedge-shaped lesion with base at cortex in a vascular distribution (in 70%) ← vasogenic + cytotoxic edema

√ mass effect (23–75%): sulcal effacement, transtentorial herniation, displaced subarachnoid cisterns + ventricles

√ "bland infarct" may be transformed into hemorrhagic infarct after 2–4 days ← leakage of blood from ischemically damaged capillary endothelium following lysis of intraluminal clot + arterial reperfusion

CECT:

√ ⇓ meningeal and ⇓ intravascular contrast enhancement

√ ⇑ parenchymal enhancement

MR:

√ ↑ SI on DWI during 1st week after onset of symptoms

√ "intravascular enhancement" sign (77%)

= Gd-pentetate enhancement of cortical arterial vessels in area of brain injury after 1–3 days ← slow arterial blood flow provided by collateral circulation via leptomeningeal anastomoses

√ "meningeal enhancement" sign (33%)

= Gd-pentetate enhancement of meninges adjacent to infarct after 2–6 days ← meningeal inflammation

Angio:

√ narrowed / occluded vessels supplying infarcted area

√ delayed filling + emptying of involved vessels

√ early draining vein

√ luxury perfusion of infarcted area (rare) = loss of small vessel autoregulation ← local increase in pH

Subacute Ischemic Infarction

Time period: 7–30 days = paradoxical phase with resolution of edema + onset of coagulation necrosis

NECT:

√ "fogging phenomenon" = less apparent low-density area

√ decrease of mass effect + ex vacuo dilatation of ventricles (in 57%)

√ ± transient calcification (especially in children)

CECT:

√ gyral blush + ring enhancement for 2–8 weeks (in 65–80% within first 4 weeks) ← breakdown of blood-brain barrier + luxury perfusion

√ NO enhancement in 20% of patients

MR:

Histo: vasogenic edema (= increased extracellular water) ← disruption of blood-brain barrier

√ ↑ SI on DWI ← T2 shine-through from infarcted tissue

√ hypointense on T1WI, hyperintense on T2WI

√ intravascular + meningeal enhancement signs resolve toward end of 1st week

√ gyriform parenchymal Gd-pentetate enhancement

◊ Gyriform parenchymal enhancement permits differentiation of subacute from chronic infarction!

√ infarction flip-flops from hyperintense lesion to iso- / hypointense lesion on ADC maps 5–10 days after ictus

Chronic Ischemic Infarction

Time period: months to years (> 30 days)

Histo: demyelination + gliosis complete

◊ Focal brain atrophy after 8 weeks!

√ cerebral atrophy + encephalomalacia + gliosis (HALLMARKS)

√ possible calcification (especially in children)

NECT:

√ cystic foci of CSF density (= encephalomalacia) in distribution of vascular territory

MR:

√ patchy region with increased intensity on T2WI

√ gliosis (hyperintense on T2WI) often surrounding encephalomalacic region

√ wallerian degeneration (= antegrade degeneration of axons ← neuronal injury) of corticospinal tracts in the wake of old large infarcts that involve the motor cortex

Hemorrhagic Infarction

Hemorrhagic transformation is rare during first 12 hours after stroke onset and usually occurs within 24–48 hours. It is almost always present 4–5 days after stroke.

Etiology: lysis of embolus / opening of collaterals / restoration of normal blood pressure following hypotension / hypertension / anticoagulation → extravasation in reperfused ischemic brain

Incidence: 6% of clinically diagnosed brain infarcts; 20% of autopsied brain infarcts

Path: petechial hemorrhages in various degrees of coalescence

Location: corticomedullary junction

CT:

√ hyperdensity (56–76 HU) appearing within a previously imaged hypodense area of acute ischemic infarction = hemorrhagic transformation (in 50–72%)

False negative: hematoma isoattenuating if hematocrit < 20%

MR:

√ hypointense area on T2WI within edema marking gyri = deoxyhemoglobin of acute hemorrhage

√ hyperintense area on T1WI = methemoglobin of subacute hematoma

◊ Early parenchymal enhancement within 6 hours of stroke has a higher risk for clinically significant hemorrhagic transformation.

Basal Ganglia Infarct

= occlusion of small penetrating arteries at base of brain (lenticulostriate / thalamoperforating arteries) = lacunar infarct (= infarct < 1 cm in size)

Cause:

(1) Embolism
(2) Hypoperfusion
(3) Carbon monoxide poisoning
(4) Drowning
(5) Vasculopathy (hypertension, microvasculopathy, aging)

√ dense homogeneous enhancement outlining caudate nucleus, putamen, globus pallidus, thalamus

√ dense round nodular enhancement / peripheral ring enhancement

Cortical Laminar Necrosis

= ischemic changes affecting deep layers of the cortex

◊ Layers 3, 5, 6 are very sensitive to oxygen deprivation

MR:

(a) acute stage
  √ linear cortical hyperintensity on T1WI
  √ contrast enhancement
  √ white matter edema on T2WI
(b) chronic stage
  √ thin hypointense cortex
  √ hyperintense white matter
  √ enlargement of CSF spaces

Lacunar Infarction

[*lacuna*, Latin = hole]

= small deep infarcts in the distal distribution of penetrating vessels (lenticulostriate, thalamoperforating, pontine perforating arteries, recurrent artery of Heubner)

Cause: occlusion of small penetrating end arteries arising from MCA, PCA, basilar, ACA and vertebral arteries at base of brain due to fibrinoid degeneration

Age: usually > 55 years; M÷F = 1÷1

Predisposed: hypertension, diabetes

Incidence: 15–20% of all strokes

Path: lacune = small hole of encephalomalacia traversed by cobweblike fibrous strands; if multiple = état lacunaire (lacunar state)

Histo: "microatheroma" = hyalinization + arteriolar sclerosis → thickening of vessel wall + luminal narrowing

- pure motor / pure sensory stroke
- ataxic hemiparesis, vascular dementia

Location: upper two-thirds of putamen > caudate > thalamus > pons > internal capsule

√ small discrete foci of hypodensity of 3–15 mm in size (most < 1 cm in diameter)

MR:

(a) acute lacunar infarction (between 12 hours and 7 days):

√ small high-signal–intensity region on T2WI + FLAIR
√ hypointense area on T1WI
√ high signal intensity on DWI + corresponding low signal intensity on ADC map

(b) chronic lacunar infarction:
√ high signal intensity on T2WI
√ low signal intensity on T1WI
√ hypointense center + hyperintense rim (= gliosis) on FLAIR
√ normal signal intensity on DWI

√ may enhance in late acute / early subacute stage (up to 8 weeks)
√ unilateral pontine infarcts are sharply marginated at midline

DDx: enlarged Virchow-Robin spaces, neurocysticercosis

TIA and RIND

√ hypodense small lesions located peripherally near / within cortex without enhancement
√ lesions detected in only 14%, contralateral lesion present in 14% (CT of marginal value)

Watershed / Border Zone Infarct

= infarct localized to border zone between 2 adjacent nonanastomosing vascular beds of major cerebral arteries

Cause: global hypoperfusion ← poor cardiac output / cervical carotid artery occlusion or severe stenosis / noncompetent circle of Willis / microembolism

Isolated cortical border zone infarcts may be embolic in nature and are less frequently associated with hemodynamic compromise.

Pathophysiology:

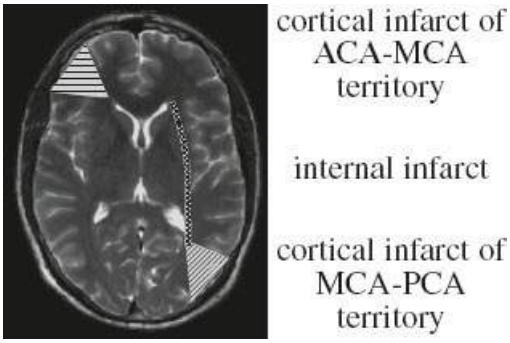
(a) repeated episodes of hypotension with severe arterial stenosis / occlusion → lower perfusion pressure → autoregulatory vasodilation → increased susceptibility to ischemia → infarction (esp. for external border zone infarcts)

› Stage I hemodynamic impairment:
√ ↑ cerebral blood volume + ↑ mean transit time

› Stage II hemodynamic impairment:
√ ↓ blood flow + ↑ oxygen extraction (measured with PET) = **misery perfusion**= chronic failure of cerebral autoregulation

Classification of Border Zone Infarcts
External (cortical) Infarct
Frontal cortex (between ACA + MCA)
Occipital cortex (between MCA + PCA)
Paramedian white matter (between ACA + MCA)
Internal (subcortical) Infarct
Between lenticulostriate + MCA
Between lenticulostriate + ACA
Between Heubner artery + ACA
Between anterior choroidal artery + MCA
Between anterior choroidal artery + PCA

(b) microemboli from heart / atherosclerotic plaques in major arteries → preferential propagation to cortical border zones secondary to lower perfusion pressure → limited ability to wash out emboli (esp for internal border zone infarcts)



Location:

(a) cortical (external) watershed

Cause: (a) Unilateral posterior external border zone infarcts ← emboli from heart / CCA
(b) Bilateral infarcts ← vascular stenosis

√ wedge-shaped / ovoid cortical "territorial" infarct
√ location of cortical border zones may vary ← development of leptomeningeal collaterals

(b) subcortical (internal) watershed

Cause: arterial stenosis / occlusion / hemodynamic compromise.

√ multiple 3-mm infarcts in rosarylike pattern arranged in linear fashion parallel to lateral ventricle in centrum semiovale / corona radiata

Small internal border zone infarcts typically represent the "tip of the iceberg" of decreased perfusion reserve and may be predictive of impending stroke.

◊ 6% of cerebral infarcts are hemorrhagic (red infarct)

- completed stroke, TIA, RIND
- amaurosis fugax = transient monocular blindness
- weakness / numbness in an extremity, aphasia, dizziness

• diplopia, dysarthria (vertebrobasilar ischemia)

INFECTION IN IMMUNOCOMPROMISED

Cause: underlying malignancy, collagen disease, cancer therapy, AIDS, immunosuppressive therapy in organ transplant

Organism: Toxoplasma, Nocardia, Aspergillus, Candida, Cryptococcus

√ poorly defined hypodense zones with rapid enlargement in size + number, particularly affecting basal ganglia + centrum semiovale (poorly localized + encapsulated infection with poor prognosis)

√ ring / nodular enhancement (sufficient immune defenses): Toxoplasma, Nocardia

√ enhancement may be blunted by steroid Rx

AIDS may be associated with:

thrombocytopenia, lymphoma, plasmacytoma, Kaposi sarcoma, progressive multifocal leukoencephalopathy

INIENCEPHALY

= complex developmental anomaly characterized by

(1) Exaggerated lordosis
(2) Rachischisis
(3) Imperfect formation of skull base at foramen magnum

M÷F = 1÷4

Associated with other anomalies in 84%:

anencephaly, encephalocele, hydrocephalus, cyclopia, absence of mandible, cleft lip / palate, diaphragmatic hernia, omphalocele, gastroschisis, single umbilical artery, CHD, polycystic kidney disease, arthrogryposis, clubfoot

√ dorsal flexion of head

√ abnormally short + deformed spine

Prognosis: almost uniformly fatal

DDx: (1) Anencephaly
(2) Klippel-Feil syndrome
(3) Cervical myelomeningocele

INTRACRANIAL HYPOTENSION

= rare cause of orthostatic headache worsening in upright position

Cause:

(a) persistent CSF leak:
diagnostic lumbar puncture, spinal anesthesia, myelography, craniotomy, spinal surgery, trauma

(b) spontaneously:
rupture of Tarlov cyst, dehydration, hyperpnea, uremia, diabetic coma

• low CSF opening pressure of < 80 mm H_2O

√ sagging of posterior fossa:

√ low-lying cerebellar tonsils

√ elongation of 4th ventricle

√ effacement of prepontine cistern
√ diffuse smooth linear pachymeningeal enhancement ← ↑ intracranial venous blood flow compensating for CSF loss
√ bilateral subdural effusions
√ enlarged pituitary gland
Rx: conservative therapy with bed rest; autologous epidural blood patch

INTRAVENTRICULAR NEUROCYTOMA

= INTRAVENTRICULAR NEUROBLASTOMA
= benign primary neoplasm of lateral + 3rd ventricles
Incidence: unknown; tumor frequently mistaken for intraventricular oligodendroglioma
Age: 20–40 years
Histo: uniform round cells with central round nucleus + fine chromatin stippling ± perivascular pseudorosettes, focal microcalcifications (closely resembling oligodendroglioma but with neuronal differentiation into synapselike junctions)
Location: body ± frontal horn of lateral ventricle, may extend into 3rd ventricle
√ entirely intraventricular well-circumscribed tumor, coarsely calcified (69%), containing cystic spaces (85%)
√ mild to moderate contrast enhancement
√ attachment to septum pellucidum CHARACTERISTIC
√ ± hemorrhage into tumor / ventricle
√ hydrocephalus
√ peritumoral edema extremely uncommon
MR:
√ isointense relative to cortical gray matter on T1WI + T2WI with heterogeneous areas due to calcifications, cystic spaces, vascular flow voids (62%)
Rx: complete surgical resection
DDx:
(1) Intraventricular oligodendroglioma (no hemorrhage)
(2) Astrocytoma (peritumoral edema in 20%)
(3) Meningioma (almost exclusively in trigone, > 30 years of age)
(4) Ependymoma (in + around 4th ventricle / trigone, in childhood)
(5) Subependymoma (in + around 4th ventricle, young adult)
(6) Choroid plexus papilloma (body + posterior horn of lateral ventricle, intense enhancement, younger patient)
(7) Colloid cyst (anterior 3rd ventricle / foramen of Monro, calcifications uncommon)
(8) Craniopharyngioma (extraventricular origin)
(9) Teratoma + dermoid cyst (fat attenuation)

ISOLATED VERMIAN HYPOPLASIA

= DANDY-WALKER VARIANT (nonpreferred term)
Genetics: usually no recurrence risk
• mild deficits in fine motor activity + receptive language
√ partial absence of inferior vermis (best on midsagittal image)

√ remainder of vermis + cerebellar hemispheres + 4th ventricle + posterior fossa of normal size and architecture

OB-US: diagnosis reliable > 18–20 weeks GA

Cave: high false-positive rate (~ 30%)

Prognosis: favorable outcome in 75%

JOUBERT SYNDROME

= rare genetic disorder affecting cerebellum

- hypotonia, ataxia
- neonatal breathing dysregulation: episodic hyperpnea
- ocular motor apraxia (abnormal eye movement)
- mental retardation (intellectual disability) of variable severity = global cognitive developmental delay

Genetics: autosomal recessive disorder with 25% recurrence risk; > 8 causative gene mutations

Systemic involvement:

√ nephronophthisis
√ congenital hepatic fibrosis
√ coloboma, retinal dystrophy
√ various forms of polydactyly

Related disorders:

COACH (**c**erebellar vermis hypoplasia / aplasia, **o**ligophrenia, **a**taxia, ocular **c**oloboma, **h**epatic fibrosis) syndrome
CORS (cerebello-oculo-renal syndrome)
OFD6 (oro-facial-digital syndrome type 6)

Path: (1) nearly total aplasia of cerebellar vermis
(2) dysplasia + heterotopia of cerebellar nuclei
(3) near total absence of pyramidal decussation
(4) anomalies in structure of inferior olivary nuclei, descending trigeminal tract, solitary fascicle, dorsal column nuclei

√ "molar tooth sign" on AXIAL image (virtually PATHOGNOMONIC):
√ elongated thickened horizontally oriented superior cerebellar peduncles
√ deep interpeduncular fossa
√ vermian hypoplasia / dysplasia

√ change in shape of 4th ventricle: triangle-shaped at mid-level + bat-wing–shaped superiorly
√ cerebellar hemispheres appose one another in midline
√ superior cerebellar peduncles surrounded by CSF
√ small isthmus + midbrain in AP diameter ← absence of decussation of superior cerebellar peduncles
√ brainstem abnormalities:
√ dysmorphic tectum + midbrain
√ thickened elongated midbrain + small pons
√ supratentorial abnormalities (30%):
√ callosal dysgenesis, cephaloceles, hippocampal malrotation, migrational disorders,

ventriculomegaly
Prognosis: renal + hepatic disease responsible for mortality
DDx: Dandy-Walker malformation

LEIGH DISEASE

= SUBACUTE NECROTIZING ENCEPHALOMYELOPATHY
= autosomal recessive disorder characterized by deficiencies in pyruvate carboxylase + pyruvate dehydrogenase complex + cytochrome c oxidase → anaerobic ATP production
• central hypotonia, ataxia, developmental regression / arrest
• ophthalmoplegia
• lactic acidosis = ↑ ratio of lactate to pyruvate in CSF + serum
Location: putamen (consistently), periaqueductal region, cerebral peduncles
√ T2 prolongation of affected areas
√ abnormally high lactate levels on MR spectroscopy

LIPOMA

= uncommon congenital malformation developing within subarachnoid space as a result of abnormal differentiation of the meninx primitiva (which differentiates into pia mater, arachnoid, inner meningeal layer of dura mater)
Incidence: < 1% of brain tumors
Age: presentation in childhood / adulthood
Associated with congenital anomalies:
(a) in anterior location: various degrees of agenesis of corpus callosum (in 50–80%)
(b) in posterior location (in < 33%)
• asymptomatic in 50%
Location: tendency to involve midline structures (usually in subarachnoid space): callosal cistern (25–50%), sylvian fissure, quadrigeminal cistern, chiasmatic cistern, interpeduncular cistern, CP angle cistern, cerebellomedullary cistern, tuber cinereum, choroid plexus of lateral ventricle
√ NO enhancement
CT:
√ well-circumscribed mass with CT density of –100 HU
√ occasionally calcified rim (esp. in corpus callosum)
MR:
√ hyperintense mass on T1WI + less hyperintense on T2WI (CHARACTERISTIC)
√ saturation on fat-suppressed sequences
Rx: insinuating mass around vessels + nerves → difficult to resect

Lipoma of Corpus Callosum

= congenital pericallosal tumor not actually involving corpus callosum ← faulty disjunction of neuroectoderm from cutaneous ectoderm during process of neurulation
Incidence: ~ 30% of intracranial lipomas
Associated with:
(1) anomalies of corpus callosum (30% with small posterior lipoma, 90% with large

anterior lipoma)
(2) frontal bone defect (frequent) = encephalocele
(3) cutaneous frontal lipoma

- in 50% symptomatic:
  - seizure disorder, mental retardation, dementia
  - emotional lability, headaches, hemiplegia

Plain film:
√ midline calcification with associated lucency of fat density

CT:
√ area of marked hypodensity immediately superior to lateral ventricles with possible extension inferiorly between ventricles / anteriorly into interhemispheric fissure
√ curvilinear peripheral / nodular central calcification within fibrous capsule (more common in anterior compared with posterior lipomas)

MR:
√ hyperintense midline mass superior + posterior to corpus callosum on T1WI
√ no callosal fibers dorsal to lipoma
√ branches of pericallosal artery frequently course through lipoma

DDx: dermoid (denser, extraaxial), teratoma

Hypothalamic Osteolipoma

Incidence: extremely rare (30 cases in literature)
Location: between mamillary bodies + infundibular stalk

- rarely symptomatic: variety of neurologic symptoms + endocrinologic disturbances

√ one / more masses directly behind infundibular stalk
√ central adipose (hyperintense on T1WI + T2WI with positive fat suppression) + peripheral osseous tissue (hypointense on T1WI + T2WI)
√ consistent size

LISSENCEPHALY

= AGYRIA-PACHYGYRIA COMPLEX
= "smooth brain" = most severe of neuronal migration anomalies; autosomal recessive disease with abnormal cortical stratification

agyria = absence of gyri on brain surface
pachygyria = focal / diffuse area of few broad flat gyri

A. COMPLETE LISSENCEPHALY = AGYRIA
most frequently parietooccipital in location

B. INCOMPLETE LISSENCEPHALY
= areas of both agyria + pachygyria, pachygyric areas most frequently in frontal + temporal regions

Histo: thick gray + thin white matter with only four cortical layers I, III, V, VI (instead of six layers)

Often associated with:
(1) CNS anomalies: microcephaly, hydrocephalus, agenesis of corpus callosum, hypoplastic thalami
(2) micromelia, clubfoot, polydactyly, camptodactyly, syndactyly, duodenal atresia,

micrognathia, omphalocele, hepatosplenomegaly, cardiac + renal anomalies
- microencephaly, severe mental retardation
- hypotonia + occasional myoclonic spasm
- early seizures refractory to medication

√ smooth thickened cortex with diminished white matter
√ figure-eight appearance of cerebrum on axial images ← shallow widened vertically oriented sylvian fissures
√ absent / shallow sulci and gyri (brain looks similar to that in fetuses of < 23 weeks GA)
√ middle cerebral arteries close to inner table of calvarium ← absence of sulci
√ small splenium + absent rostrum of corpus callosum
√ hypoplastic brainstem ← lack of formation of corticospinal + corticobulbar tracts
√ ventriculomegaly (affecting atrium + occipital horns)
√ midline round calcification in area of septum pellucidum (CHARACTERISTIC)
√ polyhydramnios (50%)

Prognosis: death by age 2
DDx: polymicrogyria (= formation of multiple small gyri mimicking pachygyria on CT + MR, most common around sylvian fissures, broad thickened gyri with frequent gliosis subjacent to polymicrogyric cortex as the most important differentiating feature)

LYMPHOID HYPOPHYSITIS

= rare inflammatory autoimmune disorder with lymphocytic infiltration of pituitary gland
Associated with: thyrotoxicosis + hypopituitarism
Age: almost exclusively in early postpartum women
- headaches, vision loss
- inability to lactate / to resume normal menses

√ enlarged homogeneously enhancing pituitary gland
Prognosis: spontaneous regression
Rx: steroids (reduction in pituitary size on follow-up)

LYMPHOMA OF BRAIN

Clues: (1) Multicentric involvement of deep hemispheres
(2) Association with immunosuppression
(3) Rapid regression with corticosteroids / radiation therapy = "ghost tumor"
Prevalence: 0.3–2% of all intracranial tumors; 7–15% of all primary brain tumors (equivalent to meningioma + low-grade astrocytoma); M > F
Peak age: 30–50 years; M÷F = 2÷1
Histo: atypical pleomorphic B-cells mixed with reactive T-cells infiltrate blood vessel walls + cluster within perivascular (Virchow-Robin) spaces simulating vasculitis
- symptoms of rapidly enlarging mass (60%)
- symptoms of encephalitis (< 25%), stroke (7%)
- cranial nerve palsy, demyelinating disease, motor dysfunction
- personality changes, headaches, seizures, cerebellar signs,
- CSF cytology positive in 4–25–43%: elevated protein, mononuclear / blast / other lymphoma cells

Location: supratentorial÷posterior fossa = 3–9÷1; paramedian structures preferentially affected; white matter + corpus callosum (55%), deep central gray matter of basal ganglia + thalamus + hypothalamus (17%), posterior fossa + cerebellum (11%), spinal cord (1%); multicentricity in 11–47%

Site: abuts ventricular ependyma + meninges (12–30%); **"butterfly lymphoma"** in frontal lobe involvement; dural involvement may mimic meningioma (rare)

Spread: typically infiltrating; may cross anatomic boundaries + midline (crosses corpus callosum); diffuse leptomeningeal spread; subependymal spread with ventricular encasement (= rim-lymphoma)

◊ Primary lymphoma is indistinguishable from secondary!

√ commonly large discrete solitary lesion (57%)
◊ A large lesion is suggestive of lymphoma!
√ small + symmetric multiple nodular lesions (43–81%)
√ diffusely infiltrating lesion with blurred margins
√ spontaneous regression (UNIQUE feature)

CT:
√ usually mildly hyperdense (33%) ← high nuclear-to-cytoplasmic ratio
√ occasionally isodense / low-density area (least common)
√ little mass effect with paucity of peritumoral edema

CECT:
√ homogeneously dense + well-defined / irregular + patchy periventricular contrast enhancement
√ commonly thick-walled ring enhancement in immuno-competent patient
◊ Steroids may inhibit contrast enhancement

MR (superior to CT):
√ well-demarcated round / oval / gyral-shaped (rare) mass
√ relatively little mass effect for size
√ isointense / slightly hypointense (← high cell density) relative to gray matter on T1WI
√ hypo- to isointense / hyperintense (less common) relative to gray matter on T2 / FLAIR (← high cellularity):
√ ring pattern (= central necrosis with densely cellular rim in hyperintense "sea of edema") typical in immunocompromised patients
√ intense ring-shaped contrast enhancement on T1WI
√ irregular sinuous / gyral-like contrast enhancement or homogeneous enhancement:
√ solid homogeneous enhancement in immunocompetent patient
√ irregular heterogeneous ringlike mass in immunocompromised patient
√ periventricular enhancement is highly SPECIFIC (DDx: CMV ependymitis)
√ elevated choline levels on MR spectroscopy

Angio:
√ avascular mass / tumor neovascularity
√ focal blush in late arterial-to-capillary phase persisting well into venous phase
√ arterial encasement
√ dilated deep medullary veins

NUC:

√ increased uptake of ^{201}Thallium on SPECT (100% sensitive, 93% specific)
√ increased uptake of 11C-methionine on PET

Prognosis: median survival of 45 days for AIDS patients; median survival of 3.3 months for immunocompetent patients; improved with radiation therapy (4.5–20 months) + chemotherapy

Rx: sensitive to radiation therapy

DDx:

A. Neoplastic disorders
   (1) Glioma (may be bilateral with involvement of basal ganglia + corpus callosum, may show dense homogeneous enhancement with vascularity)
   (2) Metastases (known primary, at gray-white matter junction)
   (3) Primitive neuroectodermal tumor
   (4) Meningioma
B. Infectious disease (multicentricity)
   (1) Abscess, especially toxoplasmosis (large edema)
   (2) Sarcoidosis
   (3) Tuberculosis
C. Demyelinating disease
   (1) Multiple sclerosis
   (2) Progressive multifocal leukoencephalopathy

Primary CNS Lymphoma (93%)

= PCNSL = RETICULUM CELL SARCOMA = HISTIOCYTIC LYMPHOMA = MICROGLIOMA
= high-grade B-cell NHL with strong association to Epstein-Barr virus infection

Prevalence: 2–10%
◊ Initial manifestation in 0.6% of AIDS patients
◊ 2nd most common cause of a CNS mass in AIDS

Risk: increased (350-fold) in immunocompromised patients: AIDS (2–10%), renal transplant, Wiskott-Aldrich syndrome, immunoglobulin deficiency A, rheumatoid arthritis, progressive multifocal leukoencephalopathy

Associated with: intraocular lymphoma

Location: anywhere; mostly periventricular; crosses corpus callosum (DDx: edema from infection will not)

√ uni- or multifocal lesions + variable mass effect
√ doubling in size within 2 weeks
√ paucity of edema

NECT:
√ often increased attenuation ← high nuclear-to-cytoplasmic ratio

MR:
√ iso- to hypointense on T1WI
√ variable intensity on T2 / FLAIR; may be hypointense ← high cell density
√ homogeneous enhancement; frequent ring enhancement in AIDS patients ← central necrosis

NUC (^{201}Tl SPECT - 100% sensitive, 93% specific):

√ uptake (DDx: toxoplasmosis not avid)
Dx: brain biopsy for unifocal lesion
Rx: sensitive to radiation therapy

Primary Dural Lymphoma
Incidence: < 1% of all CNS lymphomas
Histo: low-grade marginal zone lymphoma, follicular, Hodgkin, diffuse large B-cell subtypes; mucosa-associated lymphoid tissue (MALT) subgroup (in majority)
Age: middle-aged female
• headache, meningeal signs, cranial nerve involvement
√ ± blurred margin = indistinct brain-tumor interface
√ vasogenic edema in adjacent brain parenchyma
CT:
√ single / multiple hyperattenuating masses ← highly cellular lesion
MR:
√ iso- to hypointensity on T2WI
√ avid enhancement, sometimes heterogeneous
Prognosis: excellent
DDx: meningioma, subdural hematoma

Secondary Lymphoma of CNS (7%)
= SYSTEMIC LYMPHOMA
Type: NHL > Hodgkin disease
Location: tendency for dura mater + leptomeninges
• palsies of cranial nerves III, VI, VII
√ hydrocephalus

Spinal Epidural Lymphoma
(a) invasion of epidural space through intervertebral foramen from paravertebral lymph nodes
(b) destruction of bone with vertebral collapse (less common)
(c) direct involvement of CNS (rare)

Leukemia
CNS affected in 10% of patients with acute leukemia
√ enlargement of ventricles + sulci ← atrophy (31%)
√ sulcal / fissural / cisternal enhancement ← meningeal infiltration (in 5%)
Prognosis: 3–5 months survival if untreated

MEDULLOBLASTOMA
◊ Most malignant infratentorial neoplasm; most common neoplasm of posterior fossa in childhood (followed by cerebellar pilocytic astrocytoma)
Incidence: 15–20% of all pediatric intracranial tumors; 30–40% of all posterior fossa neoplasms in children; 2–10% of all intracranial gliomas
Origin: external granular layer of inferior medullary velum (= roof of 4th ventricle)
Histo: completely undifferentiated cells (50%), desmoplastic variety (25%), glial / neuronal

differentiation (25%)

Age: 40% within first 5 years of life; 75% in first decade; between ages 5 and 14 (⅔); between ages 15 and 35 (⅓); M÷F = 2–4÷1

• duration of symptoms < 1 month prior to diagnosis: nausea, vomiting, headache, increasing head size, ataxia

Site: (a) vermis cerebelli + roof of 4th ventricle (younger age group) in 91%
(b) cerebellar hemisphere (older age group)

Size: usually > 2 cm in diameter

√ well-defined vermian mass with widening of space between cerebellar tonsils
√ encroachment on 4th ventricle / aqueduct with hydrocephalus (85–95%)
√ shift / invagination of 4th ventricle
√ rapid growth with extension into cerebellar hemisphere / brainstem (more often in adults)
√ extension into cisterna magna + upper cervical cord, occasionally through foramina of Luschka into cerebellopontine angle cistern
√ mild / moderate surrounding edema (90%)

CT:

Classic tumor features in 53%:
√ slightly hyperdense (70%) / isodense (20%) / mixed (10%)
√ rapid intense homogeneous enhancement (97%) ← tumor usually solid

Atypical features:
√ cystic / necrotic areas (10–16%) with lack of enhancement
√ calcifications in 13%
√ hemorrhage in 3%
√ supratentorial extension

MR:
√ mixed / hypointense on T1WI
√ hypo- / iso- / hyperintense on T2WI
√ usually homogeneous Gd-DTPA enhancement with hypointense rim
√ cerebellar folia blurred

Cx: (1) Subarachnoid metastatic spread (30–100%) via CSF pathway to spinal cord + cauda equina ("drop metastases" in 40%), cerebral convexities, sylvian fissure, suprasellar cistern, retrograde into lateral + 3rd ventricle
√ continuous "frosting" of tumor on pia
(2) Metastases outside CNS (axial skeleton, lymph nodes, lung) after surgery

Rx: surgery + radiation therapy (extremely radiosensitive)

DDx of midline medulloblastoma:
ependymoma, astrocytoma (hypodense)

DDx of eccentric medulloblastoma:
astrocytoma, meningioma, acoustic neuroma

MEGACISTERNA MAGNA

= normal variant of focal enlargement of subarachnoid space in posteroinferior aspect of posterior fossa

Cause: ? delayed fenestration of Blake pouch

• incidental finding
√ cisterna magna ≥ 10 mm (on midsagittal image)
√ free communication with 4th ventricle + cervical subarachnoid space (confirmed with CSF flow study)

Pertinent negatives:
√ intact vermis + normal 4th ventricle
√ absence of hydrocephalus
√ occasionally enlarged posterior fossa

DDx: (1) Blake pouch cyst (hydrocephalus)
(2) Isolated inferior vermian hypoplasia

MELANOCYTOMA

= benign lesion arising from resident melanocytic cells found within leptomeninges

Age: any; 5th decade (majority); F > M

Path: darkly pigmented mass

Histo: tight cellular nests / whorls ± abundant melanin pigment within cytoplasm: NO mitotic activity, NO nuclear pleomorphism, NO hyperchromaticity; S-100 + melan-A + HMB-45 positivity (similar to melanoma)

• myelopathy, radiculopathy
• seizures, hydrocephalus, cranial nerve deficits

Location: posterior fossa, Meckel cave, spinal canal (cervical + thoracic spine)

√ avidly enhancing iso- to hyperattenuating mass
√ indolent growth pattern
√ typically iso- to hypointense on T2WI ± T1 hyperintensity ← melanin

Rx: surgical resection (in up to 22% recurrence within 3 years)

DDx: melanoma

MENINGIOMA

Incidence: most common extraaxial tumor: 15–18% of intracranial tumors in adults; 1–2% of primary brain tumors in children; 33% of all incidental intracranial neoplasms

Origin: derived from meningothelial cells concentrated in arachnoid villi (= "arachnoid cap cells"), which penetrate the dura (villi are numerous in large dural sinuses, in smaller veins, along root sleeves of exiting cranial + spinal nerves, choroid plexus)

Histologic classification:

› benign behavior pattern
(a) fibroblastic (fibrous) type = interwoven bands of spindle cells + collagen + reticulin fibers
(b) transitional (mixed) type
= features of meningothelial + fibroblastic forms

› aggressive imaging appearance
(c) meningothelial (syncytial) type = forming a syncytium of closely packed cells with indistinct borders
(d) angioblastic (malignant) type
= probably hemangiopericytoma / hemangioblastoma arising from vascular pericytes

Peak age: 45 (range, 35–70) years; rare < 20 years (in children > 50% malignant); M÷F = 1÷2 to 1÷4

In pediatric age group:
NO gender predilection
Higher risk of sarcomatous change
Consider association with neurofibromatosis type 2

Associated with: NF2 (multiple meningiomas, occurrence in childhood), basal cell nevus syndrome

◊ 10% of patients with multiple meningiomas have type 2 neurofibromatosis!

◊ Most common radiation-induced CNS tumor with latency period of 19–35 years varying with dosage!

Types:

(1) **Globular meningioma** (most common):
compact rounded mass with invagination of brain; flat at base; contact to falx / tentorium / basal dura / convexity dura

(2) **Meningioma en plaque**:
pronounced hyperostosis of adjacent bone, particularly along base of skull; difficult to distinguish hyperostosis from tumor cloaking the inner table (DDx: Paget disease, chronic osteomyelitis, fibrous dysplasia, metastasis)

(3) **Multicentric meningioma** (2–9%):
16% in autopsy series; tendency to localize to a single hemicranium; present clinically at earlier age; global / mixed; CSF seeding is exceptional; in 50% associated with neurofibromatosis type 2

Location:

A. Supratentorial (90%)
   (a) convexity = lateral hemisphere (20–34%)
   (b) parasagittal = medial hemisphere (18–22%):
   falcine meningioma (5%) below superior sagittal sinus, usually extending to both hemispheres
   (c) sphenoid ridge + middle cranial fossa (17–25%)
   (d) frontobasal at olfactory groove (10%)

B. Infratentorial (9–15%)
   (a) cerebellar convexity (5%)
   (b) tentorium cerebelli (2–4%)
   (c) cerebellopontine angle (2–4%)
   (d) clivus (< 1%)

C. Spine (12%)

Atypical location:

(a) cerebellopontine angle (< 5%)
(b) optic nerve sheath (< 2%)
(c) intraventricular (0.5–3.7%): 80% in atrium (L > R), 15% in 3rd, 5% in 4th ventricle ← infolding of meningeal tissue during formation of choroid plexus
   ◊ Most common trigonal intraventricular mass in adulthood!
(d) ectopic = extradural (< 1%): intradiploic space, outer table of skull, scalp, paranasal

sinus, parotid gland, parapharyngeal space, mediastinum, lung, adrenal gland

Plain film:

- √ hyperostosis at site close to / within bone (exostosis, enostosis, sclerosis):
  - ◊ Hyperostosis does NOT indicate tumor infiltration!
- √ blistering at paranasal sinuses (ethmoid, sphenoid) ± sclerosis (= pneumosinus dilatans)
- √ enlarged meningeal grooves (if location in vault)
- √ enlarged foramen spinosum
- √ calcification (= psammoma bodies)

CT:

- √ sharply demarcated well-circumscribed slowly growing mass
- √ hyperdense (70–75% ← highly cellular nature or psammomatous calcifications) / isodense lesion on NECT
- √ calcifications (15–20–25%) in circular / radial pattern (DDx: osteoma)
- √ "cortical buckling" of underlying brain
- √ "intraosseous meningioma" = permeation of bone with intra- and extracerebral soft-tissue component (DDx: fibrous dysplasia)
- √ hyperostosis of adjacent bone (18%)
- √ intense uniform enhancement on CECT ← absence of blood-brain barrier:
  - √ "dural tail" = wide attachment to adjacent dura mater
- √ minimal peritumoral edema (in up to 75%):
  - ◊ NO correlation between tumor size + amount of edema (DDx: intraaxial lesion)
- √ cystic component: major in 2%, minor in 15%

MR (100% detection rate with gadolinium DTPA):

- √ hypo- to isointense on T1WI + iso- to hyperintense on T2WI (intensity depends on amount of cellularity versus collagen elements):
  - √ tends to follow cortical signal intensity
  - √ homogeneous / heterogeneous texture (← tumor vascularity, cystic changes, calcifications)
- √ arcuate bowing of white matter + cortical effacement
- √ tumor-brain interface ← low-intensity vessels + high-intensity cerebrospinal cleft on T2WI
- √ contrast enhancement for 3–60 min on T1WI as high as 148% above enhancement of brain parenchyma
- √ "dural tail" sign (in 60–72%)
- √ encasement + narrowing of vessels
- √ elevated alanine peak (1.5 ppm) + glutamate–glutamic acid peak (2.1–2.5 ppm)

Differences between Meningioma and Schwannoma		
	Meningioma	*Schwannoma*
Angle with dura	obtuse	acute
Dural tail	frequent	rare
Calcification	20%	rare
Cystic/necrotic	rare	10%
IAC involvement	rare	80%
NECT	hyperdense	isodense
Enhancement	uniform	32% nonuniform

Angio:

√ "mother-in-law" phenomenon (contrast material shows up early and stays late into venous phase)

√ "sunburst" / "spoke-wheel" pattern of tumor vascularity with hypervascular cloudlike stain

√ early draining vein (rare: perhaps in angioblastic meningioma)

√ en plaque meningioma is poorly vascularized

Vascular supply:

A. External carotid artery (almost always):
   1. vault: middle meningeal artery
   2. sphenoid plane + tuberculum: recurrent meningeal branch of ophthalmic a.
   3. tentorium: meningeal branch of meningohypophyseal trunk of ICA
   4. clivus + posterior fossa: vertebral artery / ascending pharyngeal artery
   5. falx: partly middle meningeal artery + others

B. Internal carotid artery (rare):
   1. intraventricular: choroidal vessels

Cx: local invasion of venous sinuses

Atypical Meningioma (15%)

1. Low attenuation area of necrosis, old hemorrhage, cyst formation, fat (DDx: malignant glioma, metastasis)
   (a) **Cystic meningioma** (2–4%)
   Frequency: 55–65% in 1st year of life; 10% in children
   Type I = intratumoral central / eccentric cyst (ischemic necrosis, microcystic degeneration, breakdown of hemorrhagic products); often associated with meningothelial / microcystic / atypical / malignant histologic subtypes
   Type II = extratumoral intraparenchymal cyst (arachnoid cyst / reactive gliosis / liquefactive necrosis of adjacent brain)
   Type III = trapped CSF (DDx: cystic / necrotic glioma)
   (b) **Lipoblastic / xanthomatous meningioma** (5%) lipid-laden meningothelial cells (in 10–90%) with metaplasia of meningothelial cells into mature adipocytes
2. Heterogeneous / ring enhancement ← bland tumor infarction / necrosis in aggressive histologic variants / true cyst formation from benign fluid accumulation
3. "En plaque" morphology

4. "Comma shape" = combination of semilunar component bounded by dural interface + spherical component growing beyond dural margin
5. Sarcomatous transformation with spread over hemisphere + invasion of cerebral parenchyma (leptomeningeal supply)
6. **M eningeal hemangiopericytoma**
   √ multilobulated contour
   √ narrow dural base / "mushroom" shape
   √ large intratumoral vascular signals
   √ bone erosion
   √ prominent peritumoral edema
   √ multiple irregular feeding vessels on angiogram

Sphenoid Wing Meningioma

1. Hyperostotic meningioma en plaque
   • slowly progressive unilateral painless exophthalmos
   • numbness in distribution of cranial nerve $V_1 + V_2$
   • headaches, seizures
2. Meningioma arising from middle third of sphenoid ridge
   • headaches, seizures
   √ compression of regional frontal + temporal lobes
3. Meningioma arising from clinoid process
   √ encasement of carotid + middle cerebral arteries
   √ compression of optic nerve + chiasm
4. Meningioma of planum sphenoidale
   √ subfrontal growth + posterior growth into sella turcica and clivus
   √ hyperostotic blistering of planum sphenoidale

Suprasellar Meningioma

Incidence: 10% of all intracranial meningiomas

Origin: from arachnoid + dura along tuberculum sellae / clinoids / diaphragma sellae / cavernous sinus with secondary extension into sella; NOT from within pituitary fossa

• hypothalamic / pituitary dysfunction (rare)

√ irregular hyperostosis = blistering adjacent to sinus (HALLMARK of meningiomas at planum sphenoidale / tuberculum sellae)

√ pneumatosis sphenoidale = increased pneumatization of sphenoid in area of anterior clinoids + dorsum sellae (DDx: normal variant)

√ broad base of attachment

√ intense homogeneous enhancement (may be impossible to differentiate from supraclinoid carotid aneurysm on CT)

√ blood supply: posterior ethmoidal branches of ophthalmic artery, branches of meningohypophyseal trunk

MR:

√ large mass isointense to gray matter on T1WI + T2WI

√ hyperintense flattened pituitary gland within floor of sella

√ marked homogeneous enhancement on T1WI
DDx: metastasis, glioma, lymphoma

MENINGITIS

= infection of the pia mater + arachnoid + adjacent CSF

1. Pachymeningitis: infection of dura mater
2. Leptomeningitis: infection of pia matter / arachnoid (most common) + CSF

• headaches, stiff neck, confusion, disorientation
• positive CSF lab analysis

ROLE of CT and MR:

(1) to exclude parenchymal abscess, ventriculitis, localized empyema
(2) to evaluate paranasal sinuses / temporal bone as source of infection
(3) to monitor complications: hydrocephalus, subdural effusion, infarction

Chemical / Aseptic Meningitis

= rare complication of dermoid / epidermoid cyst ← cyst rupture into subarachnoid space

MR:

√ T1-hyperintense speckles in cortical sulci
√ fat-fluid level in ventricles

Purulent / Bacterial / Acute Septic Meningitis

Cause: otitis media / sinusitis

Organism:

(a) adults: Neisseria meningitidis, Diplococcus pneumoniae, Haemophilus influenzae, Meningococcus, Staphylococcus aureus
(b) children: group B Streptococcus (86%), S pneumonia (= Pneumococcus in 58%), Escherichia coli, Citrobacter

Incidence: 4100 cases annually in USA

• fever, headache, seizures, altered consciousness, neck stiffness

Neuroimaging most useful to:

› exclude herniation before lumbar puncture
› to detect complications

Cross-sectional imaging is neither sensitive nor specific for detection of meningitis.

NECT:

√ often normal / falsely negative due to subtlety of findings
√ sulcal effacement
√ slightly increased density in subarachnoid space ← increased vascularity, esp. in children
√ small ventricles ← diffuse cerebral edema

CECT:

√ marked curvilinear meningeal enhancement over cerebrum (frontal + parietal lobes) and interhemispheric + sylvian fissures
√ obliteration of basal cisterns with enhancement (common)

MR (most sensitive modality):

√ no abnormality (in most cases)
√ ± hyperintense obliterated basal cisterns on FLAIR ← increased protein content (NOT

specific for meningitis)
√ abnormal hyperintensity in cerebral sulci on DWI (NOT specific for meningitis) ← pyogenic (bacterial) >> lymphocytic (viral) / aseptic meningitis

CEMR (postcontrast FLAIR + delayed T1WI):
√ abnormal enhancement of pia mater + subarachnoid space (leptomeninges) ← inflammatory breakdown of blood-brain barrier (in only 50%):
√ thin linear enhancement in cerebral sulci = typical for acute pyogenic (bacterial) + lymphocytic (viral) meningitis
√ thick nodular enhancement in basal cisterns = typical of granulomatous / carcinomatous meningitis
√ leptomeningeal enhancement (in chronic infection)

Dx: CSF analysis

Cx:
(1) Cerebritis (parenchymal) / subdural infection, especially with streptococcus / staphylococcus
(2) Ventriculitis ← retrograde spread
(3) Brain atrophy
(4) Brain infarction ← arteritis, venous thrombosis (5–15% of adults, in up to 30% of neonates)
(5) Subdural effusion [sterile subdural effusion ← H. influenzae meningitis (in children) may turn into subdural empyema]
(6) Hydrocephalus ← cellular debris blocking foramen of Monro, aqueduct, 4th ventricular outlet / intraventricular septa / arachnoid adhesions
(7) Cranial nerve dysfunction

Prognosis:
◊ Cerebral infarction + edema predict poor outcome
◊ Enlargement of ventricles + subarachnoid spaces + subdural effusions have no predictive value

Mortality: 10% for H. influenza + meningococcus, 30% for Pneumococcus (5th commonest cause of death in children between 1 and 4 years of age)

DDx: meningeal carcinomatosis

Granulomatous Meningitis

Histo: thick exudate, perivascular inflammation, granulation tissue + reactive fibrosis

(1) **Tuberculous meningitis** = basilar meningitis
part of generalized miliary tuberculosis / primary tuberculous infection

(2) **Sarcoidosis** (in 5% of sarcoidosis cases)
Histo: granulomatous infiltration of leptomeninges
√ nodular pattern (DDx from bacterial causes)
√ thick meningeal plaques over convexities (mimicking meningioma)
√ marked enhancement
√ may be associated with single / multiple intracerebral mass(es)
Cx: cranial nerve palsy, hypothalamic-pituitary dysfunction, chronic meningitis

(3) **Fungal meningitis**: coccidioidomycosis (endemic), blastomycosis, mucormycosis (diabetics), nocardiosis, actinomycosis, aspergillosis (under chronic corticosteroid

therapy)

(a) yeast = unicellular eukaryotic microorganism that reproduce by asymmetric fission:
  › Cryptococcosis
  › Candidiasis

(b) mold = multicellular filaments (hyphae) that can form into macroscopic networks (mycelia); too large for meningeal microcirculation and more likely cause invasive parenchymal CNS disease in immunocompromised patients
  › Aspergillus
  › Mucormycosis

(c) dimorphic fungus = dimorphic fungus that grows as mold (yeast) at room (body) temperature; resides in soil in endemic regions and releases conidia (spores) into the air (unicellular eukaryotes at body temperature → initially misidentified as protozoa)
  › Blastomycosis
  › Coccidioidomycosis
  › Histoplasmosis

Fungal CNS diseases are usually opportunistic infections from hematogenous dissemination in susceptible hosts at extremes of age or with immunodeficiency.

• acute life-threatening process / chronic indolent disease

May be associated with: cerebritis, abscess formation

√ hydrocephalus

CT:

√ obliteration of basal cisterns, sylvian fissure, suprasellar cistern (isodense cisterns ← filling with debris)

√ intense contrast enhancement of gyri + involved subarachnoid spaces

√ calcification of meninges

√ decreased attenuation of white matter

MR:

√ high-signal intensity of basilar cisterns on T2WI

√ enhancement with gadopentetate dimeglumine

Cx: (1) Hydrocephalus ← obliteration of basal cisterns, blocking of CSF flow + blocking of CSF absorption

(2) Infarction ← arteritis

MESIAL TEMPORAL SCLEROSIS

Cause: long-standing temporal lobe epilepsy

Histo: marked neuronal loss + astrogliosis in hippocampal subfields CA1 + CA3 + CA4

Mechanism for excitotoxicity-induced neuronal death:

seizures → excessive neuronal depolarization → overproduction of excitory amino acid neurotransmitters → excessive activation of N-methyl-D-aspartate receptors → unregulated entry of $Ca2+$ → neuronal swelling with cytotoxic edema

Location: uni- / bilateral; symmetric / asymmetric

√ hippocampal atrophy + loss of internal architecture

√ increased signal intensity on T2WI

√ dilatation of temporal horn

Associated limbic system findings:
√ ipsilateral atrophy of fornix (55%)
√ ipsilateral atrophy of mamillary body (26%)
Associated extrahippocampal abnormalities:
√ increased SI of anterior temporal lobe cortex (38%)
√ cerebral hemiatrophy (1%)
Rx: amygdalohippocampectomy

METACHROMATIC LEUKODYSTROPHY

= MLD = most common hereditary (autosomal recessive) leukodystrophy (dysmyelinating disorder)
Cause: deficiency of arylsulfatase A resulting in severe deficiency of myelin lipid sulfatide within macrophages + Schwann cells
Age of presentation: before age 3 (⅔), in adolescence (⅓)
A. LATE INFANTILE FORM
Age: 2nd year of life
• gait disorder + strabismus, impairment of speech
• spasticity + tremor, intellectual deterioration
Prognosis: death within 4 years of onset
B. JUVENILE FORM
Age: 5–7 years
C. ADULT FORM
• organic mental syndrome
• progressive corticospinal, corticobulbar, cerebellar, extrapyramidal signs
√ progressive loss of hemispheric brain tissue
CT:
√ symmetric low density of white matter adjacent to ventricles (esp. centrum ovale and frontal horns)
√ progressive atrophy
√ no contrast enhancement
MR:
√ progressive symmetrical areas of hypointensity on T1WI
√ hyperintensity on T2WI (increased water)
√ early sparing of internal capsule + subcortical U-fibers
Prognosis: death within several years

METASTASIS TO BRAIN

Incidence: 14–37% of all intracranial tumors
◊ Most common intracranial neoplasm!
◊ Most common infratentorial mass in adulthood
Metastatic primary:
Six tumors account for 95% of all brain metastases:
1. Bronchial carcinoma (47%): rarely squamous cell ca.
2. Breast carcinoma (17%)

3. GI-tract tumors (15%): colon, rectum
4. Hypernephroma (10%)
5. Melanoma (8%)
6. Choriocarcinoma

In childhood:

1. Leukemia / lymphoma
2. Neuroblastoma

◊ Brain metastases from sarcomas are exceptionally rare!

Location:

(a) corticomedullary junction of brain (most characteristic)
(b) subarachnoid space = carcinomatous meningitis
(c) subependymal spread (frequent in breast carcinoma)
(d) skull (5%)

N.B.: CORTICAL METASTASES
√ minimal / no edema
√ may not be identified on T2WI
√ contrast-enhancement essential for detection

Presentation:

› multiple lesions (⅔), single lesion (⅓)
› cerebral hemispheres (57%), cerebellum (29%), brainstem (32%)
› nodular deposits to dura (common)

√ usually well-defined round masses:
√ multiple lesions of different sizes + locations
√ surrounding edema usually exceeds tumor volume
◊ Employ contrast enhancement to disclose additional lesions!

CT:

√ hypodense on NECT (unless hemorrhagic / hypercellular)
√ solid enhancement in small tumors / ringlike enhancement in large tumors

MR (combination of T2WI + contrast-enhanced T1WI offer greatest sensitivity):

√ hypointense on T1WI
√ hypointense mass relative to edema / variable intensity on T2WI ← hemorrhage, necrosis, cyst formation:
√ hypointensity more pronounced in melanoma + mucinous adenocarcinoma ← paramagnetic effect
√ homogeneous / ring / nodular mixed enhancement after Gd-DTPA; often more than one metastatic focus identified in region of colliding edema
√ asymmetric enhancement of dura with dural spread
√ leptomeningeal enhancement (eg, in metastatic ependymoma)

DDx: glioma (indistinct border, less well defined, lesser amount of vasogenic edema); multifocal inflammatory lesions

Carcinomatous Meningitis (8–15%)

= Meningeal Carcinomatosis
= metastatic involvement of leptomeninges

Source:

A. Primary CNS tumor: medulloblastoma, glioblastoma, pineal tumors
B. Secondary tumor: carcinoma of breast + lung, melanoma, NHL, leukemia

Histo: adenocarcinoma (75%)

Spread:
(a) hematogenous dissemination (most common)
(b) contiguous perineural spread
(c) lymphatic spread
(d) shedding of tumor cells from parenchymal metastases

Associated with: concurrent brain parenchymal metastases (in 20%)

◊ Simultaneous occurrence of symptoms localized to more than one area!

- headaches (50%), seizures (15%), cauda equina syndrome
- cranial nerve deficits (40%): visual disturbances, diplopia, hearing loss, facial numbness
- mental status changes: lethargy + confusion (20%)
- progressive asymmetric weakness of extremities

Dx: harvest of malignant cells ← lumbar puncture positive in 45–55% (1st puncture), 80% (after several taps)

N.B.: Perform MRI prior to lumbar puncture

◊ Lumbar puncture contraindicated if intracranial pressure increased!

Location: basal cisterns, lumbar spine (areas of CSF stasis)

√ communicating hydrocephalus ← tumor interferes with CSF reabsorption in pacchionian granulations near vertex

√ ischemic changes ← vasculitis (rare)

CEMR (abnormalities in up to ⅔):
√ linear / nodular enhancement of sulci, cisternal spaces, ventricles with associated effacement
√ diffuse / asymmetric nodular enhancement
√ hydrocephalus
√ cranial nerve enhancement

Patterns:

1. **Dural Meningeal Carcinomatosis**
   » rarely associated with positive cytology
   √ short discontinuous thin sections of enhancement localized / diffuse curvilinear underneath inner table in expected position of dura
2. **Leptomeningeal Carcinomatosis**
   » frequently associated with positive cytology
   √ thin rim of subarachnoid enhancement following convolutions of gyri "coating the surface of the brain"
   √ discrete leptomeningeal nodules
   √ invasion of underlying brain → mass effect + edema

DDx: bacterial / fungal meningitis, postoperative changes (fibrosis), previous subarachnoid hemorrhage, idiopathic cranial pachymeningitis, vasculitis, extramedullary hematopoiesis, primary leptomeningeal gliomatosis, amyloidosis, glioneural heterotopia, Castleman disease, Gaucher disease

Dural Metastasis

Origin: most common: breast, lung, prostate
others: melanoma, lymphoma, RCC, gastric cancer
√ often solitary linear dural thickening / nodular lesion: focal / diffuse involvement
√ ± dural tail
√ avid enhancement ← lack of blood-brain barrier:
√ dural enhancement adjacent to osseous involvement ← dural invasion / reactive dural response
◊ The lower the T2 signal the more hypercellular the lesion!

Dural metastases are frequently solitary, potentially leading to a misdiagnosis of meningioma and delay in care.

Hemorrhagic Metastases to Brain (in 3–4%)

1. Malignant melanoma
2. Breast cancer
3. Choriocarcinoma
4. Oat cell carcinoma of lung
5. Renal cell carcinoma
6. Thyroid carcinoma

√ hyperdense without contrast
√ hypervascular with contrast
mnemonic: MR CT BB
Melanoma
Renal cell carcinoma
Choriocarcinoma
Thyroid carcinoma
Bronchogenic carcinoma
Breast carcinoma

Cystic Metastasis to Brain

1. Squamous cell carcinoma of lung
2. Adenocarcinoma of lung

DDx: benign cyst, abscess

Calcified Metastasis to Brain

1. Mucin-producing neoplasm: GI, breast
2. Cartilage- / bone-forming sarcoma
3. Effective radio- and chemotherapy

Malignant Melanoma Metastatic to Brain

Prevalence: 39% at autopsy
Location: cerebrum > cerebellum; usually multiple lesions
• variable degree of pigmentation
√ tendency for hemorrhage
1. Melanotic pattern (in 24–54%)
√ paramagnetic property of melanin → T1-shortening effect:

√ hyperintense relative to cortex on T1WI
√ iso- / hypointense relative to cortex on T2WI

Cause: free radicals in melanin + blood products

◊ NO clear consensus on contribution of paramagnetic effect of blood products versus melanin!

2. Amelanotic pattern (38%)
   ◊ Pattern similar to other brain neoplasm
   √ hypo- / isointense on T1WI
   √ hyper- / isointense on T2WI
3. Other patterns
   √ isointense on T1WI
   √ hyperintense on T2WI

Prognosis: median survival of 113 days after discovery

DDx: primary malignant melanoma of CNS (1% of all melanoma cases; solitary lesion; leptomeningeal / choroid plexus location)

MICROCEPHALY

= clinical syndrome characterized by a head circumference below the normal range

Incidence: 1.6÷1,000 or 1÷6,200 to 1÷8,500 births

Etiology:

(1) Undiagnosed intrauterine infection (toxoplasmosis, rubella, CMV, herpes, syphilis), toxic agents, drugs, hypoxia, irradiation, maternal phenylketonuria
(2) Premature craniosynostosis
(3) Chromosomal abnormalities (trisomies 13, 18, 21)
(4) Meckel-Gruber syndrome

Often associated with:

microencephaly, macrogyria, pachygyria, atrophy of basal ganglia, decrease in dendritic arborization, holoprosencephaly

√ AC÷HC discrepancy
√ head circumference < 3 SD below the mean
√ apelike sloping of forehead
√ dilatation of lateral ventricles
√ poor growth of fetal cranium
√ intracranial contents may not be visible (rare)

Prognosis: normal to severe mental retardation (depending on degree of microcephaly)

MINERALIZING MICROANGIOPATHY

= RADIATION-INDUCED LEUKOENCEPHALOPATHY

= sequelae of radiotherapy combined with methotrexate therapy for leukemia

Incidence: in 25–30% after > 9 months after treatment

Age: childhood

Cause: deposition of calcium within small vessels of previously irradiated brain parenchyma

• 85% without neurologic deficits

CT:

√ thin reticular / serrated linear / punctate calcifications near corticomedullary junction, especially in basal ganglia + frontal and posterior parietal lobes
√ symmetric low-attenuation process in white matter near corticomedullary area

MR:

√ confluent diffuse periventricular distribution spreading peripherally with an irregular scalloped edge

Diffuse White Matter Injury

= radiation-induced demyelination of periventricular white matter

Cause: whole-brain irradiation

• subclinical

Diffuse Necrotizing Leukoencephalopathy

Cause: intrathecal methotrexate ± whole brain irradiation

• rapidly deteriorating clinical course

√ confluent pattern with scalloped margins in periventricular white matter extending out to subcortical U-fibers

MOYAMOYA DISEASE

[*moyamoya*, Japanese = puff of smoke]

= uncommon occlusive cerebral arteritis classically involving supraclinoid internal carotid arteries with relative sparing of the posterior fossa in early stages

Etiology: unknown; NO underlying cause identified

Age: bimodal distribution in 1st decade + 4th decade of life

Path: development of extensive tiny basal perforator and transdural collateral vessels (moyamoya vessels)

Histo: endothelial hyperplasia + fibrosis without associated inflammatory reaction

• headaches, behavioral disturbances

√ bilateral stenosis / occlusion of supraclinoid portion of ICA extending to proximal portions of MCA + ACA

√ large network of moyamoya vessels in basal ganglia + upper brainstem fed by basilar a. + ACA + MCA (dilatation of lenticulostriate + thalamoperforating arteries)

√ anastomoses between dural meningeal + leptomeningeal aa.

MR:

√ tiny flow voids commonly arising from basal cisterns extending into basal ganglia / thalamus

√ microbleeds (in 15–44%)

√ ischemia and infarction

√ NO nidus / dilated vessels

√ "ivy" sign = curvilinear high signal intensities along cortical sulci + brain surface = sulcal hyperintensity on FLAIR ← leptomeningeal collateral vessels

√ marked leptomeningeal enhancement along cortical sulci

◊ Angio needed for planning of revascularization procedure

Cx: in children: transient ischemic hemiparetic attacks, cerebral infarction

in ½ of adults: intracranial hemorrhage

Moyamoya Syndrome

= underlying cause for moyamoya image identified

Etiology: neurocutaneous syndromes (eg, neurofibromatosis), atherosclerosis, sickle cell anemia, periarteritis nodosa, coarctation of aorta, Down syndrome, Marfan syndrome, head trauma, tuberculosis, oral contraceptives, bacterial meningitis

MULTIPLE SCLEROSIS

= most frequent form of chronic inflammatory demyelinating disease of unknown etiology, which reduces the lipid content and brain volume; characterized by a relapsing + remitting course

Prevalence: 6÷10,000 (higher frequency in cooler climates; increased incidence with positive family history)

Cause: ? viral / autoimmune mechanism

Peak age: 25–30 (range, 20–50) years; M÷F = 2÷3

Histo:

(a) acute stage: perivenular inflammation (at junctions of pial veins) with
- › hypercellularity (= infiltration of lipid-laden macrophages + lymphocytes)
- › well-demarcated demyelination (destruction of oligodendroglia with loss of myelin sheath)
- › reactive astrocytosis (= gliosis), initially with preservation of axons (= denuded axons) → scar (= white matter plaque)

(b) chronic stage: plaques advance to fibrillary gliosis with reduction in inflammatory component

Clinical forms: (a) relapsing remitting
(b) relapsing progressive
(c) chronic progressive

- waxing and waning course with
  - numbness, dysesthesia, burning sensations
  - signs of brain neoplasm: headaches, seizures, dizziness, nausea, weakness, altered mental status, ataxia, diplopia
  - optic neuritis = retrobulbar pain, central loss of vision, afferent pupillary defect (Marcus Gunn pupil)
  - trigeminal neuralgia (1–2%)
- Schumacher criteria:
  (1) CNS dysfunction
  (2) Involvement of two / more parts of CNS
  (3) Predominant white matter involvement
  (4) ≥ 2 episodes lasting > 24 hr less than 1 month apart
  (5) Slow stepwise progression of signs + symptoms
  (6) At onset 10–50 years of age
- Rudick red flags (suggests diagnosis other than MS):
  (1) No eye findings
  (2) No clinical remission

(3) Totally local disease
(4) No sensory findings
(5) No bladder involvement
(6) No CSF abnormality

@ Brain

Location:

subependymal periventricular location (along lateral aspects of atria + occipital horns), corpus callosum, internal capsule, centrum semiovale, corona radiata, optic nerves, chiasm, optic tract, brainstem (ventrolateral aspect of pons at 5th nerve root entry), cerebellar peduncles (CLASSIC), cerebellum; rather symmetric involvement of cerebral hemispheres; subcortical U fibers NOT spared

◊ 10% of MS lesions occur in gray matter!

◊ Number + extent of plaques correlate with duration of disease + degree of cognitive impairment

√ lesion size of 1–25 (majority between 5 and 10) mm:
- √ large lesions may masquerade as brain tumors
- √ mass effect / edema in active lesions (infrequent)

√ ovoid lesions (86%) oriented with their long axis perpendicular to ventricular walls ← perivenous demyelination (pathologically described as "Dawson fingers")

√ chronic plaques do not enhance ← intact blood-brain barrier

√ diffuse cerebral atrophy (21–45–78%) in chronic MS: enlarged ventricles, prominent sulci

√ lesion enhancement ← breakdown of blood-brain barrier in demyelinating process (irrespective of clinical symptoms):
- √ peripheral enhancement of lesion
- √ occasionally central enhancement

CT:
- √ normal CT scan (18%)
- √ periventricular (near atria) multifocal nonconfluent lesions with distinct margins (lesion location does NOT always correlate well with symptoms)
  - (a) NECT: isodense / lucent
  - (b) CECT: transient enhancement during acute stage (active demyelination) for about 2 weeks; may require double dose of contrast; ultimately disappearance / permanent scar

MR (modality of choice; 95–99% specific):
- √ well-marginated discrete foci of varying size with high signal intensity on T2WI + proton density images (= loss of hydrophobic myelin produces increase in water content); hypointense on T1WI
- √ abnormally bright signal of the optic nerve + variable swelling (optic neuritis) with loss of "doughnut" sign of the normal optic nerve complex
- √ Gd-DTPA enhancement of lesions on T1WI (up to 8 weeks following acute demyelination with breakdown of blood-brain barrier)
  - √ characteristically as a solid lesion / incomplete ring
- √ lesions on undersurface of corpus callosum (CHARACTERISTIC on sagittal images)

@ Spinal cord (in up to 80%)

◊ Most common demyelinating process of spinal cord!
◊ In 12–33% without coexistent intracranial plaques!
• number + extent of plaques correlate with degree of disability
Location: predilection for cervical cord
Site: eccentric involvement of dorsal + lateral elements abutting subarachnoid space
√ atrophic plaques oriented along spinal cord axis
√ length of plaque usually less than 2 vertebral body segments + width less than half of cross section
√ acute tumefactive MS = cord swelling with enhancement
√ cord atrophy in chronic MS
DDx: (1) Acute transverse myelitis
(2) Cord tumor (follow-up after 6 weeks without decrease in size of lesion)
(3) Trauma
(4) Infarct
(3) Postviral syndromes
Rx: steroids (incite rapid decrease in size of lesions with loss of enhancement)
DDx:
(1) Acute disseminated encephalomyelitis (ADEM), subacute sclerosing panencephalitis (lesions of similar age)
(2) Lyme encephalopathy (skin rash)
(3) **Susac syndrome** (encephalopathy + branch retinal artery occlusion + hearing loss)
(4) Small vessel ischemia (patients > 50 years of age, lesions < 5 mm, NOT infratentorial)
(5) Enlarged type II Virchow-Robin spaces
(6) AIDS, CNS vasculitis, migraine, radiation injury, lymphoma, sarcoidosis, tuberculosis, systemic lupus erythematosus, cysticercosis, metastases, multifocal glioma, neurofibromatosis, contusions

NEONATAL INTRACRANIAL HEMORRHAGE

Germinal Matrix Bleed

= GERMINAL MATRIX–RELATED HEMORRHAGE
Risk factors:
(1) Prematurity
(2) Low birth weight
(3) Sex (M÷F = 2÷1)
(4) Multiple gestations
(5) Trauma at delivery
(6) Prolonged labor
(7) Hyperosmolarity
(8) Hypocoagulation
(9) Pneumothorax
(10) Patent ductus arteriosus
Etiology: hypoxia with loss of autoregulation

Pathogenesis: rupture of friable vascular bed due to

(1) Fluctuating cerebral blood flow in preterm infants with respiratory distress
(2) Increase in cerebral blood flow with
  (a) systemic hypertension (pneumothorax, REM sleep, handling, tracheal suctioning, ligation of PDA, seizures, instillation of mydriatics)
  (b) rapid volume expansion (blood, colloid, hyperosmolar glucose / sodium bicarbonate)
  (c) hypercarbia (RDS, asphyxia)
(3) Increase in cerebral venous pressure with labor and delivery, asphyxia (= impairment in exchange of oxygen and carbon dioxide), respiratory disturbances
(4) Decrease in cerebral blood flow with systemic hypotension followed by reperfusion
(5) Platelet and coagulation disturbance

Incidence: in premature neonates < 32 weeks of age; in 43% of infants < 1,500 g (in 65% of 500–700 g infants, in 25% of 701–1,500 g infants); in up to 50% without prenatal care, in 5–10% with prenatal care

Time of onset: usually during first 24 hours of life; 36% on 1st day, 32% on 2nd day, 18% on 3rd day of life; by 6th day 91% of all intracranial bleeds have occurred

Location: region of caudate nucleus and thalamostriate groove (= caudothalamic notch) remains metabolically active the longest; in 80–90% in infants < 28 weeks of MA

GRADES (**Papile classification**):

I : subependymal hemorrhage confined to germinal matrix (GMH) on one / both sides
II : subependymal hemorrhage ruptured into nondilated ventricle (IVH)
III : intraventricular hemorrhage (IVH) with ventricular enlargement: (a) mild, (b) moderate, (c) severe
IV : extension of germinal matrix hemorrhage into brain parenchyma (intraparenchymal hemorrhage = IPH)

US (100% sensitivity + 91% specificity for lesions > 5 mm; 27% sensitivity + 88% specificity for lesions ≤ 5 mm):

1. **Germinal matrix hemorrhage** (grade I)
  √ well-defined ovoid area of increased echogenicity (= fibrin mesh within clot) inferolateral to floor of frontal horn ± body of lateral ventricle
  √ bulbous enlargement of caudothalamic groove anterior to termination of choroid plexus
    DDx: choroid plexus (attached to inferomedial aspect of ventricular floor, tapers toward caudothalamic groove, NEVER anterior to foramen of Monro)
  √ resolving bleed develops central sonolucency
  √ outcome: (1) complete involution (2) thin echogenic scar (3) subependymal cyst
2. **Mild intraventricular hemorrhage** (grade II)
  √ echogenic material filling a portion of lateral ventricles (acute phase) becoming sonolucent in a few weeks
  √ clot may gravitate into occipital horns
  √ vertical band of echogenicity between thalami on coronal scans (blood in 3rd ventricle)
  √ irregular bulky choroid plexus (clot layered on surface of choroid plexus)

√ temporarily increased echogenicity of ventricular wall (= subependymal white halo between 7 days and 6 weeks after hemorrhagic event)

3. **Extensive intraventricular hemorrhage** (grade III)
   √ intraventricular cast of blood distending lateral ventricles
   √ ± extension of hemorrhage into basal cisterns, cavum septi pellucidi
   √ hemorrhage becomes progressively less echogenic
   √ temporarily thickened echogenic walls of ventricles ("ventriculitis")
4. **Intraparenchymal hemorrhage** (grade IV)
   Frequency: 5–8%
   Cause: (a) extension of hemorrhage originating from germinal matrix (unusual)
   (b) separate hemorrhage within infarcted periventricular tissue (frequent)
   = **periventricular venous infarction** ← thrombosis of medullary veins draining periventricular brain
   Location: on side of largest amount of IVH, commonly lateral to frontal horns / in parietal lobe, rare in occipital lobe + thalamus
   √ unilateral triangular hemorrhage
   √ homogeneous highly echogenic intraparenchymal mass with irregular margins
   √ central hypoechogenicity (liquefying hematoma after 10–14 days)
   √ retracted clot settles to dependent position (3–4 weeks)
   √ complete resolution by 8–10 weeks results in anechoic area (= porencephalic cyst)

Serial scans: recommended in 5–10-day intervals

CT:

√ hyperdense bleed only visible up to 7 days before it becomes isodense

DDx: subdural hemorrhage, cerebral parenchymal hemorrhage, posterior fossa lesion

MR (gradient-echo, susceptibility-weighted sequences):

√ highest sensitivity for detecting small hemorrhages
√ useful for depicting periventricular venous infarction in grade 4 germinal matrix hemorrhages

Cx:

(1) **Posthemorrhagic hydrocephalus** (30–70%)

◊ Severity of hydrocephalus directly proportional to size of original hemorrhage!

Cause:
(a) temporary blockage of arachnoid villi by particulate blood clot (within days), often transient with partial / total resolution
(b) obliterative fibrosing arachnoiditis often in cisterna magna (within weeks); frequently leads to permanent progressive ventricular dilatation (50%)

√ thickened echogenic ventricular walls

Time of onset: by 14 days (in 80%)

• delayed clinical signs because of compressible premature brain parenchyma

√ ventricular dilatation, particularly affecting the occipital horns (amount of compressible immature white matter is larger posteriorly)

DDx: ventriculomegaly ← periventricular cerebral atrophy (occurring slowly over several weeks)

(2) **Cyst formation**

(a) cavitation of hemorrhage
(b) unilocular subependymal cyst
(c) unilocular porencephalic cyst

(3) Mental retardation, cerebral palsy
(4) Death in 25%
◊ IVH is the most common cause of neonatal death!

Prognosis:
(1) Grade I + II: good with normal developmental scores (12–18% risk of handicap)
(2) Grade III + IV: 54% mortality; 30–40% risk of handicap (spastic diplegia, spastic quadriparesis, intellectual retardation)

Choroid Plexus Hemorrhage

affects primarily full-term infants
Cause: birth trauma, asphyxia, apnea, seizures
√ echogenicity of choroid plexus same as hemorrhage
√ nodularity of choroid plexus
√ enlargement of choroid plexus > 12 mm in AP diameter
√ left-right asymmetry > 5 mm
√ intraventricular hemorrhage without subependymal hemorrhage
Cx: intraventricular hemorrhage (25%)

Intracerebellar Hemorrhage

Cause:
(a) full-term infant: traumatic delivery, intermittent positive pressure ventilation, coagulopathy
(b) premature infant (in 25%): subependymal germinal matrix hemorrhage in external granule cell layer and subependymal layer of roof of 4th ventricle up to 30 weeks GA

Incidence: 16–21% of autopsies
√ echogenicity of vermis same as hemorrhage
√ echogenic mass in less echogenic cerebellar hemisphere (coronal scan most useful)
√ nonvisualization / deformity of 4th ventricle
√ asymmetry in thickness of paratentorial echogenicity is a sign of subarachnoid hemorrhage
Prognosis: poor + frequently fatal

Intraventricular Hemorrhage

Etiology:
(a) germinal matrix hemorrhage ruptures through ependymal lining at multiple sites
(b) bleeding from choroid plexus

Route of hemorrhage:
blood dissipates throughout ventricular system + aqueduct of Sylvius, passes through foramina of 4th ventricle, collects in basilar cistern of posterior fossa

• seizures, dystonia, obtundation, intractable acidosis
• bulging anterior fontanel, drop in hematocrit, bloody / proteinaceous CSF
√ IVH usually clears within 7–14 days
Cx: (1) Intracerebral hemorrhage

(2) Hydrocephalus

Periventricular Leukoencephalopathy

Periventricular Leukomalacia

= WHITE MATTER INJURY OF PREMATURITY

= PVL = perinatal hypoxic-ischemic encephalopathy

= PRINCIPAL ischemic lesion of the premature infant characterized by areas of focal coagulation necrosis of deep white matter (= cystic variant) / more diffuse injury to premyelinating oligodendrocytes (= noncystic variant)

Cause: toxic injury to premyelinating oligodendrocytes ← cerebral ischemia ± reperfusion

Location: peritrigonal area of lateral ventricles and foramen of Monro (= watershed zones in periventricular white matter) involving particularly the centrum semiovale (anterior and lateral to frontal horns + body), optic (occipital horn), and acoustic (temporal horn) radiations

Vascular supply:

(a) ventriculopetal branches penetrating cerebrum from pial surface derived from MCA ± PCA ± ACA

(b) ventriculofugal branches extending from ventricular surface derived from choroidal ± striate arteries

Incidence: 7–22% at autopsy (in 88% of infants between 900 and 2,200 g surviving beyond 6 days); in 34% of infants < 1,500 g; in 59% of infants surviving longer than 1 week on assisted ventilation; MOST FREQUENTLY in infants born < 32 weeks GA

◊ Only 28% detected by cranial sonography!

Histo: edema, white matter necrosis, evolution of cysts + cavities / diminished myelin; nonhemorrhagic÷hemorrhagic PVL = 3÷1

Risk factors: hypotension, hypocarbia, infection, prematurity, asphyxia, sepsis, patent ductus arteriosus, multiple gestation, respiratory distress, maternal hemorrhage

Pathogenesis:

immature autoregulation of periventricular vessels ← deficient muscularis of arterioles limits vasodilation in response to hypoxemia + hypercapnia + hypotension of perinatal asphyxia (hypoxic-ischemic encephalopathy); ischemia reperfusion injury of white matter → free radicals → destruction of progenitor cells of oligodendrocyte with impaired myelination

- "cerebral palsy" (in 6.5% of infants < 1,800 g):
  - spastic diplegia (81%) > quadriparesis (necrosis of descending fibers from motor cortex)
  - choreoathetosis, ataxia, ± mental retardation
- severe visual / hearing impairment, convulsive disorders

US (50% sensitivity + 87% specificity):

Early changes (2 days to 2 weeks after insult)

√ increased periventricular echogenicity (PVE) (DDx: echogenic periventricular halo / blush of fiber tracts in normal neonates, white matter gliosis, cortical infarction extending into deep white matter)

√ bilateral often asymmetric zones, occasionally extending to cortex
√ infrequently accompanied by IVH

Late changes (1–3–6 weeks after development of echodensities):
√ periventricular cystic PVL = cystic degeneration of ischemic areas (= multiple small NEVER septated periventricular cysts in relationship to lateral ventricles; the larger the echodensities, the sooner the cyst formation)
√ brain atrophy ← thinning of periventricular white matter always at trigones, occasionally involving centrum semiovale
√ ventriculomegaly (after disappearance of cysts) with irregular outline of body + trigone of lateral ventricles
√ deep prominent sulci abutting ventricles with little / no interposed white matter (DDx: schizencephaly)
√ enlarged interhemispheric fissure

CT (not sensitive in early phase):
√ periventricular hypodensity (DDx: immature brain with increased water + incomplete myelination)

MR (NOT sensitive in early phase):
√ hypointense areas on T1WI
√ hyperintense periventricular signals on T2WI in peritrigonal region ← delay in maturation / injury
DDx: normal (SI subject to interpretation)
√ thinning of posterior body + splenium of corpus callosum (= degeneration of transcallosal fibers)

Prognosis: major neurologic problem / death in up to 62%; PVL localized to frontal lobes shows relative normal development; PVL in parieto-occipital location > 10 mm in size → cerebral palsy in close to 100%

DDx: tissue damage from ventriculitis (sequelae of meningitis), metabolic disorders, in utero ischemia (eg, maternal cocaine abuse)

Periventricular Hemorrhagic Infarction

= CYSTIC PERIVENTRICULAR LEUKOMALACIA
= leukoencephalopathy resulting from pre- / perinatal hypoxic-ischemic event

Incidence: in 15–25% of infants with IVH

Pathogenesis:
(a) germinal matrix hemorrhage with intraventricular blood clot (in 80%)
(b) ischemic periventricular leukomalacia → obstruction of terminal veins with sequence of venous congestion → thrombosis → infarction

Histo: perivascular hemorrhage of medullary veins near ventricular angle

Associated with: the most severe cases of intraventricular hemorrhage

Age: peak occurrence on 4th postnatal day

• spastic hemiparesis (affecting lower + upper extremities equally) / asymmetric quadriparesis (in 86% of survivors)

Location: lateral to external angle of lateral ventricle on side of the more marked IVH: 67% unilateral; 33% bilateral but asymmetric

Stages: vascular congestion → coagulative necrosis → cavitation

US:

Early changes (hours to days after major IVH):

√ unilateral / asymmetric bilateral triangular "fan-shaped" echodensities

√ extension from frontal to parietooccipital regions / localized (particularly in anterior portion of lesion)

Late changes:

√ single large cyst = porencephaly

√ bumpy ventricle / false accessory ventricle

MR:

√ increased signal intensity in periventricular white matter on T2WI + FLAIR

√ marked loss of periventricular white matter (predominantly in periatrial region)

√ adjacent compensatory focal ventricular enlargement

√ secondary thinning of corpus callosum

√ relative sparing of overlying cortical mantle

√ surrounded by gliosis easily depicted on FLAIR

Prognosis: 59% overall mortality with echodensities > 1 cm; in 64% major intellectual deficits

DDx: enlarged Virchow-Robin spaces

Encephalomalacia

= more extensive brain damage than PVL; may include all of white matter in subcortex + cortex

Associated with:

(1) Neonatal asphyxia

(2) Vasospasm

(3) Inflammation of CNS

US:

√ small ventricles (← edema) with diffuse damage

√ increased parenchymal echogenicity making it difficult to define normal structures

√ decreased vascular pulsations

√ transcranial Doppler:

(a) group I (good prognosis)

√ normal flow profile, normal velocities, normal resistive index

(b) group II (guarded prognosis)

√ increase in peak-systolic + end-diastolic flow velocities + decreased resistive index

(c) group III (unfavorable prognosis)

√ reduced diastolic flow + decreased peak systolic and diastolic velocities + increased resistive index

√ ventricular enlargement + atrophy

√ extensive multicystic encephalomalacia with cysts often not communicating

NEUROCUTANEOUS MELANOSIS

= rare sporadic congenital syndrome characterized by large multiple melanocytic nevi (in 5–15%) + melanotic lesions of CNS (in 40–60%)

Age: first 2 years of life (most); 2nd / 3rd decade (less common); M÷F = 1÷1
Cause: abnormal migration of melanocyte precursors, abnormal expression of melanin-producing genes within leptomeningeal cells, rapid proliferation of melanin-producing leptomeningeal cells
Histo: abnormal abundance of melanotic cells (which are normally found in basilar leptomeninges) with concomitant infiltration of perivascular spaces
• increased intracranial pressure
• seizures, ataxia, cranial nerve VI + VII palsies
√ high attenuation of melanin pigments on CT scan
√ hyperintense on T1WI, hypointense on T2WI (← paramagnetic effect of oxygen-free radicals in melanin)
√ leptomeningeal melanosis = foci of abnormally thickened leptomeninges
Location: inferior surface of cerebellum; inferior surface of frontal, temporal, occipital lobes; ventral aspect of pons; cerebral peduncles; upper cervical spinal cord
√ parenchymal melanosis (less common)
Location: cerebellum, anterior temporal lobes (esp. amygdala)
√ frankly hemorrhagic necrotic invasive mass with transformation into malignant melanoma
√ hydrocephalus
√ posterior fossa cyst
√ cerebellar hypoplasia
√ Dandy-Walker malformation
√ syringomyelia
√ intraspinal arachnoid cyst
√ intraspinal lipoma
Prognosis: rapid deterioration + death within 3 years of diagnosis ← development of malignant melanoma / complication of hydrocephalus

NEUROGLIAL CYST

= GLIOEPENDYMAL CYST = NEUROEPITHELIAL CYST
= rare benign epithelium-lined lesion
Incidence: < 1% of all intracranial cysts
Cause: sequestration of developing neural tube elements during embryogenesis
Histo: rounded smooth unilocular cyst lined by ependymal (columnar epithelium) / choroid plexus cells (low cuboidal epithelium) with CSF-like content
Location: anywhere (typically in frontal lobe); intraparenchymal > extraparenchymal
Size: up to several cm in diameter
• typically asymptomatic; symptomatic if CSF flow obstructed
√ spherical / ovoid lesion of CSF signal intensity:
  √ hyperintense to CSF on T2WI with proteinaceous content
  √ smooth rounded borders
√ NO enhancement, NO adjacent edema, NO soft-tissue mass, NO gliosis
DDx: choroid plexus cyst (commonly abnormal DWI); arachnoid cyst (typically extraaxial); enlarged Virchow-Robin space (no differentiating feature on imaging, typically multiple + clustered around basal ganglia); porencephalic cyst (communication with lateral

ventricle, surrounding gliosis); epidermoid cyst; infectious cyst of neurocysticercosis (< 1 cm, partially enhancing)

NEUROFIBROMATOSIS

= autosomal dominant inherited disorder, probably of neural crest origin affecting all 3 germ cell layers, capable of involving any organ system

Path: frequently combination of

(1) pure neurofibromas (= tumor of nerve sheath with involvement of nerve, nerve fibers run through mass)
  (a) localized neurofibroma (most common, 90%)
  (b) diffuse neurofibroma mostly solitary + not associated with NF1
  (c) plexiform neurofibroma (PATHOGNOMONIC of NF1)
    ◊ Often precedes development of cutaneous neurofibromas!

(2) neurilemmomas (= nerve fibers diverge and course over the surface of the tumor mass)

Histo: proliferation of fibroblasts + Schwann cells

◊ More frequent involvement of deep large nerves (sciatic nerve, brachial plexus) in NF1 in contradistinction to isolated neurofibromas without NF1!

Peripheral Neurofibromatosis (90%)

= NEUROFIBROMATOSIS TYPE 1 = NF1 = VON RECKLINGHAUSEN DISEASE

[Friedrich von Recklinghausen (1833–1910), pathologist in Königsberg, Würzburg and Strasbourg]

= fully penetrant autosomal-dominant disorder with variable expressivity characterized by dysplasia of mesodermal + neuroectodermal tissue with potential for diffuse systemic involvement

Genetics: NF1 gene = tumor suppressor gene localized in the pericentromeric region of chromosome **17** produces neurofibromin that functions as a negative regulator of Ras signaling proteins; 50% represent new spontaneous mutations
  mnemonic: 'von Recklinghausen' has **17** letters

Incidence: 1÷3,000; M÷F = 1÷1; all races
  ◊ One of the most common genetic diseases and phakomatoses!

Predisposing factor: advanced paternal age > 35 years (2-fold increase in new mutations)

Diagnostic clinical criteria (at least two must be present):

(1) ≥ 6 "coast-of-California" café-au-lait spots
  › > 5 mm in diameter in prepubertal individuals
  › > 15 mm in diameter in postpubertal individuals
(2) ≥ 2 neurofibromas of any type / ≥ 1 plexiform neurofibroma
(3) Intertriginous freckling (Crowe sign) in axilla / inguina
(4) Optic pathway glioma
(5) ≥ 2 Lisch nodules = pigmented iris hamartomas
(6) Characteristic skeletal lesion
  › sphenoid bone dysplasia
  › dysplasia + thinning of long bone cortex

(7) 1st-degree relative (parent, sibling, child) with NF1

CLASSIC TRIAD:

(1) Cutaneous lesions
(2) Skeletal deformity
  ◊ Musculoskeletal abnormalities predominate in NF1!
(3) Mental deficiency

May be associated with:

(1) MEA IIb (pheochromocytoma + medullary carcinoma of thyroid + multiple neuromas)
(2) CHD (10 fold increase): pulmonary valve stenosis, ASD, VSD, IHSS

Cx: malignant transformation to malignant neurofibroma + malignant schwannoma (2–5–29%), glioma, xanthomatous leukemia

Rapid episodes of growth of neurofibromas:

puberty, pregnancy, malignancy

CNS Manifestations of NF1

@ Intracranial

1. Optic pathway glioma
2. **Cerebral glioma** astrocytomas of tectum, brainstem, gliomatosis cerebri (= unusual confluence of astrocytomas)
3. **Hydrocephalus** obstruction usually at aqueduct of Sylvius
   Cause: benign aqueductal stenosis, glioma of tectum / tegmentum of mesencephalon
4. **Vascular dysplasia**
   = occlusion / stenosis of distal internal carotid artery, proximal middle / anterior cerebral artery
   √ moyamoya phenomenon (60–70%)
5. **Neurofibroma** of cranial nerves III–XII (most commonly V + VIII)
   ◊ 30% of patients with solitary neurofibromas have NF1
   ◊ Virtually all patients with multiple neurofibromas have NF1
6. **Craniofacial plexiform neurofibroma**
   = locally aggressive congenital lesion composed of tortuous cords of Schwann cells, neurons and collagen with progression along nerve of origin (usually small unidentified nerves)
   Location: commonly orbital apex, superior orbital fissure
   ◊ Plexiform neurofibromas are PATHOGNOMONIC for NF1
7. **CNS hamartoma** (up to 75–90%)
   = probably dysmyelinating lesion (may resolve)
   Location: pons, basal ganglia (most commonly in globus pallidus), thalamus, cerebellar white matter
   √ multiple foci of isointensity on T1WI + hyperintensity on T2WI without mass effect (= "unidentified bright objects")
8. **Vacuolar / spongiotic myelinopathy** (in 66%)
   Location: basal ganglia (esp. in globus pallidus), cerebellum, internal capsule, brainstem
   √ nonenhancing hyperintense foci on T2WI

@ Spinal cord

1. **Cord neurofibroma**
   - √ smooth round / tubular masses of varying sizes at nearly every level throughout spinal canal
   - √ spinal cord displaced to contralateral side
   - √ enlargement of neural foramen ← "dumbbell" neurofibroma of spinal nerves (in 30%)
   - √ smooth fusiform / spherical mass:
     - √ hypoattenuating mass (20–30 HU) in up to 73% ← cystic degeneration, xanthomatous features, confluent areas of hypocellularity, lipid-rich Schwann cells
     - √ areas of higher attenuation ← densely cellular components / collagen-rich regions
     - √ slightly hyperintense to muscle on T1WI, hyper-intense periphery + hypointense core on T2WI
     - √ hypoechoic heterogeneous well-circumscribed cylindrical lesion with variable through transmission
2. **Paraspinal / presacral plexiform neurofibroma**

   = regional enlargement of nerve root trunk (plexus / multiple fascicles of medium to large nerve); exclusive to NF1

   Localized and plexiform neurofibromas of the paraspinal and sacral region are the most common abdominal neoplasm in NF1.

   Location: retroperitoneal along lumbosacral plexus adjacent to psoas muscle at single / multiple vertebral body levels

   Form: ropelike = involving non-branching nerves; "bag of worms" = in branching nerves

   - √ heterogeneous echotexture with variable through transmission
   - √ smooth round / tubular symmetric / asymmetric paraspinal masses within / adjacent to psoas m.:
     - √ homogeneously hypoattenuating (20–25 HU) in up to 73% ← myxoid + mucinous stroma
     - √ focal areas of higher attenuation ← excessive collagen
     - √ homo- / heterogeneous enhancement to 30–50 HU on CECT in 50%
   - √ enlargement of adjacent neural foramen in 30%

   Cx: malignant degeneration
3. **Lateral / anterior intrathoracic meningocele**

   = diverticula of thecal sac extending through widened neural foramina / defects in vertebra

   Cause: dysplasia of meninges focally stretched by CSF pulsations ← pressure differences between thoracic + subarachnoid space superimposed on osseous vertebral defect

   - √ erosion of bony elements with marked posterior scalloping
   - √ widening of neural foramina ← protrusion of spinal meninges

   DDx: mediastinal / lung abscess

Skeletal Manifestations of NF1 *(in 25–40%)*

= skeletal dysplasias + pseudarthroses

Age: during first year of life

@ Orbit

√ Harlequin appearance to orbit = sphenoid wing dysplasia = partial absence of greater and lesser wing of sphenoid bone + orbital plate of frontal bone ← failure of development of membranous bone

√ hypoplasia + elevation of lesser wing of sphenoid

√ defect in sphenoid bone ± extension of middle cranial fossa structures into orbit

√ concentric enlargement of optic foramen ← optic glioma

√ enlargement of orbital margins + superior orbital fissure ← plexiform neurofibroma of peripheral and sympathetic nerves within orbit / optic nerve glioma

√ sclerosis in the vicinity of optic foramen ← optic nerve sheath meningioma

√ deformity + decreased size of ipsilateral ethmoid and maxillary sinuses

@ Skull

√ macrocranium + macroencephaly

√ left-sided calvarial defect adjacent to lambdoid suture = parietal mastoid (rare)

@ Spine

• dwarfism caused by scoliosis

√ sharply angled focal kyphoscoliosis (50%) in lower thoracic + lumbar spine; kyphosis predominates over scoliosis; incidence increases with age

Cause: abnormal development of vertebral bodies

√ hypoplasia of pedicles + transverse + spinous processes

√ posterior scalloping of vertebral bodies ← dural ectasia ← weakened meninges allowing transmission of normal CSF pulsations

√ dumbbell-shaped enlargement of neural foramina

@ Appendicular skeleton

√ anterolateral bowing of lower half of tibia (most common) / fibula (frequent) / upper extremity (uncommon) secondary to deossification → thinning → pathologic fracture

√ pseudarthrosis / nonunion after bowing fracture in 1st year of life

Location: tibia, fibula

√ atrophic thinned / absent fibula

√ periosteal dysplasia = traumatic subperiosteal hemorrhage with abnormally easy stripping of periosteum from bone

√ subendosteal sclerosis

√ bone erosion from periosteal / soft-tissue neurofibroma

√ intramedullary longitudinal streaks of increased density

√ multiple nonossifying fibromas / fibroxanthomas

√ single / multiple cystic lesions within bone ← deossification / nonossifying fibroma

√ focal gigantism = unilateral overgrowth of a limb bone ← overgrowth of ossification center

Site: marked enlargement of a digit in a hand / foot

Pulmonary Manifestations of NF1

@ Lung

- exertional dyspnea

√ intrathoracic lateral + anterior meningoceles

√ peripheral pulmonary nodule = pedunculated intercostal neurofibroma

√ progressive pulmonary interstitial fibrosis with lower lung field predominance (in up to 20%)

√ large thin-walled bullae with asymmetric upper lobe predominance

@ Mediastinum

◊ Neurogenic tumors account for 9% of primary mediastinal masses in adults + 30% in children

√ mediastinal mass:

√ well-marginated smooth round / elliptic mass

√ extensive fusiform / infiltrating mass

√ paravertebral neurofibroma

@ Chest wall

√ numerous small well-defined subcutaneous neurofibromas

√ twisted "ribbonlike" ribs in upper thoracic segments ← bone dysplasia / multiple neurofibromas of intercostal nerves:

√ localized cortical notches / depression of inferior margins of ribs (DDx: aortic coarctation)

√ chest wall mass invading / eroding / destroying adjacent rib

Abdominal Tumors in NF1

A. NEUROGENIC TUMORS IN NF1
   1. Neurofibroma
   2. Plexiform neurofibroma
   3. Malignant peripheral nerve sheath tumor
   4. Ganglioneuroma
   5. Ganglioneuromatosis

B. NEUROENDOCRINE TUMORS IN NF1
   1. Periampullary carcinoid
   2. Pheochromocytoma in adults
      Location: solitary + unilateral (84%); bilateral (10%); extraadrenal (6%)
   3. Paraganglioma

C. OTHER TUMORS ASSOCIATED WITH NF1
   1. GIST
   2. Embryonal tumor
   3. Adenocarcinoma
   4. Parathyroid adenoma
      - hyperparathyroidism

Vascular Lesions in NF1

= Schwann cell proliferation within vessel wall

Age: common in childhood

1. Cranial artery stenosis
2. Renal artery stenosis: very proximal, funnel-shaped

◊ Renal artery stenosis in NF1 is one of the most common causes of hypertension in childhood!

3. Renal artery aneurysm
4. Thoracic / abdominal aortic coarctation

GI Tract Manifestations in NF1 *(10–25%)*

Neurofibromas appear as well-defined masses but frequently infiltrate into adjacent fat, muscle, or viscera → local recurrence after resection is common.

1. Neurofibroma
   - most clinically occult
   - intestinal bleeding (hematemesis, melena, hematochezia) with mucosal involvement
   - obstruction with nausea, vomiting, abdominal distension (intussusception, volvulus, simulating Hirschsprüng disease with plexiform neurofibromas of colon)

   Location: jejunum > stomach > ileum > duodenum
   Site: myenteric > mesenteric / subserosal plexus
   Associated with: increased prevalence of carcinoid tumors + GI stromal tumors
   (a) single / **solitary neurofibroma**, neuroma, ganglioneuroma, schwannoma
   √ subserosal / submucosal filling defect ("**mucosal ganglioneurofibromatosis**")
   √ displacement of intestine
   √ external mass effect on serosal surface
   √ infiltrating submucosal / mucosal polypoid masses
   √ lobular mural thickening of soft-tissue attenuation with variable amount of luminal narrowing ← infiltration through intestinal wall
   (b) **mesenteric plexiform neurofibroma**
   Location: common in perirectal space
   Site: from root of mesentery to wall of intestine
   √ mass effect on adjacent barium-filled loops
   √ multiple eccentric polypoid filling defects involving mesenteric side of small bowel
   √ mesenteric fat trapped within entangled network (15–30 HU) CHARACTERISTIC
   √ multiple leiomyomas ± mucosal ulcers
   Cx: intussusception
2. Malignant peripheral nerve sheath tumor
   ◊ Most common malignant abdominal tumor in NF1
3. Ganglioneuroma
4. Carcinoid
   - more common in NF1 than in general population

   Location: near ampulla of Vater
   Histo: psammomatous somatostatinoma
5. Gastrointestinal stromal tumor

Genitourinary Manifestations of NF1 (rare)

1. Renal artery stenosis
   √ plexiform neurofibroma with vascular narrowing

2. Urinary bladder neurofibroma
   Origin: vesicoprostatic (male) / urethrovaginal neural plexus (female)
   • symptoms of urinary tract obstruction: frequency, urgency, incontinence, hematuria, abdominal pain
   √ solitary hypoechoic bladder wall mass
   √ diffuse bladder wall thickening; mass may surround uterus, vagina, sigmoid colon
   √ scalloped contour of urinary bladder
   Cx: hydronephrosis

Ocular Manifestations in NF1 *(6%)*
- pulsatile exophthalmos / unilateral proptosis (herniation of subarachnoid space + temporal lobe into orbit)
- buphthalmos

1. Plexiform neurofibroma (most common)
2. **Lisch nodules**
   = PATHOGNOMONIC asymptomatic melanocytic iris hamartomas < 2 mm in size
   • yellow / brown pigmented nodular elevations projecting from surface of iris; mostly bilateral
   • asymptomatic
   Age: 5–10 years; > 20 years of age in > 90%
3. **Optic glioma** (in 12% of patients, in 4% bilateral)
   Age: 75% in 1st decade
   √ extension into optic chiasm (up to 25%), optic tracts, optic radiation
   √ increased intensity on T2WI if chiasm and visual pathway involved
4. Perioptic meningioma
5. Choroidal hamartoma: in 50% of patients

Skin Manifestations in NF1
1. **Café-au-lait spots**
   = tan / light brown pigmented often ovoid cutaneous macules + patches with irregular borders
   ≥ 6 in number >
   5 mm in greatest diameter prior to puberty
   > 15 mm in postpubertal individuals
   • randomly distributed
   • "**coast of California**" type (= smooth outline)
   DDx: "coast-of-Maine" spots of McCune-Albright syndrome (with more jagged borders)
   Age: usually present at birth, increase in number over first 1–2 years of life
   ◊ One of the earliest manifestations of NF1
   Histo: increased melanin pigment in basal epidermal layer
   DDx: tuberous sclerosis, fibrous dysplasia
   Extent: often parallels disease severity
2. Intertriginous freckling (= Crowe sign)
   = pigmented cutaneous macules < 5 mm in size

Age: 3–5 years
Location: intertriginous skin of axilla (in 66%), groin, submammary fold, neck

3. Dermal (cutaneous) neurofibroma
Histo: benign mixture of Schwann cells + fibroblasts + perineural cells + mast cells
Age: begins to appear around early childhood / puberty subsequent to detection of café-au-lait spots
(a) localized = **fibroma molluscum** = string of pearls along peripheral nerve
• firm well-circumscribed movable tumor
• soft compressible fleshy nodule of cutis
• firm rubbery nodule of subcutis
Cx: NO malignant degeneration!
(b) **plexiform neurofibroma** = multilobulated tortuous entanglement / interdigitating network of tumor along a nerve and its branches
◊ Exclusively seen in NF1 (in 30%)
Age: noticeable by 4–5 years
• soft gritty often hyperpigmented tumor feeling like a "bag of worms / braided ropes"
• may become very large hanging in a pendulous fashion associated with massive disfiguring enlargement of an extremity (= **elephantiasis neuromatosa**)
√ ± osseous hypertrophy ← chronic hyperemia
Cx: may transform to malignant peripheral nerve sheath tumor (MPNST = neurofibrosarcoma) in 10%!
Dx: new onset of pain / neurologic deficit / rapid growth associated with preexisting plexiform neurofibroma → FDG-PET
(c) **diffuse neurofibroma**
Location: most common in subcutaneous tissue

Neurofibromatosis with Bilateral Acoustic Neuromas

= NEUROFIBROMATOSIS TYPE 2 = NF 2 = CENTRAL NEUROFIBROMATOSIS
= rare autosomal dominant syndrome characterized by propensity for developing multiple schwannomas, meningiomas, and gliomas of ependymal derivation *mnemonic:* MISME
Multiple Inherited Schwannomas
Meningiomas
Ependymomas
Incidence: 1÷50,000 births
Etiology: deletion on the long arm of chromosome 22; in 50% new spontaneous mutation
mnemonic: Neurofibromatosis **2** is located on chromosome **22**!
Symptomatic age: during 2nd / 3rd decade of life
Diagnostic criteria:
(1) bilateral 8th cranial nerve masses
(2) first-degree relative with unilateral 8th nerve mass, neurofibroma, meningioma, glioma (spinal ependymoma), schwannoma, juvenile posterior subcapsular lenticular opacity

• NO Lisch nodules, skeletal dysplasia, optic pathway glioma, vascular dysplasia, learning disability
• café-au-lait spots (< 50%): pale and < 5 in number

• cutaneous neurofibroma: minimal in size + number / absent

@ Intracranial

1. Bilateral acoustic schwannomas (SINE QUA NON)
   Site: superior / inferior division of vestibular nerve
   √ usually asymmetric in size
2. Schwannoma of other cranial nerves
   Frequency: trigeminal nerve > facial nerve
   ◊ Nerves without Schwann cells are excluded: olfactory nerve, optic nerve
3. Multiple meningiomas: intraventricular in choroid plexus of trigone, parasagittal, sphenoid ridge, olfactory groove, along intracranial nerves
4. Meningiomatosis = dura studded with innumerable small meningiomas
5. Glioma of ependymal derivation

@ Spinal

• symptoms of cord compression

A. Extramedullary
   1. Multiple paraspinal neurofibromas
   2. Meningioma of spinal cord (esp. in thoracic region)

B. Intramedullary
   1. Spinal cord ependymomas

NEUROMA

= ambiguous term and misnomer (really a schwannoma rather than a tumor of actual nerve tissue)!

Prevalence: 8% of all intracranial tumors

Age: 20–50 years

• slow growth; not painful

Vestibular Schwannoma

= ACOUSTIC NEUROMA = ACOUSTIC SCHWANNOMA
= NEURILEMMOMA

[Theodor Ambrose Hubert Schwann (1810–1882), German anatomist and physiologist, professor of physiology and comparative anatomy in Louvain and at the State University of Liège, Belgium]

◊ Most common neoplasm of internal auditory canal / cerebellopontine angle!

Prevalence: 6–10% of all intracranial tumors; 85% of all intracranial neuromas; 60–90% of all cerebellopontine angle tumors

Age: (a) sporadic tumor: 35–60 years; M÷F = 1÷2
(b) type 2 neurofibromatosis: 2nd decade

Histo:

encapsulated neoplasm composed of proliferating fusiform Schwann cells with
(a) highly cellular dense regions (Antoni A) with reticulin + collagen, and
(b) loose areas with widely separated cells (Antoni B) in a reticulated myxoid matrix; common degenerative changes with cyst formation, vascular features, lipid-laden foam cells

May be associated with: central neurofibromatosis (NF2)

◊ Solitary intracranial schwannoma is associated with type 2 neurofibromatosis in 5–25%!
◊ Bilateral acoustic schwannomas allow a presumptive diagnosis of type 2 neurofibromatosis!

- long history of slowly progressive unilateral sensorineural hearing loss mostly for high-frequency sounds (in 95%)
- tinnitus, pain; diminished corneal reflex
- unsteadiness, vertigo, ataxia, dizziness (< 10%)

Doubling time: 2 years

Location:

(a) arises from within internal auditory canal (IAC) in 80% / cochlea
(b) may arise in cerebellopontine angle cistern at opening of IAC (= porus acusticus) with intracanalicular extension in 5%

Site: (a) in 85% from the vestibular portion of 8th nerve (around vestibular ganglion of Scarpa / at the glial-Schwann cell junction) posterior to cochlear portion
[Antonio Scarpa (1752–1832), professor of anatomy at the Università di Pavia, Lombardia, Italy]
(b) in 15% from the cochlear portion

√ round mass centered on long axis of porus acusticus forming acute angles with dural surface of petrous bone
√ funnel-shaped component extending into IAC
√ IAC enlargement / erosion (70–90%)
√ widening / obliteration of ipsilateral cerebellopontine angle cistern
√ shift / asymmetry of 4th ventricle with hydrocephalus
√ degenerative changes (cystic areas and hemorrhage) with tumors > 2–3 cm

Plain film:

√ flaring porus acusticus
√ erosion of IAC: a difference in canal heights of > 2 mm is abnormal + indicates a schwannoma in 93%

CT:

√ small isodense / large hypodense solid tumor
√ cyst formation in tumor (= central necrosis in 15% of large tumors) / coexistent extramural arachnoid cyst adjacent to tumor
√ usually uniformly dense tumor enhancement with small tumors (50% may be missed without CECT) / ring enhancement with large tumors
√ NO calcification
√ intrathecal contrast / carbon dioxide insufflation (for tumors < 5 mm)

MR (most sensitive test with Gd-DTPA enhancement):

√ iso- / slightly hypointense relative to gray matter on T1WI
√ intensely enhancing homogeneous mass / ringlike enhancement (if cystic) after Gd-DTPA
√ hyperintense on T2WI relative to gray matter (DDx: meningioma remains hypo- / isointense)

Angio:

√ elevation + posterior displacement of anterior inferior cerebellar artery (AICA) on basal view
√ elevation of the superior cerebellar artery (large tumors)

√ displacement of basilar artery anteriorly / posteriorly and to contralateral side
√ compression / posterior and lateral displacement of petrosal vein
√ posterior displacement of choroid point of PICA
√ vascular supply frequently from ECA branches
√ rarely hypervascular tumor with tumor blush
DDx: ossifying hemangioma (bony spiculations)

Trigeminal Schwannoma

= TRIGEMINAL NEUROMA
Incidence: 2–5% of intracranial neuromas, 0.26% of all brain tumors
Origin: arising from gasserian ganglion within Meckel cave at the most anteromedial portion of the petrous pyramid / trigeminal nerve root
[Johann Lorentz Gasser (1723–1765), Austrian anatomist at the Universität Wien, Österreich]
Age: 35– 60 years; M÷F = 1÷2
• symptoms of location in middle cranial fossa:
  • facial paresthesia / hypesthesia
  • exophthalmos, ophthalmoplegia
• symptoms of location in posterior cranial fossa:
  • facial nerve palsy
  • hearing impairment, tinnitus
  • ataxia, nystagmus
Location: (in any segment of trigeminal nerve)
(a) middle cranial fossa (46%) = gasserian ganglion
(b) posterior cranial fossa (29%)
(c) in both fossae (25%)
(d) pterygoid fossa / paranasal sinuses (10%)
√ erosion of petrous tip
√ enlargement of contiguous fissures, foramina, canals
√ dumbbell / saddle-shaped mass (extension into middle cranial fossa + through tentorial incisura into posterior fossa)
√ isodense mass with dense inhomogeneous enhancement ← tumor necrosis + cyst formation
√ distortion of ipsilateral quadrigeminal cistern
√ displacement + cutoff of posterior 3rd ventricle
√ anterior displacement of temporal horn
√ angiographically avascular / hypervascular mass

NEUROSYPHILIS

= consequence of hematogenous dissemination
Risk of progression: 3% if treated with penicillin; accelerated in cell-mediated immunodeficiency (HIV, AIDS)
Types:
(1) **Meningeal neurosyphilis**
Latency period: < 2 years
√ thick nodular meninges + gummas (similar to tuberculosis / sarcoidosis)

(2) **Vascular neurosyphilis**
Latency period: 5–7 years
√ alternating arterial stenoses + dilatations ← large-vessel arteritis
√ parenchymal edema ← perivascular extension of subarachnoid infection / from rare deposition of cerebral gummas
Cx: large- / small-vessel infarctions

(3) **General paresis**
Latency period: 10–20 years

(4) **Tabes dorsalis**
Latency period: 15–20 years

OLIGODENDROGLIOMA

= uncommon form of slowly growing glioma presenting with large size at time of diagnosis

Incidence: 0.3÷100,000 annually; 3rd most common glioma; 2–5% of all primary brain tumors; 5–25% of all glial neoplasms; < 1% of pediatric CNS neoplasms

Path: (a) well-differentiated oligodendroglioma
(b) anaplastic oligodendroglioma (20–54%)
(c) "mixed glioma" containing neoplastic astrocytes (9%)

Histo: monotonous "fried-egg" appearance = uniformly rounded hyperchromatic nuclei surrounded by perinuclear halo of clear cytoplasm; "chicken-wire" pattern = delicate branching network of capillaries; little mitotic activity

Genetics: deletion of alleles at chromosome loci 19q (50–80%) and 1p (40–92%) in well-differentiated tumors

Median age: 35–45 years; M÷F = 2÷1; adult÷child = 8÷1, 6% in childhood (2nd peak at 6–12 years)
◊ Older age is associated with more aggressive tumor behavior!

- long clinical presentation > 5 years
- seizures (35–85%), headache, mental status change
- paralysis (50%), visual loss (49%), papilledema (47%)
  ◊ Worse prognosis with neurologic deficit!
- ataxia (39%), abnormal reflexes (37%), meningismus (10%)

Location:
(a) supratentorial: frontal lobe (50–65%); temporal lobe (47%); parietal lobe (7–20%); occipital lobe (1–4%)
(b) infratentorial: cerebellum (3%); brainstem & spinal cord (1%)
(c) others: leptomeninges ("**oligodendrogliomatosis**"); cerebellopontine angle; cerebral ventricles (3–8%) = "**subependymal oligodendroglioma**"; retina, optic n.

Site: mostly involving cortical gray matter and subcortical white matter; occasionally through corpus callosum as "**butterfly glioma**"

√ round / oval usually sharply marginated mass
√ large nodular clumps of calcifications (in 45% on plain film; in 20–91% on CT)

CT:
√ hypodense (60%) / isodense (23%) / hyperdense (6%) mass
◊ May NOT AT ALL be detectable by CT!

√ cystic degeneration (frequent)
√ hemorrhage (uncommon)
√ ± erosion of inner table of skull (exophytic growth)

CECT:
√ may be adherent to dura (mimicking meningiomas)
√ surrounding vasogenic edema (in 50% of low-grade, in 80% of high-grade tumors)
√ subtle ill-defined enhancement (15–20%) associated with high-grade tumor

MR:
√ well-circumscribed tumor of heterogeneous intensity:
√ hypo- / isointense compared to gray matter on T1WI
√ hyperintense compared to gray matter on T2WI
√ hyperintense signal on DWI + low ADC values in solid tumor portion of high-grade tumors ← restricted water diffusion + lowered extracellular hyaluronic acid
√ little edema / mass effect (common)
√ solid / mixed moderate peripheral enhancement:
› moderate to strong for high-grade glioma
› minimal / none for low-grade glioma
N.B.: lack of enhancement does not equal low-grade
√ calcification may not be detected

SPECT (^{201}Tl) & PET (^{11}C-L–methylmethionine):
√ metabolic rate correlates with histologic grade
√ detects hypermetabolic regions within tumor

Prognosticators of malignant behavior:
› increasing age of patient
› mass effect, cyst formation, necrosis
› moderate to strong enhancement ← disruption of blood-brain barrier
<u>however:</u> up to 25% of high-grade gliomas show faint / no enhancement
› ↓ ADC values in non-enhancing solid tumor portion of high-grade tumor
› ↑ rCBV on perfusion MRI in solid portions + peritumoral region ← tumor neoangiogenesis

Cx: leptomeningeal seeding via CSF (1–15%)

Rx: gross total resection; PCV chemotherapy (procarbazine, lomustine, vincristine); irradiation reserved for chemotherapy failure

Prognosis: 46% 10-year survival rate with low-grade; 20% 10-year survival rate with high-grade; 3–17 years median postop survival

DDx: (1) Astrocytoma (no large calcifications)
(2) Ganglioglioma (in temporal lobes + deep cerebral tissues
(3) Ependymoma (enhancing tumor, often with internal bleeding producing fluid levels)
(4) Glioblastoma (infiltrating, enhancing, edema, NO calcifications)
(5) Central neurocytoma

OSMOTIC DEMYELINATION SYNDROME

= CENTRAL PONTINE MYELINOLYSIS = OSMOTIC MYELINOLYSIS

Predisposed: chronic alcoholic with liver failure (60–70%); malnourished patient; chronically debilitated transplant recipient (liver transplantation with cyclosporine use);

prolonged use of diuretics; extensive burns

Etiology: unknown; comatose patient receiving rapid correction / overcorrection of severe hyponatremia > 12 mmol/L/d (following prolonged IV fluid administration)

Pathophysiology:

rapid correction of sodium → release of myelinotoxic compounds by gray matter components → destruction of myelin sheaths of oligodendrocytes (osmotic myelinolysis with intramyelinitic splitting, vacuolization, rupture of myelin sheath); preservation of neurons + axons

Histo: abundant foamy histiocytes without lymphocytes / neutrophils; luxol fast blue staining demarcates demyelination; neurofilament staining shows preserved neuronal axons

Age: middle age; M > F

- spastic quadriplegia + pseudobulbar palsy (= head and neck weakness, dysphagia, dysarthria)
- encephalopathy with seizures + acute mental status change
- progression to pseudocoma (locked-in syndrome) in 3–5 days
- serial measurements of serum sodium

Location: (a) isolated pons lesion (most commonly)

(b) combined type = central pons + extrapontine areas: globus pallidus, putamen, thalamus, cerebellar white matter, lateral geniculate body, caudate nucleus, subcortical cerebral white matter, corona radiata, hippocampi

typically spared: ventrolateral pons; pontine portion of corticospinal tract

CT:

√ diminished attenuation in central basilar region of pons without mass effect

√ hypoattenuated areas in basal ganglia + thalamus

MR (positive 1–2 weeks post-onset of symptoms):

√ single central symmetric midline pons lesion:

√ hyperintense symmetric trident-shaped / round (coronal scan) + bat-wing configuration (sagittal scan) on T2WI + FLAIR

√ hypointense / (less commonly) isointense on T1WI

√ sparing of ventrolateral pons + pontine portions of corticospinal tracts

√ bilateral symmetric well-demarcated lesions in basal ganglia ± other extrapontine sites

√ ± restricted diffusion (24 hours after onset of symptoms)

√ no enhancement of lesions

Prognosis: 5–10% survival rate beyond 6 months; significant neurologic sequelae (in most)

DDx: hypoxia, Leigh disease, Wilson disease

PARAGONIMIASIS OF BRAIN

= Oriental lung fluke (Paragonimus westermani) producing arachnoiditis, parenchymal granulomas, encapsulated abscesses

√ isodense / inhomogeneous masses surrounded by edema

√ ring enhancement

PELIZAEUS-MERZBACHER DISEASE

[Friedrich Christoph Pelizaeus (1851–1942), neurologist and balneologist in Nassau, Ilmenau, Kreischa and Bad Oeynhausen, Germany]

[Ludwig Merzbacher (1875–1942), neuropathologist and psychiatrist in Freiburg, Heidelberg and at the University of Tübingen, Germany and chief physician at German Hospital in Buenos Aires, Argentina]
= rare X-linked sudanophilic leukodystrophy (5 types with different times of onset, rate of progression, genetic transmission)
Age: neonatal period
• bizarre pendular nystagmus + head shaking; cerebellar ataxia
• slow psychomotor development
CT:
√ hypodense white matter
√ progressive white matter atrophy
MR:
√ lack of myelination (appearance of newborn brain retained)
√ hyperintense internal capsule, optic radiations, proximal corona radiata on T1WI
√ near complete absence of hypointensity in supratentorial region on T2WI
√ mild / moderate prominence of cortical sulci
Prognosis: death in adolescence / early adulthood

PERSISTENT EMBRYONIC INFUNDIBULAR RECESS

= rare congenital malformation of neurohypophysis
• abnormal pituitary function
√ unusual expansion of anterior aspect of 3rd ventricle into sella with loss of normal contours of recesses
√ empty sella = expansion of sella + thinning of pituitary

PICK DISEASE

[Arnold Pick (1851–1924), professor of psychiatry and neurology at the German University in Prague]
= FRONTOTEMPORAL DEMENTIA
= rare form of presenile dementia similar to Alzheimer disease; may be inherited with autosomal dominant mode; M < F
• social impairment + disinhibitive and impulsive behavior
√ focal cortical atrophy of anterior frontal + anterior temporal lobes
√ dilatation of frontal + temporal horns of lateral ventricle
PET:
√ hypometabolism in frontal + anterior temporal lobes + anterior cingulate gyrus
√ temporal lobe involvement extends to anterior aspects (NOT in Alzheimer disease)
√ frontal-predominant form = sparing of temporal lobes

PINEAL CYST

= small nonneoplastic cyst of pineal gland
Incidence: 25–40% on autopsy; 4–23% on imaging
Age: any, predominantly 40–49 years; M < F
Origin:

(a) developmental = persistence of ependymal-lined pineal diverticulum
(b) degenerative = glial-lined secondary cavitation within area of gliosis

Path: uni- / multilocular cyst; inner layer = gliotic tissue, middle layer = pineal parenchymal tissue, outer layer = connective tissue; proteinaceous / hemorrhagic cyst fluid

• rarely cause of hydrocephalus (← compression / occlusion of aqueduct) with headache / visual change
• NEVER associated with Parinaud syndrome

Size: 2–15 mm, remaining stable over time; may be symptomatic if > 15 mm

√ round / oval thin-walled well-circumscribed cyst
√ ± calcification

CT:
√ normal-sized gland (80%), slightly > 1 cm in 20%, can be > 2 cm in size
√ isodense to CSF in surrounding cistern (infrequently noted)

MR:
√ isointense to CSF on T1WI; may have higher signal intensity than CSF ← high protein content
√ slightly hyperintense to CSF on T2WI ← phase coherence in cyst but not in moving CSF
√ signal not completely suppressed on FLAIR ← proteinaceous content
√ typically incomplete enhancement of cyst wall ← fragmentation of pineal parenchyma as cyst enlarges
√ appearance of a solid mass on delayed contrast images (contrast may diffuse from enhanced rim of residual pineal tissue into fluid center ← NO blood-brain barrier)
√ slight impression on superior colliculi (sagittal image)

Prognosis: lack of growth over 9 years (in 75%); rarely "pineal apoplexy" = intracystic hemorrhage

Follow-up: for cysts ≥ 10 mm

DDx: cystic tumors (astrocytoma, pineocytoma, pineoblastoma)

PINEAL TERATOCARCINOMA

= highly malignant variant of germ cell tumors

Types:
1. Choriocarcinoma
2. Embryonal cell carcinoma
3. Endodermal sinus tumor

Histo: arising from primitive germ cells, frequently containing more than one cell type

Age: < 20 years; males

• Parinaud syndrome
• tumor markers elevated in serum + CSF

√ intratumoral hemorrhage (esp. choriocarcinoma)
√ invasion of adjacent structures
√ intense homogeneous contrast enhancement

Cx: seeding via CSF

PINEAL CELL TUMORS

= TUMORS OF PINEAL PARENCHYMAL ORIGIN

Incidence: < 0.2% of intracranial neoplasms

Histo: neuroepithelial neoplasm arising from pineocytes / their precursors

√ similar imaging appearance

√ peripheral displacement of preexisting normal pineal calcification (= "exploded pineal calcification pattern")

Pineoblastoma (40%)

= highly malignant tumor derived from primitive pineal parenchymal cells

Histo: unencapsulated highly cellular primitive embryonal neoplasm composed of diffuse sheets of small round cells with scant cytoplasm (similar to medulloblastoma, neuroblastoma, retinoblastoma) ±

(a) Homer-Wright rosettes (neuroblastic differentiation), or

(b) Flexner-Wintersteiner rosettes (retinoblastic differentiation)

Age: any age, most common in first 2 decades; M÷F = 1÷1

√ usually large lobulated mass

√ obstructive hydrocephalus in almost 100%

CT:

√ poorly marginated iso- / typically hyperdense mass

√ may contain dense tumor calcifications

√ intense homogeneous contrast enhancement

MR:

√ heterogeneous with solid portion iso- / moderately T1 hypointense on T1WI + iso- / mildly T2 hyperintense

√ reduced perfusion ← increased cellularity

√ dense heterogeneous Gd-DTPA enhancement

Cx: hemorrhage, necrosis, spread

Spread:

(1) direct extension posteriorly with invasion of cerebellar vermis + anteriorly into 3rd ventricle

(2) CSF dissemination (frequent) along meninges / via ventricles as most common cause of death

N.B.: common CSF dissemination → image the entire craniospinal axis!

Prognosis: 58% 5-year survival after resection

Pineal Tumor of Intermediate Differentiation (20%)

Age: any with peak in early adulthood; M < F

Histo: diffuse sheets of uniform cells + formation of small rosettes; low to moderate levels of mitotic activity + nuclear atypia

Prognosis: 39–74% 5-year survival after resection

Pineocytoma (14–60%)

= rare slow-growing unencapsulated tumor

Histo: low-grade small uniform mature pineal parenchymal cells with lobular architecture +

pineocytomatous rosettes

Mean age: 38 years; M÷F = 1÷1

Size: < 3 cm

CT:

√ well-marginated slightly hyperdense / isodense mass

√ dense focal tumor calcifications possible

√ well-defined marked homogeneous enhancement

MR:

√ well-circumscribed hypointense / isointense mass on T1WI + hyperintense on T2WI

√ avid homogeneous / internal nodular Gd-DTPA enhancement

Cx: cystic changes: rare CSF dissemination

Prognosis: 86–100% 5-year survival after resection

DDx: pineal cyst (NO trabeculations, NO enhancement)

Trilateral Retinoblastoma *(rare variant in 1.5–5%)*

= uni- / bilateral ocular retinoblastomas + midline small cell tumor

(a) most frequently in the region of the pineal gland (= neuroectodermal pineal tumor = pineoblastoma)

(b) suprasellar region

Frequency: 6% of patients with bilateral disease

• usually family history

◊ Usually diagnosed 21 (range, 6–141) months after discovery of ocular tumor

√ enhancing midline pineal mass

√ isoattenuating relative to gray matter on CT

√ isointense relative to gray matter on T1WI

Cx: intracranial / intraspinal leptomeningeal dissemination

Prognosis: mean survival up to 19 months

PITUITARY ADENOMA

= benign slow-growing neoplasm arising from adenohypophysis (= anterior lobe); most common tumor of adenohypophysis

Prevalence: 5–10–18% of all intracranial neoplasms; < 3% of patients have underlying MEN 1

• pituitary hyperfunction / hypofunction / visual field defect

Plain film (UNRELIABLE):

√ enlargement of sella + sloping of sella floor

√ erosion of anterior + posterior clinoid processes

√ erosion of dorsum sellae

√ calcification in < 10%

√ may present with mass in nasopharynx

NECT:

√ upward convexity of gland

√ increased height > 10 mm

√ deviation of pituitary stalk (nonspecific + unreliable)

√ erosion of floor of sella with adenoma > 5 mm

√ gland asymmetry

CECT (thin section SAG + COR with dynamic bolus injection):
- √ focal hypodensity (most specific for adenoma) before + after IV contrast administration
- √ "pituitary tuft" sign = displacement / compression of visualized capillary bed (sinusoids of mid-anterior lobe) of pituitary by adenoma

MR (thin-section SAG + COR with small field of view):
- ◊ Highest sensitivity on coronal nonenhanced T1WI (70%) + 3-D FLASH sequence (69%) + combination of both (90%)
- ◊ ⅓ of lesions are missed with enhancement
- ◊ ⅓ of lesions are missed without enhancement
- √ focus of low signal intensity on T1WI
- √ focus of high-signal intensity on T2WI
- √ focal hypointensity within normally enhancing gland

DDx: simple pituitary cyst (= Rathke cleft cyst)

Functioning Pituitary Adenoma

◊ Adenoma may secrete multiple hormones!

1. PROLACTINOMA (30%)

   = most common of pituitary adenomas; ~ 50% of all cranial tumors at autopsy; M << F

   • prolactin levels do not closely correlate with tumor size

   ◊ Any mass compressing hypothalamus / pituitary stalk diminishes the tonic inhibitory effect of dopaminergic factors, which originate there → hyperprolactinemia

   Female:

   Age: 15–44 years (during childbearing age)

   • infertility, amenorrhea, galactorrhea

   • elevated prolactin levels (normal < 20 ng/mL)

   ◊ > 75% of patients with serum prolactin levels > 200 ng/mL will show a pituitary tumor!

   Male:

   • headache, visual disturbance

   • impotence + decreased libido

   √ characteristic lateral location / anteriorly / inferiorly; variable in size

   Rx: bromocriptine

2. CORTICOTROPHIC ADENOMA (14%)

   Function: ACTH-secreting tumor

   Age: 30–40 years; M÷F = 1÷3

   • Cushing disease

   √ central location; posterior lobe; usually < 5 mm in size

   √ blood sampling of inferior petrosal sinuses (95% diagnostic accuracy compared with 65% for MR)

   Rx: (1) suppression by high doses of dexamethasone of 8 mg/d

   (2) surgical resection difficult because ACTH adenomas usually require resection of an apparently normal gland (tumor small + usually not on surface of gland)

3. SOMATOTROPHIC ADENOMA (14%)

   • gigantism, acromegaly, elevated GH > 10 ng/mL, NO rise in GH after administration of

glucose / TRH

Histo: (a) densely granulated type
(b) sparsely granulated type: more aggressive

√ hypodense region, may be less well-defined, variable size

4. GONADOTROPHIC CELL ADENOMA (7%)
   secretes follicle-stimulating hormone (FSH) / luteinizing hormone (LH)
   √ slow-growing often extending beyond sella
5. THYROTROPHIC CELL ADENOMA (< 1%)
   secretes thyroid-stimulating hormone (TSH)
   √ often large + invasive pituitary adenoma
6. PLURIHORMONAL PITUITARY ADENOMA (> 5%)

Nonfunctioning Pituitary Adenoma

1. NULL CELL ADENOMA
   = hormonally inactive pituitary tumor with no histologic / immunologic / ultrastructural markers to indicate its cellular derivation
   Prevalence: 17% of all pituitary tumors
   Age: older patient
   √ slow-growing
2. ONCOCYTOMA
   Prevalence: 10% of all pituitary tumors
   • clinically + morphologically similar to null cell adenoma

Pituitary Macroadenoma

= tumor > 10 mm in size
Incidence: 10% (= 70–80% of pituitary adenomas)
Age: 25–60 years; M÷F = 1÷1

• symptoms of mass effect: hypopituitarism, bitemporal hemianopia (with superior extension), pituitary apoplexy, hydrocephalus, cranial nerve involvement III, IV, VI
• usually endocrinologically inactive

Extension into: suprasellar cistern / cavernous sinus / sphenoid sinus + nasopharynx (up to 67% invasive)

√ occasionally tumor hemorrhage
√ lucent areas ← cysts / focal necrosis
√ invasion of cavernous sinus → encasement of carotid artery (SUREST sign)

CT:
√ tumor isodense to brain tissue
√ erosion of bone (eg, floor of sella)
√ calcifications infrequent

MR: (allows differentiation from aneurysm)
√ homogeneous enhancement

Cx:
(1) Obstructive hydrocephalus (at foramen of Monro)
(2) Encasement of carotid artery
(3) Pituitary apoplexy (rare)

DDx:

(1) Metastasis (more bone destruction, rapid growth)

(2) Pituitary abscess

Pituitary Microadenoma

= very small adenoma < 10 mm in size

• usually become clinically apparent by hormone production (20–30% of all pituitary adenomas)

◊ Prolactin elevation (> 25 ng/mL in females)

4–8 x normal: adenoma demonstrated in 71%

> 8 x normal: adenoma demonstrated in 100%

• **incidentaloma** = nonfunctioning microadenoma / pituitary cyst

√ NO imaging features to distinguish between different types of adenomas

MR:

√ small nonenhancing mass of hypointensity on pre- and postcontrast T1WI

√ occasionally isointense on precontrast images + hyperintense on postcontrast images

√ enhancement on delayed images

√ focal bulge on surface of gland

√ focal depression of sellar floor

√ deviation of pituitary stalk

PITUITARY APOPLEXY

= rare clinical syndrome of acute hemorrhagic / ischemic transformation of normal / tumorous adenohypophysis

Cause: massive hemorrhage into pituitary adenoma (especially in patients on bromocriptine for pituitary adenoma) / dramatic necrosis / sudden infarction of pituitary gland

Sheehan syndrome = necrosis of anterior pituitary gland ← postpartum infarct ← hemorrhagic shock of complicated delivery

◊ Only 25% of patients with intratumoral hemorrhage will present with apoplexy!

• severe headache, stiff neck, nausea, vomiting, hypertension

• sudden visual-field defect, ophthalmoplegia

• obtundation (frequent)

• hypopituitarism (eg, secondary hypothyroidism)

◊ Area of destruction must be > 70% to produce pituitary insufficiency!

√ enlargement of pituitary gland

NECT:

√ increased density ± fluid level

MR:

◊ 20% of all pituitary adenomas show evidence of hemorrhage by MR!

√ mass lesion of heterogeneous signal intensity:

√ sellar enlargement (= macroadenoma)

√ high signal on DWI (in acute stage) ← restricted diffusion

√ predominant T1 hyperintensity + predominant T2 hypointensity ← hemoglobin

√ intermediate SI on T1WI + T2WI ← deoxyhemoglobin

√ intratumoral fluid-debris level ← sedimentation of blood products (at later stage)
DDx: Rathke cleft cyst (NO hemorrhage, NO fluid-fluid level)
√ mucosal thickening of sphenoid sinus ← venous engorgement of acute stage

PONTINE TEGMENTAL CAP DYSPLASIA

= sporadic malformation with unknown genotype
• hearing loss, facial paralysis, trigeminal anesthesia
• difficulty in swallowing
√ flattened ventral pons
√ vaulted pontine tegmentum ("cap")
√ partial absence of middle cerebellar peduncles
√ vermian hypoplasia
√ molar tooth–like aspect of pontomesencephalic junction
√ absent inferior olivary prominence

PORENCEPHALY

= focal cavity as a result of localized brain destruction

A. AGENETIC PORENCEPHALY
= SCHIZENCEPHALY = TRUE PORENCEPHALY

B. ENCEPHALOCLASTIC PORENCEPHALY
Time of injury: during first half of gestation
Histo: necrotic tissue completely reabsorbed without surrounding glial reaction (= liquefaction necrosis)
MR:
√ smooth-walled cavity filled with CSF on all pulse sequences (= porencephalic cyst)
√ lined by white matter

C. ENCEPHALOMALACIA
= PSEUDOPORENCEPHALY = ACQUIRED PORENCEPHALY
= end result of destructive process with replacement by CSF
Prevalence: 2.5% of children with perinatal brain injury
Cause: intraparenchymal hemorrhage, infection, surgery
Time of injury: after end of 2nd trimester / postnatally (brain has developed capacity for glial response)
Location: parasagittal watershed areas with sparing of periventricular region + ventricular wall

CT:
√ hypodense regions
MR:
√ hypointense on T1WI + hyperintense on T2WI
√ surrounding hyperintense rim on T2WI (= gliosis)
√ glial septa coursing through cavity identified on T1WI + proton density images
US:
√ damaged area hyperechoic (during first days to weeks) following initial hemorrhagic event
√ subsequent conversion to area with anechoic center and echogenic border ← clot retraction

√ ultimately completely anechoic cystic area ← CSF:
√ septations in cavity well visualized
√ ± discrete wall calcifications

POSTERIOR REVERSIBLE ENCEPHALOPATHY SYNDROME

= (PRES) = REVERSIBLE POSTERIOR LEUKOENCEPHALOPATHY SYNDROME = HYPERTENSIVE ENCEPHALOPATHY
= heterogeneous collection of disorders associated with a breakdown in cerebral autoregulatory perfusion mechanisms
◊ Emergency condition as patient may proceed to cerebral infarction and death if untreated!
Cause: acute rise in systemic blood pressure, preeclampsia or eclampsia, hemolytic uremic syndrome, cryoglobulinemia, SLE, following immunosuppressive treatment with cyclosporine A, cisplatin, tacrolimus (= **T**sukuba m**acrol**ide **im**m**u**no**s**uppressan = FK-506)
Pathophysiology: vasogenic edema related to sparse sympathetic innervation in posterior circulation
• headache, nausea, vomiting, visual changes
• decreased alertness, seizures
Location: white matter of posterior half of brain
√ hypodense white matter on NECT
√ lesion hypointense on T1WI + hyperintense on T2WI ← vasogenic edema (= fluid extravasation into interstitium)
√ lesion hypo- to isointense on DWI + hyperintense on ADC map (due to a net effect of elevated diffusion coefficient from vasogenic edema + T2 shine-through effect)
√ NO contrast enhancement
Cx: infarction (lesions develop high DWI signal + normal ADC signal)
Rx: rapid control of blood pressure / withdrawal of offending drug

PRIMARY ANGIITIS OF CNS

= PACNS = idiopathic inflammatory disease of medium-sized to small arteries affecting CNS / peripheral nervous system WITHOUT evidence of generalized inflammation

Age: 5–6th decade
• acute / subacute confusion, hallucinations, headache
• paresis, cranial neuropathy, loss of consciousness
• elevated inflammatory markers: ↑ ESR
• CSF analysis: ↑ opening pressure, ↑ protein level
Location: spinal cord abnormalities (5%)
◊ Nonspecific CT and MR imaging findings!
CT:
√ areas of low attenuation ← suggestive of ischemic events
MR:
√ discrete / diffuse supra- and infratentorial lesions involving deep + superficial white matter
√ ± vessel irregularities
√ ± areas of infarct + hemorrhage

√ lesion enhancement in 90%

DSA (supports diagnosis in spite of negative biopsies):

√ focal / multifocal segmental narrowing / occlusion / irregularities in both hemispheres

√ collateral vessel formation

√ prolonged circulation time

√ microaneurysm (unusual)

Subsets:

1. Hemorrhagic form (11–12%)
   Cause: hemorrhagic transformation of recent infarction / focal necrosis of intracerebral blood vessel
   √ intracerebral > subarachnoid hemorrhage
2. Pseudotumoral form (15%)
   √ nonspecific mass lesions characterized by central necrosis, surrounding edema, infiltration of adjacent structures, mass effect, variable contrast enhancement
   N.B.: often misinterpreted as malignant neoplasms
3. Rapidly progressive primary vasculitis of CNS
   √ numerous bilateral lesions of large cerebral vessels
   √ several bilateral cerebral infarctions
   Prognosis: poor, often fatal
4. Angiography-negative, biopsy-positive PACNS
   Site: small arteries / arterioles
   • cognitive dysfunction, ⇑ CSF protein
   √ meningeal / parenchymal enhancing lesions at MR
   Prognosis: good with favorable response to treatment
5. Childhood PACNS
   Site: unilateral, proximal, multifocal, supratentorial involving gray + white matter with preference for basal ganglia / lateral lenticulostriate vasculature; frequently terminal segment of ICA and proximal segments of ACA + MCA

Dx: leptomeningeal + brain parenchymal biopsies

Rx: high-dose steroids, cytotoxic agents

PRIMITIVE NEUROECTODERMAL TUMOR

= PNET = PRIMARY CEREBRAL NEUROBLASTOMA

= group of very undifferentiated tumors arising from germinal matrix cells of primitive neural tube = rare presentation of neuroblastoma

Incidence: < 5% of supratentorial neoplasms in children, 30% of posterior fossa tumors

Age: mainly in children < 5 years of age/ early adolescence; M÷F = 1÷1

Path: most undifferentiated form of malignant small cell neoplasms grouped with Ewing sarcoma, Askin tumor

Histo: highly cellular tumor composed of > 90–95% undifferentiated cells (histologically similar to medulloblastoma, pineoblastoma, peripheral neuroblastoma)

• signs of increased intracranial pressure / seizures

Location:

(a) supratentorial: deep cerebral white matter (most commonly in frontal lobe), pineal gland,

in thalamic + suprasellar territories (least frequently)
(b) posterior fossa (= medulloblastoma)
(c) outside CNS: chest wall, paraspinal region, kidney

√ large (hemispheric) heterogeneous mass with tendency for central necrosis (65%), cyst formation, hemorrhage (10%)
√ intratumoral coarse dense calcifications (71%)
√ thin rim of edema
√ mild / moderate enhancement of solid tumor portion

CT:
√ large hypodense / mixed-density mass with well-defined margins
√ solid tumor portions hyperdense ← high nuclear to cytoplasmic ratio

MR:
√ mildly hypointense on T1WI + hyperintense on T2WI
√ remarkably inhomogeneous due to cyst formation + necrosis
√ areas of signal dropout due to calcifications
√ hyperintense areas on T1WI + variable intensity (usually intermediate) on T2WI due to hemorrhage
√ inhomogeneously moderately enhancing mass with tumor nodules + ringlike areas surrounding central necrosis after Gd-DTPA

Cx: meningeal + subarachnoid seeding (15–40%)
DDx: Neuroblastoma usually NOT metastatic to brain!

Primitive Neuroectodermal Soft-tissue Tumor

√ tumor of low to intermediate attenuation
√ NO evidence of calcification
√ low to intermediate signal intensity on T1WI + high signal intensity on T2WI
√ often peripheral low-SI vascular channels ← high-flow
√ areas of hemorrhage (common)
√ well-defined tumor margins with pseudocapsule / infiltrative appearance

PROGRESSIVE MULTIFOCAL LEUKO-ENCEPHALOPATHY

= rapidly progressive fatal demyelinating disease in patients with impaired immune system (chronic lymphocytic leukemia, lymphoma, Hodgkin disease, carcinomatosis, AIDS, tuberculosis, sarcoidosis, organ transplant)
Prevalence: 4% of AIDS patients
Etiology: reactivation of ubiquitous JC papovavirus
Pathophysiology: destruction of oligodendrogliocytes leading to areas of demyelination + edema
Histo: intranuclear inclusion bodies within swollen oligodendrocytes (viral particles in nuclei); lysis of oligodendrocytes → demyelination; absence of significant perivenous inflammation

• progressive neurologic deficits, dementia, ataxia, spasticity
• speech, motor and visual disturbances; normal CSF fluid

Location: frontoparietal > temporo-occipital cerebral hemispheres; white matter tracts in cerebellum, brainstem, deep gray matter; ? predilection for parieto-occipital region

Site: subcortical white matter spreading centrally into brainstem, deep gray matter
√ bilateral white matter lesions (92%); confluent (94%); discrete (67%) in periventricular region + centrum semiovale + subcortical white matter
√ gray matter lesions in thalamus + basal ganglia (from involvement of traversing white matter tracts)
√ sparing of cortical gray matter
√ mild cortical atrophy (up to 69%)
√ ventricular dilatation (50%)
√ NO contrast enhancement
CT:
√ multicentric confluent white matter lesions of low attenuation with scalloped borders along cortex
√ NO mass effect, NO edema
MR:
√ hypointense lesions on T1WI
√ patchy hyperintense lesions of white matter away from ependyma in asymmetric distribution on T2 + FLAIR
√ NO enhancement
Prognosis: death usually within 6 months
DDx in early stages: primary CNS lymphoma

RATHKE CLEFT CYST

[Martin Heinrich Rathke (1793–1860), professor of physiology and pathology at the University of Dorpat (Tartu), Estonia and professor of zoology and anatomy in Königsberg, Germany]
= usually asymptomatic benign cystic sellar lesion
Histo: lined with single layer of epithelial cells; CSF / mucopolysaccharide content
• often asymptomatic
• hypopituitarism, visual disturbance, headache (in older patients)
Location: commonly midline at junction of anterior + posterior pituitary lobes anterior to infundibular stalk; intra- and suprasellar (71%); purely suprasellar (rare)
√ may contain thick mucinous material
√ no contrast enhancement
√ calcifications rare
MR:
√ round well-demarcated lesion
√ variable SI ranging from hypo- to hyperintense on T1WI ← dependent on biochemical content:
√ homogeneously high T1 SI (50%) ← high protein content
√ low T2 intensity (30%) ← low intracystic water content
√ simple / complex cyst content ± fluid-fluid level
√ NO central enhancement / hemorrhagic component
√ small intracystic nodules of lower T2 + higher T1 SI (75%) ← proteinaceous concretions
√ wall enhancement due to squamous metaplasia / displaced rim of pituitary tissue
DDx: craniopharyngioma, macroadenoma (hemorrhagic fluid-debris level)

REYE SYNDROME

[Ralph Douglas Kenneth Reye (1912–1977), director of pathology of the Royal Alexandra Hospital for Children in Sydney, Australia]

= hepatitis + encephalitis following viral upper respiratory tract infection with history of large doses of aspirin ingestion

Age: in children + young adults

• obtundation rapidly progressing to coma

√ initially (within 2–3 days) small ventricles

√ later progressive enlargement of lateral ventricles + sulci

√ markedly diminished attenuation of white matter

Mortality: 15–85% (from white matter edema + demyelination)

Dx: liver biopsy

RHOMBENCEPHALOSYNAPSIS

= characterized by absence of vermis + continuity of cerebellar hemispheres, dentate nuclei, superior cerebellar peduncles

Associated with: Gómez-López-Hernández syndrome (parietal alopecia, trigeminal anesthesia, craniofacial dysmorphic signs); VACTERL

• truncal ± limb ataxia, delayed motor development

• abnormal eye movements

√ agenesis or hypogenesis of vermis

√ keyhole-shaped fourth ventricle ← horseshoe-shaped arch across midline ← fusion (continuity) of cerebellar hemispheres + superior cerebellar peduncles + dentate nuclei

√ abnormal transverse orientation of cerebellar foliae

Prognosis: varying between severe impairment and normalcy

ROSAI-DORFMAN DISEASE

= rare benign histiocytosis

Etiology: reaction to infectious agents / autoimmune process

Histo: polymorphous infiltrate of lymphoplasmacytic cells and histiocytes of varying size embedded in fibrous stroma; S-100 + CD68 positive; CD1a negativity excludes Langerhans histiocytosis; CHARACTERISTIC emperipolesis (= phagocytosis of lymphocytes) in 70%
[*em*, Greek = inside, *peri* = around, *polemai* = wander about]

A. EXTRACRANIAL

Age: primarily in children + young adults; M > F

• painless bilateral cervical adenopathy + involvement of nasal cavity, bone, orbit

B. INTRACRANIAL (40%)

Age: 4th–5th decades; M÷F=3÷1

Location: cerebral convexities, parasagittal, petroclival, suprasellar regions

• headache, visual change, seizures, numbness, paraplegia

√ well-circumscribed dural-based iso- to hyperattenuating single / multiple masses

√ isointense on T1WI + iso- to hypointense on T2WI:

√ central low SI on T2WI ← release of free radicals by inflammatory macrophages

√ marked enhancement + dural tail (common)
√ edema within adjacent brain parenchyma (frequent)
DDx: meningioma (iso- to hyperintense on T2WI)

SCHISTOSOMIASIS OF CNS

Transmission: embolic distribution of ova through venous shunts / anomalous migration of adult worms
Cause: granuloma formation

Cerebral Schistosomiasis

Organism: primarily S. japonicum
• fever, focal neurologic deficits, seizures
Location: cerebellum, cerebral hemispheres, thalamus, dura
CT:
√ single / multiple variably enhancing hyperattenuated lesions ± surrounding hypoattenuated edema ← focal granulomatous reaction
√ nodular / ring / patchy enhancement
MR:
√ bilateral symmetric T1 hyperintensities of globus pallidus + substantia nigra ← manganese deposition related to portosystemic shunt
√ "arborized" T1-enhancement pattern with central linear enhancement (? specific)

Spinal Schistosomiasis

Organism: primarily S. mansoni + hematobium
• acute / subacute transverse myelitis (common): back pain, urinary retention, motor + sensory disturbances
Location: distal thoracic spinal cord, cauda equina ← presumably via vertebral venous (Batson) plexus
MR:
√ T2 hyperintensity ← granulomatous involvement
√ "arborized" T1-enhancement pattern
Cx: (1) spinal cord compression (by focal granuloma)
(2) anterior spinal artery syndrome (rare)

SCHIZENCEPHALY

= AGENETIC PORENCEPHALY = TRUE PORENCEPHALY
= "split brain"
= rare CNS malformation consisting of a <u>full-thickness</u> CSF-filled parenchymal cleft lined by gray matter extending from subarachnoid space to subependyma of lateral ventricles
Frequency: 1÷1,650
Cause: ? vascular ischemia of portion of germinal matrix / genetic mutation → segmental developmental failure of neuronal cell migration to form cerebral cortex; NOT porencephaly
Time of injury: 30–60 days of gestation
Often associated with: polymicrogyria, microcephaly, gray matter heterotopia, septooptic

dysplasia

Types:

(1) **Closed-lip schizencephaly** (type 1) = gray matter-lined lips in contact with each other (may be missed in imaging planes parallel to the plane of cleft)
√ walls appose one another obliterating CSF space

(2) **Open-lip schizencephaly** (type 2) = separated lips
√ CSF-cleft from wall of lateral ventricle to pial surface

- seizure disorder
- motor + mental deficiencies correlate with extent of defect:
  - mild / moderate developmental motor delay
  - range of normal mentation to severe mental retardation
- blindness possible (optic nerve hypoplasia in 33%)

Location: most commonly near pre- and postcentral gyri (sylvian fissure); uni- / (mostly) bilateral; in middle cerebral artery distribution

√ cleft from ependyma of lateral ventricle to pial surface of cortex:
√ cleft lined by gray matter (PATHOGNOMONIC)
√ full-thickness cleft through hemisphere with irregular margins
√ asymmetrical dilatation of lateral ventricles with midline shift
√ wide separation of lateral ventricles + squaring of frontal lobes
√ ventricle wall may be tented pointing to defect
√ absence of cavum septi pellucidi (66%)
√ absence / focal thinning of corpus callosum
√ cleft lined by polymicrogyria (66%) + heterotopias (common)
√ abnormal gyral pattern adjacent to cleft = "gyri dive into cleft"
√ polymicrogyria / pachygyria adjacent / remote to cleft
√ bilateral often symmetric intracranial cysts, usually around sylvian fissure

Prognosis: severe intellectual impairment, spastic tetraplegia, blindness

DDx: (1) Pseudoporencephaly = acquired porencephaly = local parenchymal destruction ← vascular / infectious / traumatic insult (almost always unilateral, lined by gliotic white matter on MRI)
(2) Arachnoid cyst
(3) Cystic tumor

SEPTOOPTIC DYSPLASIA

= DE MORSIER SYNDROME

[Georges de Morsier (1894–1982), professor of neurology and director of the neurological clinic of the university of Geneva, Switzerland]

= rare anterior midline anomaly with
(1) Hypoplasia of optic nerves
(2) Hypoplasia / absence of septum pellucidum

◊ Often considered a mild form of lobar holoprosencephaly

Cause: insult between 5–7th week of GA; M÷F = 1÷3

Associated with: schizencephaly (50%)

- hypothalamic hypopituitarism (66%):

diabetes insipidus (in 50%), growth retardation (← deficient secretion of growth hormone + thyroid stimulating hormone)

- diminished visual acuity (hypoplasia of optic discs), nystagmus, occasionally hypotelorism; seizures, hypotonia

√ small optic canals
√ hypoplasia of optic nerves + chiasm + infundibulum
√ dilatation of chiasmatic + suprasellar cisterns
√ fused dilated boxlike frontal horns squared off dorsally + pointing inferiorly
√ bulbous dilatation of anterior recess of 3rd ventricle
√ hypoplastic / absent septum pellucidum
√ thin corpus callosum

STURGE-WEBER-DIMITRI SYNDROME

= ENCEPHALOTRIGEMINAL ANGIOMATOSIS = MENINGOFACIAL ANGIOMATOSIS

[William Allen Sturge (1850–1919), physician and pathologist to the Royal Free Hospital in London, England
Frederick Parkes Weber (1863–1962, dermatologist and honorary physician to the German Hospital, Queen Square, London, England
Vincente Dimitri (1885–1955), Austrian dermatologist in Argentina]

= vascular malformation with capillary venous angiomas in distribution of trigeminal nerve with ipsilateral leptomeningeal malformation + atrophy + calcification of subjacent cerebral cortex, malformation of choroid of eye, and face

Cause: persistence of transitory primordial sinusoidal plexus stage of vessel development; usually sporadic

- seizures (80%) in 1st year of life: usually focal involving the side of the body contralateral to nevus flammeus
- mental deficiency (> 50%); homonymous hemianopia
- increasing crossed hemiparesis (35–65%)
- hemiatrophy of body contralateral to facial nevus ← hemiparesis

@ FACIAL MANIFESTATION

- congenital facial **port-wine stain** (nevus flammeus) = telangiectasia of trigeminal region; usually 1st ± 2nd division of 5th nerve and usually unilateral
  - › V_1 associated with occipital lobe angiomatosis
  - › V_2 associated with parietal lobe angiomatosis
  - › V_3 associated with frontal lobe angiomatosis

@ CNS MANIFESTATION

√ leptomeningeal venous angiomas confined to pia mater
Location: parietal > occipital > frontal lobes
√ cortical hemiatrophy beneath meningeal angioma ← anoxia (steal)
√ "tram track" gyriform cortical calcifications > 2 years of age; in layers 2-3 (-4-5) of opposing gyri underlying pial angiomatosis; bilateral in up to 20%
Location: temporoparieto-occipital area, occasionally frontal, rare in posterior fossa
√ subjacent white matter hypodense on CT
√ slight prolongation of T1 + T2 relaxation times (gliosis)

√ choroid plexus enlargement ipsilateral to angiomatosis
√ ipsilateral thickening of skull + orbit ← bone apposition as result of subdural hematoma ← brain atrophy
√ elevation of sphenoid wing + petrous ridge
√ enlarged ipsilateral paranasal sinuses + mastoid air cells
√ thickened calvarium (= widening of diploic space)
Angio:
√ capillary blush
√ abnormally large veins in subependymal + periventricular regions
√ abnormal deep medullary veins draining into internal cerebral vein (= venous shunt)
√ failure to opacify superficial cortical veins in calcified region ← markedly slow blood flow / thrombosis of dysgenetic superficial veins

@ ORBITAL MANIFESTATION (30%)
Site: ipsilateral to nevus flammeus
• congenital glaucoma (30%)
√ choroidal hemangioma (71%)
√ dilatation and tortuosity of conjunctival + episcleral + iris + retinal vessels
√ buphthalmos
Cx: retinal detachment

@ VISCERAL MANIFESTATION
√ localized / diffuse angiomatous malformation
Location: intestine, kidneys, spleen, ovaries, thyroid, pancreas, lungs

DDx: Klippel-Trénaunay syndrome, Wyburn-Mason syndrome

SUBARACHNOID HEMORRHAGE

= blood between pia + arachnoid membrane

Cause:

A. Spontaneous
(1) Ruptured aneurysm (72%)
(2) AV malformation (10%)
(3) Hypertensive hemorrhage
(4) Hemorrhage from tumor
(5) Embolic hemorrhagic infarction
(6) Blood dyscrasia, anticoagulation therapy
(7) Eclampsia
(8) Intracranial infection
(9) Spinal vascular malformation
(10) Cryptogenic in 6% (negative 4-vessel angiography; seldom recurrent)

B. Trauma (common)
concomitant to cerebral contusion
(1) Injury to leptomeningeal vessels at vertex
(2) Rupture of major intracerebral vessels (less common)
Location:
(a) focal, overlying site of contusion / subdural hematoma

(b) interhemispheric fissure, paralleling falx cerebri
(c) spread diffusely throughout subarachnoid space (rare in trauma): convexity sulci > basal cisterns

Pathophysiology: irritation of meninges by blood and extra fluid volume increases intracranial pressure → vasospasm in 2–41%

- acute severe headache ("worst in life"), vomiting
- altered state of consciousness: drowsiness, sleepiness, stupor, restlessness, agitation, coma
- spectrophotometric analysis of CSF obtained by lumbar puncture

NECT (60–90% accuracy of detection depending on time of scan; sensitivity depends on amount of blood; accuracy high within 4–5 days of onset, 90% sensitive within 1st day):

√ increased density in basal cisterns, superior cerebellar cistern, sylvian fissure, cortical sulci, intraventricular
√ along interhemispheric fissure = on lateral aspect irregular dentate pattern due to extension into paramedian sulci with rapid clearing after several days
√ "cortical vein" sign = visualization of cortical veins passing through extraaxial fluid collection

MR (relatively insensitive within first 48 hours):

√ hyperintense sulci and cisterns on FLAIR and T2* (more sensitive than CT for small amounts of blood)
√ "dirty" CSF isointense to brain on T1WI + T2WI
√ low signal intensity on brain surfaces in recurrent subarachnoid hemorrhages (hemosiderin deposition)

Prognosis: clinical course depends on amount of subarachnoid blood

Cx:

(1) Acute obstructive hydrocephalus (in < 1 week) ← intraventricular hemorrhage / ependymitis obstructing aqueduct of Sylvius or outlet of 4th ventricle
(2) Delayed communicating hydrocephalus (after 1 week) ← fibroblastic proliferation in subarachnoid space and arachnoid villi interferes with CSF resorption
(3) Cerebral vasospasm + infarction (develops after 72 hours, at maximum between 5–17 days, amount of blood is a prognostic parameter)
(4) Transtentorial herniation (cerebral hematoma, hydrocephalus, infarction, brain edema)

SUBDURAL HEMATOMA OF BRAIN

= accumulation of blood in potential space between pia-arachnoid membrane (leptomeninges) + dura mater (= "epiarachnoid space")

Incidence: in 5% of head trauma patients; in 15% of closed head injuries; in 65% of head injuries with prolonged interruption of consciousness

Age: accident-prone middle age; also in infants + elderly (large subarachnoid space with freedom to move in brain atrophy)

Cause: severe trauma, hemorrhagic diathesis

Source of blood:

(1) pial cortical arteries + veins: direct trauma = penetrating injury
(2) large contusions: direct / indirect trauma = "pulped brain"; occasionally in blood clotting disorder / during anticoagulation therapy

(3) torn bridging cortical veins (indirect force) ← sudden de-/acceleration; also with forceful coughing / sneezing / vomiting in elderly

Elderly predisposed: longer bridging veins in brain atrophy

◊ NO consistent relationship to skull fractures!

Pathogenesis:

differential movement of brain and adherent cortical veins with respect to skull + attached dural sinuses → tear of "bridging veins" (= subdural veins which connect cerebral cortex to dural sinuses + travel through subarachnoid and subdural space)

Location: hematoma freely extending across suture lines, limited only by interhemispheric fissure and tentorium

- nonspecific headaches, nonlocalizing signs; low-voltage EEG
- lethargy, confusion; usually negative lumbar puncture

CT:

√ hyperdense 65–90 HU (< 1 week) / isodense 20–40 HU (1–2 weeks) / hypodense 0–22 HU (3–4 weeks)

False-negative CT scan:

high-convexity location, beam-hardening artifact, volume averaging with high density of calvarium obscuring flat "en plaque" hematoma, too narrow window setting, isodense hematoma due to delay in imaging 10–20 days post injury / low hemoglobin content of blood / lack of clotting, dilution by CSF from associated arachnoid tear

◊ 38% of small subdural hematomas are missed!

Aids in detection of acute subdural hematoma:

√ perceived "thickening" of ipsilateral portion of skull (hematoma of similar pixel brightness as bone)
√ "subdural window" setting = window level of 40 HU + window width of 400 HU
√ effacement of adjacent sulci
√ sulci not traceable to brain surface
√ ipsilateral ventricular compression / distortion
√ displacement of gray-white matter interface away from ipsilateral inner table
√ midline shift (often greater than width of subdural hematoma due to underlying brain contusion)
√ contrast enhancement of cortex but not of subdural hematoma

Aids in detection of bilateral subdural hematomas:

√ "parentheses" ventricles
√ ventricles too small for patient's age

US (neonate):

√ linear / elliptical space between cranial vault + brain
√ flattened gyri + prominent sulci
√ ± distortion of ventricles, extension into interhemispheric space

Limitations:

(a) convexity hematoma may be obscured by pie-shaped display + loss of near-field resolution
◊ Use contralateral transtemporal approach!
(b) small loculations may be missed

Prognosis: poor (due to association with other lesions)
DDx: (1) Arachnoid cyst (extension into sylvian fissure)
(2) Subarachnoid hemorrhage (extension into sulci)

Acute Subdural Hematoma

Cause: usually follows severe trauma, manifests within hours after injury
Time frame: < 7 days old
Associated with: underlying brain injury (50%) with worse long-term prognosis than epidural hematoma, skull fracture (1%)
Location:
(a) over cerebral convexity, frequent extension into interhemispheric fissure, along tentorial margins, beneath temporal + occipital lobes; NO crossing of midline
(b) bilateral in 15–25% of adults (common in elderly) and in 80–85% of infants
√ extraaxial peripheral crescentic / convex fluid collection between skull and cerebral hemisphere usually with:
√ concave inner margin ← hematoma minimally pressing into brain substance
√ convex outer margin ← following normal contour of cranial vault
√ hyperdense collection of 65–100 HU
◊ Hematoma hypodense if hematocrit < 29%!
√ "swirl" sign = mixture of clotted and unclotted blood
√ occasionally with blood-fluid level
√ after surgical evacuation → underlying parenchymal injury becomes more obvious
√ after healing → ventricular + sulcal enlargement
Cx: Arteriovenous fistula ← meningeal artery + vein caught in fracture line
Prognosis: may progress to subacute + chronic stage / may disappear spontaneously
Rx: evacuation, but with poor response ← high uncontrollable intracranial pressure from associated injuries
Mortality: 35–50% (higher number due to associated brain injury, mass effect, old age, bilateral lesions, rapid rate of hematoma accumulation, surgical evacuation > 4 hours)

Interhemispheric Subdural Hematoma

Most common acute finding in child abuse ← whiplash forces on large head + weak neck muscles
√ predominance for posterior portion of interhemispheric fissure
√ crescentic shape with flat medial border
√ unilateral increased attenuation with extension along course of tentorium
√ anterior extension to level of genu of corpus callosum

Subdural Hemorrhage in Newborn

Cause: mechanical trauma during delivery (excessive vertical molding of head)
1. **Posterior fossa hemorrhage**
(a) tentorial laceration with rupture of vein of Galen / straight sinus / transverse sinus
(b) occipital osteodiastasis = separation of squamous portion from exoccipital portion of occipital bone

√ high-density "thickening" of affected tentorial leaf extending down posterior to cerebellar hemisphere (better seen on coronal view)
√ mildly echogenic subtentorial collection
Cx: death from compression of brainstem → acute hydrocephalus

2. **Supratentorial hemorrhage**
   (a) laceration of falx near junction with tentorium ← rupture of inferior sagittal sinus (less common than tentorial laceration)
   √ hematoma over corpus callosum in inferior aspect of interhemispheric fissure
   (b) convexity hematoma ← rupture of superficial cortical veins
   √ usually unilateral subdural convexity hematoma accompanied by subarachnoid blood
   √ underlying cerebral contusion
   √ sonographic visualization of convexities difficult

Subacute Subdural Hematoma

Time frame: 7–22 days

CT:
√ isodense hematoma of 25–45 HU (during 1st–3rd week), may be recognizable by mass effect:
√ effacement of cortical sulci
√ deviation of lateral ventricle
√ midline shift
√ white matter buckling
√ displacement of gray-white matter junction
√ contrast enhancement of inner membrane
Aid in Dx: contrast enhancement defines cortical-subdural interface

MR (modality of choice in subacute stage):
√ high sensitivity for Met-Hb on T1WI (<u>superior to CT during isodense phase</u> concerning small subdural hematomas + for hematomas oriented in the CT scan plane, eg, tentorial subdural hematoma):
√ hyperintense on T1WI

Chronic Subdural Hematoma

Time frame: > 22 days old

Cause: mild unremembered head trauma ?

Pathogenesis: vessel fragility accounts for repeated episodes of rebleeding (in 10–30%) following minor injuries that tear a <u>fragile capillary bed within neomembrane</u> surrounding subdural hematoma

Predisposing factors:
alcoholism, increased age, epilepsy, coagulopathy, prior placement of ventricular shunt

◊ > 75% occur in patients > 50 years of age!

Histo: hematoma enclosed by thick + vascular membrane, which forms <u>after 3–6 weeks</u>

- history of antecedent trauma often absent (25–48%)
- ill-defined neurologic signs + symptoms: cognitive deficit, behavioral abnormality,

nonspecific headache
• progressive neurologic deficit; low-voltage EEG, normal CSF
√ often biconvex lenticular = medially concave configuration, esp. after compartmentalization ← formation of fibrous septa
√ low-density lesion of 0–25 HU (= intermediate attenuation between CSF + brain):
√ different attenuations within different compartments
√ sometimes as low as CSF
√ high-density components of collection (after common rebleeding)
√ fluid-sediment levels (= sedimented fresh blood with proteinaceous fluid layered above)
√ displacement / absence of sulci, displacement of ventricles and parenchyma
√ No midline shift if bilateral (25%)
√ absent "cortical vein" sign = cortical veins seen along periphery of fluid collection without passing through it (1–4 weeks after injury)
DDx: Acute epidural hematoma (similar biconvex shape)

SUBDURAL HYGROMA

= TRAUMATIC SUBDURAL EFFUSION
= localized CSF-fluid collection within subdural space
Cause: (a) minor trauma results in separation of dura and arachnoid; proliferation of dural border cell layer results in neomembrane with hyperpermeable capillaries + efflux of serous fluid into subdural space
(b) traumatic tear in arachnoid with secondary ball valve mechanism
Age: most often in elderly + young children
Time of onset: 6–30 days following trauma
• asymptomatic in majority; headaches, drowsiness
• decreased level of consciousness, confusion
√ radiolucent crescent-shaped collection (as in acute subdural hematoma) of CSF density
√ NO evidence of blood products (DDx to subdural hematoma)
MR:
√ isointense to CSF / hyperintense to CSF on T1WI (← increased protein content)
Prognosis: often spontaneous resorption; may develop into a chronic subdural hematoma
DDx: (1) Enlarged subarachnoid space
(2) Subdural empyema
(3) Chronic subdural hematoma
(4) Brain atrophy

SUBEPENDYMAL CYST

Etiology:

1. Acquired posthemorrhagic subependymal cyst:
   - › hemorrhage
   - › hypoxic-ischemic damage

   Site: caudothalamic notch
   - • frequently in preterm infant
   - √ tear-shaped, 2–11 mm in size
2. Congenital subependymal cyst ← germinolysis
   - › neurotropic infection: CMV, rubella
   - › metabolic disorders (esp. Zellweger syndrome)
   - › chromosomal abnormalities
   - › maternal cocaine consumption
   - › idiopathic in otherwise healthy newborn

Histo: cystic cavity with pseudocapsule of aggregates of germinal cells + glial tissue; NO epithelium; macrophage-like cells within fluid ← vascular origin

TERATOMA OF CNS

Incidence: 0.5% of primary intracranial neoplasms; 2% of intracranial tumors before age 15

Histo: mostly benign; occasionally containing highly malignant primitive elements

Location: pineal + parapineal region > floor of 3rd ventricle > posterior fossa > spine (associated with spina bifida)

√ heterogeneous midline lesion, occasionally homogeneous soft-tissue mass (DDx: astrocytoma)

√ contains fat + calcium

√ hydrocephalus (common)

Pineal Teratoma

= benign tumor containing one / all three germ cell layers (pineal region most common site of teratomas)

Incidence: 15% of all pineal masses; 2nd most common tumor in pineal region

Age: < 20 years; M÷F = 2÷1 to 8÷1

- • Parinaud syndrome; hypothalamic symptoms
- • headache, somnolence (related to hydrocephalus)

Histo: (a) mature teratoma = fully differentiated tissue
- › ectoderm: skin + skin appendages
- › mesoderm: cartilage, bone, fat, smooth muscle, skeletal muscle
- › endoderm: respiratory + enteric epithelium

(b) immature teratoma = complex mixture of fetal-type tissues from all 3 germ layers + mature tissue elements

(c) teratoma with malignant transformation of mature tissues

Location: pineal, parapineal, suprasellar, 3rd ventricle

√ well-defined rounded / irregular lobulated extremely heterogeneous multiloculated mass of fat, cartilage, hair, linear / nodular calcifications + cysts

◊ Fat is absent in all other pineal tumors!

√ may show heterogeneous / rimlike contrast enhancement (limited to solid-tissue areas)

Angio:

√ elevation of internal cerebral vein

√ posterior displacement of precentral vein

CT:

√ heterogeneous mass with fat, calcification, cystic + solid areas

MR:

√ variegated appearance on all pulse sequences:

√ hyperintense areas of fat on T1WI with chemical shift artifact

√ variable signal intensity on T1WI due to calcifications

√ iso- to hypointense soft-tissue component

√ enhancement of soft-tissue component

Cx: chemical meningitis with spontaneous rupture

TOXOPLASMOSIS OF BRAIN

Organism: obligate intracellular protozoan parasite Toxoplasma gondii, can live in any cell except for nonnucleated RBCs; reservoirs in feces of house cat (felines are definite host)

Infection: ingestion of undercooked meat (eg, pork, free-range chicken) containing cysts or sporulated oocysts / transplacental transmission of trophozoites; acquired through blood transfusion + organ transplantation

◊ Disease remains dormant for as long as normal host immunity is maintained!

Forms: (1) Cyst (bradyzoite)

(2) Trophozoite

(3) Oocyst: uniquely found in intestinal mucosa of cat; outside cat it can survive for > 1 year in warm moist soil

Hosts: birds, mammals, reptiles, cockroach, flea

Geographic exposure: France (75–90%) > Central America > urban USA (17–35%)

◊ 500 million persons infected with T. gondii worldwide!

Seropositivity: up to 20% of urban adults in USA; up to 90% of European adults

Transmission:

(a) fecal-oral: fruits, vegetables, poorly cooked meat; children especially susceptible via house cat / litter box

(b) hematogenous: blood transfusion

Spread: hematogenous

Histo: inflammatory solid / cystic granulomas (← glial mesenchymal reaction) surrounded by edema and microinfarcts (← vasculitis)

Affected tissue:

@ Gray + white matter of brain

◊ Most common cause of focal CNS infection mass effect in patients with AIDS!

@ Retina: most common retinal infection in AIDS

@ Alveolar lining cells (4%):
mimics Pneumocystis carinii pneumonia

@ Heart (rare):
cardiac tamponade / biventricular failure
@ Skeletal muscle
• asymptomatic; lymphadenopathy; malaise, fever

Toxoplasmosis is the most common opportunistic infection affecting the CNS in patients with AIDS!

A. AIDS INFECTION = **toxoplasmic encephalitis**
= reactivation of a chronic latent infection in > 95%
◊ Most common cerebral mass lesion in AIDS!
◊ 2–3 times more frequent than lymphoma!
Incidence: 3–20–40% of AIDS patients; 20–70% of normal adult population is seropositive for antibodies
Path: well-localized indolent granulomatous process / diffuse necrotizing encephalitis
• fever, headaches, confusion, seizures (15–25%)
• focal neurologic deficit of subacute onset (50–89%)
• pseudotumor cerebri syndrome
Location: (a) basal ganglia (75%)
(b) subcortical at gray-white matter junction scattered throughout brain parenchyma
(c) NO involvement of corpus callosum / leptomeninges
CT:
√ multifocal abscesses with a predilection for basal ganglia:
√ multiple / solitary (up to 39%) lesions < 2 cm with nodular / thin-walled (common) ring enhancement
√ surrounding white matter edema
√ double-dose delayed CT scans with higher detection rate for multiple lesions (64–72%)
√ ± hemorrhage and calcifications after therapy
MR:
√ multiple hypo- to isointense lesions on T2WI
√ T1 hyperintense lesion + hypointensity on GRE ← hemorrhage
√ prominent associated mass effect
√ marked edema
√ increased diffusivity related to underlying acellular core on DWI (opposite to pyogenic + fungal abscess)
√ nodular / ring enhancement
√ poorly defined peripheral enhancement = poor host response
√ HIGHLY SUGGESTIVE "eccentric target" sign (30%) = small enhancing nodule along lesion margin
√ diffuse cerebral volume loss (30%)
MR spectroscopy:
√ lipid breakdown products without elevated choline levels
Dx: improvement on antitoxoplasma therapy within 2–3 weeks / biopsy
DDx: CNS lymphoma (single lesion, hyperattenuation, T2 hypointensity, restricted

diffusion, periventricular location)
◊ Multiple lesions suggest toxoplasmosis!

B. INTRAUTERINE INFECTION
= devastating effects on fetal brain because maternal antibodies passed to child will be limited by blood-brain barrier
Time of fetal infection: chances of transplacental transmission greater in late pregnancy
Screening: impractical due to high false-positive rate
• Toxoplasma gondii found in ventricular fluid
• microcephaly, mental retardation, seizures; chorioretinitis
√ thickened vault, sutures apposed / overlapping
√ hydrocephalus → return to normal / persistent large head
√ intracerebral calcifications in posterior aspect of brain
√ multiple irregular nodular / cystlike / curvilinear calcifications in periventricular area + thalamus + basal ganglia + choroid plexus (= necrotic foci); bilateral; 1–20 mm in size; increasing in number + size (usually not developed by time of birth)
OB-US (as early as 20 weeks MA):
√ sonographic findings in only 36%
√ evolving symmetric ventriculomegaly
√ intracranial periventricular + hepatic densities
√ increased thickness of placenta
√ ascites
◊ Microcephaly is NOT a feature of toxoplasmosis!
Dx: elevated toxospecific IgM levels in fetal blood

Dx: demonstration of elongated teardrop-shaped trophozoites in histologic sections of tissue
Rx: empiric therapy (pyrimethamine + sulfadiazine for 3 weeks)

TUBERCULOSIS OF CNS

= slowly dividing facultative intracellular pathogen
Prevalence: 5% (15% with immunodeficiency)
Worldwide: 1.7 million deaths per year; latent infection in 2 billion persons → 10% lifetime risk for active symptomatic tuberculosis
Transmission: through respiratory droplets → active infection usually begins as Ghon focus

Cranial Tuberculous Meningitis

◊ Most common cause of chronic meningitis!
Pathophysiology:
rupture of initial subependymal / subpial tubercle (**Rich focus**) into subarachnoid space (after earlier hematogenous dissemination) into CSF → thick gelatinous inflammatory exudate settles at base of brain along cisterns + sylvian fissure + along traversing blood vessels

Predisposed: in AIDS patients + infants + small children (part of generalized miliary tuberculosis / primary tuberculous infection)
Location: basal cisterns (around M1 segment of MCA and sylvian fissure) > sulci > cerebral convexities, interhemispheric fissure

√ characteristic thick / nodular enhancement in basal cisterns

DDx: (1) other granulomatous disease: fungus, sarcoid
(2) neoplastic disease: carcinoma, lymphoma

CT:
√ iso- / hyperattenuating meninges relative to basal cisterns
√ often homogeneous contrast enhancement of meninges

MR:
√ normal at unenhanced SE (in early stage)
√ distention of affected subarachnoid spaces with mild shortening of T1 + T2 relaxation times compared with CSF

CEMR:
√ abnormal meningeal enhancement on gadolinium-enhanced T1WI (corresponds to gelatinous exudate)
√ abnormal enhancement of choroid plexus + ependymal lining (rare)

Cx: (1) Communicating hydrocephalus (most common) ← blockage of basal cisterns by inflammatory exudate
(2) Obstructive hydrocephalus (rare) ← mass effect of tuberculoma causing obstruction of CSF flow
(3) Ischemic infarction (20–41%) in basal ganglia and internal capsule ← vasospasm of penetrating vessels / vascular compression / occlusive panarteritis (mostly in MCA distribution)
(4) Cranial neuropathy (17–70%): CN2, CN3, CN4, CN7 ← extension of cisternal inflammation along traversing cranial nerves
(5) Pachymeningitis (rare) ← seeding to bone / dura

DDx: infection (nontuberculous bacteria, virus, fungus, parasite), inflammatory disease (rheumatoid disease, sarcoidosis), neoplasia (meningiomatosis, CSF-seeding neoplasm)

Parenchymal Tuberculosis

Tuberculoma of Brain 70%

= tuberculous granuloma formation within cerebrum as most common parenchymal form of tuberculosis

Incidence: 0.15% of intracranial masses in Western countries; 30% in underdeveloped countries

Age: infant, small child, young adult

Associated with: tuberculous meningitis in 50%

• history of previous extracranial TB (in 60%)

Location: more common in posterior fossa (62%), cerebellar hemispheres (frontal + parietal lobes)

√ solitary lesion; may be multiloculated

Progression: noncaseating → caseating → solid → liquid center

NECT:
√ hypo- / iso- (72%) / hyperdense round / lobulated lesion of 0.5–4 cm in diameter with mass effect (93%)
√ moderate surrounding edema (72%) less marked than in pyogenic abscess

√ central calcification (29%)

CECT:

√ homogeneously enhancing parenchymal tuberculoma

√ homogeneous blush in tuberculoma en plaque along dural plane (6%) (DDx: meningioma en plaque)

√ ring blush (nearly all) with smooth / slightly shaggy margins + thick irregular wall around an isodense center (DDx: pyogenic abscess less thick + more regular)

√ "target" sign (⅓) = central calcification in isodense lesion with ring-blush HIGHLY SUGGESTIVE (DDx: giant aneurysm)

MR:

√ single / multiple well-defined T2 hypointensities

√ solid / ringlike enhancement

√ varying central T2 hyperintensity depending on extent of liquefaction / caseation

√ "target" sign = small focal area of calcification / enhancement in center of ring-enhancing mass

MR spectroscopy:

√ lipid level peaks at 0.9 ppm, 1.3 ppm, 2.0 ppm, 2.8 ppm

√ NO amino acid resonance at 0.9 ppm

DDx: other CNS infection (esp. toxoplasmosis, cysticercosis, fungus), lymphoma, atypical meningioma, radiation necrosis

Tuberculous Abscess of Brain (rare)

Histo: numerous tubercle bacilli in the absence of tubercular granulomatous formation

• early rapid clinical deterioration favors abscess

√ hypointense lesion core on T1WI

√ hyperintense lesion core on T2WI

√ peripheral hypointense rim (= capsule)

Miliary Tuberculosis of CNS 30–60%

Usually associated with: tuberculous meningitis

√ multiple tiny < 2 mm T2-hyperintense foci with homogeneous enhancement

Spinal Tuberculous Meningitis

MR:

√ cerebrospinal fluid loculations with cord compression

√ obliteration of spinal subarachnoid space:

√ loss of outline of spinal cord in cervicothoracic spine

√ matting of nerve roots in lumbar region

√ nodular thick linear intradural enhancement of meninges

Cx: syringomyelia, syringobulbia

Tuberculous Vasculitis

= infectious vasculitis of small and medium-sized cerebral aa. in subarachnoid space

Location: lenticulostriate arteries, posterior cerebral branches, thalamoperforating arteries

Cx: small infarctions in basal ganglia and deep white matter (in up to 41%)

TUBEROUS SCLEROSIS

= TSC = BOURNEVILLE EPIPLOIA
[Désiré-Magloire Bourneville (1840–1909), French neurologist at Salpêtrière, Bicêtre, Hôpital Saint-Louis, Pitié]

= autosomal-dominant neuroectodermal disorder characterized by multifocal systemic hamartomas + malformations that may affect CNS, eye, kidney, lung, liver, skin, heart with a spectrum of phenotypic expressions

CLASSIC TRIAD (of Vogt, 1908) in only 29% of patients:
(1) Facial angiofibromas
(2) Epileptic seizures
(3) Mental retardation
mnemonic: zits, fits, nitwits

Prevalence: 1÷6,000 to 1÷150,000 live births

• family history of TSC in 25–50%

Cause: autosomal-dominant germ line mutation inhibiting cell proliferation with low penetrance (frequent skips in generations); sporadic mutations in 50–60–80%

Genetics: gene mutations of
(a) TSC1 on chromosome 9q34 → protein hamartin
(b) TSC2 on chromosome 16p13 → protein tuberin

Dx: A. Major features
(1) Cortical / subcortical tubers
(2) Subependymal giant cell astrocytoma
(3) Cardiac rhabdomyoma
(4) Facial angiofibroma
(5) Retinal hamartoma
(6) Renal angiomyolipoma
(7) Shagreen patches
(8) Ash-leaf spots
(9) Lymphangioleiomyomatosis

B. Minor features
(1) Gingival fibroma
(2) Dental pits
(3) Hamartomatous rectal polyps
(4) Renal cysts
(5) Cerebral white matter migration lines
(6) Confetti skin lesions
(7) Bone cysts

A diagnosis is definite with 2 major / 1 major + 2 minor features!

Prognosis: 30% dead by age 5; 75% dead by age 20

Rx: antiepileptic medication; ketogenic diet

@ CNS INVOLVEMENT (> 95%)
• intractable myoclonic seizures (75–80%): often first and most common sign of tuberous sclerosis with onset at 1st–2nd year, decreasing in frequency with age
• mental retardation (50–82%): moderate to severe cognitive deficits (⅔), mild to

moderate (⅓); progressive; observed in adulthood; common if onset of seizures before age 5 years

- autism, behavioral + sleep + psychiatric disorders

1. **Subependymal hamartomas**

Location: along ventricular surface of caudate nucleus, on lamina of sulcus thalamostriatus immediately posterior to foramen of Monro (most often), along frontal + temporal horns or 3rd + 4th ventricle (less commonly)

√ multiple subependymal nodules of 1–12 mm:
  √ "candle drippings" appearance
√ periventricular calcification with increasing age (in up to 88%)

MR:
  √ subependymal nodules protruding into adjacent ventricle isointense with white matter
  √ iso- to hyperintense on T1WI + hyper- and hypointense on T2WI relative to gray and white matter
  √ minimal contrast enhancement (in up to 56%)

2. **Giant cell astrocytoma** (in 15–20%)

= SUBEPENDYMAL GIANT CELL TUMOR (SGCT)

Incidence: 5–15%; M÷F = 1÷1

Mean age: 11 years (range, birth to 5th decade); typically < 20 years

Origin: ? subependymal nodule

Histo: low-grade astrocytoma (WHO grade I lesion) with large cells resembling astrocytes / ganglion cells with abundant cytoplasm

Immunohisto: markers for both glial + neuronal proteins

Location: in the region of foramen of Monro; uncommonly in other locations

√ well-circumscribed solid intraventricular neoplasm
√ typically > 13 mm in diameter with interval growth
√ ± variable degrees of calcification ± cystic changes
√ uniform avid enhancement
√ frequent extension into frontal horn / body of lateral ventricle
√ occasionally hemorrhagic

CT:
  √ hypo- / isodense well-demarcated round mass

MR:
  √ hypo- to isointense to gray matter on T1WI
  √ iso- to hyperintense to gray matter on T2WI

Prognosis: tendency to enlarge + growth into ventricles → obstruction at foramen of Monro → progressive obstructive hydrocephalus

Cx: degeneration into higher grade astrocytoma

Surveillance: imaging every 2 (3) years with TSC2 (TSC1) mutation; once identified follow-up imaging at yearly intervals

Subependymal GCT is considered PATHOGNOMONIC for TS (rare without manifestations of TS, then likely representing somatic mosaicism of the TS gene)

3. **Cortical / subcortical tubers** (in 56%)

= CORTICAL / SUBCORTICAL HAMARTOMAS

Histo: clusters of atypical glial cells surrounded by giant cells with frequent calcifications (if > 2 years of age)

Frequency: multiple (75%); bilateral (30%)

√ large misshapen broadened gyri with central hypodense regions ← abnormal myelination

√ masslike / curvilinear calcification of cortical tubers (in 15% < 1 year of age, in 50% by age 10)

MR:

√ relaxation time similar to white matter (if uncalcified)

√ multiple nodules hyperintense on T2WI / FLAIR + iso- to hypointense on T1WI ← fibrillary gliosis / demyelination

√ enhancement extremely rare

4. **Heterotopic gray matter islands in white matter**

Histo: grouping of bizarre and gigantic neuronal cells associated with gliosis + areas of demyelination

Frequency: in up to 93%

Location: along lines of neuronal migration

√ straight / curvilinear bands extending radially from ventricular wall

√ wedge-shaped lesion with apex at ventricular wall

√ conglomerate masses

√ calcification of all / part of nodule

√ may show contrast enhancement

CT:

√ hypodense well-defined regions within cerebral white matter

MR:

√ iso- to hypointense region on T1WI + well-defined hyperintense area on T2WI relative to normal white matter

DDx of CNS lesions:

(1) Intrauterine CMV / Toxoplasma infection (smaller lesions, brain atrophy, microcephaly)

(2) Basal ganglia calcification in hypoparathyroidism / Fahr disease (different location)

(3) Sturge-Weber, calcified AVM (diffuse atrophy, not focal)

(4) Heterotopic gray matter (along medial ventricular wall, isodense, associated with agenesis of corpus callosum, Chiari malformation)

(5) Focal cortical dysplasia

(6) Subependymal heterotopia

@ SKIN INVOLVEMENT (90%)

• **Facial angiofibroma** (former misnomer: adenoma sebaceum) in 80–90%

Path: small hamartomas from neural elements with blood vessel hyperplasia = angiofibromas

Age: first discovered at age 1–5 years; family history in 30%

• wartlike nodules of red-brown / red color averaging 4 mm in size with tendency to enlarge + increase in number over time

Location: CHARACTERISTIC bimalar distribution (“butterfly rash”); initially

nasolabial folds, eventually covering nose + middle of cheeks

- **Ungual fibroma** = Koenen tumor (15–50%)
  Age: develop in adolescent / adult
  Location: sub- / periungual region of toes
  √ erosion of distal tuft
- **Shagreen rough skin patches** (80%)
  = "pigskin" = "peau d'orange"
  Histo: connective tissue nevus (collagenoma) = patches of fibrous hyperplasia
  • irregularly shaped skin-colored / brown soft plaque
  Age: early childhood
  Location: posterior trunk / buttocks + intertriginous
- **Ash leaf patches** = hypomelanotic / hypopigmented macules shaped like ash / spearmint leaf
  • may be visible only under ultraviolet light
  Age: typically present at birth, persist throughout life
  Location: trunk, lower extremity
- "Thumbprint" / "confetti" macules
- Café-au-lait spots
  Incidence: similar to that in general population
  DDx: neurofibromatosis type 1, fibrous dysplasia
- Fibrous forehead plaques

@ OCULAR INVOLVEMENT (50%)

- **Phakoma** (> 5%) = whitish disk-shaped retinal hamartoma
  = astrocytic proliferation in / near optic disc, plaques often multiple + usually in both eyes

√ small calcifications in region of optic nerve head
√ optic nerve glioma

@ RENAL INVOLVEMENT (70–90%)

- usually asymptomatic; flank pain, hematuria, hypertension
- renal failure in severe cases (5%) ← mass effect of cysts and angiomyolipomas

◊ 75% of patients die from complications of renal failure by age 20

1. **Angiomyolipoma** (55–89%): usually multiple
   Cx: spontaneous retroperitoneal hemorrhage (subcapsular / perinephric) → shock
2. **Multiple cysts** of varying size in cortex + medulla mimicking adult polycystic kidney disease (15%)
   Path: cysts lined by columnar epithelium with foci of hyperplasia projecting into cyst lumen
   √ polycystic involvement in infants
3. **Renal cell carcinoma** / **Malignant epithelioid form of angiomyolipoma** (1–3%), bilateral in 40%;
   Average age: 28 years (= 25 years younger than for RCC in general population)
   √ rapid growth + presence of calcifications

Recommendation:
US evaluation every 2–3 years before puberty + yearly thereafter to identify growing lesions

@ LUNG INVOLVEMENT (1–4%)
Age: 3rd–5th decade; in women
• progressive respiratory insufficiency
√ interstitial fibrosis in lower lung fields + miliary nodular pattern may progress to honeycomb lung (**lymphangioleiomyomatosis** = smooth muscle proliferation around blood vessels)
√ multiple bilateral small cysts in lung parenchyma on CT (26–39%)
√ repeated episodes of spontaneous pneumothorax (50%)
√ chylothorax
√ cor pulmonale
@ HEART INVOLVEMENT in children
Prevalence: decreases with increasing age ← spontaneous tumor regression + better survival of patients without cardiac tumor
• congenital cardiomyopathy; typically clinically silent
√ circumscribed / diffuse subendocardial **rhabdomyoma** (in 5–30%) of ventricle (70%) / atrium (30%)
√ aortic aneurysm
@ BONE INVOLVEMENT
√ bone cysts with undulating periosteal reaction in distal phalanges (most common), metacarpals, metatarsals of hand (DDx: sarcoidosis, neurofibromatosis)
√ "**bone islands**":
√ dense sclerotic calvarial patches (45%)
Location: frontal and parietal diploe + internal table; pelvic brim, vertebral neural arch, long bones
√ bone thickening:
√ thickening of diploe ← long-term phenytoin therapy
√ expansion + sclerosis of rib (may be isolated)
√ periosteal thickening of long bones
√ dysplasia of sphenoid body (DDx: NF1 with dysplasia of sphenoid wing)
@ OTHER VISCERAL INVOLVEMENT
1. Adenomas + lipomyomas of liver
2. Adenomas of pancreas
3. Tumors of spleen
@ VASCULAR INVOLVEMENT (rare)
√ thoracic + abdominal arterial aneurysms
Path: vascular dysplasia with intimal + medial abnormalities of large muscular + musculoelastic arteries
Prognosis: 75% mortality by 20 years

UNILATERAL MEGALENCEPHALY

= hamartomatous overgrowth of all / part of a cerebral hemisphere with neuronal migration defects
• intractable seizure disorder at early age, hemiplegia
• developmental delay

√ moderate / marked enlargement of one hemisphere
√ ipsilateral ventriculomegaly proportionate to enlargement of affected hemisphere
√ straightened frontal horn of ipsilateral ventricle pointing anterolaterally
√ neuronal migration defects:
  √ polymicrogyria
  √ pachygyria
  √ heterotopia of gray matter
  √ white matter gliosis (low density in white matter on CT, prolonged T1 + T2 relaxation times on MR)
Rx: partial / complete hemispheric resection

VEIN OF GALEN MALFORMATION / ANEURYSM

= central embryonic AVM of quadrigeminal plate cistern directly drains into a secondarily enlarged ectatic vein of Galen (aneurysm is a misnomer)
Prevalence: < 1% of all vascular brain malformations
Cause: arteriovenous fistula between primitive choroidal vessels and embryonic **median prosencephalic vein of Markowski**; fistula prevents involution of this embryonic vein + leads to development of the vein of Galen
Anatomical types:
Type 1 = AV fistula fed by enlarged arterial branches → dilatation of vein of Galen + straight sinus + torcular herophili
Type 2 = angiomatous malformation involving basal ganglia + thalami ± midbrain draining into vein of Galen
Type 3 = transitional AVM with both features
Feeding vessels:
(a) posterior cerebral artery, posterior choroidal artery (90%)
(b) anterior cerebral artery + anterior choroidal artery
(c) middle cerebral artery + lenticulostriate + thalamic perforating arteries (least common)
Age at presentation: detectable in utero > 30 weeks GA; M÷F = 2÷1
(a) neonatal pattern (0–1 month)
  • high-output cardiac failure (36%) ← massive shunting
  • cranial bruit
(b) infantile pattern (1–12 months)
  • macrocrania from obstructive hydrocephalus; seizures
(c) adult pattern (> 1 year)
  • headaches ± intracranial hemorrhage ± hydrocephalus
  • focal neurologic deficits (5%) ← steal of blood from surrounding structures
◊ Rarely diagnosed > 3 years of age
Associated with: anomalous dural sinuses + sinus stenosis
May be associated with: porencephaly, nonimmune hydrops
Location: midline posterior to 3rd ventricle
Types:
(1) Choroidal type

√ multiple prominent choroidal + pericallosal and thalamostriate feeder arteries
√ drainage into anterior aspect of intensely enhancing aneurysmal median prosencephalic vein of Markowski

(2) Mural type
√ few prominent posterior choroidal / collicular feeder arteries
√ arteries fistulize with lateral walls of an intensely enhancing median prosencephalic vein of Markowski

→ both types drain via persistent falcine sinus into superior sagittal sinus

√ prominent serpiginous network of feeding arteries in basal ganglia, thalami, midbrain + nidus + draining veins

NECT:
√ round well-circumscribed homogeneous slightly hyperdense mass posterior to indented 3rd ventricular outlet
√ hyperdense intracerebral hematoma ← ruptured AVM
√ focal hypodense zones ← ischemic changes
√ rim calcification (14%)

CECT:
√ marked homogeneous enhancement of serpentine structures + vein of Galen + dilated straight + transverse sinus + torcular herophili

US / OB-US:
√ anechoic tubular midline structure superior to cerebellum
√ cardiac enlargement ← high-output heart failure
√ dilated veins of head + neck
√ hydrocephalus with dilatation of lateral + 3rd ventricle (in 37%) ← aqueductal obstruction / posthemorrhagic impairment of CSF absorption
√ brain infarction / leukomalacia ← steal phenomenon with hypoperfusion

Doppler US:
√ median tubular cystic space with high-velocity turbulent flow
√ variable thrombus + feeding vessels
√ tortuous network of dilated arteries

MR:
√ areas of signal void

Angio:
necessary to define vascular anatomy for surgical / endovascular intervention

Cx: subarachnoid hemorrhage

Rx: ligation, excision, embolization of vessels from transtorcular / transarterial approach

Prognosis: 56% (91%) overall (neonatal) mortality: death from cardiac + multisystem failure if untreated

DDx: (1) Aneurysmal dilatation of vein of Galen (= thalamic arteriovenous malformation of brain with deep venous drainage into secondarily dilated vein of Galen)
(2) Dural AV fistula
(3) Giant developmental venous anomaly
(4) Pineal tumor
(5) Arachnoid / colloid / porencephalic cyst

VENTRICULITIS

= EPENDYMITIS = PYOCEPHALUS
= inflammation of ependymal lining of one / more ventricles
Cause: (1) rupture of periventricular abscess (thinner capsule wall medially)
(2) retrograde spread of infection from basal cisterns
CECT (necessary for diagnosis):
√ thin uniform enhancement of involved ependymal lining
√ often associated with intraventricular inflammatory exudate + septations
MR:
√ intraventricular pus shows restricted diffusion on DWI
DDx: intraventricular blood (history!)
Cx: obstructive hydrocephalus ← occlusion at foramen of Monro / aqueduct
DDx: ependymal metastases, lymphoma, infiltrating glioma

Ependymitis Granularis

= symmetric focal areas of hyperintensity on T2WI in normal individuals
Histo: patchy loss of ependyma with paucity of hydrophobic myelin (astrocytic gliosis), which allows migration of fluid out of the ventricle into interstitium
Location: anterior + lateral to frontal horns
√ punctate / up to 1 cm in diameter
√ grossly triangular in shape

Pyogenic Ventriculitis

= frequent complication of meningitis in infants (uncommon in adults)
Risk factors: craniotomy, diabetes (predisposes to staphylococcus and enterobacter infections)
√ intraventricular debris ± restricted diffusion
√ periventricular edema ± enhancement
√ ventricular dilatation

VENTRICULOPERITONEAL SHUNT MALFUNCTION

◊ The peritoneum is an efficient site of fluid absorption
Components: ventriculostomy catheter, pressure-sensitive valve + reservoir, barium-integrated silicone peritoneal catheter

- symptoms of increased intracranial pressure: seizures, headache, nausea, vomiting, lethargy, irritability
- persistent bulging of anterior fontanel
- excessive rate of head growth
- slowed refill of shunt reservoir; abdominal pain, fever

Mechanical Shunt Failure

Cause: occlusion of catheter by choroid plexus / glial tissue, discontinuity of tubes
√ sutural diastasis + increased size of cranial cavity
√ increasing ventricular size:
√ interval increase since last exam

√ enlargement of temporal horns (earliest finding)
√ preferential enlargement of temporal horns in infants
N.B.: (1) no enlargement with scarring of ventricular walls
(2) marked ventricular dilatation does not necessarily indicate shunt malfunction
√ shuntogram (by scintigram / contrast radiography) determines site of obstruction
√ brain edema tracking along shunt + within interstices of centrum semiovale (with partial obstruction)
√ formation of white matter cyst surrounding ventricular catheter

Obstruction of VP Shunt

Location: ventricular end > peritoneal end
Cause: plugging of the catheter by brain parenchyma / choroid plexus / proteinaceous material / tumor cells; adhesions within peritoneum
NUC: ^{99m}Tc-albumin colloid injected into shunt tubing proximal to reservoir:
√ no uptake within ventricles + normal peritoneal activity (= proximal obstruction)
Contrast study (injection of nonionic contrast material into shunt reservoir):
√ collection of contrast material at peritoneal end of shunt without spillage (= distal obstruction)

Disconnection & Breaks of VP Shunt

Location: connection of tubing to reservoir, at Y-connectors, areas of great mobility (neck)
DDx: pseudo-disconnection ← radiolucent tube components

Migration of VP Shunt

A. Proximal catheter: into soft tissues of neck / unusual locations within CNS
B. Distal catheter: peritoneal cavity, thorax, abdominal wall, scrotum, perforation into GI tract

Leakage of VP Shunt

= CSF escape without complete break / disconnection
• palpable cystic mass
√ contrast verifies leak site

CSF Pseudocyst of VP Shunt

√ shunt tubing coiled in an abdominal soft-tissue mass
US / CT:
√ cyst surrounding catheter tip
Cx: bowel obstruction

Infection of VP Shunt

Incidence: 1–5–38%
Time of onset: within 2 months of shunt placement
• intermittent low-grade fever
• anemia, dehydration, hepatosplenomegaly
• stiff neck; swelling + redness over shunting tract; peritonitis

√ ventriculitis (= enlarged ventricles with irregular enhancing ventricular wall ± septations)
√ meningitis (= enhancement of cerebral cortical sulci)

Abdominal Complications of VP Shunt

1. Ascites
2. Pseudocyst formation
3. Perforation of viscus / abdominal wall
4. Intestinal obstruction
5. Metastases to peritoneum: germinoma, medulloblastoma, astrocytoma, glioblastoma

Subdural Hematoma / Hygroma of VP Shunt

Cause: precipitous drainage of markedly enlarged ventricles
Age: usually seen in children > 3 years of age with relatively fixed head size
Prognosis: small hematomas resolve on their own

Granulomatous Lesion of VP Shunt

= rare granulomatous reaction adjacent to shunt tube within / near ventricle
√ irregular contrast-enhancing mass along course of shunt tube

Slit Ventricle Syndrome (0.9–3.3%)

= proximal shunt failure from ventricular collapse
Cause: overdrainage of CSF, intermittent shunt obstruction, decreased intracranial compliance, periventricular fibrosis, intracranial hypotension
Incidence: 0.9–3.3%
• intermittent / chronic headaches, vomiting, malaise
• slowed refill of shunt reservoir
√ small / slitlike ventricles

VISCERAL LARVA MIGRANS OF BRAIN

Organism: roundworm nematode (Toxocara canis)
√ small calcific nodules, especially in basal ganglia + periventricular location
DDx: tuberous sclerosis

VON HIPPEL-LINDAU DISEASE

= vHL = RETINOCEREBELLAR ANGIOMATOSIS
[Eugen von Hippel (1867–1939)], professor of ophthalmology in Heidelberg, Halle and Göttingen, Germany
Arvid Vilhelm Lindau (1892–1958), chair of general pathology, bacteriology and general health science in Lund, Sweden
= autosomal dominant inherited neurocutaneous dysplasia complex grouped under hereditary phakomatosis (although the skin is not affected)
Prevalence: 1÷31,000 – 1÷53,000 births
Genetics: mutation of VHL tumor suppressor gene located on chromosome 3p25-p26 with 80–100% high penetrance + variable delayed expressivity (ie, different subset of 40 types of lesions in 14 different organs); in 20% familial

Effect: propensity to develop multiple clear cell neoplasms like retinal and CNS hemangioblastoma, clear cell renal cell carcinoma, pheochromocytoma, pancreatic serous cystadenoma, pancreatic endocrine tumor (PET)

Age at onset: 2nd–3rd decade; M÷F = 1÷1

Diagnostic criteria:

◊ Hemangioblastoma = almost always disease-defining tumor

(a) > 1 hemangioblastoma of CNS

(b) 1 hemangioblastoma + visceral manifestation

(c) 1 manifestation + known family history

Subclassification (NIH):

Type I = renal + pancreatic cysts, high risk for renal cell carcinoma, NO pheochromocytoma

Type IIA = pheochromocytoma, pancreatic islet cell tumor (typically without cysts)

Type IIB = pheochromocytoma + renal + pancreatic disease

@ CNS MANIFESTATION

Age at presentation: 25–35 years

- signs of increased intracranial pressure: headache, vomiting
- vision changes: reactive retinal inflammation with exudate + hemorrhage, retinal detachment, glaucoma, cataract, uveitis, decreasing visual acuity, eye pain
- cerebellar symptoms: vertigo, dysdiadochokinesia, dysmetria, Romberg sign
- spinal cord symptoms (uncommon): loss of sensation, impaired proprioception

1. Retinal angiomatosis = **von Hippel tumor** (> 50%) <u>earliest</u> manifestation of disease; multiple in up to 66%, bilateral in up to 50%

   Histo: hemangioblastoma of retina

   Dx: indirect ophthalmoscopy + fluorescein angiography

   √ small tumors rarely detected by imaging studies

   √ globe distortion

   √ thick calcified retinal density (calcified angioma-induced hematoma)

   US:

   √ small hyperechoic biconvex homogeneous solid noncalcified masses, usually in temporal retina

   √ NO choroidal excavation

   Cx: (1) repeated vitreous hemorrhage (frequent)
   (2) exudative retinal detachment posteriorly

2. Hemangioblastoma of CNS = **Lindau tumor** (40%)

   = benign nonglial neoplasm as the most commonly recognized manifestation of vHL disease

   Age: 15–40 years

   Site: cerebellum (65%), brainstem (20%), spinal cord (15%); multiple lesions in 10–15% (may be metachronous)

   ◊ 4–20% of single hemangioblastomas occur in von Hippel-Lindau disease!

   CT:

√ large cystic lesion with 3–15-mm mural nodule (75%)
√ solid enhancing lesion (10%)
√ enhancing lesion with multiple cystic areas (15%)
√ intense tumor blush / blushing mural nodule
√ NO calcifications (DDx: cystic astrocytoma calcifies in 25%)

MR (modality of choice):
√ hypointense cystic component on T1WI (slightly hyperintense to CSF ← protein content); hyperintense on T2WI
√ small tubular areas of flow void within mural nodule (= enlarged feeding + draining vessels); intense contrast enhancement of mural nodule
√ slightly hypointense solid lesion on T1WI; hyperintense on T2WI; intense contrast enhancement

Angio:
√ intense staining of mural nodule ("mother-in-law phenomenon" = tumor blush "comes early and stays late", very dense)
√ presence of feeding vessels

Prognosis: most frequent cause of morbidity and mortality; frequent recurrence after incomplete resection

@ LABYRINTH

1. **Endolymphatic sac neoplasm**

= aggressive adenomatous tumor with mixed histologic features
• sensorineural hearing loss

Location: retrolabyrinthine temporal bone
Site: endolymphatic sac
√ aggressive lytic lesion containing intratumoral osseous spicules + areas of hemorrhage
√ heterogeneous enhancement with hyperintense areas on T1WI + T2WI (due to hemorrhage)

@ HEART

1. Rhabdomyoma

@ KIDNEYS

• polycythemia ← elevated erythropoietin level (in 15% with hemangioblastoma, in 10% with renal cell ca.)

1. **Cortical renal cysts** (59–63%)

multiple + bilateral (may be confused with adult polycystic kidney disease); simple appearing cysts often contain small foci of renal cell carcinoma

2. **Renal cell carcinoma** (24–45%)

Age: 20–50 years
√ multicentric in 87%, bilateral in 10–75%; many arise from cyst wall
√ sensitivity: 35% for angiography, 37% for US, 45% for CT ← inability to reliably distinguish between cystic RCC, cancer within cyst, atypical cyst
√ 50% metastatic at time of discovery
Prognosis: slower growing with higher 10-year survival rate than RCC without vHL; RCC is cause of death in 30–50% as the 2nd most frequent cause of mortality!

Screening and management strategy:
follow solid lesion every 6–12 month until the largest lesion is 3 cm → nephron-sparing surgery

3. Renal adenoma
4. Renal hemangioma

@ ADRENAL pheochromocytoma (0–60%) bilateral in up to 40%; confined to certain families

@ epididymis

1. Cystadenoma of epididymis

@ PANCREAS

1. Microcystic serous pancreatic adenoma (12–56%)
2. Microcystic serous pancreatic carcinoma (rare)
3. Pancreatic endocrine tumor (PET in 5–17%)
   Mean age: 38 years (slightly younger than sporadic PET)
   ◊ multiple mostly nonfunctioning PETs (30%) with clear cell change (60%)
   Prognosis: metastases in 1.4% with > 3 cm tumor
4. Pancreatic hemangioblastoma
5. Pancreatic cysts (in 50–91%)
   Incidence: in up to 72% (autopsies)
   Location: pancreatic body + tail
   √ usually multiple multilocular cysts (spectrum from single cyst to cystic replacement of gland)
   √ ± peripheral calcifications
   ◊ Pancreatic cysts may be only manifestation for years
   ◊ Pancreatic cysts in a patient with a family history of von Hippel-Lindau disease are DIAGNOSTIC!

@ LIVER

1. Liver hemangioma
2. Adenoma

@ OTHERS

1. Paraganglioma
2. Cysts in virtually any organ: liver, spleen, adrenal, epididymis, omentum, mesentery, lung, bone

MULTIPLE ORGAN NEOPLASMS

@ Kidney : renal cell carcinoma (up to 40%), renal angioma (up to 45%)
@ Liver : adenoma, angioma
@ Pancreas : cystadenoma / adenocarcinoma
@ Epididymis : adenoma
@ Adrenal gland : pheochromocytoma

MULTIPLE ORGAN CYSTS

(1) Kidney (usually multiple cortical cysts in 75–100% at early age, most common abdominal manifestation)
(2) Pancreas (in 9–72% often numerous cysts; second most common affected abdominal organ)

(3) Others: liver, spleen, omentum, mesentery, epididymis, adrenals, lung, bone

WERNICKE ENCEPHALOPATHY

[Karl Wernicke (1848–1905), professor of neurology and psychiatry in Breslau and Halle, Germany]

◊ MEDICAL EMERGENCY!

Cause: vitamin B1 (thiamine) deficiency

Predisposed:

malnutrition ← chronic alcoholism, GI neoplasm, hematologic neoplasm, chronic dialysis, bowel obstruction, hyperemesis gravidarum, prolonged parenteral Rx

- classic triad of
  - altered consciousness
  - ocular dysfunction (= ophthalmoplegia)
  - ataxia
- anterograde amnesia

Affected areas: medial thalami, periaqueductal gray matter, mamillary bodies, tectal plate

MR:

√ symmetric T2 prolongation
√ petechial hemorrhage
√ diffusion restriction
√ contrast enhancement

Rx: IV replacement of thiamine

WILSON DISEASE

= HEPATOLENTICULAR DEGENERATION

[Samuel Alexander Kinnier Wilson (1878–1937), professor of neurology at King's College Hospital, London and founding editor of the Journal of Neurology and Psychopathology]

= autosomal recessive disorder with increased intestinal resorption of copper → excessive copper retention (= copper toxicosis) with deposition and cell damage in liver + brain

Prevalence: 1÷33,000–200,000; 1÷90 persons is a heterozygous carrier

Cause: alteration of chromosome 13 resulting in inability of liver to excrete copper into bile; hypothetically due to

(a) lysosomal defect in hepatocytes, or
(b) deficiency of biliary copper-binding proteins, or
(c) persistence of fetal mode of copper metabolism, or
(d) hepatic synthesis of high-affinity copper-binding proteins

Age of onset: 7–50 years; hepatic manifestations predominate in children; neuropsychiatric manifestations predominate in adolescents + adults

- ↓ levels of serum copper; ↑ urinary copper excretion
- ⇓ levels of ceruloplasmin (= copper transport protein)
- ↑ copper concentration in serum ceruloplasmin (BEST SCREENING TEST)
- ↓ incorporation of orally administered radiolabeled copper into newly synthesized ceruloplasmin

Stages:

1 Asymptomatic copper accumulation in hepatocytic cytosol
2 Redistribution of copper into hepatic lysosomes + circulation from saturated hepatocytic cytosol
(a) gradual redistribution is asymptomatic
(b) rapid redistribution causes fulminant hepatic failure / acute intravascular hemolysis
3 Cirrhosis, neurologic, ophthalmologic, renal dysfunction: may be reversible with therapy

Rx: life-long pharmacologic therapy with chelation agents (penicillamine / trientine / zinc); liver transplantation

@ CNS

= excessive copper deposition in brain

Location: commonly in lenticular nucleus (= lenslike configuration of putamen + globus pallidus)
<u>perhaps also in</u>:
caudate nucleus, ventrolateral aspect of thalamus, cortical and subcortical region, mesencephalon, pons, vermis, dentate nucleus

- Kayser-Fleischer ring (= green pigmentation surrounding limbus corneae) is DIAGNOSTIC
- dysarthria, dysphagia, dystonia
- tremors, ataxia, Parkinsonian symptoms
- intellectual impairment, emotional disturbance

√ diffusion restriction (in early stages)
√ cerebral white matter atrophy
√ areas of CT hypodensities + T2 prolongation

@ Liver

- jaundice / portal hypertension (with liver cirrhosis)

Histo: macrovesicular fat deposition in hepatocytes, glycogen degeneration of hepatocyte nuclei, Kupffer cell hypertrophy

<u>in children:</u>
√ normal hepatic attenuation (fatty infiltration + copper deposition cancel each other out)
√ normal T1 relaxation time (in spite of paramagnetic effects of copper)

Cx: acute fulminant hepatitis, macronodular cirrhosis

@ Skeletal manifestations (in ⅔)

- pain, stiffness, gelling of joints (in 75%)

Location: shoulder (frequent), knee, hip, wrist, 2nd–4th MCP joints

√ subarticular cysts
√ premature osteoarthritis (narrowing of joint space + osteophyte formation)
√ osteochondritis dissecans
√ chondrocalcinosis
√ premature osteoarthrosis of spine, prominent Schmorl nodes, wedging of vertebrae, irregularities of vertebral plates
√ generalized deossification may produce pathologic fractures

Cx: rickets + osteomalacia (← renal tubular dysfunction) in minority of patients

ZELLWEGER SYNDROME

[Hans Ulrich Zellweger (1909–1990), Swiss-American pediatrician at American University in Beirut, Lebanon and University of Iowa]
= CEREBROHEPATORENAL SYNDROME
= autosomal recessive peroxisomal disorder with disturbed myelination in oligodendrocytes during neonatal + infantile period
Path: ⇑ very long–chain fatty acids in plasma and fibroblasts
Associated with:
@ CNS: cortical dysplasia, hypomyelination
@ Bile ducts: intrahepatic biliary dysgenesis
@ Kidney: polycystic renal disease
• poor feeding + failure to thrive, muscular hypotonia
• hepatomegaly + prolonged jaundice
• craniofacial dysmorphism, abnormal vision (typical)
• seizures, mental retardation
MR:
√ hypomyelination
√ diffuse microgyria + regions of pachygyria, lissencephaly
√ subependymal germinolytic cysts in caudothalamic groove
MR spectroscopy:
√ ↑ lipid levels + ↓ N-acetylaspartate levels
√ renal cortical cysts
Prognosis: death within 1st year of life

ORBIT

DIFFERENTIAL DIAGNOSIS OF ORBITAL AND OCULAR DISORDERS

OPHTHALMOPLEGIA

Lesions of

1. Oculomotor nerve (CN III)
   innervates medial rectus, superior rectus, inferior rectus, inferior oblique muscle, pupilloconstrictor, levator palpebrae
2. Trochlear nerve (CN IV)
   innervates superior oblique muscle
3. Abducens nerve (CN VI)
   innervates lateral rectus muscle

ANOPIA

[numbers refer to drawing]

A. MONOCULAR DEFECTS

1 = monocular blindness (optic nerve lesion in fracture of optic canal, amaurosis fugax)

B. BILATERAL heteronymous DEFECTS

2 = bitemporal hemianopia (chiasmatic lesion)

C. BILATERAL HOMONYMOUS DEFECTS

3 = homonymous hemianopia

4 = upper right-sided quadrantanopia

5 = central hemianoptic scotoma

3,4,5 = most common type of hemianopia (CVA, brain tumor)

Monocular Blindness In Adulthood

1. Optic neuritis
2. Vascular ischemia
   (a) Amaurosis fugax = cholesterol emboli from ICA occluding central retinal artery and its branches
   (b) Occult cerebrovascular malformation affecting the optic nerve
3. Temporal arteritis
4. Malignant optic glioma of adulthood

ORBIT

Spectrum of Orbital Disorders

A. INFLAMMATORY DISEASE

1. Tissue-specific inflammation:
   orbital cellulitis, optic neuritis, scleritis, myositis, Graves disease
2. Panophthalmitis
3. Pseudotumor of orbit

B. CYSTIC DISEASE
1. Dermoid cyst
2. Mucocele
3. Retroocular cyst (developmental)

C. VASCULAR LESIONS
(a) arterial and arteriovenous lesion
1. Ophthalmic artery aneurysm
2. Arteriovenous fistula (rare) eg, Wyburn-Mason syndrome
3. Carotid-cavernous fistula

(b) capillary lesion
4. Capillary hemangioma / benign hemangioendotheliloma

(c) venous vascular malformation
5. Cavernous hemangioma
6. Orbital varix

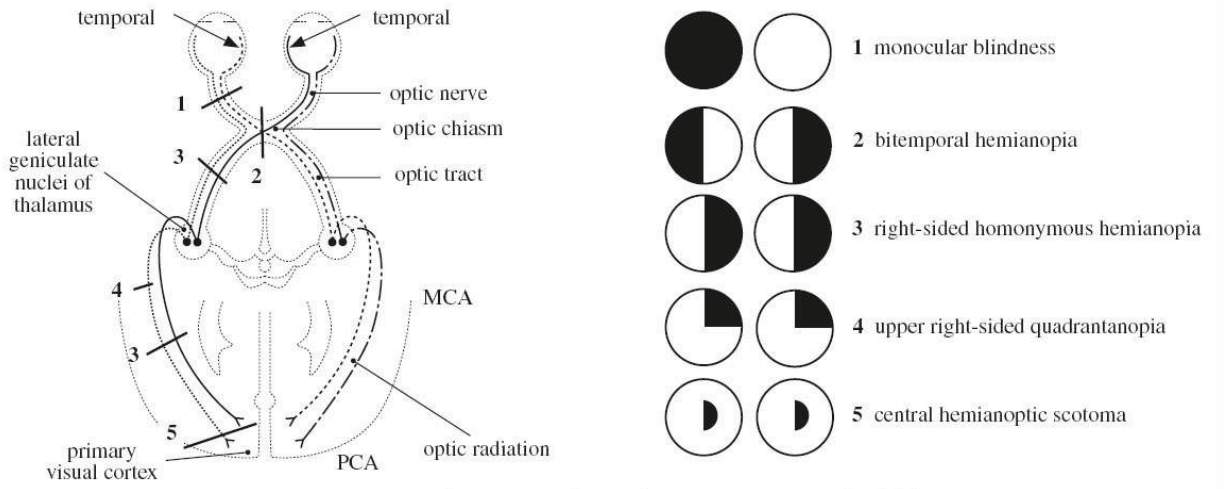
(d) venous lymphatic malformation
7. Capillary lymphangioma
8. Cavernous lymphangioma
9. Cystic lymphangioma

D. TUMORS
1. Rhabdomyosarcoma
2. Optic nerve glioma
3. Meningioma
4. Lymphoma
5. Metastasis
6. Hemangiopericytoma

Intraconal lesion

mnemonic: **M**el **M**et **R**ita **M**ending **H**ems **O**n **P**oor **C**harlie's **G**rave

Melanoma
Metastasis
Retinoblastoma
Meningioma
Hemangioma
Optic glioma
Pseudotumor
Cellulitis
Grave disease



Types of Anopia *(numbers refer to lesion location versus visual field deficits)*

Intraconal Lesion with Optic Nerve Involvement

1. Optic nerve glioma
2. Optic nerve sheath meningioma (10% of orbital neoplasm)
3. Optic neuritis
4. Inflammatory pseudotumor (may surround optic nerve)
5. Sarcoidosis
6. Intraorbital lymphoma (may surround optic nerve, older patient)
7. Elevated intracranial pressure
   → distension of optic sheath
   √ bilateral tortuous enlarged optic nerve-sheath complex

OPTIC NERVE TRAM-TRACK SIGN

1. Optic nerve sheath meningioma
2. Orbital pseudotumor
3. Perioptic neuritis
4. Perioptic hemorrhage
5. Sarcoidosis
6. Lymphoma / leukemia
7. Metastasis
8. Erdheim-Chester disease = systemic xanthogranulomatosis

Intraconal Lesion without Optic Nerve Involvement

1. Cavernous hemangioma
2. Orbital varix
3. Carotid-cavernous fistula
4. Arteriovenous malformation
   least common of orbital vascular malformations (congenital, idiopathic, traumatic)
   √ irregularly shaped intensely enhancing mass of enlarged vessels
   √ associated with dilated superior / inferior ophthalmic v.
5. Hematoma

6. Lymphangioma
7. Neurilemmoma
   √ commonly adjacent to superior orbital fissure, inferior to optic nerve
   √ local bone erosion
8. Rhabdomyosarcoma (mostly extraconal)

Extraconal lesion

Extraconal-intraorbital Lesion

A. BENIGN TUMOR
   1. Dermoid cyst
   2. **Teratoma**
      < 1% of all pediatric orbital tumors
      √ ± areas of fat, cartilage, bone
      √ expansion of bony orbit ± bone defect
   3. Capillary hemangioma
   4. Lymphangioma
   5. Plexiform neurofibroma
   6. Inflammatory orbital pseudotumor
   7. Histiocytosis X
      lesion usually arises from bone

B. MALIGNANT TUMOR
   1. Lymphoma / leukemia
   2. Metastasis
   3. Rhabdomyosarcoma

mnemonic: MOLD
Metastasis
Others (rhabdomyosarcoma, lymphangioma, sinus lesion)
Lymphoma, **L**acrimal gland tumor
Dermoid

Extraconal-extraorbital Lesion

A. FROM SINUS
   maxillary / sphenoid sinuses are rare locations of origin
   1. Tumor:
      squamous cell carcinoma (80%), lymphoma, adenocarcinoma, adenoid cystic carcinoma
   2. Mucocele
   3. Paranasal sinusitis:
      ◊ Most common cause of orbital infection!
      Origin: from ethmoid sinuses (in children), from frontal sinus (in adolescence)
      √ preseptal / orbital edema / cellulitis
      √ subperiosteal / orbital abscess
      √ mucormycosis (in diabetics) destroys bone and extends into cavernous sinus
      Cx: (1) Epidural abscess

(2) Subdural empyema
(3) Cavernous sinus thrombosis
(4) Meningitis
(5) Cerebritis
(6) Brain abscess

B. FROM SKIN
1. Orbital cellulitis

C. FROM LACRIMAL GLAND
√ mass arising from superolateral aspect of orbit

Dilatation of Superior Ophthalmic Vein

1. Carotid-cavernous sinus fistula
2. Cavernous sinus thrombosis
3. Venous varix
4. Graves disease
5. Normal variant

ORBITAL MASS

Orbital Mass in Adults

(a) vasculogenic orbital mass
1. Cavernous malformation
2. Hemangiopericytoma

(b) lymphoproliferative orbital lesion
1. Typical / atypical lymphoid hyperplasia
2. Lymphoma of orbit

(c) lacrimal gland lesion (5–14% of biopsied orbital masses)
› epithelial (largely neoplastic) lesion (40–50%)
1. Pleomorphic adenoma
2. Adenoid cystic carcinoma

› nonepithelial lesion
1. Dacryoadenitis
2. Lacrimal gland lymphoma

(d) optic nerve & meningeal lesions
1. Optic pathway glioma
2. Optic nerve sheath meningioma

(e) peripheral nerve sheath lesions
1. Schwannoma (rare)
2. Neurofibroma
3. Malignant peripheral nerve sheath tumor

(f) Primary orbital melanoma

(g) Metastasis to orbit

Orbital Mass in Childhood

1. Dermoid cyst 46%
2. Inflammatory lesion 16%
3. Dermolipoma 7%
4. Capillary hemangioma 4%
5. Rhabdomyosarcoma 4%
6. Leukemia / lymphoma 2%
7. Optic nerve glioma 2%
8. Lymphangioma 2%
9. Cavernous hemangioma 1%

mnemonic: LO VISHON

Leukemia, **L**ymphoma
Optic nerve glioma
Vascular malformation: hemangioma, lymphangioma
Inflammation
Sarcoma: ie, rhabdomyosarcoma
Histiocytosis
Orbital pseudotumor, **O**steoma
Neuroblastoma

Osseous Orbital Lesion in Children

(a) development of the osseous orbit
   1. Dermoid inclusion cyst
   2. Epidermoid inclusion cyst

(b) primary bone lesions
   1. Fibrous dysplasia
   2. Juvenile ossifying fibroma
   3. Cementifying fibroma
   4. Langerhans cell histiocytosis

(c) malignant tumors involving multiple sites
   1. Granulocytic sarcoma
   2. Hematogenous metastasis: neuroblastoma (most common primary tumor to involve orbit)

(d) primary malignant bone tumor
   1. Osteosarcoma

Nonosseous Lesion of Extraocular Orbit in Children

1. Rhabdomyosarcoma
2. Infantile hemangioma
3. Lymphangioma
4. Infantile fibromatosis

Primary Malignant Orbital Tumors

1. Retinoblastoma 86.0%
2. Rhabdomyosarcoma 8.1%

3. Uveal melanoma 2.3%
4. Sarcoma 1.7%

Pediatric Orbital Tumors

1. Retinoblastoma
2. Medulloepithelioma
3. Optic nerve glioma

Secondary Malignant Orbital Tumors

1. Leukemia 36.7%
2. Sarcoma 14.3%
3. Hodgkin lymphoma 11.0%
4. Neuroblastoma 9.2%
5. Wilms tumor 6.7%
6. Non-Hodgkin lymphoma 5.6%
7. Histiocytosis 3.9%
8. Medulloblastoma 3.5%

Orbital Cystic Lesion

1. Abscess
2. Intraorbital hematoma
3. Dermoid cyst
4. Lacrimal cyst
5. Lymphangioma
6. Hydatid cyst

Orbital Vascular Tumors

1. Orbital varix
2. Arteriovenous malformation
3. Carotid-cavernous fistula
4. Hemangioma: capillary / cavernous
5. Blood cyst
6. Arterial malformation
7. Glomus tumor
8. Hemangiopericytoma

Mass in Superolateral Quadrant of Orbit

1. Lacrimal gland tumor
2. Dermoid cyst
3. Metastasis (breast, prostate, lung)
4. Lymphoma
5. Leukemic infiltration of lacrimal gland
6. Sarcoidosis

7. Wegener granulomatosis
8. Pseudotumor
9. Frontal sinus mucocele

Granulomatous Orbital Apex Mass

√ avidly enhancing orbital soft-tissue mass with involvement of extraocular muscles + lacrimal glands

1. Granulomatosis with polyangiitis
2. Sarcoidosis

Extraocular Muscle Enlargement

A. ENDOCRINE
   1. Graves disease (50%)
   2. Acromegaly
B. INFLAMMATION
   1. **Myositis**
      • rapid onset of proptosis, erythema of lids, conjunctival injection
      Location: single muscle (in adults); multiple muscles (in children)
      √ enlarged extraocular muscle
      √ positive response to steroids
   2. Orbital cellulitis
   3. Sjögren disease, Wegener granulomatosis, lethal midline granuloma, SLE
   4. Sarcoidosis
   5. Foreign-body reaction
C. TUMOR
   1. Pseudotumor
   2. Rhabdomyosarcoma
   3. Metastasis, lymphoma, leukemia
D. VASCULAR
   1. Spontaneous / traumatic hematoma
   2. Arteriovenous malformation
   3. Carotid-cavernous sinus fistula

GLOBE

Spectrum of Ocular Disorders

A. CONGENITAL
   1. Persistent fetal vasculature
   2. Coats disease
   3. Coloboma
   4. Congenital cataract
B. VITREORETINAL
   1. Vitreous hemorrhage
   2. Retinal detachment
   3. Choroidal detachment

4. Endophthalmitis
5. Retinoschisis
6. Retrolental fibroplasia

C. TUMOR
1. Retinoblastoma
2. Choroidal hemangioma
3. Retinal angiomatosis
4. Melanocytoma
5. Choroidal osteoma

D. TRAUMA

Microphthalmia

= congenital underdevelopment / acquired diminution of globe

A. BILATERAL with cataract
1. Congenital rubella
2. Persistent hyperplastic vitreous
3. Retinopathy of prematurity
4. Retinal folds
5. Lowe syndrome
   √ small globe + small orbit

B. UNILATERAL
1. Trauma / surgery / radiation therapy
2. Inflammation with disorganization of eye (phthisis bulbi)
   √ shrunken calcified globe + normal orbit

Macrophthalmia

= enlargement of globe

A. WITHOUT INTRAOCULAR MASS

(a) generalized enlargement
1. Axial myopia (most common cause)
   √ enlargement of globe in AP direction
   √ ± thinning of sclera
2. Buphthalmos
3. Juvenile glaucoma
4. Connective tissue disorder:
   Marfan syndrome, Ehlers-Danlos syndrome, Weill-Marchesani syndrome (congenital mesodermal dysmorphodystrophy), homocystinuria
   √ "wavy" contour of sclera

(b) focal enlargement
1. Staphyloma
2. Apparent enlargement due to contralateral microphthalmia

B. WITH INTRAOCULAR MASS
(rare cause for enlargement)

(a) with calcifications:
1. Retinoblastoma

(b) without calcifications:
1. Melanoma
2. Metastasis

Posterior Wall Mass

Origin: vascular uvea

1. Melanoma
2. Metastasis
3. Melanocytic nevus
4. Choroidal hemangioma
5. Hemangioblastoma
6. Pseudomass: subretinal hematoma, granuloma

Deformity of Globe Contour

1. Open-globe injury
2. Posttraumatic orbital hematoma
3. Coloboma
4. Staphyloma

Orbital Calcifications

Extraocular Calcifications

1. Trochlear calcifications
   = aging-related normal variant / young diabetic patient
   Location: superomedial orbit

Intraocular Calcifications

1. Retinoblastoma (> 50% of all cases)
2. Astrocytic hamartoma
3. Choroidal osteoma
4. Optic drusen
5. Scleral calcifications
   (a) in systemic hypercalcemic states (HPT, sarcoidosis, hypervitaminosis D, in chronic renal disease)
   (b) in elderly: **scleral plaques** at insertion of extraocular muscles, esp. medial + lateral rectus mm.
6. Retrolental fibroplasia
7. **Phthisis bulbi**
   Cause: trauma or infection / inflammation
   √ small contracted / shrunken calcified / ossified disorganized nonfunctioning globe
7. Calcified cataract

mnemonic: NMR CT

Neurofibromatosis
Melanoma (hyperdense melanin)
Retinoblastoma
Choroidal osteoma

Tuberous sclerosis

Posttherapeutic Orbital Changes

1. Lens implant
2. **Scleral band / buckle**
   √ radiopaque / radiolucent device at midglobe level
3. Intraocular silicone oil injection
   √ silicone > 100 HU (DDx: blood < 90 HU)
   √ silicone-related chemical shift artifact
4. Pneumatic retinopexy
   √ gas within globe
5. Globe prosthesis

Noncalcified Ocular Lesion

1. Melanoma
2. Metastasis
3. Choroidal hemangioma
4. **Vitreous lymphoma**
   √ diffuse ill-defined soft-tissue density
5. Developmental anomalies
   (a) **Primary glaucoma** = enlargement of eye ← narrowing of Schlemm canal
   (b) Coloboma
   (c) Staphyloma

Vitreous Hemorrhage

Cause: trauma, surgical intervention, arterial hypertension, retinal detachment, ocular tumor, Coats disease

• visual loss frequent

US:

√ numerous irregular, poorly defined low-intensity echoes
√ echogenic material moving freely within vitreous chamber during eye movement
√ voluminous hyperechoic fibrin clots not fixed to optic nerve (DDx to retinal detachment)

Prognosis: complete absorption / development of vitreous membranes (repetitive episodes)

Cx: retinal detachment ← vitreous traction ← fibrovascular ingrowth following hemorrhage

Dense Vitreous in Pediatric Age Group

1. Retinoblastoma
2. Persistent fetal vasculature
3. Coats disease
4. Norrie disease
5. Retrolental fibroplasia
6. Sclerosing endophthalmitis

Echoes within Normal Anechoic Vitreous

1. **Vitreous degeneration**

√ usually bilateral small freely moving low-level echoes within vitreous

2. Asteroid hyalosis
3. Vitreous hemorrhage
4. Vitritis
   √ low- / medium-level echoes throughout vitreous
   √ membranes appear with progressive organization

Leukokoria

= abnormal white / pinkish / yellowish pupillary light reflex [*leuko*, Greek = white; *kore*, Greek = pupil]

Although leukokoria is suspicious for retinoblastoma, other disease processes may also cause leukokoria.

A. TUMOR
   1. Retinoblastoma 47–58%
   2. Retinal astrocytic hamartoma (3%)
      Associated with: tuberous sclerosis + von Recklinghausen disease
   3. Medulloepithelioma (rare)

B. DEVELOPMENTAL
   1. Persistent fetal vasculature 19–28%
   2. Coats disease 4–16%
   3. Retrolental fibroplasia (3–5%)
   4. Coloboma of choroid / optic disc (11%)

C. INFECTION
   1. Uveitis
   2. Larval endophthalmitis / granulomatosis 7–16%

D. DEGENERATIVE
   1. Posterior cataract (13%)

E. TRAUMA
   1. Retinopathy of prematurity 5–13%
   2. Organized vitreous hemorrhage
   3. Long-standing retinal detachment

Leukokoria in Normal-sized Eye

A. CALCIFIED MASS
   1. Retinoblastoma
   2. Retinal astrocytoma

B. NONCALCIFIED MASS
   1. Toxocara endophthalmitis
   2. Coats disease

Leukokoria with Microphthalmia

A. UNILATERAL
   1. Persistent fetal vasculature

B. BILATERAL
   1. Retinopathy of prematurity

2. Bilateral persistent hyperplastic primary vitreous

OPTIC NERVE

Optic Nerve Enlargement

A. TUMOR:
   1. Optic pathway glioma
   2. Optic nerve sheath meningioma
   3. Infiltration by leukemia / lymphoma

B. FLUID:
   1. Perineural hematoma
   2. Papilledema of intracranial hypertension
   3. Patulous subarachnoid space

C. INFLAMMATION:
   1. Optic neuritis
   2. Sarcoidosis

√ fusiform thickening of optic nerve-sheath complex
= lens-shaped thickening
(a) with central lucency: meningioma
(b) without central lucency: optic nerve glioma

√ excrescentic thickening of optic nerve-sheath complex
= single / multiple nodules along nerve-sheath complex usually due to tumor

√ tubular enlargement of optic nerve-sheath complex
= uniform enlargement of nerve-sheath complex
(a) with central lucency: subarachnoid process (metastases, perineuritis, meningioma, perineural hemorrhage)
(b) without central lucency: papilledema, leukemia, lymphoma, sarcoid, optic nerve glioma

LACRIMAL GLAND

Lacrimal Gland Lesion

A. INFLAMMATION
   1. Dacryoadenitis
   2. Mikulicz disease
   3. Sjögren syndrome
   4. Sarcoidosis
   5. Pseudotumor of orbit
   6. IgG4-related disease

B. TUMOR
   (a) benign: granuloma, cyst, benign mixed tumor (= pleomorphic adenoma)
   (b) malignant: malignant mixed tumor (= pleomorphic adenocarcinoma), adenoid cystic carcinoma, lymphoma, metastasis (rare)

Lacrimal Gland Enlargement

mnemonic: MELD

Metastasis
Epithelial tumor
Lymphoid tumor
Dermoid

Bilateral Lacrimal Gland Masses

mnemonic: LACS

Lymphoma
And
Collagen-vascular disease
Sarcoidosis

Lacrimal Sac Lesion

A. INFLAMMATION
   1. Sarcoidosis
   2. Wegener granulomatosis
B. BENIGN LESION
   1. Mucoceles
   2. Epidermoid cysts
C. MALIGNANCY
   1. Squamous cell carcinoma
   2. Lymphoma

ANATOMY OF ORBIT

ORBIT

[*orbita*, Latin = wheel track, course, path]; [*oculus*, Latin = eye]
= four-sided pyramidal space formed by 7 bones
Floor: maxilla, zygoma, palatine
Roof: orbital plate of frontal bone, lesser wing of sphenoid
Medial wall: ethmoid, lacrimal bone
Division:

A. Globe / ocular compartment
B. **Muscle cone**
   = 5 extraocular muscles (except inferior oblique m.) separating intra- from extraconal spaces
   √ converges at orbital apex to form tendinous ring (= annulus of Zinn)
   [Johann Gottfried Zinn (1727–1759), German anatomist and botanist, member of the Berlin Academy]
   Annulus of Zinn contains
   1. Optic nerve
   2. Oculomotor nerve (superior + inferior divisions)
   3. Abducens nerve
   4. Nasociliary branch of ophthalmic nerve
   5. Ophthalmic artery
C. Intraconal space
D. Extraconal space

Normal Orbit Measurements

6 extraocular muscles

medial rectus muscle	4.1 ± 0.5 mm
inferior rectus muscle	4.9 ± 0.8 mm
superior rectus muscle	3.8 ± 0.7 mm
lateral rectus muscle	2.9 ± 0.6 mm
superior oblique muscle	2.4 ± 0.4 mm
inferior oblique muscle	

Superior ophthalmic vein

axial CT	1.8 ± 0.5 mm
coronal CT	2.7 ± 1.0 mm

Optic nerve sheath

retrobulbar	5.5 ± 0.8 mm
waist	4.2 ± 0.6 mm

Globe position

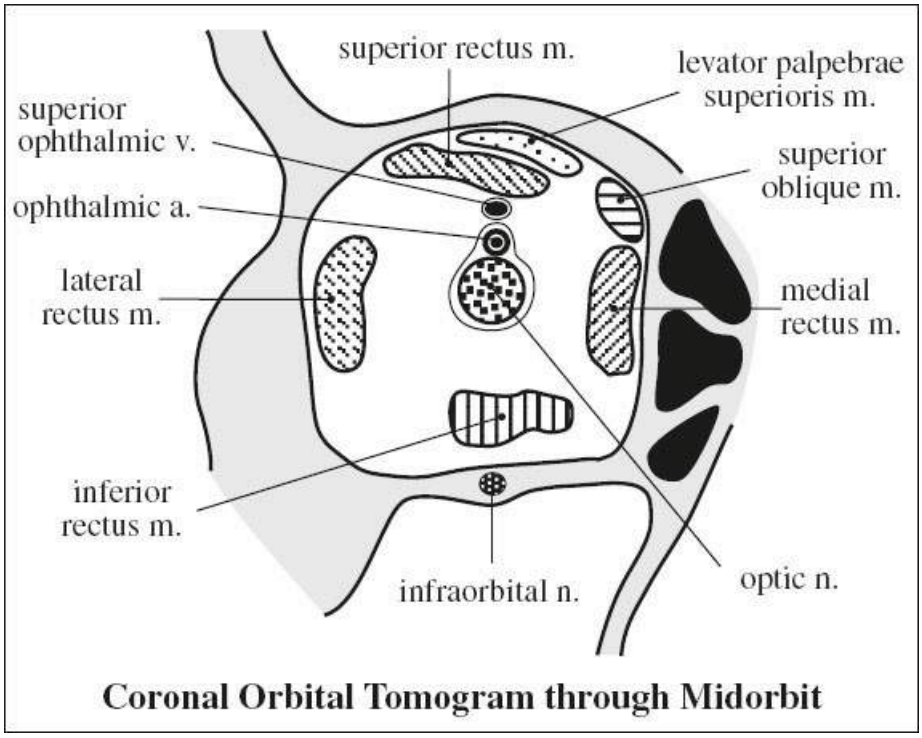
behind interzygomatic line 9.9 ± 1.7 mm

Orbital Compartments

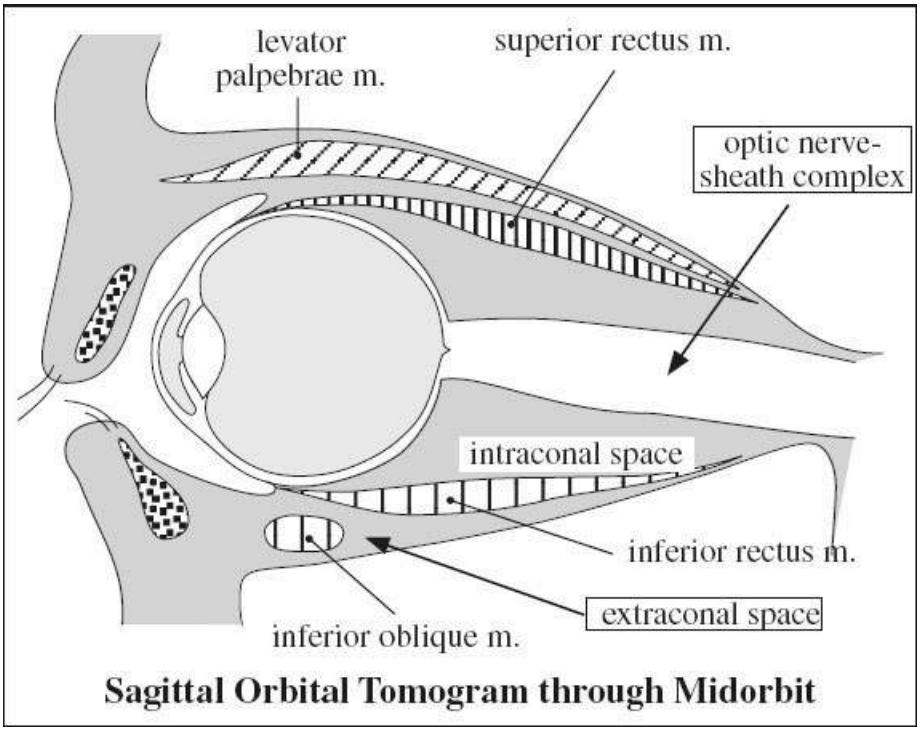
the orbital septum + globe divide orbit into

A. ANTERIOR COMPARTMENT

lids, lacrimal apparatus, anterior soft tissues



Coronal Orbital Tomogram through Midorbit



Sagittal Orbital Tomogram through Midorbit

Orbital Spaces	
globe:	subdivided into anterior + posterior segments by lens
optic nerve-sheath complex:	optic nerve surrounded by meningeal sheath as extension from cerebral meninges
intraconal space:	orbital fat, ophthalmic a., superior ophthalmic v., nerves I, III, IV, V_1, VI
conus:	incomplete fenestrated musculofascial system extending from bony orbit to anterior third of globe, consists of extraocular muscles + interconnecting fascia
extraconal space:	between muscle cone + bony orbit containing fat, lacrimal gland, lacrimal sac, portion of superior ophthalmic v.

B. POSTERIOR COMPARTMENT
= RETROBULBAR SPACE = cone consisting of extraorbital muscles + envelope of fascia divides retrobulbar space into
(a) intraconal space
(b) extraconal space

GLOBE

Ocular globe diameter: 22–25 mm
Wall: composed of 3 layers:
(a) fibrous outermost layer
Function: maintaining shape + pressure of globe
1. **Sclera** = collagenous tissue layer continuous anteriorly with cornea posteriorly with dura mater
2. **Cornea**

(b) **Uvea** = pigmented vascular middle layer
[*uvea*, Latin = grape]
3. **Iris**
4. **Ciliary body** (anteriorly)
5. **Choroid** (posteriorly) = most vascular structure of globe
Attachment: tethered to sclera by arteries + veins
◊ Most frequent site of intraocular metastases!

(c) innermost sensory layer
5. **Retina** = light-sensitive (sensory) inner layer
Attachment: firm at anterior margin (= ora serrata) and posteriorly at optic disc

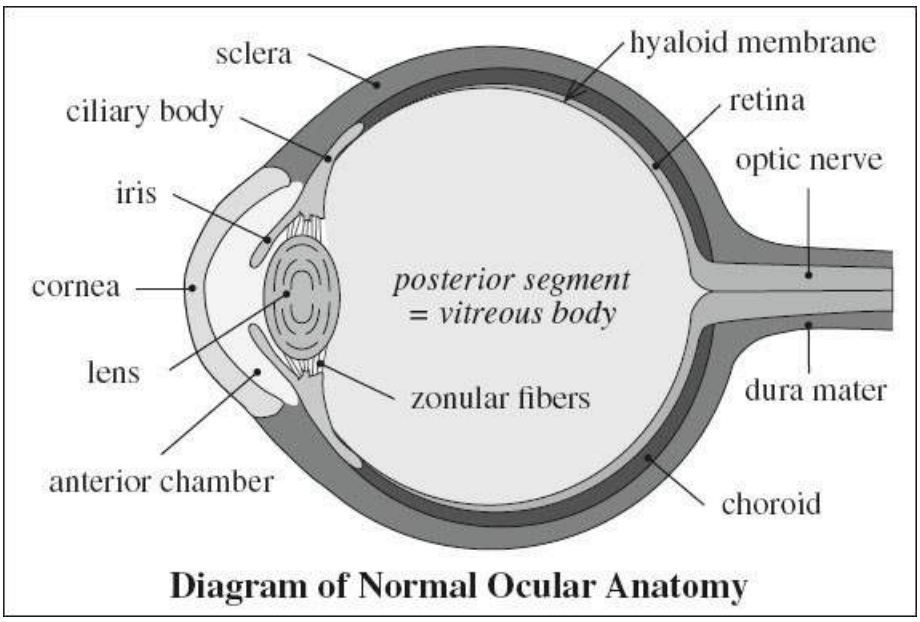


Diagram of Normal Ocular Anatomy

√ various layers of globe are NOT discernable at imaging, especially CT
√ sclera may be separated from choroid at high-res MRI
√ individually visualized in ocular (choroidal / retinal) detachments

Contents: (a) anterior segment containing
1. Aqueous humor subdivided by iris into:
› anterior chamber
› canal of Schlemm (*see below*)
› posterior chamber

(b) posterior segment containing
2. Vitreous humor

Potential ocular spaces:
(a) between retina + choroid → retinal detachment
(b) suprachoroidal space between choroid + sclera → choroidal detachment
(c) between vitreous + posterior hyaloid membrane → hyaloid detachment

Canal of Schlemm

[Friedrich Schlemm (1795–1858), German anatomist, sentenced for grave robbing, eventually

professor at the University of Berlin]
= SCLERAL VENOUS SINUS [misnomer - not a blood vessel]
= circular ringlike endothelium-lined tube lymphatic tube resembling a lymphatic vessel
Location: adjacent to outer angle of anterior chamber in pectinatum iridis (= periphery of cornea) between cornea + iris
Function: collects aqueous humor from anterior chamber and delivers it into the venous system

OPTIC NERVE SHEATH

= extension of dura mater
Content:
1. Optic nerve
2. Ophthalmic artery
3. Small veins

OPTIC NERVE (CN II)

Histo: CN II is an extension of brain = retinal ganglion cell axons myelinated by oligodendrocytes + enveloped within meninges
Segments:
A. Retinal segment leaves ocular globe through lamina cribrosa sclerae
B. Orbital segment travels in center of fat-filled orbit
√ surrounded by dural sheath containing CSF
C. Canalicular segment lies in optic canal below ophthalmic artery; frequently overlooked on radiologic images
D. Cisternal segment in suprasellar cistern leading to optic chiasm
√ anterior cerebral a. passes over superior aspect of nerve

OCULOMOTOR NERVE (CN III)

Exit: from brainstem anteriorly between posterior cerebral (PCA) + superior cerebellar arteries
Segments:
(1) cisternal segment courses through prepontine cistern
(2) cavernous sinus segment along cephalad portion of the lateral dural wall
(3) orbital segment through the superior orbital fissure
(4) division into superior + inferior branches
Function:
(a) motor fibers to
› levator palpebrae muscle
› all extraocular muscles except lateral rectus and superior oblique mm.
(b) parasympathetic fibers to
› internal eye muscles (pupillary sphincter and ciliary muscles) → constriction of pupil via Edinger-Westphal nucleus
Location: periphery of CN III → subject to compression by extrinsic masses
Disturbed function:

(1) "**pupil-sparing" oculomotor palsy** = loss of motor function in extraocular muscles with relative sparing of pupillary parasympathetic innervation ← compromised blood flow to central microvessels

(2) compression by **posterior communicating artery aneurysm** ← close association with posterior cerebral (PCA) + superior cerebellar arteries

(3) compression during transtentorial **uncal herniation** ← course over petroclinoid ligament

Nuclei:

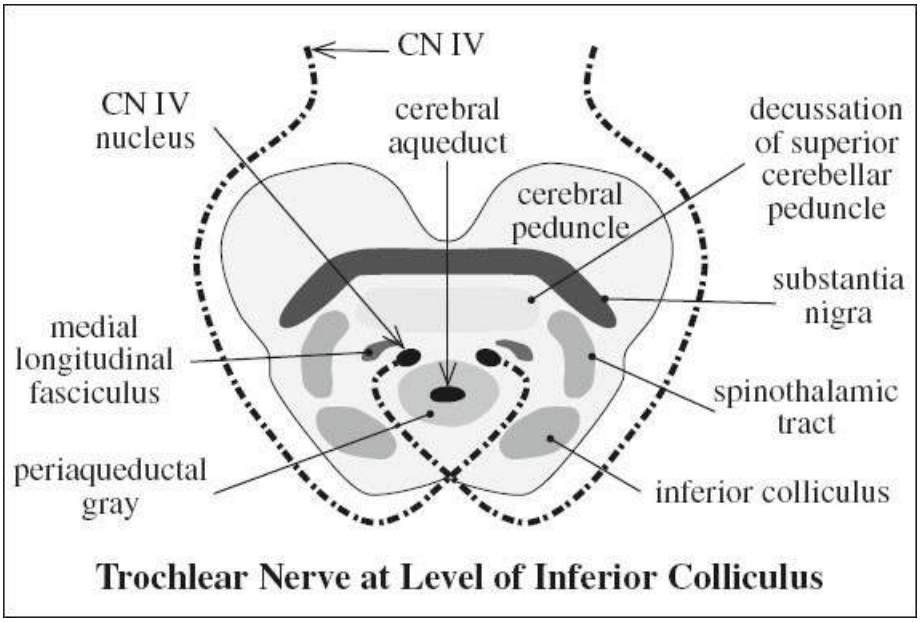
(1) Edinger-Westphal nucleus
located dorsally in periaqueductal gray matter

(2) Number of smaller nuclei arranged in an anterior and posterior group

TROCHLEAR NERVE (CN IV)

Function: pure motor nerve → innervates superior oblique m.

Nucleus: paramedian midbrain → fascicles course postero-inferiorly around cerebral aqueduct → decussation



Trochlear Nerve at Level of Inferior Colliculus

◊ Each superior oblique muscle is innervated by the contralateral cranial nerve IV nucleus!

Exit: dorsal midbrain

◊ The only cranial nerve to exit the dorsal brainstem!

Segments:

(1) Cisternal segment courses through ambient cistern traveling inferolateral to cranial nerve III between superior cerebellar and posterior cerebral arteries

(2) Cavernous sinus segment within dural investment inferior to CN III

(3) Orbital segment passes through superior orbital fissure above annulus of Zinn

ABDUCENS NERVE (CN VI)

Function: pure motor nerve for the lateral rectus muscle

Nucleus: located in pontine tegmentum near midline surrounded by a loop of the facial nerve (CN VII) causing a bulge in the floor of the 4th ventricle (= facial colliculus)

Segments:

(1) Cisternal portion exits brainstem near midline through a space between pons and pyramid of medulla oblongata

(2) Prepontine portion the nerve courses anteriorly within prepontine cistern + penetrates dura mater to enter Dorello canal

(3) Cavernous sinus portion the only nerve that travels within venous sinusoids of cavernous sinus inferolateral to cavernous ICA

◊ Cranial nerves III, IV, V_1, V_2 all lie within lateral dural wall of cavernous sinus!

Exit: enters orbit through superior orbital fissure

ORBITAL CONNECTIONS

Superior Orbital Fissure

Boundaries (Gray's Anatomy):

› medial : sphenoid body

› above : lesser wing of sphenoid = optic strut

› below : greater wing of sphenoid

› lateral : small segment of frontal bone

Contents:

(a) nerves: III oculomotor nerve
IV trochlear nerve
V_1 ophthalmic branch of trigeminal n.:
(a) lacrimal nerve
(b) frontal nerve
VI abducens nerve
sympathetic filaments of ICA plexus

(b) veins: superior + inferior ophthalmic vein

(c) arteries: 1. meningeal branch of lacrimal artery
2. orbital branch of middle meningeal artery

Inferior Orbital Fissure

Location: between floor + lateral wall of orbit; connects with pterygopalatine + infratemporal fossa

Contents:

(a) nerves: infraorbital + zygomatic nerves branches from pterygopalatine ganglion

(b) veins: connection between inferior orbital vein + pterygoid plexus

Optic Canal

completely formed by lesser wing of sphenoid
Contents:

(a) nerve: optic nerve (I) sympathetic fibers

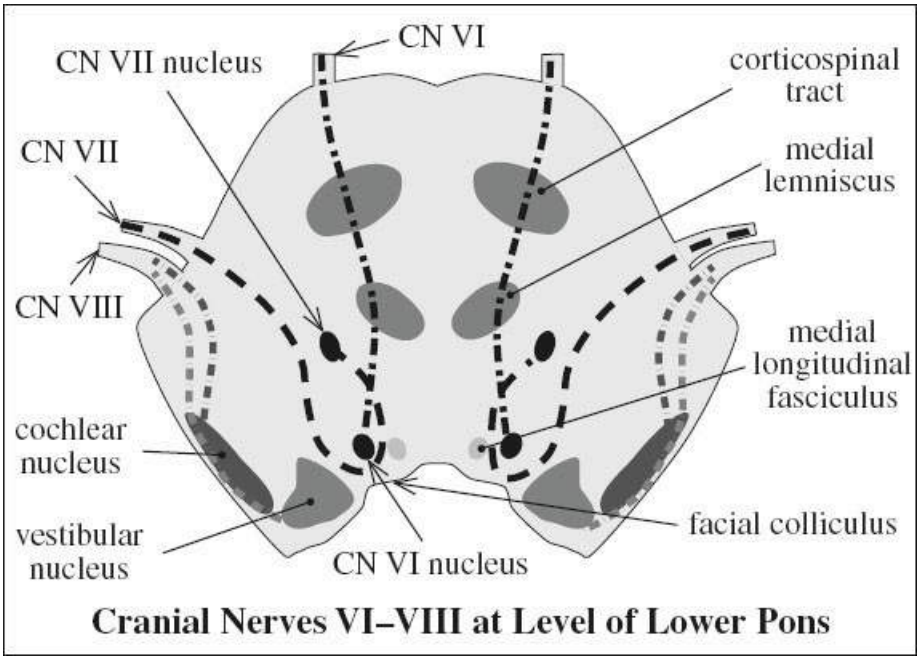
(b) vessel: ophthalmic artery

Infraorbital Canal

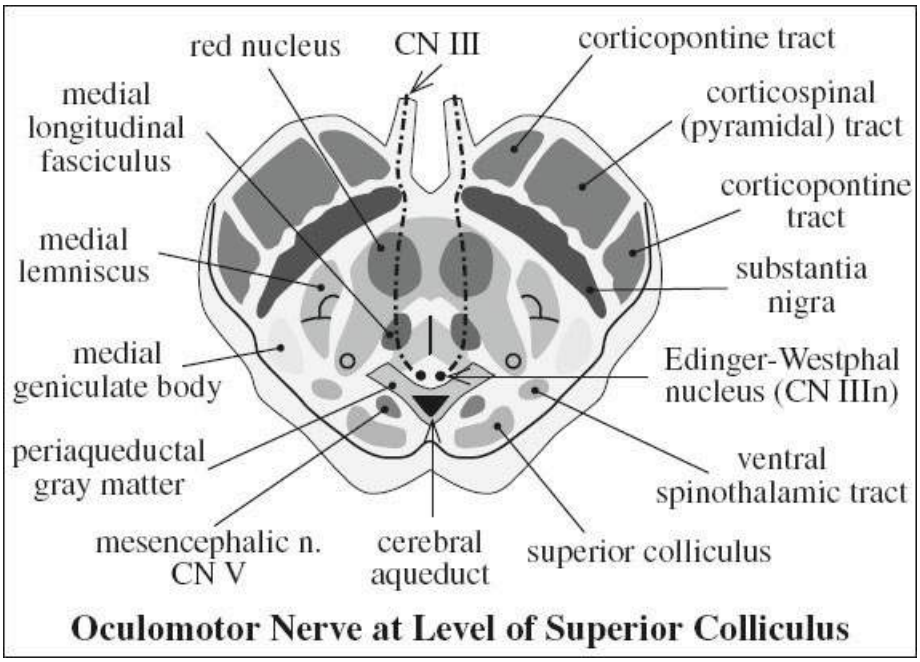
Contents:

(a) nerve: maxillary branch of trigeminal nerve

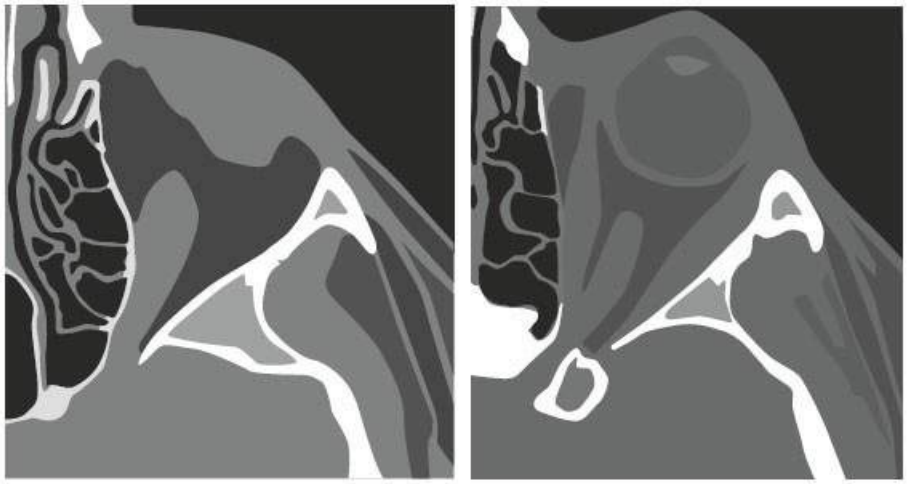
(b) vessel: infraorbital artery & vein



Cranial Nerves VI–VIII at Level of Lower Pons



Oculomotor Nerve at Level of Superior Colliculus



Superior Orbital Fissure **Optic Canal**

Axial CT of Orbital Foramina

ADENOID CYSTIC CARCINOMA

= most common malignancy of lacrimal gland

Frequency: 29% of all lacrimal epithelial neoplasms; ~ 5% of all primary orbital neoplasms
◊ 2nd most common lacrimal epithelial lesion

Age: 4th decade of life

Histo: nonencapsulated bland-appearing epithelial cells arranged in nests / chords forming a characteristic cribriform (swiss cheese–like) pattern

• pain (common presentation = indicative of malignancy)
• proptosis (may be minimal due to infiltrative pattern)
√ irregular borders with distortion of globe + orbital contents (with more advanced disease)
√ ± bone erosion + calcifications
√ perineural invasion (lacrimal branch of ophthalmic nerve)

Prognosis: poor; 20% 10-year–survival rate

ASTEROID HYALOSIS

= degenerative orbital condition with small white opacities of hydroxyl apatite (= calcium + phosphate / phospholipid deposits) attached to vitreous collagenous framework

Frequently associated with: hyperlipidemia, hypertension, diabetes mellitus

• small white vitreous opacities visible under direct illumination
√ small hyperechoic refringent mobile echoes (usually unilateral) ← calcified deposits

BUPHTHALMOS

= HYDROPHTHALMOS = MEGOPHTHALMOS
= diffuse enlargement of eye in children ← increased intraocular pressure

Cause:

1. Congenital / infantile glaucoma
2. Neurofibromatosis type 1: obstruction of canal of Schlemm by membranes / masses composed of aberrant mesodermal tissue
3. Sturge-Weber-Dimitri syndrome
4. Lowe (cerebrohepatorenal) syndrome
5. Ocular mesodermal dysplasia (eg, Axenfeld or Rieger anomalies)
6. Homocystinuria
7. Aniridia
8. Acquired glaucoma (rare)

Pathophysiology:

obstruction of canal of Schlemm located between cornea + iris → decreased resorption of aqueous humor (= anterior chamber fluid) → scleral distension

√ uniformly enlarged globe without mass of round / oval / bizarre shape

Rx: goniotomy (increases the angle of anterior chamber); trabeculotomy (lysis of adhesions)

CHOROIDAL DETACHMENT

= serous fluid / blood accumulation in potential suprachoroidal space separating choroid from sclera with sparing of optic disc due to anchoring effect of short posterior ciliary arteries and veins and nerves

Potential suprachoroidal space: extends from ora serrata to optic disc

Cause: trauma (accidental perforation), inflammation (uveitis), surgical intervention, spontaneous

Pathomechanism: ocular hypotonia → decreased pressure in suprachoroidal space → accumulation of serous / hemorrhagic transudate

US:

√ 2 convex lines projecting into the eye from periphery of globe + advancing to ciliary body with posterior fixation outside the optic disc (= macula) creating an obtuse angle

√ minimal / no choroidal membrane mobility during eye movement

CHOROIDAL HEMANGIOMA

= congenital vascular hamartoma

Mean age: 31 (range, 7–58) years (most common benign tumor in adults); M÷F = 1÷1

May be associated with: Sturge-Weber syndrome

Classification: capillary / cavernous / mixed

Location: posterior to equator, temporal to optic disc (70%)

• smoothly elevated slightly dome-shaped reddish-orange choroidal mass

√ lenticular mass of 7.5 (range, 3–11) mm

√ intense enhancement similar to choroid

√ focal thickening of posterior wall of globe

CT:

√ ill-defined mass with intense enhancement

MR:

√ hyperintense to vitreus on T1WI (rule)

√ isointense to vitreus on T2WI (rule)

US:

√ hyperechoic homogeneous mass

DDx: uveal melanoma (choroidal excavitation)

Cx: retinal detachment (frequent)

Rx: usually none; photocoagulation with retinal detachment

CHOROIDAL OSTEOMA

= rare juxtapapillary tumor of mature bone

Age: young woman

Location: may be bilateral

√ small flat very dense curvilinear mass aligned with choroidal margin of globe

DDx: calcified choroidal angioma

CMV-INDUCED RETINITIS

Frequency: in ⅓ of AIDS patents NOT on HAART (highly active antiretroviral therapy)

Location: unilateral → bilateral
√ uveal enhancement
√ retinal detachment
√ calcifications of retina
Cx: blindness ← retinal detachment within 3–6 months (in 33% prior to HAART)

COATS DISEASE

= RETINAL TELANGIECTASIA = PSEUDOGLIOMA
= congenital nonhereditary primary vascular malformation of the retina characterized by retinal telangiectasia (= multiple abnormal telangiectatic retinal vessels with aneurysm formation) and retinal exudation
Pathogenesis:
breakdown of blood-retina barrier at level of endothelial cells → leakage of lipoproteinaceous exudate of cholesterol crystals into retina + subretinal space → detachment of retina → progressive obliteration of vitreous space
Peak age: 6–8 years (range, 5 month – 75 years); M÷F = 2÷1
• ± leukokoria (if retina massively detached = 16% of leukokoria cases)
• strabismus, secondary glaucoma, loss of vision
• cholesterol crystals at funduscopy
Location: unilateral in 83–95%
Associated with: retinal detachment, slight microphthalmia
√ NO focal mass, NO calcification, NO enhancement of subretinal space (HALLMARK)
√ normal-sized / slightly smaller globe
US:
√ clumpy particulate echoes in subretinal space ← cholesterol crystals suspended in fluid
√ vitreous + subretinal hemorrhage (frequent)
CT:
√ unilateral dense vitreus ← proteinaceous subretinal exudate
√ linear V-shaped enhancement at anterior margin of subretinal exudate ← thickened retina composed of telangiectatic and aneurysmal vessels
MR:
√ subretinal exudate hyperintense on T1WI + T2WI ← mixture of protein + lipid
√ heterogeneous hypointensity on T2WI (with hemorrhage + fibrosis)
√ mild to moderate linear enhancement of retina at ora serrata and of detached retinal leaves
Cx: cataract, painful glaucoma, phthisis bulbi
Rx: photocoagulation / cryo- / laser ablation to obliterate telangiectasias (in early stages); enucleation
DDx: (1) Persistent hyperplastic primary vitreus (thick tubular retrolental mass)
(2) Retinopathy of prematurity
(3) Unilateral diffuse infiltrating noncalcifying retinoblastoma (< 3 years of age, no microphthalmia)

COLOBOMA

= COLOBOMA OF CHOROID = OPTIC DISC COLOBOMA

[*koloboun*, Greek = to mutilate]
= incomplete closure of embryonic choroidal fissure affecting eyelid / lens / iris / choroid / retina / macula (= gap in choroidal layer of globe between retina and sclera)
Genetics: autosomal dominant trait with variable penetrance (30%) and expression
Time of insult: 6th week of GA
May be associated with: encephalocele, agenesis of corpus callosum
Location: in 50–60% bilateral
• leukokoria ← exposed underlying sclera
√ cystic outpouching (= herniation) of vitreus at site of optic nerve attachment
√ scleral bulge on T2WI
√ small globe
US:
√ defect in optic disc + retroocular cyst
DDx: microphthalmos with cyst (= duplication cyst); axial (high) myopia

CATARACT

= opacification of lens
Etiology: congenital, age-related, infection, trauma

Congenital Cataract

Location: frequently bilateral
• leukokoria = white reflection with opaque lens
US:
√ increased thickness of lens
√ intralenticular echoes
√ echogenicity of posterior / both walls

DACRYOADENITIS

= infection of lacrimal gland
Organism: staphylococci (most common), mumps, infectious mononucleosis, influenza
√ homogeneous enlargement of lacrimal gland
√ ± compression of globe

DACRYOCYSTITIS

= inflammation / infection with dilatation of lacrimal sac
Cause:
(a) obstruction of nasolacrimal duct ← duct stenosis / dacryolith
(b) sarcoidosis, Wegener granulomatosis, benign lesions (eg, mucocele and epidermoid cyst), and malignant lesions (including squamous cell carcinoma and lymphoma)
Location: medial (internal / inner) canthus
• acute onset of pain, conjunctivitis
• medial canthus mass, lid swelling
• mucopurulent discharge from puncta
• conjunctivitis concurrent preseptal cellulitis

√ well-circumscribed round fluid collection along inner canthus
√ peripheral enhancement
√ adjacent inflammation + soft-tissue thickening
Cx: periorbital / orbital cellulitis

DACRYOCYSTOCELE

◊ 2nd most common cause of neonatal nasal obstruction (after choanal atresia)
Cause: congenital obstruction of nasolacrimal duct (imperforate Hasner membrane distally, reason for proximal obstruction unknown)
Location: inferomedial canthus of neonates
• tense blue-gray mass at medial canthus / in nasal cavity
CT / MR:
√ homogeneous well-defined mass of fluid attenuation extending into nasal cavity along course of nasolacrimal duct = nasolacrimal duct dilatation
√ enhancement of thin wall
√ superior displacement of inferior turbinate bone
√ contralateral shift of nasal septum
Cx: dacryocystitis, periorbital cellulitis
Rx: duct massage, duct probing with irrigation, prophylactic antibiotics, endoscopic resection, marsupialization
◊ Prompt treatment to prevent secondary infection!

INCLUSION CYST OF ORBIT

= congenital unilocular closed sac containing derivatives of single germ layer (monodermal)
Etiology: failure of surface ectoderm to separate completely from underlying developing neural tube; usually arises in fetal cleavage planes (sutures)
Prevalence: 5% of all orbital masses
◊ Most common benign developmental orbital tumor in childhood (45% of all masses)
Age: 1st decade; < ¼ diagnosed at birth
Location: in anterior extraconal orbit in close relation to frontozygomatic suture = upper temporal (outer) quadrant / lacrimal fossa (60–80%) or frontoethmoidal suture = upper nasal quadrant (25%)
Site: overwhelmingly superficial in lateral ⅓ of eyebrow
• slow progression of painless lesion
• proptosis (for deeper lesion in older child / adult)
Prognosis: slow enlargement over years / decades secondary to accumulation of debris
DDx: cephalocele (tracts leading to midline anterior cranial fossa, no lipid)

Dermoid Cyst of Orbit

= DERMOID INCLUSION CYST
Histo: thick vascularized capsule composed of stratified squamous epithelium identical to epidermis + additional ectodermal features like hair follicles / sebaceous glands containing oily secretions + proteinaceous keratin debris

√ thick surrounding capsule ± enhancement
√ ± expansion / erosion of bony orbit:
  √ periosteal and intradiploic remodeling of bone
  √ reactive sclerotic margin / shell of dense bone
US:
  √ encapsulated heterogeneous mass with variable cystic component
CT:
  √ encapsulated well-circumscribed unilocular cystic mass:
    √ ± fat-density of −60 to −90 HU
    √ ± high-attenuation foci in wall ← calcification
MR:
  √ high signal intensity on T1WI + T2WI ← lipids of sebum
  √ ↓ SI of lipid on fat-suppressed images

Epidermoid Inclusion Cyst

Path: white "pearly" tumor consisting of dry waxy / flaky keratin ← desquamated inner lining of squamous cells
Histo: exclusively squamous epithelium
√ water / CSF density ← high proteinaceous content
MR:
  √ high SI on T2WI
  √ internal signal NOT suppressed on FLAIR
  √ ↑ signal intensity on DWI + ↓ ADC map

ENDOPHTHALMITIS

Infectious Endophthalmitis

Organism: bacteria (rare in childhood, trauma, idiopathic), fungi, parasites
Cause:
  (a) exogenous endophthalmitis: most commonly related to eye injury / surgery
  (b) endogenous endophthalmitis: hematogenous spread from distant source of infection
US:
  √ medium- to high-intensity echoes dispersed throughout vitreus (DDx: vitreous hemorrhage echoes are more mobile)
CT:
  √ increased attenuation of vitreus
  √ uveal-scleral thickening
  √ decreased attenuation of lens

Sclerosing Endophthalmitis

= TOXOCARA CANIS ENDOPHTHALMITIS = OCULAR LARVA MIGRANS= NEMATODE ENDOPHTHALMITIS
= granulomatous uveitis resulting in subretinal exudate, retinal detachment, organized vitreus
Age: 2–6–12 years
Mode of infection: playing in soil contaminated by viable infective eggs from dog / cat

excrement (common in playgrounds)

Organism: helminthic nematode Toxocara canis / Toxocara cati causes visceral / ocular larva migrans (0.5 mm long, 20 μm wide); endemic throughout world; especially common in southeastern USA

Life cycle:

egg hatches into larva within intestines of definite host (dog) → develops into adult worm; alternatively dog may eat infective-stage larvae from intestines / viscera of other animals; in noncanine host (human) larvae will not develop into adult worm, but burrow through intestinal wall and migrate to liver, lung, and other tissue including brain + eye (= visceral larva migrans)

Accidental host: human

Pathophysiology: migration through human tissue produces a severe eosinophilic reaction that becomes granulomatous; spreads hematogenously to temporal choroid

Path: retina elevated + distorted + partially replaced by an inflammatory mass containing abundant dense scar tissue; subjacent choroid infiltrated with chronic inflammatory cells including eosinophils; proteinaceous subretinal exudate

Age: 5–10 years

• strabismus, red "hot" eye, pain
√ unilateral visual impairment, photophobia
• anterior chamber flare cells, keratic precipitates
• vitreous synechia; peripheral blood eosinophilia
• vitreitis = accumulation of cellular debris in vitreus
• leukokoria (16% of cases of childhood leukokoria)
• fever, hepatomegaly, pneumonitis, convulsions

Location: usually unilateral

√ eye of normal size
√ no calcifications

US:

√ hyperechoic mass in peripheral fundus / vitreus
√ ± calcifications

CT:

√ intravitreal mass
√ focal uveoscleral thickening (granulomatous reaction around larva) with contrast enhancement
√ increased density of vitreous cavity

MR:

√ granuloma isointense to vitreus on T1WI
√ mass usually hyperintense relative to vitreus on first-echo T2WI
√ mass may be isointense on second-echo T2WI compared to surrounding vitreus
√ granuloma may be of low SI ← dense fibrosis
√ moderate to marked enhancement

Cx: secondary retinal detachment (← subretinal fluid / vitreoretinal traction), cataract

Rx: antithelminthic albendazole ± vitrectomy

Dx: (1) Enzyme-linked immunosorbent assay (ELISA) on blood serum (less reliable) / vitreous aspirate

(2) Histologic identification of organism (larvae difficult to detect within inflammatory reaction)

DDx: retinoblastoma (calcifications); fascioliasis, ascariasis, ancylostomiasis, angiostrongylosis

GRAVES OPHTHALMOPATHY

= THYROID OPHTHALMOPATHY = ENDOCRINE EXOPHTHALMOS

= autoimmune disease unrelated to thyroid function with an increase in orbital pressure producing ischemia, edema, fibrosis of muscles

Etiology: produced by long-acting thyroid-stimulating factor (LATS); probably immunologic cross-reactivity against antigens shared by thyroid + orbital tissue

Age: adulthood; 5% younger than 15 years; M÷F = 1÷4

Histo: deposition of hygroscopic mucopolysaccharides + glycoprotein (early) + collagen (late); infiltration by mast cells and lymphocytes, edema, muscle fiber necrosis, lipomatosis, fatty degeneration

Time of onset: signs + symptoms usually develop within 5 years after the onset of hyperthyroidism

- proptosis
  - ◊ Most common cause of uni- / bilateral exophthalmos in adults!
- lid lag = upper eyelid retraction
- periorbital swelling, chemosis (= conjunctival swelling), conjunctivitis; progressive optic neuropathy (5%)
- ophthalmoplegia = restricted ocular motility (correlates with increase in mean muscle diameters)
- hyperthyroidism; euthyroidism (in 10–15%); severity of orbital involvement unrelated to degree of thyroid dysfunction

Staging (Werner's modified classification):

Stage I : eyelid retraction without symptoms
Stage II : eyelid retraction with symptoms
Stage III : proptosis > 22 mm without diplopia
Stage IV : proptosis > 22 mm with diplopia
Stage V : corneal ulceration
Stage VI : loss of sight

Location:

bilateral in 70–85%; single muscle in 10%; asymmetrical involvement in 10–30%; all muscles equally affected with similar proportional enlargements; superior muscle group most commonly when only single muscle involved [FORMER notion: inferior > medial > superior rectus muscle + levator palpebrae > lateral rectus muscle]

mnemonic: I'M SLow

Inferior
Medial
Superior
Lateral

√ eyelid edema

√ proptosis = globe protrusion > 21 mm anterior to interzygomatic line on axial scans at level of lens
√ "Coke-bottle" sign = swelling of muscles maximally in midportion (relative sparing of tendinous insertion at globe)
√ slight uveal-scleral thickening
√ tenting of posterior globe
√ apical crowding = orbital apex involved late → pressure on optic nerve
√ dilatation of superior ophthalmic vein ← compromised orbital venous drainage at orbital apex ← enlarged extraocular muscles
√ increase in diameter of retrobulbar optic nerve sheath ← dural distension ← accumulation of CSF in subarachnoid space ← optic neuropathy
√ stretching of optic nerve
√ increased orbital fat:
  √ increased density of orbital fat (late)
  √ intracranial fat herniation through superior ophthalmic fissure (best correlation with compressive neuropathy)
√ enlargement of lacrimal gland with anterior displacement

MR:
  √ high SI in enlarged eye muscles on T2WI (edema in acute inflammation)

Prognosis: in 90% spontaneous resolution within 3–36 months; in 10% decrease in visual acuity (corneal ulceration / optic neuropathy)

Rx: short- and long-term steroid therapy, cyclosporine, radiation, surgical decompression, correction of eyelid position

DDx: pseudotumor (usually includes tendon of eye muscles)

HEMANGIOMA OF ORBIT

◊ Most common benign orbital tumor in adults!

Location: 83–94% retrobulbar (intraconal)

√ sharply demarcated oval mass in superior-temporal portion of conus (⅔) often sparing orbital apex
√ displacement (NOT involvement) of optic nerve
√ expansion of bony orbit
√ uniform / inhomogeneous (when thrombosed) enhancement
√ small calcifications (phleboliths)
√ puddling of contrast material on angiography

US:
  √ well-defined encapsulated mass of intermediate echogenicity
  √ absent / poor predominantly venous flow

Capillary Hemangioma of Orbit

= INFANTILE HEMANGIOMA = BENIGN HEMANGIOENDOTHELIOMA

◊ Most common tumor of infancy (60% in head & neck)!

Frequency: most common vascular tumor of orbit in children; 3% of all pediatric orbital masses; 17% of vasculogenic orbital lesions

Age: first 2 weeks of life; 95% at < 6 months of age; M÷F = 2÷3

Path: nonencapsulated infiltrative mass consisting of multiple lobules separated by vascular fibrous septa

Histo: proliferation (lasting up to 10 months) of endothelial cells with multiple vessels of capillary size; involutional phase with progressive peripheral replacement by fibrofatty tissue → atrophy of mass

May be associated with: PHACES syndrome

- appears shortly after birth + rapidly increases in size for 6–12 months + then gradually involutes over 7–10 years
- proptosis, chemosis (= edema) of eyelid + conjunctiva exaggerated by crying for deep lesion
- associated with cutaneous red to bluish angiomas (90%); NO familial / hereditary association

Location: anterior part of orbit (red discoloration of skin - most frequently eyelid), subcutaneous (bluish discoloration of skin); occasionally posterior; multiple hemangiomas in 20%

Site: entirely extraconal / substantial extraconal component

√ displacement of globe (= proptosis)
√ lobulated irregularly marginated heterogeneous mass (suggesting malignant cause)
√ intense enhancement equal to / greater than orbital muscle
√ often transspatial → may extend intracranially through optic canal / superior orbital fissure
√ activity in radionuclide flow studies

US:
- √ smoothly contoured heterogeneous mass of variable (usually hyperechoic) echogenicity
- √ abundant intralesional flow decreasing with age:
  - √ high density of vessels (> 5 vessels per cm^2)
  - √ increased arterial and venous flow velocity (Doppler shift > 2 kHz)
  - √ arterial flow of low resistance

CT:
- √ fairly homogeneous mostly extraconal mass:
  - √ isoattenuating relative to muscle
  - √ hyperattenuating relative to brain ← blood in vessels
- √ scalloping / expansion of bony orbit
- √ invasion of bone (extremely rare)
- √ calcifications (rare)
- √ prompt marked uniform persistent enhancement
- √ shrinkage of mass with decrease in vascularity and progressive replacement by fat (during involution)

MR:
- √ lobulated mass with thin hypointense septa
- √ usually iso- to hyperintense to muscle on T1WI
- √ moderately hyperintense on T2WI
- √ intra- and perilesional flow voids (distinguishing feature)
- √ intense uniform enhancement (during proliferative phase)
- √ increased SI on T1WI + T2WI ← fibrofatty deposition during involutional phase

Angio (reserved for embolotherapy):

√ hypervascular mass with prolonged capillary stain and large feeding and draining vessels

Cx: profuse hemorrhage, thrombosis, calcification, corneal ulceration, optic nerve compression, amblyopia ("lazy eye"), visual axis occlusion, bone remodeling, ± visceral hemangiomas → severe consumptive thrombocytopenic coagulopathy (Kasabach-Merritt syndrome)

Rx: observation; topical / systemic oral / intralesional corticosteroids; interferon; laser; surgery

Prognosis: often increase in size for 6–10 months followed by spontaneous involution within 1–2 years

DDx: (1) Rhabdomyosarcoma (older age, may contain flow voids)
(2) Vascular malformations
(3) Infantile fibromatosis
(4) Infantile fibrosarcoma

Cavernous Hemangioma of Orbit

= CAVERNOUS MALFORMATION

= congenital vascular anomaly (1) present at birth (2) without spontaneous involution (3) slow growth over time

Frequency: low; 12–15% of all orbital masses; 1–2% of childhood orbital masses

Cavernous hemangioma is the most common benign orbital mass in adults!

Mean age: 45 (range, 18–72) years; M÷F = 2÷3

Histo: large dilated venous channels with flattened endothelial cells surrounded by fibrous pseudocapsule

- slowly progressive painless unilateral proptosis (most common presenting sign)
- visual field deficit (50%) ← mass effect on optic nerve
- acute-onset proptosis (occasionally) ← abrupt orbital enlargement ← cytokine + hormonal stimulation at puberty / during pregnancy
- recurrent episodes of diminished visual acuity (optic nerve compression)
- pain, eyelid swelling, diplopia, palpable lump (less common)

Location: lateral aspect of retrobulbar intraconal space; conal + extraconal cavernous malformation (rare)

CT:
√ well-circumscribed round / ovoid solitary homogeneously hyperattenuating mass
√ displacement of adjacent structures (extraconal muscles, optic nerve) without invasion
√ ± phleboliths (extremely rare)
√ ± bone remodeling with expansion of orbital walls
√ ± intracranial extension through superior orbital fissure (5–10%)

CECT:
√ poor enhancement during early arterial phase ← scant arterial supply
√ progressive filling from periphery to center (complete filling within 30 minutes) during delayed phase

MR:
√ mass isointense to muscle on T1WI
√ uniformly hyperintense to muscle on T2WI

√ internal septa in larger lesions
√ NO flow voids
√ progressive accumulation of contrast (late phase dynamic images / or delayed images after 1 hour!)

US:
√ well-defined borders (pseudocapsule)
√ honeycomb-like structure

Prognosis: no involution
Rx: conservative; surgical excision in cases of severe proptosis / optic nerve compression
DDx: other vascular lesions (arterial phase enhancement) like capillary hemangioma (pediatric diagnosis), hemangiopericytoma, arteriovenous malformation

PHACES Syndrome

= acronymic syndrome composed of
(1) **P**osterior fossa brain malformation (Dandy-Walker malformation, ventricular dilatation, ipsilateral cerebellar hypoplasia, cerebellar vermian hypoplasia, cortical dysgenesis)
(2) **H**emangiomas of face + neck: (segmental / plaquelike > 5 cm in diameter)
(3) **A**rterial anomalies related to ipsilateral intracranial circulation (persistent trigeminal artery, agenesis of internal carotid / vertebral artery)
(4) **C**ardiac anomalies / **C**oarctation of aorta (aortic aneurysm, aortic dissection, ASD, VSD)
(5) **E**ye abnormalities (cataract, coloboma, optic nerve hypoplasia, glaucoma)
(6) **S**ternal / ventral developmental anomalies

Incidence: > 150 cases
• endocrine abnormalities
√ occasionally absence / defect of sternum / supraumbilical raphe (= fibrous band / cleft in midline above umbilicus)

HEMANGIOPERICYTOMA OF ORBIT

= rare orbital neoplasm derived from pericytes (= contractile support cells surrounding small vessels) with cell lineage identical to solitary fibrous tumors
Frequency: 1% of all orbital masses
Mean age: 41 years; M = F
• proptosis, palpable mass (common)
• pain, diplopia, decreased visual acuity (less common)
Path: slow growing mass, may recur / metastasize (15%)
Histo: dense hypercellular tumor with spindle-shaped cells + "staghorn" vascular branching pattern, relatively bland to frankly malignant
Spread: lung
Location: extraconal (commonly adjacent to paranasal sinuses)
√ lobulated well circumscribed mass
√ ± infiltrative border + bone erosion (= aggressive lesion)
√ calcification (rare)
CECT:

√ marked enhancement during arterial + early venous phase with rapid washout

MR:

√ isointense relative to gray matter on T1WI + T2WI

DDx: cavernous malformation

INFANTILE FIBROMATOSIS OF ORBIT

= rare nonmetastasizing locally invasive fibrous proliferation with tendency to recur after surgical resection

Age: congenital (54%), < 2 years of age (in 89%)

Clinical forms: (1) solitary: M > F
(2) multicentric (= congenital generalized fibromatosis): F > M

Location: head & neck > trunk > lower extremity > upper extremity

Site: skin, subcutaneous tissue, deeper structures including visceral organs; combination of all

Mean size: 3.5 (range, 0.5–7.0) cm

• painless swelling / lump + skin discoloration ← vascularity

• proptosis

X-ray:

√ nonspecific expansion of orbit

US:

√ round well-circumscribed mass of heterogeneous texture

√ ± target appearance ← central necrosis / hemorrhage

CT:

√ ± orbital bone erosion ± small foci of calcifications

√ enhancing mass hyperattenuating to muscle

MR:

√ multilobulated / infiltrative margins

√ low to intermediate SI relative to muscle on T1WI + (frequently) foci of hyperintensity

√ heterogeneous predominantly hyperintense SI on T2WI:

√ T2 hyperintensity ← high cellularity + myxoid change

√ T2 hypointensity ← high collagen content

√ target appearance ← central hemorrhage / necrosis / cystic / myxoid change

√ intense diffuse / peripheral enhancement

Prognosis: spontaneous resolution (common); 7% recurrence rate after surgical resection

Mortality: 15% overall; 75% with visceral involvement

Rx: conservative; surgical resection for local complications

DDx of solitary disease:

(1) Rhabdomyosarcoma (occurs in older age group)

(2) Hemangioma (flow voids at tumor periphery)

INFECTION OF ORBIT

Cause: bacterial infection extending from paranasal sinuses (especially ethmoid + frontal sinuses), face, eyelid, nose, teeth, lacrimal sac through thin lamina papyracea + valveless facial veins into orbit

Organism: staphylococci, streptococci, pneumococci
• lid edema, ocular pain, ophthalmoplegia; fever, elevated WBC
Location: preseptal = periorbital soft tissue; subperiosteal; peripheral = extraconal fat; extraocular muscles; central = intraconal fat; optic nerve complex; globe; lacrimal gland
Cx: epidural abscess, subdural empyema, cavernous sinus thrombosis, cerebral abscess, osteomyelitis

Abscess of Orbit

= abscess of intraconal space
Cause: penetrating orbital injury, ocular surgery, metastatic process
• marked proptosis, chemosis, ophthalmoplegia
• impaired visual acuity
MR:
√ hyperintensity on T1WI + T2WI
Rx: surgical drainage for intraconal abscess

Subperiosteal Orbital Abscess

Cause: sinusitis, orbital inflammation
Location: along medial wall of orbit between lamina papyracea and medial rectus muscle
√ subperiosteal spindle-shaped fluid collection
√ displacement of thickened periosteal membrane + increased enhancement
√ displacement of adjacent fat + extraocular muscles
Cx: orbital abscess (extension to intraconal space)

Pott Puffy Tumor

= frontal osteomyelitis with subperiosteal abscess formation beneath galea aponeurotica
Cause: frontal sinusitis + periorbital cellulitis → thrombophlebitis of valveless emissary veins → frontal osteomyelitis
• enlarging broad swollen bump of doughy consistency in the region above brow
√ osseous destruction of frontal bone
√ frontal subgaleal fluid collection
Cx: epidural / subdural empyema; parenchymal cerebral abscess; meningitis; cavernous sinus thrombosis; thrombophlebitis; venous brain infarct

Orbital / Postseptal Cellulitis

= acute bacterial postseptal infection
Orbital septum = thin sheet of fibrous tissue originating in the orbital periosteum + inserting in palpebral tissues along tarsal plates; acts as barrier against spread of periorbital infection into posterior compartment of orbit
CT: √thin band paralleling superior orbital rim deep to facial musculature
Classification: intraconal, extraconal, subperiosteal
Source: paranasal sinusitis (most commonly) spreading via perivascular pathway
• limitation of eye movement ± proptosis
• visual acuity usually maintained

• fever
Location: mostly confined to extraconal space
√ proptosis
√ scleral thickening
√ enlargement + displacement of extraocular muscles (frequently medial rectus muscle ← ethmoid sinusitis)
√ increased attenuation of retroorbital fat + obliteration of fat planes
√ opacification of ethmoid + maxillary sinuses (extension through thin lamina papyracea into orbit)
MR (enhanced fat-suppressed images most sensitive):
√ hypointense on T1WI + hyperintense on T2WI
US:
√ diffuse hypoechoic area invading retrobulbar fat
Rx: IV antibiotics + corticosteroids
Cx: subperiosteal / intraconal abscess; thrombosis of superior ophthalmic vein / cavernous sinus; bacterial meningitis; epdidural / subdural abscess; brain abscess; loss of vision
DDx: edema, orbital pseudotumor, orbital myositis, intra- and extraorbital neoplasm (chloroma, leukemic infiltrate)

Preseptal / Periorbital Cellulitis

= preseptal infection limited to soft tissues anterior to orbital septum

Periorbital (preseptal) + orbital (postseptal) cellulitis are differentiated by location with respect to the orbital septum.

Source of infection: face, teeth, ocular adnexa, local trauma
• swelling + erythema of eyelid, chemosis
• limitation of eye movement (in severe cases) without proptosis
√ thickening of eyelids + septum
√ diffuse swelling of anterior orbital tissues with increased density + obliteration of fat planes
Rx: oral antibiotics in outpatient setting

Edema of Orbit

Location: usually confined to preseptal structures (eyelid, face); involvement of orbital structures (rare)
√ swelling of eyelids / face
√ increased attenuation of orbital fat + obliteration of fat planes
√ displacement + enlargement of extraocular muscles
MR:
√ hyperintensity on T2WI

LYMPHANGIOMA OF ORBIT

= VENOUS-LYMPHATIC MALFORMATION
= NO-FLOW / LOW-FLOW VASCULAR MALFORMATION
= LYMPHATICOVENOUS MALFORMATION

Prevalence: 3.5÷100,000; 1–2% of orbital childhood masses; 4–8% of expanding pediatric orbital lesions; 25% of vasculogenic orbital lesions

Origin: arises from a pluripotent venous anlage as a malformation (NOT neoplasm of proliferating cells!)

Path: unencapsulated diffuse multicompartmental lesion often with intra- and extraconal components insinuating between normal orbital structures

Histo: dilated lymphatics, dysplastic venous vessels, smooth muscle, areas of hemorrhage

(a) simple / capillary lymphangioma
= lymphatic channels of normal capillary size

(b) cavernous lymphangioma (most common)
= dilated microscopic channels

(c) cystic hygroma
= macroscopic multilocular cystic mass

May be associated with: intracranial vascular anomalies (70%): developmental venous anomalies (61%), AVM, cerebral cavernous malformation, sinus pericranii

Age: 1st decade or later (mean age of 6 years); M÷F = 1÷1; 43% before age of 6 years; 60% before age of 16 years

- proptosis:
  - slowly progressive proptosis with restriction of eye movement, optic nerve compression, vertical displacement of globe
  - sudden proptosis from intratumoral hemorrhage
    = CARDINAL FEATURE; often occurring spontaneously / after minor trauma / during upper respiratory infection
  - worsening proptosis from intralesional proliferation of lymphocytes during viral infection with subsequent resolution
- associated with lesions on lid, conjunctiva, cheek:
  - eyelid fullness from birth
  - purple discoloration of skin, usually in superomedial orbit
  - vesicles in conjunctiva, facial skin, oral mucosa
- restricted ocular motility (50%)
- growth with patient's growth ± accelerated growth in response to hormonal changes (during puberty / pregnancy)

Location: unilateral; usually medial to optic nerve with intra- and extraconal component, crossing anatomic boundaries (conal fascia / orbital septum)

Site: superficial (conjunctiva + eyelid) in anterior orbit (79%); deeper orbit (67%); pre- and postseptal orbit (73%)

√ poorly defined infiltrating multilobulated heterogeneous lesion
√ single / multiple cystlike areas with rim enhancement (after hemorrhage):
  √ solid-appearing microcystic component
  √ macrocystic component = cysts of 1–2 cm in size
  √ blood cyst = "chocolate cyst" associated with multiple recurrences
√ variably mild patchy low-flow enhancement (= venous channels) / ring enhancement (after hemorrhage)
√ rarely contains phleboliths (DDx: hemangioma, orbital varix)

US:
√ heterogeneous echotexture with ill-defined borders:
√ area of predominantly cystic low-level internal echoes with infiltrative borders
√ hyperechoic intracystic clot
CT:
√ poorly marginated lesion insinuating itself between normal structures:
√ well visualized ← inherent contrast between malformation + orbital fat
√ venous / solid components slightly hyperattenuating relative to brain tissue
√ macrocystic lymphatic components similar in attenuation to vitreous of globe
√ mild to moderate expansion / remodeling / hyperostotic / lytic lesion of bony orbit
√ ± widening of superior / inferior orbital fissure
√ frequent thickening of upper eyelid
MR (modality of choice):
√ iso- to slightly hyperintense relative to brain on T1WI + very hyperintense relative to brain on T2WI:
√ T1WI for lymphatic / proteinaceous fluid
√ fat-suppressed T1WI for blood / blood products
√ fat-suppressed T2WI for nonhemorrhagic fluid
√ fluid-fluid levels of hemorrhages of various ages / T2 shading in multiple cysts (almost PATHOGNOMONIC)
√ NO enlarged feeding vessels / flow voids

Prognosis: no involution; aggressive behavior with continued enlargement (in 64%) + recurrence after treatment; eventually loss of vision (in 40%); progression slows with termination of body growth

Rx: observation; intralesional injection with sclerosing agents (tetradecyl sulfate or OK-432) / steroids; surgery in case of optic nerve compression + for relieve of pain and for cosmetic improvement

DDx: orbital varix (affected by postural changes, communication with systemic circulation)

LYMPHOMA OF ORBIT

Usually presents without evidence of systemic disease; subsequent development of systemic disease frequent

Frequency: in 8% of leukemia; in 3–4% of lymphoma; 67–90% of orbital lymphoproliferative tumors; 24% of all space-occupying orbital tumors in patients > 60 years of age

Age: 50 years on average

Type: usually non-Hodgkin B-cell lymphoma; Burkitt lymphoma with orbit as primary manifestation; Hodgkin disease rare

- palpable mass, mildly restricted ocular motility
- painless swelling of eyelid (pain is uncommon)
- proptosis (late in course of disease)
  ◊ 3rd most common cause of proptosis (after orbital pseudotumor + cavernous hemangioma)

Location: extraconal (especially lacrimal gland, anterior extraconal space, retrobulbar) > intraconal > optic nerve-sheath complex; unilateral (76%)
◊ The lacrimal gland is a common site for leukemic infiltrates + lymphoma (40%)!

Growth types:
(a) well-defined high-density mass (most commonly about lacrimal gland)
√ smooth circumscribed mass (50%)
(b) diffuse infiltration (tends to involve entire intraconal region)
√ diffuse ill-defined lesion (50%)

√ tendency to mold to orbital structures (globe, optic nerve, orbital wall → ± bone remodeling

√ slight to moderate uniform enhancement
√ osseous erosion (rare)
√ isointense relative to muscle on T1WI
√ hyperintense relative to orbital fat on T2WI
US:
√ solitary / multiple hypoechoic homogeneous masses with infiltrative borders
DDx: pseudotumor (infiltration / thickening of ocular muscles, mass commonly T2-isointense relative to orbital fat, high ADC values, acute onset of pain)

MEDULLOEPITHELIOMA

= DIKTYOMA = TERATONEUROMA [*diktyon*, Greek = net]
= rare embryonal malignant (most) / benign intraocular neoplasm
Origin: primitive medullary epithelium in ciliary body
Histo: folded cords + sheets resembling a fisherman's net (diktyomatous pattern) surrounding fluid collections predominantly composed of hyaluronic acid; heteroplastic components of hyaline cartilage, rhabdomyoblasts, neuroglia, sarcomatous elements (a) teratoid (30–50%) (b) nonteratoid (50–70%)
Mean age: 5 years; M=F
• poor vision ← lens subluxation, lens notching, glaucoma, cataract formation, retinal detachment
• pain; leukokoria; mass of iris / ciliary body
• exophthalmos, buphthalmos. strabismus, ptosis
Location: ciliary body (common); optic nerve head / retina (rare); usually unilateral
√ dystrophic calcifications (in hyaline cartilage component) in 30%
US:
√ echogenic irregularly shaped /ovoid mass
CT:
√ dense irregular mass
√ moderate to marked enhancement
MR:
√ slightly to moderately hyperintense to vitreus on T1WI
√ hypointense on T2WI
√ marked homogeneous enhancement / heterogeneous (← cystic components)
Prognosis: local recurrence common; metastases rare

METASTASIS TO ORBIT

Prevalence: 1–13% of orbital tumors
Origin: source known in only in 50%

adults: carcinoma of breast + lung
children: neuroblastoma > Ewing sarcoma, leukemia, Wilms tumor

Frequency of metastases to orbit:
breast cancer (48–53% of orbital metastases) > prostate carcinoma > cutaneous melanoma > lung cancer

- proptosis, motility disturbance, pain, diplopia, ↓ vision
- **paradoxical enophthalmos** (10% of orbital lesions)
  = posterior globe retraction ← infiltrative + fibrotic contraction of orbital fat ← scirrhous breast cancer (most common) / scirrhous gastrointestinal carcinoma

Location: 12% intraorbital, 86% intraocular; bilateral in ⅓
Preferential site by type of metastasis:
› breast cancer → orbital fat + muscle
› prostate cancer → bone
› melanoma → muscle

√ diffuse enhancement of retrobulbar fat with abnormally heterogeneous hypointensity on T1WI + T2WI ← fibrotic infiltration

DDx: thyroid ophthalmopathy (bilateral, sparing tendinous insertions); orbital pseudotumor (typically painful involving tendinous insertion); sarcoidosis

Choroidal Metastasis

[choroid = posterior portion of uvea]
◊ Most common ocular malignancy in adults!
Origin: lung > breast, hypervascular + hematologic malignancy
Location: posterior half of globe near macula (access via short posterior ciliary arteries); extension along plane of choroid (in ⅓ bilateral + in ⅓ multiple)

- often asymptomatic (unless fovea involved)
- visual loss ← retinal detachment

√ small areas of broad-based flat thickening + increased density
√ subretinal fluid = retinal detachment
√ mild posterior choroidal thickening

US:
√ often multiple hyperechoic posterior wall masses: usually flat / discoid + with an irregular surface
√ higher flow than melanoma at Doppler

MR:
√ iso- to hyperintense on T1WI, hyperintense on T2WI
√ heterogeneous enhancement
√ may be T1 hyperintense + T2 hypointense ← high level of protein / hemoglobin degradation products ← metastasis from mucin-producing adenocarcinoma / hemorrhagic metastasis

NORRIE DISEASE

= RETINAL DYSPLASIA
= X-linked recessive disease: ? inherited form of persistent hyperplastic primary vitreus

- seizures, mental retardation (50%)
- hearing loss, deafness by age 4 (30%)
- bilateral leukokoria + microphthalmia
- cataract, blindness ← absence of retinal ganglion cells

√ microphthalmia
√ dense vitreus with blood-fluid level
√ cone-shaped central retinal detachment
√ calcifications

OCULAR TRAUMA

Frequency: 3% of all visits to Emergency Department in USA
Cause: blunt trauma (97%)
Mechanism: motor vehicle accident, sport-related accident, industrial accident, fall, violent trauma
Associated with: facial fractures (up to 11%), head injury (84%)

- clinical evaluation: testing of visual acuity, slit-lamp evaluation of cornea + anterior segment, intraocular pressure measurement, funduscopy

US (used if ocular media opaque due to vitreous hemorrhage / hyphema / traumatic cataract):

◊ Dynamic imaging improves visualization of the entire eye and depicts movement of vitreous echoes / lines.

√ may depict hyphema, lens dislocations, globe rupture, intraocular foreign body, vitreous + retinal hemorrhage

Contraindications for ocular US:
suspected traumatic globe rupture / recent surgery to prevent extrusion of ocular contents

CT (modality of choice):
√ especially useful for foreign body

MR:
√ CONTRAINDICATED with metallic foreign bodies
√ usually reserved for subtle open-globe injury / organic foreign body

Anterior Chamber Injury

1. Corneal laceration
   Cause: usually penetrating trauma
   √ decreased anterior-posterior dimension of anterior chamber compared to a normal globe on CT
   Cave: anterior subluxation of lens may mimick a decreased anterior chamber volume
   Cx: globe rupture with complete penetration of cornea
2. **Traumatic hyphema**
   Cause: disruption of blood vessels in iris / ciliary body
   - blood-fluid level in anterior chamber

   √ increased attenuation in anterior chamber on CT
   Cave: US NOT RECOMMENDED → excessive pressure

Lens Dislocation

Cause:
(1) Blunt trauma to eye (> 50% of all lens dislocations)
(2) Spontaneous (and often bilateral)
associated with connective tissue: Marfan syndrome, Ehlers-Danlos syndrome, homocystinuria

Pathomechanism: deformation of globe in anteroposterior direction → compensatory expansion equatorially → stretching + tearing of zonular attachments → dislocation of lens

Location of lens: posterior (common) / anterior (unusual)

Types:
(a) partial luxation = one margin of lens maintains its normal position behind iris
√ posteriorly angled position of lens
(b) complete luxation
√ lens in dependent portion of vitreous humor

In trauma associated with: echogenic lens (= traumatic cataract) + vitreous hemorrhage

Traumatic Cataract

Pathophysiology: disruption of lens capsule → edema within lens → cataract

√ hypoattenuating lens compared with nonaffected lens (in acute phase)

√ hyperattenuating / calcified lens (= mature cataract)

Open-Globe Injury = Ruptured Globe

= disruption of scleral integrity by blunt trauma / penetrating injury

Site: behind insertion of intraocular muscles (= thinnest portion of sclera)

• enlarged anterior chamber

US: CONTRAINDICATED in suspected globe rupture

CT (56–75% sensitive):
√ direct signs of globe injury:
√ change in globe contour (DDx: coloboma, staphyloma, posttraumatic orbital hematoma)
√ "flat tire" sign = loss of volume
√ scleral discontinuity with prolapse of vitreus
√ indirect signs of globe injury:
√ deep anterior chamber = mild posterior movement of lens (in spite of intact zonular fibers)
Mechanism: rupture in posterior segment → decrease in pressure + volume → allows lens to sink posteriorly
√ decreased anterior chamber depth = decreased volume in anterior segment ← severe corneal laceration

One indirect imaging finding of open-globe injuries is alteration of the anterior chamber depth.

√ intraocular air (DDx: injected perfluoropropane gas for treatment of retinal detachment)
√ intraocular foreign body (DDx: metal buckle of scleral band for treatment of retinal detachment)

◊ Consider MRI when a clinically suspected open-globe injury is not identified at CT!

Cx: blindness

Nontraumatic mimics:
coloboma, staphyloma, congenital glaucoma, elongated globe from myopia, phthisis bulbi
Altered globe contour:
mass effect from orbital mass / hematoma

Ocular Detachments / Posterior Segment Injury

1. **Traumatic retinal detachment**
   = separation of retina from choroid
   Mechanism: traumatic retinal tear → accumulation of vitreous fluid + blood between retina and choroid → detachment of retina
   (a) **Total retinal detachment**
   √ characteristic V-shaped appearance with apex at optic disc
   √ retina remains bound down at ora serrata
   (b) **Focal retinal detachment**
   √ elevated immobile line close to sclera at periphery of globe

Retinal detachments may have a characteristic V-shaped appearance with the **apex at the optic disc** !

2. **Vitreous detachment**
   = separation of vitreous from retina
   √ thin undulated mobile line moving away from posterior aspect of globe during eye motion
3. **Traumatic choroidal detachment**
   = separation of choroid from sclera by fluid accumulation in potential suprachoroidal space
   Mechanism: traumatic injury → decreased pressure in posterior segment + suprachoroidal space → accumulation of fluid / blood → detachment of choroidal layer
   Site: from vortex vein to ora serrata
   √ biconvex / lentiform fluid accumulation
   √ lentiform / biconvex shape with sparing of posterior portion of globe
   DDx: high-attenuation silicone oil injected between vitreus and retina for treatment of retinal detachment

Choroidal detachments have a lentiform / biconvex shape and **spare the posterior portion of the globe** !

Intraocular Hemorrhage

1. **Vitreous hemorrhage** (53%)
   Mechanism: disruption of retinal blood vessels → hemorrhage into vitreous humor of posterior segment
   • "black rain" / decreased visual acuity (frequent)
   US:
   √ normal / slightly increased vitreous echogenicity (= mild acute bleeding)

√ poorly defined low-level echoes / hypoechoic clots within vitreous (= abundant hemorrhage)
√ echogenic material moving freely within vitreous chamber during eye movement
CAVE: Severe vitreous hemorrhage may obscure other ocular findings!

CT:
√ hyperattenuating fluid in posterior segment

Cx: retinal detachment ← vitreous traction ← fibrovascular ingrowth following hemorrhage

Prognosis: resolution may occur within 2–8 weeks

Rx: vitrectomy

2. **Retrohyaloid hemorrhage** (2%)
√ echogenic material remaining behind detached vitreous capsule during eye movement
3. Hematoma in retroocular space

Intraocular Foreign Body

Incidence: penetrating eye injury in 3.1÷100,000 per year
◊ Intraorbital foreign bodies are present in 10–17% of all ocular injuries + in 41% of open-globe injuries!

Cause: violent trauma, motor vehicle accident, recreational accident, work-related industrial accident

Location: anywhere (commonly in posterior segment)

Type: (a) inorganic: metal, glass, plastic
(b) organic: wood → may cause a severe infection

Radiography (40–90% sensitive, depending on type of material)

US (95% sensitive for intraocular + 50% for intraorbital foreign body):
√ echogenic spot

DDx: intraocular air may mimic a foreign body

CT (up to 100% sensitive):
√ metallic fragments < 1 mm can be demonstrated
√ glass foreign body: (detection depends on location, size + type of glass)
√ 96% of > 1.5-mm glass foreign bodies
√ 48% of 0.5-mm glass foreign bodies
√ wood splinter:
√ Wood is initially of low attenuation similar to air
√ geometric margins
√ increase in density after 1–5 days

MR:

N.B.: Failure to detect a metallic foreign body before performing MR may result in blindness!

√ more sensitive than CT in depicting organic material

Cx: siderosis (if metallic), endophthalmitis, retinal toxicity, vision loss

DDx: optic drusen; scleral plaques (calcifications along insertions of medial + lateral rectus mm. in elderly); calcified cataract; material for treatment of retinal detachment (scleral bands, silicon oil, gas)

OPTIC DRUSEN

[*druse*, German = geode]
= accretions of hyaline material on / near surface of optic disc; often familial
Age: patient with macular degeneration; also in young patient
• usually asymptomatic
• headache, visual field defects
• pseudopapilledema
Location: at junction of retina + optic nerve; bilateral in 75%
US:
√ hyperechoic lesions at papilla + acoustic shadowing
CT:
√ hyperattenuating small flat / round calcification
Cx: atrophy of optic nerve

OPTIC PATHWAY GLIOMA

= JUVENILE PILOCYTIC ASTROCYTOMA = OPTIC NERVE GLIOMA
= isolated to single prechiasmatic optic nerve anywhere along optic tract ± extension to other optic nerve, chiasm, optic tract
◊ Most common › cause of optic nerve enlargement
› primary tumor of optic nerve
› intraconal tumor of childhood
› CNS neoplasm in NF1
Frequency: 1% of all intracranial tumors; 4% of orbital masses; 80% of primary tumors of optic nerve
Path: optic nerve is embryologically part of hypothalamus and develops gliomas instead of schwannomas
(a) perineural spread = fusiform enlargement of optic nerve: boundary between tumor and nerve often indistinguishable, overlying dura stretched but intact
(b) subarachnoid spread = tumor predominantly involves subarachnoid space surrounding a relatively spared nerve: infiltration through pia mater but contained by dura
Histo: proliferation of well-differentiated astrocytes
= low-grade glial neoplasm with cystic components
(a) <u>in children</u> (most common): juvenile pilocytic astrocytoma = grade 1 WHO with spindle-shaped astrocytes having hairlike (pilocytic) processes ± eosinophilic degenerative cell processes (Rosenthal fibers)
(b) <u>in adults</u>: glioblastoma
Mean age: 4–5 years; 1st decade (75%); rare in adults without NF1 (GBM); M÷F = 1÷2 to 2÷3
Associated with: neurofibromatosis type 1 (NF1) in 10–33–50% (± bilateral optic gliomas)
◊ 15–21% of children with NF1 have (often bilateral) optic nerve gliomas
◊ 10% of all optic nerve gliomas are associated with neurofibromatosis
• decreased visual acuity / visual-field deficit
• optic disc edema, pallor, atrophy (axonal damage)
• abnormal pupillary reflex; relative afferent pupillary defect

- axial proptosis with larger masses (less common)
- vision loss, strabismus
- spasmus nutans (= high-frequency nystagmus of low amplitude associated with head nodding movement)
- precocious puberty with accelerated growth (in 39% of only NF1 patients) ← involvement of optic chiasm + hypothalamus

Location: any part of optic pathway (intraorbital optic nerve in 25–48%); unilateral (most common); bilateral / multifocal (PATHOGNOMONIC for NF1); involvement of chiasma (more common in sporadic cases without NF1)

Extension to: intracanalicular + retrocanalicular optic nerve; lateral geniculate body and optic radiation (rare)

√ tubular / fusiform / excrescentic well-circumscribed homogeneous enlargement of optic nerve-sheath complex:
  √ CHARACTERISTIC kinking / buckling of nerve

√ posterior extension to involve chiasm + hypothalamus in 25–60% (indicates nonresectability)

√ ipsilateral optic canal enlargement (90%) > 3 mm / 1 mm difference compared with contralateral side

CT:
  √ iso- to slightly hypodense compared to normal optic nerve
  √ variable contrast enhancement (less intense than meningioma)
  √ calcifications (rare)

US:
  √ well-defined homogeneous mass of medium echogenicity inseparable from optic nerve

MR: more sensitive than CT in detecting intracanalicular + intracranial extent
  √ fusiform enlargement of nerve (without NF1):
    √ effacement of surrounding subarachnoid space
  √ tortuous / kinked / buckled diffusely enlarged optic nerve (NF1 patient):
    √ tumor in subarachnoid space surrounds normal-sized optic nerve
  √ lesion isointense to muscle on T1WI
  √ lesion heterogeneously hyperintense on T2WI
  √ rim of T2-hyperintensity at tumor periphery (mimicking expanded subarachnoid space) = arachnoidal gliomatosis ← leptomeningeal infiltration + proliferation
  √ ± cystic spaces
  √ calcifications (rare)
  √ nerve indistinguishable from tumor (DDx to meningioma)
  √ variable enhancement (in 50%):
  √ additional intracranial findings:
    √ other gliomas
    √ macrocephaly
    √ hydrocephalus ← aqueductal stenosis (almost exclusive to patients without NF1)
    √ neurofibromatosis spots (= foci of T2 prolongation due to myelin vacuolization)

Cx: precocious puberty ← hypothalamic impingement

Prognosis: slow growth / stability over time; 87–97% 5-year survival

Rx: conservative management; chemotherapy (for young patients), radiation therapy (for patients > 5 years of age)

DDx: optic nerve sheath meningioma (middle age, hyperattenuating mass, plaquelike calcifications, hypointense on T2WI, intense enhancement, no intracranial extension along optic pathway)

Malignant Optic Glioma of Adulthood

Prevalence: extremely rare; 30 cases in this century
Mean age: 6th decade; M÷F = 1.3÷1.0
Histo: anaplastic astrocytoma / glioblastoma multiforme
• rapidly progressive monocular visual loss culminating in monocular blindness within a few weeks
• with retrograde tumor extension: contralateral temporal hemianopia, polyuria, polydipsia
√ focal / diffuse enlargement of optic nerve
√ hypo- to isointense on T1WI + hyperintense on T2WI
√ obliteration of subarachnoid space around affected portion of nerve
√ diffuse intense enhancement of optic nerve
√ thickening + abnormal enhancement of optic nerve sheath
Tumor extension: optic chiasm, hypothalamus, basal ganglia, brain stem, medial temporal lobes, leptomeninges, ependyma
Prognosis: < 1-year survival despite aggressive therapy
DDx: (1) Optic neuritis (demyelinating plaques elsewhere)
(2) Perioptic meningioma (hypointense on T2WI, stippled calcifications, hyperostosis)
(3) Sarcoidosis, lymphoma, orbital pseudotumor (moderately / markedly hypointense on T2WI)

OPTIC NERVE SHEATH MENINGIOMA

= PERIOPTIC MENINGIOMA
Frequency: 2% of space-occupying orbital masses; < 2% of intracranial meningiomas
◊ 2nd most common optic nerve tumor!
Mean age: 49 years; M÷F = 1÷4; slightly more aggressive in children
Occasionally associated with:
neurofibromatosis type 2 (usually in teenagers)
Origin: meningothelial cells in arachnoid sheath of optic nerve in orbit / middle cranial fossa
Histo: syncytial growth pattern composed of meningioma cells with indistinct cytoplasmic margins ± multiple ringlike psammoma bodies (= round calcifications)
• classic clinical triad of retinal examination:
(1) Painless slowly progressive loss of visual acuity over months
(2) Optic nerve atrophy → progressive loss of vision
(3) Optociliary shunt vessels = dilated connections between ciliary circulation + central retinal vessels ← long-term compression of central retinal vein
• proptosis
Location:
(a) orbit = <u>intraoptic</u> nerve sheath meningioma
(b) in optic canal = <u>intracanalicular</u> meningioma
(c) <u>intracranial</u> opening of optic canal = foraminal meningioma

(d) middle cranial fossa

√ tubular (most common) / fusiform / eccentric (excrescentic) thickening of optic nerve

√ calcifications in 20–50% (HIGHLY SUGGESTIVE)

√ sphenoid bone hyperostosis

US:

√ hypoechoic tumor with irregular border

CECT: enhancement is the rule

√ tumor enhancement around nonenhancing optic n.:

√ "tram-track" configuration on axial CECT = enhancing tumor on either side of spared optic nerve

√ ringlike / doughnut configuration on coronal CECT

√ linear high-attenuation area parallel to optic nerve (= tumor spread along subarachnoid space)

√ bone remodeling ± enlargement of optic canal

√ minimal extension into optic canal (not uncommon)

MR (most valuable in determining extent of disease):

√ hypointense to fat on T1WI

√ iso- to slightly hyperintense relative to optic nerve on T2WI

√ "tram-track" sign = intensely enhancing extrinsic soft-tissue mass surrounding optic nerve on fat-suppressed T1WI

Rx: surgical intervention to prevent disease dissemination to contralateral eye if disease spreads to optic chiasm

OPTIC NEURITIS

= nerve involvement by inflammation, degeneration, demyelination

Etiology:

(1) Multiple sclerosis (involves optic nerve in ⅓)

(2) Inflammation ← ocular infection

(3) Degeneration: toxic, metabolic, nutritional

(4) Ischemia

(5) Meningitis / encephalitis (= viral infection)

(6) Systemic lupus erythematosus

(7) Radiation therapy

◊ 45–80% of patients develop multiple sclerosis within 15 years of their first episode of optic neuritis!

• ipsilateral ocular pain on eye movement

• sudden onset of unilateral loss of vision over several hours to several days

CT:

√ normal / mildly enlarged optic nerve + chiasm

√ may show enhancement

MR:

√ mild enlargement + enhancement of optic nerve best demonstrated on axial T1WI

√ hyperintense optic nerve on T2WI

Prognosis: spontaneous improvement of visual acuity within 1–2 weeks

Perioptic Neuritis

Etiology: demyelination from
(1) Multiple sclerosis
(2) Infection: measles, mumps, syphilis
(3) Sarcoidosis

√ leptomeningeal enhancement obscures lucent optic nerve

ORBITAL SCHWANNOMA

= slowly progressive benign tumor

Location: branches of trigeminal (CN V) nerve (most common) > oculomotor > trochlear > abducens > para-sympathetic > sympathetic fibers > ciliary ganglia

Site: extraconal superior orbit often abutting orbital apertures ← origin from supratrochlear and supraorbital nn. of frontal branch of ophthalmic n.

√ cone-shaped tumor ← involvement of orbital apex

√ dumbbell shape ← involvement of superior orbital fissure

MR:
√ well-circumscribed mass:
√ uniformly T1-isointense ± variations
√ T2-hyperintense heterogeneous pattern ← mixture of solid and cystic components
√ typically heterogeneous uptake of contrast medium

DDx: cavernous malformation (homogeneous pattern, progressive enhancement)

PERSISTENT FETAL VASCULATURE

= PERSISTENT HYPERPLASTIC PRIMARY VITREUS

= rare congenital nonhereditary condition with persistence + hyperplasia of fibrovascular system derived from embryonic primary vitreus + its hyaloid arterial supply ← arrest of normal regression

Embryology:

› **Hyaloid artery**
= important source of intraocular nutrition until 8th month of gestation; arises from dorsal ophthalmic artery at 3rd week of gestation; grows anteriorly with branches supplying vitreus + posterior aspect of lens

› **Primary vitreous humor**
[*vitreus*, Latin = glass; *humor*, Latin = body fluid]
= fibrillar ectodermal meshwork + mesodermal tissue consisting of embryonic hyaloid vascular system; appears during 1st month of life in posterior ocular chamber between lens + retina; involutes by 6th month of gestation

› **Secondary / adult vitreous humor**
begins to form during 3rd gestational month; watery mass of loose collagen fibers + hyaluronic acid gradually replaces primary vitreus, which is reduced to a small S-shaped remnant (hyaloid canal = Cloquet canal) and serves as lymph channel

Pathogenesis: breakdown in posterior capsule → invasion of lens → absorption of lens → cataract formation + glaucoma; hemorrhage from fibrovascular tissue (common) → folding of retina with detachment (30–56%)

May be associated with: any severe ocular malformation / optic dysplasia / trisomy 13
Age: noticed at birth / within first few weeks of life
• unilateral leukokoria (2nd most common cause)
  ◊ 19–28% of leukokoria cases
• seizures, mental deficiency, hearing loss
• ± cataract, strabismus, painful glaucoma, hyphema, uveitis
• ophthalmoscopy: S-shaped tubular mass extending between posterior surface of lens + region of optic nerve head; lens opacity may preclude diagnosis
Location: unilateral
  ◊ Bilaterality is a feature of a congenital syndrome (Norrie disease, Warburg disease)!
√ microphthalmia = small hypoplastic globe (61–92%):
  √ normal-sized globe (13%)
  √ buphthalmos (in up to 26%)
√ retinal detachment ← vitreoretinal traction in 30%
US:
  √ hyperechoic band extending from posterior pole of globe to posterior surface of lens (= embryonic rest of primary vitreus)
  √ central anechoic line (= persistent hyaloid artery) with positive Doppler signals
  √ hyperechoic band extending from papilla to ora serrata (= retinal detachment)
  √ heterogeneous increased echogenicity of vitreus ← hemorrhage
CT:
  √ enhancing cone-shaped central retrolental density extending from lens through vitreous body to back of orbit, just lateral to optic nerve (= primary vitreus)
  √ linear band / septum extending to posterior pole
  √ small optic nerve
  √ abnormally small lucent rounded lens ← absorption / swelling
  √ hyperdense vitreus (from previous hemorrhage)
  √ fluid-fluid levels from breakdown of recurrent hemorrhage in subhyaloid (between vitreus + retina) / subretinal space (between sensory + pigment epithelium)
    ◊ Blood does NOT layer in extremely viscous vitreous humor
  √ enhancement of vascular retrolental mass
  √ NO calcifications
MR:
  √ hyperintense vitreous body on T1WI + T2WI from chronic blood degradation products (methemoglobin) / proteinaceous fluid
  √ hypo- to isointense thin triangular band with base near optic disc and apex at posterior surface of lens
  √ marked enhancement of fibrovascular mass within vitreus
  √ lens abnormalities
  √ elongated ciliary process
  √ anterior tenting retina
Cx: (1) Glaucoma, cataract from recurrent spontaneous intravitreal hemorrhage (due to friable vessels)
(2) Proliferation of embryonic tissue

(3) Retinal detachment from organizing hemorrhage / traction
(4) Hydrops / atrophy of globe + resorption of lens
(5) Phthisis bulbi (scarred shrunken eye)

Rx: preservation of globe for cosmetic reasons; enucleation for retinal hemorrhage + glaucoma only

PHTHISIS BULBI

[*phthinein*, Greek = to waste away]
= "wood eye" = shrunken nonfunctioning + usually calcified eye
Cause: trauma, angiomatosis, intrauterine environmental conditions, infection, genetic disorders, retrolental fibroplasia (retinopathy of prematurity)
US:
√ shrunken eye
√ usually calcified wall
√ ± hyperechoic fibrous tracts within vitreous + resultant retinal detachment

PLEOMORPHIC ADENOMA OF ORBIT

= BENIGN MIXED TUMOR
Frequency: 57% of epithelial lesions in lacrimal gland
◊ Most common benign neoplasm of lacrimal gland
Age: 4th to 5th decade of life
• proptosis (= commonly downward displacement of globe)
• rarely painful slow-growing tumor
Histo: fibrous pseudocapsule with epithelial cells that may form nests / tubules resembling ducts; myxoid / mucinous background stroma with spindle-shaped cells ± cartilage or bone
Location: superotemporal orbit
√ well-circumscribed usually homogeneously enhancing mass
√ larger lesion heterogeneous ← cystic degeneration, hemorrhage, serous / mucous collections, necrosis
√ smooth concavity of lacrimal fossa ← bone remodeling
√ T1-hypointense + T2-hyperintense mass
DDx: lacrimal gland malignancy (infiltrative borders, nodularity, bone erosion)

PRIMARY ORBITAL MELANOMA

= UVEAL MELANOMA = Choroidal Melanoma
Most common primary intraocular neoplasm in adult Caucasian
Prevalence: 5–7÷1,000,000
Mean age: 56 (range, 50–70) years; in 65% > 50 years of age; Whites÷African Americans = 8÷1 to 15÷1
Predisposed: exposure to sunlight, fair skin complexion, light eye color, preexisting melanocytic nevi
At risk: Caucasian, light-colored iris, ocular melanocytosis
Path: mushroom-shaped tumor with broad choroidal base / flat mass / crescentic mass; range

from amelanotic to heavily pigmented lesion

Histo: (a) spindle containing varying amounts of spindle-B cells
(b) epithelioid cells with abundant cytoplasm, clear cellular borders, enlarged ovoid nuclei

Metastases to: globe, optic nerve; liver (90%), lung (24%), bone (16%), kidney, brain, subcutis

- asymptomatic (most frequently) detected on routine eye exam
- pain (uncommon), floaters, astigmatism
- visual loss ← vitreous hemorrhage
- visual field (campimetric) defect
- photopsia (perceived flashes of light) ← retinal detachment
- glaucoma (with iris location)
- accommodation impairment (with ciliary body location)

Location: choroid (85–93%) > ciliary body (4–9%) > iris (3–6%); almost always unilateral

√ initially flat growth profile, later becoming elevated, erupting through Bruch membrane (= innermost layer of choroid) into a CHARACTERISTIC mushroom shape
√ episcleral spread after infiltration of underlying sclera
√ moderate to strong contrast enhancement

US (95% diagnostic accuracy):
√ low-to-medium internal reflectivity spikes on tumor surface + vascular oscillations (A-mode US)
√ domed lobulated mushroom-shaped mass / round hyperechoic solid mass / small flat lesion
√ well-defined solid mass with smooth surface (unless hemorrhagic / necrotic)
√ NO calcification
√ choroidal excavation beneath a small posterior wall mass with retinal bowing ← local invasion (TYPICAL)

CT:
√ nonspecific ill-defined hyperdense thickening of wall of globe with inward bulge
√ diffuse moderate enhancement
√ calcifications may appear after therapy
√ diffuse moderate enhancement ← abnormal / absent blood-ocular barrier
√ restricted diffusion + low apparent diffusion coefficient

MR (superior to CT, mainly used for extraocular extension):
(a) melanotic melanoma (75%) = T1 + T2 shortening effect of paramagnetic stable free radicals with unpaired electrons in melanin pigment
√ paramagnetic effect of melanin → intrinsic T1 + T2 shortening: ⇑ T1 signal intensity + ⇓ T2 signal intensity
(b) amelanotic / slightly melanotic melanoma (25%)
√ iso- to hypointense on T1WI
√ hyperintense lesion on T2WI

Dx: indirect ophthalmoscopy, clinical history, transillumination, sequential US evaluation
Cx: retinal detachment and extrascleral spread
Rx: plaque brachytherapy, external beam radiation, transpupillary thermotherapy, surgical enucleation

N.B.: small nonprogressive melanoma < 3 mm thick can be followed every 3–6 months by US

Prognosis: 5-year survival rate for (a) small < 3 mm thick choroidal melanoma 85%, (b) medium 3–10 mm thick choroidal melanoma 68%, (c) large > 10 mm thick choroidal melanoma 47%; mean survival of 2–7 months for metastatic disease

DDx: (1) Choroidal metastasis (frequently bilateral + multiple, usually broad-based flat lesion, iso- to hyperintense on T1WI, hyperintense on T2WI, heterogeneous enhancement)

(2) Choroidal hemangioma (typically hypointense on T1WI + extremely hyperintense on T2WI, appreciable enhancement, high internal reflectivity at A-mode US)

(3) Vitreous hemorrhage / clot (typically hyperintense on T1WI + extremely hypointense on T2WI greater than for melanoma ← intracellular methemoglobin, no enhancement)

(4) Retinal detachment (similar to vitreous hemorrhage, pathognomonic V shape)

(5) Melanocytic nevus (common small flat lesion, difficult to detect at MRI, no flow at Doppler, pigmented tumor at direct examination)

(6) Orbital melanocytoma= subtype of nevus (enhancing hyperintense lesion on T1WI + extremely hypointense on T2WI, indistinguishable from uveal melanoma at MRI)

(7) Retinoblastoma (younger patient, calcifications at CT, high internal reflectivity at A-mode US, heterogeneously enhancing T1 hypointense + T2 hyperintense lesion)

(8) Retinal hamartoma = hemangioblastoma (in tuberous sclerosis, heterogeneously enhancing T1 hypointense + T2 hyperintense lesion)

(9) Osteoma (same SI characteristics as uveal melanoma, bone attenuation at CT)

PSEUDOTUMOR OF ORBIT

= INFLAMMATORY MYOFIBROBLASTIC TUMOR = IDIOPATHIC ORBITAL INFLAMMATORY SYNDROME

= idiopathic nongranulomatous inflammatory process affecting all intraorbital soft tissues

Etiology:

(a) cause not apparent at time of study: bacterial, viral, foreign body

(b) systemic disease presently not apparent: part of in IgG4-related disease, sarcoidosis, collagen, endocrine

(c) idiopathic: probably abnormal immune response

Frequency: 6% of all orbital lesions

◊ 2nd most common cause of exophthalmos (25% of all unilateral exophthalmos)

◊ 3rd most common primary tumor of the orbit

Age: young to middle-aged; M = F

Histo: myofibroblastic spindle cells with an inflammatory infiltrate of plasma cells + lymphocytes + eosinophils

May be associated with:

Wegener granulomatosis, sarcoidosis, fibrosing mediastinitis, retroperitoneal fibrosis, thyroiditis, cholangitis, vasculitis, lymphoma

- sudden acute onset of unilateral eye pain
- ophthalmoplegia (= impaired ocular movement) + diplopia
- decreased visual acuity, proptosis; eyelid swelling, chemosis

Location: retrobulbar fat (76%), commonly superior + medial extraocular muscle (57%), optic

nerve (38%), uveal-scleral area (33%), lacrimal gland (5%), thyroid gland, skull base; usually unilateral

Subcategories: often coexistence

(1) Myositic type (most common) affects extraocular muscles
- √ enlargement of one / more extraocular muscles with ill-defined margins close to insertion on globe
- √ typically at muscles + tendon insertions (DDx to Graves disease with muscle involvement only)

(2) Dacryoadenitis-related form affects lacrimal glands
(3) Neuritis-associated form affects optic nerve sheath
(4) Apical form affects orbital apex
(5) Episcleral form affects anterior orbit with sclera and preseptal soft tissues
(6) Diffuse form affects entire orbit

√ inflammatory stranding of retrobulbar fat (may involve anterior compartment)
√ SPECIFIC uveoscleral thickening (⅓) with enhancement (sclera near Tenon capsule)
√ orbital muscle thickening ← myositis
√ enhancement of optic nerve sheath
√ enlarged inflamed lacrimal gland
√ proptosis
√ bone destruction and intracranial extension (rare)

MR:
- √ lesion isointense to fat on T2WI

Prognosis:
(1) Remitting / chronic + progressive course (= intermediate malignant potential)
(2) Rapid dramatic + lasting response to steroid therapy

Cx: Tolosa-Hunt syndrome (= involvement of cavernous sinus by pseudotumor)

DDx: (1) Lymphoma (may be confused with lymphoma clinically, radiographically, pathologically)
(2) Thyroid ophthalmopathy (tapering of distal muscles, painless proptosis)
(3) Radiation therapy

RETINAL ASTROCYTOMA

= RETINAL ASTROCYTIC HAMARTOMA
= low-grade benign neoplasm / hamartoma arising from the nerve fiber layer of retina / optic nerve

Etiology: tuberous sclerosis (53%); neurofibromatosis type 1 (14%); sporadic (33%)
- ◊ 50% of patients with tuberous sclerosis develop astrocytic hamartomas (bilateral in ¼)!

Path: usually multiple + bilateral in tuberous sclerosis;
(1) small flat noncalcified semitranslucent lesion in posterior / peripheral retina
(2) "mulberry" lesion = raised white tumor in posterior retina with fine nodularity containing calcifications + cystic fluid accumulations

Histo: spindle-shaped fibrous astrocytes with small oval nuclei

Age: congenital

• leukokoria (3% of all childhood cases of leukokoria)
• asymptomatic, progressive loss of vision

Location: retina near optic disc; bilateral in 25%

√ retinal mass ± enhancement ± calcifications

√ typically unilateral (DDx to drusen)

Cx: (1) Central retinal vein occlusion + secondary hemorrhage
(2) Neovascular glaucoma
(3) Extensive tumor necrosis

Rx: not necessary

DDx: retinoblastoma

RETINAL DETACHMENT

= separation of the sensory retina from retinal pigment epithelium (RPE) = deep retinal layer adjacent to choroid

◊ MEDICAL EMERGENCY!

Cause: inflammation, neoplasm, trauma

Pathophysiology: formed vitreous gel liquefies with age, eventually separates from retina

Mechanism:

(a) rhegmatogenous / retinal tearing (most common) = tear in retina → accumulation of liquefied vitreus in subretinal space → separation of retina from underlying RPE [*rhegma*, Greek = discontinuity, break]

Predisposed: diabetic retinopathy, trauma, high myopia, congenital cataract, surgery, congenital glaucoma, sickle cell disease, leukemia, systemic lupus erythematosus, metastases

(b) tractional: pulling / tugging by vitreous membranes /fibrovascular tissue (scar)

(c) exudative: = blood / fluid / tumor within subretinal space

√ CHARACTERISTIC V-shape (= total detachment)

√ in one quadrant only (= partial detachment)

√ thick folded retina with loss of mobility (long-standing detachment)

√ subretinal space normal / occupied by blood / inflammation / tumor (depending on cause)

MR:

√ differentiation of serous vs. proteinaceous vs. hemorrhagic fluid

US:

√ curvilinear line of high echogenicity fixed at optic disc (= papilla) + extending to ora serrata forming an acute angle of V shape with apex at optic disc

√ floating echogenic line fixed at papilla extending to ora serrata (if acute)

√ thick folded fixed echogenic line (if chronic)

√ ± anechoic retinal cysts

√ fluid = anechoic; blood = anechoic / hypoechoic with low-level echoes; neoplasm = solid heterogeneous hypoechogenicity

Cx: vision loss (if macula involved)

Rx: scleral buckle, pneumatic retinopexy, laser therapy, cryotherapy, vitrectomy

DDx: proliferative vitreous membranes (lines / irregularities), choroidal detachment (point of fixation not at papilla)

DDx of partial detachment: diabetes, macular lesion, retinal ischemia

N.B.: Examine subretinal space and vitreous for blood / exudative fluid / tumor since determination of cause is usually not possible at ophthalmoscopy.

RETINOBLASTOMA

= NEUROEPITHELIOMA OF RETINA
= rare aggressive malignant congenital intraocular tumor

Prevalence: 1÷18,000 children < 5 years old in USA; 1÷17,000 – 1÷24,000 live births
◊ Most common intraocular childhood malignancy

Frequency: 1% of all pediatric malignancies; 11% of all cancers in 1st year of life; in 80% diagnosed < 3 years of age; in 95% < 5 years of age

Origin: primitive photoreceptor cells of immature retina (included in primitive neuroectodermal tumor group)

Cause: biallelic mutation (= loss of function of both alleles) in primitive neuroepithelial cells located on long arm of chromosome 13 (13q14) → inactivation of retinoblastoma tumor suppressor gene Rb1

Men age: at presentation 18 (range for bilateral tumors 7–16, range for unilateral tumors 24–29) months; M÷F = 1÷1; no race predilection

Location: bilateral in 20–34%

Classification:

(A) SPORADIC NONHERITABLE FORM (60%)

Clinical DDx to nonheritable form:
◊ Tumor typically solitary
◊ Age of onset usually > 2 years

(1) Sporadic postzygotic somatic mutation (subsequent generations unaffected)
Mean age at presentation: 23 months

(2) Chromosomal anomaly
= monosomy 13 / deletions of 13q
Associated with: microcephaly, ear changes, facial dysmorphism, mental retardation, finger + toe abnormalities, malformation of genitalia

(B) HERITABLE FORM (40%)

= autosomal dominant transmission to offspring with 90–95% penetrance
Genetics: mutation of tumor suppressor gene RB1 located on long arm of chromosome 13 (13q14)

Clinical DDx to nonheritable form:
◊ Tumors bilateral in ⅔ and multifocal
◊ Age at presentation usually < 2 years
√ multiple tumors in 60–75%

(1) Heritable sporadic form (20–25%)
= sporadic germline mutation (50% chance to occur in subsequent generations)
Mean age at presentation: 12 months
√ bilateral retinoblastomas in 66%

(2) Familial retinoblastoma (10–30%)

= autosomal dominant with 95% penetrance
Mean age at presentation: 8 months
√ usually 3–5 ocular tumors per eye
Risk of secondary nonocular malignancy (8%):
osteo-, chondro-, fibrosarcoma, malignant fibrous histiocytoma, melanoma, carcinoma (20% risk within 10 years, > 90% by 30 years of age); high risk within field of external-beam radiation (30%)
Location: head, skin, bone, brain

Trilateral retinoblastoma

Quadrilateral retinoblastoma
= trilateral retinoblastoma + 4th focus in suprasellar cistern
√ enhancing midline suprasellar mass

Path: (1) Endophytic form = centripetal tumor invasion → floating islands of tumor within semiliquid vitreus ± anterior chamber
(2) Exophytic form = growth toward sclera into subretinal space → retinal detachment + invasion of vascular choroid → hematogenous spread
(3) Mixture of endo- and exophytic growth (common)
(4) Diffuse infiltrating form = thin en-plaque lesion extending along retina (in 1–2%) → cells discharged into vitreus → seeding of anterior chamber mimicking an inflammatory process (= pseudohypopyon)
(5) Necrotic retinoblastoma with orbital cellulitis
(6) Complete spontaneous regression (rare) → phthisis bulbi (= shrunken nonfunctioning globe)

Histo:
√ primitive neuroepithelial neoplastic cells tend to outgrow blood supply → necrosis → foci of calcifications
(a) Flexner-Wintersteiner rosettes (in 50%)
= neuronal cells line up around an empty central zone filled with polysaccharides (= photoreceptor differentiation)
◊ Very specific for retinoblastomas!
(b) Homer-Wright rosettes
= neuronal cells line up around a central area containing a cobweb of filaments (also found in other primitive neuroectodermal tumors) = neuronal differentiation
(c) "fleurettes"
= flowerlike groupings of tumor cells that form photoreceptor elements (specific for retinal differentiation)

- "cat's eye" = leukokoria (white pupillary reflex) in 56–72%

◊ About 50% of all childhood leukokoria cases are caused by retinoblastoma!

- strabismus = crossed eyes = lack of binocular vision (22–24%)
- proptosis (less common)
- decreased visual acuity, heterochromia iridis, anisokoria
- spontaneous hyphema, periocular inflammation
- iris neovascularization

• ocular pain ← secondary angle-closure glaucoma

Location: posterolateral wall of globe (most commonly); 60% unilateral; 40% bilateral + frequently synchronous (90% bilateral in inherited forms)

√ normal ocular size

√ presence of calcifications

◊ Lack of calcifications OFTEN INDICATIVE of another disease!

US:

√ irregular heterogeneous hyperechoic solid intraocular mass

√ cystic areas of tumor necrosis

√ secondary retinal detachment (common)

Staging of Retinoblastoma
International Classification for Intraocular Retinoblastoma (2006)

Group	*Description*	*Features*
A	small	< 3 mm in diameter, > 3 mm from fovea, > 1.5 mm from optic disc; confined to retina (no vitreous seeding)
B	large	macular / juxtapapillary location without dissemination; subretinal fluid extends < 3 mm from tumor
C	local dissemination	vitreous / subretinal seeding < 3 mm from tumor
D	diffuse	massive tumor + diffuse / greasy vitreous seeding / fine subretinal seeds; avascular plaques / exophytic disease
E	unsalvageable / extensive	nonvascular glaucoma / intraocular or corneal hemorrhage / tumor contacting lens or in anterior segment / diffuse infiltrating tumor
F	extrascleral	extrascleral spread to optic nerve / orbit / brain; distant metastases

√ focal fine calcifications with acoustic shadowing (in 75%)

√ echogenic foci of vitreous hemorrhage (frequent)

CT (primary modality in leukokoria):

√ solid smoothly marginated lobulated retrolental hyperdense mass of endophytic type (DDx to exophytic type: retinal detachment)

√ partial punctate / nodular calcification (50–75–95%)

◊ Retinoblastoma is the most common cause of orbital calcifications!

√ dense vitreus (common)

√ extraocular extension (in 25%): optic nerve enlargement, abnormal soft tissue in orbit, intracranial extension

√ contrast enhancement (27%)

√ ± macrophthalmia

Risk: cataract formation

MR:

Advantage: assessment of extension into optic pathway + subarachnoid space + vitreous

seeding; follow-up without radiation exposure

√ mass with SI similar to gray matter:

√ mildly hyperintense on T1WI relative to vitreus
√ distinctly T2 hypointense (similar to uveal melanoma)
√ hyperintense on DWI (= reduced diffusion) with high tumor cellularity

√ heterogeneous intensity in the presence of calcifications

√ calcifications of low / high signal intensity with various pulse sequences ← dependent on proton content (susceptibility imaging for DDx to hemorrhage!)

◊ Even large calcifications may be missed on MR!

√ subretinal exudate usually hyperintense on T1WI + T2WI (proteinaceous fluid) = retinal detachment

√ assessment for 1–2 mm small vitreous seeds on high resolution T2WI 3-dimensional fast spin echo sequences

√ vitreous hemorrhage (= high SI on T1WI + low SI on T2WI) may obscure tumor

√ discontinuity within dark band of sclera = trans-scleral spread

√ tumor within orbital fat on enhanced fat-suppressed T1WI = extrascleral spread

CEMR:

√ moderate to marked enhancement

√ thinning with focal ↓ in enhancement OR thickening with focal ↑ in choroidal enhancement (= choroidal invasion)

√ thickening of enhancing choroidoretinal complex = prelaminar invasion

√ focal enhancement ± focal thickening of optic nerve (DDx: reactive gliosis)

√ leptomeningeal enhancement = dissemination into CSF

Cx: (1) Metastases to: meninges (via subarachnoid space), bone marrow, lung, liver, lymph nodes

◊ Optic nerve involvement through optic disc = port for dissemination into subarachnoid space!

◊ No risk of metastases without penetration of lamina cribrosa!

(2) Radiation-induced sarcomas develop in 15–20%

Prognosis: spontaneous regression in 1%

√ calcifications = favorable prognostic sign

√ contrast enhancement = poor prognostic sign

Mortality:

(a) choroidal invasion: 65% significant, 24% slight

(b) optic nerve invasion through optic disc:

< 10% not invaded
15% through lamina cribrosa
44% significantly posterior to lamina cribrosa

(c) margin of resection not free of tumor: > 65%

Rx: cryoablation, laser photocoagulation, chemothermotherapy, brachytherapy, plaque radiation therapy; chemoreduction and surgery; enucleation

Survival: 90–95% due to earlier detection

DDx: Pseudoretinoblastomas (in order of decreasing frequency)

(1) Persistent fetal vasculature (no calcifications, microphthalmia, vertical septum

between optic disc + posterior lens)

(2) Coats disease (subretinal exudation, no calcification, slightly older age group, no enhancement of subretinal space)

(3) Toxocara endophthalmitis (no calcification, usually > 5 years of age, contact with dogs, serology)

(4) Retrolental fibroplasia (microphthalmia, bilateral, low birth weight, periventricular leukomalacia)

(5) Giant drusen = nodular type of retinal astrocytic hamartoma (confined to sensory retina / optic disc, often lack hemorrhage / necrosis, may be associated with tuberous sclerosis / NF1)

(6) Norrie disease (retinal dysplasia)

(7) Coloboma of choroid / optic disc coloboma

(8) Retinoma = retinocytoma (benign variant)

RETROLENTAL FIBROPLASIA

= RETINOPATHY OF PREMATURITY

= bilateral often asymmetric postnatal fibrovascular organization of vitreous humor, which usually leads to retinal detachment

Pathophysiology:

retinal vascularization occurs in 4th–9th months of fetal life progressing from papilla to periphery; vascularization is incomplete in premature neonates, especially in temporal sectors

Predisposed: premature infants with respiratory distress syndrome requiring prolonged oxygen therapy

Severity directly related to:

(1) Degree of prematurity

(2) Birth weight

(3) Amount of oxygen used in therapy

- leukokoria in severe cases (traction retinal detachment, usually bilateral + temporal) [3–5% of all childhood leukokoria cases]
- Ophthalmoscopic stages:

1st stage	=	arteriolar narrowing of most immature vessels at the border of the vascular-avascular retina ← spasm as a reaction to hyperoxygenation
2nd stage	=	dilatation + elongation + tortuosity of retinal vessels (after oxygen withdrawal)
3rd stage	=	retinal neovascularization with growth into vitreus → vitreous hemorrhage
4th stage	=	fibrosis → retraction of fibrovascular tissue → retinal detachment

√ bilateral microphthalmia ± retinal detachment

US:

√ hyperechoic tracts extending from temporal side of periphery of retina to vitreus behind lens

CT:

√ dense vitreus bilaterally (neovascular ingrowth)

√ ± dystrophic calcifications in choroid + lens (late stage)

MR:

√ hyperintense vitreus on T1WI + T2WI ← chronic subretinal hemorrhage

√ hypointense retrolental mass ← apposition of detached leaves of retina displaced from retinal pigment layer

Prognosis:

(1) spontaneous regression of vitreous neovascularization (85–95%) ± retinal detachment

(2) progression to cicatricial stage characterized by formation of dense membrane of gray-white vascularized tissue in retrolental vitreus + retinal detachment + microphthalmia

DDx: Retinoblastoma (calcifications in eye of normal size)

STAPHYLOMA

= sacculation of posterior pole of globe (or berrylike protrusion of cornea)

Prevalence: increasing with size of globe

Cause: axial myopia (temporal side of optic disc / anteriorly / along equator), trauma, scleritis, necrotizing infection

√ increase of anteroposterior ocular axis > 25 mm

√ focal bulge + thinning of sclera of posterior pole

Cx: advanced chorioretinal degeneration (77%), choroid retraction from optic disc, posterior vitreous detachment, choroidal hemorrhage, retinal detachment, cataract, glaucoma

SUPERIOR OPHTHALMIC VEIN THROMBOSIS

Cause: paranasal sinusitis

• orbital pain, headache, visual disturbance, cranial nerve palsy

• periorbital edema, chemosis, proptosis

√ filling defect in superior ophthalmic vein

√ enlargement of both superior ophthalmic veins + cavernous sinus

√ periorbital edema

√ engorgement of extraocular muscles

√ exophthalmos

Cx: vision loss, thrombosis of cavernous sinus, sepsis

Rx: anticoagulation + antibiotics

TOLOSA-HUNT SYNDROME

[Eduardo Tolosa (1900–1981), Spanish neurosurgeon]

[William Edward Hunt (1921–1999), neurosurgeon at Ohio State University]

= rare disorder characterized by painful ophthalmoplegia ← cavernous sinus inflammation responsive to steroid therapy

Cause: inflammation of cavernous sinus and orbital apex

Path: lymphofibroblastic lesion (similar to orbital pseudotumor)

Age: 5th decade

• acute onset of severe retro- / periorbital pain

• ophthalmoplegia ± exophthalmos

• diplopia, ptosis, pupillary + variable extraocular muscle dysfunction

• visual loss with optic nerve involvement
• fever, chronic fatigue, vertigo, arthralgia

Location: unilateral, bilateral (5%)

CT:
- √ inflammatory soft-tissue density around orbital apex
- √ asymmetric enlargement of cavernous sinus
- √ abnormal nodular enhancement in prepontine cistern

MR (thin-section contrast-enhanced MRI + fat suppression):
- √ loss of SI of orbital fat
- √ enlargement of the cavernous sinus with convex outer margin
- √ abnormal soft tissue in cavernous sinus:
  - √ isointense to gray matter on T1WI
  - √ hypo- to isointense to gray matter on T2WI ← fibrous tissue
  - √ homogeneous enhancement
- √ extension of lesion into orbital apex through superior orbital fissure with involvement of extraocular muscles
- √ narrowing of cavernous segment of ICA (in 50%)
- √ enhancement of dura, trigeminal n., facial n. (uncommon)

Angio:
- √ narrowing of carotid siphon
- √ occlusion of superior ophthalmic vein
- √ nonvisualization of cavernous sinus

Rx: corticosteroids, immunosuppressive agents (methotrexate, azathioprine)

Dx: findings reversible with steroid use

DDx: perineural tumor spread, fungal infection, schwannoma, meningioma (no resolution with steroids), lymphoma (systemic symptoms), sarcoidosis (systemic symptoms)

VARIX OF ORBIT

◊ Most common cause of spontaneous orbital hemorrhage!

Etiology:
(a) congenital: weakness in postcapillary venous wall
(b) acquired: intraorbital / intracranial AVM
◊ Orbital veins are valveless!

Frequency: uncommon

Age: 2nd–3rd decade; M÷F = 1÷1

May be associated with: contiguous / noncontiguous intracranial venous anomalies

• stress proptosis = dramatic protrusion of eye with straining (coughing, forward bending, breath holding, Valsalva)
• frequent blindness

√ involvement of superior / inferior orbital vein; phleboliths rare
√ may produce bony erosion without sclerotic reaction
√ well-defined markedly enhancing mass
√ enlargement of mass during Valsalva maneuver / jugular vein compression

CT:

√ normal / only mild enlargement of veins in supine position (repeat scan during Valsalva maneuver / in prone position / with neck tourniquet)
√ smoothly contoured clublike / triangular tangled mass of vessels
√ intense contrast enhancement

US:
√ anechoic tubular / oval structure ± thrombus
√ venous flow increasing / reversing with Valsalva

MR:
√ flow void (rapid flow) / flow-related enhancement (slow flow)

Cx:
1. Hemorrhage
2. Spontaneous thrombosis (with rapid painful proptosis)

WARBURG DISEASE

= autosomal recessive syndrome characterized by
(1) Bilateral persistent hyperplastic primary vitreous
(2) Hydrocephalus, lissencephaly
(3) Mental retardation

• bilateral leukokoria + microphthalmia

EAR, NOSE AND THROAT

DIFFERENTIAL DIAGNOSIS OF EAR, NOSE, AND THROAT DISORDERS

FACE

Facial Swelling in Childhood

A. ACUTE SWELLING with inflammation (most common)
   1. Lymphadenitis of neck and face
      Cause: upper-airway viral (common) / bacterial infection (S. aureus, group A streptococci)
      • erythema in upper neck, submandibular, parotid region
      Cx: abscess (CECT!)
   2. Sinusitis
      • swelling around malar / brow region
      Cx: preorbital / preseptal cellulitis
   3. Odontogenic infection
      • jaw swelling, trismus ← masticator space phlegmon

B. NONPROGRESSIVE SWELLING
   (a) congenital midfacial mass
      • broad nasal bridge, glabellar swelling, hypertelorism
      1. Frontoethmoidal cephalocele
      2. Nasal glioma
      3. Nasal dermoid / epidermoid cyst
   (b) developmental
      1. Dacryocystocele
      2. Orbital dermoid
      3. First branchial cleft cyst

C. SLOWLY PROGRESSIVE SWELLING
   (a) underlying mass
      1. Neurofibroma
      2. Lymphangioma
      3. Hemangioma
      4. Plunging ranula
   (a) osseous disease
      1. Craniofacial fibrous dysplasia

D. RAPIDLY PROGRESSIVE SWELLING
   1. Rhabdomyosarcoma
   2. Langerhans cell histiocytosis
   3. Ewing sarcoma of mandible

4. Osteogenic sarcoma
5. Metastatic neuroblastoma

Facial Nerve Paralysis

A. INTRACRANIAL SEGMENT
   (a) intraaxial brainstem glioma, metastasis, multiple sclerosis, cerebrovascular accident, hemorrhage
      • cranial nerve VI also involved
   (b) extraaxial CPA tumor (acoustic neuroma, meningioma, epidermoid), CPA inflammation (sarcoidosis, basilar meningitis), vertebrobasilar dolichoectasia, AVM, aneurysm
      • cranial nerve VIII also involved
B. INTRATEMPORAL SEGMENT
   fracture, cholesteatoma, paraganglioma, hemangioma, facial nerve schwannoma, metastasis, Bell palsy, otitis media
   • loss of lacrimation, hyperacusis, loss of taste
C. EXTRACRANIAL PAROTID SEGMENT
   forceps delivery, penetrating facial trauma, parotid surgery, parotid malignancy, malignant otitis externa
   • preservation of lacrimation, stapedius reflex, taste

Bell Palsy

= facial nerve paralysis without identifiable cause
Cause: ? viral inflammation (herpes simplex virus)
• rapid onset of facial nerve paralysis progressing over a few hours to up to 3 weeks
√ enhancement of canalicular, labyrinthine, geniculate portion of facial n.
Prognosis: spontaneous improvement (in 80%); persistent Bell palsy (in 5% caused by neurinoma)
N.B.: if symptoms persist for > 3 weeks → MRI

EAR

Hearing deficit

A. CONDUCTIVE HEARING LOSS
   • decrease in air conduction via EAC, tympanic membrane, ossicular chain, oval window (sound via headphones)
   • normal bone conduction (sound via bone oscillator)
   (a) congenital (uncommon):
      1. EAC atresia / stenosis
      2. Malformed ossicles
      3. Absence of oval window
   (b) trauma: incudostapedial / malleoincudal subluxation; incus dislocation; stapes dislocation; stapes / malleus fracture
   (c) destruction of ossicular chain:
      1. Otitis media

(d) restriction of ossicular chain: fenestral otosclerosis
◊ CT is the modality of choice!

B. SENSORINEURAL HEARING LOSS (most common)
• elevated conduction thresholds for bone + air
(a) sensory / **cochlear SNHL** = damage to cochlea / organ of Corti (less common)
› bony labyrinth
» demineralization:
1. Otosclerosis (otospongiosis)
2. osteogenesis imperfecta
3. Paget disease, syphilis
» congenital deformity:
1. Cochlear dys- / aplasia
2. Michel anomaly
3. Mondini dysplasia
4. Enlarged vestibular aqueduct syndrome
5. X-linked sensorineural hearing loss
» traumatic lesion:
1. Transverse fracture
2. Perilymphatic fistula, cochlear concussion
» destructive lesion: inflammation, neoplasm
◊ High-resolution CT is the modality of choice!
› membranous labyrinth
» enhancement: labyrinthitis, Cogan syndrome (early phase of autoimmune interstitial keratitis), intralabyrinthine schwannoma, site of postinflammatory perilymphatic fistula
» obliteration: labyrinthitis ossificans, Cogan syndrome (late phase)
» hemorrhage: trauma, labyrinthitis, coagulopathy, tumor fistulization
» Ménière disease (vertigo + fluctuating sensory sensorineural hearing loss)
◊ Thin-section MR is the modality of choice!
(b) neural / **retrocochlear SNHL** (more common)
= abnormalities of neurons of spiral ganglion + central auditory pathways
› IAC / cerebellopontine angle
(1) Neoplastic lesion: vestibular / trigeminal schwannoma (acoustic neuroma in 1%), meningioma, arachnoid cyst, epidermoid cyst, leptomeningeal carcinomatosis, lymphoma, lipoma, hemangioma
(2) Nonneoplastic lesion: sarcoidosis, meningitis, vascular loop, siderosis
› intraaxial auditory pathway
(brainstem, thalamus, temporal lobe)
(1) Ischemic lesion
(2) Neoplastic lesion
(3) Traumatic lesion
(4) Demyelinating lesion
◊ MR is the modality of choice!

Pulsatile tinnitus ± Vascular Tympanic Membrane

= perception of a rhythmic cardiac synchronous sound of ringing / buzzing / roaring

A. NO ABNORMALITY (20%)

B. CONGENITAL VASCULAR VARIANTS (21%)
   1. Aberrant ICA
   2. Dehiscent jugular bulb
   3. High-riding nondehiscent jugular bulb (= jugular megabulb)
      √ high jugular bulb with diverticulum projecting cephalad into petrous temporal bone

C. ACQUIRED VASCULAR LESIONS (25%)
   1. Dural AVM
   2. Extracranial arteriovenous fistula
   3. High-grade stenotic vascular lesion:
      carotid artery atherosclerosis, fibromuscular dysplasia, carotid artery dissection
   4. Aneurysm involving horizontal segment of petrous ICA

D. TEMPORAL BONE TUMORS (31%)
   1. Paraganglioma (27%):
      glomus tympanicum, glomus jugulare
   2. Meningioma
   3. Hemangioma

E. MISCELLANEOUS
   1. Cholesterol granuloma

External Ear Masses

A. CONGENITAL
   1. Atresia

B. INFLAMMATORY
   1. Malignant external otitis
   2. Keratosis obturans
   3. Cholesteatoma

C. BENIGN TUMOR
   1. **Exostosis** = surfer's ear
      Cause: irritation by cold water
      √ bony mass projecting into EAC; often multiple + bilateral
   2. **Osteoma**
      √ may invade adjacent bone
      √ single in EAC / mastoid
   3. **Ceruminoma**
      from apocrine + sebaceous glands; bone erosion mimics malignancy

D. MALIGNANT TUMOR
   1. Squamous cell carcinoma
      • often long history of chronic suppurative otitis media = "malignant otitis"
   2. Basal cell carcinoma
   3. Melanoma, adenocarcinoma, adenoid cystic carcinoma
   4. Metastases
      (a) hematogenous: breast, prostate, lung, kidney, thyroid
      (b) direct spread: skin, parotid, nasopharynx, brain, meninges

(c) systemic: leukemia, lymphoma, myeloma

5. Histiocytosis X: in 15% of patients

Middle Ear Masses

A. CONGENITAL
   1. Aberrant internal carotid artery
   2. Dehiscent jugular bulb

B. INFLAMMATORY
   1. Cholesteatoma
   2. Cholesterol granuloma
   3. Granulation tissue
      √ linear strands partially opacifying middle ear cavity without bony erosion

C. BENIGN TUMOR
   1. Adenomatous tumor (mixed pattern type)
      √ intense enhancement
      √ no osseous destruction
   2. Glomus tumor (multiple in 10%; 8% malignant)
      (a) glomus tympanicum: at cochlear promontory
         √ seldom erodes bone
      (b) glomus jugulare: at jugular foramen
         √ invasion of middle ear from below
         √ destruction of bony roof of jugular fossa + bony spur separating vein from carotid artery
   3. Facial nerve schwannoma
   4. Ossifying hemangioma
   5. Choristoma = ectopic mature salivary tissue
   6. Endolymphatic sac tumor
   7. Meningioma

D. MALIGNANT TUMOR
   1. Squamous cell carcinoma
   2. Metastasis
   3. Rhabdomyosarcoma
      Location: orbit > nasopharynx > ear
   4. Adenocarcinoma (rare), adenoid cystic carcinoma

Mass on Promontory

[promontory = bone over basal turn of cochlea]

1. Glomus tympanicum
2. Congenital cholesteatoma
3. Aberrant carotid artery
4. Persistent stapedial artery

Inner Ear Masses

A. CONGENITAL
   1. Congenital / primary cholesteatoma

= epidermoid tumor (3rd most common CPA tumor)

B. INFLAMMATION
   1. Cholesterol granuloma
   2. Petrous apex mucocele

C. TUMOR
   1. Glomus jugulare tumor
   2. Hemangioma, fibro-osseous lesion
   3. Metastasis
   4. Facial nerve neurinoma
   5. Large CPA tumors: acoustic neuroma, meningioma (2nd most common CPA tumor)

TEMPORAL BONE

Congenital Malformation of Temporal Bone

- congenital hearing deficit

Developmental malformations affecting the EAC + middle ear may cause conductive hearing loss.

Those affecting the membranous + bony labyrinth may result in sensorineural hearing loss (SN HL).

Cause: (a) nongenetic
(b) genetic
› isolated
› associated with:
(1) **CHARGE syndrome** (= **C**oloboma, **H**eart defect, **A**tresia of nasal choanae, **R**etardation of growth ± development, **G**enital ± urinary abnormalities, **E**ar abnormalities and deafness)
(2) Klippel-Feil syndrome
(3) Trisomy 21
(4) Goldenhar syndrome
(5) Crouzon syndrome

Location: external ear, middle ear, inner ear

1. Congenital atresia of EAC
2. Otic capsule dysplasia
3. Large vestibular aqueduct syndrome

Vascular Abnormalities of Temporal Bone

1. Aberrant internal carotid artery (rare)
2. High-riding jugular bulb
3. Persistence of stapedial artery

Inflammatory Temporal Bone Lesion

The most common inflammatory condition affecting the temporal bone is acute otitis media.

@ External auditory canal
   1. EAC cholesteatoma

2. Keratosis obturans
3. Malignant otitis externa

@ Middle ear
1. Acute otitis media
2. Chronic otitis media
3. Cholesterol granuloma
4. Cholesteatoma

@ Inner ear
1. Labyrinthitis

Tumor of Temporal Bone

A. CEREBELLOPONTINE ANGLE + IAC
1. Vestibular schwannoma (most common)

B. MIDDLE EAR
◊ First exclude a vascular structure!
(a) Vascular structure
1. Persistent stapedial artery
2. Lateral / aberrant carotid artery
3. Dehiscent jugular bulb

(b) benign neoplasm

Paraganglioma (glomus tumor / chemodectoma) is the 2nd most common tumor to involve the temporal bone and most common tumor of the middle ear.

1. Paraganglioma
2. Facial nerve schwannoma
3. Geniculate hemangioma
4. Salivary choristoma
5. Meningioma
6. Middle ear adenoma

(c) malignant neoplasm (rare)
1. Carcinoma
2. Metastasis
3. Perineural spread along facial n.

C. EAC AND MASTOID
(a) malignant neoplasm (common)
1. Squamous cell carcinoma
2. Others: basal cell carcinoma, melanoma, lymphoma, myeloma, metastasis, chondro-, osteosarcoma

(b) benign process
1. Langerhans cell histiocytosis
2. Tuberculosis
3. Wegener granulomatosis
4. Malignant otitis media
5. Radiation necrosis

D. PETROUS APEX

(a) primary neoplasm
1. Chondrosarcoma: most common primary malignancy
2. Endolymphatic sac tumor

Petrous Apex Lesions	
Type	*Imaging Characteristics*
Developmental	
Cholesterol granuloma (most common)	√ hyperintense on T1 + T2WI • long Hx of otitis media
Cholesteatoma (4–9%)	√ restricted diffusion at DWI
Cephalocele (rare)	√ CSF signal intensity
Mucocele (uncommon)	
Inflammatory	
Petrous apicitis, osteomyelitis, inflammatory pseudotumor, Wegener granulomatosis	
Benign tumor	
Meningioma, schwannoma, paraganglioma	
Chondroma, chondroblastoma	√ chondroid matrix calcification
Myxoma, osteoblastoma, giant cell tumor	
Malignant tumor	
Chondrosarcoma	√ chondroid matrix calcification
Chordoma	√ honeycomb enhancement
Endolymphatic sac tumor	√ hemorrhage, bone destruction
Metastasis, plasmacytoma, lymphoma, nasopharyngeal ca., rhabdomyosarcoma, LCH	
Vascular	
Petrous carotid aneurysm	
Intraosseous dural AV fistula	√ multiple intraosseous flow voids
Osseous dysplasia	
Fibrous dysplasia	√ ground-glass matrix calcification
Paget disease	
Pseudolesion	
asymmetric marrow	√ fat signal with all sequences
pseudofracture	√ through superior semicircular canal
effusion	

(b) secondary involvement by regional tumor:
trigeminal schwannoma, jugular paraganglioma, nasopharyngeal carcinoma

Dumbbell Mass Spanning Petrous Apex

1. Large trigeminal schwannoma
2. Meningioma
3. Epidermoid cyst

Enhancing Lesion in Internal Auditory Canal

A. NEOPLASTIC
   1. Acoustic schwannoma
   2. Ossifying hemangioma
   3. Lymphoma
   4. Metastasis

B. NONNEOPLASTIC
   1. Sarcoidosis
   2. Meningitis
   3. Postmeningitic / postcraniotomy fibrosis
   4. Vascular loop of anterior inferior cerebellar artery
   5. Syphilis

Demineralization of Temporal Bone

1. Otosclerosis = otospongiosis
2. **Paget disease** = osteoporosis circumscripta
   • sensorineural / mixed hearing loss (cochlear involvement / stapes fixation in oval window)
   √ usually lytic changes beginning in petrous pyramid + progressing laterally; otic capsule last to be affected
   √ calvarial changes ± basilar impression
3. **Fibrous dysplasia** monostotic with temporal bone involvement
   Cause: inability to form mature lamellar bone owing to disordered osteoblastic activity
   • painless mastoid swelling
   • conductive hearing loss ← narrowing of EAC / middle ear
   √ homogeneously dense thickened structurally weak bone (fibro-osseous tissue less dense than calvarial bone)
   √ bone expansion with preserved cortex → osseous narrowing of vascular channels + neuroforamina
   √ lytic lesions (less frequent)
   √ sparing of membranous labyrinth, facial nerve canal, IAC is the rule
4. Osteogenesis imperfecta
   √ changes similar to otosclerosis
   van der Hoeve-de Kleyn syndrome
   = osteogenesis imperfecta + hearing loss + blue sclerae in patients in late 2nd / early 3rd decade
5. Otosyphilis: labyrinthitis + gummatous lesion of internal auditory canal + inflammatory

resorptive osteitis
√ moth-eaten permeative osteolysis of temporal bone

6. Metastasis

Mastoid Abnormality in Child

1. Acute otitis media
2. Langerhans cell histiocytosis
3. Rhabdomyosarcoma
4. Metastatic disease: most commonly neuroblastoma

SINUSES

Opacification of Maxillary Sinus

A. WITHOUT BONE DESTRUCTION
   1. **Sinus aplasia / hypoplasia**
      Age: NOT routinely visualized at birth, by age 6 antral floor at level of middle turbinate, by age 15 of adult size
      Location: uni- / bilateral
      √ depression of orbital floor with enlargement of orbit
      √ lateral displacement of lateral wall of nasal fossa with large turbinate
   2. Maxillary dentigerous cyst
      usually containing a tooth / crown; without tooth = primordial dentigerous cyst
   3. Ameloblastoma
   4. Acute sinusitis
      √ air-fluid level

B. WITH BONE DESTRUCTION
   1. Maxillary sinus tumor
   2. Infection: aspergillosis, mucormycosis, TB, syphilis
   3. Wegener granulomatosis; lethal midline granuloma
   4. Blowout fracture

Paranasal Sinus Masses

1. Mucocele
   Cause: obstruction of a paranasal sinus
   √ ± bone remodeling / sinus expansion
2. Mucus retention cyst
   Cause: obstruction of small seromucinous gland
   Location: commonly in floor of maxilla
   √ smoothly marginated soft-tissue mass
3. Sinonasal polyp
4. Antrochoanal polyp
5. Inverting papilloma
6. Sinusitis
7. Carcinoma
8. Rhabdomyosarcoma (of adulthood)

Site: ethmoid sinuses
Prognosis: poor (due to frequent intracranial extension)

Sinonasal Granulomatous Disease

√ sinus mucosal thickening
√ osseous + cartilaginous erosion (through cribriform plate)
√ nasal septal perforation
√ intraorbital extension

A. Chronic irritants
   1. Beryllium
   2. Chromate salts
B. Infection
   1. Tuberculosis
   2. Actinomycosis
   3. Rhinoscleroma
   4. Yaws
   5. Blastomycosis
   6. Leprosy
   7. Rhinosporidiosis
   8. Syphilis
   9. Leishmaniasis
   10. Glanders
C. Autoimmune disease
   1. Wegener granulomatosis
   2. Churg-Strauss syndrome
D. Lymphoma-like lesions
   1. Midline granuloma
E. Unclassified
   1. Sarcoidosis

Hyperdense Sinus Secretions

1. Inspissated secretions
2. Mycotic (fungal) sinusitis
3. Hemorrhage into sinus
4. Chronic sinusitis infected with bacteria (in particular in very long-standing disease / cystic fibrosis)

Opacified Sinus & Expansion / Destruction

mnemonic: PLUMP FACIES
Plasmacytoma
Lymphoma
Unknown etiology: Wegener granulomatosis
Mucocele
Polyp
Fibrous dysplasia, **F**ibroma (ossifying)

Aneurysmal bone cyst, **A**ngiofibroma
Cancer
Inverting papilloma
Esthesioneuroblastoma
Sarcoma: ie, rhabdomyosarcoma

Frontal Soft-tissue Swelling

1. Pott puffy tumor
2. Dermoid and epidermoid cyst
3. Cephalocele
4. Cephalhematoma
5. Mucocele
6. Destructive lesion: Langerhans cell histiocytosis, metastasis

NOSE

Nasal Vault Masses

A. BENIGN
   1. Sinonasal polyp
   2. Inverted papilloma
   3. Hemangioma
      • history of epistaxis
   4. Pyogenic granuloma
      √ pedunculated lobular mass
   5. Granuloma gravidarum
      = nasal hemangioma of pregnancy
   6. Hemangiopericytoma
   7. Juvenile nasopharyngeal angiofibroma
      √ arises in superior nasopharynx with extension into nose via posterior choana

B. MALIGNANT
   1. Squamous cell carcinoma (most common primary)
      Predisposed: nickel workers
   2. Adenocarcinoma, mucoepidermoid carcinoma, adenoid cystic carcinoma
   3. Rhabdomyosarcoma: head and neck most frequent site
   4. Lymphoma, chloroma
   5. Melanoma
   6. Metastasis

Mass in Nasopharynx

mnemonic: NASAL PIPE
Nasopharyngeal carcinoma
Angiofibroma (juvenile)
Spine / skull fracture
Adenoids
Lymphoma

Polyp
Infection
Plasmacytoma
Extension of neoplasm (sphenoid / ethmoid sinus ca.)

Congenital Midline Nasal Mass

= result of faulty regression of embryologic dural diverticulum through foramen cecum + fonticulus frontalis (= nasofrontal fontanel) from the prenasal space

Frequency: 1÷20,000 to 1÷40,000 births

1. Teratoma, dermoid, epidermoid
2. Nasal glioma = nasal cerebral heterotopia
3. Sincipital encephalocele
4. Hemangioma / lymphangioma
5. Dacryocystocele
6. Dacryocystitis

Nasal Septal Perforation / Destruction

> Nasal septal perforation due to granulomatous pressure erosions and cartilage destruction is most commonly seen in granulomatosis with polyangiitis (formerly Wegener granulomatosis), sarcoidosis and relapsing polychondritis.

A. AUTOIMMUNE DISEASE
   1. Wegener granulomatosis
   2. Relapsing polychondritis
B. IDIOPATHIC
   1. Sarcoidosis
   2. Reparative giant cell granuloma
C. INFECTION
   1. Syphilis
   2. Leprosy
D. TOXIC EXPOSURE
   1. Cocaine abuse
E. TRAUMA
   1. Rhinotillexomania (= chronic nose picking)
   2. Surgery
F. MALIGNANCY
   1. Lymphoma

ORAL CAVITY

Infections of Oral Cavity

1. Periodontal disease
2. Ludwig angina
3. Descending necrotizing mediastinitis

Cystic Lesion in Floor of Mouth

A. CYSTIC LESION
   1. Ranula
   2. Dermoid / epidermoid
B. INFLAMMATION / INFECTION
   1. Ludwig angina
   2. Dental infection: premolar / 1st molar
   3. Penetrating trauma
   4. Obstructing submandibular calculus
   5. IV drug use
C. SUBMANDIBULAR DUCT OBSTRUCTION
D. VASCULAR MALFORMATION
   1. High-flow AVM
   2. Low-flow hemangioma / venous malformation / lymphangioma
E. NEOPLASM
   (a) benign: lipoma, pleomorphic adenoma of sublingual / minor salivary gland, neural sheath tumors
   (b) malignant: SCC, salivary gland tumor
F. PSEUDOTUMOR: compensatory hypertrophy of sublingual gland, ectopic submandibular salivary gland, ectopic thyroid tissue

Primary Lesion at Root of Tongue

A. CONGENITAL (75%)
   (a) nonvascular
      1. Thyroglossal duct cyst (70%)
      2. Dermoid / epidermoid cyst
      3. Foregut duplication cyst (7%)
      4. Lingual thyroid
      5. Lipoma (0.1–5%)
      6. Capillary hemangioma
   (b) vascular
      1. Lymphatic malformation
      2. Venous malformation
      3. Venolymphatic malformation
      4. Arteriovenous malformation
B. INFECTIOUS (rare)
      1. Abscess
C. NEOPLASTIC
   (a) benign (rare)
      1. Rhabdomyoma
      2. Leiomyoma
      3. Schwannoma
      4. Neurofibroma, plexiform neurofibroma
   (b) malignant (rare)
      ◊ More aggressive than cancers of oral tongue

1. Rhabdomyosarcoma (5% of oral rhabdomyosa.)
2. Alveolar soft part sarcoma

PHARYNX

Pharyngeal Abnormalities

A. NONMALIGNANT
   (a) congenital
      1. Branchial arch anomaly
      2. Laryngeal cleft
      3. Laryngeal cyst
      4. Tracheoesophageal fistula
   (b) acquired
      1. Foreign body ingestion
      2. Perforation
      3. Laryngocele
      4. Zenker diverticulum
      5. Killian-Jamieson diverticulum
   (c) infection / inflammation:
      1. Epiglottitis, pharyngitis
      2. Granulomatous disease: tuberculosis, sarcoidosis
      3. Amyloidosis
      4. Irradiation
B. MALIGNANT
   ◊ Squamous cell carcinoma in 90%!
   @ Oropharynx
   Location: tonsils (75–80%) > tongue base > valleculae > pharyngeal wall cancer
   @ Larynx
   Location: glottic > supraglottic > subglottic cancer
   @ Hypopharynx
   Location: piriform sinus > postcricoid > posterior pharyngeal wall cancer

Parapharyngeal Space Mass

A. BENIGN
   1. Asymmetric pterygoid venous plexus
      √ racemose, enhancing area along medial border of lateral pterygoid muscle
   2. Abscess
      Origin: pharyngitis (most common), dental infection, parotid calculus disease, penetrating trauma
   3. Atypical second branchial cleft cyst
      √ exits pharynx at level of tonsillar fossa
   4. Third branchial arch anomaly
      √ exits pharynx at piriform sinus
   5. Pleomorphic adenoma of ectopic salivary tissue / of deep lobe of parotid gland (common)

6. Schwannoma, neurofibroma
   Origin: usually from cranial nerve X
   √ carotid artery pushed anteriorly
7. Paraganglioma
   √ posterior to carotid artery
   √ extremely vascular (numerous flow voids)
8. Lipoma

B. MALIGNANT
1. Squamous cell carcinoma
   √ direct extension from pharyngeal mucosal space
   √ vertical extension to skull base / hyoid bone
2. Salivary gland malignancy

Pharyngeal Mucosal Space Mass

1. Asymmetric fossa of Rosenmüller
   = lateral pharyngeal recess = asymmetry in amount of lymphoid tissue
2. Tonsillar / peritonsillar abscess
   • sore throat, fever, painful swallowing
3. Postinflammatory retention cyst
   √ 1–2-cm well-circumscribed cystic mass
4. Postinflammatory calcification
   • remote history of severe pharyngitis
   √ multiple clumps of calcification
5. Benign mixed tumor
   • pedunculated mass arising from minor salivary glands
   √ oval / round well-circumscribed mass protruding into airway
6. Squamous cell carcinoma
   √ infiltrating mass with epicenter medial to + invading parapharyngeal space
   √ middle-ear fluid (eustachian tube malfunction)
   √ cervical adenopathy
7. Non-Hodgkin lymphoma
8. Minor salivary gland malignancy
9. Thornwaldt cyst
   ◊ Most common congenital head and neck cyst in a child!

PET in Squamous Cell Carcinoma of Head and Neck

(1) Mucosal primary not identified (in 1–5%): 25–35% sensitive
(2) Staging: detection of contralateral nodal involvement
(3) Restaging (88–100% sensitive, 75–100% specific): more sensitive and specific than CT / MR

Masticator Space Mass

A BENIGN
1. Asymmetric accessory parotid gland
   Frequency: 21% of general population

Location: usually on surface of masseter muscle
√ prominent salivary gland tissue

2. Benign masseteric hypertrophy
   Cause: bruxism (= nocturnal gnashing of teeth)
   √ homogeneous enlargement of one / both masseters
3. Odontogenic abscess / mandibular cysts
   • bad dentition + trismus
4. Lymphangioma, hemangioma

B. MALIGNANT
1. Sarcoma (chondro-, osteo-, soft-tissue sarcoma, especially rhabdomyosarcoma in children)
   √ infiltrating mass with mandibular destruction
2. Malignant schwannoma
   √ tubular mass along cranial nerve V_3
3. Non-Hodgkin lymphoma
4. Infiltrating squamous cell carcinoma
   √ extending from pharyngeal mucosa
5. Salivary gland malignancy: mucoepidermoid carcinoma, adenoid cystic carcinoma
   √ extending from parotid gland

N.B.: (1) check course of V_3 to foramen ovale for skull base extension to Meckel cave area + cavernous sinus

(2) check for extension to pterygopalatine fossa + infraorbital fissure into orbit

Carotid Space Mass

A. VASCULAR LESION
1. Ectatic common / internal carotid artery
2. Carotid artery aneurysm / pseudoaneurysm
3. Asymmetric internal jugular vein
4. Jugular vein thrombosis, Lemierre syndrome

B. BENIGN TUMOR
1. Paraganglioma: carotid body tumor + glomus jugulare + glomus vagale
2. Schwannoma
   √ displacement of carotid artery anteromedially + internal jugular vein posteriorly
   √ well-encapsulated mass
3. Neurofibroma of cranial nerves IX, X, XI
4. Branchial cleft cyst

C. MALIGNANT TUMOR
1. Nodal metastasis from squamous cell carcinoma to interior jugular chain (common)
   √ encasement of carotid artery = inoperable
2. Non-Hodgkin lymphoma

Carotid Artery Aneurysm

= aneurysm of extracranial carotid artery

1. Trauma

2. Infection (mycotic aneurysm)
3. Congenital (very rare): manifestation of connective tissue disorder (Ehlers-Danlos, Marfan, Kawasaki, Maffucci syndrome)

Retropharyngeal Space Mass

A. INFECTION
   Organism: S. aureus, Haemophilus parainfluenzae, b-hemolytic Streptococcus
   1. Reactive lymphadenopathy
      √ nodes > 10 mm in diameter
   2. Suppurative lymphadenitis (common in childhood)
      √ cystic change with peripheral enhancement
   3. Retropharyngeal cellulitis
      √ retropharyngeal edema
   4. Retropharyngeal abscess
B. BENIGN TUMOR
   1. Hemangioma
   2. Lipoma
C. MALIGNANT TUMOR
   1. Metastasis to retropharyngeal nodes
      Source: nasopharyngeal squamous cell carcinoma, melanoma, thyroid carcinoma
      N.B.: **sentinel node of Rouvière** (= lateral retro pharyngeal node) = early sign of nasopharyngeal cancer before primary mass becomes obvious
   2. Non-Hodgkin lymphoma
   3. Direct invasion by squamous cell carcinoma

Prevertebral Space Mass

A. PSEUDOTUMOR
   1. Anterior disk herniation
   2. Vertebral body osteophyte
B. INFLAMMATION
   1. Vertebral body osteomyelitis
   2. Abscess
      √ extension from retropharyngeal space / osteomyelitis / diskitis / epidural abscess
C. TUMOR
   1. Chordoma
   2. Vertebral body metastasis: lung, breast, prostate, non-Hodgkin lymphoma, myeloma
      ◊ Metastases to prevertebral space = inoperable

LARYNX

Vocal Cord Paralysis

◊ Follow anatomic course of laryngeal nerve
A. INTRACRANIAL CAUSES
   √ outward bowing of ipsilateral oropharynx
   √ atrophic thinning of pharyngeal constrictor muscle

√ uvular deviation away from side of causative lesion

1. Birth injury
2. Arnold-Chiari malformation
3. Intracranial tumor
4. Medullary infarct

B. MEDIASTINAL CAUSES

(a) neoplastic: bronchogenic ca., lymphoma, esophageal ca., thyroid ca., neurogenic tumor (paraganglioma, schwannoma), thymic malignancy, nodal metastasis (breast, lung, esophagus), retrosternal goiter

(b) inflammatory: sarcoidosis, silicosis, fibrosing mediastinitis

(c) infectious: TB, histoplasmosis, coccidioidomycosis, bacterial abscess, mycotic aortic aneurysm

(d) infiltrative: amyloidosis

(e) vascular / cardiac: vascular ring, aortic dissection / pseudoaneurysm, left atrial enlargement, CHD, pulmonary artery enlargement, pulmonary embolism

(f) traumatic / surgical procedure: median sternotomy (CABG, valve repair), ligation of PDA, mediastinoscopy, radical esophagectomy, left pneumonectomy / left upper lobectomy, carotid endarterectomy, thyroidectomy, anterior cervical spine fusion, central venous line placement, endotracheal intubation, deceleration injury

C. PARALYTIC PERIPHERAL NEUROPATHY

1. Radioactive iodine ablation treatment
2. External beam radiation effect
3. Chemotherapy (vinca alkaloids)
4. Jugular vein thrombosis

Fluoroscopy

√ fixed vocal cords

CT (true axial):

√ ipsilateral dilatation of piriform sinus

√ ipsilateral dilatation of laryngeal ventricle

√ medial rotation + thickening of aryepiglottic fold

√ anteromedial displacement of ipsilateral arytenoid cartilage + medial displacement of posterior vocal cord margin

√ "sail" sign = medialization of posterior vocal cord margin + air distention of ipsilateral laryngeal ventricle

CT (oblique axial):

√ mushroom-like appearance = "stem" between posterior vocal cords + "head" tilted toward side of paralysis

PET/CT:

√ asymmetric increased uptake in normal cord

Mimics of Vocal Cord Paralysis

1. Tilted patient positioning (oblique imaging)
   √ subglottic air seen anterior to obliquely imaged vocal cord ≠ dilated laryngeal ventricle
2. Invasion of aryepiglottic cartilage by squamous cell carcinoma of larynx / piriform sinus

√ immobilization of vocal cords
√ apparent medialization of cord by thickening from enhancing tumor
√ obliteration of normal fat planes
√ sclerosis of adjacent cartilage
√ regional lymphadenopathy

3. Arytenoid cartilage dislocation / subluxation
   √ poorly defined cricoarytenoid joint
   √ disparity in height of vocal cords (coronal CT)
4. Injection laryngoplasty
   √ "medialization" of paralyzed cord (to improve glottis closure + competence)

Epiglottic Enlargement

A. NORMAL VARIANT
   1. Prominent normal epiglottis
   2. Omega epiglottis
B. INFLAMMATION
   1. Acute / chronic epiglottitis
   2. Angioneurotic edema
   3. Stevens-Johnson syndrome
   4. Caustic ingestion
   5. Radiation therapy
C. MASSES
   1. Epiglottic cyst
   2. Aryepiglottic cyst
   3. Foreign body

Aryepiglottic Cyst

1. Retention cyst
2. Lymphangioma
3. Cystic hygroma
4. Thyroglossal cyst

• may be symptomatic at birth
√ well-defined mass in aryepiglottic fold

Laryngeal Neoplasms

A. SQUAMOUS CELL CARCINOMA (95–98%)
   Location: glottic > supraglottic >> subglottic
   • endoscopically visible due to mucosal involvement
B. NON-SQUAMOUS CELL NEOPLASMS (2–5%)
   malignant÷benign = 1÷1
   (a) vasoformative tumor 33%
      BENIGN
      1. Hemangioma
      2. Lymphangioma
      3. Angiofibroma

4. Angiomatosis
5. Granuloma pyogenicum
6. Arteriovenous fistula
7. Phlebectasia, telangiectasia

MALIGNANT

1. Angiosarcoma (Kaposi sarcoma)
   Location: epiglottis (most frequent)
   √ intensely enhancing mass
2. Hemangiopericytoma

(b) chondrogenic tumor 20%
1. Chondroma
2. Chondrosarcoma
3. Osteosarcoma

(c) hematopoietic tumor 12%
1. Hodgkin / NHL / leukemia
2. Plasmacytoma
3. Pseudolymphoma

(d) salivary gland tumor 10%
1. Pleomorphic adenoma
2. Adenoid cystic carcinoma
3. Mucoepidermoid carcinoma
4. Adenocarcinoma

(e) fatty-tissue tumor 7%
1. Lipoma
2. Liposarcoma

(f) metastasis 7%
skin (melanoma) > kidney > breast > lung > prostate > colon > stomach > ovary

(g) neurogenic tumor 5%

(h) myogenic tumor 2%

(i) fibrohistiocytic tumor 2%

AIRWAYS

Inspiratory Stridor in Children

1. Croup
2. Congenital subglottic stenosis
3. Subglottic hemangioma
4. Airway foreign body
5. Esophageal foreign body
6. Epiglottitis

Airway Obstruction in Childhood

Predisposing anatomy compared to adult:

(1) Narrower nasopharynx

(2) Shorter trachea

(3) Larynx location more anterosuperiorly at level of C3–C4
(4) Cricoid cartilage = narrowest part
(5) Conus elasticus (located 1 cm below glottis): very susceptible to edema
(6) Vocal cords more anteriorly angled
(7) Epiglottis broader and longer
(8) Tongue larger
(9) Intercostal and diaphragmatic muscles weaker

In *acute **upper** airway obstruction* obtain lateral and frontal soft-tissue radiographs of the neck in upright position. If unstable, a single upright soft-tissue lateral radiograph is usually sufficiently diagnostic.

In *acute **lower** airway obstruction* → upright frontal CXR during inspiration with depiction of > 6 anterior ribs at mid-hemidiaphragmatic level + lateral neck radiograph and also expiratory CXR with possible foreign body aspiration.

Nasopharyngeal Narrowing

(a) Congenital:	choanal atresia, choanal stenosis, encephalocele
(b) Inflammatory:	adenoidal enlargement (= pharyngeal tonsils narrow pharynx), polyps
(c) Neoplastic:	juvenile angiofibroma, rhabdomyosarcoma, teratoma, neuroblastoma, lymphoepithelioma
(d) Traumatic:	foreign body, hematoma, rhinolith

Oropharyngeal Narrowing

(a) Congenital:	glossoptosis + micrognathia (Pierre Robin, Goldenhar, Treacher Collins syndrome), macroglossia (cretinism, Beckwith-Wiedemann syndrome)
(b) Inflammatory:	abscess, tonsillar hypertrophy (if tonsils occupy > 50% of oropharynx)
(c) Neoplastic:	lingular tumor / cyst
(d) Traumatic:	hematoma, foreign body

Retropharyngeal Narrowing

= potential space (normally < ¾ of AP diameter of adjacent cervical spine in infants / < 3 mm in older children)

(a) Congenital:	branchial cleft cyst, ectopic thyroid
(b) Inflammatory:	retropharyngeal abscess
(c) Neoplastic:	cystic hygroma (originating in posterior cervical triangle with extension toward midline + into mediastinum), neuroblastoma, neurofibromatosis, hemangioma
(d) Traumatic:	hematoma, foreign body
(e) Metabolic:	hypothyroidism

DDx: "pseudothickening" ← flexed position (exacerbates respiratory distress), young age, during expiration

Vallecular Narrowing

= valleys on each side of glossoepiglottic folds between base of tongue + epiglottis

(a) Congenital: congenital cyst, ectopic thyroid, thyroglossal cyst
(b) Inflammatory: abscess
(c) Neoplastic: teratoma
(d) Traumatic: foreign body, hematoma

Supraglottic Narrowing

= area between epiglottis and true vocal cords

(a) Congenital: aryepiglottic fold cyst
(b) Inflammatory: acute bacterial epiglottitis, angioneurotic edema
(c) Neoplastic: retention cyst, cystic hygroma, neurofibroma
(d) Traumatic: foreign body, hematoma, radiation, caustic ingestion
(e) Idiopathic: laryngomalacia

Glottic Narrowing

= area of true vocal cords

(a) Congenital: laryngeal atresia, laryngeal stenosis, laryngeal web (anterior commissure)
(b) Neoplastic: laryngeal papillomatosis
(c) Neurogenic: vocal cord paralysis (most common)
(d) Traumatic: foreign body, hematoma

Subglottic Narrowing

= short segment between undersurface of true vocal cords and inferior margin of cricoid cartilage = narrowest portion of child's airway

(a) Congenital: congenital subglottic stenosis
(b) Inflammatory: croup, Wegener granulomatosis
(c) Neoplastic: hemangioma, papillomatosis
(d) Traumatic: acquired stenosis ← prolonged endotracheal intubation in 5%
(e) Idiopathic: mucocele = mucous retention cyst (rare complication of prolonged endotracheal intubation)

Most Common Tracheal / Laryngeal Mass in Childhood

(a) endoluminal
    1. Recurrent respiratory papillomatosis
    2. Laryngocele
    3. Subglottic hemangioma
(b) extraluminal (compressing airway)
    1. Bronchogenic cyst
    2. Lymphadenopathy
    3. Neuroblastoma

Epiglottic and Aryepiglottic Fold Thickening

1. Epiglottitis
2. Ingestion of caustic substance / foreign body
3. Angioedema
4. Hemorrhage
5. Epiglottic cyst
6. Postirradiation edema and fibrosis

NECK

Torticollis

= "wry neck" = congenital / acquired deformity characterized by rotational deformity of the cervical spine

Congenital Torticollis

A. MUSCULAR
   1. Congenital muscular torticollis
      (a) fibromatosis colli
      (b) muscular torticollis = muscular tightness
      (c) postural torticollis
   2. Absence of sternocleidomastoid muscle (SCM)

B. SKELETAL
   1. Occipitoatlantal fusion
   2. Klippel-Feil syndrome
   3. Achondroplasia
   4. Osteogenesis imperfecta
   5. Down syndrome

C. CUTANEOUS
   1. Pterygium colli

D. NEUROLOGIC
   1. Syringomyelia
   2. Ocular abnormalities: strabismus, nystagmus

Acquired Torticollis

A. TRAUMATIC
   1. Atlantoaxial rotary fixation
   2. Occipital condyle fracture
   3. Unilateral facet dislocation
   4. Muscle spasm
   5. Spinal hematoma

B. INFECTIOUS / INFLAMMATORY → SCM SPASM
   1. Upper respiratory infection
   2. Otitis media, mastoiditis
   3. Cervical adenitis
   4. Retropharyngeal abscess
   5. Osteomyelitis, diskitis, epidural abscess, meningitis

6. Juvenile idiopathic arthritis

C. NEOPLASTIC

› CNS tumor: posterior fossa, brainstem, spinal cord

› Bone tumor:

1. Eosinophilic granuloma
2. Osteochondroma
3. Osteoid osteoma
4. Metastasis to skull base / spine

(d) miscellaneous (eg, Langerhans cell histiocytosis)

Solid Neck Mass

Soft-tissue Tumors of Head & Neck

= group of mesenchymal tumors with widely varied biologic behaviors [benign (76%), intermediate (13%), malignant (11%)]

Location: head & neck (27%)

Age: in 1st year of life (50%),; during 1st decade (71%)

◊ 12% of soft tissue tumors in children + adolescents

(a) benign

1. Fibromatosis colli
2. Infantile myofibromatosis / myofibroma
3. Nodular fasciitis
4. Giant cell angiofibroma
5. Myositis ossificans

(b) intermediate malignant potential

1. Desmoid-type fibromatosis
2. Solitary fibrous tumor
3. Hemangiopericytoma
4. Inflammatory myofibroblastic tumor

(b) malignant

1. Extraskeletal fibrosarcoma

Features of malignancy:

Malignant soft tissue tumors usually have lower ADC values than benign tumors. ADC value correlates with tumor cellularity in soft tissue sarcomas.

(a) size

√ large volume with > 5 cm in diameter

(b) internal texture

√ intratumoral hemorrhage + necrosis

√ heterogeneous texture

√ high T2 signal intensity

(c) margin

√ poorly defined margin

√ broad interface with underlying fascia

√ extracompartmental extension

(d) vascularity
√ marked primarily peripheral enhancement
(e) interaction with surroundings
√ invasion of bone + neurovascular structures

Demographics of soft-tissue tumors of head & neck:

› Child: Infantile hemangioma, lymphangioma, lipoblastoma, fibromatosis colli, myofibroma, rhabdomyosarcoma
› Adolescent: Hibernoma, desmoid-type fibromatosis, synovial sarcoma, Ewing sarcoma
› Older adult: Liposarcoma, malignant fibrous histiocytoma

Radiation-induced sarcoma of head & neck:,

1. Fibrosarcoma 41.5%
2. Osteosarcoma 22.6%
3. Malignant fibrous histiocytoma 13.2%

A mass at a previously irradiated site and average latency period of 9 (range, 3–26) years raises concern for radiation-induced sarcoma.

Solid Neck Mass in Neonate

1. Cystic hygroma
2. Hemangioma
3. Neuroblastoma
4. Teratoma
5. Fibromatosis colli

Solid Neck Mass in Childhood

1. Lymphadenopathy
2. Fibromatosis colli
3. Aggressive fibromatosis
4. Malignancy: neuroblastoma (most common), lymphoma, embryonal rhabdomyosarcoma
5. Teratoma
6. Hemangioma
7. Cervicothoracic lipoblastomatosis
8. Lipoma
9. Thyroid mass / lingual thyroid
10. Parathyroid adenoma
11. Ectopic thymus

Soft-tissue Tumors of Neck (WHO Classification 2002)				
Histology	*Benign*	*Intermediate locally aggressive*	*Intermediate rarely metastasizing*	*Malignant*
Adipocytic	Lipoma, lipoblastoma, hibernoma, lipomatosis	Atypical lipomatous tumor, well-differentiated liposarcoma	...	Liposarcoma
Fibroblastic / myofibroblastic	Fibromatosis colli, myofibroma, giant cell angiofibroma	Desmoid-type fibromatosis	Solitary fibrous tumor, hemangiopericytoma, inflammatory myofibroblastic tumor (inflammatory pseudotumor)	Fibrosarcoma
So-called fibrohistiocytic	Benign fibrous histiocytoma, diffuse-type giant cell tumor (PVNS)	...	Giant cell tumor of soft tissues	Malignant fibrous histiocytoma (undifferentiated pleomorphic sarcoma)
Skeletal muscle	Rhabdomyoma	...	...	Rhabdomyosarcoma
Smooth muscle	Leiomyoma, angioleiomyoma	...	...	Leiomyosarcoma
Vascular	Hemangioma, lymphangioma	Kaposiform hemangioendothelioma	Kaposi sarcoma	Angiosarcoma
Perivascular	Glomus tumor, myopericytoma	...	...	Malignant glomus tumor
Chondro-osseous	Soft tissue sarcoma	...	...	Mesenchymal chondrosarcoma, extraskeletal osteosarcoma
Uncertain differentiation	Myxoma	...	Ossifying fibromyxoid tumor	Synovial sarcoma, alveolar soft part sarcoma, primitive neuroectodermal tumor, Ewing sarcoma

Pediatric Neck Lesions

@ Superficial
1. Teratoma

@ Visceral
1. Retropharyngeal cellulitis
2. GI duplication cyst
3. Thyroglossal duct cyst
4. Goiter
5. Laryngocele
6. Lymphadenopathy

@ Prevertebral space
1. Descending necrotizing mediastinitis

@ Carotid space
1. Lemierre syndrome

@ Parotid space
1. Acute parotitis
2. HIV parotitis

@ Submandibular space
1. 2nd branchial cyst
2. Thyroglossal duct cyst

@ Masticator space
1. Venous malformation

@ Parapharyngeal space

1. Rhabdomyosarcoma

@ Posterior cervical space

1. Lymphatic malformation

@ Perivertebral space

1. Cervical sporadic Burkitt lymphoma
2. Cervical neuroblastoma
3. Cervical dermal sinus

@ Sternocleidomastoid muscle space

1. Fibromatosis colli

@ Multiple spaces

1. Cervical lymphadenitis

Congenital Cystic Lesions of Neck

It is critical to identify common congenital lesions like branchial cleft + thyroglossal duct cysts, and to recognize their complications (eg, superinfection)

1. Thyroglossal duct cyst
   - vertical movement with protrusion of tongue

   Location: anterior cervical triangle close to midline between foramen cecum + thyroid isthmus
2. Lateral ectopic thyroid tissue

   √ NO thyroid tissue in normal location

   √ thin fibrous band attaching it to an orthotopic gland
3. Lymphangioma / cystic hygroma

   Location: mostly in posterior cervical triangle, occasionally in floor of mouth / tongue

   √ transspatial extent containing locules

   Age: congenital lesion detected by age 2 years
4. Branchial cleft anomalies
   - often noted during upper respiratory infection

   (a) 2nd branchial cleft cyst

   Location: near mandibular angle along anterior surface of sternocleidomastoid muscle, lateral to carotid sheath structures, posterior to submandibular gland
   - painless fluctuating mass often appearing after an upper respiratory infection

   √ round mass displacing sternocleidomastoid muscle posterolaterally

   √ PATHOGNOMONIC beak insinuating itself between ICA + ECA

   (b) branchial cleft fistula

   Location: apex of piriform sinus to thyroid
5. Cervical dermoid / epidermoid cyst

   Location: base of tongue, anterior portion of neck, floor of mouth

   √ fat content / diffusion restriction
6. **Cervical thymic cyst** = persistent thymopharyngeal duct

   Location: mostly on left side of neck
7. **Cervical bronchogenic cyst**

   Cause: anomalous foregut development

Histo: columnar ciliated pseudostratified epithelial lining
M÷F = 3÷1
• draining sinus in suprasternal notch / supraclavicular area
√ cyst up to 6 cm in diameter
√ indentation of trachea

8. **Parathyroid cyst**
   Age: 30–50 years
   • hormonally inactive
   √ noncolloidal cyst near lower pole of thyroid gland
9. Obstructed laryngocele
   Location: lateral aspect of superior paralaryngeal space connecting to larynx ← originating from saccule / appendix of laryngeal ventricle
   √ well-defined smooth mass / saccular cyst
10. Lingual abscess
    = infected lingual thyroglossal duct cyst / dermoid cyst / ranula / secondary to instrumentation or tongue piercing

Midline Neck Mass

1. Thyroglossal duct cyst
2. Epidermoid / dermoid cyst
3. Lymph node
4. Abscess

Pediatric Lesions compared to Neck Compartments	
Space	*Differential Diagnosis*
Superficial fascia	teratoma, vascular malformation, cellulitis, plexiform neurofibroma, keloid, scar, SQ fat fibrosis
Visceral space	all 3: cellulitis, abscess, extension of goiter
Retropharyngeal space	lateral and medial retropharyngeal lymphadenopathy, extension of pharyngeal tumor
Retrovisceral ~	esophageal duplication
Pretracheal ~	thyroglossal cyst, laryngocele, lymphadenopathy, spondylodiskitis
Danger space	cellulitis, abscess
Carotid space	Internal jugular / retromandibular vein thrombosis or phlebitis, lymphadenopathy, paraganglioma
Submandibular / sublingual space	thyroglossal / branchial cyst, venous / lymphatic malformation, dermoid cyst, ranula, sublingual gland disease, lymphadenopathy, facial vein disease
Masticator space	venous / lymphatic malformation, cellulitis, abscess, rhabdomyosarcoma
Parapharyngeal space	cellulitis, abscess, rhabdomyosarcoma, paraganglioma
Perivertebral space	cervical dermal sinus, meningocele, rhabdomyosarcoma, lymphoma extension
Posterior cervical ~	lymphatic malformation, lymphadenopathy

Air-containing Masses of Neck

1. Laryngocele
2. Tracheal diverticulum
   arising from anterior wall of trachea close to thyroid
3. Zenker diverticulum
4. Lateral pharyngeal diverticulum
   located in tonsillar fossa / vallecula / pyriform fossa

Fat-containing Masses of Neck

1. Dermoid cyst
2. Lipoblastoma
3. Liposarcoma
   ◊ 4% of all liposarcomas
   • extremely rare < 10 years of age
   Location: neck (28%), larynx (20%), pharynx (18%)

Lymph node enlargement of neck

◊ Most common neck mass in children!

A. NORMAL LYMPH NODES
- √ few small oval hypoechoic masses
- √ ± central linear echogenicity (= invaginating hilar fat)
- √ larger in transverse than anteroposterior dimension

B. CERVICAL ADENITIS

Location: posterior cervical triangle

1. **Cat scratch disease**

   Organism: Bartonella henselae

   Mode of transfer: cat bite / lick / scratch (bacteria present in cat saliva may be transferred to paws)

   • common cause of enlarged lymph nodes in children
2. Tuberculous lymphadenitis

C. NEOPLASTIC LYMPH NODES
- • firm, nonmobile, painless

Cause: Castleman disease, lymphoma (Hodgkin disease, NHL), leukemia, metastasis
- √ increased anteroposterior diameter
- √ prominent calcifications suggestive of medullary thyroid cancer
- √ axial diameter of > 15 in jugulodigastric region / > 11 mm elsewhere (in squamous cell carcinoma)

US:
- √ loss of hilar echogenicity
- √ peripheral / mixed hypervascularity on Doppler
- √ ± intranodal cystic change

CT:
- √ irregular peripheral (marginal) enhancement
- √ central necrosis (regardless of size)
- √ fuzzy borders as sign of extracapsular extension
- √ ill-defined borders + loss of fat plane between node and adjacent structures (muscle, vasculature, bone) ← extracapsular spread

Low-density Nodes with Peripheral Enhancement

1. Suppurative adenitis
2. Tuberculosis
3. Metastatic malignancy
4. Lymphoma
5. Inflammatory conditions

Lymph Node Metastasis by Location

@ SUPRACLAVICULAR
head & neck, lung, breast, esophagus

@ INTERNAL JUGULAR
supraglottic larynx, esophagus, thyroid

@ MIDJUGULAR
tongue, pharynx, supraglottic larynx

@ JUGULODIGASTRIC

nasopharynx, oropharynx, tonsils, parotid gland, supraglottic larynx

@ SUBMANDIBULAR
skin, submandibular gland, base of tongue

@ POSTERIOR TRIANGLE
nasopharynx, base of tongue

@ LATERAL PHARYNGEAL
nasopharynx, oropharynx

Tonsillar Enlargement

1. Tonsillitis
2. Lymphoid hyperplasia
3. Mononucleosis
4. Tonsillar neoplasm: squamous cell carcinoma, lymphoma)
5. Angioedema
6. Mucositis ← Kawasaki disease

SALIVARY GLANDS

Multiple Small Hypoechoic Areas in Salivary Gland

1. Sialadenitis: chronic / acute
2. Granulomatous disease: sarcoidosis
3. Sjögren syndrome
4. Disseminated lymphoma
5. Metastases: hematogenous (uncommon)
6. Benign lymphoepithelial lesions: HIV

Anechoic Cystic Areas in Salivary Gland at US

A. BENIGN LESION
   1. Pleomorphic adenoma
   2. Basal cell adenoma
   3. Abscess
   4. Benign lymphoepithelial lesions
   5. Warthin tumor

B. MALIGNANT LESION
   1. Mucoepidermoid carcinoma
   2. Acinic cell carcinoma
   3. Necrotic metastatic node

Inflammatory Disease of Salivary Glands

1. Acute inflammation
   Organism: viral (mumps, CMV); bacterial (S. aureus)
   √ hypoechoic enlargement of gland
   √ multiple small oval hypoechoic areas
   √ enlarged lymph nodes with increased blood flow
2. Abscess

3. Chronic sialadenitis
4. Sialolithiasis
5. Sjögren syndrome

Parotid Gland Enlargement

A. LOCALIZED INFLAMMATION / INFECTION
   1. Chronic recurrent sialadenitis
   2. Sialosis
   3. Sarcoidosis
   4. Tuberculosis
   5. Cat-scratch fever
   6. Syphilis
   7. Parotid abscess ← acute bacterial (suppurative) sialadenitis
   8. Reactive adenopathy
   9. Parotitis

B. SYSTEMIC AUTOIMMUNE RELATED DISEASE
   1. Sjögren disease
   2. Mikulicz disease

C. NEOPLASM (incidence in %)
   (a) benign parotid tumor
      1. Pleomorphic / monomorphic adenoma 59%
      2. Cystadenolymphoma (= Warthin tumor) 7%
      3. Benign lymphoepithelial lesions
      4. Lipoma
      5. Facial nerve neurofibroma
      6. Oncocytoma
      7. Parotid hemangioma
      8. Angiolipoma
   (b) primary malignant parotid tumor
      1. Mucoepidermoid carcinoma 8%
      2. Adenoid cystic carcinoma (= cylindroma) 3%
      3. Malignant mixed tumor
      4. Adenocarcinoma
      5. Acinic cell carcinoma 3.5%
      6. Rhabdomyosarcoma
   (c) metastatic parotid tumor
      ◊ Parotid gland undergoes late encapsulation, which leads to incorporation of lymph nodes!
      1. Squamous cell carcinoma 2%
      2. Melanoma of periauricular region
      3. Non-Hodgkin lymphoma
      4. Thyroid carcinoma

D. LYMPHOPROLIFERATIVE DISORDER
   1. Lymphoma / leukemia
   2. Primary non-Hodgkin lymphoma (MALToma)

E. CONGENITAL
   1. First branchial cleft cyst

Bilateral Enlargement of Salivary Glands

1. Viral infection (mumps)
2. Acute phase of Sjögren syndrome
3. Mikulicz disease
4. Sarcoidosis
5. Lymphoma

Salivary Gland Neoplasm

Frequency: 90–95% occur in parotid gland, 5% in submandibular + sublingual glands; only 1% of all pediatric tumors!

◊ Most salivary gland neoplasms are benign (70%–80%) and found in parotid glands (80–90%)!

◊ The smaller the salivary gland the higher the rate of malignancy: parotid (20–25%) < submandibular (40–50%) < sublingual + minor salivary glands in tongue / floor of mouth / retromolar region (50–81%)

◊ Spread to regional lymph nodes is infrequent!

Benign Salivary Gland Neoplasm

1. Pleomorphic adenoma (80%)
2. Warthin tumor (5%–10%)

Others: oncocytoma, basal cell adenoma, hemangioma, lipoma, neurinoma, schwannoma

Malignant Salivary Gland Neoplasm

1. Mucoepidermoid carcinoma
2. Adenoid cystic carcinoma
3. Acinic cell carcinoma
4. Carcinoma ex-pleomorphic adenoma

Others: squamous cell carcinoma, adenocarcinoma

Solitary Lesion of Parotid Gland

1. Pleomorphic adenoma (80%)
2. Warthin tumor
3. Mucoepidermoid carcinoma

Multiple Lesions of Parotid Gland

1. Warthin tumor
2. Metastases to lymph nodes: squamous cell carcinoma of skin, malignant melanoma, non-Hodgkin lymphoma
3. Benign lymphoepithelial lesions (HIV)

THYROID

Congenital Dyshormonogenesis

1. Trapping defect
   = defective cellular uptake of iodine into thyroid, salivary glands, gastric mucosa
   ◊ High doses of inorganic iodine facilitate diffusion into thyroid permitting a normal rate of thyroid hormone synthesis
   ◊ Normal ratio of iodine concentration for gastric juice÷plasma = 20÷1
   √ nearly entire dose of administered radioiodine is excreted within 24 hours
2. Organification defect
   = deficient peroxidase activity, which catalyzes the oxidation of iodide by H_2O_2 to form monoiodotyrosine (MIT) / diiodotyrosine (DIT)
   • ↑ serum TSH; ↓ serum T_4
   • diffuse symmetric thyromegaly
   √ high thyroidal uptake of radioiodine / pertechnetate
   √ rapid ^{131}I turnover
   √ positive perchlorate washout test
   Pendred syndrome = autosomal recessive trait of deficient peroxidase regeneration characterized by hypothyroidism + goiter + nerve deafness
3. Deiodinase (dehalogenase) defect
   = deficient deiodination of MIT / DIT to release iodide, which is reutilized to synthesize thyroid hormone production
   • hypothyroidism; "intrinsic" iodine deficiency goiter
   • identification of MIT + DIT in serum + urine following administration of ^{131}I
   √ high thyroidal ^{131}I uptake
   √ rapid intrathyroidal turnover of ^{131}I
4. Thyroxin-binding globulin (TBG) deficiency
   • abnormal T_4 transport
   • low bound serum T_4 concentration
   • euthyroid
5. End-organ resistance to thyroid hormone
   • high serum T_4
   • euthyroid / hypothyroid; growth retardation
   √ goiter
   √ stippled epiphyses

Thyrotoxicosis

= clinical syndrome of increased systemic metabolism
• elevated free T_4, elevated free T_3, or both

Cause:

(a) increased thyroid function
   1. Graves disease
   2. Marine-Lenhart syndrome
      = nodular Graves = Graves disease coexistent in multinodular goiter
   3. Toxic autonomous nodule
   4. Toxic multinodular goiter

(b) thyroid inflammation

1. Subacute thyroiditis
2. Painless / silent thyroiditis
3. Postpartum thyroiditis

(c) iodine-induced hyperthyroidism

(d) hyperthyroidism of extrathyroidal origin

1. Factitious hyperthyroidism
2. Ectopic thyroid hormone production: metastatic thyroid cancer, toxic struma ovarii
3. Thyrotropin-induced hyperthyroidism (pituitary adenoma)

Hyperthyroidism

= excessive thyroid hormone activity

• tachycardia, weight loss, muscle weakness, anxiety, decreased temperature tolerance

Radioiodine Therapy for Hyperthyroidism

Dose:

(a) empiric: 15–30 mCi

(b) calculation (Y): 80–160 μCi/gram

Calculation:

Dose [mCi] = (gland weight [gram] x Y [μCi/gram]) divided by 24-hour uptake

Hyperthyroidism with High Radioiodine Uptake

(a) stimulation of thyrotropin receptor by specific immunoglobulin

1. Graves disease

(b) autonomous production of thyroid hormone

2. Toxic adenoma
3. Toxic multinodular goiter

(c) thyroid stimulation by endogenous hormones

4. Trophoblastic disease
   = hydatidiform mole / choriocarcinoma / testicular trophoblastic carcinoma
   • stimulation of thyroid by hCG
5. TSH-mediated hyperthyroidism

Hyperthyroidism with Low Radioiodine Uptake

1. Iodine-induced hyperthyroidism = Jod-Basedow

Mechanism of low thyroid uptake:

large serum concentration of exogenous non-radioactive iodine dilutes radioiodine tracer

Sources of iodine:

1. Foods: seaweed, sushi, Japanese cuisine, Portuguese stew
2. Health food supplement: Kelp tablets
3. Radiographic contrast agent: renografin, Gastrografin®
4. Topical antiseptic: povidone iodine, iodoform gauze
5. Medication: amiodarone, Entero-Vioform®, COMBID®, iodine-containing expectorants
6. Iodine solutions: KI, Lugol's solution, saturated solution of potassium iodide

Wolff-Chaikoff effect = continued organification of iodine is inhibited once intrathyroidal iodide stores reach a critical level

Escape from the Wolff-Chaikoff effect = intrathyroidal level of iodide decreases despite persistent high serum iodine levels → iodide organification and thyroid hormone synthesis resume

Duration: weeks – months

Hyperthyroidism with Radioiodine Uptake < 1%

1. Subacute thyroiditis
2. Ectopic hyperthyroidism
   = extrathyroidal source of thyroid hormone
   (a) **Thyrotoxicosis factitia / medicamentosa**
   = factitious surreptitious (stealthy) self-administration of thyroid hormones (eg, hamburger thyroiditis ← bovine thyroid in hamburger meat)
   (b) **Struma ovarii**
   = monodermal ovarian teratoma containing thyroid tissue
   Frequency: up to 3% of all teratomas (malignant teratoma in 24% of cases)
   Peak age: 50 years
   • hyperthyroidism in 5%
   √ multilocular cystic ovarian mass with solid components
   MR:
   √ multiple intracystic areas with low SI on T2WI + intermediate SI on T1WI
   NUC:
   √ higher uptake than thyroid gland
   DDx: thyroid cancer metastatic to the ovary
   Prognosis: > 95% benign; malignant transformation to papillary / follicular thyroid cancer (rare)
   (c) Metastatic functional thyroid cancer (very rare, 25 cases)
   • mild T_3 toxicosis

Hypothyroidism

A. PRIMARY HYPOTHYROIDISM (most common)
   = thyroid's inability to produce sufficient thyroid hormone
   • TSH >10 mU/L + FT_4 below reference range
   1. Agenesis of thyroid
   2. Congenital dyshormonogenesis
   3. Chronic thyroiditis
   4. Previous radioiodine therapy
   5. Ectopic thyroid (1÷4,000)

B. SECONDARY HYPOTHYROIDISM
   = failure of anterior pituitary to release sufficient quantities of TSH
   • low to mildly elevated TSH + low FT_4
   1. Sheehan syndrome
   2. Head trauma
   3. Pituitary tumor (primary / secondary)

4. Aneurysm
5. Surgery

C. TERTIARY / HYPOTHALAMIC HYPOTHYROIDISM
= failure of hypothalamus to produce sufficient amounts of TRH

Prominent Pyramidal Lobe

= distal remnant of thyroid descent tract
1. Normal variant: present in 10%
2. Hyperthyroidism
3. Thyroiditis
4. S/P thyroid surgery

DDx: esophageal activity from salivary excretion (disappears after glass of water)

Thyroid Calcifications

(a) microcalcifications = psammoma bodies
√ punctate hyperechoic foci without acoustic shadowing

(b) large coarse calcifications = tissue necrosis
√ spicules / fragmented plates / granular deposit within fibrous septa with posterior acoustic shadowing
◊ Common in multinodular goiter + medullary cancer
◊ Associated with 75% malignancy rate in solitary nodule

(c) peripheral calcifications
√ alignment along periphery of lesion
◊ Common in multinodular goiter ± malignancy

Psammoma Bodies

= 10–100 μm round crystalline calcific deposits
Frequency: in 29–59% of all primary thyroid cancers
◊ Most specific feature of thyroid malignancy (86–95% specific, 59% sensitive, 84% accurate, 42–94% PPV)
1. Papillary carcinoma 61%
2. Follicular carcinoma 26%
3. Undifferentiated carcinoma 13%
4. Follicular adenoma
5. Hashimoto thyroiditis

Cystic Areas in Thyroid

◊ 15–25% of all thyroid nodules!
◊ Cystic component in 13–26% of all thyroid malignancies!

A. Anechoic fluid + smooth regular wall:
1. Colloid accumulation in goiter
= colloid-filled dilated macrofollicle
2. Simple cyst (extremely uncommon)

B. Solid particles + irregular outline:
1. Hemorrhagic colloid nodule

2. Hemorrhagic adenoma (30%)
3. Necrotic papillary cancer (15%)
4. Liquefaction necrosis in adenoma / goiter
5. Abscess
6. Cystic parathyroid tumor

- bloody fluid = benign / malignant lesion
- clear amber fluid = benign lesion

Aspiration: cystic lesions often yield insufficient number of cells

Thyroid Nodule

Frequency: (increasing with age)

(a) 4–8% by palpation (> 2 cm in 2%, 1–2 cm in 5%, < 1 cm in 1%); M÷F = 1÷4
- 16% have no corresponding nodule on US
- 15% have an additional nonpalpable nodule > 1 cm

(b) 10–41% by thyroid US if clinically normal: multiple in 38%, solitary in 12% (occult small cancers found in 4%)

(c) incidental nodule in 9% by CT and MR

(d) incidental nodule in 2%–3% by PET
BOTH benign + malignant nodules show increased uptake (= 14–40% risk for malignancy) → evaluate further with US + FNAB

(e) 50% by autopsy

A. THYROID ADENOMA (most common)
1. Adenomatous nodule (42–77%)
2. Follicular adenoma (15–40%)
3. Ectopic parathyroid adenoma

B. INFLAMMATION / HEMORRHAGE
1. Thyroiditis: chronic lymphocytic (Hashimoto)
2. Inflammatory lymph node in subacute + chronic thyroiditis
3. Hemorrhage / hematoma: frequently associated with adenomas
4. Abscess

C. MALIGNANCY (5–7% of all thyroid nodules)

◊ Higher risk of malignancy if
- › patient < 15–20 and > 45–60 years of age
- › patient is male
- › Hx of radiation therapy to neck / upper chest
- › family Hx of thyroid cancer / MEN syndrome
- › new nodule in long-standing goiter
- › nodule firm / fixed to adjacent structures
- › growth rapid
- › vocal cord paralyzed
- › regional lymph nodes enlarged

1. Thyroid carcinoma
   (a) papillary carcinoma (70%)
   (b) follicular carcinoma (15%)
   - › Hürthle cell carcinoma

› Poorly differentiated carcinoma

(c) medullary carcinoma (5–10%)

(d) anaplastic / undifferentiated carcinoma (5%)

(e) primary thyroid lymphoma (5%)

2. Nonthyroidal neoplasm
   (a) Metastasis: from breast, lung, kidney, malignant melanoma
   (b) Lymphoma (uncommon):
   (usually) NHL as secondary involvement in generalized lymphoma / primary lymphoma in Hashimoto thyroiditis
3. Hürthle cell carcinoma
   √ very thin hypoechoic halo
4. Carcinoma in situ
   √ echogenic area inside a goiter nodule

Role of Fine-needle Aspiration Biopsy (FNAB):

◊ FNAB as initial test leads to a better selection of patients for surgery than any other test!

◊ Large-needle biopsy has more complications with no increase in diagnostic yield

Diagnostic adequacy:

> 6 follicular cell groups each containing 10–15 cells derived from at least 2 aspirates of the nodule

Diagnostic accuracy (70–97%):

(a) 60–70% benign (with US guidance up to 0.6% false negative rate due to sampling error)

Dx: benign follicular nodule / thyroiditis

Recommendation: clinical follow-up

Risk of malignancy: 0–3%

(b) 10% positive specimens (3–6% false-positive rate often due to Hashimoto thyroiditis)

(c) 10–20% indeterminate (follicular neoplasm, Hürthle cell neoplasm, cellular atypia / findings suggestive but not diagnostic of malignancy)

◊ FNA cannot distinguish between benign and malignant follicular lesions!

Nondiagnostic material: in up to 20%

too few follicular cells, too much blood, cyst fluid only, excessive air drying

Nondiagnostic rate: 9–30% for palpation; 4–17% for US

Technique of Fine-Needle Aspiration Biopsy

Needles: 27-gauge, 18- / 20-gauge core biopsy

Target: solid / central vascular component of nodule

6 passes for each nodule:

› 3 passes with capillary technique without suction

› 3 passes with aspiration technique = continuous 0.5–1-mL suction applied to attached 10-mL syringe

• each pass consists of ~ 50 vigorous controlled excursions of the needle through nodule for a 20-second period

If repeat biopsy inadequate: Use FNAB + core biopsy

Indeterminate result: repeat biopsy after 3 months

Role of Imaging:

◊ Imaging cannot reliably distinguish malignant from benign nodules!

Radionuclide scanning (limited role):

◊ Useful in suppressed TSH / indeterminate cytology

◊ Hyperfunctioning nodule is almost always benign!

US:

◊ Best method to determine volume of nodule

◊ Useful during follow-up to distinguish nodular growth from intranodular hemorrhage

◊ US-guidance recommended for

› nodules that are difficult to palpate

› predominantly cystic nodule

› nondiagnostic cytology from palpation-guided FNAB

› growing nodule with prior benign cytology

◊ US-follow-up recommended to ensure stability

› initially at 12 + 24 months

› subsequently at 3–5-year intervals

Discordant Thyroid Nodule

= nodule "warm" on ^{99m}Tc-pertechnetate scan + "cold" on ^{123}I scan, which indicates ^{99m}Tc trapping but no organification

Cause:

1. Malignancy: follicular / papillary carcinoma
   ◊ < 5% of thyroid carcinomas manifest as discordant nodules
2. Benign lesion: follicular adenoma / adenomatous hyperplasia
   (autonomous nontoxic nodules have accelerated iodine turnover + discharge radioiodine as hormone within 24 hr)

Rx: thyroid fine-needle aspiration biopsy

Hot / Hyperfunctioning Thyroid Nodule

Frequency: 5–8%

1. Adenoma
   (a) Autonomous adenoma = TSH-independent
   • euthyroid (80%), thyrotoxicosis (20%)
   √ partial / total suppression of remainder of gland
   (b) Adenomatous hyperplasia = TSH-dependent ← defective thyroid hormone production
2. Thyroid carcinoma (extremely rare)
   √ discordant uptake

N.B.: (1) Any hot nodule on ^{99m}Tc scan must be imaged with ^{123}I to differentiate between autonomous and cancerous lesion

(2) A hot hyperfunctioning (= low TSH level) nodule is rarely malignant → further evaluation with US / FNAB NOT NECESSARY

Increased Thyroid Uptake of Radiotracer

mnemonic: THRILLEr
Thyroiditis (early Hashimoto)
Hyperthyroidism (diffuse / nodular)
Rebound after withdrawal of antithyroid medication
Iodine starvation
Low serum albumin
Lithium therapy
Enzyme defect

Cold / Hypofunctioning Thyroid Nodule

A. BENIGN TUMOR
   1. Nonfunctioning adenoma
   2. Cyst (11–20%)
   3. Involutional nodule
   4. Parathyroid tumor

B. INFLAMMATORY MASS
   1. Focal thyroiditis
   2. Granuloma
   3. Abscess

C. MALIGNANT TUMOR (10–23%)
   1. Carcinoma
   2. Lymphoma
   3. Metastasis

US features of cold nodule:
√ hypoechoic (71%), isoechoic (22%), hyperechoic (3%)
√ mixed echogenicity (4%)
√ cystic (rarely malignant)

mnemonic: CATCH LAMP
Colloid cyst
Adenoma (most common)
Thyroiditis
Carcinoma
Hematoma
Lymphoma, **L**ymph node
Abscess
Metastasis (kidney, breast)
Parathyroid

Probability of a cold nodule to represent thyroid cancer:
(a) 5–25% for solitary cold nodule
(b) 1–6% for multiple nodules (DDx: multinodular goiter)
(c) 4% for palpable cold nodule in Graves disease
(d) with history of neck irradiation in childhood
   › 31% for solitary nodule (found in 70% of irradiations)
   › 37% for multiple nodules (found in 25% of irradiations)
   › 20% with normal thyroid scan (found in 5%)

◊ Solitary cold nodule by scintigraphy → multinodular by US in 20–25%!

Thyroid Uptake Measurements

Agents: ^{123}I / ^{131}I (easier to use), ^{99m}Tc-pertechnetate (requires calibration)

Method:

» orally administered isotope of iodine is absorbed from upper GI tract
» tracer mixes with intravascular iodine pool
» iodine is cleared by thyroid in competition with kidneys
» uptake parallels thyroidal clearance of plasma inorganic iodide
» all measurements are taken for 3 minutes at 4 and 24 hours (measurements at both 4 and 24 hours prevent missing the occasional rapid-turnover hyperthyroid patient returning to normal by 24 hours)

Radioactive Iodine Uptake (RAIU):

RAIU = Thyroid Counts* / Capsule Counts˘

* = background corrected (thigh) + decay corrected

˘ = decay corrected

Interpretation:

(a) normal: < 25% at 4 hours, < 35% at 24 hours

(b) increased: in Graves disease

(c) decreased: in subacute thyroiditis

N.B.: Uptake values do not diagnose hyperthyroidism, which is done with laboratory values (T_4, T_3, TSH) and clinical history

Decreased / No Thyroid Uptake of Radiotracer

A. BLOCKED TRAPPING FUNCTION
   1. Iodine load (most common)= dilution of tracer within iodine flooded pool
      Source of flooding:
      ◊ Suppression usually lasts for at least 4 weeks!
      ◊ A low-iodine diet for 3–10 days may be prescribed
   2. Exogenous thyroid hormone (replacement therapy) → suppresses TSH release

B. BLOCKED ORGANIFICATION
   1. Antithyroid medication (propylthiouracil [PTU] / methimazole)
   2. Goitrogenic substances

   √ ^{99m}Tc uptake not inhibited

C. DIFFUSE PARENCHYMAL DESTRUCTION
   1. Subacute thyroiditis
   2. Postpartum thyroiditis
   3. Chronic lymphocytic thyroiditis

D. HYPOTHYROIDISM
   1. Congenital hypothyroidism
   2. Surgical / radioiodine ablation
   3. Thyroid ectopia (struma ovarii, intrathoracic goiter)

mnemonic: H MITTE

Hypothyroidism (congenital)

Medications: PTU, perchlorate, Cytomel®, Synthroid®, Lugol solution
Iodine overload (eg, after IVP)
Thyroid ablation (surgery, radioiodine)
Thyroiditis (subacute / chronic)
Ectopic thyroid hormone production

Thyroxin-binding Globulin Dysfunction

A. ELEVATION OF TBG
   1. Pregnancy
   2. Estrogen administration
   3. Genetic trait
B. REDUCTION IN TBG
   1. Androgens
   2. Anabolic steroids
   3. Glucocorticoids
   4. Nephrotic syndrome
   5. Chronic hepatic disease
C. INHIBITION OF T_4 BINDING TO TBG: salicylates

Ultrasound Characterization of Thyroid Nodules

Ultrasound Features of Malignancy

√ microcalcifications = psammoma bodies
√ extension beyond thyroid margin
√ cervical lymph node metastasis (in 19%)
√ taller-than-wide shape in transverse plane
√ marked hypoechogenicity relative to thyroid parenchyma

<u>less specific:</u>

√ irregular / microlobulated / ill-defined margin
√ solid composition
√ increased central vascularity

Ultrasound Features of Benignity

√ nodule surrounded by uniform halo
√ predominantly cystic composition
√ avascularity
√ enlarged thyroid with multiple nodules

Thyroid Nodule with Halo

= hypoechoic rim around a thyroid nodule

Cause: pseudocapsule of fibrous connective tissue + compressed thyroid parenchyma + chronic inflammatory infiltrate

Cancer Risk of Thyroid Nodule by Ultrasound		
US Finding	*Low Risk*	*Increased Risk*
Echogenicity	hyperechoic	hypoechoic
Calcification	coarse + large	microcalcifications
Vascularity	in periphery	central
Internal texture	spongiform	
Margin		irregular ± vascular invasion
Edge definition	well-defined	incomplete halo
Shape	taller than wide	wider than tall
Growth	none	enlarging

(a) complete uniform halo
highly suggestive of benignity (95% specific);
BUT in 10–24% of papillary carcinomas
(b) incomplete / absent halo
in > 50% of all benign nodules

Thyroid Nodule with Ill-defined Border

= > 50% of margin not clearly demarcated with irregular jagged edges (= absence of pseudocapsule)
◊ suggests malignancy (7–97% sensitive)
◊ Unreliable sign unless frank invasion beyond capsule

Shape of Thyroid Nodule

◊ A nodule that is taller than wide suggests malignancy (93% specific)

Vascularity of Thyroid Nodule

√ marked intrinsic hypervascularity = flow in central part of nodule greater than in surrounding parenchyma
◊ in 69–74% of all thyroid malignancies
◊ > 50% hypervascular nodules are benign
√ perinodular flow = vascularity in > 25% of circumference
◊ characteristic of benign nodules
◊ in 22% of all thyroid malignancies
√ avascularity
◊ malignancy unlikely
◊ All malignant papillary carcinomas show some vascularity

Echogenicity of Thyroid Nodule

√ hypoechoic solid nodule less than thyroid parenchyma (87% sensitive + 15–27% specific for carcinoma / lymphoma)
◊ in 55% of benign nodules
√ hypoechogenicity less than infrahyoid / strap muscles (12% sensitive + 94% specific for malignancy)

Cystic Thyroid Nodule

= hemorrhagic / cystic degeneration

Features associated with cancer:

1. > 50% solid tissue component
2. Eccentricity of cystic space
3. Microcalcifications

Growth of Thyroid Nodule

= 2 mm / 10% increase (if > 20 mm) in 2 dimensions

◊ 40% of benign nodules grow at least 15% by volume over 5 years

Size of Thyroid Nodule

Papillary carcinomas < 1 cm are usually nonaggressive

Follicular carcinomas < 2 cm are usually nonaggressive

◊ Papillary microcarcinoma (< 1 cm) are incidentally detected in 10% of surgical specimens for benign disease + in 12% at autopsies

◊ The rate of metastases + invasion is the same for lesions of 8–10 mm as for lesions of 11–15 mm

Likely Benign Thyroid Nodule

1. Entirely cystic nodule
2. Predominantly cystic nodule < 2 cm, its solid part without flow / calcifications
3. Honeycomb / spongiform nodule < 2 cm
4. Pseudonodule of autoimmune thyroiditis
5. Mixed nodule with functioning solid component

ANATOMY AND FUNCTION OF NECK ORGANS

PARANASAL SINUSES

Mucus production of 1 L/d (Liter/day); mucus blanket turns over every 20–30 minutes; irritants are propelled toward nasopharynx at a rate of 1 cm/minute

Maxillary Sinus

Size: 6–8 cm at birth

Walls: roof = floor of orbit; posterior wall abuts pterygopalatine fossa

Extension: 4–5 mm below level of nasal cavity by age 12

Ostium: maxillary ostium + infundibulum enter middle meatus within posterior aspect of hiatus semilunaris; additional ostia may be present

Plain film: present at birth; visible at 4–5 months; completely developed by 15 years of age

Variations: sinus hypoplasia in 9%; aplasia in 0.4%

Ethmoid Sinuses

Size: adult size by age 12; 3–18 air cells per side

Walls: roof = floor of anterior cranial fossa; lateral wall = lamina papyracea

Plain film: very small at birth; visible at 1 year of age; completely developed by puberty

(a) anteromedial ethmoid air cells

2–8 cells with a total area of 24 x 23 x 11 mm

Ostia: opening into anterior aspect of hiatus semilunaris of middle meatus (anterior group), opening into ethmoid bulla (middle group)

Agger nasi cell

[*agger*, Latin = mound, heap]

= anteriormost ethmoid air cell in front of the attachment of middle turbinate to cribriform plate near the lacrimal duct = intranasal portion of frontal process of maxilla

Frequency: 78–99%

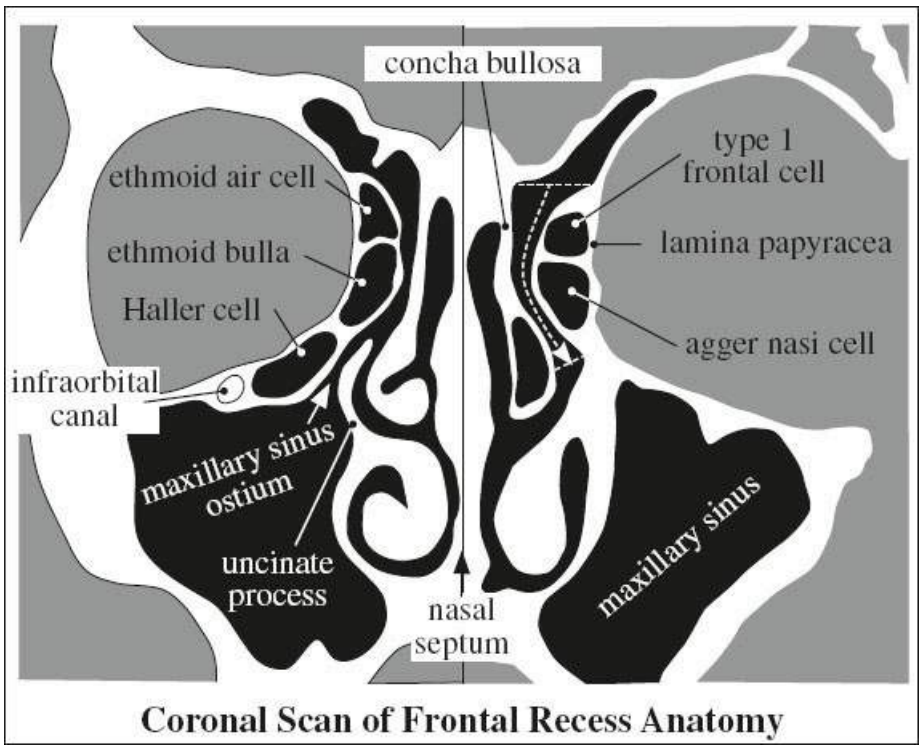
Location: anterior, lateral + inferior to frontoethmoidal recess = on lateral nasal wall at leading edge of middle turbinate

Prevalence: present in > 90%

Ethmoidal bulla

= ethmoidal air cell above + posterior to infundibulum + hiatus semilunaris, located outside the lamina papyracea at the lateral wall of the middle meatus

Haller cells



Coronal Scan of Frontal Recess Anatomy

= INFRAORBITAL ETHMOIDAL AIR CELL = MAXILLOETHMOIDAL / ORBITOMAXILLARY CELL
= anterior ethmoid air cells inferolateral to ethmoidal bulla, on lateral wall of infundibulum, along inferior margin of orbit / roof of maxillary sinus, protruding into maxillary sinus

Prevalence: 2–10–45%

Significance: may narrow ipsilateral ostiomeatal complex if large → obstruction of ipsilateral maxillary antrum

(b) posterior ethmoid air cells

1–8 cells, larger cells, total area smaller than that of anteromedial group

Location: behind the basal (= ground) lamella of the middle turbinate

Ostium: into superior meatus / supreme meatus, ultimately draining into sphenoethmoidal recess of nasal cavity

Onodi cell

= most posterior ethmoid air cell pneumatized into sphenoid bone ± surrounding the optic canal

Location: superolateral to sphenoid sinus

Frontal Sinus

Size: 28 x 24 x 20 mm in adults, rapid growth until late teens

Walls: posterior wall = anterior cranial fossa; inferior wall = anterior portion of roof of orbit

Ostium: into frontal recess of middle meatus via frontoethmoidal recess (= nasofrontal duct)

Outflow tract: frontal infundibulum + frontal ostium + frontal recess

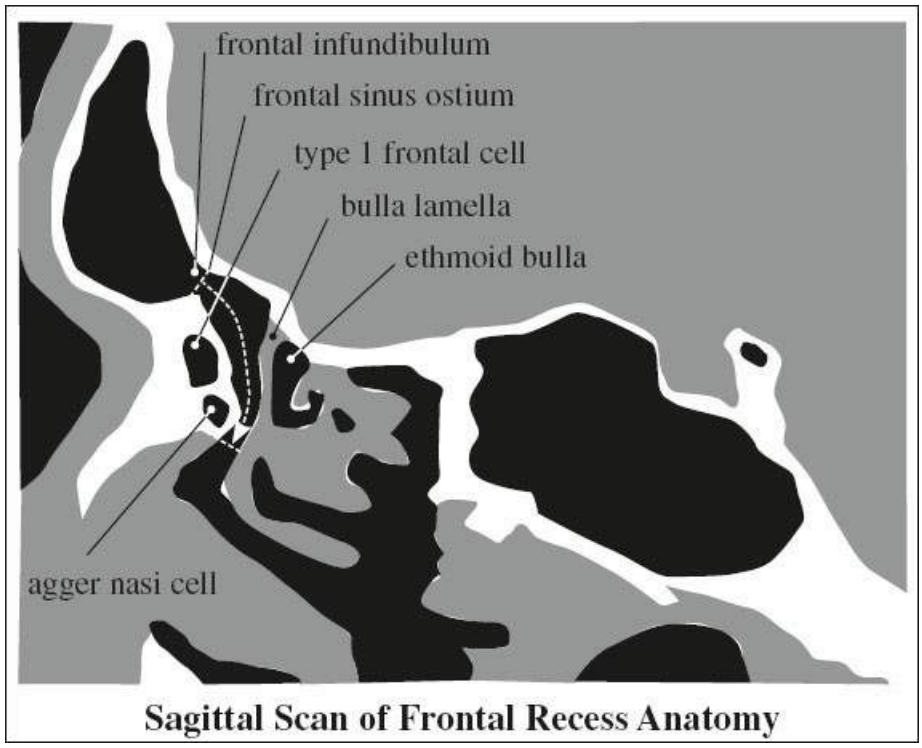
Plain film: visible at age 6 years
Variations: sinus aplasia in up to 4% (in 90% with Down syndrome)

Frontal Recess = Frontoethmoidal Recess

Walls: agger nasi cell anteriorly; lamina papyracea laterally; middle turbinate medially; ethmoid cell with bulla lamella posteriorly

Frontal Recess Cells *(20–33%)*

= pneumatization of frontal recess by various anterior ethmoid cells
Relevance: obstruction of frontal sinus outflow



Sagittal Scan of Frontal Recess Anatomy

(a) anterior group
- › Type 1 frontal cell (in up to 37%)
  = single anterior ethmoid cell within frontal recess above agger nasi cell
- › Type 2 frontal cell (in up to 19%)
  = tier of > 2 anterior ethmoid cells above agger nasi cell
- › Type 3 frontal cell (in up to 7%)
  = single massive cell above agger nasi pneumatizing into frontal sinus
- › Type 4 frontal cell (2%)
  = isolated air cell along anterior wall of frontal sinus not abutting the agger nasi cell

(b) posterior group
1. Supraorbital ethmoid cell (in up to 15%)
   = pneumatized orbital plate of frontal bone posterior to frontal recess mimicking septated frontal sinus = anterior ethmoid air cell extending from frontal recess superiorly + laterally over orbit

2. Frontal bullar cell
   = pneumatized anterior skull base atop ethmoid bulla with extension into frontal sinus as part of posterior boundary of frontal recess + sinus
3. Suprabullar cell
   = atop ethmoid bulla but below level of frontal sinus ostium without extension into frontal sinus as part of posterior boundary of frontal recess
4. Interfrontal sinus septal cell
   = pneumatized interfrontal sinus septum; may extend into crista galli

Sphenoid Sinus

Size: 20 x 23 x 17 mm in adults, small evagination of sphenoethmoidal recess at birth, invasion of sphenoid bone begins at age 5 years; aerated extensions into pterygoid plates (44%) + into clinoid processes (13%)

Walls: roof = floor of sella turcica; anterior wall shared with ethmoid sinuses; posterior wall = clivus; inferior wall = roof of nasopharynx

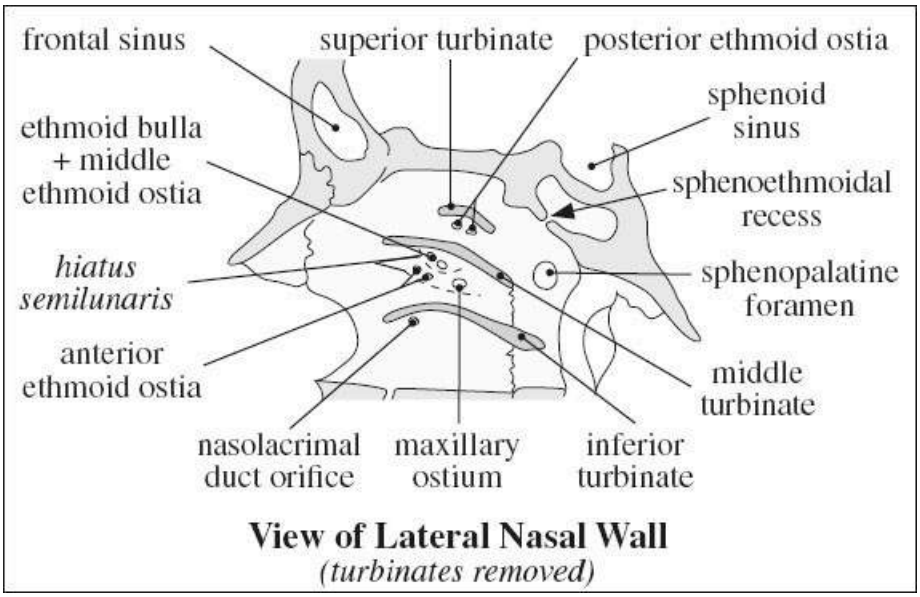
Ostium: 10 mm above sinus floor into sphenoethmoidal recess posterior to superior meatus at level of sphenopalatine foramen

Plain film: appears by 3 years of age; continues to grow posteriorly + inferiorly into the sella until adulthood

OSTIOMEATAL UNIT

= area of superomedial maxillary sinus + middle meatus as the common mucociliary drainage pathway of frontal maxillary, and anterior + middle ethmoid air cells into the nose

Coronal CT: visualized on two or three 3-mm–thick sections



View of Lateral Nasal Wall
(turbinates removed)

Components:

Infundibulum

= flattened conelike passage between inferomedial border of orbit / ethmoid bulla (laterally) + uncinate process (medially) + maxillary sinus (inferiorly) + hiatus

semilunaris (superiorly)

Uncinate process

= key bony structure in lateral nasal wall below hiatus semilunaris in middle meatus defines hiatus semilunaris together with adjacent ethmoid bulla

Attachment: skull base / middle turbinate / lamina papyracea / agger nasi

√ pneumatized in < 2.5% of patients

Ethmoid bulla

√ located in cephalad recess of middle meatus

Hiatus semilunaris

= final segment for drainage of maxillary sinus; located just inferior to ethmoid bulla in middle meatus

Ostia:

(1) Multiple ostia from anterior ethmoid air cells (at its anterior aspect)

(2) Maxillary ostium infundibulum (at its posterior aspect)

Anatomic variations predisposing to ostiomeatal narrowing:

1. **Concha bullosa** (4–15%) = aerated / pneumatized middle turbinate
2. **Intralamellar cell** = air cell within vertical portion of middle turbinate
3. Oversized ethmoid bulla
4. Haller cell
5. Uncinate process bulla
6. Bowed nasal septum
7. **Paradoxical middle turbinate** = convexity of turbinate directed toward lateral nasal wall (10–26%)
8. Deviation of uncinate process

◊ These conditions are not disease states per se!

FACIAL BUTTRESSES

= areas of relatively increased bone density that support functional units of the face (muscles, eyes, dental occlusion, airways)

› sufficient bone thickness to accommodate metal screw fixation

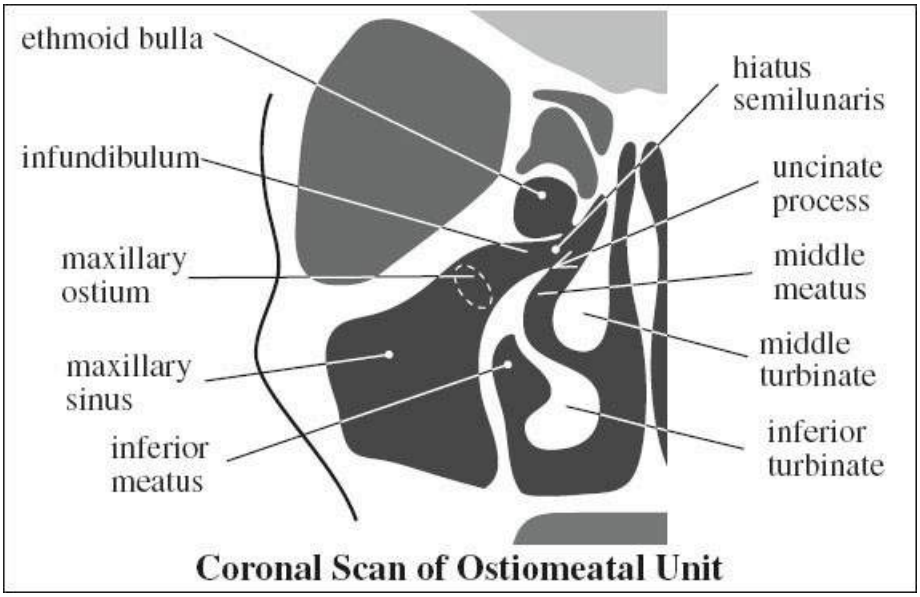
› linked directly / through another buttress to cranium / skull base

(a) horizontal buttresses

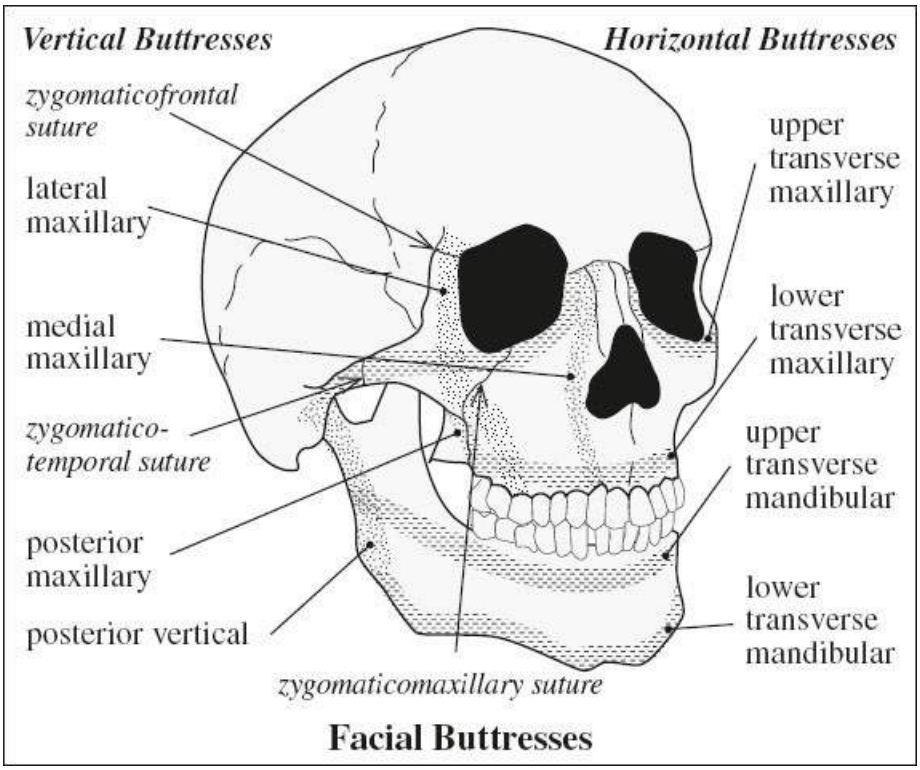
• responsible for facial height

(1) Upper transverse maxillary buttress: temporal squamosa → zygomatic arch → inferior orbital rim → nasofrontal junction

Posterior extension: orbital floor



Coronal Scan of Ostiomeatal Unit



Facial Buttresses

(2) Lower transverse maxillary buttress: maxilla above alveolar ridge
Posterior extension: hard palate
(3) Upper transverse mandibular
(4) Lower transverse mandibular

(b) vertical buttresses
- responsible for facial profile and width

(1) Medial maxillary buttress: anterior nasal spine → rim of piriform aperture → frontal process of maxilla → nasofrontal junction → frontal bone

Posterior projection: medial orbital wall
Anterior projection: lateral nasal wall

(2) Lateral maxillary buttress: above posterior maxillary molar → zygomaticomaxillary suture → body of zygoma → lateral orbital rim → zygomaticofrontal suture → frontal bone
Posterior projection: lateral orbital wall, lateral wall of maxillary sinus

(3) Posterior maxillary buttress: pterygomaxillary junction

(4) Posterior vertical buttress

BRANCHIAL CLEFT DEVELOPMENT

Branchial apparatus: branchial arches, pharyngeal pouches, branchial grooves, branchial membranes

› 6 paired branchial arches are responsible for formation of lower face + neck; recognizable by 4th week GA
› each branchial arch contains a central core of cartilage + muscle, a blood vessel, and a nerve
› 5 ectodermal "clefts" / grooves on outer aspect of neck + 5 endodermal pharyngeal pouches separate the 6 arches with a closing membrane located at the interface between pouches and clefts

Formation: during 4th–6th week of embryonic development

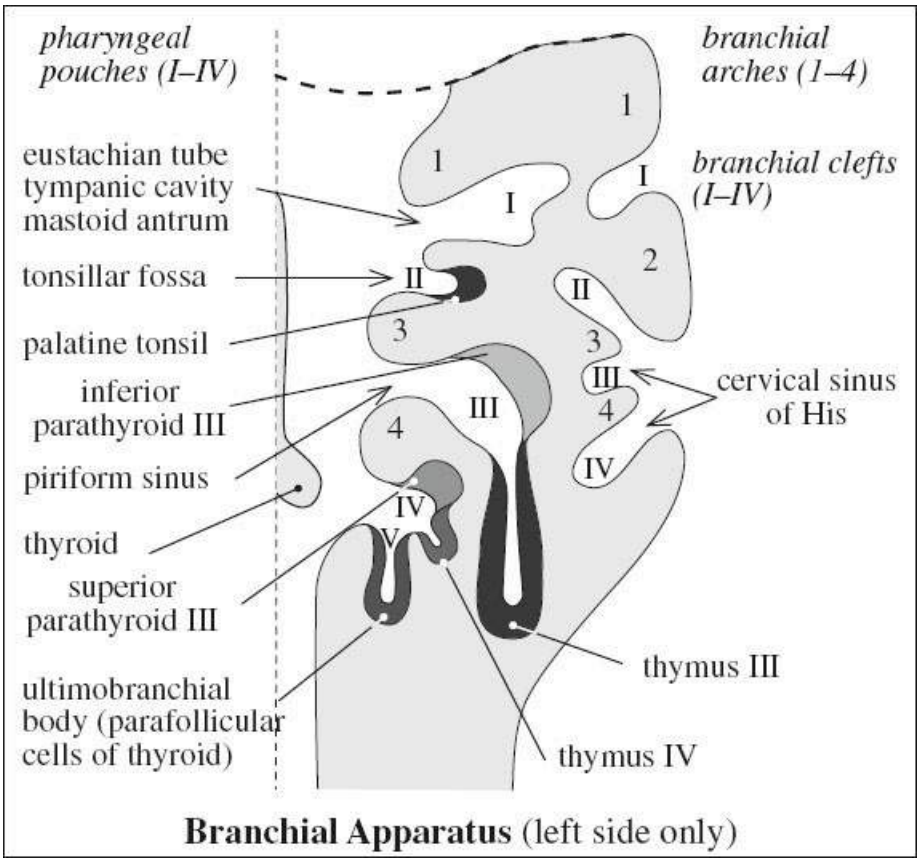
1st Branchial Arch = maxillomandibular arch

(a) large ventral / mandibular prominence
forms: mandible, incus, malleus, muscles of mastication

(b) small dorsal / maxillary prominence
forms: maxilla, zygoma, squamous portion of temporal bone, cheek, portions of external ear
nerve: mandibular division of trigeminal nerve (CN V_3)
pouch forms: mastoid air cells + eustachian tube
cleft forms: external auditory canal + tympanic cavity

2nd Branchial Arch = hyoid arch

nerve: facial nerve (CN VII)



Branchial Apparatus (left side only)

arch forms: thyroid gland, stapes, portions of external ear, muscles of facial expression
pouch forms: palatine tonsil + tonsillar fossa
→ cleft involutes completely by 9th fetal week; 2nd arch overgrows 2nd + 3rd + 4th clefts to form cervical sinus, which creates a tract that runs from the supraclavicular area just lateral to carotid sheath, turns medially at mandibular angle between external + internal carotid artery, and terminates in tonsillar fossa

3rd Branchial Arch

sinks into retrohyoid depression
nerve: glossopharyngeal nerve (CN IX)
arch forms: glossoepiglottic fold, superior constrictor m., internal carotid a., parts of hyoid bone
pouch forms:
(a) thymus gland, which descends into mediastinum by 9th fetal week
(b) inferior parathyroid glands passing down with the thymus

4th Branchial Arch

sinks into retrohyoid depression
nerve: superior laryngeal branch of vagus nerve (CN X)
arch forms: epiglottis + aryepiglottic folds, thyroid cartilage, cricothyroid m., left component of aortic arch, right component of right proximal subclavian a.
pouch superior parathyroid glands, apex of piriform fossa

forms:

cleft ultimobranchial body, which provides parafollicular ("C") cells of thyroid *forms:*

5th + 6th Branchial Arches

cannot be recognized externally

nerve: recurrent laryngeal branch of vagus nerve (CN X)

TONGUE

= complex of muscle groups + fibrous scaffolding

A. FIBROUS SCAFFOLDING

1. Hyoglossal membrane
   anchors inferior posterior edge of tongue to hyoid bone
2. Midline lingual septum
   inserts into hyoglossal membrane + extends superiorly along midline of tongue dividing tongue into halves + providing attachments for transverse intrinsic muscles

B. INTRINSIC MUSCLES (named for their orientation):

Function: wide range of motion for mobile tongue

› vertical + transverse

› inferior + superior longitudinal

C. EXTRINSIC MUSCLES

Function: raising + lowering of tongue, forward + backward motion

1. Genioglossus m.
   Origin: symphysis menti on back of mandible
   Insertion: dorsum of tongue (interdigitating with intrinsic tongue muscles); hyoid bone (few inferolateral fibers)
2. Geniohyoid m.
   Origin: symphysis menti on back of mandible
   Insertion: hyoid bone
3. Hyoglossus m.
   Origin: hyoid bone
   Insertion: lateral aspect of tongue
4. Styloglossus m.
5. Palatoglossus m.

Anatomic subdivision:

(A) Mobile tongue (part of oral cavity)
= frenulum to circumvallate papillae

› "**Root of tongue**"
= region deep to mobile tongue + anterior to base of tongue

Parts: (1) Lingual septum
(2) Genioglossus-geniohyoid complex
= both genioglossus m. + geniohyoid m.

Borders:
(a) anterior: mandible

(b) lateral: sublingual space
(c) inferior: U-shaped mylohyoid m. underneath geniohyoid m.
(c) superior: indistinct ← genioglossus m. fans out and blends with intrinsic tongue muscles

(B) **Base of tongue** (part of oropharynx)
= posterior to circumvallate papillae

ORAL CAVITY

= most ventral portion of aerodigestive tract

Borders:

(a) inferior: circumvallate papillae
(b) superior: soft palate
(c) lateral: anterior tonsillar pillars

Anatomic subdivisions:

lips; floor of mouth; oral tongue (= anterior ⅔ of tongue); buccal mucosa; upper + lower gingiva; hard palate;
retromolar trigone

Sites of squamous cell carcinoma: lower lip > oral tongue > floor of mouth (in 75%)

Floor of Mouth

= horizontally aligned U-shaped space situated in the part of the oral cavity that lies beneath the tongue between mucosal surface and mylohyoid muscle sling

Anatomic components:

1. Squamous epithelium of mucosal surface
2. Mylohyoid muscle sling (paired)
   [*mylai*, Greek = molar (mill) teeth]
   separates floor of mouth from R + L submandibular spaces and midline submental space
   Origin: inner surface of mandible from symphysis menti to last molar posteriorly
   Insertion: fibrous median raphe (medially), posterior aspect of hyoid bone (midline); free edge (posterolaterally) allowing communication between sublingual + submandibular space
   • palpable lump ← herniated sublingual salivary gland mylohyoid defect into adjacent submandibular space
   √ boutonniere = defect in mylohyoid m. (77% of CTs)
3. **Sublingual space**
   = located on both sides of tongue, superomedial to mylohyoid m. and lateral to midline geniohyoid-genioglossus muscle complex
   Content:
   › lingual artery (medial to hyoglossus m.)
   › lingual vein + main submandibular duct (lateral to hyoglossus m.) coursing between hyoglossus + mylohyoid mm.
   √ higher T1 + T2 signal ← higher fat + connective tissue content
4. Submandibular space
5. Submental space

Content: salivary glands (see below); nerves (lingual n. = branch of mandibular division of trigeminal nerve with input from chorda tympani branch of facial n.), distal portions of hypoglossal n. and glossopharyngeal n.

Salivary Glands at Floor of Mouth

1. Sublingual glands
   Excretion via:
   (a) **Rivinus ducts** = numerous small ducts that open at mucosa of floor of mouth
   (b) **Bartholin duct** = formation of a common duct from joining of several of more anterior ducts typically emptying into main submandibular duct
2. Deep portion of submandibular glands
   Excretion via: **Wharton duct** = main submandibular duct coursing anteriorly through sublingual space from deep aspect of submandibular gland
   Orifice: sublingual papilla on ipsilateral side of frenulum, anterior to sublingual gland
3. Subepithelial minor salivary glands

PHARYNX

Barium Pharyngography:

Patient maneuvers:

(a) modified Valsalva maneuver = patient puffs out cheeks as if blowing a trumpet
(b) phonation = patient phonating letter E → widening of oropharynx + deepening of valleculae with forward movement of tongue

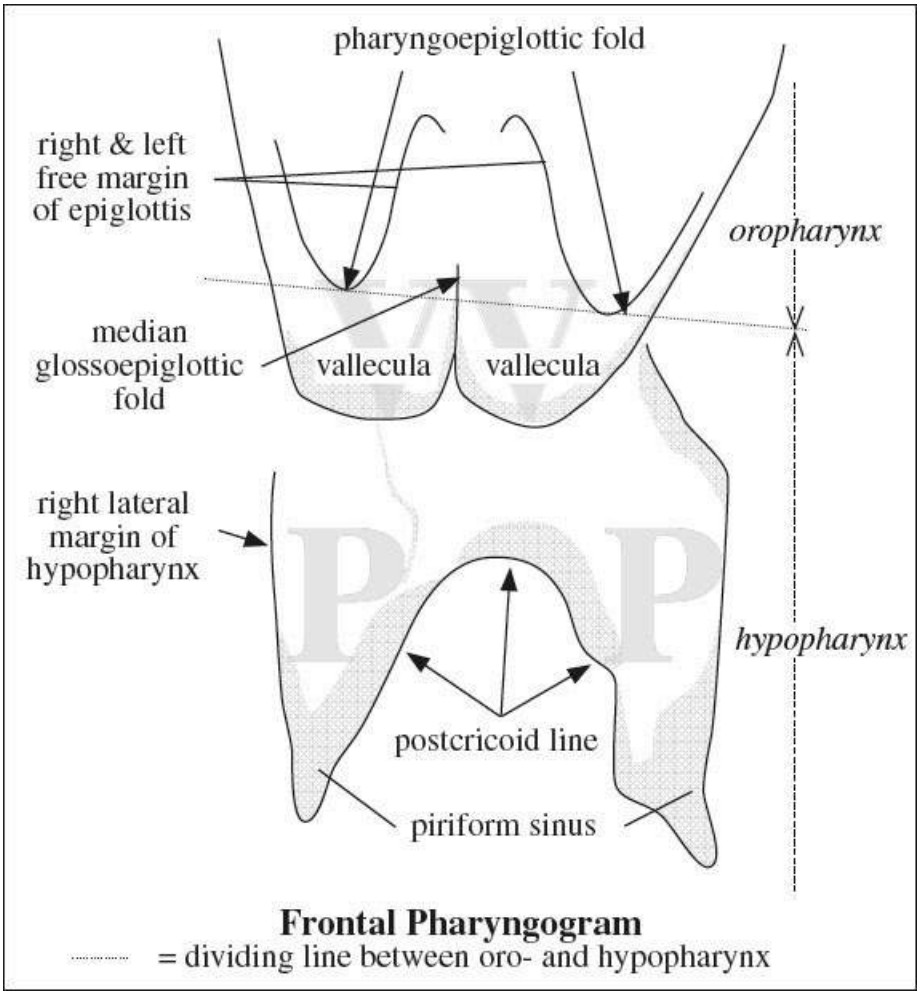
Technique: videofluoroscopic recording

› patient standing in upright position
› initial swallow with high-density barium assessing for aspiration, leak, stricture, obstruction, delayed emptying on lateral view
› second swallow to coat oro- and hypopharynx in LAT + AP projection during maneuvers
› solid-column evaluation for inferior hypopharynx

The pharynx is divided into oropharynx and hypopharynx by the pharyngoepiglottic fold, which is not seen at barium pharyngography. Instead the base of the free margin of the epiglottis / hyoid bone are used as a proxy landmark.

Normal variants:

1. Lateral protrusion of superior ⅓ of lateral hypopharyngeal wall



Cause: weakening of thyrohyoid membrane in elderly / glassblower / trumpet player

√ symmetric bilateral outward bulge of superior aspect of lateral wall of piriform sinus, more pronounced during modified Valsalva maneuver

2. Mild asymmetry of vallecular pouches due to lymphoid tissue

Structural abnormalities of the pharynx are diagnosed by a change in the normal coated surfaces / an alteration in density.

Oropharynx

consists of

(a) oropharyngeal mucosa (pharyngeal wall between nasopharynx + pharyngoepiglottic fold)
(b) soft palate
(c) palatine tonsils
(d) base of tongue (= posterior ⅓ of tongue)

Borders:

(a) superior: soft palate and **Passavant ridge** (= ridge of pharyngeal muscle that opposes the soft palate when soft palate is elevated)
[Philippas G. Passavant, German surgeon, 1815–1893]

(b) anterior: plane formed by the posterior border of soft palate, anterior tonsillar pillars, circumvallate papillae
(c) posterior: posterior pharyngeal wall
(d) inferior: valleculae
[*valles*, Latin = valley → *vallecula* = little valley]
(e) lateral: tonsillar region consisting of anterior tonsillar pillar (= palatoglossus m.) + palatine / faucial tonsil + posterior tonsillar pillar (= palatopharyngeus muscle)

Anatomic subdivisions: base of tongue; tonsils

Tonsillar complex: tonsillar fossa + tonsillar pillars

Barium Pharyngography:

√ valleculae = paired symmetric structures divided by median glossoepiglottic fold posteroinferior to tongue base
√ free margin of epiglottis projects posterior + superior to valleculae
√ cornua of hyoid project on end with change in position during swallowing
√ slightly nodular surface of base of tongue superior to valleculae
√ aryepiglottic fold covers posterior surface of arytenoid cartilage

Hypopharynx

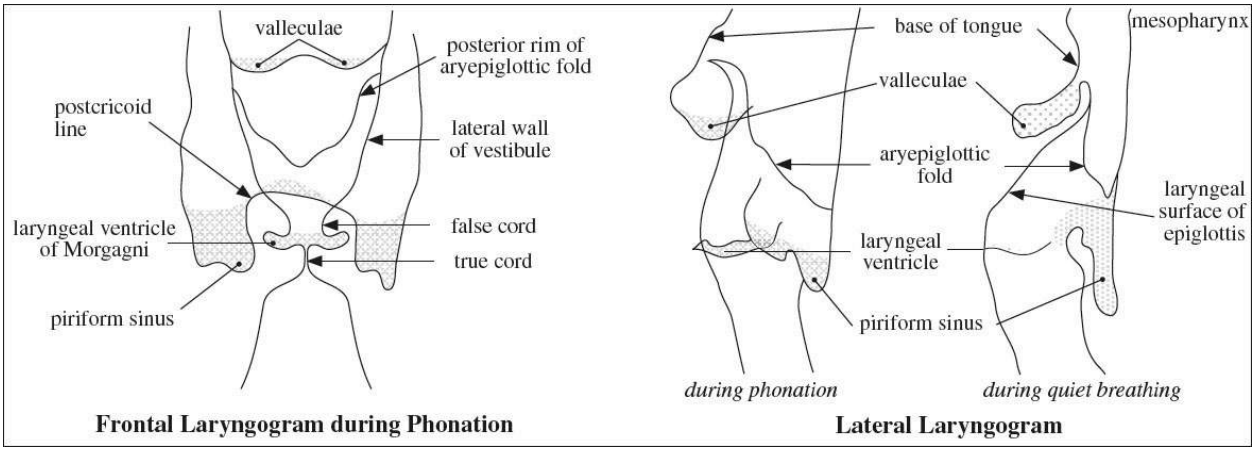
= LARYNGOPHARYNX
= compartment of aerodigestive tract posterior to supraglottic larynx bridging oropharynx above + esophagus below

Origin: derived from 4th branchial arch (= buccopharyngeal bud) → rich lymphatic drainage directed cranially to upper deep jugular chain (levels II + III)

Superior boundary: valleculae at level of hyoid bone

Inferior boundary: lower edge of cricopharyngeus m. = lower edge of cricoid cartilage

1. Piriform sinus [*pirum*, Latin = pear; *forma*, Latin = shape → pear-shaped]
= two symmetric lateral stalactites of air hanging from hypopharynx behind larynx
› inferior wall: level of cricoarytenoid joint
› anteromedial wall: lateral wall of aryepiglottic fold
› lateral wall: abuts posterior ala of thyroid cartilage
› posterior wall: most lateral aspect of posterior hypopharyngeal wall
2. Postcricoid area = pharyngoesophageal junction extends from level of arytenoid cartilages to inferior border of cricoid cartilage
› anterior wall of hypopharynx = posterior wall of lower larynx = "party wall"



3. Posterior hypopharyngeal wall extends from level of valleculae to cricoarytenoid joints

Barium Pharyngography:

√ lateral walls of piriform sinuses = lateral margins of hypopharynx

√ "postcricoid line" = coated mucosal surface ← larynx pressing on anterior wall of hypopharynx

√ barium coating of inner anterior surface of laryngeal vestibule ± laryngeal ventricle ← laryngeal penetration + aspiration

LARYNX

Vertical length: 44 mm (males), 36 mm (females), at 4th–6th cervical vertebrae (from tip of epiglottis to lower end of cricoid cartilage)

Function: (1) Protection against aspiration

(2) Phonation

Lymphatic drainage:

(a) supraglottis: rich drainage directed cranially to upper deep jugular chain (levels II + III)

(b) glottis + subglottis: sparse drainage directed inferiorly to lower deep jugular + paratracheal nodes (levels IV + VI)

Supraglottis

extends from tip of epiglottis to laryngeal ventricle

derived from 4th branchial arch (= buccopharyngeal bud)

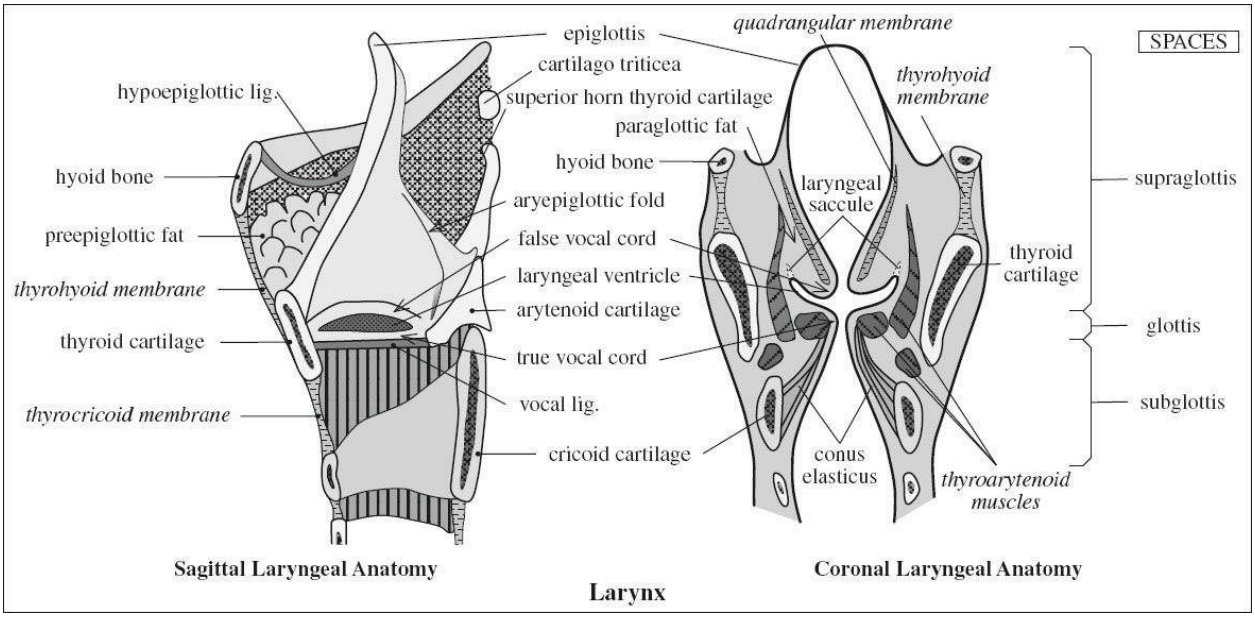
1. Vestibule = airspace within supraglottic larynx
2. **Epiglottis**
   = leaf-shaped cartilage that functions as a lid to endolarynx
   (a) petiole = stem of epiglottis
   (b) thyroepiglottic ligament = connects petiole to thyroid cartilage inferiorly
   (c) hyoepiglottic ligament = connects epiglottis to hyoid bone anteriorly, covered by a mucosal fold between the valleculae (glossoepiglottic fold)
   (d) "free margin" = superior portion of epiglottis
3. **False vocal cords**
   = ventricular folds = inferior continuation of aryepiglottic folds = mucosal surface of ventricular ligaments; forming superior border of laryngeal ventricle

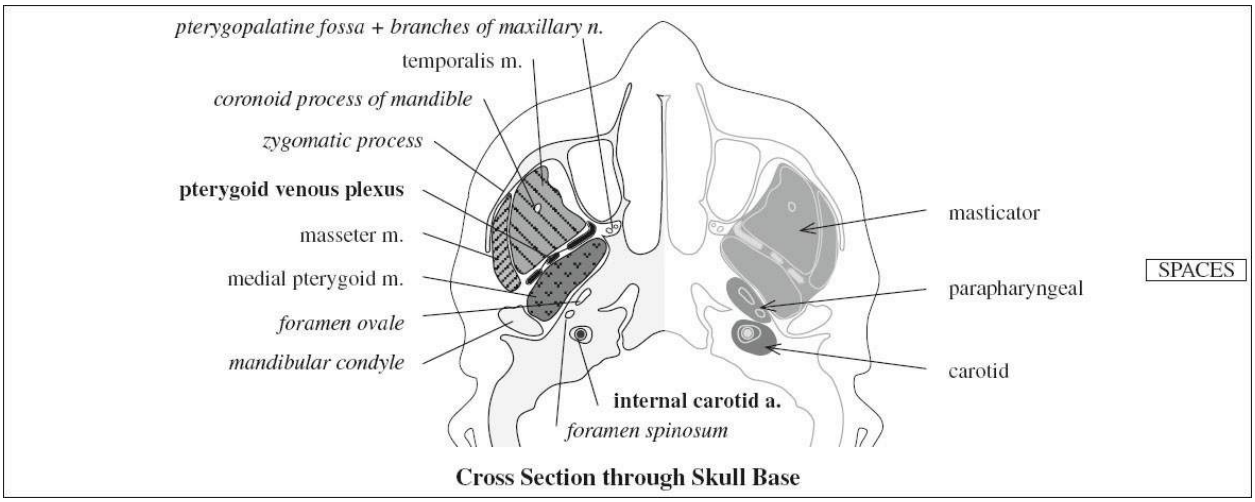
4. Arytenoid cartilages
5. Aryepiglottic folds
   = mucosal reflections between cephalad portion (= arytenoid processes) of arytenoid cartilage + inferolateral margin of epiglottis
   √ soft-tissue folds forming border between lateral piriform sinuses + central laryngeal lumen
6. **Laryngeal ventricle of Morgagni**
   = slitlike fusiform cavity between true + false cords
   Boundary: crescentic edge of false cords superiorly + straight margin of true cords inferiorly
   √ generally not visible on axial scans
7. Laryngeal saccule of Hilton = laryngeal appendix
   = small conical mucosa-lined blind pouch (diverticulum) arising from anterosuperior third of laryngeal ventricle
   Boundary: superiorly between ventricular fold (= false vocal cord) and aryepiglottic fold medially + inner surface of thyroid cartilage laterally
   Function: lubrication of vocal folds
   √ relatively large in infancy
   √ usually involutes by 6th year of life
8. Preepiglottic space
   Boundary: hypoepiglottic lig. (superiorly), thyrohyoid membrane (anteriorly), thyroepiglottic lig. (inferiorly), epiglottis (posteriorly)
9. Paraglottic (paralaryngeal) space
   Boundary: quadrangular membrane + medial piriform sinus wall (superiorly), conus elasticus (inferiorly), thyroid cartilage (laterally)
   √ low-density tissue between true + false cords
   √ contiguous with preepiglottic space anterosuperiorly + aryepiglottic folds superiorly

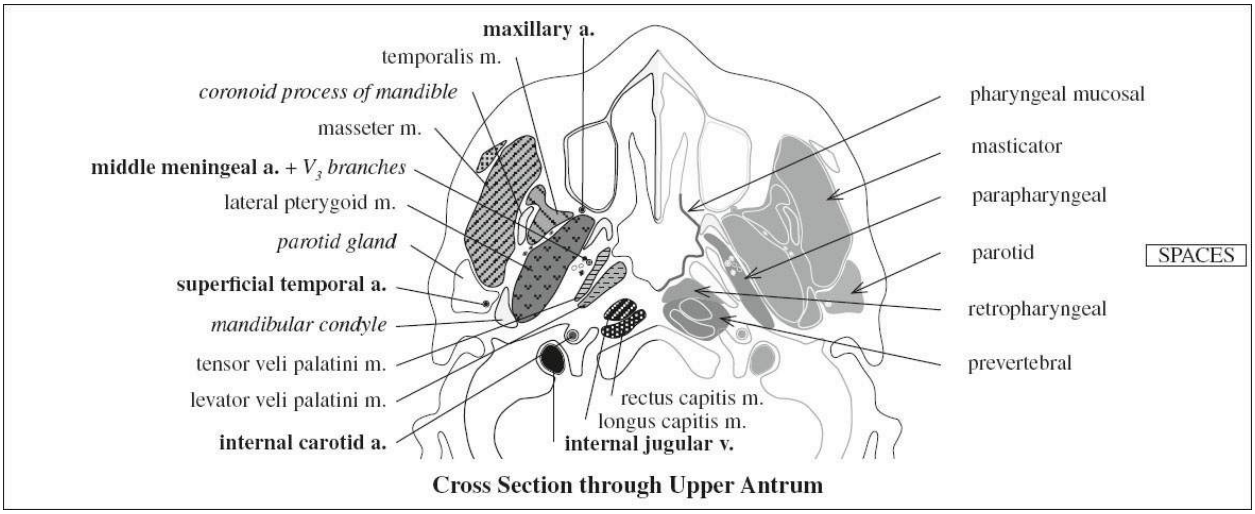
Glottis

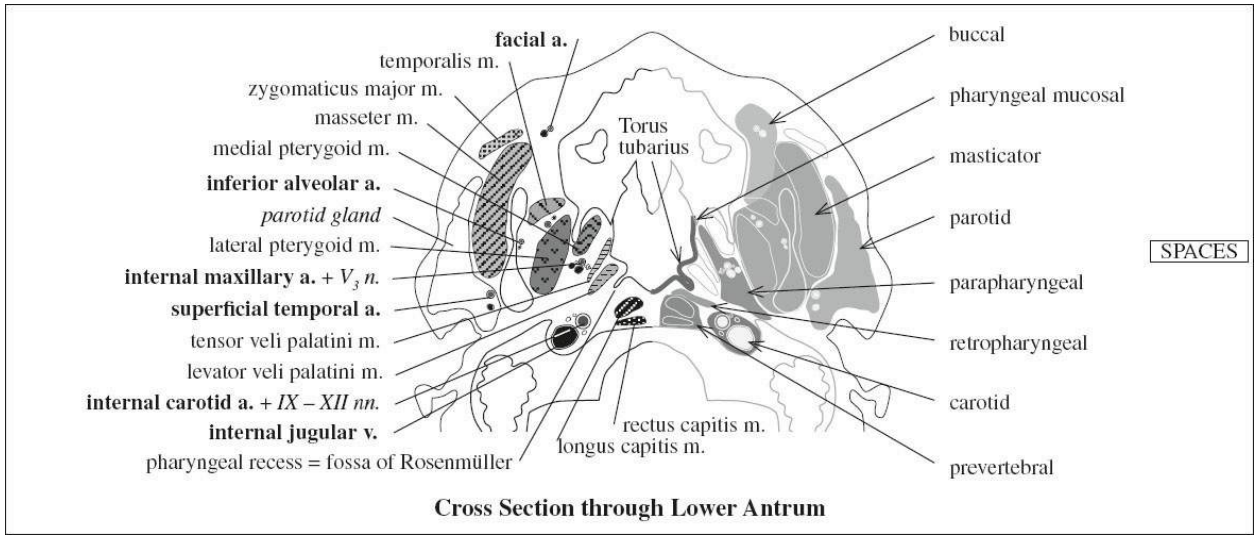
Boundary: from laryngeal ventricles to imaginary plane 1 cm below laryngeal ventricles
Origin: 5th branchial arch (= tracheobronchial bud)

1. **True vocal cords**
   = extend from vocal process of arytenoid cartilage to anterior commissure
   √ vocal cords adduct during phonation of "E" / breath holding

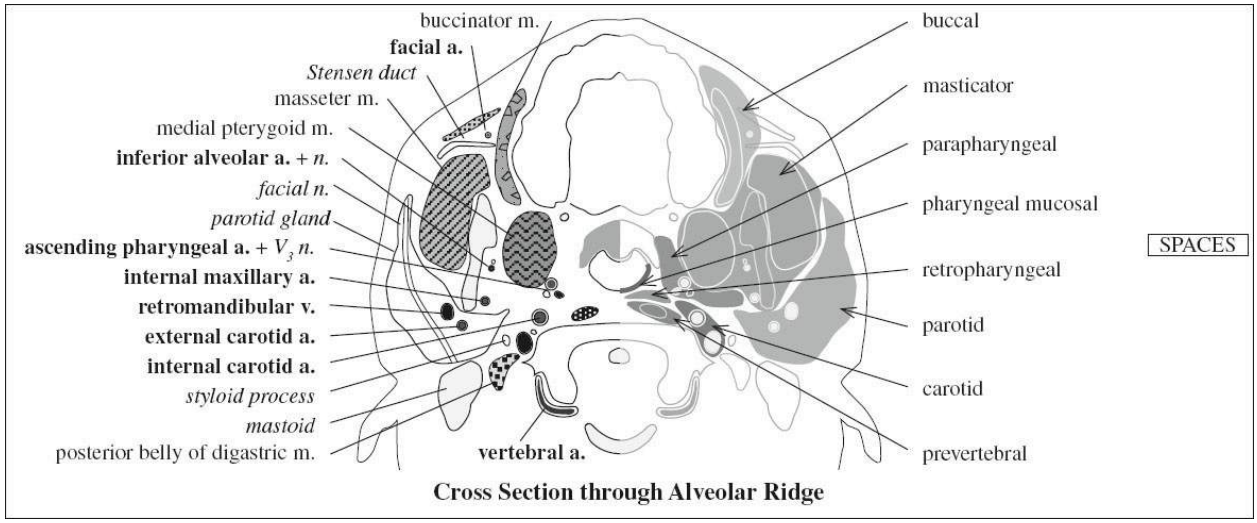

epiglottis
cartilago triticea
superior horn thyroid cartilage
paraglottic fat
hyoid bone
aryepiglottic fold
false vocal cord
laryngeal ventricle
arytenoid cartilage
true vocal cord
vocal lig.
cricoid cartilage
hypoepiglottic lig.
hyoid bone
preepiglottic fat
thyrohyoid membrane
thyroid cartilage
thyrocricoid membrane
quadrangular membrane
thyrohyoid membrane
laryngeal saccule
thyroid cartilage
conus elasticus
thyroarytenoid muscles
SPACES
supraglottis
glottis
subglottis
Sagittal Laryngeal Anatomy
Coronal Laryngeal Anatomy
Larynx


pterygopalatine fossa + branches of maxillary n.
temporalis m.
coronoid process of mandible
zygomatic process
pterygoid venous plexus
masseter m.
medial pterygoid m.
foramen ovale
mandibular condyle
internal carotid a.
foramen spinosum
masticator
parapharyngeal
carotid
SPACES
Cross Section through Skull Base

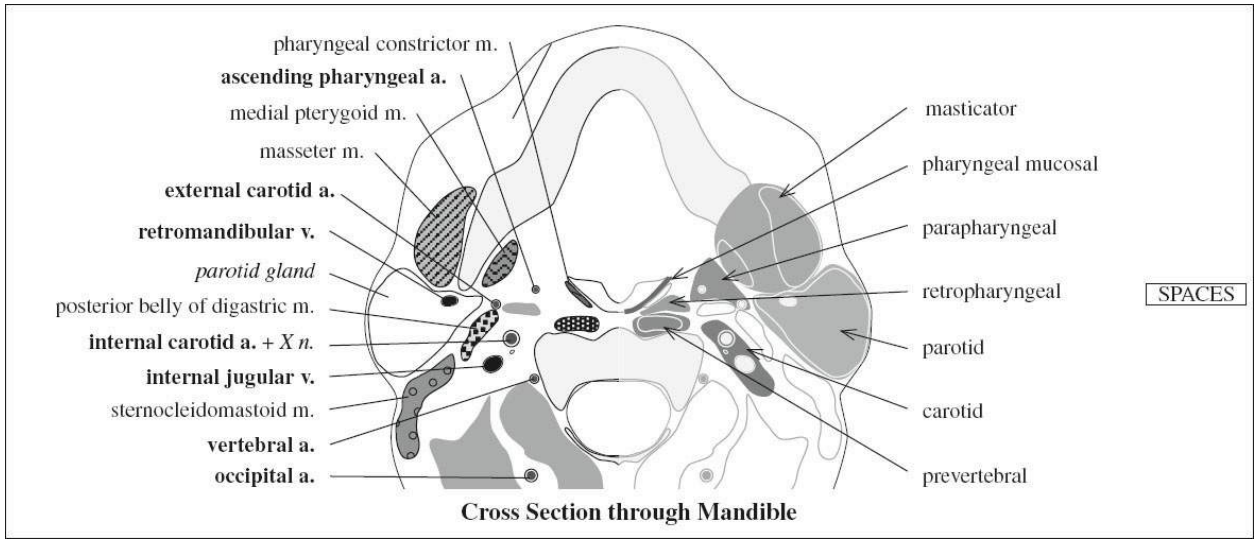

maxillary a.
temporalis m.
coronoid process of mandible
masseter m.
middle meningeal a. + V3 branches
lateral pterygoid m.
parotid gland
superficial temporal a.
mandibular condyle
tensor veli palatini m.
levator veli palatini m.
internal carotid a.
rectus capitis m.
longus capitis m.
internal jugular v.
pharyngeal mucosal
masticator
parapharyngeal
parotid
retropharyngeal
prevertebral
SPACES
Cross Section through Upper Antrum



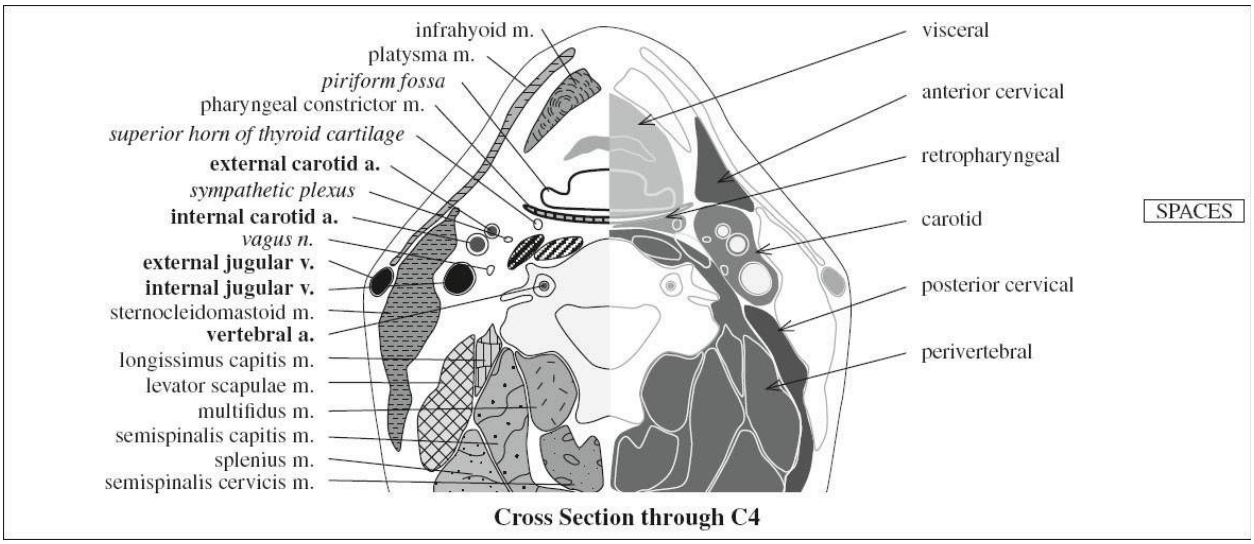
Cross Section through Lower Antrum



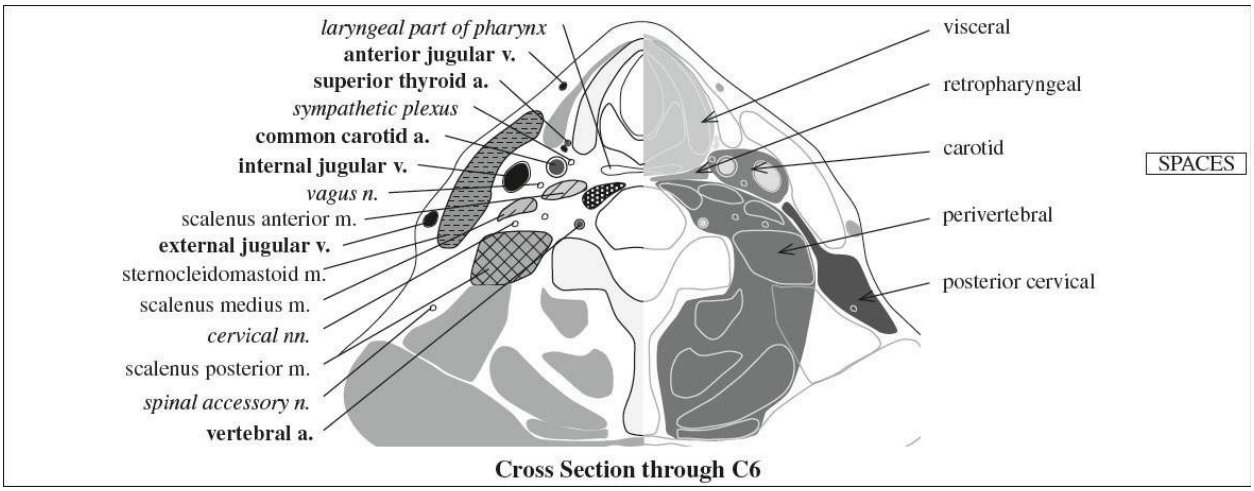
Cross Section through Alveolar Ridge



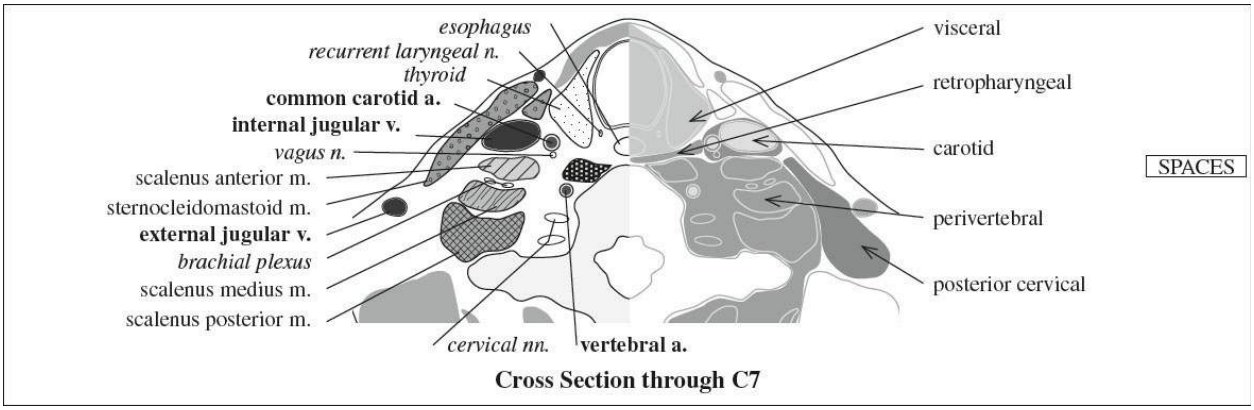
Cross Section through Mandible



Cross Section through C4



Cross Section through C6



Cross Section through C7

2. Anterior commissure
   = midline laryngeal mucosa covering anterior portions of the true vocal cords where they abut the laryngeal surface of the thyroid cartilage
   √ < 1 mm soft tissue behind thyroid cartilage (during abduction of vocal cords with quiet breathing)

3. Posterior commissure
   = midline laryngeal mucosal surface between attachment of true vocal cords and the arytenoid cartilages

Subglottis

extends from undersurface of true vocal cords to inferior edge of cricoid cartilage
derived from 6th branchial arch (= tracheobronchial bud)

1. Conus elasticus
   = fibroelastic membrane extending from cricoid cartilage to medial margin of true vocal cords; forming lateral wall of subglottis

FASCIAE OF THE NECK

= well-defined sheets of fat + fibrous tissue that circumscribe several compartments / spaces

A. Superficial cervical fascia
B. Deep cervical fascia
   (a) superficial layer
   (b) middle layer
   (c) deep layer

DEEP SPACES OF SUPRAHYOID HEAD & NECK

Masticator Space

= lateral to parapharyngeal space

Fascia: superficial layer of deep cervical fascia encloses muscles of mastication

Contents:

› muscles of mastication (medial + lateral pterygoid muscles, masseter, temporalis muscle)
› ramus + body of mandible
› cranial nerve V_3

Pharyngeal Mucosal Space

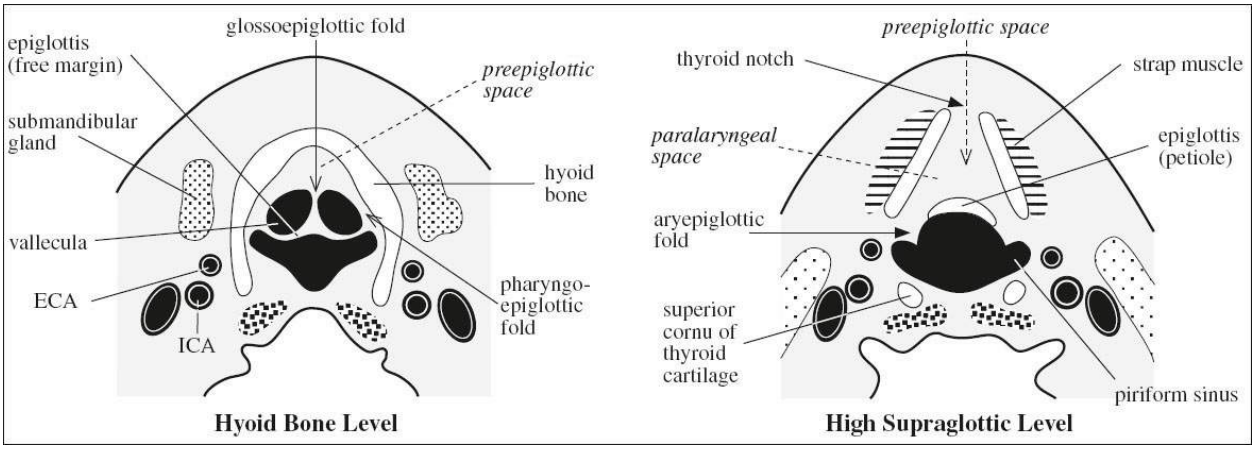
Components:

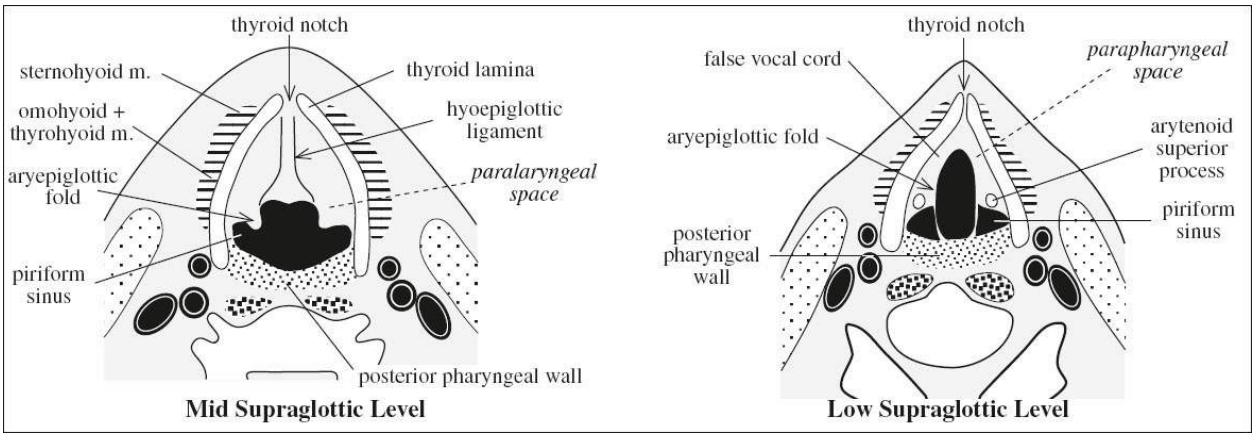
› **Waldeyer ring** = adenoids, faucial + lingual tonsils + submucosal lymphatics
  [Heinrich Wilhelm Gottfried Waldeyer-Hartz (1836–1921), professor of pathology in Breslau, Strasbourg and Berlin]
› superior + middle constrictor muscles
› salpingopharyngeal muscle
› levator palatini muscle underneath torus tubarius
› torus tubarius = prominent ridge between orifice of eustachian tube anteroinferiorly + fossa of Rosenmüller posterosuperiorly
› pharyngeal recess = **fossa of Rosenmüller**
  [Johann Christian Rosenmüller (1771–1820), professor of anatomy and surgery at University of Leipzig]

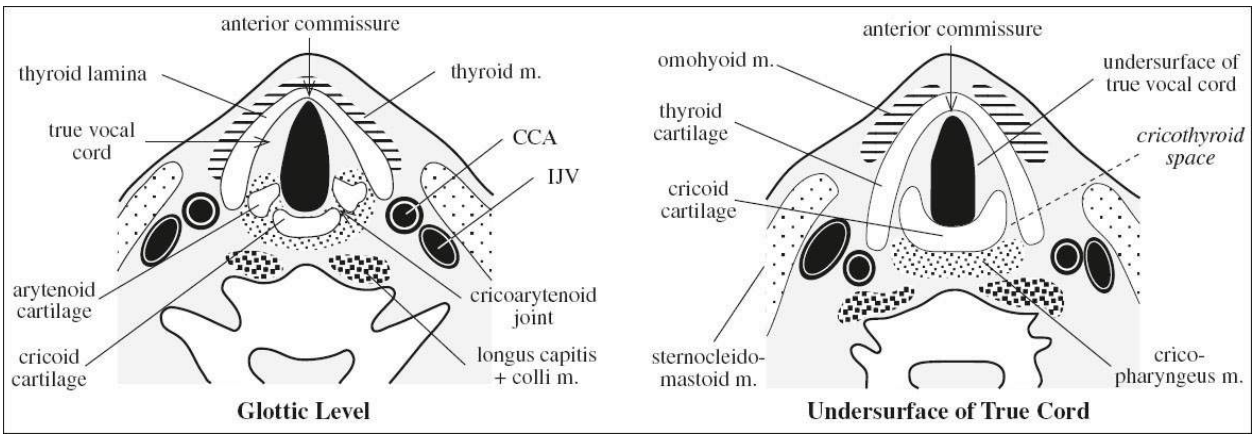
Contents: squamous mucosa, lymphoid tissue, minor salivary glands

Parapharyngeal Space

= triangular-shaped centrally located space; major vertical highway extending from skull base to hyoid







Fascial borders:

medial = middle layer of deep cervical fascia

lateral = superficial layer of deep cervical fascia

posterior = carotid sheath

Contents:
- › fat
- › internal maxillary artery
- › ascending pharyngeal artery
- › pharyngeal venous plexus
- › branches of cranial nerve V3

Vectors: if parapharyngeal fat is effaced

anteriorly = lesion in masticator space
medially = lesion in pharyngeal mucosal space
laterally = lesion in parotid space
posteriorly = lesion in carotid space

Retropharyngeal Space

= potential space posterior to pharyngeal mucosal space + anterior to prevertebral space; major vertical highway from skull base to T4

Fascial borders:

mid + deep layers of cervical fascia; alar fascia laterally

Contents:
- › fat
- › medial + lateral retropharyngeal nodes

Prevertebral Space

= major highway from skull base to T4; posterior to retropharyngeal space

Fascial borders:

(a) anterior compartment of deep cervical fascia:
from one transverse process to the other anteriorly in front of longus colli muscle

(b) posterior compartment of deep cervical fascia:
from transverse process posteriorly to spinous process

Contents:
- › prevertebral muscles (longus colli)
- › scalene muscles
- › vertebral artery + vein
- › brachial plexus
- › phrenic nerve

Carotid Space

Carotid fascia extends from skull base to aortic arch

Contents:

(a) below hyoid bone:
- › common carotid artery
- › internal jugular vein
- › cranial nerve X (= vagus nerve)
- › cervical sympathetic plexus

(b) at level of nasopharynx:

› internal carotid artery
› internal jugular vein
› cranial nerves IX–XII
› internal jugular chain of nodes

Parotid Space

Contents:

› parotid gland with Stensen duct
› intraparotid lymph nodes
› external carotid + internal maxillary arteries
› retromandibular vein
› facial nerve

Submandibular Space

Contents:

› submandibular gland with Wharton duct
› facial artery + vein
› cranial nerve XII

TEMPORAL BONE

A. SQUAMOUS PORTION
= lateral wall of middle cranial fossa + floor of temporal fossa

B. MASTOID PORTION

1. **Mastoid antrum**
[*mastos*, Greek = woman's breast; *eidos*, Greek = form / shape]; [*oeides*, Greek = like; *mastoeides*, Greek = resembling a nipple]
[*antron*, Greek / *antrum*, Latin = cave]
2. **Aditus ad antrum**
connects epitympanum (= attic) of middle ear cavity to mastoid antrum
[*ad* + *ire*, Latin = to go to; *aditus*, Latin = entrance]
[*tympanum*, Latin / *tympanon*, Greek = drum]
3. **Körner septum**
= small bony projection extending inferiorly from roof of mastoid antrum as part of petrosquamosal suture between lateral + medial mastoid air cells posteriorly from epitympanum

C. PETROUS PORTION = inner ear

1. **Tegmen tympani**
[*tegmina*, Latin (pl) = covering structure or roof]
= roof of tympanic cavity
2. **Arcuate eminence**
= prominence of bone over superior semicircular canal
3. Internal auditory canal (IAC)
4. Vestibular aqueduct
5. Cochlear aqueduct
6. Otic capsule = densest portion of temporal bone that surrounds osseous labyrinth

7. Petrous apex
   = separated from clivus by petrooccipital fissure + foramen lacerum

D. TYMPANIC PORTION
   1. External auditory canal (EAC)

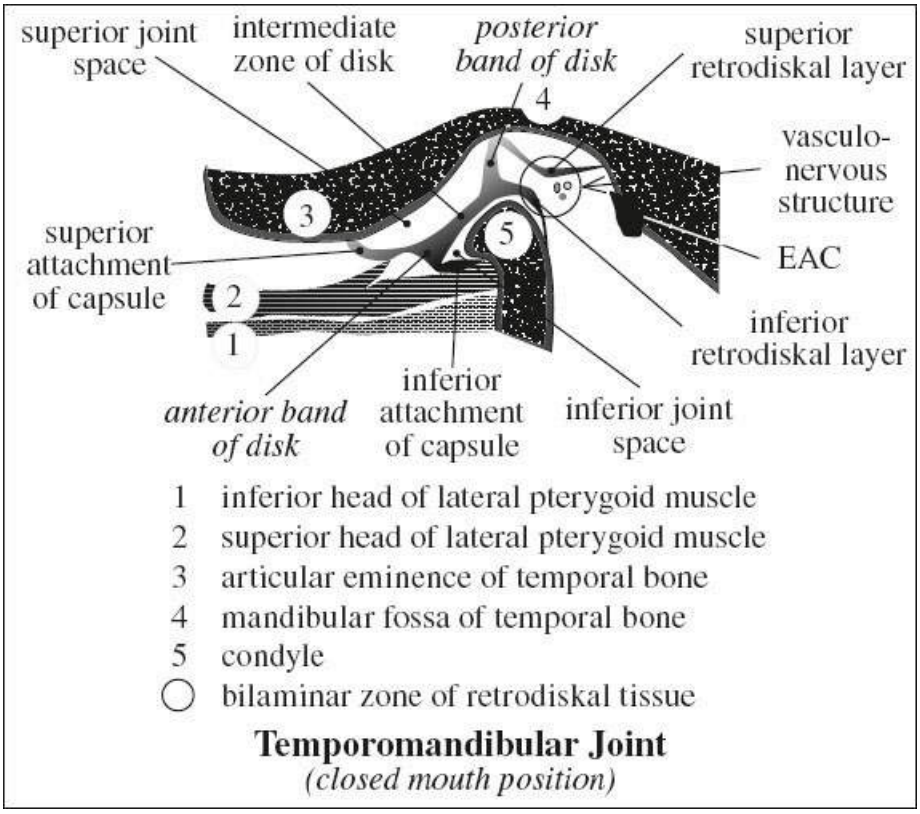
E. STYLOID PORTION

TEMPOROMANDIBULAR JOINT

Components:

1. **Meniscus** = articular disk
   = biconcave fibrocartilaginous structure that divides the synovial TMJ into superior + inferior compartments
   Location: between mandibular condyle and temporal bone component of TMJ
   Shape: round / oval
      (a) thin center (= intermediate zone)
      (b) thicker periphery (= bands of disk)
   Function: interposition of thinnest part between condyle and temporal bone prevents articular damage (in closed- or open-mouth position)
   (a) hyperintense **anterior band of disk** attached to
      › superior attachment of capsule
      › inferior attachment of capsule
      √ lies immediately in front of condyle + junction of bilaminar zone
      √ may form bulge (? normal variant)
   (b) hyperintense **intermediate zone**
      √ lies at superior part of the condyle
   (c) mildly hyperintense **posterior band of disk** formed by
      › superior retrodiskal layer
      › inferior retrodiskal layer
      √ best depicted in open-mouth position
2. **Retrodiskal tissue** = **bilaminar zone** composed of
   (a) retrodiskal layers
   (b) vasculonervous structures
   √ best depicted in open-mouth position

Muscles:



Temporomandibular Joint
(closed mouth position)

1. Lateral pterygoid m.
   (a) superior lateral pterygoid m.
   (a) inferior lateral pterygoid m.
2. Digastric muscle

Motion:

1. **Rotation** around horizontal axis through condylar heads
2. **Translation** = <u>condyle + meniscus</u> move together anteriorly to lie beneath articular eminence
   → central part of disk interposed between condyle and articular tubercle

Closed-mouth position:

√ thick posterior band of meniscus lies immediately above condyle near 12 o'clock position
√ junction of posterior band + bilaminar zone should fall within 10° of vertical

Open-mouth position:

√ best depiction of posterior band + retrodiskal tissue
√ anterior band lies immediately in front of condyle + junction of bilaminar zone
√ condyle may lie beneath anterior band of meniscus when mouth is fully opened
√ disk lies at superior part of condyle
√ anterior band may be seen as a bulge

EXTERNAL (OUTER) EAR

Origin: 1st branchial cleft and 1st + 2nd branchial arches during 6th–12th weeks of intrauterine life

A. Auricle

B. External auditory canal (EAC)

Origin: meatal plate (= solid core of epithelium) that migrates toward 1st pharyngeal pouch and hollows out during 2nd–7th months of intrauterine life

Wall of lateral ⅓: fibrocartilage

Wall of medial ⅔: tympanic portion of temporal bone

Anterior wall: posterior aspect of glenoid fossa

Posterior wall: anterior margin of mastoid

Medial border: tympanic membrane,

MIDDLE EAR / TYMPANIC CAVITY

= air-filled cavity within petrous portion of temporal bone containing ossicular chain

Borders:

› anterior wall = carotid wall

› posterior wall = mastoid wall including from lateral to medial

(a) facial nerve recess for descending facial nerve

(b) pyramidal eminence overlying stapedius muscle (inserting onto head of stapes)

(c) sinus tympani (clinically blind spot)

(d) round window niche

› superior wall = tegmen tympani (= thin bony plate separating dura of middle cranial fossa from middle ear)

› inferior wall = jugular wall

› lateral wall = tympanic membrane

› medial wall = labyrinthine wall

A. EPITYMPANUM (= **attic**)

= tympanic cavity superior to level of tympanic membrane above a line drawn between the inferior tip of drum spur (= scutum) + tympanic portion of facial nerve

[*scutum*, Latin = shield; tympanum, Latin = semicircular area enclosed by the arch above the horizontal portion of a portal]

Contents: malleus head, body + short process of incus, **Prussak space** (= superior recess between incus + lateral wall of epitympanum)

Communication: with mastoid via aditus ad antrum

B. MESOTYMPANUM (= tympanic cavity proper)

= tympanic cavity at level of tympanic membrane between inferior tip of scutum + line drawn parallel to inferior aspect of bony EAC

Contents: manubrium of malleus, long process of incus, stapes, tensor tympani muscle (innervated by V_3), stapedius muscle (innervated by VII)

C. HYPOTYMPANUM

= shallow trough in floor of middle ear inferior to tympanic membrane

Contents: opening of eustachian tube

Medial margin: ICA

D. TYMPANIC MEMBRANE (**eardrum**)

= thin cone-shaped membrane separating external from middle ear

Origin: ectoderm from 1st branchial groove; mesoderm and endoderm from 1st branchial

pouch
√ may be faintly discerned on CT
Diameter: 10 mm
Function: transmission of sound from air to malleus
Attachment: superiorly at scutum (=sharp bony projection); inferiorly at tympanic annulus
Regions:
(a) pars flaccida (= **Shrapnell membrane**)
= small triangular fragile 2-layered membrane in upper region loosely attached to petrous bone
Location: above malleolar folds; forms superior ⅛ of drum circumference
Relationship: chorda tympani crosses on inner surface
(b) pars tensa
= larger robust tightly attached region consisting of 3 layers (skin + fibrous tissue + mucosa)

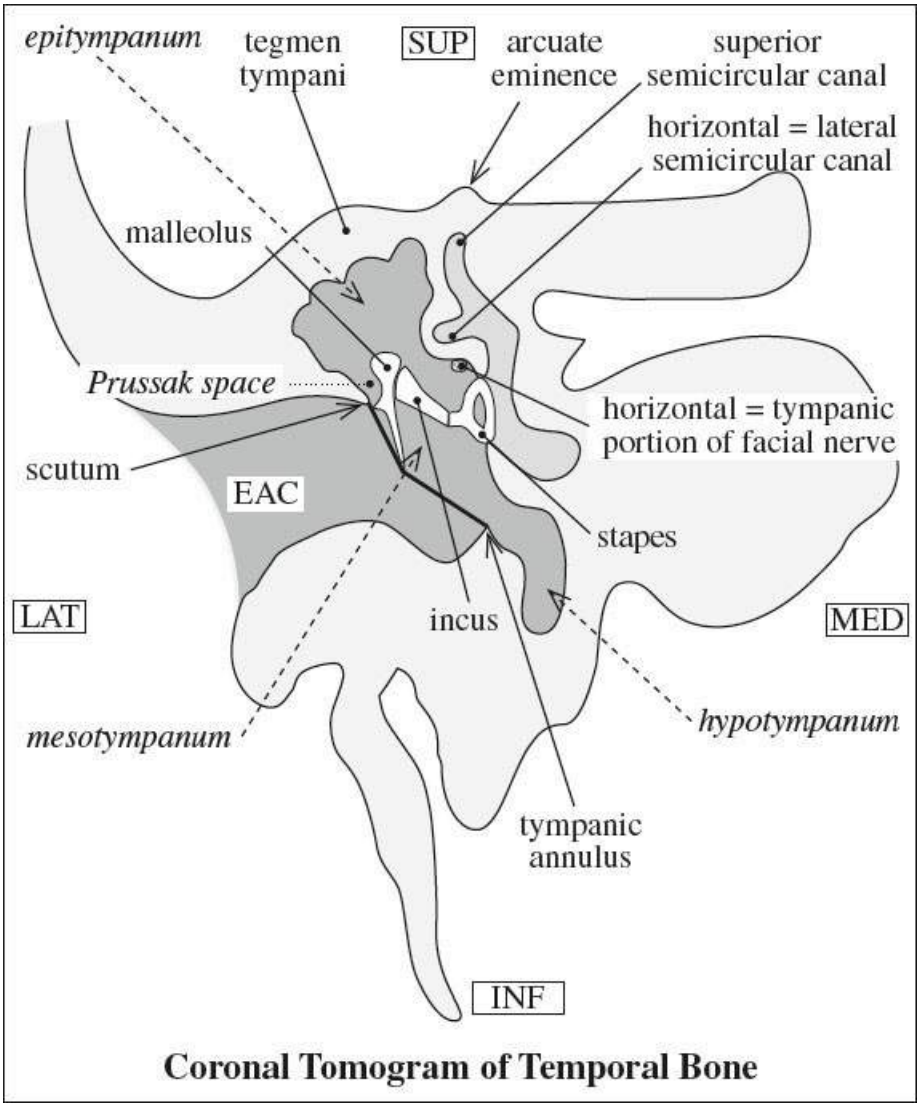
E. TYMPANIC CAVITY & EUSTACHIAN TUBE
Origin: from 1st pharyngeal pouch during 10–30 weeks EGA

Wall Ridges of Tympanic Cavity

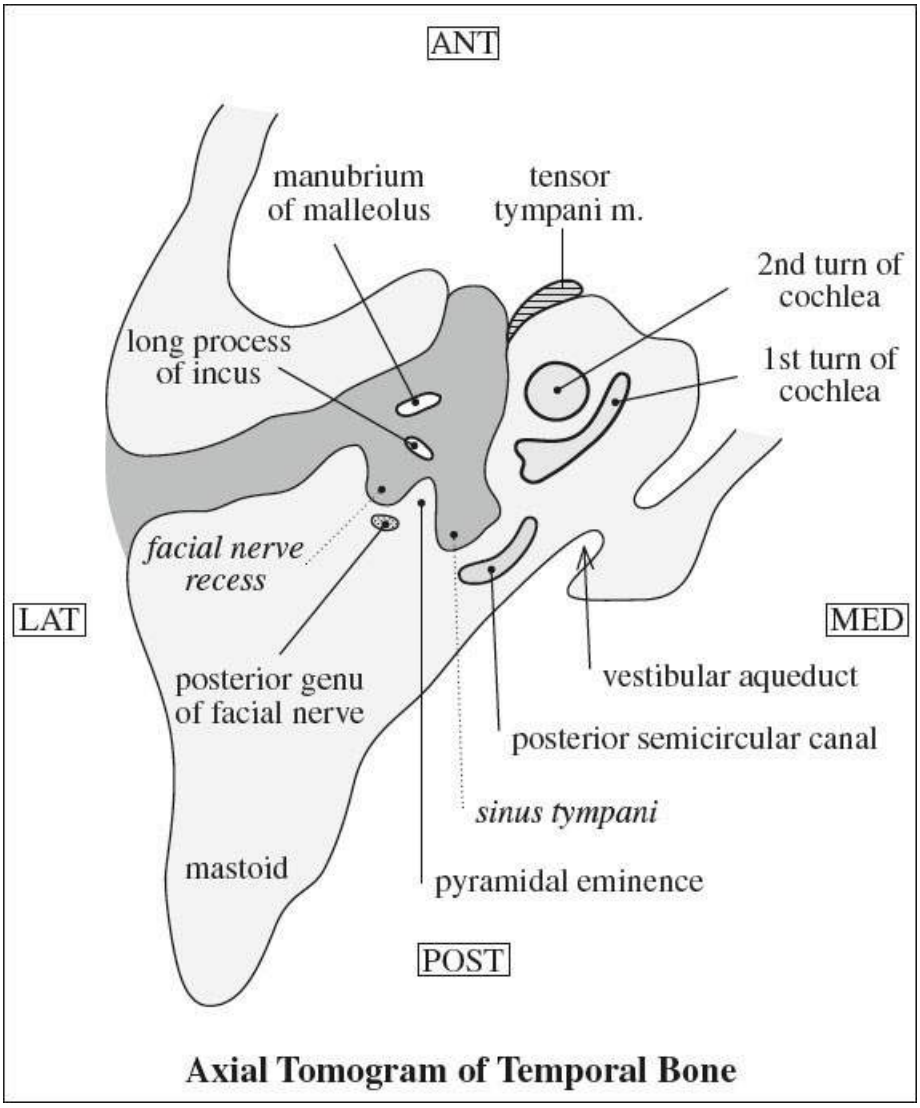
on medial & posterior wall of tympanic cavity produced by:
» MEDIAL WALL:
(1) Anterior limb of lateral semicircular canal
√ wall prominence posteriorly + superiorly
(2) Bony canal for facial nerve
√ wall prominence inferior and anterior to (1)
(3) Terminus of septum canalis musculotubarii
= landmark for geniculate ganglion
√ wall prominence anterior to (2)
(4) **Oval window**
√ inferior to (3)
(5) **Basal turn of cochlea**
√ convexity inferior + slightly anterior to (4)
= rounded promontory
» POSTERIOR WALL:
(6) **Sinus tympani**
= landmark for ampulla of posterior semicircular canal
√ recess on posterior wall
(7) **Facial nerve recess**
= important surgical landmark when tympanic cavity is entered via mastoid approach
√ recess on posterior wall lateral to (6)
(8) **Pyramidal eminence**
= protrusion that gives rise to stapedius muscle
√ situated between sinus tympani + facial nerve recess

Embryology of Stapedial Artery (complex & simplified)

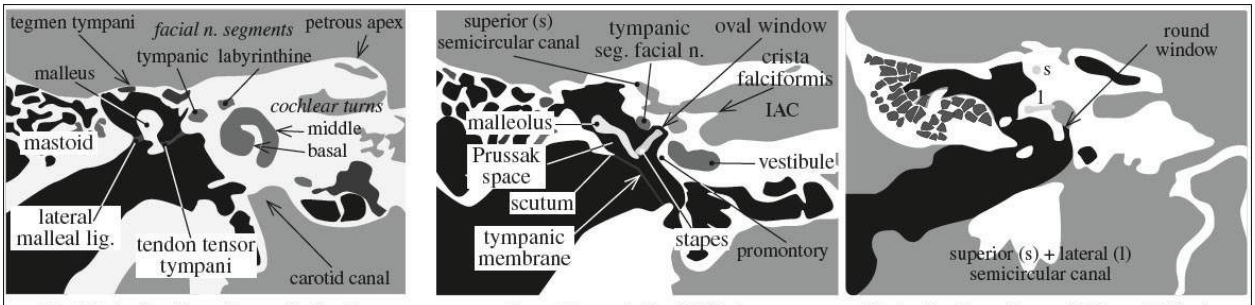
› 2nd aortic arch becomes hyoid artery and persists as caroticotympanic branch of the ICA



Coronal Tomogram of Temporal Bone



Axial Tomogram of Temporal Bone

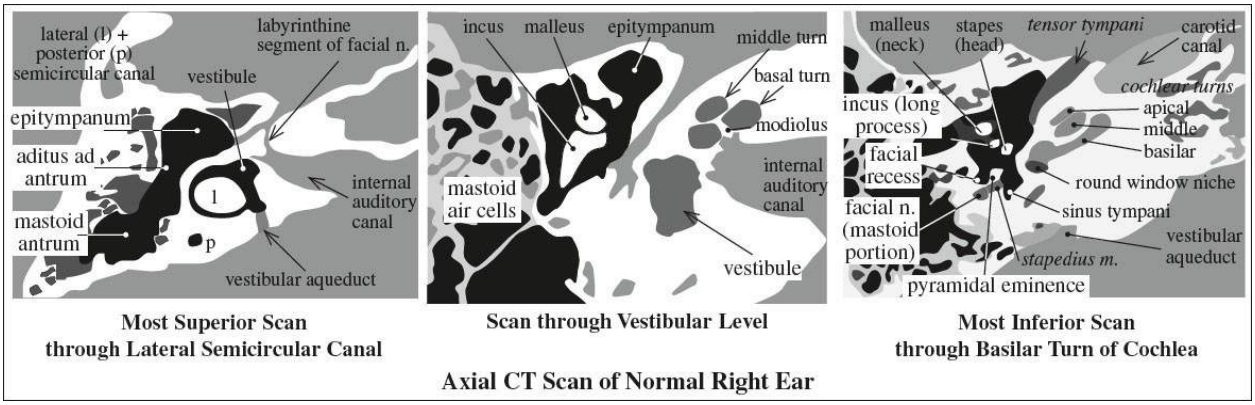


Most Anterior Scan through Cochlea
"snake eyes" = two facial n. segments

Scan through Oval Window

Posterior Scan through Round Window

Coronal CT Scan of Normal Right Ear



› **stapedial artery** arises from hyoid artery near its origin from the proximal ICA (3rd arch) at 4–5 weeks of fetal life following regression of 1st + 2nd aortic arches
  » stapedial artery extends cranially to pass through obturator foramen of stapes and branches into
    (a) upper supraorbital branch with its posterior division that becomes middle meningeal artery
    (b) lower maxillofacial branch forms an anastomosis with ventral pharyngeal artery (precursor of external carotid artery) and exits through foramen spinosum
› as ventral pharyngeal artery supplies flow to middle meningeal artery, stapedial artery regresses leaving a small caroticotympanic artery

OSSICULAR CHAIN

[*malleus*, Latin = hammer; *manubrium*, Latin = handle ← manus = hand; *incus*, Latin = anvil; *stapia*, Latin = stand; *pes*, Latin = foot; *stapes*, Latin = stirrup; *umbo*, Latin = boss at center of a circular shield]

Origin: from 1st + 2nd branchial arches

Function: transmits + amplifies vibrations incident on tympanic membrane across middle ear cavity → deflection of oval window (area of tympanic membrane is 30 x greater than that of oval window)

A. **Malleus**

Location: anterolateral to incus and stapes

Attachment: manubrium to tympanic membrane

Articulation: diarthrodial **incudomalleal joint** between facet on posterior surface of head of malleus and body of incus
√ "ice cream cone" configuration on axial CT

Components:
› head: articulating facet on posterior surface
› neck: at inferior aspect of club-shaped head; provides attachment for tensor tympani m.
› **manubrium**: long process that lies further inferiorly; tip attaches to tympanic membrane at **umbo**
› anterior + lateral processes: small bony spicules that project from upper portion of manubrium; provide attachment for anterior + lateral malleal ligaments that support malleus within middle ear cavity

√ lateral process with ligament may be visible on CT

B. **Incus**

shaped like a premolar tooth

Articulation:

(1) facet on anterior surface of body of incus → head of malleus

(2) lenticular process of incus → head of stapes

Components:

› body

› short process: directed posterolaterally

› long process: directed inferiorly parallel to manubrium; tip of long process bends medially to end in lenticular process (rounded projection) articulating with stapes

› lenticular process: for articulation with head of stapes

C. **Stapes**

most medial ossicle resembling a stirrup

Attachment: footplate to oval window of vestibule (= **incudostapedial joint**)

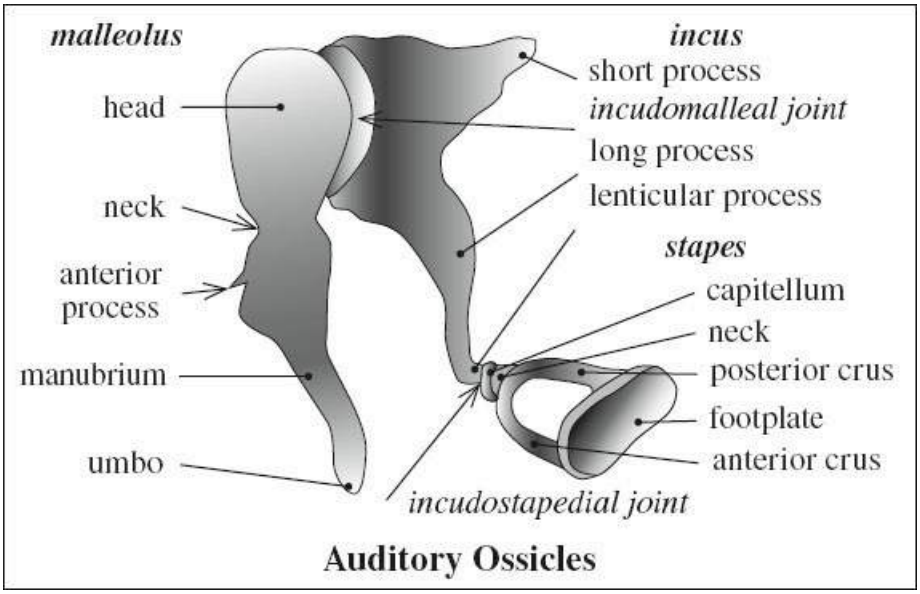
Articulation: with lenticular process of incus

Components:

› head / capitellum

› neck: provides insertion for stapedius muscle at its posterior aspect

› anterior + posterior crus



Auditory Ossicles

› footplate: attached to margins of oval window by annular ligament

D. Suspensory ligaments

1. Superior malleal
2. Lateral malleal
3. Posterior malleal
4. Posterior incudal

√ sometimes visible on CT as thin linear structures (most commonly lateral malleal lig.)

INNER EAR

A. OSSEOUS LABYRINTH

encloses membranous labyrinth = **otic capsule**

◊ Densest bone in entire body

Embryology: develops from mesenchyme around membranous labyrinth between 4–8 weeks EGA → continued growth between 8–16 weeks EGA → ossification by 24th week EGA

Location: petrous portion of temporal bone

1. **Cochlea**

[*kokhlias*, Greek; probably related to *konkhe* = conch]

[*modiolus*, diminutive of *modius*, Latin = hub of a wheel]

= spiral-shaped structure with 2½ – 2¾ turns encircling central bony axis (= **modiolus**) like conical snail shell

› basal first turn opens into round window posteriorly

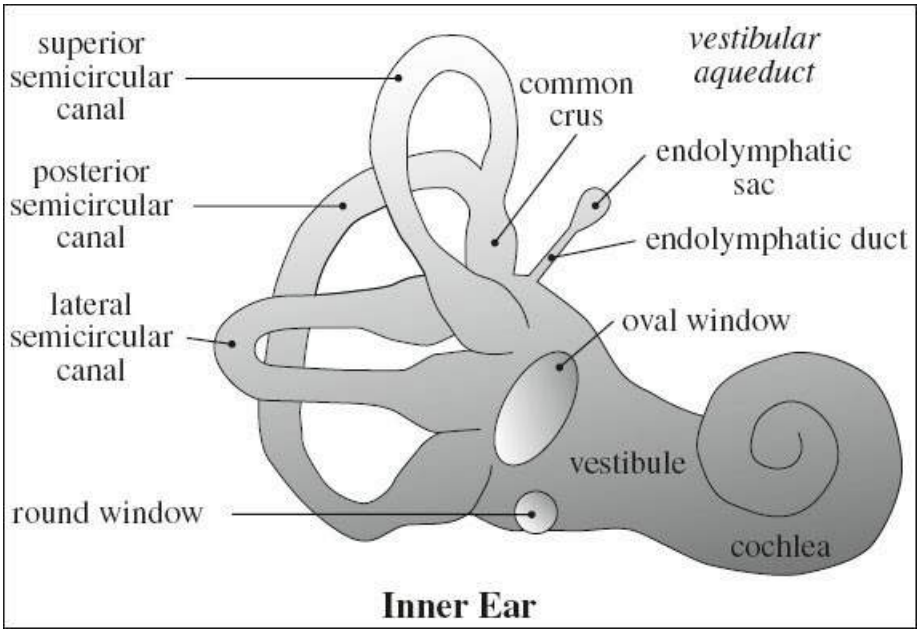
› lateral aspect of basal turn bulges into middle ear cavity forming cochlear promontory

› nerve of Jacobson = tympanic branch of glossopharyngeal n. (CN IX) courses over promontory

Division by interscalar septum:

(a) **scala vestibuli** (upper compartment)

(b) **scala tympani** (lower compartment)



Inner Ear

(c) **scala media** / cochlear duct contains organ of Corti (sensory organ of hearing)

helicotrema = open communication between scala vestibuli + tympani at cochlear apex

[*scala*, Latin = stair, slope]

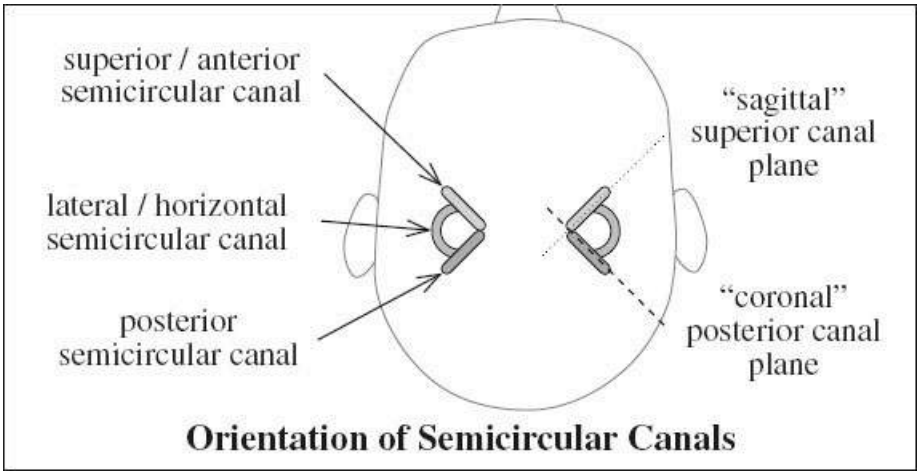
[*helix*, Greek = coil and *trema*, Greek = hole]

2. **Vestibule**

= central and most capacious ovoid part of bony labyrinth posterior to cochlea
› continuous anteriorly with cochlea
› continuous posteriorly with semicircular canals
› separated from middle ear by oval window
Subunits: (not separately visualized)
(a) utricle [*utriculus*, Latin = little bag]
Location: in elliptical recess superiorly and posteriorly on medial wall of vestibule
(b) saccule [diminutive of *saccus*, Latin = bag]
Location: in spherical recess inferiorly + anteriorly
Function: both involved with balance

3. **Semicircular canals** (SCC)
= 3 canals oriented orthogonal to each other
› each canal has a dilatation at one end (= ampulla)
› common crus ← junction of posterior end of superior SCC + upper end of posterior SCC
Function: detection of angular acceleration
(a) **lateral** / horizontal (external) SSC
• detects rotation in transverse plane around vertical axis (ie, left-right movement of head)
Location: lateral
Arch direction: horizontal backward
√ juts into epitympanum
(b) **superior** / anterior SCC
• detects rotation in sagittal plane around lateral axis (ie, nodding of head)
Location: anteromedial
Arch direction: superiorly
√ vertical orientation transverse to long axis of petrous part of temporal bone
√ forms convexity of arcuate eminence
(c) **posterior** SCC
• detects rotation in coronal plane around anterior-posterior axis (ie, head touching shoulder)
Location: posteromedial
Arch direction: superiorly
√ nearly parallel to posterior surface of petrous bone

4. **Cochlear aqueduct**
= thin osseous canal containing 8-mm–long perilymphatic duct
Size: ≤ 0.1–0.2 mm
Course: from basal turn of cochlea (anterior to round window) to lateral border of jugular foramen paralleling IAC inferiorly



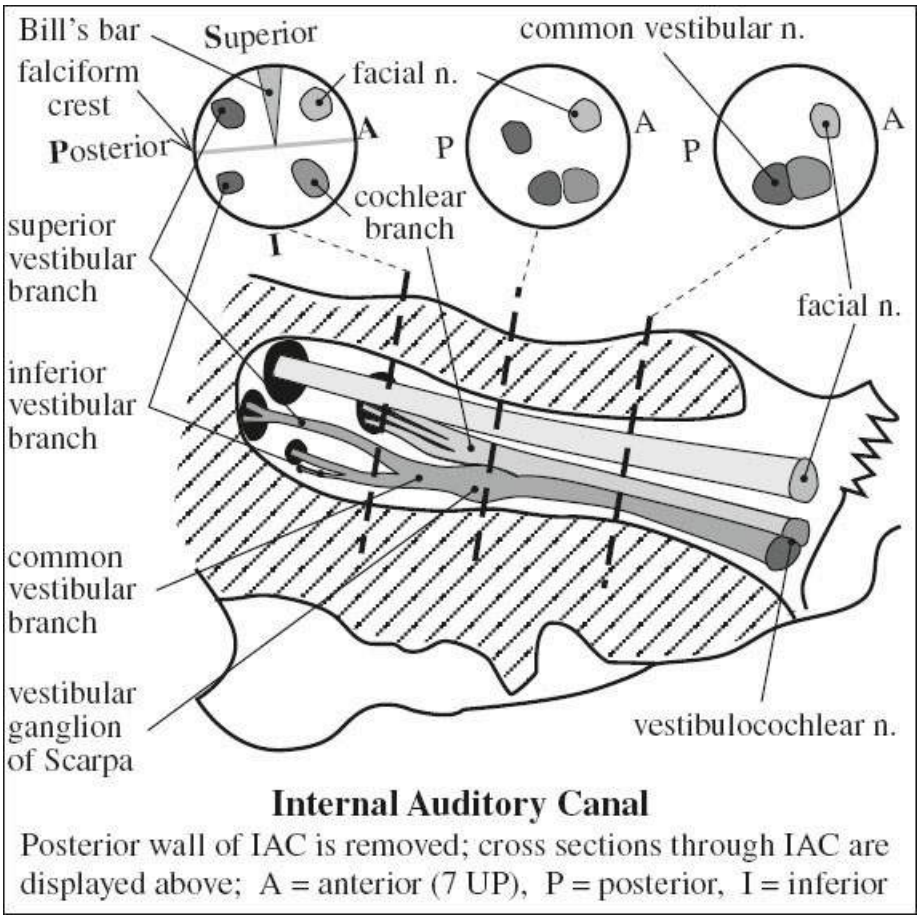
Orientation of Semicircular Canals

Function: regulates CSF + perilymphatic fluid pressure

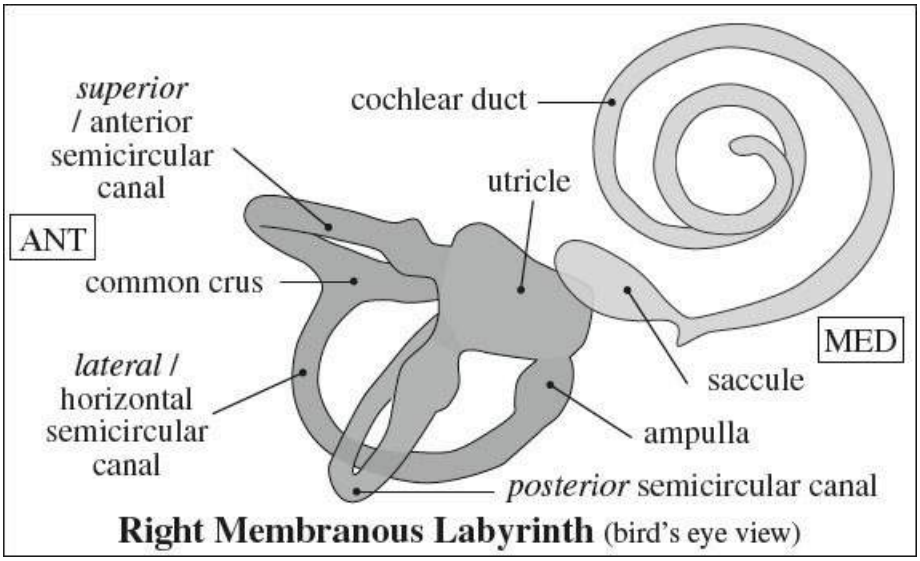
5. **Vestibular aqueduct**
   = curvilinear duct connected to utricle + saccule
   Size: ≤ 1 mm at midpoint; ≤ 2 mm at operculum
   Content: endolymphatic duct and sac
   Course: from vestibule to endolymphatic sac
   Function: equilibration of endolymphatic fluid pressure
   Location: along posteroinferior surface of petrous bone to the medial wall of vestibule in a course parallel + posterior to posterior SCC
6. **Internal auditory canal** (IAC)
   traverses petrous portion of temporal bone; extends from labyrinth to cerebellopontine angle
   Content:
   (a) 7th (facial) CN (anterosuperior quadrant)
   (b) 8th (vestibulocochlear) CN
   › superior vestibular branch (posterosuperior)
   Innervation: utricle, superior + lateral SCC
   › inferior vestibular branch (posteroinferior)
   Innervation: saccule, posterior SCC
   › cochlear branch (anteroinferior quadrant)
   Innervation: cochlea
   Borders:
   (a) medial opening = **porus acusticus** internus
   (b) lateral opening abutting labyrinth = **fundus;** separated from inner ear by **lamina cribrosa** (= perforated vertical plate of bone) allowing passage of facial + vestibulocochlear nerves
   › **crista falciformis** (= falciform crest)
   = horizontal bony septum dividing IAC into superior and inferior compartments
   » superoposteriorly: superior vestibular n.
   » inferoposteriorly: inferior vestibular n.
   › **"Bill's bar"** = vertical crest divides superior compartment into anterior + posterior areas

» anterosuperiorly: facial n. (CN VII)
» anteroinferiorly: cochlear n.
mnemonic: "Seven Up Coke Down"

B. PERILYMPH
= fluid within space between osseous + membranous labyrinth
Osseous openings:



Internal Auditory Canal
Posterior wall of IAC is removed; cross sections through IAC are displayed above; A = anterior (7 UP), P = posterior, I = inferior



(a) **oval window**: compresses perilymph in scala vestibuli via stapes excursions
(b) **round window**: pressure-relief diaphragm that bulges outward with each pressure wave in scala tympani

C. MEMBRANOUS LABYRINTH
Origin: arises from neuroectoderm in 4th week EGA
Embryology: **otic placode** (neuroectoderm) invaginates → **otic pit** → otic vesicle (**otocyst**); otocyst divides into superior (dorsal pars) + inferior (ventral pars) pouches = precursors to utricle, semicircular canals, cochlear duct, saccule
√ filled with endolymph
1. Cochlear duct
2. Utricle
3. Saccule
4. Semicircular ducts
5. Endolymphatic duct
Course: from posterior aspect of vestibule toward posterior cranial fossa
6. Endolymphatic sac
Location: posterior margin of petrous ridge

D. ENDOLYMPH
= fluid within membranous labyrinth

SALIVARY GLANDS

US:
√ homogeneous texture varying from markedly hyperechoic to slightly hyperechoic (compared to adjacent muscles)

Parotid Gland

Embryology:
glandular component arises from ingrowth of local proliferation of oral epithelium, which

creates ducts by 10th week GA; secretions begin by 18th week GA

◊ Epithelial buds branch around divisions of facial nerve thus incorporating it into parotid parenchyma

◊ The only salivary gland that becomes encapsulated after development of the lymphatic system resulting in intraglandular lymph nodes and lymph vessels

Location: mainly in upper + lower poles of parotid

Features of normal intraparotid lymph nodes:

√ short axis–to–long axis ratio > 0.5 (in 60%)

√ short axis diameter < 5–6 mm

√ hyperechoic hilum

Location: retromandibular fossa; wraps around mandibular angle (within parotid space)

Anatomic divisions:

(a) superficial lobe = main bulk of gland superficial and posterior to masseter muscle; separated by invisible facial nerve / (in its place) retromandibular vein

(b) deep lobe = small extension of gland deep to angle of mandible

(c) accessory lobe (20%) = superficial and lateral to masseter muscle + anterior to superficial lobe along course of Stenon duct draining directly into parotid duct

Drainage route: Stensen / Stenon duct

Stensen / Stenon Duct

[Stensen, Niels aka Steensen, Latin: Nicolaus Stenonius, Italian: Stenone, French *:* Stenon (1638–1686), Danish anatomist, natural scientist, theologist in Holland, France, Italy and Germany]

= main excretory duct of parotid gland

Length: 3–5 cm

Course: lies on masseter muscle about 1 cm below zygomatic arch → crosses buccal muscle

Orifice: parotid papilla above upper 2nd molar tooth

√ normal duct sonographically not visible

Submandibular Gland

Location: in posterior part of submandibular triangle (created by anterior + posterior bellies of the digastric muscle and body of the mandible)

√ may be connected to parotid / sublingual glands by glandular processes

Drainage route:

5-cm long submandibular duct (Wharton duct) forms at hilum superiorly; runs forward between mylohyoid m., hyoglossus m. and genioglossus m.; bends around margin of mylohyoid muscle; exits through orifice (= sublingual caruncle) along medial aspect of sublingual gland

[Thomas Wharton (1614–1673), English anatomist, in 1956 published "Adenographia", a description of the glands of the entire body, associated with St. Thomas's Hospital, London]

√ duct sonographically not visible

Relationship to adjacent vessels:

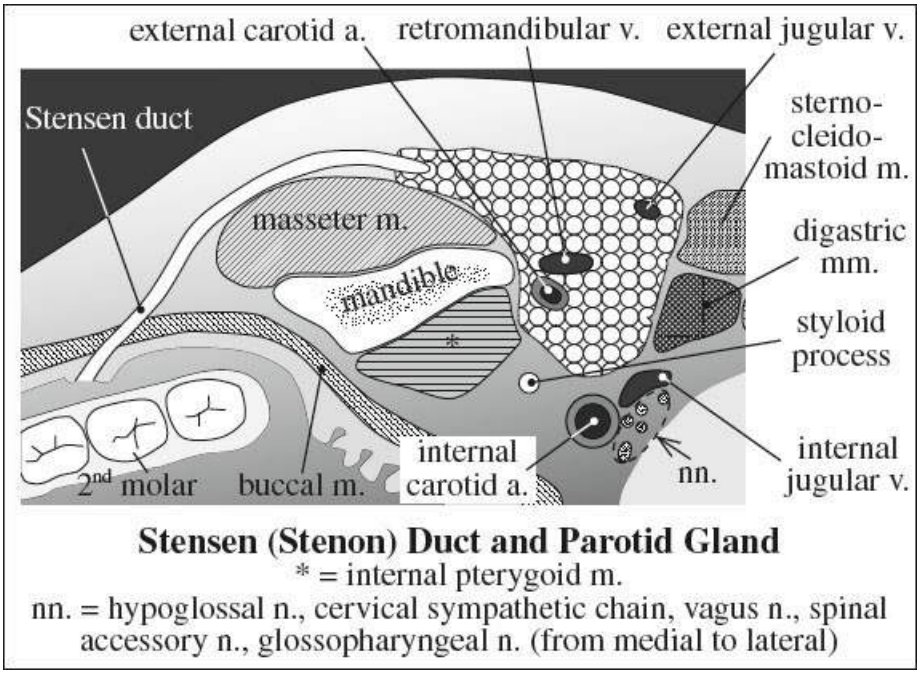
› tortuous facial artery may cross through parenchyma

› facial vein runs along anterosuperior part of gland
› ± branch vein connecting to retromandibular v. in posterior portion
› lingual artery and vein medial to gland

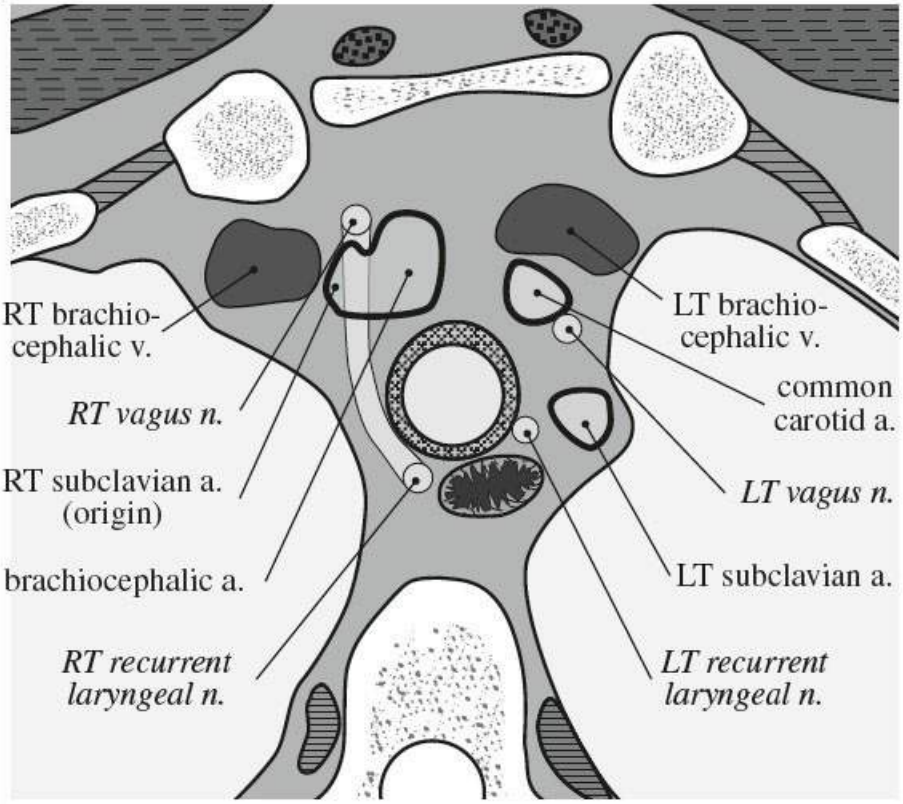
Sublingual Gland

Location: between geniohyoid m., intrinsic muscles of tongue, hyoglossal m. (medially) + mylohyoid m.; medial to mandible

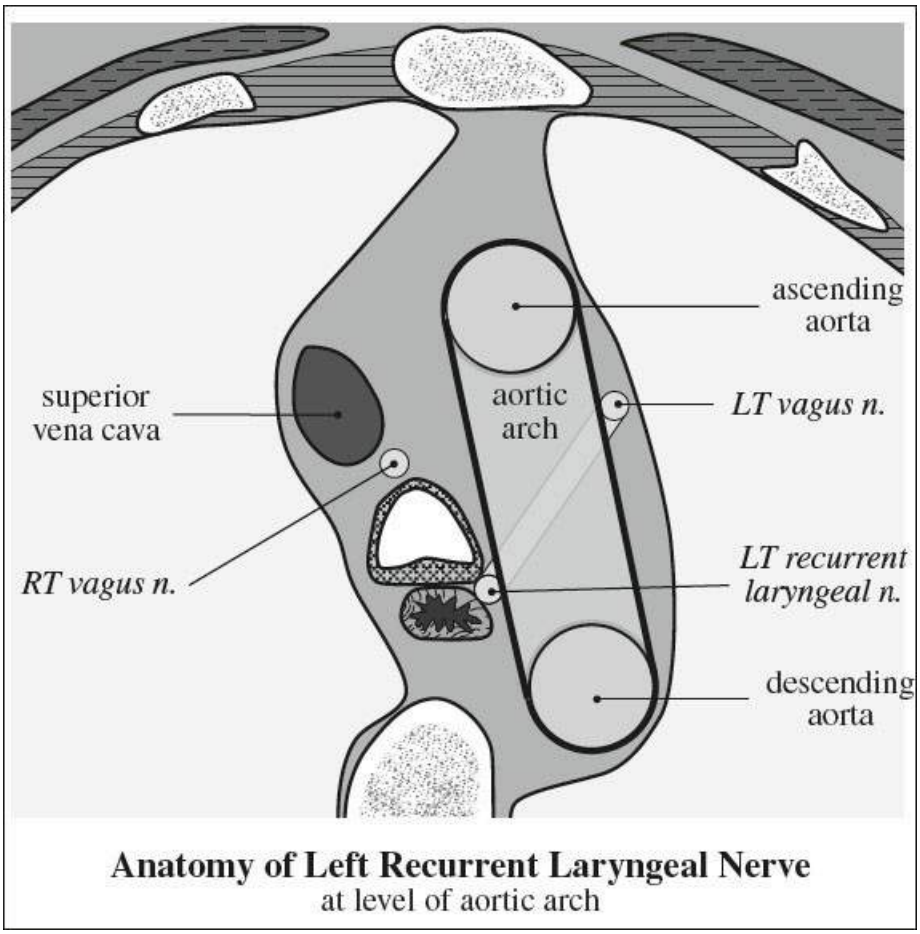
Drainage route: 8–20 excretory ducts with orifices on either side of frenulum; some form major sublingual duct of Bartholin connecting to submandibular duct



Stensen (Stenon) Duct and Parotid Gland
* = internal pterygoid m.
nn. = hypoglossal n., cervical sympathetic chain, vagus n., spinal accessory n., glossopharyngeal n. (from medial to lateral)

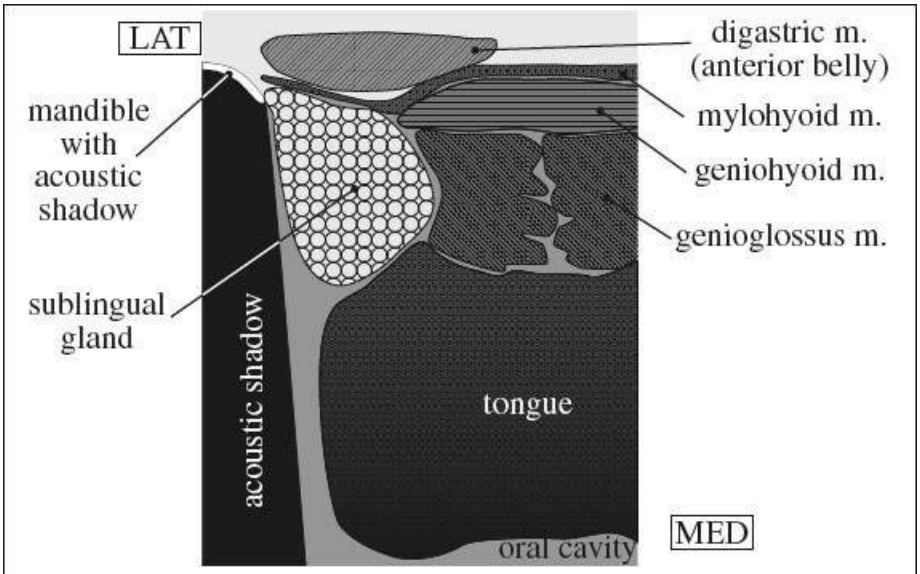


Anatomy of Right Recurrent Laryngeal Nerve
at level of origin of right subclavian artery



Anatomy of Left Recurrent Laryngeal Nerve
at level of aortic arch

Thyroid Hormones		
Thyroxin	T_4	4.5 – 12.0 µg/dL
Triiodothyronine	T_3	90 – 200 ng/dL
Thyroid stimulating hormone	TSH	0.4 – 4.5 µIU/mL
Free T_4 (0.03% of T_4)	FT_4	0.7 – 1.6 ng/dL
Free T_3 (0.4% of T_3)	FT_3	230 – 420 ng/L
Thyroxin-binding globulin	TBG	binds 70% of T_4
		binds 38% of T_3
Thyroxin-binding prealbumin	TBPA	binds 10% of T_4
		binds 27% of T_3
Albumin		binds 20% of T_4
		binds 35% of T_3
Radioiodine uptake	RAIU	8 – 35% @ 24 hr



US of Sublingual Gland
transverse image from inferiorly via floor of mouth

RECURRENT LARYNGEAL NERVE (RLN)

not directly visualized on CT

Origin: nucleus ambiguus in medulla of brainstem within vagus n.

Course:

crosses lateral in cerebellomedullary cistern → exits skull base via pars vascularis of jugular foramen (located within dural sheath shared by spinal accessory n. [CN XI]) → superior ganglion within jugular foramen → inferior ganglion immediately below jugular foramen → exit point of pharyngeal branches (containing sensory fibers of glossopharyngeal n. [CN IX]) + superior laryngeal n. → descends within carotid sheath posterolateral to internal carotid a. + posteromedial to jugular v.

(a) RT RLN:

Exit: from vagus n. anterior to subclavian a.

courses posteriorly beneath the subclavian a. at level of brachiocephalic bifurcation → right tracheoesophageal groove over surface of apical parietal pleura

Length to cricothyroid joint: 5–6 cm

(b) LT RLN:

Exit: from vagus at level of aortic arch

courses posteromedial beneath aortic arch through aorticopulmonary window + posterior to ligamentum arteriosum → ascends vertically to reach left tracheoesophageal groove

Length to cricothyroid joint: 12 cm

Innervation by superior laryngeal nerve:

motor fibers to cricothyroid + superior pharyngeal constrictor mm.

Innervation by recurrent laryngeal nerve:

intrinsic laryngeal mm. (posterior cricoarytenoid m. = main vocal cord abductor)

THYROID GLAND

Normal size: 4.0–4.8 cm (L) x 1.0–1.8 cm (W) x 0.8–1.6 (H) cm
Volume: L x W x H x π/6
Normal weight: 10–25 g
Physiology: hypothalamic TRH → anterior pituitary TSH → T_4 (= main hormone produced by thyroid); T_3 mainly produced by peripheral conversion of T_4; T_3 and T_4 are largely protein-bound in plasma to (mainly) TBG; only the unbound free portion (FT_3, FT_4) is active → increased cell metabolism by binding to nuclear receptors

√ intense homogeneous enhancement

CT:

√ homogeneous mildly hyperattenuating relative to surrounding neck musculature with an average attenuation of 80–100 (range, 70–120) HU

MR:

√ slightly hyperintense on T1WI + iso- to slightly hyperintense on T2WI relative to the neck musculature

NUC (^{99m}Tc pertechnetate / ^{123}I / ^{131}I):

√ symmetric uniform uptake in both lobes

N.B.: intravenous contrast medium impairs thyroid uptake of radioactive iodine for 4–8 weeks

Embryogenesis of Thyroid

Origin: derived from median thyroid anlage = endodermal thickening between 1st + 2nd pharyngeal arches → forming small pit at 24th day GA = **thyroid bud** → elongates into bilobate diverticulum → descends caudally while in contact with aortic primordium → reaches final location by 7 weeks GA

Cells: (a) thyroid **follicular cells** ← median thyroid anlage

(b) **parafollicular cells** (C cells) ← arise laterally from 4th pharyngeal pouch ← lateral thyroid anlagen (= ultimobranchial bodies) merge with products of median anlage after descent into infrahyoid portion of neck → dispersion of parafollicular cells throughout thyroid gland

Ectopic Thyroid Tissue

Location: (a) base of the tongue (90%);

(b) infrahyoid portion of neck (< 10%);

(c) lateral to midline = superficial to strap muscle (rare)

(d) beyond usual path of migration: mediastinum, heart, adrenal, bowel, ovary

Mean age at presentation: 40.5 years

√ absence of orthotopic thyroid tissue (in 70–80%)

NUC (^{99m}Tc-pertechnetate, ^{123}I, ^{131}I):

√ thyroid tissue identified in usual thyroid bed / at ectopic sites

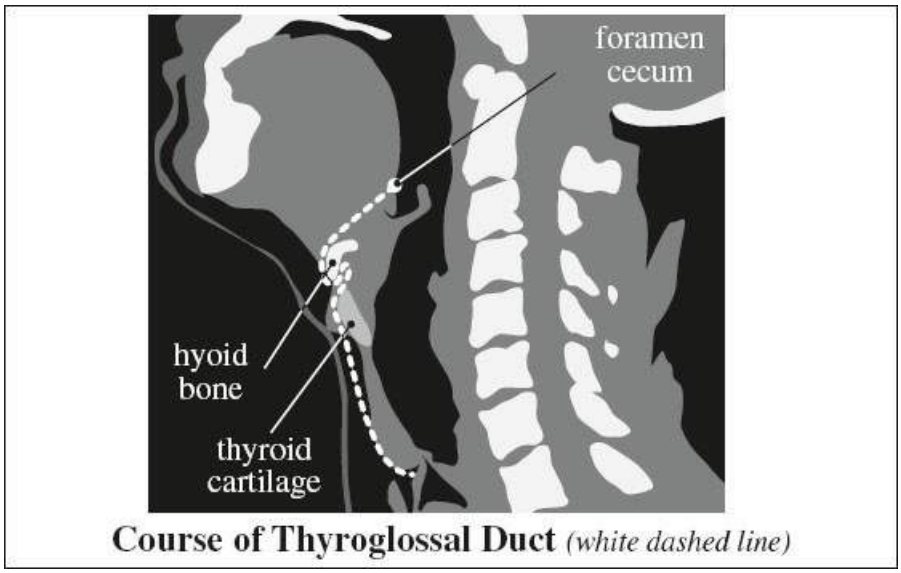
N.B.: normal thyroid gland may trap majority of radionuclide making identification of small ectopic rests difficult!

CT:

√ mildly increased attenuation of 70 HU ± 10 relative to adjacent muscle ← intrinsic iodine content

√ well-circumscribed homogeneous avidly enhancing mass
√ islands of low attenuation within ectopic thyroid tissue = clue to diagnosis of ectopic thyroid tissue

MR:
√ isointense to mildly hyperintense relative to musculature on T1WI
√ mildly hyperintense with variable enhancement on T2WI



Course of Thyroglossal Duct *(white dashed line)*

Embryogenesis of Thyroglossal Duct

= small temporary channel along which thyroid primordium descends in midline of neck to its final position → forms in 3rd week GA → usually involutes by 8th–10th week of fetal life prior to definite formation of thyroid

Origin: **foramen cecum** at base of tongue (= vertex of sulcus terminalis linguae formed by circumvallate papillae)

Course: passes from foramen cecum anterior to primordial hyoid bone → makes a recurrent loop through / posterior to precursor of hyoid bone → finally descends to infrahyoid portion of neck anterior to thyrohyoid membrane + thyroid cartilage + trachea + strap muscles

Inferior end: becomes **pyramidal lobe** of thyroid

Biosynthesis of Thyroid Hormone

(1) Uptake of iodide by thyrocytes

NIS (natrium-iodide symporter) gene:

› located on chromosome 9p12-13.2 → intrinsic thyrocyte-based plasma membrane glycoprotein NIS

Sodium iodide symporter (NIS):

driven by Na+/K+ ATPase cotransports two Na+ and one I- into follicular cell raising cytoplasmic iodine concentration to 20–40 times that of plasma (**iodide trapping**)

Biodistribution of NIS expression:

thyroid, salivary gland (ductal cell), gastric mucosa (parietal + mucus cells), lactating

mammary gland (nonlactating breast in 6%), lacrimal gland, choroid plexus, ciliary body, skin, placenta, thymus [lower levels in prostate, ovary, adrenal gland, lung, heart, colon, orbital fibroblasts, nasopharyngeal mucosa]

(2) Efflux into follicular lumen

(3) Organification onto thyroglobulin thyroid peroxidase → oxidisation of two I- to nonreactive I2 and very reactive I0 → iodinates tyrosyl residue of thyroglobulin within colloid

Thyroglobulin

produced in endoplasmic reticulum of follicular cell → secreted into colloid of thyroid follicle by exocytosis

PARATHYROID GLANDS

Embryology: parathyroid glands develop by 6 weeks GA + migrate into neck at 8 weeks

Size: 6 x 3–4 x 1–2 mm = 29.5 ± 17.8 (range, 25–65) mg

Histo: gland composed of chief cells (secretion of parathyroid hormone), oxyphil cells (packed with mitochondria of unknown function), transitional oxyphil cells mixed with adipose tissue

A. SUPERIOR PARATHYROID GLANDS

Embryology: derived from 4th pharyngeal pouches, descending together with thyroid gland in close relationship to its posterolateral lobes

Eutopic location:

posterior to superior / middle third of thyroid gland in tracheoesophageal groove on dorsal surface of thyroid / intracapsular (> 90%); posterior to inferior thyroid artery + recurrent laryngeal n.

◊ Fairly constant position due to minimal descent

Ectopic location:

› above upper pole of thyroid lobe (< 1%)

› posterior to pharynx / esophagus, on either side of neck or superior mediastinum (1%–4%)

› intrathyroidal (< 3%)

B. INFERIOR PARATHYROID GLANDS

Embryology: derived from 3rd pharyngeal (branchial) pouches migrating caudally with thymus

Eutopic location:

anterior / lateral / posterior to inferior third of thyroid (61%); anterior to inferior thyroid artery + recurrent laryngeal nerve

◊ More variable position ← descent over greater distance

Ectopic location:

› in neck, inferior to lower pole of thyroid lobe: either in thyrothymic ligament / associated with cervical portion of thymus (26%)

› on / adjacent to the posterior aspect of the middle third of the thyroid lobe (7%)

› in anterior mediastinum (4%–5%): within thymus / at posterior aspect of thymic capsule / in contact with great vessels

› along the carotid sheath (< 1%–2%)

› intrathyroidal (< 3%)

C. SUPERNUMERARY PARATHYROID GLANDS

5^{th} / 6^{th} gland may occupy an ectopic site

◊ Up to 12 parathyroids may be present!

D. ABSENCE OF 1 PARATHYROID GLAND

Surgical success rates for finding parathyroid glands:

› 95% for initial cervical exploration

› 60% for repeat surgical exploration

Cause for failure: overlooking an adenoma, multiple abnormal glands, diffuse hyperplasia

Localization technique:

US (75% sensitivity), thallium-technetium subtraction scintigraphy, MR (88% sensitivity)

LYMPH NODES OF THE NECK

Imaging of normal lymph nodes:

Shape: oval similar to a lima bean

CT:

√ iso- or hypoattenuating to muscle

MR:

√ low to intermediate signal intensity on T1WI

√ intermediate to high signal intensity on T2WI

US:

√ hypoechoic in comparison with muscle

√ ovoid shape with echogenic fatty hilum

Reactive lymph nodes:

Organism:

(a) bacterium

√ greater enlargement + inflammation of surrounding tissue

Cx: progression to suppurative adenopathy

(b) virus (CMV, infectious mononucleosis, HIV)

√ diffuse enlargement + little surrounding inflammation

(c) inflammatory cause: sarcoidosis

(d) idiopathic:

Kimura, Kawasaki, Kikuchi-Fujimoto disease

• signs of local or systemic infection

• painful mobile nodes at physical examination

√ normal to slightly enlarged in size

√ ± enhancement ← increased vascularity

A. CENTRAL COMPARTMENT

= between right and left carotid arteries

1. Delphian (prelaryngeal) / pretracheal

[The Delphic Oracle in the Greek world was consulted before all major undertakings. An enlarged Delphian node is ominously evidence of metastatic thyroid cancer.]

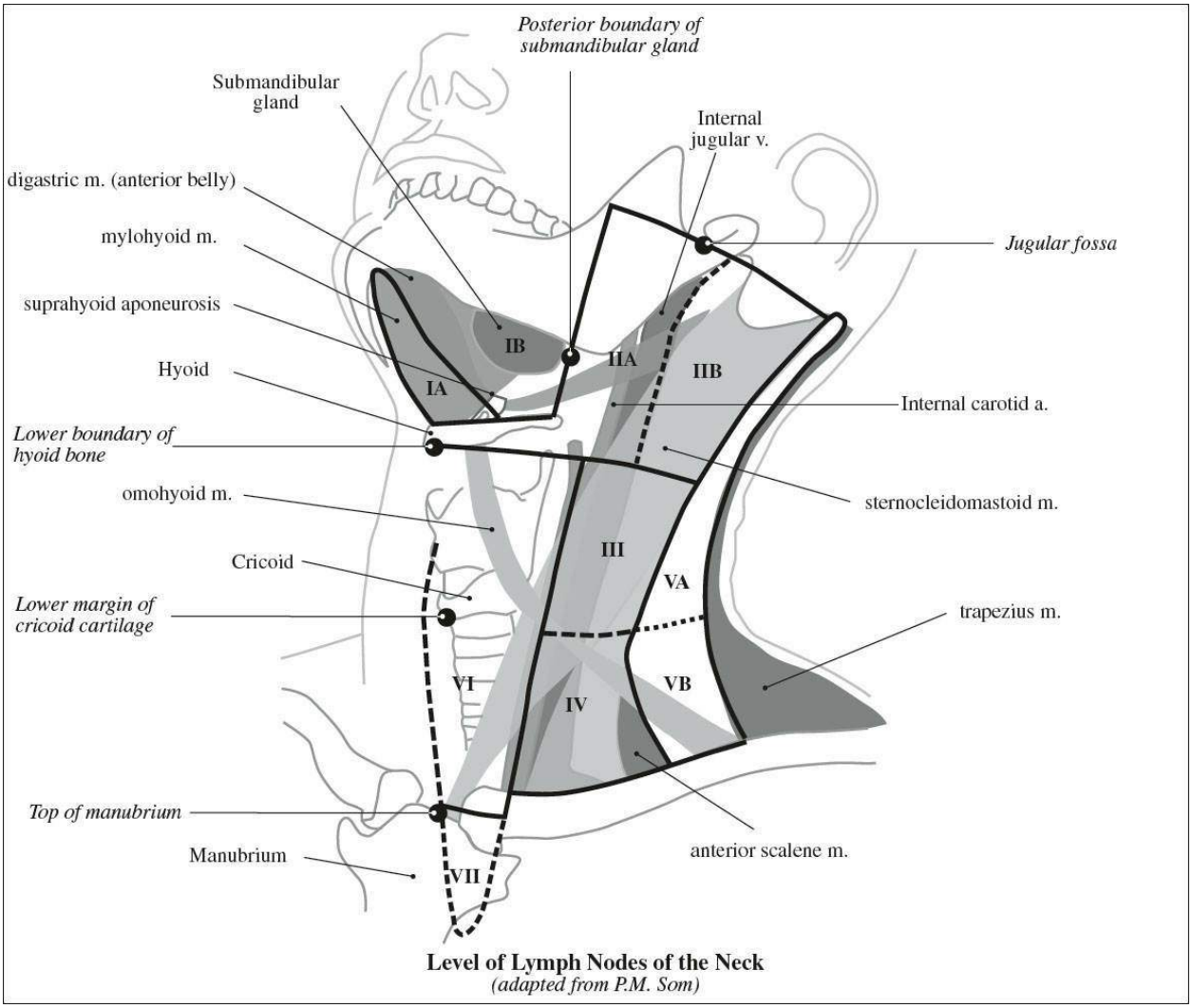
= level VI node (not routinely excised during radical neck dissection)

Involvement with: thyroid carcinoma, squamous cell carcinoma, laryngeal cancer

2. Paratracheal: alongside recurrent laryngeal nerve
3. Thymic / perithymic: within fatty tissue in the lower anterior part of neck

B. LATERAL COMPARTMENT

1. Internal jugular
   - › jugulodigastric node: < 15 mm maximal longitudinal diameter, < 10 mm axial diameter
   - › retropharyngeal: < 8 mm maximal longitudinal, < 10 mm axial diameter
   - › others: < 10 mm maximal longitudinal diameter, < 10 mm axial diameter
2. Spinal accessory: posterior triangle
3. Transverse cervical: supraclavicular



Level of Lymph Nodes of the Neck
(adapted from P.M. Som)

Essential anatomic landmarks:

jugular fossa of skull base, bottom of hyoid body, bottom of cricoid arch, top of manubrium, back edge of submandibular gland, back edge of sternocleidomastoid m., lateral posterior edge of anterior scalene m., anterior edge of trapezius m., internal + common carotid a., internal jugular v., clavicle, medial margin of anterior belly of digastric m., mylohyoid m.

I	above hyoid + below mylohyoid m. + anterior to posterior edge of submandibular gland (**submandibular nodes**); IA = between medial edge of anterior bellies of both digastric mm. (**submental nodes**)
II	skull base at jugular fossa + lower body of hyoid bone + anterior to posterior edge of sternocleidomastoid m. + posterior to posterior edge of submandibular gland; IIA = anterior to internal jugular vein (**upper internal jugular nodes**); IIB = posterior to internal jugular v. (**upper spinal accessory nodes**); **retropharyngeal node** = level II node medial to internal carotid a.; **jugulodigastric node** = where posterior belly of digastric muscle crosses internal jugular vein
III	lower body of hyoid + lower margin of cricoid arch + posterior edge of sternocleidomastoid m. (**midjugular nodes**)
IV	lower margin of cricoid + clavicle + posterior edge of sternocleidomastoid m. + posterolateral edge of anterior scalene m. + medial aspect of common carotid a. (**jugular nodes**)
V	behind posterior edge of sternocleidomastoid m.
VI	lower body of hyoid + top of manubrium + between common carotid aa. (**visceral nodes**)
VII	top of manubrium to innominate v. + between common carotid aa. (**superior mediastinal nodes**)

Supraclavicular nodes = level IV & VB nodes; **Internal jugular nodes of Rouvière** = level II or III or IV nodes

ABERRANT INTERNAL CAROTID ARTERY

= collateral pathway = anastomosis of enlarged inferior tympanic artery with enlarged caroticotympanic artery (= remnant of embryonic hyoid artery) ← involution of normal cervical portion (1st embryonic segment) of ICA

• vascular tympanic membrane, sensation of fullness in ear

• pulsatile tinnitus, hearing loss, vertigo

√ tubular soft-tissue density entering middle ear cavity posterolateral to cochlea → crossing mesotympanum along cochlear promontory → exiting anteromedial to become horizontal portion of carotid canal

√ protrusion into middle ear without bony margin

Cave: catastrophic hemorrhage from tympanotomy / biopsy

DDx: neoplastic process (eg, paraganglioma); inflammation (eg, effusive otitis media)

ADENOID CYSTIC CARCINOMA

= CYLINDROMA

Frequency: 4–15% of salivary gland cancers; 1–3% of all head & neck malignancies

Histo: (a) cribriform subtype, grade 1
(b) tubular subtype, grade 2
(c) solid / basaloid subtype, grade 3
◊ Perineural invasion is typical!

Age: 3rd–9th decade; maximum between 40 and 70 years; M=F

• slowly growing with pain ← tendency to infiltrate nerves

Location:

◊ Most often found in minor salivary glands

@ Minor salivary glands (most common; 25–31% of malignant neoplasms occur in minor salivary glands)
◊ Most common tumor of the minor salivary glands!
• nasal obstruction + swelling
Site: oral cavity > pharynx > nose > paranasal sinuses > trachea > larynx

@ Submandibular gland (15% of tumors affecting this gland)

@ Parotid gland (2–6% of tumors in this gland; arises from peripheral parotid ducts with propensity for perineural spread along facial nerve)
• hard mass + facial nerve pain / paralysis
√ infiltrating parotid mass

@ Trachea

MR:

√ hypo- to hyperintense (high signal corresponds to low cellularity with a better prognosis) on T2WI

√ adenoid cystic carcinomas have the highest relative incidence of perineural invasion (up to 56%)

Metastases to: lung, cervical lymph nodes, bone, liver, brain

Prognosis: slow growing but relentless malignant course with repeat recurrences; the greater the cellularity, the worse the prognosis (requires entire tumor); 60–69% 5-year survival rate; 40% 10-year survival rate

Rx: repeat surgical excision + radiation therapy

Laryngeal Adenoid Cystic Carcinoma

0.25–1% of all malignant laryngeal tumors

Histo: uniform small basaloid cells with large deeply staining ovoid nuclei arranged in anastomosing cords or islands

- coughing attacks, wheezing, hemoptysis
- CHARACTERISTIC paralysis of recurrent laryngeal nerve ← propensity to invade nerves
- absent history of cigarette smoking

Location: subglottis at junction with trachea (80%)

√ extensive submucosal tumor spread of entire larynx

√ invasion of cricoid cartilage, thyroid + esophagus

√ regional neck nodes hardly ever involved

ANGIOFIBROMA

Giant Cell Angiofibroma

= benign tumor with rapid growth mimicking malignancy / with slow growth over many years

Mean age: 45 years

Histo: pseudovascularized spaces within stromal matrix

Location: orbital region / eyelid (most common); buccal mucosa, submandibular region, parapharyngeal space

√ NO osseous erosion

CT:

√ circumscribed enhancing mass

MR:

√ usually hyperintense relative to muscle on T2WI

√ isointense relative to muscle on unenhanced T1WI

√ heterogeneous mass with stippled areas of low signal intensity / signal void ← multiple pseudovascular spaces

√ intense enhancement

Juvenile Angiofibroma

= most common benign nasopharyngeal tumor, can grow to enormous size and locally invade vital structures

Frequency: 0.5% of all head and neck neoplasms

Mean age: 15 years; almost exclusively in males

- recurrent + severe epistaxis (59%)
- nasal speech ← nasal obstruction (91%)
- facial deformity (less common)

Location: nasopharynx / posterior nares; center of mass within sphenopalatine foramen
Extension: posterolateral wall of nasal cavity; via pterygopalatine fossa into retroantral region / orbit / middle cranial fossa; laterally into infratemporal fossa
Vascular supply: primarily by ipsilateral internal maxillary / ascending pharyngeal / palatine artery
√ widening of pterygopalatine fossa (90%) with anterior bowing of posterior antral wall
√ osseous erosion of nasal cavity, hard palate, pterygoid plates
√ invasion of sphenoid sinus (⅔) from tumor erosion through floor of sinus
√ widening of inferior + superior orbital fissures → spread into orbit via inferior orbital fissure + into middle cranial fossa via superior orbital fissure
√ highly vascular nasopharyngeal mass
CECT:
√ avid enhancement of mass (only enhances on CT scan immediately after bolus injection)
MR (best for tumor extension into skull base / intracranially):
√ low to intermediate SI on T1WI with discrete punctate areas of hypointensity ← highly vascular stroma
√ heterogeneous intermediate SI on T2WI
√ avid enhancement with flow voids
Angio (to define vascular supply):
√ may involve branches of contralateral ICA + ECA
NOTE: Biopsy contraindicated!

ANGIOLIPOMA OF PAROTID GLAND

= benign nodular lesion similar to ordinary lipomas except for associated angiomatous proliferation
Age: rare before puberty
CT:
√ circumscribed (more common) / infiltrating mass
√ marked enhancement around fatty components
DDx: hemangioma with fatty degeneration

APICAL PETROSITIS

= PETROUS APICITIS = PETROSITIS
= infectious process caused by medial extension of acute otitis media into pneumatized petrous air cells
Frequency: chronic > acute apicitis
Etiology: spread from middle ear + mastoid infection; requires presence of air cells in petrous apices (which is normally found in 9–30% of population)
Organism: Streptococcus pneumoniae, Haemophilus influenzae, Staphylococcus aureus
• **Gradenigo syndrome** = classic triad of
  • deep facial (retroorbital) pain in distribution of cranial nerve V_1 (trigeminal pain) ← focal meningitis over petrous apex with irritation of gasserian ganglion in Meckel cavity
  • diplopia ← 6th nerve palsy
  • ipsilateral otorrhea ← otitis media

[Giuseppe Conte Gradenigo (1859–1926), Italian otolaryngologist in Wien, Torino and Napoli]

√ opacification of aerated petrous apex + air-fluid levels
√ osseous erosion
√ fluid in ipsilateral middle ear + mastoid

MR:
√ hyperintense signal on T2WI + hypointense on T1WI
√ avidly enhancing mass in pneumatized petrous apex
√ enhancing meninges ← adjacent meningeal inflammation

Cx: meningitis; epidural / brain abscess (ring enhancement, restricted DWI); venous sinus thrombosis; cranial nerve palsy (abducens, trigeminal, vagus nn.)

Mortality: up to 20% (prior to antibiotic era)

Rx: intravenous antibiotics, myringotomy, surgery

DDx: petrous apex osteomyelitis (nonpneumatized petrous apex, septal + cortical destruction, predisposing diabetes mellitus); neoplastic disease (rhabdomyosarcoma, metastasis); epidermoid tumor

BENIGN LYMPHOEPITHELIAL LESIONS

= BLL = HIV-ASSOCIATED LYMPHOEPITHELIAL CYSTS
= painless idiopathic swelling of one / both parotid glands characterized by chronic progression in the absence of retroviral therapy

Prevalence: 5% of HIV population

Cause: serves as index lesion for diagnosis of HIV infection without AIDS; NOT an AIDS defining illness

Pathogenesis: cystic dilatation of terminal salivary ducts

Age: 6th decade; M÷F = 2÷3 to 4÷5

Histo: polyclonal CD8+ lymphoid hypertrophy → obstruction + dilatation of intraglandular ducts

Location: one / both (20%) parotid glands

US:
√ cystic lesions with multiple small septations + small mural nodules (in 40%)
√ ± vascular pedicle entering the cystic region
√ moderately vascular (79%), hypervascular (14%), avascular (7%) on color Doppler

CT:
√ numerous (rarely isolated single) mixed cystic + solid lesions
√ reactive cervical lymphadenopathy
√ tonsillar hypertrophy

CECT:
√ rimlike enhancement around cystic parotid lesions
√ heterogeneous enhancement of solid parotid lesions

Cx: transformation into B-cell lymphoma (rare)

DDx: acute phase of Sjögren syndrome (lesions predominantly solid, of decreased echogenicity, smaller, more numerous), sarcoidosis, lymphoma, viral infection (mumps), Warthin tumor (frequently multicentric or bilateral, internal cystic elements, no cervical

adenopathy)

BRANCHIAL CLEFT ANOMALIES

= BRANCHIAL CLEFT CYST
= failure of involution of branchial cleft
Frequency: 2nd most common congenital lesion of head & neck after thyroglossal duct cyst!
• neck mass / cyst; respiratory compromise, dysphagia (if large)
Barium pharyngography:
√ performed for localization of a fistulous tract in 2nd + 3rd arch anomalies
Cx: high incidence of infection

First Branchial Cleft Cyst (5–8%)

= PAROTID LYMPHOEPITHELIAL CYST
Frequency: 5–8% of all branchial cleft anomalies (rare)
Age: middle-aged women
• enlarging mass near lower pole of parotid gland
• recurrent parotid abscesses near ear / angle of mandible
• otorrhea (if cyst drains into EAC) ± facial nerve palsy
Spectrum: branchial cyst (68%) / sinus (16%) / fistula (16%)
Location: from submandibular triangle (posterior / inferior to angle of mandible) near branches of facial nerve within parotid gland to preauricular region extending anterior / posterior to pinna to junction of cartilaginous + bony external auditory canal
Pathologic classification (Work):
Type 1 duplication anomaly of membranous EAC; derived from ectoderm + lined with squamous epithelium; no skin appendages
Site: postauricular region = course parallel to EAC; medial to concha of ear
Type 2 parotid cyst containing ectoderm and mesoderm involving EAC + pinna; skin appendages (hair follicles, sweat and sebaceous glands)
• otorrhea without otitis media
√ cystic mass within parotid or immediate periparotid region (superficial to / deep to parotid gland)
√ may extend into adjacent fat-containing parapharyngeal space ± connection to EAC
DDx: inflammatory parotid cyst, benign cystic parotid tumor, necrotic metastatic lymphadenopathy

Second Branchial Cleft Cyst (95%)

= incomplete obliteration of 2nd branchial cleft tract (cervical sinus of His) resulting in sinus tract / fistula / cyst (75%)
Frequency: 95% of all branchial cleft anomalies
◊ Most common branchial cleft abnormality!
Age: 10–40 years; M = F
Classification (Bailey):
Type I along anterior surface of sternocleidomastoid muscle, just deep to platysma

Type II: along anterior surface of sternocleidomastoid muscle, lateral to carotid space, posterior to submandibular gland adhering to the great vessels (most common)

Type III: extension medially between bifurcation of external and internal carotid arteries to lateral pharyngeal wall

Type IV: within pharyngeal mucosal space

Path: 1–10-cm large thin-walled cyst, lined by stratified squamous epithelium overlying lymphoid tissue, filled with turbid yellowish fluid ± cholesterol crystals

- skin openings with sinus / fistula
- painless fluctuant mass at mandibular angle
- history of multiple parotid abscesses unresponsive to drainage + antibiotics
- otorrhea (if connected to external auditory canal)

Location:
anywhere along a line from the oropharyngeal tonsillar fossa to supraclavicular region of neck; CLASSICALLY at anteromedial border of sternocleidomastoid muscle + lateral to carotid space + at posterior margin of submandibular gland; may be in parapharyngeal space (after extension through stylomandibular tunnel + middle constrictor muscle)

Internal opening: oropharyngeal tonsillar fossa

√ oval / round cyst near mandibular angle

√ displacement of sternocleidomastoid muscle posteriorly, carotid artery + jugular vein posteromedially, submandibular gland anteriorly

√ cyst may enlarge after upper respiratory tract infection / injury

US:

√ well-marginated thin-walled ovoid compressible hypoechoic mass:

√ occasionally fine internal echoes = internal debris (due to hemorrhage / infection) obscuring its cystic nature

√ lack of internal flow

CT / MR:

√ "beak" sign = curved rim of tissue pointing medially between internal + external carotid arteries (PATHOGNOMONIC)

√ slight enhancement of capsule

DDx: necrotic neural tumor, cervical abscess, submandibular gland cyst, cystic lymphangioma, necrotic metastatic / inflammatory lymphadenopathy

Atypical Second Branchial Cleft Cyst

Age: child / young adult

- protruding parotid gland
- bulging posterolateral pharyngeal wall

√ cystic mass projecting from deep margin of faucial tonsil toward skull base

Third Branchial Fistula / Cyst

= above superior laryngeal nerve

Frequency: extremely rare

Internal opening: piriform sinus anterior to fold formed by internal laryngeal nerve

Course: fistula pierces thyrohyoid membrane; passes anterior to vagus nerve + above

hypoglossal nerve + below glossopharyngeal nerve; between internal + external carotid arteries; caudolateral / posterolateral to proximal ICA + CCA

External opening: at base of neck anterior to sternocleidomastoid muscle

√ unilocular cystic mass within posterior cervical space

Fourth Branchial Fistula

= below superior laryngeal nerve

Frequency: extremely rare (R > L)

Internal opening: apex of piriform sinus

Course: between cricoid + thyroid cartilage, below cricothyroid muscle, caudal course between trachea + carotid vessels, deep to clavicle into mediastinum, looping forward below aorta (left side) / right subclavian artery (right side), ascending along ventral surface of common carotid artery, passing over hypoglossal nerve

External opening: at base of neck anterior to sternocleido-mastoid m. + anteroinferior to subclavian a.

• recurrent episodes of "suppurative thyroiditis'" / neck abscesses

Site: 90% on left side

CALCIFIC LONGUS COLLI TENDINITIS

= ACUTE CALCIFIC RETROPHARYNGEAL TENDINITIS

= calcification anterior to C1–C2 ← deposition of calcium hydroxyapatite

Location: near insertion of longus colli tendon in close proximity to anterior arch of C1

Site: superior oblique tendon fibers of the longus colli muscle

• recent history of upper respiratory infection / minor trauma to head or neck, acute to subacute onset of neck pain and stiffness

• dysphagia, odynophagia

• low-grade fever, mildly elevated WBC count

√ prevertebral / retropharyngeal soft-tissue swelling

√ amorphous calcification anterior to C1–C2 (CT most sensitive)

√ fluid originating in prevertebral space ± extension to retropharyngeal space:

√ retropharyngeal space smoothly expanded in all directions from C1 tapering inferiorly to C5-6

√ effusions may involve both lateral atlantoaxial joints

√ no rimlike enhancement

Rx: antiinflammatory medication

DDx: retropharyngeal abscess (similar clinical manifestation, enhancing wall), suppurative retropharyngeal lymphadenitis (low-attenuation centers), traumatic injury, infectious spondylitis

CAROTID ARTERY STENOSIS

High-grade ICA stenosis is associated with increased risk for TIA, stroke, carotid occlusion, embolism arising from thrombi forming at site of narrowing

Increased risk for stroke:

(a) significant ICA stenosis → compromised blood flow:

◊ Reduction of blood flow occurs at 50–60% diameter stenosis / 75% area stenosis
◊ 2% risk of stroke with nonsignificant stenosis
◊ 16% incidence of stroke with significant stenosis
◊ 2% incidence of subsequent stroke following endarterectomy

(b) intraplaque hemorrhage → embolic stroke

Histo:

Arteriosclerosis = generic term for all structural changes resulting in hardening of the arterial wall

1. **Diffuse intimal thickening**
   = growth of intima ← migration of medial smooth muscle cells into subendothelial space through fenestrations in internal elastic lamella associated with increasing amounts of collagen, elastic fibers, glycosaminoglycans
   Age: beginning at birth slowly progressing to adult life
2. **Atherosclerosis**
   = intimal pool of necrotic, proteinaceous + fatty substances within hardened arterial wall
   Location: large + medium-sized elastic and muscular arteries
   (a) <u>fatty streak</u> = superficial yellow-gray flat intimal lesion characterized by focal accumulation of subendothelial smooth muscle cells + lipid deposits
   (b) <u>fibrous plaque</u> = *whitish protruding lesion* consisting of central core of lipid + cell debris surrounded by smooth muscle cells, collagen, elastic fibers, proteoglycans; fibrous cap separates lipid core (= atheroma) from vessel lumen
   (c) <u>complicated lesion</u> = fibrous plaque with degenerative changes such as calcification, plaque hemorrhage, intimal ulceration / rupture, mural thrombosis
   Plaque hemorrhage = vascularized plaque may cause ulceration, thrombosis + embolism, and luminal narrowing
   ◊ In 93% of symptomatic patients
   ◊ In 27% of asymptomatic patients
   Plaque ulceration exposes thrombogenic subendothelial collagen + lipid-rich material
   ◊ Frequent in plaques occupying > 85% of lumen
   ◊ 12.5% stroke incidence per year
3. **Mönckeberg sclerosis** = medial calcification
4. **Hypertensive arteriosclerosis**

Temporal course of carotid artery stenosis:

1. Stable stenosis (68%)
2. Progressive stenosis to > 50% diameter reduction (25%)

Angiography:

@ Extracranial
√ smooth asymmetrical excrescence encroaching upon vessel lumen
√ crater / niche = ulceration
√ mound within base of crater = mural thrombus
√ **Holman "carotid slim" sign** = diffuse narrowing of entire contrasted ICA distal to high-grade stenosis ← decrease in perfusion pressure
√ occlusion of ICA

@ Intracranial
√ carotid siphon stenosis

- √ retrograde flow in ophthalmic artery filled via ECA
- √ small vessel occlusion
- √ focal areas of slow flow
- √ early draining vein = reactive hyperemia = "luxury perfusion" ← shunting between arterioles + venules surrounding an area of ischemia
- √ ICA-MCA slow flow = delayed arrival + washout of ICA-MCA distribution in comparison to ECA

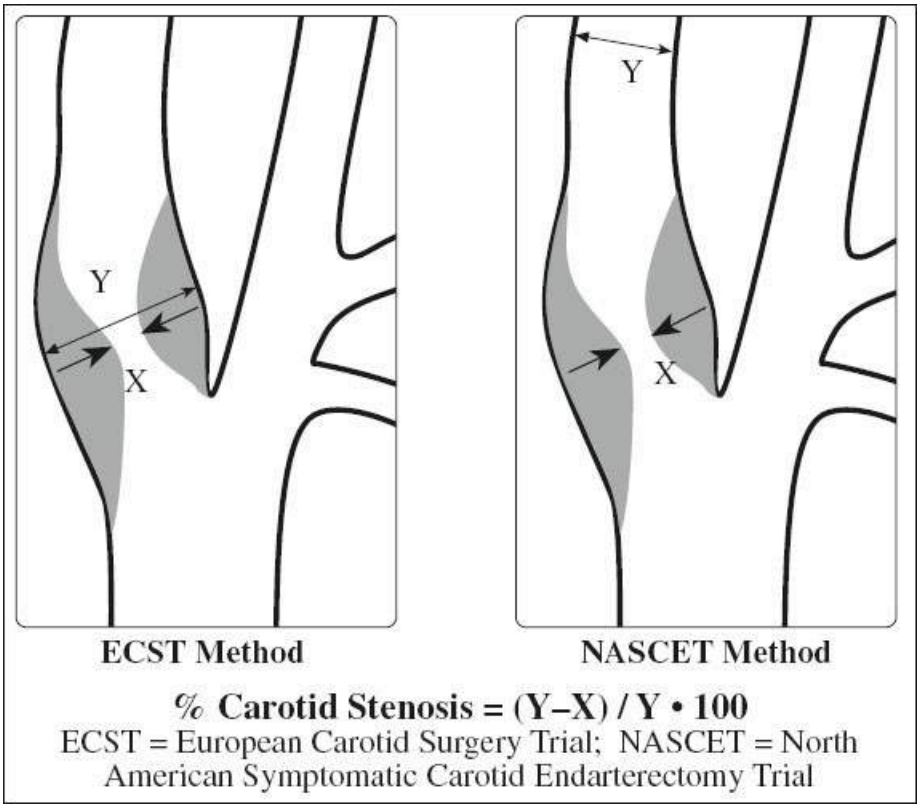
Carotid endarterectomy:

Benefit: 17% reduction of ipsilateral stroke at 2 years in patients with > 70% carotid stenosis (NASCET = North American Symptomatic Carotid Endarterectomy Trial)

Risk: 1% mortality; 2% risk of intraoperative neurologic deficit

Predilection Sites of Arterial Stenosis

	Incidence of Lesions	
	Stenosis	*Occlusion*
Right ICA origin	33.8%	8.6%
Left ICA origin	34.1%	8.7%
Right vertebral artery origin	18.4%	4.8%
Left vertebral artery origin	22.3%	2.2%
Right carotid siphon	6.7%	9.0%
Left carotid siphon	6.6%	9.2%
Basilar artery	7.7%	0.8%
Right MCA	3.5%	2.2%
Left MCA	4.1%	2.1%



Carotid Duplex Ultrasound

Indications for carotid duplex US:

(1) Screening for suspected extracranial carotid disease
  (a) high-grade flow-limiting stenosis
  (b) low-grade stenosis with hemorrhage
(2) Nonhemispheric neurologic symptomatology
(3) History of transient ischemic attack / stroke
(4) Asymptomatic carotid bruit
(5) Retinal cholesterol embolus
(6) Preoperative evaluation before major cardiovascular surgery
(7) Intraoperative monitoring of vascular patency during endarterectomy
(8) Sequential evaluation after endarterectomy
(9) Monitoring of known plaque during medical treatment

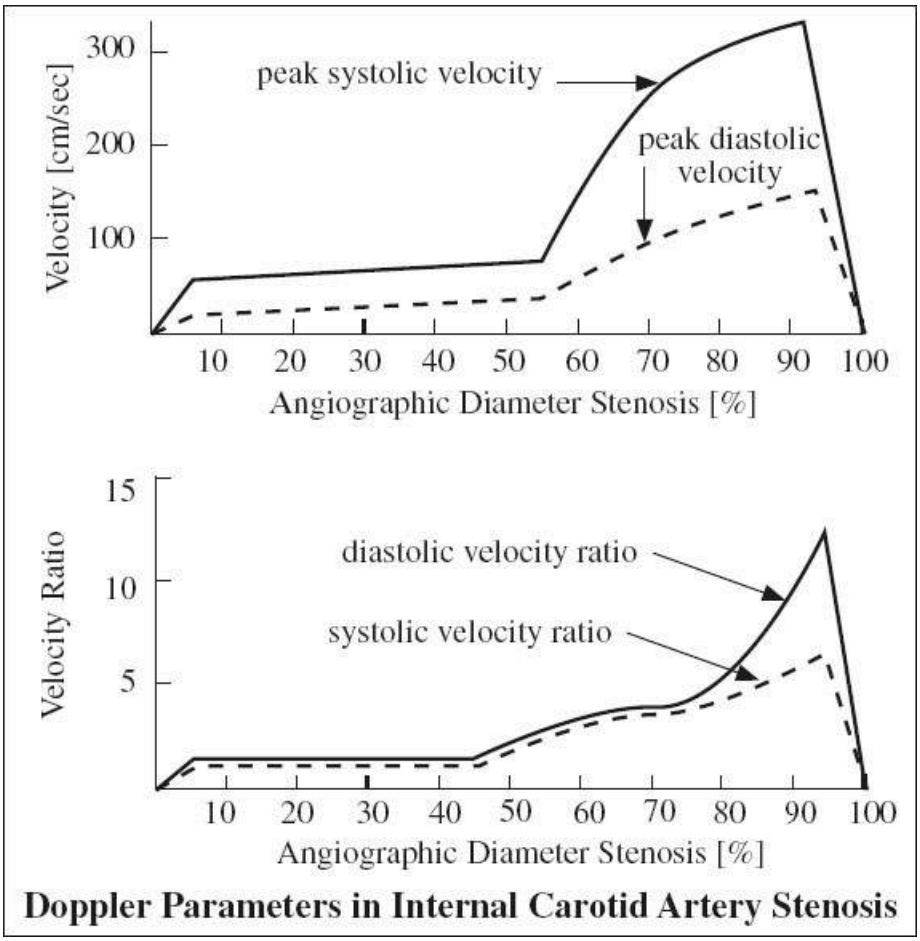
Grading of Internal Carotid Stenosis

= severity of stenosis is primarily graded as a ratio of lumen diameter narrowing NOT reduction in cross sectional area

Decrease in Luminal Diameter vs. Cross-sectional Area	
Decrease in Lumen Diameter	*Decrease in Cross-sectional Area*
20%	36%
40%	64%
60%	84%
80%	96%

Limitations of assessment by US:

1. Calcification > 1 cm in length obscures vessel lumen
   ◊ A jet associated with a stenosis of > 70% usually travels at least 1 cm downstream allowing conclusion about degree of obscured stenosis!
2. Contralateral high-grade stenosis
   = ipsilateral ICA functions as collateral → increased blood flow velocities
   ◊ Use velocity ratios to compensate for this effect!
3. Tortuosity of artery
4. Increased depth of artery
5. "High" bifurcation → possibly obscured by mandible



Doppler Parameters in Internal Carotid Artery Stenosis

Accuracy of duplex scans (compared to arteriography) for ICA lesions:

91–94% sensitivity, 85–99% specificity, 90–95% accuracy for > 50% ICA diameter stenosis

A. NORMAL (0% diameter reduction)
   √ no evidence of plaque
   √ peak systolic velocity (PSV) < 125 cm/sec
   √ no spectral broadening (= clear window under systole)
B. MINIMAL DISEASE (0–15% diameter reduction)
   √ minimal amount of plaque
   √ PSV < 125 cm/sec
   √ minimal spectral broadening in deceleration phase of systole
C. MODERATE DISEASE (16–49% diameter reduction)
   √ moderate amount of plaque
   √ peak systole < 125 cm/sec
   √ end-diastolic velocity (EDV) < 40 cm/sec
   √ poststenotic spectral broadening throughout systole
D. SEVERE DISEASE = hemodynamically SIGNIFICANT LESION
   (a) 50–69% stenosis
      √ PSV 125–230 cm/sec
      √ EDV 40–100 cm/sec
   (b) > 70% stenosis (→ benefit of endarterectomy documented in NASCET study)
      √ peak systole > 230 cm/sec
      √ end diastole > 100 cm/sec
      √ peak systolic velocity ratio of ICA÷CCA > 4.0
E. CRITICAL STENOSIS (> 95% diameter reduction)
   √ PSV + EDV return to <u>normal</u> range / flow undetectable
   √ "string" sign on color Doppler with slow-flow sensitivity setting
F. OCCLUSION
   √ NO signal in ICA on longitudinal / transverse images (color sensitivity + velocity scale must be set low enough to clearly discern flow signals within internal jugular vein)
   √ absence of diastolic flow / diastolic flow reversal in CCA (= high impedance flow)
   √ increased diastolic flow in ECA (if ECA assumes the role of primary supplier of blood to brain)
   √ increase in peak systolic velocities in contralateral ICA ← collateral flow

Common Carotid Waveform Analysis

A. DISTAL OBSTRUCTION
   √ high-pulsatility waveform
      ◊ Pulsatility changes occur only with > 80% stenosis
   √ reduced amplitude
B. PROXIMAL OBSTRUCTION
   √ low-amplitude damped waveform

Hemodynamic Variations of Carotid Stenosis

A. MORPHOLOGY OF STENOSIS

1. Degree of stenosis: velocities increase up to a luminal diameter of 1.0–1.5 mm
2. Length of stenosis: peak velocities decrease with length of stenosis

√ use the same angle + beam steering direction when following a patient for disease progression

B. PHYSIOLOGIC VARIABILITY

◊ A range of velocities may be encountered with a given degree of stenosis!
◊ ICA÷CCA ratio obviates effects of physiologic variability!
◊ Compare left with right waveforms to avoid errors!
◊ Measure volume flow (more sensitive because of contralateral compensatory flow increase)

Cause:

1. Cardiac output
2. Pulse rate
3. Flow velocity: ↑ with obstruction in collateral vessels, ↓ with proximal obstruction in same vessel
4. Normal helical nature of blood flow with many different velocity vectors + nonaxial blood flow NOT detectable by color Duplex imaging
5. Peripheral resistance
6. Arterial compliance
7. Hypertension
8. Blood viscosity

Doppler Spectrum Analysis
(Consensus Conference of Society of Radiologists in Ultrasound 2002)

Diameter Stenosis (%)	*ICA Peak Systolic Velocity (cm/sec)*	*ICA/CCA Peak Systolic Velocity Ratio*	*ICA End-Diastolic Velocity (cm/sec)*	*Plaque*
Normal	< 125	< 2.0	< 40	none
< 50	< 125	< 2.0	< 40	< 50% diameter reduction
50–69	125–230	2.0–4.0	40–100	≥ 50% diameter reduction
> 70	> 230	> 4.0	> 100	≥ 50% diameter reduction
Critical stenosis	low / undetectable	variable	variable	massive, detectable lumen
Occlusion	undetectable	not applicable	undetectable	no detectable lumen

Carotid Plaque

1. Asymptomatic patients with diffuse atherosclerotic disease:
   Prevalence of > 50% stenosis: 18–20%
2. Symptomatic patients with stroke, TIA, amaurosis fugax ← emboli from atheromas at carotid bifurcation
   Prevalence of > 50% stenosis: 14%

Formation Theory of Carotid Plaque

1. Stagnant eddy that rotates at outer vessel margin (away from and opposite to flow divider = area of flow separation + low shear stress) → net influx of fluid into subendothelial tissue with progressive deposition of lipids + smooth muscle cell proliferation
2. Increased likelihood of intraplaque hemorrhage ← vascularization of plaque with fragile vessels derived from vasa vasorum / from lumen) + fissuring at a critical size
   ◊ As the degree of stenosis increases, it is more likely that plaques become denser +

more heterogeneous demonstrating an irregular luminal surface!

Density of Carotid Plaque

1. Hypoechoic = low-echogenicity plaque
   = fibrofatty plaque / hemorrhage
   √ echogenicity less than sternocleidomastoid muscle
   √ flow void / flow disturbance on color Duplex
2. Isoechoic plaque
   = smooth muscle cell proliferation / laminar thrombus
   √ echogenicity equal to sternocleidomastoid muscle + lower than adventitia
3. Hyperechoic = moderately echogenic (fibrous) plaque
   √ echogenicity higher than sternocleidomastoid muscle + similar to adventitia
4. Calcification = strongly echogenic plaque
   √ acoustic shadow impairs visualization of intima

Texture of Carotid Plaque

1. Homogeneous (stable) plaque
   Histo: deposition of fatty streaks + fibrous tissue; rarely shows intraplaque hemorrhage / ulcerations
   √ homogeneous uniform echo pattern with smooth surface (acoustic impedance similar to blood)
2. Heterogeneous (unstable) plaque
   = mixture of high, medium, and low-level echoes with smooth / irregular surface; may fissure / tear resulting in intraplaque hemorrhage / ulceration + thrombus formation → embolus / increasing stenosis
   B-mode ultrasound has 90–94% sensitivity, 75–88% specificity, 90% accuracy for intraplaque hemorrhage!
   MRI depicts intraplaque hemorrhage (methemoglobin) on T1 fat-suppressed SPGR / FLASH sequence
   Histo: lipid-laden macrophages, monocytes, leukocytes, necrotic debris, cholesterol crystals, calcifications
   √ anechoic areas within plaque (= hemorrhage / lipid deposition / focal plaque degeneration)
   √ heterogeneous complex echo pattern

Plaque Texture vs. Prognosis

Consequences	*Homogeneous*	*Heterogeneous*
Neurologic deficit	4%	27%
Ipsilateral infarction by CT	12%	24%
Ipsilateral symptoms	22%	50%
Progressive stenosis	18%	77%

Surface Characteristics of Carotid Plaque

◊ US unreliable due to poor visualization of intima

4 Categories: › smooth

› mildly irregular
› markedly irregular
› ulcerated

1. Intimal thickening
   Histo: fatty streaks
   √ wavy / irregular line paralleling vessel wall extending > 1 mm into vessel lumen
2. Ulcerated plaque
   Accuracy: 60% sensitive, 60–70% specific
   ◊ The presence of intraplaque hemorrhage is much more common than normally appreciated (neither arteriography nor US has proved reliable)!
   √ isolated crater of > 2 mm within surface of plaque demonstrated on transverse + longitudinal images
   √ reversed flow vortices extending into plaque crater demonstrated by color Doppler
   √ proximal + distal undercutting of plaque
   √ anechoic area within plaque extending to surface

Errors In Duplex Ultrasound

1. Error in proper localization of stenosis (6%)
   Cause: ECA stenosis placed into ICA / carotid bifurcation or vice versa
2. Mistaking patent ECA branches for carotid bifurcation (4%)
   Cause: complete occlusion of ICA not recognized
   √ disparity in position of bifurcation between left and right
   √ no difference in waveform pulsatility
   √ high-resistance waveform in CCA
3. Interpreter error in estimating severity of stenosis (2.5%):
   » usually overestimation, rarely underestimation
   √ absence of one / more components for diagnosis which are
   (a) significant elevation of peak velocity
   (b) poststenotic turbulence
   (c) extension of high velocity into diastole
4. Superimposition of ECA + ICA (2%)
   Cause: strict coronal orientation of ECA + ICA
   √ superimposition can be avoided by rotation of patient's head to opposite side
5. Severe stenosis mistaken for occlusion
   √ minimal flow not detectable
   √ angiogram necessary with delayed images
6. Weak signals misinterpreted as occlusion
7. Normal / weak signals in severe stenosis
   Cause: severe stenosis causes a decrease in blood flow and peak velocity → return to normal velocity levels
   √ high resistivity in CCA
8. Point of maximum frequency shift not identified
   Cause: extremely small lumen / short segment of stenosis
   √ unexplained (poststenotic) coarse turbulence

√ collateral flow in ipsilateral ECA
√ abnormal CCA resistivity

9. Stenosis obscured by plaque / strong Doppler shift in overlying vessel
10. Inaccessible stenosis
    √ abnormal CCA resistivity
    √ abnormal oculoplethysmography
11. Unreliable velocity measurements
    (a) higher velocities: HTN, severe bradycardia, obstructive contralateral carotid disease, anemia, hyperthyroidism
    (b) lower velocities: arrhythmia, aortic valvular lesion, CHF, severe cardiomyopathy, proximal obstructive carotid lesion ("tandem lesion"), > 95% ICA stenosis
    (c) **aliasing** = high velocities are displayed in reversed direction below zero baseline due to Doppler frequency exceeding half the pulse repetition frequency
    Remedy: shift zero baseline; increase pulse repetition frequency; increase Doppler angle; decrease transducer frequency; use continuous-wave Doppler probe
    (d) misalignment of Doppler "Angle Correct" cursor
    = cursor not aligned with blood stream line introducing a wrong Doppler angle
    ◊ Doppler angle larger than actual angle means velocity measurement are higher than actual velocity!

Error in Doppler "Angle Correct Cursor" Alignment
at an Actual Velocity of 50 cm/sec

Actual Angle	*Erroneous Angle*	*Estimated Velocity*	*Percent Error*
0°	5°	50.2 cm/sec	0.4%
20°	25°	51.8 cm/sec	3.6%
40°	45°	54.2 cm/sec	8.4%
60°	65°	59.2 cm/sec	18.3%
80°	85°	99.6 cm/sec	99.0%

CHOANAL ATRESIA

◊ Most common cause of neonatal nasal obstruction!

Frequency: 1÷5,000 to 1÷8,000 neonates; M < F

Etiology: failure of perforation of buccopharyngeal + oronasal membrane, which normally perforates by 7th week EGA

Associated anomalies (in 50–75%):
acrophalyngosyndactyly, amniotic band syndrome, malrotation of bowel, Crouzon syndrome, fetal alcohol syndrome, DiGeorge syndrome, Treacher-Collins syndrome, chromosome 18 / 12 anomalies, polydactyly, coloboma, facial cleft, CHD, tracheoesophageal fistula, craniosynostosis

Location: bilateral÷unilateral atresia = 3÷2 to 2÷1

- respiratory distress in bilateral choanal atresia (relieved by crying in neonates who are obligatory nasal breathers during first 2–6 months)
- nasal stuffiness, rhinorrhea, infection in unilateral choanal atresia

Types:

A. OSSEOUS / BONY SEPTATION (85–90%)
Cause: incomplete canalization of choanae
√ fusion of hard palate + vomer + ventral clivus with nasopharyngeal atresia
B. MEMBRANOUS SEPTATION (10–15%)
Cause: incomplete resorption of epithelial plugs
C. OSSEOMEMBRANOUS

CT (preceded by vigorous suctioning + administration of topical decongestant):
√ narrowing of choanal orifice to a width of < 3.4–3.7 mm (in children < 2 years of age)
√ inward bowing of posterior maxilla
√ deviation / bowing of nasal septum
√ fusion / thickening of vomer
√ bone / soft-tissue septum extending across posterior choanae
Dx: nasal catheter cannot be advanced to beyond 32 mm
Cx: bilateral choanal atresia is LIFE-THREATENING
Rx: endoscopic perforation, choanal reconstruction

CHOLESTEATOMA

= KERATOMA = EPIDERMOID
= epithelium-lined sac characterized by accumulation of desquamated keratin epithelium → bone destruction by pressure + increase in osteoclastic activity
Location: middle ear cavity, other pneumatized portions of temporal bone
Histo: (a) acellular keratin debris = content of sac
(b) matrix = biologically active sac lining consisting of
› inner layer of keratinizing squamous epithelium
› outer layer of subepithelial connective tissue (= perimatrix) producing proteolytic enzymes → bone resorption
√ NO enhancement
• pearly white lesion diagnosed otoscopically in 95%
Cx: (1) Infection → malodorous discharge
(2) Erosion of ossicular chain, scutum, mastoid bone, Körner septum

DDx of soft-tissue attenuation:
(1) Fluid attenuation of chronic otitis media
(2) Inflammation / infection (NO restricted diffusion)

Primary Cholesteatoma (2%)

= CONGENITAL CHOLESTEATOMA = EPIDERMOID CYST
= derived from aberrant embryonic ectodermal rests in temporal bone (commonly petrous apex) / epidural space / meninges
• conductive hearing loss (hypoacusis) in child with NO history of otorrhea, membrane perforation, otologic procedure
• cholesteatoma seen through intact tympanic membrane (usually difficult due to stenosis of EAC)
Associated with: dysplasia / atresia / stenosis of EAC /middle ear cavity
Location:

(a) epitympanum (commonly in anterior superior quadrant of middle ear cavity just above opening of eustachian tube)
(b) petrous pyramid: internal auditory canal first involved
(c) meninges: scooped out appearance of petrous ridge
(d) cerebellopontine angle: erosion of porus, shortening of posterior canal wall
(e) jugular fossa: erosion of posteroinferior aspect of petrous pyramid

Cx: facial palsy, mastoiditis, intracranial disease

Secondary Cholesteatoma (98%)

= INFLAMMATORY CHOLESTEATOMA = ACQUIRED EPIDERMOID

Pathophysiology:

(a) invagination theory = eustachian tube dysfunction → vacuum phenomenon in middle ear cavity → formation of posterosuperior retraction pocket in pars flaccida → repeated episodes of ear inflammation (= chronic otitis media)
(b) epithelial invasion theory = marginal perforation of eardrum → ingrowth of keratinizing stratified squamous epithelium

Location: middle ear cavity

Age: usually > 40 years

- chronic foul-smelling otorrhea
- facial paralysis ← compression of nerve VII at geniculate ganglion
- conductive hearing loss ← compromise of CN VIII in internal auditory canal / involvement of cochlea or labyrinth
- severe vertigo (labyrinthine fistula)

Type:

1. **Pars flaccida cholesteatoma** (80%)
   = PRIMARY ACQUIRED CHOLESTEATOMA
   = **Attic cholesteatoma**
   Site: centered in Prussak space (pars flaccida invaginates toward Prussak space)
   √ rounded expansile lobulated lesion
   √ increasing width of attic
   √ initially destruction of lateral wall of attic, particularly erosion of drum spur (scutum)
   √ medial displacement + erosion of auditory ossicles
   √ extension superiorly into attic + mastoid air cells through aditus ad antrum
   √ destruction of Körner septum
2. **Pars tensa cholesteatoma** (20%)
   = SECONDARY ACQUIRED CHOLESTEATOMA
   Site: centered in sinus tympani / facial recess
   √ lateral displacement of auditory ossicles
   √ erosion of ossicular chain: first affecting long process of incus

CT:

√ nondependent homogeneous mass
√ perforation of tympanic membrane posterosuperiorly (= pars flaccida)
√ poorly pneumatized mastoid (frequent association)
√ erosion of tegmen tympani (with more extensive cholesteatoma) → extradural mass ±

formation of meningoencephalocele
√ destruction of labyrinthine capsule (less common) involving the lateral semicircular canal first → labyrinthine / perilymphatic fistula
√ erosion of bony facial canal in its tympanic / mastoid pars

MR (adjunct to CT ONLY if doubt in diagnosis):
√ iso- / hypointense relative to cortex on T1WI
CAVE: occasional T1-hyperintensity similar to "white" epidermoid cyst ← high protein content
√ mildly hyperintense lesion on T2WI + FLAIR
√ restricted diffusion (highly hyperintense) on DWI ← high keratin content
FN: mural / evacuated cholesteatoma, lesion < 2–3 mm
FP: residual hemorrhage after recent surgery; silastic sheet; bone pâté; cerumen in EAC; cholesterol granuloma; artifact ← dental brace; middle ear / mastoid abscess
√ relatively hypointense ADC map (DDx: cholesterol granuloma very hyperintense)
√ NO delayed enhancement 45–60 min after Gd-DTPA (DDx: cholesterol granuloma enhances ← inflammatory / granulation / scar tissue)

Cx: (1) Intratemporal: ossicular destruction; facial nerve paralysis (1%); labyrinthine fistula; automastoidectomy; complete hearing loss
(2) Intracranial: meningitis; cerebritis; subdural / epidural empyema; temporal lobe abscess; sigmoid sinus thrombosis; CSF rhinorrhea

Rx: canal-wall-down / canal-wall-up tympanoplasty with recurrence rates of 7% and 20%, respectively

DDx: chronic otitis media; granulation tissue (= cholesterol granuloma); brain herniation through tegmen defect; neoplasm (rhabdomyosarcoma, squamous cell carcinoma)

Cholesteatoma of External Auditory Canal

Incidence: 0.1–0.5%
Cause: spontaneous (most), prior trauma, surgery, radiation
Path: local invasion of EAC by squamous epithelial lining into underlying bone → periostitis, canal wall erosion
Age: older age group
• chronic dull pain, otorrhea

CT:
√ focal soft-tissue within EAC (typically inferior wall)
√ canal wall erosion into underlying bone

DDx: carcinoma, otitis externa

CHOLESTEROL GRANULOMA

= CHOLESTEROL CYST
= acquired benign chronic inflammatory mass in petrous bone
◊ Most common lesion arising in petrous apex!

Pathophysiology:
mucosal edema → exposure of bone marrow → hemorrhage + obstruction → breakdown of

erythrocytes + tissue → release of cholesterol → foreign body giant cell reaction (= chronic granuloma) → cyst formation + bone expansion

Histo: cholesterol crystals surrounded by foreign-body giant cells; embedded in fibrous connective tissue with varying proportions of hemosiderin-laden macrophages, chronic inflammatory cells and blood vessels; brownish cyst fluid contains cholesterol crystals + blood (= **"chocolate cyst"** = **"blue-domed cyst"**)

Location: in pneumatized petrous apex; (occasionally in)mastoid segment, middle ear, orbitofrontal region

- blue (vascular) tympanic membrane without pulsatile tinnitus
- hemotympanum; conductive hearing loss, headache
- long-standing history of otitis media

√ bone gaps ← bone remodeling
√ ossicles remain intact
√ NO enhancement

CT:
√ expansile homogeneous middle ear lesion with smooth well-defined / imperceptible bone margins
√ nonenhancing mass

MR:
√ hyperintense signal on T1WI ← methemoglobin
√ heterogeneously hyperintense signal on T2WI ← cholesterol crystals + methemoglobin from repeated hemorrhage
√ remains hyperintense with fat-suppression
√ ± hypointense rim on T2WI ← hemosiderin deposition / preserved rim of bone

DDx: (1) Asymmetric petrous apex pneumatization (hyperintense fatty marrow on T1WI, hypointense with fat suppression)
(2) Petrous apex effusion (no expansion / destruction of petrous air cells)
(3) Cholesteatoma (isointense to brain on T1WI)

Rx: conservative Rx for asymptomatic lesion; surgical drainage / cyst resection for large symptomatic lesion
◊ Loss of T1-hyperintensity after successful drainage!

CHRONIC SIALADENITIS

- often painful intermittent swelling of gland

√ normal-sized / small hypoechoic heterogeneous texture
√ multiple small round / oval hypoechoic areas

Chronic Sclerosing Sialadenitis

= KÜTTNER TUMOR = IgG4-RELATED SIALADENITIS
[Hermann Küttner (1870–1932), German surgeon in Breslau]
= non-neoplastic uni / bilateral hard swelling of submandibular gland considered part of IgG4-related disease

Histo: markedly fibrous sclerotic lesion containing IgG4-positive plasma cells

√ diffuse / focal swelling of both submandibular glands

US:
√ multiple small hypoechoic foci scattered on a heterogeneous background of salivary tissue
CT:
√ homogeneous attenuation
MR:
√ low to intermediate SI on T2WI
√ intermediate SI on T1WI + homogeneous enhancement
DDx: lymphoma, acute Sjögren syndrome

Granulomatous Sialadenitis

Organism: TB, actinomycosis
√ single / multiple hypoechoic areas in enlarged / normal-sized gland of diffusely low echogenicity
√ ± increased blood flow

COGAN SYNDROME

= AUTOIMMUNE INTERSTITIAL KERATITIS
= rare autoimmune multisystem disease characterized by nonsyphilitic interstitial keratitis + audiovestibular dysfunction + vascular inflammation
Age: young white adult
• eye redness. photophobia, eye pain (from interstitial keratitis)
• audiovestibular manifestations (similar to Ménière syndrome)
• nerve deafness
@ Cardiovascular (10–15%%)
Histo: prominent lymphocytic infiltration of aortic wall, destruction of media elastica, fibrosis, aneurysm formation, neovascularization
√ aortitis → aortic insufficiency
√ necrotizing vasculitis → coronary / iliac / renal artery stenosis
@ CNS (29%)
• psychosis, headache, convulsion, stroke, coma
√ ischemic change or infarction, meningoencephalitis, cerebral venous sinus thrombosis, cranial neuropathy
MR:
√ membranous labyrinthine obliteration / narrowing
√ enhancement of membranous labyrinth

CONGENITAL ATRESIA OF EAC

= failure of EAC to fully develop
Prevalence: ~ 1÷10,000
Often associated with: abnormalities of pinna
Classification: osseous / membranous / mixed
Location: unilateral > bilateral
Imaging assessment:

(1) Size + pneumatization of middle ear
(2) Abnormalities of ossicles
(3) Location of mastoid segment of facial nerve (often displaced anteriorly)

CROUP

= ACUTE LARYNGOTRACHEOBRONCHITIS = ACUTE VIRAL SPASMODIC LARYNGITIS
= lower respiratory tract infection
◊ Most common cause of airway obstruction in young children!
Organism: parainfluenza, respiratory syncytial virus
Season: fall and winter months
Age: > 6 months of age; peak incidence 2–3 years
• prodromal symptoms of viral infection
• "brassy / barking" cough → worse at night and while crying
• inspiratory difficulty with stridor, fever, hoarse cry
√ thickening of vocal cords
√ distension of cervical trachea on expiration
AP radiograph (most helpful image):
√ "**steeple**" / subglottic "inverted V" sign = symmetrical funnel-shaped narrowing 1–1.5 cm below lower margins of pyriform sinuses (= loss of lateral convexities / normal "shouldering" of air column)
Cause: subglottic mucosal edema affecting most severely the conus elasticus + external restriction by cricoid
√ accentuated on expiration
√ paradoxical inspiratory collapse → less pronounced during expiration
LAT radiograph:
√ NORMAL epiglottis + aryepiglottic folds (→ NO epiglottitis)
√ subglottic narrowing + increased density of subglottic region
√ narrow + indistinct subglottic trachea
√ inspiratory ballooning of hypopharynx (= nonspecific sign of any acute upper airway obstruction)
DDx: normal at end of inspiratory phase in a crying child

With clinically suspected croup imaging is performed to determine if another cause of inspiratory stridor is present.
Viral croup is unlikely to occur in children > 3 years of age. With radiographic findings of croup outside this age range, consider membranous croup and foreign-body aspiration.

Prognosis: usually self-limiting
Rx: supportive

DERMOID / EPIDERMOID OF HEAD AND NECK

= benign congenital or acquired (eg, posttraumatic) inclusions of dermal elements at site of embryonic 1st + 2nd branchial arches
◊ Dermoids of the head and neck comprise 7% of all dermoids
Definition:

Teratoma = neoplasm whose tissue is foreign to the part of the body from which the tumor arises

Teratoid cyst

Origin: ectoderm + mesoderm + endoderm

Histo: inclusion cyst lined by squamous / respiratory epithelium containing derivatives of ectoderm + endoderm + mesoderm (skin appendages, nervous / GI / respiratory tissue)

Dermoid cyst

Origin: ONLY ectoderm = epidermis + dermal substructure of subcutaneous tissue + skin appendages (= annexa consisting of hair follicles, sebaceous glands, sweat glands)

Histo: inclusion cyst lined by a thick keratinizing squamous epithelium containing a variable number of skin appendages ± dystrophic calcifications; lumen filled with keratin + sebaceous material + hair (occasionally)

Path: cheesy tumor, fat content often collects in globules

√ greater signal heterogeneity ← combination of solid and cystic elements

√ intralesional fat = DISTINGUISHING feature:

√ "sack-of-marbles appearance" = globules of coalesced fat (nearly PATHOGNOMONIC)

Epidermoid cyst

Origin: ONLY epithelial elements WITHOUT skin appendages

Histo: inclusion cyst lined by thin simple squamous epithelium ± calcifications (rarely); lumen filled with debris of keratin and some cholesterol

Path: "pearly tumor" = shiny smooth waxy character

√ usually lacks observable solid components

√ ± CHARACTERISTIC restriction at DWI (= high diffusion + moderately low apparent diffusion coefficient)

Mean age: 30 years (range, 5–50 years); M÷F = 3÷1

Location:

(1) Periorbital (50%): lateral eyebrow (most common)
(2) Oral cavity (25%): floor of mouth (12%), root of tongue
(3) Nasal cavity (13%)
(4) Submental: neck

√ well-circumscribed lesions of high T2 signal

√ NO / only rim enhancement

Nasal Dermoid

= dermal inclusion in cranium through patent suture

Age: infants (most common)

Associated with: craniofacial malformation (in 41%)

Location: anywhere between *glabella* (= depressed space between eyebrows above nose) and *columella* (= fleshy external part of nasal septum); lower third of bridge of nose (most commonly)

- nasal pit (skin dimple) / fistula / fluctuant swelling
- hair protruding from cyst / sinus tract (< 50%)

√ bone defect in cranium (= dermal sinus)
MR:
√ variable nonspecific appearance of sinus ± cyst
Cx: infection with abscess in nasal septum
DDx: normal fat in crista galli / nasal septum

Cervical Dermoid / Epidermoid Cyst

Age: 2nd–3rd decades; M = F
• slowly growing soft mobile mass in the suprahyoid midline (no movement with tongue protrusion!)
Site: (a) sublingual space (superior to mylohyoid muscle) = intraoral surgical approach (more frequent)
Type: frequently epidermoid cyst
(b) submandibular (inferior to mylohyoid muscle) = external surgical approach
Type: frequently dermoid cyst
Size: few mm – up to 12 cm
√ thin-walled unilocular mass
CT:
√ homogeneous fluid material of 0–18 HU
√ heterogeneous mass ← various germinal components
√ fluid-fluid level ← supernatant lipid
√ rim enhancement frequent
MR:
√ hypointense / hyperintense (sebaceous fluid) / isointense relative to muscle on T1WI
√ hyperintense on T2WI + internally heterogeneous
Prognosis: malignant degeneration into squamous cell carcinoma in 5%
DDx: ranula

DISSECTION OF CERVICOCEPHALIC ARTERIES

= CRANIOCERVICAL ARTERIAL DISSECTION
= hematoma within media splitting off vessel wall → false lumen within media
Incidence: 5÷100,000 per year; responsible for 5–20% of strokes in young and middle-aged adult
Etiology:
A. SPONTANEOUS
(1) trivial trauma (frequent): nonrecalled minor trauma like coughing, vomiting, sports (bowling, tennis, archery)
(2) primary arteriopathy (rare): fibromuscular dysplasia (in 15%), Marfan syndrome, Ehlers-Danlos syndrome type IV, autosomal dominant polycystic kidney disease, osteogenesis imperfecta type I, cystic medial necrosis, collagen vascular disease, homocystinuria
Indirect evidence of arteriopathy:
intracranial aneurysm, widened aortic root, arterial redundancy
Associated with: hypertension (36%), smoking (47%), migraine (11%)
B. TRAUMATIC (rare)

severe blunt head and neck trauma / penetrating trauma (automobile accident, boxing, accidental hanging, diagnostic carotid compression, chiropractic cervical manipulation)

Arteriographic Injury Grading	
Grade	*Type of Lesion*
I	√ irregularity of vessel wall √ dissecting intramural hematoma with < 25% stenosis
II	√ intraluminal thrombus / raised intimal flap √ small arteriovenous fistula √ dissection / intramural hematoma ≥ 25% stenosis
III	√ pseudoaneurysm
IV	√ occlusion
V	√ transection √ hemodynamically significant AV fistula

Pathophysiology:

primary intramural hematoma / penetration of blood into arterial wall via primary intimal tear → dissection usually extends cranially (same direction as blood stream) → narrowing of vessel lumen + enlargement of external diameter → pseudoaneurysm = dissecting aneurysm (with extension of hematoma into adventitia) → nidus for distal thromboembolism

Location: cervical ICA (68%), vertebral artery (27%), both ICA + vertebral artery (5%); multiple simultaneous dissections (28%)

Site: (a) subintimal dissection = close to intima
(b) subadventitial dissection = close to adventitia

√ arterial narrowing / occlusion
√ intimal flap
√ pseudoaneurysm
√ embolic distal branch occlusion of intracranial artery

US (low sensitivity due to location, 50% accuracy):
- √ wall hematoma = thickened hypoechoic vessel wall (DDx: intraluminal thrombus)
- √ echogenic intimal flap floating in lumen (rarely depicted)
- √ echogenic thrombus

Color Doppler (71–95% sensitive):
- √ separation of 2 lumina with different Doppler signals
- √ dampened / high-resistance Doppler waveform

DDx of increased ICA flow:

ICA redundancy, fibromuscular dysplasia, vasospasm, brain AVM, carotid cavernous sinus fistula, persistent trigeminal artery, anemia, hyperthyroidism

DDx of decreased ICA flow:

ipsilateral severe stenosis / occlusion of carotid siphon or intracranial ICA or M1 segment

NECT:
- √ crescent-shaped hyperattenuating acute wall hematoma

CECT (50–100% sensitive, 67–100% specific):
- √ target picture = narrow eccentric lumen surrounded by crescent-shaped mural thickening +

peripheral thin annular enhancement (enhancing vasa vasorum)
√ increase in external diameter
√ intramural hematoma becomes isoattenuating to muscle with correct window settings (DDx: atherosclerotic plaque, thrombus)
√ intimal flap
√ dissecting aneurysm
√ arterial occlusion

MR (50–100% sensitive, 58–99% specific):
√ cross-sectional T1WI imaging ± fat saturation:
√ increase in external diameter of artery
√ narrowing of lumen
√ intramural hematoma:
√ isointense to surrounding structures during early / chronic stage
√ crescent-shaped hyperintense hematoma around eccentric flow void between 7 days and 2 months
√ iso- to hyperintense on T2WI around flow void of artery

3-D TOF MR angiography:
√ pseudoenlargement of lumen in subacute dissection = flow-simulating intramural hematoma

DDx: pseudodissection (= high SI of turbulent flow in aneurysmal dilatation)

Rx: best therapy not clear; anticoagulation (primary treatment) in absence of subarachnoid hemorrhage / dissecting aneurysm; surgery; endovascular stent placement

Carotid Artery Dissection

◊ Twice as common as vertebral artery dissection!

Frequency: 2–5–20% of strokes in persons aged 40–60 years

Age: 18–76 years (66% between 35 and 50 years)

• unremitting unilateral anterior headache (47–86%), neck pain (25%), facial pain
• TIA / stroke (49–82%), amaurosis fugax (12%):
• completed stroke usually during first 7 days after onset of symptoms, may occur up to 1 month later
• oculosympathetic paresis = Horner syndrome (52%)
• cranial nerve palsy, bruit (48%), pulsatile tinnitus

Location: cervical ICA usually at level of C1-2 (60%) within a few cm of carotid bifurcation > supraclinoid segment of ICA; bilateral carotid dissections (15%)

Length: a few centimeters

Angiography / DSA (gold standard):
√ "string" sign = long tapered usually eccentric irregular luminal stenosis beginning distal to carotid bulb + extending to base of skull (76%)
√ "string and pearl" sign = focal narrowing + distal site of dilatation
√ abrupt luminal reconstitution at level of bony carotid canal (42%)
√ fingerlike / saccular aneurysm (40%), often in upper cervical / subcranial region
√ intimal flap (29%)
√ double-barrel lumen similar to aortic dissection (rare)
√ slow ICA-MCA flow

√ tapered "flamelike" / "radish taillike" occlusion (17%) that spares the carotid bulb

Cx: (1) Thromboemboli due to stenosis
(2) Subarachnoid hemorrhage (with intracranial location)
(3) Secondary aneurysm

Prognosis: complete / excellent recovery (8%) with normalization in a few months; worsening in 10%

DDx:
(1) Fibromuscular dysplasia ("string of beads" sign, young woman, adjacent to C1-2, bilateral in 65%)
(2) Dysgenesis of ICA (hypoplastic / absent carotid canal)
(3) Atherosclerosis (carotid bifurcation + bulb)
(4) Radiation treatment (circumferential wall thickening in radiation field)
(5) Takayasu arteritis (long-segment wall thickening of aorta + side branches on both sides, young woman, common in Asia + Mexico)
(6) Giant cell (temporal) arteritis (extradural carotid siphon most severely affected, > 50 years of age)
(7) Behçet disease

Vertebral Artery Dissection

= hemorrhage into wall of vertebral artery

Prevalence: unknown; up to 15% of strokes in young adults

- headache: occipital (> 50%), frontal (20%), orbital (20%)
- neck pain (30%), ischemia of posterior circulation (57–84%)
- ischemia of cervical spinal cord, cervical root impairment

Location: in pars transversaria at level of C1/2 = V_2 (35%); atlas loop = V_3 (34%); bilateral vertebral artery dissections (5%); site of direct trauma

CT:
√ subarachnoid hemorrhage ← rupture of adventitia

MR (modality of choice):
√ decreased arterial lumen
√ diminished flow void
√ periarterial rim SI changes with time (hemoglobin)

Angio:
√ tapering of artery / intimal flap / complete occlusion

Cx: stroke (in up to 95%) after hours / weeks

Prognosis: full recovery with some residual deficit (88%); recurrence within 4–6 weeks involving multiple cervical arteries in sequence

EPIGLOTTITIS

= ACUTE BACTERIAL EPIGLOTTITIS= SUPRAGLOTTITIS

= life-threatening infection characterized by edema of supraglottic structures (= epiglottis + aryepiglottic folds)
[*glottis*, Greek = mouth of windpipe ↔ *glotta / glossa* = tongue]

Cause:

(a) infectious

Organism: Haemophilus influenzae type B, Pneumococcus, Streptococcus group A

◊ Less prevalent since introduction of vaccine against H. influenzae!

(b) noninfectious: angioedema, trauma, ingestion of caustic agent, anaphylaxis

Peak age: formerly 6 (range, 1–5) years; now more prevalent among adults + children of > 15 years

- toxic appearance, high fever, posturing with neck extension
- abrupt onset of inspiratory stridor + respiratory distress
- sore throat, drooling, severe dysphagia

Location: purely supraglottic lesion; associated subglottic edema in 25%

Lateral radiograph (preferred modality, frontal view irrelevant):

◊ Radiograph should be taken in erect position only!

√ "thumb" sign = bulbous thickening of epiglottis

√ thickening of aryepiglottic folds

√ circumferential narrowing of subglottic portion of trachea during inspiration

√ ± supraglottitis = additional swelling of supraglottic larynx

√ ballooning of hypopharynx + pyriform sinuses

√ cervical kyphosis

CT (NOT recommended in acute setting):

√ enlarged edematous epiglottis with mucosal enhancement

√ edema of entire supraglottic larynx + tongue base + tonsils

√ phlegmonous collection in adjacent soft tissues

Cx: necrotizing epiglottitis, deep neck abscess (4–25%)

Prognosis: in children mortal danger of suffocation ← hazard of complete airway closure; patient needs to be accompanied by physician experienced in endotracheal intubation

Rx: broad-spectrum antibiotics, steroids, direct laryngoscopy, emergent intubation (in children) may be required

EXTERNAL AUDITORY CANAL DYSPLASIA

Frequency: 1÷10,000 births; family history in 14%

Etiology:

(a) isolated
(b) Trisomy 13, 18, 21
(c) Turner syndrome
(d) maternal rubella
(e) craniofacial dysostosis
(f) mandibulofacial dysostosis

Spectrum:

1. Stenosis of EAC
2. Fibrous atresia of EAC
3. Bony atresia (in position of tympanic membrane)
4. Decreased pneumatization of mastoid (mastoid cells begin to form in 7th fetal month)
5. Decreased size / absence of tympanic cavity
6. Ossicular changes (rotation, fusion, absence)

7. Ectopic facial nerve = anteriorly displaced vertical (mastoid) portion of facial nerve canal
8. Decrease in number of cochlear turns / absence of cochlea
9. Dilatation of lateral semicircular canal

Location: bilateral in 29%; M÷F = 6÷4

• pinna deformity; stenotic / absent auditory canal

Cx: congenital cholesteatoma (infrequent)

EXTRACARDIAC RHABDOMYOMA

= benign tumor consisting of immature striated muscle cells

Location: 70%–90% in head & neck

1. **Adult** rhabdomyoma
   Age: 5th decade; M > F
   Location: larynx, pharynx, oral cavity
   Size: large ← slow rate of growth
2. **Fetal** rhabdomyoma
   Median age: 4 years; M > F
   Location: subcutaneous tissue with a particular predilection for postauricular region

√ signal intensity similar to muscle on T1WI and T2WI

√ usually enhancement after contrast administration

EXTRAMEDULLARY PLASMACYTOMA

= EXTRAOSSEOUS PLASMACYTOMA

Uncommon form of plasmacytoma (3–4%); questionable if precursor to multiple myeloma

Age: 40–60 years; M÷F = 2÷1

Location: air passages (50%) predominantly in upper nose and oral cavity; larynx; conjunctiva (37%); lymph nodes (3%); perirenal

• usually not associated with increased immunoglobulin titer or amyloid deposition

√ mass of one to several cm in size with well-defined lobulated border

Classification:

A. OSSEOUS
   1. Medullary plasmacytoma
   2. Multiple myeloma:
      (a) scattered involvement of bone
      (b) myelomatosis of bone

B. EXTRAOSSEOUS
   3. Extramedullary plasmacytoma

Dx: requires exclusion of multiple myeloma by:

› bone marrow biopsy with normal results
› normal plasma electrophoresis
› negative skeletal survey
› negative bone marrow imaging with MR

Prognosis: relatively benign course (dissemination may be found months / years later or not at all); better than solitary bone plasmacytoma; progression to multiple myeloma in 50%

DDx:

(1) MULTIPLE MYELOMA
= malignant course with soft-tissue involvement in 50–73%:
(a) microscopic infiltration
(b) enlargement of organs
(c) formation of tumor mass (⅓)
• usually associated with protein abnormalities
• may have amyloid deposition
Age incidence: 50–85 years
◊ Extramedullary plasmacytoma tends to occur late in the course of multiple myeloma → indicates a poor prognosis (0–6% 5-year survival)

FIBROMATOSIS COLLI

= PSEUDOTUMOR OF INFANCY = STERNOCLEIDOMASTOID TUMOR OF INFANCY = CONGENITAL MUSCULAR TORTICOLLIS
= rare form of benign self-limiting benign fibrous mass within sternocleidomastoid muscle associated with torticollis in neonates and infants
Prevalence: 0.4% of live births
Cause: in > 60–90% associated with birth trauma during difficult breech / forceps delivery; positive family history (11%)
Path: compartment syndrome with pressure necrosis + secondary fibrosis of sternocleidomastoid m.
Histo: myoblasts + fibroblasts + myofibroblasts in various stages of differentiation
Associated congenital abnormalities:
developmental hip dysplasia, rib anomalies, talipes equinovarus (clubfoot), thoracic scoliosis, metatarsus adductus, mental retardation, seizure disorder
Associated skeletal abnormalities:
ipsilateral lateral mandibular asymmetry, cervicothoracic scoliosis, facial deformity, ipsilateral mastoid process hypertrophy, ipsilateral elevation of clavicle / shoulder
Age: 2nd to 4th week of life; M > F
• unilateral firm soft-tissue mass in mid to lower ⅓ of sternocleidomastoid muscle; typically unaffected at birth; enlarging neck mass over the course of 2–6 weeks
• torticollis (14–30%) tilting toward lesion ← muscle contraction
Location: lower ⅓ of sternocleidomastoid muscle affecting sternal + clavicular heads of the muscle; usually unilateral (R > L)
Average size: 1–3 cm
√ focal / diffuse enlargement of sternocleidomastoid muscle
√ NO extramuscular extension / associated soft tissue abnormality
√ mild mass effect on surrounding structures
X-ray (NOT indicated):
√ normal in 98%
√ lytic lesion in clavicular head at insertion of sternocleidomastoid muscle
US:
√ unilateral diffuse fusiform homogeneous expansion of sternocleidomastoid muscle
√ well- / ill-defined focal mass within muscle:

√ homogeneous echotexture (51%)
√ hypo- to iso- to hyperechoic depending on duration
√ mass moves synchronously with muscle at real-time

MR:

Indication: atypical sonographic features, NO resolution within 12 months

√ isointense lesion to normal muscle on T1WI
√ hyperintense lesion relative to normal muscle on T2WI
√ subtle patchy and linear areas of decreased signal intensity
√ heterogeneous enhancement

CT:

√ focal / diffuse homogeneous enlargement isoattenuating to other muscle

Prognosis: gradual spontaneous regression over 2–3 months; spontaneous resolution during next 4–8 months in 90% with / without treatment

Rx: (1) Muscle stretching exercise
(2) Surgery in 10%

DDx: (1) Neuroblastoma (heterogeneous solid mass with calcifications)
(2) Rhabdomyosarcoma
(3) Lymphoma (well-defined round /oval masses along cervical lymph node chain)
(4) Cystic hygroma (anechoic region with septations)
(5) Branchial cleft cyst
(6) Hematoma

EXTRASKELETAL FIBROSARCOMA

= malignant tumor of fibroblasts of classic herringbone-like architecture

Prevalence: 1–3% of sarcomas in adults; 11–12% of sarcomas in infants

May be associated with: prior irradiation of head & neck

Age: 40 –70 years; M÷F = 3÷2

• painful / painless enlarging mass

Subtypes: storiform-pleomorphic (50–60%), myxoid (25%), giant cell (5–10%), inflammatory (5%)

Location: sinonasal cavity, larynx, neck

MR:

√ heterogeneous mass of predominantly low signal intensity with variable enhancement on T1WI
√ heterogeneous high signal intensity on T2WI

Prognosis: infantile extraskeletal fibrosarcoma better than adult fibrosarcoma

GENICULATE HEMANGIOMA

= venous malformation in region of facial nerve

Site: geniculate ganglion > IAC > posterior genu

CT:

√ expansile honeycomb appearance
√ intratumoral bone spicules

√ bone forming / growth among bone trabeculae (= **ossifying hemangioma**)

MRI:

√ mass of heterogeneous signal intensity

√ avid enhancement

DDx: meningioma with intraosseous involvement

GLOMUS TUMOR

◊ Distinct from head & neck paragangliomas!

= composed of cells closely resembling modified smooth muscle cells of glomus bodies of dermis

Prevalence: < 2% of all soft tissue tumors

Location: distal extremities, head & neck (15–30%)

Sinonasal Glomus Tumor (5%)

= GLOMANGIOPERICYTOMA = SINONASAL-TYPE HEMANGIOPERICYTOMA

Origin: modified perivascular glomuslike myoid cells in nasal cavity + paranasal sinuses

Path: well-delineated unencapsulated cellular tumors

Histo: closely packed cells (= high cellularity) forming short fascicles, sometimes exhibiting storiform / whorled / palisaded patterns with multiple interspersed vascular channels of staghorn configuration; NO hemorrhage, NO necrosis

Peak age: 7th decade; M = F

- nasal obstruction / congestion, epistaxis
- difficulty breathing, sinusitis, headache

Site: nasal cavity

CT:

√ soft tissue mass with strong enhancement

√ extension into orbits + intracranial compartment and destruction of adjacent bone (if large)

MR:

√ tumor isointense relative to muscle on T1WI

√ hypo- to isointense relative to muscle on T2WI

√ variable degrees of (usually marked) enhancement

Prognosis: low tendency for metastasis (5%)

GOITER

[*gutteria*, Latin = throat]

Definition: visible enlargement of thyroid gland

Volume definition: > 18 mL for women; > 25 mL for men

Clinical classification:

Class I:	palpable but not visible in normal posture of head
Class II:	palpable and easily visible
Class III:	very large + retrosternal with compression marks

Adenomatous Goiter

= MULTINODULAR GOITER

US: (89% sensitive, 84% specific, 73% positive predictive value, 94% negative predictive value)

√ increased size + asymmetry of gland

√ multiple 1–4-cm solid nodules

√ areas of hemorrhage + necrosis

√ coarse calcifications may occur within adenoma ← hemorrhage + necrosis

Cx: compression of trachea

Diffuse Goiter

US:

√ increase in glandular size, R lobe > L lobe

√ NO focal textural changes

√ calcifications not associated with nodules

Iodine-deficiency Goiter

Not a significant problem in USA because of supplemental iodine in food

Etiology: chronic TSH stimulation

• low serum T4

√ high ^{131}I uptake

Jod-Basedow Phenomenon *(2%)*

= development of thyrotoxicosis (= excessive amounts of T_4 synthesized + released) if normal dietary intake is resumed / iodinated contrast medium administered

Frequency: most common in individuals with long-standing multinodular goiter

Age: > 50 years

√ multinodular goiter with in- / decreased uptake (depending on iodine pool)

Toxic Nodular Goiter

= PLUMMER DISEASE

= autonomous function of one / more thyroid adenomas

Peak age: 4th–5th decade; M÷F = 1÷3

• elevated T_4, suppressed TSH

√ nodular thyroid with hot nodule + suppression of remainder of gland

√ stimulation scan will disclose normal uptake in remainder of gland

√ ~ 80% increased radioiodine uptake by 24 hours

Rx: (1) ^{131}I treatment with empirical dose of 25–29 mCi → hypothyroidism in 5–30%

(2) Surgery → hypothyroidism in 11%

(3) Percutaneous ethanol injection → hypothyroidism in < 1%, → transient damage of recurrent laryngeal nerve in 4%

Intrathoracic Goiter

= extension of cervical thyroid tissue / ectopic thyroid tissue (rare) into mediastinum

Frequency: 5% of resected mediastinal masses; most common cause of mediastinal masses;

2% of all goiters

- mostly asymptomatic
- symptoms of tracheal + esophageal + recurrent laryngeal nerve compression

Location:

(a) retrosternal (80%) in front of trachea

(b) posterior descending (20%) = behind trachea but in front of esophagus, caudal extent limited by arch of azygos vein, exclusively on right side of trachea

√ continuity with cervical thyroid / lack of continuity (with narrow fibrous / vascular pedicle)

√ frequent focal calcifications

CT:

√ mass of high HU + well-defined margins

√ inhomogeneous texture with low-density areas (= degenerative cystic areas)

√ marked + prolonged enhancement

GRAVES DISEASE

= DIFFUSE TOXIC GOITER

= autoimmune disorder antibodies binding to TSH receptors (LATS) with inhibitory + stimulatory effects producing hyperplasia + hypertrophy of thyroid gland

Prevalence: 5÷10,000; most common form of hyperthyroidism (60–80%)

Peak age: 3rd–4th decade; M÷F = 1÷7

- ↑ T_3 and T_4, ↓ TSH production
- elevated levels of thyroid-peroxidase antibodies (75%)
- positive thyroid stimulating immunoglobulins
- **ophthalmopathy** (50%) = periorbital edema, lid retraction, ophthalmoplegia, proptosis, malignant exophthalmos
- **dermopathy** = pretibial myxedema (5%)
- **acropachy** = bulbous swelling of hands + feet (rare)

√ diffuse thyroid enlargement

√ gland may be normal in size in early stage

√ uniformly increased uptake

√ incidental nodules superimposed on preexisting adenomatous goiter (5%)

US: (identical to diffuse goiter)

√ global enlargement of 2–3 times the normal size

√ normal / diffusely hypoechoic pattern

√ "thyroid inferno" = diffuse hyperemia on color Doppler

Rx: ^{131}I treatments (for adults):

Dose: 80–120 μCi/g of gland with 100% uptake (taking into account estimated weight of gland + measured radioactive iodine uptake for 24 hours)

Cx: 10–30% develop hypothyroidism within 1st year + 3% per year rate thereafter

HYPOPHARYNGEAL CARCINOMA

Histo: squamous cell carcinoma (95%)

Metastases: common (50–75%) due to rich lymphatic drainage

May be associated with:

Plummer-Vinson syndrome (= atrophic mucosa of tongue, achlorhydria, sideropenic anemia) affecting women in 90%

- sore throat, intolerance to hot / cold liquids (early signs)
- dysphagia, weight loss (late signs)
- cervical adenopathy (in 50% at presentation)

Stage:

T1 tumor limited to one subsite of hypopharynx ≤ 2 cm

T2 tumor involves > 1 subsite / adjacent site without fixation of hemilarynx measuring 2–4 cm

T3 same as T2 with fixation of hemilarynx > 4 cm in size

T4 invasion of thyroid / cricoid cartilage / hyoid bone / esophagus / strap muscles / SQ fat

Pyriform Sinus Carcinoma (60%)

- may escape clinical detection if located at inferior tip = often cause of "cervical adenopathy with unknown primary" (next to primaries in lingual + faucial tonsils and nasopharynx)

√ invasion of posterior ala of thyroid cartilage, cricothyroid space, soft tissue of neck in T4 lesion

Prognosis: poor ← early soft-tissue invasion

Postcricoid Carcinoma (25%)

√ difficult assessment due to varying thickness of inferior constrictor + prevertebral muscles

Prognosis: 25% 5-year survival (worst prognosis)

Posterior Pharyngeal Wall Carcinoma (15%)

√ invasion of retropharyngeal space with extension into oro- and nasopharynx

√ retropharyngeal adenopathy

Staging of Cervical Nodes in SCC of Head & Neck

N Stage	*Definition*
Nx	cannot assess regional lymph nodes
N0	no regional lymph node metastasis
N1	single ipsilateral node ≤ 3 cm
N2a	single ipsilateral node 3–6 cm
N2b	multiple ipsilateral nodes, each ≤ 6 cm
N2c	bi- / contralateral nodes, each ≤ 6 cm
N3	any nodal mass > 6 cm

IMMUNOGLOBULIN IGG4-RELATED DISEASE

= IGG4-RELATED SCLEROSING DISEASE (ISD) = HYPER-IGG4 DISEASE = MULTIFOCAL FIBROSCLEROSIS

= systemic disease with multiorgan involvement and elevated IgG4 levels

Major diagnostic criteria:

(1) Diffuse / localized swelling / masses in ≥ 1 organ

(2) Elevated serum IgG4 concentrations ≥ 135 mg/dL
(3) Marked lymphoplasmacytic infiltration + storiform fibrosis with organ infiltration by IgG4-positive plasma cells

Multiorgan involvement in IgG4-related disease make whole-body CT, MRI, and PET important diagnostic tools.

Histo: diffuse lymphoplasmacytic infiltration (by T-lymphocytes and plasma cells staining positive for IgG4) + irregular fibrosis + occasional eosinophilic infiltration + obliterative phlebitis

Head and neck are commonly involved in IgG4-related disease, most commonly salivary glands, lacrimal glands, orbits, thyroid gland, lymph nodes, sinonasal cavities, pituitary stalk.

@ Orbit: fibrotic orbital pseudotumor
@ Salivary gland
1. Mikulicz disease
2. Sclerosing sialadenitis (Küttner tumor)

@ Lacrimal gland
1. Inflammatory pseudotumor (IPT)
Location: mostly bilateral symmetric; unilateral lacrimal gland lesions may occur
CT:
√ intermediate soft-tissue attenuation
MR:
√ low T1 signal intensity (= isointense to muscle)
√ homogeneous low to intermediate SI on T2WI ← increased cellularity + fibrosis
2. Lymphoid hyperplasia

@ Thyroid
1. Hashimoto thryoiditis
2. Riedel fibrosing thyroiditis

@ Pituitary gland: hypophysitis
@ Lung: interstitial pneumonia
@ Mediastinum: mediastinal fibrosis
@ Abdomen
1. Autoimmune pancreatitis (most commonly affected organ)
2. Sclerosing cholangitis
3. Sclerosing cholecystitis
4. Sclerosing mesenteritis
5. Retroperitoneal fibrosis (RPF)
6. Prostatitis

INVERTED PAPILLOMA

= INVERTING PAPILLOMA = ENDOPHYTIC PAPILLOMA
= SQUAMOUS CELL PAPILLOMA = TRANSITIONAL CELL PAPILLOMA = CYLINDRICAL EPITHELIOMA
= SCHNEIDERIAN PAPILLOMA

Frequency: 4% of all nasal neoplasms; most common of epithelial papillomas; commonly

occurring after nasal surgery

Cause: unknown; association with human papillomavirus-11

Age: 40–60 years; M÷F = 3–5÷1

Path: vascular mass with prominent mucous cyst inclusions interspersed throughout epithelium

Histo: hyperplastic epithelium inverts into underlying stroma rather than in an exophytic direction; high intracellular glycogen content

◊ Squamous cell carcinoma coexistent in 5.5–27%!

Location: uniquely unilateral (bilateral in < 5%)

(a) most often arising from the lateral nasal wall with extension into ethmoid / maxillary sinuses, at junction of antrum + ethmoid sinuses

(b) paranasal sinus (most frequently maxillary antrum)

(c) nasal septum (5.5–18%)

• unilateral nasal obstruction, epistaxis, postnasal drip, recurrent sinusitis, sinus headache

• distinctive absence of allergic history

√ commonly involves antrum + ethmoid sinus

√ widening of infundibulum / outflow tract of antrum

√ destruction of medial antral wall / lamina papyracea of orbit, anterior cranial fossa (pressure necrosis) in up to 30%

√ septum may be bowed to opposite side (NO invasion)

√ homogeneous enhancement

MR:

√ may have intermediate to low intensity on T2WI (DDx: squamous cell carcinoma, olfactory neuroblastoma, melanoma, small cell carcinoma)

Cx: (1) Cellular atypia / squamous cell carcinoma (10%)

(2) Recurrence rate of 15–78%

Rx: complete surgical extirpation (lateral rhinotomy with en bloc excision of lateral nasal wall)

KERATOSIS OBTURANS

= expansile accumulation of keratin debris within EAC

Age: younger patient < 40 years

• severe pain, conductive hearing loss, (rarely) otorrhea

Associated with: chronic sinusitis, bronchiectasis

Location: usually bilateral process

√ diffuse widening of EAC by epidermal plug

√ ± smooth scalloping of surrounding bone

DDx: EAC cholesteatoma (periostitis, bone erosion)

LABYRINTHITIS

Acute Labyrinthitis

Cause: viral infection (mumps, measles) > bacterial infection > syphilis, autoimmune disease, toxins

• sudden hearing loss, vertigo, tinnitus

MR:
√ faint diffuse enhancement of labyrinth on T1WI (HALLMARK)

Tympanogenic Labyrinthitis
Cause: agent enters through oval / round window in middle ear infection

Meningogenic Labyrinthitis
Cause: agent propagates along IAC / cochlear aqueduct in meningitis
Location: often bilateral

Fibrous Labyrinthitis
= cochlear obstruction

Ramsay-Hunt Syndrome
= HERPES ZOSTER OTICUS
Cause: reactivation of varicella zoster virus latent in geniculate ganglion
Predisposition: immunocompromised, systemic disease, aging
• burning pain in ear, facial paralysis, hearing loss, vertigo
• mucosal vesicles of external auditory canal 1–4 days later
√ enhancement of 7th + 8th nerve, labyrinth ± pontine nucleus

Labyrinthitis Ossificans
= LABYRINTHITIS OBLITERANS = SCLEROSING LABYRINTHITIS = CALCIFIC / OSSIFYING COCHLEITIS
Cause: suppurative infection (tympanogenic, meningogenic, hematogenic) in 90%, trauma, surgery, tumor, severe otosclerosis
◊ Meningitis is the most likely etiology!
Pathophysiology: progressive fibrosis + ossification of granulation tissue within labyrinth
• bi- / unilateral profound deafness
√ loss of normal fluid signal within labyrinth on T2WI (early in course of disease)
√ inner ear structures filled with bone: most common region of cochlear ossification = scala tympani of basal turn

LARYNGEAL CARCINOMA
Frequency: 98% of all malignant laryngeal tumors; 1% of all cancers; 89,081 cases in USA (2013)
Age: 5th / 6th decade of life; M > F
Risk factors: tobacco, alcohol, airborne irritants
◊ High risk to develop 2nd primary malignancy of lung + upper aerodigestive tract (in 8%)
Histo: squamous cell carcinoma (95%)
Negative prognostic factors:
√ nodal involvement
√ invasion of cricoid / thyroid cartilage:
√ tumor within fatty medullary cavity
√ tumor on outer extralaryngeal side of thyroid cartilage

◊ Assessment made difficult by natural asymmetric ossification of thyroid cartilage!

N.B.: Reactive periostitis may lead to sclerosis of cartilage

√ invasion of pre- and paraepiglottic fat (clinically not detectable!)

√ fixation of carotid artery

√ extranodal spread

Suggestive of lymph node metastasis:

√ uptake on PET-CT (50–94% sensitive, 82–100% specific depending on lymph node size)

√ enlarged lymph node:

(a) > 15 mm in cross section for level I / II nodes

(b) > 8 mm in cross section for retropharyngeal node

(c) > 10 mm in greatest dimension for all other node levels

√ round lymph node with loss of reniform shape

√ necrotic lymph node (= central low attenuation)

√ amorphous node with spiculated / indistinct border suggests extracapsular spread

√ proximity to laryngeal mass

√ cluster of > 3 lymph nodes 6–15 mm in size

Distant metastasis (in 5–15%): lung > bone > abdomen

Prognosis: 64% 5-year survival (2013)

Rx: conservative laryngectomy (partial laryngectomy preserving speech + control of aspiration)

Supraglottic Carcinoma (20–30%)

Metastases: early to lymph nodes of deep cervical chain (levels II + III), in 25–55% at time of presentation

• symptomatic late in course of disease (often T3 / T4)

Stage:

T1 tumor confined to one supraglottic subsite

T2 involvement of adjacent supraglottic subsite / glottis without cord fixation

T3 tumor limited to larynx with cord fixation or extension to postcricoid area / medial wall of pyriform sinus / preepiglottic space

T4 extension beyond larynx with involvement of oropharynx (base of tongue) / prevertebral space / encasement of carotid a. / thyroid cartilage

A. ANTERIOR COMPARTMENT

1. **Epiglottic carcinoma**

√ circumferential relatively symmetric growth

√ extension into preepiglottic space ± base of tongue ± paraglottic space

Prognosis: better than for tumors of posterolateral compartment

B. POSTEROLATERAL COMPARTMENT

1. **Aryepiglottic fold (marginal supraglottic) carcinoma**

√ exophytic growth from medial surface of aryepiglottic fold

√ growth into fixed portion of epiglottis + paraglottic (= paralaryngeal) space

2. **False vocal cord / laryngeal ventricle carcinoma**

√ submucosal spread into paraglottic space

√ ± destruction of thyroid cartilage

√ ± involvement of true vocal cords

Prognosis: poorer than for cancer of anterior compartment

Glottic Carcinoma (50–60%)

• early detection due to hoarseness

Metastases: uncommon (< 10%) ← sparse lymphatic drainage to lower deep jugular chain (levels IV + VI)

Stage:

T1 tumor confined to vocal cord with normal mobility

T1a tumor limited to one vocal cord

T1b tumor involving both vocal cords

T2 supra- / subglottic extension + impaired mobility

T3 fixation of true vocal cord ± invasion of paraglottic space ± inner cortex of thyroid cartilage

T4 destruction of thyroid cartilage / extension outside larynx

Patterns of tumor invasion:

(1) Anterior extension into anterior commissure
- √ > 1 mm thickness of anterior commissure
- √ invasion of contralateral vocal cord via anterior commissure
- √ FDG uptake in opposite cord at PET

(2) Posterior extension to arytenoid cartilage, posterior commissure, cricoarytenoid joint

(3) Subglottic extension
- √ tumor > 5 mm inferior to level of vocal cords

(4) Deep lateral extension into paralaryngeal space

Prognosis: T1 carcinoma rarely metastasizes (0–2%) due to absence of lymphatics within true vocal cords

Subglottic Carcinoma (5%)

• late detection due to minimal symptomatology (stridor)

Stage:

T1 confined to subglottis

T2 extension to vocal cords ± impaired mobility

T3 tumor confined to larynx + cord fixation

T4 cartilage destruction / extension beyond larynx

√ any tissue seen on airway side of cricoid cartilage

Prognosis: poor due to early metastases to cervical lymph nodes (in 25% at presentation)

LARYNGEAL CHONDROSARCOMA

◊ The most common sarcoma of the larynx

Age: 50–70 years; M >> F

• lobulated submucosal mass

Location: posterior lamina of cricoid cartilage (50–70%), thyroid cartilage (20–35%)

√ coarse / stippled intratumoral calcifications

√ ± locally invasive
MR:
√ very high SI of tumor matrix on T2WI (= hyaline cartilage)
Rx: function-preserving laryngeal resection (local recurrence may be seen 10 years or more)
DDx: benign chondroma

LARYNGEAL CLEFT

= rare sagittal communication between trachea + esophagus ← lack of separation between laryngotracheal and pharyngoesophagеal systems
Cause: failure of fusion of posterior cricoid lamina
Classification: based on downward extent of cleft (ranging from submucosal interarytenoid cleft to a cleft that extends into thoracic trachea)
• swallowing difficulty, stridor, recurrent pneumonia, weak cry
• clinical suspicion of TE fistula
Associated with other congenital anomalies:
(1) CHARGE syndrome
(2) VACTERL (VATER) association; esophageal atresia; imperforate anus
√ simultaneous barium opacification of esophagus + trachea
Dx: endoscopic visualization

LARYNGEAL CYST

= rare benign pharyngeal cyst of vallecula / vocal cord / epiglottis
Age: any; most common in 6th decade
• dysphonia, airway obstruction, foreign body sensation in throat
Classification: ductal and saccular types
A. Ductal cyst (more common)
Cause: submucosal gland duct obstruction
Involvement of: valleculae, vocal cords, epiglottis
B. Saccular cyst
Cause: mucus retention within laryngeal saccule from obstruction / loss of patency of saccular orifice
√ smoothly hemispheric mass ± distortion of coated surfaces of pharyngeal / laryngeal supraglottic anatomy
DDx: laryngocele, branchial cleft cyst, oncocytic papillary cystadenoma

LARYNGEAL HEMANGIOMA

Histo: cavernous / capillary type
• dark bluish red / pale red compressible swelling on endoscopy
√ strong contrast enhancement
CT:
√ phleboliths (PATHOGNOMONIC for cavernous type)
MR:
√ very high signal intensity on T2WI
DDx: paraganglioma, hypervascular metastasis (renal adenocarcinoma)

Infantile Laryngeal Hemangioma (10%)

= SUBGLOTTIC HEMANGIOMA

◊ Most common subglottic soft-tissue mass causing upper respiratory tract obstruction in neonates

Age: < 6 months; M÷F = 1÷2

• crouplike symptoms (dyspnea, stridor) in neonatal period

• hemangiomas elsewhere (skin, mucosal membranes) in 50%

Location: subglottic region

Neck X-ray:

√ posterolateral subglottic airway narrowing (AP view)

√ eccentric thickening of subglottic portion of trachea (AP view)

√ subtle endoluminal mass arising from posterior wall below true cords (LAT view)

N.B.: CECT required to depict full extent

Rx: tracheostomy (waiting for spontaneous regression)

Adult Laryngeal Hemangioma

Location: supraglottic region (isolated); associated with extensive cervicofacial angiodysplasia

M > F

Rx: laser excision, cryotherapy, selective embolization

LARYNGEAL PAPILLOMATOSIS

= RECURRENT RESPIRATORY PAPILLOMATOSIS

◊ Squamous papilloma is the most common benign tumor of the larynx!

Etiology: human papilloma virus serotypes 6 + 11 (papova virus causing genital condyloma acuminatum)

Histo: core of vascular connective tissue covered by stratified squamous epithelium

Age of onset: 1–54 years; M÷F = 1÷1; bimodal distribution

(a) < 10 years (diffuse involvement) = juvenile laryngotracheal papillomatosis

Cause: transmission from mother to child via birth canal

(b) 21–50 years (usually single papilloma)

• signs of upper respiratory tract obstruction:

  • progressive hoarseness / aphonia, asthmalike symptoms

  • repeated episodes of respiratory distress, inspiratory stridor

• cough, hemoptysis, recurrent pneumonia

Location: (a) uvula, palate

(b) vocal cord

(c) subglottic extension (50–70%)

(d) pulmonary involvement (1–6%): lower lobe and posterior part of lung

√ thickened lumpy cords

√ bronchiectasis

Cx:

(1) **Tracheobronchial papillomatosis** (2–5%)

Cause: tracheostomy

Location: lower lobe + posterior predilection
√ solid pulmonary nodules in mid + posterior lung fields
√ 2–3 cm large thin-walled cavity with 2–4 mm thick nodular wall (foci of squamous papillomas enlarge centrifugally, undergo central necrosis, cavitate)
√ peripheral atelectasis + obstructive pneumonitis
HRCT:
√ tree-in-bud opacities

(2) **Pulmonary papillomatosis**
from aerial dissemination (bronchoscopy, laryngoscopy, tracheal intubation) 10 years after initial diagnosis
√ irregularities of tracheal / bronchial walls
√ noncalcified granulomata progressing to cavitation

(3) Malignant transformation into invasive squamous cell carcinoma

Rx: CO_2 laser resection / surgical excision

LARYNGEAL PLASMACYTOMA

Age: 50–70 years; M >> F
Histo: large sheets of uniform cells indistinguishable from normal plasma cells; marked amyloid deposition (20%)
• pedunculated / slightly prominent mass that bleeds easily
Location: epiglottis, true and false vocal cords
CT:
√ large smoothly marginated homogeneous mass
√ no significant contrast enhancement

LARYNGOCELE

= dilated appendix / saccular cyst of the laryngeal ventricle that contains air ← maintaining communication with laryngeal lumen + extending beyond superior border of thyroid cartilage
Prevalence: 1÷2,500,000
Age: middle-aged men
Pathogenesis: chronic increase in intraglottic pressure
Cause: excessive coughing, shouting, playing wind instrument, blowing glass, obstruction of appendicular ostium (= secondary laryngocele) by chronic granulomatous disease / laryngeal neoplasm (15%)

N.B.: Almost 50% of laryngoceles detected with plain radiography contain a laryngeal carcinoma!

Histo: lined by pseudostratified columnar ciliated epithelium + mixture of submucosal serous and mucous glands
Types: based on relationship to thyrohyoid membrane

(a) internal (40%) = in parapharyngeal space confined <u>within</u> thyrohyoid membrane
√ confined within larynx between false vocal cord and medial surface of thyrohyoid membrane

(b) external (26%) = protrusion through thyrohyoid membrane at the point of insertion of the neurovascular bundle (superior laryngeal nerve + vessels) presenting as lateral neck mass near hyoid bone with normal size inside the membrane

√ extension upward and laterally

(c) mixed (44%) = internal + external dilatation of saccule on both sides of thyrohyoid membrane

• visible in 10% of adults during phonation
• hoarseness / dysphagia / stridor (internal laryngocele)
• compressible anterior neck mass just below angle of mandible (external laryngocele)
• Bryce sign = gurgling / hissing sound on compression

Site: unilateral (80%), bilateral (20%)

√ sharply defined round / oval radiolucent area within paralaryngeal soft tissues:
√ increase in size during Valsalva maneuver
√ decrease in size during compression

√ cystic mass that can be followed to level of ventricle
√ may be filled with fluid / contain air-fluid level
√ DIAGNOSTIC = connection between air sac + airway

Cx: infection (laryngopyocele) in 8–10%, formation of mucocele

DDx: (1) Laryngeal cyst (lined by squamous epithelium)
(2) Lateral pharyngeal diverticulum (fills with barium)

LARYNGOMALACIA

= immaturity of cartilage;
most common cause of stridor in neonate + young infant

• only cause of stridor to get worse at rest

√ hypercollapsible larynx during inspiration (supraglottic portion only)
√ backward bent of epiglottis + anterior kink of aryepiglottic folds during inspiration

Prognosis: transient (disappears by age 1 year)

LEMIERRE SYNDROME

= SEPTIC JUGULAR VEIN THROMBOPHLEBITIS = POSTANGINAL SEPSIS = NECROBACILLOSIS

= uncommon potentially life-threatening complication of acute oropharyngeal infection (pharyngotonsillitis)

Age: adolescent, teenager, young adult > infant, child

Organism: anaerobic Fusobacterium necrophorum (81%, part of the normal oropharyngeal flora), other Fusobacterium species (11%), other gram-negative organisms (8%)

• acute pharyngitis followed by fever 3–10 days later
• pain and swelling over the sternocleidomastoid muscle
• hoarseness, dysphagia ← cranial nerve involvement
• septicemia with rigors, malaise, trismus

US / CT:
√ internal jugular venous thrombosis
√ edema of the surrounding soft tissues + wall of jugular vein

CT of chest:
√ patchy consolidation = bronchopneumonia
√ septic pulmonary emboli:

√ multiple peripheral round / wedge-shaped opacities
√ "feeding vessel" sign = vessel leading into nodule
√ peripheral enhancement with central areas of reduced attenuation = cavitation
√ pleural effusion → empyema

Cx: systemic dissemination of infection: pleuropulmonary septic emboli (97%), septic arthritis (15%), hepatic and splenic abscesses, osteomyelitis, meningitis, epidural abscess, diffuse encephalopathy

Rx: prolonged IV antibiotics with anaerobic activity, anticoagulation

LINGUAL THYROID

= solid embryonic rest of thyroid tissue, which remains ectopic along the tract of thyroglossal duct

Frequency: in 10% of autopsies (within tongue < 3 mm); M << F

- may be the only functioning thyroid tissue (in 70–80%)
  N.B.: resection of ectopic thyroid will render patient athyroid
- asymptomatic (usually), may enlarge causing dysphagia / dyspnea

Location: midline dorsum of tongue near foramen cecum (90%), thyroglossal duct, trachea; ± multifocal

CT:
√ small hyperattenuating focus relative to muscle ← iodine content + moderate contrast enhancement

MR:
√ solid avidly enhancing lesion mildly T1 hyper- / isointense relative to muscle

NUC:
√ SPECIFIC high uptake of ^{123}I and ^{99m}Tc

Cx: in 3% malignant (papillary carcinoma) / goitrous transformation

LIPOMATOSIS

= condition caused by diffuse overgrowth of mature adipocytes

Age: children < 2 years of age; may affect adults

Types:

(1) **Infiltrating congenital lipomatosis of the face**
= infiltrative nonencapsulated accumulations of mature fat cells
- lesion growth → facial asymmetry, parotid involvement, osseous hypertrophy, macroglossia

May be associated with: cutaneous capillary blush and mucosal neuromas

(2) **Encephalocraniocutaneous lipomatosis**
= infiltrative lipomatous process

Location: commonly temporofrontal area unilaterally, cerebral + leptomeningeal tissue, skull; occasionally eye and heart

May be associated with: cerebral malformations and calcifications

(3) **Madelung disease**

LUDWIG ANGINA

[Wilhelm Friedrich von Ludwig, 1790–1865, German surgeon and obstetrician in Tübingen]
[*angina* = *ankhon*, Greek = strangling]
= serious potentially life-threatening necrotizing infection of floor of mouth rapidly involving both submandibular spaces
Cause: odontogenic / gum infection (90%) surrounding a partially erupted tooth (= pericoronitis) usually of 2nd / 3rd mandibular molar; frenulum piercing
Predisposing factors: poor dental hygiene, dental extraction from lower jaw a few days prior, compromised immune status, diabetes, IV drug abuse
Spread: by direct extension of infection = tooth apices of 2nd / 3rd molar of jaw extend inferiorly to mandibular insertion of mylohyoid muscle → fascial planes of neck → mediastinitis → airway compromise
Organism: Streptococcus, Actinomyces israelii, Pseudomonas aeruginosa
Age: usually in young adults
Location: bilateral sublingual and submandibular spaces
• swelling of the submandibular (and sublingual) spaces
• brawny (firm hard) painful edema ± crepitation of submandibular tissue → elevation of tongue
• malaise, fever, laryngeal edema, stridor, difficulty breathing
• displacement of tongue → drooling, dysphagia, difficulty swallowing or speaking
Imaging: (1) Assessment of airway patency
(2) Presence of gas-forming organism
(3) Location of underlying dental infection
√ underlying dental disease
√ local skin thickening, muscle enlargement
√ increased attenuation of subcutaneous fat
√ loss of fat planes within submandibular space
√ soft tissue emphysema
√ ill-defined abscesses in submandibular / sublingual spaces
CT:
√ inflammatory change with small cystic spaces = serosanguinous accumulation in floor of mouth
√ ± extension deep into submandibular + parapharyngeal spaces + pharynx → airway narrowing / obstruction
√ well-defined fluid collection with rimlike enhancement
Cx: mandibular osteomyelitis, spread of infection into deep fascial spaces of neck, thrombophlebitis of IJV (Lemierre syndrome)
Mortality: up to 10%
Rx: IV antibiotics, aggressive drainage, surgical airway creation

LYMPHANGIOMA

= congenital lymphatic malformation
Frequency: 5.6% of all benign tumors of infancy + childhood
Age: present at birth in 50–65%, in 80–90% evident by age 2 (time of greatest lymphatic growth); M = F
Lymphatic development:

endothelial buds from veins in jugular region form confluent plexuses, which develop into rapidly enlarging bilateral juguloaxillary lymph sacs (7.5 weeks GA); these fused lymph sacs extend craniad and dorsolateral with extensive outgrowth of lymph vessels in all directions; connection with internal jugular vein at level of confluence + external jugular vein persists on left side

Pathogenesis:

(1) Early sequestration of embryonic lymphatic tissue with failure to join central lymphatic channels

(2) Congenital obstruction of lymphatic drainage ← abnormal budding of lymph vessels (= loss of connection / noncommunication of primordial jugular lymphatic sac with jugular vein)

Classification (based on size of lymphatic spaces):

(1) **Cystic lymphangioma** = cystic hygroma (see below)

(2) **Cavernous lymphangioma**
= mildly dilated cavernous lymphatic spaces with cysts of intermediate size
Location: tongue, floor of mouth, salivary glands
√ penetration of contiguous structures
√ same signal intensities as cystic lymphangioma + fibrous stromal component of low intensity on T1WI + T2WI

(3) **Capillary / simple lymphangioma** (least common)
= capillary-sized lymphatic channels
Location: epidermis + dermis of proximal limbs

(4) **Vasculolymphatic malformation**
composed of lymphatic + vascular elements, eg, lymphangiohemangioma

Histo: endothelial-lined lymphatic channels containing serous / milky fluid + separated by connective tissue stroma

- asymptomatic (in majority) soft / semifirm mass
- rapid increase in size (from infection / hemorrhage)
- ± dyspnea / dysphagia with encroachment upon trachea, pharynx, esophagus

Location: anywhere in developing lymphatic system; mostly in posterior cervical triangle, occasionally in floor of mouth / tongue

(a) posterior triangle of neck (75%), with extension into mediastinum in 3–10%
- visible at birth in 65%
- clinically apparent by end of 2nd decade in 90%

(b) anterior mediastinum (< 1%)

(c) axilla (20%), chest wall, groin

(d) retroperitoneum (1%), abdominal organs, bone

√ multilocular thin-walled cysts separated by fibrous tissue

√ well-marginated small lesions / ill-defined infiltrative large lesions with transspatial growth pattern

Cx: infection, airway compromise, chylothorax, chylopericardium

Prognosis: spontaneous regression (10–15%)

Rx: surgical excision (treatment of choice but difficult since mass does not follow tissue planes) with recurrence rate of up to 15%

Cystic Hygroma

= CYSTIC LYMPHANGIOMA

= single / multiloculated fluid-filled cavities on either side of fetal neck + head (localized form) ± trunk (generalized form) as the most common form of lymphangioma developing within loose connective tissue

Frequency: 1÷6,000 pregnancies

Path: multiple enormously dilated cystic lymphatic channels; variation in size between a few mm to > 10 cm in diameter containing chylous fluid; separated by minimal intervening stroma; may invade adjacent soft tissues / muscle and surround vessels

Histo: cystic spaces lined by endothelial cells + supporting connective tissue stroma

Associated with:

(a) chromosomal abnormalities in 60–80% (in particular when detected in 2nd trimester)
  (1) Turner syndrome (45 XO, mosaic) in 40–80%
  (2) Trisomies 13, 18, 21, 13q, 18p, 22
  (3) Noonan syndrome
  (4) Distichiasis (= second row of hair behind eyelash) -lymphedema syndrome [*stichos*, Greek = row]
  (5) Familial pterygium colli
  (6) Roberts, Cumming, Cowchock syndrome
  (7) Achondrogenesis type II
  (8) Lethal pterygium syndrome

(b) exposure to teratogens
  (1) Fetal alcohol syndrome
  (2) Aminopterin
  (3) Trimethadione

Types:

(1) Cystic hygroma with abnormal peripheral lymphatic system
  √ lymphangioma in posterior compartment of neck
  √ septations (indicate high probability for aneuploidy, development of hydrops, and perinatal death)

(2) Diffuse lymphangiectasia
  √ lymphangioma of chest + extremities
  √ peripheral lymphedema + nonimmune hydrops

(3) Isolated cystic hygroma
  (a) axillary lymph sac malformation
    √ lymphangioma restricted to axilla
  (b) jugular lymph sac malformation
    √ lymphangioma restricted to lateral neck
  (c) internal thoracic + paratracheal lymph sac malformation
    √ lymphangioma within mediastinum
  (d) combined lymph sac malformation
  (e) thoracic duct malformation
    √ thoracic duct cyst

• AF-AFP / MS-AFP may be elevated

Location: neck (frequently posterior cervical space) and lower portions of face (75–80%);

mediastinum (3–10%, in ½ extension from neck); axilla (20%); chest wall (14%); face (10%); retroperitoneum (kidneys); abdominal viscera (colon, spleen, liver); groin; scrotum; skeleton

US:
- √ thin-walled fluid-filled structure with multiple septa of variable thickness + solid cyst wall components
- √ fluid-fluid level with layering hemorrhagic component
- √ isolated nuchal cysts
- √ webbed neck (= pterygium colli) following later communication with jugular veins
- √ nonimmune hydrops (43%)
- √ progressive peripheral edema
- √ fetal ascites
- √ oligo- / polyhydramnios / normal amount of fluid
- √ bradycardia

CT:
- √ poorly circumscribed multiloculated masses
- √ homogeneous attenuation of fluid values / higher (after infection)

MR (allows the best differentiation between lymphatic malformations and surrounding soft tissues):
- √ low signal intensity on T1WI
- √ high SI lesion with low-SI septations of variable thickness on T2WI
- √ may be hyperintense on T1WI ← clotted blood / high chylous lipid content / high protein content
- √ ± fluid-fluid level (if hemorrhage present)

DDx: hemangioma (different location, feeding vessels, contrast enhancement)

Cx: (1) Compression of airways / esophagus
(2) Slow growth / sudden enlargement (hemorrhage, inflammation)

Prognosis:
(1) Intrauterine demise (33%)
(2) Mortality of 100% with hydrops
(3) Spontaneous regression (10–15%)
- ◊ Favorable prognosis for localized lesions of anterior neck and axilla
- ◊ Only 2–3% of fetuses with posterior cystic hygroma become healthy living children!

DDx: twin sac of blighted ovum; cervical meningocele; encephalocele; cystic teratoma; nuchal edema; branchial cleft cyst; vascular malformation; lipoma; abscess

Pseudocystic Hygroma
- = PSEUDOMEMBRANE
- = anechoic space bordered by specular reflection on posterior aspect of fetal neck during 1st trimester

Cause: ? developing integument
- √ NO prominent posterior bulge / internal septations

MADELUNG DISEASE

= BENIGN SYMMETRICAL LIPOMATOSIS = MULTIPLE SYMMETRIC LIPOMATOSIS

= rare benign condition characterized by symmetric proliferation of adipose tissue
Location: head, neck, shoulders (periscapular), upper chest; NO involvement of anterior mediastinal / cardiophrenic / paraspinal areas
Age: 25–60 years; white men
May be associated with:
history of alcohol abuse, dyslipidemia, diabetes mellitus, hyperthyroidism, liver disease, hypertension, hyperuricemia, renal tubular acidosis, macrocytic anemia, polyneuropathy
Cx: respiratory compromise ← tracheal compression at neck
DDx: obesity (different fat distribution)

MALIGNANT EXTERNAL OTITIS

= NECROTIZING EXTERNAL OTITIS
= severe bacterial infection of the soft tissues + bones at base of skull
Organism: almost always Pseudomonas aeruginosa
Age: elderly
Predisposed: diabetes mellitus / immunocompromised
• unrelenting severe otalgia, headache
• purulent otorrhea unresponsive to topical antibiotics
• ± malfunction of nerves VII, IX, X, XI ← skull base osteomyelitis; granulation tissue within external auditory canal
Location: at bone-cartilage junction of EAC
Spread of infection:
via fissures of Santorini (= 2–3 vertical fissures in cartilaginous portion of EAC anteroinferiorly) →
(a) inferiorly into soft tissues inferior to temporal bone, parotid space, nasopharyngeal masticator space
(b) posteriorly into mastoid
(c) anteriorly into temporomandibular joint
(d) medially into petrous apex of skull base
√ osseous erosion of external auditory canal
CT:
√ soft-tissue density in external auditory canal (100%)
√ fluid in middle ear / mastoid air cells (89%)
√ disease around eustachian tube (64%)
√ obliteration of fat planes beneath temporal bone (64%)
√ involvement of parapharyngeal space (54%)
√ masticator space disease (27%)
√ mass effect in nasopharynx (54%)
√ bone erosion of clivus (9%)
√ intracranial extension (9%)
MR (method of choice for soft-tissue complications):
√ abnormal signal intensity + obliteration of fat within stylomastoid foramen
Cx: bone destruction; skull base osteomyelitis (clivus, jugular foramen); abscess of epidural space + brain parenchyma + prevertebral space

Prognosis: 20% recurrence rate; high mortality rate

DDx: nasopharyngeal carcinoma (with obstruction of eustachian tube and secondary otomastoiditis); nonnecrotizing external otitis (no osseous erosion); cholesteatoma of EAC; squamous cell carcinoma of EAC

MIKULICZ DISEASE

= painless bilateral symmetric swelling of lacrimal and salivary glands (parotid (80%), submandibular, sublingual)

[Jan Mikulicz-Radecki (1850–1905), Polish-Austrian surgeon at universities in Kraków, Königsberg and Wrocław]

Age: 6th decade; M÷F = 2÷3 to 4÷5

Histo: "epimyoepithelial islands" = marked lymphoplasmacytic infiltration surrounding epithelial nests, excess hyaline basement membrane material, acinar atrophy and destruction

Often associated with: IgG4-related disease, Sjögren syndrome

√ homogeneous attenuation + enhancement of involved glands

CT:

√ intermediate soft-tissue attenuation

MR:

√ low signal intensity (= isointense to muscle) on T1WI

√ homogeneous low to intermediate SI on T2WI ← increased cellularity + fibrosis

DDx: viral infection (mumps), acute phase of Sjögren syndrome, sarcoidosis, lymphoma, leukemia

MUCOCELE

= end stage of a chronically obstructed sinus

Frequency: increased incidence in cystic fibrosis

◊ Most common lesion to cause expansion of paranasal sinus!

Etiology: chronic obstruction of paranasal sinus ostium

Path: expanded sinus cyst lined by mucosa + filled with accumulated secretions and desquamations

Age: usually adulthood

- history of chronic nasal polyposis + pansinusitis
- commonly present with unilateral proptosis
- ↓ visual acuity, visual field defect, intractable headaches
- palpable mass in superomedial aspect of orbit (frontal mucocele)

Location:

mnemonic: fems

frontal (60%) > **e**thmoid (30%) > **m**axillary (10%) > **s**phenoid (rare)

√ expanded airless sinus filled with homogeneous mucoid material

N.B.: Presence of air in an affected sinus effectively rules out a mucocele!

√ sinus cavity expansion (DDx: never in sinusitis)

√ bone demineralization + remodeling at late stage but NO bone destruction (impossible DDx

from neoplasm)
√ surrounding zone of bone sclerosis / calcification at edges of mucocele (from chronic infection)
√ macroscopic calcification in 5% (especially with superimposed fungal infection)
√ uniform enhancement of thin rim

US:
√ homogeneous hypoechoic mass

MR:
√ expansive well-delineated mass with homogeneously hyperintense T1 and T2 signal:
√ signal intensity varies with state of hydration, protein content, hemorrhage, air content, calcification, fibrosis
√ hypointense on T1WI + signal void on T2WI ← inspissated debris + fungus
√ NO enhancement / peripheral enhancement pattern (DDx from solid enhancement pattern of neoplasms)

Cx: (1) Protrusion into orbit displacing medial rectus muscle laterally
(2) Expansion into subarachnoid space → CSF leak
(3) Mucopyocele = superimposed infection (rare)

Rx: followed (if asymptomatic); surgical drainage (if symptomatic)

DDx: paranasal sinus carcinoma, mucus retention cyst, Aspergillus infection (enlargement of medial rectus muscle + optic nerve, focal / diffuse areas of increased attenuation), chronic infection, inverting papilloma

MUCOEPIDERMOID CARCINOMA

Path: arises from intercalated ducts of seromucinous glands

Histo: composed of a mixture of 3 cells: mucin-secreting cells + squamous cells + mucous cells; arranged in cords / sheets / cystic configuration

Age: 30–50 years

Prognosis: variable (well-encapsulated low-grade to infiltrating highly aggressive malignancy)

Rx: complete surgical removal

Parotid Mucoepidermoid Carcinoma

◊ Most common malignant lesion of parotid gland
◊ <u>In children</u>: up to 35% of all salivary gland tumors are malignant (60% are mucoepidermoid carcinomas)
• rock-hard mass; facial nerve paralysis
• pain / itching along course of facial nerve

CT:
√ may contain cystic low-attenuating areas
√ focal calcifications (rare)

(a) low-grade lesion:
√ well-circumscribed parotid mass
√ hypo- to isointense on T1WI
√ hyperintense on T2WI
Rx: wide local excision

(b) high-grade lesion:
√ infiltrating poorly marginated, more solid, relatively homogeneous lesion with few cystic areas
Rx: wide block excision + radical neck dissection

Laryngeal Mucoepidermoid Carcinoma

Prevalence: ~100 cases
M÷F = 6÷1
Location: epiglottis (most common)

MUCOUS RETENTION CYST

= obstructed submucosal mucinous gland
√ partially surrounded by air
DDx: indistinguishable from polyps, mucocele (NEVER surrounded by air)

NASAL GLIOMA

misnomer (no neoplastic features) = NASAL CEREBRAL HETEROTOPIA
= rare congenital mass composed of dysplastic sequestered neurogenic tissue (= distal part of a cephalocele in extracranial location) that has become isolated from the subarachnoid space (= disrupted central connection); analogous to nasoethmoidal encephalocele
Age: usually identified at birth
Location: (a) extranasal (60%)
Site: paramedian at bridge of nose external to nasal passage
(b) intranasal (30%)
Site: within nasal passage medial to middle turbinate
(c) combination of intra- and extranasal (10%)
Site: root of nose; unilateral right > left side
• smooth firm noncompressible mass, covered by skin
• no change in size during crying
√ no growth / very little growth / growth similar to brain
√ attached to middle turbinate bone / nasal septum
√ foramen cecum may be deeper than normal
√ ± small and bifid crista galli (intracranial extension likely)
√ soft-tissue mass of glabella
√ attached to brain by stalk of tissue (in 1–15–30%)
◊ NO communication with subarachnoid space by fluid-filled tract as in encephalocele
MR (method of choice):
√ iso- / hypointense relative to normal gray matter on T1WI
√ hyperintense on T2WI (as a result of gliosis)
√ contrast enhancement may depict tract to frontobasal region
DDx: encephalocele (communicates with subarachnoid space)

ODONTOGENIC INFECTION

Spread:

(1) dental caries → bacteria enter tooth and spread to apex (root) → apical periodontitis, granuloma, abscess, radicular cyst formation
(2) bacterial overgrowth + inflammation in space between tooth and gum → destruction of periodontal ligaments → erosion of bone

Odontogenic Abscess

- fever, tooth pain, facial swelling, dysphagia, trismus
- possibly dyspnea

CT:
√ periodontal lucency with focal cortical break / fistula
√ extraosseous fluid collection with rimlike enhancement
Cx: spread of infection into deep spaces of neck and orbit, airway compromise, internal jugular vein thrombosis, intracranial extension of infection

OLFACTORY NEUROBLASTOMA

= very malignant tumor arising from olfactory mucosa
Types:
1. Esthesioneuroepithelioma
2. Esthesioneurocytoma
3. Esthesioneuroblastoma

√ mass in superior nasal cavity with extension into ethmoid + maxillary sinuses
Cx: distant metastases in 20%

Esthesioneuroblastoma

= OLFACTORY NEUROBLASTOMA
Origin: olfactory epithelium
Age peaks: young men + 50–60 years

- hyposmia, anosmia, nasal congestion, epistaxis, facial pain
- headache, personality change (with frontal lobe involvement)
- exophthalmos, ophthalmoplegia, visual loss

Location: centered on cribriform plate
√ erosion of cribriform plate and nasal septum
MR:
√ tumor hypointense to brain on T1WI
√ tumor iso- or hyperintense to brain on T2WI
√ cysts along the superior tumor margin within anterior cranial fossa (CHARACTERISTIC)

OTIC CAPSULE DYSPLASIA

Single-cavity Cochlea

= cochlear cavity malformation
= saccular defect / cavity in otic capsule in the position normally occupied by cochlea without recognizable modiolus, osseous spiral lamina, interscalar septum

- profound hearing loss discovered in early childhood

May be associated with: recurrent bacterial meningitis, perilymphatic fistula of oval window

√ cystic cochlea (= developed basal turn, middle + apical turn occupy common nondeveloped space)

Type: (a) incomplete partition type I
= cystic cochleovestibular malformation
= complete lack of partitioning of cochlea
√ cystic structure at CT

(b) incomplete partition type II (see below)
= classic Mondini malformation

Insufficient Cochlear Turns

= normal basilar turn + varying degrees of hypoplasia of middle and apical turns

Mondini Malformation

Cause: in utero insult at 7 weeks GA

Frequency: 2nd most common imaging finding in children with sensorineural hearing loss

- some high-frequency hearing preserved; vertigo
- otorrhea, rhinorrhea, recurrent meningitis (perilymphatic fistula caused by absence / defect of stapes footplate)

√ cochlea contains 1½ turns:
√ normal basal turn
√ cystic-appearing dilated apical portion

√ absence of cochlear apex

May be associated with: deformity of vestibule + semicircular canals + vestibular aqueduct

Labyrinthine Aplasia

= **Michel aplasia** = Michel anomaly = agenesis of osseous + membranous labyrinth (rare)

Cause: arrested development at 4 weeks GA

- total sensorineural hearing loss

√ region of otic capsule normally occupied by cochlea is replaced by dense labyrinthine + pneumatized bone

√ flat medial wall of middle ear (= undeveloped horizontal semicircular canal)

√ hypoplasia of internal auditory canal

√ dysplasia of vestibule = marked enlargement into region of lateral + superior semicircular canals

DDx: labyrinthitis obliterans (no loss of lateral convexity of medial wall of middle ear)

Anomalies of Membranous Labyrinth

Scheibe dysplasia = abnormal cochlea + saccule

Alexander dysplasia = dysplasia of basal turn

√ normal CT findings

Small Internal Auditory Canal

= decrease in the diameter of IAC ← hypoplasia / aplasia of cochlear nerve (portion of

cranial nerve VIII)
• total sensorineural hearing loss
√ hypoplastic anteroinferior quadrant of IAC

Large Vestibule

Associated with: underdeveloped lateral semicircular canal
• sensorineural hearing loss (most common cause)
√ lateral semicircular canal smaller
√ vestibule extends further into lateral + superior aspects of otic capsule

Large Vestibular Aqueduct

= ENLARGED VESTIBULAR AQUEDUCT SYNDROME
Age: manifests around 3 years
Frequency: most common imaging abnormality detected in children with sensorineural hearing loss (SNHL)
May be associated with: other inner ear abnormalities
• unilateral congenital deafness (commonly missed)
◊ in 12% of children with congenital SNHL
• vertigo, tinnitus (in 50%)
Location: bilateral in 50–66%
√ vestibular aqueduct > 1.4–2 mm in diameter (measured at halfway point between posterior petrous bone + common crus at level of vestibule)
√ vestibular aqueduct larger than normal semicircular canals
√ CLASSIC funnel-shaped deformity of dilated vestibular aqueduct ← enlarged endolymphatic sac housed within dorsal vestibular aqueduct

OTITIS MEDIA

Cx: (1) Otomastoiditis
(2) Development of acquired middle ear cholesteatoma

Acute Otitis Media

◊ Most common infection of the temporal bone!
◊ Most common infection in first 5 years of life!
Cause: viral upper respiratory infection with disruption of the mucosal barrier → bacteria in nose and nasopharynx spread to middle ear
Age: infants + young children > adults
Organism: Streptococcus species, Haemophilus influenzae
• fever, otalgia, otorrhea; red bulging tympanic membrane
√ partial / total fluid-attenuation opacification of middle ear ± fluid level
√ opacification of mastoid air cells

Chronic Otitis Media

= CHRONIC OTOMASTOIDITIS
= long-term damage to middle ear
Cause: long-standing eustachian tube dysfunction, perforation of tympanic membrane

Sequelae:
√ middle ear effusion
√ granulation tissue (no displacement / destruction)
√ cholesterol granuloma
√ cholesteatoma

OTOMASTOIDITIS

= serious complication of acute otitis media in children
Anatomy: tympanic cavity communicates with mastoid air cells via the tympanic antrum (subject to viral and bacterial invasion by way of eustachian tube)
Age: young children
Organism: Streptococcus pneumoniae, Haemophilus influenzae, Staphylococcus aureus
• retroauricular swelling + erythema, protrusion of auricle
• history of recent otitis media
Temporal bone CT (87%–100% sensitive):
√ increased attenuation of the middle ear cavity (= middle ear effusion)
√ increased attenuation of the mastoid cells
√ ± fluid levels
Intratemporal Cx:
(1) **Coalescent mastoiditis** = empyema of mastoid
Pathomechanism: suppuration under pressure → local acidosis + ischemia → osseous decalcification + osteoclasis of pneumatic cell walls
√ loss of internal bone septa of the mastoid air cells ← erosion of mastoid septa / cortex with periosteal reaction
√ fluid or soft-tissue opacification of mastoid air cells
√ subperiosteal abscess located postauricular / in external auditory canal / along zygomatic bone
Rx: myringotomy, mastoidectomy
(2) Petrositis = petrous apicitis
(3) Labyrinthitis
• vertigo, nystagmus
√ abnormal labyrinthine enhancement
(4) Facial nerve paralysis
(5) Hearing loss
Cervical Cx:
(1) Carotid artery involvement: arteritis, occlusion, pseudoaneurysm, rupture
(2) **Bezold abscess** = inflammatory collection that may spread along plane of sternocleidomastoid muscle to lower neck
Location: inferior to mastoid tip + medial to insertion of posterior belly of digastric muscle
√ erosion of mastoid tip
√ adjacent involvement of posterior digastric muscle insertion
Cx: mediastinitis ← extension of infection inferiorly along fascial planes
Intracranial Cx:

(1) Meningitis
(2) Epidural abscess
› perisinus abscess = erosion of the cortical plate overlying the sigmoid sinus
(3) **Dural sinus / Sigmoid sinus thrombophlebitis**
Cause: erosion of sigmoid plate / thrombophlebitic spread via emissary veins
Location: (commonly) sigmoid + transverse sinus
• headache, otalgia, papilledema, fever
√ sinus of low attenuation on NECT and CECT
√ absence of normal flow void on spin-echo MR
√ no flow-related enhancement on gradient-echo MR
√ occlusion on MRV
DDx: aberrant arachnoid granulation
(4) **Subdural empyema**
Route: communication through intact bone and dura with vessels in subarachnoid space + brain parenchyma
Location: along posterior interhemispheric fissure; tentorium cerebelli
• meningismus, focal neurologic deficits, focal seizures
√ widening of extracerebral space
√ compression of adjacent sulci
Rx: prompt neurosurgical drainage
(5) Intraparenchymal brain abscess and empyema

OTOSCLEROSIS

= OTOSPONGIOSIS
= replacement of dense otic capsule by highly vascular spongy bone in active phase (otosclerosis = misnomer!) with restoration of density during reparative sclerotic phase
Etiology: unknown; frequently hereditary
Age: adolescent / young adult Caucasian; M÷F = 1÷2
Histo: otosclerosis limited to endochondral layer
DDx: Paget disease, osteogenesis imperfecta, syphilis

Stapedial = Fenestral Otosclerosis (80–90%)
Location: lateral wall of bony labyrinth, including oval and round windows, promontory, facial nerve canal
Site: anterior oval window margin (= fissula ante fenestrum); bilateral in 85%
• tinnitus early in course (⅔)
• progressive conductive hearing loss (stapes fixation in oval window)
√ oval window too wide (lytic phase)
√ new bone formation on anterior oval window margin ± posterior oval window margin ± round window
√ complete plugging of oval window = obliterative otosclerosis (in 2%)

Cochlear = Retrofenestral Otosclerosis (10–20%)
Location: otic capsule
Invariably associated with: fenestral otosclerosis

- progressive sensorineural hearing loss (involvement of otic capsule / cytotoxic enzyme diffusion into fluid of membranous labyrinth)
- Schwartze sign = reddish hue behind tympanic membrane when promontory involved

√ "double ring / double lucent" = lucent halo around cochlea (may appear as 3rd turn to cochlea) in early phase

√ bony proliferation in reparative sclerotic phase difficult to diagnose because of same density as cochlea

PAPILLARY ENDOLYMPHATIC SAC TUMOR

= HEFFNER TUMOR
= locally invasive papillary cystadenomatous tumor of temporal bone
Origin: epithelial lining of endolymphatic sac
Associated with: von Hippel-Lindau disease (in 7%), which may have bilateral papillary endolymphatic sac neoplasms
• hearing loss, facial nerve palsy, vestibular dysfunction
Location: along posterior petrous apex (retrolabyrinthine petrous bone) typically involving vestibular aqueduct
CT:
√ moth-eaten lytic appearance of invaded bone surrounded by thin shell of reactive bone:
√ solid + cystic components
√ intratumoral calcifications = "bone sequestra" from destruction of petrous bone
√ may be hypervascular (supplied by branches of external carotid artery)
MR:
√ speckled pattern of hyperintensity on T1WI (mimicking glomus tumor)
√ commonly contains blood products (hyperintense on T1WI + hypointense on T2WI)
√ areas of low SI may represent hemosiderin
√ heterogeneous enhancement
DDx: paraganglioma, cystic and papillary adenocarcinoma, chondroid lesions (benign chondroma, low-grade chondrosarcoma, chondromyxoid fibroma), cholesterol granuloma, metastatic disease

PARAGANGLIOMA

= NONCHROMAFFIN PARAGANGLIOMA = GLOMUS TUMOR (describes the rich arborization of blood vessels and nerves) = CHEMODECTOMA (reflective of chemoreceptor tissue of origin) = GLOMERULOCYTOMA = ENDOTHELIOMA = PERITHELIOMA = SYMPATHOBLASTOMA = FIBROANGIOMA = SYMPATHETIC NEVI
= rare neuroendocrine tumor arising from paraganglionic tissue found between base of skull and floor of pelvis; belongs to amine-precursor-uptake decarboxylation (APUD) system characterized by cytoplasmic vesicles containing catecholamines
Paraganglion = collection of tissue of the extraadrenal neuroendocrine system, frequently located near nerves and vessels with special chemoreceptor function
Origin: arises from nonchromaffin paraganglion cells of neuroectodermal origin (= neural crest cells found in adrenal medulla + parasympathetic ganglia + chemoreceptors); differs from adrenal medulla only in its nonchromaffin feature
Terminology of Neuroendocrine System:
(a) Adrenal paraganglioma arising from adrenal medulla = **pheochromocytoma**
(b) **Extraadrenal pheochromocytoma**
= pheochromocytoma arising from organs of Zuckerkandl
(c) **Paraganglioma** (10%)
= pheochromocytoma arising in other extraadrenal locations like retroperitoneum, bladder, GI tract

1. Aorticosympathetic paraganglioma associated with sympathetic chain + retroperitoneal ganglia
2. Parasympathetic paraganglioma including branchiomeric chemodectoma, vagal + visceral autonomic paraganglioma

Classification of extraadrenal paragangliomas (Glenner):

A. BRANCHIOMERIC DISTRIBUTION
   1. Associated with great vessels of chest + neck including carotid body, glomus jugulare, glomus tympanicum

B. PARASYMPATHETIC DISTRIBUTION
   2. Associated with vagal nerve
   3. Associated with aorticosympathetic chain in thoracolumbar region from aortic arch to urinary bladder, including organ of Zuckerkandl at origin of inferior mesenteric artery
   4. Associated with visceral organs

Histo: acidophil-epithelioid cells in contact with endothelial cells of a vessel; storage of catecholamines (usually nonfunctioning); histologically similar to pheochromocytoma

Peak age: 5th–6th decade (range, 6 months to 80 years); M÷F = 1÷1

- tumor may secrete catecholamine in 40% (= **functional paraganglioma**); proportion of hormonally active tumors high for pheochromocytomas, intermediate for aorticosympathetic paragangliomas, low for parasympathetic paragangliomas
- **p**aroxysmal / **p**ermanent hypertension ← secretion of vasopressor amines responsible for:
  - › **p**ain in head (headache)
  - › **p**allor
  - › **p**erspiration (excessive sweating)
  - › **p**alpitations
- elevated urinary metanephrine / vanillylmandelic acid
- pheochromocytomas secrete norepinephrine + epinephrine, extraadrenal paragangliomas secrete only norepinephrine, some paragangliomas produce dopamine
- determination of free norepinephrine most sensitive with gas chromatography / high-pressure liquid chromatography (HPLC) performed on 24-hour urine specimens

Location of functioning paragangliomas:

(a) adrenal medulla (> 80%)
(b) extraadrenal intraabdominal (8–16%)
(c) extraadrenal in head & neck (2–4%)

Four primary sites in head & neck:

1. Carotid body
2. Jugular foramen
3. Path of vagus nerve
4. Middle ear

Less common sites in head & neck:

sella turcica, pineal gland, cavernous sinus, larynx (laryngeal branches of vagus nerve), orbit (ciliary ganglion of the eye), thyroid gland, nasopharynx, mandible, soft palate, face, cheek

(d) spinal paraganglioma

(e) multiple paragangliomas, particularly in hereditary disorders (multiple endocrine neoplasia syndromes (MEN 2a and 2b) + neuroectodermal disorders of neurofibromatosis type 1, von Hippel-Lindau syndrome):
synchronous multicentricity in 3–26%:
› autosomal dominant in 25–35%
› nonhereditary in < 5%

√ highly vascular tumor with intense early blush that persists into late arterial + venous phases
√ well-circumscribed iso- to hyperintense mass on T2WI
√ flow voids ← multiple small serpentine + arborizing vessels
√ frequent hemorrhage with "cap" sign (= hypointense rim)
Cx: malignant transformation in 2–10%

Carotid Body Tumor

Embryology:
derived from mesoderm of 3rd branchial arch + neural crest ectoderm cells, which differentiate into sympathogonia (= forerunner of paraganglionic cells)
◊ Chemodectoma is misnomer (NOT derived from chemoreceptor cells)!

Histo: nests of epithelioid cells ("Zellballen") with granular eosinophilic cytoplasm separated by trabeculated vascularized connective tissue
◊ Chromaffin-positive granules (= catecholamines) may be present

Function of carotid body:
5 x 3 x 2 mm carotid body regulates pulmonary ventilation through afferent input by way of glossopharyngeal nerve to the medullary reticular formation
Chemoreceptor: detects changes in arterial partial pressures of O_2 + CO_2 + pH
Stimulus: hypoxia > hypercapnia > acidosis
Effect: increase in respiratory rate + tidal volume; increase in sympathetic tone (heart rate, blood pressure, vasoconstriction, elevated catecholamines)

• painless pulsatile firm neck mass below the angle of the jaw, laterally mobile but vertically fixed

Location: within / outside adventitial layer of CCA at level of carotid bifurcation, commonly along posteromedial wall; bilateral in 5% with sporadic occurrence, in 32% with autosomal dominant transmission
√ enhancing oval mass with splaying of ICA + ECA above CCA bifurcation
√ no narrowing of ICA / ECA caliber
Extension: inferiorly to lower cranial nerves + pharynx; superiorly to skull base + intracranial cavity
Growth rate: about 5 mm per year
Cx: malignant transformation in 6% with metastases to regional lymph nodes, brachial plexus, cerebellum, lung, bone, pancreas, thyroid, kidney, breast

Jugulotympanic Paraganglioma

= large glomus tumor with 2 components in the middle ear + jugular foramen
Age: 4th–6th decade; M÷F = 1÷4
Location: margin of jugular foramen
NUC:

√ ^{111}In-octreotide (higher sensitivity)
√ ^{123}I-metaiodobenzylguanidine (lower sensitivity)
Rx: embolization of larger tumor prior to surgery

Glomus Tympanicum Tumor

Most common tumor in middle ear
- hearing loss, pulsatile tinnitus
- reddish purple mass behind tympanic membrane

Origin: nerve of Jacobson = jugulotympanic paraganglia cells along tympanic branch of glossopharyngeal n.
Location: tympanic plexus on cochlear promontory of <u>middle ear</u>
CT (bone algorithm preferred):
√ globular soft-tissue mass abutting promontory
√ intense enhancement
√ usually small at presentation (but with early involvement of ossicles)
√ erosion + displacement of ossicles
√ inferior wall of middle ear cavity intact
Angio:
√ difficult to visualize because of small size

Glomus Jugulare Tumor

◊ Most common tumor in jugular fossa with intracranial extension
Origin: adventitia of jugular vein arising from paraganglia cells along nerves of Jacobson / Arnold
- tinnitus, hearing loss; vascular tympanic membrane

Location: at <u>dome of jugular bulb</u>
√ soft-tissue mass in jugular bulb region / hypotympanum / middle ear space
√ intense enhancement
√ destruction of posteroinferior petrous pyramid + corticojugular spine of jugular foramen
√ destruction of ossicles (usually incus), otic capsule, posteromedial surface of petrous bone
MR:
√ "salt and pepper" appearance on T1WI + T2WI ← multiple small serpentine + arborizing tumor vessels in large tumor
√ intense enhancement in small tumor
Angio: (film entire neck for concurrent glomus tumors!)
√ enlarge feeding arteries + rapidly draining veins:
√ arteriovenous shunting
√ hypervascular mass with persistent homogeneous reticular stain
√ invasion / occlusion of jugular bulb by thrombus / tumor
√ supplied by tympanic branch of ascending pharyngeal artery, meningeal branch of occipital artery, posterior auricular artery via stylomastoid branch, internal carotid artery, internal maxillary artery
Cx: malignant transformation with metastases to regional lymph nodes (in 2–4%)

Glomus Vagale Tumor

= PARAGANGLIA OF VAGUS NERVE = VAGAL BODY TUMOR

Histo: dispersed within perineurium / below nerve sheath / between nerve fiber fascicles; not organized into a compact mass

Location:

(1) within inferior ganglion (= ganglion nodosum), inferior to base of skull close to jugular foramen (most common location)

(2) within superior ganglion (= ganglion jugulare) within base of skull at level of jugular bulb

(3) elsewhere along course of vagus nerve

Inferior Nodose Paraganglion

√ spindle-shaped mass

√ compression of internal jugular vein

√ displacement of carotid vessels anteromedially

√ displacement of lateral pharyngeal wall medially

√ minimal destruction of skull base

Superior Jugular Paraganglion

√ dumbbell-shaped mass

√ may encase / displace ICA

Location in temporal bone:

(1) dome of jugular bulb = intravagal paraganglia inferior to jugular foramen

(2) mucosa of cochlear promontory related to tympanic branch of glossopharyngeal nerve (**Jacobson nerve**)

(3) auricular branch of vagus nerve (**Arnold nerve**)

Extension:

(a) superiorly into posterior cranial fossa ± compression of brainstem

(b) inferiorly into infratemporal / parapharyngeal space (⅔)

(c) medially to involve arch of atlas

(d) laterally into middle ear structures

(e) posteriorly into mastoid air cells

• slow growing + asymptomatic

√ spherical / ovoid / spindle-shaped mass with sharp interfacing margins and homogeneous enhancement

√ highly vascular mass + neovascularity + intense tumor blush

Cx: malignant transformation + metastases in 15% to regional lymph nodes + lung (for other paragangliomas in 10%)

PARANASAL SINUS CARCINOMA

Location: maxillary sinus (80%), nasal cavity (10%), ethmoid sinus (5–6%), frontal + sphenoid sinus (rare)

Maxillary Sinus Carcinoma (80%)

Histo: squamous cell carcinoma (80%)

Age: > 40 years in 95%; M÷F = 2÷1
• asymmetry of face, tumor in oral / nasal cavity
√ bone destruction (in 90%) predominates over expansion
√ nodal metastases in 10–18%

Nasopharyngeal Carcinoma (10%)

Frequency: 0.25–0.5% of all malignant tumors in whites; M > F
Predisposed: Chinese population
Histo: squamous cell carcinoma (> 85%), nonkeratinizing carcinoma, undifferentiated carcinoma
Mean age: 40 years
• asymptomatic for a long time; unilateral nasal obstruction
• history of chronic sinusitis / nasal polyps (15%)
Location: turbinates (50%) > septum > vestibule > posterior choanae > floor
Extension:
(a) lateral + superior: through sinus of Morgagni (= natural defect in superior portion of lateral nasopharyngeal wall) into cartilaginous portion of eustachian tube + levator veli palatini muscle
± masticator space and pre- and poststyloid parapharyngeal spaces
± involvement of levator + tensor veli palatini muscle, 3rd division of nerve V, petroclinoid fissure
± foramen lacerum of skull base encasing ICA
± cavernous sinus (along ICA / mandibular nerve / direct skull base invasion)
(b) anterior: posterior nasal cavity + pterygopalatine fossa
(c) inferior (⅓): submucosal spread along lateral pharyngeal wall + anterior and posterior tonsillar pillars
√ polypoid or papillary (⅔)
√ bone invasion (⅓)
MR:
√ asymmetric thickening of nasopharyngeal mucosa
√ homogeneous intermediate SI similar to that of adjacent mucosa on T2WI
√ moderate contrast enhancement less than that of normal mucosa on T1WI
√ focal homogeneous enhancing mass

Ethmoid Sinus Carcinoma (5–6%)

Histo: squamous cell carcinoma (> 90%), sarcoma, adenocarcinoma, adenoid cystic carcinoma; frequently secondarily involved from maxillary sinus carcinoma
• nasal obstruction, bloody discharge
• anosmia, broadening of nose

PARATHYROID ADENOMA

Location: posterior to thyroid gland; ectopic in 5–15%
US (82% sensitive):
◊ Often used after localization with ^{99m}Tc-MIBI scintigraphy
√ well-defined oval hypoechoic mass

√ multilobulated mass ± echogenic areas (in large adenoma)

CT:

Indication: ectopic mediastinal adenoma (detected in 50%)

MR:

√ hypointense on T1WI, hyperintense on T2WI + STIR

NUC (^{99m}Tc-MIBI):

√ increased radiotracer uptake

PAROTID HEMANGIOMA

Frequency: 90% of parotid gland tumors during 1st year of life; M < F

Histo: capillary type >> cavernous type (in older children)

- soft-tissue mass developing shortly after birth with progressive growth peaking at age 1–2 years
- gradual spontaneous regression usually complete by adolescence

US:

√ hypoechoic mass relative to parotid tissue

√ variable degree of abnormal flow

CT:

√ occasionally phleboliths

√ well-defined mass with uniform intense enhancement

MR:

√ low to intermediate signal intensity on short TR

√ bright signal intensity on long TR

√ flow voids due to prominent vasculature

Rx: surgery, sclerotherapy, laser ablation (therapy only with large size + encroachment on adjacent structures due to spontaneous regression)

PENDRED SYNDROME

[Vaughan Pendred (1869–1946), English general practitioner]

= autosomal recessive disorder of chromosome 7 characterized by dyshormonogenic goiter associated with sensory-neural deafness

Cause: deficient protein that functions as a membrane-bound chloride-iodine transporter

- slowly progressive + fluctuating / profound hearing loss
- prelingual deafness (= hearing loss prior to the age at which speech is acquired)
- vestibular symptoms
- euthyroid / variable degrees of hypothyroidism
- positive perchlorate discharge test (= 10–80% of iodine taken up by thyroid is discharged by perchlorate ← organification defect)

√ multinodular goiter

√ absence of interscalar septum of modiolus (= central bony spiral of cochlea) in 20–75%; bilateral in 80%

√ enlargement of vestibular duct in 80–100%

PERIODONTAL DISEASE

• facial swelling, pain, dysphagia, dysphonia

Location:

(a) submandibular space: roots of 2nd / 3rd molar tooth reach inferior to mylohyoid muscle

(b) sublingual space: roots of teeth anterior to 2nd / 3rd molar remain above mylohyoid muscle

CT:

√ rimlike enhancement of fluid collection (abscess), cellulitis, myositis

√ cortical dehiscence commonly on lingual aspect of mandible

√ permeative bone changes, osseous destruction, periosteal reaction

Cx: descending necrotizing mediastinitis

Rx: tooth extraction, abscess drainage, IV antibiotics

PERITONSILLAR ABSCESS

= complication of untreated / incompletely treated tonsillitis

◊ Most commonly encountered deep neck infection among adolescents + young adults!

Prevalence: ⅓ of all soft-tissue abscesses of head & neck

Organism: β-hemolytic Streptococcus, Staphylococcus aureus, pneumococcus, Haemophilus influenzae

• severe unilateral sore throat, dysphagia, otalgia, trismus

• tender cervical lymphadenopathy

• pharyngotonsillar exudate, fever

Imaging: (1) Diagnosis uncertain

(2) Limited clinical examination (severe trismus)

(3) Suspected infection of deep neck space

(4) Failed response to therapy

Location: between tonsillar capsule and pillar

CECT (75% specific, 99% sensitive):

√ tonsillar enlargement: √ "kissing tonsils" = medial apposition of enlarged tonsils

√ mass effect on oropharynx

√ linear striated enhancement of palatine tonsil + posterior pharyngeal soft tissue

√ central liquefaction + surrounding rimlike enhancement

◊ Commonly FP due to phlegmon!

Site: peritonsillar abscess typically along superior tonsillar pole (= potential space between tonsillar capsule + superior constrictor muscle)

√ true tonsillar abscess (rare)

Cx: extension of infection into parapharyngeal + masticator + submandibular space

Rx: needle aspiration, surgical drainage

DDx: tonsillitis; phlegmonous infection; necrotic retropharyngeal lymph node

PERSISTENCE OF STAPEDIAL ARTERY

= rare congenital vascular anomaly due to failure of regression of the embryonic stapedial artery that connects branches of the future external carotid artery to internal carotid artery

Prevalence: 1÷5,000

May be associated aberrant ICA

with:

Origin: petrous segment of ICA / aberrant ICA

Course: anteriorly and superiorly through middle ear to supply the middle meningeal artery

- pulsatile tinnitus
- conductive hearing loss ← ankylosis of stapes
- sensorineural hearing loss ← erosion of otic capsule (rare)

√ enlarged / separate tympanic segment of facial nerve canal
√ abnormal linear soft-tissue density crossing over cochlear promontory
√ absent / hypoplastic ipsilateral foramen spinosum
√ absence of normal origin of middle meningeal artery

PHARYNGEAL ABSCESS

Etiology: spread of infection from tonsils / pharynx
Age: children > adults

- trismus (most common presenting symptom) from involvement of pterygoid muscle, sore throat, low-grade fever

√ isodense / low-density mass with unsharp margins
√ rim enhancement
Cx: mycotic aneurysm of carotid artery (within 10 days)

PINDBORG TUMOR

[Jens Pindborg (1921–1995), Danish oral pathologist in Copenhagen]
= CALCIFYING EPITHELIAL ODONTOGENIC TUMOR
Frequency: 0.17–1.8% of all odontogenic tumors
Age: 20–60 years; M÷F = 1÷1
Histo: epithelial cells in a fibrous stroma
Associated with: crown of impacted tooth
Location: premolar / molar region of mandible (⅔), maxilla (⅓)
√ perichondral lucencies
√ radiolucent with scattered calcified components
CT:
√ diffuse highly attenuated foci = intralesional calcifications
MR:
√ predominantly low signal intensity on T1WI
√ high signal intensity on T2WI
√ heterogeneous contrast enhancement

PLEOMORPHIC ADENOMA

= BENIGN MIXED TUMOR OF PAROTIS
Frequency: 80% of all benign parotid tumors; 3rd most common tumor in pediatric parotid gland (after hemangioma + lymphangioma)
Histo: mixture of epithelial + myoepithelial cells
Age: usually > 50 (range, 30–70) years; M < F

• slow-growing asymptomatic hard painless lump in cheek
Location: usually solitary + unilateral
mnemonic: 80% in parotid gland
80% in superficial lobe
80% benign
√ lobulated round / oval sharply marginated mass
√ rarely dystrophic calcifications
√ variable, usually mild contrast enhancement
US:
√ hypo- to isoechoic well-defined lobulated mass
√ posterior acoustic enhancement
√ homogeneous well-defined tumor (if small)
√ less well-defined with low-density center if large (mucoid matrix, hemorrhage, necrosis)
√ ± hyperechogenic shadowing foci of calcifications
√ often poor / absent / occasionally abundant vascularity
MR:
√ hypointense on T1WI + hyperintense mass on T2WI
√ hyperintense areas in center (mucoid matrix)
Cx: malignant transformation after decades (= carcinoma ex pleomorphic adenoma, typically after 10–15 years); usually multifocal recurrence after inadequate surgery
Rx: facial nerve-sparing partial parotidectomy

RANULA

= mucus retention cyst / mucocele ← obstruction of sublingual / adjacent minor salivary gland
Classification:
(a) simple: confined to sublingual space; occasionally in submandibular space ← herniation through mylohyoid defect / arising from ectopic sublingual gland
(b) diving: extends to below mylohyoid muscle into submandibular space
Cause: trauma / inflammation of salivary gland
Origin: sublingual gland / minor salivary gland
• swelling in floor of mouth
US:
√ simple cystic (anechoic) lesion deep to mylohyoid muscle
√ ± fine internal echoes ← debris
MR:
√ lesion of high SI in sublingual space on T2WI
√ ± abnormally high SI on T1WI ← high protein content

Plunging / Diving Ranula

= pseudocyst (= no epithelial lining) in submandibular space
Cause: ruptured sublingual gland retention cyst
• gradually enlarging painless mass in submental / submandibular triangle
Location: posterior extension into submental / submandibular space with narrow tail to

floor of mouth

Size: < 6 cm in largest diameter

√ continuous cystic mass of comet-tail shape:

√ head of the comet = submandibular space component

√ tail of the comet = component pointing toward sublingual space

√ constriction at myohyoid muscle

RETROPHARYNGEAL ABSCESS / HEMORRHAGE

= PREVERTEBRAL ABSCESS

= spread of infection within retropharyngeal space

◊ In neck 2nd most common location after peritonsillar abscess

Etiology: tonsillitis, suppurative lymphadenitis, pharyngitis, otitis media, infection of oral cavity, dental infection, sinusitis, penetrating trauma of pharynx / esophagus, diskitis, osteomyelitis

Organism: Staphylococcus aureus, H influenzae, Streptococcus pneumoniae, Streptococcus pyogenes, Bacteroides melaninogenicus, typically mixed polymicrobial flora

Path: cellulitis > abscess

Age: usually 2–4 (range, 1–6) years (atrophy of nodes with age)

- history of upper respiratory tract infection
- fever, sore throat, neck stiffness, dysphagia, cough, sepsis

Lateral neck radiograph:

√ thickness of retropharyngeal space > ¾ of AP diameter of vertebral body:

√ may contain locules of gas / gas-fluid levels

√ reversal of cervical lordosis

√ anterior bowing / displacement of airway

N.B.: look carefully for possible ingested foreign body

DDx: "pseudothickening" (common in pediatric patients) ← neck flexion / incomplete inspiration

US:

√ hypoechoic areas + adenopathy

CECT (obligatory with concern for abscess):

√ hypoattenuating ovoid fluid collection

√ loss of normal bow-tie shape of retropharyngeal space

√ complete irregular circumferential rimlike enhancement (HALLMARK)

DDx: partial / NO enhancement = phlegmon

Cx: (1) Inferior extension through anatomic "danger space" into mediastinum

N.B.: ensure that at least part of mediastinum is imaged to exclude descending mediastinitis

(2) Direct extension to spine / epidural or carotid space

(3) Compromised airway

(4) IJV thrombosis = Lemierre syndrome

(5) Narrowing of ICA

(6) Pseudoaneurysm of ICA

Rx: aggressive treatment with IV antibiotics, airway management, surgical drainage

DDx: retropharyngeal space edema; suppurative retropharyngeal lymph node

> The differentiation of retropharyngeal abscess from retropharyngeal edema or cellulitis is critical but difficult in the absence of rimlike enhancement.

RHINOCEREBRAL MUCORMYCOSIS

= paranasal sinus / orbital infection caused by nonseptated fungi Rhizopus arrhizus and Rhizopus oryzae

Spread: fungus first involves nasal cavity, then extends into maxillary / ethmoid sinuses / orbits / intracranially along ophthalmic artery / cribriform plate (frontal sinuses are spared)

Predisposed:

(1) Poorly controlled diabetes mellitus
(2) Chronic renal failure
(3) Cirrhosis
(4) Malnutrition
(5) Cancer
(6) Prolonged antibiotic therapy
(7) Steroid therapy
(8) Cytotoxic drug therapy
(9) AIDS
(10) Extensive burns

- black crusting of nasal mucosa (in diabetics)
- small ischemic areas (invasion of arterioles + small arteries)

√ propensity for vascular invasion by fungal hyphae ← production of elastase

Cx: cerebral infarction, hemorrhage, mycotic aneurysm

√ nodular thickening involving nasal septum + turbinates
√ mucoperiosteal thickening + clouding of ethmoids
√ focal areas of bone destruction

Cx: (1) Blindness
(2) Cranial nerve palsy
(3) Hemiparesis

Prognosis: high mortality rate

SIALADENITIS

Organism: S. aureus
Location: submandibular gland, parotid gland
Site: typically unilateral

Acute Submandibular Sialadenitis

- "salivary colic" = painful swelling exacerbated by eating

US:

√ may depict ductal obstruction + calculi as small as 3 mm

CT:

√ enlargement of submandibular gland
√ ductal dilatation ← obstructive calculus / stenosis:

√ calculus in submandibular duct (80–90%) / parotid duct (10–20%) = radiographically visible in 80–90%

√ cellulitis + myositis in sublingual + submandibular space

Sialography:

√ may demonstrate cause of ductal stricture ← calculus, recurrent infection, autoimmune disease, trauma (rare)

Chronic Recurrent Sialadenitis

A. PAROTID GLAND

- painful periodic unilateral enlargement of parotid gland
- milky discharge may be expressed

Sialography:

√ Stensen duct irregularly enlarged / sausage-shaped

√ pruning of distal parotid ducts

√ ± calculi

CT:

√ diffusely enlarged dense gland

√ dilated Stensen duct ± calculi

Cx: Mucocele

B. SUBMANDIBULAR GLAND

- firm painless submandibular gland

√ unilateral atrophy + fatty infiltration

Acute Parotitis

Cause: bacterial, viral, calculus-induced

- toxic appearance, high fever, tenderness
- sudden onset of pain, swelling, tenderness

Acute Suppurative Parotitis

- purulent material expressed from Stenson duct

Organism: S. aureus (> 50%), anaerobic bacteria

At risk: elderly, debilitated, intubated + dehydrated patient

CT:

√ diffusely enlarged + enhancing parotid gland

√ ill-defined margins

√ intraparotid hypoattenuating abscess

HIV Parotitis

Histo: benign lymphoepithelial lesion consisting of an intranodal cyst lined with epithelial cells

US:

√ multiple hypoechoic / anechoic areas without posterior acoustic enhancement (70%)

√ anechoic cysts (30%)

CT / MR:

√ bilateral parotid gland enlargement with intraglandular cystic + solid masses

√ cervical lymphadenopathy + enlarged adenoids typically associated

Prognosis: parotid involvement is associated with a better prognosis in HIV-positive children!

Viral Parotitis

- self-limiting condition with prodromal symptoms

Peak age: 5–9 years
Organism: paramyxovirus (mumps) > influenzavirus, parainfluenzavirus, coxsackievirus, cytomegalovirus, adenovirus
Site: bilateral in 75%
Associated with: systemic viral illness ± involvement of submandibular and sublingual glands

Calculus-induced Parotitis

Site: typically unilateral
X-ray: √calculus radiolucent in 90%
CT: √majority of calculi visible

SIALOLITHIASIS

- recurrent swelling of salivary gland during eating
- palpable stone in floor of mouth = in distal part of submandibular (Wharton) duct

Location: submandibular gland (60–90%), parotid gland (10–20%); may be multiple
X-ray:
√ stones radiopaque (in only 20%)
Sialography (digital / MR)
US:
√ strongly hyperechoic line + distal acoustic shadowing
√ dilated excretory ducts
Cx: partial / total mechanical obstruction of salivary duct, bacterial infection, loss of glandular function

SIALOSIS

= usually bilateral nontender <u>noninflammatory</u> recurrent enlargement of parotid gland
Cause: cirrhosis, alcoholism, diabetes, malnutrition, hormonal insufficiency (ovarian / pancreatic / thyroid), drugs (sulfisoxazole, phenylbutazone), radiation therapy
Histo: serous acinar hypertrophy + fatty replacement of gland
Sialography:
√ sparse peripheral ducts
CT:
√ enlarged / normal-sized gland
√ diffusely dense gland in end stage
US:
√ enlarged hyperechoic salivary gland
√ NO focal lesion / increased blood flow

SINONASAL POLYPOSIS

= benign sinonasal mucosal lesions

Frequency: in 25% of patients with allergic rhinitis;
in 15% of patients with asthma
◊ Most frequent complication of sinusitis!

Pathogenesis: expansion of fluid in deep lamina propria of sinonasal mucosa

Cause: infectious rhinosinusitis; allergic fungal rhinitis (atopic hypersensitivity); cystic fibrosis (child); asthma; Kartagener syndrome; nickel exposure; aspirin intolerance; nonneoplastic hyperplasia of inflamed mucous membranes

Location: commonly maxillary antrum

√ multiple homogeneous soft-tissue masses with smooth convex borders within nasal cavity enlarging sinus ostium

√ remodeling / expansion of sinus with enlargement
◊ Most common expansile lesion in nasal cavity!

√ thinning of bony trabeculae ± erosive changes at anterior skull base

√ usually peripheral / occasionally solid heterogeneous enhancement

DDx: neoplasm, mucocele, mucus retention cyst

Prognosis: 75% surgical failure rate

Antrochoanal Polyp

= benign antral polyp, which widens the sinus ostium and extends into nasal cavity; 5% of all nasal polyps

Age: teenagers + young adults

√ antral clouding

√ ipsilateral nasal mass

√ smooth mass enlarging the sinus ostium

√ NO sinus expansion

Angiomatous Polyp

= derivative of choanal polyp (following ischemia of polyp with secondary neovascularity along its surface)

DDx: juvenile angiofibroma (involvement of pterygopalatine fossa)

SINONASAL PSEUDOTUMOR

Location: nasal cavity, nasopharynx, skull base, temporal bone, maxillary sinus, larynx, trachea, thyroid gland, salivary gland

√ more aggressive appearance than orbital pseudotumors:
√ osseous erosion, remodeling, sclerosis (common)

√ ± perineural spread along maxillary, mandibular, hypoglossal nn.

Cx: internal carotid occlusion

Prognosis: good after complete resection

Rx: less responsive to steroid therapy than orbital pseudotumors

SINUSITIS

Incidence:

most common paranasal sinus problem; most common chronic disease diagnosed in USA (31,000,000 persons per year); complicating common colds in 0.5% (3–4 colds per year in adults, 6–8 colds per year in children)

Pathogenesis:

viral infection → mucosal congestion → apposition of mucosal surfaces → retention of secretions → bacterial superinfection

(1) Obstruction of major ostia
  (a) middle meatus draining frontal, maxillary, anterior ethmoid sinus
  (b) sphenoethmoidal recess draining posterior ethmoid sphenoid sinus
(2) Ineffective mucociliary clearing ← contact of two mucosal surfaces

Predisposing anatomic variants:

(1) Greater degree of nasal septal deviation
(2) Horizontally oriented uncinate process NOT concha bullosa, paradoxical turbinate, Haller cells, uncinate pneumatization

Location:

(1) Infundibular pattern (26%)
  = isolated obstruction of inferior infundibulum just above the maxillary sinus ostium
  √ limited maxillary sinus disease
(2) Ostiomeatal unit pattern (25%)
  √ middle meatus opacification
(3) Sphenoethmoidal recess obstruction (6%)
  √ sphenoid / posterior ethmoid sinus inflammation
(4) Sinonasal polyposis pattern
  √ enlargement of ostia, thinning of adjacent bone
  √ air-fluid levels

Plain films (Waters, Caldwell, lateral, submental vertex views):

1. **Acute sinusitis**

   Dx: rests on clinical rather than radiologic findings!

   • "cold" symptoms (cough), fever, purulent nasal discharge
   √ mucosal thickening + enhancement
   √ air-fluid level ← retention of secretions ← ostial dysfunction ← mucosal swelling
   √ total sinus opacification
   √ hyperintense secretions on T2WI (95% water content + 5% proteinaceous macromolecules)

   DDx: mucus retention cyst

2. **Chronic sinusitis**

   √ mucosal swelling > 5 mm thick on Waters view (99% sensitive, 46% specific in maxillary sinus)
   √ bone remodeling + sclerosis ← osteitis
   √ polyposis
   √ hyperattenuating lesion on NECT ← inspissated secretions / fungal disease
   √ hypointense secretions on T1WI + T2WI ← inspissated material with chronic obstruction (DDx: air)

CT and MR lack specificity to diagnose acute sinusitis.
Either modality may be used to identify complications.

CT:
mapping bony anatomy for surgical planning

MR:
√ sinus thickening with high SI on T2WI + low SI on T1WI
√ near solid secretions with > 28% protein concentration are hypointense on both T1WI + T2WI simulating air
√ rim gadolinium enhancement (DDx to neoplasms, which enhance centrally)

Cx:
(1) Mucous retention cyst (10%)
(2) Mucocele
(3) Orbital extension through neurovascular foramina, dehiscences, or thin bones: orbital cellulitis
(4) Pott puffy tumor
(5) Septic thrombophlebitis
(6) Intracranial extension: meningitis, epidural abscess, subdural empyema, venous sinus thrombosis, cerebral abscess

Rx: functional endoscopic sinus surgery (amputation of uncinate process; enlargement of infundibulum + maxillary ostium; creation of common channel for anterior ethmoid air cells; complete / partial ethmoidectomy

Bacterial Sinusitis

Organism:
(a) acute phase: Streptococcus pneumoniae + Haemophilus influenzae (> 50%), beta-hemolytic streptococcus, Moraxella catarrhalis
(b) chronic phase: staphylococcus, streptococcus, corynebacteria, Bacteroides, fusobacteria

√ solitary antral disease (obstruction of sinus ostium)
√ uniform enhancement

Mycotic = Fungal Sinusitis

Organism: Aspergillus fumigatus, mucormycosis, bipolaris, Drechslera, Curvularia, Candida

√ polypoid lesion / fungus ball (= extramucosal infection ← saprophytic growth on retained secretions, usually caused by Aspergillus)
√ infiltrating fungal sinusitis (in immune-competent host)
√ fulminant fungal sinusitis (aggressive infection in immune-compromised individual / diabetics)

CT:
√ punctate calcifications (= calcium phosphate / calcium sulfonate deposition near mycelium)

MR:
√ dark on T2WI ← high fungal mycelial iron, magnesium, manganese content from amino acid metabolism (DDx: inspissated secretions / polypoid disease)

Dx: failure to respond to antibiotic therapy

Noninvasive Fungal Sinusitis

FUNGAL MYCETOMA / FUNGUS BALL OF SINUS

= uncommon manifestation as a tangled collection of fungal hyphae without allergic mucin

Organism: Aspergillus fumigatus, (rarely) Pseudallescheria boydii and Alternaria

Cause: deficient mucociliary clearance

Age: older individual; M < F

- asymptomatic
- minimal symptoms: chronic pressure, nasal discharge, cacosmia [*kakos*, Greek = bad, *osme* = smell]

√ nonenhancing intraluminal mass (usually limited to one sinus)

NECT:

√ hyperattenuating mass ← dense matted fungal hyphae
√ ± punctate calcifications
√ hypoattenuating mucosal lining ← inflammation
√ sclerotic thickened bony sinus walls
√ ± sinus expansion with focally thinned wall ← pressure necrosis

MR:

√ hyperintense mucosal lining on T2WI
√ hypointense intraluminal mass on T1WI + T2WI ← absence of free water
√ areas of signal void on T2WI ← calcifications and paramagnetic metals (iron, magnesium, manganese)

N.B.: NO invasion of sinus mucosa, blood vessels, bone

ALLERGIC FUNGAL SINUSITIS

◊ Most common form of fungal sinusitis characterized by presence of "allergic mucin" (= inspissated yellow-green / white-tan / gray / brown / black mucin of peanut butter consistency)

Prevalence: 5–10% of surgical patients with chronic hypertrophic sinus disease

Region: northern India, southern USA (warm humid climate)

Cause: IgE–mediated type I immediate hypersensitivity and type III delayed hypersensitivity reaction to inhaled fungal organisms (similar to allergic bronchopulmonary aspergillosis)

Organism: Bipolaris, Curvularia, Alternaria (dematiaceous pigmented fungi), Aspergillus, Fusarium (hyaline molds)

Histo: eosinophils + Charcot-Leyden crystals

Age: immunocompetent patient in 3rd decade

- chronic headaches, nasal congestion, chronic sinusitis
- history of sinus surgery

Often associated with: atopy (allergic rhinitis, asthma)

Location: multiple / all sinuses (bilateral); nose

√ near-complete opacification
√ high concentration of various metals (iron, magnesium, manganese) concentrated by

fungal organisms + high protein concentration + low free-water content:
√ hyperattenuating allergic mucin
√ mixed low / intermediate / high SI on T1WI
√ characteristic low SI / signal void on T2WI
√ inflamed mucosal lining:
√ hypointense on T1WI + hyperintense on T2WI
√ enhancement after administration of gadolinium
√ no central enhancement (DDx to neoplasm)
√ ± expansion of sinus and smooth bone erosion
√ ± intracranial and intraorbital extension

Invasive Fungal Sinusitis

Predisposed: immunocompromised
Pathophysiology: vascular invasion → rapid spread to maxillofacial soft tissues, orbit, pterygo-palatine fossa, anterior cranial fossa
MR signs of invasion:
√ obliteration of periantral fat = subtle sign of invasion
√ intraorbital invasion:
√ inflammation of orbital fat + extraocular muscle → proptosis
√ intracranial invasion:
√ leptomeningeal enhancement (initial stage)
√ adjacent cerebritis, granuloma, cerebral abscess
Cx: thrombosis of veins + cavernous sinus, meningitis, epidural + cerebral abscess, intraorbital extension, osteomyelitis, carotid artery invasion / occlusion / pseudoaneurysm → fatal cerebral infarct and intracranial hemorrhage
DDx: malignant neoplasm

ACUTE INVASIVE FUNGAL SINUSITIS

= INVASIVE FUNGAL RHINOSINUSITIS
= rapidly progressive most lethal form of sinusitis with hyphae within mucosa / submucosa / bone / blood vessels of paranasal sinuses
Predisposed: immunocompromised, poorly controlled diabetes
Organism:
(a) zygomycosis in diabetics with varied species: Rhizopus, Rhizomucor, Absidia, Mucor
(b) neutropenia (= neutropenic sinusitis) with hematologic malignancy, systemic chemotherapy, systemic steroid Rx, bone marrow transplantation, organ transplantation, AIDS : Apergillus in 80%
Associated with: nasal infection (⅔ in middle turbinate)
• painless necrotic nasal septal ulcer (eschar), sinusitis
CT:
√ aggressive bone destruction of sinus walls on CT
√ severe unilateral nasal cavity soft-tissue thickening (nonspecific)
Mortality: 50–80% among neutropenic patients
Rx: aggressive surgical débridement, systemic antifungal medication

CHRONIC INVASIVE FUNGAL SINUSITIS

= persistent + recurrent disease → invasion develops over months to years

Organism: Mucor, Rhizopus, Aspergillus, Bipolaris, Candida

• chronic rhinosinusitis: paranasal sinus pain, fever, serosanguinous nasal discharge, epistaxis, nasal polyposis

CT:

√ hyperattenuating soft-tissue collection

√ mottled lucencies / irregular bone destruction

√ sclerotic changes in osseous sinus walls (chronic)

MR:

√ decreased signal intensity on T1WI + T2WI

Odontogenic Sinusitis

Incidence: 5–38% of maxillary sinusitis

• purulent nasal discharge, facial pressure, cheek and facial pain

◊ Infection decompressed through patent ostiomeatal unit!

◊ Sinus floor mucosal inflammation may manifest with toothache!

√ sinus mucosal thickening above a carious tooth

√ focal ballooning / dehiscence above a carious tooth

√ unerupted tooth in maxillary sinus

Rx: root canal therapy, tooth extraction, antibiotics

SJÖGREN SYNDROME

= MYOEPITHELIAL SIALADENITIS

= chronic autoimmune multisystem disorder (= collagen-vascular disease) characterized by inflammation + destruction of exocrine glands (by T-lymphocytes, mainly CD4+ cells, and autoantibodies from hyperstimulated B cells) → dryness of mucous membranes affecting

(1) Salivary + lacrimal glands

(2) Mucosa + submucosa of pharynx

(3) Tracheobronchial tree

(4) Reticuloendothelial system

(5) Joints

Frequency: 0.1% of population; 3% of older adults

Cause:

A. PRIMARY SJöGREN SYNDROME

= autoimmune exocrinopathy in isolation

(a) recurrent parotitis in children

(b) **Sicca syndrome** = Mikulicz disease = xerophthalmia + xerostomia

B. SECONDARY SJöGREN SYNDROME

as a complication of other autoimmune disorders

Associated with:

(a) connective tissue diseases

1. Rheumatoid arthritis (55%)
2. Systemic lupus erythematosus (2%)
3. Progressive systemic sclerosis (0.5%)

4. Psoriatic arthritis, primary biliary cirrhosis (0.5%)
5. Polymyositis

(b) lymphoproliferative disorders

1. Lymphocytic interstitial pneumonitis (LIP)
2. Pseudolymphoma (25%)
3. Lymphoma (5%; 44 x increased risk): mostly B-cell lymphoma
4. Waldenström macroglobulinemia

Mean age: 57 (range, 35–70) years; M÷F = 1÷9

Path: benign lymphoepithelioma

Histo: lymphocytic infiltrate associated ductal dilatation, acinar atrophy, interstitial fibrosis (= parotid destruction)

- **xerostomia** (most common symptom) = atrophy of salivary + parotid glands → diminished saliva production and dryness of mouth + lips
- **xerophthalmia** = dryness of eyes = keratoconjunctivitis sicca = desiccation of cornea + conjunctiva ← decreased lacrimation
- **xerorhinia** = dryness + crusting of nasal mucosa

  Cx: epistaxis, nasal septal perforation
- decreased sweating, decreased vaginal secretions
- swelling of parotid gland:
  - › recurrent acute episodes with tenderness; usually unilateral
  - › chronic glandular enlargement with superimposed acute attacks of painless progressive swelling
- rheumatoid factor (positive in up to 95%)
- ANA (positive in up to 80%); mitochondrial antibodies (6%)

Location: lacrimal + salivary glands; mucous glands of conjunctivae, nasal cavity, pharynx, larynx, trachea, bronchi; extraglandular involvement in 5–10%

@ Lung (9–75%)

affected by airway abnormalities, interstitial pneumonias, and lymphoproliferative disorders

- chronic dry cough, recurrent bronchitis, dyspnea on exertion

Histologic pattern of interstitial lung disease:

LIP, NSIP, UIP, cryptogenic organizing pneumonia, follicular bronchiolitis, diffuse interstitial amyloidosis

√ pulmonary fibrosis (10–14%, most common finding)
√ reticulonodular pattern (3–33–52%) involving lower lobes (= lymphocytic interstitial pneumonitis)
√ patchy consolidation
√ inspissated mucus
√ atelectasis
√ recurrent pneumonia
√ bronchiectasis of both lower lobes
√ acute focal / lipoid pneumonia ← oils taken to combat dry mouth
√ ± pleural effusion (uncommon)

HRCT (usually required for detection):

√ poorly defined centrilobular nodules + branching linear opacities = tree-in-bud appearance

√ bronchiectasis + bronchiolectasis
√ bronchial wall thickening ← bronchiolar inflammation
√ groundglass opacities + air trapping
√ thickening of interlobular septa
√ cysts ← bronchiolar obstruction ← follicular bronchiolitis (= lymphocytic wall infiltration)

@ Mediastinum
√ lymph node enlargement
√ thymic lymphoid hyperplasia
√ multilocular thymic cyst
√ MALT lymphoma

@ Parotid gland
Sialogram:
√ nonobstructive sialectasia (ducts + acini destroyed by lymphocytic infiltrates / infection)
Stage I : punctate contrast collection < 1 mm
Stage II : globular contrast collection 1–2 mm
Stage III : cavitary contrast collection > 2 mm
Stage IV : destruction of gland parenchyma

US:
√ enlarged heterogeneous gland with punctate areas of increased echogenicity (= mucus-filled ducts)
√ multiple small oval usually well-defined scattered hypo- / anechoic areas bilaterally (= sialectasis ← cystic dilatation of intraparotid ducts + glands)
√ increased parenchymal vascularity on color Doppler

MR:
√ inhomogeneous "honeycomb" / "salt and pepper" appearance (= areas of low intensity between nodular parenchyma of high SI) on T2WI / Gd-enhanced T1WI

@ CNS involvement (in 25–30%)
• trigeminal neuropathy, recurrent aseptic meningoencephalitis, cerebral parenchymatous lesions

MR:
√ extensive uni- / multifocal white and gray matter lesions + infarctions + microbleeds
√ multiple arterial narrowings

Prognosis: generally good (morbidity from decreased function of exocrine organs)

Cx: **Sjögren syndrome-associated B-cell lymphoma** (occurs in salivary glands + mucosa-associated lymphatic tissue in stomach + lung in a significant number of patients + follows an aggressive course)

Dx: biopsy for fast-growing lesions > 2 cm

SUBGLOTTIC STENOSIS

A. CONGENITAL SUBGLOTTIC STENOSIS
• crouplike symptoms, often self-limiting disease
Location: 1–2 cm below vocal cords

√ circumferential symmetrical narrowing of subglottic portion of trachea during inspiration
√ NO change in degree of narrowing with expiration

B. ACQUIRED SUBGLOTTIC STENOSIS
following prolonged endotracheal intubation (in 5%)

TERATOMA OF HEAD & NECK

= GERM CELL TUMOR OF NECK

Prevalence: 1÷20,000 to 1÷40,000 live births; 5% of newborn teratomas in lateral + anterior neck

◊ 80% of mediastinal germ cell tumors are benign!

Origin: thyrocervical area / palate / nasopharynx

Spectrum:

1. Dermoid cyst (with skin appendages):
   Site: orbit, nasal region, at floor of the mouth
2. Epidermoid cyst
3. Teratoid cyst (with tissues from CNS, GI, respiratory system)

OB-US:

√ polyhydramnios in 30% ← esophageal obstruction
√ large bulky complex cystic + solid mass in cervical region
√ calcifications (in 50%)

CT:

√ hypoattenuating thin-walled unilocular mass:
  √ nodules frequent in dermoid cysts
  √ heterogeneous contents in teratomas

MR:

√ hypo- to isointense on T1WI + hyperintense on T2WI:
  √ dermoid cysts may be hyperintense on T1WI ← lipid-containing areas
  √ coronal imaging useful to depict relationship to mylohyoid muscle

Cx: airway obstruction, compromised swallowing

Rx: ex utero intrapartum treatment (EXIT) procedure

DDx: cystic hygroma (septated fluid-filled collection, posterior location), goiter, branchial cleft cyst, cervical meningo-cele, neuroblastoma of neck, hemangioma of neck

Cervical Teratoma

= usually benign; malignant transformation possible

Prevalence: 5% of teratomas in newborn

Location: anteriorly (thyroid gland) with extension to trapezius muscle (posteriorly), mastoid (superiorly), clavicle / mediastinum (inferiorly)

√ hyperextension of neck
√ solid + cystic structures within heterogeneous mass
√ calcifications (more frequent than cartilage / bone)

Cx: malpresentation, dystocia

Teratoma of Mouth

= EPIGNATHUS

Origin: hard / soft palate
√ mass filling oral cavity + extending out through mouth
DDx: frontal encephalocele, myoblastoma

TEMPOROMANDIBULAR JOINT DYSFUNCTION

= internal derangement = abnormal relationship of disk to condyle
Incidence: affects up to 28% of population
Cause: disk injury
√ intrinsic disk lesion (change in shape + signal intensity):
  √ irregular biconvex / rounded disk ← thickening of posterior band + reduction in mass of anterior band and central thin area
  √ flattening of disk
  √ reduction in normal intermediate to high SI of disk
√ disk displacement:
  √ anterior (in up to 34% of asymptomatic volunteers), anterolateral, anteromedial, lateral, medial, posterior disk displacement
  √ anterior displacement of posterior band in front of condyle with abnormal stretching of bilaminar zone
  √ anterior displacement of meniscus without reduction at maximum mouth opening
  √ "stuck disk" = fixed position of disk relative to glenoid fossa and articular eminence during closed- and open-mouth positions
  √ "locked jaw" = posterior band displaced beyond 1 o'clock position
√ joint effusion
√ osteoarthritis: flattening, osteophytes, erosions, sclerosis

THYROGLOSSAL DUCT CYST

= failure of complete involution of embryonic thyroglossal duct
Frequency: most common congenital neck mass (70% of all congenital neck anomalies); 2nd most common benign neck mass after benign lymphadenopathy; 90% of nonodontogenic congenital cysts
Histo: cyst lined by stratified squamous epithelium / ciliated pseudostratified columnar epithelium ± mucous glands; ectopic thyroid tissue in 5–62%
Age: < 10 years in 50%; 2nd peak at 20–30 years; M=F
• gradually enlarging painless midline neck mass
• cyst moves vertically / upward during protrusion of tongue / swallowing ← close relationship of cyst to hyoid bone + foramen cecum (= most SPECIFIC physical finding)
• ± history of previous incision and drainage of an "abscess" in area of cyst
Location: suprahyoid (15–25%), at level of hyoid (15–50%), infrahyoid (20–65%)
Site: midline (75%), paramedian within 2 cm of midline frequently on left (25%)
Size: 1.5–3.0 (range, 0.5–6.0) cm
√ cyst with occasional septation within 2 cm of midline
√ infrahyoid cyst embedded within / deep to strap muscle:
  √ infrahyoid strap muscles beaks over edge of cyst
  √ thin connecting stalk to midline

√ paramedian cyst with a tail that dives into hyoid bone

US:

- √ anechoic cyst (42%) in midline
- √ hypoechoic mass with fine to coarse internal echoes (= proteinaceous material) + increased through transmission

Scintigraphy:

- √ uptake in functional thyroid tissue of thyroglossal duct cyst

CT:

- √ smooth well-circumscribed midline mass with thin wall
- √ homogeneous mucoid attenuation of 0–20 HU / occasionally higher ← increased protein content
- √ thin peripheral rim of enhancement
- √ tract of thyroid tissue between cystic mass + thyroid

MR:

- √ cyst of low to intermediate SI on T1WI + high SI on T2WI
- √ NO restricted diffusion
- √ nonenhancing / enhancing very thin rim (unless inflamed)
- √ heterogeneous complex cyst with infection:
  - √ thick irregular rim of enhancement
  - √ variable SI of fluid ← infection / hemorrhage
  - √ profuse surrounding soft-tissue edema

Cx: (1) Infection → thick external wall ± internal septa
(2) Fistulous communication to the skin (15–33%)
(3) Thyroid carcinoma (1–4%): in 80% papillary ca.
(4) Squamous cell carcinoma (even rarer)

Dx: close association with hyoid bone (60–80%)

Rx: Sistrunk procedure (= resection of central portion of hyoid bone + core of tissue following the expected course of entire thyroglossal duct to foramen cecum) with 2.6% recurrence rate

DDx: (1) Ectopic thyroid (no thyroid tissue in normal location)
(2) Obstructed laryngocele (well-defined smooth mass / saccular cyst in lateral aspect of superior paralaryngeal space connecting to larynx originating from saccule / appendix of laryngeal ventricle)
(3) 2nd branchial cleft cyst (round mass near mandibular angle along anterior surface of sternocleidomastoid muscle / displacing muscle posterolaterally, lateral to carotid sheath structures (carotid artery + internal jugular vein), posterior to submandibular gland, PATHOGNOMONIC beak insinuating itself between ICA + ECA)
(4) Thymic cyst = persistent thymopharyngeal duct (mostly on left side of neck)
(5) Lymphatic malformation (mostly in posterior cervical triangle, transspatial, containing locules, congenital lesion detected by age 2 years)
(5) Lingual abscess (← infected lingual thyroglossal duct cyst / dermoid cyst / ranula / secondary to instrumentation or tongue piercing)

THYROID ADENOMA

√ round / oval mass of low attenuation with enhancement

Adenomatous Nodule (42–77%)
= COLLOID NODULE = ADENOMATOUS HYPERPLASIA
= DEGENERATIVE INVOLUTED NODULE
Cytology: abundant colloid + benign follicular cells with uniform slightly large nuclei, arranged in a honeycomb pattern (difficult DDx from follicular tumors)
√ often multiple nodules by US / scintigraphy / surgery
√ mostly hypofunctioning, rarely hyperfunctioning
√ solid form = incompletely encapsulated, poorly demarcated nodules merging with surrounding tissue
√ cystic form (= colloid cyst) = anechoic areas in nodule ← hemorrhage / colloid degeneration
√ calcific deposits

Follicular Adenoma (15–40%)
= monoclonal tumor arising from follicular epithelium
Path: single lesion with well-developed fibrous capsule
Histo subtypes:
(a) Simple colloid (macrofollicular) adenoma: most common form
(b) Microfollicular (fetal) adenoma
(c) Embryonal (trabecular) adenoma
(d) Hürthle-cell (oxyphil / oncocytic) adenoma: large single polygonal cells with abundant granular cytoplasm + uniform eccentric nuclei + no colloid
(e) Atypical adenoma
(f) Adenoma with papillae
(g) Signet-ring adenoma
◊ 5% of microfollicular adenomas, 5% of Hürthle-cell adenomas, 25% of embryonal adenomas prove to be follicular cancers in carefully performed study!
Functional status:
(1) Toxic adenoma
(2) Toxic multinodular goiter = hyperfunctioning adenoma within multinodular goiter; usually occurs in nodule > 2.5 cm in size
(3) Nonfunctioning adenoma
√ mass with increased / decreased echogenicity
√ "halo" sign = complete hypoechoic ring with regular border surrounding isoechoic solid mass
Rx: surgical hemithyroidectomy (→ 15–30% risk of malignancy if diagnosed on FNAB)

THYROID CARCINOMA

Incidence: 25,000 new cancers per year in USA (2005); clinically silent cancers in up to 35% at autopsy / surgery (usually papillary carcinomas of < 1.0 cm in size); 3.6÷100,000 (1973), 8.7÷100,000 (2002)
Age: < 30 years; M÷F = 1÷3 to 1÷2
Risk factors: age < 20 years or > 60 years; history of neck irradiation; family history of thyroid

cancer
◊ Lifetime risk of thyroid cancer < 1% in USA

Types (in order of worsening prognosis):
papillary (50–80%) > follicular (10–20%) > medullary (6–10%) > anaplastic

• history of neck irradiation, rapid growth
• stone-hard nodule:
◊ 5–7% of all thyroid nodules are malignant!

√ hypoechoic / hypoattenuating mass
√ irregular ill-defined border without / disrupted halo
√ NO hemorrhage / liquefaction necrosis
√ ancillary findings:
√ lymphadenopathy (in 19%)
Frequency: papillary carcinoma (in up to 40–90%) > medullary carcinoma (in up to 50%) > follicular carcinoma (rare)
√ increased size with round bulging shape
√ replaced fatty hilum
√ heterogeneous echotexture
√ irregular margins
√ psammomatous calcifications
√ cystic change (70% in metastatic papillary carcinoma)
√ color Doppler vascularity throughout instead of central hilar vessels only
√ destruction of adjacent structures
√ loss of fat planes
√ distant metastasis

PET:
√ well-differentiated thyroid carcinomas are not FDG-avid

Mortality: 0.5 deaths÷100,000 (unchanged over decades)

Radiation-induced Thyroid Cancer

Incidence: increases with doses of thyroidal irradiation from 6.5–1,500 rad (higher doses are associated with hypothyroidism)

Peak occurrence: 5–30 (up to 50) years post irradiation

Thyroid abnormalities in 20%:
(a) in 14% adenomatous hyperplasia, follicular adenoma, colloid nodules, thyroiditis
(b) in 6% thyroid cancer

◊ Nondetectable microscopic foci of cancer in 25% of patients operated on for benign disease!
◊ In patients with multiple cold nodules frequency of cancer is 40%

Diagnostic Whole-body ^{131}I Scintigram

Indication: to detect metastases of thyroid carcinoma after total thyroidectomy; for skeletal metastases preferred over bone scan (that only detects 40%)

◊ Metastases not detectable in presence of normal functioning thyroid tissue because uptake is much less in metastases
◊ ^{99m}Tc-pertechnetate is useless because of high background activity + lack of organification

◊ False-negative ^{131}I scan in 24% ← nonfunctioning metastases

Technique:

» low iodine diet for 7 days = avoid iodized salt; milk and diary products; eggs; seafood; bread made with iodate dough conditioners; red food dyes; restaurant food; food containing iodized salt, sea salt, iodates, iodines, algin, alginates, agar agar

» T_4 replacement therapy discontinued for 6 weeks

» short-acting T_3 is administered for 4–6 weeks

» T_3 replacement therapy discontinued 10–14 days prior to whole-body scan

» measurement of TSH level to confirm adequate elevation (TSH > 30–50 mIU/mL; administration of exogenous TSH not desirable because of uneven stimulation)

» oral administration of 1–5–10 mCi ^{131}I

» whole-body scan after 24–48–72 hours (low background activity) with high-energy collimator + 20% energy window centered at 364 keV

N.B.: posttherapy scan (1 week after therapeutic dose) identifies more lesions than diagnostic scan; CONTRAINDICATED during pregnancy!

Treatment for Follicular / Papillary Cancer

(1) Surgery: total thyroidectomy + modified radical neck dissection

(2) Postoperative radioiodine treatment with ^{131}I if diagnostic scan positive (multiple treatments are usually necessary)

◊ Radioiodine therapy only appropriate for papillary / mixed / follicular thyroid carcinomas (NOT for medullary or anaplastic carcinomas)

(a) **Ablation of thyroid tissue remnants**

Time interval: 6 weeks after surgery

• no thyroid hormone replacement for 3–4 weeks

Calculated dose:

= {(thyroid weight [g] x 80–120 μCi/g) π % uptake of ^{123}I by 24 hours} x 100

Estimated dose: 30–100 mCi ^{131}I orally

» rescan after 3–7 days

√ no change from pre-ablation: on suppression therapy

√ new foci (in up to 16%): consider therapy

√ decreased uptake: may be due to "stunning"

(b) **Treatment of metastases**

Middle-of-the-road dose:

» 100 mCi for residual neck activity

» 150 mCi for regional lymph node metastases

» 175 mCi for lung metastases

» 200 mCi for bone metastases

Tumor dose:

150 mCi of ^{131}I with an uptake of 0.5% per gram of tumor tissue and a biologic half-life of 4 days will produce 25,000 rad to tumor

◊ Rapid turnover rates may exist in some metastases (lower dose advisable)

◊ Treatment of large tumors incomplete (range of beta radiation is a few mm only)

Cx: radiation thyroiditis; radiation parotitis; GI symptoms (nausea, diarrhea); minimal

bone marrow depression; leukemia (2%); anaplastic transformation (uncommon); lung fibrosis (with extensive pulmonary metastases and dose > 200 mCi)

(3) Thyroid replacement therapy: exogenous thyroid hormone to suppress TSH stimulation of metastases

(4) External radiation therapy for anaplastic carcinoma + metastases without iodine uptake

FOLLOW-UP: thyroglobulin > 50 ng/mL indicates functioning metastases after complete ablation of thyroid tissue

Papillary Carcinoma of Thyroid (60–80%)

Peak age: 5th decade; F > M

Histo: unencapsulated well-differentiated tumor

(a) purely papillary

(b) mixed with follicular elements (more common, especially under age 40)

Metastases:

(1) Lymphogenic spread to regional lymph nodes (40%, in children almost 90%)

(2) Hematogenous spread to lung (4%), bone (rare)

• carcinoma elaborates thyroglobulin

NUC:

√ tumor usually concentrates radioiodine (even some purely papillary tumors) → ^{131}I whole-body scintigraphy to assess for recurrence after thyroidectomy / ablation

US:

√ psammoma bodies = punctate echogenic foci less than 1 mm in size WITHOUT acoustic shadowing

√ tumor of decreased echogenicity

√ purely solid / complex mass with areas of necrosis, hemorrhage, cystic degeneration

X-ray:

√ punctate / linear psammomatous calcifications at tumor periphery

Rx: total thyroidectomy (← commonly multifocal); radioactive iodine ablation

Prognosis: 90–95% 20-year survival; 60% 10-year survival for extrathyroidal cancer; worse prognosis with increasing age

Follicular Carcinoma of Thyroid (11–20%)

Peak age: 5th decade; F > M

Path: encapsulated well-differentiated tumor without papillary elements; in 25% multifocal

Histo: follicular cells with capsular / vascular invasion; cytologically impossible to distinguish between well-differentiated follicular carcinoma + follicular adenoma (vascular invasion is the only criteria)

Early hematogenous spread to:

(a) lung

(b) bone (30%): almost always osteolytic lesion (more frequent than in papillary carcinoma)

• carcinoma elaborates thyroglobulin

√ psammoma bodies + stromal calcium deposits

NUC:

√ usually concentrates pertechnetate, but fails to accumulate ^{123}I

US:
√ indistinguishable from benign follicular adenoma
Prognosis: slow growing; 75% 20-year survival; 90% 10-year survival with slight / equivocal angioinvasion; 35% 10-year survival with moderate / marked angioinvasion
Rx: total thyroidectomy (for invasive cancer); ± subsequent radioactive iodine ablation; lobectomy + isthmusectomy (for minimally invasive cancer)

Anaplastic / Undifferentiated Carcinoma of Thyroid

Prevalence: 2–15%
Age: 6–7th decade; M÷F = 1÷1
√ intrathoracic extension in up to 50%
√ ± invasion of carotid artery, internal jugular vein, larynx
NUC:
√ NO radioiodine uptake
CT:
√ mass with inhomogeneous attenuation
√ areas of necrosis (74%)
√ calcifications (58%)
√ regional lymphadenopathy (74%)
Prognosis: 5% 5-year survival; average survival time of 6–12 months

Medullary Carcinoma of Thyroid (1–5–10%)

sporadic (80%) / familial
Histo: arises from parafollicular C-cells, associated with amyloid deposition in primary + metastatic sites
Hormone activity: calcitonin, VIP, somatostatin, CEA
Mean age: 60 years for sporadic variety;
during adolescence in MEN 2
In 20% associated with:
(1) MEN 2a = pheochromocytoma + parathyroid hyperplasia (Sipple syndrome)
(2) MEN 2b = without parathyroid component
Metastases: early spread to lymph nodes (50%), lung, liver, bone
• elevated calcitonin (= primary tumor marker from tumor production) stimulated by pentagastrin + calcium infusion
• elevated carcinoembryonic antigen (CEA)
√ mass of 2–26 mm
√ granular calcifications within fibrous stroma / amyloid masses (50%)
√ local invasion (common)
√ nodal spread to neck + mediastinum (in up to 50%) at time of presentation
√ distant metastases to liver, lung, bone (15–25%)
NUC:
√ NO uptake by radioiodine / pertechnetate
√ frequently shows increased uptake of ^{201}Tl
√ concentrates ^{123}I-MIBG, pentavalent ^{99m}Tc-DMSA, ^{111}In-pentetreotide (41% sensitive)

√ FDG-PET (96% sensitive)

CT:

√ mass of low attenuation (no iodine concentration)

Prognosis: 90% 10-year survival without nodal metastases; 42% 10-year survival with nodal metastases

Rx: total thyroidectomy + modified radical neck dissection

THYROIDITIS

DeQuervain Thyroiditis

= SUBACUTE GRANULOMATOUS THYROIDITIS

= distinct clinical syndrome characterized by exquisite thyroid tenderness, goiter, and thyrotoxicosis

Etiology: probably viral / postviral process (Coxsackie, mumps) frequently occurring in seasonal clusters

Histo: infiltrate of neutrophils and lymphocytes + characteristic multinucleated giant cells

Peak age: 2nd–5th decade; M÷F = 1÷5

- upper respiratory tract infection, fever, and systemic flulike symptoms precede onset of symptoms by 2–3 weeks
- tender gland with pain radiating to jaw / ear
- firm tense mild thyroid gland enlargement
- CHARACTERISTIC elevation of ESR > 50 mm/hour
- hyperthyroidism (50%) ← severe gland destruction
- short-lived hypothyroidism (25%) ← hormone depletion

US:

√ areas of hypoechogenicity

NUC:

√ abnormally low 24-hour radioiodine uptake with clinical and laboratory evidence of hyperthyroidism

√ poor visualization of thyroid (initially)

√ single / multiple hypofunctional areas (occasionally)

√ increased uptake during phase of hypothyroidism (late event)

Cx: permanent hypothyroidism (rare)

Rx: treatment of pain with NSAID / prednisone

Prognosis: usually full recovery

Hashimoto Thyroiditis

= CHRONIC LYMPHOCYTIC THYROIDITIS = GOITROUS AUTOIMMUNE THYROIDITIS

Incidence: 0.3–1.5÷1,000 population per year

Most frequent cause of goitrous hypothyroidism in adults in the USA (iodine deficiency is the more common cause worldwide)

Etiology: autoimmune process with marked familial predisposition (antibodies are typically present); functional organification defect

Histo: diffuse lymphocytic infiltration; occasional germinal centers; small thyroid follicles

containing sparse colloid; fibrosis; Hürthle / Askanazy cells = large thyroid cells with pink cytoplasma ("oxyphil change")

Peak age: 4–5th decade; M÷F = 1÷15

- firm rubbery possibly asymmetric lobular goiter
- decreased thyroid reserve (= injection of TSH does not result in expected increase in radioiodine uptake / release of hormone from the gland)
- FT_4 most typically normal / low
- antithyroid peroxidase + antithyroglobulin antibodies

Clinical course:

- gradual painless enlargement resulting in neck tightness
- periods of mild thyrotoxicosis (4%) / subclinical to overt hypothyroidism (20%) at presentation
- progression from euthyroidism to hypothyroidism
- return to normal function over several years (in 25%)

√ moderate enlargement of both lobes (usually 2–4 x normal volume) + prominent pyramidal lobe

NUC:

√ characteristically normal / elevated tracer uptake
√ low tracer uptake with poor visualization (4%)
√ positive perchlorate washout test
√ patchy tracer distribution
√ multiple (40%) / single cold defects (28%) / normal thyroid (8%)

US:

√ enlarged thyroid (77% greater volume compared with normal size)
√ initially heterogeneous nonspecific diffusely decreased echogenicity (in 18–77%)
√ irregular surface with slight lobulation of contour
√ marked hyperemia on color Doppler
√ later densely echogenic (fibrosis) + acoustic shadowing
√ ± satellite lymph nodes (Delphian node above isthmus)

Cx: hypothyroidism

Dx: (1) Diffuse firm bosselated goiter with pyramidal lobe enlargement
(2) NO signs of thyrotoxicosis
(3) Positivity for antibodies against thyroid microsomes / peroxidase / thyroglobulin
(4) Lymphocytic infiltrates

DDx (1) Atrophic chronic autoimmune thyroiditis (small gland)
(2) Painless thyroiditis (transient disorder, painless goiter, hyperthyroidism / hypothyroidism)
(3) Graves disease (diffuse goiter, hyperthyroidism, ophthalmopathy)

Painless / Silent Thyroiditis

= SUBACUTE LYMPHOCYTIC THYROIDITIS

Frequency: up to 23% of hyperthyroid patients in USA (many cases misdiagnosed as Graves disease)

Etiology: autoimmune process frequently in postpartum period (**postpartum thyroiditis**) +

under cytokine / lithium therapy

Histo: resembles chronic lymphocytic thyroiditis (Hashimoto) with paucity of lymphocyte germinal centers and fibrosis

- clinical presentation similar to subacute thyroiditis + clinically indistinguishable from Graves disease
- anti-thyroid peroxidase antibodies (in 60%)
- small NOT painful / tender goiter (in 50–60%)
- mild thyrotoxicosis lasting for a few months

√ 24-hour radioiodine uptake < 1%

Prognosis: recovery of thyroid function (majority); persistent goiter (33%); permanent hypothyroidism (20%); recurrent episodes of subacute lymphocytic thyroiditis (10%)

Acute Infectious / Suppurative Thyroiditis

= rare entity since the introduction of antibiotics

- ill febrile usually euthyroid patient

US:

√ focal / diffuse enlargement; possibly abscess

√ decreased echogenicity

Subacute Thyroiditis

= inflammatory destruction of thyroid follicles with release of preformed hormone into the circulation

Classification:

1. Subacute granulomatous thyroiditis (de Quervain)
2. Subacute lymphocytic thyroiditis
   (a) postpartum thyroiditis:
      ◊ Enable radioiodine uptake test by suspending breast-feeding for 1 week, during which time the radioiodine-contaminated breast milk should be pumped and discarded
   (b) cytokine-associated thyroiditis (interferon-alpha for chronic hepatitis B/C, interleukin-2 as adjunctive therapy for metastatic cancer and leukemia)
   (c) lithium-associated thyroiditis
3. Subacute thyroiditis due to cellular injury
   ← amiodarone-induced thyroiditis
4. Subacute thyroiditis due to trauma
   Cause: palpation, parathyroid surgery, direct surgical trauma, thyroid biopsy, seatbelt injury
5. Subacute thyroiditis due to radiation
   Cause: radioiodine treatment, external beam radiation

Phases:

1. Hyperthyroid phase
   = initial inflammatory stage → leakage of T_4 and T_3 into the circulation → suppression of pituitary TSH production → virtually absent 24-hour uptake
   - $T_3 \div T_4$ ratio (ng/dL ÷ mg /dL) < 20

√ virtually absent radioiodine uptake (usually < 1%)
Duration: several weeks – several months
√ marked decrease in echogenicity (the lowest of all thyroid disorders)
√ normal vascularity
Rx: beta-adrenergic blocking agents; ipodate or iopanoic acid

2. Hypothyroid phase
= inflammation subsides → thyroid hormone levels decrease to euthyroid + into hypothyroid range
√ normalization of 24-hour radioiodine uptake
Duration: 4 weeks – 6 months
√ regaining of isoechogenicity during recovery phase
√ ± slightly increased vascularity
Rx: levothyroxine dose adjusted to TSH level

US:
√ discrete nodules (50%)

Riedel Thyroiditis

= IgG4-RELATED THYROIDITIS
= rare chronic inflammatory process with extensive fibrosis
• rock-hard painless mass involving thyroid parenchyma and surrounding tissues
Associated with: fibrosclerosis in other organs (in ⅓)
US:
√ heterogeneously hypoechoic thyroid mass
CT:
√ focal / diffuse low-attenuation mass of thyroid
√ minimal contrast enhancement relative to normal thyroid
PET:
√ avid uptake
Rx: steroid therapy → marked reduction of thyroid mass

TORNWALDT CYST

= midline congenital pouch / cyst lined by ectoderm within nasopharyngeal mucosal space
[Gustav Ludwig Tornwaldt (1843–1910), physician in Danzig, Germany]
Origin: persistent focal adhesion between notochord + ectoderm extending to pharyngeal tubercle of occipital bone
Frequency: 4% of autopsies
◊ Most common congenital head and neck cyst in childhood!
Peak age: 15–30 years
• asymptomatic incidental finding
• persistent nasopharyngeal drainage
• halitosis, foul taste in mouth
Location: posterior roof of nasopharynx
√ smoothly marginated cystic mass of few mm to 3 cm in size
√ low density, not enhancing
√ NO bone erosion

Cx: infection of cyst
DDx: Rathke pouch (occurs in craniopharyngeal canal located anteriorly + cephalad to Thornwaldt cyst)

TOXIC AUTONOMOUS NODULE

= PLUMMER DISEASE = TOXIC ADENOMA
= hyperthyroidism caused by one / two hyperfunctioning nodules independent of normal pituitary-thyroid control mechanism
◊ All toxic nodules are autonomous;
HOWEVER, not all autonomous nodules are toxic
Cause: gene mutation of TSH receptors of adenoma surface (not autoimmunity) result in continuous activation
Histo: adenoma
• excessive serum levels of thyroid hormone
• suppressed TSH production, clinically hyperthyroid
√ radioiodine uptake (RAIU) mildly to moderately elevated
√ concentration of radiopharmaceutical to a far greater degree than surrounding extranodular thyroid tissue
DDx: Graves disease (RAIU significantly elevated)

TOXIC MULTINODULAR GOITER

= multinodular goiter associated with hyperthyroidism
Cause: several of nodules have gradually formed areas of hyperplasia that eventually grew into autonomously functioning nodules
Age: elderly
• mildly elevated thyroid levels, suppressed TSH
√ RAIU normal / slightly elevated
√ multiple "hot" nodules in thyroid with suppressed extranodular thyroid tissue
DDx: Graves disease (younger patient, milder degree of thyrotoxicosis)

TUBERCULOSIS OF HEAD & NECK

Frequency: 15% of extrapulmonary tuberculosis; initial presentation in 1.5% of all new cases
Site: (a) lymph nodes: multiple nodal chains
(b) extranodal disease (rare): larynx > temporal bone > pharynx; sinonasal cavity, thyroid gland, skull base
√ soft-tissue thickening + infiltration of preepiglottic + paraglottic spaces
DDx of low-density node: necrotic lymph node metastasis from squamous cell carcinoma
DDx of calcified node: metastatic thyroid cancer

Tuberculous Lymphadenitis = Scrofula

Organism: Mycobacterium scrofulaceum (in children), M. tuberculosis (in adults)
Predisposed: HIV, AIDS
• bilateral chronic painless lymphadenitis growing with time
• "cold abscess" = no accompanying local color or warmth (overlying skin acquires a

violaceous color)
√ initially homogeneous nodes, later with central necrosis:
√ multichambered centrally hypoattenuating mass
√ central T1-hypointensity and T2 -hyperintensity
√ thick enhancing peripheral rim
√ peripheral nodal calcifications (in late TB)

WARTHIN TUMOR

= PAPILLARY CYSTADENOMA LYMPHOMATOSUM = ADENOLYMPHOMA = CYSTADENOLYMPHOMA

Frequency: 2nd most common benign tumor of parotid gland; 5%–10% of all benign salivary neoplasms: bilateral in 10%

Age: 5–6th decade; M > F

Origin: from heterotopic salivary gland tissue within parotid lymph nodes (direct result of incorporation of lymphatic elements + heterotopic salivary gland ductal epithelium within intraparotid + periparotid nodes during embryonic development

Histo: CHARACTERISTIC double layer of oncocytes (= epithelial cells) resting on a dense lymphoid stroma

• slow-growing painless mass

Associated with: history of smoking

Location: usually solitary + unilateral; bilateral + multifocal (±metachronous) in 10–60%
◊ Most common lesion to manifest as unilateral + multifocal masses
◊ Most common salivary neoplasm to manifest as multiple masses in one / both parotid glands

Site: often in tail of parotid gland

√ well-circumscribed single / multiple cystic / solid lesion in parotid region usually 3–4 cm in size

MR:
√ hypointense compared with fat / surrounding parotid tissue on T2WI

US:
√ oval hypoechoic well-defined tumor
√ frequently multiple anechoic areas
√ increased vascularity

NUC:
√ increased uptake with ^{99m}Tc, ^{201}Tl, FDG

Cx: sporadically malignant transformation of epithelial component

Rx: surgical resection

DDx: lymphoma, inflammatory disease

CHEST

DIFFERENTIAL DIAGNOSIS OF CHEST DISORDERS

PULMONARY HEMORRHAGE

A. WITHOUT RENAL DISEASE
   1. Bleeding diathesis: leukemia, hemophilia, disseminated intravascular coagulation (DIC)
   2. Pulmonary embolism, thromboembolism
   3. Blunt trauma: contusion
   4. Idiopathic pulmonary hemosiderosis
   5. Limited Wegener granulomatosis
   6. Drugs: amphotericin B, mitomycin, high-dose cyclophosphamide, cytarabine (ara-C), D-penicillamine, anticoagulants, lymphangiography

B. WITH RENAL DISEASE
   (a) medium-sized vessel vasculitis
      1. Polyarteritis nodosa
   (b) ANCA-associated small-vessel vasculitis:
      1. Wegener granulomatosis
      2. Churg-Strauss syndrome
   (c) immune-complex small vessel vasculitis:
      1. Goodpasture syndrome = antibasement membrane antibody disease with a linear pattern on tissue stains
      2. Henoch-Schönlein purpura
      3. Behçet disease
   (d) Collagen vascular disease:
      1. Systemic lupus erythematosus: granular pattern of immune complexes on tissue stains, noncaseating granulomas, malar rash
      2. Rheumatoid arthritis
      3. Seronegative juvenile rheumatoid arthritis
   (e) others
      1. Rapidly progressive glomerulonephritis ± immune complexes
      2. Immunoglobulin A nephropathy
      3. Idiopathic pulmonary hemorrhage
      4. Idiopathic glomerulonephritis

C. HEMORRHAGIC PNEUMONIA
   1. Bacteria: Legionnaires' disease
   2. Viruses: CMV, herpes, Rocky Mountain spotted fever, infectious mononucleosis
   3. Fungi: aspergillosis, mucormycosis

D. BLEEDING METASTASIS, eg, choriocarcinoma

• acute respiratory distress, hemoptysis (uncommon)

CXR:
√ bilateral heterogeneous + homogeneous opacities
√ multifocal patchy segmental / lobar consolidation
HRCT:
√ bilateral patchy / confluent ground-glass opacities / consolidation
√ ground-glass centrilobular nodules
√ may delineate underlying etiology (bronchiectasis, lung cancer, TB, pulmonary embolism)
NUC:
√ typically matched defect on V/Q scan in bronchial artery bleeding

Hemoptysis

= bleeding from lower respiratory tract
• frothy sputum, bright red blood, alkaline pH
• massive hemoptysis = expectoration of greater than 300–600 mL of blood in 24 hours

Risk: airway compromise

Source:
(a) bronchial artery (90–95%)
(b) pulmonary artery
(c) nonbronchial systemic aa. (brachiocephalic, intercostal, inferior phrenic, gastric, celiac, internal mammary, subclavian aa. as contributing source in 41–88%)

Pathophysiology:
(a) chronic thromboembolic disease / Takayasu arteritis → ⇓ pulmonary arterial perfusion → vasodilatation of bronchial-pulmonary arterial anastomotic connections → rupture of thin-walled anastomoses under systemic blood pressure into alveolus / bronchus
(b) chronic inflammation (eg, bronchiectasis and TB) / neoplasm → release of angiogenic growth factors → ⇑ collateral vascular supply and neovascularization → fragile + leaky new vessels prone to rupture into alveolus / bronchus

Etiology:
◊ The 2 <u>most common</u> causes (in adults) are bronchial carcinoma + bronchiectasis and (in children) cystic fibrosis + CHD!
◊ Most <u>clinically significant</u> cases of hemoptysis are due to entities that increase bronchial + systemic pulmonary blood flow: bronchiectasis, lung cancer, chronic bronchitis, cavitary infection, cavitary sarcoidosis, bronchial artery malformation

A. TUMOR
1. Carcinoma (35%)
2. Bronchial carcinoid
3. Endobronchial metastasis

B. BRONCHIAL WALL INJURY
1. Foreign body erosion
2. Bronchoscopy / biopsy

C. VASCULAR
1. COPD
2. Pulmonary embolus with infarction
√ bronchial blood flow may increase by 300% in the weeks following pulmonary artery embolization

3. Venous hypertension (most common): mitral stenosis
4. Arteriovenous malformation
5. Rupture of pulmonary artery aneurysm: TB, vasculitis, trauma, neoplasm, abscess, septic embolus, indwelling catheter

D. INFECTION (pneumonia)
1. Chronic bronchitis
Dieulafoy disease = abnormally dilated submucosal vessels of pulmonary artery prone to hemorrhage
[Paul Georges Dieulafoy (1839–1911), chief of medical services at the Hôtel-Dieu, Paris, France]
2. Bronchiectasis, mouthful (15%)
3. Tuberculosis (Rasmussen aneurysm)
4. Aspergillosis
5. Abscess
6. Cystic fibrosis

E. CRYPTOGENIC (3–10–42%)
◊ 6–10% of patients who smoke present with unresectable lung cancer within subsequent 3 years!

CT:
√ cluster of avidly enhancing "nodular" bronchial arteries in posterior mediastinum below level of aortic arch paralleling bronchial anatomy
√ abnormal bronchial arteries show tortuosity, dilatation, hypervascularity, neovascularity, aneurysms, shunts
N.B.: multidetector CT mapping prior to angiography reduces the rate of catheterization failures and the number of patients needing surgical intervention!

Angio:
√ vasodilated enlarged tortuous bronchial arteries → bronchial-to-pulmonary-artery shunting, hypervascularity, parenchymal staining

Prognosis: 50–100% mortality rate of conservatively treated massive hemoptysis; death usually from asphyxiation rather than from exsanguination

Rx: transcatheter particulate embolization of bronchial aa. using polyvinyl alcohol (PVA) + Gelfoam® pledgets (effective in 70–95%; recurrent bleeding in 20–30%)
N.B.: identify arteria radicularis (= artery of Adamkiewicz) at T5–L2 (in 75% T9–T12) to avoid postembolization transverse myelitis

DDx: hematemesis (containing food particles, dark blood, acid pH)

ASPIRATION

= intake of solid / liquid materials into the airways and lungs

Predisposing factors:
1. Alcoholism (most common in adults)
2. General anesthesia, loss of consciousness
3. Structural abnormalities of pharynx / esophagus (congenital / acquired tracheoesophageal + tracheopulmonary fistula), laryngectomy
4. Neuromuscular disorders

5. Deglutition abnormalities

Substrate:

(a) solids
- › foreign bodies
- › lentils

(b) liquids
- › gastric acid = Mendelson syndrome
- › water = near drowning
- › barium, water-soluble contrast material
- › liquid paraffin / petroleum = acute exogenous lipoid pneumonia / fire-eater pneumonia
- › mineral oil / cod liver oil = chronic exogenous lipoid pneumonia

(c) contaminated substances from oropharynx / GI tract

Acute Lower Airway Obstruction in Childhood

Location: intrathoracic trachea + bronchi

(a) infectious / inflammatory:
- • fever, cough, wheeze
- › < 2 years old:
  1. Bronchiolitis
     √ bronchial wall thickening + hyperinflation
- › > 2 years old:
  2. Lower respiratory tract inflammation
     √ bronchial wall thickening
  3. Reactive airways disease
     √ bronchial wall thickening + hyperinflation

(b) others:
1. Aspirated foreign body

PULMONARY DISEASE & CIGARETTE SMOKING

1. Bronchogenic carcinoma
2. Chronic bronchitis
3. Centrilobular emphysema
4. Panacinar emphysema with α-1 antitrypsin deficiency
5. **S**moking-related interstitial lung disease
   - › Respiratory bronchiolitis ILD (RB-ILD)
   - › Desquamative interstitial pneumonitis (DIP)
   - › Pulmonary Langerhans cell histiocytosis (PLCH)
   - › Idiopathic pulmonary fibrosis (IPF)

HYPERSENSITIVITY TO ORGANIC DUSTS

A. TRACHEOBRONCHIAL HYPERSENSITIVITY

large particles reaching the tracheobronchial mucosa (pollens, certain fungi, some animal / insect epithelial emanations)

1. Extrinsic asthma

2. Hypersensitivity aspergillosis
3. Bronchocentric granulomatosis
4. Byssinosis in cotton-wool workers

B. ALVEOLAR HYPERSENSITIVITY
= HYPERSENSITIVITY PNEUMONITIS
= EXTRINSIC ALLERGIC ALVEOLITIS
small particles of < 5 μm reaching alveoli

DRUG-INDUCED PULMONARY DAMAGE

Histopathologic manifestations:

(a) Diffuse alveolar damage:
bleomycin, busulfan, carmustine, mitomycin, cyclophosphamide, melphalan, gold salts

(b) Nonspecific interstitial pneumonia:
amiodarone, methotrexate, carmustine, chlorambucil

(c) Bronchiolitis obliterans organizing pneumonia: gold salts, bleomycin, methotrexate, amiodarone, nitrofurantoin, penicillamine, sulfasalazine, cyclophosphamide

(d) Eosinophilic pneumonia:
penicillamine, sulfasalazine, nitrofurantoin, nonsteroidal anti-inflammatory drugs, para-aminosalicylic acid

(e) Pulmonary hemorrhage:
anticoagulants, amphotericin B, cytarabine (ara-C), penicillamine, cyclophosphamide

A. CYTOTOXIC DRUGS (most important group)

1. **Cyclophosphamide**
Use: variety of malignancies, Wegener granulomatosis, glomerulonephritis
Toxicity: after 2 weeks – 13 years (mean, 3.5 years), no relationship to dose / duration of therapy
Prognosis: good after discontinuation of therapy
√ diffuse alveolar damage (most common)
√ nonspecific interstitial pneumonia
√ BOOP (least common)

2. **Busulfan** = Myleran® (for CML)
Toxicity: dose-dependent, after 3–4 years on the drug in 1–10%
√ diffuse linear pattern (occasionally reticulonodular / nodular pattern)
√ partial / complete clearing after withdrawal of drug
DDx: Pneumocystis pneumonia, interstitial leukemic infiltrate

3. **Nitrosoureas** = carmustine (BCNU), lomustine (CCNU)
Use: CNS glioma, lymphoma, myeloma
Toxicity: in 50% after doses > 1500 mg/m2; sensitivity increased after radiation Rx
√ diffuse alveolar damage (most common)
√ nonspecific interstitial pneumonia:
√ linear / finely nodular opacities (following treatment of 2–3 years)
√ high incidence of pneumothorax

4. **Bleomycin**
Use: squamous cell carcinoma of neck / cervix / vagina, Hodgkin lymphoma,

testicular carcinoma

Toxicity: at doses > 300 mg (in 3–6%); increased risk with age + radiation therapy + high oxygen concentrations

Prognosis: death from respiratory failure within 3 months of onset of symptoms

√ diffuse alveolar damage (most common)

√ nonspecific interstitial pneumonia / BOOP:

√ subpleural linear / nodular opacities (5–30 mm) in lower lung zones occurring after 1–3 months following beginning of therapy

DDx: metastases

5. **Taxoid derivatives** = paclitaxel, docetaxel, gemcitabine, topotecan, vinorelbine

Use: breast cancer, lung cancer, ovarian cancer

√ interstitial pneumonitis

B. NONCYTOTOXIC DRUGS

1. **Amiodarone**

= triiodinated benzofuran

Use: refractory ventricular tachyarrhythmia

Toxicity: in 5–10%; risk increased with daily dose > 400 mg + in elderly

Prognosis: good after discontinuation of drug

• pulmonary insufficiency after 1–12 months in 14–18% on long-term therapy

√ nonspecific interstitial pneumonia (most common) + associated BOOP:

√ alveolar + interstitial infiltrates (chronic presentation)

√ focal homogeneous peripheral consolidation (acute presentation):

√ attenuation values of iodine ← incorporation of amiodarone into type II pneumocytes

√ pleural thickening (inflammation) adjacent to consolidation

√ associated high-attenuation of liver relative to spleen

2. **Gold salts**

Use: inflammatory arthritis

Toxicity: in 1% within 2–6 months

• mucocutaneous lesions (30%)

√ diffuse alveolar damage (common)

√ nonspecific interstitial pneumonia (common)

√ BOOP (less common)

3. **Methotrexate**, procarbazine

Use: lung cancer, breast cancer, head and neck epidermoid cancer, nonmetastatic osteosarcoma, advanced stage NHL, AML, recalcitrant psoriasis, severe rheumatoid arthritis, pemphigus

Toxicity: in 5–10%; not dose-related

Prognosis: usually self-limited despite continuation of therapy

• blood eosinophilia (common)

√ nonspecific interstitial pneumonia (most common)

√ BOOP (less frequent)

√ linear / reticulonodular process (time delay of 12 days to 5 years, usually early)

√ acinar filling pattern (later)

√ transient hilar adenopathy + pleural effusion (on occasion)

DDx: Pneumocystis pneumonia

4. **Nitrofurantoin** (Macrodantin®)
   Use: urinary tract infection
   Toxicity: rare
   • positive for ANA + LE cells
   (a) acute disorder within 2 weeks of administration:
      • fever, dyspnea, cough
      • peripheral eosinophilia (more common)
      Prognosis: prompt resolution after withdrawal from drug
      √ diffuse bilateral predominantly basal heterogeneous opacities
   (b) chronic reaction with interstitial fibrosis (less common)
      • insidious onset of dyspnea + cough
      • may not be associated with peripheral eosinophilia
      √ nonspecific interstitial pneumonia (common)
         √ bilateral basilar interstitial opacities

C. OTHERS
1. **Heroin, propoxyphene, methadone**
   Toxicity: overdose followed by pulmonary edema in 30–40%
   √ bilateral widespread airspace consolidation
   √ aspiration pneumonia in 50–75%
2. **Salicylates**
   • asthma
   √ pulmonary edema (with chronic ingestion)
3. **Intravenous contrast material**
   √ pulmonary edema

LYMPHOPROLIFERATIVE MALIGNANCIES

= subgroup of hematologic malignancies comprising 4 different types:

1. Lymphoma (Non-Hodgkin Lymphoma)
   > 30 subtypes of lymphoma
2. Hodgkin disease
3. Lymphocytic leukemias (acute or chronic)
4. Plasma cell myeloma (multiple myeloma)

PULMONARY DISEASE AND OTHER ORGAN MANIFESTATIONS

Disorders with Hepatic & Pulmonary Manifestations

1. Alpha-1-antitrypsin deficiency
2. Cystic fibrosis
3. Hereditary hemorrhagic telangiectasia
4. Autoimmune disease: primary biliary cirrhosis, rheumatoid arthritis, Hashimoto thyroiditis, Sjögren syndrome, scleroderma, sarcoidosis
5. Drugs with toxic effects on lung and liver: methotrexate, phenytoin, amiodarone

Pulmonary-Renal Syndromes

1. Wegener granulomatosis = granulomatosis with polyangiitis
2. Goodpasture syndrome
3. Systemic lupus erythematosus
4. Mixed connective tissue disease
5. Microscopic polyangiitis

PULMONARY EDEMA

= abnormal accumulation of fluid in the extravascular compartments of the lung

Pathophysiology (Starling equation):

transcapillary flow dependent on

(1) Hydrostatic pressure
(2) Oncotic (= colloid osmotic) pressure
(3) Capillary permeability (the endothelial cells are relatively impermeable to protein but remain permeable to water and solutes; the tight intercellular junctions of alveolar epithelium remain nearly impermeable to water and solutes)

$$Q_{filt} = K_{filt} (HP_{iv} - HP_{ev}) - t(OP_{iv} - OP_{ev})$$

Q_{filt} = amount of fluid filtered per unit area per unit time

HP_{iv} = intravascular hydrostatic pressure

HP_{ev} = extravascular hydrostatic pressure

OP_{iv} = intravascular oncotic pressure

OP_{ev} = extravascular oncotic pressure

K_{filt} = conductance of capillary wall = water resistance of capillary endothelial cell junction

t = oncotic reflection coefficient = permeability of capillary membrane to macromolecules

Cause: disturbed equilibrium of net flow F_{net} between fluid transudation / exudation Q_{filt} and lymphatic absorption Q_{lymph}

$$F_{net} = Q_{filt} - Q_{lymph}$$

A. INCREASED HYDROSTATIC PRESSURE

(a) cardiogenic (most common)
= PULMONARY VENOUS HYPERTENSION
1. Heart disease: left ventricular failure, mitral valve disease, left atrial myxoma
2. Pulmonary venous disease: acute / chronic pulmonary embolism, primary venoocclusive disease, mediastinal fibrosis
3. Pericardial disease: pericardial effusion, constrictive pericarditis (extremely rare)
4. Drugs: antiarrhythmic drugs; drugs depressing myocardial contractility (beta-blocker)

(b) noncardiogenic
1. Renal failure
2. Massive IV fluid overload
3. Hyperosmolar fluid (eg, contrast medium)

(c) neurogenic
? sympathetic venoconstriction in cerebrovascular accident, head injury, CNS tumor,

postictal state

B. DECREASED COLLOID OSMOTIC PRESSURE
   1. Hypoproteinemia
   2. Transfusion of crystalloid fluid
   3. Rapid reexpansion of lung

C. INCREASED CAPILLARY PERMEABILITY
   Endothelial injury from
   (a) physical trauma: parenchymal contusion, radiation therapy
   (b) aspiration injury:
      1. Mendelson syndrome (gastric contents)
      2. Near drowning in sea water / fresh water
      3. Aspiration of hypertonic contrast media
   (c) inhalation injury:
      1. Nitrogen dioxide = silo-filler's disease
      2. Smoke (pulmonary edema may be delayed by 24–48 hours)
      3. Sulfur dioxide, hydrocarbons, carbon monoxide, beryllium, cadmium, silica, dinitrogen tetroxide, oxygen, chlorine, phosgene, ammonia, organophosphates
   (d) injury via bloodstream
      1. Vessel occlusion: shock (trauma, sepsis, ARDS) or emboli (air, fat, amniotic fluid, thrombus)
      2. Circulating toxins: snake venom, paraquat
      3. Drugs: heroin, morphine, methadone, aspirin, phenylbutazone, nitrofurantoin, chlorothiazide
      4. Anaphylaxis: transfusion reaction, contrast medium reaction, penicillin
      5. Hypoxia: high altitude, acute large airway obstruction

mnemonic: ABCDEFGHI - PRN
Aspiration
Burns
Chemicals
Drugs (heroin, nitrofurantoin, salicylates)
Exudative skin disorders
Fluid overload
Gram-negative shock
Heart failure
Intracranial condition
Polyarteritis nodosa
Renal disease
Near drowning

Atypical pulmonary edema = lung edema with an unusual radiologic appearance
Unusual form of pulmonary edema = lung edema from unusual causes

Increased Hydrostatic Pressure Edema

- Pulmonary capillary wedge pressure (PCWP):
  = reflects left atrial pressure and correlates well with radiologic features of CHF + pulmonary venous HTN

◊ In acute CHF radiologic features are delayed in onset and resolution

√ **flow inversion** = "cephalization of pulmonary vessels" is ONLY seen in longstanding left heart failure, NEVER in pulmonary edema of renal failure / overhydration / low oncotic pressure

HRCT:

√ smooth interlobular septal + peribronchovascular thickening

√ ground-glass opacities in a perihilar / dependent distribution, which may progress to consolidation

√ centrilobular ground-glass nodules

Radiographic Signs in Pressure Edema	
PCWP [mmHg]	*Findings*
5–12	normal
12–17	cephalization of pulmonary vessels (only in chronic conditions)
17–20	Kerley lines, subpleural effusions
> 25	alveolar flooding edema

Interstitial Pulmonary Edema

= 1st phase of pressure edema with increase in quantity of extracellular fluid

Cause: increase in mean transmural arterial pressure of 15–25 mmHg

√ mild enlargement of peribronchovascular spaces

√ appearance of Kerley lines

√ subpleural effusions

√ early loss of definition of subsegmental + segmental vessels

√ progressive blurring of vessels ← central migration of edema at lobar + hilar levels

√ small peripheral vessels difficult to identify ← decrease in lung radiolucency

◊ Often marked dissociation between clinical signs + symptoms + roentgenographic evidence

◊ Nothing differentiates it from other interstitial lesions

◊ Does not necessarily develop before alveolar pulmonary edema

◊ NOT typical for bacterial pneumonia

Alveolar Flooding Edema

= 2nd phase of pressure edema

Cause: increase in mean transmural arterial pressure of > 25 mmHg ± pressure-induced damage to alveolar epithelium

√ tiny nodular / acinar areas of increased opacity

√ frank consolidation

Bat-Wing Edema *(in < 10%)*

= central nongravitational distribution of alveolar edema

Cause: rapidly developing severe cardiac failure (acute mitral insufficiency associated with papillary muscle rupture, massive MI, valve leaflet destruction by septic endocarditis) or renal failure

√ lung cortex spared from fluid (due to pumping effect of respiration / contractile property of alveolar septa / mucopolysaccharide-filled perivascular matrix)

Asymmetric Distribution of Pressure Edema

Cause: morphologic lung changes in COPD, hemodynamics, patient position

√ lung apices spared (= lung emphysema in heavy smokers)
√ upper + middle portions of lung spared (= end-stage TB, sarcoidosis, asbestosis)
√ predominantly RUL involvement (= mitral regurgitation refluxes preferentially into right upper pulmonary vein)
√ anteroposterior gradient on CT in recumbent position
√ unilateral edema in lateral decubitus position

Pulmonary Edema with Acute Asthma

Cause: air trapping maintains a positive intraalveolar pressure and thus decreases hydrostatic pressure gradient

Pathogenesis: associated with severity of Müller maneuver

√ heterogeneous edema ← nonuniform airway obstruction
√ peribronchial cuffing
√ ill-defined vessels
√ enlarged ill-defined hila
√ patency of narrowed airways maintained ← high negative pleural pressure in forced inspiration

Postobstructive Pulmonary Edema

Cause: following relief from an upper airway obstruction (impacted foreign body, laryngospasm, epiglottitis, strangulation)

Pathogenesis:

(a) forced inspiration causes a high negative intrathoracic pressure (Müller maneuver) and increases venous return
(b) obstruction creates high positive intrathoracic pressure that impairs development of edema

√ septal lines, peribronchial cuffing
√ central alveolar edema
√ normal heart size

Prognosis: resolution within 2–3 days

Edema with Pulmonary Embolism *(< 10%)*

Cause: occlusion of pulmonary arterial bed causes redirection of blood flow and hypertension in uninvolved areas

√ areas of ground-glass attenuation
√ sharply demarcated from areas of transparency distal to occluded arteries
√ associated with dilated pulmonary arteries (70%)

Edema & Pulmonary Venoocclusive Disease

Cause: organized thrombi in small veins causes an increase in peripheral resistance and hydrostatic pressure

• rapidly progressive dyspnea, orthopnea ± hemoptysis
• normal / low pulmonary capillary wedge pressure
√ enlarged pulmonary arteries
√ diffuse interstitial edema + numerous Kerley lines
√ peribronchial cuffing
√ dilated right ventricle

Permeability Edema

Heroin-induced Pulmonary Edema

Hx: overdose of opiates (almost exclusively with heroin, rarely with cocaine / "crack")
Frequency: 15% of cases of heroin overdose
Pathophysiology: depression of medullary respiratory center leading to hypoxia + acidosis
√ widespread patchy bilateral airspace consolidations
√ ill-defined vessels + peribronchial cuffing
√ markedly asymmetric gravity-dependent distribution of edema (motionless recumbent position for hours / days)
√ resolution within 1 or 2 days in uncomplicated cases
Cx:
(1) Extensive crush injuries with associated muscle damage and ensuing renal insufficiency (from motionless recumbency)
(2) Aspiration of gastric contents
Prognosis: 10% mortality rate

Edema following Administration of Cytokines

(a) intravenous interleukin 2 (IL–2):
enhances tumoricidal activity of natural killer cells in metastatic melanoma + RCC
(b) intraarterial tumor necrosis factor:
increases production + release of IL–2
Frequency: in 75% of IL–2 therapy;
in 20% of tumor necrosis factor therapy;
in 25% of recombinant IL–2 therapy
Pathophysiology: permeability disruption of capillary endothelial cells
• 12 mmHg increase in pulmonary capillary wedge pressure (= direct toxic effect on myocardium)
√ pulmonary edema 1–5 days after start of therapy:
√ bilateral symmetric interstitial edema with thickened septal lines
√ peribronchial cuffing (75%)
√ small pleural effusions (40%)
√ NO alveolar edema (unless associated cardiac insufficiency)

High-altitude Pulmonary Edema

Predisposed: young males after rapid ascent to > 3,000 m
Cause: prolonged exposure to low partial oxygen atmospheric pressure
Pathophysiology: acute persistent hypoxia with endothelial leakage

- prodromal acute mountain sickness
- dyspnea at rest, cough with frothy pink sputum
- neurologic disturbances ← brain edema
- arterial oxygen levels as low as 38%

√ central interstitial pulmonary edema
√ peribronchial cuffing
√ ill-defined vessels
√ patchy airspace consolidation

Mixed Hydrostatic & Permeability Edema

Neurogenic Pulmonary Edema

Frequency: in up to 50% of severe brain trauma, stroke, subarachnoid hemorrhage, status epilepticus

Pathophysiology: modification in neurovegetative pathways causes sudden ↑ in pressure in pulmonary venules with reduced venous outflow

- dyspnea, tachypnea, cyanosis shortly after brain insult + rapid disappearance

√ bilateral inhomogeneous / homogeneous airspace consolidations, in 50% affecting predominantly the apices, disappearing within 1–2 days

Dx: by exclusion

DDx: fluid overload, postextubation edema

Reperfusion Pulmonary Edema

Frequency: in up to 90–100%

Cause: pulmonary thrombendarterectomy for massive pulmonary embolism / for webs and segmental stenosis

Pathophysiology: rapid increase in blood flow + pressure

- dyspnea, tachypnea, cough during the first 24–48 hours after reperfusion

√ pulmonary edema within 2 days after surgery:
  √ heterogeneous airspace consolidation, predominantly in areas distal to recanalized vessels
  √ random distribution in up to 50%

Reexpansion Pulmonary Edema

Cause: rapid reexpansion of a collapsed lung following evacuation of hydro-, hemo- or pneumothorax

Pathophysiology: prolonged local hypoxic event, abrupt restoration of blood flow, sudden marked increase in intrapleural pressure, diffuse alveolar damage

- frank respiratory insufficiency: cough, dyspnea, tachypnea, tachycardia, frothy pink sputum; may be asymptomatic

√ pulmonary edema within reexpanded entire lung within 1 hour (in 64%)
√ increase in severity within 24–48 hours with slow resolution over next 5–7 days

Prognosis: 20% mortality

Pulmonary Edema due to Air Embolism

Cause: usually iatrogenic complication (neurosurgical procedure in sitting position,

placement / manipulation of central venous line), rare in open / closed chest trauma

Pathophysiology: embolized air bubbles cause mechanical obstruction of pulmonary microvasculature

- sudden onset of chest pain, tachypnea, dyspnea
- hypotension

√ air bubbles in right-sided cardiac chambers on echocardiography
√ interstitial edema
√ bilateral peripheral alveolar areas of increased opacity, predominantly at lung bases

Postpneumonectomy Pulmonary Edema

= life-threatening complication in early postoperative period after pneumonectomy (rare in lobectomy / lung reduction surgery)

Frequency: 2.5–5%; R > L pneumonectomy

Risk factors: excessive administration of fluid during surgery, transfusion of fresh frozen plasma, arrhythmia, marked postsurgical diuresis, low serum colloidal osmotic pressure

Pathophysiology: increased capillary hydrostatic pressure, altered capillary permeability

- marked dyspnea during first 2–3 postop days

√ ARDS-like picture

Prognosis: very high mortality rate

Pulmonary Edema after Lung Transplantation

Frequency: in up to 97% during first 3 days after surgery

Pathophysiology: tissue hypoxia, disruption of pulmonary lymphatic drainage, lung denervation

√ progressive diffuse confluent areas of increased opacity, most pronounced on postop day 5
√ return to normal 2 weeks after surgery

Unilateral Pulmonary Edema

A. IPSILATERAL = on side of preexisting abnormality
   (a) filling of airways
      1. Unilateral aspiration / pulmonary lavage
      2. Drowned lung (bronchial obstruction)
      3. Pulmonary contusion
   (b) increased pulmonary venous pressure
      1. Unilateral venous obstruction
      2. Prolonged lateral decubitus position
   (c) pulmonary arterial overload
      1. Systemic artery-to-pulmonary artery shunt (Waterston, Blalock-Taussig, Pott procedure)
      2. Rapid thoracentesis (rapid reexpansion)
B. CONTRALATERAL = opposite to side of abnormality
   (a) pulmonary arterial obstruction

1. Congenital absence / hypoplasia of pulmonary a.
2. Unilateral arterial obstruction
3. Pulmonary thromboembolism

(b) loss of lung parenchyma

1. Swyer-James syndrome
2. Unilateral emphysema
3. Lobectomy
4. Pleural disease

C. RIGHT UPPER LOBE
PATHOGNOMONIC for mitral valve regurgitation

Pulmonary Edema with Cardiomegaly

1. Cardiogenic
2. Uremic (cardiomegaly ← pericardial effusion / hypertension)

Pulmonary Edema without Cardiomegaly

mnemonic: U DOPA

Uremia
Drugs
Overhydration
Pulmonary hemorrhage
Acute myocardial infarction, **A**rrhythmia

Noncardiogenic Pulmonary Edema

mnemonic: The alphabet

ARDS, **A**lveolar proteinosis, **A**spiration, **A**naphylaxis
Bleeding diathesis, **B**lood transfusion reaction
CNS (increased pressure, trauma, surgery, CVA, cancer)
Drowning (near), **D**rug reaction
Embolus (fat, thrombus)
Fluid overload, **F**oreign-body inhalation
Glomerulonephritis, **G**oodpasture syndrome, **G**astrografin® aspiration
High altitude, **H**eroin, **H**ypoproteinemia
Inhalation (SO2, smoke, CO, cadmium, silica)
-
Narcotics, **N**itrofurantoin
Oxygen toxicity
Pancreatitis
-
Rapid reexpansion of pneumothorax / removal of pleural effusion
-
Transfusion
Uremia

PNEUMONIA

"Classic" pneumonia pattern:

1. Lobar distribution: Streptococcus pneumoniae
2. Bulging fissure: Klebsiella
3. Pulmonary edema: Viral / Pneumocystis pneumonia
4. Pneumatocele: Staphylococcus
5. Alveolar nodules: Varicella, bronchogenic spread of TB

Distribution:

A. SEGMENTAL / LOBAR
   - › Normal host: S. pneumoniae, Mycoplasma, virus
   - › Compromised host: S. pneumoniae

B. BRONCHOPNEUMONIA
   - › Normal host: Mycoplasma, virus, Streptococcus, Staphylococcus, S. pneumoniae
   - › Compromised host: gram-negative, Streptococcus, Staphylococcus
   - › Nosocomial: gram-negative, Pseudomonas, Klebsiella, Staphylococcus
   - › Immunosuppressed: gram-negative, Staphylococcus, Nocardia, Legionella, Aspergillus, Phycomycetes

C. EXTENSIVE BILATERAL PNEUMONIA
   - › Normal host: virus (eg, influenza), Legionella
   - › Compromised host: candidiasis, Pneumocystis, TB

D. BILATERAL LOWER LOBE PNEUMONIA
   - › Normal host: anaerobic (aspiration)
   - › Compromised host: anaerobic (aspiration)

E. PERIPHERAL PNEUMONIA
   - › Noninfectious eosinophilic pneumonia

Transmission:

A. **Community-acquired pneumonia**
   Organism: viruses, S. pneumoniae, Mycoplasma
   Mortality: 10%

B. **Nosocomial pneumonia**
   [*nosos*, Greek = disease; *kamnein*, Greek = to suffer; *nosocomium*, Latin = hospital]
   (a) gram-negative organism (> 50%): Klebsiella pneumoniae, P. aeruginosa, E. coli, Enterobacter
   (b) gram-positive organism (10%): S. aureus, S. pneumoniae, H. influenzae

Complications:

1. Empyema
2. Pulmonary abscess
3. Cavitary necrosis
4. Pneumatocele
5. Pneumothorax
6. Pyopneumothorax
7. Bronchopleural fistula

Bacterial Pneumonia

Lobar Pneumonia

= ALVEOLAR PNEUMONIA

= pathogens reach peripheral air space, incite exudation of watery edema into alveolar space, centrifugal spread via small airways, pores of Kohn + Lambert into adjacent lobules + segments

√ nonsegmental sublobar consolidation

√ round pneumonia (= uniform involvement of contiguous alveoli)

(a) Streptococcus pneumoniae

(b) Klebsiella pneumoniae (more aggressive); in immunocompromised + alcoholics

(c) any pneumonia in children

(d) atypical measles

√ expansion of lobe with bulging of fissures

√ lung necrosis with cavitation

√ lack of volume loss

DDx: aspiration; pulmonary embolus

Lobular Pneumonia

= BRONCHOPNEUMONIA

= combination of interstitial + alveolar disease (injury starts in airways, involves bronchovascular bundle, spills into alveoli, which may contain edema fluid, blood, leukocytes, hyaline membranes, organisms)

Organism:

(a) Staphylococcus aureus, Pseudomonas pneumoniae: thrombosis of lobular artery branches with necrosis and cavitation

(b) Streptococcus (pneumococcus), Klebsiella, Legionnaires' bacillus, Bacillus proteus, E. coli, anaerobes (Bacteroides + Clostridia), Nocardia, actinomycosis

(c) Mycoplasma

√ small fluffy ill-defined acinar nodules, which enlarge with time

√ lobar + segmental densities with volume loss from airway obstruction ← bronchial narrowing + mucus plugging

Atypical Bacterial Pneumonia

= bacterial infection with radiographic appearance of viral pneumonia

Organism:

(1) Mycoplasma

(2) Pertussis

(3) Chlamydia trachomatis

Gram-negative Pneumonia

In 50% cause of nosocomial necrotizing pneumonias (including staphylococcal pneumonia)

Predisposed: elderly, debilitated, diabetes, alcoholism, COPD, malignancy, bronchitis, gram-positive pneumonia, treatment with antibiotics, respirator therapy

Organism:

1. Klebsiella
2. Pseudomonas

3. E. coli
4. Proteus
5. Haemophilus
6. Legionella

√ airspace consolidation (Klebsiella)
√ spongy appearance (Pseudomonas)
√ affecting dependent lobes (poor cough reflex without clearing of bronchial tree)
√ bilateral
√ cavitation common

Cx: (1) Exudate / empyema
(2) Bronchopleural fistula

Mycotic Lung Infection

A. IN HEALTHY SUBJECTS
1. Histoplasmosis
2. Coccidioidomycosis
3. Blastomycosis

B. OPPORTUNISTIC INFECTION
1. Aspergillosis
2. Mucormycosis (phycomycosis)
3. Candidiasis

Growth: (a) mycelial form
(b) yeast form (depending on environment)

Source of contamination:
(a) soil
(b) growth in moist areas (apart from Coccidioides)
(c) contaminated bird / bat excreta

Viral Lung Infection

= VIRAL PNEUMONIA = BRONCHIOLITIS = PERIBRONCHIAL PNEUMONIA = INTERSTITIAL PNEUMONIA = LOWER RESPIRATORY TRACT INFECTION
[terms used in an attempt to differentiate from airspace pneumonia]

= infection of bronchi + peribronchial tissues

Organism:

◊ The cause of infection cannot be reliably ascertained from its imaging appearance!

A. RNA VIRUSES
(a) Influenza A: more common during infancy, may lead to severe lower respiratory tract infection; mild URI in adults
1. Avian flu (H5N1 subtype): 1997 Hong Kong; 60% fatality rate
2. Swine influenza A (H1N1): 2009 in Mexico; pandemic; 1% fatality rate

(b) Parainfluenza 1–4: common cause of seasonal URI
(c) RSV = respiratory syncytial virus: most frequent viral cause of lower respiratory tract infection in infants
(d) Human metapneumovirus (HMPV): clinically indistinguishable from RSV
(e) Rubeola (measles): highly contagious; 1–36% mortality; febrile illness before /

with onset of rash

(f) Enterovirus, Coxsackie virus, ECHO virus: summertime URI

(g) Human T-cell lymphotropic virus type 1 (HTLV-1): retrovirus associated with leukemia / lymphoma; transmission by sexual contact + blood transfusion + breast feeding

(h) Hantavirus (hantavirus pulmonary syndrome): 1993 in southwestern USA

(i) Coronavirus (SARS = severe acute respiratory syndrome): 2002 Guangdong Province / China; 10% mortality rate

B. DNA VIRUSES

(a) Adenovirus: associated with Swyer-James-MacLeod syndrome in children

(b) Herpes simplex virus: in immunocompromised

(c) Varicella (chickenpox)-zoster virus: common in childhood; in 10% of adults; 2–5 days after rash

(d) Cytomegalic inclusion virus: features suggestive of bronchopneumonia

(e) Epstein-Barr virus

Path: necrosis of ciliated epithelial cells, goblet cells, bronchial mucous glands with frequent involvement of peribronchial tissues + interlobular septa

Clinical syndromes:

1. (**Common) cold** = mild upper respiratory tract symptoms ← tonsillopharyngitis, pharyngitis, epiglottitis, sinusitis, otitis media, conjunctivitis
   - sore throat, runny nose, congestion, sneezing, cough
   - headache, fever (milder than for influenza)

   Cause: > 200 different viruses other than influenza; Most common: rhinovirus (30–80%), coronavirus (15%), influenza virus (10–15%)
2. **Influenza**
   - abrupt fever > 100° F (38° C), chills and sweats, headache, myalgias, malaise, fatigue, weakness
   - nasal congestion, sore throat, dry persistent cough

   Cause: influenza virus types A, B, C constantly changing (= antigenic drift + shift)

Viral Pneumonia in Childhood

Pathophysiology:

tracheitis, bronchitis, bronchiolitis with peribronchial infiltrates → increased secretion of mucus + constriction of bronchi → narrowing of airways → increased resistance to air flow → air trapping → increase in residual volume; injury to alveolar cells with hyaline membranes; necrosis of alveolar walls with blood, edema, fibrin, macrophages within alveoli

Age: most common cause of pneumonia in children < 5 years of age; adults have usually acquired immunity

- retractions, tachypnea, air hunger, respiratory distress

Distribution: usually bilateral

Accuracy of CXR: 92% NPV, 30% PPV

√ hyperaeration + air trapping (best indicator!):

√ depression of diaphragm on both views:

(a) projects below anterior 6th rib

(b) projects below posterior 8th/10th rib on lordotic view
(c) loss of diaphragmatic dome on lateral view
√ increase in transverse diameter of chest
√ bowing of sternum upward + outward
√ increased anteroposterior diameter on lateral view

√ "**dirty chest**" = peribronchial cuffing + opacification:
√ symmetric parahilar peribronchial linear densities ← patchy atelectasis
√ bronchial wall thickening
√ interstitial pattern

√ segmental + subsegmental atelectasis with frequently changing distribution ← dislodgement of mucus plugs (common):
√ wedge-shaped / triangular densities

√ airspace pattern (50%) ← hemorrhagic edema
√ pleural effusion (20%)
√ hilar adenopathy (3%)
√ striking absence of pneumatoceles, lung abscess, pneumothorax
√ radiographic resolution lags 2–3 weeks behind clinical

Cx: (1) Bacterial superinfection (child becomes toxic after a week of sickness, peripheral consolidations + air bronchograms + pleural effusion)
(2) Bronchiectasis
(3) Unilateral hyperlucent lung, bronchiolitis obliterans

◊ Atypical measles pneumonia does NOT show the typical radiographic findings of viral pneumonias!

Viral Pneumonia in Adulthood

Clinical groups:
(a) atypical pneumonia in healthy host
(b) viral pneumonia in immunocompromised host

Risk factors: very young & old age, malnutrition, immunologic disorders

Histo:
(a) diffuse alveolar damage (intraalveolar edema, fibrin, variable cellular infiltrate with hyaline membrane)
(b) intraalveolar hemorrhage
(c) interstitial (intrapulmonary / airway) inflammatory cell infiltration

CXR:
√ unilateral / patchy bilateral areas of consolidation
◊ Lobar consolidation is uncommon!
√ nodular opacities
√ bronchial wall thickening
√ small pleural effusion

CT:
√ disturbances of parenchymal attenuation:
√ patchy inhomogeneities = mosaic attenuation (= bronchiolar inflammation / cicatricial scarring → bronchiolar obstruction → alveolar hypoventilation):

√ area of decreased attenuation persists during expiration ← air trapping
√ lobular ground-glass opacities (= thickening of interstitium + partial filling of airspaces)
√ pulmonary consolidation:
√ patchy + poorly defined (bronchopneumonia)
√ focal + well defined (lobar pneumonia)
√ nodules < 10 mm
√ centrilobular micronodules
√ tree-in-bud of small airway disease
= dilated centrilobular bronchioles, their lumina impacted with mucus / fluid / pus
√ widespread smooth interlobular septal thickening ± crazy paving pattern
√ bronchial ± bronchiolar wall thickening
Cx: acute pneumonia with rapid progression to ARDS

Round Pneumonia

= NUMMULAR PNEUMONIA
= fairly spherical pneumonia caused by pyogenic organisms
Pathophysiology: in young children only few intraalveolar pores of Kohn + bronchoalveolar channels of Lambert have developed to allow collateral air drift
Organism: Haemophilus influenzae, Streptococcus, Pneumococcus
Age: children >> adults
• cough, chest pain, fever of ≥ 104° F (40° C)
Location: always posterior, usually in lower lobes
√ spherical infiltrate with slightly fluffy borders + air bronchogram
√ triangular infiltrate abutting a pleural surface (usually seen on lateral view)
√ rapid change in size and shape

Cavitating Pneumonia

1. Staphylococcus aureus
2. Haemophilus influenzae
3. S. pneumoniae

other gram-negative organisms (eg, Klebsiella)

Cavitating Opportunistic Infection

◊ Repeated infections in same patient are not necessarily due to same organism!

A. FUNGAL INFECTIONS
   1. Aspergillosis
   2. Nocardiosis
   3. Mucormycosis (= phycomycosis)

B. STAPHYLOCOCCAL ABSCESS
C. TUBERCULOSIS (nummular form)
D. SEPTIC EMBOLI
   1. Anaerobic organisms

DDx: Metastatic disease in carcinoma / Hodgkin lymphoma

Recurrent Pneumonia in Childhood

A. IMMUNE PROBLEM
   1. Immune deficiency
   2. Chronic granulomatous disease of childhood (males)
   3. Alpha 1-antitrypsin deficiency

B. ASPIRATION
   1. Gastroesophageal reflux
   2. H-type tracheoesophageal fistula
   3. Disorder of swallowing mechanism
   4. Esophageal obstruction, impacted esophageal foreign body

C. UNDERLYING LUNG DISEASE
   1. Sequestration
   2. Bronchopulmonary dysplasia
   3. Cystic fibrosis
   4. Atopic asthma
   5. Bronchiolitis obliterans
   6. Sinusitis
   7. Bronchiectasis
   8. Ciliary dysmotility syndromes
   9. Pulmonary foreign body

NEONATAL LUNG DISEASE

Parenchymal Lung Disease on 1st Day of Life

◊ Radiographic findings overlap!

1. Transient tachypnea of newborn
2. Respiratory distress syndrome
3. Neonatal pneumonia
4. Meconium aspiration syndrome
5. Prematurity with accelerated lung maturity (see below)

Air Leaks in Neonatal Chest

= intrathoracic extra-alveolar gas

1. Pulmonary interstitial emphysema
2. Pneumomediastinum
3. Pneumothorax
4. Gas below visceral pleura
   √ gas at lung base / against fissure
5. Pneumopericardium
6. Gas embolus to cardiac chambers / blood vessels

Mediastinal Shift & Abnormal Aeration in Neonate

A. SHIFT TOWARD LUCENT LUNG
   1. Congenital diaphragmatic hernia
   2. Chylothorax

3. Cystic adenomatoid malformation

B. SHIFT AWAY FROM LUCENT LUNG
1. Congenital lobar emphysema
2. Persistent localized pulmonary interstitial emphysema
3. Obstruction of mainstem bronchus (by anomalous or dilated vessel / cardiac chamber)

Pulmonary Infiltrates in Neonate

mnemonic: I HEAR

Infection (pneumonia)
Hemorrhage
Edema
Aspiration
Respiratory distress syndrome

Reticulogranular Densities in Neonate

1. Respiratory distress syndrome (90%): premature infant, inadequate surfactant
2. **Prematurity with Accelerated Lung Maturity** (PALM)
   = IMMATURE LUNG SYNDROME:
   premature infant with normal surfactant ← maternal steroid therapy / intrauterine stress
   √ lung granularity (= almost clear chest)
   √ small thymus (stress / steroids)
3. Transient tachypnea of the newborn
4. Neonatal group-B streptococcal pneumonia
5. Idiopathic hypoglycemia
6. Congestive heart failure
7. Early pulmonary hemorrhage
8. Infant of diabetic mother

CONGENITAL LUNG ABNORMALITIES

= SEQUESTRATION SPECTRUM

A. BRONCHOPULMONARY (LUNG BUD) ANOMALY
1. Lung agenesis-hypoplasia complex
2. Congenital pulmonary airway malformation
3. Congenital lobar overinflation / emphysema
4. Bronchial atresia
5. Bronchogenic cyst

B. VASCULAR ANOMALY
1. Absence of main pulmonary artery
2. Pulmonary sling = Anomalous origin of left pulmonary a.
3. Anomalous pulmonary venous drainage
4. Pulmonary arterial / AV malformation

C. COMBINED LUNG & VASCULAR ANOMALY
1. Scimitar / hypogenetic lung / congenital pulmonary venolobar syndrome
2. Bronchopulmonary sequestration
3. Congenital pulmonary airway malformation = cystic adenomatoid malformation

Hypogenetic Lung Syndrome

= collective name for congenital underdevelopment of one / more lobes of a lung separated into 3 forms:

1. **Pulmonary agenesis**
   = complete absence of a lobe + its bronchus
   CT:
   √ missing bronchus + lobe(s)
2. **Pulmonary aplasia**
   = rudimentary bronchus ending in blind pouch + absence of parenchyma + vessels
   Incidence: 1÷10,000; R÷L = 1÷1
   CT:
   √ absence of ipsilateral pulmonary artery
   √ bronchus terminates in dilated blind pouch
   √ absence of ipsilateral pulmonary tissue
3. **Pulmonary hypoplasia**
   = completely formed but congenitally small bronchus with rudimentary parenchyma + small vessels
   Developmental causes:
   resulting in intrauterine compression of chest
   (a) Idiopathic (rare)
   (b) Extrathoracic compression (= Potter syndrome)
      1. Oligohydramnios (renal agenesis, bilateral cystic renal disease, obstructive uropathy, premature rupture of membranes)
      2. Fetal ascites
   (c) Thoracic cage compression
      1. Thoracic bone dysplasia: Ellis-van Creveld, Jeune, thanatophoric dystrophy, severe achondroplasia
      2. Muscular disease
   (d) Intrathoracic compression
      1. Diaphragmatic defect
      2. Excess pleural fluid
      3. Large intrathoracic cyst / tumor

ABNORMAL LUNG PATTERN

1. Mass
   = any localized density not completely bordered by fissures / pleura
2. Consolidative (alveolar) pattern
   = commonly produced by filling of air spaces with fluid (transudate / exudate) / cells / other material, ALSO by alveolar collapse, airway obstruction, confluent interstitial thickening
   ground glass = hazy area of increased attenuation not obscuring bronchovascular structures
   consolidation = marked increase in attenuation with obliteration of underlying anatomic features

3. Interstitial pattern
4. Vascular pattern
   (a) increased vessel size: CHF, pulmonary arterial hypertension, shunt vascularity, lymphangitic carcinomatosis
   (b) decreased vessel size: emphysema, thromboembolism
5. Bronchial pattern
   √ wall thickening: bronchitis, asthma, bronchiectasis
   √ density without air bronchogram (= complete airway obstruction)
   √ lucency of air trapping (= partial airway obstruction with ball-valve mechanism)

ALVEOLAR (CONSOLIDATIVE) PATTERN

Classic appearance of airspace consolidation:

mnemonic: A2BC3

- √ **A**cinar rosettes: rounded poorly defined nodules of acinus size (6–10 mm), best seen at periphery of opacity
- √ **A**ir alveologram / bronchogram
- √ **B**utterfly / bat-wing distribution: perihilar / bibasilar
- √ **C**oalescent / confluent cloudlike ill-defined opacities
- √ **C**onsolidation in diffuse, perihilar / bibasilar, segmental / lobar, multifocal / lobular distribution
- √ **C**hanges occur rapidly (labile / fleeting)

HRCT:

- √ poorly marginated densities within primary lobule (up to 1 cm in size)
- √ rapid coalescence with neighboring lesions in segmental distribution
- √ predominantly central location with sparing of subpleural zones
- √ air bronchograms

Diffuse Airspace Disease

= alveoli filled with

A. INFLAMMATORY EXUDATE = "PUS"
   1. Lobar pneumonia
   2. Bronchopneumonia: especially gram-negative organisms
   3. Unusual pneumonia
      (a) viral: extensive hemorrhagic edema especially in immunocompromised patient with hematologic malignancy + transplant
      (b) Pneumocystis
      (c) fungal: Aspergillus, Candida, Cryptococcus, Phycomycetes
      (d) tuberculosis
   4. Complication of pneumonia = lung abscess

B. HEMORRHAGE = "BLOOD"
   1. Trauma: contusion
   2. Pulmonary embolism, thromboembolism
   3. Bleeding diathesis: leukemia, hemophilia, anticoagulants, DIC, immune thrombocytopenia (ITP)
   4. Vasculitis:

Wegener granulomatosis, Goodpasture syndrome, SLE, mucormycosis, aspergillosis, Rocky Mountain spotted fever, infectious mononucleosis

5. Idiopathic pulmonary hemosiderosis
6. Bleeding metastasis: eg, choriocarcinoma

C. TRANSUDATE = "WATER" = PULMONARY EDEMA / ARDS

1. Cardiac edema
2. Neurogenic edema
3. Hypoproteinemia
4. Fluid overload
5. Renal failure
6. Radiotherapy
7. Shock
8. Toxic inhalation
9. Drug reaction
10. Drowning
11. Aspiration
12. Adult respiratory distress syndrome

D. SECRETIONS = "PROTEIN"

1. Phospholipoprotein: Pulmonary alveolar proteinosis
2. Mucus plugging

E. "CELLS"

(a) malignant: bronchioloalveolar cell carcinoma, lymphoma
(b) T4 lymphocytes: sarcoidosis
(c) Neutrophils: infection
(d) Eosinophils: eosinophilic pneumonia
(e) Plasma cells, mast cells: hypersensitivity pneumonitis

F. INTERSTITIAL DISEASE
simulating airspace disease, eg, "alveolar sarcoid"

mnemonic: AIRSPACED

Aspiration
Inhalation, Inflammatory
Renal (uremia)
Sarcoidosis
Proteinosis (alveolar)
Alveolar cell carcinoma
Congestive (CHF)
Emboli
Drug reaction, **D**rowning

Air-space Opacification in Trauma

A. ACUTE PHASE

1. Pulmonary contusion
2. Pulmonary laceration
3. Aspiration pneumonia
4. Atelectasis ← splinting / mucous plug

5. Pulmonary edema: cardiogenic / noncardiogenic

B. SUBACUTE PHASE (> 24 hours) add
   1. Fat embolism
   2. Adult respiratory distress syndrome

Localized Airspace Disease

mnemonic: 4P's & TAIL

Pneumonia
Pulmonary edema
Pulmonary contusion
Pulmonary interstitial edema
Tuberculosis
Alveolar cell carcinoma
Infant
Lymphoma

Acute Alveolar Infiltrate

mnemonic: I 2 CHANGE FAST

Infarct
Infection
Contusion
Hemorrhage
Aspiration
Near drowning
Goodpasture syndrome
Edema
Fungus
Allergic sensitivity
Shock lung
Tuberculosis

Chronic Alveolar Infiltrate

mnemonic: STALLAG

Sarcoidosis
Tuberculosis
Alveolar cell carcinoma
Lymphoma
Lipoid pneumonia
Alveolar proteinosis
Goodpasture syndrome

CT Angiogram Sign

= homogeneous low attenuation of lung consolidation, which allows vessels to be clearly seen

1. Lobar bronchioloalveolar cell carcinoma

2. Lobar pneumonia
3. Pulmonary lymphoma
4. Extrinsic lipid pneumonia
5. Pulmonary infarction
6. Pulmonary edema

Migratory / Fleeting Pulmonary Opacities

1. Simple pulmonary eosinophilia
2. Pulmonary hemorrhage
3. Pulmonary vasculitis
4. Cryptogenic organizing pneumonia
5. Recurrent aspiration / infection

INTERSTITIAL LUNG DISEASE

= thickening of lung interstices (= interlobular septa)

A. MAJOR LYMPHATIC TRUNKS
   1. Lymphangitic carcinomatosis
   2. Congenital pulmonary lymphangiectasia
   3. Pulmonary edema
   4. Alveolar proteinosis

B. PULMONARY VEINS (↑ pulmonary venous pressure)
   1. Left ventricular failure
   2. Venous obstructive disease

C. SUPPORTING CONNECTIVE TISSUE NETWORK
   1. Interstitial edema
   2. Chronic interstitial pneumonia
   3. Pneumoconioses
   4. Collagen-vascular disease
   5. Interstitial fibrosis
   6. Amyloid
   7. Tumor infiltration within connective tissue
   8. Desmoplastic reaction to tumor

Path: stereotypical inflammatory response of alveolar wall to injury
   (a) acute phase: fluid + inflammatory cells exude into alveolar space, mononuclear cells accumulate in edematous alveolar wall
   (b) organizing phase: hyperplasia of type II pneumocytes attempt to regenerate alveolar epithelium, fibroblasts deposit collagen
   (c) chronic stage: dense collagenous fibrous tissue remodels normal pulmonary architecture

Characterizing criteria:
(a) distribution:
   › vertical distribution: upper / lower lung zones
   › horizontal distribution : axial (core) / parenchymal (middle) / peripheral compartment
(b) volume loss
(c) time course

(d) interstitial lung pattern

Classification scheme:

A. Interstitial pneumonia
   1. Usual interstitial pneumonia (UIP)
   2. Nonspecific interstitial pneumonia (NSIP)
   3. Acute interstitial pneumonia (AIP)
   4. Alveolar macrophage pneumonia (AMP) = desquamative interstitial pneumonia (DIP)
   5. Bronchiolitis obliterans organizing pneumonia

B. Diffuse infiltrative disease with granulomas
   1. Sarcoidosis
   2. Hypersensitivity pneumonitis

C. Lymphocytic interstitial pneumonia (LIP)

D. Pneumoconiosis

E. Interstitial lung disease with cysts
   1. Langerhans cell histiocytosis
   2. Lymphangioleiomyomatosis

F. Interstitial lung disease with interlobular septal thickening
   1. Lymphangitic carcinomatosis
   2. Interstitial pulmonary edema
   3. Alveolar proteinosis

G. Eosinophilic syndrome

H. Pulmonary hemorrhage

I. Vasculitis

Interstitial Lung Pattern on CXR

1. LINEAR PATTERN
   (a) Kerley lines = septal lines = thickened connective septa
   Path: accumulation of fluid / tissue
   √ **Kerley A lines** = relatively long fine linear shadows in upper lungs, deep within lung parenchyma radiating from hila
   √ **Kerley B lines** = short horizontally oriented peripheral lines extending + perpendicular to pleura in costophrenic angles + retrosternal clear space
   (b) reticulations
   = innumerable interlacing linear opacities suggesting a mesh / network
   √ **Kerley C lines** = fine "spider web / lacelike" polygonal opacities distributed primarily in a peripheral / subpleural location
   Path: pulmonary fibrosis (lower lobes), hypersensitivity pneumonitis (upper lobes)
   √ thick linear opacities in a central / perihilar distribution
   Path: (a) dilated thick-walled bronchi of bronchiectasis
   (b) cysts of lymphangioleiomyomatosis / tuberous sclerosis
2. NODULAR / MILIARY PATTERN
   = small well-defined innumerable uniform 3–5-mm nodules with even distribution
   Path: diffuse metastatic disease, infectious granulomatous disease (TB, fungal), noninfectious granulomatous disease (pneumoconioses, sarcoidosis, eosinophilic

granuloma)

3. DESTRUCTIVE FORM = honeycomb lung

Signs of Acute Interstitial Disease

√ peribronchial cuffing = thickened bronchial wall + peribronchial sheath (when viewed end on)
√ thickening of interlobular fissures
√ Kerley lines
√ perihilar haze = blurring of hilar shadows
√ blurring of pulmonary vascular markings
√ increased density at lung bases
√ small pleural effusions

Signs of Chronic Interstitial Disease

◊ HRCT ~ 60% more sensitive than CXR
√ irregular visceral pleural surface
√ **reticulations**:
  √ fine reticulations
    = early potentially reversible / minimal irreversible alveolar septal abnormality
    (1) Idiopathic pulmonary fibrosis (basilar predominance)
  √ coarse reticulations
    in 75% related to environmental disease, sarcoidosis, collagen-vascular disorders, chronic interstitial pneumonia
√ **nodularity**:
  in 90% related to infectious / noninfectious granulomatous process, metastatic malignancy, pneumoconioses, amyloidosis
√ **linearity**:
  (1) Cardiogenic / noncardiogenic interstitial pulmonary edema
    √ symmetric linearity
  (2) Lymphangitic malignancy
    √ asymmetric linearity
  (3) Diffuse bronchial wall disorders: cystic fibrosis, bronchiectasis, hypersensitivity asthma
√ **honeycombing**
  = usually subpleural clustered cystic air spaces < 1 cm in diameter with thick well-defined walls set off against a background of increased lung density (end-stage lung)

Distribution of Interstitial Disease

Perihilar Interstitial Lung Disease

(a) acute rapidly changing
  1. Pulmonary edema
  2. Pneumocystis pneumonitis
  3. Early extrinsic allergic alveolitis
(b) chronic slowly progressive
  1. Lymphangitic carcinomatosis:

often unilateral, associated with adenopathy, pleural effusion

Peripheral Interstitial Lung Disease

(a) acute rapidly changing
   1. Interstitial pulmonary edema with Kerley B lines (most common)
   2. Active fibrosing alveolitis

(b) chronic slowly progressive
   1. Secondary pulmonary hemosiderosis

Upper Interstitial Lung Disease

(a) chronic slowly progressive ± volume loss
   1. Postprimary TB (common)
   2. Silicosis (common)

(b) chronic slowly progressive with volume loss
   1. Sarcoidosis (common)
   2. Ankylosing spondylitis (rare)
   3. Sulfa drugs (rare)

(c) chronic slowly progressive without volume loss
   1. Extrinsic allergic alveolitis
   2. Eosinophilic granuloma
   3. Aspiration pneumonia
   4. Postradiation pneumonitis
   5. Recurrent Pneumocystis carinii pneumonia (PCP) under aerosolized pentamidine prophylaxis

mnemonic: SHIRT CAP
Sarcoidosis
Histoplasmosis
Idiopathic
Radiation therapy
Tuberculosis (postprimary)
Chronic extrinsic alveolitis
Ankylosing spondylitis
Progressive massive fibrosis

Chronic Diffuse Infiltrative Lung Disease

= CHRONIC INTERSTITIAL LUNG DISEASE = GENERALIZED INTERSTITIAL LUNG DISEASE

Prevalence: up to 15% of pulmonary conditions

Cause: > 200 described disorders; in only 25–30% known / established etiology; 15–20 diseases comprise > 90% of cases

- dyspnea (primary complaint)
- dry basilar rales / crackles that fail to clear with coughing

CXR:

◊ Difficult to characterize due to similar findings

◊ Differentiation into alveolar + interstitial disease is unreliable as "interstitial disease"

invariably involves alveoli + vice versa
√ ± nonspecific abnormality

mnemonic: HIDE FACTS
Hamman-Rich, **H**emosiderosis
Infection, **I**rradiation, **I**diopathic
Dust, **D**rugs
Eosinophilic granuloma, **E**dema
Fungal, **F**armer's lung
Aspiration (oil), **A**rthritis (rheumatoid, ankylosing spondylitis)
Collagen vascular disease
Tumor, TB, **T**uberous sclerosis
Sarcoidosis, **S**cleroderma

Zonal Predilection of Chronic Diffuse Parenchymal Lung Disease (DPLD)

CHRONIC DPLD OF UPPER LUNG ZONE

= zone with higher oxygen tension and pH, but less efficient lymphatic drainage

(a) inhalational disease
1. Silicosis
2. Coal worker pneumoconiosis
3. Extrinsic allergic alveolitis
4. Aspiration pneumonia

(b) granulomatous disease
1. Sarcoidosis
2. Langerhans cell histiocytosis (EG)
3. Postprimary TB (common)

(c) others
1. Cystic fibrosis
2. Ankylosing spondylitis
3. Chronic interstitial pneumonia
4. Sulfa drugs (rare)
5. Radiation pneumonitis
6. Recurrent Pneumocystis carinii pneumonia (PCP) under aerosolized pentamidine prophylaxis

mnemonic: CASSET
Cystic fibrosis
Ankylosing spondylitis
Silicosis
Sarcoidosis
Eosinophilic granuloma
Tuberculosis, fungus

CHRONIC DPLD OF LOWER LUNG ZONE

lower lung zone = zone with greater ventilation, perfusion, and lymphatic drainage
1. Idiopathic pulmonary fibrosis: usual interstitial pneumonia (common)
2. Lymphangitic carcinomatosis

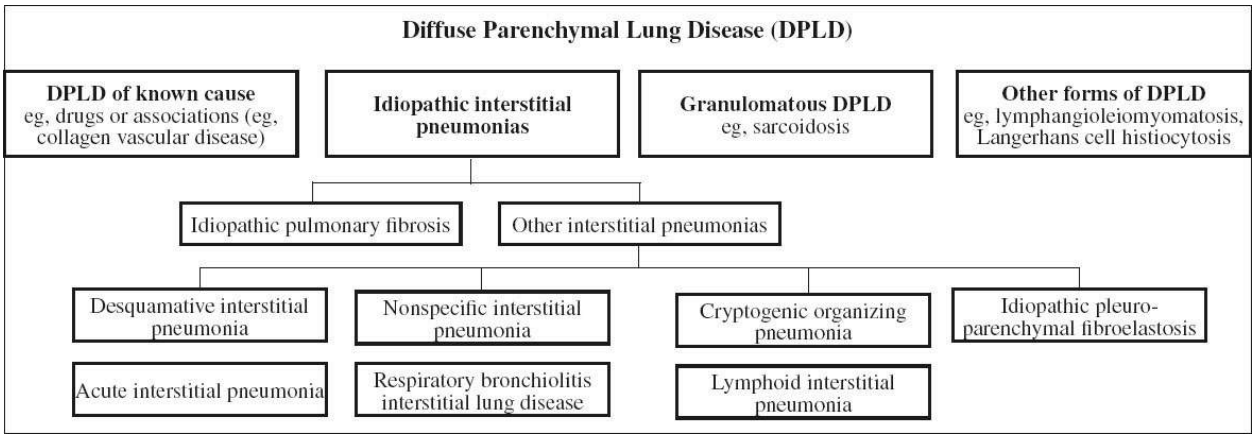
3. Collagen vascular disease: scleroderma (common)
4. Asbestosis (posterior aspect of lung base)
5. Lymphangioleiomyomatosis
6. Chronic aspiration pneumonia with fibrosis (often regional + unilateral)

mnemonic: BAD LASS RIF

Bronchiectasis
Aspiration
Dermatomyositis
Lymphangitic spread
Asbestosis
Sarcoidosis
Scleroderma
Rheumatoid arthritis
Idiopathic pulmonary fibrosis
Furadantin®

Compartmental Predilection of Chronic DPLD

A. AXIAL / CORE COMPARTMENT
= peribronchial vascular bundles + lymphatics
1. Sarcoidosis
2. Lymphangitic carcinomatosis
3. Lymphoma



B. MIDDLE / PARENCHYMAL COMPARTMENT
= formed by alveolar walls
1. Sarcoidosis
2. Lymphangitic carcinomatosis
3. Chronic medications
4. Neurofibromatosis
5. Vasculitis
6. Silicosis

C. PERIPHERAL COMPARTMENT
= pleura with subpleural connective tissue, interlobular septa, pulmonary veins,

lymphatics, walls of cortical alveoli

1. Sarcoidosis
2. Lymphangitic carcinomatosis
3. Idiopathic pulmonary fibrosis
4. Collagen vascular disease
5. Rheumatoid arthritis

Lung Volumes in Chronic DPLD

CHRONIC DPLD WITH NORMAL LUNG VOLUME

1. Sarcoidosis
2. Langerhans cell histiocytosis (in 66%)

CHRONIC DPLD WITH INCREASED LUNG VOLUME

mnemonic: ELECT

Emphysema with interstitial lung disease
Lymphangioleiomyomatosis
Eosinophilic granuloma (Langerhans) in 33%
Cystic fibrosis
Tuberous sclerosis

CHRONIC DPLD WITH REDUCED LUNG VOLUME

due to fibrotic process

1. Systemic lupus erythematosus
2. Collagen vascular disease (eg, scleroderma, dermatomyositis, polymyositis)
3. Idiopathic pulmonary fibrosis
4. Chronic interstitial pneumonias
5. Asbestosis

Pleural Disease in Chronic DPLD

CHRONIC DPLD WITH PNEUMOTHORAX

1. Lymphangioleiomyomatosis
2. Langerhans cell histiocytosis
3. End-stage lung disease

CHRONIC DPLD WITH PLEURAL EFFUSION

1. Lymphangioleiomyomatosis
2. Rheumatoid arthritis
3. Systemic lupus erythematosus
4. Mixed connective tissue disorder
5. Wegener granulomatosis
6. Lymphangitic carcinomatosis
7. Pulmonary edema

CHRONIC DPLD WITH PLEURAL THICKENING

1. Asbestosis
2. Collagen vascular disease

Lymphadenopathy in Chronic Diffuse Lung Disease

1. Silicosis
2. Sarcoidosis
3. Lymphoma
4. Lymphangitic carcinomatosis

Diffuse Fine Reticulations

Acute Diffuse Fine Reticulations

A. ACUTE INTERSTITIAL EDEMA
   1. Congestive heart failure
   2. Fluid overload
   3. Uremia
   4. Hypersensitivity

B. ACUTE INTERSTITIAL PNEUMONIA
   1. Viral pneumonia (Hantavirus, CMV)
   2. Mycoplasma pneumonia
   3. Pneumocystis carinii pneumonia

mnemonic: HELP
Hypersensitivity
Edema
Lymphoproliferative
Pneumonitis (viral)

Chronic Diffuse Fine Reticulations

A. VENOUS OBSTRUCTION
   1. Atherosclerotic heart disease
   2. Mitral stenosis
   3. Left atrial myxoma
   4. Pulmonary venoocclusive disease
   5. Sclerosing mediastinitis

B. LYMPHATIC OBSTRUCTION
   1. Lymphangiectasia (pediatric patient)
   2. Mediastinal mass (lymphoma)
   3. Lymphoma / leukemia
   4. Lymphangitic carcinomatosis:
      predominantly basilar distribution
      (a) bilateral (breast, stomach, colon, pancreas)
      (b) unilateral (lung tumor)
   5. Lymphocytic interstitial pneumonitis

C. INHALATIONAL DISEASE
   1. Silicosis: small nodules + reticulations
   2. Asbestosis: basilar distribution, pleural thickening + calcifications
   3. Hard metals
   4. Allergic alveolitis

D. GRANULOMATOUS DISEASE
from a nodular to a reticular pattern if
(a) nodules line up along bronchovascular bundles
(b) interlobular septa show fibrotic changes
1. Sarcoidosis:
√ hilar + mediastinal adenopathy (may have disappeared)
2. Eosinophilic granuloma: upper lobe distribution

E. CONNECTIVE-TISSUE DISEASE
√ reticulations in late stages
1. Rheumatoid lung
2. Scleroderma
3. Systemic lupus erythematosus

F. DRUG REACTIONS

G. IDIOPATHIC
1. Usual interstitial pneumonitis (UIP)
2. Desquamative interstitial pneumonitis (DIP)
3. Tuberous sclerosis: smooth muscle proliferation
4. Lymphangiomyomatosis
5. Idiopathic pulmonary hemosiderosis
6. Alveolar proteinosis (late complication)
7. Amyloidosis
8. Interstitial calcification (chronic renal failure)

mnemonic: LIFE lines
Lymphangitic spread
Inflammation / infection
Fibrosis
Edema

Coarse Reticulations

= architectural destruction of interstitium = end-stage scarring of lung = interstitial pulmonary fibrosis = **honeycomb lung**

√ coarse reticular interstitial densities with intervening cystic spaces
√ rounded radiolucencies < 1 cm in areas of increased lung density
√ small lung volume (decreased compliance)

Cx: (1) Intercurrent pneumothoraces
(2) Bronchogenic carcinoma = scar carcinoma

Cause:

A. INHALATIONAL DISEASE
(a) Pneumoconiosis
1. Asbestosis: basilar distribution, shaggy heart, pleural thickening + calcifications
2. Silicosis: upper lobe predominance ± pleural thickening ± hilar and mediastinal adenopathy
3. Berylliosis
(b) Chemical inhalation (late)

1. Silo-filler's disease (nitrogen dioxide)
2. Sulfur dioxide, chlorine, phosgene, cadmium

(c) Extrinsic allergic alveolitis
← hypersensitivity to organic dusts

(d) Oxygen toxicity
← sequelae of RDS therapy with oxygen

(e) Chronic aspiration
eg, mineral oil: localized process in medial basal segments / middle lobe

B. GRANULOMATOUS DISEASE
1. Sarcoidosis
2. Eosinophilic granuloma

C. COLLAGEN-VASCULAR DISEASE
1. Rheumatoid lung
2. Scleroderma
3. Ankylosing spondylitis: upper lobes
4. SLE: rarely produces honeycombing

D. IATROGENIC
1. Drug hypersensitivity
2. Radiotherapy

E. IDIOPATHIC
1. Usual interstitial pneumonitis (UIP)
√ honeycombing in 50%
√ severe volume loss in 45%
2. Desquamative interstitial pneumonitis (DIP)
√ honeycombing in 12.5%
√ severe volume loss in 23%
3. Lymphangiomyomatosis
4. Tuberous sclerosis (rare)
5. Neurofibromatosis (rare)
6. Pulmonary capillary hemangiomatosis (rare)

DDx: bronchiectasis, cavitary metastases (rare)

Reticulations & Pleural Effusion

A. ACUTE
1. Edema
2. Infection: viral, Mycoplasma (very rare)

B. CHRONIC
1. Congestive heart failure
2. Lymphangitic carcinomatosis
3. Lymphoma / leukemia
4. SLE
5. Rheumatoid disease
6. Lymphangiectasia
7. Lymphangiomyomatosis
8. Asbestosis

Reticulations & Hilar Adenopathy

1. Sarcoidosis
2. Silicosis
3. Lymphoma / leukemia
4. Lung primary: particularly oat cell carcinoma
5. Metastases: lymphatic obstruction / spread
6. Fungal disease
7. Tuberculosis
8. Viral pneumonia (rare combination)

End-stage Lung Disease

= evidence of honeycombing / cystic change / conglomerate fibrosis

A. DISTRIBUTION
   1. Usual interstitial pneumonia
      √ subpleural distribution + lower lobe predominance
   2. Asbestosis
      √ subpleural distribution + lower lobe predominance + pleural thickening
   3. Sarcoidosis
      √ subpleural honeycombing
      √ central cystic bronchiectasis
      √ conglomerate fibrosis
      √ peribronchovascular distribution
      √ upper lobe predominance
   4. Extrinsic allergic alveolitis
      √ diffuse random distribution + patchy areas of ground-glass attenuation

B. CYSTIC SPACES WITH WELL-DEFINED WALLS
   1. Langerhans cell histiocytosis
      √ upper lobe predominance
   2. Lymphangioleiomyomatosis
      √ no zonal predominance

C. CONGLOMERATE FIBROTIC MASSES
   1. Sarcoidosis
      √ peribronchovascular distribution
   2. Silicosis
      √ bronchi splayed around masses
   3. Talcosis
      √ areas of high attenuation (= talc deposits)

Honeycomb Lung

mnemonic: SHIPS BOATS

Sarcoidosis
Histiocytosis X = Langerhans cell histiocytosis
Idiopathic (UIP)
Pneumoconiosis
Scleroderma

Bleomycin, **B**usulfan
Oxygen toxicity
Arthritis (rheumatoid), **A**myloidosis, **A**llergic alveolitis
Tuberous sclerosis, **T**B
Storage disease (Gaucher)

Chronic Interstitial Disease Simulating Airspace Disease

A. REPLACEMENT OF LUNG ARCHITECTURE BY AN INTERSTITIAL PROCESS
   (a) neoplastic: Hodgkin disease, histiocytic lymphoma
   (b) benign cellular infiltrate: lymphocytic interstitial pneumonia, pseudolymphoma
   (c) granulomatous disease: alveolar sarcoidosis
   (d) fibrosis
B. EXUDATIVE PHASE OF INTERSTITIAL PNEUMONIA
   1. UIP
   2. Adult respiratory distress syndrome
   3. Radiation pneumonitis
   4. Drug reaction
   5. Reaction to noxious gases
C. CELLULAR FILLING OF AIR SPACE
   1. Desquamative interstitial pneumonia
   2. Pneumocystis carinii pneumonia

Reticulonodular Lung Disease

mnemonic: Please Don't Eat Stale Tuna Fish Sandwiches Every Morning
Pneumoconiosis
Drugs
Eosinophilic granuloma
Sarcoidosis
Tuberculosis
Fungal disease
Schistosomiasis
Exanthem (measles, chickenpox)
Metastases (thyroid)

Reticulonodular Pattern & Lower Lobe Predominance

mnemonic: CIA
Collagen vascular disease
Idiopathic
Asbestosis

Nodular Lung Disease

= round moderately well marginated opacity < 3 cm in maximum diameter

A. GRANULOMATOUS LUNG DISEASE
   (a) infection: eg, tuberculosis
   (b) fungal disease: eg, histoplasmosis

(c) silicosis
(d) vasculitis: eg, Wegener granulomatosis

B. NEOPLASM
(a) metastatic lung diseases: eg, thyroid cancer
(b) lymphoma
(c) bronchioloalveolar cell carcinoma

C. OTHER DISEASE
(a) drug-induced: methotrexate
(b) nongranulomatous vasculitis
(c) sarcoidosis

Macronodular Lung Disease

√ nodules > 5 mm in diameter

mnemonic: GAMMA WARPS

Granuloma (eosinophilic granuloma, fungus)
Abscess
Metastases
Multiple myeloma
AVM
Wegener granulomatosis
Amyloidosis
Rheumatoid lung
Parasites (Echinococcus, paragonimiasis)
Sarcoidosis

Micronodular Lung Disease

= discrete 3–5–7-mm small round focal opacity of at least soft-tissue attenuation

1. Granulomatous disease: miliary TB, histoplasmosis
2. Hypersensitivity (organic dust)
3. Pneumoconiosis (inorganic dust, thesaurosis = prolonged hair spray exposure)
4. Sarcoidosis
5. Metastases (thyroid, melanoma)
6. Langerhans cell histiocytosis
7. Chickenpox

DIFFUSE FINE NODULAR DISEASE & MILIARY NODULES

√ very small 1–4-mm sharply defined nodules of interstitial disease

(a) Inhalational disease
    1. Silicosis + coal worker's pneumoconiosis
    2. Berylliosis
    3. Siderosis
    4. Extrinsic allergic alveolitis (chronic phase)
(b) Granulomatous disease
    1. Langerhans cell histiocytosis = eosinophilic granuloma
    2. Sarcoidosis (with current / previous adenopathy)
(c) Infectious disease

1. Bacteria: salmonella, nocardiosis
2. TB
3. Fungus: histoplasmosis, coccidioidomycosis, blastomycosis, aspergillosis (rare), cryptococcosis (rare)
4. Virus: varicella (more common in adults), Mycoplasma pneumonia

(d) Metastases:
thyroid carcinoma, melanoma, adenocarcinoma of breast, stomach, colon, pancreas

(e) Alveolar microlithiasis (rare)

(f) Bronchiolitis obliterans

(g) Gaucher disease

mnemonic: TEMPEST

Tuberculosis + fungal disease
Eosinophilic granuloma
Metastases (thyroid, lymphangitic carcinomatosis)
Pneumoconiosis, Parasites
Embolism of oily contrast
Sarcoidosis
Tuberous sclerosis

Fine Nodular Disease in Afebrile Patient

1. Inhalational disease
2. Eosinophilic granuloma
3. Sarcoidosis
4. Metastases
5. Fungal infection (late stage)
6. Miliary tuberculosis (rare)

Fine Nodular Disease in Febrile Patient

1. Tuberculosis
2. Fungal infection (early stage)
3. Pneumocystis
4. Viral pneumonia

DIFFUSE LUNG DISEASE ON HRCT

Patterns of Diffuse Lung Disease on HRCT

maximum resolution = 300 μm

1. **Linear densities**
   = thickening of interlobular septa + bronchovascular interstitium
   Cause: interstitial fluid / fibrosis / cellular infiltrates
   (a) intralobular septal thickening
   = weblike network of fine lines in secondary pulmonary lobule
   (b) interlobular septal thickening
   = fine linear opacities perpendicular to pleural surface / in a polygonal pattern in a more central location

√ smooth septal thickening: pulmonary edema, lymphangitic carcinomatosis
√ beaded septa / septal nodules: lymphangitic carcinomatosis
√ irregular septa imply fibrosis
› distorted lobules: fibrosis
› no architectural distortion of lobules: edema / infiltration

2. **Reticular densities**
= clustered areas of septal thickening producing intricate network of crisscross lines in subpleural location
(a) predominantly subpleural small reticular elements of 6–10 mm in diameter with collection of small cystic airspaces with well-defined walls ("honeycombing")
Associated with: interstitial fibrosis, lymphangio- leiomyomatosis, amyloidosis
(b) fine diffusely distributed network of 2–3-mm basic elements
Associated with: miliary TB, reactions to methotrexate
Distribution:
› lower lung zones in subpleural areas: idiopathic pulmonary fibrosis, collagen vascular disease, asbestosis
› mid lung zone / all lung zones: chronic extrinsic allergic alveolitis
› mid + upper lung zones: sarcoidosis

3. **Nodules**
(a) interstitial nodules lymphangitic carcinomatosis, sarcoidosis, Langerhans cell histiocytosis, silicosis, coal worker pneumoconiosis, tuberculosis, hypersensitivity pneumonitis, metastatic tumor, amyloidosis
√ perihilar, peribronchovascular, centrilobular, interlobular septa, subpleural nodules
(b) airspace nodules lobular pneumonia, transbronchial spread of TB, bronchiolitis obliterans organizing pneumonia (BOOP), pulmonary edema
√ ill-defined nodules, a few mm to 1 cm in size
√ peribronchiolar + centrilobular
Size:
› small (< 5 mm): centrilobular location (separated by several mm from pleural surface, fissures, interlobular septa)
› large (> 5 mm): well / poorly defined occasionally surrounded by a halo of ground-glass opacity
Distribution:
› along bronchoarterial bundles + interlobular septa + subpleural: sarcoidosis
› upper zone: silicosis, coal-worker's pneumoconiosis
› centrilobular: extrinsic allergic alveolitis
DDx: vessel on cross section

4. **Ground-glass attenuation**
= hazy increase in lung opacity without obscuration of underlying vessels ← parenchymal abnormalities below spatial resolution of HRCT

◊ Often indicative of an acute, active, and potentially treatable process!

Histo:
(a) alveolar wall inflammation / thickening
(b) partial filling of air-spaces

(c) combination of both

Common cause: "water, blood, cells, no air"

A. Interstitial pulmonary edema = increased capillary blood volume
   √ perihilar + gravitational distribution
   √ cardiomegaly and pleural effusion

B. Diffuse inflammation / infection
   (a) alveolitis = minimal airspace filling as in
      1. Viral / mycoplasmal pneumonia
      2. Pneumocystis pneumonia in immunocompromised patient
      3. ARDS
   (b) early interstitial lung disease = minimal alveolar wall thickening (NSIP, DIP, RB-ILD, LIP)

C. Hypersensitivity pneumonitis
   √ centrilobular densities + air trapping
   • history of exposure to certain antigen

D. Pulmonary alveolar hemorrhage
   • hemoptysis, anemia, coagulopathy, vasculitis

E. Alveolar collapse
   1. Partial atelectasis = partial collapse of alveoli
   2. Normal during expiration

Distribution:

› peripheral in lower lung zones: DIP, UIP
› mid + upper lung zones: sarcoidosis
› "crazy paving" pattern
› mosaic perfusion

5. **Consolidation**

= homogeneous increase in pulmonary attenuation with obscuration of underlying vessels
√ ± air-bronchogram
√ sharp border at major fissure
√ advancing margin of ground-glass opacity
√ vessels visible only on enhanced CT

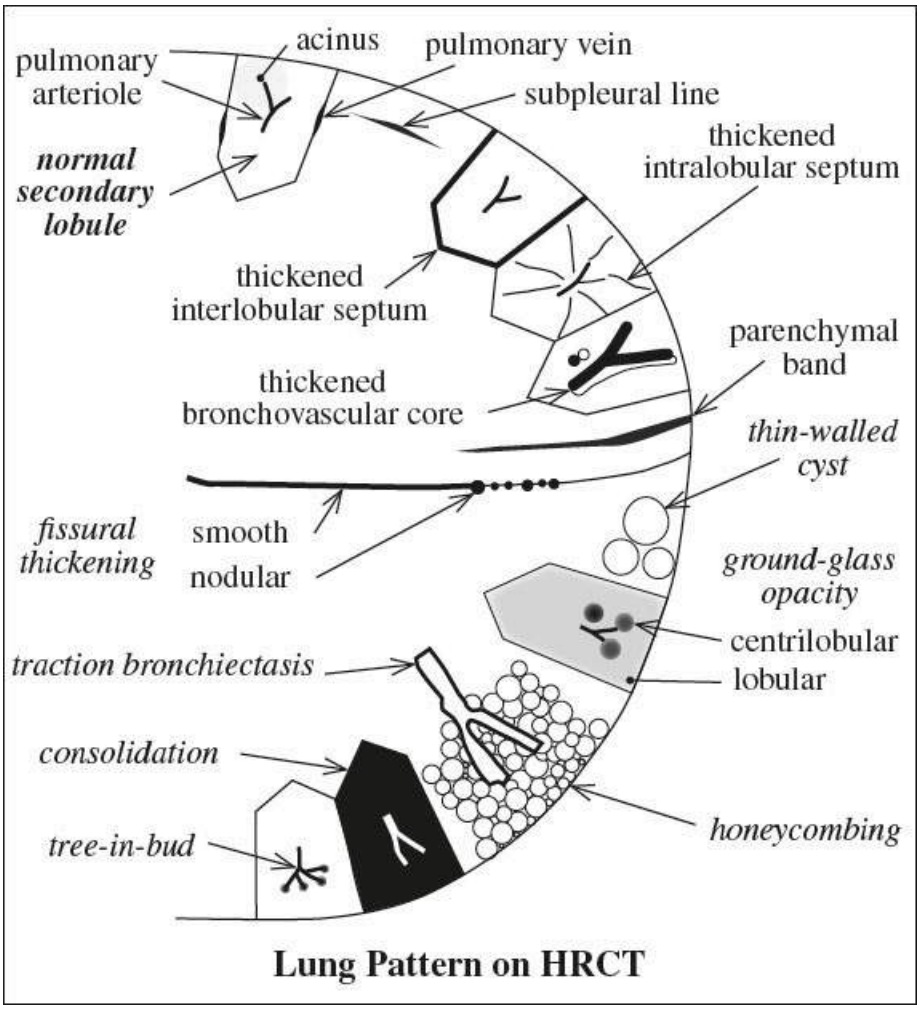
Cause:

(a) any process filling airspaces with blood, fluid, inflammatory cells, tumor cells
(b) alveolar collapse = atelectasis

› subpleural in mid + upper lung zones: chronic eosinophilic pneumonia
› subpleural + peribronchial: BOOP
› focal: bronchioloalveolar cell carcinoma, lymphoma
› random: infectious pneumonia

6. **Cystic airspaces**

= circumscribed round structure filled with air



(a) with well-defined walls:
lymphangioleiomyomatosis, pulmonary Langerhans-cell granulomatosis, DIP, LIP, honeycomb lung, cystic bronchiectasis

(b) without well-defined walls:
centrilobular, panlobular (panacinar), paraseptal emphysema

Cause:

(a) focally clustered: cystic bronchiectasis

(b) subpleural location: honeycombing, Langerhans cell histiocytosis, lymphangioleiomyomatosis

Centrilobular Nodules

A. Acute / chronic bronchiolar infection
   1. Bacterial infection
   2. Viral infection
   3. Fungal infection

B. Inflammation
   1. Hypersensitivity pneumonia
   2. Respiratory bronchiolitis-interstitial lung disease

3. Bronchiolitis obliterans organizing pneumonia
4. Bronchiolitis obliterans
5. Sarcoidosis
6. Asthma
7. Autoimmune / immunodeficiency disease

C. Pneumoconiosis

Peribronchial / Peribronchiolar Nodules

1. Metastatic calcifications
2. Endobronchial spread of infection
3. Hypersensitivity pneumonia
4. Sarcoidosis
5. Silicosis
6. Langerhans cell histiocytosis
7. Respiratory bronchiolitis

Centrilobular Nodules Without Ground-Glass Opacities

1. Endobronchial TB
2. Chronic bronchiolitis
3. Silicosis
4. Langerhans cell histiocytosis

Centrilobular Nodules with Ground-Glass Opacities

1. Hypersensitivity pneumonia
2. Bronchiolitis obliterans organizing pneumonia

Random Nodules

1. Hematogenous metastases: thyroid, kidney, breast
2. Miliary infection
3. Langerhans cell histiocytosis
4. Sarcoidosis
5. Silicosis

Thickened Bronchovascular, Interlobular Septal & Pleural Interstitium

A. Uni- / bilateral
   1. Lymphangitic tumor
   2. Lymphoma

B. Bilateral
   3. Kaposi sarcoma
   4. Edema

Parenchymal Bands & Architectural Distortion

1. Asbestos-related lung disease
2. Atelectasis
3. Tuberculosis

Classification of Bronchiolar (Small Airways) Disorders
Primary bronchiolar disorders
Constrictive bronchiolitis
Acute bronchiolitis
Diffuse panbronchiolitis
Respiratory bronchiolitis
Mineral dust airway disease
Follicular bronchiolitis
Interstitial lung disease + prominent bronchiolar involvement
Hypersensitivity pneumonitis
Respiratory bronchiolitis - interstitial lung disease
Desquamative interstitial pneumonia
Organizing pneumonia
Bronchiolar involvement in large airway disease
Chronic bronchitis
Asthma
Bronchiectasis

4. Sarcoidosis
5. Diffuse pulmonary fibrosis

Smooth Thickening of Interstitium

1. Lymphangitic tumor
2. Edema
3. Lymphoma
4. Kaposi sarcoma
5. Sarcoidosis (uncommon)

HRCT of Bronchiolitis

[CT findings are nonspecific and must be interpreted in the appropriate clinical context]

Cause:

(a) infection via endobronchial spread (acute bronchiolitis):

◊ Most common cause of tree-in-bud appearance.

› bacterial (most common)
› mycobacterial: classic TB, M. avium-intracellulare
› viral: acute infectious bronchiolitis in infants and young children due to RSV, adenovirus, mycoplasma
› parasitic
› fungal

(b) inhalation of organic / inorganic antigens: hypersensitivity pneumonitis, mineral dust airways disease

(c) immunologic deficiency or impaired host defense: cystic fibrosis, dyskinetic cilia syndrome

(d) cigarette smoking
1. Respiratory bronchiolitis
2. Respiratory bronchiolitis-interstitial lung disease

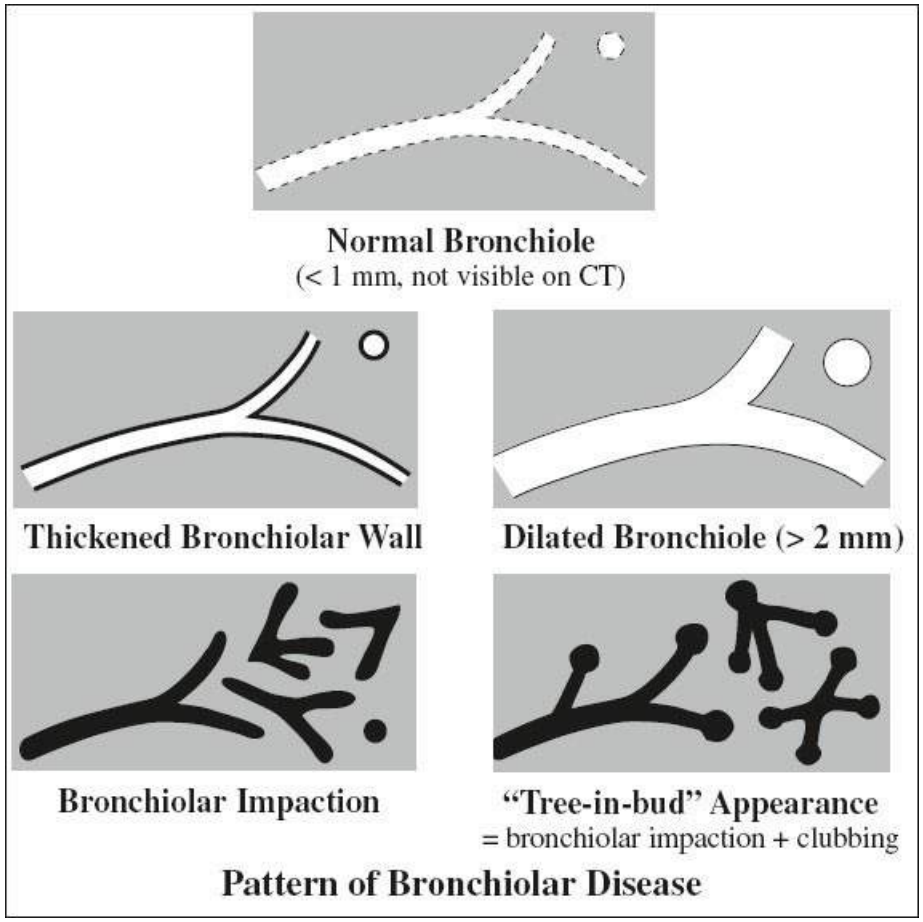
(e) idiopathic
1. Diffuse panbronchiolitis in Asians
2. Follicular bronchiolitis (← lymphoid hyperplasia): rheumatoid arthritis, Sjögren syndrome
3. Asthma
4. Bronchiolitis obliterans = constrictive bronchiolitis
5. Cryptogenic organizing pneumonia = bronchiolitis obliterans with organizing pneumonia (BOOP) = proliferative bronchiolitis

A. DIRECT SIGNS

√ ringlike tubular structures in lung periphery

Cause: wall thickening

√ dilatation of bronchioles



Cause: bronchiolectasis

√ 2- to 4-mm nodules / branching linear structures in lung periphery

Cause: bronchiolar luminal impaction with pus, mucus, granulomas, inflammatory exudate, fibrosis

B. INDIRECT SIGNS

√ subsegmental atelectasis = wedge-shaped area of ground-glass attenuation

√ air trapping = area of decreased attenuation from collateral air drift / ball-valve effect distal to occluded / stenotic airway <u>more prominent on expiration</u>:

DDx: physiologic air trapping with a few lucent secondary pulmonary lobules

√ mosaic perfusion = scattered areas of air trapping

√ centrilobular emphysema = destruction of small airways + surrounding parenchyma in the center of the pulmonary lobule

√ centrilobular airspace nodule = acinar nodule = < 1 cm ill-defined nodule of ground-glass attenuation (from inflammation within alveolar space) <u>less prominent on expiration</u>

Cause: extrinsic allergic alveolitis, sarcoidosis (perivenular nodules), pneumoconiosis (asbestosis, silicosis)

DDx: (1) Cystic lung disease (thin septum surrounds area of air attenuation, central vessel not present)

(2) Panlobular emphysema (distortion of vascular + septal architecture, bullae)

Tree-in-bud Appearance

= peripheral (within 5 mm of pleural surface) small (2–4 mm) centrilobular well-defined soft-tissue nodules connected to linear branching opacity (single stalk) with more than one contiguous branching sites

◊ Direct sign of treatable exudative bronchiolitis!

Histo: dilated centrilobular bronchioles → lumina impacted with mucus / fluid / pus + peribronchiolar inflammation (analogous to "gloved finger" appearance)

√ depiction of the normally invisible branching course of the intralobular bronchiole on HRCT

√ ± air trapping ± subsegmental consolidation

A. AIRWAY INFECTION (most common)
   1. Bacterial: Mycobacterium tuberculosis (endobronchial spread of active TB), atypical mycobacteria (M avium- intracellulare complex, M fortuitum, M chelonei), Staphylococcus aureus, Haemophilus influenzae
   2. Viral: CMV, Respiratory syncytial virus
   3. Fungal: invasive aspergillosis (A fumigatus)
   4. Parasitic

B. IMMUNOLOGIC DISORDER
   1. Allergic bronchopulmonary aspergillosis
   2. Congenital immunodeficiencies

C. CONGENITAL DISORDER
   1. Cystic fibrosis
   2. Kartagener syndrome
   3. Yellow nail syndrome

D. CONNECTIVE TISSUE DISORDER
   1. Rheumatoid lung
   2. Sjögren syndrome

E. IDIOPATHIC DISORDER
   1. Bronchiolitis obliterans
   2. Panbronchiolitis

F. NEOPLASM
   1. Primary pulmonary lymphoma
   2. Laryngotracheal papillomatosis
   3. Tumor embolism

G. TUMOR EMBOLI
   1. Gastric cancer
   2. Breast cancer
   3. Ewing sarcoma
   4. Renal cancer

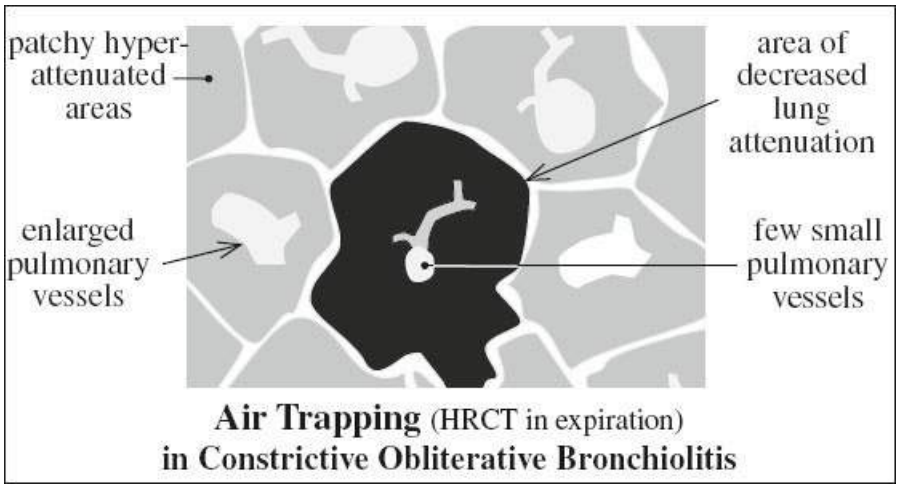
H. ASPIRATION of irritant substance
   1. Aspiration pneumonitis

I. INHALATION of toxic fumes + gases
   = alveolocapillary damage → pulmonary edema + bronchitis + bronchiolitis ± complicated by atelectasis + pneumonia

Mosaic Attenuation / Perfusion

= CT imaging pattern consisting of a heterogeneous patchwork of normal and air-attenuated segments

Mosaic Attenuation due to Ground-Glass Opacities
Acute causes
Pulmonary edema
Pulmonary hemorrhage
Infection
Pneumocystis pneumonia
Cytomegalovirus pneumonia
Herpes simplex pneumonia
Diffuse alveolar damage
Acute respiratory distress syndrome
Acute interstitial pneumonia
Acute eosinophilic pneumonia
Subacute to chronic causes
Organizing pneumonia
Hypersensitivity pneumonitis
Infection
Pneumocystis pneumonia
Diffuse alveolar damage (organizing + fibrotic changes)
Nonspecific interstitial pneumonia



Air Trapping (HRCT in expiration)
in Constrictive Obliterative Bronchiolitis

√ hypoattenuated areas with small vessels in 94% ← diminished blood flow
√ hyperattenuated areas with normal / dilated arteries and enhancement in 77% ← increased perfusion

The best method to differentiate between causes of mosaic attenuation is to perform expiratory imaging → thus allowing identification of areas trapping air.

Pathophysiology:

(a) air trapping

Cause: any obstructive lung disease

1. Chronic bronchitis / bronchiolitis obliterans
2. Bronchiectasis
3. Emphysema
4. Asthma
5. also: sarcoidosis, hypersensitivity pneumonia

√ attenuation differences are accentuated on expiratory HRCT

◊ Indirect sign of constrictive obliterative bronchiolitis without reversibility / improvement!

(b) vascular obstruction

Cause:

1. Chronic thromboembolic pulmonary hypertension (common)
2. Pulmonary venoocclusive disease
3. Idiopathic pulmonary hypertension

√ increase in lung attenuation in low- and high-attenuation areas on expiratory **HRCT**

(c) diffuse ground-glass opacities

Focal Air-trapping on HRCT

1. Asthma
2. Bronchiolitis obliterans
3. Bronchiectasis

Ground-glass Attenuation

Cause:

(a) partial airspace filling
(b) interstitial thickening with
  › inflammation
  › edema
  › fibrosis
(c) neoplastic proliferation
  › bronchioloalveolar cell carcinoma
  › lymphoma

1. Desquamative interstitial pneumonia
2. Extrinsic allergic alveolitis
3. Sarcoidosis
4. Usual interstitial pneumonia
5. Alveolar proteinosis
6. Cryptogenic organizing pneumonia

Large Symmetric Regions of Ground-glass Opacities

A. WATER
  1. Pulmonary edema
  2. Uremic lung
  3. Acute interstitial pneumonia
  4. Adult respiratory distress syndrome
B. PROTEIN
  1. Alveolar proteinosis
  2. Nonspecific interstitial pneumonia
C. RBCs
  1. Pulmonary hemorrhage
D. WBCs
  1. Hypersensitivity pneumonia
  2. Acute / chronic eosinophilic pneumonia
  3. Desquamative interstitial pneumonia
  4. Churg-Strauss syndrome
  5. Atypical pneumonia (viral, pneumocystis, mycoplasma)
E. TUMOR
  1. Bronchioloalveolar cell carcinoma

Nodular Ground-glass Opacity

A. MALIGNANCY
  1. Atypical adenomatous hyperplasia (in 2.8% of general population)
  2. Bronchioloalveolar cell carcinoma (in 5.2% of non-small cell lung cancer population)
  3. Adenocarcinoma
  4. Lymphoma
B. BENIGN CONDITION
  (a) idiopathic

1. Focal interstitial fibrosis
2. BOOP

(b) infection
1. Aspergillosis
2. Cryptococcus

(c) eosinophilic lung disease
1. Simple eosinophilic pneumonia (Löffler syndrome)
2. Idiopathic hypereosinophilic syndrome
3. Collagen vascular disease
4. Sarcoidosis
5. Parasitic infection
6. Drug reaction

(d) hemorrhagic nodule
1. Thoracic endometriosis
2. Focal traumatic lung injury
3. Wegener granulomatosis
4. Henoch-Schönlein purpura

C. TECHNICAL (false positive + false negative)
1. Excessive noise due to low tube current
2. Volume averaging

Ground-glass Opacities & Interlobular Septal Lines

A. ACUTE / SUBACUTE
1. Hypersensitivity pneumonia
2. Pulmonary edema
3. Diffuse alveolar hemorrhage
4. Viral, pneumocystis, mycoplasmal pneumonia

B. CHRONIC
1. Hypersensitivity pneumonia
2. Pulmonary alveolar proteinosis
3. Usual interstitial pneumonia
4. Bronchioloalveolar cell carcinoma

Ground-glass Opacity & Reticular Change

1. Nonspecific interstitial pneumonia
2. Desquamative interstitial pneumonia
3. Acute interstitial pneumonia
4. BOOP
5. Chronic eosinophilic pneumonia
6. Churg-Strauss syndrome

Reversed Halo / Atoll Sign

= focal area of ground-glass opacity surrounded by a complete / incomplete ring of denser consolidation initially thought to be specific for organizing pneumonia

Cause: (a) variety of infections
(b) noninfectious granulomatous disease

(c) malignancy

Airspace Nodules & Ground–glass-opacity Halo

(a) infection
1. Invasive pulmonary aspergillosis
2. Mucormycosis
3. Candidiasis

(b) noninfectious disease
1. Wegener granulomatosis
2. Bronchioloalveolar carcinoma
3. Hemorrhagic tumors (primary, metastatic)
4. Pulmonary lymphoma

Crazy-paving Pattern

= smooth thickening of interlobular septa + intralobular lines superimposed on a background of patchy ground-glass opacities in a geographic distribution
1. Pulmonary alveolar proteinosis
2. Pneumocystis carinii pneumonia
3. Mucinous bronchioloalveolar cell carcinoma
4. Sarcoidosis
5. Nonspecific interstitial pneumonia
6. Organizing pneumonia
7. Exogenous lipoid pneumonia
8. ARDS
9. Pulmonary hemorrhage syndromes
10. Bacterial pneumonia
11. Acute eosinophilic pneumonia
12. Cardiogenic edema

PULMONARY NODULE / MASS

Solitary Pulmonary Nodule (SPN) / Mass

Definition: any pulmonary / pleural sharply defined discrete nearly circular opacity

2–30 mm in diameter = nodule

> 30 mm in diameter = mass (> 90% prevalence of malignancy)

Incidence: 150,000 annually in USA on CXR

(a) roentgenographic survey of low-risk population: < 5% of nodules are cancerous

(b) on surgical resection: 40% malignant tumors (lung primaries + metastases), 40% granulomas

International Early Lung Cancer Action Project:

(1) CT detection of nodules vs chest x-ray: 23%÷7%

(2) CT detection of malignancy vs chest x-ray: 2.7%÷0.7%; stage I malignancy: 2.3%÷0.4%)

(3) Cancers: 96% resectable; 85% stage I, 83% not on CXR

Controversy:

» 80% estimated 10-year survival rate ← high proportion of stage I lung cancer (National Lung Screening Trial, 2011)

» NO mortality benefit from CT lung cancer screening (JAMA 2007)

A. INFLAMMATION / INFECTION

(a) inflammatory

1. **Granuloma** (<u>most common lung mass</u>):
   sarcoidosis (⅓), tuberculosis, berylliosis, leprosy, hypersensitivity pneumonitis, fungal disease (histoplasmosis, coccidioidomycosis, nocardiosis, cryptococcosis), gumma, atypical measles infection, Dirofilaria immitis (dog heartworm), talc, Crohn disease, primary biliary cirrhosis
2. Fluid-filled cavity: abscess, hydatid cyst, bronchiectatic cyst, bronchocele
3. Mass in preformed cavity: fungus ball, mucoid impaction
4. Rounded atelectasis
5. Inflammatory pseudotumor: fibroxanthoma, histiocytoma, plasma cell granuloma, sclerosing hemangioma
6. Paraffinoma = lipoid granuloma
7. Focal organizing pneumonia
8. Round pneumonia

(b) noninflammatory

1. Rheumatoid arthritis
2. Wegener granulomatosis

B. MALIGNANT TUMORS (< 30%)

◊ A solitary pulmonary nodule is the initial radiographic finding in 20–30% of patients with lung cancer!

(a) Malignant primaries of lung:

1. Bronchogenic carcinoma (66%, <u>2nd most common mass</u>)
2. Primary pulmonary lymphoma
3. Primary sarcoma of lung
4. Plasmacytoma (primary / secondary)
5. Clear cell carcinoma, carcinoid, giant cell carcinoma

(b) Metastases (4th most common cause)

in adults: kidney, colon, ovary, testes

in children: Wilms tumor, osteogenic sarcoma, Ewing sarcoma, rhabdomyosarcoma

C. BENIGN TUMORS

(a) lung tissue : hamartoma (6%, <u>3rd most common lung mass</u>), chondroma

(b) fat tissue : lipoma (usually pleural lesion)

(c) fibrous tissue : fibroma

(d) muscle tissue : leiomyoma

(e) neural tissue : schwannoma, neurofibroma, paraganglioma

(f) lymph tissue : intrapulmonary lymph node

(g) deposits : amyloid, splenosis, endometrioma, extramedullary hematopoiesis

D. VASCULAR

1. Arteriovenous malformation (AVM), hemangioma

2. Hematoma
3. Organizing infarct
4. Pulmonary venous varix
5. Pseudoaneurysm of pulmonary artery

E. DEVELOPMENTAL / CONGENITAL
1. Bronchogenic cyst (fluid-filled)
2. Pulmonary sequestration
3. Bronchial atresia

F. INHALATIONAL
1. Silicosis (conglomerate mass)
2. Mucoid impaction (allergic aspergillosis)

G. MIMICKING DENSITIES (20%)
(a) Pseudotumor
1. Fluid in fissure
2. Composite area of increased opacity

(b) Mediastinal mass

(c) Chest wall lesion
1. Nipple
2. Skin tumor: mole, neurofibroma, lipoma, keloid
3. Bone island, rib osteochondroma
4. Rib fracture / osteophyte
5. Pleural plaque / mass (mesothelioma)

(d) External object
1. Electrocardiographic lead attachment
2. Buttons, snaps

mnemonic: **B**ig **S**olitary **P**ulmonary **M**asses **C**ommonly **A**ppear **H**opeless **A**nd **L**onely

Bronchogenic carcinoma
Solitary metastasis, **S**equestration
Pseudotumor
Mesothelioma
Cyst (bronchogenic, neurenteric, echinococcal)
Adenoma, **A**rteriovenous malformation
Hamartoma, **H**istoplasmosis
Abscess, **A**ctinomycosis
Lymphoma

Morphologic Evaluation of Solitary Pulmonary Nodule

A. SIZE
◊ The smaller the nodule the more likely it is benign!
√ < 3 mm nodule: in 99.8% benign
√ 4–7 mm nodule: in 99.1% benign
√ 8–20 mm nodule: in 82% benign
√ > 20 mm nodule: in 50% benign
√ > 30 mm nodule: in > 93% malignant

B. MARGIN / EDGE

√ smooth well-defined margin = likely benign
◊ Mostly benign, in 21% malignant
√ corona radiata = irregular spiculated margin
◊ In 89% malignant, in 10% benign
√ pleural tag
◊ In 25% malignant, in 9% benign
√ "halo" sign (= nodule surrounded by ground-glass opacity)
◊ In neutropenic patient suggests aspergillosis
√ vessels feeding a smooth / lobulated nodule
◊ in arteriovenous malformation

C. CONTOUR
√ sharply marginated nodule: benign in 79%
√ lobulated nodule: malignant in 58%

Probability of Malignancy for Indeterminate Solitary Pulmonary Nodule	
Characteristic / Feature	*Likelihood Ratio*
spiculated margin	5.54
size > 3 cm	5.23
> 70 years of age	4.16
malignant growth rate	3.40
smoker	2.27
upper lobe location	1.22
size < 10 mm	0.52
smooth margin	0.30
30–39 years of age	0.24
never smoked	0.19
20–29 years of age	0.05
benign calcification	0.01
benign growth rate	0.01

(a) organizing mass
(b) tumor with multiple cell types growing at different rates (malignancy, hamartoma)

◊ A lobulated contour occurs in 25% of benign nodules
√ vessel leading to mass: pulmonary varix, AVM

D. SATELLITE LESION
= nodule(s) in association with larger peripheral nodule
› in 99% due to inflammatory disease (often TB)
› in 1% due to primary lung cancer

E. LOCATION
√ attached nodule = length of contact surface of nodule > 50% of nodule diameter OR major part of nonspherical nodule attached to fissure / pleura / vessel
Histo: scar, pleural plaque, post-infarction fibrosis, intrapulmonary lymph node

◊ 1-year follow-up is sufficient

√ perifissural nodule = oval / lentiform / triangular homo- generous nodule with smooth margins attached to fissure

Prevalence: 20% in lung cancer screening trial in heavy smokers

Prognosis: ± growth; almost uniformly benign

√ purely intraparenchymal = malignant

F. ENHANCEMENT PATTERN

G. INTERNAL ATTENUATION

H. CALCIFICATION

INTERNAL ATTENUATION OF SPN

√ entirely solid nodule in 15% malignant

√ nonsolid nodule of pure groundglass opacity in 34% malignant

√ partially solid nodule in 40–50% malignant

√ pseudocavitation (= small focal hypodense region) with air bronchogram suggests bronchioloalveolar cell carcinoma / lymphoma / resolving pneumonia

◊ Air bronchogram in nodules of < 2 cm: in 65% malignant, in 5% benign

√ bubblelike areas of low attenuation: bronchiolo-alveolar cell carcinoma (in 50%)

(a) CAVITATION

√ a thin (≤ 4 mm) smooth wall is benign in 94%

√ a thick (> 16 mm) irregular wall suggests malignancy

(b) Intranodular fat (–40 to –120 HU)

◊ Fat is a reliable indicator of a hamartoma!

√ fat density in up to 50% of hamartomas

CALCIFICATION IN SOLITARY PULMONARY NODULE

Sensitivities of HRCT > CT > CXR:

22–36% of nodules considered noncalcified on CXR contain calcium on thin-section CT; HRCT is 10–20 times more sensitive than CXR and detects more calcium by 24% compared to standard CT

◊ 38–63% of benign nodules are not calcified!

√ > 200 HU at CT densitometry indicates calcification within a nodule (66% sensitive, 98% specific for benign disease)

√ diffuse amorphous, eccentric, stippled = malignant pattern

√ central, completely solid, laminated: granuloma of prior infection (TB / histoplasmosis)

√ popcornlike = chondroid calcification in a hamartoma in 5–50%

√ peripheral calcification: granuloma, tumor

Calcifying malignant lung tumors:

carcinoid (up to 33%), lung cancer (up to 6%), osteosarcoma, chondrosarcoma, metastatic mucinous adenocarcinoma

ENHANCEMENT PATTERN OF SPN

(98% sensitive, 73% specific, 75–85% accurate)

√ nodule enhancement of < 15 HU suggests benign lesion

√ nodule enhancement of > 20 HU indicates malignancy

Growth Rate Assessment of Indeterminate SPN

= size comparison of nodule on current versus prior image

General recommendation for follow-up:

3-month intervals for up to 1 year and 6-month intervals for another year

Best method (quite imprecise):

early repeat HRCT (resolution in x and y planes of 0.3 mm) in 1–4 weeks for nodules > 5 mm measuring volume / area / diameter of nodule

Doubling time (= time required to double in volume):

(a) for most malignant nodules: 30–400 days = 26% increase in diameter

~ 30 days: aggressive small cell cancer

~ 90 days: squamous cell carcinoma

~ 120 days: large cell carcinoma

~ 150 days: aggressive adenocarcinoma

~ 1–80 days: average adenocarcinoma

(b) for benign nodules: < 30 and > 400 days

◊ Absence of growth over a 2-year period implies a doubling time of > 730 days

Disadvantage:

(1) only 65% positive predictive value

› very slow growth: hamartoma, bronchial carcinoid, inflammatory pseudotumor, granuloma, low-grade adenoca., metastasis from renal cell carcinoma

› very rapid growth: osteosarcoma, choriocarcinoma, testicular neoplasm, organizing infectious process, infarct (thromboembolism, Wegener granulomatosis)

(2) unreliable growth perception in nodules < 10 mm:
eg, a nodule with a doubling time of 6 months increases its diameter from 5 mm to only 6.25 mm remaining radiologically "stable"

<u>better:</u> volumetric growth assessment

(3) delay can worsen the prognosis

√ decrease in size with time: benign lesion

◊ Bronchogenic carcinoma may show temporary decrease in size due to infarction - necrosis - fibrosis - retraction sequence!

Clinical Assessment of Indeterminate SPN

- by patient age (prevalence of cancer < 30 years is low)
- history of prior malignancy
- presenting symptoms, smoking history

Management Strategies of Indeterminate SPN

A. Bayesian Analysis

◊ Analysis of patient characteristics + selected radiologic features is superior to evaluation by experienced radiologist in stratification of benign from malignant nodules!

Likelihood ratio (LR) = probability of malignancy

= LR of 1.0 means a 50% chance of malignancy

Odds of malignancy ($Odds_{ca}$) = sum of LR of radiologic features or patient characteristics

Probability of malignancy:

$pCa = Odds_{ca} / (1 + Odds_{ca})$

B. Decision Analysis

= cost-effective strategy for management decision determined by pCa

pCa < 0.05 observation

pCa > 0.05 and < 0.6 biopsy

pCa ≥ 0.60 immediate surgical resection

C. **Contrast-enhanced thin-section CT**

= degree of enhancement directly related to vascularity + likelihood of malignancy

Technique:

- 300 mg/mL iodine at 2 mL/sec (total dose 420 mg/kg)
- delay of 20 sec from onset of injection
- contiguous sections through the nodule obtained at 1, 2, 3, and 4 minute after onset of injection
- scan of chest and upper abdomen obtained between 1 and 2 minute after onset of injection

D. **^{18}F-FDG Positron Emission Tomography (PET)**

Size: 94% sensitive + 83% specific for nodules of 1–3 cm; NOT useful for nodules < 8 mm

◊ Detectable size of metabolically active lesion: (4–)7 mm

› benign nodule

√ no uptake = benign nodule (92–100% sensitive, 52–100% specific, 94% accurate)

√ SUV of 0.4 – 2.0 indicates a benign lesion

Incidental Pulmonary Nodule Follow-up by CT for Persons > 35 years
(Fleischner Society Recommendation)

*Average Nodule Size**	*Low-Risk Patient (Hx of minimal smoking; no malignancy)*	*High-Risk Patient (Hx of smoking & malignancy)*
≤ 4 mm	no f/u needed	f/u @ 12 mo
> 4–6 mm	f/u @ 12 mo	f/u @ 6–12 mo; if stable @ 18–24 mo
> 6–8 mm	f/u @ 6–12 mo; if stable @ 18–24 mo	f/u @ 3–6 mo; if stable @ 9–12 mo and @ 24 mo
> 8 mm	f/u @ 3 mo; if stable @ 9 mo and 24 mo	f/u @ 3 mo; if stable @ 9 mo and @ 24 mo

* average of length + width

Subsolid Pulmonary Nodule Follow-up by CT (*Fleischner Society Recommendation*)	
Nodule Type	*Management*
Solitary pure GGN	
≤ 5 mm	NO f/u needed
> 5 mm	f/u @ 3 mo; if persistent @ yearly intervals for 3 up to years
Solitary part-solid GGN	
solid component < 5 mm	f/u @ 3 mo; if persistent @ yearly intervals for up to 3 years
solid component ≥ 5 mm	biopsy / resection
Multiple subsolid nodules	
pure GGNs ≤ 5 mm	f/u @ 2 and 4 years
pure GGNs > 5 mm; NO dominant lesion	f/u @ 3 mo; if persistent @ yearly intervals for up to 3 years
part-solid GGNs > 5 mm; WITH dominant lesion	f/u @ 3 mo; if persistent biopsy / resection
GGN = ground-glass nodule; requires CT with contiguous 1-mm–thick sections; PET/CT for nodules only > 10 mm	

› inflammatory / infectious nodule
√ low FDG uptake = active TB, fungal infection (histoplasmosis), rheumatoid nodule, sarcoidosis, silicosis
√ gradual washout of FDG after initial increase suggests benign inflammatory lesion
› malignant nodule
√ increased FDG uptake = cancer (94–97% sensitive, 78–92% specific, 92% accurate)
√ intensity greater than mediastinum / SUV (standardized uptake value) > 2.5 indicates malignancy (95–100% sensitive, 80–89% specific, 92% accurate for nodules > 15 mm)
√ continually increasing FDG uptake over time is indicative of malignancy

FN: elevated serum glucose level > 250 mg/dL, low-grade malignancy (bronchioloalveolar carcinoma in up to 57% undetectable), carcinoid tumor, mucinous neoplasm; malignant lesion < 7 mm

FP: sarcoidosis, active TB, fungal infection (histoplasmosis, aspergillosis, coccidioidomycosis), silicoanthracosis, lipoid pneumonia, rheumatoid nodule, Wegener, radiation pneumonitis

E. **Transthoracic Needle Aspiration Biopsy**

95–100% sensitive for 10–15-mm malignancies;
50% sensitive for 5–7-mm malignancies; improved with the addition of a core
up to 91% sensitive for establishing a benign diagnosis

Cx: pneumothorax (5–30%) with chest tube placement in 1–15%; self-limiting hemorrhage

F. Bronchoscopy

10% diagnostic yield for nodules < 20 mm;

40–60% diagnostic yield for nodules 20–40 mm
Cx: lower than transthoracic needle biopsy

Decision Algorithm for Solitary Pulmonary Nodule

A. COMPARISON WITH OLD STUDY
√ growth → needle aspiration biopsy
√ no growth > 2 years → no action

B. COMPARISON NOT AVAILABLE
√ benign calcification or fat → no action
√ nodule of any size → further workup
(a) immunocompromised / fever
→ follow-up in 4–6-week intervals to resolution
→ or intervention
(b) history of malignancy
→ follow-up at 3, 6, 12 months
→ if growth consider intervention
(c) no history of malignancy ± smoking
micronodule ≤ 4 mm
→ follow-up at 12 and 24 months for age ≥ 35
→ follow-up at 12 months for age 18–35
→ if growth consider intervention
nodule of > 4–8 mm
→ follow-up at 3, 9 and 24 months for age ≥ 35
→ follow-up at 6, 12 and 24 months for age 18–35
→ if growth consider intervention
nodule of > 8 mm
→ consider PET / intervention
ground-glass nodule
→ longer follow-up for all ages
√ if no growth then no intervention

CT Halo Sign

√ central area of soft-tissue attenuation surrounded by a halo of ground-glass attenuation

A. HEMORRHAGIC PULMONARY NODULE
(a) hemorrhagic infarction (angioinvasion)
1. Early invasive aspergillosis
2. Mucormycosis
3. Hematogenous candidiasis
4. Coccidioidomycosis
(b) necrotizing vasculitis
1. Wegener granulomatosis
(c) fragility of neovascular tissue
1. Metastatic angiosarcoma
2. Metastatic choriocarcinoma
3. Metastatic osteosarcoma

4. Kaposi sarcoma

(d) trauma

1. Following lung biopsy
2. Lung transplant

B. LEPEDIC TUMOR GROWTH

1. Bronchioloalveolar carcinoma
2. Metastatic extrapulmonary adenocarcinoma
3. Lymphoma

C. OTHERS

1. Eosinophilic pneumonia
2. Bronchiolitis obliterans organizing pneumonia
3. Tuberculoma associated with hemoptysis
4. Mycobacterium avium complex
5. Herpes simplex, CMV, varicella-zoster virus

Benign Lung Tumor

A. CENTRAL LOCATION

1. Bronchial polyp
2. Bronchial papilloma
3. Granular cell myoblastoma

B. PERIPHERAL LOCATION

1. Hamartoma
2. Leiomyoma:
   benign metastasizing leiomyoma, history of hysterectomy
3. Amyloid tumor: not associated with amyloid of other organs / rheumatoid arthritis / myeloma
4. Intrapulmonary lymph node
5. Arteriovenous malformation
6. Endometrioma, fibroma, neural tumor, chemodectoma

C. CENTRAL / PERIPHERAL

1. Lipoma: (a) subpleural, (b) endobronchial

D. PSEUDOTUMOR

1. Fibroxanthoma / xanthogranuloma
2. Plasma cell granuloma
3. Sclerosing hemangioma: middle-aged woman, RML / RLL (most commonly), may be multiple
4. Pseudolymphoma
5. Round atelectasis
6. Pleural pseudotumor = accumulation of pleural fluid within interlobar fissure

Lung Tumor in Childhood

1. Metastatic (common)
2. Blastoma
3. Mucoepidermoid carcinoma
4. Bronchogenic carcinoma

5. Hemangiopericytoma
6. Rhabdomyosarcoma

Solid Intrathoracic Neonatal Mass

1. Type 3 / fluid-filled cystic adenomatoid malformation
2. Sequestration
3. Solid (high-grade) pleuropulmonary blastoma
4. Bronchial atresia

Differential Diagnosis of Airspace Opacities

Disease	*Presentation*	*Distribution*	*Adenopathy*	*Tree-in-bud*	*Cavitation*
Wegener granulomatosis	most often acute	multifocal, bilateral perihilar + peribronchovascular	rare	rare	rare
Bacterial pneumonia	acute	lobar + patchy	reactive	yes	rare
Aspiration	most often acute	dependent, associated with bronchiectasis in lower lobes	reactive	yes	sometimes
Organizing pneumonia	chronic	multifocal, peripheral, migratory, atoll sign	rare	no	no
Rheumatoid arthritis	solitary / multiple	5–7 mm	usually peripherally	rare	waxing and waning; SQ nodules
Adenocarcinoma	chronic	uni- / multifocal, ranging from ground-glass opacity to consolidation	yes	no	pseudocavitation

Differential Diagnosis for Nodules and Masses

Disease	*Number*	*Size*	*Distribution*	*Cavitation*	*Ancillary Findings*
Wegener granulomatosis	multiple	5–100 mm	usually bilateral, random (peribronchovascular, subpleural, angiocentric	in up to 50% of lesions > 2 cm	CT halo / atoll sign, radiating linear scarring, pleural tags
Metastasis	multiple	variable	bilateral, random	uncommon; if present suggestive of squamous / sarcoma / TCC primary	lymphadenopathy
Infection	variable	usually < 10 mm	peripheral (septic emboli), miliary (TB, fungus)	rare	tree-in-bud opacities, consolidation, reactive lymphadenopathy
Sarcoidosis	multiple	2 –10 mm	perilymphatic	rare	architectural distortion, symmetric adenopathy
Rheumatoid arthritis	solitary / multiple	5–7 mm	usually peripherally	rare	waxing and waning; subcutaneous nodules

5. Neuroblastoma

Large Pulmonary Mass

mnemonic: CAT PIES

Carcinoma (large cell, squamous cell, cannon ball metastasis
Abscess
Toruloma (Cryptococcus)
Pseudotumor, **P**lasmacytoma
Inflammatory
Echinococcal disease
Sarcoma, **S**equestration

Cavitating Lung Nodule

A. NEOPLASM
   (a) Lung primary:
      1. Squamous cell carcinoma (10%)
      2. Adenocarcinoma (9.5%)
      3. Bronchioloalveolar carcinoma (rare)
      4. Hodgkin disease (rare)
   (b) Metastases (4% cavitate):
      1. Squamous cell carcinoma (⅔):
         nasopharynx (males), cervix (females), esophagus
      2. Adenocarcinoma (colorectal)
      3. Sarcoma: Ewing sarcoma, osteo-, myxo-, angiosarcoma
      4. Melanoma
      5. Seminoma, teratocarcinoma
      6. Wilms tumor
B. COLLAGEN-VASCULAR DISEASE
   1. Pulmonary angiitis + granulomatosis
      › Wegener granulomatosis + Wegener variant
   2. Rheumatoid nodules + Caplan syndrome
   3. SLE
   4. Periarteritis nodosa (rare)
C. GRANULOMATOUS DISEASE
   1. Langerhans cell histiocytosis
   2. Sarcoidosis (rare)
D. VASCULAR DISEASE
   1. Pulmonary embolus with infarction
   2. Septic emboli (Staphylococcus aureus)
E. INFECTION
   1. Bacterial: pneumatoceles from staphylococcal / gram-negative pneumonia
   2. Mycobacterial: TB
   3. Fungal: nocardiosis, cryptococcosis, coccidioidomycosis (in 10%), aspergillosis
   4. Parasitic: echinococcosis (multiple in 20–30%), paragonimiasis
F. TRAUMA
   1. Traumatic lung cyst (after hemorrhage)
   2. Hydrocarbon ingestion (lower lobes)
G. BRONCHOPULMONARY DISEASE
   1. Infected bulla
   2. Cystic bronchiectasis
   3. Communicating bronchogenic cyst

mnemonic: CAVITY

Carcinoma (squamous cell), **C**ystic bronchiectasis
Autoimmune disease (Wegener granulomatosis, rheumatoid lung)
Vascular (bland / septic emboli)
Infection (abscess, fungal disease, TB, Echinococcus)
Trauma
Young = congenital (sequestration, diaphragmatic hernia, bronchogenic cyst)

mnemonic: WEIRD HOLES
Wegener's syndrome
Embolic (pulmonary, septic)
Infection (anaerobes, pneumocystis, TB)
Rheumatoid (necrobiotic nodules)
Developmental cysts (sequestration)
Histiocytosis
Oncological
Lymphangioleiomyomatosis
Environmental, occupational
Sarcoid

Pulmonary Mass with Air Bronchogram

1. Bronchioloalveolar carcinoma
2. Lymphoma
3. Pseudolymphoma
4. Kaposi sarcoma
5. Blastomycosis

Air-crescent Sign

= air in a crescentic shape separating the outer wall of a nodule / mass from an inner sequestrum

A. INFECTION
   1. Invasive pulmonary aspergillosis
   2. Noninvasive mycetoma
   3. Echinococcal lung cyst
   4. Tuberculoma
   5. Rasmussen aneurysm (most too small to be identified on CXR)
   6. Bacterial lung abscess ± pulmonary gangrene

B. CAVITATING NEOPLASM
   1. Primary / metastatic carcinoma / sarcoma
   2. Bronchial adenoma
   3. Cystic hamartoma

C. TRAUMA
   1. Pulmonary hematoma

D. THROMBOEMBOLISM

Shaggy Pulmonary Nodule

mnemonic: **S**haggy **S**ue **M**ade **L**oving **A** **R**eally **W**ild **F**antasy **T**oday
Sarcoidosis, alveolar type
Septic emboli
Metastasis
Lymphoma, **L**ung primary, **L**ymphomatoid granulomatosis
Alveolar cell carcinoma
Rheumatoid lung

Wegener granulomatosis
Fungus
Tuberculosis

Multiple Pulmonary Nodules and Masses

√ homogeneous masses with sharp borders
√ no air alveolo- / bronchogram

A. TUMORS
   (a) malignant
      1. Metastases:
         from breast, kidney, GI tract, uterus, ovary, testes, malignant melanoma, sarcoma, Wilms tumor
      2. Lymphoma (rare)
      3. Multiple primary bronchogenic carcinomas (synchronous in 1% of all lung cancers)
   (b) benign
      1. Hamartoma (rarely multiple)
      2. Benign metastasizing leiomyoma
      3. AV malformations
      4. Amyloidosis

B. VASCULAR LESIONS
   1. Thromboemboli with organizing infarcts
   2. Septic emboli with organized infarcts

C. COLLAGEN-VASCULAR DISEASE
   1. Wegener granulomatosis: vasculitis with organizing infarcts
   2. Wegener variants
   3. Rheumatoid nodules: tendency for periphery, occasionally cavitating

D. INFLAMMATORY GRANULOMAS
   1. Fungal: coccidioidomycosis, histoplasmosis, cryptococcosis
   2. Bacterial: nocardiosis, tuberculosis
   3. Viral: atypical measles
   4. Parasites: hydatid cysts, paragonimiasis
   5. Sarcoidosis: large accumulation of interstitial granulomas
   6. Inflammatory pseudotumors: fibrous histiocytoma, plasma cell granuloma, hyalinizing pulmonary nodules, pseudolymphoma

mnemonic: SLAM DA PIG
Sarcoidosis
Lymphoma
Alveolar proteinosis
Metastases
Drugs
Alveolar cell carcinoma
Pneumonias
Infarcts
Goodpasture syndrome

Progressive Massive Fibrosis Pattern

1. Sarcoidosis
2. Tuberculosis
3. Silicosis
4. Berylliosis
5. Talcosis

Multiple Cavitating Nodules / Masses

A. PULMONARY VASCULITIS
    1. Wegener granulomatosis
    2. Necrotizing sarcoid granulomatosis
    3. Bronchocentric granulomatosis
B. METASTATIC DISEASE
    particularly squamous histologic type
C. MULTIFOCAL INFECTION
    1. Pseudomonas
    2. Tuberculosis
    3. Septic abscesses
D. MULTIPLE PULMONARY INFARCTS
E. BRONCHIECTASIS
F. NEOPLASMS
    1. Lymphoma
    2. Multicentric bronchioloalveolar carcinoma
G. COLLAGEN-VASCULAR DISEASE
    1. Rheumatoid nodules
H. GRANULOMATOUS DISEASE
    1. Cystic form of sarcoidosis
    2. Langerhans cell histiocytosis

Patchy Airspace Consolidations

1. Pneumonia
2. Sarcoidosis
3. Tuberculosis
4. Bronchiolitis obliterans organizing pneumonia

Small Pulmonary Nodules

mnemonic: SMALT
Sarcoid
Metastases (esp. thyroid)
Alveolar cell carcinoma
Lymphoma, **L**eukemia
TB

Pulmonary Nodules & Pneumothorax

1. Osteosarcoma
2. Wilms tumor

3. Histiocytosis

Pleura-based Lung Nodule

√ ill-defined / sharply defined lesion mimicking a true pleural mass
√ associated linear densities in lung parenchyma

1. Granuloma (fungus, tuberculosis)
2. Inflammatory pseudotumor
3. Metastasis
4. Rheumatoid nodule
5. Pancoast tumor
6. Lymphoma
7. Infarct: Hampton hump
8. Atelectatic pseudotumor

Intrathoracic Mass of Low Attenuation

A. CYSTS
   1. Bronchogenic / neurenteric / pericardial cyst
   2. Hydatid disease
B. FATTY SUBSTRATE
   1. Hamartoma
   2. Lipoma
   3. Tuberculous lymph node
   4. Lymphadenopathy in Whipple disease
C. NECROTIC MASSES
   1. Resolving hematoma
   2. Treated lymphoma
   3. Metastasis from ovary, stomach, testes

PNEUMOCONIOSIS

= tissue reaction to the presence of an accumulation of inhaled particulates (= dust) in lungs

Path: 1. Fibrosis
(a) focal / nodular = silicosis
(b) diffuse = asbestosis
Cause: silicosis, coal worker pneumoconiosis, asbestosis, berylliosis, talcosis
2. Nonfibrotic aggregates of particle-laden macrophages in inert dusts
Cause: siderosis (iron oxide), stannosis (tin oxide), and baritosis (barium)

Types:

1. Silicosis
2. Coal worker pneumoconiosis
3. Berylliosis
4. Talcosis
5. Siderosis
6. Carbon black pneumoconiosis
7. Hard-metal pneumoconiosis
8. Asbestos-related disease

Pneumoconiosis Categories

according to ILO (International Labour Office) useful for epidemiologic purposes

A. TYPE OF OPACITIES
1. Silicosis, coal worker's pneumoconiosis
nodular (round) opacities: p = < 1.5 mm; q = 1.5–3 mm; r = 3–10 mm
2. Asbestosis
linear (irregular) opacities: s = fine; t = medium; u = coarse / blotchy

B. PROFUSION / SEVERITY
(= concentration of small opacities in affected area) 0 = normal; 1 = slight; 2 = moderate; 3 = advanced
intermediate grading: 2/2= definitely moderate profusion
2/3 = moderate possibly advanced profusion

C. ZONAL DISTRIBUTION: upper / middle / lower

D. PLEURAL THICKENING: diffuse / circumscribed

Pneumoconiosis with Mass

Anthracosilicosis with:

1. Granuloma (histoplasmosis, TB, sarcoidosis)
2. Bronchogenic carcinoma (incidence same as in general population)
3. Metastasis
4. Progressive massive fibrosis
5. Caplan syndrome (rheumatoid nodules)

PULMONARY CALCIFICATIONS

Multiple Pulmonary Calcifications

A. INFECTION
   1. Histoplasmosis
   2. Tuberculosis
   3. Chickenpox pneumonia

B. INHALATIONAL DISEASE
   1. Silicosis

C. MISCELLANEOUS
   1. Hypercalcemia
   2. Mitral stenosis
   3. Alveolar microlithiasis

Calcified Pulmonary Nodules

mnemonic: HAM TV Station

Histoplasmosis, **H**amartoma
Amyloidosis, **A**lveolar microlithiasis
Mitral stenosis, **M**etastasis (thyroid, osteosarcoma, mucinous carcinoma)
Tuberculosis
Varicella
Silicosis

◊ Central / laminated / popcorn / diffuse calcifications are characteristic of benign solitary lung nodules!

DENSE LUNG LESIONS

Opacification of Hemithorax

mnemonic: FAT CHANCE

Fibrothorax
Adenomatoid malformation
Trauma (ie, hematoma)
Collapse, **C**ardiomegaly
Hernia
Agenesis of lung
Neoplasm (ie, mesothelioma)
Consolidation
Effusion

Atelectasis

A. TUMOR
   1. Bronchogenic carcinoma (⅔ of squamous cell carcinomas occur as an endobronchial mass with persistent or recurrent atelectasis / recurrent pneumonia)
   2. Bronchial carcinoid
   3. Metastasis: primary tumor of kidney, colon, rectum, breast, melanoma
   4. Lymphoma (usually as a late presentation)
   5. Lipoma, granular cell myoblastoma, amyloid tumor, fibroepithelial polyp

B. INFLAMMATION
   1. Tuberculosis (endobronchial granuloma, broncholith, bronchial stenosis)
   2. Right middle lobe syndrome (chronic right middle lobe atelectasis)
   3. Sarcoidosis (endobronchial granuloma – rare)

C. MUCUS PLUG
   1. Severe chest / abdominal pain (postoperative patient)
   2. Respiratory depressant drug (morphine; CNS illness)
   3. Chronic bronchitis / bronchiolitis obliterans
   4. Asthma
   5. Cystic fibrosis
   6. Bronchopneumonia (peribronchial inflammation)

D. OTHER
   1. Large left atrium: mitral stenosis + LLL atelectasis
   2. Foreign body: food aspiration, endotracheal intubation
   3. Broncholithiasis
   4. Amyloidosis
   5. Wegener granulomatosis
   6. Bronchial transection

Signs:

√ local increase in lung density
√ crowding of pulmonary vessels
√ bronchial rearrangement
√ displacement of fissures
√ displacement of hilum
√ mediastinal shift
√ elevation of hemidiaphragm
√ cardiac rotation
√ approximation of ribs
√ compensatory overinflation of normal lung

Obstructive Atelectasis

RESORPTIVE ATELECTASIS

Pathophysiology:
sum of partial gas pressures in venous blood perfusing atelectatic region is less than atmospheric pressure, → gradual resorption of air trapped distal to site of obstruction; continuing secretion into small airways leads to consolidation → postobstructive pneumonitis / bacterial infection

Cause: bronchiolar obstruction by
1. Tumor
2. Stricture
3. Foreign body
4. Mucus plug
5. Bronchial rupture

• airless collapse within minutes to hours

MR:
√ high signal intensity on T2WI in atelectatic area

Nonobstructive Atelectasis

Pathophysiology:
bronchi less compliant than lung parenchyma → bronchi + pathway between bronchial system + alveoli remain patent → elimination of secretions continues with preservation of convective airflow to distal bronchioles

• collapsed lung NOT completely airless (up to 40% residual air)

MR:
√ low-signal intensity on T2WI in atelectatic area

PASSIVE ATELECTASIS

= pleural space-occupying process

1. Pneumothorax
2. Hydrothorax / hemothorax
3. Congenital diaphragmatic hernia
4. Pleural masses: metastases, mesothelioma

ADHESIVE ATELECTASIS

= decrease in surfactant production

1. Respiratory distress syndrome of the newborn (hyaline membrane disease)
2. Pulmonary embolism: edema, hemorrhage, atelectasis
3. Intravenous injection of hydrocarbon

CICATRIZING ATELECTASIS

= parenchymal fibrosis causing decreased lung volume

1. Tuberculosis / histoplasmosis (upper lobes)
2. Silicosis (upper lobes)
3. Scleroderma (lower lobes)
4. Radiation pneumonitis (nonanatomical distribution)
5. Idiopathic pulmonary fibrosis

DISCOID ATELECTASIS

mnemonic: EPIC
Embolus
Pneumonia
Inadequate inspiration
Carcinoma, obstructing

ROUNDED ATELECTASIS

Cause: any type of pleural inflammatory reaction (asbestos as leading cause)

Pathomechanism:
thickening of visceral pleura with progressive wrinkling + folding of subpleural lung

Location: posterobasal subpleural

√ round / lentiform mass incompletely surrounded by lung

√ increased attenuation in periphery of mass

√ pleural thickening in vicinity of mass
√ curving of vessels + bronchi toward mass
√ air bronchogram within mass
√ lesion may be stable / enlarge

Left Upper Lobe Collapse

PA view:

√ "**Luftsichel**" sign = sharply marginated paraaortic crescent of hyperlucency (= hyperexpanded superior segment of LLL extending toward lung apex + between aortic arch and atelectatic LUL)
√ hazy opacification of left hilum + cardiac border
√ elevation of left hilum
√ near horizontal course of left main bronchus
√ posterior + leftward rotation of heart

Lateral view:

√ retrosternal opacity
√ major fissure displaced anteriorly paralleling anterior chest wall

DDx: (1) Herniation of right lung across midline (leftward displacement of anterior junction line)
(2) Medial pneumothorax

Multifocal Ill-defined Densities

= densities 5–30 mm resulting in airspace filling

A. INFECTION
1. Bacterial bronchopneumonia
2. Fungal pneumonia:
histoplasmosis, blastomycosis, actinomycosis, coccidioidomycosis, aspergillosis, cryptococcosis, mucormycosis, sporotrichosis
3. Viral pneumonia
4. Tuberculosis (primary infection)
5. Rocky Mountain spotted fever
6. Pneumocystis carinii

B. GRANULOMATOUS DISEASE
1. Sarcoidosis (alveolar form ← peribronchial granulomas)
2. Eosinophilic granuloma

C. VASCULAR
(a) thromboembolic disease
(b) septic emboli
(c) vasculitis
1. Wegener granulomatosis
2. Wegener variants: limited Wegener, lymphomatoid granulomatosis
3. Infectious vasculitis = invasion of pulmonary arteries: mucormycosis, invasive form of aspergillosis, Rocky Mountain spotted fever
4. Goodpasture syndrome
5. Scleroderma

D. NEOPLASTIC
   1. Bronchioloalveolar cell carcinoma
      = only primary lung tumor to produce multifocal ill-defined densities with air bronchograms
   2. Alveolar type of lymphoma
      = massive accumulation of tumor cells in interstitium with compression atelectasis + obstructive pneumonia
   3. Metastases
      (a) Choriocarcinoma: hemorrhage (however rare)
      (b) Vascular tumors: malignant hemangiomas
   4. Waldenström macroglobulinemia
   5. Angioblastic lymphadenopathy
   6. Mycosis fungoides
   7. Amyloid tumor
E. IDIOPATHIC INTERSTITIAL DISEASE
   1. Lymphocytic interstitial pneumonitis (LIP)
   2. Desquamative interstitial pneumonitis (DIP)
   3. Pseudolymphoma = localized form of LIP
   4. Usual interstitial pneumonitis (UIP)
F. INHALATIONAL DISEASE
   1. Allergic alveolitis: acute stage (eg, farmer's lung)
   2. Silicosis
   3. Eosinophilic pneumonia
G. DRUG REACTIONS

Diffuse Infiltrates in Immunocompromised Patient

mnemonic: FOLD
Failure (CHF)
Opportunistic infection
Lymphangitic tumor spread
Drug reaction

Segmental & Lobar Densities

A. PNEUMONIA
   1. Lobar pneumonia
   2. Lobular pneumonia
   3. Acute interstitial pneumonia
   4. Aspiration pneumonia
   5. Primary tuberculosis
B. PULMONARY EMBOLISM
   (rarely multiple / larger than subsegmental)
C. NEOPLASM
   1. Obstructive pneumonia
   2. Bronchioloalveolar cell carcinoma
D. ATELECTASIS

Chronic Infiltrates

Chronic Infiltrates in Childhood

mnemonic: ABC'S

Asthma, **A**gammaglobulinemia, **A**spiration
Bronchiectasis
Cystic fibrosis
Sequestration, intralobar

Chronic Multifocal Ill-defined Opacities

1. Organizing pneumonia
2. Granulomatous disease
3. Allergic alveolitis
4. Bronchioloalveolar cell carcinoma
5. Lymphoma

SUBACUTE / CHRONIC CONSOLIDATION & GROUND-GLASS OPACITIES

1. BOOP
2. Chronic eosinophilic pneumonia
3. Churg-Strauss syndrome
4. Desquamative interstitial pneumonia
5. Nonspecific interstitial pneumonia
6. Chronic hypersensitivity pneumonia
7. Mycoplasma pneumonia
8. Lymphoma
9. Lipoid pneumonia

Chronic Diffuse Confluent Opacities

1. Alveolar proteinosis
2. Hemosiderosis
3. Sarcoidosis

Ill-defined Opacities with Holes

A. INFECTION
   1. Necrotizing pneumonias:
      Staphylococcus aureus, ß-hemolytic streptococcus, Klebsiella pneumoniae, E. coli, Proteus, Pseudomonas, anaerobes
   2. Aspiration pneumonia:
      mixed gram-negative organisms
   3. Septic emboli
   4. Fungus:
      histoplasmosis, blastomycosis, coccidioidomycosis, cryptococcosis
   5. Tuberculosis
B. NEOPLASM
   1. Primary lung carcinoma
   2. Lymphoma (cavitates very rarely)

C. VASCULAR + COLLAGEN-VASCULAR DISEASE
   1. Emboli with infarction
   2. Wegener granulomatosis
   3. Necrobiotic rheumatoid nodules
D. TRAUMA
   1. Contusion with pneumatoceles

Recurrent Fleeting Infiltrates

1. Löffler disease
2. Bronchopulmonary aspergillosis / bronchocentric granulomatosis
3. Asthma
4. Subacute bacterial endocarditis with pulmonary emboli

Tubular Density

A. Mucoid impaction
B. Vascular malformation
   1. Arteriovenous malformation
   2. Pulmonary varix

Mucoid Impaction

= BRONCHIAL MUCOCELE = BRONCHOCELE
= V-/Y-shaped branching tubular opacities of dilated bronchi filled with inspissated mucus surrounded by aerated lung (collateral air drift circumvents obstructed bronchi)
√ "gloved finger / **finger-in-glove**" sign
√ usually associated with bronchial dilatation
CT:
√ bronchiectasis
√ low-attenuation mucus inspissated in bronchi
√ clear connection with central airway

A. BRONCHIAL OBSTRUCTION
   (a) congenital
      1. Bronchial atresia
      2. Interlobar sequestration
      3. Intrapulmonary bronchogenic cyst
   (b) endobronchial tumor
      1. Endobronchial hamartoma
      2. Endobronchial lipoma
      3. Bronchogenic carcinoma / adenoma
      4. Carcinoid tumor
      5. Laryngeal papillomatosis
      6. Metastasis: breast, kidney, colon, rectum, uterus, skin
   (c) others
      1. Tuberculous stricture
      2. Broncholithiasis
      3. Foreign body aspiration

B. WITHOUT BRONCHIAL OBSTRUCTION
   (a) congenital
      1. Cystic fibrosis
   (b) inflammatory / infectious
      1. Allergic bronchopulmonary aspergillosis: central perihilar + upper lobe bronchiectasis
      2. Asthma (most frequent cause): esp. during acute attack or convalescent phase
      3. Chronic bronchitis
      4. Fluid-filled bronchiectasis: history of childhood pneumonia; peripheral distribution

Perihilar "Bat-wing" Infiltrates

mnemonic: **P**lease, **P**lease, **P**lease, **S**tudy **L**ight, **D**on't **G**et **A**ll **U**ptight

Pulmonary edema
Proteinosis
Periarteritis
Sarcoidosis
Lymphoma
Drugs
Goodpasture syndrome
Alveolar cell carcinoma
Uremia

Peripheral "Reverse Bat-wing" Infiltrates

mnemonic: REDS

Resolving pulmonary edema
Eosinophilic pneumonia
Desquamative interstitial pneumonia
Sarcoidosis

LUCENT LUNG LESIONS

Pulmonary Oligemia

Generalized Oligemia

= reduction in pulmonary blood volume

1. Aortic valve disease
   indicative of ⇓ stroke volume + cardiac output
   √ LV enlargement
2. Overpenetration of film = artifact
3. Deep inspiration + Valsalva maneuver
4. Positive pressure ventilation

Regional Oligemia

A. DECREASE IN BLOOD VOLUME
   1. Pulmonary arterial hypoplasia

2. Mitral valve disease
3. Pulmonary embolism
4. Flow inversion (= oligemic bases + hyperemic upper lobes in longstanding elevation of left heart pressure)

B. INCREASE IN AIR SPACES
1. Swyer-James syndrome
2. Regional emphysema
3. Valvular air trapping

Hyperlucent Lung

Bilateral Hyperlucent Lung

A. FAULTY RADIOLOGIC TECHNIQUE
1. Overpenetrated film

B. DECREASED SOFT TISSUES
1. Thin body habitus
2. Bilateral mastectomy

C. CARDIAC CAUSE of ↓ pulmonary blood flow
1. Right-to-left shunt:
Tetralogy of Fallot (small proximal pulmonary vessels), pseudotruncus, truncus type IV, Ebstein malformation, tricuspid atresia
2. Eisenmenger physiology of left-to-right shunt:
ASD, VSD, PDA (dilated proximal pulmonary vessels)

D. PULMONARY CAUSE of ↓ pulmonary blood flow
(a) decrease of vascular bed:
1. Pulmonary embolism:
bilaterality is rare; localized areas of hyperlucency (Westermark sign)

(b) increase in air space:
1. Air trapping (reversible changes):
acute asthmatic attack, acute bronchiolitis (pediatric patient)
2. Emphysema
3. Bulla
4. Bleb
5. Interstitial emphysema

Unilateral Hyperlucent Lung

A. FAULTY RADIOLOGIC TECHNIQUE
1. Rotation of patient

B. CHEST WALL DEFECT
1. Mastectomy
2. Absent pectoralis muscle (Poland syndrome)

C. INCREASED PULMONARY AIR SPACE
with decreased pulmonary blood flow
(a) large airway obstruction with air trapping
@ Bronchial compression:

1. Hilar mass (rare)
2. Cardiomegaly compressing LLL bronchus

@ Endobronchial obstruction with air trapping (collateral air drift):

1. Foreign body
2. Broncholith
3. Bronchogenic carcinoma
4. Carcinoid
5. Bronchial mucocele

(b) small airway obstruction

1. Bronchiolitis obliterans
2. Swyer-James / MacLeod syndrome
3. Emphysema (particularly bullous emphysema)
4. Emphysema + unilateral lung transplant

(c) Pneumothorax (in supine patient)

D. PULMONARY CAUSE of ↓ pulmonary blood flow

1. Pulmonary artery hypoplasia
2. Pulmonary embolism
3. Congenital lobar emphysema
4. Compensatory overaeration

UNILATERAL HYPERLUCENT LUNG IN CHILD

(a) hyperattenuating contralateral hemithorax

(b) pulmonary parenchyma

1. Idiopathic bullous emphysema
2. Bronchopulmonary dysplasia
3. Pulmonary interstitial emphysema
4. Pneumatocele

(c) airway

1. Aspiration of foreign body
2. Swyer-James syndrome
3. Congenital lobar overinflation
4. Bronchial atresia
5. Endobronchial mass (carcinoid)
6. Extrinsic bronchial compression
7. Accidental bronchial intubation

(d) pulmonary vasculature

1. (Unilateral) pulmonary agenesis
2. Pulmonary hypoplasia
3. Interruption of pulmonary artery
4. Scimitar syndrome
5. Unilateral pulmonary venous atresia
6. Unilateral congenital pulmonary lymphangiectasia
7. Unilateral massive central pulmonary embolism

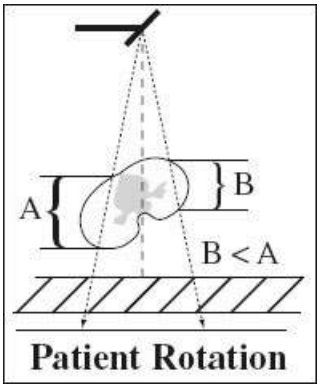
(e) pleural space

1. Anterior pneumothorax

2. Contralateral layering pleural effusion
3. Diaphragmatic hernia / rupture

(f) chest wall
1. Poland syndrome
2. Scoliosis

(g) technical
1. Patient rotation (1% of CXR)
√ hyperlucent lung on side which patient rotates toward tube / away from film ← asymmetric absorption of x-ray beam by chest wall



2. Lateral decentering = positioning of x-ray tube lateral to patient's midline

Hyperinflation in Newborn
√ level of inflation beyond 8th rib posteriorly
√ depressed configuration of hemidiaphragms best judged on LAT view
1. Fetal aspiration syndrome
2. Neonatal pneumonia
3. Pulmonary hemorrhage
4. Congenital heart disease
5. Transient tachypnea (mild)

Hyperinflation in Child
mnemonic: BUMP FAD
Bronchiectasis / **B**ronchiolitis (viral) / **B**ronchopulmonary dysplasia
Upper airway obstruction (vascular ring, laryngitis)
Mucoviscidosis (cystic fibrosis)
Pneumonia (esp. staph)
Foreign body inhalation / ingestion
Asthma (reactive airway disease)
Dehydration (diarrhea, acidosis)

Localized Lucent Lung Defect

Lung Cavity
= tissue necrosis with bronchial drainage

A. INFECTION
   (a) bacterial pneumonia
      1. Pyogenic infection = necrotizing pneumonia = abscess: Staphylococcus, Klebsiella, E. coli, Pseudomonas, anaerobes, β-hemolytic streptococcus, mixed gram-negative organisms
      2. Aspiration pneumonia = gravitational pneumonia: mixed gram-negative organisms, anaerobes
   (b) granulomatous infection
      1. TB: cavitation indicates active infectious disease with risk for hematogenous / bronchogenic dissemination
      2. Fungus: coccidioidomycosis, nocardiosis (in immunocompromised), histoplasmosis, blastomycosis, mucormycosis, sporotrichosis, aspergillosis, cryptococcosis
         √ very thin-walled cavities less likely to follow the apical distribution of TB / histoplasmosis
      3. Sarcoidosis (stage IV, upper lobe predominance)
      4. Angioinvasion → septic lung infarction followed by cavity formation: Aspergillus, Mucorales, Candida, torulosis, P. aeruginosa
   (c) parasitic infestation: hydatid disease
B. NEOPLASM
   (a) primary lung tumor: 16% of peripheral lung cancers (in particular squamous cell carcinoma (30%); also in bronchioloalveolar cell carcinoma
   (b) metastasis (usually multiple)
      1. Squamous cell carcinoma (in ⅔): nasopharynx, esophagus, cervix
      2. Adenocarcinoma: lung, breast, GI
      3. Osteosarcoma (rare)
      4. Melanoma
      5. Lymphoma (rare): with adenopathy; cavities often ← opportunistic infection with nocardiosis + cryptococcosis
C. VASCULAR OCCLUSION
   1. Infarct (thromboembolic, septic)
   2. Wegener granulomatosis
   3. Rheumatoid arthritis
D. INHALATION
   1. Silicosis with coal worker's pneumoconiosis
      › complicating tuberculosis
      › ischemic necrosis of center of conglomerate mass (rare)

MASS WITHIN CAVITY

1. Mycetoma = aspergilloma
2. Tissue fragment within carcinoma
3. Necrotic lung within abscess
4. Disintegrating hydatid cyst
5. Intracavitary blood clot

Lung Cyst

= round circumscribed space surrounded by an epithelial / fibrous wall of uniform / varied thickness containing air / liquid / semisolid / solid material

A. CONGENITAL CYST (rare)
   1. Bronchogenic cyst
   2. Intralobar sequestration: multicystic structure in lower lobes
   3. Congenital cystic adenomatoid malformation (CCAM) type I
   4. Congenital lobar emphysema
   5. Diaphragmatic hernia (congenital / traumatic)
   6. Bronchial atresia

B. ACQUIRED CYST
   (a) centrilobular / bullous emphysema
      1. **Bleb** = cystic air collection within visceral pleura; mostly apical with narrow neck
      2. **Bulla** = sharply demarcated dilated air space within lung parenchyma > 1 cm in diameter with epithelialized wall < 1 mm thick due to destruction of alveoli (= air cyst in localized / centrilobular / panlobular emphysema)
         • usually asymptomatic
         √ typically at lung apex
         √ slow progressive enlargement
         Cx:
            (1) Spontaneous pneumothorax
            (2) "Vanishing lung" = large area of localized emphysema causing atelectasis + dyspnea
         Rx: surgical resection if bulla > ⅓ of hemithorax
   (b) pneumatocele
      1. Postinfectious pneumatocele
      2. Traumatic pneumatocele: lung hematoma / hydrocarbon inhalation
   (c) cystic bronchiectasis
      1. Cystic fibrosis (more obvious in upper lobes)
      2. Agammaglobulinemia (predisposed to recurrent bacterial infections)
      3. Recurrent bacterial pneumonias
         √ multiple thin-walled lucencies with air-fluid levels in lower lobes
      4. Childhood infection: tuberculosis, pertussis
      5. Allergic bronchopulmonary aspergillosis (in asthmatic patients)
         √ involvement of proximal perihilar bronchi
      6. Kartagener syndrome (ciliary dysmotility)
   (d) infection
      1. Hydatid disease
   (e) interstitial emphysema
      1. Pseudocyst

LARGE CYSTIC NEONATAL LUNG LESION

1. Type 1 / type 4 cystic adenomatoid malformation
2. Bronchogenic cysts

3. Low-grade cystic pleuropulmonary blastoma
4. Congenital diaphragmatic hernia
5. Cavitary necrosis complicating pneumonia
6. Congenital lobar overinflation
7. Cystic lymphangioma

Small Cystic Neonatal Lung Lesion

1. Type 2 cystic adenomatoid malformation
2. Pneumonia
3. Pulmonary sequestration
4. Bronchial atresia

Multiple Lucent Lung Lesions

Multiple Lung Cavities

A. INFECTION
   1. Bacteria: cavitating pneumonia, lung abscess
   2. Granulomatous infection: TB, sarcoidosis
   3. Fungal infection: coccidioidomycosis
   4. Parasitic infection: echinococcosis
   5. Protozoan infection: pneumocystosis

B. NEOPLASM

C. VASCULAR
   1. Thromboembolic + septic infarcts
   2. Wegener granulomatosis
   3. Rheumatoid arthritis
   4. Angioinvasive organism (→ septic lung infarction followed by → cavity formation): Aspergillus, Mucorales, Candida, torulosis, P. aeruginosa

Multiple Thin-walled Cavities

mnemonic: BITCH

Bullae + pneumatoceles
Infection (TB, cocci, staph)
Tumor (squamous cell carcinoma)
Cysts (traumatic, bronchogenic)
Hydrocarbon ingestion

Multiple Lung Cysts

A. CONGENITAL
   1. Multiple bronchogenic cysts
   2. Intralobar sequestration:
      multicystic structure in lower lobes
   3. Congenital cystic adenomatoid malformation (CCAM) type I
   4. Diaphragmatic hernia (congenital / traumatic)

B. INFECTION
   1. Tuberculosis

2. Pneumocystis carinii pneumonia in AIDS

C. VASCULAR-EMBOLIC
   1. Cavitating septic emboli
      √ often seen at end of feeding vessel
   2. Angioinvasive infection: invasive pulmonary aspergillosis, candida, P. aeruginosa
   3. Pulmonary vasculitis: Wegener granulomatosis

D. DILATATION OF BRONCHI = cystic bronchiectasis
   √ bronchial wall thickening
   1. Cystic fibrosis (more obvious in upper lobes)
   2. Agammaglobulinemia (predisposed to recurrent bacterial infections)
   3. Recurrent bacterial pneumonias
   4. Tuberculosis
   5. Allergic bronchopulmonary aspergillosis (in asthmatic patients)

E. DISRUPTION OF ELASTIC FIBER NETWORK
   1. Centrilobular emphysema
      √ imperceptible walls
      √ chiefly in upper lung zones
   2. Panlobular emphysema
      √ lobular architecture preserved with bronchovascular bundle in central position, areas of lung destruction without arcuate contour
   3. Paraseptal emphysema
      √ cysts with walls arrayed in a single subpleural tier
   4. Lymphangioleiomyomatosis
      √ randomly scattered cysts surrounded by normal lung
      √ normal / increased lung volumes
   5. Tuberous sclerosis
      • skin abnormalities, mental retardation, epilepsy
   6. Air-block disease: adult respiratory distress syndrome, asthma, bronchiolitis, viral / bacterial pneumonia

F. REMODELING OF LUNG ARCHITECTURE
   = honeycombing of idiopathic pulmonary fibrosis (= fibrosing alveolitis)
   √ 3–10-mm small irregular thick-walled cystic air spaces usually of comparable diameter surrounded by abnormal + distorted lung parenchyma
   √ predominantly peripheral + basilar distribution
   √ bibasilar reticular opacities
   √ progressive reduction in lung volumes

G. MULTIFACTORIAL / UNKNOWN
   1. Langerhans cell histiocytosis
      √ cysts with walls of variable thickness + irregular shape
      √ in combination with nodules ± cavitation
      √ septal thickening
      √ predilection for upper lung zones with relative sparing of lung bases
   2. Lymphocytic interstitial pneumonia
      √ thickening of interlobular septa + bronchovascular bundles
      √ enlarged mediastinal nodes

3. Klippel-Trénaunay syndrome
4. Juvenile tracheolaryngeal papillomatosis
5. Neurofibromatosis
   √ cystic air spaces predominantly apical
6. Pneumatoceles

Cystlike Pulmonary Lesions

mnemonic: C.C., I BAN WHIPS

Coccidioidomycosis
Cystic adenomatoid malformation
Infection
Bronchogenic cyst, **B**ronchiectasis
Abscess
Neoplasm
Wegener granulomatosis
Hydatid cyst, **H**istiocytosis X
Infarction
Pneumatocele
Sequestration

PLEURA

Pneumothorax

= accumulation of air within pleural space

Pathophysiology: disruption of visceral pleura / trauma to parietal pleura

• pleuritic back / shoulder pain, dyspnea (in 80–90%)

Cause:

mnemonic: THE CHEST SET

Trauma
Honeycomb lung, **H**amman-Rich syndrome
Emphysema, **E**sophageal rupture
Chronic obstructive pulmonary disease
Hyaline membrane disease
Endometriosis
Spontaneous, **S**cleroderma
Tuberous sclerosis
Sarcoma (osteo-), **S**arcoidosis
Eosinophilic granuloma
Tuberculosis + fungus

Types:

1. Closed pneumothorax = intact thoracic cage
2. Open pneumothorax = "sucking" chest wound
3. **Tension pneumothorax** (clinical diagnosis)
   = accumulation of air within pleural space ← free ingress + limited egress of air
   Pathophysiology:

intrapleural pressure exceeds atmospheric pressure in lung during expiration (check-valve mechanism)

Frequency: in 3–5% of patients with spontaneous pneumothorax, higher in barotrauma

• compromised venous return

√ hyperexpanded ipsilateral chest

√ mediastinal shift to contralateral side

√ contralateral displacement of anterior junction line

√ "deep sulcus" sign = on frontal view larger lateral costodiaphragmatic recess than on opposite side

√ flattening / inversion of ipsilateral hemidiaphragm

√ total / subtotal collapse of ipsilateral lung

√ collapse of SVC / IVC / right heart border ← decreased systemic venous return + decreased cardiac output

√ sharp delineation of visceral pleural by dense pleural space

N.B.: Medical emergency!

4. **Tension hydropneumothorax**

√ air-fluid level in pleural space on erect CXR

Pneumothorax size:

Average Interpleural Distance (AID) = (A + B + C) ÷ 3 [in cm] converts to percentage of pneumothorax

(see nomogram in drawing)

CXR signs in upright position:

√ white margin of visceral pleura separated from parietal pleura

DDx: skin fold, air trapped between soft tissues of chest wall, hair braid, overlying tubing / dressing / line, prior chest tube track

√ absence of vascular markings beyond visceral pleural margin

CXR signs in supine position:

◊ "occult pneumothorax" = 10–30–50% of pneumothoraces go undetected on supine radiographs!

1. Anteromedial pneumothorax (earliest location)

√ outline of medial diaphragm under cardiac silhouette

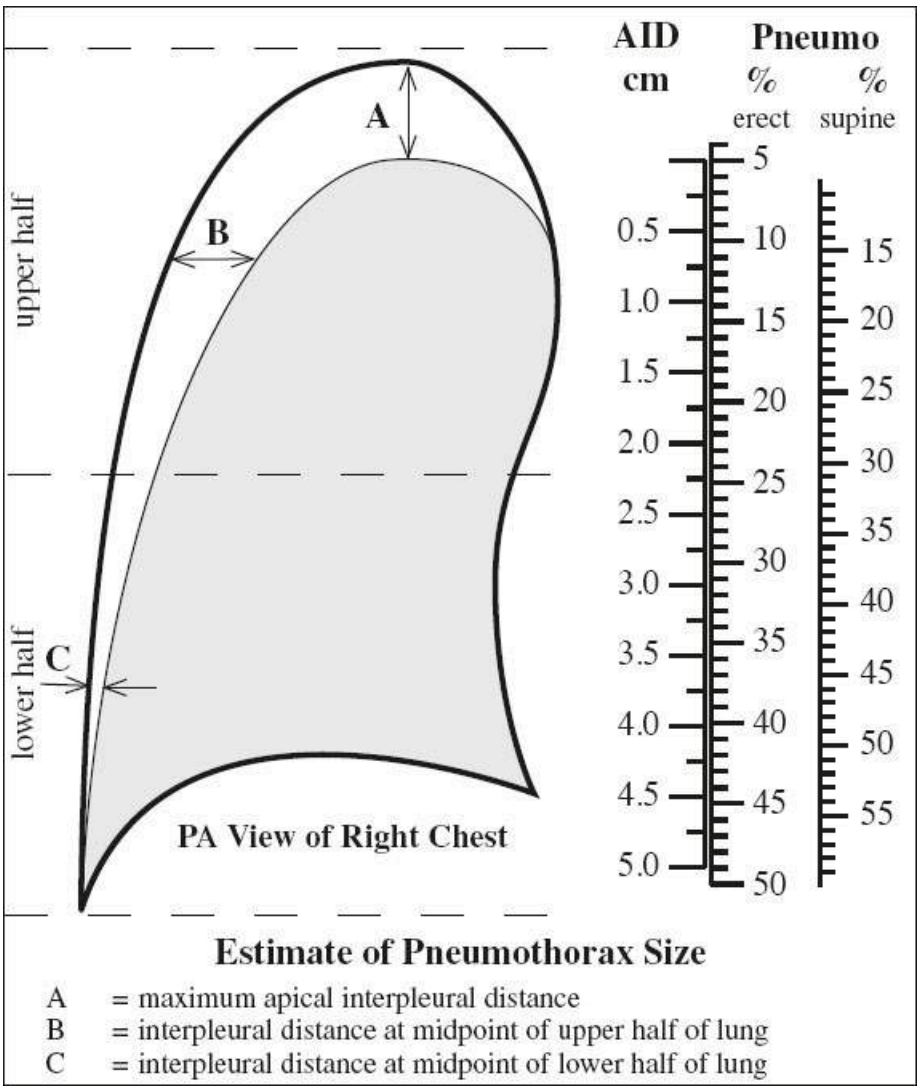
√ improved definition of mediastinal contours (SVC, azygos vein, left subclavian artery, anterior junction line, superior pulmonary vein, heart border, IVC, pericardial fat-pad)

√ relative lucency of entire lung:

√ "large hyperlucent hemithorax" sign (most common in neonates)

√ depression of ipsilateral diaphragm

√ band of air in minor fissure bounded by two visceral pleural lines



- √ outline of anterior junction line (in bilateral pneumothoraces)
- √ "figure 8" / "pseudomass" = compression of malleable lobes of thymus (in bilateral pneumothoraces)

2. Subpulmonic / anterolateral pneumothorax (2nd most common location)
   - √ "deep sulcus" sign = lucency of abnormally deep lateral costophrenic angle extending toward hypochondrium (DDx: COPD)
   - √ hyperlucent upper abdominal quadrant / hypochondrial region
   - √ increased lucency of lung base = sharply outlined diaphragm / inferior surface of lung in spite of parenchymal disease / collapsed lower lobe
   - √ "double-diaphragm" sign = air outlining anterior costophrenic sulcus + aerated lung outlining diaphragmatic dome
   - √ visible lateral edge of right middle lobe ← medial retraction
3. Apicolateral pneumothorax (least common location)
   - √ visualization of visceral pleural line
   - √ displacement of minor fissure from chest wall
4. Posteromedial pneumothorax (in presence of lower lobe collapse)

√ lucent triangle with vertex at hilum
√ V-shaped base delineating costovertebral sulcus

5. Pneumothorax → outlines pulmonary ligament

Prognosis: resorption of pneumothorax occurs at a rate of 1.25% per day (accelerated by increasing inspired oxygen concentrations)

Rx: A pneumothorax > 35% usually requires management with a chest tube!

Traumatic Pneumothorax

A. PENETRATING TRAUMA

B. BLUNT TRAUMA

Frequency: 15-40% of blunt chest trauma

Pathophysiology: ruptured alveoli (sudden increase in intrathoracic pressure), blunt crushing force, deceleration force

1. Rib fracture
2. Increased intrathoracic pressure against closed glottis: lung contusion / laceration
3. Bronchial fracture
   √ "fallen lung" sign = hilum of lung below expected level within chest cavity
   √ persistent pneumothorax with functioning chest tube
   √ mediastinal pneumothorax

C. IATROGENIC

tracheostomy, central venous catheter, PEEP ventilator (3–16%), thoracic irradiation

Rx: indication for chest tube placement dependent on symptoms + physiologic response

Spontaneous Pneumothorax

1. **Primary / idiopathic spontaneous pneumothorax** (80%)

Cause: rupture of subpleural blebs in lung apices

Age: 20–40 years; M÷F = 8÷1; esp. in patients with tall asthenic stature; mostly in smokers

• chest pain (69%), dyspnea

Prognosis: recurrence in 30% on same side, in 10% on contralateral side

Rx: simple aspiration (in > 50% success) / tube thoracostomy (in 90% effective)

2. Secondary spontaneous pneumothorax (20%):

(a) Air-trapping disease: spasmodic asthma, diffuse emphysema, Langerhans cell histiocytosis, lymph-angiomyomatosis, tuberous sclerosis, cystic fibrosis

◊ Chronic obstructive pulmonary disease is the most common predisposing disorder of secondary spontaneous pneumothorax.

(b) Pulmonary infection: lung abscess, necrotizing pneumonia, hydatid disease, pertussis, acute bacterial pneumonia, Staphylococcus aureus, Pneumocystis carinii pneumonia

(c) Granulomatous disease: tuberculosis, coccidioidomycosis, sarcoidosis, berylliosis

(d) Malignancy: primary lung cancer, lung metastases (esp. osteosarcoma, pancreas, adrenal, Wilms tumor)

(e) Connective tissue disorder: scleroderma, rheumatoid disease, Marfan syndrome, Ehlers-Danlos syndrome

(f) Pneumoconiosis: silicosis, berylliosis

(g) Vascular disease: pulmonary infarction
(h) Catamenial pneumothorax
(i) Neonatal disease: meconium aspiration, respirator therapy for hyaline membrane disease
(j) Cx of honeycomb lung: pulmonary fibrosis, cystic fibrosis, sarcoidosis, scleroderma, eosinophilic granuloma, interstitial pneumonitis, Langerhans cell histiocytosis, rheumatoid lung, idiopathic pulmonary hemosiderosis, pulmonary alveolar proteinosis, biliary cirrhosis

Pleural Effusion

A. TRANSUDATE (protein level = 1.5–2.5 g/dL)
Pathophysiology: systemic abnormality → outpouring of low-protein fluid
(a) ⇑ hydrostatic pressure
1. **Congestive heart failure** (in 65%):
bilateral (88%); right-sided (8%); left-sided (4%); least amount on left side ← stimulated lymphatic resorption ← cardiac movement
2. **Constrictive pericarditis** (in 60%)
(b) ⇓ colloid-oncotic pressure
› decreased protein production
1. **Cirrhosis with ascites** (in 6%): on right side (in 67%)
› protein loss / hypervolemia
1. **Nephrotic syndrome** (21%), overhydration, glomerulonephritis (55%), peritoneal dialysis
2. Hypothyroidism
(c) **Chylous effusion**

◊ Most frequent cause of isolated pleural effusion in newborn → 15–25% mortality rate!

• chylomicrons + lymphocytes in fluid

B. EXUDATE
Pathophysiology: increased permeability of abnormal pleural capillaries with release of high-protein fluid into pleural space
Criteria:
• pleural fluid total protein ÷ serum total protein ratio of > 0.5
• pleural fluid LDH ÷ serum LDH ratio of > 0.6

◊ Most frequent cause of isolated pleural effusion in newborn with 15–25% mortality!

• pleural fluid LDH > ⅔ of upper limit of normal for serum LDH (upper limit for LDH ~ 200 IU)
• pleural fluid specific gravity > 1.016
• protein level > 3 g/dL
√ effusion with septation / low-level echoes
√ "split pleura" sign on CECT = thickened enhancing visceral + parietal pleura separated by fluid
√ extrapleural fat thickening of > 2 mm + increased attenuation (edema / inflammation)
Cause:
(A) INFECTION

1. **Empyema necessitatis** = chronic empyema attempting to decompress through chest wall (in TB, nocardiosis, actinomycosis, aspergillosis, blastomycosis)
2. Parapneumonic effusion (in 40%)
   = any effusion associated with pneumonia / lung abscess / bronchiectasis WITHOUT criteria for an empyema
3. Tuberculosis (in 1%): high protein content (75 g/dL), lymphocytes > 70%, positive culture (only in 20–25%)
4. Fungi: Actinomyces, Nocardia
5. Parasites: amebiasis (→ liver abscess in 15–20%), Echinococcus
6. Mycoplasma, rickettsia (in 20%)

(B) MALIGNANT DISEASE (in 60%)

• positive cytologic results

Pathogenesis:

› pleural metastases → ⇑ pleural permeability
› lymphatic obstruction ← pleural vessels, mediastinal nodes, thoracic duct disruption
› bronchial obstruction → loss of volume + resorptive surface
› hypoproteinemia ← tumor cachexia

Cause: lung cancer (26–49%), breast cancer (8–24%), lymphoma (10–28% with chylothorax in ⅔), ovarian cancer (10%), malignant mesothelioma containing hyaluronic acid (5%)

Rx: sclerosing agents: doxycycline, bleomycin, talc

(C) VASCULAR

Pulmonary emboli (in 15–30% of all embolic events):

• often serosanguinous

(D) ABDOMINAL DISEASE

1. Pancreatitis / pancreatic pseudocyst / pancreaticopleural fistula (in ⅔):
   √ usually left-sided pleural effusion
   • high amylase levels
2. Boerhaave syndrome:
   left-sided esophageal perforation
3. Subphrenic abscess
   √ pleural effusion (79%)
   √ elevation + restriction of diaphragmatic motion (95%)
   √ basilar platelike atelectasis / pneumonitis (79%)
4. Abdominal tumor with ascites
5. **Meigs-Salmon syndrome**
   = primary pelvic neoplasms (ovarian fibroma, thecoma, granulosa cell tumor, Brenner tumor, cystadenoma, adenocarcinoma, fibromyoma of uterus) cause pleural effusion in 2–3%; ascites + hydrothorax resolve with tumor removal
6. Endometriosis
7. Bile fistula

(E) COLLAGEN-VASCULAR DISEASE

1. Rheumatoid arthritis (in 3%):
   unilateral; R > L (in 75%), recurrent alternating sides; pleural effusion relatively

unchanged in size for months; predominantly in men; LOW GLUCOSE content of 20–50 mg/dL (in 70–80%) without increase following IV infusion of glucose (DDx: TB, metastatic disease, parapneumonic effusion)

2. SLE (in 15–74%)
   most common collagenosis to give pleural effusion, bilateral in 50%; L > R
   √ ⇑ size of cardiovascular silhouette (in 35–50%)
3. Wegener granulomatosis (in 50%)
4. Sjögren syndrome
5. Mixed connective tissue disease
6. Periarteritis nodosa
7. Postmyocardial infarct syndrome

(F) TRAUMATIC

- hemorrhagic, chylous

Cause: esophageal rupture, thoracic / abdominal surgery, intrapleural infusion = "**infusothorax**" (0.5%), radiation pneumonitis

(G) MISCELLANEOUS

1. Sarcoidosis
2. Uremic pleuritis (in 20% of uremic patients)
3. Drug-induced effusion

CXR:

√ first 300 mL not visualized on PA view (collect in subpulmonic region first, then spill into posterior costophrenic sinus)
√ lateral decubitus views may detect as little as 25 mL
√ hemidiaphragm + costophrenic sinuses obscured
√ extension upward around posterior > lateral > anterior thoracic wall (mediastinal portion fixed by pulmonary ligament + hilum)
√ meniscus-shaped semicircular upper surface with lowest point in midaxillary line
√ associated collapse of ipsilateral lung

Massive pleural effusion:

√ enlargement of ipsilateral hemithorax
√ displacement of mediastinum to contralateral side
√ severe depression / flattening / inversion of ipsilateral hemidiaphragm
√ visible air bronchogram

Subpulmonic / subdiaphragmatic / infrapulmonary pleural effusion:

√ peak of dome of pseudodiaphragm laterally positioned
√ acutely angulated costophrenic angle
√ increased distance between stomach bubble and lung
√ blunted posterior costophrenic sulcus
√ thin triangular paramediastinal opacity (mediastinal extension of pleural effusion)
√ flattened pseudodiaphragmatic contour anterior to major fissure (on lateral CXR)

CT:

√ fluid outside diaphragm
√ fluid elevating crus of diaphragm
√ indistinct fluid-liver interface
√ fluid posteromedial to liver (= bare area of liver)

CAVE: "central oval" sign of ascites may be seen in subpulmonic effusion with inverted diaphragm

Unilateral Pleural Effusion

◊ The majority of massive unilateral pleural effusions are malignant (lymphoma, metastatic, primary lung cancer)!

1. Neoplasm
2. Infection: TB
3. Collagen vascular disease
4. Subdiaphragmatic disease
5. Pulmonary emboli
6. Trauma: fractured rib
7. Chylothorax

LEFT-SIDED PLEURAL EFFUSION

1. Spontaneous rupture of esophagus
2. Dissecting aneurysm of aorta
3. Traumatic rupture of aorta <u>distal</u> to left subclavian a.
4. Transection of distal thoracic duct
5. Pancreatitis: left-sided (68%), right-sided (10%), bilateral (22%)
6. Pancreatic + gastric neoplasm

RIGHT-SIDED PLEURAL EFFUSION

1. Congestive heart failure
2. Transection of <u>proximal</u> thoracic duct
3. Pancreatitis

Pleural Effusion & Large Cardiac Silhouette

1. Congestive heart failure (most common)
   - √ cardiomegaly
   - √ prominence of upper lobe vessels + constriction of lower lobe vessels
   - √ prominent hilar vessels
   - √ interstitial edema (fine reticular pattern, Kerley lines, perihilar haze, peribronchial thickening)
   - √ alveolar edema (perihilar confluent ill-defined densities, air bronchogram)
   - √ "**phantom tumor**" = fluid localized to interlobar pleural fissure (in 78% in right horizontal fissure)
2. Pulmonary embolus + right heart enlargement
3. Myocarditis / pericarditis with pleuritis
   (a) viral infection
   (b) tuberculosis
   (c) rheumatic fever (poststreptococcal infection)
4. Tumor: metastatic, mesothelioma
5. Collagen-vascular disease
   (a) SLE (pleural + pericardial effusion)
   (b) rheumatoid arthritis

Pleural Effusion & Hilar Enlargement

1. Pulmonary embolus
2. Tumor: bronchogenic carcinoma, lymphoma, metastasis
3. Tuberculosis
4. Fungal infection (rare)
5. Sarcoidosis (very rare)

Pleural Effusion & Subsegmental Atelectasis

1. Postoperative (thoracotomy, splenectomy, renal surgery) ← thoracic splinting + mucous plugging of small airway
2. Pulmonary embolus
3. Abdominal mass
4. Ascites
5. Rib fractures

Pleural Effusion & Lobar Densities

1. Pneumonia with empyema
2. Pulmonary embolism
3. Neoplasm: bronchogenic carcinoma > lymphoma
4. Tuberculosis

Hemothorax

= blood in pleural space

• massive hemothorax = blood exceeding 1 L + clinical signs of shock and hypoperfusion

√ rapidly enlarging pleural effusion of 35–70 HU attenuation

√ heterogeneous attenuation

√ hyperattenuating areas of debris

√ fluid-hematocrit level

A. TRAUMA
   (a) thoracic injury
      1. Closed / penetrating injury to lung, chest wall, heart, great vessels
      2. Surgery
      3. Interventional procedures: thoracentesis, pleural biopsy, catheter placement
   (b) abdominal injury with diaphragmatic rupture: trauma to liver / spleen

B. BLEEDING DIATHESIS
   1. Anticoagulant therapy
   2. Thrombocytopenia
   3. Factor deficiency

C. VASCULAR
   1. Pulmonary infarct
   2. Arteriovenous malformation
   3. Aortic dissection
   4. Leaking atherosclerotic aneurysm

D. MALIGNANCY
   1. Mesothelioma

2. Lung cancer
3. Metastasis
4. Leukemia

E. OTHER
1. Catamenial hemorrhage
2. Extramedullary hematopoiesis

Solitary Pleural Mass

CXR:
√ "incomplete border" sign (= mass density with partly invisible border)
√ obtuse angle with chest wall

CT:
√ displacement of pulmonary vessels
√ centered in pleural space
√ NO involvement of chest wall
√ ± outward displacement of extrapleural fat

DDx: (1) Chest wall mass (rib destruction reliable sign of chest wall mass)
(2) Peripheral lung mass (centered within lung tissue, acute angle with chest wall, engulfs pulmonary vessels)

Malignant Pleural Tumor

1. Metastasis (most common)
   Origin: lung, breast, GI tract
   √ tumor nodule + pleural effusion
2. Drop metastasis from thymoma / thymic carcinoma
   √ anterior mediastinal mass
3. Mesothelioma

Benign Pleural Tumor

1. Loculated pleural effusion ("vanishing tumor")
2. Organized empyema
3. Local benign mesothelioma
4. Subpleural lipoma: may erode adjacent rib
5. Mesothelial cyst
6. Neural tumor: schwannoma, neurofibroma
7. Solitary fibrous tumor of pleura (rare)
8. **Fibrin bodies**
   = 3–4 cm large tumorlike concentrations of fibrin forming in serofibrinous pleural effusions; usually near lung base
9. Hematoma

Focal Tumorlike Condition of Pleura

1. Pleural plaque
2. Thoracic splenosis
3. Catamenial pneumothorax
4. Pleural pseudotumor

= pleural fluid (frequently transudate) collected within lung fissure (most frequently minor fissure)

5. Extrapleural hematoma
   = injury to internal mammary / intercostal vessels without disruption of parietal pleura
   ◊ May expand rapidly causing respiratory / circulatory collapse
   √ "extrapleural fat" sign = inward displacement of extrapleural fat

Diffuse Tumorlike Condition of Pleura

1. Diffuse pleural thickening
   = inflammatory pleuritis fusing leaves of pleura
   Cause: empyema, hemothorax, connective tissue disorder, asbestos exposure
   • ± restrictive lung physiology
   √ ill-defined irregular thickening spanning multiple ribs
   √ costophrenic angle blunting
   √ often undergoing calcification
2. Erdheim-Chester disease
3. Diffuse pulmonary lymphangiomatosis

Multiple Pleural Densities

√ diffuse pleural thickening with lobulated borders

1. Loculated pleural effusion: infectious, hemorrhagic, neoplastic
2. Pleural plaques
3. Metastasis (most common cause)
   Origin: lung (40%), breast (20%), lymphoma (10%), ovary, melanoma, uterus, GI tract, pancreas, sarcoma
   ◊ Metastatic adenocarcinoma histologically similar to malignant mesothelioma!
4. Diffuse malignant mesothelioma:
   almost always unilateral, associated with asbestos exposure
5. Invasive thymoma (rare)
   √ contiguous spread, invasion of pleura, spreads around lung
   √ NO pleural effusion
6. Thoracic splenosis

mnemonic: **M**ary **T**yler **M**oore **L**ikes **L**emon
Metastases (especially adenocarcinoma)
Thymoma (malignant)
Malignant mesothelioma
Loculated pleural effusion
Lymphoma

Pleural Thickening

A. TRAUMA
   1. **Fibrothorax** (most common cause)
      = organizing effusion / hemothorax / pyothorax
      √ dense fibrous layer of ~ 2 cm thickness; almost always on visceral pleura
      √ frequent calcifications on inner aspect of pleural peel

B. INFECTION
   1. Chronic empyema: at bases; history of pneumonia; parenchymal scars
   2. Tuberculosis / histoplasmosis: lung apex; associated with apical cavity
   3. Aspergilloma: in preexisting cavity concomitant with pleural thickening
C. COLLAGEN-VASCULAR DISEASE
   1. Rheumatoid arthritis: pleural effusion fails to resolve
D. INHALATIONAL DISORDER
   1. Asbestos exposure: lower lateral chest wall; basilar interstitial disease (< 25%); thickening of parietal pleura + typically sparing of visceral pleura
   2. Silicosis (advanced disease)
   3. Talcosis
E. NEOPLASM
   1. Metastases: often nodular appearance; may be obscured by effusion
   2. Diffuse malignant mesothelioma
   3. Pancoast tumor
F. OTHER
   1. **Pleural hyaloserositis**
      Path: hyaline sclerotic tissue = cartilagelike whitish sugar icing appearance (Zuckerguss) with occasional calcification
   2. Mimicked by extrathoracic musculature, 1st + 2nd rib companion shadow, subpleural fat, focal scarring around old rib fractures

mnemonic: TRINI
Trauma (healed hemothorax)
Rheumatoid arthritis (collagen vascular disease)
Inhalation disease (asbestosis, talcosis)
Neoplasm
Infection

Circumferential Pleural Thickening
1. Mesothelioma
2. Adenocarcinoma
3. Lymphoma
4. Thymoma
5. Asbestos-related benign pleural disease
6. Infection

Apical Cap
1. Inflammatory process: TB, healed empyema
2. Postradiation fibrosis
3. Neoplasm
4. Vascular abnormality
5. Mediastinal hemorrhage
6. Mediastinal lipomatosis
7. Peripheral upper lobe collapse

Pleural Calcification

A. INFECTION
   1. Healed empyema
   2. Tuberculosis (and therapy for TB: pneumothorax / oleothorax), histoplasmosis
B. TRAUMA
   1. Healed hemothorax = fibrothorax:
      • history of significant chest trauma
      √ irregular plaques of calcium usually in visceral pleura
      √ healed rib fracture
   2. Radiation therapy
C. PNEUMOCONIOSIS
   1. Asbestos-related pleural disease (most common):
      √ combination of basilar reticular interstitial disease (< ⅓) + pleural thickening
      √ calcifications of parietal pleura frequently diagnostic (diaphragmatic surface of pleura, bilateral but asymmetric), visceral pleura typically spared
   2. Talcosis: similar to asbestos-related disease
   3. Bakelite
   4. Muscovite mica
D. HYPERCALCEMIA
   1. Pancreatitis
   2. Secondary hyperparathyroidism of chronic renal failure / scleroderma
E. MISCELLANEOUS
   1. Mineral oil aspiration
   2. Pulmonary infarction

√ FDG-avid pleural lesions at PET/CT with corresponding high attenuation at CT suggests pleurodesis, because < 10% of pleural malignancies develop calcifications!

mnemonic: TAFT
Tuberculosis
Asbestosis
Fluid (effusion, empyema, hematoma)
Talc

Chest Wall Tumor

A. BONE TUMOR
   (a) malignant osseous chest wall tumor
      ◊ Primary bone tumors of the chest wall represent only 5–8% of all skeletal masses!

◊ Sternal tumors are usually malignant!

      1. Metastasis
      2. Chondrosarcoma (33% of primary rib tumors)
      3. Myeloma
      4. Ewing sarcoma
   (b) benign osseous chest wall tumor
      1. Fibrous dysplasia
      2. Enchondroma

3. Osteochondroma (8% of all rib tumors)
4. Chondroblastoma
5. ABC
6. GCT
7. Langerhans cell histiocytosis

B. SOFT-TISSUE TUMOR

(a) adipocytic tumor
1. Lipoma
2. Liposarcoma

(b) vascular tumor
1. Hemangioma
2. Lymphangioma
3. Angiosarcoma

(c) fibroblastic-myofibroblastic tumor
1. Elastofibroma
2. Fibromatosis

(d) fibrohistiocytic tumor
1. Undifferentiated pleomorphic sarcoma

(e) peripheral nerve sheath tumor (PNST)
1. Schwannoma
2. Neurofibroma
3. Malignant PNST

(f) cutaneous lesion
1. Epidermal inclusion cyst
2. Pilomatricoma
3. Dermatofibrosarcoma protuberans (DFSP)

MEDIASTINUM

Conventional Radiographic Mediastinal Signs

used in the interpretation of single frontal CXR

1. "**Silhouette**" sign
   = obscured margin (ie, silhouette) of the normal air-soft tissue interface of a mediastinal structure (heart, aortic arch, hilum, azygoesophageal recess) / diaphragm
   Cause: any intrathoracic opacity of the same density as the adjacent normal structure (eg, pneumonia, atelectasis, mass, fluid)
2. "**Hilum overlay**" sign
   = normal hilar structures project through a mass → mass is not in contact with hilum but posterior / anterior to hilum
3. "**Hilum convergence**" sign
   = convergence of pulmonary arteries into the lateral border of a hilar density → enlarged pulmonary artery
   DDx: nodule / mass → vessels course through opacity
4. "**Cervicothoracic**" sign
   = uppermost border of anterior mediastinum ends at level of clavicles while middle

(higher) + posterior (highest) mediastinum project above clavicles

Use: localizing a mediastinal mass

√ posterior superior mediastinal masses are sharply outlined by apical lung

√ anterior superior mediastinal masses extending into neck have unsharp borders

Acute Mediastinal Widening

1. Rupture of aorta / brachiocephalic arteries
2. Venous hemorrhage: traumatic / iatrogenic (malpositioning of central venous line)
3. Congestive heart failure (venous dilatation)
4. Rupture of esophagus
5. Rupture of thoracic duct
6. Atelectasis abutting the mediastinum
7. Magnification + geometric distortion on supine radiograph (attempt at suspended full inspiration, no rotation, 10–15° caudal angulation of central beam)

Mediastinal Hematoma

- dyspnea, dysphagia, dysphonia, chest pain
- neck + chest wall ecchymosis, tachycardia

√ mediastinal widening

√ abnormal aortic contour

√ > 5 mm widening of right paratracheal stripe

√ deviation of nasogastric tube to right of T4 spinous process

CT:

√ soft-tissue mass > 60 HU

√ focal heterogeneous mass / ill-defined soft-tissue thickening with extension to cervical region

√ compression of trachea, main bronchi, great vessels

Mediastinal Shift

= displacement of heart, trachea, aorta, hilar vessels

◊ Expiration film, lateral decubitus film (expanded lung down), fluoroscopy helps to determine side of abnormality

A. DECREASED LUNG VOLUME

1. Atelectasis
2. Postoperative (lobectomy, pneumothorax)
3. Hypoplastic lung / lobe
   - √ small pulmonary artery + small hilum
   - √ decreased peripheral pulmonary vasculature
   - √ irregular reticular vascular pattern (bronchial origin) without converging on the hilum
4. Bronchiolitis obliterans = Swyer-James syndrome

B. INCREASED LUNG VOLUME

= **air trapping** = retention of excess gas in all / part of the lung, especially during expiration, as a result of

(a) complete / partial airway obstruction, or

(b) local abnormalities in pulmonary compliance

@ Major bronchus

1. Foreign body obstructing main-stem bronchus (common in children) with ball-valve mechanism + collateral air drift
   √ contralateral mediastinal shift → increasing with expiration

@ Emphysema

1. Bullous emphysema (localized form)
   √ large avascular areas with thin lines
2. Congenital lobar emphysema: only in infants
3. Interstitial emphysema
   Cause: Cx of positive pressure ventilation therapy
   √ pattern of diffuse coarse lines

@ Cysts / masses

1. Bronchogenic cyst: with bronchial connection + check-valve mechanism
2. Cystic adenomatoid malformation
3. Large mass (pulmonary, mediastinal)

C. PLEURAL SPACE ABNORMALITY

1. Large unilateral pleural effusion:
   √ opaque hemithorax ← empyema, congestive heart failure, metastases
2. Tension pneumothorax:
   NOT always complete collapse of lung
3. Large diaphragmatic hernia:
   usually detected in neonatal period
4. Large pleural mass

D. Partial absence of pericardium / pectus excavatum
   √ shift of heart WITHOUT shift of trachea / aorta / mediastinal border

Pneumomediastinum

= free air around mediastinal structures

Frequency: in 1% of patients with pneumothorax

Source of air:

A. INTRATHORACIC

1. Trachea, major bronchi: blunt chest trauma
2. Esophagus
3. Lung
   (a) narrowed / plugged airways (most common) = air trapping in small airways as in asthma
   (b) straining against closed glottis: vomiting, parturition, weight-lifting
   (c) blunt / penetrating chest trauma
   (d) alveolar rupture
4. Pleural space

B. EXTRATHORACIC

1. Head and neck: sinus fracture, dental extraction
2. Intra- and retroperitoneum: perforated hollow viscus

Pathophysiology:

after alveolar rupture → air tracks along bronchovascular sheath → ruptures through fascial sheath at lung root into mediastinum + facial planes of the neck → produces subcutaneous emphysema

• chest pain, breathlessness, subcutaneous emphysema

◊ NOT a life-threatening condition!

√ subcutaneous emphysema

√ streaky lucencies of air in mediastinum (look at thoracic inlet on PA + retrosternal space on LAT film)

√ "ring around artery" sign = air surrounding intramediastinal segment of right pulmonary artery (LAT view)

√ "tubular artery" sign = air adjacent to major aortic branches, eg, left subclavian + left common carotid aa.

√ "continuous diaphragm" sign = air trapped posterior to pericardium produces lucency connecting both domes of hemidiaphragms (frontal view)

√ "double bronchial wall" sign = clear depiction of bronchial wall by air next to and within a bronchus

√ "V" sign of Naclerio / "extrapleural" sign = mediastinal air extends laterally between mediastinal pleura / lower thoracic aorta + diaphragm

√ "spinnaker sail" / "thymic sail" / "angel wing" sign in children = air outlining the thymus

√ air in azygoesophageal recess

√ air in pulmonary ligament = triangular gas collection in low mid chest

DDx:

(a) other air collections:
medial / subpulmonary pneumothorax (simulating "extrapleural" sign); pneumoperitoneum (simulating "extrapleural" sign); pneumopericardium

(b) mistaken normal anatomic structures:
superior aspect of major fissure (on lordotic view); anterior junction line; Mach band effect

Spontaneous Pneumomediastinum

Age: neonates (0.05-1.00%), 2nd–3rd decade

Cause:

1. Rupture of marginally situated alveoli: sudden / prolonged rise in intraalveolar pressure → subsequent dissection of air centrally along bronchovascular bundles to hila (interstitial emphysema) → rupture into mediastinum:
   Valsalva maneuver, status asthmaticus, aspiration pneumonia, hyaline membrane disease, measles, giant cell pneumonia, coughing, vomiting, strenuous exercise, parturition, diabetic acidosis, crack cocaine inhalation = free-basing (mixing solid cocaine salt with a solvent to render it "smokeable")
2. Tumor erosion of trachea / esophagus
3. Pneumoperitoneum / retropneumoperitoneum
   = extension from peritoneal / retroperitoneal / deep fascial planes of the neck

Traumatic Pneumomediastinum *(rare)*

Cause:

1. Pulmonary interstitial emphysema
   = disruption of marginal alveoli with gas traveling toward mediastinum ← positive pressure ventilation
2. Bronchial / tracheal rupture
   √ commonly associated with pneumothorax
3. Esophageal rupture: diabetic acidosis, alcoholic, Boerhaave syndrome
4. Iatrogenic - accidental:
   neck / chest / abdominal surgery, subclavian vein catheterization, mediastinoscopy, bronchoscopy, gastroscopy, rectosigmoidocolonoscopy, electrosurgery with intestinal gas explosion, positive pressure ventilation, intubation, barium enema

Tension Pneumomediastinum

◊ MEDICAL EMERGENCY!

Pathophysiology:

increased intramediastinal pressure → compression of heart → decreased venous return + compression of tracheobronchial tree → sudden profound cardiovascular + respiratory collapse

- sudden development of severe hypoxia, hypotension, tachycardia, metabolic acidosis, high ventilation pressure

CXR:

√ thin line outlining the borders of the heart (in 50%)

CT (modality of choice):

√ substantial amount of mediastinal free air
√ flattening of anterior cardiac contour
√ uplifting of heart off the diaphragm
√ compression of right atrium
√ compression of mediastinal vessels
√ distension of IVC
√ flattening of main bronchi

Rx: percutaneous needle aspiration / CT-guided catheter placement

Tension Pneumopericardium

◊ MEDICAL EMERGENCY!

- chest pain, dyspnea, cyanosis, hypotension, tachycardia
- "mill wheel" murmur, metallic sounds of high frequency, muffled heart sounds
- ECG: elevated ST segment, low-voltage waveform

Cause:

(a) traumatic: blunt / penetrating trauma; iatrogenic (eg, occurring during or after cardiac surgery); barotrauma from positive pressure ventilation

a) nontraumatic: pericarditis with gas-forming organism; direct extension of inflammation from adjacent structures; fistulous communication with air-containing structures (eg, stomach, esophagus, airway, lung); extension of pneumomediastinum into pericardial cavity

√ intrapericardial pressure > 265 mm H_2O

CXR:

√ "halo" sign = continuous rim of air outlining left and right heart borders
√ "small heart" sign on frontal view = sudden marked decrease in size of cardiac silhouette

CT:
√ substantial amount of air in pericardial cavity
√ compression + displacement of heart:
√ collapse of heart chambers
√ flattening of anterior heart border
√ distention of inferior vena cava

Cx: cardiac tamponade → hemodynamic compromise

Rx: immediate pericardial decompression ← needle pericardiocentesis / placement of pericardial drain

Mediastinal Fat

A. MEDIASTINAL LIPOMATOSIS
B. FAT HERNIATION
= omental fat herniating into chest
1. Foramen of Morgagni
= sternocostal triangle mass, R >> L side
2. Foramen of Bochdalek
= lumbocostal triangle mass, almost always on left
3. Paraesophageal hernia
= perigastric fat through phrenicoesophageal membrane

CT:
√ fat with fine linear densities (= omental vessels)

C. LIPOMA
= un- / encapsulated fatty tissue with variable amount of fibrous septa
√ smooth + sharply defined boundaries
DDx: liposarcoma, lipoblastoma (infancy), fat-containing teratoma, thymolipoma (inhomogeneous, higher CT numbers, poor demarcation, ± invasion of surrounding structures)
D. MULTIPLE SYMMETRIC LIPOMATOSIS

Low-attenuation Mediastinal Mass

A. FLUID
1. Foregut cyst
2. Lymphocele
3. Seroma
4. Hematoma
5. Abscess
6. Hydatid disease

B. LYMPH NODE
1. Tuberculous lymph nodes
2. Metastasis from thyroid / testicular tumor
3. Lymphoma: treated / untreated

C. PRIMARY NEOPLASM
   1. Neurogenic tumor
   2. Fat-containing neoplasm

Mediastinal Cyst

= 21% of all primary mediastinal tumors

@ Anterior mediastinum
   1. Thymic cyst
   2. Dermoid cyst
   3. Parathyroid cyst (uncommon as mediastinal mass)

@ Middle mediastinum
   1. Pericardial cyst
   2. Bronchogenic cyst

@ Posterior mediastinum
   1. Esophageal duplication cyst
   2. Neurenteric cyst
   3. Thoracic duct cyst
   4. Transdiaphragmatic jejunal duplication
   5. Cystic hygroma
   6. Lateral thoracic meningocele
   7. Posttraumatic lymphocele
      = contained pleural / mediastinal lymph collection
      • history of prolonged chylous chest tube drainage
      Time of onset: several months after injury
   8. **Hydatid cyst**
      Location: paravertebral gutter
      √ erosion of ribs + vertebrae

Frequency of Developmental Mediastinal Cyst

1. Enterogenous cyst = Foregut cyst 45%
   (a) bronchogenic cyst (30%)
   (b) esophageal duplication cyst (15%)
   (c) neurenteric cyst (least common)
2. Pericardial cyst 30%
3. Thymic cyst 10%
4. Nonspecific mesothelial cyst 10%
5. Cystic hygroma 5%

Mediastinal Mass

(excluding hyperplastic thymus gland, granuloma, lymphoma, metastasis)

1. Neurogenic tumor (28%): malignant in 16%
2. Teratoid lesion (19%): malignant in 15%
3. Enterogenous cyst (16%)
4. Thymoma (13%): malignant in 46%
5. Pericardial cyst (7%)

A. BENIGN MEDIASTINAL MASS
◊ 66–75% of all mediastinal tumors are benign (in all age groups)
◊ 88% discovered incidentally on routine chest x-ray
B. MALIGNANT MEDIASTINAL MASS
◊ 57–80% of malignant tumors are symptomatic (pain, cough, shortness of breath)

Thoracic Inlet Lesion

1. Thyroid mass
   1–3% of all thyroidectomies have a mediastinal component; ⅓ of goiters are intrathoracic
   Location: anterior (80%) / posterior (20%) mediastinum
   √ displacement of trachea posteriorly and laterally ← anterior goiter
   √ displacement of trachea anteriorly and laterally + esophagus posteriorly ← posterior goiter
   √ inhomogeneous density ← cystic spaces + high-density iodine contents of > 100 HU
   √ focal calcifications (common)
   √ marked + prolonged contrast enhancement
   √ connection to thyroid gland
   √ vascular displacement + compression
   NUC (rarely helpful as thyroid tissue may be nonfunctioning):
   √ ± uptake on ^{123}I / ^{131}I scan (pertechnetate is sufficient with modern gamma cameras, SPECT imaging may be helpful)
2. Cystic hygroma
   3–10% involve mediastinum; childhood
3. Lymphoma
4. Other tumors: adenoma, carcinoma, ectopic thymoma

MASS IN RAIDER TRIANGLE

Raider triangle (= retrotracheal triangle) on LAT CXR formed by posterior wall of trachea (anteriorly) + thoracic spine (posteriorly) + aortic arch (inferiorly) + thoracic inlet superiorly)
[Louis Raider (1913–1999), professor of radiology in Mobile, AL at the University of South Alabama Medical Center]

1. Aberrant right subclavian artery
2. Aberrant left subclavian a. with right aortic arch
3. Aneurysm
4. Posterior descending goiter
5. Enlarged lymph node
6. Esophageal mass / duplication cyst

Anterior Mediastinal Mass

◊ Lymphoma is the most common anterior mediastinal mass in children + the 2nd most common in adults!

√ posterior junction line preserved
√ anterior junction line obliterated

√ "hilum overlay" sign present
√ no interface with lung above level of clavicle

mnemonic: 4 T's

Thymoma
Teratoma
Thyroid tumor / goiter
Terrible lymphoma

A. SOLID THYMIC LESIONS
   1. Thymoma (benign, malignant): most common
   2. Normal thymus (neonate)
   3. Thymic hyperplasia (child)
   4. Thymic carcinoma
   5. Thymic carcinoid
   6. Thymolipoma
   7. Lymphoma

B. SOLID TERATOID LESIONS = germ cell tumors
   1. Teratoma
   2. Embryonal cell carcinoma
   3. Choriocarcinoma
   4. Seminoma

C. THYROID / PARATHYROID
   1. Substernal thyroid / intrathoracic goiter
      (10% of all mediastinal masses)
   2. Thyroid adenoma / carcinoma
   3. **Ectopic parathyroid adenoma**:
      ectopia in 1–3% (62–81% in anterior mediastinum / thymus, 30% within thyroid tissue, 8% in posterior superior mediastinum)

D. LYMPH NODES
   1. Lymphoma (Hodgkin, NHL): may arise in thymus, more common in young adults
   2. Metastasis
   3. Benign lymph node hyperplasia
   4. Angioblastic lymphadenopathy
   5. Mediastinal lymphadenitis: sarcoidosis / granulomatous infection

E. CARDIOVASCULAR
   1. Tortuous brachiocephalic artery
   2. Aneurysm of ascending aorta
   3. Aneurysm of sinus of Valsalva
   4. Dilated SVC
   5. Cardiac tumor
   6. Epicardial fat-pad
      √ low-density mass obliterating cardiac silhouette

F. CYSTS
   1. Cystic hygroma
   2. Bronchogenic cyst
   3. Extralobar sequestration

4. Thymic cysts / dermoid cysts
5. Pericardial cyst: true cyst; pericardial diverticulum
6. Pancreatic pseudocyst

G. OTHERS
1. Neural tumor: vagus, phrenic nerve
2. Paraganglioma
3. Hemangioma / lymphangioma
4. Mesenchymal tumor: fibroma, lipoma
5. Sternal tumors
   (a) metastasis from breast, bronchus, kidney, thyroid
   (b) malignant primary: chondrosarcoma, myeloma, lymphoma
   (c) benign primary: chondroma, aneurysmal bone cyst, giant cell tumor
6. Primary lung / pleural tumor (invading mediastinum)
7. Mediastinal lipomatosis:
   (a) Cushing disease
   (b) Corticosteroid therapy
8. Morgagni hernia / localized eventration
   √ presence of bowel gas
9. Abscess

FAT-CONTAINING MEDIASTINAL MASS

1. Mature cystic teratoma
2. Mediastinal lipoma
3. Mediastinal lipomatosis
4. Thymolipoma
5. Liposarcoma

PREVASCULAR MEDIASTINAL MASS

1. Lymphadenopathy
2. Retrosternal goiter
3. Thymic lesion
4. Germ cell tumor

PRECARDIAC MASS IN CONTACT WITH DIAPHRAGM

1. Epicardial fat pad
2. Diaphragmatic hump
3. Morgagni hernia
4. Pleuropericardial cyst
5. Lymph node enlargement

Middle Mediastinal Mass

mnemonic: HABIT5

Hernia, **H**ematoma
Aneurysm
Bronchogenic cyst / duplication cyst

Inflammation: sarcoidosis, histoplasmosis, coccidioidomycosis, primary TB in children
Tumors – remember the 5 L's:
Lung, especially oat cell carcinoma
Lymphoma
Leukemia
Leiomyoma
Lymph node hyperplasia

A. LYMPH NODES

◊ 90% of middle mediastinal masses are malignant

(a) neoplastic adenopathy
1. Lymphoma: Hodgkin÷NHL = 2÷1
2. Leukemia (in 25%): lymphocytic > granulocytic
3. Metastasis: bronchus, lung, upper GI, prostate, kidney
4. Angioimmunoblastic lymphadenopathy

(b) inflammatory adenopathy
1. Tuberculosis / histoplasmosis → may lead to fibrosing mediastinitis
2. Blastomycosis (rare) / coccidioidomycosis
3. Sarcoidosis (predominant involvement of paratracheal nodes)
4. Viral pneumonia
(particularly measles + cat-scratch fever)
5. Infectious mononucleosis / pertussis pneumonia
6. Amyloidosis
7. Plague / tularemia
8. Drug reaction
9. Giant lymph node hyperplasia = Castleman dz.
10. Connective tissue disease: rheumatoid, SLE
11. Bacterial lung abscess

(c) inhalational disease adenopathy
1. Silicosis (eggshell calcification also in sarcoidosis + tuberculosis)
2. Coal worker's pneumoconiosis
3. Berylliosis

B. FOREGUT CYST
1. Bronchogenic / respiratory cyst (cartilage, respiratory epithelium)
2. Enteric cyst = esophageal duplication cyst
3. Extralobar sequestration (anomalous feeding vessel)
4. Hiatal hernia
5. Esophageal diverticula: Zenker, traction, epiphrenic

C. PRIMARY TUMORS (infrequent)
1. Carcinoma of trachea
2. Bronchogenic carcinoma
3. Esophageal tumor:
leiomyoma, carcinoma, leiomyosarcoma
4. Mesothelioma
5. Granular cell myoblastoma of trachea (rare)

D. VASCULAR LESIONS
   1. Aneurysm of transverse aorta
   2. Distended veins: SVC, azygos vein
   3. Hematoma

E. VASCULAR VARIANTS
   1. Right aortic arch (in 0.5% of general population)
      √ absence of aortic knuckle
   2. Left SVC (in 0.3% of general population)
   3. Azygos continuation of IVC

Subcarinal Space Lesion

1. Enlarged lymph nodes
2. Bronchogenic cyst
3. Pericardial effusion
4. Enlarged left atrium
5. Esophageal mass
6. Aortic aneurysm

Aorticopulmonary Window Mass

1. Adenopathy
2. Aneurysm: traumatic aortic pseudoaneurysm, pulmonary artery aneurysm, ductus Botalli aneurysm, bronchial artery aneurysm
4. Bronchogenic cyst
5. Tumor of tracheobronchial tree
6. Esophageal tumor
7. Neurogenic tumor
8. Mediastinal abscess

Widening of Paratracheal Space

Normal width: < 5 mm

1. Dilated tortuous vessels: brachiocephalic artery, SVC, azygos vein
2. Enlarged lymph node
3. Bronchogenic carcinoma
4. Mediastinal lipomatosis
5. Mediastinal hematoma
6. Bronchogenic cyst

Retrocardiac Space of Holzknecht Lesion

[Guido Holzknecht (1872–1931), pioneer in radiology and director of the X-ray laboratory at Vienna General Hospital in 1905, adjuvantly irradiated Sigmund Freud for an oral cavity squamous cell carcinoma unsuccessfully]

1. Hiatal hernia
2. Esophageal lesion
3. Left ventricular aneurysm
4. Pericardial cyst
5. Bronchogenic cyst

6. Aortic aneurysm
7. Vagal / phrenic nerve neurofibroma

Posterior Mediastinal Mass

A. NEOPLASM

› NEUROGENIC TUMOR (largest group): 30% malignant

(a) tumor of peripheral nerve origin

• more common in adulthood

√ 80% appear as a round mass with sulcus

√ lower attenuation than muscle (in 73%)

1. Schwannoma = neurilemmoma (32%)
2. Neurofibroma (10%): contains Schwann cells + nerve cells, 3rd + 4th decade
3. Malignant schwannoma

(b) tumor of sympathetic ganglia origin

• more common in childhood

√ 80% are elongated with tapered borders

1. Ganglioneuroma (23–38%): second most common tumor of posterior mediastinum after neurofibroma
2. Neuroblastoma (15%): highly malignant undifferentiated small round cell tumor originating in sympathetic ganglia, < 10 years of age
3. Ganglioneuroblastoma (14%): both features, spontaneous maturation possible

(c) tumor of paraganglia origin (rare)

1. Chemodectoma = paraganglioma (4%)
2. Pheochromocytoma

√ rib spreading, erosion, destruction

√ enlargement of neural foramina (dumbbell lesion)

√ scalloping of posterior aspect of vertebral body

√ scoliosis

CT:

√ low-density soft-tissue mass (lipid contents)

› SPINE TUMOR: metastasis (eg, bronchogenic carcinoma, multiple myeloma), ABC, chordoma, chondrosarcoma, Ewing sarcoma

› LYMPHOMA

› INVASIVE THYMOMA

› MESENCHYMAL TUMOR: fibroma, lipoma, leiomyoma

› HEMANGIOMA

› LYMPHANGIOMA

› THYROID TUMOR

B. INFLAMMATION / INFECTION

1. Infectious spondylitis: pyogenic, tuberculous, fungal

√ destruction of endplates + disk space

√ paravertebral soft-tissue mass

2. Mediastinitis

5. Pancreatic pseudocyst
3. Lymphoid hyperplasia
4. Sarcoidosis (in 2%, typically asymptomatic patient)

C. VASCULAR MASS
1. Aneurysm of descending aorta (curvilinear calcification; elderly)
2. Enlarged azygos + accessory hemiazygos vein
3. Esophageal varices
4. Congenital vascular anomalies:
aberrant subclavian artery, double aortic arch, pulmonary sling, interruption of IVC with azygos / hemiazygos continuation

D. TRAUMA
1. Aortic aneurysm / pseudoaneurysm
2. Hematoma
3. Loculated hemothorax
4. Traumatic pseudomeningocele

E. FOREGUT CYST
√ cysts may demonstrate peripheral rimlike calcifications
1. Bronchogenic cyst
2. Enteric cyst
3. Neurenteric cyst
4. Extralobar sequestration

F. FATTY MASS
1. Bochdalek hernia
2. Mediastinal lipomatosis
3. Fat-containing tumors: lipoma, liposarcoma, teratoma (rare)

G. OTHER
1. Loculated pleural effusion
2. Pancreatic pseudocyst
3. Lateral meningocele: neurofibromatosis; enlarged neural foramen
4. Extramedullary hematopoiesis:
in chronic bone marrow deficiency; paraspinal area rich in RES-elements
√ splenomegaly; widening of ribs
5. "Pseudomass" of the newborn

mnemonic: BELLMAN
Bochdalek hernia
Extramedullary hematopoiesis
Lymphadenopathy
Lymphangioma
Meningocele (lateral)
Aneurysm
Neurogenic tumor

Deviation / Disruption of Azygoesophageal Line

1. Left atrial enlargement
2. Subcarinal adenopathy

3. Esophageal disease
4. Bronchogenic cyst
5. Hiatal hernia

Cardiophrenic-angle Mass

A. LESION OF PERICARDIUM
   1. Pericardial cyst
   2. Intrapericardiac bronchogenic cyst
   3. Benign intrapericardiac neoplasm:
      teratoma, leiomyoma, hemangioma, lipoma
   4. Malignant neoplasm:
      mesothelioma, metastasis (lung, breast, lymphoma, melanoma)

B. CARDIAC LESION
   1. Aneurysm
   2. Congenital absence of pericardium = pericardial defect
      √ apparent elevation of cardiac apex
      √ prominent pulmonary artery segment
      √ lucency between aorta + main pulmonary artery caused by interposed lung

C. OTHERS
   1. Mass of lung, pleura, diaphragm, abdomen
   2. Cardiophrenic angle varices

RIGHT CARDIOPHRENIC-ANGLE MASS

A. HEART
   1. Aneurysm: cardiac ventricle, sinus of Valsalva
   2. Dilated right atrium

B. PERI- / EPICARDIUM
   1. **Epicardial fat-pad** in obesity / lipoma (most common cause)
      √ triangular opacity in cardiophrenic angle less dense than heart
      √ increase in size under corticosteroid treatment
   2. Pericardial cyst

C. DIAPHRAGM
   1. Diaphragmatic hernia of Morgagni
   2. Diaphragmatic lymph node (esp. in Hodgkin disease + breast cancer)

D. ANTERIOR MEDIASTINAL MASS: thymolipoma
E. PRIMARY LUNG MASS
F. PARACARDIAC VARICES
G. ENLARGED LYMPH NODE: lymphoma, metastasis (lung, breast, colon, ovary, melanoma)

FATTY CARDIOPHRENIC-ANGLE MASS

1. Diaphragmatic hernia (congenital > traumatic)
2. Pericardial fat necrosis
   • acute pleuritic chest pain
   √ encapsulated fatty lesion with inflammatory changes similar to epiploic appendagitis

√ local thickening of adjacent pericardium

Prognosis: benign self-limiting course with spontaneous resolution / improvement

3. Thymolipoma
4. Teratoma
5. Lipoma / liposarcoma (no diaphragmatic defect)

CYSTIC CARDIOPHRENIC-ANGLE MASS

1. Pericardial cyst
2. Thymic tumor with predominantly cystic content
3. Hydatid cyst

SOLID CARDIOPHRENIC-ANGLE MASS

1. Lymphadenopathy: lymphoma > metastasis (lung cancer, mesothelioma, several abdominal cancers)
2. Malignant / benign thymic tumor (connection with superior mediastinum maintained)

Hypervascular Mediastinal Mass

1. Paraganglioma
2. Metastasis: typically renal cell carcinoma
3. Castleman disease
4. Hemangioma
5. Sarcoma
6. Tuberculosis
7. Sarcoidosis

Popcorn-type Calcification

1. Hamartoma (lung)
2. Histoplasmosis (mediastinum)
3. Sarcoidosis (mediastinum)

Hilar Mass

A. LARGE PULMONARY ARTERIES

√ enlargement of main pulmonary artery
√ abrupt change in vessel caliber
√ enlarged pulmonary artery compared with bronchus (in same bronchovascular bundle)
√ cephalization
√ enlargement of right ventricle (RAO 45°, LAO 60°)

Cause:

1. Chronic obstructive disease: emphysema
2. Chronic restrictive interstitial lung disease: idiopathic fibrosis, cystic fibrosis, rheumatoid arthritis, sarcoidosis
3. Pulmonary embolic disease (acute massive / chronic)
4. Idiopathic pulmonary hypertension
5. Left-sided heart failure + mitral stenosis
6. Congenital heart disease with left-to-right shunt
   (a) acyanotic: ASD, VSD, PDA

(b) cyanotic (admixture lesions): transposition of great vessels, truncus arteriosus

Differential Diagnosis for Lymphadenopathy of Chest	
Disease	*Description*
Sarcoidosis / other granulomatous disease	√ symmetric hilar + mediastinal involvement
Primary lung cancer	√ usually asymmetric involvement √ following course of lymphatic drainage
Lymphoma	√ bulky anterior and middle mediastinal mass
Infection	√ hypoattenuating (TB, mycobacterium avium complex) √ calcific (TB, fungal infection)

B. DUPLICATION CYST

C. UNILATERAL HILAR ADENOPATHY

(a) neoplastic

1. Bronchogenic carcinoma (most common)
2. Metastases (lack of mediastinal involvement exceptional)
3. Lymphoma

(b) inflammatory

1. Tuberculosis (primary) in 80%
2. Fungal infection: histoplasmosis, coccidioidomycosis, blastomycosis
3. Viral infection: atypical measles
4. Infectious mononucleosis
5. Drug reaction
6. Sarcoidosis (in 1–3%)
7. Bilateral lung abscess

mnemonic: Fat Hila Suck

Fungus
Hodgkin disease
Squamous / oat cell carcinoma

D. BILATERAL HILAR ADENOPATHY

◊ Most common cause in the absence of specific symptoms / signs is sarcoidosis (in 75%)

(a) neoplastic

1. Lymphoma (in 50% Hodgkin disease)
2. Metastasis
3. Leukemia
4. Primary bronchogenic carcinoma
5. Plasmacytoma

(b) inflammatory

1. Sarcoidosis (in 70–90%)
2. Silicosis
3. Langerhans cell histiocytosis
4. Idiopathic pulmonary hemosiderosis

5. Chronic berylliosis

(c) infectious

1. Rubella, ECHO virus, varicella, mononucleosis

mnemonic: **P**lease **H**elen **L**ick **M**y **P**opsicle **S**tick

Primary TB
Histoplasmosis
Lymphoma
Metastases
Pneumoconiosis
Sarcoidosis

Bilateral Hilar Lymphnode Enlargement

in the absence of specific symptoms / signs

1. Sarcoidosis (75%)
2. Fungal / mycobacterial infection
3. Malignancy: lymphoma

Eggshell Calcification of Nodes

A. PNEUMOCONIOSIS
   1. Silicosis (5%)
   2. Coal worker's pneumoconiosis (1.3–6%) not seen in: asbestosis, berylliosis, talcosis, baritosis

B. SARCOIDOSIS (5%)

C. FUNGAL + BACTERIAL INFECTION (rare)
   1. Tuberculosis
   2. Histoplasmosis
   3. Coccidioidomycosis

D. FIBROSING MEDIASTINITIS

E. LYMPHOMA FOLLOWING RADIATION THERAPY

Enlargement of Azygos Vein

Normal azygos vein (on upright CXR): ≤ 7 mm

√ round / oval opacity at right tracheobronchial angle marks terminal portion of azygos vein

A. COLLATERAL CIRCULATION
   1. Portal hypertension
   2. SVC obstruction / compression below azygos vein
   3. IVC obstruction / compression
   4. Interrupted IVC with azygos continuation
   5. Partial anomalous venous return (rare)
   6. Pregnancy
   7. Hepatic vein occlusion

B. RIGHT ATRIAL HYPERTENSION
   1. Right-sided heart failure
   2. Tricuspid insufficiency
   3. Constrictive pericarditis

4. Large pericardial effusion

Enlargement of Bronchial Artery

= > 2 mm in diameter

N.B.: visualization of dilated bronchial arteries should initiate a search for thoracic problems

CT / MR (best with multiplanar / 3-D volumetric images):

√ undulating nodular / linear enhancing structures

√ tortuous mediastinal course

A. CONGENITAL PULMONARY ARTERY OBSTRUCTION / ANOMALIES
   1. Tetralogy of Fallot
   2. Proximal interruption of pulmonary artery
   3. Anomalous origin of LCA from pulmonary artery

B. ACQUIRED PULMONARY ARTERY OBSTRUCTION
   (a) intrinsic
      1. Chronic thromboembolic disease
      2. Takayasu arteritis
   (b) extrinsic
      1. Fibrosing mediastinitis

C. CHRONIC / ACUTE INFLAMMATION
   1. Bronchiectasis
   2. Infection: TB, nontuberculous mycobacterial infection, cystic fibrosis, chronic fungal infection
   3. Malignancy

D. PULMONARY HYPERTENSION

THYMUS

Thymic Mass

1. Thymoma
2. Thymolipoma
3. Thymic cyst
4. Thymic carcinoid

Neoplasia in Thymus

1. Epithelial thymic tumor: thymoma, thymic carcinoma
2. Thymic lymphoma: Hodgkin disease, NHL
3. Langerhans cell histiocytosis
4. Thymolipoma
5. Carcinoid tumor
6. Germ cell tumor
7. Sarcoma
8. Metastasis

Diffuse Thymic Enlargement

A. BENIGN

1. Thymic hyperplasia
2. Intrathymic hemorrhage
3. Hemangioma
4. Lymphangioma

B. MALIGNANT THYMIC INFILTRATION

• presence of adenopathy elsewhere
√ no pleural implants

1. Leukemia
2. Hodgkin disease / non-Hodgkin lymphoma
3. Langerhans cell histiocytosis

TRACHEA & BRONCHI

Malignant Central Airway Obstruction

1. Primary lung cancer
2. Lymphoma
3. Metastatic mediastinal adenopathy
4. Bronchial carcinoid
5. Endobronchial metastasis
6. Primary tracheal tumor: chondroma, adenoid cystic ca.

Tracheal Narrowing

A. ANTERIOR COMPRESSION

(a) congenital

1. Congenital goiter
2. Innominate artery syndrome

• ablation of right radial pulse by rigid endoscopic pressure
√ posterior tracheal displacement
√ focal collapse of trachea at fluoroscopy
√ pulsatile indentation of anterior tracheal wall by innominate artery on MR
Rx: surgical attachment of innominate artery to manubrium

(b) inflammatory

1. Cervical / mediastinal abscess

(c) neoplastic

1. Cervical / intrathoracic teratoma

√ amorphous calcifications + ossifications

2. Thymoma
3. Thyroid tumors
4. Lymphoma

(d) traumatic: hematoma

B. POSTERIOR TRACHEAL COMPRESSION

(a) congenital

1. Vascular ring

› complete: double aortic arch, right aortic arch
› incomplete: anomalous right subclavian a.

√ posterior indentation of esophagus + trachea

2. Pulmonary sling
   = anomalous left pulmonary artery arising from right pulmonary artery, passing between trachea + esophagus en route to left lung
3. Bronchogenic cyst most commonly between esophagus + trachea at level of carina
   (a) inflammatory: abscess
   (b) neoplastic: neurofibroma
   (c) traumatic: esophageal foreign body, esophageal stricture, hematoma

C. INTRINSIC TRACHEAL CAUSES

(a) congenital:

1. Congenital tracheal stenosis (generalized / segmental)
   = complete cartilaginous ring (instead of horseshoe shape)
2. Congenital tracheomalacia = immaturity of tracheal cartilage = chondromalacia
   • expiratory stridor
   √ tracheal collapse on expiration

(b) neoplastic: papilloma, fibroma, hemangioma

(c) traumatic: acquired stenosis (endotracheal + tracheostomy tubes), granuloma, acquired tracheomalacia (cartilage degeneration after inflammation, extrinsic pressure, bronchial neoplasia, tracheoesophageal fistula, foreign body)

Tracheal Wall Thickening

1. Wegener granulomatosis
   √ involvement of posterior membrane
2. Relapsing polychondritis
   √ thickening of cartilaginous trachea + tracheal wall
3. Tracheobronchopathia osteochondroplastica
   √ calcified / ossified nodules in cartilaginous trachea
4. Amyloidosis
   √ nodular concentric calcified / ossified wall thickening
   √ no posterior sparing

Tracheal Tumor

• asthma symptomatology, hoarseness, cough, hemoptysis
• wheeze: <u>inspiratory</u> with extrathoracic lesion, <u>expiratory</u> with intrathoracic lesion

A. PRIMARY MALIGNANT

(a) from surface epithelium

1. Squamous-cell carcinoma (commonest primary)
   ◊ 50% of all malignant tracheal lesions
2. Adenocarcinoma
3. Neuroendocrine tumor = carcinoid

(b) from salivary gland

1. Cylindroma = adenoid cystic ca.
2. Mucoepidermoid carcinoma

(c) from mesenchyme

1. Sarcoma

2. Lymphoma
3. Plasmacytoma

B. SECONDARY MALIGNANT
(a) direct invasion: thyroid, lung, larynx, esophagus
(b) hematogenous: malignant melanoma, breast cancer, renal cell carcinoma, colon cancer

C. BENIGN TUMOR
(a) from surface epithelium
1. Squamous-cell papilloma
2. Pleomorphic adenoma
3. Oncocytoma
4. Mucous gland adenoma

(b) from mesenchyme
1. Cartilaginous tumor (hamartoma)
2. Leiomyoma
3. Fibroma / lipoma
4. Hemangioma
5. Granular cell myoblastoma
6. Neurogenic tumor

D. INFLAMMATION
1. Granulomatous disease:
TB, sarcoidosis, Wegener granulomatosis
2. Inflammatory myoblastic pseudotumor
3. Amyloid tumor
4. Pseudotumor: inspissated mucus, foreign body

Tracheobronchial Tumor

Frequency: < 0.4% of all body tumors

A. PRIMARY MALIGNANT (90%)
(a) surface epithelium
1. Squamous cell carcinoma (most common)
2. Adenocarcinoma
3. Neuroendocrine tumor: carcinoid, large / small cell carcinoma

(b) salivary gland
1. Adenoid cystic carcinoma (2nd most common)
2. Mucoepidermoid carcinoma

(c) mesenchyme
1. Sarcoma
2. Lymphoma

B. SECONDARY MALIGNANT (uncommon)
(a) directly invading: thyroid cancer, laryngeal cancer, lung cancer, esophageal cancer
(b) hematogenous: melanoma, breast cancer, renal cell carcinoma, colon cancer

C. BENIGN (< 10%)
(a) surface epithelium: papilloma, papillomatosis, pleomorphic adenoma. oncocytoma
(b) mesenchyme: hamartoma, leiomyoma, lipoma, fibroma, neurogenic tumor

Endobronchial Tumor

1. Neuroendocrine tumor (typical / atypical carcinoid)
2. Mucoepidermoid carcinoma
3. Adenoid cystic carcinoma
4. Hamartoma
5. Leiomyoma
6. Myoblastoma
7. Mucous gland adenoma
8. Squamous cell carcinoma

Bronchial Obstruction

1. Foreign body: most commonly in young children
2. Granulomatous disease: granuloma formation in bronchial wall / extrinsic compression by lymphadenopathy
3. Broncholith
4. Stenosis / atresia
5. Neoplasm
   (a) Bronchogenic carcinoma
   (b) Adenoid cystic carcinoma
   (c) Mucoepidermoid tumor
   (d) Hamartoma

mnemonic: MEATFACE

Mucus plug
Endobronchial granulomatous disease
Adenoma
Tuberculosis
Foreign body
Amyloid, **A**tresia (bronchial)
Cancer (primary)
Endobronchial metastasis

Bronchial Wall Thickening

◊ Apparent thickness of bronchial wall varies with lung window chosen on CT: a mean window that is too low can make the bronchial wall appear abnormal!

Differential Diagnosis of Airway Thickening		
Disease	*CT appearance*	*Differentiating Features*
Wegener granulomatosis	√ circumferential tracheal wall thickening (mostly subglottic)	• history of sinus / renal disease √ subglottic tracheal narrowing √ involvement of posterior wall √ pulmonary cavitary nodules / pulmonary hemorrhage √ NO wall calcifications
Relapsing polychondritis	√ thickening of cartilaginous trachea + tracheal wall	• cartilaginous abnormalities of ears + nose √ sparing of posterior tracheal wall √ tracheal narrowing √ occasional wall calcifications
Trachebronchopathia osteochondroplastica	√ calcified / ossified nodules in cartilaginous trachea	√ nodular calcified / ossified tracheal wall with wall thickening √ sparing of posterior tracheal membrane + superior trachea
Amyloidosis	√ calcified / ossified nodular concentric tracheal wall thickening	√ possible involvement of larynx + upper trachea √ nodular concentric calcified / ossified tracheal wall with wall thickening √ NO sparing of posterior membrane of trachea

Windowing: level at -250 to -700 HU, width at > 1000 HU

A. PERIBRONCHOVASCULAR
   1. Sarcoidosis
   2. Lymphangitic carcinomatosis
   3. Kaposi sarcoma
   4. Lymphoma
   5. Pulmonary edema

B. BRONCHIAL WALL
   1. Airway disease
   2. Relapsing polychondritis
   3. Wegener granulomatosis
   4. Amyloidosis

C. MUCOSAL INFECTION
   1. Croup
   2. Tuberculosis
   3. Fungal disease
   4. Aspergillosis

Circumferential Tracheobronchial Wall Thickening

1. Wegener granulomatosis
2. Sarcoidosis
3. Inflammatory bowel disease
4. Post-intubation stenosis
5. Amyloidosis
6. Infection: Klebsiella rhinoscleromatis, fungal infection, TB

Signet-ring Sign

= cross section of usually thick-walled dilated ringlike bronchus + normal branch of pulmonary artery as adjacent round soft-tissue opacity

1. Bronchiectasis
2. Multifocal bronchioloalveolar carcinoma
3. Metastatic adenocarcinoma

Broncholithiasis

Broncholith = erosion of calcified peribronchial lymph node extruded into bronchial lumen → bronchial obstruction

1. Histoplasmosis
2. Tuberculosis
3. Cryptococcosis
4. Actinomycosis
5. Coccidioidomycosis

√ calcified lymph node within / adjacent to affected bronchus
√ bronchial obstruction → atelectasis, mucoid impaction, bronchiectasis, air trapping, airspace disease (obstructive pneumonia)
√ absence of associated soft-tissue mass

Distribution of Bronchiectasis

A. Bronchiectasis with upper / midlung predominance

= less effective lymphatic clearance in upper zones (← gravitational gradient of blood flow and lower respiratory excursions) may account for upper lobe predominance of certain inhalational- and perilymphatic-predominant diseases.

1. Cystic fibrosis
2. Sarcoidosis
3. Silicosis and other pneumoconioses
4. Allergic bronchopulmonary aspergillosis
5. Tuberculosis

B. Bronchiectasis with anterior predominance
1. Atypical mycobacterial infection
2. Acute respiratory distress syndrome

C. Bronchiectasis with lower lung predominance
1. Chronic aspiration
2. Pulmonary fibrosis: UIP, NIP
3. Primary ciliary dyskinesia = immotile cilia syndrome
4. Immunodeficiency
5. α1-antitrypsin deficiency

D. Bronchiectasis with central predominance
1. Tracheobronchomegaly
2. Williams-Campbell syndrome

E. Focal bronchiectasis
1. Endo- / peribronchial tumor
2. Swyer-James syndrome

F. Diffuse bronchiectasis
1. Bronchiolitis obliterans

DIAPHRAGM

Bilateral Diaphragmatic Elevation

A. Shallow inspiration (most frequent)
B. Abdominal causes:
obesity, pregnancy, ascites, large abdominal mass
C. Pulmonary causes
(1) Bilateral atelectasis
(2) Restrictive pulmonary disease: SLE
D. Neuromuscular disease
(1) Myasthenia gravis
(2) Amyotrophic lateral sclerosis

Unilateral Diaphragmatic Elevation

1. Subpulmonic pleural effusion
√ dome of pseudodiaphragm migrates toward the costophrenic angle and flattens
2. Altered pulmonary volume
(a) Atelectasis
√ associated pulmonary density
(b) Postoperative lobectomy / pneumonectomy
√ rib defects, metallic sutures
(c) Hypoplastic lung
√ small hemithorax (more often on the right), crowding of ribs, mediastinal shift, absent / small pulmonary artery, frequently associated with dextrocardia + anomalous pulmonary venous return
3. Phrenic nerve paralysis
(a) primary lung tumor
(b) malignant mediastinal tumor
(c) iatrogenic
(d) idiopathic
√ diagnosed fluoroscopically by paradoxic diaphragmatic motion (with patient asked to sniff in lateral projection)
4. Abdominal disease
(a) subphrenic abscess (history of surgery, accompanied by pleural effusion)
(b) distended stomach / colon
(c) interposition of colon
(d) liver mass: tumor, echinococcal cyst, abscess
5. Diaphragmatic hernia
6. Eventration of diaphragm
7. Traumatic rupture of diaphragm associated with rib fractures, pulmonary contusion, hemothorax
8. Diaphragmatic tumor: mesothelioma, fibroma, lipoma, lymphoma, metastases

Diaphragmatic Paralysis

A. PHRENIC NERVE INJURY
1. Birth trauma
2. Cardiac surgery
3. Resection of thoracic tumor

B. INFECTION
   1. West Nile virus
   2. Lyme disease
C. TUMOR
   1. Mediastinal tumor
   2. Neck tumor

Diaphragmatic Tumor in Children

A. MALIGNANT (80%)
   1. Rhabdomyosarcoma
   2. Undifferentiated sarcoma
   3. Germ cell tumor
   4. Ewing sarcoma
B. BENIGN (20%)
   1. Lymphangioma
   2. Hemangioma
   3. Lipoma
   4. Myofibroma
   5. Neurofibroma

Cystic Lesion of Diaphragm

1. Mesothelial cyst
   Location: between liver + posterolateral thoracic wall
2. Bronchogenic cyst
3. Cystic teratoma
4. Pleuropulmonary blastoma
5. Hydatid cyst

RETROCRURAL NEOPLASM

A. NEUROGENIC TUMOR
   › ganglion cell tumor
      1. Neuroblastoma (most common)
      2. Ganglioneuroblastoma
      3. Ganglioneuroma
   › nerve / nerve sheath tumor
      1. Neurofibroma
      2. Neurilemmoma
   › tumor of paraganglia
      1. Paraganglioma
B. MESENCHYMAL TUMOR
   › benign
      1. Lipoma, leiomyoma, lymphangioma
      3. Hemangiopericytoma, hemangioma
   › malignant
      1. Liposarcoma, leiomyosarcoma

2. Rhabdomyosarcoma, fibrosarcoma
3. Malignant fibrous histiocytoma

C. GERM CELL TUMOR
1. Teratoma
2. Seminomatous + nonseminomatous tumors

D. LYMPHOID TUMOR
√ enlarged = lymph node > 6 mm in diameter
1. Lymphoma
2. Extramedullary hematopoiesis

CHEST WALL

Chest Wall Lesions

√ "incomplete border" sign ← obtuse angle
√ smooth tapering borders (tangential views)
√ tumor pedicle suggests a benign tumor

A. EXTERNAL
1. Cutaneous lesion: moles, neurofibroma
2. Nipples
3. Artifact

B. NEOPLASTIC

C. TRAUMATIC
1. Hematoma
2. Rib fracture

D. INFECTIOUS
cellulitis, pyomyositis, abscess, necrotizing fasciitis
1. Actinomycosis (parenchymal infiltrate, pleural effusion, chest wall mass, rib destruction, cutaneous fistulas)
2. Aspergillosis, nocardiosis, blastomycosis, tuberculosis (rare)
3. Pyogenic: Staphylococcus, Klebsiella

E. CHEST WALL INVASION
1. Peripheral lung cancer (eg, Pancoast tumor)
2. Recurrent breast cancer
3. Lymphomatous nodes

Pancoast Syndrome

[Henry Khunrath Pancoast (1875–1939), the first professor of radiology in the USA at the Hospital of the University of Pennsylvania in Philadelphia in 1912]
= superior sulcus tumor invading brachial plexus + sympathetic stellate ganglion
CLINICAL TRIAD:
1. Ipsilateral arm pain
2. Muscle wasting of hand
3. Horner syndrome = enophthalmos, ptosis, miosis, anhidrosis

Cause: lung cancer (most common), breast cancer, multiple myeloma, metastases, lymphoma, mesothelioma

Lung Disease with Chest Wall Extension

A. INFECTIOUS
   1. Actinomycosis
   2. Nocardia
   3. Blastomycosis
   4. Tuberculosis

B. MALIGNANT TUMOR
   1. Bronchogenic carcinoma
   2. Lymphoma
   3. Metastasis
   4. Mesothelioma
   5. Breast carcinoma
   6. Internal mammary node

C. BENIGN TUMOR
   1. Capillary hemangioma of infancy
   2. Cavernous hemangioma
   3. Extrapleural lipoma
   4. Abscess
   5. Hematoma

Chest Wall Tumor

Location of primary tumors: ribs (95%) > sternum

A. OSSEOUS TUMOR
   (a) secondary tumor
      1. Metastasis: most common type of skeletal tumor, particularly in older patients
         √ absence of mineralization
   (b) primary malignant tumor
      Frequency: 5–8% of all skeletal masses
      1. Chondrosarcoma (33% of primary rib tumors)
         √ arc-and-ring / flocculent / stippled chondroid mineralization
      2. Myeloma
         √ absence of mineralization
      3. Osteosarcoma
         √ dense / cloudy / ivorylike osteoid mineralization greatest at center + least at periphery
      4. Parosteal osteosarcoma
      5. Ewing sarcoma
   (c) primary benign
      1. Fibrous dysplasia (in 30%)
         √ amorphous mineralization
      2. Enchondroma
         √ benign osteolytic lesion + chondroid calcification
      3. Osteochondroma
         √ continuity of medullary cavity between lesion and affected bone
      4. Chondroblastoma

5. Aneurysmal bone cyst
6. Giant cell tumor

B. SOFT TISSUE TUMOR

(a) adipocytic

1. Lipoma (common):
   Location: intrathoracic + subcutaneous
   √ deep seated growing mass between ribs
   √ mature fat tissue on CT + T1WI
2. Liposarcoma (2nd most common soft-tissue malignancy)
   √ prominent internal septa > 2 mm in thickness
   √ nodular nonadipose areas

(b) vascular

1. Hemangioma
   √ high SI on T2WI ← vascular tissue
   √ variable amounts of fat tissue on T1WI
   √ phleboliths on CT
2. Lymphangioma
   √ commonly in neck + axilla
   √ high SI greater than that of fat on T2WI
3. Angiosarcoma
   Associated with: postmastectomy lymphedema
4. Hemangioendothelioma, hemangiopericytoma
   √ usually deep seated
5. Aneurysm, false aneurysm

(c) fibroblastic-myofibroblastic

1. Elastofibroma dorsi
   √ fibrous mass located under serratus anterior / latissimus dorsi muscle
2. Fibromatosis = desmoid tumor

(d) fibrohistiocytic

1. Malignant fibrous histiocytoma = undifferentiated pleomorphic sarcoma (most common soft-tissue malignancy)

(e) peripheral nerve sheath tumor

√ "target "sign on T2WI (in 50–70% of neurofibromas, in 0–54% of schwannomas)
√ fascicular" sign on T2WI (in 63% of schwannomas and 25% of neurofibromas)

1. Schwannoma
2. Neurofibroma (may erode ribs inferiorly with sclerotic bone reaction), neuroma, neuroblastoma
3. Malignant PNST (5–10% of all soft-tissue sarcomas)
   Associated with: NF 2 (in 25–70%)

(f) cutaneous lesions

1. Epidermal cyst
   √ NO high signal intensity on T2WI
2. Pilomatricoma
   √ calcified subdermal nodule + peritumoral edema
4. Dermatofibrosarcoma protuberans

Chest Wall Tumor in Children

MALIGNANT TUMORS OF CHEST WALL IN CHILDREN

◊ More common than benign primary chest wall tumors!

1. Ewing sarcoma of rib (most common)
   (a) older child: rib involvement in 7%, predominant involvement of pelvis + lower extremity
   (b) child < 10 years: rib involvement in 30%
   DDx: osteomyelitis, unusual-appearing fracture, callus, direct spread of lung infection
2. Rhabdomyosarcoma
   relatively common in children + adolescents
   √ sclerosis / destruction / scalloping of cortex (local extension to contiguous bone)
   √ may calcify
   Metastases to: lung, occasionally lymph nodes
   Prognosis: infiltrative growth with high risk of local recurrence
3. Metastasis
   (a) Neuroblastoma
   • 10% present as chest wall mass
   √ may calcify
   (b) Leukemia
4. Askin tumor
5. Chondro- / osteosarcoma (quite rare in pediatric patients)

BENIGN TUMORS OF CHEST WALL IN CHILDREN

A. OSSEOUS
   1. Aneurysmal bone cyst
   2. Chondroblastoma
   3. Enchondroma
   4. Osteoblastoma
   5. Osteochondroma
   6. Osteoid osteoma

   Often associated with systemic syndrome: neurofibromatosis, histiocytosis, osteochondromatosis

   √ cortical rib destruction + soft-tissue mass

B. SOFT TISSUE
   1. Lipoma
   2. Hemangioma
   3. Lymphangioma
   4. Teratoma

BEDSIDE CHEST RADIOGRAPHY

Benefit:

Unexpected findings: in 37–43–65%

Change in diagnostic approach / therapy: in 27%

Indications:

A. APPARATUS POSITION + COMPLICATIONS

1. **Malposition of tracheal tube** (12%)
   √ tip of tube 4–6 cm above carina with neck in neutral position:
   √ migration by 2 cm inferiorly with flexion
   √ migration by 2 cm superiorly with extension
   √ tube diameter should be ½ to ⅔ of tracheal lumen
   √ diameter of inflated balloon should be less than diameter of trachea
   Cx:
   (a) Tracheal damage (stenosis / rupture) if ratio of cuff to tracheal lumen > 1.5
   (2) Aspiration (in 8%)
   (3) Disloding of teeth / fillings
2. **Malposition of central venous line** (9%) into internal jugular vein, azygos arch, internal mammary vein, congenital anomaly (eg, persistent left SVC), artery
   Cx: placement into branch vein / anomalous vein (eg, persistent left SVC), intraarterial placement, extravascular placement
   FDA Recommendation:
   (1) Tip of CVC within extrapericardial portion of SVC, 2 cm from cavoatrial junction = 85% of distance from sternoclavicular junction to carina = 9 mm above carina
   (2) Tip of tunneled hemodialysis catheter at junction of SVC and right atrium / in RA
   (3) Tip of nontunneled upper extremity catheter at superior cavoatrial junction = 4 cm below carina
   • fibrin sheath occlusion is suspected when a well-positioned CVC fails to function normally (confirmed at conventional catheter venography)
3. **Malposition of nasogastric tube**
   › esophageal malposition
   › bronchial intubation
   › esophageal perforation
   √ may not be on film if coiled in hypopharynx
4. **Swan-Ganz line** (= balloon-directed line)
   • 25% of catheters malpositioned on initial CXR
   √ tip should be in main / right / left pulmonary artery (NOT distal to proximal interlobar pulmonary a.)
   Cx: pulmonary infarction, pulmonary artery rupture, hemorrhage, cardiac perforation, pseudoaneurysm formation, malposition, intracardiac knot, arrhythmia
5. **Thoracostomy tube**
   √ break in radiopaque material (= most proximal side hole should be intrathoracic)
   √ intrafissural placement makes tube ineffective
6. **Tracheostomy**
   ◊ Position NOT affected by flexion / extension of neck!
   √ tube diameter should be ⅔ of tracheal lumen
   √ tip should be at level of T3

7. **Intraaortic balloon pump** (IABP)
   - tip of pump should be just distal to left subclavian artery in proximal descending aorta = 1–2 cm below top of aortic arch

   √ balloon inflates in diastole, deflates in systole
8. Retained catheter / implantable cardioverter-defibrillator lead **fragments**
9. **Calcified** fibrin sheath / calcified thrombus

B. CARDIOPULMONARY DISEASE

1. **Atelectasis**
   - most common CXR abnormality in ICU

   Incidence increased:
   after general anesthesia, thoracic / upper abdominal surgery, pre-existing lung disease, smoking, obesity, elderly

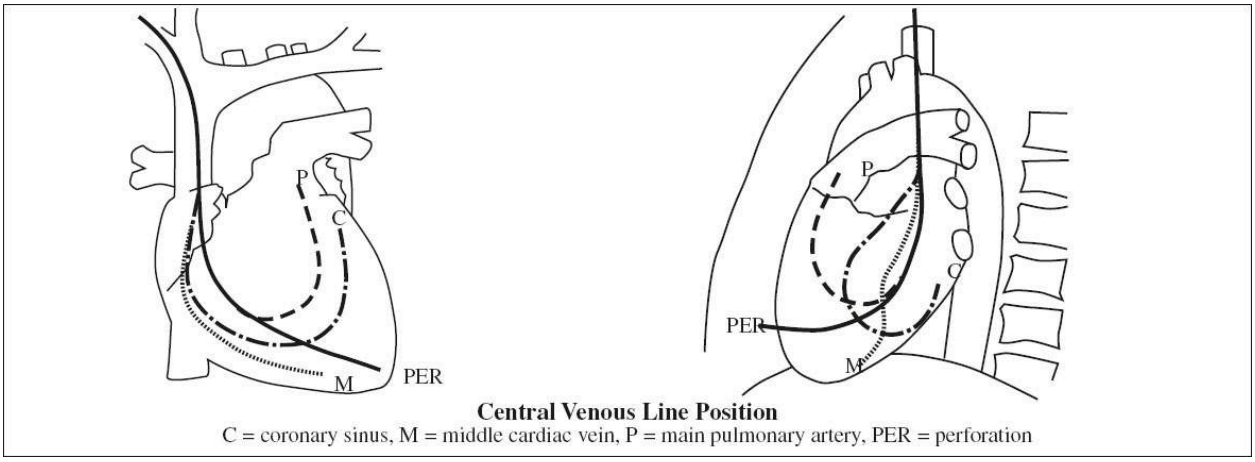
   Location: left lung base (most frequent)

   √ linear / platelike subsegmental

   √ lobar / segmental:

   √ air bronchogram present = collapse of small airways → bronchoscopy not beneficial

   √ air bronchogram absent = central mucoid impaction → bronchoscopy therapeutic



Central Venous Line Position
C = coronary sinus, M = middle cardiac vein, P = main pulmonary artery, PER = perforation

√ patchy density mimicking pneumonia

√ rapid temporal change possible

2. Pulmonary edema

(a) cardiac (hydrostatic)
including CHF, overhydration, renal failure

N.B.: cephalization of vasculature NOT helpful in supine position

√ usually cardiomegaly (cardiothoracic ratio ≥ 55%)

√ enlarged vascular pedicle (mediastinal width at SVC ≥ 70 mm)

√ Kerley lines

√ pleural effusion frequent

√ central / diffuse lung opacity

√ rapid onset + resolution

Accuracy of both CT ratio+ vascular pedicle width: 70% for pulmonary

wedge pressure > 18 mmHg

(b) noncardiac (permeability edema)
including ARDS, sepsis, drug reaction, near drowning, smoke inhalation, neurogenic edema, aspiration, fat embolism

√ cardiomegaly rare
√ Kerley lines absent
√ pleural effusions unusual + small
√ decreased lung volumes frequent
√ diffuse / peripheral lung opacity
◊ Patchy peripheral distribution in 58% of permeability edema vs. in 13% of hydrostatic edema
√ delayed onset + resolution
√ barotrauma common

3. Pleural effusion (due to CHF)
Location: bilateral / right-sided

◊ A solely left-sided effusion suggests a superimposed process / gravity!

√ homogeneous density over lower lung
√ fluid over apex / in fissures
√ intrafissural pseudotumor
√ not visible in 30%

DDx: atelectasis, empyema (loculated nonmobile effusion), postpericardiotomy syndrome (increasing effusion beyond 3rd postop. day)

4. Alveolar disease = pneumonia
• in 10% of ICU patients, in 60% with ARDS
• commonly related to aspiration
√ slowly progressing, often multifocal patchy areas of consolidation / poorly defined opacities
√ air bronchograms
√ cavitation (most specific finding)
Impossible DDx: ARDS, lobar atelectasis

5. Interstitial disease
DDx: (a) interstitial pulmonary edema changes daily
(b) pneumonia (CMV, pneumocystis)

6. Barotrauma (in 4–15% of ventilated patients)
Increased risk: underlying lung disease (ARDS, pneumonia), peak inspiratory pressure > 40 cm H_2O, use of PEEP, large tidal volume
√ pulmonary interstitial edema (initially)
√ anteromedial / subpulmonic location
√ tension pneumothorax (in 60–96%) with mediastinal shift masked by PEEP

7. Aspiration
Increased risk: general anesthesia, depressed consciousness, neuromuscular disorder, esophageal disease, presence of NG / ET tube
Location: posterior aspect of upper lobes, superior segments + posterior basilar segments of lower lobes

√ focal / multifocal consolidation in dependent location with central predominance
√ aspiration pneumonitis (may progress over first day but clearing within a few days)
√ aspiration pneumonia (lack of clearing / progression)

8. Thoracic bleeding
9. Mediastinal disease

MEDICAL DEVICES ON CXR

Cardiac Devices

Coronary Artery Bypass Grafting (CABG)

√ median sternotomy wires
√ vascular clips
√ anastomotic markers

Coronary Artery Stent

with self / balloon / thermally expandable stents

Cardiac Conduction Devices

Circulatory Assist Devices

› Intraaortic Counterpulsation Balloon Pump (IACB) inflated with CO_2 during ventricular diastole to augment perfusion of coronary arteries
› Ventricular Assist Device (VAD)

Heart Valve Replacement

(a) mechanical: Starr-Edwards, Björk-Shiley, Medtronic Hall, St. Jude Medical, Sorin Bicarbon, CarboMedics
(b) biologic: homograft (from human cadaver), xenograft from porcine aortic cusps, bovine pericardium, Carpentier-Edwards, Tissue Med, Hancock

Vascular Devices

Central Venous Pressure Catheter

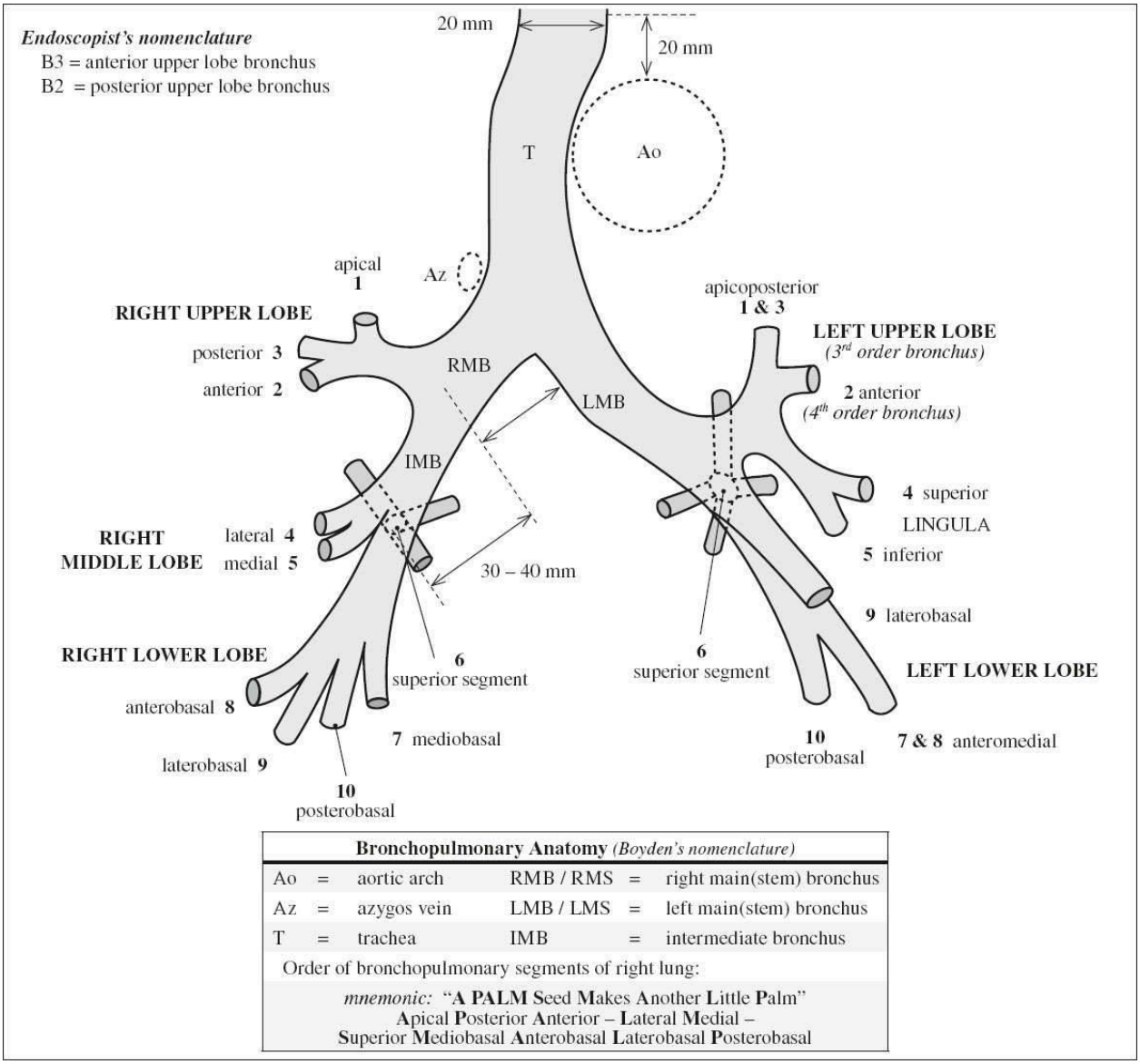
= CVP = CENTRAL CATHETER = CENTRAL LINE
Types: Hickman, Broviac, Leonard, Hohn, Cordis Sheath, Swan-Ganz (= pulmonary artery catheter), Groshong

Implantable Access Devices

= SUBCUTANEOUS PORT
Types: Port-A-Cath, SlimPort, Dialock, LifeSite

Peripheral Inserted Central Catheter (PICC)

ANATOMY AND FUNCTION OF LUNG



Bronchopulmonary Anatomy *(Boyden's nomenclature)*

Ao	=	aortic arch	RMB / RMS	=	right main(stem) bronchus
Az	=	azygos vein	LMB / LMS	=	left main(stem) bronchus
T	=	trachea	IMB	=	intermediate bronchus

Order of bronchopulmonary segments of right lung:

mnemonic: "**A PALM** Seed **M**akes **A**nother **L**ittle **P**alm"
Apical **P**osterior **A**nterior – **L**ateral **M**edial –
Superior **M**ediobasal **A**nterobasal **L**aterobasal **P**osterobasal

ORDER OF BRONCHOPULMONARY SEGMENTS OF RIGHT LUNG:

AIRWAYS

The carina is normally at the level of T4/T5.

Embryology of Airways & Maldevelopment

first 5 weeks GA	lung buds grow from ventral aspect of primitive foregut (from caudal end of laryngotracheal groove of primitive pharyngeal floor)
abnormal:	pulmonary agenesis
5th week GA	separation of trachea + esophagus
5–16 weeks	formation of tracheobronchial tree with bronchi, bronchioles, alveolar ducts, alveoli

abnormal: bronchogenic cyst ← abnormal budding;
pulmonary hypoplasia ← fewer than expected bronchi

16–24 weeks dramatic increase in number + complexity of airspaces and blood vessels

abnormal: small airways ← reduction in number and size of acini

Anomalous Bronchial Division

Branching anomalies:

(a) displaced (replaced) bronchus

√ bronchus with abnormal origin while normal bronchus ventilating corresponding parenchyma is absent

(b) supernumerary (accessory) bronchus

√ may end blindly in parenchyma of corresponding normal bronchus = congenital bronchial diverticulum

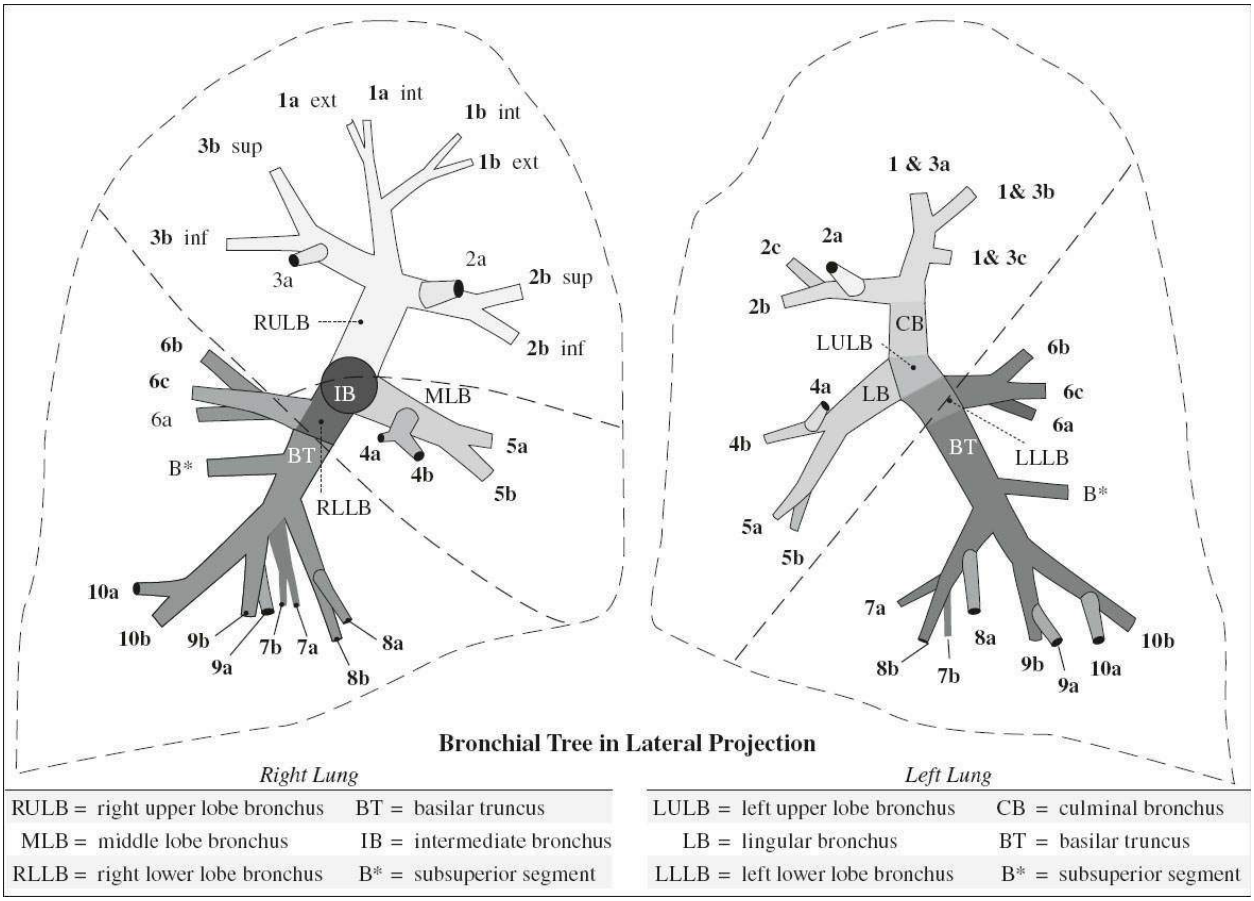
√ may ventilate additional lung parenchyma, possibly delineated by an accessory fissure

Tracheal Bronchus *(0.1–2.0%)*

= bronchus of variable length arising from lower trachea

Frequency: 0.1–1.3% in adults; 1.5–2% in childhood

In 78% associated with:



Bronchial Tree in Lateral Projection

Right Lung		*Left Lung*	
RULB = right upper lobe bronchus	BT = basilar truncus	LULB = left upper lobe bronchus	CB = culminal bronchus
MLB = middle lobe bronchus	IB = intermediate bronchus	LB = lingular bronchus	BT = basilar truncus
RLLB = right lower lobe bronchus	B* = subsuperior segment	LLLB = left lower lobe bronchus	B* = subsuperior segment

Down syndrome; malformation of thoracic cage / foregut / lung; tracheal stenosis; other

tracheobronchial branching anomalies

Type: displaced in 75%; supernumerary in 25% → ventilating intra- / extralobar tracheal lobe (NOT related to azygos lobe)

Location: almost invariably on right; bilateral (rare)

Site: distal trachea < 2 cm from carina

- recurrent pneumonia, respiratory distress in childhood
- almost invariably asymptomatic in adults

√ blind-ending pouch (= congenital right tracheal diverticulum) / aeration of a portion or all of RUL

√ early origin of apicoposterior LUL bronchus (less common)

√ "pig bronchus" = entire RULB displaced on trachea

Right Preeparterial Bronchus

= any bronchus directed toward RUL that arises abnormally from RMB above level of right eparterial ULB

Frequency: 0.9%

Type: 82% displaced

- mostly asymptomatic

DDx: accessory cardiac bronchus

Right Posteparterial Bronchus

= any bronchus directed toward RUL that arises abnormally from right bronchial tree below level of right eparterial ULB

Left Eparterial Bronchus

= any bronchus directed toward LUL that arises from posterolateral / lateral wall of LMB above level where left pulmonary artery crosses LMB

Left Prehyparterial Bronchus

= anomalous bronchus directed toward LUL that arises from LMB between level of left pulmonary artery crossing and hyparterial LULB

Accessory Cardiac Bronchus (ACB)

= true supernumerary anomalous bronchus

The only bronchus originating from medial wall of either RMB or IMB (occasionally on left side)

M÷F = 2.8÷1

√ arises from medial wall of bronchus intermedius prior to origin of apical segmental RLL bronchus

√ caudal course toward pericardium

√ blind-ending pouch / ventilation of an accessory lobe

Bridging bronchus

= aberrant bronchus that partially / totally supplies the right lung but originates from LMB

√ carina at T4–T5

√ pseudocarina in the shape of an inverted T at T6-T7

Paracardiac Bronchus

= normal bronchus arising from medial aspect of lower lobe

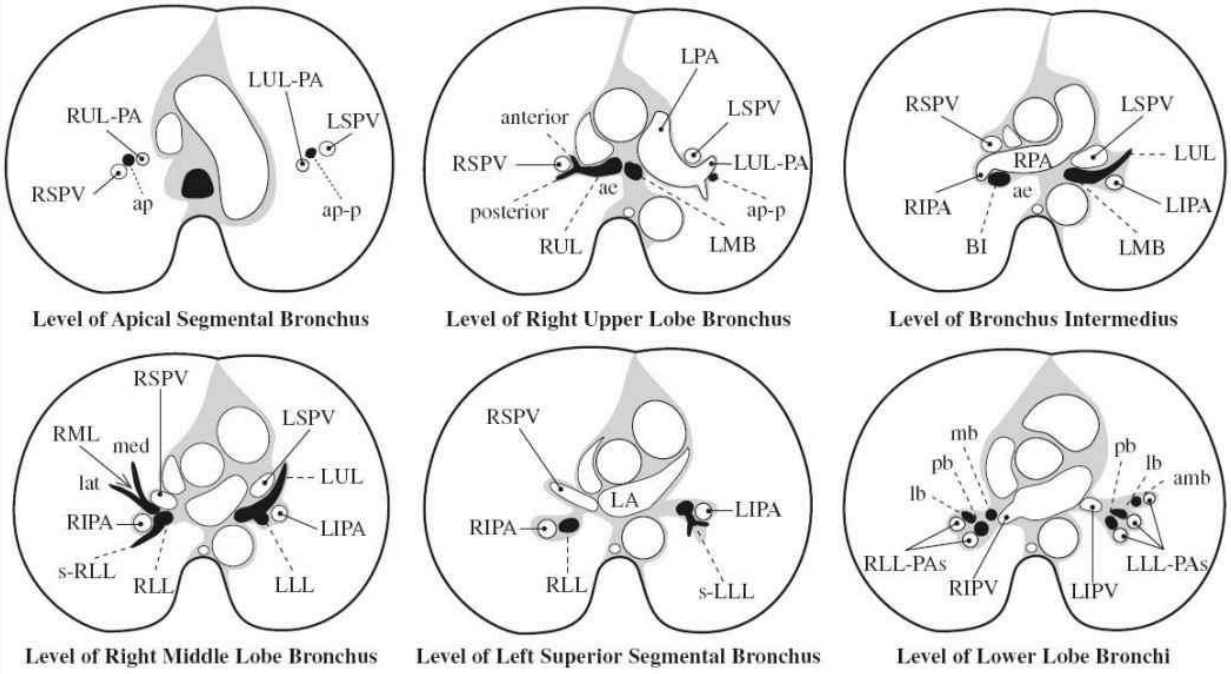
Prevalence: 5% of patients

Airway

= conducting branches for the transport of air; ~ 300,000 branching airways from trachea to bronchiole with an average of 23 airway generations

Definition:

bronchus = cartilage in wall



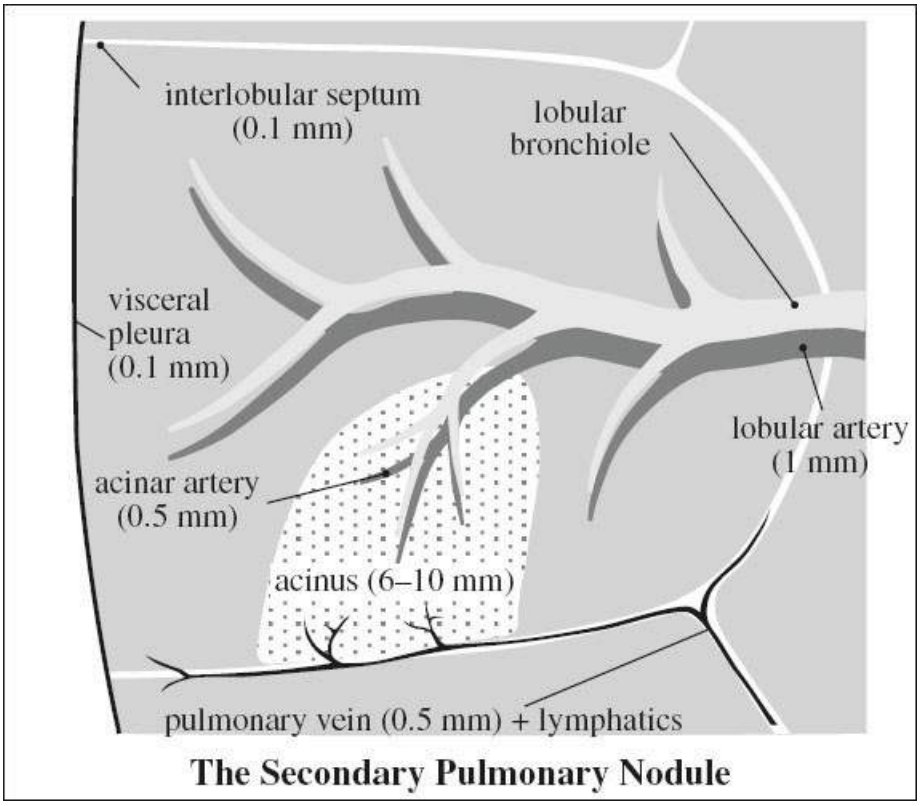
Cross-sectional Anatomy of Bronchovascular Divisions

Right Lung

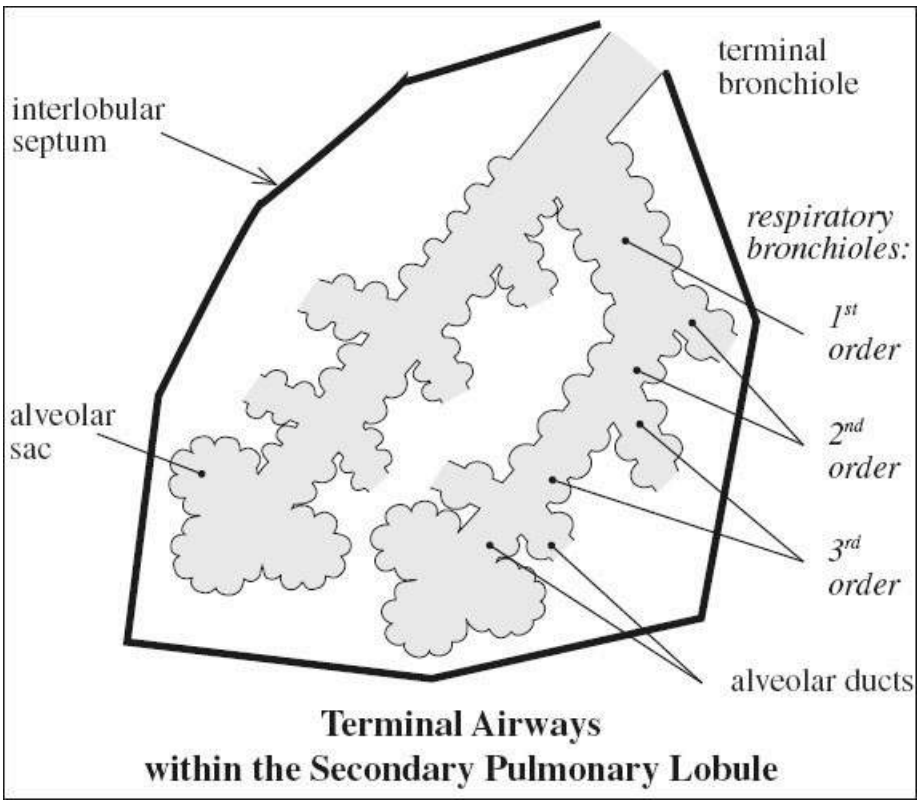
ant	=	anterior RUL	pb	=	posterobasal RLL
ap	=	apical RUL	post	=	posterior RUL
BI	=	bronchus intermedius	RLL	=	right lower lobe
lat	=	lateral RML	RML	=	right middle lobe
mb	=	mediobasal RLL	RUL	=	right upper lobe
med	=	medial RML	s-RLL	=	superior segment
RUL-PA / LUL-PA	=	R / L upper lobe pulmonary artery			
RLL-PAs / LLL-PAs	=	R / L pulmonary artery			
RIPV / LIPV	=	R / L inferior pulmonary vein			
RPA	=	R pulmonary artery			

Left Lung

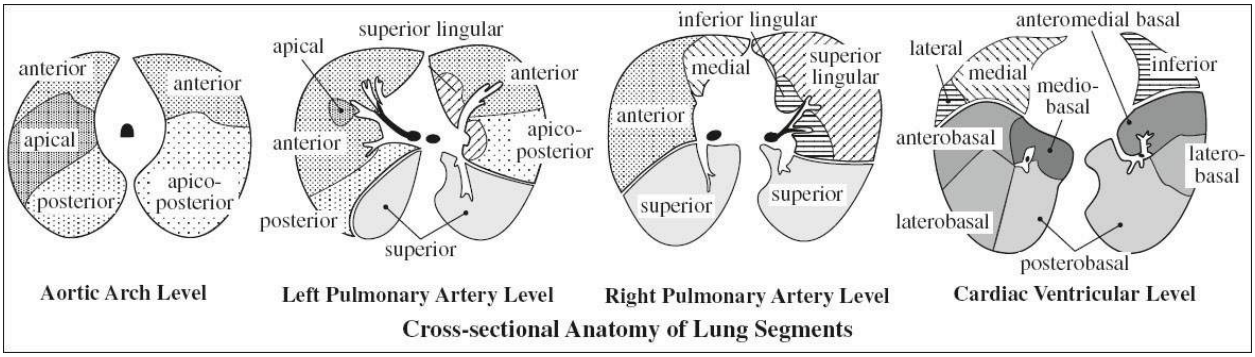
amb	=	anteromediobasal LLL	ap-p	=	apicoposterior LUL
lb	=	laterobasal LLL	LLL	=	left lower lobe
LMB	=	left main bronchus	LUL	=	left upper lobe
pb	=	posterobasal LLL	s-LLL	=	superior segment
ae	=	azygoesophageal recess			
RIPA / LIPA	=	R / L inferior pulmonary artery			
RLL-PAs / LLL-PAs	=	R / L lower lobe pulmonary arteries			
RSPV / LSPV	=	R / L superior pulmonary vein			



The Secondary Pulmonary Nodule



Terminal Airways
within the Secondary Pulmonary Lobule



Cross-sectional Anatomy of Lung Segments

bronchiole = absence of cartilage (after 6–2 divisions of segmental bronchus)
- › **membranous** bronchiole = purely air conducting
- › **respiratory** bronchiole = contains alveoli in its wall
- › **lobular** bronchiole = supplies secondary pulmonary lobule; may branch into 3 or more terminal bronchioles
- › **terminal** bronchiole = last generation of purely conducting bronchioles without alveoli; each supplying one acinus

small airways = internal diameter < 2 mm = small noncartilaginous membranous and respiratory bronchioles; account for 25% *of airway resistance*

large airways = diameter > 2 mm; account for 75% *of airway resistance*

HRCT of normal lung (window level –700 HU, window width 1,000–1,500):
- √ –875 ± 18 HU at inspiration
- √ –620 ± 43 HU at expiration
- √ 8th order bronchi visible = bronchi > 2 mm in diameter
- ◊ Normal lobular bronchioles NOT visible!

Acinus

◊ Functionally most important subunit of lung!

= all parenchymal tissue <u>distal to one terminal bronchiole</u> comprising 2–5 generations of respiratory bronchioles + alveolar ducts + alveolar sacs + alveoli

• gas exchange

√ radiologically NOT visible

Cells of Lung Parenchyma *75% of all lung cells*

1. Air-blood barrier
   - › epithelial cells (25%) = lining of air space
   - › endothelial cells (25%) = lining of vessels
   - › interstitial cells (35%), collagen fibres (15%)
2. Alveolar epithelium
   - › lining cells (type I pneumocyte) → tight junctions, no mitosis
   - › secretory cells (type II pneumocyte) → synthesis + storage + secretion of surfactant
   - › brush cells

[Primary Pulmonary Lobule]

= alveolar duct + its connected air spaces

Secondary Pulmonary Lobule

= REID LOBULE

[Lynne McArthur Reid (1923–?), experimental pathologist and dean of Cardiothoracic Institute, London University, Harvard Medical School, pathologist-in-chief emeritus at Children's Hospital in Boston]

= smallest portion of lung surrounded by connective tissue septa; supplied by 3–5 terminal bronchioles

√ basic anatomic + functional pulmonary unit appearing as an irregular polyhedron containing 3–24 acini

√ separated from each other by thin fibrous interlobular septa (100 μm)

Size: 10–25 mm in diameter

• visible on surface of lung

Contents:

› centrally = lobular core:

» branches of terminal bronchioles with a 0.1 mm wall thickness = below the resolution of HRCT

√pulmonary arterioles (1 mm)

› peripherally (within interlobular septa):

√pulmonary vein + lymph vessels

HRCT:

√ barely visible fine lines of increased attenuation in contact with pleura (= interlobular septa); best developed in subpleural areas of

› UL + ML: anterior + lateral + juxtamediastinal

› LL: anterior + diaphragmatic regions

√ dotlike / linear / branching structures (= pulmonary arterioles)

Site: near center of secondary pulmonary lobule; 3–5 mm from pleura

Interstitial Anatomy

1. **Bronchovascular** interstitium
   surrounding bronchovascular bundle
2. **Centrilobular** interstitium
   surrounds distal bronchiolovascular bundle
   √ line extending to the center of a lobule
3. **Interlobular** septal interstitium
   √ lines perpendicular to pleura surrounding a lobule
4. **Pleural** interstitium

Lung Interstitium	
Division	*Components*
Axial	bronchovascular sheaths, lymphatics
Middle (parenchymal)	alveolar wall (interalveolar septum)
Peripheral	pleura, subpleural connective tissue interlobular septa (enclosing pulmonary veins, lymphatics, walls of cortical alveoli)

Lung Development

› *embryonic phase*
respiratory diverticulum (= laryngotracheal bud) originates from ventral wall of primitive foregut
→ elongation of lung bud → lateral invagination of mesoderm → tracheoesophageal septum
→ bifurcation of laryngotracheal bud at 5–7 weeks EGA → R + L mainstem bronchi
→ mainstem bronchi branch further into lobar bronchi
→ pulmonary arteries arise from 6th aortic arch
Time: 26 days to 7 weeks EGA

› *pseudoglandular phase* development of segmental + subsegmental bronchi, respiratory bronchioles + terminal bronchioles, alveolar ducts + alveoli
Time: 7–16 weeks EGA

› *canalicular / acinar phase* development of distal acinar units + canalization of further airspaces; airspaces are approximated by network of capillaries; type II alveolar cells capable of surfactant synthesis
Time: 16–24 weeks EGA

› *saccular phase* increase in number of terminal sacs + thinning of intervening interstitium + beginning of alveolar septation
Time: 24–36 weeks EGA

› *alveolar phase* development of true fully mature alveoli with progressive formation throughout first 2 years of life
Time: 36 weeks EGA – 18th postnatal month

mnemonic: **E**very **P**remature **C**hild **T**akes **A**ir
Embryonic phase
Pseudoglandular phase
Canalicular phase
Terminal sac phase
Alveolar phase

Surfactant

= surface-active material essential for normal pulmonary function

Substrate: phospholipids (dipalmitoylphosphatidylcholine, phosphatidylglycerol), other lipids, cholesterol, lung-specific proteins

Production: type II pulmonary alveoli synthesize + transport + secrete lung surfactant; earliest production around 18th week of gestation (in amniotic fluid by 22nd week

of gestation)

Action: increases lung compliance, stabilizes alveoli, enhances alveolar fluid clearance, reverses surface tension, protects against alveolar collapse during respiration, protects epithelial cell surface, reduces opening pressure + precapillary tone

PULMONARY CIRCULATION

Primary Pulmonary Circulation

⇒ supplies 99% of blood flow to lungs pulmonary arteries travel along lobar + segmental bronchi down to subsegmental level matching caliber of airways

(a) **large elastic** pulmonary arteries (500 to > 1,000 μm) accompany lobar + segmental bronchi matching caliber of airways
- › main pulmonary artery / trunk: ≤ 28 mm
- › right / left pulmonary artery
- › lobar pulmonary artery
- › segmental pulmonary artery

(b) **muscular** arteries (50–1,000 μm) accompany subsegmental airways + terminal bronchioles
- √ provide active vasodilatation + constriction

(c) **arterioles** (15–150 μm) accompany respiratory bronchioles + alveolar ducts

(d) **capillary** network in alveolar walls

(e) venules

(f) pulmonary veins course through interlobular fibrous septa

Function: gas exchange

Bronchial Circulation

⇒ supplies 1% of blood flow to lungs = 1% of cardiac output

Pressure: systemic high-pressure system (6 x that of normal pulmonary circulation); bronchial arteries are resistant to arteriosclerosis

Origin:

(a) orthotopic bronchial artery (64%): anteriorly from proximal to mid-descending thoracic aorta at level of left main bronchus between superior endplate of T5 and inferior endplate of T6

Angio landmark: 1 cm above / below level of left main bronchus as it crosses descending thoracic aorta

(b) at least one ectopic bronchial artery (36%):
- › from undersurface of aortic arch (15%)
- › distal descending thoracic aorta, subclavian artery, thyrocervical trunk, costocervical trunk, brachiocephalic trunk, internal mammary artery, pericardiophrenic a., inferior phrenic a., coronary a.

(c) left bronchial artery: most commonly directly from aorta toward left side of esophagus

(d) right bronchial artery: most commonly originating from another artery, typically intercostal artery toward right side of esophagus

Variants of vascular anatomy (9 types):

(1) 1 right bronchial a. arising posteromedially from a common **I**nter**C**ostal **B**ronchial

Artery **T**runk (ICBAT) + 2 left bronchial a. anteriorly (41%)

(2) 1 bronchial artery on each side, the right bronchial artery originating from an ICBAT (21%)

(3) 2 bronchial aa. on each side, 1 right bronchial artery originating from an ICBAT (21%)

(4) 1 right bronchial a. + 1 right ICBAT + 2 left bronchial arteries (10%)

Course: behind trachea and main-stem bronchi; enter lung via hila; tortuous path along peribronchial sheath of mainstem airway to terminal bronchioles

Function:

⇒ nourishment for supporting structures
- › extra- and intrapulmonary airways
- › vasa vasorum of pulmonary arteries
- › nerves, pulmonary veins, lymph nodes within thorax

⇒ systemic blood supply to
- › trachea, bronchi, bronchial branches, visceral pleura
- › esophagus

The bronchial circulation + other collateral vessels (eg, intercostal, internal mammary, inferior phrenic aa.) respond to chronic pulmonary ischemia and ↓ pulmonary blood flow → vessel hypertrophy / enlargement → maintenance of blood flow to affected lung + participation in gas exchange through systemic-pulmonary arterial anastomoses beyond the pulmonary artery obstruction.

Bronchial-to-Pulmonary Artery Anastomoses

= microvascular connections (= capillary communications) at level of alveoli and respiratory bronchioles

⇒ normal L-to-R shunt accounting for 5% of cardiac output

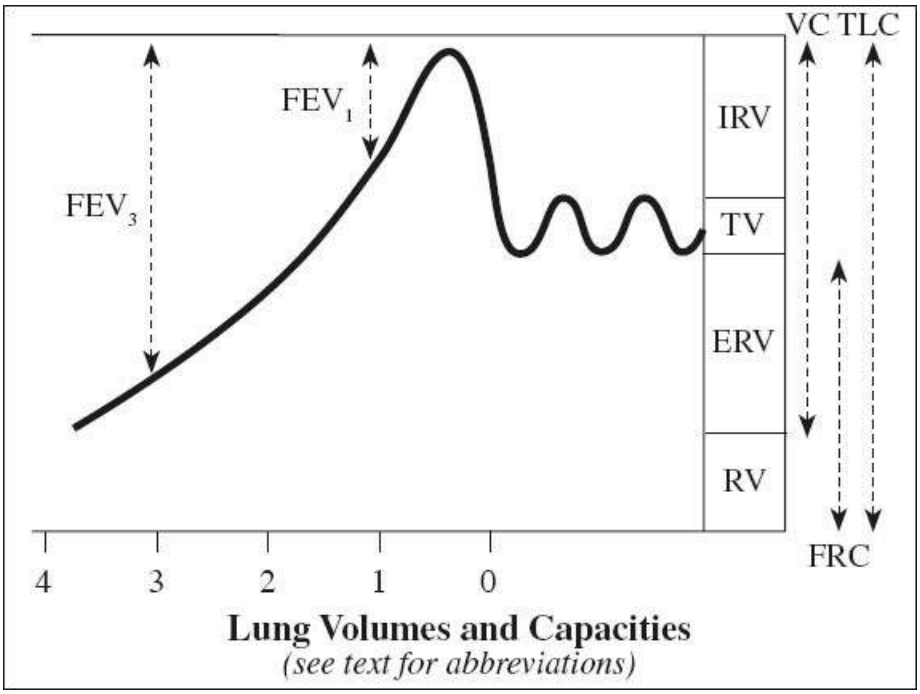
√ normal bronchial arteries NOT usually visible on thoracic angiography

LUNG FUNCTION

Lung Volumes & Capacities

1. Tidal volume (**TV**)

= amount of gas moving in + out with each respiratory cycle



2. Residual volume (**RV**)
   = amount of gas remaining in lung after maximal expiration
3. Total lung capacity (**TLC**)
   = gas contained in lung at end of maximal inspiration
4. Vital capacity (**VC**)
   = amount of gas that can be expired after a maximal inspiration without force
5. Functional residual capacity (**FRC**)
   = volume of gas remaining in lungs at end of quiet expiration

Changes In Lung Volumes

A. DECREASED VITAL CAPACITY:
   1. Reduction in functioning lung tissue due to
      (a) space-occupying process (eg, pneumonia, infarction)
      (b) surgical removal of lung tissue
   2. Process reducing overall volume of the lungs
      (eg, diffuse pulmonary fibrosis)
   3. Inability to expand lungs due to
      (a) muscular weakness (eg, poliomyelitis)
      (b) increase in abdominal volume (eg, pregnancy)
      (c) pleural effusion

B. INCREASED FRC and RV:
   = characteristic of air trapping and overinflation (eg, asthma, emphysema)
   Associated with: increased TLC
   √ normal level of inflation to 8th posterior rib

C. DECREASED FRC and RV:
   1. Process reducing overall volume of lungs

(eg, diffuse pulmonary fibrosis)

2. Process that occupies volume within alveoli
   (eg, alveolar microlithiasis)
3. Process that elevates diaphragm (eg, ascites, pregnancy), usually associated with decreased TLC

Flow Rates

A. Spirometric measurements:

1. **Forced expiratory volume** (FEV)
   = amount of air expired during a certain period (usually 1 + 3 seconds)
   Normal values: **FEV_1** = 83%; **FEV_3** = 97%
2. **Maximal midexpiratory flow rate** (MMFR)
   = amount of gas expired during middle half of forced expiratory volume curve (largely effort independent)
   Indicator of small airway resistance
3. **Flow-volume loop**
   = gas flow is plotted against the actual volume of lung at which this flow is occurring
   Useful in identifying obstruction in large airways

B. Resistance in small airways

Closing volume = lung volume at which dependent lung zones cease to ventilate because of airway closure in small airway disease or loss of lung elastic recoil

- decrease in FEV, MMFR, MBC:
  (a) expiratory airway obstruction (reversible as in spasmodic asthma / irreversible as in emphysema)
  (b) respiratory muscle weakness

Diffusing Capacity

= rate of gas transfer across alveolocapillary membrane in relation to constant pressure differences across it; measured by carbon monoxide diffusion method DLCO.

Technique:

» patient inspires maximally a gas with a known small concentration of CO
» breath-holding for 10 seconds followed by slow expiration to residual volume (RV)
» an aliquot of the end-expired (alveolar) gas is analyzed for amount of CO absorbed during breath

Measurement: in mL of CO absorbed/min/mmHg

Causes of reduction:

1. Ventilation / perfusion inequality: less CO is taken up by poorly ventilated or poorly perfused areas (eg, emphysema)
2. Reduction of total surface area (eg, emphysema, surgical resection)
3. Reduction in permeability from thickening of alveolar membrane (eg, cellular infiltration, edema, interstitial fibrosis)
4. Anemia with lack of hemoglobin

Arterial Blood Gas Abnormalities

- decreased pulmonary arterial O2:

1. Alveolar hypoventilation
2. Impaired diffusion
3. Abnormal ventilation / perfusion ratios
4. Anatomic shunting

- elevated pulmonary arterial CO_2:
  1. Alveolar hypoventilation
  2. Impaired ventilation / perfusion ratios

V/Q Inequality

A. NORMAL
   (a) blood flow decreases rapidly from base to apex
   (b) ventilation decreases less rapidly from base to apex
   ◊ V/Q is low at base and high at apex
   ◊ Pulmonary arterial O2 is substantially higher at apex
   ◊ Pulmonary arterial CO_2 is substantially higher at base

B. ABNORMAL
   chiefly resulting from non- / underventilated lung regions
   ◊ Non- / underperfused regions do NOT result in blood gas disturbances!

Compliance

= relationship of the change in intrapleural pressure to the volume of gas that moves into the lungs

A. DECREASED COMPLIANCE
   edema, fibrosis, granulomatous infiltration

B. INCREASED COMPLIANCE
   emphysema (faulty elastic architecture)

√ height of diaphragm at TLC can provide some indication of lung compliance, particularly valuable in sequential roentgenograms for comparison in:
1. Diffuse interstitial pulmonary edema
2. Diffuse interstitial pulmonary fibrosis

LUNG ZONES

Pressure Gradients in Upright Position (Erect Lung)

Gravity	20 mmHg blood pressure gradient between top and bottom for erect lung
$P_{alveolar}$	0 ± 2 cm H_20 (1.5 mmHg) at zero flow at end expiration equal to atmospheric pressure
P_{venous}	~ 5 (–5 at apex → +15 mmHg at base) mmHg
$P_{arterial}$	15 (range, 5 at apex → 25 mmHg at base) mmHg

Vertical Zonal Distribution

Zone 1: $P_{alveolar} > P_{arterial} > P_{venous}$
positive pressure ventilation / lung hemorrhage → complete vascular collapse → cessation of blood flow (= alveolar dead space)

Zone 2: $P_{arterial} > P_{alveolar} > P_{venous}$
about 3 cm above the heart → cyclical capillary blood flow (= no flow in diastole to maximum flow during systole = starlings resistor or waterfall effect)

Zone 3: $P_{arterial} > P_{venous} > P_{alveolar}$
lung in health → continuous blood flow throughout cardiac cycle determined by arteriovenous pressure difference; transmural pressure increases due to gravity → increase in vessel caliber

Zone 4: $P_{arterial} > P_{interstitial} > P_{venous} > P_{alveolar}$
lung base at low lung volumes or pulmonary edema → interstitial pressure rises with ⇓ in lung volume (← reduced radial tethering of lung) OR fluid leakage from lung vessels; pressure is highest at lung base due to weight of lung above → increase in resistance to flow → ⇓ caliber of extra-alveolar blood vessels

Effect on V/Q ratio
- highest in zone 1 of lung apex in erect person because perfusion is nearly absent
- lower in zone 3 with both high ventilation, perfusion and lymphatic drainage in erect chest

MEDIASTINUM

Terminology: coined by Spigelius "Quod per medium stat" = "what sits in the middle"

A. SUPERIOR MEDIASTINAL COMPARTMENT
= thoracic inlet

B. INFERIOR MEDIASTINAL COMPARTMENT

(1) Anterior mediastinum = retrosternal region
Anterior boundary: sternum
Posterior boundary: pericardium, aorta, brachiocephalic vessels
Superior boundary: thoracic inlet
Inferior boundary: diaphragm
Contents: thymus, lymph nodes, adipose tissue, internal mammary vessels

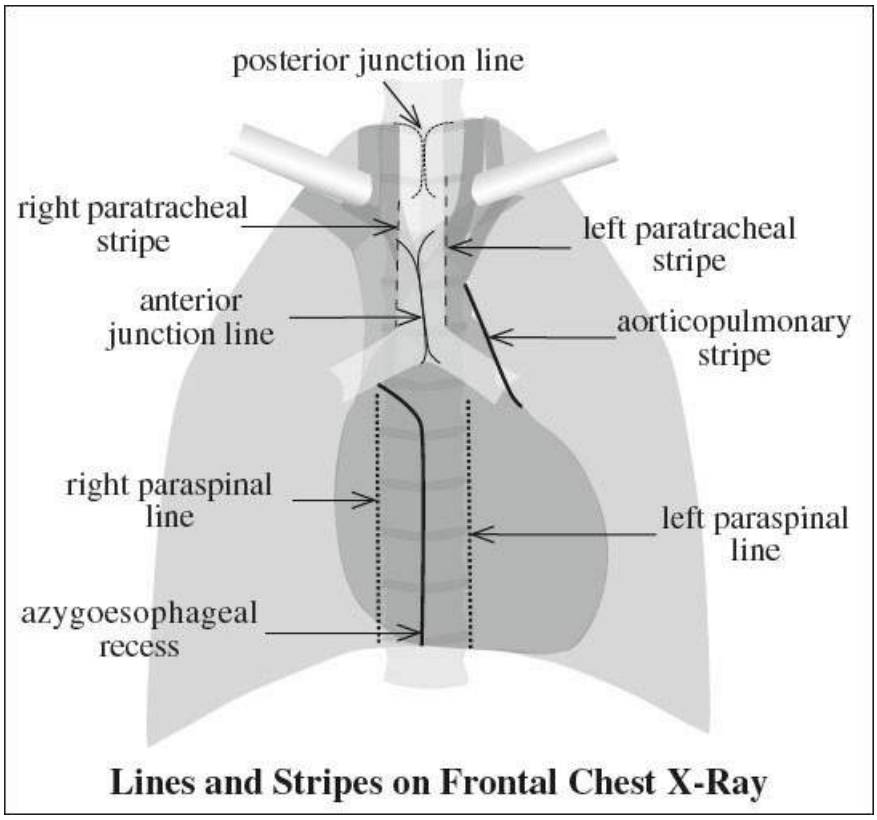
(2) Middle mediastinum = visceral region
Anterior boundary: pericardium
Posterior boundary: pericardium, posterior tracheal wall
Superior boundary: thoracic inlet
Inferior boundary: diaphragm
Contents: heart, pericardium, ascending + transverse aorta, SVC, IVC, brachiocephalic vessels, pulmonary vessels, trachea + main bronchi, lymph nodes, phrenic n., vagus n., left recurrent laryngeal n.

(3) Posterior mediastinum = contains esophagus, descending aorta, paraspinal region
Anterior boundary: posterior trachea, pericardium
Posterior boundary: line 1 cm posterior to the anterior edge of vertebral column
Superior boundary: thoracic inlet
Inferior boundary: diaphragm
Contents: esophagus, descending aorta, azygos + hemiazygos veins, thoracic duct, vagus n., splanchnic n., lymph nodes, fat

Lung-Mediastinal Interfaces on Frontal CXR

1. **Anterior junction line**
   = apposing pleural reflections
   Location: anterior to aorta behind upper ⅔ of sternum; does not extend above manubriosternal junction
   Thickness: 4 layers of pleura separated by variable amount of fat
   Course: obliquely from upper right to lower left
   Visualization in: 25–57%
   Abnormal in: thyroid mass, lymphadenopathy, neoplasm, thymic mass, lipomatosis
2. **Posterior junction line**
   = apposing 4 layers of pleural reflections
   Location: posterior to esophagus and anterior to spine (between 3rd–5th thoracic vertebrae); typically projecting through trachea
   Course: vertically from lung apices to top of aortic arch (above suprasternal notch)
   Visualization in: 32%
   Abnormal in: esophageal mass, lymphadenopathy, aortic disease, neurogenic tumor
3. **Right paratracheal stripe**
   = 1–4 mm uniformly thick line between tracheal air column and right lung
   Location: undersurface of right clavicle to azygos arch
   Course: vertical
   Visualization in: 94–97%
   Abnormal in: paratracheal lymphadenopathy, tracheal ca. + stenosis, thyroid + parathyroid neoplasm
4. **Left paratracheal stripe**
   = uniformly thick line between tracheal air column and left upper lobe
   Location: superiorly from aortic arch to left subclavian a.
   Course: vertical
   Visualization in: 21–31%
   Abnormal in: left pleural effusion, left paratracheal lymphadenopathy, neoplasm, mediastinal hematoma
5. **Azygoesophageal recess**
   = right lung abutting the azygos vein posteriorly and esophagus anteriorly
   Location: undersurface of azygos arch to aortic hiatus
   Course: vertical straight / mild leftward convexity
   Abnormal in: lymphadenopathy, hiatal hernia, bronchopulmonary foregut malformation, esophageal neoplasm, pleural abnormalities, cardiomegaly with left atrial enlargement
6. **Right paraspinal line**
   = lung abutting the lateral margins of thoracic vertebral bodies (left paraspinal line more often seen than right)
   Location: from 8th to 12th thoracic vertebra
   Course: straight vertical
   Visualization in: 23%
   Abnormal in: osteophytes, prominent mediastinal fat, neoplasm, mediastinal hematoma, extramedullary hematopoiesis

7. **Left paraspinal line**



= lung abutting the lateral margins of thoracic vertebral bodies, mediastinal fat, paraspinal muscles

Location: aortic arch to diaphragm, typically medial to lateral wall of descending thoracic aorta

Course: straight vertical

Visualization in: 41%

Abnormal in: osteophytes, prominent mediastinal fat, neoplasm, mediastinal hematoma, extramedullary hematopoiesis, tortuosity of descending thoracic aorta, esophageal varices

8. **Aorticopulmonary stripe**

= interface of anterior left lung + mediastinal fat anterolateral to left pulmonary artery + aortic arch

Course: straight / mildly convex

Abnormal in: pneumomediastinum, thyroid + thymic mass, prevascular lymphadenopathy

9. **Aortic-pulmonary (AP) window** / stripe

= space between inferior wall of aortic arch + superior wall of left pulmonary artery

Border:

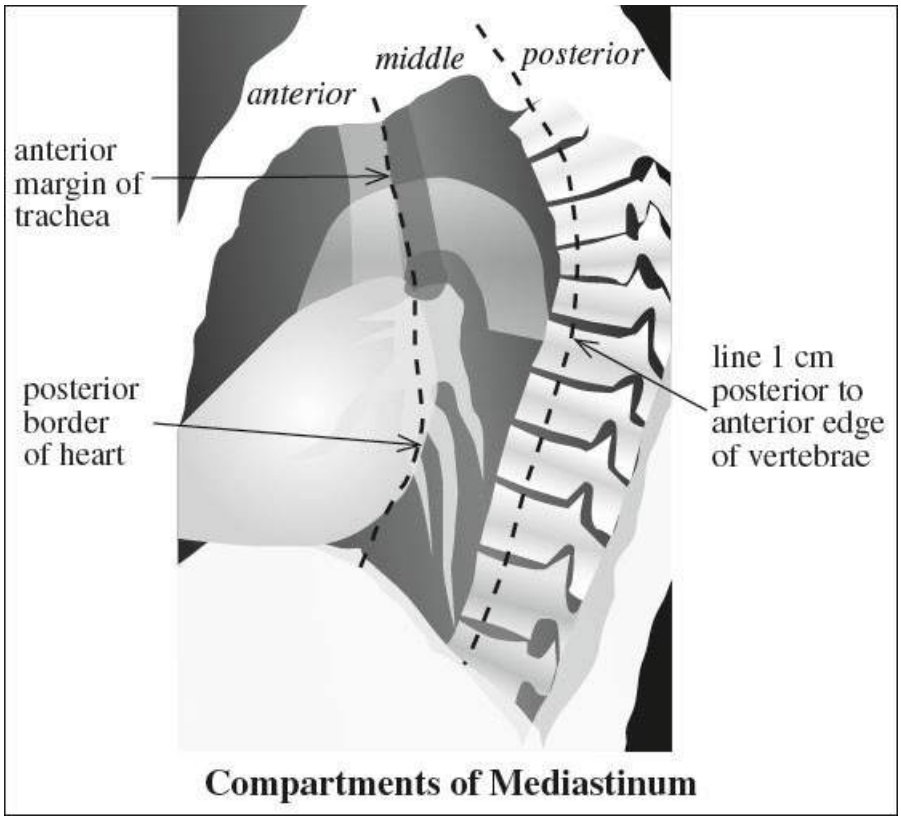
- superior: inferior wall of aortic arch
- inferior: superior wall of left pulmonary artery
- posterior: anterior wall of ascending aorta

- › anterior: posterior wall of ascending aorta
- › lateral: left lung + pleura
- › medial: trachea, lateral wall of LMB, esophagus

Location: posterior to aorticopulmonary stripe
Course: straight / concave reflection along mediastinum
Abnormal in: mediastinal fat, lymphadenopathy, aneurysm of aorta / bronchial artery, nerve sheath tumor (recurrent laryngeal nerve, left vagus nerve)

Lung-Mediastinal Interfaces on Lateral CXR

1. **Tracheoesophageal / posterior tracheal stripe**
   = formed by air within trachea and right lung
   Location: anterior border of retrotracheal space (= Raider triangle)
   Thickness: up to 2.5 mm; up to 5.5 mm (if wall of air-containing esophagus included)
   Course: vertical
   Abnormal in: congenital developmental anomalies of aortic arch, acquired vascular lesion, esophageal lesion, lymphatic malformation, mediastinitis, posttraumatic hematoma



Compartments of Mediastinum

2. **Posterior wall of bronchus intermedius**
   = formed by air in bronchus intermedius, which descends for 3–4 cm, and lung within azygoesophageal recess
   Course: thin vertical / slightly oblique stripe that projects through the radiolucent area created by left upper lobe bronchus

Thickness: 0.5–3.0 mm
Visualization in: 90–95%
Abnormal in: pulmonary edema, lung neoplasm, lymphadenopathy

THYMUS

[*thymos*, Greek = warty excrescence, soul, spirit]

Embryogenesis:

dorsal + ventral wings of 3rd (and possibly 4th) pharyngeal (branchial) pouch begin to form elongated cylindrical primordia during 7th week (= thymopharyngeal ducts); both ducts migrate caudally and medially into anterior mediastinum pulling inferior parathyroid glands along; thymic primordia fuse at their lower poles inferior to thyroid gland during 8th week; thymic tail thins + disappears by 8th week of GA

◊ Residual thymic tissue in neck in 1.8–21%

Histo: contains elements of all 3 germinal layers; until 9th week EGA purely epithelial; during 10th week EGA lymphoid cells migrate from fetal liver + bone marrow into primordia causing thymic lobulation; differentiation into cortex and medulla completed by 16th week EGA

Cortex: primarily lymphocytes = thymocytes

Medulla: more epithelial cells = nurse cells (essential for maturation of T lymphocytes); Hassall corpuscles (round keratinized formations with mature epithelial cells)

Function: development + maturation of immune system during childhood, ie, T-cells (regulating cellular immunity) and B cells (regulating humoral immunity)

Thymic weight:

increases from birth to age 11–12 years (22 ± 13 g in neonate, 34 ± 15 g at puberty); ratio of thymic weight to body weight decreases with age (largest during infancy, fatty involution after puberty, total fatty replacement after age 60)

Extent: from manubrium to 4th costal cartilage; may bulge into neck / extend down to diaphragm

√ normal thymus visible in 50% of neonates 0–2 years of age
√ "notch" sign = indentation at junction of thymus + heart
√ "sail" sign = triangular density extending from superior mediastinum
√ "wave" sign = rippled border due to indentation by ribs
√ shape changes with respiration + position

CXR:

√ prominent normal thymus visible in 50% of neonates + infants 0–3 years of age
√ **"notch" sign** = indentation at junction of thymus + heart
√ **"sail" sign** (5%) = triangular slightly right-convex density extending from superior mediastinum, usually on right side with sharply demarcated base caused by minor fissure
√ "wave" sign = rippled / undulated / scalloped / wavy lateral border due to indentation by ribs
√ shape changes with respiration + position

DDx: mediastinal mass, upper lobe pneumonia, atelectasis

CT:

√ measurement (perpendicular to axis of aortic arch):

› mean thickness of 11 (5) mm at < 20 (> 50) years
› maximal thickness of < 18 (< 13) mm at < 20 (> 20) years
√ visualization of thymus:
√ detected in 83% (17%) of subjects < 50 (> 50) years of age
√ shape of thymus:
√ quadrilateral with convex borders in child < 5 years
√ triangular like an arrowhead (62%), bilobed (32%), single lobe (6%) in older child
√ density of thymus:
√ muscular density of 30 HU (before puberty)
√ flat / concave borders with abundant fat (after puberty)

US (supra-, trans-, parasternal approach in infants):
√ homogeneous finely granular echotexture with multiple linear / branching echogenic foci
√ mildly hypoechoic (25%) / isoechoic (75%) to liver, spleen, thyroid
√ smooth well-defined margin ← fibrous capsule
√ hypo- / avascular
N.B.: pliable organ WITHOUT causing compression / displacement of adjacent structures

MR:
√ homogeneous texture hyperintense to muscle on T1WI
√ signal intensity close to fat on T2WI

PET:
√ usually barely visible
√ striking FDG avidity in rebound hyperplasia

Ectopic Thymus

√ solid mass of identical attenuation / signal as normal thymus
√ often connected to normal thymus
√ cystic mass (= endodermal-lined cavity of thymopharyngeal duct / cystic degeneration of Hassall corpuscles or glandular epithelium)

(1) Unilateral failure of thymic primordium to descend
√ neck mass of thymic tissue on one side of neck
√ ipsilateral absence of normal thymic lobe
√ parathyroid tissue within ectopic thymus

(2) Small rest of thymus left behind within thymopharyngeal tract during migration ← failure to involute
√ neck mass (32%)
√ normally positioned bilobed thymus

(3) Atypical location ← sequestration: trachea, skull base, intrathyroidal, behind thyroid (26%), adjacent to SVC / brachiocephalic vessels / aorta, posterior mediastinum, dermis
√ widened superior mediastinum

Rx: no treatment unless symptomatic

DIAPHRAGM

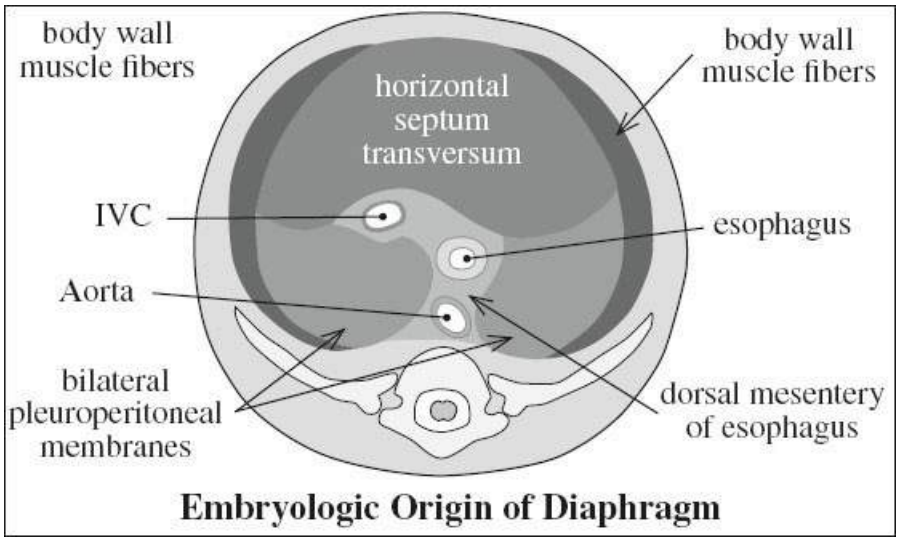
= musculofibrous septum separating abdominal + thoracic cavities

Time of formation: 4th–12th weeks of embryonic life

Embryologic precursors & final structures:

ventral septum transversum → gradually extends posteriorly around esophagus + great vessels → fuses with foregut mesentery → forms posteromedial portions by 8th week → lateral margins of diaphragm from muscles of thoracic wall → posterolaterally located pleuroperitoneal foramina close last

(1) Septum transversum ventrally during 3rd–5th week → central tendon
(2) Pleuroperitoneal membrane → muscular diaphragm
(3) Dorsal mesentery of esophagus → median portion of diaphragm and crura
(4) Body wall → peripheral muscle fibers of diaphragm attached to
    (a) sternum
    (b) costal margin of inferior ribs
    (c) lumbar portion
        › arcuate ligaments = 2 pairs of medial + lateral lumbocostal arches
            » **medial arcuate ligament**: arches over psoas major m. + attaches to anterior aspect of transverse process of L1
            » **lateral arcuate ligament**: arches over quadratus lumborum m. + attaches laterally to 12th rib + medially to anterior aspect of transverse process of L1
        › diaphragmatic crura = bilateral musculotendinous pillars attaching to anterolateral surface of lumbar vertebrae + intervertebral fibrocartilage:
            » L1-L3 for longer + broader **right crus**
            » L1-L2 for shorter **left crus**
            [*crus*, Latin = shin, leg, pillar support of a bridge]
            » medial fibers of ascending crura join to form an arch ventral to aorta just above celiac trunk = **median arcuate ligament**



Embryologic Origin of Diaphragm

Function: major respiratory muscle for quiet breathing (in concert with accessory muscles of respiration); contraction → expansion of thoracic cavity → ⇓ intrathoracic pressure → drawing of air into lungs

Openings: (1) aortic hiatus at T12 behind median arcuate lig.
(2) esophageal hiatus at T10
(3) vena cava hiatus at T8 through central tendon

(4) Medial arcuate ligament covering psoas muscle
(5) Lateral arcuate ligament covering quadratus lumborum muscle

Innervation: both phrenic nerves (C3-C5) + lower intercostal nn.

Blood supply: aorta → internal thoracic a. + inferior phrenic aa. → pericardiophrenic a. + musculophrenic artery

Pleuroperitoneal pressure gradient: negative 7–22 cm H_2O

US:

√ thick echogenic line = specular reflection from air-diaphragm interface
√ thin hypoechoic line = diaphragmatic muscle
√ both domes are visualized together (on oblique transverse subxiphoid view obtained from midline position)

CXR:

@ Infant / young child:
√ right dome of diaphragm at level of anterior 6th rib
√ left dome of diaphragm at level of anterior 7th rib (= one intercostal space lower)

@ Adult
√ right dome at 9.7 ± 0.8 (range, 7.4–11.3) thoracic vertebral levels below the top of 1st thoracic vertebra
√ left dome at 10.2 +/- 0.8 (range, 8.1–11.8) thoracic vertebral levels below the top of 1st thoracic vertebra
◊ Position of diaphragm tends to be <u>lower</u> with higher age, lower weight, smaller thoracic dimensions; <u>flatter</u> with higher age, weight, transverse thoracic dimension, pack-years smoked, and male gender

Diaphragmatic Variants

1. Diaphragmatic slip
   = fold / strip of muscle bundle protruding from inferior surface of diaphragm ± indentation of liver or spleen
   DDx: peritoneal implant, lymph node, mass
2. Hypertrophic median arcuate ligament
   = fibrous arch uniting diaphragmatic crura passing over aorta
   (a) superior to origin of celiac trunk (85%)
   (b) crossing over proximal portion of celiac trunk → vessel indentation (15%) → celiac artery compression / median arcuate ligament syndrome
3. Partial duplication of diaphragm (R > L)
   Associated with: cardiovascular malformations, ipsilateral pulmonary maldevelopment
   √ duplicated accessory diaphragm extends obliquely upward + backward to attach to 3rd–7th ribs posteriorly
   √ lower lung lobe may be partially / completely contained within accessory diaphragm + true hemidiaphragm
4. Diaphragmatic discontinuity (11%)
   Location: between crura + lateral arcuate ligaments
   DDx: diaphragmatic rupture

Retrocrural Space

= triangular region forming the most inferior portion of the posterior mediastinum

Boundaries:

› anteriorly and laterally: diaphragmatic crura decussating in front of aorta

› posteriorly: ventral aspect of vertebral bodies

Communication: posterior mediastinum + retroperitoneum

Contents:

› vessels:

» aorta and its arterial branches (= lower posterior intercostal + subcostal arteries)

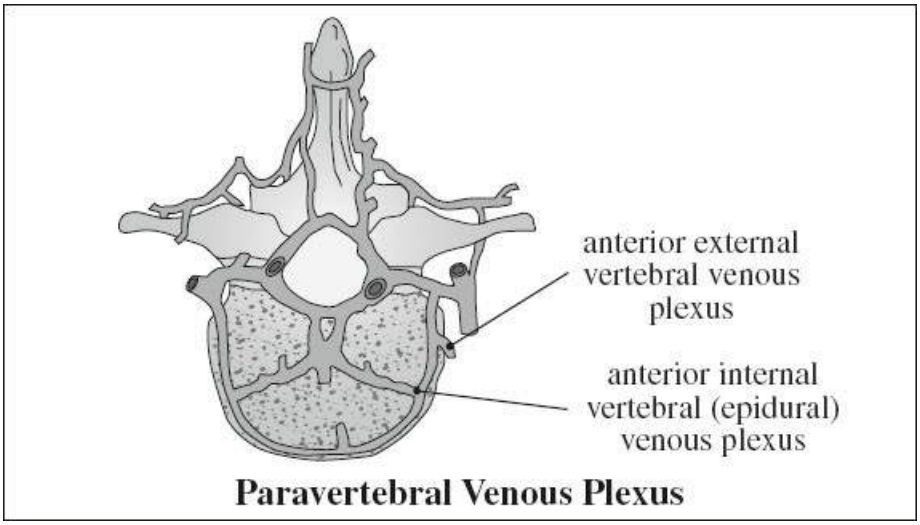
» azygos vein (R), hemiazygos vein (L)

» ascending lumbar venous plexus = valveless venous system freely communicating along entire extent of spine

› nerves: sympathetic trunks + splanchnic nerves

› lymphatics: lymph nodes (draining stations for posterior diaphragm, posterior mediastinum, lumbar spine), thoracic duct, cisterna chyli

› fat



Paravertebral Venous Plexus

Cisterna Chyli

= bulbous dilatation formed by convergence of lymphatic channels at level of upper lumbar vertebral bodies

Location: usually to right of aorta (occasionally left-sided / retroaortic)

› receives 2 afferent lumbar and intestinal lymphatic trunks

› ascends as thoracic duct

√ tubular shape (most common, in 30–43%) / rounded / oval / plexiform / fusiform:

Lymphangiography: visualized in 52%

CT: visualized in 1.7%

√ low near-water attenuation

√ delayed enhancement after oral ingestion of ethiodized oil / IV injection of contrast material

MR: visualized in 15%–96%

Thoracic Duct

Origin: arises from cisterna chyli anterior to L1-L2 (10–15 mm in diameter and 5–7 cm long)

Course: enters thorax through aortic hiatus; ascends in right prevertebral location (between azygos vein and descending aorta); swings to left at T4–6 posterior to esophagus; ascends for a short distance along right of aorta; crosses behind aortic arch; runs ventrally at T3 between left common carotid artery + left subclavian artery

Termination: 3–5 cm above clavicle at venous angle (= junction of left subclavian + internal jugular veins)

Variation: two (33%) or more (in up to 50%) main ducts each consisting of up to 8 separate channels

Azygos Vein

= major tributary of SVC

Origin: arises from junction of lumbar azygos with right ascending lumbar + subcostal vein

Course: travels along right anterior borders of thoracic vertebrae up to level of carina → traverses middle mediastinum → arches over right tracheobronchial angle → drains posteriorly into distal SVC

Azygos arch: on PA CXR at tracheobronchial angle = inferior margin of right paratracheal stripe

Transverse diameter: 6–7 mm (normal); 10 mm (upper limits); up to 15 mm (in pregnancy)

CHEST DISORDERS

AIDS

= ACQUIRED IMMUNE DEFICIENCY SYNDROME

= ultimately fatal disease characterized by HIV seropositivity, specific opportunistic infections, specific malignant neoplasms (Kaposi sarcoma, Burkitt lymphoma, primary lymphoma of brain)

= patient with CD4 cell count < 200 cells/μL (normal range, 800–1,200 cells/μL)

Prevalence: 36.9 million HIV infections worldwide with 2 million new infections (2014); 47,352 North Americans newly infected with HIV with 13,712 deaths from AIDS (2013); 13% unaware of infection; > 50% develop pulmonary disease

Organism: human immunodeficiency virus (HIV) = human T-cell lymphotropic virus type III (HTLV III) = lymphadenopathy-associated virus (LAV)

Pathomechanism:

HIV retrovirus attaches to CD4 molecule on surface of T-helper lymphocytes + macrophages + microglial cells; after cellular invasion HIV genetic information is incorporated into cell's chromosomal DNA; virus remains dormant for weeks to years; after an unknown stimulus for viral replication CD4 lymphocytes are destroyed (normal range of 800–1,000 cells/mm^3) and others become infected leading to impairment of the immune system; CD4 lymphocyte number and function decreases (at a rate of ~ 50–80 cells/year)

AIDS-defining illness related to CD4 T-lymphocyte count [cells/μL]:

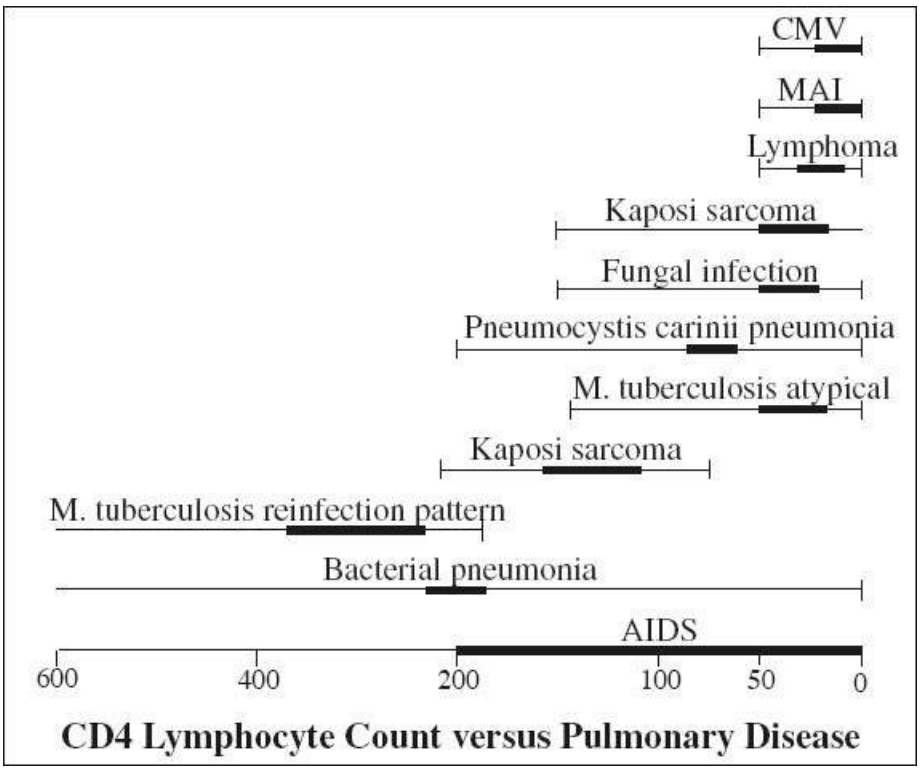
< 400	extrapulmonary Mycobacterium tuberculosis, Kaposi sarcoma
< 200	Candida albicans (thrush, hairy leukoplakia), Histoplasma capsulatum, Cryptosporidium species, Pneumocystis carinii pneumonia, non-Hodgkin lymphoma
< 150	cerebral toxoplasmosis
< 100	Cytomegalovirus, Herpes simplex virus, Mycobacterium avium complex (intestinal CMV + MAI infection)
< 50	AIDS-related lymphoma

Prognosis: median survival with a CD4 lymphocyte count of < 50 cells/mm^3 is 12 months

Transmission by: intimate sexual contact, exposure to contaminated blood / bloody body secretions

Groups at risk:

1. Homosexual males (74%)
2. IV drug abusers (16%)



CD4 Lymphocyte Count versus Pulmonary Disease

3. Recipients of contaminated blood products (3%)
4. Sexual partner of drug abuser + bisexual man
5. Infants born to a woman infected with HIV virus

◊ HIV antibodies present in > 50% of homosexuals + 90% of IV drug abusers!

◊ Rate of heterosexual transmission is increasing!

Clinical classification:

group I acute HIV infection with seroconversion

group II asymptomatic HIV infection

group III persistent generalized lymphadenopathy

group IV other HIV disease

- › subgroup A constitutional disease
- › subgroup B neurologic disease
- › subgroup C secondary infectious disease
- › subgroup D secondary cancers
- › subgroup E other conditions

AIDS-defining pulmonary conditions (CDC, 1993):

(1) Tracheal / bronchial / pulmonary candidiasis
(2) Pulmonary CMV infection
(3) Herpes simplex bronchitis / pneumonitis
(4) Kaposi sarcoma
(5) Immunoblastic / Burkitt lymphoma
(6) Pneumocystis carinii pneumonia

(7) Mycobacterium tuberculosis / avium complex / kansasii
(8) Recurrent pneumonia

A. LYMPHADENOPATHY

Cause: reactive follicular hyperplasia = HIV adenopathy (50%), AIDS-related lymphoma (20%), mycobacterial infection (17%), Kaposi sarcoma (10%), metastatic tumor, opportunistic infection with multiple organisms, drug reaction

Location: mediastinum, axilla, retrocrural

B. OPPORTUNISTIC INFECTION

accounts for majority of pulmonary disease

◊ Pulmonary infection is often the first AIDS-defining illness!

1. **Pneumocystis jirovecii pneumonia** (60–80%) (formerly Pneumocystis carinii pneumonia)

20–40% develop > 1 episode during disease

- CD4+ T helper lymphocyte cell count ≤ 200/mm³
- subacute insidious onset with malaise, minimal cough

√ bilateral ground-glass infiltrates without effusion / adenopathy
√ bilateral perihilar interstitial infiltrates
√ diffuse bilateral alveolar infiltrates
√ frequently associated with pneumatoceles
√ apical predominance (in patients on prophylactic aerosolized pentamidine)

Mortality: in 25% fatal

2. Fungal disease (< 5%)

(a) **Cryptococcus neoformans pneumonia** (2–15%) usually associated with brain / meningeal disease
√ segmental infiltrate + superimposed pulmonary nodules ± lymphadenopathy ± pleural effusion

(b) **Histoplasma capsulatum**
√ typically diffuse nodular / miliary pattern at time of diagnosis
√ normal CXR in up to 35%

(c) Coccidioides immitis
√ diffuse infiltrates + thin-walled cavities

(d) Candida albicans

(e) Aspergillus: less common + less invasive ← relative preservation of neutrophilic function
› invasive pulmonary aspergillosis
› chronic necrotizing aspergillosis
› necrotizing tracheobronchitis
› obstructing bronchopulmonary aspergillosis

3. Mycobacterial infection (10% per year)

(a) **M. tuberculosis** (increasing frequency)
◊ AIDS patients are 500 times more likely to become infected than general population!
√ postprimary TB pattern with upper-lobe cavitating infiltrate
- CD4 lymphocyte count of 200–500 cells/mm³

√ primary TB pattern with lung infiltrate / lung masses + hilar / mediastinal

lymphadenopathy + pleural effusion
• CD4 lymphocyte count of 50–200 cells/mm³)
√ atypical TB pattern with diffuse reticular / nodular infiltrates (CD4 lymphocyte count of < 50 cells/mm³)
√ adenopathy of low attenuation + rim enhancement

(b) **M. avium-intracellulare** (5%)
• in patients with low CD4 lymphocyte count only
√ diffuse bilateral reticulonodular infiltrates
√ adenopathy, miliary disease

(c) M. kansasii and others

4. Bacterial pneumonia (5–30%):

(a) Haemophilus influenzae, Streptococcus pneumoniae, Staphylococcus aureus
√ frequently multilobar distribution
• bacteremia (common)

(b) Nocardia pneumonia (< 5%)
usually occurs in cavitating pneumonia
√ segmental / lobar alveolar infiltrate ± cavitation ± ipsilateral pleural effusion

(c) Rhodococcus equi (aerobic, Gram-negative)
√ cavitary pneumonia

(d) Bartonella henselae (Gram-negative)
= bacillary angiomatosis
• cutaneous lesions
√ highly vascular small pulmonary nodules
√ dramatic enhancement of enlarged lymph nodes

5. **CMV pneumonia**
most frequent infection found at autopsy (49–81%), diagnosed before death in only 13–24%;
high prevalence combined with Kaposi sarcoma
• fever, nonproductive cough, dyspnea, hypoxia
√ bilateral hazy infiltrates, focal nodules, masses
√ scattered widespread ground-glass opacities
√ thickening of bronchovascular bundles
√ tree-in-bud pattern
√ bronchiectasis / bronchial wall thickening

6. Toxoplasmosis
√ coarse interstitial / nodular pattern
√ focal areas of consolidation ± cavities
DDx: indistinguishable from PCP

C. TUMOR

1. Kaposi sarcoma (15%)
2. **AIDS-related lymphoma** of B-cell origin (2–5%) primarily immunoblastic NHL / Burkitt lymphoma / non-Burkitt lymphoma; occasionally Hodgkin disease
Location: pulmonary involvement (8–15%), CNS, GI tract, liver, spleen, bone marrow
Site: primarily extranodal
√ pleural effusion (50%)

√ hilar / mediastinal adenopathy (25%) ± axillary / supraclavicular / cervical adenopathy
√ solitary / multiple well-defined pulmonary nodules (occasionally with doubling times of 4–6 weeks)
√ diffuse bilateral reticulonodular heterogeneous opacities
√ alveolar infiltrates
√ paraspinal masses

D. LYMPHOID INTERSTITIAL PNEUMONITIS
Age: in children < 13 years of age

E. SEPTIC EMBOLI

F. PREMATURE DEVELOPMENT OF BULLAE (40%) with disposition to spontaneous pneumothorax

AIDS-related Complex (ARC)

= GENERALIZED LYMPHADENOPATHY SYNDROME
= prodromal phase of HIV seropositivity, generalized lymphadenopathy, CNS diseases other than those associated with AIDS
Time interval: ~ 10 years between seroconversion + clinical AIDS
• weight loss, malaise, diarrhea
• fever, night sweats, lymphadenopathy
• lymphopenia with selective decrease in helper T-cells

ADULT RESPIRATORY DISTRESS SYNDROME

= SHOCK LUNG = POSTTRAUMATIC PULMONARY INSUFFICIENCY = HEMORRHAGIC LUNG SYNDROME = RESPIRATOR LUNG = STIFF LUNG SYNDROME = PUMP LUNG = CONGESTIVE ATELECTASIS = OXYGEN TOXICITY = ACUTE RESPIRATORY DISTRESS SYNDROME
= severe unexpected life-threatening acute respiratory distress characterized by abrupt onset of marked dyspnea, increased respiratory effort, severe hypoxemia associated with widespread airspace consolidation

Etiology:
◊ ARDS is the most severe form of permeability edema associated with diffuse alveolar damage

A. PRIMARY = DIRECT INJURY (← pulmonary disease)
= exposure to chemical agents, infectious pathogens, gastric fluid, toxic gas
Associated with: pulmonary consolidation

B. SYSTEMIC CONDITION (← extrapulmonary disease)
= sepsis, pancreatitis, severe trauma, blood transfusion → systemic biochemical cascade creating oxidating agents, inflammatory mediators, enzymes
Associated with: interstitial edema, alveolar collapse

Histo:
› up to 12 hr: fibrin + platelet microemboli
› 12–24 hr: interstitial edema
› 24–48 hr: capillary congestion, extensive interstitial + alveolar proteinaceous edema + hemorrhage, widespread microatelectasis, destruction of type I alveolar

epithelial cells

› 5–7 d: extensive hyaline membrane formation, hypertrophy + hyperplasia of type II alveolar lining cells

› 7–14 d: extensive fibroblastic proliferation in interstitium + within alveoli, rapidly progressing collagen deposition + fibrosis; almost invariably associated with infection

Predisposed:

hemorrhagic / septic shock, massive trauma (pulmonary / general body), acute pancreatitis, aspiration of liquid gastric contents, heroine / methadone intoxication, massive viral pneumonia, traumatic fat embolism, near-drowning, conditions leading to pulmonary edema

mnemonic: DICTIONARIES

Disseminated intravascular coagulation
Infection
Caught drowning
Trauma
Inhalants: smoke, phosgene, NO_2
O$_2$ toxicity
Narcotics + other drugs
Aspiration
Radiation
Includes pancreatitis
Emboli: amniotic fluid, fat
Shock: septic, hemorrhagic, cardiogenic, anaphylactic

- initially few / no symptoms
- rapidly progressive dyspnea, tachypnea, cyanosis
- hypoxia unresponsive to oxygen therapy ← AV shunting
- NO increase in pulmonary capillary pressure

Stages (often overlapping):

1st (early / exudative) stage

= interstitial edema with high protein content rapidly filling the alveolar spaces associated with hemorrhage → ensuing hyaline membrane formation

√ interstitial edema (with high protein content) initially
√ perihilar areas of increased opacity following rapidly
√ widespread alveolar consolidation with predominantly peripheral cortical distribution
√ air bronchogram
√ gravitational gradient (best seen on CT) ← dependent atelectasis

DDx: cardiogenic edema (cardiomegaly, apical vascular distribution, Kerley lines)

2nd (proliferative) stage

= organization of fibrinous exudate + subsequent regeneration of alveolar lining + thickening of alveolar septa

√ inhomogeneous areas of patchy / diffuse ground-glass opacities

3rd (fibrotic) stage (after days to weeks)

= varying degrees of scarring
√ dependent gradient of consolidation (often)

√ bronchial dilatation with improvement / even resolution
√ ± progression to irreversible varicoid bronchial enlargement
√ subpleural and intrapulmonary cysts
Cx: pneumothorax

CXR:
√ NO cardiomegaly / pleural effusion
› up to 12 hours:
√ characteristic 12-hour delay between clinical onset of respiratory failure and CXR abnormalities
› 12–24 hours:
√ patchy ill-defined opacities throughout both lungs
› 24–48 hours:
√ massive airspace consolidation of both lungs
› 5–7 days:
√ consolidation becomes inhomogeneous ← resolution of alveolar edema
√ local areas of consolidation ← pneumonia
› > 7 days:
√ reticular / bubbly lung pattern ← diffuse interstitial + airspace fibrosis

ALPHA-1 ANTITRYPSIN DEFICIENCY

= rare autosomal recessive disorder
Source: alpha-1 antitrypsin (glycoprotein) is to > 90% synthesized in hepatocytes + released into serum
Gene: codominant gene expression on chromosome 14 with > 100 genetic variants of the protein; most severe hepatopulmonary manifestations result from homozygous PiZZ phenotype
Action: proteolytic inhibitor of neutrophil elastase, trypsin, chymotrypsin, plasmin, thrombin, kallikrein, leukocytic + bacterial proteases; neutralizes circulating proteolytic enzymes
Mode of injury from deficiency:
PMNs + alveolar macrophages sequester into lung during recurrent bacterial infections + release neutrophil elastase, which acts unopposed + digests basement membrane
Age: early age of onset (20–30 years); M÷F = 1÷1
• rapid + progressive deterioration of lung function:
• dyspnea in 4th and 5th decade
◊ 20% of homozygotic individuals never develop clinically apparent emphysema
• chronic sputum production (50%)
√ severe panacinar emphysema with basilar predominance ← gravitational distribution of pulmonary blood flow:
√ ↓ in size + ↓ in number of pulmonary vessels in lower lobes
√ redistribution of blood flow to unaffected upper lung zones
√ bullae at both lung bases
√ marked flattening of diaphragm
√ minimal diaphragmatic excursion
√ multilobar cystic bronchiectasis (40%)

√ hepatopulmonary syndrome
Cx: hepatic cirrhosis (in homozygotic individuals)
◊ Most common metabolic liver disease in children
Prognosis: 15–20-year decrease in longevity in smokers relative to nonsmokers

ALVEOLAR MICROLITHIASIS

= very rare disease of unknown etiology characterized by myriad of calcospherites (= microliths composed of calcium + phosphorus) within alveoli
Cause: autosomal recessive inheritance of a gene mutation preventing production of a transporter protein for sodium-dependent transfer of phosphate into type II pneumocytes → phosphorus ions stay in alveolar space
Age peak: 30–50 years; begins in early life; has been identified in utero; M÷F = 1÷1; in 50% familial (in at least one sibling)
• usually asymptomatic (70%)
• progressive dyspnea on exertion, cyanosis, clubbing of fingers
• striking discrepancy between marked radiographic findings and mild clinical symptoms
• NORMAL serum calcium + phosphorus levels
• restrictive lung disease (↓ in residual volume and ↓ diffusion capacity)
Distribution: predisposition for posterior segments of lower lobes + anterior segments of upper lobes; medial lung >> lateral lung
√ very fine, sharply defined, sandstorm-like micronodular (< 1 mm) pattern
√ diffuse involvement of both lungs
√ obscuration of mediastinal + diaphragmatic reflections
√ vertical linear radiolucency between ribs + lung parenchyma ← subpleural cystic changes
√ intense uptake on bone scan
HRCT:
√ thickening + micronodulation of interlobular septa ← innumerable microliths within periphery of secondary pulmonary lobule
√ thickened micronodular appearance of bronchovascular + subpleural interstitium
√ pleural calcifications
√ ground-glass appearance (of microliths < 1 mm) ± "crazy paving" pattern
Prognosis:
(a) late development of pulmonary insufficiency ← interstitial fibrosis + cor pulmonale
(b) disease may become arrested
(c) microliths may continue to form / enlarge
Rx: NO effective treatment aside from lung transplant
Dx: open lung biopsy
DDx: (1) Pulmonary alveolar proteinosis, sarcoidosis, pneumoconiosis, pulmonary hemosiderosis, amyloidosis, miliary tuberculosis, metastatic pulmonary calcifications of renal failure
(2) "Mainline" pulmonary granulomatosis (IV abuse of talc-containing drugs such as methadone, rarely as numerous + scarring + loss of volume)

ALVEOLAR PROTEINOSIS

= PULMONARY ALVEOLAR PROTEINOSIS (PAP)
= rare disorder characterized by accumulation of lipoproteinaceous material in alveoli ← altered surfactant homeostasis

Forms:

A. CONGENITAL PAP
B. PRIMARY ACQUIRED PAP (90%)
   Age: median 39 years; M>> F
   Predisposed: smoking in 72%
C. SECONDARY PAP
   Cause: hematologic cancers, pharmacologic immunosuppression, inhalation of inorganic dust (eg, silica), toxic fumes, certain infections
   Pathophysiology: functional impairment / reduced number of alveolar macrophages

Etiology: ?; associated with dust exposure (eg, silicoproteinosis is histologically identical to PAP), immunodeficiency, hematologic + lymphatic malignancies, AIDS, chemotherapy

Pathophysiology:

(a) overproduction of surfactant by granular pneumocytes
(b) defective clearance of surfactant by alveolar macrophages

Histo: alveoli filled with proteinaceous material (the ONLY pure airspace disease), normal interstitium

Age peak: 39 years (range, 2–70 years); M÷F = 3÷1

• asymptomatic (10–20%), gradual onset of dyspnea + cough
• weight loss, weakness, hemoptysis, defect in diffusing capacity

√ bilateral air-space disease with ill-defined nodular / confluent ground-glass pattern:
  √ perihilar predominance of "bat-wing" configuration WITHOUT signs of left-sided heart failure
√ small acinar nodules + coalescence + consolidation
√ patchy peripheral / primarily unilateral infiltrates (rare)
√ reticular / reticulonodular / linear interstitial pattern with Kerley B lines (late stage)
√ slow clearing over weeks or months
√ slow progression (⅓), remaining stable (⅔)
√ NO adenopathy, NO cardiomegaly, NO pleural effusion

HRCT:

√ crazy-paving pattern = combination of patchy ground-glass opacities + smooth interlobular septal thickening often in geographic distribution
√ sharp demarcation between normal + abnormal lung
√ consolidation

Cx: susceptible to pulmonary infections ← poorly functioning macrophages + excellent culture medium for opportunistic pathogens (esp. Nocardia asteroides), other common respiratory pathogens

Prognosis:

highly variable course with clinical and radiologic episodes of exacerbation + remissions

(a) 50% improvement / recovery
(b) 30% death within several years under progression

Dx: bronchoalveolar lavage, transbronchial / open lung biopsy
Rx: bronchopulmonary lavage
DDx:
(a) during acute phase: pulmonary edema, diffuse pneumonia, ARDS
(b) in chronic stage:
1. Idiopathic pulmonary hemosiderosis (boys, symmetric involvement of mid + lower zones, progression to nodular + linear pattern)
2. Hemosiderosis (bleeding diathesis)
3. Pneumoconiosis
4. Hypersensitivity pneumonitis
5. Goodpasture syndrome (more rapid changes, renal disease)
6. Desquamative interstitial pneumonia ("ground-glass" appearance, primarily basilar + peripheral)
7. Pulmonary alveolar microlithiasis (widespread discrete intraalveolar calcifications primarily in lung bases, rare familial disease)
8. Sarcoidosis (usually with lymphadenopathy)
9. Lymphoma
10. Bronchioloalveolar cell carcinoma (more focal, slowly enlarging with time)

AMNIOTIC FLUID EMBOLISM

= most common cause of maternal peripartum death
• dyspnea, shock during / after labor + delivery
Pathogenesis: amniotic debris enters maternal circulation resulting in:
(1) Pulmonary embolization
(2) Anaphylactoid reaction
(3) DIC
√ usually fatal before radiographs obtained
√ may demonstrate pulmonary edema

AMYLOIDOSIS OF THE CHEST

= disease characterized by an extracellular deposition of insoluble fibrillar proteins aggregating into twisted ß-pleated sheets of great chemical diversity
Histo: protein (immunoglobulin) / polysaccharide complex; affinity for Congo red stain

Pulmonary Amyloidosis

Frequency: 1° amyloidosis (in up to 70%), 2° amyloidosis (rare)
A. NODULAR PARENCHYMAL TYPE (most common)
Age: 50–60 years of age; M÷F = 1÷1
• usually asymptomatic, incidental discovery on CXR
Size: 5–15 cm
Site: subpleural / peripheral
Distribution: concentrated in lower lobes
√ solitary mass = **amyloidoma** (60%)
√ multiple pulmonary nodules:

√ smooth lobulated / spiculated margins
√ cavitation (rare)
√ ± central calcification / ossification (in up to 50%)
DDx: chronic renal failure
√ mediastinal / hilar adenopathy
Dx: AL amyloid (= amyloid light chain) on biopsy
Prognosis: excellent with slow progression over years; incurable; treatment rarely required
Rx: low-dose prednisone, colchicine
DDx: metastatic disease, granulomatous disease (fungal, TB), rheumatoid lung, sarcoidosis, mucoid impaction, bronchogenic carcinoma, chondroma

Classification of Amyloidosis

Subtype	*Common Anatomic Distribution*	*Fibrillar protein*	*Common Disease Associations*	*Treatment*
Primary amyloidosis	multiple organs	amyloid light chain (AL)	plasma cell dyscrasias (eg, multiple myeloma)	chemotherapy (melphalan, steroids), stem cell transplantation
Secondary amyloidosis	single organ	serum amyloid A (AA)	chronic infection (eg, osteomyelitis), chronic systemic inflammation (eg, rheumatoid arthritis)	symptomatic (eg, diuresis in cardiac amyloidosis, surgery in tracheal amyloidosis), treatment of underlying condition

B. DIFFUSE ALVEOLAR SEPTAL TYPE (least common)
◊ Most commonly associated with systemic amyloidosis
Age: > 60 years of age
May be associated with: concurrent systemic involvement
• usually asymptomatic with normal CXR
• cough + dyspnea with abnormal CXR

CT:
√ well-defined scattered 2–4 mm micronodules
√ reticulations = widespread small irregular densities (exclusively interstitial involvement) ± calcification
√ interlobular septal thickening
√ may become confluent ± honeycombing
Distribution: basal + peripheral predominance

√ punctate lung calcifications
√ pleural thickening
√ ± pleural effusion
√ rarely associated with thin-walled cysts (most commonly in Sjögren syndrome)
Dx: AL amyloid (= amyloid light chain) on biopsy
Prognosis: median survival of 16 months ← pulmonary hypertension, respiratory failure
DDx: pneumoconiosis (especially asbestosis), idiopathic pulmonary fibrosis, rheumatoid lung, Langerhans cell histiocytosis, scleroderma, cancer with lymphangitic spread

Airway Amyloidosis (2nd most common manifestation)
= TRACHEOBRONCHIAL TYPE
= diffuse / solitary (rarely) submucosal deposition of amyloid in trachea + segmental airways
Age: 50–70 years; M > F

Rarely associated with: systemic amyloidosis
- hemoptysis (most frequent complaint)
- stridor, cough, dyspnea, hoarseness, wheezing

CXR: notoriously insensitive

CT:
√ diffuse rigid narrowing of a long tracheal segment (best depicted on COR and SAG reconstructions)

√ calcified / ossified tracheal wall also affecting posterior membrane of trachea (DDx to tracheobronchopathia osteochondroplastica / relapsing polychondritis)
√ luminal narrowing by multiple nodules protruding from wall of trachea / large bronchi
√ prominent bronchovascular markings
√ obstruction with consolidation
√ atelectasis
√ hyperinflation
√ bronchiectasis
√ destructive pneumonitis

PET/CT:
√ increased FDG uptake may allow detection of early amyloidosis + response to treatment

Cx: recurrent pneumonia
Rx: local bronchoscopic resection, laser therapy, stent placement, radiation therapy
Prognosis: 30–50% 5-year survival; worse for proximal disease
DDx: endobronchial neoplasm

Mediastinal Amyloidosis (3rd most common manifestation)
Commonly associated with: systemic amyloidosis
Location: multistation lymphadenopathy / anatomically localized isolated tumefactive amyloidoma
- asymptomatic lymphadenopathy (frequent)

√ enhancing lymphadenopathy
√ punctate / diffuse / eggshell lymph node calcifications

ASBESTOS-RELATED DISEASE

[*asbestos*, Greek = inextinguishable = several fibrous silicate minerals sharing the property of heat resistance]

Substances:

Aspect (length-to-diameter) ratio effects carcinogenicity:
eg, aspect ratio of 32 = 8 µm long x 0.25 µm wide

› commercial <u>amphiboles</u>: straight, rigid, needlelike
  - crocidolite = blue / black asbestos
  - amosite = brown asbestos

› commercial <u>serpentines</u> (= nonamphiboles):
  - chrysotile = white asbestos (the only mineral in the serpentine group accounting for > 90% of asbestos used in the USA)

› noncommercial contaminated amphiboles

- actinolite; anthophyllite; tremolite

(a) relatively benign:
  (1) Chrysotile in Canada
  (2) Anthophyllite in Finland, North America
  (3) Tremolite

(b) relatively malignant:
  (1) Crocidolite in South Africa, Australia
  (2) Amosite

◊ Very fine fibers (crocidolite) are associated with the largest number of pleural disease!

◊ Asbestos fibers up to 100 μm in length

Occupational exposure:

(a) asbestos mining, milling, processing

(b) insulation manufacturing, textile manufacturing, construction and demolition, pipe fitting, shipbuilding, gaskets, brake linings

Pathophysiology:

asbestos-activated macrophages produce a variety of growth factors that interact to induce fibroblast proliferation; oxygen-free radicals released by macrophages damage proteins + lipid membranes sustaining the inflammatory process

Asbestos-related Pleural Disease

1. **Pleural Effusion** (21%)

= earliest asbestos-related pleural abnormality, frequently followed by diffuse pleural thickening + rounded atelectasis

Prevalence: 3% (higher with increasing levels of asbestos exposure)

Latency period: 8–10 years after exposure

- **benign asbestos pleurisy**:
  - may be associated with chest pain (⅓)
  - usually small sterile serous / hemorrhagic exudate

√ recurrent bilateral effusions

√ ± plaque formation

DDx: TB, mesothelioma

2. **Focal Pleural Plaques** (65%)

= hyalinized collagen in submesothelial layer of parietal pleura

◊ Most useful marker of asbestos exposure!

Frequency: most common manifestation of exposure; 6% of general population will show plaques; 3–14% of dockyard workers; 58% of insulation workers

Latency period: in 10% (50%) after 20 (40) years

Histo: dense hypocellular undulating collagen fibers often arranged in a "basket weave" pattern ± focal / massive calcifications; may contain large numbers of asbestos fibers (almost exclusively chrysotile)

Location: bilateral + multifocal; posterolateral chest wall between 7th–10th rib following rib contours; lateral chest wall between 6th–9th rib; aponeurotic dome of diaphragm; mediastinum

◊ Apices + costophrenic angles are spared!

◊ RARE in fissures of lung (visceral pleura)

Site: parietal pleura (visceral pleura typically spared)

• asymptomatic, no functional impairment

CXR:

√ geographic / holly leaf-shaped veil-like opacity

√ localized sharply marginated pleural thickening

CT (more sensitive + specific):

√ usually focal nodular area of pleural thickening (< 1 cm thick) with edges thicker than central portions of plaque; in 48% only finding; in 41% with parenchymal changes; stable over time

√ thin layer of extrapleural fat separates plaque from underlying rib + intercostal muscle

√ "hairy plaque" = visceral pleural plaque + underlying short interstitial lines radiating from plaque (rare)

√ no hilar adenopathy

√ calcified (in 10–15% by X-ray, in 15–20% by CT)

Prognosis: NO risk of malignant degeneration; increased risk of developing mesothelioma + bronchogenic carcinoma

DDx: chest wall fat, rib fractures, rib companion shadow

3. **Pleural Calcification** (21–25–60%)

◊ HALLMARK of asbestos exposure!

◊ detected by CXR (CT) in 25% (60%)

Latency: 20% (40%) become visible in > 20 (40) years

Histo: calcification starts in parietal pleura; calcium deposits may form within center of plaques

√ dense lines paralleling the chest wall, mediastinum, pericardium, diaphragm

◊ Bilateral diaphragmatic calcifications with clear costophrenic angles are PATHOGNOMONIC!

√ advanced calcifications are leaflike with thick-rolled edges

DDx: talc exposure, hemothorax, empyema, therapeutic pneumothorax for TB (often unilateral, extensive sheetlike, on visceral pleura)

4. **Diffuse Pleural Thickening** (17%)

= smooth uninterrupted diffuse thickening of parietal pleura extending over at least ¼ of chest wall (visceral pleura involved in 90%, but difficult to demonstrate)

• may cause restriction of pulmonary function

May be associated with: rounded atelectasis

√ bilateral process with "shaggy heart" appearance (20%)

√ smooth (difficult to assess when viewed en face)

√ thickening of interlobar fissures

√ focally thickened diaphragm

√ obliterated costophrenic angles (minority of cases)

DDx: pleural thickening from parapneumonic effusion, hemothorax, connective tissue disease

Pulmonary Asbestosis

= (term "asbestosis" reserved for) chronic progressive diffuse interstitial pulmonary fibrosis

← inhalation of asbestos fibers

Frequency: in 49–52% of industrial asbestos exposure; 1,229 new cases annually in USA (2013)

Latency period: 40–45 years; dose-effect relationship

Histo: interstitial fibrosis begins around respiratory bronchioles, then progresses to involve adjacent alveoli

Diagnostic criteria:

1. Reliable history of exposure
2. Appropriate time interval between exposure + detection
3. Radiographic opacities classified as ILO s,t,u
4. Restrictive pattern of lung impairment
5. Diffusing capacity below normal range
6. Bilateral crackles at posterior lung bases, NOT cleared by cough

- dyspnea
- restrictive pulmonary function tests: progressive reduction of vital capacity + diffusing capacity
- asbestos bodies in macrophages from bronchoalveolar lavage (BAL) fluid (= single asbestos fiber surrounded by segmented protein-iron coat)

Location: lower posterior bases > apices

Site: most severe in subpleural zones (asbestos fibers concentrate beneath visceral pleura)

CXR:

√ small irregular linear opacities (NOT rounded as in coal / silica) progressing from fine to coarse reticulations:
  √ confined to lung bases, progressing superiorly
  √ septal lines (= fibrous thickening around 2ndary lobules)
  √ honeycombing (uncommon)

√ "shaggy" (obscured) heart border ← parenchymal + pleural changes

√ ill-defined outline of diaphragm

√ rarely massive fibrosis, predominantly at lung bases without migration toward hilum (DDx from silicosis / CWP)

√ ABSENCE of hilar / mediastinal adenopathy (if present consider other diagnosis)

HRCT:

◊ Obtain scan in prone position to differentiate from gravity-related physiologic phenomena

√ thickened intralobular lines as initial finding ← centrilobular peribronchiolar fibrosis:
  √ multiple subpleural curvilinear branching lines ("subpleural pulmonary arcades") = dotlike reticulonodularities connected to the most peripheral branch of pulmonary artery
  Site: most prominent posteriorly parallel to and within 1 cm of pleura

√ thickened interlobular septal lines (= interlobular fibrotic / edematous thickening):
  √ reticulations = network of linear densities, usually posteriorly at lung bases
  √ architectural distortion of lobule

√ parenchymal band formation = linear < 5 cm long + several mm wide opacity, often extending to pleura, which may be thickened + retracted at site of contact

√ subpleural curvilinear lines
√ patchy areas of ground-glass attenuation (= alveolar wall thickening due to fibrosis / edema)
√ honeycombing = multiple cystic spaces < 1 cm in diameter with thickened walls
NUC:
√ ^{67}Ga uptake gives a quantitative index of inflammatory activity
Cx: pulmonary fibrosis, pleuropulmonary malignancy (latency period of > 20 years)
DDx: idiopathic pulmonary fibrosis (NO parietal pleural thickening)

Atelectatic Asbestos Pseudotumor

= ROUND ATELECTASIS = "FOLDED LUNG"
= infolding of redundant pleura accompanied by segmental / subsegmental atelectasis
◊ Most common of benign masses caused by asbestos exposure!
Location: posteromedial / posterolateral basal region of lower lobes (most common); frequently bilateral
√ 2.5–8 cm focal subpleural mass abutting a region of thickened pleura
√ size + shape show little progression, occasionally ↓ in size
CT:
√ rounded / lentiform / wedge-shaped peripheral mass
√ pleural thickening ± calcification always present and frequently greatest near mass
√ **"crow's feet"** = linear bands radiating from mass into lung parenchyma (54%)
√ **"vacuum cleaner"** / "comet" sign
= bronchovascular markings emanating from nodular subpleural mass + coursing toward ipsilateral hilum
√ **"Swiss cheese"** air bronchogram (18%)
√ partial interposition of lung between pleura + mass
√ volume loss of affected lobe ± hyperlucency of adjacent lung

Asbestos-related Malignancy

Estimated yearly asbestos-related deaths in USA (2013):
12,000–15,000 annually

Lung Cancer

Incidence: 180,000 new cases annually in USA; 20–25% of workers heavily exposed to asbestos
Occurrence related to:
(a) cumulated dose of asbestos fibers
(b) smoking (synergistic carcinogenic effect)
◊ 100-fold increased risk in smokers versus a 7-fold increased risk in nonsmokers!
(c) preexisting interstitial disease
(d) occupational exposure to known carcinogen
Latency period: 25–35 years
Associated with: increased incidence of gastric carcinoma
Histo: bronchioloalveolar cell carcinoma (most common); bronchogenic carcinoma (adenocarcinoma + SCC)

Location: at lung base / in any location if associated with smoking

Malignant Mesothelioma

Incidence: 2,686 new cases annually in USA (2013); 7,000-fold increase in incidence
Risk: 10% over lifetime of an asbestos worker; household members of asbestos worker; residents near asbestos mines and plants
Latency period: 20–40 years

Gastrointestinal Neoplasm

= pancreatic, liver, gallbladder, colon, rectal, stomach cancer
Frequency: 3-fold increase (weak link)

ASKIN TUMOR

= EXTRASKELETAL EWING SARCOMA = PRIMITIVE NEUROECTODERMAL TUMOR (PNET)
= uncommon tumor probably arising from intercostal nerves
Mean age: 14.5 years; M÷F = 1÷3; Caucasian
Path: neuroectodermal small cell tumor containing neuron-specific enolase (may also be found in neuroblastoma)
• chest wall mass with / without pain
• constitutional symptoms: fever, anorexia, weight loss
√ large tumor involving chest wall + pleura
√ high tumor vascularity
√ rib destruction (occasionally arising from rib) in 25–63%
√ often large malignant pleural effusion
√ pulmonary parenchymal disease (25%)
√ calcifications (10%)
√ ipsilateral hilar + mediastinal lymphadenopathy
√ ± pneumothorax ← pulmonary involvement
CT:
√ large unilateral heterogeneous chest wall mass with intra- and extrathoracic components
√ ± pleural, pericardial, diaphragmatic, vertebral, spinal extension and involvement
MR:
√ predominantly intermediate SI on T1WI + high SI on T2WI
√ prominent areas of high SI on T2WI ← hemorrhage + necrosis
√ commonly invasion of chest wall musculature + mediastinum + lung
NUC:
√ ↑ activity on bone scan + 111In-pentetreotide + ^{99m}Tc-MIBI
√ NO uptake on FDG PET
Metastatic to: lung, mediastinal nodes, bone (25%), CNS, liver, adrenal
◊ At presentation pulmonary metastases (in 38%) + mediastinal lymphadenopathy (in 25%)
Prognosis: median survival of 8 months
DDx: Ewing sarcoma, lymphoma, chest wall hamartoma in infancy

ASPERGILLOSIS

Organism:

Aspergillus fumigatus = intensely antigenic ubiquitous fungus in soil, water, decaying vegetable and animal matter existing as

(a) conidiophores = reproductive form releasing thousands of spores

(b) hyphae (= matured spores) characterized by 45° dichotomous branching pattern

Occurrence:

commonly in sputum of normal persons, ability to invade arteries + veins facilitating hematogenous dissemination

M÷F = 3÷1

Transmission: spore inhalation

Predisposed:

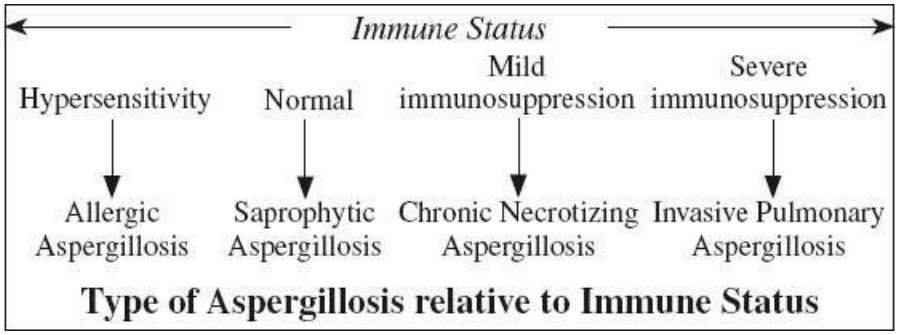
(a) preexisting lung disease (tuberculosis, bronchiectasis)

(b) impairment of immune system (alcoholism, advanced age, malnutrition, concurrent malignancy, poorly controlled diabetes, cirrhosis, sepsis)

- tracheo-bronchitis, bronchiolitis, bronchopneumonia
- fungal hyphae in lumen of airways
- positive precipitin test to Aspergillus antigen
- elevated Aspergillus-specific IgE, IgG-ELISA, polymerase chain reaction identification

Cx: dissemination to heart, brain, kidney, GI tract, liver, thyroid, spleen

◊ Sputum cultures are diagnostically unreliable because of normal (saprophytic) colonization of upper airways!



Type of Aspergillosis relative to Immune Status

Noninvasive Aspergillosis = Mycetoma Formation

= SAPROPHYTIC ASPERGILLOSIS

= noninvasive colonization of preexisting cavity / cyst in <u>immunologically normal</u> patients with cystic / cavitary lung disease like:

granulomatous disease [sarcoidosis (common), remote TB, atypical mycobacterial infection, Pneumocystis jirovecii], bronchiectasis, cystic fibrosis, abscess, bullous emphysema, carcinoma, traumatic pneumatocele, ankylosing spondylitis, Marfan syndrome, neurofibromatosis type 1

- blood-streaked sputum / severe hemoptysis (45–95%)
- elevated serum precipitins level for Aspergillus (50%)

√ solid round gravity-dependent mass within preexisting spherical / ovoid thin-walled cavity (= **Monad sign**):

[*monas*, Greek = single, alone; - *ad*, Greek suffix = group, unit]

Histo: **mycetoma** = aspergilloma = **fungus ball** = masslike collection of intertwined hyphae matted together with fibrin, mucus, cellular debris colonizing a pulmonary cavity

√ "air-crescent" sign = crescent-shaped air space separating fungus ball from nondependent cavity wall

√ fungus ball may calcify in scattered / rimlike fashion

√ pleural thickening adjacent to preexisting cyst / cavity = commonly first sign before visualizing mycetoma

Cx: life-threatening hemoptysis with mycetoma

N.B.: search for hypertrophied bronchial arteries as road map for bronchial artery embolization

Dx: transthoracic needle biopsy / bronchial washings

DDx of other organisms causing fungus ball:

Candida albicans, Pseudallescheria boydii, Coccidioides immitis, Nocardia, Actinomyces

Semiinvasive Aspergillosis

= CHRONIC NECROTIZING ASPERGILLOSIS

= chronic cavitary slowly progressive disease in patients with preexisting lung injury (COPD, radiation therapy), mild immune suppression, or debilitation (alcohol, diabetes)

• symptoms mimicking pulmonary tuberculosis

√ progressive consolidation (usually upper lobe)

√ development of air crescent and fungus ball over a period of months

Dx: pathologic examination demonstrating local tissue invasion

Invasive Pulmonary Aspergillosis

= often fatal form in severely immunocompromised patients with absolute neutrophil count of < 500

Predisposed: most commonly in lymphoma / leukemia patients with prolonged granulocytopenia; after organ transplantation

Path: endobronchial fungal proliferation followed by trans- bronchial vascular invasion eventually causes widespread hemorrhage + thrombosis of pulmonary arterioles and ischemic tissue necrosis with systemic dissemination; fungus ball = devitalized sequestrum of lung infiltrated by fungi

• history of series of bacterial infections + unremitting fever

• pleuritic chest pain (mimicking emboli)

• dyspnea, nonproductive cough

• progression of pulmonary infiltrates not responding to broad-spectrum antibiotics

(a) early signs

Frequency: 96% (19%) on day 0 (day 14)

√ single / multiple ill-defined peripheral opacities abutting the pleural surface

√ "CT halo" sign = single / multiple 1–3-cm peripheral nodules (= necrotic lung) with halo of ground-glass attenuation (= hemorrhagic edema)

√ patchy localized bronchopneumonia

(b) later signs of progression

√ enlargement of nodules into diffuse bilateral consolidation

√ development into large wedge-shaped pleural-based lesions
√ "air-crescent" sign (in up to 50%) = cavitation of existing nodule (air crescent between retracting sequestered necrotic tissue and surrounding rim of hemorrhagic lung parenchyma) 1–3 weeks after recovery from neutropenia
◊ has better prognosis than consolidation without cavitation (= feature of resolution phase)

Prognosis: mortality rate of 50–90%
Dx: biopsy showing branching hyphae at tissue examination; sputum culture positive in only 10%
Rx: amphotericin B

Allergic Bronchopulmonary Aspergillosis

= ABPA = hypersensitivity reaction to aspergillus antigens released by colonization of tracheobronchial tree by Aspergillus fumigatus in patients with long-standing asthma / cystic fibrosis
◊ Most common + clinically important form of aspergillosis!
Prevalence: in 2–32% of patients with asthma; in 2–15% of patients with cystic fibrosis
Age: mostly young patients (begins in childhood); may be undiagnosed for 10–20 years
Path: bronchocentric granulomas within bronchi and bronchioles with associated mucoid impactions
Histo: deposition of immune complexes + inflammatory cells in bronchial mucosa → necrosis + eosinophilic infiltrates
Pathogenesis: IgE-mediated type I hypersensitivity reaction + specific IgG-mediated type III hypersensitivity
Pathophysiology:
inhaled spores trapped in segmental bronchi of individuals with asthma → germinate and form hyphae → aspergillus antigen reacts with IgG antibodies → immune complexes activate complement → release of proteolytic enzymes → inflammatory infiltrates → bronchial wall damage → central bronchiectasis
Staging (Patterson):
I acute phase with all primary diagnostic criteria
II remission = clearing of pulmonary infiltrates with declining IgE levels
III exacerbation = all criteria of stage I reappear after remission
IV corticosteroid dependency

Criteria for Diagnosis of ABPA *(adapted Rosenberg-Patterson Criteria)*
Major diagnostic criteria
acronym: ARTEPICS
Asthma (present in 84–96%)
Roentgenographic fleeting / fixed pulmonary infiltrates
Test for A. fumigatus positive: immediate skin reaction (type I hypersensitivity)
Eosinophilia in blood (8–40%)
Precipitating antibodies (IgG) in serum to A. fumigatus (70%)
IgE in serum elevated > 1000 IU/mL
Central bronchiectasis (late manifestation proves diagnosis)
Serum A. fumigatus-specific IgG + IgE (> 2 x the value of pooled serum samples from asthmatics with Aspergillus hypersensitivity)
Minor diagnostic criteria
Aspergillus fumigatus mycelia in sputum
Expectoration of brown sputum plugs (54%)
Arthus reaction (= late skin reactivity with erythema and induration) to Aspergillus antigen

V irreversible lung fibrosis

A. ACUTE ABPA

Type I reaction = immediate hypersensitivity (IgE-mediated mast cell degranulation)

Histo: alveoli filled with eosinophils

- bronchoconstriction, mucus production
- bronchial wall edema ← ⇑ vascular permeability

B. CHRONIC ABPA

Type III reaction = delayed immune complex response = Arthus reaction (IgG-mediated)

Histo: bronchocentric granulomas + mucoid impaction; fungal hyphae without tissue invasion

- flulike symptoms: fever, headache, malaise, weight loss, fleeting pleuritic chest pain
- wheezing, expectoration of brown mucous plugs
- positive skin test to A. fumigatus; peripheral eosinophilia
- elevated IgE level correlates well with disease activity!

CXR:

√ initial CXR normal in up to 50%

√ NORMAL peripheral bronchi

√ hyperinflation ← bronchospasm / emphysema

(a) early stage:

√ migratory pneumonitis = ill-defined homogeneous transient recurrent **"fleeting"** alveolar patchy subsegmental / lobar opacities (in up to 90%)

Location: upper lobes (50%), lower lobes (20%), middle lobe (7%); both lungs (65%)

Duration: may persist for > 6 months

(b) later stage of bronchial wall damage:

√ central varicose / cystic bronchiectasis with thickened bronchial walls:

√ "tramline" / parallel line bronchial walls ← edema

√ 1–2-cm ring shadows (= bronchus on end)

√ "finger in glove / gloved finger / **toothpaste shadow"** = V- or Y-shaped branching and tapering tubular opacities arising centrally and extending peripherally remaining for months + growing in size

Location: perihilar + upper lobes

Path: plugging of airways by hyphal masses with mucoid impaction distally in 2nd order bronchi of 2.5–6 cm in length

√ perihilar opacities simulating hilar and/or mediastinal lymphadenopathy ←mucus-filled dilated central bronchi

√ isolated lobar / segmental atelectasis (in 14%) with collateral air drift

√ lobar consolidation (in 32%)

√ cavitation (in 14%) ± air-fluid levels ← postobstructive / eosinophilic abscess

√ UNUSUAL: aspergilloma in cavity (7%), empyema, pneumothorax

(c) chronic stage:

√ pulmonary fibrosis + retraction

√ hilar elevation ← lobar shrinkage

CT:

√ bronchiectasis of segmental + subsegmental bronchi affecting > 3 lobes

√ CHARACTERISTIC highly opaque mucus within dilated bronchi ← calcium salts / metals (iron and manganese) / desiccated mucus / calcifications (in 30%)

√ tree-in-bud appearance = centrilobular nodules connected to branching linear structures (more common in asthmatics)

√ patchy areas of mosaic attenuation ← concomitant small-airway disease + areas of air trapping

√ atelectasis, consolidation, air trapping

Prognosis: end-stage pulmonary fibrosis → respiratory and right heart failure (if untreated)

DDx: hypersensitivity pneumonitis or allergic asthma (no hyphae in sputum, normal levels of IgE + IgG to A. fumigatus), tuberculosis, lipoid pneumonia, Löffler syndrome, bronchogenic carcinoma

Cerebral Aspergillosis

Transmission:

(1) hematogenous dissemination from distant pulmonary infection

(2) angiotropic / perineural spread from paranasal sinus / orbital infection (rhinocerebral disease)

(3) direct traumatic implantation

√ ring-enhancing cerebral abscesses ← hematogenous dissemination

√ hypoattenuating intracavitary projections without associated enhancement on T2WI + ADC map ← proliferating hyphae

√ propensity for vascular invasion by fungal hyphae ← production of elastase

√ zones of low T2 signal intensity ← iron, manganese, magnesium in paranasal fungal

concretions

Cx: cerebral infarction, hemorrhage (25%), mycotic aneurysm ← invasion of vessel wall

Prognosis: in immunocompromised ~ 100% mortality

Pleural Aspergillosis

= Aspergillus empyema in patients with pulmonary tuberculosis, bacterial empyema, bronchopleural fistula

√ pleural thickening

Renal Aspergillosis

= uncommon renal infection

Renal aspergillosis occurs in immunocompromised patients with diabetes / HIV infection / on corticosteroid therapy.

Route: hematogenous dissemination (most common) / ascending infection / Aspergillus casts in renal pelvis

√ mimicks complex renal mass / cyst / abscess

CT:

√ hypoattenuating mass with thick enhancing wall

√ internal septations

√ ± features of focal pyelonephritis in surrounding renal parenchyma with delayed enhancement

Dx: urinalysis, aspiration of lesion

ASPIRATION OF SOLID FOREIGN BODY

In suspected foreign-body ingestion the initial standard imaging protocol includes frontal and lateral radiographs of the chest, neck (often included on CXR) and abdomen.

CXR (frontal + lateral view):

√ apparently normal radiograph (20–35%) ← radiolucent foreign body (in 80%)

√ overdistension of hypopharynx

√ prevertebral soft-tissue swelling

√ ipsilateral lobar / segmental overinflation despite expiration:

√ ipsilateral hyperlucency ← obstructive overinflation (68%) + reflex vasoconstriction (= decrease in perfusion of compromised segment ← air trapping)

√ air trapping → needs expiratory / bilateral decubitus views

√ chronic volume loss of affected lobe ← atelectasis

√ recurrent pneumonia / infiltrate (11%)

√ bronchiectasis

√ pleural effusion

CT (indicated to assess for residual foreign body after bronchoscopy / with suspected serious complication):

√ intrabronchial foreign body:

√ intrabronchial low-attenuation material (SUGGESTIVE)

√ radiopaque foreign body (9%)

√ thickened bronchial wall adjacent to foreign body → chronic inflammatory reaction around aspirated material
√ ipsilateral hilar adenopathy
√ hyperlucency
√ bronchiectasis
√ atelectasis (14–53%), lobar collapse
√ mucoid impaction, tree-in-bud pattern
√ ipsilateral pleural effusion

NUC (V/Q scan):
√ ventilation defect (initial breath) + retention (washout)

Cx: bronchiectasis (from long retention), hemoptysis, bronchial stricture, development of inflammatory polyps, abscess

@ Childhood
Age: peak prevalence 6 month–3 years; in 50% < 3 years; in 70% < 15 years
Delay of diagnosis: within 2–3 days (usual) / > 24 hours; weeks to months (rare)
Source:
(a) young child: in 85% vegetable origin (peanut, seed, bean, lentil, pea, barley grass); disk battery
(b) older child: nonfood items like broken fragments of tooth

Disk batteries lodged in esophagus → battery-generated current → potential leakage of caustic material → esophageal perforation within hours
N.B.: upper GI examination must follow to evaluate for esophageal stricture, erosion, tracheoesophageal / aortoesophageal fistulas

Location: R main-stem bronchus (almost exclusively in lower lobes), larynx (3%), valleculae, epiglottis, vocal folds, subglottis, trachea; R÷L = 2÷1
• varying degrees of cough mimicking asthma / bronchitis / chronic pneumonia
• respiratory difficulty, wheezing, hemoptysis, recurrent pneumonia
Technique: inspiratory + expiratory phase images (in older cooperative child) / lateral decubitus images (in young less cooperative child)

√ hyperinflation is the most common finding in children ← "ball-valve" mechanism ← increased compliance of pediatric airway

DDx: impacted esophageal foreign body may also contribute to respiratory compromise; ingestion of dishwasher / laundry detergent "pods" → severe caustic injury to esophagus and surrounding tissues

@ Adulthood (unusual)
Contributing factors: CNS disorder, alcoholism, dental procedure
Source: animal bones, nutshells, medications, metallic denture parts, needles
Delay of diagnosis: for long periods of time
• often clinically silent / recurrent pneumonia
• massive life-threatening hemoptysis
Location: RLL, intermediate bronchus, left main bronchus

Lower Airway Foreign Body in Childhood

= 75% of foreign bodies aspirated into airways below larynx

Location: trachea (13%), right lung (60%), left lung (23%); bilateral (2%)
Source: mostly organic material (ie, food)
• episode of choking followed by asymptomatic period
N.B.: consider aspirated / ingested occult foreign body with chronic cough / recurrent pneumonia
√ aspirated foreign body radiolucent (90%) / radiopaque (10%)
√ unilateral hyperinflation, atelectasis, mediastinal shift
√ affected lung will remain lucent in expiration

With partial airway occlusion, expiratory view shows an increase in diagnostic accuracy ← airway narrowing ← air trapping ← ball-valve mechanism

N.B.: lateral decubitus view is WITHOUT an increase in diagnostic accuracy
Cx: pneumomediastinum, pneumothorax
Rx: bronchoscopy = reference standard for diagnosis and management of aspirated foreign bodies

Aspiration Bronchiolitis

= chronic inflammatory reaction to repeated aspiration of foreign particles into bronchioles
Predisposed: achalasia, Zenker diverticulum, hiatal hernia, gastroesophageal reflux, esophageal carcinoma
Histo: resembling diffuse panbronchiolitis
• dysphagia, regurgitation, aspiration
√ moderate / marked dilatation of esophagus
√ lobar / segmental / disseminated small nodules
CT:
√ uni- / bilateral foci of branching areas of increased attenuation:
√ tree-in-bud appearance = centrilobular nodules + uni- / bilateral branching areas of increased attenuation
√ mottled poorly defined opacified acinar areas

ASPIRATION PNEUMONIA

Frequency: 4–8÷1000 inpatients in USA → 50,000 deaths each year from Cx of aspiration
Predisposing conditions:
(1) CNS disorders / intoxication: alcoholism, mental retardation, seizure disorders, recent anesthesia
(2) Swallowing disorders: esophageal motility disturbances, head + neck surgery

Cough may be a potential indicator of aspiration due to oropharyngeal dysphagia. However, in up to 55% aspiration can be silent producing no reflexive cough.

• low-grade fever, choking on swallowing, productive cough
Location: gravity-dependent portions of lung, posterior segments of upper lobes + lower lobes in bedridden patients; frequently bilateral; right middle + lower lobe with sparing of left lung is common
Prognosis: 20–65% mortality in patients > 65 years of age

Acute Aspiration Pneumonia

Cause: gastric acid, food particles, anaerobic bacteria from GI tract provoke edema, hemorrhage, inflammatory cellular response, foreign-body reaction

Organism: Gram-negative bacteria; Pseudomonas aeruginosa, Actinomyces israelii

√ patchy bronchopneumonic pattern

√ lobar / segmental consolidation in dependent portion

√ necrotizing pneumonia

√ abscess formation

Aspiration of high-osmolar water-soluble contrast agents can lead to severe pulmonary edema. Iso-osmolar or low-osmolar agents should be used in patients at increased risk for aspiration.

Chronic Aspiration Pneumonia

Cause: repeated aspiration of foreign material from GI tract over long time / mineral oil (eg, in laxatives)

Associated with: Zenker diverticulum, esophageal stenosis, achalasia, tracheoesophageal fistula, neuromuscular disturbances in swallowing

√ recurring segmental consolidation

√ progression to interstitial scarring (= localized honeycomb appearance)

√ bronchopneumonic infiltrates of variable location over months / years

√ residual peribronchial scarring

Upper GI:

√ abnormal swallowing / aspiration

Mendelson Syndrome

= aspiration of gastric acid with a pH < 2.5

Associated with: vomiting, gastroesophageal reflux, achalasia, hiatal hernia

Pathophysiology:

acid rapidly disseminates throughout bronchial tree + lung parenchyma → incites chemical pneumonitis within minutes; extent of injury from mild bronchiolitis to hemorrhagic pulmonary edema depends on pH + aspirated volume

Location: posterior upper lobe segments + superior lower lobe segments (with patient in recumbent position)

√ bilateral perihilar ill-defined alveolar consolidations

√ multifocal patchy infiltrates

√ segmental / lobar consolidation localized to one / both lung bases

Prognosis: 30% mortality with massive aspiration; > 50% with initial shock, apnea, secondary pneumonia, or ARDS

ASTHMA

= chronic episodic reversible bronchoconstriction (= airflow obstruction) ← hypersensitivity / hyperresponsiveness of airways to a variety of stimuli

Terminology:

Reactive airway disease = clinical diagnosis of asthma not yet established, usually in children between 2 and 6 years of age

A. INTRINSIC ASTHMA

Age: middle age

Pathogenesis:

probably autoimmune phenomenon caused by viral respiratory infection and often provoked by infection, exercise, pharmaceuticals; NO environmental antigen

B. EXTRINSIC ASTHMA = ATOPIC ASTHMA

Pathogenesis:

antigens produce an immediate hypersensitivity response (type I); reagin sensitizes mast cells → histamine release → increased vascular permeability, edema, small muscle contraction; effects primarily bronchi causing airway obstruction

Nonoccupational allergens:

pollens, dog + cat fur, tamarind seed powder, castor bean, fungal spores, grain weevil

Occupational allergens:

(a) natural substances: wood dust, flour, grain, beans
(b) pharmaceuticals: antibiotics, ASA
(c) inorganic chemicals: nickel, platinum

Path: bronchial plugging with large amounts of viscid tenacious mucus (eosinophils, Charcot-Leyden crystals), edematous bronchial walls, hypertrophy of mucous glands + smooth muscle

ACUTE SIGNS:

- during asthmatic attack low values for FEV + MMFR and abnormal V/Q ratios; normal diffusing capacity
- increased resistance to airflow due to
  (a) smooth muscle contraction in airway walls
  (b) edema of airway wall caused by inflammation
  (c) mucus hypersecretion with airway plugging

√ hyperexpansion of lungs = severe overinflation + air trapping:
  √ increased anteroposterior chest diameter
  √ flattening of diaphragmatic domes
  √ increased retrosternal air space
√ peribronchial cuffing ← inflammation of airway wall
√ bronchial dilatation
√ localized areas of hypoattenuation / atelectasis
√ peripheral oligemia

CHRONIC CHANGES:

Normal chest x-ray in 73%, findings of abnormalities depend on
(a) age of onset (< 15 years of age in 31%; > 30 years of age in none)
(b) severity of asthma

√ central ring shadows = bronchiectasis
√ scars (from recurrent infections)

Cx:

(1) Pneumonia (2 x as frequent as in nonasthmatics)
  √ peripheral pneumonic infiltrates ← blocked airways
(2) Atelectasis (5–15%) ← mucoid impaction

(3) Barotrauma in children (often overlooked on radiographs)pneumomediastinum (5%), pneumothorax, subcutaneous emphysema
(4) Emphysema
(5) Allergic bronchopulmonary aspergillosis with central bronchiectasis

ATYPICAL MEASLES PNEUMONIA

= clinical syndrome in patients who have been previously inadequately immunized with killed rubeola vaccine and are subsequently exposed to the measles virus (= type III immune complex hypersensitivity); noted in children who have received live vaccine before 13 months of age
• 2- to 3-day prodrome of headache, fever, cough, malaise
• maculopapular rash beginning on wrists + ankles (sometimes absent); history of exposure to measles
• postinfectious migratory arthralgias
√ extensive nonsegmental consolidation, usually bilateral
√ hilar adenopathy (100%)
√ pleural effusion (0–70%)
√ nodular densities of 0.5–10 cm in diameter in peripheral location, may calcify and persist up to 30 months

BARITOSIS

= inhalation of nonfibrogenic barium sulfate
• asymptomatic; normal pulmonary function (benign course)
√ bilateral nodular / patchy opacities, denser than bone ← high atomic number
√ similar to calcified nodules
√ NO cor pulmonale, NO hilar adenopathy
√ regression if patient removed from exposure

BERYLLIOSIS

= chronic granulomatous disorder caused by exposure to beryllium dust / fumes (= acid salts from extraction of beryllium oxide)
Substance: one of the lightest metals (atomic weight 9), marked heat resistance, great hardness, fatigue resistance, no corrosion
Occupational exposure: fluorescent light bulb factories, ceramics manufacture, nuclear weapon production, aerospace industry
Immunology: cell-mediated immune response (= delayed hyper-sensitivity reaction) → accumulation of CD4+ T helper cells + macrophages in lower respiratory tract
Histo: noncaseating granulomas within interstitium + along vessels + in bronchial submucosa → fibrosis
DDx: indistinguishable from other granulomatous disorders like sarcoidosis
• positive beryllium lymphocyte transformation test (= sample of blood / bronchoalveolar lavage tested for T-lymphocyte transformation + proliferation to beryllium)

Acute Berylliosis (25%)

√ pulmonary edema following an overwhelming exposure (in 54%)
Cx: pulmonary carcinoma

Chronic Berylliosis

= widespread systemic disease of liver, spleen, lymph nodes, kidney, myocardium, skin, skeletal muscle
Metabolism: removed from lungs → excreted via kidneys
Latent period: 5–15 years
Associated with: granulomatous hepatitis, hypercalcemia, kidney stones
• dyspnea, cough, fever, anorexia, weight loss, skin lesions
Location: middle + upper lung zones
CXR:
√ fine irregular reticulonodular opacities (granulomas similar to sarcoidosis) sparing apices + bases
√ progression to interstitial fibrosis, honeycombing
√ ± mass lesions ← coalescence of granulomas
√ moderate hilar + mediastinal adenopathy (may calcify)
√ emphysema in upper lobes
√ pneumothorax in 10%
HRCT:
√ diffuse small parenchymal nodules (57%) along bronchovascular bundles
√ interlobular septal lines (50%)
√ patches of ground-glass attenuation (32%)
√ hilar / mediastinal lymphadenopathy (21–39%), only in the presence of parenchymal abnormalities
√ bronchial wall thickening (46%)
√ pleural irregularities (25%)
√ honeycombing (7%), conglomerate mass (7%)
Rx: prolonged treatment with corticosteroids ± oxygen
DDx: (1) Nodular pulmonary sarcoidosis (indistinguishable)
(2) Asbestosis (no hilar adenopathy)

BLASTOMYCOSIS

= NORTH AMERICAN BLASTOMYCOSIS = GILCHRIST DISEASE = CHICAGO DISEASE
= rare systemic mixed pyogenic + granulomatous fungal infection mimicking many other diseases (TB, bacterial pneumonia, malignancy)
Organism: soil-born saprophytic dimorphic fungus Blastomyces dermatitidis; mycelial phase in soil; round thick-walled yeast form with broad-based budding in mammals
Geographic distribution:
worldwide; endemic in midwest + southeastern USA (Ohio + Mississippi river valleys), vicinity of Great Lakes, St. Lawrence River valley, Canada (northern Ontario), Africa, India, Israel, Saudi Arabia, Central + South America
Prevalence: 1–40÷100,000 persons in endemic regions
Peak age: 25–50 (range, several months to 80) years; M÷F = 10÷1

Mode of infection:
inhalation (primary portal of entry) of fungal conidia growing in warm wet soil of decayed vegetation + decomposing wood acquired through activities in woods (hunting, camping, logging); spread to extrapulmonary sites (in 17–30%) → eg, skin, bone (often direct extension from skin lesion resembling actinomycosis), joints

Pathophysiology:
conidia are usually destroyed by a granulomatous reaction mediated by neutrophils, monocytes and macrophages;
if host defenses are overwhelmed conidia transform into yeast form, which is more resistant to destruction

Predisposed: elderly, immunocompromised

Histo:
(a) exudative phase: accumulation of numerous neutrophils with infecting organism
(b) proliferative phase: proliferation of epithelioid granulomas + giant cells with central microabscesses containing neutrophils and yeast forms

- acute: fever, chills, cough similar to community-acquired pneumonia
- chronic: intermittent low-grade fevers, mild persistent productive cough, chest pain, hemoptysis, malaise, fatigue, weight loss
- mouth ulcers

@ Lung (100%)
- clinical patterns following pulmonary infection:
  (a) severe pulmonary symptoms
  (b) asymptomatic pulmonary infection with spontaneous resolution
  (c) disseminated disease to single / multiple organs indolent for several years
  (d) extrapulmonary manifestation involving male GU system, skeleton, skin

◊ Highly variable imaging features!
√ segmental / lobar patchy ill-defined airspace disease in lower lobes in acute illness (26–76%)
√ solitary / multiple irregular masses of 3–10 cm in diameter (31%) / satellite lesions in paramediastinal / perihilar location
√ air bronchogram in area of consolidation (87%)
√ solitary / multiple nodules of 0.5–3.0 cm in diameter (6%)
√ bilateral diffuse reticulonodular interstitial disease (6–9%) with tree-in-bud pattern on HRCT
√ miliary disease (11–28%) with nodules of < 3 mm in diameter in fulminant course
√ cavitary lesions (13%) mimicking TB / other granulomatous disease if located in upper lobes
√ hilar / mediastinal lymph node enlargement (< 25%)

@ Skin (20–40% in disseminated disease)
- crusted verrucous lesions on exposed body areas
- skin ulcers

√ subcutaneous areas of soft-tissue + fluid attenuation with associated skin thickening

@ Bone (25%)
Location: spine, pelvis, sacrum, skull, ribs, long bones
√ marked destruction ± surrounding sclerosis

√ periosteal reaction in long bones, but NOT in short bones
√ multiple osseous lesions (frequent)
√ destruction of vertebral bodies + intervertebral disks (similar to tuberculosis)
√ psoas abscess
√ lytic skull lesions + soft-tissue abscess
√ usually monoarticular arthritis: knee > ankle > elbow > wrist > hand
@ GU tract (20%): prostatitis, epididymoorchitis
@ CNS (5–10%): epidural / parenchymal abscess, meningitis

Dx: (1) Culture of organism
(2) Silver stain microscopy of tissues

Prognosis: spontaneous resolution of acute disease in up to 4 weeks; disease may reactivate for up to 3 years; acute respiratory distress within 1 week (in rare fulminant course)

Rx: (1) Amphotericin B IV: 8–10 weeks for noncavitary + 10–12 weeks for cavitary lesions
(2) Ketoconazole

DDx: other pneumonias (ie, bacterial, tuberculous, fungal), pseudolymphoma, malignant neoplasm (ie, alveolar cell carcinoma, lymphoma, Kaposi sarcoma)

BLUNT CHEST TRAUMA

Incidence: 100,000 hospital admissions / year (in USA)

Prevalence: 3rd most common site (after injury to head and extremities)

Cause: high-speed motor vehicle accidents (70%), fall, blow to chest

Type of injury:

1. Pneumothorax 69%
2. Lung contusion 67%
3. Rib fracture 66%
4. Hemothorax 28%
5. Flail chest 14%
6. Thoracic spine fracture 13%
7. Clavicle fracture 13%
8. Scapula fracture 8%
9. Sternal fracture 5%
10. Sternoclavicular dislocation
11. Diaphragmatic injury 5%
12. Tracheobronchial tear 2%
13. Vascular injury 2%
14. Esophageal rupture 1%

Prognosis: 10.1% fatality rate (especially due to cardiac and tracheobronchial-esophageal injury)

Fracture of Trachea / Bronchus

= TRACHEOBRONCHIAL TEAR

Prevalence: 0.2–1.5–8.0% of all blunt chest injuries

• delayed diagnosis is common

Location: (a) mainstem bronchus within 2.5 cm of carina (80%); R > L

(b) just above carina (20%)

Orientation of tear: longitudinal at junction of cartilaginous and membranous portion of trachea / parallel to cartilage rings of bronchus

Associated injuries:

√ fracture of first 3 ribs (53–91%), rare in children

√ fracture of clavicle, sternum, scapula (40%)

√ pneumothorax (70%) without improvement after chest tube placement + suction

√ increasing pneumomediastinum ± subcutaneous emphysema of neck

√ absence of pleural effusion

√ **"fallen lung"** sign = collapsed lung droops to dependent position posterolaterally away from hilum (loss of anchoring support in complete bronchial transection)

√ inadequate reexpansion of lung despite adequate placement of one / more chest tubes ← large size of air leak

√ elevation of hyoid bone above level of C3 vertebra / elevation of greater cornu to < 2 cm from angle of mandible (on LAT radiograph of spine) ← infrahyoid muscle rupture + unopposed action of suprahyoid muscles

√ atelectasis (may be late development)

CT:

√ focal peribronchial collection of air

√ discontinuity / irregularity of bronchial wall

√ abnormal position of endotracheal tube:

√ overdistension of tube cuff

√ protrusion of tube wall beyond expected margins of trachea

√ extraluminal position of tip of tube

Dx: bronchoscopy

Prognosis: 30% mortality (in 15% within 1 hour)

Long-term Cx: airway stenosis / bronchomalacia; recurrent atelectasis / pneumonia; abscess; empyema

Pulmonary Contusion

= acute traumatic injury to alveoli

Prevalence: 17-70% (most common manifestation of blunt chest trauma, esp. deceleration trauma)

Path: exudation of edema + hemorrhage into airspace + interstitium

At risk for: pneumonia, RDS

Time of onset: apparent within 6 hours after trauma

• may be clinically inapparent; hemoptysis (50%)

Location: posterior (in 60%)

Distribution: nonsegmental

Site: in lung periphery at site of impact ± contrecoup lesion

◊ Frequently not visible on CXR < 6 hours after injury

√ irregular patchy / diffuse extensive homogeneous consolidation

√ opacity may enlarge for 48–72 hours

√ rapid resolution beginning after 24–48 hours

√ complete clearing in 3-10 days
√ overlying rib fractures (frequent)
CT (more sensitive than CXR):
◊ Immediately visible!
√ nonsegmental coarse ill-defined crescentic (50%) / amorphous (45%) opacification of lung parenchyma without cavitation
√ "subpleural sparing" = 1–2-mm rim of nonopacified clear lung between contusional lesion and pleura
Cx: pneumothorax
DDx: aspiration, pneumonia, fat embolism (1–2 days after injury)

Pulmonary Laceration

= disruption / tear of lung parenchyma resulting in lung cavity ← elastic recoil of lung
Predisposed: children + young adults (greater flexibility of chest wall with higher likelihood of lung injury in blunt trauma)
Type:
1 **Compression rupture injury** (most common)
= direct compressive force
Location: deep portions of lung
2 **Compression shear injury**
= severe sudden blow to lower thorax → shift of lower lobes across spine
Location: paraspinous portion of lung
3 **Rib penetration tear**
= rib fracture + pneumothorax
Location: periphery of lung
4 **Adhesion tear**
= laceration at preexisting pleuroparenchymal adhesion
Prognosis: tear fills gradually with blood → slow regression lasting up to several months
√ single / multiple uni- / multilocular pulmonary lesions consisting of round / oval lung cavity filled with:
(a) air = **traumatic pneumatocele**
(b) blood = **traumatic hematocele** / pulmonary hematoma
(c) both = traumatic hematopneumatocele with air-fluid level
◊ On CXR laceration often obscured by surrounding contusion!

Traumatic Lung Cyst

Age: children + young adults are particularly prone
√ thin-walled air-filled cavity (50%) ± air-fluid level preceded by homogeneous well-circumscribed mass (= hematoma)
√ oval / spherical lesion of 2–14 cm in diameter
√ single / multiple lesions; uni- or multilocular
√ usually subpleural under point of maximal injury
√ persistent up to 4 months + progressive decrease in size (apparent within 6 weeks)

Traumatic Lung Herniation

= pleura-covered part of lung extruding through a traumatic defect in the chest wall
Associated with: rib fracture

BONE MARROW TRANSPLANTATION

= intravenous infusion of hematopoietic progenitor cells from patient's own marrow (autologous transplant) / HLA-matched donor (allogenic transplant) to reestablish marrow function after high-dose chemotherapy and total body irradiation for lymphoma, leukemia, anemia, multiple myeloma, congenital immunologic defects, solid tumors

Cx: pulmonary complications in 40–60%

Neutropenic-Phase Pulmonary Complications

Time: 2–3 weeks after transplantation

1. **Angioinvasive aspergillosis**
   - √ nodule surrounded by halo of ground-glass attenuation (= fungal infection spreading into lung parenchyma with surrounding area of hemorrhagic infarction)
   - √ segmental / subsegmental consolidation (= pulmonary infarction)
   - √ cavitation of nodule with "air-crescent" sign (during recovery phase with resolving neutropenia)
   - √ < 5-mm centrilobular nodules to 5-cm peribronchial consolidation (= airway invasion with surrounding zone of hemorrhage / organizing pneumonia)
2. **Diffuse alveolar hemorrhage** (20%)
   - • hemosiderin-laden macrophages on lavage
   - √ bilateral areas of ground-glass attenuation / consolidation
3. **Pulmonary edema**
   Cause: infusion of large volumes of fluid combined with cardiac + renal dysfunction
   - √ prominent pulmonary vessels, interlobar septal thickening, ground-glass attenuation, pleural effusions
4. **Drug toxicity**
   Cause: bleomycin, busulfan, bischloronitrosurea (carmustine), methotrexate
   - √ bilateral areas of ground-glass attenuation / consolidation / reticular attenuation (= fibrosis)

Early-Phase Pulmonary Complications

Time: up to 100 days after transplantation

1. CMV pneumonia (23%)
   - √ multiple small nodules + associated areas of consolidation + ground-glass attenuation (= hemorrhagic nodules)
2. Pneumocystis carinii pneumonia
   - √ diffuse / predominantly perihilar / mosaic pattern of ground-glass attenuation with sparing of some secondary pulmonary lobules
3. Idiopathic interstitial pneumonia (12%)
   - √ nonspecific findings (diagnosis of exclusion)

Late-Phase Pulmonary Complications

Time: after 100 days post transplantation

1. Bronchiolitis obliterans (in up to 10%)
2. BOOP
3. Chronic graft-versus-host disease:
   infections, chronic aspiration, bronchiolitis obliterans, lymphoid interstitial pneumonia

BRONCHIAL ADENOMA

= misnomer due to locally invasive features + tendency for recurrence + occasional metastasis to extrathoracic sites (in 10%) = low-grade malignancy

Path: arises from duct epithelium of bronchial mucous glands (predominant distribution of Kulchitsky cells at bifurcations of lobar bronchi)

Frequency: 6–10% of all primary lung tumors

Mean age: 35–45 (range, 12–60) years; 90% occur < 50 years of age; most common primary lung tumor < 16 years of age; M÷F = 1÷1; Whites÷Blacks = 25÷1

Types:

mnemonic: CAMP

Carcinoid 90%
Adenoid cystic carcinoma = cylindroma 6%
Mucoepidermoid carcinoma 3%
Pleomorphic carcinoma 1%

Location: most commonly near / at bifurcation of lobar / segmental bronchi; central÷peripheral = 4÷1

› 48% on right: RLL (20%), RML (10%), main right bronchus (8%), RUL (7%), intermediate bronchus (3%)

› 32% on left: LLL (13%), LUL (12%), main left bronchus (6%), lingular bronchus (1%)

• hemoptysis (40–50%), atypical asthma, persistent cough
• recurrent obstructive pneumonia; asymptomatic (10%)
√ complete obstruction / air trapping in partial obstruction (rare) / nonobstructive (10–15%)
√ obstructive emphysema
√ recurrent postobstructive infection: pneumonitis, bronchiectasis, abscess
√ atelectasis / consolidation of a lung / lobe / segment (78%)
√ collateral air drift may prevent atelectasis
√ solitary round / oval slightly lobulated pulmonary nodule (19%) of 1–10 cm in size
√ hilar enlargement / mediastinal widening = central endo- / exobronchial mass

CT:

√ well-marginated sharply defined mass
√ in close proximity to an adjacent bifurcation with splaying of bronchus
√ coarse peripheral calcifications in ⅓ (cartilaginous / bony transformation)
√ may exhibit marked homogeneous enhancement

Biopsy: risky ← high tumor vascularity

Prognosis: 95% 5-year survival rate; 75% 15-year survival rate after resection

Cylindroma

= ADENOID CYSTIC CARCINOMA (7%)

◊ 2nd most common primary tumor of trachea
◊ Most common carcinoma of minor salivary tissue
Path: mixed serous + mucous glands; resembles salivary gland tumor
Histo:
Grade 1: tubular + cribriform; no solid subtype
√ entirely intraluminal
Grade 2: tubular + cribriform; < 20% solid subtype
√ predominantly intraluminal
Grade 3: solid subtype > 20%
√ predominantly extraluminal
Age peak: 4th–5th (range, 3rd–9th) decade; M=F
• typical history of refractory "asthma", hoarseness
• hemoptysis, cough, stridor, wheezing, chest pain, dysphagia
√ endotracheal mass with extratracheal extension
Malignant potential: more aggressive than carcinoid with propensity for local invasion + distant metastases (lung, bone, brain, liver) in 25%
Rx: tracheal resection + adjunctive radiotherapy
Prognosis: 8.3 years mean survival

Mucoepidermoid Carcinoma

Path: squamous cells + mucus-secreting columnar cells; resembles salivary gland tumor
√ may involve trachea = locally invasive tumor
√ sessile / polypoid endobronchial lesion

Pleomorphic Adenoma

= MIXED TYPE (extremely rare)

BRONCHIAL ATRESIA

= rare anomaly resulting from focal obliteration of proximal lumen of a lobar / segmental / subsegmental bronchus
Proposed causes:
(a) local interruption of bronchial arterial perfusion > 16 weeks GA (when bronchial branching is complete)
(b) tip of primitive bronchial bud separates from bud and continues to develop
Path: normal bronchial tree distal to occlusion is patent and filled with mucus; alveoli distal to occlusion are air-filled and mildly overinflated through collateral air drift
Associated with: lobar emphysema, cystic adenomatoid malformation
Mean age: 17 years; M÷F = 2÷1
• minimal symptoms, apparent later in childhood (most by age 15) / adult life
• recurrent pulmonary infections (in 20%)
Location: apicoposterior segment of LUL (>> RUL / ML)
CXR:
√ lobular / ovoid / round / branching perihilar mass:
√ CHARACTERISTIC **"gloved finger"** sign ← accumulation of mucus in dilated central bronchus distal to atretic lumen (= mucus impaction = bronchocele / mucocele)

√ overexpanded hyperlucent lung segment (collateral air drift with expiratory air-trapping)

CT:

√ mucus-filled bronchus near hilum WITHOUT connection between mucocele + hilum

√ air trapping in surrounding area

√ decreased perfusion with focal parenchymal oligemia

OB-US (detected > 24 weeks MA):

√ large echogenic fetal lung mass ← lung fluid-filled distal to occlusion (indistinguishable from other lung masses)

√ dilated fluid-filled bronchus

Fetal MR:

√ focal lung mass of homogeneously high SI on T2WI

Rx: no treatment in asymptomatic patients; segmentectomy in symptomatic infected patients

DDx: allergic bronchopulmonary aspergillosis; cystic fibrosis; congenital lobar emphysema (no mucus plug)

DDx in fetus: congenital cystic adenomatoid malformation, bronchopulmonary sequestration

BRONCHIECTASIS

= localized mostly irreversible dilatation of bronchi often with thickening of the bronchial wall

Pathophysiology:

"vicious cycle" hypothesis = airway damage + infection play reinforcing roles in the development of bronchiectasis. Host factors that predispose to infection are impaired glandular secretion (cystic fibrosis), impaired ciliary function (ciliary dyskinesia), or systemic immune dysfunction.

Etiology:

A. Chronic or recurrent infection
   (a) congenital
      1. Structural defect of bronchi: bronchial atresia, Williams-Campbell syndrome
         Distribution: midorder bronchi
         √ cartilage deficiency
      2. Abnormal mucociliary transport: Kartagener syndrome = primary ciliary dyskinesia
         Distribution: middle lobe, lingula
         √ situs inversus, chronic sinusitis, bronchiectasis
      3. Abnormal secretions: cystic fibrosis
         Distribution: central upper lung zone
         √ extensive cystic + cylindrical bronchiectasis
      4. Mounier-Kuhn syndrome
         Distribution: central
         √ absence / atrophy of elastic fibers + muscle in trachea and main bronchial walls
   (b) congenital / acquired immune deficiency (usually IgG deficiency):
      1. Chronic granulomatous disease of childhood
      2. Alpha-1 antitrypsin deficiency
   (c) postinfectious childhood pneumonias (after necrotizing viral / bacterial bronchitis):
      1. Measles
      2. Whooping cough

3. Swyer-James syndrome
   Distribution: focal unilateral
   √ increased lucency of smaller lung ← air trapping
4. Allergic bronchopulmonary aspergillosis
   Distribution: central upper lung zone
   √ high-attenuation mucus plugging
5. Chronic granulomatous infection (TB)
   Distribution: asymmetric upper lobe involvement
   √ tree-in-bud nodules

(d) fibrosing lung disease

1. Sarcoidosis
   Distribution: central upper lung zone
   √ bihilar lymphadenopathy, perilymphatic nodules
2. Pulmonary fibrosis
   Distribution: peripheral lower lung zone
   √ varicoid bronchiectasis, architectural distortion
   √ honeycombing in UIP
3. Acute respiratory distress syndrome
   Distribution: middle lobe and lingula
   √ varicoid bronchiectasis, diffuse ground-glass opacities

B. Distal to bronchial obstruction ← accumulation of secretions: neoplasm, inflammatory nodes, foreign body

C. Aspiration / inhalation: gastric contents / inhaled fumes (late complication) / foreign object
   Distribution: periphery of lower lung zone
   √ hiatal hernia

D Bronchiolitis obliterans
   Distribution: diffuse
   √ diffuse air trapping, post transplantation

E. **"Traction bronchiectasis"** ← increased elastic recoil with bronchial dilatation + mechanical distortion of bronchi: advanced pulmonary fibrosis / radiation-induced lung injury

F. Increased inflationary pressure

The distribution and morphologic features of bronchiectasis, architectural distortion and findings of fibrosis, mosaic attenuation, presence and pattern of diffuse nodular lung disease can provide clues to the diagnosis.

Classification of anatomical abnormality: often in combination
◊ Of little value for illuminating etiology / pathogenesis!
◊ Little interobserver agreement as to bronchiectatic classes
Normal lung: 17–20 bronchial subdivisions between lung periphery + hilum

1. **Cylindrical / tubular / fusiform bronchiectasis**
   = mildly uniformly dilated bronchi (least severe type)
   ◊ reversible if associated with pulmonary collapse
   Path: bronchial subdivisions between lung periphery + hilum reduced to 16
   √ square abrupt ending with lumen of uniform diameter and same width as parent

bronchus

HRCT:

√ "tram lines" of nontapering air ways (horizontal course)

√ "signet-ring" sign (vertical course) = cross section of dilated bronchus + branch of pulmonary artery

√ Y- or V-shaped areas of attenuation = mucous plugs filling bronchiectatic segments

2. **Varicose / varicoid bronchiectasis**

= moderately dilated and beaded bronchi (rare)

Associated with: Swyer-James syndrome, interstitial fibrosis → bronchial traction

Path: bronchial subdivisions between lung periphery + hilum reduced to 4–8

√ alternating segments of bronchial dilatation + narrowing with normal pattern distally

3. **Saccular / cystic bronchiectasis**

= marked cystic dilatation = focal pouch-like areas of enlargement (most severe type)

Associated with: cystic fibrosis, severe bronchial infection

Path: bronchial subdivisions between lung periphery + hilum reduced to < 5

√ progressive ballooning dilatation toward periphery with diameter of saccules > 1 cm

√ irregular constrictions may be present

√ dilatation of bronchi on inspiration, collapse on expiration

√ contains variable amounts of pooled secretions

HRCT:

√ string of cysts = "string of pearls" (horizontal course) / cluster of cysts = "cluster of grapes"

√ air-fluid level (frequent)

Age: predominantly pediatric disease

- chronic productive cough, excess sputum production
- recurrent infection with expectoration of purulent sputum
- shortness of breath
- hemoptysis (50%) ← bronchial artery dilatation and neovascularity ← recurrent airway inflammation
  - ◊ Most common cause of massive hemoptysis!
- frequent exacerbations + resolutions ← superimposed infections
- Spirometry often reveals an obstructive physiologic condition that worsens over time

Associated with: obliterative + inflammatory bronchiolitis (in 85%)

Location: posterior basal segments of lower lobes, bilateral (50%); middle lobe / lingula (10%); central bronchiectasis in bronchopulmonary aspergillosis

CXR (37% sensitive):

√ tramlines = dilated air-filled wall-thickened bronchi:

√ parallel + ringlike opacities

√ increased background density ← parenchymal volume loss:

√ crowding of lung markings (if associated with atelectasis)

√ increase in size of lung markings (mucous plugs)

√ loss of definition of lung markings (peribronchial fibrosis)

√ cystic spaces ± air-fluid levels < 2 cm in diameter (dilated bronchi)

√ honeycomb pattern (in severe cases)

√ compensatory hyperinflation of uninvolved ipsilateral lung

HRCT (87–97% sensitive, 93–100% specific):

√ lack of bronchial tapering (in 80% = most sensitive finding)

√ bronchial wall thickening

√ "signet ring" sign = internal diameter of bronchus larger than adjacent pulmonary artery (in 60%)

√ bronchi visible within 1 cm of pleura (in 45%) implies bronchiolectasis (DDx: honeycombing)

√ mucus-filled dilated bronchi (in 6%)

√ small bronchial arterial diameter with an increase in bronchoarterial ratio ← vasoconstriction ← small-vessel / small-airways disease

√ dilatation of bronchial arteries ← pulmonary hypertension → pseudo-normalization of bronchoarterial ratio

Cx: frequent respiratory infections

Prognosis: 20% 5-year mortality rate

Rx: antibiotics for superimposed infection, bronchodilator, nasal oxygen therapy, chest physiotherapy, inhaled steroids

DDx of CT appearance:

(1) Emphysematous blebs (no definable wall thickness, subpleural location)

(2) "Reversible bronchiectasis" = temporary dilatation during pneumonia with return to normal within 4–6 months

BRONCHIOLITIS

= LOWER RESPIRATORY TRACT INFLAMMATION

Cause: inflammation of small airways ←viral antigen (usually respiratory syncytial virus / rhinovirus)

Terminology:

› **bronchiolitis:** child < 2 years of age

› **lower respiratory tract inflammation:** child > 2 years of age

√ small airways ← perihilar bronchial wall thickening ← edema

√ hyperinflation:

√ > 6 anterior rib ends depicted on frontal projection

√ downward sloping + flattening of hemidiaphragms

√ increased retrosternal airspace

√ ± lung tissue herniating through intercostal spaces

Cx: atelectasis, consolidation

Prognosis: development of asthma later in life

BRONCHIOLITIS OBLITERANS

= CONSTRICTIVE BRONCHIOLITIS = OBLITERATIVE BRONCHIOLITIS

= concentric narrowing of bronchial lumen

• decrease in forced expiratory volume in 1 second > 20%

Path: irreversible submucosal and peribronchiolar fibrosis of small airway walls (respiratory bronchiole, alveolar duct, alveoli) → narrowing / obliteration of airway lumina by

granulation tissue of immature fibroblastic plugs (Masson bodies)

Etiology:

(1) Idiopathic (most frequent) / cryptogenic: in immunocompetent patient
(2) Inhalation: 1–3 weeks after exposure to toxic fumes (nitrogen dioxide, isocyanates, phosgene, ammonia, sulfur dioxide, chlorine, diacetyl (buttery flavor of popcorn)
(3) Postinfectious: Mycoplasma (children), virus (older individual); cystic fibrosis (as a complication of repeated episodes of pulmonary infections)
(4) Drugs: bleomycin, gold salts, cyclophosphamide, carmustine, methotrexate, D-penicillamine, cocaine
(5) Collagen vascular disorder: rheumatoid arthritis (especially after treatment with penicillamine / gold salts), systemic sclerosis (= scleroderma), systemic lupus erythematosus, mixed connective tissue disease
(6) Transplantation: chronic graft-versus-host disease in bone marrow transplant, lung transplant, heart-lung transplant (30–56% after 3 years)
(7) Miscellaneous: ulcerative colitis, diffuse idiopathic pulmonary neuroendocrine cell hyperplasia (DIPNECH)Stevens-Johnson syndrome, paraneoplastic pemphigus

Peak age: 40–60 years; M÷F = 1÷1

• insidious onset of dyspnea over many months
• obstructive pulmonary function tests
• no response to antibiotics, persistent nonproductive cough, fever

√ normal CXR (in up to 40%)
√ hyperinflated lungs = limited disease with connective tissue plugs in airways
√ oligemia = decreased vascularity ← reflex vasoconstriction
√ bilateral scattered heterogeneous + homogeneous opacities: typically peripheral in distribution; equally distributed between upper + lower lobes
√ bronchiectasis

HRCT (paired expiration-inspiration images):

√ patchy <u>air trapping</u> on expiratory scan ← collateral air drift into postobstructive alveoli = failure of change in attenuation (ie, volume) between expiration + inspiration
√ "mosaic perfusion" of lobular air trapping (85–100%)
= patchy areas of decreased lung attenuation alternating with areas of normal attenuation:
√ areas of ↓ attenuation = vessels of decreased caliber ← secondary vasoconstriction of alveoli distal to bronchiolar obstruction ← alveolar hypoventilation
√ areas of ↑ attenuation = vessels of increased caliber ← compensatory increased perfusion in uninvolved areas
√ bronchial wall thickening (87%)
√ central + peripheral bronchiectasis (66–80%)
√ poorly defined nodular areas of consolidation
√ "tree-in-bud" appearance of bronchioles
= centrilobular branching structures and nodules caused by peribronchiolar thickening + bronchiolectasis with secretions (the only direct, but UNCOMMON sign)
√ centrilobular ground-glass opacities

Rx: steroids may stop progression

DDx: (1) Bacterial / fungal pneumonia (response to antibiotics, positive cultures)

(2) Chronic eosinophilic pneumonia (young female, eosinophilia in ⅔)
(3) Usual interstitial pneumonia (irregular opacities, decreased lung volume)

BRONCHIOLOALVEOLAR CARCINOMA

= BAC = ALVEOLAR CELL CARCINOMA = BRONCHIOLAR CARCINOMA
= type of adenocarcinoma showing lepedic growth pattern without surrounding stromal / vascular invasion

Frequency: 1.5–6% of all primary lung cancers (increasing incidence to ? 20–25%)
Etiology: development from type II alveolar epithelial cells
Age: 40–70 years; M÷F = 1÷1 (strikingly high in women)
Path: peripheral neoplasm arising beyond a recognizable bronchus with tendency to spread locally using lung structure as a stroma (= **lepedic** growth)
Histo: subtype of well-differentiated adenocarcinoma; cuboidal / columnar cells grow along alveolar walls + septa without disrupting the lung architecture or pulmonary interstitium (serving as "scaffolding" for tumor growth)
Subtypes:
(a) mucinous (80%): mucin-secreting tall columnar peglike bronchiolar cells; more likely multicentric; 26% 5-year survival rate
(b) nonmucinous (20%): cuboidal type II alveolar pneumocytes with production of surfactant / nonciliated bronchiolar (Clara) cells; more localized + solitary; 72% 5-year survival rate
Risk factors: localized pulmonary fibrosis (tuberculous scarring, pulmonary infarct) in 27%, diffuse fibrotic disease (scleroderma), previous exogenous lipid pneumonia

- history of heavy smoking (25–50%)
- often asymptomatic (even in disseminated disease) with insidious onset
- pleuritic chest pain (← peripheral location)
- cough (35–60%), hemoptysis (11%)
- bronchorrhea = abundant white mucoid / watery expectoration (5–27%); can produce hypovolemia + electrolyte depletion; unusual + late manifestation only with diffuse bronchioloalveolar carcinoma
- shortness of breath (15%), weight loss (13%), fever (8%)

Location: peripherally, beyond a recognizable bronchus
Spread: tracheobronchial dissemination = cells detach from primary tumor + attach to alveolar septa elsewhere in ipsi- / contralateral lung; lymphogenous and hematogenous dissemination
Metastases: involving almost any organ (in 50–60%); 33% of skeletal metastases are osteoblastic

A. LOCAL FORM (60–90%)
1. **Ground-glass attenuation**
= early stage (← lepedic growth pattern along alveolar septa with relative lack of acinar filling)
√ ground-glass haziness
√ bubblelike hyperlucencies / pseudocavitation
√ airway dilatation

√ lesion persists / progresses within 6–8 weeks

Spectrum of Adenocarcinoma of Lung (formerly Bronchioloalveolar Carcinoma *2011*)

Term	*Pathology*	*CT*
Adenocarcinoma in situ (AIS)	noninvasive ≤ 3 cm mass, purely lepedic growth	nonsolid mass ± small scattered sites of low attenuation
Minimally invasive adenoca. (MIA)	invasive ≤ 3 cm mass with lepedic growth (depth of invasion ≤ 5-mm)	nonsolid mass + 5-mm central solid component
Lepedic adenocarcinoma	invasive nonmucinous adenocarcinoma with predominantly lepedic growth	partly solid mass + bubblelike component
Acinar / papillary / micropapillary / solid adenoca.	invasive nonmucinous adenocarcinoma + small proportion of lepedic growth	usually solid mass ± small nonsolid component
Invasive mucinous adenocarcinoma	invasive mucinous adenocarcinoma + lepedic growth as predominant component	solid / mostly solid / part solid / nonsolid mass

2. **Single mass** (43%)
   √ well-circumscribed focal mass in peripheral / subpleural location arising beyond a recognizable bronchus
   √ "open bronchus" sign = air bronchogram = tumor / mucus surrounding aerated bronchus ± narrowing / stretching / spreading of bronchi
   √ "rabbit ears" / pleural tags / triangular strand / "tail" sign (55%) = linear strands extending from nodule to pleura (desmoplastic reaction / scarring granulomatous disease / pleural indrawing)
   √ spiculated margin = sunburst appearance (73%)
   √ solitary cavity ← central necrosis (7%)
   ◊ 2nd most common cell type associated with cavitation after squamous cell carcinoma
   √ pseudocavitation (= dilatation of intact air spaces from desmoplastic reaction / bronchiectasis / focal emphysema) in 50–60%
   √ heterogeneous attenuation (57%)
   √ confined to single lobe
   √ rarely evolving into diffuse form
   √ slowly progressive growth on serial radiographs
   √ NO atelectasis
   √ negative FDG PET results in 55%
   Prognosis: 70% surgical cure rate for tumor < 3 cm; 4–15-years survival time with single nodule

B. DIFFUSE FORM = Pneumonic form (10–40%)
   1. **Diffuse consolidation** (30%)
      √ acinar airspace consolidation + air bronchogram + poorly marginated borders
      √ airspace consolidation may affect both lungs (mucus secretion)

√ ± cavitation within consolidation
√ "CT angiogram" sign = low-attenuation consolidation does NOT obscure vessels (mucin-producing subtype)

2. **Lobar form**
√ ± expansion of a lobe with bulging of interlobar fissures

3. **Multinodular form** (27%)
√ multiple bilateral poorly / well-defined nodules similar to metastatic disease
√ multiple poorly defined areas of ground-glass attenuation / consolidation

• consolidation despite treatment with antibiotics
√ pleural effusion (8–10%)
Prognosis: worse with extensive consolidation / multifocal / bilateral disease; death within 3 years with diffuse disease

BRONCHOCENTRIC GRANULOMATOSIS

= rare disorder characterized by destructive necrotizing granulomatous inflammation of bronchial + bronchiolar walls and surrounding parenchyma
Peak age: 4th–7th decade
• asthma with underlying allergic bronchopulmonary aspergillosis (33–50%)
• fever, night sweats, cough, dyspnea, pleuritic chest pain
• seropositive arthritis (rare), ocular scleritis (rare)
Path: thick-walled ectatic bronchi + bronchioles containing viscous material of mucopurulent / caseous character
Histo: necrotizing granulomas surrounding small airways; pulmonary arteritis as a secondary phenomenon
(1) large masses of eosinophils in necrotic zones, associated with endobronchial mucus plugs, eosinophilic pneumonia, Charcot-Leyden crystals, fungal hyphae in granulomas (with asthma) in ⅓
(2) polymorphonuclear cell infiltrate in necrotic zones (without asthma) in ⅔
Location: unilateral (75%); upper lung zones (60%)
√ branching opacities / atelectasis ← mucoid impaction
√ solitary > multiple nodules / masses (in 60%)
Location: unilateral with upper lobe predominance
√ ill-defined parenchymal consolidation (in 27%)
√ ± cavitation
Rx: corticosteroid therapy

BRONCHOGENIC CARCINOMA

= LUNG CANCER = LUNG CARCINOMA
◊ Most frequent cause of cancer deaths in males (35% of all cancer deaths) and females (21% of all cancer deaths); most common malignancy of men in the world; 6th leading cancer in women worldwide
Prevalence: 225,000 new cases + 160,000 deaths (2012)
Age at diagnosis: 55–60 years (range 40–80 years); M÷F = 1.4÷1
• asymptomatic (10–50%) usually with peripheral tumors

- symptoms of central tumors:
  - cough (75%), wheezing, pneumonia
  - hemoptysis (50%), dysphagia (2%)

    ◊ Most common cause of massive hemoptysis at age > 40.
- symptoms of peripheral tumors:
  - pleuritic / local chest pain, dyspnea, cough, hoarseness
  - Pancoast syndrome, superior vena cava syndrome
- symptoms of metastatic disease (CNS, bone, liver, adrenal gland)
- paraneoplastic syndromes:
  - cachexia of malignancy, migratory thrombophlebitis
  - clubbing + hypertrophic osteoarthropathy
  - nonbacterial thrombotic endocarditis
  - ectopic hormone production: hypercalcemia, syndrome of inappropriate secretion of antidiuretic hormone (SIADH), Cushing syndrome, gynecomastia, acromegaly

Risk factors:

(1) Cigarette smoking (squamous cell carcinoma + SSC)
   › related to number of cigarettes smoked, depth of inhalation, age at which smoking began
   ◊ 85% of lung cancer deaths are attributable to cigarette smoking!
   ◊ Passive smoking may account for 25% of lung cancers in nonsmokers!

(2) Radon gas: may be the 2nd leading cause for lung cancer with up to 20,000 deaths annually

(3) Industrial exposure: asbestos, uranium, arsenic, chlormethyl ether

(4) Concomitant disease: chronic pulmonary scar + pulmonary fibrosis

Scar carcinoma

◊ 45% of all peripheral cancers originate in scars!

Frequency: 7% of lung tumors; 1% of autopsies

Origin: related to infarcts (> 50%), tuberculosis scar (< 25%)

Histo: adenocarcinoma (72%), squamous cell ca. (18%)

Location: upper lobes (75%)

Location:

◊ 60–80% arise in segmental bronchi

› central: small cell carcinoma, squamous cell carcinoma (sputum cytology positive in 70%); arises in central airway often at points of bronchial bifurcation, infiltrates circumferentially, extends along bronchial tree

mnemonic: **S**mall **c**ell **a**nd **S**quamous are **S**entral

› peripheral: adenocarcinoma, large cell carcinoma

› upper lobe÷lower lobe = right lung÷left lung = 3÷2

› most common site: anterior segment of RUL

› **Pancoast tumor** (3%) = superior sulcus tumor, frequently squamous cell carcinoma
- atrophy of muscles of ipsilateral upper extremity ← lower brachial plexus involved
- Horner syndrome (enophthalmos, miosis, ptosis, anhidrosis) ← sympathetic chain + stellate ganglion involved

√ apical pleural thickening / mass

√ ± soft-tissue invasion / bone destruction

√ coronal + sagittal MR images improve evaluation

› SVC obstruction (5%): often in small cell carcinoma

Presentation:

√ solitary peripheral mass with corona radiata / "pleural tail" sign / satellite lesion

√ cavitation (16%): usually thick-walled with irregular inner surface; in 80% squamous cell carcinoma, followed by bronchioloalveolar carcinoma

√ central mass (38%): common in small cell carcinoma

√ unilateral hilar enlargement ← primary tumor / enlarged lymph nodes

Histologic Classification of Lung Cancer
(WHO 2004)

Categories	*[%]*
Non-small cell lung cancer (NSCLC)	**85**
Adenocarcinoma	32–50
Adenocarcinoma (not otherwise specified)	
Bronchioloalveolar carcinoma	4–10
Squamous cell lung carcinoma	25–35
Large cell lung carcinoma	5–9
Others (carcinoid (1–2%), sarcomatoid, adenosquamous, salivary gland tumor, etc.)	
Small cell lung cancer (SCLC)	**15**
Limited disease / stage LS-SCLC (1/3) = confined to hemithorax, mediastinum, supraclavicular nodes *Rx:* curative intent chemo- + radiation therapy	5
Extensive disease / stage ES-SCLC (2/3) = hematogenous metastatic disease at presentation *Rx:* chemotherapy	10

√ calcified enlarged nodes frequently benign

√ nodes in short axis diameter:

› 0–10 mm normal (CAVE: micrometastases)

› > 10 mm (65% sensitive + specific for tumor)

› 20–40 mm (37% NOT involved by tumor)

√ PET (89% sensitive, 99% specific)

√ anterior + middle mediastinal widening (suggests small cell carcinoma)

√ segmental / lobar / lung atelectasis (37%) ← airway obstruction (particularly in squamous cell carcinoma):

√ postobstructive lung enhances to a greater extent than tumor

√ distal lung atelectasis has a higher SI on T2WI than the central mass (in 77%) ← accumulation of secretions in obstructed lung

√ **"(reverse) S"** sign of Golden on PA CXR = combination of:

√ RUL collapse (inferiorly concave margin of lateral portion of minor fissure, which moved superiorly and medially with compensatory expansion of RML)

√ bulge of central tumor (inferiorly convex margin of medial portion of minor fissure)

√ rat tail termination of bronchus

√ "bronchial cuff "sign = focal / circumferential thickening of bronchial wall imaged end-on

(early sign)
√ local hyperaeration ← check-valve type endobronchial obstruction (best on expiratory view)
√ mucoid impaction of segmental / lobar bronchus ← endobronchial obstruction
√ persistent peripheral infiltrate (30%) = postobstructive pneumonitis
√ NO air bronchogram
√ pleural effusion (8–15%): most commonly due to adenoca.
√ chest wall invasion:
• localized chest wall pain = most sensitive predictor
√ tumor interdigitation with chest wall musculature on T2WI
√ obliteration of high-intensity extrathoracic fat on T1WI
√ bone erosion of ribs / spine (9%)
√ involvement of main pulmonary artery (18%); lobar + segmental arteries (53%) may result in additional peripheral radiopacity ← lung infarct
√ calcification in 7% on CT (histologically in 14%) usually eccentric / finely stippled
(a) preexisting focus of calcium engulfed by tumor
(b) dystrophic calcium within tumor necrosis
(c) calcium deposit from secretory function of carcinoma (eg, mucinous adenocarcinoma)

PET-CT:
√ lung nodule > 1 cm (97% sensitive, 78% specific)
Spatial resolution: 4 mm diameter
Metabolic resolution: 1 mm diameter = 1,000,000 cells
False positive: infection, granulomatous disease, other inflammatory disease
False negative: partial volume effect, small tumor size < 1 cm, respiratory motion blurring, low glycolytic activity (bronchioloalveolar carcinoma, carcinoid tumor)

(1) Staging (PET-CT better than any other modality)
◊ Occult metastases detected in up to 40% of cases!
(a) intrathoracic lymph nodes
√ lymph node with short-axis diameter > 1 cm by CT + NOT FDG avid = 100% NPV
√ small lymph node by CT + intense FDG uptake = 100% PPV
√ cancerous mediastinal nodes (91% sensitive, 86% specific) better than CT alone (75% sensitive, 66% specific)
◊ 21% of normal-sized nodes harbor metastatic dz

T-Staging of Lung Cancer
7th edition of TNM in Lung Cancer by International Association for the Study of Lung Cancer (2009)

Stage	*Diameter*	*Endoscopy*	*Atelectasis / obstructive pneumonia*	*Invasion of*	*Separate nodule(s)*
T1	T1a ≤2 cm T1b >2 to ≤3 cm	no invasion proximal to lobar bronchus			
T2	T2a >3 to ≤5 cm T2b >5 to ≤7 cm	main bronchus (≥2 cm distal to carina)	to hilus but not entire lung	visceral pleura	
T3	tumor >7 cm	main bronchus (≥2 cm distal to carina)	entire lung	parietal pleura, chest wall, diaphragm, mediastinal pleura, pericardium	within same lobe
T4	any tumor size			mediastinum / trachea / heart / great vessels / esophagus / vertebral body / carina	within different lobe

Anatomic Definition of Lymph Node Stations
International Association for the Study of Lung Cancer (IASLC)

Name	*Location*	*Upper Border*	*Lower Border*
supraclavicular	low cervical, supraclavicular, sternal notch	cricoid	clavicles; manubrium
superior mediastinal	upper paratracheal	apex of right lung; manubrium	intersection of innominate v. + trachea (RT); aortic arch (LT)
	prevascular, retrotracheal	apex of chest	carina
	lower paratracheal = para- and pretracheal	intersection of innominate v. + trachea (RT); aortic arch (LT)	azygos v. (RT); Lt pulmonary artery (LT)
aortic	subaortic = aortopulmonary window	lower aortic arch	Lt pulmonary artery
	paraaortic = ascending aorta / diaphragm	upper aortic arch	lower aortic arch
inferior mediastinal	subcarinal	carina	bronchus intermedius (RT); lower lobe bronchus (LT)
	paraesophageal = below carina	bronchus intermedius (RT); lower lobe bronchus (LT)	diaphragm
	pulmonary ligament	inferior pulmonary v.	diaphragm
N1 nodes	hilar, interlobar, lobar, segmental, subsegmental		

◊ 40% of enlarged nodes are free of metastatic dz

(b) adrenal metastasis
- √ PET scan: 100% sensitive, 80–95% specific
- √ FDG can differentiate adrenal "incidentaloma" from metastasis

(c) bone metastasis
- √ bone scan: 80–94% sensitive, 67–75% specific
- √ PET scan: 92–96% sensitive, 98% specific

(2) Recurrent disease (restaging) = residual tumor versus posttreatment changes
- ◊ radiotherapy + chemotherapy alter morphology causing confusion for CXR, CT, MR
- √ increased FDG uptake at sites of residual radiographic abnormality > 8 weeks after completion of therapy

False positive: radiation pneumonitis (evaluation must be postponed for 2–4 months)

Angio:
- √ bronchogenic carcinoma supplied by bronchial arteries
- √ distortion / stenosis / occlusion of pulmonary arterial circulation

Cx:

(1) Diaphragmatic elevation (phrenic nerve paralysis)
(2) Hoarseness (laryngeal nerve involvement, left > right)
(3) SVC obstruction (5%): lung cancer is cause of all SVC obstructions in 90%

(4) Pleural effusion (10%): malignant, parapneumonic, lymphoobstructive
(5) Dysphagia: enlarged nodes, esophageal invasion
(6) Pericardial invasion: pericardial effusion, localized pericardial thickening / nodular masses
(7) massive hemoptysis ← neovascularity, parenchymal destruction, angioinvasion by tumor

Prognosis: mean survival time < 6 months; 15% overall 5-year survival; survival at 40 months: squamous cell 30% > large cell 16% > adenocarcinoma 15% > oat cell 1%

Rx:

(1) Surgical resection for non-small cell histologic types
Unresectable: involvement of heart, great vessels, trachea, esophagus, vertebral body, malignant pleural effusion
(2) Adjuvant chemotherapy + radiation therapy in extensive resectable disease
(3) Chemotherapy for small cell carcinoma + radiation therapy for bulky disease, CNS metastases, spinal cord compression, SVC obstruction
(4) Embolization of bronchial artery

MULTIPLE PRIMARY LUNG CANCERS

Frequency: 0.72–3.5%; in ⅓ synchronous, in ⅔ metachronous

◊ 10–32% of patients surviving resection of a lung cancer will develop a second primary!

Dx: biopsy mandatory for proper therapy because tumors may have / develop a different cell type

PARANEOPLASTIC MANIFESTATIONS OF LUNG CANCER

1. Carcinomatous neuromyopathy (4–15%)
2. Migratory thrombophlebitis
3. Hypertrophic pulmonary osteoarthropathy (3–5%)

NM-Staging of Lung Cancer
7th edition of TNM in Lung Cancer IASLC (2009)

Stage	*Description (node ≥1 cm in short axis)*
N1	peribronchial / ipsilateral hilar nodes
N2	ipsilateral superior + inferior mediastinal nodes
N3	contralateral hilar / mediastinal nodes; scalene / supraclavicular nodes on either side
M1a	*intrathoracic spread*: malignant pleural / pericardial effusion, separate tumor nodule(s) in contralateral lung
M1b	*disseminated (extrathoracic) disease*: liver, bone, brain, adrenal gland, etc.

4. Endocrine manifestations (15%) usually with small cell carcinoma: Cushing syndrome, inappropriate secretion of ADH, HPT, excessive gonadotropin secretion

SPREAD OF LUNG CANCER

1. Direct local extension
2. Hematogenous (small cell carcinoma)
3. Lymphatic spread (squamous cell carcinoma)
   ◊ Normal-sized lymph nodes harbor tumor in 10%
4. Transbronchial spread – least common

DISTANT METASTASES OF LUNG CANCER

Likelihood: small cell > adeno > large cell > squamous

@ Bone

(a) marrow: in 40% at time of presentation

(b) gross lesions in 10–35%:

Location: vertebrae (70%), pelvis (40%), femora (25%)

√ osteolytic metastases (¾)

√ osteoblastic metastases (¼) in small cell carcinoma / adenocarcinoma

√ occult metastases in 36% of bone scans

@ Adrenals: in 37% at time of presentation

◊ 50% of adrenal masses in lung cancer patients are benign!

@ Brain: asymptomatic metastases on brain scan in 7% (30% at autopsy), in ⅔ multiple

@ Kidney, GI tract, liver, abdominal lymph nodes

@ Lung-to-lung metastases (in up to 10%, usually in late stage)

Adenocarcinoma of Lung (32–50%)

◊ Most common histologic subtype of lung cancer (2011)!

= intermediate malignant potential → slow growth, high incidence of early metastases

Doubling time: ~ 150–180 days

Histo: formation of glands / intracellular mucin

Subtype: bronchioloalveolar carcinoma

Location: almost invariably develops in periphery; frequently found in scars (tuberculosis, infarction, scleroderma, bronchiectasis) + in close relation to preexisting bullae

√ solitary peripheral subpleural mass (52%) / alveolar infiltrate / multiple nodules

√ may invade pleura + grow circumferentially around lung mimicking malignant mesothelioma

√ upper lobe distribution (69%)

√ air bronchogram / bronchiologram on HRCT (65%)

√ calcification in periphery of mass (1%)

√ smooth margin / spiculated margin ← desmoplastic reaction with retraction of pleura

Large Cell Carcinoma of Lung (5–9%)

= most heterogeneous of primary lung cancers

Path: difficult DDx from poorly differentiated adenoca. / SCC

Subtype: large cell = LC

› LC rhabdoid carcinoma

› LC basaloid carcinoma

› LC lymphoepithelioma

› LC neuroendocrine carcinoma (LCNEC, 2–3%)

› LC undifferentiated carcinoma

Large Cell Undifferentiated Carcinoma of Lung

◊ Strongly associated with smoking

Malignant potential: intermediate → rapid growth + early distant metastases

Doubling time: ~ 120 days

Histo: tumor cells with abundant cytoplasm + large nuclei + prominent nucleoli; diagnosed per exclusion due to lack of squamous / glandular / small cell differentiation

Subtype: giant cell carcinoma with very aggressive behavior + poor prognosis

√ large bulky usually peripheral mass > 6 cm (50%)
√ large area of necrosis
√ pleural involvement
√ large bronchus involved in central lesion (50%)

Squamous Cell Carcinoma of Lung (25–35%)

= EPIDERMOID CARCINOMA

◊ Strongly associated with cigarette smoking

Histo: mimics differentiation of epidermis by producing keratin ("epidermoid carcinoma"); central necrosis is common

Histogenesis: chronic inflammation with squamous metaplasia → progression to dysplasia + carcinoma in situ

• positive sputum cytology

◊ Most common cell type that is radiologically occult!

• hypercalcemia from tumor-elaborated parathyroid hormone-like substance

◊ Slowest growth rate, lowest incidence of distant metastases

Doubling time: ~ 90 days

(a) Central location in main / lobar / segmental bronchus (⅔)
√ large central mass ± cavitation
√ distal atelectasis ± bulging fissure ← mass effect
√ postobstructive pneumonia
◊ All cases of pneumonia in adults should be followed to complete radiologic resolution!
√ airway obstruction with atelectasis (37%)

(b) Solitary peripheral nodule (⅓)
√ characteristic cavitation (in 7–10%)
√ invasion of chest wall

◊ Squamous cell carcinoma is the most common cell type to cavitate and to cause Pancoast tumor!

Small Cell Undifferentiated Lung Carcinoma (13–20%)

= OAT-CELL CARCINOMA = SMALL CELL LUNG CANCER

◊ Most common primary pulmonary neuroendocrine neoplasm!

The prevalence of SCLC in the USA has been declining over the past 30 years to 13%–15%!

Cause: associated with cigarette smoking (in 95%)

Biologic behavior:
more aggressive than non-SCLC; rapid growth (= short doubling time); high growth fraction (= ratio of proliferating cells to total cells); high metastatic potential (early metastases in 60–70% at time of diagnosis); should be regarded as systemic disease

regardless of stage; virtually never resectable

Doubling time: ~ 30 days

Path: arises from bronchial mucosa with growth in submucosa + subsequent invasion of peribronchial connective tissue

Histo: small blue cells of round / oval / fusiform shape with scant cytoplasm, ill-defined borders, finely granular nuclear chromatin, absent / inconspicuous nucleoli; high cellularity with very high mitotic rate → large areas of necrosis; positive for neurosecretory granules (chromogranin, synaptophysin); in 20% coexistent with non-small cell histologic types (most frequently squamous cell)

Immunohistochemistry:

pancytokeratin antibodies (AE1/AE3, CD56), chromogranin– synaptophysin, thyroid transcription factor 1 (TTF-1 in 80%), Ki-67 proliferation index (in 80–100%) most helpful in separating SCLC from carcinoids

Age: 60–70 years; M÷F = 2.6÷1 to 1÷1

- weight loss, fatigue, anorexia, dyspnea, persistent cough
- chest pain, hemoptysis, postobstructive pneumonia
- symptoms of SVC syndrome (10%)

◊ Most common primary lung cancer causing superior vena cava obstruction ← extrinsic compression / endoluminal thrombosis / invasion!

- dysphagia ← esophageal invasion
- hoarseness ← invasion of recurrent laryngeal nerve
- smooth-appearing bronchial mucosal surface endoscopically
- paraneoplastic syndrome (= ectopic hormone production):
  - inappropriate secretion of ADH → ↓ concentration of urine, ↓ plasma osmolarity, euvolemic hyponatremia
  - Cushing syndrome ← ectopic ACTH production
  - acromegaly ← ectopic GHRP
  - hypercalcemic hyperparathyroidism
  - Eaton-Lambert myasthenia syndrome (= autoimmune neuropathy) → muscle weakness of limbs
  - encephalomyelitis, limbic encephalitis

Signs of extrapulmonary metastases:

bone marrow suppression, bone pain, pruritus, jaundice, seizures, mental status changes, ataxia

Location: 90–95% central within lobar / mainstem bronchus (primary tumor rarely visualized)

The most common manifestation of SCLC is a large centrally located lung mass or a mediastinal mass involving a hilum!

CT:

√ typically large hilar / perihilar parenchymal mass involving at least one hilum (85%):

√ extensive necrosis + hemorrhage

√ central mass often produced by a combination of primary neoplasm + mediastinal lymphadenopathy

√ centrally obstructing lesion → atelectasis of entire lung / major lobar atelectasis (30%)

√ "bronchus cut-off" sign

√ lobulated peripheral nodule without adenopathy (5%):
  √ fine spiculations ← vascular or lymphatic invasion / irregular intraalveolar spread
  √ marginal ground-glass opacity ← focal edema / hemorrhage / intraalveolar invasion
  √ enhancement reflecting tumor angiogenesis
√ intratumoral calcification (in up to 23%)
√ large confluent mediastinal (92%) / hilar 84%) adenopathy
√ displacement / narrowing of tracheobronchial tree (68%) or major vessels (68%)
√ atelectasis of entire lung / major lobar atelectasis (30%)
√ pleural effusion (38%) / thickening ± nodules

PET:

Useful for: initial tumor staging, treatment planning, prognosis (high SUV suggests poor survival)

√ avid FDG uptake (100%)

PET modifies management in up to 27% of patients!

Staging evaluation:

CT of abdomen + head, bone scintigraphy, bilateral bone marrow biopsies

Veterans Administration Lung Study Group (VALSG) Staging:

◊ Evaluate with CECT of chest (through adrenals) + brain MRI + PET/CT ± bone marrow biopsy

Limited disease / stage (LS-SCLC):

= without extrathoracic extension

1. Encompassed within single radiation port
2. Ipsilateral mediastinal / supraclavicular lymph nodes
3. Contralateral mediastinal / supraclavicular nodes
4. Ipsilateral (benign / malignant) pleural effusion

Extensive disease / stage (ES-SCLC in 60–70%):

= hematogenous metastatic disease at presentation

1. Not confined to single radiation port
2. Metastatic disease: contralateral lung, bone (19–38%), liver (17–34%), adrenal gland (10–17%), bone marrow (17–23%), CNS (8–15%), retroperitoneum (11%), other lymph nodes

Prognosis: 2–4 months median survival without treatment; 60–70% initial response to chemotherapy with relapse and death within 2 years; 5-year survival rate of 10–15% for LS-SCLC + 1–5% for ES-SCLC (unchanged for 30 years!)

Rx: (a) chemoradiation + prophylactic cranial irradiation + surgical resection (for LS-SCLC)

(b) etoposide + cisplatin (for ES-SCLC)

BRONCHOGENIC CYST

= CONGENITAL BRONCHOGENIC CYST

= fluid-filled blind pouch of ventral primitive foregut

◊ Belongs to spectrum of foregut duplication cysts!

Cause: abnormal budding / branching of primitive foregut between 26th and 40th day of

embryogenesis forming ventral diverticulum for tracheobronchial tree (dorsal segment = esophagus)

Frequency: most common intrathoracic foregut cyst (54–63% in surgical series)

Histo: thin-walled cyst filled with mucinous material, lined by columnar respiratory epithelium, mucous glands, cartilage, elastic tissue, smooth muscle

Location: mediastinum (near carina) >> lung parenchyma > pleura > diaphragm

- mostly incidental
- wheezing, stridor, dyspnea, dysphagia (in infants)

√ sharply outlined round / oval mass

√ may contain air-fluid level ← infection / communication with airway or GI tract

CT:

√ hypoattenuating lesion with smooth imperceptible wall

√ cyst contents of water density (50%) / higher density (50%) ← proteinaceous-mucoid material / milk of calcium

OB-US:

√ single unilocular fluid-filled pulmonary cyst in middle / posterior mediastinum

◊ Most common cystic lesion in fetal chest!

√ echogenic distended lung obstructed by bronchogenic cyst

Fetal MR:

√ hyperintense signal relative to lung + CSF on T2WI

√ occasionally hyperintense signal relative to lung on T1WI (mucoid / hemorrhagic content)

√ hyperintense obstructed lobe on T2WI

DDx: esophageal duplication cyst (middle / posterior mediastinum), neurenteric cyst (posterior mediastinum, vertebral defect)

Mediastinal Bronchogenic Cyst (86%)

Associated with: spinal abnormalities

M÷F = 1÷1

- asymptomatic (usually) vs. stridor, dysphagia

Location: pericarinal (52%), paratracheal (19%), esophageal wall (14%), retrocardiac (9%); usually on right

√ rarely communicates with tracheal lumen

√ may show esophageal compression

Intrapulmonary Bronchogenic Cyst (14%)

M > F

- infection (75%), dyspnea, hemoptysis (most common)

Location: lower÷upper lobe = 2÷1; usually medial third

√ 36% will eventually contain air

DDx: solitary pulmonary nodule, cavitated neoplasm, cavitated pneumonia, lung abscess

BRONCHOPULMONARY DYSPLASIA

= RESPIRATOR LUNG = BPD

= complication of respirator therapy (PPV or nasal CPAP) treated with > 21% oxygen for > 28 days

Cause: oxygen toxicity (lung damage by oxygen radicals) + barotrauma (bronchopulmonary injury from assisted ventilation)

- chronic oxygen dependency in premature neonates:
  - mild BPD = breathing room air
  - moderate BPD = need for < 30% oxygen
  - severe BPD = need for ≥ 30% oxygen ± PPV or nasal CPAP

Pathogenesis: hypoxia + oxygen toxicity

› capillary wall damage, leakage of fluid into interstitium and pulmonary edema

Stage I (0–3 days):

Path: loss of ciliated cells + necrosis of bronchiolar mucosa

√ RDS pattern of hyaline membrane disease

Stage II (4–10 days):

Path: hyaline membranes, eosinophilic exudate, squamous metaplasia, interstitial edema

Associated with: congestive failure from PDA

√ complete opacification with air bronchogram

› fibrosis of interstitium + groups of emphysematous alveoli

Stage III (10–20 days):

Path: fewer hyaline membranes, persistent injury of alveolar epithelium, exudation of macrophages

√ small round cystic lucencies alternating with regions of irregular opacity

Stage IV (after 1 month):

Path: septal wall thickening, dilated + tortuous lymphatics

√ "spongy" / "bubbly" coarse linear densities, esp. in upper lobes

√ hyperaeration of lung

√ lower lobe emphysema

CT:

√ regional air trapping

√ thickened interlobular septa

√ subsegmental atelectasis

√ reduced bronchoarterial diameter ratios

√ bronchial wall thickening

√ bullae + pneumatoceles

Prognosis: 40% mortality if not resolved by 1 month

Cx: (1) Increased airway reactivity = increased frequency of lower respiratory tract infections

(2) Obstructive airway disease = asthmalike clinical picture

(3) Focal atelectasis

(4) Cor pulmonale

(5) Rib fractures, rickets, renal calcifications (← chronic furosemide therapy)

(6) Cholelithiasis (← hyperalimentation ± ? furosemide)

(7) Focal areas of tracheomalacia, tracheal stenosis, acquired lobar emphysema

Rx: supportive

Prognosis:

(1) Complete clearing over months / years (⅓)

(2) Retained linear densities in upper lobe emphysema (29%)

DDx:

(a) conditions present at birth:
  (1) Diffuse neonatal pneumonia
  (2) Meconium aspiration
  (3) Total anomalous pulmonary venous return
  (4) Congenital pulmonary lymphangiectasia

(b) conditions developing over time:
  (1) Recurrent pneumonias with scarring (gastroesophageal reflux, tracheoesophageal fistula, immune deficiency, etc)
  (2) Cystic fibrosis
  (3) Idiopathic pulmonary fibrosis

(c) conditions not apparent at birth:
  (1) Wilson-Mikity syndrome
  (2) Pulmonary interstitial emphysema
  (3) Patent ductus arteriosus (uncommon appearance)
  (4) Overhydration
  (5) Perinatally acquired viral infection (especially CMV)

BRONCHOPLEURAL FISTULA

= BRONCHOPULMONARY FISTULA

= communication between the bronchial system / lung parenchyma + pleural space

Cause:

A. TRAUMA
  1. Complication of resectional surgery (pneumonectomy, lobectomy, bullectomy)
  2. Blunt / penetrating trauma
  3. Barotrauma

B. LUNG NECROSIS
  1. Putrid lung abscess
  2. Necrotizing pneumonia: Klebsiella, H. influenzae, Staphylococcus, Streptococcus; tuberculosis; fungus; Pneumocystis
  3. Infarction

C. AIRWAY DISEASE
  1. Bronchiectasis (very rare)
  2. Emphysema complicated by pneumonia / pneumothorax

D. MALIGNANCY: lung carcinoma with postobstructive pneumonia / tumor necrosis following therapy

• large / persistent air leak; acute / chronic empyema

HRCT:

√ direct visualization of bronchopleural fistula (in 50%)

√ peripheral air + fluid collection (indirect sign)

Dx: (1) Introduction of methylene blue into pleural space, in 65% dye appears in sputum
(2) Sinography
(3) Bronchography

Rx: tube thoracostomy, open drainage, decortication, thoraco-plasty, muscle-pedicle closure, transbronchial occlusions

BRONCHOPULMONARY SEQUESTRATION

= congenital malformation consisting of
(1) Nonfunctioning bronchopulmonary tissue
(2) No communication with tracheobronchial tree
(3) Systemic arterial supply

Frequency: 0.15–6.4% of all congenital lung malformations; 1.1–1.8% of all pulmonary resections

◊ 2nd most common lung lesion found in utero after congenital pulmonary airway malformation!

Etiology: formation of supernumerary tracheobronchial foregut bud caudad to normal lung bud
(a) before development of pleura = intralobar
(b) after development of pleura = extralobar

◊ Pulmonary sequestration with communication to GI tract is termed **bronchopulmonary foregut malformation**!

Size: usually > 6 cm
√ round / oval, smooth, well-defined solid homogeneous mass near diaphragm with mass effect
√ occasionally fingerlike appendage posteriorly + medially (= anomalous vessel)
√ contrast enhancement of sequestration at the same time as thoracic aorta (on rapid sequential CT scans)
√ multiple / single air-fluid levels if infected
√ surrounded by recurrent pulmonary consolidation in a lower lobe that never clears completely
√ may communicate with esophagus / stomach

OB-US:
◊ The vast majority of sequestrations in fetuses are extralobar!
Age: usually in 2nd trimester
√ conical / triangular homogeneously hyperechoic mass (many interfaces from multiple microscopically dilated structures) in a paraspinal location
√ color duplex may demonstrate feeding artery from descending aorta
√ polyhydramnios (? esophageal compression, excessive fluid secretion by sequestration)
√ fetal hydrops (? venous compression):
√ edema, ascites
√ hydrothorax (obstructed lymphatics + veins in torsed sequestration)
Rx: prenatal thoracoamniotic shunt

Fetal MR:
√ solid well-defined uniform hyperintense mass on T2WI

DDx: bronchiectasis, lung abscess, empyema, bronchial atresia, congenital lobar emphysema, cystic adenomatoid malformation, intrapulmonary bronchogenic cyst, Swyer-James syndrome, pneumonia, arteriovenous fistula, primary / metastatic neoplasm, hernia of Bochdalek

Intralobar Sequestration (75–86%)

= shares pleural investment with affected normal pulmonary lobe but separated from

bronchial tree

Etiology: controversial

(1) Possibly acquired through repeated lung inflammation → hypertrophy of vessels in pulmonary ligament

(2) Early appearance of congenital accessory tracheobronchial bud → incorporation within one pleural investment

Path: chronic inflammation fibrosis: multiple irregular cordlike adhesions to mediastinum, diaphragm, parietal pleura; vascular sclerosis; multiple cysts filled with fluid / thick gelatinous / purulent material

hybrid lesion = intralobar sequestration + type II cystic adenomatoid malformation usually associated!

Age at presentation: adulthood (50% > 20 years); M÷F = 1÷1

Associated with congenital anomalies in 6–12%:

skeletal deformities (4%): scoliosis, rib + vertebral anomalies; esophagobronchial diverticula (4%); diaphragmatic hernia (3%); cardiac anomalies (including tetralogy of Fallot); failure of renal ascent + rotation; cerebral anomalies; congenital pulmonary venolobar syndrome

- about 50% have symptoms by age 20; asymptomatic in 15%
- pain, repeated infection in same location (eg, recurrent acute lower lobe pneumonias)
- high-output congestive heart failure (in neonatal period) from L-to-L shunt
- cough + sputum production, hemoptysis

Location: posterobasal segments, rarely upper lung / within fissure; L÷R = 3÷2

CXR:

√ recurrent / persistent pneumonia localized to lower lobe

√ cavitation and cysts ± fluid levels

◊ Sequestered lung is aerated via pores of Kohn / communication with tracheobronchial tree!

Bronchogram:

√ NO communication of rudimentary bronchial system of sequestration with tracheobronchial tree (rare exceptions)

Angio:

√ usually single large artery (mean diameter of 6 mm) coursing through inferior pulmonary ligament from

› distal thoracic aorta (73%)
› proximal abdominal aorta (22%)
› celiac / splenic artery
› intercostal artery (4%)
› anomalous branch of coronary artery
› subclavian artery

√ multiple arteries in 16% (with vessel diameter of < 3 mm)

√ combined systemic + pulmonary arterial supply

√ <u>venous drainage via</u>

› <u>normal pulmonary veins</u> to L atrium (in 95%)
› azygos / hemiazygos vv. / intercostal vv. / SVC into R atrium (in 5%)

CT:
- √ single / multiple thin-walled cysts containing fluid / mucus / pus / air-fluid level / air alone
- √ mucus-impacted ectatic bronchi (= fat density) in sequestered lung
- √ emphysema bordering normal lung (37%) = postobstructive hyperinflation of sequestered lung
- √ homogeneous / inhomogeneous soft-tissue mass with irregular borders
- √ irregular enhancement (rare)
- √ one / two anomalous systemic arteries arising from aorta (DDx: AVM, interrupted pulmonary artery, isolated anomaly, chronic infection / inflammation of lung or pleura, surgically created shunt)
- √ premature atherosclerosis of anomalous arteries
- ◊ Mucoid impaction of bronchus surrounded by hyperinflated lung is CHARACTERISTIC!

Cx: massive spontaneous nontraumatic pleural hemorrhage, chronic inflammation, fibrosis

DDx of mass: neurogenic tumor, lateral thoracic meningocele, extramedullary hematopoiesis, pleural tumor, CPAM type III

Bronchopulmonary Sequestrations

	Intralobar	*Extralobar*
Prevalence	75%	25%
Pleural investment	visceral pleura	own pleura
Venous drainage	pulmonary veins	systemic veins
Symptomatic	adulthood	first 6 months
Etiology	acquired	developmental
Congenital anomalies	15%	50%

DDx of cavity: lung abscess, necrotizing pneumonia, fungal / mycobacterial pneumonia, cavitating neoplasm, empyema

DDx of cysts: pulmonary abscess, empyema, bronchiectasis, emphysema, bronchogenic foregut cyst, pericardial cyst, eventration of diaphragm, congenital cystic malformation

Extralobar Sequestration (14–25%)

= accessory lobe with its own pleural sheath (= "Rokitansky lobe") preventing collateral air drift → airless round mass

[Karl Freiherr von Rokitansky (1804–1878), professor of pathological anatomy at Allgemeines Krankenhaus, Wien, Austria]

Etiology: anomalous accessory / supernumerary tracheo-bronchial foregut bud develops after formation of pleura

Path: single ovoid / rounded / pyramidal airless lesion

Histo: resembles normal lung with diffuse dilatation of bronchioles + alveolar ducts + alveoli; dilatation of subpleural + peribronchiolar lymph vessels; covered by mesothelial layer overlying fibrous connective tissue

Frequency: 0.5–6.0% of all congenital lung lesions

Age: neonatal presentation; 61% within first 6 months of life; occasionally in utero; M÷F =

4÷1

Associated with congenital anomalies in 15–65%:

@ Lung: congenital diaphragmatic hernia (20–30%), eventration / diaphragmatic paralysis (up to 60%), congenital cystic adenomatoid malformation type II (15–25%), lobar emphysema, bronchogenic cyst, pectus excavatum, congenital pulmonary venolobar syndrome
  ◊ May coexist / form part of spectrum with CAM
@ Heart: anomalous pulmonary venous return, cardiac / pericardial anomalies (8%)
@ GI tract: epiphrenic diverticula (2%), tracheoesophageal fistula (1.5%), intestinal duplication cyst, ectopic pancreas
@ Others: renal anomaly, vertebral anomaly

• respiratory distress + cyanosis + CHF in newborn ← shunting of blood
  ◊ Lower lobe pneumonia that does NOT clear with antibiotics!
• feeding difficulties
• asymptomatic (rarely becomes infected) in 10%

Location: L÷R = 4÷1; typically within pleural space in posterior costodiaphragmatic sulcus between diaphragm + lower lobe (63–77%); mediastinum; within pericardium; within / below diaphragm (5–15%)

Size: 3–6 (range, ½ – 15) cm in diameter

√ airless (NO communication with bronchial tree); presence of air → connection with GI tract is inferred
√ may contain cystic areas
√ mediastinal shift (if large)

Angio (diagnostic):
√ arterial supply from
  › aorta as single / several small branches (80%)
  › splenic, gastric, subclavian, intercostal branches (15%)
  › pulmonary artery (5%)
√ venous drainage via
  › systemic veins in 80% (IVC, azygos, hemiazygos, SVC, portal vein) to right heart
  › pulmonary vein (25%)

CXR:
√ single well-defined homogeneous triangular mass (most commonly located adjacent to posterior medial hemidiaphragm)
√ NO air bronchograms
√ small "bump" on hemidiaphragm / inferior paravertebral region
√ opaque hemithorax ± ipsilateral pleural effusion (if sequestration large)
√ ± air-fluid level

CT:
√ homogeneous well-circumscribed soft-tissue density mass (no bronchial communication)

NUC (radionuclide angiography):
√ lack of perfusion during pulmonary phase followed by rapid perfusion in systemic phase

DDx: intrathoracic kidney, scimitar syndrome (with systemic supply to affected lung), hepatic herniation through diaphragm

DDx for chest lesion:
congenital cystic adenomatoid malformation, neuroblastoma, teratoma, diaphragmatic hernia
DDx for infradiaphragmatic lesion:
neuroblastoma, teratoma, adrenal hemorrhage, mesoblastic nephroma, foregut duplication
Cx: infection (in case of communication with bronchus / GI tract)
Rx: resection (delineation of vascular supply helpful)
Prognosis: favorable (worse if pulmonary hypoplasia present); decreases in size / disappears in up to 65% before birth

Esophageal / Gastric Lung
= rare variant of pulmonary sequestration
Age: infancy (as it is symptomatic)
• cough related to feeding; recurrent pulmonary infections
√ communication of bronchial tree of sequestered lung with esophagus / stomach

CANDIDIASIS

= CANDIDOSIS
◊ Most common nosocomial fungal infection
Organism: ubiquitous human saprophyte (Candida albicans most commonly) characterized by blastospheres (yeasts) admixed with hyphae / pseudohyphae (conventional stains)
◊ Normal constituent of gut flora
Manifestation: (1) Superficial overgrowth (thrush)
(2) Invasive systemic disease
At risk: particularly common in patients receiving immuno-suppressive therapy / with indwelling catheters
Entry:
(a) aspiration
(b) hematogenous dissemination from GI tract / infected central venous catheter
• prolonged fever despite broad-spectrum antibacterial coverage
• cough, hemoptysis
√ patchy airspace consolidation in lower lobe distribution
√ interstitial pattern
√ diffuse micro- / macronodular disease
√ pleural effusion (25%)

Cerebral Candidiasis

= disseminated disease
√ scattered cerebral microabscesses of < 3 mm
√ macroabscess + meningitis (uncommon)
Cx: angioinvasion → thrombosis and hemorrhage

CARDIOPULMONARY SCHISTOSOMIASIS

= form of parasitic embolism
Organism: Schistosoma mansoni (endemic in Middle East, Africa, Atlantic coast of South

America, Caribbean; S. japonicum and S. haematobium (less commonly)

At risk: > 5 years of continuous ova secretion

Prerequisite: portal hypertension with periportal hepatic fibrosis

Cycle: eggs travel as emboli via portosystemic collateral pathways to lodge in pulmonary muscular arteries and arterioles (50–150 μm in diameter)

Pathogenesis:

eggs trapped in pulmonary arteries are antigenic → incite an obliterative endarteritis (due to delayed host hypersensitivity) → pulmonary hypertension

Path: intra- and perivascular granulomas, intimal hyperplasia, medial hypertrophy, concentric collagen deposition and fibrosis of vessel walls; localized alveolitis with eosinophilic infiltration; pulmonary infarction

Age: 25–35 (range, 1–93) years

- gradually worsening hepatosplenomegaly
- dyspnea, cough, chest pain
- severe hypoxemia, cyanosis, digital clubbing

CXR:

√ cardiomegaly
√ central pulmonary arterial enlargement
√ tiny scattered lung nodules occasionally

HRCT:

√ nodules of 2–15 mm, interstitial thickening
√ larger nodules surrounded by ground–glass-opacity halo
√ dilatation of right atrium + right ventricle + central pulmonary arteries

Cx: cor pulmonale (2–33%)

Rx: praziquantel, oxamniquine

CASTLEMAN DISEASE

= ANGIOFOLLICULAR LYMPH NODE HYPERPLASIA = BENIGN GIANT LYMPH NODE HYPERPLASIA = ANGIOMATOUS LYMPHOID HAMARTOMA = LYMPHOID HAMARTOMA

[Benjamin Castleman (1906–1982), chief of anatomic pathology at Massachusetts General Hospital, Boston]

= diverse group of rare nonclonal lymphoproliferative disorders of differing histopathologic properties + biologic behavior

Etiology: lymphoid-hamartomatous hyperplasia, autoimmune disease, immunodeficiency, chronic low-grade inflammation

Associated with: unregulated overproduction of interleukin-6

Histopathogenetic classification:

(a) **hyaline-vascular Castleman disease** (76–91%) nonclonal hyaline vascular lymph follicles; expanded mantle zones of small lymphocytes forming concentric rings ("onionskin"); prominent capillary proliferation with endothelial hyperplasia in interfollicular areas; involuted germinal centers often penetrated by single capillary vessel ("lollipop" appearance)

Age: 3rd– 4th decade

- asymptomatic

√ unicentric intensely enhancing mass (in 90%)
√ calcification + central fibrosis
Prognosis: benign course
Rx: curative surgical resection, steroids ± chemotherapy

(b) **plasma cell Castleman disease** (4–9–24%) sheets of plasma cells between normal / enlarged follicles; paucity of capillaries
Prevalence: < 10% of Castleman disease
Age: 6th decade
• systemic manifestations: fever, night sweats, malaise
• anemia, thrombocytopenia, hyperglobulinemia
√ multicentric / unicentric (9–24%) mass
√ splenomegaly
Prognosis: worse than hyaline vascular Castleman
Rx: systemic chemotherapy, antiproliferative agents

(c) **HHV-8–associated Castleman Disease**
[HHV= **H**uman **H**erpes **V**irus]
= plasmablastic variant (= microlymphoma) in immunosuppressed patients with positive HIV status
• generalized lymphadenopathy; constitutional symptoms
• hematologic ± immunologic abnormalities
Prognosis: poor with several months of survival
Rx: systemic chemotherapy, antiviral + antiproliferative regimens (rituximab)

(d) multicentric not otherwise specified

Morphologic classification: unicentric versus multicentric
Location: chest / mediastinum (46–70%), neck (15%), abdomen & pelvis (15%)
extralymphatic: lung, larynx, parotid, pancreas, meninges, muscle
Mean size: 5 cm
√ enlarged lymph node with preserved architecture

Localized / Unicentric Angiofollicular Lymph Node Hyperplasia

Cause: chronic viral antigenic stimulation with reactive lymphoid hyperplasia / developmental growth disturbance of lymphoid tissue
Age: all age groups (peaks in 4th decade); M÷F = 1÷4
Histo: mostly hyaline-vascular cell type (95%)
Location:
(a) middle mediastinum + hila
(b) cervical lymph nodes
(c) mesenteric + retroperitoneal lymph nodes
(d) extralymphatic sites: lung, larynx, parotid gland, pancreas, meninges, muscle
Morphologic types:
(a) solitary well-circumscribed mass without associated lymphadenopathy (50%)
(b) dominant mass displacing / surrounding / invading contiguous structures + lymphadenopathy (40%)
(c) multiple enlarged matted lymph nodes confined to one mediastinal compartment (10%)
• asymptomatic in 58–97%; growth retardation

- cough, dyspnea, hemoptysis, lassitude, weight loss, fever
- ↑ sedimentation rate, refractory microcytic anemia
- IgG, IgM, IgA hypergammaglobulinemia (50%)

Size: up to 16 cm in diameter

US:
- √ well-defined homogeneous hypoechoic mass
- √ increased vascularity on color Doppler with large vessels at periphery extending centrally

CT:
- √ sharply marginated smooth / lobulated homogeneous solitary mass of muscle density
- √ spotty coarse peripheral / central branching calcifications (10–31%)
- √ enhancing rim (vascular capsule)
- √ intense enhancement almost equal to aorta (in hyaline vascular type)
- √ slight enhancement (in plasma cell type)
- √ nonenhancing central areas ← fibrosis / cystic necrosis
- √ pleural effusion (uncommon)

MR:
- √ heterogeneous mass iso- / hyperintense to muscle on T1WI
- √ markedly hyperintense on T2WI
- √ T2-hypointense stellate scar = central area / linear web of hypointensity ← fibrosis / fibrous septa reminiscent of stellate scar of hepatic fibrolamellar carcinoma
  - √ scar hypointense on early phase dynamic T1WI
- √ peripheral flow voids of feeding vessels surrounding mass (in hyaline vascular type)

Angio:
- √ hypervascular mass with intense homogeneous blush (hyalin-vascular type)
- √ enlarged feeding vessels arising from bronchial / internal mammary / intercostal arteries
- √ some hypervascularity (plasma cell type)

DDx: indistinguishable from lymphoma

Prognosis: good with treatment; ~ 100% curative

Rx: (1) Complete surgical resection
(2) Radiation + steroid therapy

DDx: thymoma, lymphoma, sarcoma, hemangiopericytoma, paraganglioma, neurofibroma, schwannoma, chest wall tumor, bronchial adenoma, mesenteric fibromatosis, inflammatory myofibroblastic tumor, microcystic lymphatic malformation

Disseminated / Generalized / Multicentric Angiofollicular Lymph Node Hyperplasia

= potentially malignant lymphoproliferative disorder

Cause: disordered immunoregulation with polyclonal plasma cells from viral infection with uncontrolled B-cell proliferation + interleukin-6 dysregulation

Mean age: 40–60 years; M÷F = 2÷1

Histo: mostly plasma cell type (66%) with infiltration of nodes by sheets of mature plasma cells

Associated with:

(a) hyperplasia without neuropathy

- fatigue, anorexia, skin lesions, CNS disorders

(b) hyperplasia with POEMS syndrome

(c) osteosclerotic myeloma, HHV-8 (Kaposi sarcoma, AIDS)

√ 1–6 cm large homogeneous lymph nodes in multiple mediastinal compartments
√ variable mild contrast enhancement
√ peripheral multicentric adenopathy
√ hepatosplenomegaly
√ salivary gland enlargement
√ ascites
√ lymphocytic interstitial pneumonitis (LIP):
  √ ± ill-defined centrilobular nodules
  √ ground-glass attenuation
  √ air-space consolidation
  √ cysts ← partial airway obstruction by peribronchial + peribronchiolar LIP
  √ thickening of bronchovascular bundles

Rx: surgical resection, irradiation, systemic chemotherapy + corticosteroids

Prognosis: mean survival of 24–33 months

CATAMENIAL PNEUMOTHORAX

[*kata*, Greek = according to; *men*, Greek = month]

= recurrent spontaneous pneumothorax during menstruation associated with endometriosis of the diaphragm; R >> L

• right scapular / thoracic pain within 24–72 hours after onset of menstruation

Frequency: 24–33% of recurrent spontaneous pneumothoraces in women of reproductive age referred for surgery

◊ Coexistent abdominal endometriosis in 60–80%

Dx: brown nodules on video-assisted thoracoscopic surgery (VATS)

Rx: (1) Suppression of endometrial implants by hormonal manipulation
(2) Resection of endometrial implants with closure of diaphragmatic holes

CHEMICAL PNEUMONITIS

= inhalation of noxious chemical substances

A. ORGANIC: organophosphates, paraquat, polyvinyl chloride, polymer fumes, smoke
B. NONORGANIC: ammonia, hydrogen sulfide, nitrogen oxide, sulfur dioxide
C. METAL: cadmium, mercury, nickel, vanadium

Carbamates

= agricultural insecticides functioning as cholinesterase inhibitor (similar to organophosphates) but with poor penetration into CNS

√ pulmonary edema with respiratory failure

Paraquat

= agricultural herbicide

Exposure: often intentional ingestion

Pathophysiology: rapid accumulation in lungs with production of superoxide radicals damaging pulmonary cells

CXR (wide radiographic variability:
√ no abnormality
√ increased interstitial / granular opacities
√ pulmonary edema
√ pneumomediastinum

HRCT:
√ bilateral diffuse areas of ground-glass attenuation evolving into consolidation with bronchiectasis, irregular lines, traction bronchiectasis of interstitial fibrosis

Hydrogen Sulfide

= irritant + chemical asphyxiant gas

Industries: coal mines, tanneries, petroleum manufacturing plants, geothermal power plants, aircraft factories, sewer works, rubber works

Effect: toxic for respiratory (large quantities → inhibition of medullary respiratory center) + neurologic systems

• "knockdown" = brief loss of consciousness ← bronchial hyperresponsiveness

• determination of urine thiosulfate levels (to monitor occupational exposure); smell of rotten eggs
√ pulmonary edema

Ammonia

= highly soluble corrosive gas acts as a mucosal irritant
Industries: production of explosives, petroleum, agricultural fertilizer, plastics
√ pulmonary edema
Prognosis: complete recovery; bronchiectasis + bronchiolitis obliterans may develop

Hydrocarbon

Exposure: ingestion / aspiration (eg, accidental poisoning in children; fire-eating performers)
Path: (a) acute phase: intraalveolar, intrabronchial, peribronchial, interstitial accumulation of inflammatory cells + edema
(b) chronic phase (1–2 weeks after initial onset): proliferative bronchiolitis, parenchymal fibrosis, pneumatocele formation
√ uni- / bilateral consolidation, well-defined nodules
√ pneumatoceles (from coalescing areas of bronchiolar necrosis / partial obstruction of bronchial lumen)

Mercury

Exposure: inhalation of mercury vapor
Industries: electrolysis, manufacture of thermometers, cleaning of boilers, smelting silver from dental amalgam containing mercury
Pathophysiology: acute chemical bronchiolitis + pneumonitis followed by diffuse alveolar damage with hyaline membrane formation
• pulmonary function impairment
√ perivascular haziness + fine reticular opacities
√ pulmonary interstitial fibrosis
Prognosis: acute inhalation poisoning usually fatal

CHYLOTHORAX

= leakage of chyle (= lymph containing chylomicrons of suspended fat) from thoracic duct or its branches into pleural space ← obstruction / disruption of thoracic duct (in 2%)

Etiology:

A. Developmental defects
   1. Thoracic duct atresia
   2. Lymphangiectasia
   3. Lymphangioma
   4. Lymphangiomatosis (rare): mediastinal / thoracic cystic hygroma of neck growing into mediastinum
   5. Lymphangioleiomyomatosis ± tuberous sclerosis

B. Trauma
   1. Closed / penetrating chest trauma / birth trauma (25%): latent period of 10 days

2. Surgery (2nd most common cause):
   esophagectomy / cardiovascular surgery, esp. coarctation repair (0.5%), retroperitoneal surgery, neck surgery
3. Subclavian venous catheter

C. Neoplasm (54%)
1. Lymphoma (most common cause)
2. Metastatic cancer

D. Fibrosing conditions
1. Mediastinitis
2. Tuberculosis
3. Filariasis (rare)

E. Obstruction of central venous system / thoracic duct

F. Idiopathic / cryptogenic (15%): most common cause in neonatal period

G. Transdiaphragmatic passage of chylous ascites

Age: in full-term infants; may be present in utero; M÷F = 2÷1

Frequency: 1÷10,000 deliveries

May be associated with:
trisomy 21, tracheoesophageal fistula, extralobar lung sequestration, congenital pulmonary lymphangiectasia

- high in neutral fat + fatty acid (low in cholesterol):
  - triglyceride level > 110 mg/dL
- milky viscoid fluid (chylomicrons) after ingestion of milk / formula and clear during fasting

√ usually unilateral loculated pleural effusion
(a) right chylothorax ← duct disruption inferior to T5–6 (more common)
(b) left-sided chylothorax if duct disrupted above T5–6

√ low attenuation (fat) / high attenuation (protein content)

√ ± leakage of lymphangiographic contrast

√ polyhydramnios (? result of esophageal compression)

Cx: (1) Pulmonary hypoplasia
(2) Hydrops (congestive heart failure ← impaired venous return)

Rx: (1) Thoracentesis → loss of calories, lymphocytopenia, hypogammaglobulinemia
(2) Total parenteral nutrition
(3) Thoracic duct ligation (if drainage exceeds 1,500 mL/d for adults or 100 mL/year-age/day for children > 5 years of age; drainage > 14 days)
(4) Pleuroperitoneal shunt; tetracycline pleurodesis; mediastinal radiation; intrapleural fibrin glue; pleurectomy

COAL WORKER PNEUMOCONIOSIS

= CWP = ANTHRACOSIS = ANTHRACOSILICOSIS

Prevalence: 3%

Coal dust: inert, HOWEVER admixed silica is fibrogenic

Coal rank (= carbon content of coal):
anthracite (highest risk) > bituminous coal > lignite coal; washed coal = nearly free of silica

Pathophysiology of clearance:

inhaled coal dust deposited predominantly in respiratory bronchioles (slower air flow) + alveoli

(a) cleared by lymphatic flow (majority)
(b) cleared by mucociliary action (particle size > 5 μm)
(c) taken up by alveolar / interstitial macrophages = anthracosis (seen also in smokers + urbanites)

May be associated with: Caplan syndrome (in 1%)

DDx: silicosis, mycobacterial infection, sarcoidosis, subacute hypersensitivity pneumonitis

Simple CWP

coal macule = aggregate of centrilobular carbon-containing macrophages around bronchioles surrounded by network of collagen fibers + fibroblasts (about 1–5 mm in diameter)

◊ NO progression in absence of further exposure

Path: development of reticulin fibers associated with bronchiolar dilatation (focal emphysema) + bronchiolar artery stenosis (↓ capillary perfusion); with disease progression nodules may coalesce + become centrally necrotic ← ischemia

• poor correlation between symptoms + physiologic findings + roentgenogram

Location of coal macules:
around respiratory bronchioles in upper lobes >> lower lobes (higher pulmonary arterial gradient in lower portions of lung → higher lymphatic flow → coal dust particles clear more rapidly → particle deposition less prominent in lower lobes)

Size of nodules: < 10 mm

CXR:
√ small round 1–5-mm nodular interstitial opacities (only seen by superposition after an exposure of > 10 years):
√ granular appearance with poor definition of margins
√ nodularity correlates with amount of collagen (NOT amount of coal dust)
√ nodules calcify (in 10–20%) as central nodular dot
√ occasionally reticular / reticulonodular opacities

CT:
√ small round nodules diffusely involving both lungs in a perilymphatic distribution:
√ calcifications within nodules in 30%
√ pleural pseudoplaques (= coalescent macules in subpleural region)
√ hilar / mediastinal lymph node enlargement in 30%

Cx: (1) Chronic obstructive bronchitis
(2) Focal emphysema
(3) Cor pulmonale

Rx: reducing exposure, cessation of smoking, supplemental oxygen, bronchodilators, corticosteroids

DDx: silicosis (nodules diffusely calcified with well-defined margins, eggshell calcifications in only 1.3%)

Progressive Massive Fibrosis

= COMPLICATED PNEUMOCONIOSIS
= CONGLOMERATE ANTHRACOSILICOSIS

May develop / progress after cessation of dust exposure

Path: avascular amorphous central fibrotic mass of haphazardly arranged insoluble proteins stabilized by cross-links + ill-defined bundles of coarse hyalinized collagen at periphery; numerous pigment-laden macrophages and abundant free pigment; foci of frank necrosis, cholesterol clefts, chronic inflammatory cellular infiltrates

Location: almost exclusively restricted to posterior segment of upper lobe / superior segment of lower lobe

Size of nodules: > 10 mm

- cough (blackened sputum), dyspnea
- low FEV_1 (may not correlate with radiograph!)

√ large opacities initially at periphery of lung in middle + upper lung zones:
- √ irregular border + surrounding pericicatricial emphysema
- √ radiation toward hila starting at lung periphery; bilateral symmetry
- √ discoid contour (44%) = mass flat from front to back (thin opacity on lateral view, large opacity on PA view), medial border often ill-defined, lateral borders sharp + parallel to rib cage
- √ cavitation (occasionally) ← ischemic necrosis / superimposed TB infection

√ apparent decrease in nodularity ← incorporation of nodules from surroundings

√ bullous scar emphysema

√ pulmonary hypertension

√ ± enlargement + calcifications of mediastinal + hilar lymph nodes

MR:
- √ low SI on T1WI + T2WI compared to muscle ← fibrosis
- √ peripheral contrast enhancement

PET:
- √ hypermetabolic nodules (majority)

N.B.: Exposure reduction to coal dust does not stop progression of disease!

DDx: lung cancer (increased SI on T2WI), sarcoidosis, berylliosis, tuberculosis, talcosis

Carbon Black Pneumoconiosis

= burning of natural gas + petroleum products (filler in rubber, plastics, phonograph records, inks, carbon paper, carbon electrodes)

√ fine reticulonodular pattern with lower zone predominance

COCCIDIOIDOMYCOSIS

Organism: dimorphic soil fungus Coccidioides immitis and its close relative Coccidioides posadasii; arthrospores in desert soil spread by wind aerosolized in dry dust; highly infectious

Geographic distribution:

endemic in southwest desert of USA (San Joaquin Valley, central southern Arizona, western Texas, southern New Mexico) + northern Mexico + in parts of Central + South America; similar to histoplasmosis

Mode of infection:

arthrospores deposited in alveoli after inhalation; maturation into large thick-walled

spherules → rupture with release of hundreds of endospores (instead of budding)

Dx: (1) Culture of organism
(2) Spherules in pathologic material (demonstrated with Gomori-methenamine silver stain)
(3) Positive skin test
(4) Complement fixation titer

Primary Pulmonary Coccidioidomycosis (40%)

= ACUTE RESPIRATORY COCCIDIOIDOMYCOSIS

- 60–80% asymptomatic
- "valley fever" = influenza-like symptoms
- desert rheumatism (33%) most commonly in ankle
- rash, erythema nodosum / multiforme (5–20%)

√ segmental / lobar consolidation
√ patchy infiltrates mainly in lower lobes (46–80%) frequently subpleural + abutting fissures
√ peribronchial thickening
√ hilar adenopathy (20%)
√ pleural effusion (10%)

Chronic Respiratory Coccidioidomycosis (5–10%)

Prevalence: 5% of infected patients

- symptoms of postprimary tuberculosis, hemoptysis in 50%

√ one / several well-defined nodules (= coccidioidomycoma) of 5–30 mm in size (in 50–70%)
√ persistent / progressive consolidation
√ "grape skin" thin-walled cavities (in 10–15%), in 90% solitary, 70% in anterior segment of upper lobes (DDx: TB), 3% rupture into pleural space due to subpleural location (pneumothorax / empyema / persistent bronchopleural fistula
√ bronchiectasis
√ mediastinal adenopathy (10–20%)

Disseminated Coccidioidomycosis (1%)

= secondary phase of hematogenous spread to meninges, bones, skin, lymph nodes, subcutaneous tissue, joints (except GI tract)

- skin granulomas / abscesses

√ micronodular "miliary" lung pattern
√ pericardial effusion

Cerebral Coccidioidomycosis

= fungal meningitis (in 50%)
√ thick exudate + abnormal enhancement in basal cisterns + subarachnoid space

Cx: (1) Hydrocephalus
(2) Vasculitis (in up to 40%) involving small perforators → deep brain infarct
(3) Subarachnoid hemorrhage ← granulomatous inflammation of large vessels
(4) Cerebritis (especially in immunocompromised patients) → fungal extension

along vessel walls / in perivascular spaces

CONGENITAL HIGH AIRWAY OBSTRUCTION SYNDROME (CHAOS)

Cause: complete / near-complete obstruction of fetal airway → trapping of lung fluid + hyperplasia of pulmonary alveoli

√ tracheal dilatation

√ flattened / everted hemidiaphragm

√ massive ascites

Fetal MR:

√ enlarged hyperintense lungs on T2WI

Cx: hydrops fetalis ← cardiac compression + obstructed venous return

Prognosis: poor

CONGENITAL HYDROTHORAX

Prevalence: 1÷15,000 pregnancies

Cause: disequilibrium across pleural membranes due to

(a) primary cause: lymphatic duct abnormality → chylothorax → defective chest drainage

(b) secondary cause: generalized fluid retention related to immune / nonimmune fetal hydrops

Associated abnormalities (in 40%):

congenital cystic adenomatoid malformation, congenital diaphragmatic hernia, bronchopulmonary sequestration cardiac anomalies, Turner syndrome, Down syndrome, cystic hygroma, infection

Fetal MR:

√ lungs surrounded by fluid collection = hypointense on T1WI + hyperintense on T2WI

Rx: fetal intervention (thoracentesis / thoracoamniotic shunting) reserved for hydrothorax with marked mass effect

CONGENITAL LOBAR OVERINFLATION

= CONGENITAL LOBAR EMPHYSEMA (technically inaccurate term)

= progressive overdistension of one / multiple lobes

M÷F = 3 ÷1

Etiology:

(a) bronchomalacia: deficient / dysplastic / immature bronchial cartilage

(b) endobronchial obstruction: mucosal fold / web

(c) extrinsic bronchial compression: PDA, aberrant left pulmonary artery, pulmonary artery dilatation, bronchogenic cyst

(d) polyalveolar / macroalveolar hyperplasia

Histo: airspace enlargement without maldevelopment

Pathophysiology:

(a) collapsed airway acts as 1-way valve → air trapping with expansion of alveoli but intact alveolar wall

(b) bronchial obstruction → hyperinflated lung ← collateral air drift

Associated with: CHD in 12–15% (PDA, VSD)
• respiratory distress (90%) + progressive cyanosis within first 6 months of life; during first 2 days of life (50%)
Location: LUL (42–43%) > RML (32–35%) > RUL (20%) > either lower lobe (< 1%)
√ hazy masslike dense opacity immediately following birth ← delayed clearance of lung fluid in emphysematous lobe over 1–14 days
√ hyperlucent overinflated lobe (after clearing of fluid via lymphatic + capillary system)
√ air trapping:
  √ compression atelectasis of adjacent ipsilateral lobes
  √ contralateral mediastinal shift
  √ widening of rib spaces
  √ depression of ipsilateral hemidiaphragm
  √ widely separated but organized vascular markings
OB-US / MR:
  √ homogeneously hyperechoic mass
  √ mass of homogeneously high SI on T2WI
Mortality: 10%
Rx: ventilatory support (low-volume, low-pressure); surgical resection
DDx: pneumothorax, pulmonary cyst

CONGENITAL LYMPHANGIECTASIA

Primary Pulmonary Lymphangiectasia (⅔)

= CONGENITAL PULMONARY LYMPHANGIECTASIA
= abnormal development of lungs between 14th–20th week of GA characterized by anomalous dilatation of (pulmonary, subpleural, interlobar, perivascular, peribronchial) lymphatic vessels of chest
Path: subpleural cysts, ectatic tortuous lymph channels in pleura, interlobular septa + along bronchoarterial bundles; NO obstruction
Age: usually manifest at birth; 50% stillborn; M = F
May be associated with:
total anomalous pulmonary venous return, hypoplastic left heart, Noonan syndrome, Turner syndrome, Ehlers-Danlos syndrome, Down syndrome
• respiratory distress within few hours of birth
Site: diffuse involvement of both lungs, occasionally only in one / two lobes (with good prognosis)
√ marked prominence of coarse interstitial markings (simulating interstitial edema)
√ hyperinflation
√ scattered radiolucent areas (dilated airways)
√ patchy areas of pneumonia + atelectasis
√ pneumothorax
√ ± pleural effusion
Fetal MR:
  √ bilateral inhomogeneity of the lung parenchyma on T2WI

√ high SI in pulmonary interstitium on T2WI

Prognosis: with diffuse involvement invariably fatal at < 2 months of age

Generalized Lymphangiectasia

= DIFFUSE LYMPHANGIOMA

= proliferation of mainly lymphatic vascular spaces with relentless systemic progression

Age: children, young adults

Location: widespread visceral + skeletal involvement

√ diffuse pulmonary interstitial disease

√ chylous effusions in pleural + pericardial spaces

√ ± lytic bone lesions

√ lymphangiographic pooling of contrast material in dilated lymphatic channels / lymph nodes

Localized Lymphangioma

= rare benign usually cystic lesion

Histo: collection of dilated + proliferated lymph vessels (? hamartoma / benign neoplasm / focal sequestration of ectatic lymph tissue)

Age: first 3 years of life; M = F

• asymptomatic (33%); dyspnea ← tracheal compression

Location: neck (80%), mediastinum, axilla, extremity

√ discrete featureless mass

√ may have chylous / pleural effusion

√ may have lytic lesion in contiguous skeleton

Prognosis: propensity for local recurrence

DDx: hemangioma

Secondary Pulmonary Lymphangiectasia

Cause: surgery, infection, tumor genesis, pulmonary venous obstruction (← total anomalous pulmonary venous return, hypoplastic left heart syndrome)

CONGENITAL PULMONARY AIRWAY MALFORMATION (CPAM)

= CONGENITAL CYSTIC ADENOMATOID MALFORMATION (CCAM)

= congenital abnormality of the lung characterized by an intralobar mass of disorganized pulmonary tissue communicating with bronchial tree; normal vascular supply + drainage (pulmonary artery + vein) with delayed clearance of fetal lung fluid

Prevalence: 1÷25,000–35,000 pregnancies; 25% of congenital lung disorders; 30–40% of all congenital diseases 95% of congenital cystic lung lesions

◊ Most common fetal lung mass diagnosed in neonatal period / in utero!

Cause: arrest of normal bronchoalveolar differentiation (= branching) between 5th–7th week of gestation with overgrowth of terminal bronchioles

Path: proliferation of bronchial structures at the expense of alveolar saccular development; modified by inter-communicating cysts of various size (adenomatoid overgrowth of terminal bronchioles, proliferation of smooth muscle in cyst wall, absence of cartilage)
<u>hybrid lesion</u> = features of CPAM + bronchopulmonary sequestration with systemic arterial supply

Connections:
(a) proximal airways: abnormal communication
(b) blood supply: pulmonary artery
Exception: hybrid lesion → systemic blood supply
(c) blood drainage: pulmonary veins

Modified Stocker classification (2002):

Type 0 (< 3%, added later):
= ACINAR DYSPLASIA OF THE LUNG (previous designation)
= severe global arrest of lung development
Origin: trachea / bronchus
Histo: acinar dysgenesis / dysplasia = no cysts / very small ones (<0.5 cm)
Location: in any lobe
• incompatible with life

Type 1 = **large cyst CPAM** (60–70%):
Origin: bronchus / bronchiolus
Histo: (a) single large cyst > 20 mm
(b) 1–10 cm intercommunicating cysts surrounded by multiple smaller cysts lined by ciliated pseudo- stratified columnar epithelium, mucigenic (mucus-producing) cells in ⅓; small amount of supporting fibrous tissue + smooth muscle; NO cartilage
√ numerous variable-sized anechoic spaces of 1–10 cm in diameter intermixed with echogenic soft tissue on US
√ hyperintense uni- / multilocular lesion with discrete walls on T2WI
√ mass of variable density ± mediastinal shift on postnatal radiograph
√ round soft-tissue mass gradually filling with air on neonatal radiographs ← delayed clearance of fetal lung fluid through abnormal airway:
√ solitary well-defined air-filled cyst with thin wall
√ multiple air-filled cysts of varying sizes
√ ± air fluid levels
√ well-defined air-filled spaces on CT
√ ± abnormal systemic arterial supply
Prognosis: excellent following resection

Type 2 = **small cyst CPAM** (15–20%):
Origin: bronchiolus
Histo: multiple cysts / bronchiole-like structures < 20 mm in diameter lined by ciliated cuboidal / columnar epithelium without normal lung airspaces (similar to pulmonary hyperplasia associated with laryngeal atresia)
Strong association with: tracheoesophageal fistula, renal agenesis, intestinal atresia, diaphragmatic hernia
√ echogenic mass with multiple small 5–20 mm cysts
√ variable appearance with cystic + solid T2 components
√ heterogeneous intrapulmonary mass with small air-filled cystic areas on postnatal radiograph / CT
√ ± abnormal systemic arterial supply = hybrid lesion demonstrating features of CPAM + bronchopulmonary sequestration

Prognosis: poor secondary to associated abnormalities

Type 3 = **microcystic solid CPAM** (5–10%):

Origin: bronchiolar-alveolar duct (adenomatoid type)

Histo: solitary large bulky firm mass of bronchuslike structures lined by ciliated cuboidal epithelium with 3–5-mm small microcysts / solid type

√ large homogeneously echogenic mass compared with liver WITHOUT discernible cystic spaces

√ homogeneously hyperintense solid mass on T2WI

√ ill-defined area of increased attenuation on CT

Prognosis: poor ← pulmonary hypoplasia / hydrops

Type 4 (10–15%, added later):

Histo: type of "unlined" peripheral lung cyst

Unique association with: tension pneumothorax

√ large cyst up to 10 cm in diameter indistinguishable from a low-grade cystic pleuropulmonary blastoma / type 1 CPAM (clinically / radiologically)

In 25% associated with:

cardiac malformation, pectus excavatum, renal agenesis, prune-belly syndrome, jejunal atresia, chromosomal anomaly, bronchopulmonary sequestration

Age of detection: childhood, neonate, fetus; M÷F = 1÷1

• respiratory distress + severe cyanosis in 1st week of life (66%) / within 1st year of life (90%) ← compression of normal lung + airways

• superimposed chronic recurrent infection (10%) after 1st year

Location: equal frequency in all lobes (rare in middle lobe); more than one lobe involved in 20%; L÷R = 1÷1

◊ Mostly unilateral affecting an entire lobe!

CXR:

√ may appear normal due to prenatal regression

√ almost always unilateral expansile mass with well-defined margins (80%) ← retained fetal lung fluid / type III lesion

√ multiple air-filled cysts ← progressive expansion of cysts ← communication with tracheobronchial tree

√ effects of compression of adjacent lung:

√ contralateral shift of mediastinum (87%)

√ ipsilateral hypoplasia of uninvolved lung

√ proper position of abdominal viscera

√ spontaneous pneumothorax (late sign)

CT:

◊ Postnatally becoming obstructed and filled with air

√ solitary / multiple thin-walled cysts filled with fluid / air ± air-fluid / gas-liquid levels

√ surrounding focal emphysematous changes

OB-US (detectable at about 20 weeks GA):

√ lesion with single large / multiple large / multiple small cysts

√ echogenic (= nondiscernible microcystic) solid mass

√ rapid growth at 20–26 weeks GA followed by stabilization

√ contralateral mediastinal shift (89%)
√ polyhydramnios (25–75%) ? ← compression of esophagus / increased fluid production by abnormal lung
√ normal amniotic fluid (28%) / oligohydramnios (6%)
√ fetal ascites (62–71%)
√ fetal hydrops in 33–81% ← ⇓ venous return ← compression of heart / vena cava (= most important prognostic factor):
Predictable by: mass-thorax ratio > 0.56; CPAMvol ÷HC ratio > 1.6

Risk of recurrence: none

Cx: ipsi- / bilateral pulmonary hypoplasia

Prognosis: 50% premature, 97% survival rate (in absence of associated anomalies)
◊ Polyhydramnios, ascites, hydrops indicate a poor outcome!
◊ Postnatally lesions may regress / persist / remain stable: CPAM becomes smaller in fetuses in many cases + resolves spontaneously with < 60% of total lung volume!

Rx: (1) Thoracoamniotic shunting for single large cyst with fetal hydrops
(2) EXIT (ex utero intra partum) procedure after 32 weeks
(3) Surgical resection > 1 month of life (reason: risk of infection / small risk of malignancy)

DDx: (1) Congenital lobar emphysema
(2) Diaphragmatic hernia
(3) Bronchogenic cyst (small solitary cyst near midline)
(4) Neurenteric cyst
(5) Bronchial atresia
(6) Bronchopulmonary sequestration (less frequently associated with polyhydramnios / hydrops)
(7) Mediastinal / pericardial teratoma

CONGENITAL PULMONARY VENOLOBAR SYNDROME

= SCIMITAR SYNDROME
= unique form of congenital lung underdevelopment affecting one / more lobes in a constellation of distinctly different congenital anomalies of the thorax that often occur together; M÷F = 1÷1.4

◊ The most constant components of the syndrome are hypogenetic lung + partial anomalous pulmonary venous return

A. MAJOR COMPONENTS
1. Hypogenetic lung (69%): pulmonary lobar agenesis / aplasia / hypoplasia
√ hypoplasia / aplasia of one / more lobes of the lung with errors in lobation (= bilateral left bronchial branching pattern / horseshoe lung)
√ solid mass along posterior right hemidiaphragm (if trapped lung is unaerated)
√ large ipsilateral apical cap + blunted costophrenic angle
√ diminished radiolucency on involved side
√ small ipsilateral hemithorax + mediastinal shift
√ elevated hemidiaphragm
√ heart shifted toward involved side → cardiac dextroposition in right lung hypoplasia

2. Ipsilateral partial anomalous pulmonary venous return (PAPVR) → L-to-R shunt
   √ "**scimitar vein**" (90%) commonly connecting to infradiaphragmatic or suprahepatic portion of IVC / portal vein / hepatic vein / coronary sinus / R atrium
   √ on CXR seen only in 31%
3. Absence of pulmonary artery (14%)
   √ reticular densities (enlarged bronchial / transpleural arterial collaterals)
   √ indistinct hazy cardiomediastinal border on involved side
   √ small hilum ← absent / small pulmonary artery
   √ diminished pulmonary vascularity on involved side
4. Pulmonary sequestration (24%)
5. Systemic arterialization of lung without sequestration (10%)
   √ systemic arterial supply to abnormal segment from
   › thoracic aorta: bronchial, intercostal, transpleural
   › abdominal aorta: celiac artery, transdiaphragmatic
   √ rib notching
6. Absence / interruption of inferior vena cava (7%)
7. Duplication of diaphragm = accessory diaphragm (7%)
   = thin membrane in right hemithorax fused anteriorly with the diaphragm coursing posterosuperiorly to join with the posterior chest wall + trapping all / part of RML / RLL
   √ accessory fissurelike oblique line above right posterior costophrenic sinus (if trapped lung is aerated)
   √ broad retrosternal band of opacity (LAT view)
   CT:
   √ ovoid area of increased density in posterior right hemithorax (= dome of accessory diaphragm)

B. MINOR COMPONENTS

1. Tracheal trifurcation (extremely rare): 2 mainstem bronchi supplying the right lung
2. Eventration of diaphragm
3. Partial absence of diaphragm
4. Phrenic cyst
5. Horseshoe lung
6. Esophageal / gastric lung
7. Anomalous superior vena cava
8. Absence of left pericardium

Associated with:

(1) Vascular anomalies: hypoplastic artery, anomalous venous return, systemic arterial supply
(2) Anomalies of hemidiaphragm on affected side:
   √ retrosternal band on lateral CXR ← mediastinal rotation
   √ phrenic cyst
   √ diaphragmatic hernia
   √ accessory hemidiaphragm
(3) Hemivertebrae + scoliosis
   √ rib hypoplasia / malsegmentation
   √ anomalies of bony thorax / thoracic soft tissues

(4) CHD (25–50%): sinus venosus ASD, VSD, tetralogy of Fallot, PDA, coarctation of aorta, hypoplastic left heart, double-outlet right ventricle, double-chambered right atrium, endocardial cushion defect, persistent left SVC, pulmonary stenosis

May be associated with:
congenital tracheal stenosis, bronchogenic cyst, accessory diaphragm, diaphragmatic hernia, bronchitis, bronchiectasis

- usually asymptomatic in isolated hypogenetic lung (40%)
- may have exertional dyspnea / recurrent infections

Location: R÷L = 3÷1; RML (65%) > RUL (40%) > RLL (20%) > LUL (20%) > LLL (15%); multiple lobes (45%)

OB-US:
√ isolated cardiac dextroposition + normal abdominal situs
√ polyhydramnios
√ mild narrowing of right pulmonary artery

CXR:
√ curvilinear RLL density directed toward right hemidiaphragm

CT:
√ small bronchus + lobe
√ small hemithorax + mediastinal shift
√ abnormalities of bronchial branching
√ anomalously located pulmonary fissure
√ discontinuity of hemidiaphragm
√ pulmonary arterial hypoplasia
√ arterial supply from thoracic / abdominal aorta ← absent / hypoplastic pulmonary artery
√ hyparterial (instead of eparterial) right bronchus
√ one / more vessels increasing in diameter toward diaphragm
√ rind of subpleural fatty tissue in affected hemithorax
√ lack of normal venous confluence of right lung
√ venous drainage into IVC, hepatic vein, portal vein, right atrium, coronary sinus

DDx: meandering pulmonary vein, dextrocardia, hypoplastic lung, Swyer-James syndrome

Horseshoe Lung

= uncommon variant of hypogenetic lung syndrome in which RLL crosses midline between esophagus and heart + fuses with opposite LLL
√ oblique fissure in left lower hemithorax (if both lungs separated by pleural layers)
√ pulmonary vessels + bronchi crossing midline

COSTOCHONDRITIS

= musculoskeletal infection

Frequency: increased with IV drug abuse

Agents: Staphylococcus epidermidis, Streptococcus pneumoniae, Candida albicans, Aspergillus

CT:
√ soft-tissue swelling
√ cartilage fragmentation, bone destruction
√ low-attenuation cartilage

√ focal peripheral cartilaginous calcification

Rx: surgical excision

CRYPTOCOCCOSIS

= TORULOSIS = EUROPEAN BLASTOMYCOSIS

Organism: encapsulated unimorphic yeastlike fungus Cryptococcus neoformans; spherical single-budding yeast cell with thick capsule; stains with India ink; often in soil contaminated with pigeon excreta

Histo: granulomatous lesion with caseous necrotic center

Predisposed: opportunistic invader in diabetics + immunocompromised patients

• low-grade meningitis (affinity to CNS); M÷F = 4÷1

@ Lung

√ well-circumscribed mass (40%) of 2–10 cm in diameter, usually in peripheral location

√ lobar / segmental consolidation (35%)

√ cavitation (15%)

√ hilar / mediastinal adenopathy (12%)

√ calcifications (extremely rare)

√ interstitial pneumonia (rare, in AIDS patients)

@ Musculoskeletal

√ osteomyelitis (5–10%)

√ arthritis (rare, usually from extension of osteomyelitis)

CYSTIC FIBROSIS

= CF = MUCOVISCIDOSIS = FIBROCYSTIC DISEASE

= common autosomal recessive multisystem disease of exocrine gland dysfunction characterized by

(a) mucous plugging (= thick tenacious material obstructing conducting system)

(b) reduced mucociliary clearance

Frequency: 1÷2,500 livebirths; almost exclusively in Caucasians affecting 70,000 persons worldwide (5% carry a CF mutant gene allele); unusual in Blacks (1÷17,000), Orientals, Polynesians

Genetics: mutation of cystic fibrosis transmembrane regulator gene (CFTR) on long arm of chromosome 7 (usually necessary for absorption + secretion of salt and water); > 1000 different gene mutations (in 90% DF508)

◊ Most common lethal autosomal recessive disease in white population (highest rate is in Ireland!)

Pathophysiology:

faulty CFTR protein at cell surface → defective epithelial ion channel → abnormal transmembrane conductance / block for Cl- into bronchial lumen and excessive resorption of Na+ → decrease in osmotic forces and luminal water → mucous plugging in small + large airways → increased incidence of bacterial airway infections

Screening (for 6 most common mutations of CF gene):

85% carrier detection rate for Northern Europeans, 90% for Ashkenazi Jews, 50% for American Blacks

Mean age at diagnosis: 2.9 years (70% in 1st year of life, 80% by age 4 years, 90% by age 12 years); 50% are now adults (2012); M÷F = 1÷1

Affected organs: lung, pancreas, hepatobiliary system, kidney, GI tract

- chronic sinusitis with nasal polyposis; infertility in males
- elevated concentrations of sodium + chloride (> 40 mmol/L for infants) in sweat, decreased urinary PABA excretion
- increased susceptibility to infection by Staphylococcus aureus + Pseudomonas aeruginosa

Rx: aggressive nutrition and physiotherapy programs + antimicrobial and corticosteroid therapy, pancreatic enzyme supplementation, lung transplantation

Median survival: 41.1 years (in 2012)

@ Lung

- recurrent lung infections (reduced mucociliary clearance encourages Pseudomonas colonization), chronic cough
- progressive respiratory insufficiency ← obstructive lung disease

Location: predilection for apical + posterior segments of upper lobes

√ "gloved finger" sign = <u>mucous plugging</u> = mucoid impaction in dilated bronchi within 1st month of life

√ subsegmental / segmental / lobar <u>atelectasis</u> with right upper lobe predominance (10%)

√ progressive cylindrical / cystic <u>bronchiectasis</u> (in 100% at > 6 months of age) ± air-fluid levels ← prolonged mucous plugging preponderant in upper lobes

√ parahilar linear densities + peribronchial cuffing

√ focal peripheral / generalized hyperinflation ← collateral air drift into blocked airways with <u>air trapping</u>

√ hilar adenopathy

√ large pulmonary arteries ← pulmonary arterial hypertension

√ recurrent local <u>pneumonitis</u> (initiated by Staphylococcus aureus / Haemophilus influenza, succeeded by Pseudomonas aeruginosa)

√ allergic bronchopulmonary aspergillosis (with bronchial dilatation + mucoid impaction)

HRCT:

√ mosaic attenuation ← air trapping in early stage (on lateral decubitus HRCT in dependent lung)

√ bronchial + peribronchial thickening

√ cylindrical (varicose / cystic) bronchiectasis + bronchiolectasis

◊ in 30% of children with normal lung function!

√ bronchiectatic cyst (= bronchus directly leading into sacculation) in 56%

√ interstitial cysts in 32%

√ emphysematous bulla (= peripheral air space with long pleural attachment + NO communication to bronchus) in 12%

√ periseptal emphysema

√ mucous plugs = tubular structures ± branching pattern → centrilobular nodules + tree-in-bud pattern

√ subsegmental / segmental atelectasis / consolidations

NUC:

√ matched patchy areas of decreased ventilation + perfusion

Cx: (1) Pneumothorax (← rupture of bulla / bleb) common + recurrent
(2) Hemoptysis (parasitized bronchial arteries connect to pulmonary vessels resulting in AV fistulae)
(3) Cor pulmonale
(4) Hypertrophic pulmonary osteoarthropathy (rare)

Cause of death: massive mucous plugging (95%)

DDx: Immotile cilia syndrome (predominantly affecting middle lobe)

Rx: (1) Intratracheal instillation of aerosolized adenoviral + liposomal vector-CFTR gene preparations
(2) Lung transplant (using forced expiratory volume + body mass index as predictors of necessity)

@ GI tract (85–90%)
• chronic obstipation, failure to thrive
@ Esophagus
√ gastroesophageal reflux (21–39%) ← elevated abdominal pressures from chronic cough, hyperinflation, diaphragm depression, lower esophageal sphincter relaxation from long-term use of medication (eg, aminophylline):
√ esophagitis, reflux stricture, Barrett metaplasia
@ Small bowel
√ thickened nodular gastric + duodenal mucosal folds ± peptic ulcers ← unbuffered gastric acid, production of abnormal mucus, Brunner gland hypertrophy
√ mild generalized small bowel dilatation with diffuse distortion + thickening of mucosal folds (at times involving colon + rectum)
√ Crohn disease (increased frequency)
√ ileocecal intussusception (in 1%): often intermittent with spontaneous resolution / asymptomatic transient
Lead point: inspissated secretions, lymphoid tissue, chronically distended appendix
@ Colon
√ <u>meconium ileus</u> (10–13–16% at birth)
◊ Earliest clinical manifestation of cystic fibrosis!
√ <u>meconium plug syndrome</u> (25%, most common cause of colonic obstruction in the infant)
√ <u>distal intestinal obstruction syndrome</u>
√ proximal colonic wall thickening, pericolonic fat proliferation, mesenteric fat infiltration
√ large distended colon with mottled appearance (retained bulky dry stool) = acquired megacolon
√ "microcolon" = colon of normal length but diminished caliber
√ <u>fibrosing colonopathy</u> (in children) = stricture of right colon with longitudinal shortening ← submucosal fibrosis ← high-dose lipase supplementation
√ pneumatosis intestinalis of colon (5%) ← air block phenomenon of obstructive pulmonary disease:
√ cystic submucosal + subserosal foci of air lining up along dependent portion of bowel wall

√ "jejunization of colon" = coarse redundant hyperplastic colonic mucosa ← distended crypt goblet cells
√ rectal prolapse between 6 months and 3 years (in 18–23%) ← frequent bulky stools and diminished muscle tone in undiagnosed patient

@ Appendix
√ chronically > 6 mm distended appendix ← swollen appendix filled with inspissated secretions
√ acute appendicitis (1–4%)

Cx: gastrointestinal perforation with meconium peritonitis (in 50%), volvulus of dilated segments, bowel atresia, colon cancer (odds ratio 20÷1)

@ Liver (in up to 72% of adult patients)

Pathophysiology:
absent / dysfunctional activity of CFTR protein → impaired secretory function of biliary epithelium → accumulation + precipitation of hyperviscous biliary secretions → cholangiocyte injury → hepatic parenchymal injury

• asymptomatic / abnormal liver function tests
√ hepatic steatosis (23–67%) ← untreated malabsorption, dietary deficiencies, hepatic dysfunction, medications (= initial manifestation in infants):
√ diffuse / focal fatty infiltration
√ multilobulated pseudomasses = 1–2 cm lobulated fatty lesions with hyperechoic center surrounded by a hypoechoic ring → heterogeneity of liver echotexture + irregularity of hepatic contour
√ diffuse increase in liver echogenicity + posterior acoustic attenuation + decreased depiction of vessel walls
√ diffuse low hepatic attenuation and prominent vessels
√ hepatic T1-hyperintensity + suppression on fat saturation
√ focal biliary cirrhosis (40–78%):
√ focal portal fibrosis and cholestasis
√ > 2 mm thick hyperechoic periportal tissue
√ high signal intensity on T1WI
√ multilobular cirrhosis (5–15%) ← inspissated bile:
= multiple regenerative nodules with diffuse involvement
• signs of portal hypertension in multilobular form (clinically in 4–8%, autoptic in up to 50%)

Cx: dysplastic nodules, HCC

√ portal hypertension (in 1% of biliary cirrhosis) + hepatosplenomegaly + hypersplenism

Multilobular cirrhosis is the 3rd leading cause of death associated with CF (after cardiorespiratory + transplant complications) accounting for 2.5% of overall mortality.

@ Gallbladder

Histo: mucus-containing cysts in gallbladder wall

• symptoms of gallbladder disease (3.6%)
√ sludge (33%)
√ cholelithiasis (12–24%): mostly cholesterol stones ←
(a) interrupted enterohepatic circulation after ileal resection

(b) ileal dysfunction in distal intestinal obstruction syndrome

√ gallbladder atony

√ microgallbladder (4–45% at autopsy) ← cystic duct atresia / stenosis ← inspissated material:

√ false positive results in hepatobiliary scintigraphy

√ gallbladder atrophy

√ thickened trabeculated gallbladder wall ← cirrhosis, ascites, hypoalbuminemia, nutritional deficiencies

√ subepithelial cysts of gallbladder wall

@ Bile ducts

• cholestasis ← CBD obstruction

√ strictures + beading + dilatation of intra- and extrahepatic bile ducts similar to sclerosing cholangitis (in 50%)

√ choledocholithiasis + intrahepatic calculi

√ sclerosing cholangitis

√ hyperechoic periportal thickening ← fibrosis / focal fat

√ ductal abnormalities at MRCP in (65%)

@ Pancreas

The pancreas is the most commonly involved abdominal organ in cystic fibrosis.

Pathophysiology:

inspissated secretions in proximal pancreatic ducts → luminal obstruction with increase in fluid pressure → mild inflammatory reaction + acinar disruption → widespread loss of acinar cells → replacement with fibrous tissue + fat (= complete pancreatic atrophy / lipomatous pseudohypertrophy); increased pancreatic lobulation; recurrent acute and chronic pancreatitis → diffuse fibrosis + with microcystic transformation

Histo: progressive ductectasia = dilatation of acini + ducts

Classification of dysfunction:

(1) Exocrine insufficiency (85–90%) ← fat malabsorption ← deficient pancreatic enzyme production ← duct obstruction ← inspissated secretions ← precipitation of relatively insoluble proteins (= protein plugs)

• malnutrition, steatorrhea, fat intolerance, deficiency of fat-soluble vitamins

The degree of pancreatic fatty infiltration correlates with the severity of exocrine dysfunction. CF is the most common cause of exocrine pancreatic insufficiency in patients < 30 years of age!

(2) Endocrine gland dysfunction (30–50%) ← CF-related diabetes mellitus (unique combination of type 1 and 2) ← fibrosis and gland atrophy

• abdominal pain, bloating, flatulence, failure to thrive

• diabetes mellitus ← pancreatic fibrosis increasing with age (in 1% of children + 13% of adults):

• glucose intolerance in 30–50%

• 1–2% require insulin therapy

• acute (1.2%) by age 20 / recurrent acute (10%) pancreatitis

√ partial (in 16%) / complete (in 42%) fatty replacement of pancreas by fibrofatty tissue by age 17 years:

√ density of –90 to –120 HU on CT (in up to 93%) similar to retroperitoneal fat
√ generalized increased echogenicity (70–100%)
√ loss of fine lobular pattern of pancreas on US
√ focal hypoechoic areas + cyst formation
√ variable T1 hyper- and hypointensity depending on proportion of fatty infiltration + fibrosis
√ lipomatous pseudohypertrophy of pancreas = markedly enlarged pancreas ← complete fibrofatty replacement
√ diffuse pancreatic atrophy without fatty replacement (in 24%)
√ periductal chronic calcific pancreatitis (7%)
√ pancreatic duct strictures, beading, dilatation, obstruction
√ **pancreatic cystosis** (extremely rare) = mostly 1–3-mm small cysts completely replacing pancreas, occasionally macroscopic cysts up to 12 cm in diameter
• low levels of amylase + CEA in cyst fluid

@ Kidney
• immunoglobulin A nephropathy, amyloidosis
• symptomatic renal stones (3–6% vs. 2% in general population)
√ nephrocalcinosis, nephrolithiasis (in 90% at autopsy)

@ Skull
√ sinusitis with opacification of well-developed maxillary, ethmoid, sphenoid sinuses
√ hypoplastic frontal sinuses

OB-US:
√ hyperechogenic bowel (in up to 60–70% of fetuses affected with cystic fibrosis)

Prognosis: median survival of 41 years (2012); pulmonary Cx are the most predominant cause of morbidity and death (90%); 2.3 deaths per 100 patients from cardiorespiratory causes (78%) / hepatic disease (4%)

DIAPHRAGMATIC HERNIA

Congenital Diaphragmatic Hernia

= CDH = absence of closure of the pleuroperitoneal fold by 9th week of gestational age

Frequency: 1÷ 2,200–4,000 livebirths (0.04%); M÷F = 2÷1
◊ Most common intrathoracic fetal anomaly
◊ Delayed closure following group B streptococcal infection!

Etiology:
(1) Delayed fusion of diaphragm (spontaneous self-correction may occur) / premature return of bowel from its herniated position within the umbilical coelom
(2) Insult that inhibits / delays normal migration of the gut + closure of the diaphragm between 8th and 12th week of embryogenesis

Classification (Wiseman):
I. herniation early during bronchial branching → severe bilateral pulmonary hypoplasia; uniformly fatal
II. herniation during distal bronchial branching → unilateral pulmonary hypoplasia; survival possible
III. herniation late in pregnancy with compression of otherwise normal lung; excellent

prognosis

IV. postnatal herniation with compression of otherwise normal lung; excellent prognosis

Associated anomalies in 20% of liveborn and in 90% of stillborn fetuses:

1. CNS (28%): neural tube defects, hydrocephalus
2. Cardiovascular (9–23%): VSD, ASD, tetralogy of Fallot
3. Gastrointestinal (20%): particularly malrotation, oral cleft, omphalocele, esophageal atresia
4. Genitourinary (15%): cryptorchidism
5. Chromosomal abnormalities (4%): trisomy 21, 18, 13; tetrasomy 12p
6. Limb anomalies: polydactyly, syndactyly, reduction defects
7. Spinal defects
8. Genetic syndromes: Fryns, Lange, Marfan
9. IUGR (with concurrent major abnormality in 90%)

Location: L÷R = 85%÷13%; 2% bilateral

◊ Right-sided hernias are frequently fatal!

- respiratory distress in neonatal period = life-threatening deficiency of small airways + alveoli; scaphoid abdomen

Herniated organs:

small bowel (90%), stomach (60%), large bowel (56%), spleen (54%), pancreas (24%), kidney (12%), adrenal gland, liver (major prognostic factor), gallbladder

√ bowel loops in chest
√ contralateral shift of mediastinum + heart
√ complete (1–2%) / partial absence of diaphragm
√ absence of stomach + small bowel in abdomen
√ passage of nasogastric tube under fluoroscopic control entering intrathoracic stomach
√ incomplete rotation + anomalous mesenteric attachment of bowel

OB-US (diagnosis possible by 18 weeks GA):

√ solid / multicystic / complex chest mass
√ mediastinal shift
√ nonvisualization of fetal stomach below diaphragm
√ fetal stomach at level of fetal heart
√ peristalsis of bowel within fetal chest (inconsistent)
√ paradoxical motion of diaphragm with fetal breathing (defect in diaphragm sonographically not visible)
√ scaphoid fetal abdomen with reduced abdominal circumference
√ herniated liver frequently surrounded by ascites
√ polyhydramnios (common, due to partial esophageal obstruction or heart failure) / normal fluid volume / oligohydramnios
√ swallowed fetal intestinal contrast appears in chest (CT amniography confirms diagnosis)
√ fetal lung volume < 15–25%, decreased lung-head ratio

OB-MR:

√ calculation of relative fetal lung volume:

< 14.3% = postnatal death, > 32.8% = survival

> 44.0% = ECMO not required

Cx: (1) Bilateral pulmonary hypoplasia
(2) Persistent fetal circulation → postsurgical pulmonary hypertension
(3) PROM (47%), chorioamnionitis, premature labor

Prognosis: (1) Stillbirth (35–50%)
(2) Neonatal death (35%)

◊ Survival is determined by size of defect + time of entry + associated anomalies (34% survival rate if isolated, 7% with associated anomalies)

Indicators of poor prognosis:
large intrathoracic mass with marked mediastinal shift, IUGR, polyhydramnios, hydrops fetalis, detection < 25 weeks MA, intrathoracic liver, dilated intrathoracic stomach, other malformations

Mortality: in 10% death before surgery; 40–50% operative mortality;
(a) stomach intrathoracic vs. intraabdominal = 60% vs. 6%
(b) polyhydramnios vs. normal amniotic fluid = 89% vs. 45%

Rx: Fetal endotracheal balloon occlusion (29–34 weeks)

DDx: bronchopulmonary foregut malformation, mediastinal cyst (bronchogenic, neurenteric, thymic), sequestration, congenital adenomatoid malformation, pulmonary agenesis / hypoplasia

***Bochdalek Hernia* (85–92%)**

[Vincent Alexander Bochdalek (1801–1883), professor of anatomy in Prague]

= posterolateral hernia caused by maldevelopment of pleuroperitoneal folds / failure of fusion of folds and transverse septum with intercostal muscles
◊ 90% of congenital diaphragmatic hernias; L > R

Age: antenatal ultrasound @ 24 weeks GA; late presentation in 11%

Frequency: 1÷2,000–1÷5,000 live births

- respiratory distress
- asymptomatic with late presentation (in 11%)

Location: left (80%), right (15%), bilateral (3–5%)

Herniated organs:
(a) on left: omental fat (6%), bowel, spleen, left lobe of liver, stomach (rare), kidney, pancreas
(b) on right: part of liver, gallbladder, small bowel, kidney

mnemonic: 4 B's
Bochdalek
Back (posterior location)
Babies (age at presentation)
Big (usually large)

Morgagni Hernia (9–12% of CDH)

[Giovanni Battista Morgagni (1682–1771), professor of anatomy and theoretical medicine in Padua, Italy]

= anteromedial parasternal defect = space of Larrey / foramen of Morgagni

◊ < 10% of congenital diaphragmatic hernias

Cause: failure of fusion between septum transversum and lateral body wall where internal mammary artery crosses the diaphragm

Location: between sternum medially + 8th rib laterally; R÷L = 9÷1 (mostly unilateral)

Time of defect: between 3rd and 7th week of GA

Age: children; incidental finding in adults

Frequency: 1÷4,800 live births; M > F

Herniated organs:

(a) abdominal viscera: omentum, liver, transverse colon

(b) heart may herniate into upper abdomen

(c) fat may herniate into pericardial sac

Often associated with:

congenital heart disease (component of pentalogy of Cantrell), pericardial deficiency, bowel malrotation, chromosomal abnormality (Down syndrome, Turner syndrome), mental retardation

mnemonic: 4 M's

Morgagni

Middle (anterior + central location)

Mature (tend to present in older children)

Minuscule (usually small)

- asymptomatic (majority), epigastric discomfort
- chronic cough, choking, shortness of breath
- respiratory distress, cyanosis (in neonates)
- abdominal pain, nausea, vomiting

√ cardiophrenic angle mass

√ anteriorly located gas-filled loops of bowel on lateral chest x-ray (PATHOGNOMONIC)

Cx: bowel incarceration + strangulation

DDx on CXR: thymoma, teratoma, germ cell tumor, lymphoma, thyroid lesion, pericardial cyst, lymphangioma

DDx on CT: lipoma, liposarcoma (no omental vessels)

Septum Transversum Defect

= defect in central tendon

Hiatal Hernia (9% of CDH)

= congenitally large esophageal orifice with herniation of a portion of the stomach into mediastinum

Eventration *(5%)*

= congenital thinning of diaphragmatic muscle that causes an abnormal elevation of part (= focal bulge) / entire otherwise intact hemidiaphragm into chest cavity → upward displacement of abdominal contents

Cause: ? congenitally thinned hypoplastic / absent muscle fibers consisting only of pleura + peritoneum; focal dyskinesia; neuromuscular dysfunction; weakness from ischemia / infarct

Unilateral eventration may be associated with:
Beckwith-Wiedemann syndrome, trisomy 13, 15, 18
Bilateral eventration may be associated with:
toxoplasmosis, CMV, arthrogryposis
Location: R÷L = 5÷1; anteromedial on right; complete involvement on left (M > F)
√ small diaphragmatic excursions
√ often lobulated diaphragmatic contour
DDx for right anteromedial eventration:
Morgagni hernia, paraesophageal hernia, pericardial cyst, bronchogenic cyst, tumor
DDx for complete eventration: diaphragmatic paralysis

Traumatic Diaphragmatic Hernia

= DIAPHRAGMATIC RUPTURE = DIAPHRAGMATIC INJURY
Prevalence: 0.8–8% in blunt trauma patients; 5% of all diaphragmatic hernias, but 90% of all strangulated diaphragmatic hernias
Etiology of traumatic rupture of diaphragm:
(a) blunt trauma (5–50%) ← sudden increase in intraabdominal / intrathoracic pressure against a fixed diaphragm: motor vehicle accident (> 90%), fall from height, bout of hyperemesis; L÷R = 3÷1, bilateral rupture in < 3.6%
◊ 7–66% undiagnosed at initial presentation!
(b) penetrating trauma (50%): bullet > knife, repair of hiatus hernia
◊ 1–4 cm in length; often only detected at surgery
• may be asymptomatic for months / years following trauma, onset of symptoms may be so long delayed that traumatic event is forgotten
• virtually all become ultimately symptomatic, 80% in < 3 years
• **Bergqvist triad**:
(1) Rib fractures
(2) Fracture of spine / pelvis
(3) Traumatic rupture of diaphragm
Location: 77–90–98% on left side; right hemidiaphragm has greater strength and is relatively protected by liver; L÷R = 1.5÷1 to 7÷1
Site: posterolateral central portion medial to spleen / medial central tendon with intrapericardial hernia (3.4%) / sites of attachments of diaphragm / esophageal hiatus (rare)
Size: most tears are > 10 cm in length
Herniation of organs (32–58%) in order of frequency:
(a) right: liver, small bowel, large bowel
(b) left: stomach, colon, spleen, omentum, small bowel, kidney, pancreas
CXR:
◊ The first posttraumatic CXR is abnormal in 46–77% but nonspecific!
◊ Positive intrathoracic pressure from ventilation may delay herniation!
◊ Serial CXRs may show progressive changes!
√ nonvisualization (loss) of diaphragmatic contour
√ elevated asymmetric / irregular contour of hemidiaphragm > 4–6 cm above level of contralateral hemidiaphragm + contralateral shift of mediastinum

Cave: cephalad margin of bowel may simulate an elevated diaphragm (look for haustra)

√ herniation of air-filled viscus: stomach, colon
√ shift of mediastinum + lung to opposite side
√ lower lobe mass / consolidation (herniated solid organ / omentum / airless bowel loop)
√ inhomogeneous mass with air-fluid level in left hemithorax
√ mushroomlike mass of herniated liver in right hemithorax
√ hydrothorax / hemothorax suggests strangulation
√ "collar" sign = hourglass constriction of afferent + efferent bowel loops at orifice
√ multiple fractures of lower ribs + spine
√ abnormal U-shaped course of nasogastric tube above suspected level of hemidiaphragm

N.B.: tube first dips below diaphragm (rent spares esophageal hiatus with gastroesophageal junction remaining in its normal position)

√ location of diaphragm may be documented by

1. Gas-filled bowel constricted at site of diaphragmatic laceration
2. Barium study

CT (71% sensitive, 100% specific, 70% accurate for right side; 80–87% sensitive, 100% specific, 88% accurate for left side):

◊ Best detected on reformatted SAG + COR images!

Associated with: abdominal + pelvic injury in 90–94%

(a) direct signs:
- √ segmental diaphragmatic defect = abrupt discontinuity of hemidiaphragm (73–82%)
- √ "absent diaphragm" sign = failure to see diaphragm
- √ "dangling diaphragm" sign = free edge of injured diaphragm curls inwards + away from chest wall
- √ "curled diaphragm" sign = irregularity + thickening of diaphragmatic leaflet ← contracted torn muscle
- √ contiguous (= transdiaphragmatic) injury on either side of diaphragm in case of penetrating trauma
- √ wound trajectory crossing diaphragm

(b) indirect signs:
- √ intrathoracic herniation of omentum / bowel / abdominal organs (55%)
- √ visualization of peritoneal fat / abdominal viscera lateral to lung or diaphragm / posterior to crus of hemidiaphragm
- √ "collar" sign = waistlike constriction of viscera at level of diaphragmatic rent (27%):
  - √ "hump" sign = rounded portion of superior liver protrudes through diaphragmatic rent
  - √ "band" sign = linear area of hypoattenuation at level of torn free edge of diaphragm causing linear indentation of herniated liver edge
- √ "dependent viscera" sign = abdominal viscera (bowel loops / stomach) no longer supported posteriorly by torn diaphragm fall dependently against posterior chest wall
- √ "sinus cutoff" sign = herniated abdominal content prevents expected layering of pleural fluid

√ abdominal organ / fatty tissue peripheral to diaphragm / posterior to crura
√ elevated / cephalad displacement of abdominal organs: hemidiaphragmatic elevation by > 5 cm (RT) and > 4 cm (LT)
√ concurrent pneumothorax, pneumoperitoneum, hemothorax, hemoperitoneum

MR:
√ interruption of hypointense band of diaphragmatic muscle outlined by hyperintense abdominal + mediastinal fat

Associated injuries (in 44–81–100%):
√ head injury
√ fractures of lower ribs / pelvis (42%)
√ intraabdominal injuries (72%):
√ perforation of hollow viscus
√ rupture of spleen / kidney

Reasons for diagnostic misses:
(1) Left-sided defect covered by omentum
(2) Right-sided defect sealed by liver
(3) Positive pressure ventilation
(4) Associated injuries mask tear: atelectasis, pleural effusion, lung contusion, phrenic nerve paralysis

Cx: (1) Incarceration of herniated organs
(2) Life-threatening strangulation of bowel / stomach occurs in majority

◊ 90% of strangulated hernias are posttraumatic!

(3) Bowel perforation

Prognosis: 30% mortality in unrecognized cases

DDx: congenital hernia, acquired defect = fenestration, diaphragmatic eventration, diaphragmatic paralysis, hiatal hernia, congenital Bochdalek hernia (6–11%)

DIAPHRAGMATIC PARALYSIS

= absent orthograde diaphragmatic excursion on quiet deep breathing with paradoxical motion on sniffing

Diaphragmatic weakness = reduced / delayed orthograde excursion on deep breathing ± paradoxical motion on sniffing

Cause:
(1) Phrenic nerve injury during birth trauma / cardiac surgery / resection of thoracic tumors
(2) Infection: West Nile virus, Lyme disease
(3) Tumor of mediastinum / neck

• difficulty in weaning from mechanical ventilation, ventilatory failure (common)
• respiratory distress, tachypnea, increased oxygen requirements

› Static imaging:
√ elevation of one hemidiaphragm on CXR (not sensitive or specific)

› Functional imaging (= evaluation of diaphragmatic motion):
Fluoroscopy:
√ evaluate comparative movement of domes, excursion of individual dome, and shift of mediastinum

√ sniff test:
√ both normal hemidiaphragms move downward
√ reduced excursion of weakened hemidiaphragm
√ absent / paradoxical motion (= elevation during inspiration and vice versa) of paralyzed hemidiaphragm

M-mode US (SAG view, transducer position anteriorly, ventilator temporarily disconnected):
◊ US has replaced fluoroscopy in children!
√ diaphragm moves toward transducer during inspiration by < 4 mm
√ > 50% difference in excursion between domes

Cx: pneumonia, atelectasis, pulmonary collapse

DIFFUSE PULMONARY LYMPHANGIOMATOSIS

= rare condition consisting of proliferation + dilatation of communicating lymphatic channels in pleura + interlobular septa + mediastinum

Cause: congenital developmental abnormality of lymphatic channels

Age: teenager, young adult

Path: resembles lymphangioma

• progressive dyspnea → pulmonary failure

Location: predominantly upper lobes of lung

CT:
√ smooth symmetric thickening of interlobular septa + peribronchovascular bundles
√ diffuse increased attenuation of mediastinal fat
√ mild perihilar infiltration
√ diffuse pleural thickening
√ pleural effusion
√ pericardial effusion

Dx: biopsy; findings persist under diuretic therapy

DROWNED LUNG

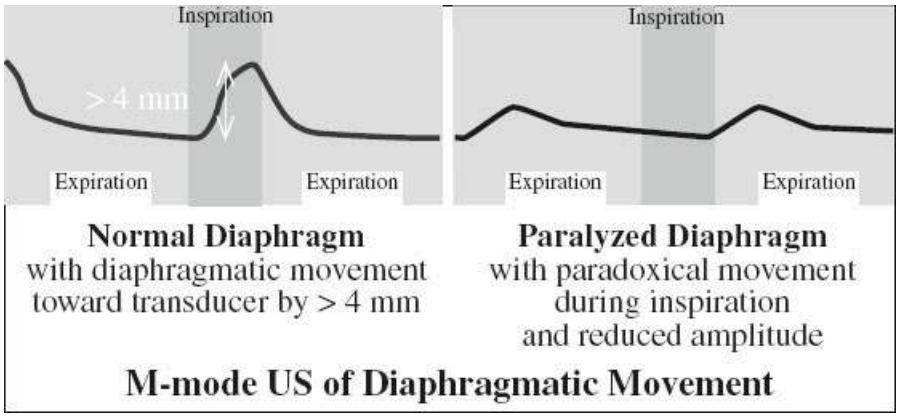
= abnormal increase in lobar / rarely whole lung volume

Pathophysiology: bronchial obstruction → acute collapse of airspaces → rapid filling of alveoli + bronchi with secretions / fluid

Cause: bronchogenic carcinoma, carcinoid, foreign body, mucus plug

• bronchial obstruction that persists beyond 3–4 weeks

√ bulging interlobar fissure
√ little / no mediastinal shift to contralateral side
√ obliteration of bronchial lumen leading to obstructed lobe



√ absence of air bronchogram
√ hilar mass + regional lymphadenopathy

CT:
√ postobstructive consolidation
√ mucus bronchogram = bronchi filled with low-attenuation material

CECT:
√ delineates enhancing tumor + lymph nodes from consolidated lung of low attenuation (= drowned lung)

MR:
√ T2WI differentiates drowned lung from obstructing tumor

PET:
√ high tumor activity centrally

Cx: necrosis, cavitation, secondary infection

DDx: resorptive atelectasis, obstructive pneumonitis, endogenous "golden" lipoid pneumonia, Gram-negative pneumonia, large pleural effusion (marked mediastinal shift to contralateral side), unilateral veno-occlusive disease, unilateral aspiration

EMPHYSEMA

= group of pulmonary diseases characterized by permanently enlarged air spaces distal to terminal bronchioles accompanied by destruction of alveolar walls + local elastic fiber network

◊ The clinical term "chronic obstructive pulmonary disease (COPD)" should not be used in image interpretation! It encompasses: asthma, chronic bronchitis, emphysema!

Prevalence: 12.7 million people in USA (2002)

Cause: imbalance in elastase-antielastase system ← increase in elastase activity in smokers / α1-antiprotease deficiency (causing proteolytic destruction of elastin resulting in alveolar wall destruction)

- irreversible expiratory airflow obstruction ← decreased elastic recoil from parenchymal destruction; dyspnea on exertion
- decreased carbon monoxide diffusing capacity

CXR (moderately sensitive, highly specific):
√ hyperinflated lung (most reliable sign):

√ low hemidiaphragm (= at / below 7th anterior rib)
√ flat hemidiaphragm (= < 1.5 cm distance between line connecting the costo- and cardiophrenic angles + top of midhemidiaphragm)
√ retrosternal air space > 2.5 cm
√ "barrel chest" = enlarged anteroposterior chest diameter
√ saber-sheath trachea
√ pulmonary vascular pruning + distortion (± pulmonary arterial hypertension)
√ right-heart enlargement
√ bullae

HRCT:
√ well-defined areas of abnormally decreased attenuation without definable wall (< –910 HU)
◊ Centrilobular + panacinar forms of emphysematous lung destruction tend to coexist!

Rx: lung volume reduction surgery

Centrilobular Emphysema

= CENTRIACINAR EMPHYSEMA = PROXIMAL ACINAR EMPHYSEMA
= emphysematous change selectively affecting the acinus at the level of 1st + 2nd generations of respiratory bronchioles (most common form)

Path: normal + emphysematous alveolar spaces adjacent to each other
Histo: enlargement of respiratory bronchioles + destruction of centrilobular alveolar septa in the center of the secondary pulmonary lobule; CHARACTERISTICALLY surrounded by normal lung; distal alveoli spared; severity of destruction varies from lobule to lobule
Predisposed: smokers (in up to 50%), coal workers
Cause: excess protease with smoking (elastase is contained in neutrophils + macrophages found in abundance in lung of smokers)

• blue bloater

Site: apical and posterior segments of upper lobe + superior segment of lower lobe (relatively greater ventilation-perfusion ratio in upper lobes favors deposition of particulate matter and release of elastase in upper lungs)

CXR (80% sensitivity for moderate / severe stages):
√ irregular scattered area of radiolucency (best appreciated if lung opacified by edema / pneumonia / hemorrhage) = area of bullae, arterial depletion + increased markings
√ hyperinflated lung

HRCT:
√ "emphysematous spaces" (= focal round area of air attenuation) > 1 cm in diameter with central dot / line = centrilobular location (representing the centrilobular artery of secondary pulmonary lobule) without definable wall and surrounded by normal lung
√ pulmonary vascular distortion + pruning with lack of juxtaposition of normal lung (advanced stage)

Panacinar Emphysema

= PANLOBULAR EMPHYSEMA = DIFFUSE EMPHYSEMA = GENERALIZED EMPHYSEMA
= emphysematous change involving the entire acinus
= uniform nonselective destruction of all air spaces throughout both lungs (rare)

Path: uniform enlargement of acini from respiratory bronchioles to terminal alveoli (from center to periphery of secondary pulmonary lobule) ← destruction of lung distal to terminal bronchiole

Cause: autosomal recessive a-1 antitrypsin deficiency in 10–15% (proteolytic enzymes carried by leukocytes in blood gradually destroy lung unless inactivated by a-1 protease inhibitor)

Age: 6th–7th decade (3rd–4th decade in smokers)

• pink puffer

Site: affects whole lung, but more severe at lung bases ← greater blood flow

CXR:

√ hyperinflated lung

√ decreased pulmonary vascular markings

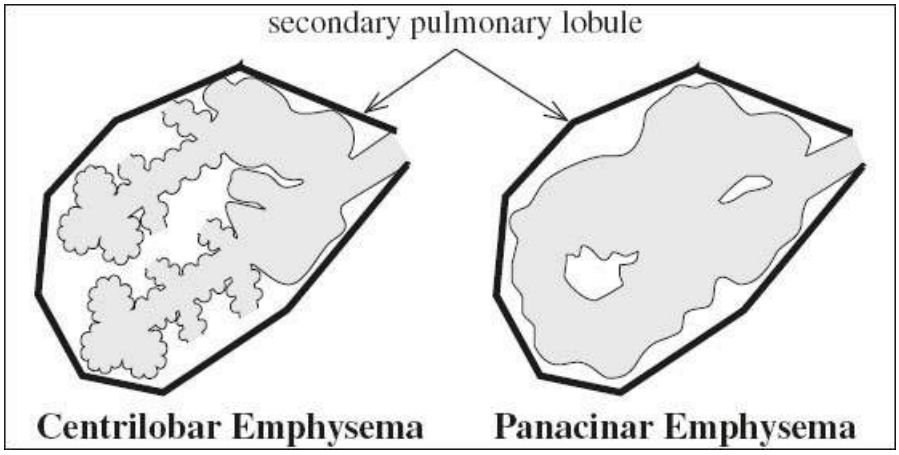
√ lung destruction extremely uniform

HRCT:

√ diffuse simplification of lung architecture with pulmonary septal and vascular distortion + pruning (difficult to detect early, ie, prior to considerable lung destruction for lack of adjacent normal lung)

√ paucity of vessels

√ bullae



Paracicatricial Emphysema

= PERIFOCAL / IRREGULAR EMPHYSEMA

= airspace enlargement + lung destruction developing adjacent to areas of pulmonary scarring

Usual cause: granulomatous inflammation, organized pneumonia, pulmonary infarction

Path: no consistent relationship to any portion of secondary lobule / acinus; frequently associated with bronchiolectasis producing honeycomb lung

• little functional significance

CXR (rarely detectable):

√ fine curvilinear reticular opacities + interposed radiolucent areas

HRCT:

√ low-attenuation areas adjacent to areas of fibrosis (diagnosable only in the absence of other forms of emphysema)

Paraseptal Emphysema

= DISTAL ACINAR / LOCALIZED / LINEAR EMPHYSEMA
= focal subpleural enlargement + destruction of air spaces in one site of otherwise normal lung
Path: predominant involvement of alveolar ducts + sacs
Site: characteristically within subpleural lung and adjacent to interlobular septa + vessels
CXR:
√ area of lucency, frequently sharply demarcated from normal lung
√ bands of radiopacity (residual vessels / interstitium) may be present
HRCT:
√ peripheral low-attenuation area with remainder of lung normal
Cx: spontaneous pneumothorax; bullae formation

EMPYEMA

= parapneumonic effusion characterized by presence of pus ± positive culture
Organism: S. aureus, Gram-negative + anaerobic bacteria
• positive Gram stain
• positive culture (anaerobic bacteria most frequent)
Stage:
I **Exudative phase** = inflammation of visceral pleura results in increased capillary permeability with weeping of proteinaceous fluid into pleural space = sterile exudate
• pH > **7.20**
• glucose > 40 mg/dL (2.2 mmol/L)
• LDH < 1,000 IU/L
II **Fibrinopurulent phase** = accumulation of inflammatory cells and neutrophils within pleural space + fibrin deposition on pleural surfaces
› early stage II empyema
• WBCs > 5 x 109/mm^3, but no gross pus
• pH between **7.0 and 7.2**
• glucose level > 40 mg/dL
• LDH < 1,000 IU/L
› late stage II empyema
• gross pus (WBC > 15,000/cm^3) = frank pus
• pH < **7.0**
• glucose level < **40 mg/dL**
• LDH > **1,000 IU/L**
Cx: multiloculation
Rx: chest tube drainage
III **Organizing phase** = recruitment of fibroblasts + capillaries results in deposition of collagen and granulation tissue on **pleural surfaces** = pleural fibrosis = **"pleural peel / pleural rind"**
Cx: limited expansion of lung
Rx: decortication (with persistent sepsis despite appropriate antibiotic Rx + drainage / persistent thick pleural rind trapping underlying lung)

CT:
- √ thickening of parietal pleura in 60% on NECT, in 86% on CECT
- √ increased thickness + density of paraspinal subcostal tissue (= inflammation of extrapleural fat)
- √ curvilinear enhancement of chest wall boundary in 96% (= inflammatory hyperemia of pleura)
- √ "split pleura" sign = pleural fluid between enhancing thickened parietal + visceral pleura
- √ gas bubbles in pleural space (gas-forming organism / bronchopleural fistula)

DDx: simple / complicated parapneumonic effusion (negative Gram + culture stain), malignant effusion after sclerotherapy, malignant invasion of chest wall, mesothelioma, pleural tuberculosis, reactive mesothelial hyperplasia, pleural effusion of rheumatoid disease

ENDOBRONCHIAL LIPOMA

Prevalence: 0.1–0.5% of lung tumors

Age: middle-aged men

• cough, hemoptysis, fever, dyspnea

Location: usually segmental bronchus

√ atelectasis, consolidation, or both

√ mass or nodule:

- √ homogeneous fatty mass without enhancement is DIAGNOSTIC (may not be large enough to characterize)
- √ high SI on T1WI + intermediate SI on T2WI

EOSINOPHILIC PNEUMONIA

= PULMONARY INFILTRATION WITH BLOOD / TISSUE EOSINOPHILIA (PIE)

Classification:

A. IDIOPATHIC EOSINOPHILIC LUNG DISEASE
   = eosinophilic lung disease of unknown cause
   1. Simple Pulmonary Eosinophilia
   2. Acute eosinophilic pneumonia
   3. Chronic eosinophilic pneumonia
   4. Idiopathic hypereosinophilic syndrome

B. EOSINOPHILIC LUNG DISEASE OF SPECIFIC ETIOLOGY
   = eosinophilic lung disease of known cause
   (a) drug induced:
   nitrofurantoin, penicillin, sulfonamides, ASA, tricyclic antidepressants, hydrochlorothiazide, cromolyn sodium, mephenesin
   1. Toxic-oil syndrome
      = oral ingestion of food-grade rapseed oil contaminated with aniline derivatives
   2. Eosinophilia-myalgia syndrome
      = ingestion of L-tryptophan
   3. Toxic epidermal necrolysis
   4. Drug rash with eosinophilia and systemic symptoms (DRESS)

   √ nonspecific peripheral airspace consolidation with ground–glass-opacity

√ reticulonodular densities
√ hilar adenopathy
√ pleural effusion

(b) parasite induced:
tropical eosinophilia (ascariasis, schistosomiasis), strongyloidiasis, ancylostomiasis (hookworm), filariasis, Toxocara canis (visceral larva migrans), Dirofilaria immitis, amebiasis (occasionally – in RLL + RML), clonorchis infestation
• peripheral blood eosinophil counts > 3000/mL
• average BAL fluid eosinophilia of 50%

(c) fungus induced:
1. Allergic bronchopulmonary aspergillosis
√ bronchiectasis ± mucoid impaction in central upper lungs
2. Bronchocentric granulomatosis
√ nonspecific focal mass / lobular consolidation with atelectasis

(d) Pulmonary eosinophilia with asthma

C. EOSINOPHILIC LUNG DISEASE ASSOCIATED WITH ANGIITIS ± GRANULOMATOSIS
= eosinophilic vasculitis
1. Allergic angiitis
2. Churg-Strauss syndrome
√ subpleural consolidation in a lobular distribution
√ centrilobular nodules
3. Wegener granulomatosis
4. Lymphomatoid granulomatosis
5. Necrotizing sarcoid granulomatosis
6. Polyarteritis nodosa
7. Rheumatoid disease
8. Scleroderma
9. Dermatomyositis
10. Sjögren syndrome
11. CREST

Maybe associated with: rheumatoid arthritis
M÷F = 1÷2
√ pulmonary opacities
• pulmonary eosinophilia (regardless of eosinophilia in peripheral blood / in bronchoalveolar lavage)

Simple Pulmonary Eosinophilia

= TRANSIENT PULMONARY EOSINOPHILIA = LöFFLER SYNDROME
[Wilhelm Löffler (1887–1972), extraordinary professor of medicine at the University of Zurich, Switzerland]
= benign disorder of unknown etiology characterized by local areas of transient parenchymal consolidation associated with blood eosinophilia
Cause: unknown (in ⅓); parasites, drug reaction, allergic bronchopulmonary aspergillosis (in some)

Path: interstitial + alveolar edema containing a large number of eosinophils
- no / mild symptoms, history of asthma + atopy (common)
- high WBC + peripheral eosinophilia

CXR:
√ peripheral patchy migratory / fleeting (= transient and shifting) noncavitary pleural-based pulmonary infiltrates changing within one to several days

√ NO associated lymphadenopathy, NO pleural effusion
Location: mainly middle and upper lobes
Distribution: uni- or bilateral, nonsegmental distribution, predominantly in lung periphery

HRCT:
√ peripheral ground-glass and/or airspace consolidation with upper and middle lobe predominance
√ solitary / multiple pulmonary nodular opacities with surrounding ground-glass halo (rare)

Prognosis: typically spontaneous resolution within 1 month
DDx: cryptogenic organizing pneumonia, pulmonary hemorrhage, multifocal pneumonia, atypical infection

Acute Eosinophilic Pneumonia

Etiology: idiopathic (no evidence of infection / exposure to potential antigens) with abrupt increase in lung cytokines; strong association with cigarette smoking
Age: 32 ± 17 years; M > F
Histo: eosinophilic infiltrates + pulmonary edema ← release of eosinophilic granules altering vascular permeability
- acute febrile illness peaking in 1–5 days, myalgia, chest pain
- acute life-threatening respiratory failure within a few hours in previously healthy individuals
- restrictive pulmonary function
- DIAGNOSTIC markedly elevated levels of eosinophils of > 25% in bronchoalveolar lavage (BAL) fluid
- no peripheral eosinophilia

√ diffuse bilateral reticular opacities mimicking pulmonary interstitial edema
√ peripheral air space opacities (rare)
HRCT:
√ bilateral patchy areas of ground-glass opacities
√ smooth interlobular septal thickening (frequent)
√ crazy-paving pattern (= ground-glass attenuation with intralobular reticular opacities)
√ small pleural effusion
uncommon:
√ poorly defined centrilobular nodules
√ airspace consolidation
√ thickening of bronchovascular bundle
√ enlarged lymph nodes

Rx: IV corticosteroids
Prognosis: prompt + complete response to steroids; no relapse after discontinuation of

steroids

DDx: hydrostatic pulmonary edema (cardiomegaly), ARDS, acute interstitial pneumonia, atypical bacterial / viral pneumonia

Chronic Eosinophilic Pneumonia

Etiology: unknown (NO underlying cause like parasites)

Histo: accumulation of numerous eosinophils, macrophages, histiocytes, lymphocytes, PMNs within lung interstitium + alveolar sacs with interstitial fibrosis

Age: middle age; M < F

- insidious onset of fever, malaise, cough, chest pain, dyspnea develops over 4–8 months (DDx to Löffler syndrome)
- common history of atopy in ~ 50% (may occur during therapeutic desensitization procedure)
- history of allergic rhinitis
- adult-onset asthma (wheezing) in 50%
- usually mild / moderate peripheral blood eosinophilia (with rare exceptions) of > 1000/µL
- increased serum IgE levels (in up to 75%)
- > 25% (usually > 40%) of eosinophils in BAL fluid
- restrictive / obstructive (asthma) pulmonary function

√ (CLASSIC) homogeneous peripheral airspace consolidation:

- √ frequently multifocal bilateral > unilateral nonsegmental with predilection for upper lung zones
- √ CHARACTERISTIC photographic negative of pulmonary edema (in 25–34%)
- √ unchanged for many days to weeks (DDx to Löffler syndrome)
- √ fast regression of infiltrates under steroids

CT:

- √ patchy consolidation / nodules with peripheral and upper lobe predominance
- √ ground-glass opacities with crazy paving
- √ subpleural reticulations (less common early, but frequent in later stages of disease)
- √ linear bandlike opacities parallel to pleural surface (> 2 months after onset of symptoms)
- √ pleural effusion (in < 10%)

Prognosis: chronic and progressive clinical features

Rx: dramatic response to steroid therapy (within 3–10 days)

DDx:
1. Churg-Strauss syndrome (lobular distribution of peripheral consolidation, centrilobular nodules within ground-glass opacities)
2. Löffler syndrome (shifting and transient pulmonary opacities in identical distribution)
3. Cryptogenic organizing pneumonia

Idiopathic Hypereosinophilic Syndrome

= rare disorder characterized by overproduction of eosinophils (= primary hypereosinophilia) that eventually leads to organ injury

Age: 3rd–4th decade; M÷F = 7÷1

Histo: striking eosinophilic infiltration of involved organs associated with necrosis

Diagnostic criteria:

(1) Persistent eosinophilia of > 500 eosinophils/mm³ for more than 6 months

(2) Absence of known causes of eosinophilia
(3) Evidence of eosinophil-mediated end organ damage (heart, CNS) with multiorgan system dysfunction

@ Heart
• restrictive cardiomyopathy
√ endocardial fibrosis
√ valvular damage (= mitral + tricuspid insufficiency)
√ formation of mural cardiac thrombus

@ Lungs (involved in 40%)
• BAL fluid eosinophilia (as high as 73%)
√ congestive heart failure with pulmonary edema
√ nonspecific focal / diffuse interstitial or alveolar nonlobar opacities
√ occasionally peripheral pulmonary opacities
√ pleural effusion (in 50%)
CT:
√ nodules ± surrounding ground-glass opacities
√ focal / diffuse areas of ground-glass opacities in a patchy + peripheral distribution
√ interlobular septal thickening

@ CNS
√ peripheral neuropathy + encephalopathy

@ Skin
• urticaria, angioedema

DDx: (1) Churg-Strauss syndrome (vasculitis)
(2) Eosinophilic leukemia (immature eosinophils)

ERDHEIM-CHESTER DISEASE

= LIPOID GRANULOMATOSIS = POLYOSTOTIC SCLEROSING HISTIOCYTOSIS

[Jakob Erdheim (1874–1937), chief of the pathological-anatomical institute of the Vienna City Hospital, Austria]

[William Chester (1903–1974), in 1930 pathology fellow under Erdheim, later American cardiologist]

= rare multisystem non–Langerhans cell histiocytosis (non-LCH) of unknown cause characterized by xanthomatous infiltration of organs by foamy lipid-laden histiocytes, commonly involving skin + long bones

Mean age: 53 (range, 7–84) years; M÷F = 3÷1

Histo: mononuclear histiocytes with clear, foamy cytoplasm (xanthoma cells) and immunohistochemical reaction positive for CD68 + negative for CD1a and S-100 immunostaining protein or Birbeck granules (DDx to LCH)

• fever, weight loss, malaise, heart failure

@ Appendicular skeleton (95% long bone involvement)
• periarticular bone pain (mostly) in lower extremity (47%)

Location: commonly distal femoral metadiaphyses

Distribution: diaphyses + metaphyses similar to progressive diaphyseal dysplasia

√ symmetric patchy long bone medullary osteosclerosis in metadiaphyseal region with

sparing of epiphyses

√ lesser involvement of flat bones + axial skeleton
√ loss of the corticomedullary junction
√ coarsened trabecular pattern
√ patchy areas of T2-signal hyperintensity
√ sparing of epiphyses + hands and feet + axial skeleton
Associated with: bone infarcts, periostitis

@ Retroperitoneum (29%)
• progressive renal failure ← fibrous perinephritis
√ perirenal rind of soft tissue with a hairy appearance encasing kidneys, ureters ± aorta
DDx: lymphoma, retroperitoneal fibrosis
√ low SI on T1WI + T2WI with minimal contrast enhancement
√ hydronephrosis
Cx: renal failure
Rx: ureteral stent placement, steroids, chemo- and immunotherapy, radiation, surgery

@ Lung (14–23%)
Age: elderly men
• dyspnea (5%) ← pulmonary fibrosis
√ circumferential pleural thickening / effusion
√ smooth interlobular septal thickening
√ centrilobular nodules ± lung cysts
√ pericardial thickening
√ mediastinal infiltration
Prognosis: significant contributor to morbidity & mortality

@ CNS (< 30%)
Types:
(a) infiltrative: widespread nodules / masses predominantly involving cerebellum + brainstem
(b) meningeal: meningioma-like nodular thickening along dura / dural xanthoma
(c) composite
Associated with: osteosclerosis of sinus walls, orbital masses

Intracranial lesions that also involve facial bones / orbits are suggestive of Erdheim-Chester disease.

• painless bilateral exophthalmos (27%); diabetes insipidus
√ retro-orbital infiltration / mass → exophthalmos
√ single / multiple dura-based extra-axial masses (particularly in sellar region) ± diffuse pachymeningeal thickening
√ iso- to slightly hypointense on T1WI
√ avid homogeneous enhancement for up to 8 days after injection
√ iso- to hypointense on T2WI

@ Heart
√ cardiac fibrosis → cardiomyopathy
√ pericardial thickening / effusion

@ Skin: xanthelasma of eyelids, xanthoma (in 15%)

Rx: corticosteroid therapy, chemotherapy, radiation, surgery

EXTRINSIC ALLERGIC ALVEOLITIS

= HYPERSENSITIVITY PNEUMONITIS

= characterized by an inappropriate host response to repeatedly inhaled organic allergens often related to patient's occupation

Cause: inhalation of organic dust (= particulate organism / protein complex) typically of 1–2 µm (always < 5 µm) particle size deposited in distal airspaces of lung acting as antigen for a type III + type IV immune reaction

Manifestation: after months / years of continuous / intermittent inhalation of inciting agent

Histo:
1. Cellular bronchiolitis = chronic inflammatory cells lining small airways
2. Diffuse chronic interstitial inflammatory infiltrate of lymphocytes, plasma cells, neutrophils, mast cells
3. Poorly circumscribed interstitial nonnecrotizing (noncaseating) granulomas < 1 mm in diameter
4. Individual giant cells in alveoli / interstitium

- asymptomatic (10–40%); recurrent episodes of fever, chills, dry cough, dyspnea following exposure after 6-hour interval
- resolution of episodic symptoms after cessation of exposure, abate spontaneously over 1–2 days
- insidious onset of gradually progressive dyspnea
- reduction in vital capacity, diffusing capacity, arterial pO2
- intracutaneous injection of antigen results in delayed hypersensitivity reaction
- presence of serum precipitins against antigen
- positive aerosol provocation inhalation test
- markedly increased cell count with often > 50% T-lymphocytes on bronchoalveolar lavage

Location: predominantly midlung zones, occasionally lower lung zones, rarely upper lung zones

Specific antigens for immune complex disease (type III = Arthus reaction):

1. **Farmer's lung** from damp moldy hay (Thermoactinomyces vulgaris or Micropolyspora faeni)
2. **Pandora's pneumonitis** from heating / humidifying / forced air conditioning systems (thermophilic actinomycetes)
3. **Bird-fancier's lung,** pigeon breeder's lung from protein in bird serum / excrements / feathers

   Average duration of exposure: 9 years
4. **Mushroom worker's lung** from mushroom compost (Thermoactinomyces vulgaris or Micropolyspora faeni)

   Average duration of exposure: 5 years
5. **Bagassosis** from moldy sugar cane in sugar mill (contamination with Thermoactinomyces sacchari /vulgaris and Micropolyspora faeni)
6. **Malt worker's lung** from malt dust (Aspergillus clavatus)
7. **Maple bark disease** from moldy maple bark in saw mill (Cryptostroma corticale)
8. **Suberosis** from moldy cork dust (Penicillium frequentans)
9. **Sequoiosis** from redwood dust (Graphium species)
10. **Mollusk shell** pneumonitis

    Average duration of exposure: 11 years

11. **Hot tub lung** from colonization of heated water by M. avium
Average duration of exposure: 2 years
Thermophilic actinomycetes:
= bacteria < 1 μm in diameter with morphologic characteristics of fungi; found in soil, grains, compost, fresh water, forced-air heating, cooling system, humidifier, air-conditioning system
Isocyanates: used for large-scale production of polyurethane polymers in the manufacture of flexible / rigid foams, elastomers, glue, adhesives, surface coating, spray paint
◊ Principal cause of occupational asthma!
Mycobacterium avium:
colonization of heated water in hot tub / lubrication of metalworking machinery
Aspergillus: in corn and malt workers
Penicillium: in production of cheese, cork, peat moss
Rx: mask, filter, industrial hygiene, alterations in forced-air ventilatory system, change in patient's habits / occupation / environment

Acute / Episodic Extrinsic Allergic Alveolitis

= renewed exposure to antigen with improvement between attacks usually within enclosed spaces with poor ventilation
Histo: filling of air spaces by polymorph neutrophils + lymphocytes
Onset of symptoms: 4–12 hours after exposure
- fever, chills, myalgia, malaise, frontal headache
- chest tightness, cough, dyspnea, scanty mucoid expectoration
- arthralgia (common)

√ No CXR abnormalities in 30–95%
√ diffuse acinar consolidative pattern (edema + exudate filling alveoli) resolving within a few days
√ lymph node enlargement (30%, more common with recurrence)
HRCT (abnormal in > 90%):
√ "headcheese" sign (= type of terrine with bits of meat scavenged from a calf or pig) = combination of patchy ground-glass opacities + normal regions + air trapping
√ usually bilateral symmetric homogeneous patchy ground-glass opacities concentrated in middle part and base of lungs
√ numerous round centrilobular ground-glass opacities usually < 5 mm in diameter with indistinct border and small central lucency (= patent bronchiole)
√ hypoattenuation + hypovascularity of scattered secondary lobules ← air trapping
√ diffuse dense airspace consolidation (= confluent collections of intraalveolar histiocytes, interstitial + intraalveolar edema)
Dx: classical presentation of a known exposure history + typical symptoms + detection of serum precipitins to suspected antigen + positive bronchoalveolar lavage (lymphocytes > 20–50%)
DDx: UIP, NSIP

Subacute Extrinsic Allergic Alveolitis

= less intense but continuous exposure to inhaled antigens, usually in domestic environment

Histo: predominantly interstitial lymphocytic infiltrate, poorly defined granulomas, cellular bronchiolitis

Onset of symptoms after exposure: weeks – months

- recurrent respiratory / systemic symptoms:
  - breathlessness upon exertion, fever + cough
  - weight loss, muscle + joint pain

√ changes may be completely reversible if present for < 1 year

√ interstitial nodular / reticulonodular pattern

HRCT:

√ widespread patchy / diffuse ground-glass attenuation in 52% (obstructive pneumonitis, filling of alveoli by large mononuclear cell infiltrates)

√ poorly defined centrilobular micronodules < 5 mm (cellular bronchiolitis + small granulomas)

√ areas of decreased attenuation + mosaic perfusion (86%)

√ irregular reticular changes, septal lines, parenchymal bands

Chronic Extrinsic Allergic Alveolitis

= prolonged insidious dust exposure

Onset of symptoms after exposure: months to years

- insidious progressive exertional dyspnea indistinguishable from idiopathic pulmonary fibrosis

Histo: proliferation of epithelial cells + predominantly peribronchiolar interstitial fibrosis

Location: usually in mid zones, relative sparing of lung apices + costophrenic sulci

√ irregular linear opacities (= fibrosis)

√ loss of lung volume ← cicatrization atelectasis

√ pleural effusion (rare)

√ lymph node enlargement may occur

CT:

√ fibrosis of middle + lower lung zones with relative sparing of lung bases:

√ intralobular interstitial thickening

√ irregular interlobular septal thickening

√ honeycombing

√ traction bronchiectasis

√ focal air trapping / diffuse emphysema

√ coexistent subacute changes ← continuing exposure

FAT EMBOLISM

= obstruction of pulmonary vessels by fat globules followed by chemical pneumonitis from unsaturated plasma fatty acids producing hemorrhage / edema

Frequency: in 67–97% of necropsy series in patients with major skeletal trauma; however, symptomatic fat embolism syndrome in < 10% (M > F)

Onset: 24–72 hours after trauma

- dyspnea (progressive pulmonary insufficiency), fever
- systemic hypoxemia; mentation changes: headaches, confusion
- petechiae (50%) from coagulopathy ← release of tissue thromboplastin

√ initial chest film usually negative (normal up to 72 hours)
√ platelike atelectasis
√ bilateral diffuse alveolar infiltrates
√ consolidation (may progress to ARDS)
NUC:
√ mottled peripheral perfusion defects (1–4 days after injury), later enlarging ← pneumonic infiltrates

FOCAL ORGANIZING PNEUMONIA

= unresolving pneumonia / pneumonia with incomplete resolution beyond 8 weeks

Pattern of organizing pneumonia: (a) unilateral / focal (10–38%)

(b) diffuse (majority)

Cause: infection (most common), collagen-vascular disease, immunologic disorders, drug reaction, aspiration, toxic inhalation, radiation, organ transplantation, idiopathic (= cryptogenic organizing pneumonia)

Prevalence: 5–10% of all pneumonias (87% of pneumonias resolve within 4 weeks, 12% within 4–8 weeks)

Predisposing factors: ? age, diabetes mellitus, chronic bronchitis, overuse of antibiotics

Path: intraalveolar exudate → transformed into connective tissue as nonspecific response to lung injury

Histo: organizing fibroblastic plugs of tissue composed of spindle-shaped cells in a pale staining matrix

Location: within airspace, alveolar septa, bronchial mucosa, bronchioles

• cough, sputum, fever, hemoptysis (in ¼)
√ ill-defined localized parenchymal abnormality with irregular margin:
√ solitary pulmonary nodule
√ focal area of consolidation / ground-glass opacity in peribronchial distribution
√ associated bronchiectasis / architectural distortion
√ "reverse halo" sign = focal area of ground-glass opacity surrounded by a complete ring of denser consolidation
√ "atoll" sign = incomplete ring of denser consolidation
√ decrease in size of mass within 3–4 weeks
HRCT:
√ flat / ovoid lesion with irregular margin in subpleural location / along bronchovascular bundle
√ ± satellite lesions (44%) + air bronchograms (22%)

DDx: acute pneumonia, pulmonary hemorrhage, lung cancer (organizing pneumonia may be adjacent to malignancy)

GIANT CELL INTERSTITIAL PNEUMONIA

◊ ALMOST PATHOGNOMONIC for hard metal pneumoconiosis
√ diffuse micronodular pattern
√ reticular pattern; in advanced disease coarse and accompanied by small cystic spaces

√ ± lymph node enlargement
HRCT:
√ bilateral areas of ground-glass attenuation
√ areas of consolidation
√ extensive reticulations
√ traction bronchiectasis

GOODPASTURE SYNDROME

[Ernest William Goodpasture (1886–1960), chair of pathology at the medical school of Vanderbilt University, developed a method for cultivating viruses and rickettsiae]
= ANTI-GLOMERULAR BASEMENT MEMBRANE ANTIBODY DISEASE
= autoimmune disease characterized by
(1) Glomerulonephritis
(2) Circulating antibodies against glomerular + alveolar basement membrane
(3) Pulmonary hemorrhage

Pathogenesis:
cytotoxic antibody-mediated disease = type II hypersensitivity; alveolar basement membrane becomes antigenic (perhaps viral etiology); IgG / IgM antibody with complement activation → cell destruction + pulmonary hemorrhage → hemosiderin deposition and pulmonary fibrosis

Age peak: 26 (range, 17–78) years; M÷F = 7÷1
• iron-deficiency anemia, systemic hypertension
√ hepatosplenomegaly
@ Lung
• preceding upper respiratory infection (in ⅔) + renal disease
• mild hemoptysis (72%) with hemosiderin-laden macrophages in sputum, commonly precedes the clinical manifestations of renal disease by several months
• cough, mild dyspnea, basilar rales
√ extensive bilateral air-space consolidation:
√ symmetric consolidation of perihilar area + lung bases with sparing of lung apices
√ air bronchogram
√ consolidation replaced by interstitial pattern within 2–3 days → organization of hemorrhage resulting in interlobular septal thickening
√ hilar lymph nodes may be enlarged during acute episode
@ Kidney
• glomerulonephritis with IgG deposits in characteristic linear pattern in glomeruli; hematuria

Prognosis: death within 3 years (average 6 months) because of renal failure
Rx: cytotoxic chemotherapy, plasmapheresis, bilateral nephrectomy
DDx: idiopathic pulmonary hemosiderosis

GRANULOMA OF LUNG

Cause:
A. SARCOIDOSIS

B. NON-SARCOID GRANULOMATOUS DISEASE

(a) infectious

› bacterial: TB, gumma
› opportunistic: cryptococcosis
› parasitic: Dirofilaria immitis (dog heartworm)
› fungal: histoplasmosis, coccidioidomycosis, nocardiosis

(b) noninfectious

› foreign body: talc, beryllium, algae, pollen, cellulose, lipids, abuse of nasally inhaled drugs, aspiration of medication
› angiocentric lymphoproliferative disease
› vasculitides
› extrinsic allergic alveolitis
› Langerhans cell histiocytosis
› pulmonary hyalinizing granuloma
› peribronchial granuloma
› chronic granulomatous disease of childhood

Histo: epithelial cells, lymphocytes, macrophages, giant cells of Langhans type
[Theodor Langhans (1839–1915), professor of pathology at the University of Bern, Switzerland, and Giessen, Germany, discoverer of multi-nucleated giant cell = Langhans giant cell]

Frequency: constitutes majority of solitary pulmonary nodules

• nonproductive cough, shortness of breath
√ spontaneous pneumothorax

CXR:

◊ CXR detection requires multiple granulomas / clusters of granulomas (individual granuloma too small)!
√ central nidus of calcification in a laminated / diffuse pattern
√ absence of growth for at least 2 years

CT (most effective in nodules ≤ 3 cm of diameter with smooth discrete margins):

√ 50–60% of pulmonary nodules demonstrate unsuspected calcification by CT

DDx: carcinoma (in 10% eccentric calcification in preexisting scar / nearby granuloma / true intrinsic stippled calcification in larger lesion)

HAMARTOMA OF CHEST WALL

= MESENCHYMOMA (incorrect as it implies neoplasm)
= focal overgrowth of normal skeletal elements with a benign self-limited course; extremely rare

Age: 1st year of life

√ moderate / large extrapleural well-circumscribed mass affecting one / more ribs
√ ribs near center of mass partially / completely destroyed
√ ribs at periphery deformed / eroded
√ significant amount of calcification / ossification (DDx: aneurysmal bone cyst)
√ mass compresses underlying lung

Rx: resection curative

HAMARTOMA OF LUNG

= most common benign tumor of the lung

Frequency: 0.25% in population (autopsy); 6–8% of all solitary pulmonary neoplasms; 77% of all benign lung tumors

Etiology:

1. Congenital malformation of a displaced bronchial anlage
2. Hyperplasia of normal structures
3. Cartilaginous neoplasm
4. Response to inflammation

Path: solitary mass composed of tissues normally found in this location in abnormal quantity, mixture, and arrangement

Histo: columnar, cuboidal, ciliated epithelium, fat (in 50%), bone, cartilage (predominates), muscle, vessels, fibrous tissue, calcifications, plasma cells originating in fibrous connective tissue beneath mucous membrane of bronchial wall

Age peak: 5th and 6th decade; M÷F = 2÷1 – 3÷1

May be associated with:

Carney triad (pulmonary chondromatous lesion, gastric leiomyosarcoma, functioning extraadrenal paraganglioma); pulmonary hamartoma syndrome

- mostly asymptomatic; fever ← postobstructive pneumonitis
- cough, hemoptysis (rare), vague chest pain

Location: ⅔ peripheral; endobronchial in 1%; multiplicity (rare)

√ round smooth lobulated mass < 4 cm (average of 2.5 cm)
√ calcification in 15–20% (ALMOST PATHOGNOMONIC if of chondroid "popcorn" type)
√ fat density in 50% (DIAGNOSTIC)
√ cavitation (extremely rare)
√ growth patterns: slow / rapid / stable with later growth
√ usually diameter increase by 1.5 mm/year doubling in size every 14 years

HRCT:

√ fat density detectable in 34% (–80 to –120 HU)
√ calcium + fat detectable in 19%

Transthoracic needle biopsy: 85% diagnostic accuracy

DDx: lipoid pneumonia (ill-defined mass / lung infiltrate); granulomatous disease, carcinoid tumor; metastatic mucinous adenocarcinoma, amyloidoma

HARD-METAL PNEUMOCONIOSIS

= alloy of tungsten, carbon and cobalt

Occupational exposure: processing of tungsten carbide + cobalt (occasionally adding titanium, tantalum, nickel, chromium)

Main cause: cobalt (= cytotoxic + allergic agent)

Histo: obliterative bronchiolitis (earliest manifestation), subacute fibrosing alveolitis (= desquamation of epithelial cells + accumulation of macrophages in alveolar space), PATHOGNOMONIC giant cell interstitial pneumonia (multinuclear giant cells), chronic interstitial lung disease = diffuse mural fibrosis with honeycombing (several years after initial exposure)

- asthma, shortness of breath, chronic cough
- dyspnea on exertion over prolonged period
- restricted / obstructive pulmonary function tests

√ diffuse small reticulonodular pattern + small cystic spaces
√ panlobular bilateral ground-glass opacities / consolidation
√ parenchymal distortion, honeycombing, traction bronchiectasis

DDx: idiopathic pulmonary fibrosis, non-specific interstitial pneumonia

HEREDITARY HEMORRHAGIC TELANGIECTASIA

= RENDU-OSLER-WEBER SYNDROME

[Henri Jules Louis Marie Rendu (1844–1902), Head of the Department of Medicine at the Hôpital Necker, Paris]
[Sir William Osler (1849–1919), first professor of medicine at Johns Hopkins University Medical School in Baltimore, USA]
[Frederick Parkes Weber (1863–1962), dermatologist, London]

= group of autosomal dominant inherited disorders that result in a variety of systemic fibrovascular dysplasias affecting mucous skin, membranes, lung, brain, GI tract:

Phenotypes of Rendu-Osler-Weber Syndrome

Type	*Gene mutation*	*Description (lesions = AVMs + AVFs)*
HHT1	ENG	most common phenotype; prevalence of pulmonary lesions
HHT2	ALK1	prevalence of hepatic lesions; frequently pulmonary hypertension
HHT3	unknown	hepatic > pulmonary lesions
HHT4	unknown	lesions in lung, brain, nose
JPHT	SMAD4	lesions in various sites + juvenile polyposis

(1) Telangiectasias
(2) Arteriovenous malformations (AV hemangiomas)
(3) Aneurysms

Etiology: gene mutation that encodes a protein binding transforming growth factor (TGF)-β controlling cell proliferation + differentiation + death → abnormal vascular remodeling into fibrovascular dysplasia

Prevalence: 1–20÷100,000; M = F

Age: manifestation usually during adulthood

Path: direct connections between arteries + veins with absence of capillaries (telangiectases are small AVMs)

(a) small telangiectasis = focal dilatation of postcapillary venules with prominent stress fibers in pericytes along luminal borders
(b) fully developed telangiectasis = markedly dilated + convoluted venules with excessive layers of smooth muscle without elastic fibers directly connecting to dilated arterioles

Histo: absence of cellular intervals in vascular endothelial cells

Diagnostic criteria: ≥ 3 of the following conditions
(1) Recurrent epistaxis
(2) Multiple vascular dilatations in face + oral cavity
(3) AVMs / AVFs in internal organs
(4) 1st-degree relative with this condition

• frequent bleeding into mucous membranes, skin, lungs, GU system, GI system ← vascular weakness

@ Nose (= telangiectasis of nasal mucosa)
• recurrent epistaxis (32–85%): more severe over time in 66%; begins by age 10, present by age 21 in most cases; up to 45 episodes per month

@ Skin
• telangiectases = small red vascular blemishes
Age: present in most cases by age 40; increase in number + size with age
Location: lips, tongue, floor of oral cavity, palate, fingers, face, conjunctiva, trunk, arms, nail beds

@ Lung (5–15%)
◊ 5–15% of patients with hereditary hemorrhagic telangiectasia have pulmonary AVMs
◊ Up to 60% of patients with pulmonary AVMs have hereditary hemorrhagic telangiectasia

@ CNS (= cerebral or spinal AVMs)
• headache; seizure; paraparesis (less common)
√ subarachnoid hemorrhage

@ GI tract (stomach, duodenum, small bowel, colon)
= dilatation of small mucosal blood vessels
May be associated with: AVMs / angiodysplasia
• recurrent GI bleeding (in 5th–6th decade)

@ Liver (8–74%)
√ hepatomegaly
√ presence of multiple AVMs (between hepatic artery branches + branches of hepatic / portal veins):
√ heterogeneous liver enhancement with mosaic perfusion
√ simultaneous enhancement of hepatic arteries + veins
√ multiple areas of transient hepatic attenuation differences on hepatic arterial phase:
(a) arterioportal shunt (65%)
(b) telangiectasia (63%)
(c) confluent vascular mass (25%)
√ dilated tortuous hepatic arteries
√ early enhancement of dilated hepatic veins
√ diffuse mottled capillary blush on angio
Cx: atypical cirrhosis, hyperdynamic portal hypertension, variceal GI hemorrhage, ascites, hepatic portosystemic encephalopathy

Cx: (1) Congestive heart failure ← AV shunting
(2) Cerebral abscess ← paradoxical emboli

HISTOPLASMOSIS

Prevalence: nearly 100% in endemic area; up to 30% in Central + South America, Puerto Rico, West Africa, Southeast Asia; annually 500,000 infected in USA; up to 30% of US population has positive skin reaction

Organism: Histoplasma capsulatum = ubiquitous dimorphic fungus; worldwide most often in temperate climates; widespread in soil enriched by bird droppings of central North America (endemic in Ohio, Mississippi, St. Lawrence River valley; exists as a spore in soil + transforms into yeast form at normal body temperature

Vector: fowl + other birds (passes through feces without infection due to high body temperature); bats

Infection: inhalation of wind-borne spores (microconidia of 2–6 μm, macroconidia of 6–14 μm), which germinate within alveoli releasing yeast forms, which are phagocytized but not killed by macrophages; invasion of pulmonary lymphatics with spread to hilar + mediastinal lymph nodes; hematogenous dissemination of parasitized macrophages throughout reticuloendothelial system (spleen!)

Path: spores incite formation of epithelioid granulomas, necrosis, calcification

Dx: (1) Culture (sputum, lung tissue, urine, bone marrow, lymph node)
(2) Identification of yeast forms stained with PAS / Gömöri methenamine silver
(3) Complement fixation test (absolute titer of 1÷64 or 4-fold rise in convalescent titer suggest active / recent infection)
(4) Serum immunodiffusion: agar gel diffusion test (H precipitin band)

Rx: ketoconazole

Pulmonary Histoplasmosis

A. ACUTE HISTOPLASMOSIS
- mostly asymptomatic and self-limiting illness (in 99.5%)
- fever, cough, malaise simulating viral upper respiratory infection 3 weeks after massive inoculum / in debilitated patients (infants, elderly)
- positive skin test for histoplasmosis; hypersensitivity develops in 1–2 weeks

√ generalized lymphadenopathy
√ bilateral nonsegmental bronchopneumonic pattern with tendency to clear in one area + appear in another
√ multiple nodules changing into hundreds of punctate calcifications (usually > 4 mm) after 9–24 months
√ "target lesion" = PATHOGNOMONIC central calcification
√ hilar / mediastinal lymph node enlargement (DDx: acute viral / bacterial pneumonia)
√ "popcorn" calcification of mediastinal lymph nodes > 10 mm (80% probability of being caused by histoplasma)
√ > 5 splenic calcifications (40%)

CT:
√ paratracheal / subcarinal mass with regions of low attenuation (necrosis) + enhancing septa

B. CHRONIC HISTOPLASMOSIS (0.03%)

Predisposed: individuals with chronic obstructive pulmonary disease + cigarette smoking

Age: middle-aged white men

Pathophysiology: hyperimmune reaction

- cough, low-grade fever, night sweats simulating postprimary tuberculosis

√ segmental wedge-shaped peripheral consolidation of moth-eaten appearance from scattered foci of emphysematous lung

√ fibrosis in apical posterior segments of upper lobes (indistinguishable from postprimary TB) adjacent to emphysematous blebs

C. DISSEMINATED HISTOPLASMOSIS

Predisposed: impaired T-cell immunity; AIDS; immunosuppression after organ transplant

Prevalence: 1÷50,000 exposed individuals

Pathophysiology: progression of exogenous infection / reactivation of latent focus

- acute rapidly fatal infection:
  - fever, weight loss, anorexia, malaise, cough (< 50%)
  - abdominal pain, nausea, vomiting, diarrhea
- chronic intermittent illness:
  - low-grade fever, weight loss, fatigue
  - adrenal insufficiency

√ normal CXR (> 50%)

√ miliary nodules of < 3 mm

√ linear irregular reticulonodular opacities

√ segmental / lobar / diffuse airspace opacities

√ hilar + mediastinal adenopathy (uncommon in immunocompromised patients)

√ hepatosplenomegaly

@ GI tract (cecum, small bowel)

√ mucosal nodularity + strictures ← ulceration

Cx: arthritis (most often knee), tenosynovitis, osteomyelitis

D. DELAYED MANIFESTATIONS

◊ Organism recovered in only 50%!

√ **histoplasmoma** (= continued growth of primary focus at 0.5–2.8 mm/year) adjacent to pleura + typically with laminated calcific rings ("lung stone")

In 20% associated with: mediastinal granulomas

√ broncholithiasis = erosion of peribronchial calcified lymph node into bronchus:

- hemoptysis, fever, chills, productive cough

√ change in position of stone on serial radiographs

√ **mediastinal granuloma** (more common)

= direct infection of mediastinal lymph nodes

Histo: involved nodes with varying degrees of central caseation ± calcification

- usually asymptomatic

Location: subcarinal / right paratracheal / hilar lymph nodes

√ widened mediastinum (enlarged nodes + veins)

√ lobulated mass of low-density lymph nodes 3–10 cm in thickness surrounded by a 2–5-mm thick fibrous capsule crisscrossed by irregularly shaped enhancing septa (CHARACTERISTIC)

√ displacement of SVC / esophagus

√ **fibrosing mediastinitis** (less common)

HODGKIN DISEASE

= HODGKIN LYMPHOMA

[Thomas Hodgkin (1798–1866), English physician and pathologist, first appointed physician at London Dispensary and curator of Pathology Museum at Guy's Hospital Medical School]

= disease of T cells

Frequency: 0.75% of all cancers diagnosed each year; 40% of all lymphomas

Age: bimodal peaks at age 25–30 years and 75–80 years; very rare in children < 5 years; M÷F = 1÷1

Histo: Hodgkin and Reed-Sternberg cells = binucleate cells with prominent centrally located nucleoli (= activated pre-B cells) scattered in infiltrate of inflammatory cells

- positive for CD30, CD15, EBV

(1) Nodular sclerosis (78%)

= lymph nodes traversed by broad bands of birefringent collagen separating nodules, which consist of normal lymphocytes, eosinophils, plasma cells, and histiocytes

- ⅓ with systemic symptoms

√ typically localized anterior mediastinal involvement

Prognosis: good

(2) Mixed cellularity (17%)

= diffuse effacement of lymph nodes with lymphocytes, eosinophils, plasma cells + relative abundance of atypical mononuclear and Reed-Sternberg cells; more commonly advanced stage at presentation and older age

√ more commonly abdominal than mediastinal

Prognosis: less favorable

(3) Lymphocyte predominance (5%)

= abundance of normal-appearing lymphocytes + relative paucity of abnormal cells

- often diagnosed in younger people < 35 years
- systemic symptoms are uncommon
- frequently in early stage + localized disease

Prognosis: most favorable natural history

(4) Lymphocyte depletion (1%)

= paucity of normal-appearing lymphocytes + abundance of abnormal mononuclear and Reed-Sternberg cells; least common subtype with worst prognosis

Age: older patients

- systemic symptoms

√ disseminated advanced stage

Prognosis: rapidly fatal

- painless lymphadenopathy: cervical > supraclavicular > inguinal > axillary
- alcohol-induced pain, generalized pruritus
- unexplained fevers, drenching night sweats, weight loss

@ CHEST

At presentation: 67% with intrathoracic disease

Sites of lymphoid aggregates:

1. Lymph nodes in mediastinum
2. Lymph nodes at bifurcation of 1st + 2nd order bronchi

3. Encapsulated lymphoid collections on thoracic surface deep to parietal pleura
4. Unencapsulated nodules at points of divisions of more distally situated bronchi, bronchioles, pulmonary vessels
5. Unencapsulated lymphoid aggregates within peribronchial connective tissue
6. Small accumulations of lymphocytes in interlobular septa + lymphatic channels

Ann Arbor Staging Classification for HD (1971)	
Stage	*Description*
I	one anatomic region / lymphoid structure (eg, spleen, thymus, Waldeyer ring) or single extralymphatic site
II	≥ 2 lymph node regions / localized contiguous involvement of extranodal site + lymph node region on same side of diaphragm (number of sites indicated by subscript, eg, II_2)
III	lymph node regions on both sides of diaphragm ± spleen (Stage III_S) / Waldeyer ring / localized contiguous involvement of one extranodal site
III_1	± splenic / hilar / celiac / portal nodes
III_2	+ paraortic / iliac / mesenteric nodes
IV	diffuse / disseminated involvement of ≥ 1 extranodal organs lymph nodes
A*	no symptoms
B*	temperature > 38°C, drenching night sweats, unexplained loss of > 10% of body weight within preceding 6 months
E*	single extranodal site contiguous to nodal site
X*	bulky disease (mediastinum widened > 1/3) OR nodal mass > 10 cm
CS*	clinical stage
PS*	pathologic stage (as determined by laparoscopy)
* these designations are applicable to any stage	

A. INTRAPULMONARY MANIFESTATIONS

Frequency: 6–11%; in 4.3% bilateral (more frequent in recurrent disease)

◊ Most commonly in nodular sclerosing type

◊ Subsequent to hilar adenopathy in ipsilateral lung

1. Bronchovascular form (most common type)
   - √ coarse reticulonodular pattern contiguous with mediastinum = direct extension from mediastinal nodes along lymphatics
   - √ nodular parenchymal lesions
   - √ miliary nodules
   - √ endobronchial involvement
   - √ lobar atelectasis ← endobronchial obstruction (rare)
   - √ cavitation ← necrosis (rare)
2. Subpleural form
   - √ circumscribed subpleural masses
   - √ pleural effusion (20–50%) ← lymphatic obstruction
3. Massive pneumonic form (68%)

√ diffuse nonsegmental infiltrate (pneumonic type)
√ massive lobar infiltrates (30%)
√ homogeneous confluent infiltrates with shaggy borders
√ air bronchogram

4. Nodular form
   √ multiple nodules < 1 cm in diameter (DDx: metastatic disease)

DDx in treated patients:
relapse, infection, radiation pneumonitis, drug-induced lung disease

B. EXTRAPULMONARY MANIFESTATIONS

1. Mediastinal + hilar lymphadenopathy
   most common manifestation, present in 90–99%, in thorax commonly multiple lymph node groups involved
   Location:
   anterior mediastinal + retrosternal nodes commonly involved (DDx: sarcoidosis); confined to anterior mediastinum in 40%; 20% with mediastinal nodes have hilar lymphadenopathy also; hilar lymph nodes involved bilaterally in 50%
   Spread from anterior mediastinum to:
   other mediastinal locations, pleura, pericardium, chest wall
   ◊ Involvement of multiple lymph node groups in 95%!
   √ CXR: on initial film adenopathy identified in 50%
   √ necrotic lymph nodes (commonly nodular sclerosing type)
   √ lymph nodes may calcify following radiation / chemotherapy
2. Pleural effusion (13%)
   ◊ NOT of prognostic significance
   Prognosis: usually resolves following treatment
3. Pleural masses + plaques
   √ sternal erosion
   √ invasion of anterior chest wall
4. Thymic involvement
   √ thymic enlargement (in 56%)

Cx:

1. Superimposed infection
   √ consolidation with bulging borders: necrotizing bacterial pneumonia
   √ multiple nodular foci: aspergillosis + nocardiosis
   √ bilateral diffuse consolidation: Pneumocystis carinii
   √ rapidly developing cavitation within consolidation: anaerobes / fungus
   Dx: by culture, sputum cytology, lung biopsy
2. Drug toxicity

Extranodal Hodgkin Disease (15–30%)

@ BONE (5–20%)
◊ During course of disease 5–32% develop bone marrow involvement
At presentation: 1–4%; indicative of widespread aggressive disease with poor prognosis
Location: dorsolumbar spine > pelvis > ribs > femora > sternum

NUC: recommended only with bone pain + elevated serum alkaline phosphatase
√ solitary (33%) / polyostotic (66%) lesions:
√ usually wide ill-defined lesion edge / sclerotic margin
√ lamellated / "sunburst" periosteal reaction
√ predominantly osteolytic with blurred borders; rarely sclerotic / mixed lytic-sclerotic
√ fractures occur rarely at presentation
√ vertebral osteolysis with collapse / patchy sclerosis / "ivory vertebra" / mixed lytic + blastic lesion
√ gouge defect of anterior vertebral body margin ← erosion by lymph nodes
√ osteolysis of sternum ← proximity to thoracic lymph ducts

@ HEAD & NECK (< 1%)
• nasopharyngeal biopsy positive in 20%
√ thyroid mass as secondary involvement (2%)

@ CNS (uncommon)
Frequency: secondary hematogenous involvement in 0.2–0.5%; usually not part of standard staging without CNS symptoms / signs
Location: supratentorial cerebral cortex + meninges in inferior aspect of brain (most frequent)
√ leptomeningeal + choroid plexus masses
√ white matter mass, typically periventricular / basal ganglionic / cerebellar
√ paraneoplastic cerebellar atrophy
√ epidural mass with spinal cord compression (in 3.0–7.6%) from extension of paraspinal nodes through intervertebral neural foramen:
√ concomitant vertebral bone involvement (in 32–42%)

@ THYMUS (30–56%)
◊ Considered a "lymph node" in staging
√ remains enlarged after treatment in 33% ← recurrent disease / rebound hyperplasia / persistence of thymic cysts

@ CHEST WALL (6.4%)
√ infiltration of parasternal soft tissues by direct extension from internal mammary nodes
√ mass beneath / between pectoralis muscles (rare)

@ HEART (7.5% at autopsy)
√ pericardial effusion (with large mediastinal mass)
√ invasion of pericardium + SVC
√ pericardial nodular mass

@ LIVER (6–20%)
◊ Primary involvement is very rare
Associated with: splenic disease (almost invariably)
√ discrete nodules (10%) = miliary lesions of < 10 mm
√ diffuse disease (87%) = patchy irregular infiltrates in portal areas

@ SPLEEN
◊ Considered a "nodal organ"
Frequency: 30–40% at staging laparotomy
√ diffuse involvement (not detectable by imaging) ± splenomegaly

√ hypoechoic hypoattenuating nodules with reduced contrast enhancement

MR:

√ hypo- / isointense nodules on T1WI + hyperintense on T2WI

√ reduced enhancement compared with normal spleen

DDx: reactive splenomegaly (in 30%)

@ PANCREAS (extremely rare)

◊ secondary to contiguous lymph node disease

@ GI TRACT (10–15%)

= rarely affecting GI tract → mostly 2ndary involvement by tumor extension from adjacent lymph nodes

◊ primary HD in < 1% of all primary gastric + small bowel lymphomas

Barium:

√ diffuse fold thickening / ulcerated mass in stomach

√ irregular luminal narrowing + nodularity in esophagus, small bowel, colon

CT:

√ concentric thickening of affected bowel wall

› Stomach (9% of all intestinal lymphomas):

√ narrow rigid obstructive lesion (DDx: scirrhous ca.)

√ wall thickening + smoothly lobulated outer border

› Small intestine:

• spruelike symptoms, steatorrhea

√ abundance of desmoplastic reaction (DDx from NHL)

√ infiltrating (60%); polypoid (26%); ulcerated (14%)

Prognosis: poorer 5-year survival rate than with other forms of this disease

› Esophagus (extremely rare):

√ esophageal nodules / irregular narrowing

Cx: focal stenosis, obstruction ← greater degree of fibrosis than lymphoma

@ GU TRACT (extremely rare)

√ perirenal / renal masses ← invasion from surrounding nodes

Cx: increased risk for other malignancies from aggressive therapy (acute leukemia, NHL, radiation-induced sarcoma)

Clinical & HRCT Features of Idiopathic Interstitial Pneumonias
American Thoracic Society and European Respiratory Society (2001)

Type	*Onset [y]*	*Gender*	*Onset*	*Smoking*	*Prognosis*	*Steroids*	*Distribution*	*HRCT*
UIP (IPF)	> 50	M > F	gradual	?	poor	poor	apicobasal, subpleural	macrocystic honeycombing, reticular opacities, traction bronchiectasis, architectural distortion, focal ground-glass opacity , spatial + temporal heterogeneity
NSIP	40–50	M = F	gradual / subacute	no	variable	good	no gradient, symmetric, subpleural	ground-glass opacities, irregular linear / reticular opacities, micronodules, consolidation, microcystic honeycombing
COP	55	M = F	subacute	+	complete recovery	excellent	basal patchy, peripheral / peribronchial	airspace consolidation, mild bronchial dilatation, ground-glass opacities, large nodules (rare)
RB-ILD	30–40	M > F	gradual	+++	good after smoking cessation	good	diffuse / upper lobes	centrilobular nodules, patchy ground-glass opacities, bronchial wall thickening
DIP	30–40	M > F	insidious	++	good after smoking cessation	good	apicobasal, peripheral	ground-glass opacities, irregular linear / reticular opacities, sometimes cysts
LIP	40–50	F > M	slow	no	variable	variable	basal / diffuse	ground-glass opacities, perivascular cysts, septal thickening, centrilobular nodules
AIP	50	M = F	acute	no	> 50 % mortality	unclear	lower lung, symmetric, bilateral	exudative: ground-glass opacities, airspace consolidation organizing: bronchial dilatation, architectural distortion

CT Features and Differential Diagnosis of Idiopathic Interstitial Pneumonias
American Thoracic Society and European Respiratory Society (2013 revision)

Group & Diagnosis	*CT Pattern*	*CT Distribution*	*Typical CT Findings*	*DDx of CT Morphology*
Chronic fibrosing IIPs				
Idiopathic pulmonary fibrosis	Usual interstitial pneumonia (UIP)	√ peripheral √ subpleural √ basal	√ reticular opacities √ honeycombing √ traction bronchiectasis / bronchiolectasis √ architectural distortion √ focal ground-glass attenuation	(1) Collagen vascular disease (2) Hypersensitivity pneumonitis (3) Asbestosis (4) Sarcoidosis
Idiopathic NSIP	Nonspecific interstitial pneumonia (NSIP)	√ peripheral √ basal √ symmetric	√ ground-glass attenuation √ irregular lines √ traction bronchiectasis √ consolidation	(1) UIP (2) DIP (3) Cryptogenic organizing pneumonia (4) Hypersensitivity pneumonitis
Smoking-related IIPs				
Desquamative interstitial pneumonia	Desquamative interstitial pneumonia (DIP)	√ lower zone √ (mostly) peripheral predominance	√ ground-glass attenuation √ reticular lines √ cysts	(1) RB-ILD (2) NSIP (3) Hypersensitivity pneumonitis
RB-ILD	Respiratory bronchiolitis	√ (often) upper lung predominant √ centrilobular	√ bronchial wall thickening √ centrilobular nodules √ patchy ground-glass opacity	(1) DIP (2) NSIP (3) Hypersensitivity pneumonitis
Acute / subacute IIPs				
Cryptogenic organizing pneumonia	Organizing pneumonia	√ subpleural √ peribronchial	√ patchy consolidation / nodules √ perilobular pattern √ reverse halo sign	(1) Infection (2) Aspiration (3) Eosinophilic pneumonia (4) NSIP (5) Vasculitis (6) Sarcoidosis (7) Mucinous adenocarcinoma (8) Lymphoma

Group & Diagnosis	*CT Pattern*	*CT Distribution*	*Typical CT Findings*	*DDx of CT Morphology*
Acute interstitial pneumonia	Diffuse alveolar damage	√ diffuse / patchy	√ consolidation and ground-glass opacity (often with lobular sparing) √ traction bronchiectasis (late)	(1) Hydrostatic edema (2) Pneumonia (3) Pulmonary hemorrhage (4) Acute eosinophilic pneumonia
Rare IIPs				
Lymphoid interstitial pneumonia	Lymphoid interstitial pneumonia	√ lower lung predominant	√ centrilobular nodules √ ground-glass attenuation √ septal + bronchovascular thickening √ thin-walled cysts	(1) NSIP (2) Sarcoidosis (3) Langerhans cell histiocytosis (4) Other cystic lung disease
Idiopathic pleuroparenchymal fibroelastosis	Idiopathic pleuro-parenchymal fibroelastosis	√ peripheral √ upper lung predominant	√ pleural thickening √ subpleural fibrotic changes	(1) Sarcoidosis (2) Pneumoconiosis (3) Pulmonary fibrosis (4) Connective tissue disease (5) Hypersensitivity pneumonitis

Classification of Idiopathic Interstitial Pneumonias
American Thoracic Society and European Respiratory Society (2001)

#	*Entities (in order of frequency)*	*Abbrev.*
1	Idiopathic Pulmonary Fibrosis	IPF
2	Nonspecific Interstitial Pneumonia	NSIP
3	Cryptogenic Organizing Pneumonia	COP
4	Desquamative Interstitial Pneumonia*	DIP
5	Respiratory Bronchiolitis-associated Interstitial Lung Disease*	RB-ILD
6	Acute Interstitial Pneumonia	AIP
7	Lymphoid Interstitial Pneumonia	LIP

** smoking -related*

DDx: sarcoidosis, vasculitis, collagen vascular (connective tissue) disease, drug reaction, asbestosis, chronic hypersensitivity pneumonitis

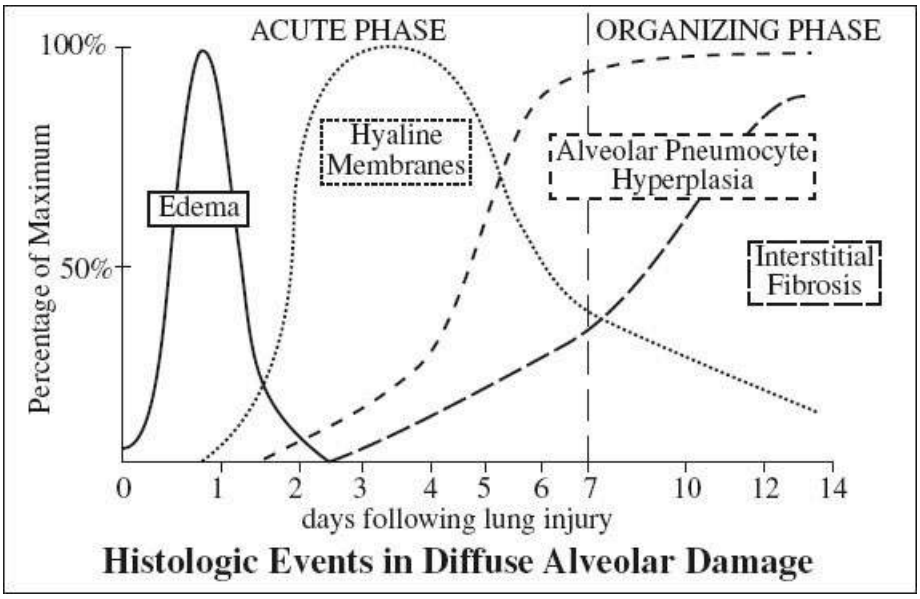
IDIOPATHIC INTERSTITIAL PNEUMONIA (IIP)

Acute Interstitial Pneumonia

= AIP = [ACCELERATED INTERSTITIAL PNEUMONIA] = DIFFUSE ALVEOLAR DAMAGE = IDIOPATHIC ARDS = ACUTE DIFFUSE INTERSTITIAL FIBROSIS = HAMMAN-RICH SYNDROME

= rapidly progressive fulminant disease of unknown etiology that usually occurs in previously healthy subjects + produces diffuse alveolar damage

Cause: diffuse alveolar damage of unknown origin from a variety of toxic insults such as infection, drugs, sepsis, shock, aspiration, toxic inhalation / ingestation, exacerbation of idiopathic pulmonary fibrosis, etc.



Histologic Events in Diffuse Alveolar Damage

Path: temporally homogeneous organizing diffuse alveolar damage; little mature collagen deposition / architectural distortion / honeycombing (as opposed to UIP); indistinguishable from ARDS caused by sepsis + shock

Histo: extensive diffuse alveolar damage

(a) acute exudative phase: alveolar + interstitial edema; hyaline membrane formation (most prominent in 1st week after lung injury); diffuse alveolar infiltrates by lymphocytes

(b) chronic organizing phase: uniform alveolar wall thickening ← marked interstitial (alveolar septal) fibroblast proliferation with stabilizing nonprogressive scarring + pneumocyte hyperplasia

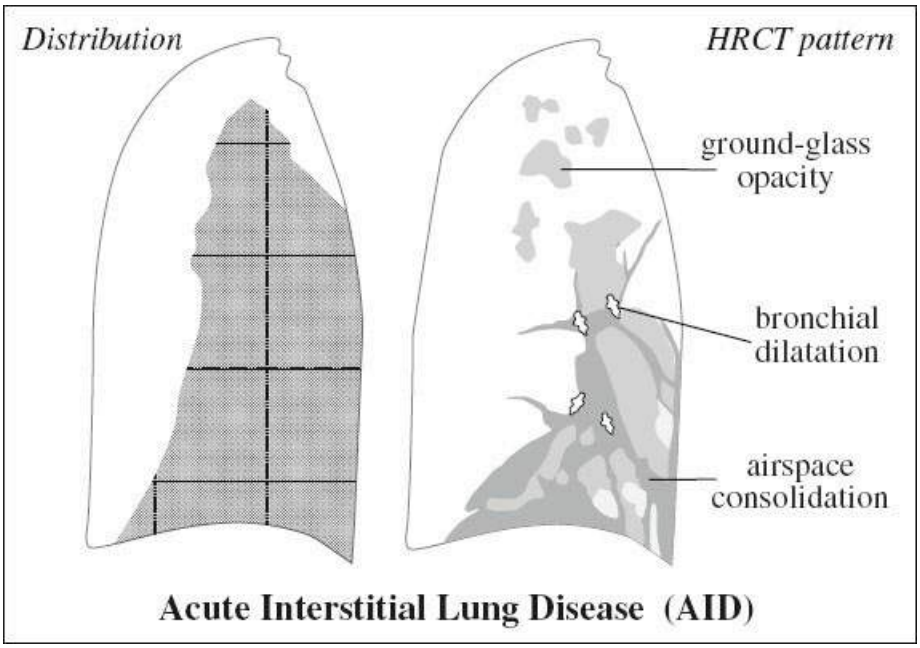
Mean age: 50 years (wide range); M = F

- prodromal viral upper respiratory infection: cough, fever
- rapidly increasing dyspnea + acute respiratory failure
- requires ventilation within days to 1–4 weeks (= "outpatient ARDS")
- decreased diffusing capacity for carbon monoxide
- pulmonary capillary wedge pressure of < 18 mmHg

AIP is the only entity of idiopathic interstitial pneumonias with acute onset of symptoms!

Location: bilateral symmetric mainly in lower lung zones

Site: predominantly central / subpleural (in 22%); anteroposterior lung attenuation gradient; costophrenic angles often spared



CXR:

√ progressive extensive bilateral hetero- / homogeneous airspace opacification: symmetric, bilateral, basilar

HRCT:

√ bilateral ground-glass opacities (in exudative phase) ← alveolar septal edema and hyaline membranes:

- √ patchy geographic (67%) / diffuse (38%)
- √ diffuse bilateral airspace consolidation (in 67%) limited to dependent area of lung (similar to ARDS) ← intraalveolar edema and hemorrhage ← alveolar closure from weight + hydrostatic pressure of more-superior lung tissue
- √ geographic focal sparing of lobules
- √ bronchial dilatation

√ architectural distortion (in organizing phase) more severe in nondependent areas of lung (atelectasis + consolidation protect from damaging effect of mechanical ventilation):

- √ airspace consolidation ← intraalveolar fibrosis
- √ distortion of bronchovascular bundles
- √ traction bronchiectasis
- √ honeycomb lung

Radiographic features of AIP are similar to ARDS with a symmetric bilateral distribution of lower lobe predominance!

Dx: NEGATIVE bacterial / viral / fungal cultures;
NO inhalational exposure to noxious agents;
NO pulmonary drug toxicity

Prognosis: death within 1–6 months (60–90%); recovery in 12%; frequently progression to fibrosis after survival in acute phase

Rx: supportive with oxygen supplementation; corticosteroids in early phase

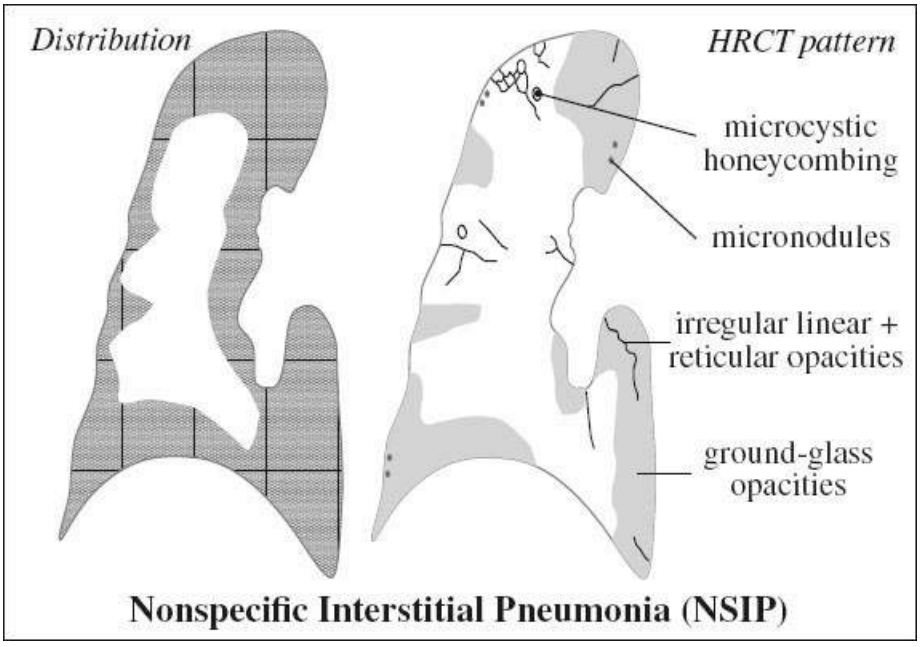
DDx: (1) ARDS (less symmetric, no lower lobe predominance)
(2) Widespread pneumonia" esp. Pneumocystis jirovecii pneumonia
(3) Hydrostatic edema (substantial interlobular septal thickening, pleural effusions)
(4) Acute eosinophilic pneumonia (substantial interlobular septal thickening, pleural effusions)
(5) Diffuse pulmonary hemorrhage
(6) Acute hypersensitivity pneumonitis (profuse centrilobular nodules / mosaic attenuation)
(7) Alveolar proteinosis

Subacute Interstitial Pneumonia

Nonspecific Interstitial Pneumonia

= NSIP = IDIOPATHIC NONSPECIFIC INTERSTITIAL PNEUMONIA = NONCLASSIFIABLE INTERSTITIAL PNEUMONIA

= provisional diagnosis for a probably heterogeneous group of interstitial pneumonia that cannot be easily classified as UIP / DIP / AIP / COP



Frequency: 14–36% (second most common IIP)

Path: spatially + temporally homogeneous alveolar wall thickening caused by inflammation and/or fibrosis

Histo: (I) cellular NSIP (48%) = mild to moderate cellular interstitial infiltrate with little / no fibrosis
(II) fibrotic NSIP (52%) = dense / loose fibrosis of uniform appearance

Clinical conditions associated with NSIP pattern:
(1) Idiopathic
(2) Collagen vascular disease (16%): scleroderma, polymyositis, dermatomyositis,

Sjögren syndrome, rheumatoid arthritis, mixed connective tissue disease, systemic lupus erythematosus

(4) Drug-induced pneumonitis

(3) Hypersensitivity pneumonitis: inhalational exposure to noxious agents (17%)

(5) Infection (8%)

(6) Immunodeficiency including HIV

Age: 40–50 years (1 decade younger than IPF); M = F

- gradually worsening dyspnea (1-week to 5-year history)
- dry cough, low-grade fever, fatigue, weight loss
- decreased diffusing capacity for carbon monoxide (less severe than idiopathic pulmonary fibrosis)

Location: lower lobe predominance (92%); symmetric involvement of both lungs

Site: peribronchovascular / subpleural distribution (21–64%)

√ normal CXR in 14%

√ bibasilar irregular linear opacities + diffuse heterogeneous airspace consolidation

√ volume loss in lower lobe (91%)

HRCT (70% sensitive, 63% specific):

√ fibrosis:

√ <u>irregular fine linear / reticular opacities</u> (87%)

√ traction bronchiectasis (82%)

√ lobar volume loss (77%)

√ relative subpleural sparing

√ bilateral symmetric areas of scattered <u>patchy ground-glass opacities</u> (44%) without zonal preference ← homogeneous interstitial inflammation

√ areas of low attenuation (34%)

√ microcystic honeycombing (inconspicuous, 30%)

√ airspace consolidation (uncommon)

√ diffuse micronodules (very infrequent)

√ mildly enlarged mediastinal lymphadenopathy (80%)

√ follow-up (stable in 35%):

√ decrease in ground-glass attenuation

√ persistence of reticular abnormalities

√ marked increase in fibrosis

Consider NSIP in homogeneous lung involvement without apicobasal gradient, a fine reticular pattern, and micronodules without progression to honeycombing!

Prognosis: substantially better than idiopathic pulmonary fibrosis; 11% overall mortality

Dx: surgical lung biopsy necessary

Rx: systemic corticosteroids combined with cytotoxic drugs (cyclophosphamide, cyclosporine) → clinical + functional + radiographic improvement in 50–86%

DDx: usual interstitial pneumonia (irregular reticular pattern + macrocystic honeycombing involving subpleural + lower lung zones); desquamative interstitial pneumonia; cryptogenic organizing pneumonia; chronic hypersensitivity pneumonitis

Respiratory Bronchiolitis-Interstitial Lung Disease

= RB-ILD = interstitial pneumonia of smokers in which respiratory bronchiolitis is associated with limited peribronchiolar interstitial inflammation; considered early and mild manifestation of DIP

Mean age: 36 (range, 30–40) years; M÷F = 2÷1

Cause: heavy cigarette smoking > 30 pack years

◊ Most common form of smoking-related lung injury

Histo: bronchiolocentric intraluminal accumulation of brown-pigmented alveolar macrophages and mild interstitial inflammation in 1st and 2nd order respiratory bronchioles + neighboring alveoli; mild peribronchial thickening with contiguous extension into alveolar septa but without significant fibrosis

- history of excessive smoking (> 30 pack year)
- usually asymptomatic / mild dyspnea + cough
- inspiratory crackles (50%)
- pulmonary function test: normal / mixed restrictive + obstructive + reduced diffusing capacity

Location: diffuse / upper lobe predominance

CXR (insensitive for detection):

√ normal CXR (21%)

√ fine bilateral reticulonodular opacities ← thickening of central + peripheral bronchial walls (71%)

√ bibasilar atelectasis (12%)

HRCT:

√ scattered patchy ground-glass opacities (66%) ← macrophage accumulation in alveolar ducts + spaces

√ inconspicuous poorly defined centrilobular micronodules (upper lobe predominance) ← peribronchial distribution of intraluminal infiltrates

√ scattered lobules of reduced attenuation ← lobular air trapping at expiration (upper lobe predominance)

√ mild interlobular septal thickening

√ bronchial wall thickening

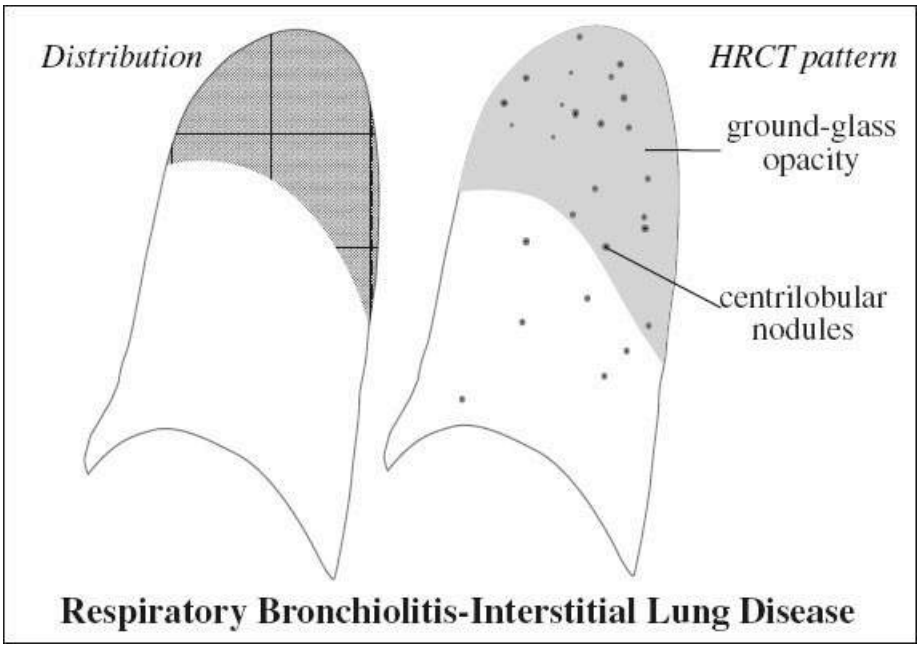
√ upper lobe centrilobular + paraseptal emphysema (rarely severe)

√ NO fibrosis

Prognosis: excellent (after cessation of smoking / corticoid therapy) without progression to end-stage lung fibrosis

Rx: smoking cessation (most important therapy!), corticosteroids

DDx: (1) Subacute hypersensitivity pneumonitis (more profuse + more diffuse poorly defined centrilobular nodules, exposure history, nonsmoker, lymphocytosis in BAL)



(2) Desquamative interstitial pneumonia (more extensive ground-glass attenuation, uncommon / sparse centrilobular nodules, lower lobe predominance)
(3) Nonspecific interstitial pneumonia (NSIP)
(4) Infectious bronchiolitis

Cryptogenic Organizing Pneumonia

= COP = BRONCHIOLITIS OBLITERANS ORGANIZING PNEUMONIA (BOOP) = IDIOPATHIC BOOP = PROLIFERATIVE BRONCHIOLITIS

Prevalence: 20–30% of all chronic infiltrative lung disease

Cause: pulmonary manifestation of collagen vascular disease, postobstructive pneumonia, organizing adult respiratory distress syndrome, pulmonary drug toxicity, extrinsic allergic alveolitis, silo filler disease, lung cancer, idiopathic (50%)

Path: temporally uniform homogeneous mild / moderate inflammation with preservation of lung architecture characterized by granulation tissue polyps filling the lumina of alveolar ducts and respiratory bronchioles (bronchiolitis obliterans) + variable degree of infiltration of interstitium and alveoli with macrophages (organizing pneumonia) [formerly known as bronchiolitis obliterans organizing pneumonia (BOOP)]

Histo: patchy distribution of intraluminal organizing fibrosis in distal airspaces = plugs of immature intraalveolar fibroblast proliferations (Masson bodies) covered with low cuboidal epithelium, which may spread through collateral air drift pathways

May be associated with: rheumatoid arthritis, polymyositis

Mean age: 55 (range, 40–70) years; M÷F = 1÷1

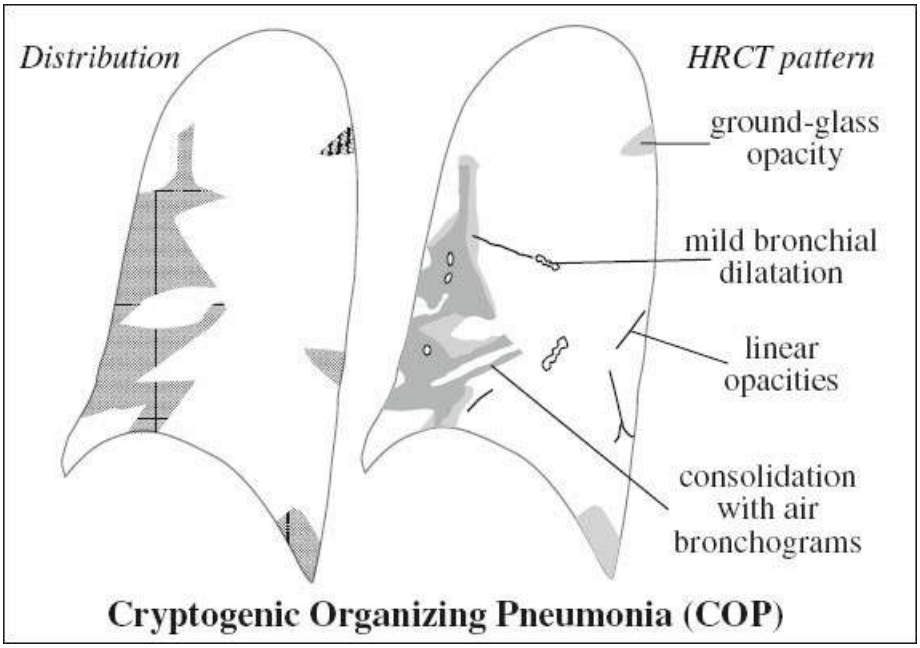
- nonproductive cough + mild dyspnea of 1–4-month duration preceded by a brief flulike illness with sore throat (40%), low-grade fever, malaise (in 33%)
- NO association with cigarette smoking

- restrictive pulmonary function tests + diminished diffusing capacity on pulmonary function tests
- consolidation often diagnosed as pneumonia with failure to respond to broad-spectrum antibiotic treatment

Location: lower lobe predominance

Site: CHARACTERISTIC peripheral (= subpleural in 50%) + peribronchial distribution (in 30–50%); tendency to expand and migrate over time

CXR: frequently a mixture of



√ preserved lung volumes
√ uni- / bilateral patchy alveolar airspace consolidation (25–73%), often subpleural, resembling pneumonic infiltrates
√ 3–5 mm nodules (up to 50%)
√ irregular linear opacities (15–42%)
√ unilateral focal / lobar consolidation (5–31%)
√ pleural thickening (13%)
√ cavitation / pleural effusion (< 5%)

HRCT: far more extensive than suggested on CXR

√ uni- / bilateral patchy airspace consolidation of triangular / polygonal shape (80–90%) a few cm in size
√ patchy ground-glass opacities ← alveolitis (60%):
  √ **"atoll"** sign = "reverse halo" sign if surrounded by 10-mm thick crescentic / ring-shaped opacities
  √ air bronchograms with mild cylindrical bronchial dilatation (in 36–70%)
√ large nodules (rare)
√ reticular opacities ← fibrosis (less common)
√ pleural effusion (28–35%)

√ adenopathy (27%)

Four distinctive HRCT patterns:

(1) Multiple bilateral symmetric patchy airspace opacities
(2) Diffuse bilateral reticular / nodular opacities
(3) Focal airspace consolidation
(4) Multiple large masses / nodules ± cavitation

Dx: tissue examination from open lung biopsy

Prognosis: radiologic improvement / resolution under steroids (in 84% of patients with idiopathic form); persistent abnormalities (30%); 10% mortality ← progressive / recurrent disease

DDx: bronchioloalveolar cell carcinoma; lymphoma; vasculitis; sarcoidosis; chronic eosinophilic pneumonia; infection; nonspecific interstitial pneumonia

Chronic Interstitial Pneumonia

= ORGANIZING INTERSTITIAL PNEUMONIA = CHRONIC DIFFUSE SCLEROSING ALVEOLITIS

Lymphoid Interstitial Pneumonia

= LIP = LYMPHOCYTIC INTERSTITIAL PNEUMONITIS

= benign lymphoproliferative disorder of lung parenchyma characterized by diffuse dense interstitial lymphoid infiltrate (probably immunologic disorder) with highly variable course

Frequency: extremely rare

Age: 50–80 years; M < F

Histo: extensive diffuse infiltration of alveolar interstitium (bronchovascular bundles, interlobular septa) and pleura by polyclonal mature small lymphocytes (predominantly T cells intermixed with some polytypic B cells) + plasma cells + histiocytes → expansion of the alveolar septa; reactive lymphoid follicles along peribronchiolar region; lymphoid hyperplasia frequent; many cases reclassified as lymphoma

Clinical conditions associated with LIP pattern:

(a) immune related
1. Immunodeficiency
2. Collagen vascular disease: Sjögren syndrome, rheumatoid arthritis, systemic lupus erythematosus
3. Immunologic disorders: autoimmune hemolytic anemia, Hashimoto thyroid disease, Castleman disease, myasthenia gravis, pernicious anemia, chronic active hepatitis, primary biliary cirrhosis, celiac sprue, Crohn disease, dysproteinemia

(b) infectious
1. HIV /AIDS
   ◊ Indicative of AIDS when present in child < 13 years of age!
2. Epstein-Barr virus (EBV) infection
3. Human herpesvirus 8
4. Chronic active hepatitis
5. Legionella pneumonia

6. Pneumocystis jirovecii
7. Tuberculosis

(c) miscellaneous

1. Drugs / toxic exposure: eg, Dilantin (phenytoin)-induced
2. Allogenic bone marrow transplant
3. Graft-versus-host disease

- slowly progressive dyspnea + cough over > 3 years
- occasionally fever, night sweats, weight loss
- cyanosis + clubbing (50%)
- enlargement of salivary glands (20%)
- NO lymphocytosis or history of atopy
- dysproteinemia (60%): hypergammaglobulinemia > hypogammaglobulinemia
- monoclonal gammopathy (usually IgM)

Distribution: bilateral; diffusely involving all lung zones / basilar predominance

LIP is suggested by thin-walled perivascular cysts in mid lung zones in combination with ground-glass opacities!

CXR (nonspecific):

√ absence of findings
√ fine reticulonodular pattern in both lower lungs
√ resembling airspace disease (in severe form)

HRCT:

√ ill-defined centrilobular nodules of varying size (100%)
√ ground-glass opacities (100%) ← diffuse interstitial inflammation
√ subpleural small nodules (in majority)
√ peribronchovascular thin-walled 1–30 mm cysts (68%) predominantly in lower lung ← air trapping ← ball-valve mechanism ← obstruction of small bronchioles ← peribronchiolar lymphocytic infiltration
√ mild patchy thickening of bronchovascular bundles + interlobular septal thickening (in majority) ← infiltration of interlobular septa with lymphocytes + plasma cells
√ mediastinal lymph node enlargement (50%)
√ pleural effusion / airspace consolidation (extremely uncommon)

N.B.: pleural effusion and > 11 mm large / growing nodules concerning for coexisting lymphoma

Prognosis:

(a) recovery / slowly improving / stable disease
(b) progression to fibrosis (in 33%)

Cx: malignant lymphoma (in 5%)

Rx: responsive to steroids

DDx: infection; primary pulmonary lymphoma; pulmonary amyloidosis; hypersensitivity pneumonitis (ground-glass attenuation, small centrilobular nodules, NOT cystic airspaces / thickening of interlobular septa or bronchovascular bundles); sarcoidosis; lymphangitic carcinomatosis; Langerhans cell histiocytosis; lymphangioleio-myomatosis; emphysema; desquamative interstitial pneumonia with cysts

Localized form = PSEUDOLYMPHOMA

Usual Interstitial Pneumonia

= UIP = MURAL TYPE OF FIBROSING ALVEOLITIS
= CRYPTOGENIC FIBROSING ALVEOLITIS

= commonest (90%) form of idiopathic interstitial pneumonia (may represent late stage of DIP)

Clinical conditions associated with UIP pattern:

(1) Idiopathic pulmonary fibrosis (IPF) / cryptogenic fibrosing alveolitis (50%)
(2) Collagen vascular disease / immunologic disorder (mostly rheumatoid arthritis) (20–30%)
(3) Drug toxicity: bleomycin, cyclophosphamide (Cytoxan®), busulfan, nitrofurantoin
(4) Chronic hypersensitivity pneumonitis
(5) Asbestosis
(6) Familial idiopathic pulmonary fibrosis (25%)

Mean age: 64 years (usually > 50 years); M> F

Path: patchy scattered fibrotic lesions of different stages (fibroblastic foci + mature fibrosis + honeycombing) mixed with areas of normal lung tissue (= temporal + spatial variegation (heterogeneity)

Dx: biopsy samples from > 1 lobe (because UIP pattern rules independent of other coexisting patterns) ← HRCT serves as a guide for appropriate biopsy sites

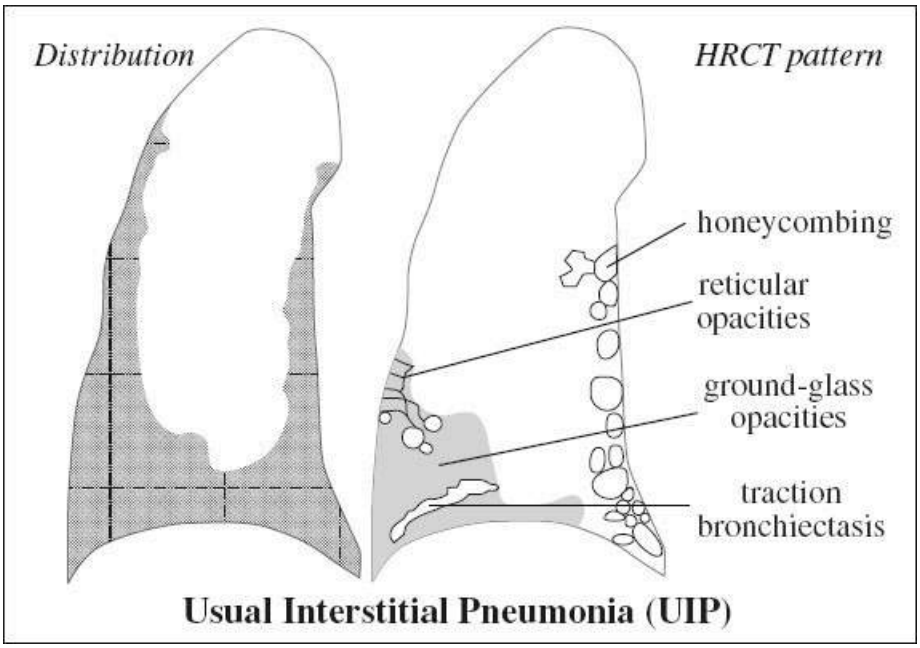
Histo: proteinaceous exudate in interstitium + hyaline membrane formation in alveoli; necrosis of alveolar lining cells followed by cellular infiltration of mono- and lymphocytes + regeneration of alveolar lining; intraalveolar histiocytes; proliferation of fibroblasts + deposition of collagen fibers + smooth muscle proliferation; progressive disorganization of pulmonary architecture

- progressive dyspnea, dry cough, fatigue (over 1–3 years)
- bibasilar fine inspiratory crackles = "Velcro" rales
- clubbing of fingers (83%)
- lymphocytosis on bronchoalveolar lavage (= marker of alveolitis)
- pulmonary function tests: restrictive defects + decreased diffusing capacity for carbon monoxide

Consider UIP with low lung volumes, subpleural reticular opacities, macrocystic honeycombing and traction bronchiectasis with apicobasal gradient!

CXR:

√ occasionally ground-glass pattern in early stage of alveolitis (= alveolar wall injury, interstitial edema, proteinaceous exudate, hyaline membranes, infiltrate of monocytes + lymphocytes) in 15–62%
√ bilateral diffuse linear / small irregular reticulations (100%); basilar (85%) + peripheral (59%)



Usual Interstitial Pneumonia (UIP)

Differentiation UIP vs. NSIP

UIP	*NSIP*
Obvious apicobasal gradient	No obvious apicobasal gradient
Heterogeneous	Homogeneous
Honeycombing	Ground-glass opacities
Traction bronchiectasis	Micronodules

√ reticulonodular pattern = superimposition of linear opacities
√ heart border "shaggy"
√ macrocystic honeycombing = numerous cystic spaces (up to 74%)
√ elevated diaphragm = progressive loss of lower-lobe lung volume (45–75%)
√ 1.5–3-mm diffusely distributed nodules (15–29%)
√ pleural effusion (4–6%), pleural thickening (6%)
√ pneumothorax in 7% (in late stages)
√ normal CXR (2–8%)

HRCT (88% sensitive, 70–100% PPV):

The primary role of CT is to separate chronic fibrosing lung diseases with a UIP pattern from those with non-UIP lesions, including those with findings associated with other idiopathic interstitial pneumonias like RB-ILD, lymphoid interstitial pneumonia, and idiopathic pleuroparenchymal fibroelastosis.

Location: apicobasal gradient affecting lung bases in 68–80%
Site: predominantly subpleural regions (79%)

√ patchy distribution with areas of normal parenchyma, active alveolitis, early + late fibrosis present at the same time (HALLMARK)
√ reticular opacities (82%)
√ small peripheral convoluted cysts (= traction bronchiectasis) in 50%
√ prominent architectural distortion of secondary pulmonary lobule (= lung fibrosis)
√ minimal focal ground-glass opacities (= diffuse inflammatory mononuclear cell infiltrates of active disease + fibroblast proliferation) in 65–76% progressing to fibrosis
√ subpleural areas of macrocystic honeycombing with cystic spaces outlined by thick fibrous walls (up to 96%) enlarging slowly over time
√ subpleural lines (= fibrosis / functional atelectasis)
√ interlobular septal thickening (10%)

NOT: micronodules, air trapping, nonhoneycomb cysts, extensive ground-glass opacification, consolidation, predominantly peribronchovascular distribution

Cx: bronchogenic carcinoma (10–15%), opportunistic infections with therapy, accelerated deterioration

Rx: usually no response to steroids (only in 10–15%)

Prognosis: median survival of 2.5–3.5 years; 43% 5-year survival rate, 15% 10-year survival rate; 87% overall mortality; no recovery

DDx: collagen vascular disease, chronic hypersensitivity pneumonitis, asbestosis

Desquamative Interstitial Pneumonia

= DIP = DESQUAMATIVE TYPE OF FIBROSING ALVEOLITIS = ALVEOLAR MACROPHAGE PNEUMONIA

= end spectrum of RB-ILD; 2nd most common (although rare) form of idiopathic interstitial pneumonia of a more benign course than UIP; may be self-limited disease or lead to UIP

Cause: cigarette smoking (history in up to 90%), lung infection, exposure to organic dust

Mean age: 42 (range, 30–40) years (~ 8 years younger than in UIP); M÷F = 2÷1

Path: spatially homogeneous thickening of alveolar septa + intraalveolar accumulation of macrophages; relative preservation of lung architecture + mild interstitial fibrosis (temporally uniform)

Histo: alveoli lined by large cuboidal cells + filled with heavy accumulation of mononuclear cells (pigmented macrophages, NOT desquamated alveolar cells); histologic uniformity from field to field

- average smoking history of 18 pack-years
- asymptomatic, weight loss
- insidious onset of dyspnea + nonproductive dry cough (for 6–12 months)
- inspiratory crackles (60%), clubbing of fingers (40%)
- markedly ⇓ diffusing capacity + restrictive defects

Distribution: lower lung lobe predominance, peripheral; more diffuse + uniform compared to RB-ILD

CXR (nonspecific):
√ normal chest x-ray (3–22%)
√ ground-glass alveolar pattern sparing costophrenic angles (25–33%), diffuse ground-glass opacities (15%)

√ linear irregular opacities (60%), bilateral + basilar (46–73%)
√ lung nodules (15%)
√ honeycombing (13%)
√ preserved lung volume

HRCT:

Location: apicobasal gradient affecting mainly middle + lower lung zones (73%); bilateral + symmetric (86%)

Site: predominantly subpleural distribution (59%); random distribution (23%)

√ bilateral peripheral patchy / diffuse ground-glass opacities (23%) ← spatially homogeneous intraalveolar accumulation of macrophages and thickening of alveolar septa:
  √ progression to reticular pattern (in 20%)
  √ round thin-walled cysts < 2 cm within ground-glass opacities
√ some irregular linear / limited reticular opacities (= fibrosis) + architectural distortion (59%) confined to subpleural lung bases
√ little peripheral honeycombing + traction bronchiolectasis (32%)
√ ± coexistent centrilobular emphysema
√ fibrosis of lower lung zones in late stage

Prognosis: better response to corticosteroid Rx than UIP (in 60–80%); improvement with smoking cessation; median survival of 12 years; 5% 5-year mortality rate (overall 16–27%); 70% 10–year survival

DDx: (1) RB-ILD (centered on respiratory bronchiole, ground-glass opacities less extensive, more patchy, more poorly defined)
(2) Acute interstitial pneumonia
(3) NSIP (fibrotic features like traction bronchiectasis + lower lobe volume loss)
(4) Acute / subacute hypersensitivity pneumonitis
(5) P. carinii pneumonia
(6) Sarcoidosis

Idiopathic Pleuroparenchymal Fibroelastosis

= rare condition consisting of a form of fibrosis rich in elastic fibers involving pleura and subpleural lung parenchyma, predominantly of upper lobes

Distribution: striking apical subpleural predominance

CT:

√ irregular pleural thickening + tags in upper zones merging with fibrotic changes in subjacent lung
√ substantial upper lobe volume loss: architectural distortion, traction bronchiectasis, hilar elevation

Prognosis: disease progression (60%), death (40%)

DDx: (1) Familial pulmonary fibrosis
(2) Connective tissue disease (esp. ankylosing spondylitis)
(3) Fibrotic sarcoidosis
(4) Chronic hypersensitivity pneumonitis

IDIOPATHIC PULMONARY FIBROSIS

= USUAL INTERSTITIAL PNEUMONIA
= specific form of chronic progressive fibrosing interstitial pneumonia of unknown cause
= clinical syndrome associated with morphologic pattern of UIP and related to cigarette smoking (in 41–83%)
◊ Most common form of idiopathic interstitial lung disease!

Histo: UIP pattern = cluster of fibroblasts + immature connective tissue within pulmonary interstitium → remodeling of lung architecture with honeycombing; temporal + spatial heterogeneity of fibrotic lesions of different stages (= fibroblastic foci, mature fibrosis, honeycombing)

Distribution: bibasilar peripheral + subpleural

Age: 50–70 years; M = F

- chronic dry cough, gradually progressing exertional dyspnea
- basilar "Velcro-type" inspiratory crackles
- digital clubbing (in ⅔)
- PFTs: restrictive defect + ⇓ diffusing capacity for CO
- decreased total lung capacity + functional residual capacity + residual volume

Distribution: lung periphery with apicobasal gradient, often patchy, asymmetric (in 25%)

CXR:

√ decreased lung volume, progressive over time
√ bibasilar subpleural reticular opacities
√ honeycombing (30%)
√ bibasilar ground-glass appearance (uncommon)
√ small nodules (< 10%), occasionally ossified

HRCT (95–100% PPV):

(a) classic:
√ lower zone macrocystic honeycombing (90%) often combined with traction bronchiectasis

(b) possible:
√ irregular reticular opacities (= intralobular interstitial thickening) in peripheral basal distribution
√ ground-glass opacities in area of fibrosis (occasionally)
√ discrete nodules (occasionally)
√ mild mediastinal lymph node enlargement (70%)

√ coexisting emphysema (common) makes Dx less reliable

Criteria for Diagnosis of IPF (without Surgical Biopsy) *American Thoracic Society and European Respiratory Society (2001)*
Major criteria
• exclusion of other causes of interstitial lung disease: toxic effects of certain drugs, environmental exposures, connective tissue disease
• abnormal PFT: reduced vital capacity, ↑ FEV_1/FVC ratio
• impaired gas exchange: $PAO_2 - PaO_2$, PaO_2 with rest / exercise, ↓ DLCO
√ lower zone macrocystic honeycombing (90%) often combined with traction bronchiectasis
√ bibasilar irregular reticular opacities
√ minimal ground-glass opacities
Minor criteria
Age: > 50 y
• insidious onset of otherwise unexplained dyspnea on exertion
• duration of illness < 3 months
• bibasilar inspiratory crackles (dry / "Velcro" type)

CT's primary role is to separate chronic fibrosing lung disease with a UIP pattern from non-UIP lesions associated with other IIPs (eg, RB-ILD, lymphoid interstitial pneumonia, and idiopathic pleuroparenchymal fibroelastosis).

Dx: (a) exclusion of other known causes of interstitial lung dz
(b) UIP pattern on CT in appropriate clinical setting = sufficient for diagnosis in > 50%
(c) on follow-up subpleural reticular opacities in upper lung zones = fibrosis creeping up along lung periphery

Rx: cyclosporine A + corticosteroids (for acute exacerbations only); lung transplantation

Prognosis: poor with invariable deterioration and a mean survival of 2.5–3.5 years (30–50% 5-year survival)
◊ Substantially poorer prognosis than NSIP, COP, RB-ILD, DIP, LIP

DDx: (1) Connective tissue disease
(2) Asbestosis (exposure history, pleural plaques, diffuse pleural thickening, subpleural dotlike / branching opacities, less-coarse reticular shadows)
(3) Chronic hypersensitivity pneumonitis (poorly defined fine micronodules, multilobular decreased attenuation / air trapping, sparing of lung bases)
(4) Sarcoidosis (large cysts, peribronchovascular nodules)
(5) Coal workers pneumoconiosis (less traction bronchiectasis, more subpleural homogeneous attenuation, more random distribution of fibrosis)

IDIOPATHIC PULMONARY HEMOSIDEROSIS

= IPH = probable autoimmune process with clinical + radiologic remissions + exacerbations characterized by eosinophilia + mastocytosis, immunoallergic reaction, pulmonary hemorrhage, iron deficiency anemia

Age: (a) chronic form: most commonly < 10 years of age
(b) acute form (rare): in adults; M÷F = 2÷1

Histo: hemosiderin-laden macrophages in bronchoalveolar lavage
- recurrent episodes of severe hemoptysis, clubbing of fingers
- hepatosplenomegaly (25%), bilirubinemia
- iron deficiency anemia

Distribution: perihilar + lower lung zone predominance
√ bilateral patchy alveolar-filling pattern (= blood in alveoli); initially for 2–3 days with return to normal in 10–12 days unless episode repeated
√ reticular pattern (= deposition of hemosiderin in interstitial space) later
√ moderate fibrosis after repeated episodes
√ hilar lymph nodes may be enlarged during acute episodes
CT:
√ diffuse homogeneous areas of ground-glass attenuation (during exacerbation)
√ nodules + patchy areas of ground-glass attenuation (subacute phase)

Prognosis: death within 2–20 years (average survival 3 years)
DDx:
1. Secondary pulmonary hemosiderosis
   Cause: mitral valve disease
   √ septal lines (NOT in idiopathic form)
   √ lung ossifications (NOT in idiopathic form)
2. Goodpasture syndrome
   - antiglomerular basement membrane antibodies

INFLAMMATORY PSEUDOTUMOR

= INFLAMMATORY MYOBLASTIC PSEUDOTUMOR = PLASMA CELL GRANULOMA = PLASMACYTOMA = (FIBROUS) HISTIOCYTOMA = XANTHOGRANULOMA = XANTHOMA = XANTHOFIBROMA = SCLEROSING HEMANGIOMA = PSEUDOLYMPHOMA
= rare mass characterized by fibroblastic / myofibroblastic spindle cell proliferation with varying degrees of inflammatory cell infiltration (lymphocytes, plasma cells, histiocytes)
Cause: ? low-grade malignancy versus primary inflammation
Associated with: minor trauma, surgery, malignancy, occult infection (Epstein-Barr virus, Mycobacterium, Actinomyces), IgG4-related sclerosing disease
Prevalence: < 1% of all tumors of lung + airways
Path: nonencapsulated circumscribed nodular mass, occasionally with infiltrative margins
Histo: mixture of inflammatory cells (plasma cells, lymphocytes, eosinophils, neutrophils) + myofibroblastic proliferation (fibroblasts, blood vessels); foamy histiocytes + multinucleated giant cells + spindle cells (70% of tumor) grouped in CHARACTERISTIC pinwheel / whorled pattern
DDx: malignancy ← highly cellular areas with mitoses
Age: young patient
- asymptomatic
- airway obstruction (symptoms often attributed to asthma / pneumonia), fever, malaise, weight loss, abdominal pain

Location: described in all major organs
@ Chest: lung > bronchus / trachea > pleura

@ Orbit
@ Abdomen: liver (2nd most common), spleen, pancreas, adrenal gland, kidney, retroperitoneum, diaphragm, mesentery GI tract, GU tract
√ well-defined smoothly marginated / infiltrating mass
US:
√ solid process with variable echogenicity ± Doppler flow
CT:
√ variable heterogeneous attenuation ± central calcification
√ no / heterogeneous / peripheral enhancement
MR:
√ hypointense lesion ← fibrotic component
√ NO restricted diffusion
Rx: surgical excision
DDx: any soft-tissue tumor

KARTAGENER SYNDROME

= IMMOTILE / DYSMOTILE CILIA SYNDROME
[Manes Kartagener (1897–1975), internist at the University department of medicine in Zurich, Switzerland]
= uncommon autosomal recessive disease characterized by congenital impairment of mucociliary transport
Frequency: 1÷40,00; high familial incidence
Etiology: abnormal mucociliary function ← generalized deficiency of dynein arms of cilia affecting respiratory epithelium, auditory epithelium, sperm
Triad: (1) Situs inversus (in 50%)
◊ Kartagener syndrome is present in 20% of patients with situs inversus!
(2) Nasal polyposis with chronic sinusitis
(3) Bronchiectasis
• chronic respiratory tract infections beginning in early childhood → chronic bronchitis + rhinosinusitis
• otitis → deafness; male infertility (abnormal sperm tails)
Location: middle lobe, lingula, lower lobes
√ ground-glass opacity / pulmonary consolidation (60%)
√ peribronchial / bronchial wall thickening (96%)
√ mucous plug (85%) + atelectatic areas
√ bronchiectasis (73%) / bronchiolectasis
√ air trapping (38%) = hyperinflation
√ ± small centrilobular opacities = tree-in-bud pattern
Associated anomalies:
transposition of great vessels, trilocular / bilocular heart, pyloric stenosis, postcricoid web, epispadia, pectus excavatum, polysplenia (8%)
DDx: cystic fibrosis (predominantly upper lobe lesions)

KLEBSIELLA PNEUMONIA

◊ Most common cause of Gram-negative pneumonias; community acquired

Frequency: responsible for 5% of adult pneumonias

Organism: Friedländer bacillus = Klebsiella pneumoniae = encapsulated, nonmotile, Gram-negative rod

[Carl Friedländer (1847– 1887), German pathologist and microbiologist at Städtische Krankenhaus Am Friedrichshain, Berlin, introduced the ampoule, also first described thromboangiitis obliterans]

Predisposed: elderly, debilitated, alcoholic, chronic lung disease, malignancy

• bacteremia in 25%

√ propensity for posterior portion of upper lobe / superior portion of lower lobe

√ dense lobar consolidation

√ bulging of fissure (large amounts of inflammatory exudate) CHARACTERISTIC but unusual

√ empyema (one of the most common causes)

√ patchy bronchopneumonia may be present

√ uni- / multilocular cavities (50%) appearing within 4 days

√ pulmonary gangrene = infarcted tissue (rare)

Cx: meningitis, pericarditis

Prognosis: 25–50% mortality rate

DDx: Acute pneumococcal pneumonia (bulging of fissures, abscess + cavity formation, pleural effusion / empyema frequent)

LEGIONELLA PNEUMONIA

= LEGIONNAIRES' DISEASE

Organism: Legionella pneumophila, 1–2 µm, aerobic, Gram-negative bacillus, weakly acid-fast, silver-impregnation stain

Predisposed: middle-aged / elderly, immunosuppressed, alcoholism, chronic obstructive lung disease, diabetes, cancer, cardiovascular disease, chronic renal failure, transplant recipients

Transmission: direct inhalation (air conditioning systems)

Prevalence: 6% of community-acquired pneumonias

Histo: leukocytoclastic fibrinopurulent pneumonia with histiocytes in intraalveolar exudate

• fever; absence of sputum / lack of purulence (22–75%)

Clue: involvement of other organs with

- diarrhea (0–25%), myalgia, toxic encephalopathy
- liver + renal disease; hyponatremia (20%)
- elevated serum transaminase / transpeptidase levels
- lack of quick response to penicillin / cephalosporin / aminoglycoside

Concomitant infection (in 5–10%):

Streptococcus pneumoniae, Chlamydia pneumoniae, Mycobacterium tuberculosis, Pneumocystis carinii

Location: unilateral / bilateral (less frequent); lobar / segmental

√ patchy bronchopneumonia (= multifocal consolidation)

√ moderate volume of pleural effusion (6–30–63%)

√ cavitation (rare)

Cx: progressive respiratory failure (most common cause of death; 6% mortality in otherwise healthy patients)

Rx: erythromycin

LIPOID PNEUMONIA

Acute Exogenous Lipoid Pneumonia

= FIRE-EATER PNEUMONIA

Material: liquid paraffin, petroleum (hydrocarbons)

Cause: accidental poisoning in children, fire-eaters

√ ill-defined nodular areas of increased radiopacity

√ pneumatoceles / thin-walled collections of air

Chronic Exogenous Lipoid Pneumonia

Etiology: aspiration / inhalation of fatlike material

Types of oils:

(a) vegetable oil: sesame oil used in medical suspensions for the treatment of constipation

(b) animal oil: cod liver oil (commonly given to children); squalene = derivative of shark liver oil (folk remedy in some Asian countries); milk

(c) mineral oil (most common): as liquid paraffin in nose drops (taken at bedtime) / oral laxatives = inert pure hydrocarbon that does not initiate cough reflex

Predisposed: elderly, debilitated, neuromuscular disease, swallowing abnormalities (eg, scleroderma)

Path: pool of oil emulsified by lung lipase + surrounded by giant cell foreign body reaction (mineral oil aspiration) / necrotizing hemorrhagic bronchopneumonia (higher content of free fatty acid in animal fat aspiration)

◊ The degree + type of tissue reaction depend on the frequency of aspiration + chemical character of oil

Histo: numerous lipid-laden macrophages distending alveolar walls + interstitium, accumulation of lipid material, inflammatory cellular infiltration, variable amount of fibrosis

- mostly asymptomatic; fever, constitutional symptoms
- lipid-laden macrophages in sputum / lavage fluid
- oil droplets in bronchial washing / needle aspirate

Location: predilection for RML + lower lobes

√ homogeneous segmental airspace consolidation (most common)

√ interstitial reticulonodular pattern (rare)

√ paraffinoma = circumscribed peripheral mass (granulomatous reaction + fibrosis often causing stellate appearance)

√ slow progression / no change

CT:

√ diffuse ground-glass opacity of centri- / panlobular distribution (= acinar pattern) + thickening of interlobular septa as earliest finding

√ airspace consolidation (filling of alveoli with exudate + inflammatory cells) at 1 week

√ return to ground-glass opacity ← expectoration + lymphatic drainage of lipid droplets + inflammatory cells at 2–4 weeks

√ volume loss + fibrosis of interlobular septa and pleura at 14–16 weeks

√ mass of low-attenuation approaching that of subcutaneous fat (–150 to 50 HU)

Dx: bronchoalveolar lavage, transbronchial biopsy

LUNG TRANSPLANT

Indications for transplantation:

emphysema / COPD (39%), idiopathic pulmonary fibrosis (17%), cystic fibrosis (16%), alpha-1 antitrypsin deficiency (9%), CHD, primary pulmonary hypertension, sarcoidosis, pneumoconiosis, malignancy (lung cancer contraindicated)

Unilateral lung transplants:

in selected cases of emphysema, pulmonary fibrosis

Contraindicated in: cystic fibrosis; bronchiectasis ← cross-contamination

Operative mortality: up to 8%

Common causes of mortality: bacterial infection, chronic graft dysfunction

Recurrence of primary disease:

sarcoidosis (in 35%); others (in 1%): lymphangioleiomyomatosis, Langerhans cell histiocytosis, talc granulomatosis, diffuse panbronchiolitis, alveolar cell proteinosis

Survival rate: 75% for 1 year, 50% for 5 years, 35% for 10 years, 25% for 15 years

Immediate Complications of Lung Transplant (< 24 hours)

A. Malpositioned monitoring tubes and lines

B. Donor-recipient mismatch

C. **Hyperacute Rejection of Lung Transplant**

= rejection in cases of an immunoglobulin G donor-specific HLA antibody positive crossmatch

Path: acute diffuse alveolar damage

√ diffuse homogeneous infiltrate of entire allograft

Early Complications of Lung Transplant (24 hours to 1 week)

Acute Pleural Complications of Lung Transplant

Frequency: 22%

Types:

1. Pneumothorax (most common)
2. Postoperative effusion (resolves by 2 weeks)
3. Air leaks ← airway ischemia, bronchial dehiscence

Reperfusion Edema

= ISCHEMIA-REPERFUSION INJURY = PULMONARY REIMPLANTATION RESPONSE

= noncardiogenic pulmonary edema = infiltrate appearing within 48 hours after transplantation unrelated to fluid overload, LV failure, infection, atelectasis, or rejection; diagnosed by exclusion

◊ Most frequent immediate postoperative complication!

Risk factors: poor organ preservation, prolonged ischemic time, unsuspected donor pathology (contusion, aspiration), interrupted lymphatic flow, cytokine-mediated injury

Pathogenesis: permeability edema ← lymphatic disruption, pulmonary denervation, organ ischemia, surgical trauma

Histo: fluid accumulation in interstitium consistent with noncardiogenic pulmonary edema

Time course: manifests after 24 hours, peaks on 4th postoperative day, generally resolves by end of 1st week (up to 6 months)

• increasing hypoxia before extubation; poor correlation between radiographic severity + physiologic parameters

Location: perihilar areas + basal regions in transplanted lung

√ perihilar haze / rapid uni- or bilateral heterogeneously dense interstitial and/or airspace disease

√ small pleural effusions

Dx: per exclusion (radiographic changes not due to LV failure, hyperacute rejection, fluid overload, infection, atelectasis)

Prognosis: usually resolves over 7–10 days

Rx: diuresis, mechanical support

Intermediate Complications (8 days – 2 months)

Acute Rejection of Lung Transplant

Cause: cell-mediated immune response

Histo: mononuclear cell infiltrate around arteries, veins, bronchioles, alveolar septa with alveolar edema (initially) + fibrinous exudate (later)

Frequency: 60–80% with 2–3 significant episodes in first 3 months

◊ Most patients will have at least 1 episode in the year following transplantation!

Time of onset: first episode 5–10 days after transplantation; occasionally by 48 hours

• drop in arterial oxygen pressure WITHOUT infection /airway obstruction / fluid overload

• pyrexia, fatigue, decreased exercise tolerance

√ heterogeneous opacities in perihilar areas

√ peribronchial cuffing

√ ground-glass attenuation on HRCT

√ new increasing pleural effusion + septal thickening (most common, 90% specific, 68% sensitive) WITHOUT concomitant signs of LV dysfunction (= increase in cardiac size / vascular pedicle width / vascular redistribution)

√ subpleural edema, peribronchial cuffing, airspace disease

Dx: (1) Transbronchial biopsy

(2) Rapid improvement of radiologic abnormalities after treatment with IV bolus of corticosteroids for 3 days

Rx: methylprednisolone, polyclonal T-cell antibody (antithymocyte globulin), monoclonal antibodies (CD3, OKT3), lymphoid irradiation

Delayed Lung Transplant Complications (> 4 months)

Chronic Rejection of Lung Transplant

= BRONCHIOLITIS OBLITERANS SYNDROME (BOS)

Prevalence: 50% at 5 years
◊ Probably develops in all transplant patients given sufficient time!
Risk factor: frequent / severe bouts of acute rejection, gastroesophageal reflux
Path: obliterative bronchiolitis (36%), interstitial pneumonitis, rejection-mediated vasculopathy
Time of onset: 3–6–75 months after transplantation

- persistent coughing and wheezing
- slowly worsening exertional dyspnea
- physiologic airflow obstruction + decline in forced expiratory volume at 1 second

CXR:
√ frequently normal
√ increased lung volumes (= hyperinflation)
√ regional volume contraction
√ diminished peripheral lung markings (= decreased peripheral vascularity)
√ thin irregular areas of increased opacity (= subsegmental atelectasis)
√ bronchiectasis
√ pleural thickening
√ nodular / reticular opacities associated with peribronchial thickening

HRCT:
√ air trapping on expiratory HRCT (HALLMARK)
√ mosaic lung attenuation (= regions of mixed hypo- and hyperattenuation)
√ central + peripheral cylindrical bronchiectasis
√ bronchial wall thickening

Complications of Lung Transplant (any time)

Anastomotic Complications of Lung Transplant

Prevalence: 15%

1. Bronchial dehiscence (2–8%)
   Time of onset: within 1 month
   √ presence of extraluminal air collections at anastomotic site (80%)
   √ bronchial wall defect / narrowing / irregularity
   DDx: telescoped anastomosis
2. Airway stricture / stenosis
   Definition: stenosis = ≥ 50% diameter reduction
   DDx: telescoped anastomosis
   Rx: laser resection, balloon bronchoplasty
3. Bronchomalacia
   √ transient airway narrowing on expiratory CT
4. Vascular stenosis
5. Diaphragmatic hernia from omentopexy
   Procedure: omental pedicle is harvested at time of transplantation through a small diaphragmatic incision + wrapped around anastomosis to prevent dehiscence

Posttransplantation Infection

Cause: immunosuppression, reduced mucociliary clearance, interruption of lymphatic drainage, direct contact of transplant with environment via airways

◊ May occur at any time during postoperative period!

Frequency: 35–86% of transplant recipients

A. INFECTION OF LUNG TRANSPLANT

Prevalence: 35–50%; major cause of morbidity + mortality in early postoperative period

Cause: absent cough reflex, impaired mucociliary transport in denervated lung, interruption of lymphatics, immunosuppressive drugs

Organism: bacteria (23%): Staphylococcus, Pseudomonas, Klebsiella > CMV > Aspergillus (6%) > Pneumocystis

(1) within 1st month: Gram-negative bacteria, fungi (candidiasis, aspergillosis)

(2) after 1st month: viruses (CMV [50%], community-acquired viruses [RSV, parainfluenza, influenza, adenovirus]); Pneumocystis carinii; bacteria; fungi

• fever, leukocytosis

√ lobar / multilobar consolidation ← bacterial > fungal pathogens

√ diffuse heterogeneous air-space / ground-glass opacities ← parainfluenza + RSV + adenovirus / disseminated fungal pathogens

√ bronchial wall thickening ← adenovirus, influenza virus, RSV

√ bronchial dilatation ← RSV

√ nodules ← fungal / unusual bacterial pathogens / CMV / septic emboli

√ septal lines

√ pleural effusion

Cx: may progress rapidly to respiratory failure + death

Dx: transbronchial / open biopsy (80% accurate)

B. EXTRAPULMONARY INFECTION

thoracotomy wound infection, bacteremia, sepsis, empyema, central venous line infection

Prognosis: primary cause of postoperative mortality in up to 50%; 2–12% mortality for CMV; 50% mortality for Aspergillus

LYMPHANGIOMYOMATOSIS

= LAM = LYMPHANGIOLEIOMYOMATOSIS

= rare disorder characterized by

(1) Gradually progressive diffuse interstitial lung disease

(2) Recurrent chylous pleural effusions

(3) Recurrent pneumothoraces

Prevalence: 1÷400,000; 1,300 women in USA (in 2001)

Etiology: unknown; hamartomatous proliferation of a particular form of HMB-45 positive smooth muscle (? forme fruste of tuberous sclerosis)

Mean age: 34 (range, 17–62) years, exclusively in women of childbearing age

Path: enlarged lungs with extensive diffuse air- / fluid-filled 5–20 mm cysts affecting both lungs + distorting pleural surfaces; ± involvement of lymph nodes

Histo: abnormal proliferation of atypically short + plump smooth muscle cells with a high nuclear-to-cytoplasmic ratio (LAM cells) in pulmonary lymphatic vessels, blood vessels, walls of airways; NO atypia / mitoses; positive staining for human melanin black-45 (HMB-45)

Pathogenesis:

proliferation of immature smooth muscle cells in a haphazard fashion causes obstruction of

(a) bronchioles → trapping of air, overinflation, formation of cysts, pneumothorax
(b) venules → venous occlusion → hemorrhage (hemoptysis), hemosiderosis
(c) lymphatics → thickening of lymphatics, chylous effusions of thorax + abdomen

Hormonal influence: menstruation, pregnancy, exogenous estrogen treatment may result in exacerbation of symptoms

Cause of thin-walled lung cysts:

(a) air trapping distal to small airways narrowed by smooth muscle proliferation
(b) destruction of collagen + elastin in the interstitium from metalloproteinases elaborated by LAM cells

In 1% associated with: tuberous sclerosis

- progressive exertional dyspnea (59%) + cough (39%)
- hemoptysis (30–40%), chyloptysis (rare)
- combination of restrictive + obstructive ventilatory defects:
  - radiologic-physiologic discrepancy = severe airflow obstruction in 100% (reduced FEV_1, reduced ratio of FEV_1 / FVC) despite relatively normal findings on CXR
  - decreased DLCO (= diffusing capacity for lung carbon monoxide) in 54%
- hypoxemia without hypercapnia on arterial blood gas
- positive immunohistochemical staining of LAM cells with HMB-45 (monoclonal antibody for melanocytic lesion)

CXR:

√ classic signs:
  √ coarse reticular / reticulonodular interstitial pattern diffusely + equal in all lung zones caused by summation of multiple cyst walls (80–90%)
  √ recurrent unilateral pneumothorax (39–53% at presentation; in up to 81% during course of disease)
  √ recurrent uni- / bilateral chylothorax (14% at presentation; in up to 39% during course of disease)
√ normal (55–78%) / increased (22–45%) lung volume

◊ The only interstitial lung disease to develop an increase in lung volume!

√ Kerley B lines = interlobular septal thickening ← dilated lymphatics (7–9%)
√ pulmonary cysts (visible if > 1 cm) + honeycombing
√ pericardial effusion / chylous pericardial effusion (rare)
√ mediastinal + retroperitoneal adenopathy ← smooth muscle proliferation

CT:

√ numerous randomly scattered thin-walled (< 2 mm) cysts of various sizes (typically 2–5 mm, up to 30 mm) surrounded by normal lung parenchyma

Parenchymal Involvement		*Cyst Size*
mild	< 25%	< 5 mm
moderate	25–80%	5–10 mm
severe	> 80%	> 10 mm

√ patchy areas of ground-glass attenuation ← hemorrhage following destruction of pulmonary microvasculature
√ dilated thoracic duct
√ pleural effusion: proteinaceous / chylous (-17 HU)
√ chylous pericardial effusion (rare)
√ hilar + mediastinal lymphadenopathy (in up to 50%)

NUC (V/Q scan):
√ "speckling" = well-defined hot spots on ventilation scan (presumably due to accumulation of coalescing droplets of DTPA aerosol trapped in peripheral cysts) in 66%

@ Abdomen (in 76% positive findings)
• bloating, increased abdominal girth, abdominal pain
• flank / pelvic pain
• perineal swelling, chylous vaginal discharge
• lower-extremity lymphedema, paresthesias
√ **lymphadenopathy** of up to 4 cm (33%):
Histo: replacement of lymph node with smooth muscle
Location: retroperitoneum (77%) > pelvis (11%) > mesentery > posterior mediastinum > axilla > neck
√ central hypoattenuating areas of –72 to +50 HU (due to chylous lymph collections / fat) ± fat-fluid level
√ **lymphangioleiomyoma** (5–21%) = well-defined lobulated complex lymphatic mass:
Path: smooth muscle proliferation in walls of lymphatics resulting in lymphatic dilatation + mural thickening
Site: retroperitoneum near aorta + renal arteries, posterior mediastinum, mesentery
√ thin- / thick-walled mass with hypoattenuating center of 3–25 HU ± fat-fluid level
√ volumes of 10–1,500 mL
√ anechoic irregularly shaped thin-walled cysts with intraluminal septa (= ectatic lymphatic vessels)
√ diurnal variations in size (↑ over course of day)
√ **chylous ascites** (10–33%): low-density ascites of -10 to +21 HU ← rupture of overdistended lymph cysts
√ dilatation of thoracic duct (10%)
√ fatty liver masses (5%): AML / lipoma
√ uterine leiomyomas
√ lymphaticoureteric, lymphaticovenous communication

@ Kidneys
• flank pain, hematuria, severe hypotension, chyluria (with > 4 cm large angiomyolipoma)
√ **angiomyolipoma** (in 20–70%):
√ occasionally lacking fat
√ multiplicity in < 20%

√ simple cysts (occasionally large enough to lead to renal insufficiency)

Dx: open / transbronchial lung biopsy; image-guided biopsy of an extrapulmonary mass

Rx: hormone therapy, oophorectomy, lung transplantation

Prognosis: survival rate of 91% at 5-year, 79% at 10 years, 71% at 15 years; death from progressive respiratory failure + cor pulmonale

DDx:

(1) Tuberous sclerosis (cortical tubers, subependymal nodules, retinal hamartomas, facial angiofibromas, periungual fibromas, mental retardation, epilepsy, multiple renal AML in 40–80%)

(2) Langerhans cell histiocytosis (irregular cysts in upper ⅔ of lung with sparing of costophrenic angles, cyst walls more variable in thickness, pulmonary nodules and cavitation, septal thickening)

(3) Centrilobular emphysema (imperceptible cyst walls, cysts chiefly distributed in upper lobes, lobular architecture preserved with bronchovascular bundle in central position, areas of lung destruction without arcuate contour)

(4) Paraseptal emphysema (evident walls, arrayed in a single subpleural tier)

(5) Idiopathic pulmonary fibrosis = fibrosing alveolitis (small irregular thick-walled cysts in a predominantly peripheral subpleural + basilar distribution, surrounded by abnormal distorted lung parenchyma)

(6) Neurofibromatosis (cystic air spaces predominantly in apical location)

LYMPHANGITIC CARCINOMATOSIS

= INTERSTITIAL CARCINOMA = LYMPHANGITIS CARCINOMATOSA

= tumor cell accumulation within connective tissue (bronchovascular bundles, interlobular septa, subpleural space, pulmonary lymphatics) from tumor embolization of blood vessels followed by lymphatic obstruction, interstitial edema, and collagen deposition (fibrosis from desmoplastic reaction when tumor cells extend into adjacent pulmonary parenchyma)

Frequency: 7% of all pulmonary metastases

Tumor origin: bronchogenic carcinoma, carcinoma of breast (56%), stomach (46%), thyroid, pancreas, larynx, cervix

mnemonic: **C**ertain **C**ancers **S**pread **B**y **P**lugging **T**he **L**ymphatics

Cervix
Colon
Stomach
Breast
Pancreas
Thyroid
Larynx

Path: (a) interstitial edema
(b) interstitial fibrotic changes
(c) lymphatic dilatation
(d) tumor cells within connective tissue planes

- dyspnea (often preceding radiographic abnormalities)
- rarely dry cough + hemoptysis

Location: bilateral; unilateral if secondary to lung primary

CXR (accuracy 23%):

√ normal chest radiograph
√ reticular / reticulonodular opacities
√ coarsened bronchovascular markings
√ Kerley A + B lines
√ small lung volume
√ hilar (20–50%) / mediastinal lymphadenopathy
√ pleural effusion

HRCT:

√ normal lung architecture without distortion
√ focal / diffuse, uni- / bilateral distribution
√ well-defined smoothly thickened polygonal reticular network of 10–25 mm in diameter (= thickened interlobular septa)
√ irregular / nodular = "beaded" thickening of interlobular septa
√ central dot within secondary pulmonary lobule = thickened centrilobular bronchovascular bundle
√ smooth / nodular thickening of fissures
√ subpleural thickening
√ pleural effusion (30–50%)
√ hilar / mediastinal lymphadenopathy (30–50%)

Prognosis: death within 1 year

DDx: (1) Fibrosing alveolitis (peripheral predominance)
(2) Extrinsic allergic alveolitis (no polygonal structures, pleural changes rare)
(3) Sarcoidosis (nodules of irregular outline more frequent in upper lobes, polygonal structures uncommon)
(4) pulmonary edema (smooth septal thickening)

LYMPHOMA

= NON-HODGKIN LYMPHOMA (NHL) = MALIGNANT LYMPHOMA

= most common primary hematopoietic malignancy

◊ 7th leading cause of death from cancer in USA

Pathogenesis: ? viral cause

Frequency: 4.3% of all newly diagnosed cancers (2015); 3rd most common cancer in childhood (behind leukemia + CNS neoplasms); 4 times more common than Hodgkin disease

Predisposed: (40–100 times greater risk) congenital immuno-deficiency syndromes, immunosuppressed organ transplant recipients, patients with HIV infection, collagen vascular disease

Age: all ages; median age of 55 years; M÷F = 1.4÷1

• chest / shoulder pain, dyspnea, dysphagia
• CHF, hypotension, SVC syndrome

Modified Rappaport Classification:

= categorization according to histologic distribution of lymphomatous cells

A. Nodular form = organized in clusters

1. Poorly differentiated lymphocytic (PDL)
2. Mixed lymphocytic / histiocytic (mixed cell)
3. Large cell (histiocytic)

B. Diffuse form = distortion of tissue architecture
1. Well-differentiated lymphocytic (WDL)
2. Intermediate-differentiated lymphocytic (IDL)
3. Poorly differentiated lymphocytic (PDL)
4. Mixed lymphocytic / histiocytic large cell (histiocytic) (DLCL); undifferentiated Burkitt lymphoma; undifferentiated non-Burkitt lymphoma (pleiomorphic); lymphoblastic (LBL); unclassified

Working Formulation Classification (Kiel / Lennert):

= categorization by grade

A. Low grade
1. Small lymphocytic (3.6%)
2. Follicular, small cleaved cell (22.5%)
3. Follicular, mixed (7.7%)

B. Intermediate grade
1. Follicular, large cell (3.8%)
2. Diffuse, small cleaved cell (6.9%)
3. Diffuse, mixed (6.7%)
4. Diffuse, large cell (19.7%)

C. High grade
1. Large cell, immunoblastic (7.9%)
2. Lymphoblastic (4.2%)
3. Small noncleaved cell (5%)

D. Miscellaneous (12%)
composite, mycosis fungoides, histiocytic, extramedullary plasmacytoma

Luke and Collins Classification:

= categorization by morphologic characteristics of cell + cell of origin (T cell, B cell, non-B, non-T cell)

Histologic types:

A. B-cell
1. **Diffuse large B-cell lymphoma**
◊ The largest subtype of NHL
Prognosis: extranodal involvement frequent at presentation, rapid spread to nodes, curable in < 50%
2. **Mantle cell lymphoma**
◊ 4–8% of all NHL
√ extranodal involvement of GI tract + bone marrow
Prognosis: poor
3. **Follicular lymphoma**
FDG PET reliable for staging + follow-up (98% sensitive, 94% specific, 95% PPV, 98% NPV)
√ potential for upstaging in a high number of patients with apparent early-stage disease

Prognosis: good response to initial therapy, pattern of repeated relapses, tendency to progress to diffuse large B-cell lymphoma

4. **Burkitt Lymphoma**

   [Denis Parsons Burkitt (1911–1993), Irish surgeon who served with the Royal Army Medical Corps in England and later in Kenya and Somaliland settling in Uganda]

   (a) endemic type (Africa)

   (b) Non-African Burkitt lymphoma sporadic type (Europe, US, Japan) and immunodeficiency type (HIV-infected patients)

   √ often in abdominal location

   √ extremely hypermetabolic

5. **Mucosa-associated lymphoid tissue (MALT)**

   ◊ Subtype related to chronic inflammation and autoimmune disease

   √ orbital MALT (low metabolism) + pulmonary MALT (metabolism similar to pneumonia) + gastric MALT (physiologic FDG accumulation) → difficult to diagnose

B. T-cell

1. **Lymphoblastic lymphoma**

   Prevalence: higher in Far East than Western nations

   Age: young adults

   √ usually manifests with a mediastinal mass

   √ < 25% leukemia cells in bone marrow (DDx to acute lymphoblastic leukemia with > 25%)

2. **Peripheral T-cell lymphoma**

   FDG PET only 40% sensitive

3. **Adult T-cell lymphoma-leukemia**

   Geography: Japan (Kyushu region), Caribbean, Central African Republic, Central & South America

   • positive human adult T-lymphotropic virus type 1 (HTLV-1)

4. **Malignancy associated with Epstein-Barr virus**

   Epstein-Barr virus (= human herpesvirus 4) may induce natural killer cell (NK) and T-cell lymphoproliferative disorders; associated with infectious mononucleosis, chronic active Epstein-Barr virus infection

Malignancy Grade vs. Type of Lymphoma at FDG PET

Malignancy Grade	*B-Cell Lymphoma*	*T-Cell Lymphoma*
Indolent	Follicular lymphoma (grade 1–3a); MALT lymphoma; chronic lymphocytic leukemia; nodal marginal zone B-cell lymphoma	Adult T-cell leukemia-lymphoma (chronic); mycosis fungoides; large granular T-cell lymphocytic leukemia
Aggressive	Follicular lymphoma (grade 3b); diffuse large B-cell lymphoma; plasma cell myeloma; intravascular large B-cell lymphoma; primary effusion lymphoma; Burkitt lymphoma; mantle cell lymphoma	Peripheral T-cell lymphoma; extranodal T-cell lymphoma; T-cell prolymphocytic leukemia; angioimmunoblastic T-cell lymphoma, aggressive natural killer-cell leukemia; enteropathy-type T-cell lymphoma;hepatosplenic T-cell lymphoma
Very aggressive	Burkitt lymphoma; lymphoblastic lymphoma	Adult T-cell leukemia-lymphoma (acute); lymphoblastic lymphoma

5. **Nasal type extranodal NK/T-cell lymphoma (angiocentric lymphoma)**

   Age: 40 years

Geography: frequent in Asia
Histo: angiocentric invasion
Prognosis: poor

PET/CT (88–100% sensitive):
◊ Most useful tool for primary diagnosis + assessment of response to treatment + prognosis

CT / MR:
√ homogeneous attenuation / signal intensity
√ vascular penetration = "sandwich" sign (CHARACTERISTIC for mesenteric lymphoma)
√ spread across existing structure ← permeative nature

Staging: same Ann Arbor system as for Hodgkin disease
Rx: involved-field radiation (stage I or II); chemotherapy (stage III and IV)
Prognosis: 64% 5-year survival; death rate of 8.9/100,000 males + 5.7/100,000 females

Extranodal Involvement in Lymphoma (NHL)

Sites other than: nodal (see below)
Frequency: NHL (in 20–40%); Hodgkin disease (4–5%)

A. FOCAL / MULTIFOCAL SOLID ORGAN DISEASE

CT:
√ discrete round well-defined homogeneous solid nodules in focal / multifocal disease
√ ± heterogeneous appearance ← central necrosis
√ mild uniform contrast enhancement

US:
√ homogeneously hypoechoic nodules resembling cysts
√ ± bull's-eye appearance
√ absence of posterior acoustic enhancement

MR:
√ nodules of low to intermediate SI on T1WI + moderately high SI on T2WI
√ moderate uniform contrast enhancement

DDx: metastases, primary cancer, infection, granulomatous disease

B. DIFFUSE SOLID ORGAN DISEASE

CT / MR:
√ NO structural abnormality → detection difficult
√ organomegaly → very low sensitivity & specificity for diagnosis of lymphoma
√ uniform infiltration of involved site
√ subtle heterogeneous areas after contrast administration, NOT visible on unenhanced images
√ uptake on PET
√ CHARACTERISTIC amorphous infiltration of tissues outside involved organ with minimal mass effect

@ Chest (40–50%):
lung (6%), pleural fluid (3.3%), pericardial fluid (0.7%), heart (0.2%)
√ hilar + mediastinal adenopathy (DDx: sarcoidosis; anterior nodes favor lymphoma)
◊ Nodes frequently not involved!
√ isolated lymph nodes may enhance (DDx: Castleman dz)
√ lung nodules + air bronchograms

√ pleural effusion

Prognosis: unfavorable

@ Spleen (41%)
@ Pancreas (30%)
@ Liver (14%)
@ GI tract: stomach (3%), small bowel (5%), large bowel (2%), peritoneal nodules + ascites (1.4%)
@ GU tract (10%): kidneys (6%), testes (1.2%), ovaries (1.8%), uterus (1.2%)
@ Skin (6.4%)
@ Bone (3.8%)
@ CNS (2.4%)
  • cranial nerve palsy / spinal cord compression
@ Head and neck (1.7%)
@ Breast (1.2%)

Nodal Involvement in Lymphoma (NHL)

Sites: lymph nodes, spleen, thymus, tonsils, pharyngeal lymphatic (Waldeyer throat) ring

@ Mesenteric lymph nodes (51%): predominantly in middle mediastinum, cardiophrenic angle
  ◊ Single lymph node involvement is often the only manifestation of intrathoracic disease!
@ Splenic hilar lymph nodes (53%)
  ◊ Lymphography 89% sensitive + 86% specific
@ Paraaortic lymph nodes (49%)

Differences between NHL and Hodgkin Disease

HD: contiguous spread → scan only abnormal area

NHL: noncontiguous spread → requires scanning of chest, abdomen, pelvis

@ Thoracic lymphadenopathy anterior mediastinal, pretracheal, hilar, subcarinal, axillary, periesophageal, paracardiac, superior diaphragmatic, internal mammary lymph nodes
  › anterior mediastinum: nodular sclerosing type of HD (75%); M < F
  › posterior mediastinum: NHL
@ Spleen

Differences between NHL and Hodgkin Disease

Organ Involvement	*NHL*	*HD*
Thoracic involvement	45%	85%
Mediastinal nodes	posterior	anterior
Lung involvement	4%	12%
Lymphadenopathy		
Periaortic adenopathy	49%	25%
Mesenteric adenopathy	51%	4%
Liver involvement	14%	8%
Hepatomegaly	57%	< 30%
Splenic involvement	41%	37%

Differences between Adult and Childhood NHL		
Characteristics	*Adult NHL*	*Childhood NHL*
Primary site	nodal	extranodal
Histology	50% follicular, 50% diffuse	diffuse
Grade	low, intermediate, high	high
Histologic subtype	many	three
Sex predilection	none	70% male

HD: most common site of abdominal involvement

NHL: 3rd most common site of abdominal involvement; may be initial manifestation in large cell NHL

@ Gastrointestinal involvement in 10% of patients with abdominal lymphoma (uncommon in HD, common in histiocytic NHL); NHL accounts for 80% of all gastric lymphomas

@ Renal involvement late manifestation, most commonly in NHL

@ Adrenal involvement more common in NHL

@ Extranodal involvement more frequent with histologically diffuse forms of NHL

Lymphoma (NHL) in Childhood

Frequency: 3rd most common childhood malignancy (after leukemia + CNS tumors); 7% of all malignancies in children < 15 years of age

Origin: B or T cell (in 90%) located outside marrow; (rarely) non-B and non-T cells located within bone marrow

Median age: 10 years; < 15 years of age (most common); unusual < 5 years of age; M÷F = 2÷1

- chest pain, back pain, cough, dyspnea, fever
- anorexia, weight loss, ± peripheral blood involvement
- bone marrow involvement:
  < 25% = lymphoma; > 25% = leukemia

Histo: Burkitt lymphoma (most common), Burkitt-like lymphoma, large B-cell lymphoma, lymphoblastic lymphoma, anaplastic large cell lymphoma, peripheral T-cell lymphoma

Prognosis: 80% cure rate with multiple-agent chemotherapy

DDx: (1) Acute lymphocytic leukemia (> 25% lymphoblasts within bone marrow)
(2) Hodgkin disease (contiguous spread, nodes are site of origin)

Undifferentiated / Small Noncleaved NHL *(39%)*

Path: non-Burkitt lymphoma; Burkitt lymphoma

- abdominal mass ± ascites
- pain similar to appendicitis / intussusception

Primary site: abdomen (distal ileum, cecum, appendix); ovaries

St. Jude Children Hospital Staging Classification for NHL	
Stage	*Description*
I	single extranodal tumor / single nodal area outside abdomen and mediastinum
II	single tumor with regional node involvement; ≥ 2 tumors / nodal areas on same side of diaphragm; primary resected GI tumor ± regional node involvement
III	tumors / nodal involvement on both sides of diaphragm; any intrathoracic / extensive intraabdominal disease; any paraspinal / epidural tumor
IV	bone marrow* / CNS^ disease regardless of other sites
* 5% malignant cells with normal peripheral blood cell count; in lymphoblastic lymphoma with > 25% malignant cells = leukemia	
^ in lymphoblastic lymphoma a WBC ≥ 5/µL with malignant cells	

Common site: mesenteric, inguinal, iliac nodes; CNS; bone marrow; kidney
Rare site: orbit, supradiaphragmatic paraspinal region, mediastinum, paranasal sinuses, bone, testes, pulmonary parenchyma
Cx: "leukemic transformation" (= extensive bone marrow involvement)

Lymphoblastic** (T-cell) **NHL (28%)

Primary site: mediastinum (66%)
Common site: neck, thymus, liver, spleen, CNS, bone marrow, gonads
Rare site: subdiaphragmatic (ileum, cecum, kidney, mesentery, retroperitoneum), orbit, paranasal sinus, thyroid, parotid

- respiratory distress, dysphagia
- SVC syndrome, pericardial tamponade

Large Cell** (histiocytic) **NHL (26%)

Origin: B cell, T cells (small percentage)
Location: nodal + extranodal
Primary site: variable (Waldeyer ring, Peyer patches)
Common site: peripheral lymph nodes, lung, bone, brain, skin
Rare site: hard palate, esophagus, trachea
PET - SUV measurement: 92% sensitive, 90% specific

LYMPHOMATOID GRANULOMATOSIS

= angioinvasive + angiodestructive oligo- / monoclonal lymphoproliferative + granulomatous disease
Cause: combination of Epstein Barr virus infection and immunosuppression
Mean age: 48 (range, 7–85) years; M÷F = 2÷1
Path: multiple sharply marginated masses adjacent to a bronchus causing obstructive pneumonitis
Histo: angiocentric infiltrate of atypical lymphoid cells (CD20-positive B-cells, some infected with Epstein-Barr virus); necrotic lung parenchyma in higher grade lesions; giant cells absent (DDx to Wegener granulomatosis)

• malaise, weight loss (35%); NO specific serum markers
◊ Less commonly found in lymph nodes, bone marrow, spleen
◊ Involvement of upper respiratory tract + sinuses is very unusual
@ Lung (100%)
• fever (60%), cough (56%), dyspnea (29%)
√ normal CXR
√ diffuse reticulonodular opacities (= granulomas)
√ large masslike opacities (= granulomas + pulmonary infarcts)
√ multiple bilateral nodules in middle + lower lobes (80%)
√ unilateral involvement (21%)
√ small pleural effusions (40%)
√ hilar lymphadenopathy (25%)
CT:
Distribution: peribronchovascular
√ peripheral subpleural 0.6–8.0 cm large nodules / masses
√ reticular / nodular airspace opacities (10–43%):
√ central cavitation (30%)
√ peripheral ground-glass halo ± air bronchogram
@ Skin (39–53%)
• nodules, ulcers, maculopapular rash (20–39%)
@ CNS (37–53%) → very poor prognosis
• neurologic complaints (21%)
@ Kidneys (32–40%)
Cx: lymphoma (12–47%)
Mortality: in 53–90% from sepsis, respiratory failure, pulmonary embolism, massive hemoptysis, CNS lesions

LYMPHOPROLIFERATIVE DISEASE AFTER TRANSPLANTATION

= POSTTRANSPLANT LYMPHOPROLIFERATIVE DISEASE (PTLD)

PTLD encompasses a group of lymphoproliferative disorders post stem cell and organ transplantation that ranges from benign polyclonal proliferation to malignant monoclonal disease. PTLD is intimately associated with EBV infection.

Cause: sequelae of chronic immunosuppression with limited ability to suppress neoplastic activity ← oral secretion transmission of virus, residual EBV DNA within bronchus-associated lymphoid tissue, lymphocytes of donated allograft, blood transfusion containing EBV-infected B cells

Pathogenesis:
90–95% of adults are Epstein-Barr virus (EBV) seropositive → T cells fight initial EBV infection by eradicating B cells that display EBV antigens → EBV-specific cytotoxic T cells may be completely lost within 6 months of transplantation

In a state of T-cell–depletion latently infected B cells can proliferate and result in PTLD. Immunosuppressive therapy in transplant recipients is responsible for a 3- to 8-fold increase in malignancies.

Pathophysiology of B-cell origin:

1. Infection of B lymphocytes (in 85%) with EBV (Epstein-Barr virus) → increased proliferation of B cells (= polyclonal B-cell expansion)

PTLD *[in %]* **with Various Organ Transplantations**

PTLD	All Tx	Pancreas Tx	Liver Tx	Heart Tx	Kidney Tx	Lung Tx
GI tract	5–15	33	12–30	14–24	11–22	20
Liver		22–40	30–45	9–23	5	5–10
Spleen	10–40		+++			
Kidney	10–30		0	0.6	10–75	1.4
Adrenal	5					
Pancreas		10–75				
Abd. nodes	15–20					
Chest			4–24	16–32	4–15	69–100
CNS	3–16	16	4	4–13	12–13	
Any PTLD			2–8	2–3	1–5	2–8

2. Loss of protective immune control by T cells allows for uncontrolled proliferation of EBV-infected B lymphocytes (= oligoclonal B-cell expansion)
3. Genetic mutation transforms some B cells into malignant cells

Frequency: PTLD in 2% of all allograft recipients (different rates likely related to differences in degree and regimen of immunosuppression)

bone marrow transplantation 0.6%
kidney transplantation 1–5%
cardiac transplantation 1.8–3.4%
lung transplantation 1.8–7.9%
liver transplantation 2.2–8.4%
heart-lung transplantation 9.4%
multivisceral transplantation 13–33%
bowel transplantation 13–33%

◊ Prevalence of NHL is 35 x greater than in general population!

The incidence + prognosis of PTLD vary according to the organ transplanted, recipient age, and intensity of immuno-suppression therapy. The risk is greatest within 1st year of transplantation, declining thereafter.

Risk factor: pretransplantation seronegative for EBV, autoimmune hepatitis, Langerhans cell histiocytosis, chronic interstitial nephritis

Time of onset: as early as 1 month after transplantation with very aggressive immunosuppressive regimen; mean of 2–5 months after bone marrow, lung, heart-lung transplantation; mean of 23–32 months after kidney, heart, liver transplantation

◊ Under cyclosporine / OKT3 within 1 month

Categories by location:

› nodal
  » mediastinal
  » retroperitoneal
› extranodal
  » GI tract
  » solid organ
    – obstructive: kidney, liver
    – hilar / solitary mass: kidney, liver, spleen, lung
    – scattered parenchymal: kidney, liver, spleen, lung
    – infiltrative: solid organ / abdominal wall
  » CNS: basal ganglia, subcortical white matter

Unique features:

(a) high propensity for extranodal involvement (80%): liver (50%), small bowel (25%), kidney (17%)

Features of Posttransplant Lymphoproliferative Disorder (PTLD)	
Clinical data:	Post stem cell and organ transplant patients Associated with EBV infection
Histopathology:	Proliferation of EBV-infected B cells Spectrum of poly- to monoclonal proliferation
Imaging findings:	*Distribution:* peribronchovascular, subpleural √ multiple pulmonary nodules / masses / airspace consolidation √ ± ground-glass halo √ air bronchograms √ septal thickening √ mediastinal + hilar lymphadenopathy √ ± pleural effusion √ invasion of adjacent structures √ avidly hypermetabolic on PET/CT
DDx:	Angioinvasive aspergillosis

(b) varied morphologic appearance
(c) strong causal association with EBV infection
(d) frequent absence of immunophenotypic / genotypic evidence of monoclonality
(e) poor response to cytolytic chemotherapy / irradiation

• unexplained fever / lymphadenopathy
• illness resembling infectious mononucleosis = pharyngitis, fever, lymphadenopathy, hepatosplenomegaly

Anatomic distribution:

◊ Frequency of location varies with type of allograft!
@ Thorax (most commonly involved in 1st year)
  √ pulmonary mass (50%)
  √ multiple / solitary discrete well-circumscribed pulmonary nodules (40–50%) (DDx: cryptococcosis, fungus, Kaposi sarcoma):

√ ± low-attenuation center ± ground-glass halo
√ patchy airspace consolidation (7–10%) (DDx: edema, infection, rejection)
√ mediastinal / hilar lymphadenopathy (in up to 50%)
√ pleural masses

@ Lymph nodes (in 2–10% of various allografts)

@ Gastrointestinal tract

Location: distal jejunum + ileum > duodenum > colon (prox > distal) > stomach > esophagus

√ bowel wall thickening + dilatation
√ eccentric mass, luminal ulceration
√ short-segment intussusception

Cx: visceral perforation (frequent)

@ Gallbladder

√ gallbladder thickening, biliary obstruction

@ Liver

Site: intrahepatic / extrahepatic (frequently extranodal)

√ discrete hypoattenuating hypovascular nodular lesion:
√ single / multiple parenchymal lesions
√ diffuse ill-defined infiltrative pattern of hepatic involvement → hepatomegaly
√ hypoechoic heterogeneous soft tissue mass encasing hilar structures
Cx: narrowing of bile duct, hepatic artery, portal vein
√ periportal adenopathy
√ portal vein constriction / focal thrombus (15%)

In posttransplant lymphoproliferative disease extrahepatic involvement is frequently extranodal and appears at US / CT as ill-defined hypoechoic / hypoattenuating periportal heterogeneous soft tissue that encases the hilar structures.

@ Spleen

√ splenomegaly

WHO Histopathologic Classification of Posttransplant Lymphoproliferative Disorder (PTLD)

Category	*Subtypes*
Hyperplastic PTLD (early)	Infectious mononucleosis-like plasmacytic hyperplasia
Polymorphic PTLD	Polymorphic diffuse B-cell hyperplasia Polymorphic diffuse B-cell lymphoma
Monomorphic (lymphomatous) PTLD	Diffuse large B-cell lymphoma Burkitt lymphoma Plasma cell myeloma Plasmacytoma-like PTLD T-cell neoplasm (up to 14%) Natural killer cell neoplasm
Hodgkin-like PTLD	Hodgkin disease, Hodgkin-like variants

√ multiple focal hypoattenuating lesions (less frequent)

@ Kidney
√ heterogeneous mass surrounding hilar vessels
√ multifocal discrete round hypovascular parenchymal masses (almost always unilateral)
√ diffuse infiltrative disease → renal enlargement
@ CNS
√ solitary hyperdense typically periventricular mass usually surrounded by vasogenic edema
@ Disseminated disease (10–14% of various allografts)
PET (modality of choice for disease staging + assessment of therapy response)
√ extremely hypermetabolic active lesions
@ Others: skin, eye, area of prior trauma / surgery, bone marrow (uncommon)

Dx: tissue sampling for DDx from invasive aspergillosis

DDx: posttransplant opportunistic infection, lymphoid hyperplasia (spontaneous resolution)

Rx: (1) Antiviral agents (controversial)
(2) Reduction / cessation of immunosuppressive agent (first-line treatment for patients with early polymorphic lesions)
(3) Rituximab = monoclonal antibody against B-cell receptor CD20 (60% response rate)
(4) Surgical resection of tumor mass (complete resolution in 63%)

MALARIA

[*mala aria*, Italian = bad air] [*anophelos*, Greek = useless]
= mosquito-borne infectious disease by Plasmodium species

Type of Malaria	*Organism*	*Fever spikes*
malignant tertian fever	P falciparum	irregular
benign tertian fever	P vivax, P ovale	every 48 h
quartan fever	P malariae	every 72 h

Prevalence: 400–500 million new cases annually worldwide

Prognosis: 2.2–2.7 million deaths annually in mostly young children

◊ Most deadly parasitic infection in the world!

Endemic to: sub-Saharan Africa, South America, southern Asia

Transmission: bite by female Anopheles mosquito (definite host)

Transmission vector: sporozoite = motile infective form

Secondary host: vertebrate (human)

Life cycle:

(a) with a mosquito's bite the motile infective form (**sporozoite**) travels through blood vessels to hepatocytes → asexual reproduction (= tissue schizogony) → thousands of merozoites
(b) **merozoites** infect new RBCs initiating a series of asexual multiplication cycles (= blood schizogony) producing 8–24 new infective merozoites → bursting of RBC (= hemolysis) at different time intervals depending on species
(c) other merozoites develop into immature **gametocytes** (= precursors of male + female gametes); during bite of an infected person by fertilized mosquito, gametocytes are taken up with blood and mature in mosquito gut
(d) male + female gametocytes fuse and form an **ookinete** (= fertilized motile zygote) → develop into new sporozoites that migrate to salivary glands of insect → transmission

during mosquito bite

• fever with chills, sweating, anemia, leukopenia, splenomegaly

@ Lung

Adult respiratory distress syndrome (ARDS)

Cause: (a) RBC sequestration + destruction → vascular injury
(b) release of parasite + erythrocyte material into circulation
(c) host response to these events

√ noncardiogenic diffuse interstitial pulmonary edema
√ pleural effusion
√ lobar consolidation

Dx: identification of trophozoites / other parasitic forms within RBCs (thin blood smear) / parasites (thick smear)

Cerebral Malaria *(2%)*

Cause: sequestration of infected erythrocytes in microcirculation

• encephalopathy, coma, retinal whitening at fundoscopy
√ diffuse cerebral edema ← microvascular occlusion
√ cortical infarcts
√ nonspecific white matter hyperintensity ← small-vessel ischemia
Location: cerebral cortex, thalamus, basal ganglia, splenium of corpus callosum
√ petechial hemorrhages, hemorrhagic infarctions

Prognosis: 15–25% mortality rate

Rx: quinine (from cinchona bark), artemisinin (from sweet wormwood)

MECONIUM ASPIRATION SYNDROME

= most common cause of neonatal respiratory distress in full term / postmature infants (hyaline membrane disease most common cause in premature infants)

Etiology: fetal circulatory accidents / placental insufficiency / postmaturity → perinatal hypoxia + fetal distress → defecation of meconium in utero

Pathogenesis: severe hypoxemia induces gasping reflex with inhalation of tenacious meconium that produces medium and small airway obstruction + chemical pneumonitis

Frequency: 10% of all deliveries have meconium-stained amniotic fluid; 1% of all deliveries have respiratory distress

• cyanosis (rare)
• **persistent fetal circulation syndrome** = neonatal pulmonary hypertension (← thick-walled pulmonary arterioles) + R-to-L shunt through PDA and foramen ovale + severe cyanosis

Rx: extracorporeal membrane oxygenation (major indication besides diaphragmatic hernia + neonatal pneumonia)

√ large infant
√ bilateral diffuse grossly patchy opacities (atelectasis + consolidation)
√ hyperinflation with areas of emphysema ← air trapping
√ spontaneous pneumothorax + pneumomediastinum (25–40%) requiring no therapy
√ small pleural effusions (10–20%)
√ NO air bronchograms

√ rapid clearing usually within 48 hours
Cx: morbidity from anoxic brain damage is high

MEDIASTINAL LIPOMATOSIS

= excess unencapsulated fat deposition
Etiology:
A. exogenous steroids (average daily dose of > 30 mg prednisone):
(1) Chronic renal disease, renal transplant (5%)
(2) Collagen vascular disease, vasculitis
(3) Hemolytic anemia
(4) Asthma
(5) Dermatitis
(6) Crohn disease
(7) Myasthenia gravis
B. endogenous steroid elevation
(1) Adrenal tumor
(2) Pituitary tumor / hyperplasia = Cushing disease
(3) Ectopic ACTH-production (carcinoma of the lung)
C. obesity
• moon facies, buffalo hump, supraclavicular + episternal fat
Location: upper mediastinum (common), cardiophrenic angles + paraspinal areas (less common)
√ upper mediastinal widening
√ paraspinal widening
√ increase in epicardial fat-pads
√ symmetric slightly lobulated extrapleural deposits extending from apex to 9th rib laterally
OTHER FEATURES:
√ osteoporosis
√ fractures
√ aseptic necrosis
√ increased rectosacral distance

MEDIASTINITIS

Acute Mediastinitis

= life-threatening condition with high mortality + morbidity
Cause: acute inflammation of connective tissues + fat surrounding mediastinal structures secondary to
(a) surgery (= postoperative)
(b) transmural esophageal perforation
(c) osteomyelitis of adjacent bone
(d) direct extension of head & neck infection
(e) hematogenous spread of any infection
• acute chest pain, high fever, chills, shortness of breath

• leukocytosis

CXR:

√ widening + loss of normal contours of mediastinum

√ diffuse / focal gas bubbles within mediastinum

CT (modality of choice):

√ increased attenuation of mediastinal fat

√ free gas bubbles in mediastinum

√ localized fluid collections

√ enlarged lymph nodes, pleural effusions, empyema

Postoperative Mediastinitis

Frequency: 0.5–5.0% after median sternotomy

Organism: Staphylococcus aureus

Risk factors: obesity, insulin-dependent diabetes, internal mammary artery graft

Frequently associated with: sternal dehiscence

CXR:

√ displacement, rotation, fracture of sternal wires

√ midsternal lucent stripe (rare)

CT:

√ midsternal lucent stripe > 3 mm = sternal dehiscence

√ pleural / pericardial effusion

N.B.: mediastinal gas bubbles + fluid collections after 14th postoperative day (almost 100% sensitive and specific)

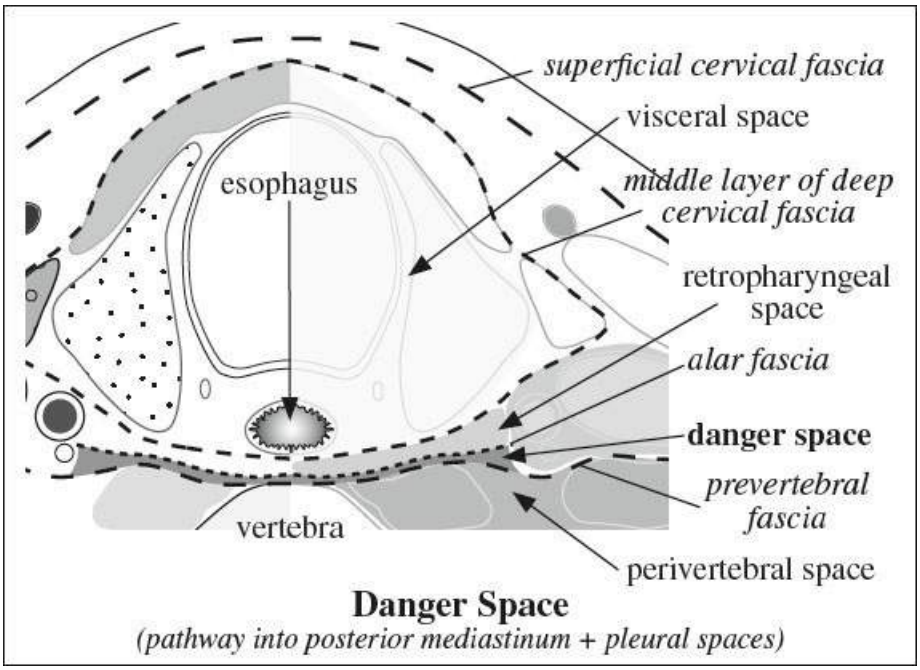
Mortality rate: 7–80%

Descending Necrotizing Mediastinitis

= DNM = rare acute emergent polymicrobial infection of mediastinum

Source: oropharyngeal / cervical / odontogenic infection

Pathways: (a) pretracheal route → anterior mediastinum



Danger Space
(pathway into posterior mediastinum + pleural spaces)

(b) lateral pharyngeal route (via carotid space) → middle mediastinum
(c) retropharyngeal-retrovisceral route → posterior mediastinum (most common)
(d) "**danger space**" = between cervical alar fascia and prevertebral fascia from skull base → posterior mediastinum and diaphragm (posterior to retropharyngeal space)

Classification of disease extent:

type 1 = localized above carina
type 2A = extends to lower anterior mediastinum
type 2B = extension to anterior + posterior mediastinum

X-Ray:

√ subcutaneous emphysema
√ prevertebral soft-tissue swelling
√ mediastinal air
√ widening of superior mediastinum

CT:

√ thickening of subcutaneous tissues of neck
√ thickening + enhancement of cervical fascia + muscles
√ increased attenuation of mediastinal fat
√ mediastinal fluid collections
√ locules of gas within mediastinum
√ pericardial / pleural effusion
√ enlarged lymph nodes

Mortality: 25–50% ← delayed diagnosis ← nonspecific subtle symptoms and findings
Rx: aggressive airway management, early mediastinal exploration, débridement, drainage

Chronic Mediastinitis

Etiology:

(1) Granulomatous infection: histoplasmosis (most frequent), tuberculosis, actinomycosis, Nocardia
(2) Mediastinal granuloma
(3) Fibrosing mediastinitis
(4) Radiation therapy

Mediastinal Granuloma

= relatively benign massive coalescent adenitis with caseating / noncaseating lesions
Cause: primary lymph node infection (commonly tuberculosis / histoplasmosis)
Histo: thin fibrous capsule surrounding granuloma
√ lymphadenopathy
DDx: fibrosing mediastinitis (infiltrative, rare)

Fibrosing Mediastinitis

= SCLEROSING MEDIASTINITIS = MEDIASTINAL COLLAGENOSIS = MEDIASTINAL FIBROSIS
= uncommon benign disorder characterized by progressive proliferation of dense fibrous tissue within mediastinum
Types:

1. Granulomatous fibrosing mediastinitis
   = focal granulomatous form
   Cause: idiosyncratic reaction to Histoplasma capsulatum antigens (organisms recovered in 50%, risk of < 1÷20,000 patients), TB, cryptococcosis, aspergillosis, sarcoidosis

The most common focal granulomatous form of fibrosing mediastinitis is caused by idiopathic proliferation of fibrous tissue in response to Histoplasma capsulatum antigen stimulation.

   √ often calcified focal mediastinal mass
   √ calcified hepatic + splenic granulomas
2. Nongranulomatous fibrosing mediastinitis
   = diffuse form
   Cause: autoimmune disorders / radiation therapy / reaction to drugs (eg, methysergide)
   Associated with:
   retroperitoneal fibrosis, orbital pseudotumor, systemic lupus erythematosus, sclerosing thyroiditis, Riedel thyroiditis, IgG4-related disease
   √ noncalcified diffuse mediastinal infiltration
   √ smooth lobulated contours

Path: ill-defined soft-tissue mass with minimal / NO apparent granulomatous foci
Histo: abundant paucicellular fibrous tissue infiltrating + obliterating adipose tissue
Age: 2nd–5th decade of life; M = F
Most common narrowed mediastinal structures:
airways, pulmonary arteries + veins, esophagus, SVC

- symptoms of central airway obstruction:

- cough (41%), dyspnea (32%)

- symptoms of pulmonary venous occlusion:
  - "pseudo-mitral stenosis syndrome" = progressive exertional dyspnea, hemoptysis (31%)
  - cor pulmonale ← pulmonary arterial hypertension ← compression of pulmonary arteries / veins
- dysphagia (2%)
- superior vena cava syndrome (6–39%)
- low left atrial pressure + widely differential elevation of pulmonary capillary wedge pressures

Location: middle mediastinum (subcarinal and paratracheal regions) + hila; right > left side of mediastinum

CXR:

√ nonspecific widening of mediastinum:
- √ distortion of normally recognizable interfaces
- √ lobulated (in 86% calcified) paratracheal / hilar mass

√ typically unilateral pulmonary artery obstruction:
- √ enlargement of main pulmonary artery + right heart
- √ diminution in size + quantity of vessels of affected lung
- √ localized regional oligemia of affected lung

√ pulmonary venous obstruction:
- √ peribronchial cuffing, septal thickening
- √ ipsilateral Kerley B lines
- √ pulmonary infarct

√ central airway narrowing:
- √ segmental / lobar atelectasis
- √ recurrent pneumonia

UGI:

√ circumferential narrowing / long-segment stricture of esophagus at junction of upper + middle ⅓

√ "downhill" esophageal varices

CT:

√ focal mediastinal mass (82%):
- √ dense / stippled calcifications (in 63%) in right paratracheal / subcarinal / hilar locations
- √ distortion and narrowing of adjacent structures
- √ calcified granulomas in lymph nodes, lung, liver, spleen

√ diffusely infiltrative mediastinal mass (18%) involving several mediastinal compartments:
- √ soft-tissue attenuation, NO calcification
- √ obliteration of normal mediastinal fat planes
- √ encasement / invasion of adjacent structures (vascular stenosis / obstruction)
- √ generally NO signs of remote granulomatous infection

√ wedge-shaped peripheral consolidation of venous / arterial infarction

√ ipsilateral bronchial artery dilatation ← critical narrowing / encasement of pulmonary artery

MR:
√ heterogeneous infiltrative mass of intermediate SI on T1WI
√ mixture of regions of increased + markedly decreased SI on T2WI

NUC:
√ unilateral decreased / absent perfusion with normal ventilation (in focal hilar fibrosis)
√ large segmental / smaller subsegmental unmatched perfusion defects
√ ventilation defects in lobar / segmental occlusion

PET:
√ variable activity → not routinely performed

Angio (with therapeutic intent):
√ unilateral / asymmetric narrowing of central pulmonary arteries / distal arterial cutoffs
√ funnel-like pulmonary vein stenosis / obstruction / focal dilatation near left atrium

Cx: (1) Compression of SVC (64%) + pulmonary veins (4%)
(2) Chronic obstructive pneumonia (narrowing of trachea / central bronchi) in 5%
(3) Esophageal stenosis (3%)
(4) Pulmonary infarcts + fibrosis ← narrowing of pulmonary artery
(5) Prominent intercostal arteries ← narrowing of pulmonary artery

Dx: tissue diagnosis is essential to diagnose malignancy

Rx: resection (laser therapy, venous graft), ketoconazole, steroid therapy (limited success); stent insertion

DDx: (1) Bronchogenic carcinoma
(2) Lymphoma
(3) Metastatic carcinoma
(4) Mediastinal sarcoma

MESOTHELIOMA OF CHEST

Benign Pleural Mesothelioma

= LOCALIZED FIBROUS MESOTHELIOMA = LOCALIZED FIBROUS TUMOR OF THE PLEURA = SOLITARY FIBROUS TUMOR OF PLEURA = BENIGN LOCALIZED MESOTHELIOMA = BENIGN PLEURAL FIBROMA = FIBROSING MESOTHELIOMA = PLEURAL FIBROMYXOMA

= slowly growing, primary pleural neoplasm unrelated to asbestos exposure

Frequency: < 5% of all pleural tumors

◊ No recognized association with asbestos exposure!

Mean age: 50–60 years (range, 3rd–8th decade); M÷F = 1÷1

Path: usually solitary mass arising from visceral pleura in 80% + parietal pleura in 20%

Histo: tumor originates from submesothelial fibroblasts, lined by layer of mesothelial cells
(a) relatively acellular fibrous tissue
(b) rounded spindle-shaped densely packed cells
(c) resembling hemangiopericytoma of lung

- asymptomatic in 50%; episodic hypoglycemia (4%)
- cough, fever, dyspnea, chest pain (larger mass)
- digital clubbing (rare) + hypertrophic pulmonary osteoarthropathy in 20–35%

Location: near lung periphery / adjacent to pleural surface / within fissure
Size: 2–30 cm in diameter
√ sharply circumscribed spherical / ovoid lobular mass:
  √ sessile with smooth tapered margin (common) / pedunculated (almost 50%)
  √ obtuse angle toward chest wall (rare, benign feature)
  √ tumor may change in shape + location upon alteration of patient's position / during respiration (if pedunculated)
  √ areas of hemorrhage / necrosis may be present (favors malignancy)
√ ipsilateral pleural effusion (rare) containing hyaluronic acid
√ mass effect on adjacent lung + mediastinum
CT:
  √ homogeneous mass of intermediate to high attenuation
  √ calcification (7%) associated with necrosis in large tumor
CECT:
  √ substantial contrast enhancement
  √ heterogeneous enhancement with central areas of low attenuation in large tumor ← myxoid changes / hemorrhage / necrosis / cystic degeneration
MR:
  √ hypointense on T1WI + hyperintense on T2WI
Cx: malignant degeneration in 37%
DDx: metastatic deposit
Rx: excision is curative (recurrence rate lower for pedunculated versus nodular tumor)

Malignant Pleural Mesothelioma

= DIFFUSE MALIGNANT MESOTHELIOMA
= uncommon fatal neoplasm of serosal lining of pleura
◊ Most common primary neoplasm of pleura!
Prevalence: 7–13÷1,000,000 persons per year; 2,000–3,000 cases per year in USA
Etiology: asbestos exposure (13–100%); zeolite (nonasbestos mineral fiber); chronic inflammation (TB, empyema); irradiation
Carcinogenic potential:
proportional to aspect ratio of asbestos fibers (= length-to-diameter) of fiber and durability in human tissue:
crocidolite > amosite > chrysotile > actinolite, anthophyllite, tremolite
◊ Occupational exposure of asbestos found in only 40–80% of all cases!
◊ 5–10% of asbestos workers will develop mesothelioma in their lifetime (risk factor of 30 compared with general population)
◊ No relation to duration / degree of exposure or smoking Hx!
Latency period: 20–35–45 years (earlier than asbestosis; later than asbestos-related lung cancer)
Peak age: 50–70 years (66%); M÷F = 2–4–6÷1
Path: multiple tumor masses involving predominantly the parietal pleura + to a lesser degree

the visceral pleura; progression to thick sheetlike / confluent masses resulting in rindlike tumoral encasement of lung

Histo: (a) epithelioid (60%), (b) sarcomatoid (15%), (c) biphasic (25%); intracellular asbestos fibers in 25%; positive stain for epithelial membrane antigen, calretinin, Wilms tumor I antigen, cytokeratin 5/6, HBME-1, mesothelin

Associated with: peritoneal mesothelioma; hypertrophic osteoarthropathy (10%)

Staging (Boutin modification of Butchart staging):

IA confined to ipsilateral parietal / diaphragmatic pleura

IB + visceral pleura, lung, pericardium

II invasion of chest wall / mediastinum (esophagus, heart, contralateral pleura) or metastases to thoracic lymph nodes

III penetration of diaphragm with peritoneal involvement or metastases to extrathoracic lymph nodes

IV distant hematogenous metastases

Stage at presentation: II in 50%, III in 28%, I in 18%, IV in 4%

- nonpleuritic (56%) / pleuritic chest pain (6%), dyspnea (53%)
- fever + chills + sweats (30%), cough (24%), weight loss (22%)
- weakness, fatigue, malaise (30%), anorexia (10%)
- expectoration of asbestos bodies (= fusiform segmented rodlike structures = iron-protein deposition on asbestos fibers [a subset of ferruginous bodies])
- elevated serum mesothelin-related protein (84%)

Spread:

(a) contiguous: chest wall, mediastinum, contralateral chest, pericardium, diaphragm, peritoneal cavity; lymphatics, blood, lung

(b) lymphatic: hilar + mediastinal (40%), celiac (8%), axillary + supraclavicular (1%), cervical nodes

(c) hematogenous: lung, liver, kidney, adrenal gland

√ extensive irregular lobulated bulky pleural-based masses typically > 5 cm / pleural thickening (60%)

√ recurrent exudative / hemorrhagic <u>unilateral</u> pleural effusion (30–60–80%) without mediastinal shift ("frozen hemithorax" = fixation by pleural rind of neoplastic tissue); bilateral effusions (in 10%) contain hyaluronic acid in 80–100%

√ distinct pleural mass without effusion (< 25%)

√ associated pleural plaques in 50% = HALLMARK of asbestos exposure

√ pleural calcifications (20%)

√ circumferential rindlike encasement of entire lung = involvement of all pleural surfaces (mediastinum, pericardium, fissures) as late manifestation

√ extension into interlobar fissures (40–86%)

√ superficial invasion of underlying lung (primarily as extension into interlobular septa)

√ rib destruction in 20% (in advanced disease)

√ ascites (peritoneum involved in 35%)

CT:

√ circumferential + nodular pleural thickening > 1 cm (92%)

√ thickening of mediastinal pleura

√ thickening of interlobar fissure (86%)
√ unilateral pleural effusion (74%) → level of fluid accumulation diminishes with advanced disease
√ contraction of affected hemithorax (42%):
√ ipsilateral mediastinal shift
√ narrowed intercostal spaces
√ elevation of ipsilateral hemidiaphragm
√ calcified pleural plaques (20%)
MR (best modality to determine resectability):
√ minimally hyperintense relative to muscle on T1WI
√ moderately hyperintense relative to muscle on T2WI
PET-CT (useful in identifying occult distant metastases)
Metastases to:
ipsilateral lung (60%), hilar + mediastinal nodes, contralateral lung + pleura (rare), extension through chest wall + diaphragm, pericardium
√ invasion of chest wall:
√ obscured fat planes in chest wall
√ invasion of intercostal muscles
√ separation / destruction of ribs by tumor
√ invasion of mediastinum:
√ obliteration of fat planes around heart, great vessels, esophagus, trachea
Prognosis: 10% of occupationally exposed individuals die of mesothelioma (in 50% pleural + in 50% peritoneal mesothelioma); 5–12 months mean survival time
DDx: pleural fibrosis from infection (TB, fungal, actinomycosis), fibrothorax, empyema, asbestos-related benign pleural disease, pleural lymphoma, metastatic adenocarcinoma (differentiation impossible)
Dx: video-assisted thoracoscopic surgery (postprocedural radiation therapy of all entry ports for tumor seeding of needle track [21%])

METASTASIS TO LUNG

Pulmonary metastases occur in 30% of all malignancies; mostly hematogenous
Age: > 50 years (in 87%)
Incidence of pulmonary metastases:
mnemonic: CHEST
Choriocarcinoma 60%
Hypernephroma / Wilms tumor 30 / 20%
Ewing sarcoma 18%
Sarcoma (rhabdomyo- / osteosarcoma) 21 / 15%
Testicular tumor 12%
Common primaries of intravascular metastases:
breast, stomach, liver, kidney, lung, prostate, choriocarcinoma
◊ Right atrial myxoma + RCC tend to embolize to large central + segmental pulmonary arteries
• progressive dyspnea, subacute pulmonary hypertension

• symptoms of acute pulmonary thromboembolism
√ multiple nodules (in 75%), 82% subpleural:
  √ often smooth + well-defined
  √ varying sizes (most typical)
  √ usually in random distribution
√ fine micronodular pattern: highly vascular tumor (renal cell, breast, thyroid, prostate carcinoma, bone sarcoma, choriocarcinoma)
√ pneumothorax (2%): especially in children with sarcoma + frequently with osteosarcoma ← bronchopleural fistula ← subpleural metastasis

Frequency of Pulmonary Metastases

Origin of pulmonary mets		*Probability of pulmonary mets*	
Breast	22%	for Kidney cancer	75%
Kidney	11%	for Osteosarcoma	75%
Head and neck	10%	for Choriocarcinoma	75%
Colorectal	9%	for Thyroid cancer	65%
Uterus	6%	for Melanoma	60%
Pancreas	5%	for Breast cancer	55%
Ovary	5%	for Prostate cancer	40%
Prostate	4%	for Head and neck CA	30%
Stomach	4%	for Esophagus CA	20%

CT:
  √ noncalcified multiple (> 10) round lesions > 2.5 cm likely to be metastatic
  √ lesions connected to pulmonary arterial branches (75%):
    √ filling defects in large pulmonary arteries (tumor thromboemboli)
    √ multifocal dilatation / beading of subsegmental arteries
    √ tree-in-bud appearance of arterioles in secondary pulmonary lobules

Solitary Metastatic Lung Nodule

◊ A solitary lung nodule represents a primary lung tumor in 62% in patients with known history of neoplasm
◊ 0.4–5.0–9.0% of all solitary nodules are metastatic; most likely origin: colon carcinoma (30–40%), melanoma, osteosarcoma, renal cell carcinoma, bladder cancer, testicular cancer, breast carcinoma

Calcifying Lung Metastases (< 1%)

mnemonic: BOTTOM
Breast
Osteo- / chondrosarcoma
Thyroid (papillary)
Testicular
Ovarian
Mucinous adenocarcinoma (colon)
+ *others:* synovial sarcoma, giant cell tumor of bone, lung metastases following radiation

/ chemotherapy

Cavitating Lung Metastases

Frequency: 4% (compared with 9% in primary bronchogenic carcinoma)
Histo: squamous cell carcinoma (10%), adenocarcinoma (9.5%)
mnemonic: Squamous Cell Metastases Tend to Cavitate
Squamous cell carcinoma, **S**arcoma
Colon
Melanoma
Transitional cell carcinoma
Cervix, during **C**hemotherapy

Hemorrhagic Lung Metastases

CT: √ill-defined nodules with fuzzy margin + "halo" sign (= surrounding ground-glass opacity)

1. Angiocarcinoma
2. Choriocarcinoma
3. Renal cell carcinoma
4. Melanoma
5. Thyroid carcinoma

Endobronchial Metastasis

Frequency: 1%
√ subsegmental / segmental atelectasis or atelectasis of entire unilateral lung
√ round endobronchial lesion on CT

1. Bronchogenic carcinoma
2. Lymphoma
3. Colorectal carcinoma
4. Breast cancer
5. Renal cell carcinoma

Lung Metastases in Childhood

mnemonic: ROWE
Rhabdomyosarcoma
Osteosarcoma
Wilms tumor
Ewing sarcoma

Metastases with Airspace Pattern

= lepedic growth along intact alveolar walls similar to bronchioloalveolar carcinoma mimicking pneumonia
√ airspace nodules
√ consolidation with air bronchogram
√ focal /extensive ground-glass opacities

1. Adenocarcinoma of GI tract (10%)

2. Adenocarcinoma of breast / ovary

Sterilized Metastasis

= persistence of metastatic nodule without significant change in size after adequate chemotherapy

Histo: necrotic nodule ± fibrosis without viable tumor cells

1. Choriocarcinoma
2. Testicular cancer
   - √ growing teratoma syndrome = conversion to a benign mature teratoma
   - √ pulmonary lacunae (= transformation into thin-walled cavity) may persist for years

Metastasis of Benign Tumor to Lung

1. Leiomyoma of uterus
2. Hydatidiform mole of uterus
3. Giant cell tumor of bone
4. Chondroblastoma
5. Pleomorphic adenoma of salivary gland
6. Meningioma

METASTASIS TO PLEURA

1. Lung (36%)
2. Breast (25%)
3. Lymphoma (10%)
4. Ovary (5%)
5. Stomach (2%)

MIXED CONNECTIVE TISSUE DISEASE

= OVERLAP SYNDROME

= disorder that shares distinctive features of ≥ 2 different connective tissue diseases in same patient (overlapping features of SLE, RA, scleroderma (PSS), poly- / dermatomyositis)

Age peak: 2nd + 3rd decade; M÷F = 1÷10

- Raynaud phenomenon, swollen hands, acrosclerosis
- arthritis / arthralgia, esophageal dysmotility + GERD, myositis
- high titer of speckled fluorescent antinuclear antibodies
- moderate to high serum level of antibodies against ribonucleoprotein (anti-U1-RNP)

@ Chest involvement (in 20–85%)

- √ interstitial lung disease (21–66%):
  Pattern: NSIP, UIP, LIP
  - √ groundglass opacities predominantly in lower lung fields
- √ pulmonary arterial hypertension (in 10–45%):
  Cause: interstitial pulmonary fibrosis / intimal proliferation of pulmonary arterioles
  - decrease in CO diffusing capacity
- √ pleural thickening / effusion (<10%)
- √ pulmonary vasculitis, thromboembolism

√ alveolar hemorrhage
√ respiratory muscle dysfunction

Cx: aspiration pneumonia ← esophageal dysmotility

MYCOPLASMA PNEUMONIA

= PRIMARY ATYPICAL PNEUMONIA (PAP)

◊ Varied radiographic + clinical picture!

◊ Commonest cause of community-acquired nonbacterial pneumonia with a mild course (only 2% require hospitalization), usually lasts 2–3 weeks; only 10% of infected subjects develop pneumonia

Frequency: 10–33% of all pneumonias; autumn peak

Organism: Eaton agent = pleuropneumonia-like organism = 350 μm long pleomorphic Mycoplasma pneumoniae with lack of cell wall

Spread: direct contact / aerosol

Age: 5–20 years (most common, esp. in closed populations)

Histo: peribronchial mononuclear cell infiltrates (similar to viral lower respiratory infection)

• incubation period: 1–2 weeks
• gradual onset beginning with pharyngitis, headache, myalgia (rhinorrhea + nasal congestion uncommon)
• mild symptoms of dry cough + low fever, malaise, otitis
• sputum with PMNs but few bacteria, mild leukocytosis (20%)
• most common respiratory cause of cold agglutinin production (60%)

◊ Severity of radiologic findings discrepant to mild clinical condition with pulmonary infiltrates having a significant lag time

√ focal reticular <u>interstitial infiltrate</u>:
  √ unilobar from hilum into lower lobe as earliest change (52%), bilobar (10%)
  √ parahilar peribronchial opacification (12%)
  √ atelectasis (29%)
√ <u>alveolar infiltrates</u>:
  √ patchy inhomogeneous unilateral (L > R) airspace consolidation in segmental lower lobe in 50%, bilateral in 10–40%
√ small pleural effusions in 20%
√ hilar adenopathy (7–22%)

Rx: erythromycin, azithromycin, tetracycline

Cx: ? as an autoimmune response
  (1) Acute disseminated encephalomyelitis
  (2) Cerebral arteriovenous occlusion
  (3) Erythema nodosum, erythema multiforme, Stevens-Johnson syndrome
  (4) pulmonary: Swyer-James syndrome, pulmonary fibrosis, bronchiolitis obliterans, ARDS

Prognosis: 20% with recurrent symptoms of pharyngitis + bronchitis ± infiltrations

DDx: viral infection of lower respiratory tract, pertussis, chlamydia (indistinguishable)

NEAR DROWNING

= asphyxiation ← water inhalation followed by survival for a minimum of 24 hour

Stage 1:

(a) acute laryngospasm after inhalation of a small amount of water
√ NO roentgenographic abnormality

(b) prolonged laryngospasm = "dry drowning" ← negative pressure edema arising from a prolonged episode of the Müller maneuver as in postobstructive pulmonary edema
√ Kerley lines, peribronchial cuffing
√ patchy perihilar alveolar airspace consolidation
Prognosis: resolution within 24–48 hours (under therapy)

Stage 2:

= laryngospasm + swallowing of water into the stomach

Stage 3:

(a) persistent laryngospasm with dry drowning (10–15%)
√ pressure edema

(b) aspiration of water after hypoxia-induced relaxation of laryngospasm (85–90%)
√ permeability edema ← hypoxia + diffuse alveolar damage
Cx: ARDS, aspiration of gastric fluid, infection by fresh-water saprophytic bacteria

1. **Sea-water drowning**
   • hemoconcentration, hypovolemia
2. **Fresh-water drowning**
   • hemodilution, hypervolemia, hemolysis
3. **Secondary drowning**
   (a) pneumonia ← toxic debris
   (b) progressive pulmonary edema
4. **Dry drowning** (20–40%)
   = laryngeal spasm prevents water from entering
   √ no roentgenographic abnormality

Similarities of all 4 types:

• hypoxemia, metabolic acidosis
√ central extensive fluffy areas of increased opacity (alveolar edema indistinguishable from other types):
√ tendency for opacities to coalesce
√ hyaline membrane formation = considerable loss of protein from blood
Cx: pneumonia ← aspirated bacteria / fungi /mycobacteria

NECROTIZING SARCOID GRANULOMATOSIS

Etiology: ? variant of sarcoidosis

Mean age: 49 years (range, 3rd–7th decade); M÷F = 1÷2.2

Path: pleural + subpleural + peribronchovascular scattered nodules / conglomerate masses ± central cavitation

Histo: confluent noncaseating granulomas, extensive necrosis, vasculitis of muscular pulmonary arteries + veins with frequently total vascular occlusion, bronchiolar obstruction, bronchiolitis obliterans, obstructive pneumonitis

• asymptomatic (15–40%)

• cough, chest pain, dyspnea, fever, weight loss, fatigue
• uveitis, hypothalamic insufficiency (13%)
◊ Almost exclusively affects lungs
√ multiple bilateral subpleural + peribronchovascular pulmonary nodules
√ numerous ill-defined parenchymal opacities
√ ± cavitation
√ hilar lymphadenopathy (8–79%)
√ pleural thickening
◊ NO upper airway disease / glomerulonephritis / systemic vasculitis
Rx: corticosteroid therapy alone
DDx: sarcoidosis (high prevalence of mediastinal + hilar lymphadenopathy, little propensity for cavitation)

NEONATAL PNEUMONIA

Pathogenesis:
(a) in utero infection: ascending from premature rupture of membranes or prolonged labor / transplacental route) = major risk factor
(b) aspiration of infected vaginal secretions during delivery
(c) infection after birth

Organism:
(1) Group B streptococcus (GBS) = most common cause: in low–birth-weight premature infants; 50% mortality
√ pulmonary opacities (87%):
√ appearance identical to RDS (in 52%)
√ appearance suggests retained lung fluid / focal infiltrates (35%)
√ normal CXR (13%)
√ cardiomegaly (common)
√ pleural effusions (in ⅔, but RARE in RDS)
Associated with: delayed onset of diaphragmatic hernia (evidenced by clinical deterioration)
Prognosis: often lethal
(2) Pneumococci: RDS-like
(3) Listeria: RDS-like
(4) Candida: progressive consolidation + cavitation
(5) Chlamydia trachomatis: bronchopneumonic pattern
(6) *others:* H. influenzae, Staphylococcus aureus, E. coli, CMV, Pneumocystis
• afebrile, lower ventilatory pressure requirements
√ bilateral focal / diffuse areas of opacities (may initially appear similar to fetal aspiration syndrome)
√ hyperaeration
√ may cause lobar atelectasis
√ may cause pneumothorax / pneumomediastinum
√ pleural effusion (exceedingly rare)

NEUROENDOCRINE TUMOR OF LUNG

= tumors arising from Kulchitsky cells (normally present in bronchial mucosa)

Incidence: 25% of all pulmonary neoplasms

Histo: neuroendocrine morphology = organoid nesting, palisading, rosettes, trabecular growth pattern

Classification of Pulmonary Neuroendocrine Neoplasms (WHO 2004)
Histologic Categories
Low-grade malignant neoplasm
Typical carcinoid
Intermediate-grade neoplasm
Atypical carcinoid
High-grade neoplasm
Large cell neuroendocrine tumor
Small cell lung cancer (SCLC)

Classification (Travis):

1. Carcinoid (25%)
2. Large cell neuroendocrine carcinoma
3. Small cell lung cancer

Carcinoid Tumor of Lung

= NEUROENDOCRINE CARCINOMA / NEOPLASM

◊ 2nd most common location after GI tract

Frequency: 1–2% of all pulmonary neoplasms; 20–30% of all carcinoid tumors; 20–25% of all invasive primary lung cancers

◊ Most common primary pulmonary neoplasm in children!

DDx of Typical Carcinoid versus Atypical Carcinoid		
Criterion	*Typical Carcinoid (80–90%)*	*Atypical Carcinoid (10–20%)*
Path	well-differentiated	intermediate grade npl.
Histo	NO necrosis; < 2 mitoses÷10 HPFs / 2 mm^2	areas of punctate necrosis; 2–10 mitoses÷10 HPFs
Association		cigarette smoking (83–94%)
Age	younger patient; M÷F = 1÷10 (?)	~ 1 decade older patient; M÷F = 2÷1 to 3÷1
Location	central: endobronchial growth	peripheral > central
Mean size	2.3 cm	3.6 cm
Spread	rare: to lymph node in 3%	adrenal gland, brain, liver, skin, bone (osteoblastic) in 30%; lymph node (25–50%)
Prognosis	5 (10)-year survival of 87–100% (82–94%)	5 (10)-year survival of 44–88% (18–64%)

Mean age: 46 (range, 4–95) years; 4% occur in children + adolescents; M÷F = 1÷1; very uncommon in Blacks

Associated with: MEN 1 in < 4% (almost all hormonally inactive)

Path:

well-defined pulmonary nodule / mass that originates from neurosecretory cells of bronchial mucosa (= Kulchitsky cells = argentaffin cells); part of APUD (amine precursor uptake and decarboxylation) system = chromaffin paraganglioma, which produces serotonin, ACTH, norepinephrine, bombesin, calcitonin, ADH, bradykinin

Histo: neuroendocrine morphology = organoid nesting, palisading, rosettes, trabecular growth pattern; uniform cells separated by prominent vascular stroma + numerous thin-walled blood vessels

Immunohisto: positive for neuron-specific enolase, CD56, Ki-67, chromogranin A, synaptophysin

- asymptomatic (20–50%) ← peripheral tumor
- recurrent unifocal pneumonitis, hemoptysis
- wheezing, persistent cough, dyspnea, chest pain
- paraneoplastic syndromes (rare):
  (a) Cushing syndrome: in 2% of bronchial carcinoids
  (b) carcinoid syndrome: in 0.7% of pulmonary carcinoids
- endobronchial exophytic mass at endoscopy

Location:

› 70–90% in main / lobar / segmental bronchi, often near bifurcation; R÷L lung = 3÷2

Site: relationship to central bronchus
(a) completely endobronchial / endoluminal
(b) partially endoluminal ("tip of iceberg" sign)
(c) abutting airway

› 10–42% peripheral in lung parenchyma

Site: no relationship to bronchus

Average size: 3 (range, 2–5) cm; atypical carcinoid is larger + more peripheral

CXR:

√ well-defined <u>central</u> hilar / perihilar mass:
√ ± consolidation ← atelectasis / postobstructive pneumonitis / recurrent pneumonia
√ ± mucus plugging = "gloved finger" appearance

√ solitary well-defined round / ovoid <u>peripheral</u> nodule / mass distal to segmental bronchus
√ ± lobulated borders < 3 cm in size

CT:

√ spherical / ovoid polypoid nodule / mass (with long axis parallel to adjacent bronchovascular bundle):
√ well-defined slightly lobulated border
√ "bronchus sign" (= bronchus leading directly to the tumor) may allow diagnosis prospectively
√ "collar button" lesion = extension through bronchial wall involving bronchial lumen + parenchyma

√ diffuse scattered eccentric punctate calcifications / dense ossification (26–33%): central carcinoid÷peripheral carcinoid = 10%÷43%
√ cavitation (rare)
√ intense > 30 HU net enhancement ← vascular tumor supplied by bronchial circulation
√ bronchiectasis, mucoid impaction, atelectasis, air trapping
√ postobstructive pneumonia
√ hilar / mediastinal lymphadenopathy (6–25%) ← metastasis / reactive hyperplasia ← recurrent pneumonia
√ metastases in liver, bone, adrenal glands

MR:
√ mass of high T2 + STIR signal intensity
√ intense enhancement during systemic circulatory phase

NUC:
Agents: 111In-octreotide / lanreotide (short-acting / long-acting somatostatin analogs), MIBG = meta-iodobenzylguanidine (norepinephrine analog)
√ typically for staging / assessing response to therapy
√ helpful in detecting occult tumor (depending on degree of somatostatin-receptor expression rather than hormonal hypersecretion)
√ MIBG less sensitive than octreotide

PET (high false-negative rate):
√ NO (most often) / increased activity (occasionally)

Prognosis: death from valvular disease
Rx: lobectomy, pneumonectomy, endobronchial resection, bronchial sleeve resection, segmentectomy
DDx: lung cancer, pulmonary hamartoma, bronchial gland tumor, metastasis

Large Cell Neuroendocrine Carcinoma

= poorly differentiated high-grade neuroendocrine tumor as a variant of large-cell carcinoma
Prevalence: 3% of all resected lung cancers; 19% of pulmonary endocrine tumors; 12% of all large cell undifferentiated carcinomas
Histo: high mitotic rate of > 10 per 10 HPFs; large cell size, polygonal shape, low nuclear-cytoplasmic ratio, finely granular eosinophilic cytoplasm, coarse nuclear chromatin, frequent nucleoli; positive neuroendocrine marker (chromogranin A, synaptophysin, neural cell adhesion molecule [NCAM/CD56], thyroid transcription factor (TTF)-1 [41–75%], Ki-67 proliferation index [50–100%])
Mean age: 65 (range, 44–82) years; M÷F = 2.5÷1
Associated with: heavy smoking (30–62 pack-years) in 60%

- asymptomatic (25%)
- chest pain, hemoptysis, cough, dyspnea, weight loss, fever

Location: peripheral (70–80%) / central (20–30%)
Mean size: 3.7 (range, 1.3–9.2) cm

CXR:
√ 3.7-cm peripheral pulmonary mass

CT:

√ nonspecific well-defined lobulated nodule / mass:
√ ± air bronchogram, cavity, bubbly lucency, necrosis
√ intratumoral calcifications (9%)
√ homo- / heterogeneous enhancement
√ attendant atelectasis / distal mucus plugging
√ pleural effusion (24%)
PET:
√ avid FDG uptake; SUV > 13.7 suggests shortened survival
Spread: mediastinal lymphadenopathy (27%); extrathoracic metastasis (36%)
Prognosis: 5-year survival rate of 15–57%; recurrence in supraclavicular / mediastinal lymph nodes within 2 years
DDx: small cell lung cancer, atypical carcinoid

NOCARDIOSIS

Organism: Gram-positive acid-fast bacterium resembling fungus
Predisposed: immunocompromised
√ multiple poorly / well-defined nodules ± cavitation
√ lobar consolidation
√ empyema without sinus tracts
√ SVC obstruction (rare)

NODULAR LYMPHOID HYPERPLASIA

= PSEUDOLYMPHOMA = LOCALIZED MASSLIKE FORM OF LIP
= reactive benign lesion = uncommon localized lymphoid hyperplasia; no progression to lymphoma
Path: usually single involvement of small area of lung
Histo: aggregates of polymorphous large + small lymphoid cells (B and T cells); multiple germinal centers; infiltration and expansion of alveolar interstitium by lymphocytes (T cells) and plasma cells, occasional giant cell; variable fibrosis; common lymphoepithelial lesions (= invasion of bronchial epithelium by lymphoid cells)
May be associated with: collagen vascular disease, Sjögren syndrome, dysgammaglobulinemia
• mostly asymptomatic / cough, dyspnea
Location: subpleural / ± peribronchial
CXR:
√ well-demarcated dense infiltrate(s) as nodule / mass / masslike consolidation
CT:
√ infiltrate typically in central location extending to visceral pleura
√ prominent central air bronchogram
√ NO invasion of adjacent bronchus / pleural space
√ NO hilar / mediastinal lymphadenopathy
√ NO pleural effusion
Prognosis: occasionally progression to non-Hodgkin lymphoma
Rx: most patients respond well to steroids initially
Dx: surgical biopsy

DDx: LIP (diffuse involvement of lung)

NONTUBERCULOUS MYCOBACTERIAL LUNG INFECTION

= ATYPICAL TUBERCULOSIS = ATYPICAL MYCOBACTERIAL INFECTION

Organism:

M. kansasii: lung infection in subjects with good immune status
M. marinum: "swimming pool granuloma"
M. ulcerans: "Buruli ulcer" in tropical areas
M. scrofulaceum: cervical lymphadenitis in infants
M. avium intracellulare: esp. in AIDS (most common)

Organism causing pulmonary disease (Runyon classification):

ubiquitous organisms as part of normal environmental flora

1. Photochromogens M. kansasii, M. simiae, M. asiaticum
   - colonies turn yellow with exposure to light
   - ◊ 70–80% of individuals from rural areas test positive on PPD-B (= antigen from M. kansasii)!
2. Scotochromogens M. scrofulaceum, M. xenopi, M. szulgai, M. gordonae
   - yellow colonies turn orange with exposure to light
3. Nonchromogens M. avium-intracellulare, M. malmoense, M. terrae
   - white / beige colonies without color change
4. Rapid growers M. fortuitum-chelonei
   - appear in culture in 3–5 days (all other groups appear in culture in 2–4 weeks)

Histo: lesions indistinguishable from M. tuberculosis

Source: soil, water, dairy products, bird droppings

Infection: inhalation of aerosolized water droplets (M. avium-intracellulare complex), food aspiration in patients with achalasia (M. fortuitum-chelonei), GI tract (in AIDS)

- cough (60–100%), hemoptysis (15–20%), asthma, dyspnea
- fever distinctly uncommon (10–13%)
- weakness + weight loss (up to 50%)
- weekly positive tuberculin skin test

A. CLASSIC FORM

Age: 6th–7th decade; in Whites (80–90%); M > F

Predisposing factors:

COPD (25–72%), previous TB (20–24%), interstitial lung disease (6%), smoking > 30 pack-years (46%), alcohol abuse (40%), cardiovascular disease (36%), chronic liver disease (32%), previous gastrectomy (18%)

Location: apical + anterior segments of upper lobes

√ chronic fibronodular / fibroproductive apical opacities (indistinguishable from reactivation TB)
√ cavitation in 80–95%
√ apical pleural thickening in 37–56%
√ additional patchy nodular alveolar opacities in ipsi- / contralateral lung in 40–70% ← bronchogenic spread
√ adenopathy (0–4%)

√ pleural effusion (5–20%)
√ typically NO hilar elevation

B. NONCLASSIC FORM (20–30%)

Age: 7th–8th decade; 86% in Whites; M÷F = 1÷4

- chronic cough, hemoptysis, malaise, weight loss, fatigue
- older woman with thin body habitus = "Lady Windermere syndrome":
  [Oscar Wilde's Victorian-era play Lady Windermere's Fan exemplifies the fastidious behavior believed to cause the syndrome by suppressing cough and never displaying any signs of illness]
  - pectus excavatum chest wall deformity, thoracic scoliosis
  - mitral valve prolapse
- older men with chronic obstructive pulmonary disease

Predisposing factors: NONE

Location: predominantly in middle lobe + lingula

√ multiple bilateral centrilobular nodules throughout both lungs in random distribution
√ irregular curvilinear interstitial opacities
√ mild to moderate cylindrical bronchiectasis
√ atelectasis / scarring

HRCT:

√ bronchiectasis, bronchial wall thickening
√ mucoid bronchial impaction
√ scattered tree-in-bud nodules
√ areas of segmental + subsegmental atelectasis + scarring

C. ASYMPTOMATIC GRANULOMAS

√ cluster of similar-sized nodules

D. ACHALASIA-RELATED INFECTION

with M. fortuitum-chelonei

E. DISSEMINATED DISEASE

in immunocompromised patients: AIDS, transplant patients, lymphoproliferative disorders (esp. hairy cell leukemia), steroid + immunosuppressive therapy

CT:

√ multifocal bronchiectasis (79–94%), esp. middle lobe + lingula
√ centrilobular nodules of varying sizes, usually < 1 cm (= micronodules) in 76–97%
√ bronchial wall thickening (97%)
√ airspace disease (76%)
√ cavitation (21%), esp. in upper lobes
√ interlobular septal thickening (12%)

◊ Unfavorable response to antituberculous therapy is suspicious for atypical TB!

Rx: multidrug regimen typically prescribed for at least 1 year

DDx: M. tuberculosis (bronchiectasis less common + less extensive), bronchiolitis obliterans, sarcoidosis, fungal disease

PANBRONCHIOLITIS

= DIFFUSE PANBRONCHIOLITIS

= progressive inflammatory lung disease characterized by chronic inflammation of paranasal sinuses + respiratory bronchioles, prevalent in Asians but rare in Europeans + North Americans

Pathogenesis: unknown

Histo: thickening of respiratory bronchiole wall + transmural infiltration of lymphocytes + plasma cells + histiocytes

Location: predominantly in lung bases

HRCT:

√ tree-in-bud pattern = small centrilobular nodules of < 5 mm connected to centrilobular branching structures (= segments of bronchiolectasis filled with secretions)

√ bronchial wall thickening

√ mosaic perfusion

√ bronchiectasis

√ cystic lesions + air trapping (in later stage)

DDx: bronchiolitis obliterans

PARAGONIMIASIS OF LUNG

= PLEUROPULMONARY PARAGONIMIASIS

= parasitic disease caused by trematode Paragonimus (usually P. westermani = lung fluke / P. kellicotti)

Prevalence: 20.7 million infected

Endemic to: certain areas of East + Southeast Asia (China, Korea, Japan, Thailand, Laos, Philippines, India); Latin America (primarily Peru); Africa (primarily Nigeria); in US among Indo-Chinese and Latin American immigrants

Infection: ingestion of raw / incompletely cooked freshwater crustaceans (crab / crayfish) infected with metacercariae; larva exists in small intestine → penetrates intestinal wall → enters peritoneal cavity; → penetrates diaphragm + pleura → enters lung (target organ)

Cycle:

from final host (tiger, cat, dog, fox, weasel, opossum, wild boar, human) eggs of worm pass to the outside with blood-streaked sputum; in fresh water ciliated embryos (miracidia) develop → become tailed larvae (cercariae) after invading a fresh-water snail; when infected snail is eaten by a crustacean, their tails detach and they become 300 µm encysted larvae (metacercariae)

- parasitic eggs in sputum / BAL fluid / pleural fluid / feces
- intradermal and serologic tests

@ Chest

- fever, chest pain, chronic cough, hemoptysis

Location: pulmonary lesions in 83%, pulmonary + pleural lesions in 44%, pleural lesions in 17%)

Early findings (lesions occur 3–8 weeks after ingestion when organisms migrate to pleural space)

√ uni- / bilateral pneumo- / hydropneumothorax (17%)

√ uni- / bilateral pleural effusion (3–54%) / empyema ± pleural thickening

√ focal patchy migrating airspace consolidation (= worm migration causes focal exudative / hemorrhagic pneumonia) in 45%:
√ ± cavitation
√ lobar / segmental collapse ← airway obstruction from egg granuloma / intrusion of worm
√ 2–4-mm thick and 2–7-cm long linear opacities / hyperattenuation abutting the pleura (41%) ← peripheral atelectasis / worm migration track (visible in up to 50%)

CT:
√ hypoattenuating fluid-filled cysts surrounded by hyperattenuating consolidation in adjacent lung
√ mediastinal lymphadenopathy

Late findings when organisms reside and reproduce in lung parenchyma:
√ lung cyst ← cyst formation ← infarction ← arteriolar / venous obstruction by worm or egg / expansion of small airway by intraluminal parasite:
√ thick-walled cyst ← fibrosis
√ "eclipse effect" = eccentric thickening of cyst wall ← one / two intracystic worms
√ < 3 mm thin-walled cyst ← cyst connected to airway
√ 10–15-mm poorly marginated subpleural / subfissural worm cyst (= nodules + masslike consolidation in 24%):
√ cyst initially masked by pericystic airspace consolidation
√ ± cyst filled with chocolate-colored necrotic fluid of low opacity
√ adjacent bronchiectasis (35%)
√ cavity formation
√ high radiotracer uptake on PET

@ CNS
• meningoencephalitis (in 25%)
√ shell-like / soap–bubble-like calcifications of varying size (~ 50%)

Dx: eggs of parasite in sputum or in pleural / BAL fluid

DDx: tuberculosis (nodular slowly changing lesion, residual fibrosis after treatment, no subpleural linear opacities), cryptococcosis, bacterial infection with abscess formation, vasculitis

PNEUMATOCELE

= discrete thin-walled cystic air collection within lung parenchyma ← obstructive overinflation
= regional obstructive emphysema
◊ Does not indicate destruction of lung parenchyma
◊ Occurs during healing phase
◊ Appears to enlarge while patient improves
◊ Frequently multiple

Developmental theories:
(1) small bronchioles undergo severe distension ← check-valve endobronchial / peribronchial obstruction
(2) focus of necrotic lung → evacuates through a bronchus narrowed by edema / inflammation → subsequent airspace enlargement due to check-valve mechanism from enlarging

pneumatocele / inflammatory exudate

(3) air from ruptured alveoli / bronchioles dissects along interstitial interlobular tissue and accumulates between visceral pleura and lung parenchyma = subpleural emphysematous bulla = subpleural air cyst

√ well-defined thin-walled pulmonary parenchymal cyst
√ may be entirely filled with gas / air-fluid level
√ ± contralateral mediastinal shift + compressive atelectasis
Cx: rupture → tension pneumothorax

Pneumatocele Associated with Infection

Organism: Staphylococcus (in childhood), Pneumococcus, Escherichia coli, Klebsiella pneumoniae, Haemophilus influenzae
Age: infant + young child; < 3 years of age in up to 70%
√ appears within 1st week, disappears within 6 weeks
√ thin-walled + completely air-filled cavity
√ ± air-fluid level + wall thickening (during infection)
√ pneumothorax
√ spontaneous resolution over several weeks to months

Traumatic Pneumatocele = Pneumatocyst

Cause: blunt chest trauma

(a) air trapped within area of pulmonary laceration is initially obscured by surrounding contusion (hematoma):
√ pneumatocyst appears within hours after trauma
√ cyst spontaneously resolves within 3 weeks

(b) intensive inflammatory response from hydrocarbon (furniture polish, kerosene) inhalation / ingestion

√ single / multiple pneumatoceles with sparing of apices

"Pulverized Lung"

Cause: severe chest trauma
√ multiple 5–10-mm air cysts in an area of airspace opacification

PNEUMOCOCCAL PNEUMONIA

Most common Gram-positive pneumonia (90% community-acquired, 10% nosocomial)
Frequency: 15% of all adulthood pneumonias, uncommon in childhood; peaks in winter + early spring; increased during influenza epidemics
Organism: Streptococcus pneumoniae (formerly Diplococcus pneumoniae, Gram-positive, in pairs / chains, encapsulated, capsular polysaccharide responsible for virulence + serotyping)
Susceptible: elderly, debilitated, alcoholics, CHF, COPD, multiple myeloma, hypogammaglobulinemia, functional / surgical asplenia

- rusty blood-streaked sputum, left-shift leukocytosis
- impaired pulmonary function

Location: usually involves one lobe only; bias for lower lobes + posterior segments of upper

lobes ← bacteria flow under gravitational influence to most dependent portions as in aspiration

√ extensive airspace consolidation abutting against visceral pleura (lobar / beyond confines of one lobe through pores of Kohn) CHARACTERISTIC
√ slight expansion of involved lobes
√ prominent air bronchograms (20%)
√ patchy bronchopneumonic pattern (in some)
√ pleural effusion (parapneumonic transudate) uncommon with antibiotic therapy
√ cavitation (rare, with type III)

Variations (pneumonia modified by bronchopulmonary disease, eg, chronic bronchitis, emphysema):

√ bronchopneumonia-like pattern
√ effusion may be only presentation (esp. in COPD)
√ empyema (with persistent fever)
› in children:
√ round pneumonia = sharply defined round lesion

Prognosis: prompt response to antibiotics (if without complications); 5% mortality rate

Dx: blood culture (positive in 30%)

Cx: meningitis, endocarditis, septic arthritis, empyema (now rarely seen)

PNEUMOCYSTOSIS

= PNEUMOCYSTIS CARINII PNEUMONIA

◊ Most common cause of interstitial pneumonia in immuno-compromised patients, which quickly leads to airspace disease

Organism:

ubiquitous obligate extracellular protozoan / fungus Pneumocystis carinii

(a) trophozoite develops into a cyst
(b) cyst produces up to eight daughter sporozoites, which are released at maturity + develop into trophozoites

Pathomechanism:

trophozoite attaches to cell membrane of type I alveolar pneumocytes → cell death + leakage of proteinaceous fluid into alveolar space

Predisposed:

(a) debilitated premature infants, children with hypogammaglobulinemia (12%)
(b) AIDS (60–80%)
(c) other immunocompromised patients: congenital immuno-deficiency syndrome, lymphoproliferative disorders, organ transplant recipients (renal transplant patients in 10%), patients on long-term corticosteroid therapy (nephrotic syndrome, collagen vascular disease), patients on cytotoxic drugs [under therapy for leukemia (40%), lymphoma (16%)]
◊ Often associated with simultaneous infection by CMV, Mycobacterium avium-intracellulare, herpes simplex

• severe dyspnea + cyanosis over 3–5 days
• subacute insidious onset of malaise + minimal cough (frequent in AIDS patients), respiratory failure (5–30%)

- WBC slightly elevated (PMNs)
- lymphopenia (50%) heralds poor prognosis

√ normal CXR in 10–39%
√ bilateral diffuse symmetric finely granular / reticular interstitial / airspace infiltrates (in 80%) with perihilar + basilar distribution (CHARACTERISTIC central location)
√ response to therapy within 5–7 days
√ rapid progression to diffuse alveolar homogeneous consolidation (DDx: pulmonary edema)
√ air bronchogram
√ fine / coarse linear / reticular pattern = thickened coarse interstitial lung markings (in healing phase)
√ pleural effusion + hilar lymphadenopathy (uncommon)
√ <u>atypical pattern</u> (in 5%):
  √ isolated lobar disease / focal parenchymal opacities
  √ lung nodules ± cavitation
  √ hilar / mediastinal lymphadenopathy
  √ thin- / thick-walled regular / irregular cysts / cavities with predilection for upper lobes + subpleural regions
√ <u>effect of prophylactic use of aerosolized pentamidine</u>:
  √ redistribution of infection to upper lobes
  √ cystic lung disease
  √ spontaneous pneumothorax, frequently bilateral (6–7%)
  √ disseminated extrapulmonary disease (1%)
  √ punctate / rimlike calcifications in enlarged lymph nodes + abdominal viscera

CT:
  √ patchwork pattern (56%)
    = bilateral asymmetric patchy mosaic appearance with sparing of segments / subsegments of pulmonary lobe
  √ ground-glass pattern (26%)
    = bilateral diffuse / perihilar airspace disease (fluid + inflammatory cells in alveolar space) in symmetric distribution
  √ interstitial pattern (18%)
    = bilateral symmetric / asymmetric, linear / reticular markings (thickening of interlobular septa)
  √ air-filled spaces (38%):
    (a) pneumatoceles = thin-walled spaces without lobar predilection resolving within 6 months
    (b) subpleural bullae (due to premature emphysema)
    (c) thin-walled cysts (? check-valve obstruction of small airways from aerosolized pentamidine)
    (d) necrosis of PCP granuloma
  √ pneumothorax (13%)
  √ lymphadenopathy (18%)
  √ pleural effusion (18%)
  √ pulmonary nodules usually due to malignancy (leukemia, lymphoma, Kaposi sarcoma,

metastasis) / septic emboli
√ pulmonary cavities / cyst formation (chronic) usually due to superimposed fungal / mycobacterial infection

NUC:
√ bilateral and diffuse 67Ga uptake without mediastinal involvement prior to roentgenographic changes
DDx: TB / MAI infection (with mediastinal involvement)

Dx: (1) Sputum collection
(2) Bronchoscopy with lavage
(3) Transbronchial / transthoracic / open lung Bx

Prognosis: rapid fulminant disease; death within 2 weeks

Rx: co-trimoxazole IV, nebulized pentamidine

PNEUMONECTOMY CHEST

Early signs (within 24 hours):
√ partial filling of thorax
√ ipsilateral mediastinal shift + diaphragmatic elevation

Late signs (after 2 months):
√ complete obliteration of space

N.B.: Depression of diaphragm / shift of mediastinum to contralateral side indicates a bronchopleural fistula / empyema / hemorrhage!

POLAND SYNDROME

= congenital chest wall anomalies

May be associated with: hypo- / aplasia of mamilla / breast

Autosomal recessive

√ unilateral partial / complete absence of muscles:
› pectoralis major (absence of sternocostal head) + minor
› latissimus dorsi
› serratus anterior
› intercostal muscles

√ ipsilateral syndactyly + brachydactyly

√ hypoplasia / absence of ribs

√ ± scoliosis

POSTOBSTRUCTIVE PNEUMONIA

= chronic inflammatory disease distal to bronchial obstruction; despite the name coexistent infection is uncommon

Cause:
1. Bronchogenic carcinoma (most commonly)
2. Bronchial adenoma
3. Granular cell myoblastoma (almost always tracheal lesion)
4. Bronchostenosis

Histo: "golden pneumonia" = cholesterol pneumonia = endogenous lipid pneumonia ←

mixture of edema, atelectasis, round cell infiltration, bronchiectasis, liberation of lipid material from alveolar pneumocytes ← inflammatory reaction

√ frequently associated with some degree of atelectasis
√ persists unchanged for weeks
√ recurrent pneumonia in same region after antibiotic Rx

PRIMARY PULMONARY LYMPHOMA

= monoclonal lymphoid proliferation within lung parenchyma

Frequency of primary lung lymphomas:

› MALT lymphoma (most common)
› diffuse large B-cell NHL (2nd most common)
› Hodgkin disease (least common)

Pulmonary MALT Lymphoma

= low-grade marginal zone B-cell lymphoma of mucosa-associated lymphoid tissue

◊ Most common type of lymphoma involving the pulmonary parenchyma (in up to 90%)

Prevalence: 3–4% of extranodal lymphomas; 1% of lung malignancies

Cause: chronic inflammation of bronchus-associated lymphoid tissue (BALT)

Age: 6th decade

Associated with:
autoimmune disease (eg, Sjögren syndrome, rheumatoid arthritis, immunodeficiency); chronic inflammation from smoking; infections (eg, HIV, hepatitis C)

Histo: sheets of monoclonal lymphocytes + occasional interspersed plasma cells (containing intranuclear inclusions of immunoglobulins = Dutcher bodies); often additional cells causing confusion, like giant cells, granulomas, reactive germinal centers

• cough, dyspnea, hemoptysis, weight loss
• asymptomatic (50%)

Location: bi- / unilateral

√ multiple nodules / masses / consolidations
√ areas of ground-glass attenuation / consolidation in bronchovascular distribution
√ air bronchograms (frequent) ± dilatation
√ patchy large areas of ground-glass attenuation throughout lungs (rare)
√ mosaic attenuation ← infiltration along airways
√ hilar / mediastinal lymphadenopathy (in up to 30%)
√ pleural effusions (uncommon)
√ hypermetabolic at PET/CT (50%)

Prognosis: 84–88% 5–10-year survival rate

DDx: granulomatosis with polyangiitis (= Wegener granulomatosis), sarcoidosis, perilymphatic spread of metastatic disease, infection

PSEUDOMONAS PNEUMONIA

= most dreaded nosocomial infection because of resistance to antibiotics in patients with debilitating diseases on multiple antibiotics + corticosteroids; rare in community

Organism: Pseudomonas aeruginosa, Gram-negative
- bradycardia, temperature with morning peaks

√ widespread patchy bronchopneumonia ← bacteremia (unlike other Gram-negative pneumonias)
√ predilection for lower lobes
√ extensive bilateral consolidation
√ "spongelike pattern" with multiple nodules > 2 cm (= extensive necrosis with formation of multiple abscesses)
√ small pleural effusions

PULMONARY ARTERIAL MALFORMATION

= PULMONARY ARTERIOVENOUS ANEURYSM = PAVM
= PULMONARY ARTERIOVENOUS FISTULA = PULMONARY ARTERIOVENOUS MALFORMATION = PULMONARY ANGIOMA = PULMONARY TELANGIECTASIA

= abnormal vascular communication between pulmonary artery and vein (95%) or systemic artery and pulmonary vein (5%)

Etiology:
(a) congenital defect of capillary structure (common)
(b) acquired in cirrhosis (hepatogenic pulmonary angiodysplasia), cancer, trauma, surgery (Glenn and Fontan procedure), schistosomiasis, actinomycosis, TB (Rasmussen aneurysm)

Path: hemangioma of cavernous type

Pathophysiology:
low-resistance extracardiac R-to-L shunt (which may result in paradoxical embolism); quantification with ^{99m}Tc–labeled albumin microspheres by measuring fraction of dose reaching kidneys

Age: 3rd–4th decade; manifest in adult life, 10% in childhood

Occurrence:
(a) isolated single abnormality (in ⅔)
(b) multiple (in ⅓)
Associated with: Rendu-Osler-Weber syndrome (in 30–60–88%) = hereditary hemorrhagic telangiectasia
◊ 15–50% of Rendu-Osler-Weber patients have pulmonary AVMs!

Types:
1. Simple type (79%)
   = single feeding artery empties into a bulbous nonseptated aneurysmal segment with a single draining vein
2. Complex type (21%)
   = more than one feeding artery empties into a septated aneurysmal segment with more than one draining vein

- asymptomatic in 56% (until 3rd–4th decade) if AVM single and < 2 cm
- orthodeoxia = with lesion in lower lobes increase in arterial hypoxemia (= PaO_2 < 85 mmHg) in erect position ← L-to-R shunting larger in sitting or standing position ← gravitational shift of pulmonary blood flow to base of lung
- cyanosis with normal-sized heart (R-to-L shunt) in 25–50%, clubbing

- audible bruit over lesion (increased during inspiration)
- dyspnea on exertion (60–71%), tachypnea, palpitation, chest pain, hemoptysis (10–15%); No CHF

Location: lower lobes (60–70%) > middle lobe > upper lobes; bilateral (8–20%); medial third of lung

√ "coin lesion" = sharply defined, lobulated oval / round mass (90%) of 1 to several cm in size
√ cordlike bands from mass to hilum (= feeding artery + draining veins)
√ enlargement with advancing age
√ change in lesion size:
  √ decrease: expiration, Valsalva maneuver, recumbent position
  √ increase: inspiration, Müller maneuver (= forced inspiration against a closed glottis after full expiration), erect position
√ phleboliths (occasionally)
√ increased pulsations of hilar vessels

CT (98% detection rate):
  √ homogeneous circumscribed noncalcified nodule / serpiginous mass up to several cm in diameter
  √ vascular connection of mass with enlarged feeding artery + draining vein
  √ sequential enhancement of feeding artery + aneurysmal part + efferent vein on dynamic CT

MR (if contraindication to contrast material / if flow slow due to partial thrombosis / for follow-up):
  √ irregular T2-hypointense lesion, usually adjacent to hilum
  √ signal void on standard spin echo / high SI on GRASS images

Angio (mostly obviated by MR / CT unless surgery or embolization contemplated):
  ◊ 100% sensitive for detection of vessels > 2 mm

Cx: CNS symptoms are commonly the initial manifestation
  (1) Cerebrovascular accident: stroke (18%), transient ischemic attack (37%) ← paradoxical bland emboli
  (2) Brain abscess (5–9%) ← loss of pulmonary filter function for septic emboli
  (3) Hemoptysis (13%) ← rupture of PAVM into bronchus, most common presenting symptom
  (4) Hemothorax (9%) ← rupture of subpleural PAVM
  (5) Polycythemia

Prognosis: 26% morbidity, 11% mortality

Recommendation: screening of first-degree relatives

DDx: solitary / multiple pulmonary nodules

Rx: embolization with coils / detachable balloons

PULMONARY CAPILLARY HEMANGIOMATOSIS

= bilateral pulmonary disease behaving like a low-grade nonmetastatic vascular neoplasm with slowly progressive pulmonary hypertension

Histo: sheets of thin-walled capillary blood vessels infiltrating pulmonary interstitium + invading pulmonary vessels, bronchioles, and pleura

Pathomechanism of pulmonary hypertension (pHTN):

(a) venoocclusive phenomenon ← invasion of small pulmonary veins
(b) progressive vascular obliteration ← in situ thrombosis + infarction
(c) pulmonary scar formation ← recurrent pulmonary hemorrhage

Age: 20–40 years

- cor pulmonale: jugular venous distension, pedal edema, ECG signs of RV failure (DDx: pulmonary venoocclusive disease)
- elevated PA pressures + normal pulmonary wedge pressure
- dyspnea on exertion; hemoptysis + pleuritic chest pain in ⅓ (DDx: pulmonary thromboembolic disease)

CXR:
√ diffuse reticulonodular pattern
√ focal areas of interstitial fibrosis (recurrent episodes of pulmonary hemorrhage + thrombotic infarction)

CT:
√ thickening + nodularity of interlobular septa + walls of pulmonary veins
√ poorly defined centrilobular ground-glass nodules
√ pleural effusions
√ lymphadenopathy

Angio:
√ combination of increased flow (to hemangiomatous areas) + decreased flow (to regions of thrombosis, infarction, and scarring)

Prognosis: death after 2–12-year interval from onset of symptoms

Rx: bilateral lung transplantation

Pulmonary capillary hemangiomatosis may develop fatal pulmonary edema if treated with vasodilators!

Dx: open lung biopsy → extremely hazardous with pHTN

DDx: (1) Pulmonary venoocclusive disease
(2) Idiopathic interstitial fibrosis
(3) Primary pulmonary hypertension (no increase in lung markings)
(4) Pulmonary hemangiomatosis (only in children, cavernous hemangiomas involving several organs)

PULMONARY INFARCTION

= ischemic coagulative necrosis of lung parenchyma

Frequency: rare due to protective effect of collateral blood flow from bronchial circulation

Path: dark necrotic material (with faint ghostlike structures of lung tissue remaining evident on histology) surrounded by a narrow rim of hyperemia + inflammation

Cause: pulmonary artery occlusion (medium- to small-sized vessel)

Pathogenesis:
ischemic capillary endothelial injury → increased vascular permeability + reperfusion via bronchial circulation causes intraalveolar extravasation of blood cells in a confined area with possible progression to infarction

Co-condition to progress to infarction:
CHF, high embolic burden, underlying malignancy, diminished bronchial flow (due to shock, hypotension, chronically impaired circulation), vasodilator use, elevated pulmonary venous

pressure, interstitial edema

Prognosis: replacement by vascular fibrous tissue folding into a collagenous platelike mass → pleural retraction

PULMONARY INTERSTITIAL EMPHYSEMA

= PIE = complication of respirator therapy with PEEP

Pathogenesis:

gas escapes from overdistended alveolus → dissects into perivascular sheath surrounding arteries, veins, and lymphatics → tracks into mediastinum forming clusters of blebs

• sudden deterioration in patient's condition during respiratory Rx

√ meandering tubular + cystic lucencies following distribution of bronchovascular tree

√ bilateral symmetrical distribution

√ pseudocysts (localized form of PIE) = multiple circular well-defined air collections with uniformly thin walls

Location: right parahilar region

√ lobar overdistension (occasionally)

Cx: (1) pneumothorax (77%) ← rupture of cyst
(2) pneumomediastinum (37%)
(3) subcutaneous emphysema, pneumopericardium, intracardiac air, pneumoperitoneum, pneumatosis intestinalis
(4) **air-block phenomenon** = buildup of pressure in mediastinum / pericardial tamponade impeding blood flow in low-pressure pulmonary veins → diminished blood return to heart (obstruction esp. during expiration); esp. common in neonatal period
√ microcardia

Rx: (1) High-frequency jet / oscillatory ventilation
(2) Placing affected side of infant down for 24–48 hours
(3) Selective bronchial intubation

DDx: air bronchograms (branching / tapering)

PULMONARY LANGERHANS CELL HISTIOCYTOSIS

= PLCH = LCH

= rare pulmonary disorder that typically affects the young adult in isolation and is associated with cigarette smoking

Associated with: extrapulmonary manifestation (in 5–15%):
bone lesions, diabetes insipidus (10–25%), skin lesions

Prevalence: in 3.4% of chronic diffuse infiltrative lung disease

Incidence: 0.05–0.50÷100,000 per year

Age: most frequently in 3rd–5th decade (range, 3 months to 69 years); M÷F = 1÷1; Caucasians >> Blacks
◊ All children with PLCH show multisystem involvement
◊ In 30% of adolescents with PLCH lung affected alone

Pathogenesis:

heavy cigarette smoking in young men → accumulation + activation of Langerhans cells (in

90–100% current / former smokers) as a result of excess neuroendocrine cell hyperplasia + secretion of bombazine-like peptides

◊ 90–100% of patient with PLCH smoke

◊ 3–5% of smokers get PLCH

Path:

multifocal granulomatous infiltration centered on walls of bronchioles (= bronchiolitis) often extending into surrounding alveolar interstitium (< 1 cm) → bronchiolar destruction → thick-walled cysts presumably caused by check-valve bronchial obstruction + pneumothorax (NO necrosis); in end-stage disease foci of PLCH are replaced by fibroblasts forming CHARACTERISTIC stellate "starfish" scars with central remnants of persisting inflammatory cells

- asymptomatic (in up to 25%); occasionally crackles + wheezes
- nonproductive cough (75%), dyspnea (40%)
- normal or mild obstructive / restrictive / mixed abnormalities on pulmonary function tests
- ↓ CO diffusing capacity (in up to 90%)
- constitutional symptoms (in up to ⅓): fatigue, fever, night sweats, weight loss, anorexia
- chest pain (15–25%) ← spontaneous pneumothorax / eosinophilic granuloma in rib
- lymphocytosis with predominance of T-suppressor cells on bronchoalveolar lavage (DDx: excess of T-helper cells in sarcoidosis)

Location: usually bilaterally symmetric, upper + mid lung predominance, sparing of bases + costophrenic angles

Evolutionary sequence on radiography:

nodule → cavitated nodule → thick-walled cyst → thin-walled cyst (secondary to progressive enlargement + air trapping of original cavitary nodule)

◊ CXR abnormalities more severe than clinical symptoms + pulmonary function tests!

√ diffuse fine reticular / reticulonodular pattern ← cellular infiltrate with predilection for apices:

√ nodules 1–10 mm (granuloma stage):

√ ill-defined / stellate with irregular borders

√ cavitation of large nodules (in up to 10%)

√ may develop into "honeycomb lung" = multiple 1–5-cm cysts + subpleural blebs (fibrotic stage)

√ lung volume increased in ⅓ or normal (DDx: most other interstitial lung diseases have decreased lung volumes!)

√ pleural effusion (8%), hilar adenopathy (unusual)

√ thymic enlargement ← infiltration

CT (CLASSIC manifestation):

√ < 10-mm small cysts with varying wall thickness → often coalescing to form irregular larger cysts / bullae

√ multiple small scattered bilateral peribronchiolar nodules with early signs of cavitation

HRCT:

The combination of nodules + cysts in correlation with demographic + clinical factors are considered DIAGNOSTIC for PLCH and obviate a lung biopsy.

√ complex / branching perivascular thin-walled (< 1 mm) cysts individually < 5 mm in size:

√ confluent contiguous cysts 2–3 cm in size
√ equally distributed in central + peripheral zones of upper + mid lung while sparing the bases
◊ As cysts become more numerous in later stages nodules occur less frequently!
√ thick-walled cysts
√ 1–5-mm centrilobular ± cavitary nodules with irregular borders in peribronchiolar distribution associated with cysts
√ fine reticular opacities (50%)
√ ground-glass opacities
√ perivascular honeycombing
√ thickening of bronchovascular bundles + interlobular septa
√ intervening lung appears normal

DDx for nodules:
sarcoidosis, hypersensitivity pneumonitis, berylliosis, TB, atypical TB, metastases, silicosis, coal worker's pneumoconiosis

DDx for cysts:
emphysema (no definable wall), bronchiectasis (communicating branching pattern), idiopathic pulmonary fibrosis, lymphangio-myomatosis (almost exclusively in women, diffuse involvement of entire lung)

DDx: sarcoidosis (equal sex distribution, always multisystem disease, not related to smoking, erythema nodosum, bilateral hilar lymphadenopathy, lung cavitation + pneumothorax rare, epithelioid cells)

Cx:
1. Recurrent pneumothoraces in 25% (from rupture of subpleural cysts) CHARACTERISTIC
2. Pulmonary hypertension ← severe diffuse pulmonary vasculopathy involving pulmonary muscular arteries and interlobar veins
3. Superimposed Aspergillus fumigatus infection

Prognosis: poor with multisystem disease + organ dysfunction (especially with skin lesions)
(a) complete / partial regression (50%)
(b) stable symptoms of variable severity (30–40%)
(c) rapid progression (10–20%) to air-flow obstruction + impaired diffusing capacity + respiratory failure + cor pulmonale
◊ May recur in transplanted lung if smoking is continued or resumed!

Mortality: 2–25%

Rx: smoking cessation; chemotherapy (vincristine sulfate, prednisone, methotrexate, 6-mercaptopurine); lung transplant

PULMONARY MAINLINE GRANULOMATOSIS

= PULMONARY TALCOSIS

= pulmonary microembolism in drug addicts ← chronic IV injection of suspensions prepared from crushed tablet compounds (talc is a common insoluble additive)

Drugs: amphetamines, methylphenidate hydrochloride ("West coast"), tripelen amine ("blue velvet"), methadone hydrochloride, Dilaudid®, meperidine, pentazocine, propylhexedrine, hydromorphone hydrochloride

Pathogenesis: talc (= magnesium silicate) particles incite a pronounced granulomatous foreign-body reaction + subsequent fibrosis in perivascular distribution

Path: multiple scattered whitish nodules of 0.3–3 mm converging into gritty fibrotic masses in central + upper lungs measuring several cm in diameter

Histo: widespread granulomas packed with doubly refractile talc particles expanding the walls of muscular pulmonary arteries and arterioles + perivascular connective tissue + alveolar septa

- talc retinopathy (80%) = small glistening crystals
- angiothrombotic pulmonary hypertension + cor pulmonale

Early changes:

√ widespread micronodularity of "pinpoint" size (1–2–3 mm) with perihilar / basilar predominance

√ well-defined nodules predominantly in middle zones

Late changes:

√ loss of lung volume of upper lobes + hilar elevation + hyperlucency at lung bases

√ indistinctly marginated coalescent opacities similar to progressive massive fibrosis (DDx: in silicosis slightly further away from pulmonary hila + distinct margin)

Cx: mycotic pulmonary artery aneurysm; right-sided endocarditis with septic emboli; chronic respiratory failure; emphysema; systemic talc breakthrough to liver + spleen + kidneys + retina

DDx of late changes:

(1) Progressive massive fibrosis of silicosis / coal worker's pneumoconiosis
(2) Chronic sarcoidosis

Dx: lung biopsy

PULMONARY THROMBOEMBOLIC DISEASE

= PULMONARY EMBOLISM (PE)

Incidence: 600,000 Americans / year (0.23%) with missed / delayed diagnosis in 400,000, causing death in 100,000; diagnosed in 1% of all hospitalized patients; in 12–64% at autopsy; in 9–56% of patients with deep venous thrombosis

Age: 60% > 60 years of age

Cause: deep vein thrombosis (DVT) of extremities / pelvis (> 90%), right atrial neoplasia / thrombus, thrombogenic intravenous catheters, endocarditis of tricuspid / pulmonic valves

Time of onset: PE usually occurs within first 5–7 days of thrombus formation

Predisposing factors:

primary thrombophlebitis (39%), immobilization (32%), recent surgery (31%), venous insufficiency (25%), recent fracture (15%), myocardial infarction (12%), malignancy (3–8%) with higher frequency in gynecologic malignancies + melanoma (hypercoagulability ← direct thrombogenic effects of malignancy / chemotherapy), CHF (5%), no predisposition (6%)

Pathophysiology: A clot from the deep veins of the leg breaks off → fragments in right side of heart → showers lung with emboli of varying size

◊ On average > 6–8 vessels are embolized!

◊ Clinical presentation is protean + nonspecific!

◊ False-positive clinical diagnosis in 62%

- Classic triad (< 33%):
  (1) Hemoptysis (25–34%)
  (2) Pleural friction rub
  (3) Thrombophlebitis
  - symptoms (nonfatal PE versus fatal PE):
    - pleuritic chest pain (88% versus 10%)
    - acute dyspnea (84% versus 59%)
    - apprehension (59% versus 17%)
    - cough (53% versus. 3%); hemoptysis (30% versus. 3%)
    - sweats (27% versus. 9%); syncope (13% versus 27%)
  - signs (nonfatal PE versus fatal PE):
    - respiratory rate > 16 (92% versus. 66%)
    - rales due to loss of surfactant (58% versus 42%)
    - tachycardia > 100 bpm (44% versus 54%)
    - temperature > 37.8°C (43% versus 30%)
    - diaphoresis (36% versus 10%)
    - heart gallop (34% versus 10%); phlebitis (32% versus 7%)
    - heart murmur (23%); cyanosis (19% versus 12%)
  - ECG changes (83%), mostly nonspecific: P-pulmonale, right-axis deviation, right bundle branch block, classic S1Q3T3 pattern
  - elevated levels of fibrinopeptide-A = small peptide split off of fibrinogen during fibrin generation
  - positive D-dimer assay (generated during clot lysis)

Location of PE: bilateral emboli (in 45%), R lung only (36%), L lung only (18%); multiple emboli (3–6 on average) in 65%

Distribution: RUL (16%), RML (9%), RLL (25%), LUL (14%), LLL (26%)

Site: central = segmental / larger (in 58%);
peripheral = subsegmental / smaller (in 42%);
in subsegmental branches <u>exclusively</u> (in 30%)

◊ Emboli are occlusive in 40%!

A. EMBOLISM WITHOUT INFARCTION (90%)
Histo: hemorrhage + edema

B. EMBOLISM WITH INFARCTION (10–60%)
= any opacity developing as a result of thromboembolic disease; more likely to develop in presence of cardiopulmonary disease with obstruction of pulmonary venous outflow (diagnosed in retrospect)

Clinical Probability of PE: Wells Score	
Variable	*Points*
clinically suspected DVT	3.0
alternative diagnosis is less likely than PE	3.0
tachycardia	1.5
immobilization / surgery in previous four weeks	1.5
history of DVT or PE	1.5
hemoptysis	1.0
malignancy (treatment for within 6 months, palliative)	1.0
Interpretation	
Score > 6.0	High (59% probability)
Score 2.0 to 6.0	Moderate (29% probability)
Score < 2.0	Low (15% probability)

Histo: (1) incomplete infarction = reversible transient hemorrhagic congestion / edema usually resolving over several days to weeks
(2) complete infarction = hemorrhagic infarction with necrosis of lung parenchyma remaining permanently

Prognosis: majority of pulmonary thromboemboli resolve with appropriate therapy

Acute Pulmonary Thromboembolism

◊ Hypertension disappears as emboli lyse

Mortality:

3÷1,000 surgical procedures; 200,000 deaths in 1975; 7–10% of all autopsies (death within first hour of PE in most patients); 26–30% if untreated; 3–10% if treated; 50–58% / 8–15% with hemodynamic instability / stability

◊ Healthy patients may survive obstruction of 50–60% of vascular bed, fatal if > 60% of pulmonary bed obstructed

- sudden onset of chest pain, acute dyspnea
- hemoptysis occasionally
- enzyme-linked immunosorbent D-dimer assay test (detects one of the products of fibrin breakdown) > 500 µg/L

Assessment of severity of PE:

ECG:

√ straightening / leftward bowing of IVS
√ paradoxical motion of interventricular septum
√ "empty LV" appearance = ↓ LV volume
√ loss of inspiratory collapse of IVC
√ tricuspid regurgitation + dilatation of PA
√ McConnell sign = regional RV wall motion abnormality with sparing of apex

CT:

√ RV÷LV diameter ratio > 1 on 4-chamber view
√ leftward septal bowing (with RV wall < 6 mm thick)
√ ↑ size of azygos v. + SVC ← ↑ R heart pressure

√ contrast reflux into IVC ← tricuspid valve insufficiency

CXR (33% sensitive, 59% specific):

◊ Abnormal nonspecific CXR in 84%; a normal CXR has a negative predictive value of only 74%!

√ general findings (patients with PE versus no PE):

√ atelectasis / infiltrate (68% versus 48%)
√ pleural effusion (48% versus 31%)
√ pleural opacity (35% versus 21%)
√ elevated diaphragm (24% versus 19%)
√ decreased vascularity (21% versus 12%)
√ prominent pulmonary artery (17% versus 28%)
√ cardiomegaly (12% versus 11%)
√ pulmonary edema (4% versus. 13%)

√ local findings:

√ Westermark sign = area of oligemia in 2–7% ← vasoconstriction distal to embolus
√ Fleischner sign = local widening of artery by impaction of embolus ← distension by clot / developing pulmonary hypertension ← peripheral embolization
√ "knuckle" sign = abrupt tapering of an occluded vessel distally
√ Fleischner lines = long-line shadows (fibrotic scar) from invagination of pleura at the base of the collapse resulting in pseudofissure
√ Hampton hump = segmentally distributed pleura-based shallow wedge-shaped consolidation with base against pleural surface + convex medial border:
√ NO air-bronchogram ← hemorrhage into alveoli
√ ± cavitation
√ "melting" sign = within few days to weeks regression from periphery toward center
√ subsequent nodular / linear scar

√ thoracentesis: bloody (65%), predominantly PMNs (61%), exudate (65%)

NECT (purpose):

√ depiction of acute changes of PE:

√ atelectasis / linear bands (100%)
√ pleural effusion (87%)
√ consolidation (57%)
√ ground-glass opacification (57%)
√ Hampton's hump (50%)
√ intraluminal area of high attenuation (= hyperdense artery) measuring 33 ± 15 HU
√ dilated central / segmental pulmonary artery

√ depiction of chronic changes of PE
√ chest findings leading to alternative diagnosis
√ localization of volume-of-interest for CECT

CT angio (method of choice):

N.B.: CT (2.2–6.0 mSv) has a 1.6–4.3 times higher radiation dose than a V/Q scan (1.4 mSv)!

◊ Helical CT equal to angio in detection of emboli within proximal arteries of ≤ 5th / 6th generation
◊ Subsegmental intraluminal filling defects (in 2–30%) usually not detectable!

◊ Detection poor in middle lobe + lingular branches (in 18%)!

N.B.: evaluate the vessel adjacent to a bronchus

√ complete filling defect of low attenuation occupying entire arterial section creating convex interface with the contrasted lumen

√ ± enlargement of thrombosed artery

√ "railway track" sign = partial filling defect = embolus floating freely within lumen surrounded by areas of intravascular contrast enhancement

√ eccentric mural filling defect forming acute angles with arterial wall

√ RV dysfunction (ratio RV÷LV ≥ 1÷1)

Pseudo-filling defects:

(1) Breathing artifact in tachypneic patient
(2) Too short / long scanning delay
(3) Unilateral increase in vascular resistance
(4) R-to-L shunt
(5) Window setting
(6) Partial voluming

Anatomic pathologic mimics:

(1) Peribronchial lymph node
(2) Unopacified veins
(3) Mucus-filled bronchi
(4) Perivascular edema

Technical failure rate: 3–4% due to severe dyspnea

CT of lung parenchyma:

√ peripheral wedge-shaped area of infarct / hemorrhage in arteries of < 3 mm in diameter

√ linear parenchymal band

MR:

√ filling defect in pulmonary artery on coronal contrast-enhanced 3-D maximum intensity projection

Angio (> 95% sensitive & specific):

Indication for pulmonary angiography:

(1) Indeterminate V/Q scan with high clinical suspicion + risky anticoagulation therapy (angio within 24 hours)
(2) Mismatch between interpretation + clinical findings
(3) Significant risk for anticoagulation + high probability for PE
(4) Specific diagnosis necessary for proper management (vasculitis, drug induced, lung cancer with predominant vascular involvement)
(5) Prior to intervention: pulmonary embolectomy, caval ligation, caval filter placement
(6) Patients too ill to undergo V/Q scan

Technique: AP & ipsilateral posterior oblique projection

√ intraluminal defect (94%)

√ abrupt termination of pulmonary arterial branch

√ pruning + attenuation of branches

√ wedge-shaped parenchymal hypovascularity

√ absence of draining vein in affected segment

√ tortuous arterial collaterals

Risks of pulmonary angiography:

(1) left bundle branch block: requires temporary pacing wire prior to right heart catheterization

(2) marginal cardiac function: therapy must be available to treat frank pulmonary edema

(3) Right ventricular end diastolic pressure > 20 mmHg: selective catheterization with occlusion balloon

Cx of pulmonary angiography (1–2%):

arrhythmia, endocardial injury, cardiac perforation, cardiac arrest, contrast reaction

Mortality rate of pulmonary angiography: 0.2–0.5%

Clinical Classification of Pulmonary Thromboembolic Disease according to Severity

Signs & Symptoms	*Class 1*	*Class 2*	*Class 3*	*Class 4*
Occlusion of pulmonary arteries	< 20%	20–30%%	30–50%	> 50%
Symptoms	asymptomatic	anxiety, hyperventilation	dyspnea, collapse	shock, dyspnea
Arterial pO_2	normal	< 80 torr	< 65 torr	< 50 torr
Arterial pCO_2	normal	< 35 torr	< 30 torr	< 30 torr
Central venous pressure	normal	normal	elevated	elevated
Mean PA pressure	normal	–	–	> 20 mmHg
Systolic blood pressure	normal	–	–	< 100 mmHg

False-negative rate:

1–4–9% due to difficulty in visualizing subsegmental emboli (with only 30% interobserver agreement about presence of subsegmental emboli)

NUC (V/Q scan = guide for angiographic evaluation) interpreted in reference to Biello or PIOPED criteria:

Indication:

(1) Allergy to iodinated contrast media

(2) Renal insufficiency

(3) Weight limit of CT table exceeded

√ low- / intermediate-probability scans in 50–70%:

◊ results in recommending additional studies; although only 12–14% will undergo angiography

◊ 25–30% disagreement between expert readers in interpreting intermediate- and low-probability V/Q scans

√ high-probability scan: in 12% normal angiogram

N.B.: V/Q abnormalities vary over time ← autoregulation (hypoxic vasoconstriction, hypercapneic bronchoconstriction) and resolution

Prognosis:

◊ Resolution less favorable with increasing age + cardiac disease

◊ Resolution improved with urokinase > heparin

(a) total resolution (90%) within 30 days after treatment ← mechanical fragmentation + endogenous fibrinolysis

(b) no resolution in 10%: organization of thromboembolus leading to retraction with total / partial obstruction, recanalization, stenosis, fibrous webs / cords and vessel atrophy

Cx: pulmonary arterial hypertension (in 4%)

Rx:

1. Heparin IV: 10,000–15,000 units as initial dose; 8,000–10,000 units/hour during diagnostic evaluation; continued for 10–14 days
2. Streptokinase: better results with massive PE
3. Urokinase: slightly better than streptokinase
4. Coumadin: maintained for at least 3 months (15% complication rate)

Acute Pulmonary Embolism in Pregnancy

Risk: increased x 4 during pregnancy

- D-dimer frequently elevated

◊ Lung scintigraphy + CTA have comparable diagnostic performances

Indeterminate results in 19%:

similar for V/Q scan and CTA (mostly poor arterial opacification ← increase in maternal blood volume)

Advantage of CT over Lung Scintigraphy:

(1) Better interobserver agreement

(2) Unsuspected alternative diagnosis in 12 % (eg, bronchopneumonia, pericardial effusion)

Dose comparison CT versus V/Q:

(a) radiation exposure of mother

› mean dose from CTA (7.3 mSv) is higher than for lung scintigraphy (0.9 mSv)

› CTA (10–70 mGy) has a higher dose to breast than low-dose perfusion scan (0.11–0.30 mGy)

(b) radiation exposure of fetus

V/Q scan (640–800 mSv) has a 5–267 times higher radiation dose than a CT scan (3–131 mSv) during all trimesters!

Iodine exposure: contrast during pregnancy

Chronic Pulmonary Thromboembolism

= CHRONIC THROMBOEMBOLIC DISEASE

Frequency: 1–5% of patients with acute pulmonary thromboembolism, especially in patients with large emboli / recurrent episodes

At risk: underlying malignancy, cardiovascular disease, pulmonary disease, splenectomy, ventriculoatrial shunt for hydrocephalus, permanent central venous line, chronic inflammatory bowel disease, myeloproliferative syndromes; M < F

Path: fibrous webs and bands (= organized thromboemboli), often with overlying recent thrombosis; embolic material is incorporated into vessel wall + covered over by a thin layer of endothelial cells

Pathogenesis:

patent pulmonary arteries develop medial hypertrophy + intimal thickening + atherosclerotic plaques in response to pressure elevation; bronchial arteries may dilate + form extensive collateral pathways to minimize areas of lung infarction

- may be clinically silent / asymptomatic for years ("honeymoon period")

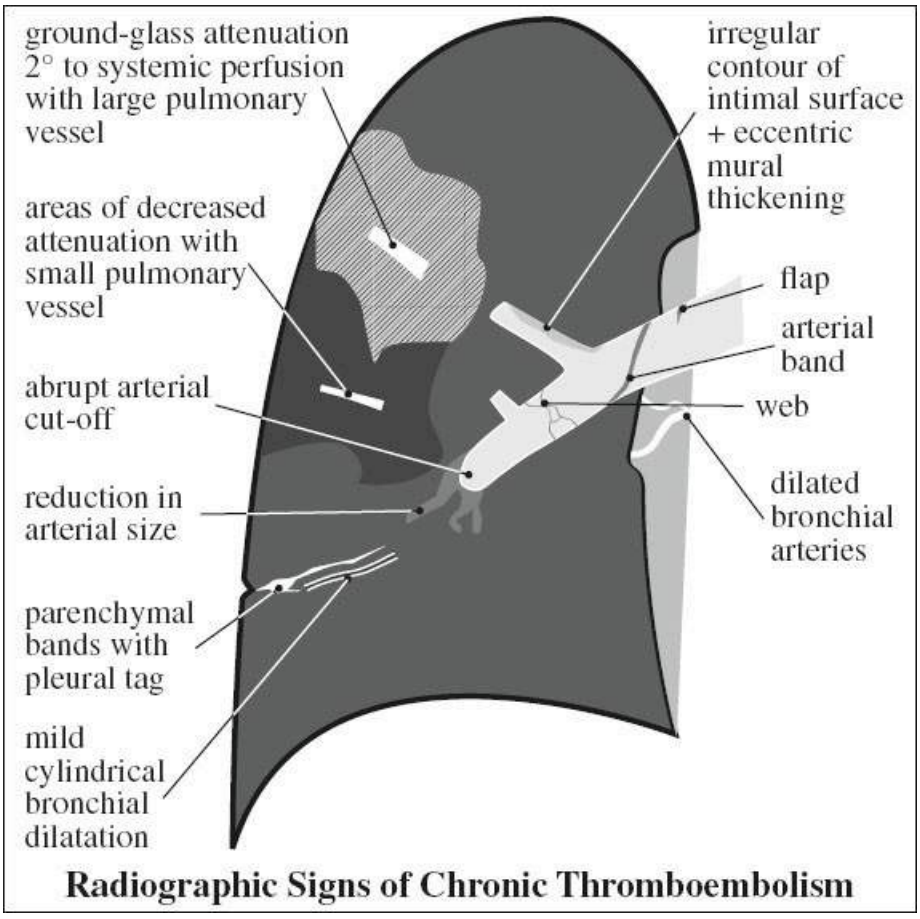
◊ To become symptomatic at least 60% of the arterial bed must be obstructed!

- history of previous embolic episodes; 63% lack a history of acute thromboembolism
- recurrent acute / gradual progressive exertional dyspnea (DDx: interstitial lung disease)

- chronic nonproductive cough, atypical chest pain
- tachycardia, syncope
- loss of RV functional capacity: elevated pulmonary arterial pressure (36–78 mmHg), normal pulmonary capillary wedge pressure; high right atrial pressures, reduced cardiac output
- lupus anticoagulant = anticardiolipin (11–24%)
- elevated plasma levels of thrombophilic factors (factor VIII + antiphospholipid antibodies)

CXR:

√ prominence of right side of heart
√ asymmetric enlargement of central pulmonary arteries
√ oligemic vascularity in patchy distribution
√ triangular / rounded opacity + adjacent pleural thickening ← pulmonary infarction
√ patchy bilateral perihilar alveolar opacities of "reperfusion edema" after thrombendarterectomy



Radiographic Signs of Chronic Thromboembolism

CT angio (77% sensitive):

◊ CT angio rivals conventional angiography!
@ Heart
√ enlargement + hypertrophy of RA + RV:
√ RV myocardial thickness > 4 mm
√ cardiomegaly ← chamber dilatation

- √ transverse diameter of RA > 35 mm
- √ transverse diameter of RV > 45 mm

√ RV÷LV > 1÷1 with leftward bowing of interventricular septum into LV

√ ± opacification of IVC + suprahepatic veins ← tricuspid valve regurgitation ← dilatation of tricuspid valve annulus

√ mild pericardial thickening

√ small pericardial effusion

@ Pulmonary vessels

√ <u>pulmonary hypertension</u> (secondary signs):

- √ pulmonary trunk diameter > 29 mm measured in scan plane of its bifurcation at right angle to long axis lateral to ascending aorta
- √ diameter ratio of main pulmonary artery to aorta > 1÷1
- √ right + left pulmonary arteries > 18 mm in diameter measured in their intrapericardial portion 1 cm beyond origin: often asymmetric in size

√ <u>visualization of chronic thrombus</u> (most specific):

- √ flattened eccentric incomplete filling defect of organized thrombus forming obtuse angles with arterial wall
- √ irregular contour of intimal surface
- √ completely obstructing thrombus:
  - √ abrupt termination / narrowing / obliteration of a pulmonary artery
  - √ convex margin of contrast column (= "pouch defect") best appreciated on reformatted images
  - √ occlusion of main pulmonary artery (3%)
- √ thrombus of increased density (87 ± 30 HU) ←
  - (a) enhancement of organizing thrombus
  - (b) thrombus retraction with concentration of hemoglobin + iron
- √ clot may become calcified = atherosclerotic pulmonary artery plaque (rare)
- √ postobstructive signs:
  - √ absence of contrast in distal vessel segment
  - √ abrupt persistent decrease in caliber of artery distal to occlusion compared to accompanying bronchus ← retraction of thrombus
  - √ poststenotic dilatation / aneurysm / tortuosity

√ <u>recanalized thrombus</u>:

- √ thickened walls of arteries with irregular contour of intimal surface in vessel parallel to scan plane / peripheral crescent-shaped intraluminal filling defect in vessel transverse to scan plane
- √ arterial band (= 1–3-mm linear structure attached at both ends to vessel wall) / flap (= attached at one end to vessel wall) / web (= network of multiple branching bands)

√ <u>collateral systemic supply</u> of occluded pulmonary arterial bed ← participation in gas exchange:

- √ bronchial artery dilatation ≥ 1.5 mm + tortuosity (47–77%) within mediastinum supplied by inferior phrenic, intercostal + internal mammary arteries

@ <u>Parenchymal abnormalities</u>:

√ mosaic perfusion on HRCT (77–100%) in segmental / subsegmental distribution:

√ scattered geometric areas of low attenuation with vessels of small cross-sectional diameter ← oligemic hypoperfusion / small-vessel arteriopathy
√ regional sharply demarcated enhancing areas of high attenuation with enlarged vessels ← compensatory hyperperfusion of lung + collateral blood flow
√ NO air trapping on expiratory scan
DDx: primary pulmonary hypertension (more diffuse pattern of mosaic perfusion)
√ isolated focal areas of ground-glass attenuation in perihilar region ← systemic perfusion
√ infarcted tissue replaced by scar (72–87%):
Location: lower lung (70%), often multiple
√ wedge-shaped pleura-based opacities with tip pointing to hilum
√ linear opacities (= parenchymal bands)
√ peripheral nodule / cavity
√ often accompanied by pleural thickening
√ cylindrical bronchial dilatation of segmental and subsegmental bronchi (64%) adjacent to severely stenosed / completely occluded + retracted pulmonary arteries ← hypoxic bronchodilatation

MR:
√ discrete fixed areas of low-to-medium SI on T1WI
Disadvantage: slow flow in central vessels may obscure fixed signal of emboli

NUC:
• A history of prior PE decreases the probability of acute embolism because small V/Q mismatches never resolve!
√ V/Q scan characteristically of high probability with multiple unmatched segmental perfusion defects

Angio (reference standard with highest specificity):
√ webs, bands
√ stenotic / absent arterial segments
√ pouchlike filling defects = convex margin of contrast material bolus
√ abrupt cutoffs often confined to one / two lung segments
√ unilateral occlusion / hypoperfusion
√ selective bronchial arteriography shows dilated bronchial artery collaterals (up to 30% of systemic blood flow) filling pulmonary arteries downstream from sites of occlusion

◊ Bronchial artery dilatation suggests chronic rather than acute thromboembolic disease!

• measurement of pulmonary artery pressure → quantification of disease severity + postoperative prognosis

Disadvantage: sensitivity for central emboli lower than for CT angio

Prognosis: partial or complete obstruction of the pulmonary vascular bed → pulmonary hypertension → cor pulmonale; 30% 5-year survival with a mean PA pressure of > 30 mmHg

Rx:
(1) Thrombendarterectomy for main / lobar / proximal segmental arteries (4–14% operative mortality) in patients with hemodynamic / ventilatory impairment
(2) Lifelong supplemental warfarin anticoagulation therapy (to avoid recurrent / growth of

thromboembolism) ± vasodilators

DDx:

(1) Idiopathic pulmonary hypertension (arteries rarely enlarged)
(2) Acute thromboembolism (diameter of pulmonary artery may be increased, nonobstructive filling defect in central location, eccentric filling defect forms acute angles with vessel wall, no dilatation of bronchial arteries, lower attenuation of thrombus, no hypertrophy of RV)
(3) Interruption of pulmonary artery (associated with congenital cardiovascular anomaly, smooth abrupt tapering of pulmonary artery blindly ending at hilum, NO endoluminal changes)
(4) Takayasu arteritis (concentric inflammatory mural thickening, mainly segmental + subsegmental arteries affected in 50–80% of late stage disease, involvement of aorta + its branches, delayed mural contrast enhancement, increased FDG uptake)
(5) Primary sarcoma of pulmonary artery (unilateral filling defect spans entire luminal diameter ± expansion of main / proximal pulmonary artery / RV, extension into lung parenchyma / mediastinum)

Ventilation-Perfusion (V/Q) Scan

Indication:

(1) Allergy to iodinated contrast media
(2) Renal insufficiency
(3) Weight limit of CT table exceeded

Rationale for Perfusion Scan:

perfusion images will detect

› 90% of surface perfusion defects > 2 x 2 cm
› 90% of emboli completely occluding a vessel > 1 mm in diameter
› 26% of emboli partially occluding a vessel

◊ A pulmonary embolus (PE) presents as segmentally hypo-perfused but normally ventilated lung (= V/Q mismatch)
◊ A normal perfusion scan excludes PE for practical purposes

Rationale for Adding Ventilation Scan & Chest X-ray

◊ A perfusion defect requires further evaluation with a ventilation scan + CXR to determine the most likely etiology
◊ If ventilation scan + CXR are normal an embolus must be suspected
◊ A ventilation scan detects obstructive lung disease because a CXR is insensitive for this entity.

Terminology:

Nonsegmental	=	does not conform to a lung segment (eg, enlarged hilar structures / aorta, small pleural effusion, elevated hemidiaphragm, cardiomegaly)
Subsegmental	=	involves 26–75% of a known bronchopulmonary segment
Segmental	=	involves > 75% of a known bronchopulmonary segment
V/Q match	=	area of abnormal ventilation identical to perfusion defect in size, shape, a location
Triple match	=	matched ventilation-perfusion defect with an associated matching area of increased opacity on CXR

V/Q mismatch = normal ventilation / normal CXR in region of perfusion defect or perfusio defect larger than ventilation defect / CXR abnormality

Reverse mismatch = area with better perfusion than ventilation suggestive of non-thromboemb cause

Interpretation: refer to Biello or PIOPED (Prospective Investigation of Pulmonary Embolism Diagnosis) criteria

Interpretive algorithm:

√ no perfusion defect

Diagnosis: normal

Interpretation: no PE

√ perfusion defect WITHOUT lung disease (= normal ventilation + normal CXR = V/Q mismatch)

Diagnosis: PE

Interpretation: high probability for PE; > 1 perfusion defect is necessary to increase certainty

√ perfusion defect WITH lung disease:

(a) ventilation abnormality + clear CXR:

Diagnosis: COPD

Interpretation: low probability for PE

◊ COPD does not diminish usefulness of V/Q scan, but increases likelihood of an indeterminate result!

(b) absent ventilation + consolidation on CXR:

Diagnosis: pneumonia, pulmonary embolism with infarction, segmental atelectasis

√ perfusion defect larger than CXR opacity

Interpretation: high probability for PE

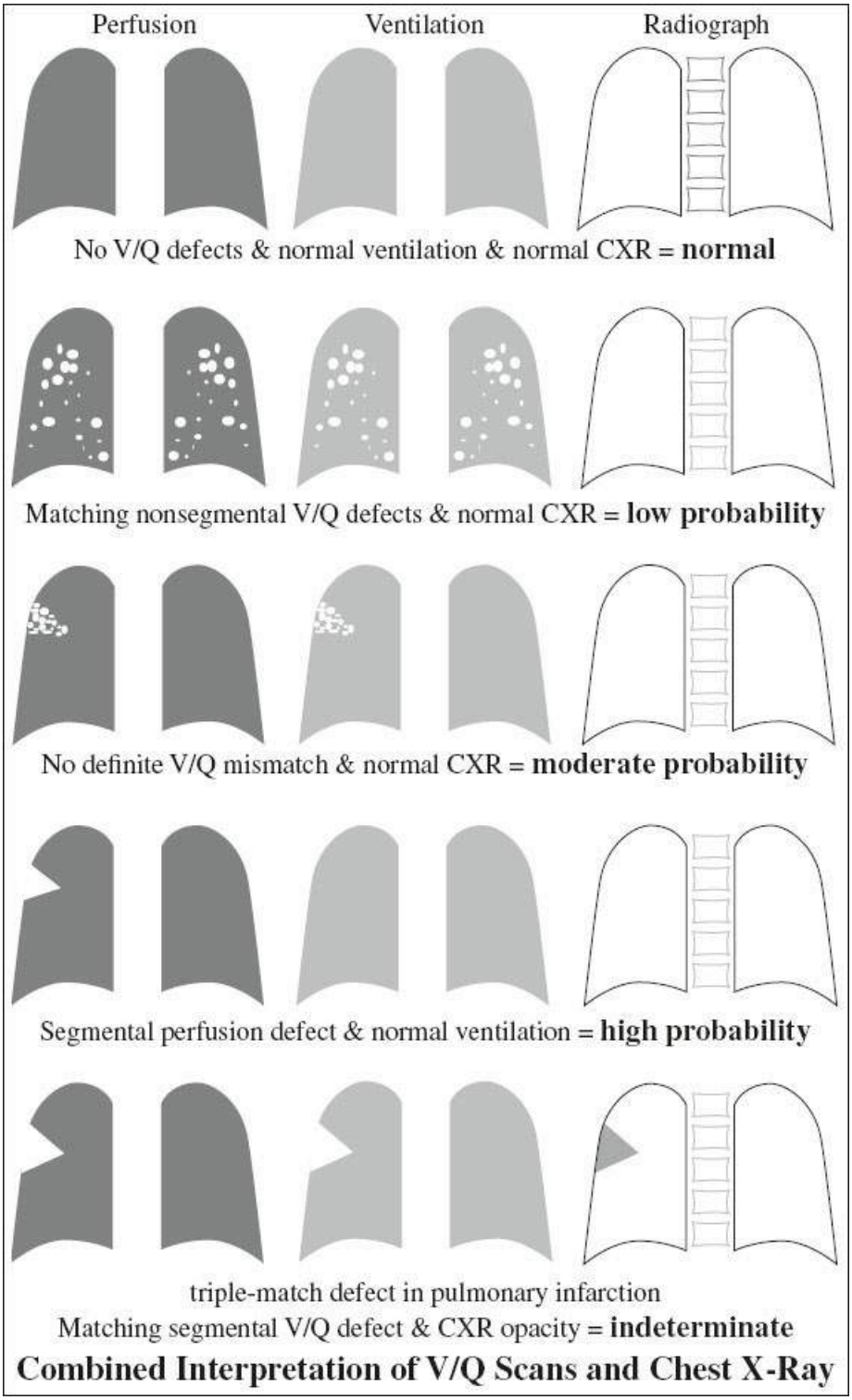
√ perfusion defect substantially smaller than opacity

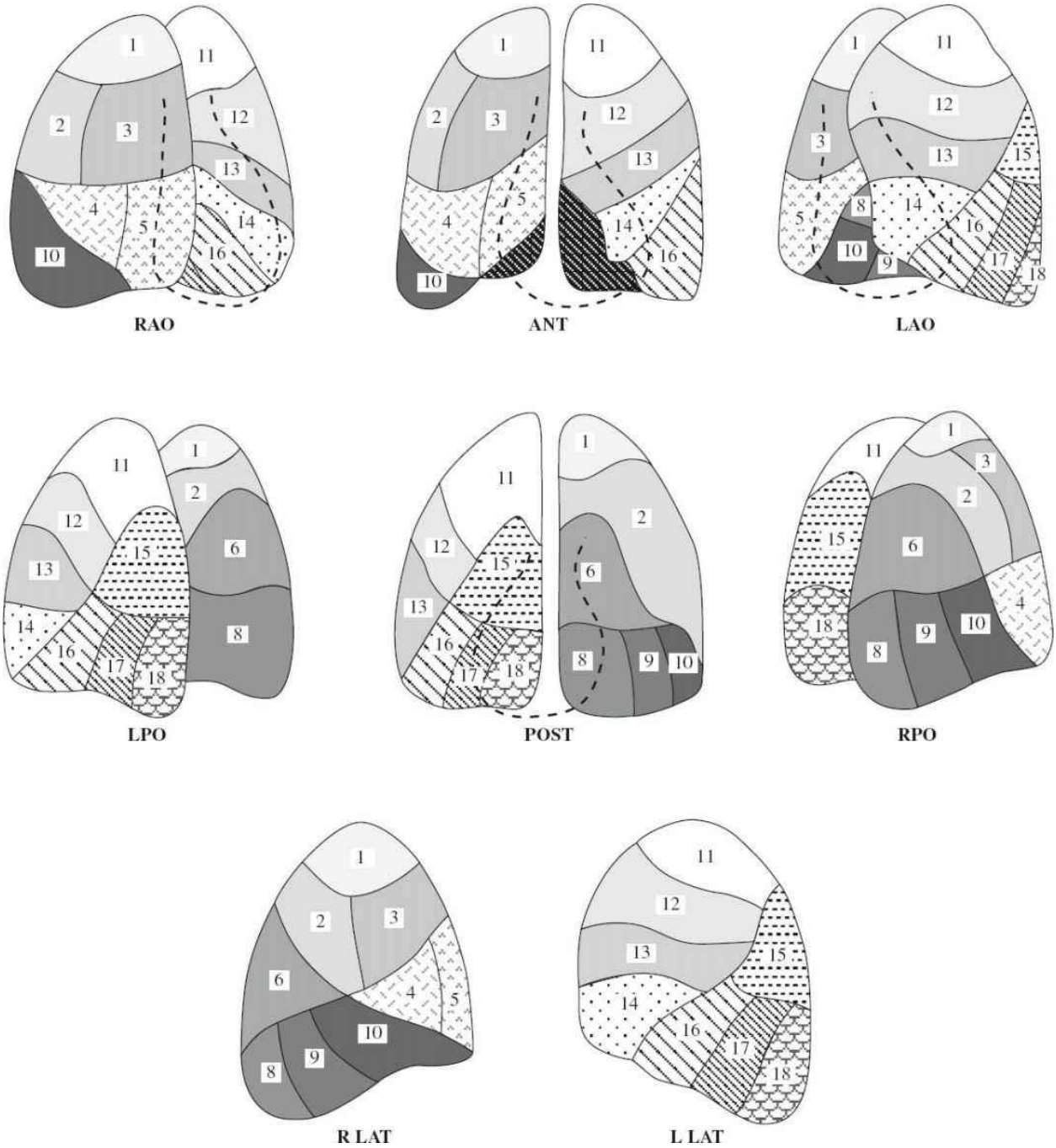
Interpretation: low probability for PE

√ perfusion defect of comparable size

Interpretation: intermediate probability

√ "stripe" sign = rim of preserved peripheral activity around a perfusion defect usually indicates


Perfusion
Ventilation
Radiograph
No V/Q defects & normal ventilation & normal CXR = normal
Matching nonsegmental V/Q defects & normal CXR = low probability
No definite V/Q mismatch & normal CXR = moderate probability
Segmental perfusion defect & normal ventilation = high probability
triple-match defect in pulmonary infarction
Matching segmental V/Q defect & CXR opacity = indeterminate
Combined Interpretation of V/Q Scans and Chest X-Ray



RUL		RML		RLL		LUL		LLL	
1	apical	4	lateral	6	superior	11	apicoposterior	15	superior
2	posterior	5	medial	7	mediobasal	12	anterior	16	anteromedial basal
3	anterior			8	posterobasal	13	superior lingual	17	laterobasal
				9	laterobasal	14	inferior lingual	18	posterobasal
				10	anterobasal				

Correlation between V/Q Scan and Chest X-Ray (CXR should be taken within 6–12 hours of scan)	
CXR Category	*Nondiagnostic V/Q Scan*
No acute abnormality	12%
Linear atelectasis	12%
Pulmonary edema	12%
Pleural effusion	36%
Parenchymal consolidation	82%

Criteria for Very Low Probability Interpretation of V/Q Lung Scans (< 10% PPV for thromboembolism)	
Criterion	*PPV*
√ nonsegmental perfusion abnormality	8%
√ perfusion defect smaller than corresponding radiographic defect	8%
√ stripe sign	7%
√ triple matched defect in upper / middle lung zone	4%
√ matched ventilation-perfusion defects in 2 / 3 zones of a single lung + normal CXR	3%
√ 1 to 3 small segmental perfusion defects	1%

Study Results of Prospective Investigation of Pulmonary Embolism Diagnosis (PIOPED)		
Probability of PE	*in*	*Angiogram Positive in*
High	13%	88%
Intermediate	39%	33%
Low	34%	16%
Normal	14%	9%

Probability Estimate for Pulmonary Thromboembolism	
indeterminate	lungs cannot be adequately evaluated due to underlying consolidation / obstructive disease; impossible to give a probability estimate
high	> 85% (more than one segmental mismatch) → 12% normal angiogram!
intermediate	~ 30% = perfusion abnormality falling short of diagnostic confidence for PE (eg, single segmental mismatch)
low	< 15%
normal	< 1%
N.B.:	low- / intermediate-probability scans are diagnosed in 50–70% of all V/Q scans with disagreement between expert readers in 25–30% → recommendation of additional studies (but only 12–14% will undergo angiography)

Effect of Clinical Probability for PE on Presence of PE		
V/Q scan	*Clinical Probability*	*PE Present*
High-probability	> 80%	96%
Low-probability	< 20%	4%
Indeterminate	DVT present	93%

Indeterminate V/Q Lung Scans	
Criterion	*PPV*
√ Q defect << CXR consolidation	14%
√ Q defect equal to CXR	26%
√ Q defect >> CXR consolidation	89%

Interpretation Criteria for V/Q Lung Scans		
Probability of PE	*Modified Biello Criteria*	*Modified PIOPED Criteria*
Normal	√ normal perfusion	√ normal perfusion
Low (0–19%)	√ small (< 25% segment) V/Q mismatches	√ small perfusion defects regardless of number / ventilation scan finding / CXR finding
	√ focal V/Q matches without corresponding CXR consolidation	√ perfusion defect substantially smaller than CXR abnormality; ventilation findings irrelevant
	√ perfusion defects substantially smaller than CXR abnormality	√ V/Q match in ≤ 50% of one lung / ≤ 75% of upper / mid / lower lung zone; CXR normal / nearly normal
		√ single moderate perfusion defect with normal CXR; ventilation findings irrelevant
		√ nonsegmental perfusion defects
Indeterminate Intermediate (25 – 50%)	√ severe COPD with perfusion defects	√ 1 large (segmental) ± 1 moderate (subsegmental) V/Q mismatch
	√ perfusion defect with corresponding CXR consolidation	√ 1–3 moderate (subsegmental) V/Q mismatches
	√ single moderate / large V/Q mismatch without corresponding CXR abnormality	√ 1 matched V/Q with normal CXR
High (> 85%)	√ perfusion defects substantially larger than CXR abnormalities	√ ≥ 2 large (segmental) perfusion defects without match
	√ ≥ 2 moderate (25–90% segment) / ≥ 2 large (> 90% segment) V/Q mismatches; no corresponding CXR abnormality	√ > 2 large (segmental) perfusion defects substantially larger than matching ventilation / CXR abnormality
		√ ≥ 2 moderate (subsegmental) + 1 large (segmental) perfusion defect without match
		√ ≥ 4 moderate (subsegmental) perfusion defects; ventilation + CXR findings normal

(a) nonembolic cause
(b) old / resolving pulmonary embolism

√ focal lung opacity:
√ not ventilated + not perfused = "indeterminate scan"
√ not changed > 1 week + not ventilated + not perfused = low probability for PE

N.B.: With a lung opacity, evaluate well-aerated areas for perfusion defects!

◊ 75% of patients with pulmonary edema + without pulmonary embolism have a normal perfusion scan!

Effect of a priori suspicion for pulmonary embolus:

› increased in patients with risk factors (immobilization, recent surgery, known hypercoagulable state, malignancy, previous pulmonary embolus, DVT, estrogen therapy)

› incidence of PE for a low probability scan increases from 15% to 40% in patients with a high clinical risk!

Therapeutic implications:

(a) high probability scan : treat for PE
(b) indeterminate scan : pulmonary angiogram
(c) low probability scan : consider other diagnosis, unless clinical suspicion very high

Overall accuracy:

68% for perfusion scan only
84% for ventilation-perfusion scan

◊ 100% sensitivity in detection of PE ← occurrence of multiple emboli (usually > 6–8), at least one of which causes a perfusion defect!
◊ A normal perfusion scan virtually excludes PE!
◊ In an individual < 45 years of age a subsegmental perfusion defect + pleuritic chest pain in the same region is indicative of pulmonary embolism in 77%! (DDx: idiopathic / viral pleurisy)
◊ 73–82% of patients have equivocal perfusion scans (ie, low and intermediate probability)!
◊ Interobserver variability for intermediate- and low-probability scans is 30%!

False-positive scans: nonthrombotic emboli, IV drug abuse, vasculitis, redistribution of flow, acute asthma (due to mucus plugging)

False-negative scans: saddle embolus

Temporal Resolution of V/Q Scan

N.B.: V/Q abnormalities vary over time ← autoregulation (hypoxic vasoconstriction, hypercapneic bronchoconstriction) and resolution

(1) Abnormality resolves within weeks / months (in most)
(2) Abnormality may last permanently

◊ Baseline study necessary to detect new emboli!

Characteristic V/Q Pattern of Nonthromboembolic Disease

1. Reverse mismatch
   Cause: mucus plugging, atelectasis
   Associated with: functional venous-to-systemic shunt contributing to hypoxemia
2. Matched perfusion-ventilation defect
   Cause: chronic obstructive pulmonary disease, asthma exacerbation
3. Peripheral perfusion defects of microembolic disease
   Cause: fat / amniotic fluid / tumor cell emboli

Cause of Unilateral Lung Perfusion

Frequency: 2%

A. PULMONARY EMBOLISM (23%)
B. AIRWAY DISEASE
   (a) Unilateral pleural / parenchymal disease (23%)
   (b) Bronchial obstruction

1. Bronchogenic carcinoma (23%)
2. Bronchial adenoma
3. Aspirated endobronchial foreign body

C. CONGENITAL HEART DISEASE (15%)

D. ARTERIAL DISEASE
1. Swyer-James syndrome (8%)
2. Congenital pulmonary artery hypoplasia / stenosis
3. Shunt procedure to pulmonary artery (eg, Blalock-Taussig)

E. ABSENCE OF LUNG
1. Pneumonectomy (8%)
2. Unilateral pulmonary agenesis

mnemonic: SAFE POEM
Swyer-James syndrome
Agenesis (pulmonary)
Fibrosis (mediastinal)
Effusion (pleural)
Pneumonectomy, **P**neumothorax
Obstruction by tumor
Embolus (pulmonary)
Mucous plug

Cause of Perfusion Defect

A. VASCULAR DISEASE
(a) Acute / previous pulmonary embolus
1. Pulmonary thromboembolic disease
2. Fat embolism
√ nonsegmental perfusion defect
3. Air embolism
√ characteristic decortication appearance in uppermost portion on perfusion scintigraphy
4. Embolus of tumor / cotton wool / balloon for occlusion of AVM / obstruction by Swan-Ganz catheter, other foreign body
5. Dirofilaria immitis (dog heartworm): clumps of heartworms break off cardiac wall + embolize pulmonary arterial tree
6. Sickle cell disease

(b) Vasculitis
1. Collagen vascular disease: sarcoidosis
2. IV drug abuse
3. Previous radiation therapy:
√ defect localized to radiation port
4. Tuberculosis

(c) Vascular compression
1. Bronchogenic carcinoma:
√ perfusion defect depending on tumor size + location
2. Lymphoma / lymph node enlargement

3. Pulmonary artery sarcoma
4. Fibrosing mediastinitis ← histoplasmosis
5. Idiopathic pulmonary fibrosis:
   √ small subsegmental defects in both lungs
6. Aortic aneurysm (large saccular / dissecting)
7. Intrathoracic stomach

(d) Altered pulmonary circulation

1. Absence / hypoplasia of pulmonary artery
2. Peripheral pulmonary artery stenosis
3. Bronchopulmonary sequestration
4. Primary pulmonary hypertension
   √ upward redistribution + large hilar defects
   √ multiple small peripheral perfusion defects
5. Pulmonary venoocclusive disease
6. Mitral valve disease
   √ predilection for right middle lobe + superior segments of lower lobes
7. Congestive heart failure
   √ diffuse nonsegmental V/Q mismatch
   √ enlargement of cardiac silhouette + perihilar regions
   √ reversed distribution: more activity anteriorly than posteriorly
   √ accentuation of fissures
   √ flattening of posterior margins of lung (lateral view)
   √ pleural effusion

B. AIRWAY DISEASE

◊ Nearly all pulmonary disease produces decreased pulmonary blood flow to affected lung zones = autoregulatory reflexive vasoconstriction!

1. Asthma, chronic bronchitis, bronchospasm, mucus plugging
2. Bronchiectasis (bronchiolar destruction)
3. Emphysema (bulla / cyst)
4. Pneumonia / lung abscess
5. Lymphangitic carcinomatosis

√ perfusion defects in area of hypoxia
√ abnormal ventilation to a similar / more severe degree
√ mostly multiple nonanatomic defects (in 20%)

Tumor Embolism

◊ Diagnosis frequently missed until postmortem exam!

Frequency: 2–26% of patients with known malignancy

Primary: gastric carcinoma (most common), breast, liver, kidney, prostate, lung, ovarian, osteosarcoma, lymphoma, choriocarcinoma

◊ Right atrial myxoma + RCC tend to embolize to large central + segmental pulmonary arteries!

Pathogenesis: tumor cells form emboli in vena cava subsequently occlude small muscular pulmonary arteries + arterioles

Histo: intravascular malignant cells, acute and organizing platelet-fibrin thrombi, small

artery intimal fibrosis, adjacent intralymphatic tumor

- progressive dyspnea, cough, pleuritic chest pain
- hemoptysis, syncope; hypoxemia < 50 mmHg

CXR:

√ enlarged central pulmonary arteries
√ cardiomegaly
√ ill-defined nodular / confluent peripheral parenchymal opacities (with multiple pulmonary infarcts)
√ focal / diffuse heterogeneous opacities = lymphangitic carcinomatosis

CT:

√ subpleural linear + wedge-shaped opacities (at sites of pulmonary infarctions)
√ companion manifestations: lymphadenopathy, pulmonary venous hypertension, lymphangitic carcinomatosis:
  √ multifocal dilatation / beading of vessels
  √ thickening of interlobular septa
√ tree-in-bud pattern ← filling of centrilobular arteries with tumor cells / carcinomatous endarteritis ← fibrocellular intimal hyperplasia initiated by tumor microemboli

CECT:

√ filling defects in main pulmonary artery branches
√ multifocal beading + dilatation of subsegmental pulmonary arteries

NUC (V/Q scan):

√ multiple small subsegmental unmatched perfusion defects

Angio:

√ delayed arterial phase
√ filling defects / occlusions of subsegmental arterial branches
√ arterial wall irregularities
√ peripheral pruning of smaller arteries

Cx: subacute cor pulmonale (heralds death within 4–12 weeks)

Mercury Embolism

Cause: accidental / suicidal IV injection

Pathomechanism: intravascular mercury becomes encased in thrombus or migrates into pulmonary interstitium / alveolar spaces resulting in significant granulomatous response

√ high-density fine-caliber branching structures in symmetric distribution
√ mercury collection within apex of right ventricle

PULMONARY VENO-OCCLUSIVE DISEASE

= fibrous narrowing / occlusion of pulmonary venules + small veins; the postcapillary counterpart of primary pulmonary arterial hypertension

Pulmonary veno-occlusive disease may develop fatal pulmonary edema if treated with vasodilators!

Prevalence: 01.–0.2 per 1,000,000 persons

Age: < 20 years in 30–50% (range, 9 days to 70 years); M÷F = 1÷1

Cause: idiopathic (rare condition); venous thrombosis initiated by infection / toxic exposure /

immune complex deposition

May be associated with:

pregnancy, transplantation, drug toxicity (carmustine, bleomycin, mitomycin)

Hemodynamics:

- ↑ pressure in right atrium + pulmonary artery (PAH)
- normal / low / variably elevated pulmonary capillary wedge pressure (PCWP); decreased cardiac output
- normal pressure in left atrium + left ventricle (excludes cardiac disease as the cause for venous hypertension)

Histo:

(a) specific changes: webs, recanalized thrombus (in up to 95%), intimal fibrosis with narrowing / occlusion of pulmonary veins of all sizes; "capillary hemangiomatosis" = sheets and nodular collections of thin-walled capillaries invading pulmonary arteries + veins + bronchioles + pleura

(b) nonspecific changes of venous hypertension: venous medial hypertrophy, edematous interlobular septa with dilated lymphatic spaces, paraseptal venous infarction, interstitial + pleural lymphatic dilatation, intraalveolar hemosiderin-laden macrophages; muscularized arterioles + medial hypertrophy of muscular pulmonary arteries

- progressive dyspnea and fatigue, hemoptysis, digital clubbing
- antecedent flulike symptoms; dry / productive chronic cough
- chest pain, syncope; episodes of acute pulmonary edema

CXR:

√ enlargement of main pulmonary artery (PAH)
√ prominent Kerley B lines
√ pulmonary veins of normal caliber
√ normal contours of LA + LV
√ ± pleural effusions
√ diffuse interstitial ± alveolar pulmonary edema:
  √ central and gravity-dependent parenchymal ground-glass attenuation
√ multifocal airspace consolidation ← parenchymal hemorrhage, pulmonary edema, pulmonary infarction
√ mediastinal lymphadenopathy ← vascular transformation of lymph node sinus with various degrees of sclerosis

CT:

√ markedly small central pulmonary veins
√ dilated central pulmonary arteries
√ smoothly thickened interlobular septa
√ peribronchovascular thickening
√ diffuse / geographic / mosaic / perihilar / patchy / centrilobular ground-glass opacity
√ right heart enlargement + normal-sized left atrium
√ pleural effusions

◊ The combination of signs of pulmonary arterial hypertension + interstitial / alveolar pulmonary edema is virtually DIAGNOSTIC of pulmonary venoocclusive disease!

NUC:

√ patchy distribution of ^{99m}Tc-MAA (of "upstream" pulmonary arterial hypertension)

Angio:

√ enlarged right ventricle + central pulmonary arteries

√ prolonged parenchymal phase enhancement

√ delayed filling of normal pulmonary veins

√ normal to small left atrium

Cx: potentially fatal pulmonary edema following administration of vasodilators for misdiagnosed presumed precapillary pulmonary hypertension

Dx: often missed initially (clinical presentation + radiographic findings mimic interstitial lung disease)

Prognosis: death within 3 years ← NO effective therapy

Rx: lung / heart-lung transplant (only curative option); supportive diuretics, anticholinesterase (ACE) inhibitors, cardiac glycosides (digoxin), oxygen supplementation, pulmonary vasodilators (calcium channel blockers, prostacyclin), immunosuppressive agents

PULMONARY VEIN VARIX

= abnormal tortuosity + focal dilatation of pulmonary vein just before entrance into left atrium

Etiology: congenital / associated with chronic pulmonary venous hypertension or mitral valve disease

• usually asymptomatic

• hemoptysis ← rupture / thromboembolic disease

Location: medial ⅓ of either lung below hila close to left atrium

√ well-defined lobulated round / oval mass without Ca2+

√ change in size during Valsalva / Müller maneuver

√ opacification at same time as LA (on CECT)

Risk: (1) Death upon rupture during worsening heart failure

(2) Source of cerebral emboli

DDx: pulmonary arteriovenous malformation, pulmonary nodule, hilar lymphadenopathy

RADIATION PNEUMONITIS

= damage to lungs after radiation therapy depends on:

(a) irradiated lung volume (most important):

• asymptomatic in < 25% of lung volume

(b) radiation dose (almost always exceeds critical value for tumoricidal doses):

› pneumonitis unusual if < 20 Gy given in 2–3 weeks

› pneumonitis common if > 60 Gy given in 5–6 weeks

› significantly increased risk for pneumonitis if daily dose fraction > 2.67 Gy

(c) fractionation of dose

(d) concurrent / later chemotherapy

Pathologic phases:

(1) Exudative phase = edema fluid + hyaline membranes

(2) Organizing / proliferative phase

(3) Fibrotic phase = interstitial fibrosis

Time of onset: usually 4–6 months after treatment

Location: confined to radiation portals

Acute Radiation Pneumonitis

Onset: within 4–8 (range, 1–12) weeks after radiation Rx
Path: depletion of surfactant (1 week to 1 month later), plasma exudation, desquamation of alveolar + bronchial cells
• asymptomatic (majority), acute respiratory failure (rare)
• nonproductive cough, shortness of breath, weakness, fever (insidious onset)
√ changes usually within portal entry fields
√ patchy / confluent consolidation, may persist up to 1 month (exudative reaction)
√ atelectasis + air bronchogram
√ spontaneous pneumothorax (rare)
CT:
√ mild hazy homogeneous increase in attenuation obscuring vessel outlines (2–4 months after Rx)
√ coalescing patchy consolidations (1–12 months after therapy) not conforming to shape of portals
√ nonuniform discrete consolidation (most common; 3 months to 10 years after therapy) forming sharp edges and conforming to treatment portals
Prognosis: recovery / progression to death / fibrosis
Rx: steroids

Chronic Radiation Pneumonitis

Onset: 9–12 (range, 6–24) months after radiation therapy; stabilized by 1–2 years after therapy
Histo: permanent damage of endothelial + type I alveolar cells
May be associated with:
(1) Thymic cyst
(2) Calcified lymph nodes (in Hodgkin disease)
(3) Pericarditis + effusion (within 3 years)
√ severe loss of volume
√ dense fibrous strands from hilum to periphery
√ thickening of pleura
√ pericardial effusion
CT:
√ solid consolidation with parenchymal distortion ← radiation fibrosis + atelectasis
√ traction bronchiectasis
√ mediastinal shift
√ pleural thickening

RESPIRATORY DISTRESS SYNDROME OF NEWBORN

= RDS = SURFACTANT DEFICIENCY DISORDER = HYALINE MEMBRANE DISEASE
= acute pulmonary disorder characterized by generalized atelectasis, intrapulmonary shunting, ventilation-perfusion abnormalities, reduced lung compliance
Frequency: 6÷1,000 neonates (in 2002); M÷F = 1.8÷1

Cause: relative lack of mature type II pneumocytes → deficiency of endogenous surfactant (production usually begins at 18–20 weeks of gestational age) → increased alveolar surface tension + decreased alveolar distensibility → acinar atelectasis (persistent collapse of alveoli) + dilatation of terminal airways

Histo: uniformly collapsed alveoli + variable distension of alveolar ducts + terminal bronchioles; lined by fibrin ("hyaline membranes") ← protein seepage from damaged hypoxic capillaries

Predisposed: perinatal asphyxia; maternal / fetal hemorrhage, term infants of diabetic mothers, multiple gestations, premature infants (< 1,000 g in 66%; 1,000 g in 50%; 1,500 g in 16%; 2,000 g in 5%; 2,500 g in 1%)

Onset: < 2–5 hours after birth, increasing in severity from 24–48 hours, gradual improvement after 48–72 hours

- nonspecific tachypnea, nasal flaring
- expiratory grunting (expiratory breathing against a partially closed glottis to augment alveolar distension)
- circumoral cyanosis (carbon dioxide retention)
- substernal + intercostal retraction of chest wall

√ decreased lung expansion (counteracted by respirator therapy)

√ symmetric generalized consolidation of variable severity:

- √ complete "white out" of lung
- √ diffuse reticulogranular texture (coincides with onset of clinical signs, maximum severity at 12–24 hours of life) = summation of collapsed alveoli, transudation of fluid into interstitium, air distension of terminal bronchioles + alveolar ducts
- √ evolving hazy opacities to clearing over several days

√ effacement of normal pulmonary vessels

√ prominent air bronchograms (distension of compliant airways)

Prognosis: spontaneous clearing within 7–10 days (mild course in untreated survivors); death in 18%

Rx:
(1) Antenatal maternal corticosteroid therapy
(2) Surfactant replacement therapy (liquid bolus of exogenous surfactant delivered into tracheobronchial tree
(3) Nasal continuous positive airway pressure (CPAP)
(4) High-frequency oscillatory ventilation (HFOV)
(5) Extracorporeal membrane oxygenation (ECMO)

DDx:
(1) Diffuse pneumonia accompanying sepsis
(2) Retained fetal lung fluid (first few hours)
(3) Pulmonary hemorrhage
(4) Pulmonary venous congestion (eg, TAPVR, pulmonary vein atresia, hypoplastic left heart)
(5) Premature with accelerated lung maturity (PALM baby)

Causes of Asymmetric Clearing after Surfactant

(a) maldistribution of surfactant into right mainstem bronchus
(b) insufficient surfactant requiring additional application
(c) regional differences in aeration before surfactant treatment

DDx: neonatal pneumonia, meconium aspiration, unilateral tension pneumothorax, hemorrhagic pulmonary edema

Acute & Subacute Complications of RDS

(a) persistent patency of ductus arteriosus (PDA) with oxygen stimulus missing to close duct; gradual ↓ in pulmonary resistance (by end of 1st week) → significant L-to-R shunt
(b) barotrauma with air-block phenomena
(c) hemorrhage
    1. Pulmonary hemorrhage
    2. Cerebral hemorrhage
(d) focal atelectasis (usually from mucus plug)
(e) persisting fetal circulation
(f) myocardial ischemia
(g) diffuse opacity
    1. Worsening RDS (first 1–2 days only)
    2. Congestive heart failure (PDA, fluid overload)
    3. Pulmonary hemorrhage
    4. Superimposed pneumonitis
    5. Massive aspiration
    6. Stage II bronchopulmonary dysplasia
    7. "Weaning effect" from removal of endotracheal tube / diminished ventilator pressure
    8. Extracorporeal membrane oxygenation
(h) disseminated intravascular coagulopathy
(i) necrotizing enterocolitis
(j) acute renal failure
(k) metabolic disturbance (eg, hyperbilirubinemia, hypocalcemia)

Chronic Complications of RDS

1. Bronchopulmonary dysplasia (10–20%)
2. Subglottic stenosis (intubation)
3. Localized interstitial emphysema
4. Hyperinflation
5. Retrolental fibroplasia
6. Malnutrition, rickets
7. Lobar emphysema
8. Delayed onset of diaphragmatic hernia
9. Recurrent inspiratory tract infections

Complication of Continuous Positive Pressure Ventilation

Cause: airway overdistension (**volutrauma**) rather than high airway pressure (**barotrauma**)
Path:
(a) rupture of alveoli along margins of interlobular septa + vascular structures (= parenchymal pseudocyst)
(b) air dissecting along interlobular septa + perivascular spaces = pulmonary interstitial emphysema (PIE)

√ "pseudoclearing" of RDS

(c) interstitial air migrating centripetally into pleural space (= pneumothorax) / mediastinum (= pneumomediastinum) / pericardial cavity (= pneumopericardium)

(d) interstitial air rupturing into peritoneal space (= pneumoperitoneum) / retroperitoneal space (= pneumoretroperitoneum)

(e) air dissecting into skin (= subcutaneous emphysema)

(f) air rupturing into vessel (= gas embolism)

√ streaky / mottled lucencies radiating from hila without branching / tapering often outlining bronchovascular bundles (DDx: air bronchogram)

√ large subpleural cysts without definable wall usually at diaphragmatic + mediastinal surface compressing adjacent lung

√ pneumothorax (in up to 25%)

Rx: mechanical ventilatory assistance with positive end-expiratory pressure (to increase oxygen diffusion)

RETAINED FETAL LUNG FLUID

= NEONATAL WET LUNG DISEASE = TRANSIENT RESPIRATORY DISTRESS OF THE NEWBORN = TRANSIENT TACHYPNEA OF THE NEWBORN

Frequency: 6%; most common cause of respiratory distress in newborn

Cause: cesarean section, precipitous delivery, breech delivery, prematurity, maternal diabetes

Pathophysiology:

delayed resorption of fetal lung fluid (normal clearance occurs through capillaries (40%), lymphatics (30%), thoracic compression during vaginal delivery (30%); stiff lungs cause labored ventilation until fluid is cleared

Onset: within 6 hours of life; peaks at 1st day of life

- increasing respiratory rates during first 2–6 hours of life
- intercostal + sternal retraction
- normal blood gases during hyperoxygenation

√ linear opacities + perivascular haze + thickened fissures + interlobular septal thickening (interstitial edema):

√ symmetric perihilar radiating congestion

√ mild hyperaeration

√ mild cardiomegaly

√ small amount of pleural fluid

Prognosis: resolving within 1–2–4 days (retrospective Dx)

DDx: (1) Normal (during first several hours of life)

(2) Diffuse pneumonitis / sepsis

(3) Mild meconium aspiration syndrome

(4) Alveolar phase of RDS

(5) "Drowned newborn syndrome" = clear amniotic fluid aspiration

(6) Pulmonary venous congestion (eg, left heart failure, overhydration, placental transfusion)

(7) Pulmonary hemorrhage

(8) Hyperviscosity syndrome = thick blood

(9) Immature lung syndrome = premature with accelerated lung maturity (PALM baby)

RHEUMATOID LUNG

= autoimmune disease of unknown pathogenesis

Frequency: 2–54% of patients with rheumatoid arthritis; M÷F = 5÷1 (although incidence of rheumatoid arthritis: M÷F = 1÷3)

◊ Lung disease is 2nd most common cause of death after infection!

• rheumatoid arthritis

Stage 1: multifocal ill-defined alveolar infiltrates

Stage 2: fine interstitial reticulations (histio- and lymphocytes)

Stage 3: honeycombing

A. PLEURAL DISEASE (38–73%)

◊ Most frequent thoracic manifestation!

◊ NOT related to pulmonary disease!

• history of pleurisy (21%)

Associated with: pericarditis, subcutaneous nodules

◊ Usually late in the disease, but may antedate rheumatoid arthritis

• exudate (with protein content > 4 g/dL)

• low in sugar content (< 30 mg/dL) without rise during glucose infusion (75%); low WBC high in lymphocytes

• positive for rheumatoid factor, LDH, RA cells

√ pleural thickening, usually bilateral

√ pleural effusion (3–5%) with little change for months:

√ unilateral (92%), usually small, may be loculated

√ tendency to resolve spontaneously

√ usually not associated with parenchymal disease

B. BRONCHIAL ABNORMALITIES

√ cystic bronchiectasis on HRCT (30%)

√ bronchiolitis obliterans (may be transient regardless of penicillamine / gold therapy):

√ mosaic pattern (= areas of decreased attenuation + vascularity ← air trapping in small airways) on end-expiratory HRCT

√ bronchiolitis obliterans organizing pneumonia (BOOP):

√ bilateral air-space consolidation in peripheral / peribronchial distribution

√ follicular bronchiolitis (in 66%):

Histo: hyperplasia of peribronchial + peribronchiolar lymphatic follicles

√ multiple small centrilobular nodules with patchy areas of ground-glass attenuation

C. DIFFUSE INTERSTITIAL FIBROSIS

Prevalence: 2–5–9% of patients with rheumatoid arthritis

• restrictive ventilatory defect

Location: lower lobe predominance

Histo: deposition of IgM in alveolar septa (DDx to IPF)

Patterns: UIP > NSIP, cryptogenic organizing pneumonia, follicular bronchiolitis, bronchiolitis obliterans

√ punctate / nodular densities (mononuclear cell infiltrates in early stage)

√ reticulonodular densities
√ medium to coarse reticular opacities (mature fibrous tissue in later stage):
  √ irregular interlobular septal thickening on HRCT, predominantly in periphery of lower lung zones
  √ traction bronchiectasis
√ honeycomb lung (uncommon in late stage)
√ architectural distortion + progressive lower-lobe volume loss (advanced disease)
√ ± groundglass opacities (less extensive / impressive)

D. NECROBIOTIC (RHEUMATOID) NODULES (rare)
= well-circumscribed nodular mass in lung, pleura, pericardium identical to subcutaneous nodules associated with advanced rheumatoid arthritis
Path: central zone of eosinophilic fibrinoid necrosis surrounded by palisading fibroblasts; nodule often centered on necrotic inflamed blood vessel (? vasculitis as initial lesion)
M > F
• subcutaneous nodules (same histology)
• frequently seen in smokers with subcutaneous nodules + high rheumatoid factor titers
• may arise before manifestation of rheumatoid arthritis
Associated with: interstitial lung disease
Distribution: commonly in lung periphery of upper and middle lung regions
Size: 3–70 mm
√ usually multiple well-circumscribed nodules
√ may increase in size / resolve spontaneously
√ new ones may arise while older ones resolve
√ ± cavitation with thick symmetric walls + smooth inner lining (in 50%)
√ ± central calcification (very rare)
Cx: rupture into pleural space: pneumothorax, pleural effusion, empyema

E. CAPLAN SYNDROME
= RHEUMATOID PNEUMOCONIOSIS SYNDROME
= hyperimmune reactivity to irritating silica inhalation (of coal workers with rheumatoid arthritis)
Frequency: 2–6% of all men affected by pneumoconioses (exclusively in Wales)
Path: disintegrating macrophages deposit a pigmented ring of dust surrounding the central necrotic core + zone of fibroblasts palisading the zone of necrosis
◊ NOT necessarily evidence of long-standing pneumoconiosis
• concomitant with joint manifestation (most frequent) / may precede arthritis by several years
• concomitant with systemic rheumatoid nodules
√ rapidly developing well-defined nodules of 5–50 mm in size with a tendency to appear in crops predominantly in upper lobes + in periphery of lung
√ nodules may remain unchanged / increase in number / calcify / result in thick-walled cavities
√ background of pneumoconiosis
√ pleural effusion (may occur)

F. PULMONARY ARTERITIS
= fibroelastoid intimal proliferation of pulmonary arteries
• pulmonary arterial hypertension + cor pulmonale

G. CARDIAC ENLARGEMENT
(pericarditis + carditis / congestive heart failure)

H. BONE ABNORMALITIES ON CXR
√ erosive arthritis of acromioclavicular joint, sternoclavicular joint, shoulder joint:
√ resorption of distal end of clavicles
√ ankylosis of vertebral facet joints
√ vertebral body collapse ← steroid use
√ cricoarytenoid arthritis (frequently overlooked!)
• foreign body sensation, soreness / fullness in throat, hoarseness, dyspnea, pain radiating into ears, stridor, dysphagia, odynophagia, pain with speech

I. DRUG-INDUCED LUNG DISEASE
Gold, penicillamine: diffuse alveolar damage, obliterative bronchiolitis
Methotrexate: pneumonitis

SARCOIDOSIS

= BOECK SARCOID [*sarkos*, Greek = flesh; *sarcoid* = sarcoma-like]
[Caesar Peter Möller Boeck (1845–1917), Norwegian dermatologist describes skin lesions in 1899]

= immunologically mediated multisystem granulomatous disease of unknown etiology with variable presentation, progression and prognosis characterized by noncaseating nonnecrotic epitheloid cell granulomas

Bilateral hilar lymphadenopathy is the most common radiologic finding. Adenopathy in the right paratracheal nodes, left aortic-pulmonary window, and subcarinal nodes can also be seen, often with associated pulmonary infiltrates.

Prevalence: 10–48÷100,000 in USA in 2010 (highest in African-Americans, Swedes, Danes); Blacks÷Whites in USA = 3÷1 to 10÷1 (rare in African / South American Blacks); more common in blood group A

Age peak: 20–40 years; M÷F = 1÷3

Epidemiology: found with varying frequency in every country in the world; prevalence higher in temperate climates than tropical regions (< 10÷100,000)

Immunology:
unknown environmental antigen(s) activate <u>alveolar macrophages</u> in a genetically susceptibel host releasing
› interleukin-1 (T-cell activator)
› fibronectin (fibroblast chemotactic factor)
› alveolar macrophage-derived growth factor (stimulates fibrosis)
and activate <u>T-lymphocytes</u> releasing
› interleukin-2 (stimulates growth of T-helper / cytolytic cells)
› immune interferon (polyclonal B-cell activator)
› monocyte chemotactic factor (attracts circulating monocytes and stimulates granuloma formation)

Path: (a) acute phase: lymphocytes + scattered macrophage giant cells + small granulomas
(b) intermediate phase: well=formed granulomas + minimal scarring
(c) late phase: predominant fibrosis + few granulomas + chronic inflammation

Histo: noncaseous granulomas composed of central core (histiocytes, epitheloid cells, multinucleated giant cells) surrounded by lymphocytes, scattered plasma cells, fibroblasts and collagen; occasional minimal central coagulative necrosis

DDx: indistinguishable from granulomas of berylliosis, treated TB, leprosy, fungal disease, hypersensitivity pneumonitis, Crohn disease, primary biliary cirrhosis

Laboratory:

- **angiotensin-converting enzyme** (ACE) elevated in 70% (ACE is a product of macrophages and an indicator for the granuloma burden of the body)
  DDx: tuberculosis, leprosy, histoplasmosis, berylliosis, cirrhosis, hyperthyroidism, diabetes
- CD4÷CD8 ratio in blood serum commonly decreased
- hypercalcemia + hypercalciuria in 2–15% ← increased intestinal resorption of calcium ← hydroxylation of 1,25-dihydroxy vitamin D in macrophages
- Kveim-Siltzbach test (positive in 70%) = intracutaneous injection of 0.1–0.2 mL of a previously validated saline suspension of human sarcoid spleen / lymph nodes; no longer considered specific → rarely used
- functional pulmonary impairment (even with NO radiographic abnormality):
  (a) restrictive ventilatory defect
  › reduced VC + FRC + TLC ← generalized reduction in lung volume
  › low lung compliance ← diffuse interstitial disease
  (b) obstructive ventilatory defect (6%) ← endobronchial lesions / peribronchial fibrosis
- NO identification of infectious / inflammatory agent

Dx: based on a combination of clinical + radiological + histologic features after exclusion of other infectious / inflammatory entities

Diagnostic criteria:

(1) Compatible clinical + radiologic picture
(2) **Noncaseous epithelioid granulomas** on bronchial / transbronchial US-guided biopsy (diagnostic results in 60–95% and 80–95% respectively) or from extrapulmonary sites like cervical lymph nodes and liver
(3) Negative results of special stains / cultures for other entities

Assessment of activity:

(1) ACE titer (= angiotensin I converting enzyme)
(2) Bronchoalveolar lavage (BAL): 20–50% lymphocytes with T-suppressor lymphocytes 4–20 times above normal
(3) Gallium scan
√ uptake in lymph nodes + lung parenchyma + salivary glands (correlates with alveolitis + disease activity); monitor of therapeutic response (indicator of macrophage activity)
(4) PET
√ degree of FDG uptake correlates well with disease activity for monitoring response to therapy

Clinical Forms:

A. ACUTE FORM
- fever + malaise + arthralgia of large joints
- erythema nodosum; (occasionally) uveitis + parotitis

Löfgren Syndrome (17%)
= (1) erythema nodosum (2) periarticular ankle inflammation (3) mediastinal lymphadenopathy
Prognosis: self-limiting course with spontaneous resolution

B. CHRONIC FORM
= insidious onset (especially with involvement of lung or multiple extrapulmonary lesions) that may be followed by progressive fibrosis of lung and other organs
- asymptomatic (30–50%); fever, malaise, weight loss
- dry cough + shortness of breath (25%)
- hemoptysis in 4% (from endobronchial lesion / vascular erosion / cavitation)

Extrathoracic involvement (most commonly of skin and eyes) can be an initial manifestation in ½ of symptomatic patients.

Rx: inhaled / oral corticosteroids; immunosuppressive drugs (methotrexate, cyclophosphamide) with aggressive disease / frequent recurrence

Abdominal Sarcoidosis (30%)
- strikingly elevated ACE levels in 91%

Scattered hypoattenuating nodules involving liver and spleen suggest a diagnosis of sarcoidosis or lymphoma.

@ Liver (24–59%):
Prevalence: autoptic (50–80%), bioptic (24–59%)
√ mild homogeneous hepatomegaly (18–29%)
√ cirrhotic appearance (rare) ← diffuse granulomatous involvement along periportal tracts followed by fibrosis

CT:
√ scattered 2–5-mm hypoattenuating nodular lesions in liver (in 5–15%) ← coalescent granulomata occurring within 5 years of diagnosis
√ hypoenhancing lesions relative to background on early phase + minimal enhancement on delayed phase

MR:
√ heterogeneous nodular hepatic texture hypointense on all pulse sequences
√ lesions most conspicuous on fat-saturated T2WI

@ Spleen (pathologic involvement in 24–59%)
√ splenomegaly (20–33%)
√ scattered hypoattenuating nodular lesions (18%): more common + larger than in liver

@ Abdominal lymphadenopathy (10–31%)
- frequently associated with thoracic adenopathy

Location: mesenteric (periportal, perisplenic), retroperitoneal
Mean size: 2.6 cm
DDx: tumor-related sarcoid-like reaction = development of noncaseating granulomas in

treated malignancy

@ Pancreas

√ mass + pain mimicking pancreatic carcinoma

Cardiac Sarcoidosis (5%)

Frequency: 5% clinically, 20–50% at autopsy

1. Global / regional hypokinesis with systolic dysfunction → ↓ LV ejection fraction + ↑ end-diastolic LV diameter
2. Ventricular arrhythmia
3. Cardiomyopathy, congestive failure, angina

- may be asymptomatic throughout life
- CHF (25%) ← diffuse myocardial involvement
- cor pulmonale ← pulmonary hypertension
- conduction disturbances (in 23–30%): isolated bundle branch block to complete heart block
  - heart block (= CLASSIC clinical presentation)
- supraventricular + ventricular arrhythmias
- sudden cardiac death (in 12–65%) ← dysrhythmia

Distribution: basal portion of septum, LV wall

N.B.: rare in papillary muscle / RV

Echo (nonspecific):

√ wall motion abnormalities

√ thinning of basal septum

√ LV dilatation (30%)

CT:

√ cardiomegaly (25%)

√ pericardial effusion

√ ventricular aneurysm (10%)

MR (75–100% sensitive, 77–79% specific):

CAVE: often contraindicated ← cardiac pacemakers (unless device is MR compatible)

√ myocardial thickening

√ nodular / patchy areas of high SI on T2WI / SSFP (bright-blood steady-state free precession) ← edema

√ late gadolinium-induced enhancement (LGE) of myocardium ← expansion of extracellular space

Location:

(a) transmural

(b) nontransmural: subepi- / midmyocardial along basal or midventricular septum (in 67%)

DDx: ischemic heart disease (subendocardial distribution in vascular territory)

√ focal wall thinning + regional wall motion abnormalities ← myocardial fibrosis + scarring:

√ subepicardial > midmyocardial > subendocardial scars in random distribution

√ LV thinning with transmural involvement

NUC (^{99m}Tc, ^{201}Th SPECT, ^{82}Rb PET):

√ resting perfusion defects ← inflammation-induced tissue damage

PET (89% sensitive,78% specific):

N.B.: useful in patients with cardiac pacemakers!

√ increased FDG-uptake (SUV range, 2.5–15.8) in nonperivascular distribution ← active necrotizing granulomatous disease

also involvement of:

√ mediastinal + hilar lymph nodes (39%)

√ lung parenchymal nodules (15%) in peribronchovascular distribution

√ spleen, liver, muscle, salivary glands, subcutaneous tissue, bone (less frequent)

Cx: ventricular aneurysm, pericardial effusion

Dx: treatment-responsive cardiomyopathy, conduction defects at ECG, abnormal imaging findings, endomyocardial biopsy (on right side of heart)

Endomyocardial biopsy is rarely performed because of its diagnostic yield of only 20–50% and lack of information about cardiac distribution.

Rx: based on symptoms, ECG, imaging findings and disease course, rather than histologic confirmation

DDx: (1) Dilated cardiomyopathy (dilated LV with global dysfunction, linear stripe of LGE in ventricular septum)

(2) Hypertrophic cardiomyopathy (LV hypertrophy > 15 mm, scattered patchy midmyocardial involvement)

(3) Arrhythmogenic right ventricular cardiomyopathy (RV dilatation + dysfunction, fibrofatty infiltration of RV, dyskinetic free wall of RV + RV aneurysm)

(4) Myocarditis (patchy epicardial LGE in often inferolateral distribution, hyperemia)

(5) Amyloidosis (biventricular hypertrophy, global + diffuse LGE, LA enhancement, diffuse myocardial nulling abnormality)

Gastrointestinal Sarcoidosis (< 1%)

Location: anywhere from esophagus to rectum

@ Stomach (most common)

√ polypoid / nodular mass frequently in antrum

√ ± ulcer (simulating peptic ulcer disease)

√ diffuse fold thickening (mimicking Ménétrier disease)

√ circumferential narrowing + loss of antral compliance (resembling scirrhous carcinoma)

@ Colon (2nd most common)

√ plaque-like lesions / ulcers

√ fold thickening, focal nodularity

√ annular segmental narrowing with obstruction

@ Esophagus

√ plaquelike lesions, narrowing, aperistalsis

@ Small bowel

√ circumferential thickening of terminal ileum (rare)

Genitourinary Sarcoidosis (0.2–5%)

@ Kidney

• interstitial nephritis, glomerulonephritis (rare)
√ renal calculi
CT:
√ striated nephrograms in case of interstitial nephritis
√ multiple low-attenuation tumorlike nodules (rare)

@ Scrotum (0.5%) = Testicular sarcoid
√ diffuse enlargement of epididymis
√ hypoechoic lesions in epididymis (bilateral in ⅓)
√ multiple hypoechoic lesions in testis (typically bilateral)
MR:
√ T2-hypointense nodules with enhancement on T1WI
Ethnicity: African-American÷white males = 20÷1

◊ Strongly consider sarcoidosis in cases of multiple masses simultaneously affecting epididymis and testis.

Musculoskeletal Sarcoidosis (6–20%)

◊ Portends a more chronic + adverse prognosis!
◊ Usually accompanied by cutaneous manifestations!

@ Joint (up to 40%)
• unimpaired joint function
Location: knee, ankle, elbow, wrist
√ inflammatory arthralgia

@ Muscle
√ increased T2 signal intensity of involved muscle
√ sarcoid nodules with centrally low signal intensity on all sequences (= area of fibrosis)
√ granulomas peripherally hyperintense on T2WI with contrast-enhancement on T1WI

@ Bone (5–10%)
Histo: medullary granulomas infiltrate cortical bone → bone destruction / reactive sclerosis
Location: hands + feet (metaphyseal ends of distal + middle phalanges, metacarpals, metatarsals); vertebrae; skull
• pain and swelling
√ sharply marginated cystlike lesions of varying size:
√ reticulated "lacelike" trabecular pattern
√ neuropathy-like destruction of terminal phalanges (DDx: scleroderma)
√ extensive bone erosion with pathologic fractures
√ phalangeal endosteal sclerosis + periosteal new bone (infrequent)
√ densely sclerotic lesions in spine, pelvis, ribs:
√ vertebral involvement unusual: destructive lesions with sclerotic margin
√ diffuse sclerosis of multiple vertebral bodies
√ paravertebral soft-tissue mass (DDx: indistinguishable from tuberculosis)
√ preservation of disk spaces
√ osteolytic changes in skull
NUC (bone scan):

√ positive before radiographic manifestation

Neurosarcoidosis (9%)

= SARCOIDOSIS OF CNS

= dural / leptomeningeal noncaseating granulomas

Incidence: CNS involvement clinically in 1–5–10% (in up to 25% of autopsies)

Age: bimodal distribution: initial peak around 20–29 years + 2nd peak > 50 years more common in women + people of West African descent; black÷white = 3÷1 to 10÷1

Suspected neurosarcoidosis is difficult to confirm without evidence of systemic disease; chest imaging may be helpful to evaluate for pulmonary involvement.

- cranial neuropathy (facial > acoustic > optic > trigeminal nerves) ← granulomatous infiltration + leptomeningeal fibrosis (50–75%) of rapid onset with spontaneous resolution
- peripheral neuropathy + myopathy
- aseptic meningitis (20%)
- diffuse encephalopathy, dementia
- pituitary + hypothalamic dysfunction (eg, diabetes insipidus in 5–10%)
- generalized / focal seizures (herald poorer prognosis)
- multiple sclerosislike symptoms (from multifocal parenchymal involvement)
- prompt improvement following therapy with steroids
    - spinal fluid: normal (in up to 30%) or nonspecific (↑ protein, ↑ leukocyte count, ↔ / ↓ glucose)

Location: leptomeninges, dura mater, subarachnoid space, peripheral nerves, brain parenchyma, ventricular system

◊ Affects meninges + cranial nerves more often than brain!

Neurosarcoidosis has a strong predilection for the base of the brain.

@ Meningeal / ependymal invasion

√ diffuse meningeal thickening + enhancement (most common) / meningeal nodules (less common)

Site: particularly in basal cisterns (suprasellar, sellar, subfrontal regions) with extension to optic chiasm, hypothalamus, pituitary gland, cranial nerves at points of exit from brainstem

Cx: communicating / obstructive hydrocephalus (most common finding) ← arachnoiditis / adhesions

DDx: carcinomatous / fungal / tuberculous meningitis

√ dense enhancement of falx + tentorium (granulomatous invasion of dura)

√ solitary / multiple dura-based small enhancing nodules / masses on brain surface + in perivascular spaces

DDx: granulomatous meningitis, TB, carcinomatous meningitis

√ ependymal enhancement

√ meningeal lesions usually imperceptible on unenhanced MR: T1-isointense + T2-hypointense relative to gray matter

√ intense diffuse meningeal enhancement

@ Parenchymal disease ← extension from meningeal / ventricular surfaces

√ single / multiple ringlike nodules / masses (= invasion of brain parenchyma via perivascular spaces of Virchow-Robin):
√ T2-hyperintense
√ iso- to hyperdense
√ homogeneously enhancing (if biologically active)
Site: periphery of parenchyma, periventricular, deep white matter, intraspinal
Cx: stenosis / occlusion of blood vessels
DDx: glioblastoma, metastases
√ small vessel ischemic change
√ lacunar infarction (especially brain stem + basal ganglia)
√ focal / widespread infarcts of peripheral gray matter / at gray-white matter junction ← periarteritis
√ reactive subcortical vasogenic edema
√ usual hyperintensity of posterior pituitary lobe no longer identifiable on unenhanced T1WI ← depletion of intracellular neurosecretory granules

@ Spinal cord
√ hyperintense enlargement of spinal cord (common) on T2WI ← edema
√ intramedullary lesion of decreased T2-signal
√ enhancing focus of sarcoid granuloma on T1WI

Skin / Cutaneous Sarcoidosis (25%)

(1) **Erythema nodosum** = nongranulomatous panniculitis:
= multiple bilateral tender erythematous nodules mostly on anterior surface of lower extremities
• often associated with fever + arthralgia (= painful swollen adjacent joints)
Onset: typically associated with benign self-limiting acute sarcoidosis (eg, Löfgren syndrome)
Prognosis: remission in 6–8 weeks

(2) **Lupus pernio** = indurated red-brown to violaceous (= bluish purple) papules + plaques
Location: nasal alae, cheeks, ear lobes, fingers, toes
Associated with: pulmonary fibrosis, lytic lesions of phalanges

(3) Asymptomatic pink-yellow / red-brown papules + plaques
Onset: typically associated with chronic sarcoidosis
Location: face, posterior neck, previous trauma site
• characteristic "apple jelly" color on diascopy (= pressure applied with glass slide)

• skin plaques / scars

Thoracic Sarcoidosis (90%)

◊ Extrathoracic manifestations without intrathoracic involvement in < 10%!

Silzbach CXR stage versus percentage at presentation:
0 normal chest radiograph 5–10%
1 hilar + mediastinal lymphadenopathy only 50%
2 lymphadenopathy + parenchymal disease 25–30%
3 diffuse parenchymal disease only 10–12%
4 pulmonary fibrosis 5%

◊ Progression to pulmonary fibrosis in 25%!

Spontaneous remissions versus Siltzbach stage:

60–90% for stage 1 disease
40–70% for stage 2 disease
10–20% for stage 3 disease
0% for stage 4 disease

- mild symptoms in spite of extensive radiographic changes (DIAGNOSTICALLY SIGNIFICANT):
  - dry cough, dyspnea, hyperreactivity
  - fatigue, night sweats, weight loss, erythema nodosum
  - pulmonary arterial hypertension (50%)

Associated with: tuberculosis in up to 13%

@ intrathoracic lymphadenopathy (85% by CT):

Typical patterns of lymphadenopathy:

√ symmetric enlargement of bilateral hilar nodes + right paratracheal and aortopulmonary window nodes (75–95%) = "1-2-3" sign = **Garland triad**

Clinical Diagnostic Criteria of Cardiac Sarcoidosis *established by Japanese Ministry of Health and Welfare (2007)*
Major criteria
• advanced atrioventricular block
√ basal thinning of interventricular septum
√ positive cardiac gallium uptake
√ LV ejection fraction depressed by < 50%
Minor criteria
• abnormal ECG: ventricular arrhythmias, complete right bundle branch block axis deviation, abnormal Q wave
√ abnormal echo: abnormality of regional wall motion / morphology (ventricular aneurysm, wall thickening)
√ perfusion defect on ^{201}Th / ^{99m}Tc myocardial scintigraphy
√ late / delayed Gd-enhancement of myocardium
• endomyocardial Bx: interstitial fibrosis / monocyte infiltration

√ enlargement of middle mediastinal nodes = left paratracheal, subcarinal, aortopulmonary (50%)

Atypical patterns of lymphadenopathy:

√ asymmetric lymph node enlargement
√ isolated unilateral hilar nodal enlargement (< 5%)
√ lymphadenopathy in unusual locations: internal mammary, paravertebral, retrocrural
√ mediastinal lymphadenopathy without hilar nodes
√ calcification of lymph nodes (in 3% after 5 years, in 20% after 10 years): amorphous, punctate, popcornlike, eggshell-like

Prognosis: adenopathy commonly ↓ as parenchymal disease ↑; subsequent parenchymal disease in 32%; adenopathy does NOT develop subsequent to parenchymal disease

@ parenchymal disease (in 60% by CT):

Location: usually bilateral + symmetric; predominantly in upper lung + mid-zone

◊ NOT associated with lymphadenopathy in 16–20%
◊ Parenchymal granulomas are invariably present on open lung biopsy!
Typical parenchymal manifestations:
√ multiple bilateral symmetric micronodules (75–90%)
Cause: noncaseous epitheloid cell granulomas deposited along course of lymphatics
Distribution: subpleural peribronchovascular > interlobular septal sites
Size: 2–4 mm
√ macronodules ≥ 5 mm
Cause: coalescence of micronodules
√ bilateral perihilar consolidations radiating from hilum toward periphery ± air bronchogram
√ progressive patchy fibrosis in 20%:
√ linear reticular opacities
√ traction bronchiectasis
√ architectural distortion
√ volume loss

Pattern of distribution + upper lung predominance with coexistent mediastinal lymphadenopathy strongly favor sarcoidosis differentiating it from other nodular lesions (EG, miliary TB, metastasis).

Atypical parenchymal manifestations:
√ airspace consolidation (15–25%):
√ multiple bilateral 1–4 cm pulmonary nodules and masses:
√ ± air bronchograms
√ cavitation (0.6%)
Cause: coalescent interstitial granulomas
Distribution: in perihilar and peripheral regions
√ conglomerate masses
√ nonspecific **"galaxy" sign** = small satellite nodules at periphery of masses
Cause: coalescent parenchymal lesions
DDx: progressive massive fibrosis
√ **"sarcoid cluster"** = cluster of multiple micronodules distributed along lymph vessels
√ solitary lung nodule / mass (rare)
√ **"alveolar sarcoidosis"** = bilateral symmetric patchy airspace consolidation ± air bronchograms fading into a nodular pattern peripherally (10–20%)
Cause: confluence of acinar + interstitial micro-nodules compressing surrounding alveoli
DDx: pneumonia, tuberculosis, BOOP
√ patchy ground-glass opacities (40%)
Cause: confluence of micronodular granulomatous + fibrotic interstitial lesions → airway compression without airspace filling
DDx: bronchoalveolar cell carcinoma, lymphoma, pneumoconiosis, pneumonia, BOOP
√ reticulolinear opacities (50%)

Cause: interlobular + intralobular septal thickening
DDx: lymphangitic carcinomatosis
√ fibrocystic changes = cyst, bulla, bleb, paracicatricial emphysema
Cause: advanced stage of chronic fibrosis
√ honeycomb-like cysts
√ cavitation / pseudocavitation of parenchymal lesion (10% of end-stage sarcoidosis / primary cavitary sarcoidosis in < 1%)
√ mycetoma formation of stage 4 cystic sarcoidosis (1–3%)
√ miliary opacities (<1%)
DDx: tuberculosis, pneumoconiosis, metastases, histoplasmosis, chickenpox, Langerhans cell histiocytosis

@ <u>airway disease</u> by CT:
√ mosaic attenuation = inhomogeneous attenuation at inspiratory CT
Cause: patchy interstitial disease, obstructed small airways, vascular disease
√ air trapping = focal areas of ↓ attenuation on expiratory CT (95%)
√ tracheobronchial stenosis (2%):
√ atelectasis ← compression by large lymph nodes / endobronchial granulomas
√ bronchiectasis ← scarring / fibrosis

@ <u>pleural disease</u> (1–4%) by CT:
√ usually small pleural effusion (transudative / exudative, hemorrhagic, chylous) clearing within 2–3 months
√ pneumothorax
Cause: rupture of emphysematous bleb, necrosis of subpleural sarcoid granuloma
√ pleural plaquelike opacities
Cause: multiple subpleural coalescent micronodules

HRCT:
(a) reversible ← granulomatous inflammation resolving with time (in 80%):
√ micronodules, macronodules
√ airspace consolidation / confluent alveolar opacities
√ ground-glass opacities
√ interlobular septal thickening
√ intralobular linear opacities
(b) irreversible ← chronic interstitial fibrosis (in 20%):
√ honeycomb-like opacities, cysts, bullae, emphysema
√ architectural distortion
√ traction bronchiectasis / bronchiolectasis
√ volume loss in upper lobes with retraction of hila
√ mycetoma (in 10% of preexisting cavity)

NUC:
√ FDG uptake in lung parenchyma + mediastinal nodes ← regional inflammation + sarcoid lesions

Atypical manifestations (25%):
√ bronchostenosis (2%) with lobar / segmental atelectasis

Cx: (1) pneumothorax ← chronic lung fibrosis (rare)
(2) cardiomegaly ← cor pulmonale (rare)

(3) aspergilloma formation in apical bulla

Prognosis:

80% spontaneous remission of stage 1 + 2 disease

75% complete resolution of hilar adenopathy

33% complete resolution of parenchymal disease

30% significant improvement

20% irreversible pulmonary fibrosis (may persist unchanged for > 15 years)

5% mortality: cor pulmonale (← lung fibrosis), CNS, liver cirrhosis, pulmonary hemorrhage (← mycetoma); in Japan death from cardiac involvement in 80%

25% relapse (in 50% detected by CXR)

5% recurrence after remission lasting > 1 year

Factors effecting poor prognosis: stage 2 / 3 at time of initial diagnosis, disease onset > 40 years of age, black race, hypercalcemia, splenomegaly, osseous involvement, chronic uveitis, lupus pernio

Factors effecting good prognosis: fever, polyarthritis, erythema nodosum, bilateral hilar lymphadenopathy (Löfgren syndrome)

DDx: mycobacterial / fungal infection, malignancy, pneumoconiosis (silicosis, berylliosis)

◊ "The great mimic" = initially broad imaging DDx

Sarcoidosis of Head & Neck

√ granulomas may enhance

@ Cervical lymph nodes (rare)

• palpable peripheral lymphadenopathy (⅓): discrete, nontender and movable

@ Ophthalmic sarcoidosis (25–80%)

• typically bilateral uveitis, photophobia, blurred vision, glaucoma (rare)

√ commonly bilateral enlarged enhancing lacrimal glands ← chronic dacryoadenitis

√ masslike appearance of optic nerve / nerve sheath

√ enlargement of optic canal ← optic neuritis

√ avidly enhancing orbital soft-tissue masses with involvement of extraocular muscles + lacrimal glands

@ Larynx (5%)

√ thickening of larynx with enhancement of granulomas

@ Nose

√ multiple small granulomas of septum + turbinates

@ Parotid gland (6%), other salivary glands (30%)

CT:

√ multiple diffusely dense noncavitating nodules within parotid gland

√ enlargement of intraparotid lymph nodes

NUC:

√ **"panda" sign** = 67Ga uptake in both parotid glands + both lacrimal glands + nose

Heerfordt Syndrome

(1) Parotid enlargement (6%)

◊ May be the initial and only manifestation of sarcoid

- diffuse bilateral painless enlargement (10–30%)
- xerostomia

(2) Uveitis
(3) Facial nerve paralysis

Uveoparotid Fever

(1) Parotitis
(2) Uveitis
(3) Fever

Sarcoidosis of Other Organs

@ Peripheral lymph node enlargement (30%)
@ Muscle (25%): myopathy

SEPTIC PULMONARY EMBOLI

= lodgement of an infected thrombus in a pulmonary artery
Organism: S. aureus, Streptococcus
Predisposed: IV drug abusers, alcoholism, immunodeficiency, CHD, dermal infection (cellulitis, carbuncles)
Source:
(a) infected venous catheter / pacemaker wires, arteriovenous shunts for hemodialysis, drug abuse producing septic thrombophlebitis (eg, heroin addicts), pelvic thrombophlebitis, peritonsillar abscess, osteomyelitis
(b) tricuspid valve endocarditis (most common cause in IV drug abusers)
Age: majority < 40 years
• sepsis, cough, dyspnea, chest pain
• shaking chills, high fever, severe sinus tachycardia
Location: predilection for lung bases
√ multiple nondescript pulmonary infiltrates (initially)
√ migratory infiltrates (old ones heal, new ones appear)
√ cavitation (frequent), usually thin-walled
√ pleural effusion (rare)
CT (more sensitive than CXR):
√ multiple peripheral parenchymal nodules ± cavitation / air bronchogram (83%)
√ wedge-shaped subpleural lesion with apex of lesion directed toward pulmonary hilum (50%)
√ **"feeding vessel" sign** = pulmonary artery leading to nodule (67%)
√ cavitation (50%), esp. in staphylococcal emboli
√ air bronchogram within pulmonary nodule (28%)
Cx: empyema (39%)

SIDEROSIS

= ARC WELDER PNEUMOCONIOSIS
= inhalation of inert iron oxide / metallic iron deposits
Occupational exposure:

electric arc welding, oxyacetylene torch workers (iron oxide in fumes), mining + processing of iron ores, cutting / burning of iron + steel, foundry workers, grinders, fettlers, silver polishers (jewelry industry)

Path: iron phagocytized by macrophages in alveoli / respiratory bronchioles, elimination from lung by lymphatic circulation; NOT associated with fibrosis unless admixed with silica

Location: middle ⅓ of lung, perihilar region

• asymptomatic (for pure siderosis)

√ small nodules / diffuse fine reticulonodular opacities ← radiopaque accumulation of iron particles in macrophages aggregated in lymphatics along bronchovascular bundles:

√ may disappear after exposure is discontinued

√ small round opacities (indistinguishable from silica / coal)

√ NO secondary fibrosis + NO hilar adenopathy (unless mixed dust inhalation as in **siderosilicosis** / **silicosiderosis** = mixed-dust pneumoconiosis)

HRCT:

√ widespread poorly defined centrilobular micronodules (71%)

√ ± branching linear structures ← deposition of minute iron oxide particles along perivascular + peribronchial lymphatic vessels

√ extensive ground-glass attenuation + reticulation without zonal predominance

√ emphysematous changes (33%) likely due to smoking

√ honeycombing resembling usual interstitial pneumonia

√ pleural irregularity (suggestive of exposure to asbestos)

√ conglomerate masses with areas of high attenuation (= organizing pneumonia with siderosis)

DDx: silicosis (nodular opacities more dense + profuse)

SILICOSIS

= inhalation of crystalline silicon dioxide (= silica, one of the most widespread elements on earth); most prevalent silicosis of progressive nature after termination of exposure; similar to CWP (because of silica component in CWP)

Substance: crystalline silica (quartz); tridymite / cristbalite (less fibrogenic)

Occupational exposure:

tunneling, mining, quarrying, stone cutting, polishing, glass manufacturing, foundry work, sandblasting, pottery, brick lining, boiler scaling, vitreous enameling, ceramic industry

Dust deposition: dependent on

(a) airflow: deposition of 1–5-µm particles predominantly around respiratory bronchioles in a centrilobular location within secondary pulmonary lobule

(b) lymphatic clearance: related to pulmonary arterial pressure (gravity-related vertical gradient) + blood flow (higher blood flow through LUL) + passive milking of lymphatics by respiratory motion (lateral > anterior > posterior chest wall)

Path: small particles engulfed by macrophages; liberation of silica results in cell death; 2–3-mm nodules with layers of laminated connective tissue around smaller vessels

Clinical classification:

1. Acute silicosis = alveolar silicoproteinosis
2. Classic silicosis = chronic interstitial reticulonodular

Radiographic classification:
(a) simple = small + round / irregular opacities
(b) complicated = progressive massive fibrosis

Cx: predisposes to tuberculosis + carcinoma

DDx: coal worker pneumoconiosis (identical radiographs)

Acute Silicosis

= ALVEOLAR SILICOPROTEINOSIS

= heavy exposure to respirable free silica in enclosed space with minimal / no protection of airways (sandblasters!)

Histo: alveolar filling with PAS-positive staining substance; proliferation of type II pneumatocytes + profuse surfactant production

Exposure time: as short as 6–8 months

Associated with: increased risk to develop autoimmune disease

Distribution: lung periphery; predominantly lower lung zones; bilateral

√ diffuse bilateral perihilar airspace / ground-glass disease

√ air bronchograms

HRCT:

√ numerous bilateral patchy centrilobular nodular ground-glass opacities

√ multifocal patchy ground-glass opacities + consolidation

√ "crazy paving" = airspace filling + fine interlobular septal thickening ← edematous + fibrous tissue

Cx: infection with TB + atypical mycobacteria

Prognosis: often rapidly progressive with death from respiratory failure + cor pulmonale

DDx: alveolar proteinosis

Classic Silicosis

= chronic interstitial reticulonodular disease

Path: silicotic nodules = mature collagen centrally + peripheral zone of particle laden macrophages

Histo: birefringent silicate crystals of 1–3 μm in length

Chronic Simple Silicosis

Lag time: at least 10–20 years of dust exposure before appearance of roentgenographic abnormality

Location: posterior portion of upper lobes bilaterally

CXR:

√ multiple small 2–5 (range, 1–10)-mm round well-defined opacities:

√ typically central calcifications in 10–20%

√ hilar + mediastinal lymphadenopathy, may calcify in 5% **("eggshell pattern")**

√ ± reticulonodular pattern

HRCT:

√ multiple small calcified nodules of 2–5 mm in size:

Distribution: perilymphatic (= centrilobular, paraseptal, subpleural)

√ "pleural pseudoplaques" = aggregate of subpleural nodules in round / triangular

configuration
√ thickened intra- and interlobular lines
√ subpleural curvilinear lines ← peribronchiolar fibrosis
√ ground-glass pattern = mild thickening of alveolar wall + interlobular septa ← fibrosis / edema
√ parenchymal fibrous bands
√ traction bronchiectasis
√ honeycombing

Complicated Silicosis

= PROGRESSIVE MASSIVE FIBROSIS
= appearance of large opacities > 1 cm in diameter ← expansion + confluence of individual silicotic nodules
Location: mid lung zone / peripheral ⅓ of upper lung migrating toward hilum
Distribution: often bilateral symmetric + nonsegmental
√ focal conglomerate sausage-shaped masses with ill-defined / irregular margins (in advanced stages):
√ lateral interface typically parallels lateral chest wall
√ surrounding compensatory emphysema in unaffected portion between mass + pleura
√ slow change over years
√ may calcify + cavitate ← ischemic necrosis

Silicotuberculosis

= synergistic relationship between silicosis + primary tuberculosis (in 25%)
• intermittently positive sputa
√ asymmetric nodules / consolidation
√ cavitation (strongest indicator of associated TB)
√ rapid disease progression

Caplan Syndrome

More common in coal worker's pneumoconiosis

SOLITARY FIBROUS TUMOR

= rare benign ubiquitous spindle cell neoplasm; frequently misdiagnosed as hemangiopericytoma
Origin: neoplasm of submesothelial origin (primitive mesenchymal cell)
Path: well-defined pseudoencapsulated lobulated neoplasm of whorled fibrous tissue WITHOUT necrosis / cyst formation / hemorrhage
◊ Most solitary fibrous tumors are benign!
Histo: (a) fibrous type: hypercellular areas composed of spindle cells resembling fibroblasts + variable amount of hypocellular fibrous areas (= hyalinized collagen)
(b) cellular type: monotonous moderate to high cellularity + little intervening fibrous tissue
CHARACTERISTIC strong CD34 immunoreactivity + EMA negativity
Mean age: 54 years; M > F

Location:
(a) visceral pleura (most common)
(b) extrapleural location: lung, mediastinum, pericardium, extraperitoneal spaces, nose, paranasal sinuses, orbit, kidney, liver, skin

Extrapleural solitary fibrous tumor: mesentery, peritoneum

• hypertrophic osteoarthropathy (35%), hypoglycemia (4%)
√ solitary well-circumscribed unencapsulated lobulated mass
√ mobile mass if pedunculated
√ heterogeneous texture if large
√ ± dystrophic calcifications and enhancing internal vessels
√ intense arterial enhancement ← hypervascularity

MR:
√ intermediate SI on T1WI
√ heterogeneous SI + multiple flow voids representing prominent vascular channels on T2WI (common)

CEMR:
√ SUGGESTIVE avidly enhancing areas of low T2 signal ← fibrosis with abundant collagen
√ persistent delayed enhancement ← fibrous tumor component

Prognosis: 10–15% of extrapleural solitary fibrous tumors show malignant behavior (← recurrence after resection / metastatic disease)

DDx: (1) Hypervascular neoplasm: angiosarcoma, hemangioendothelioma, angiomyxoma
(2) Fibrous neoplasm: malignant fibrous histiocytoma, fibrosarcoma, leiomyoma, desmoid tumor

Solitary Fibrous Tumor of CNS

Mean age: 57 years; (?) F >> M
• headache
Location: dura (falx, occipital + spinal dura, tentorium, cerebellopontine angle), ventricle
√ hyperattenuating mass ± dural tail
√ diffuse / heterogeneous enhancement
√ smooth erosion of adjacent skull
√ lipid + lactate peaks + elevated myo-inositol (3.5 ppm)
DDx: meningioma (hyperostosis)

Solitary Fibrous Tumor of Pelvis

Age: 5th decade (range, 20–70 years); M = F
Location: pelvic peritoneum / retroperitoneum
• mostly asymptomatic, pressure, hypoglycemia (< 5%)
Rx: complete surgical resection ± preoperative embolization; surgical cytoreduction + intraoperative chemotherapy + radiation therapy

√ well-defined mass with intense heterogeneous enhancement that persists into delayed phase
√ areas of central low attenuation ← necrosis / hemorrhage / cystic change

Staphylococcal pneumonia

◊ Most common cause of bronchopneumonia!
(a) common nosocomial infection (patients on antibiotic drugs most susceptible)
(b) accounts for 5% of community-acquired pneumonias (esp. in infants + elderly)
◊ Secondary invader to influenza (commonest cause of death during influenza epidemics)
Organism: Staphylococcus aureus = Gram-positive, appears in coagulase-producing clusters
√ rapid spread through lungs
√ empyema (esp. in children)
√ pneumothorax, pyopneumothorax
√ abscess formation
√ bronchopleural fistula
A. in CHILDREN:
√ rapidly developing lobar / multilobar consolidation
√ pleural effusion (90%)
√ pneumatocele (40–60%)
B. in ADULTS:
√ patchy often confluent bronchopneumonia of segmental distribution, bilateral in > 60%
√ segmental collapse (air bronchograms absent)
√ late development of thick-walled lung abscess (25–75%)
√ pleural effusion / empyema (50%) (DDx from other pneumonias)
Cx: meningitis, metastatic abscess to brain / kidneys, acute endocarditis

STREPTOCOCCAL PNEUMONIA

Frequency: 1–5% of bacterial pneumonias (rarely seen); most common in winter months
Organism: Group A ß-hemolytic streptococcus
= Streptococcus pyogenes, Gram-positive cocci appearing in chains
Predisposed: newborns, following infection with measles
Associated with: delayed onset of diaphragmatic hernia (in newborns)
• rarely follows tonsillitis + pharyngitis
√ patchy bronchopneumonia
√ lower lobe predominance (similar to staphylococcus)
√ empyema
Cx: (1) Residual pleural thickening (15%)
(2) Bronchiectasis
(3) Lung abscess
(4) Glomerulonephritis

SWYER-JAMES SYNDROME

= MACLEOD SYNDROME = UNILATERAL LOBAR EMPHYSEMA = IDIOPATHIC UNILATERAL HYPERLUCENT LUNG
= chronic complication of infectious obliterative bronchiolitis in infancy or childhood as early as 9 months after initial infectious insult
Etiology: acute viral bronchiolitis in infancy / early childhood (adenovirus, RSV, mycoplasma) preventing normal development of lung
Path: variant of postinfectious constrictive bronchiolitis with acute obliterative bronchiolitis,

bronchiectasis, distal airspace destruction (developing in 7–30 months)
- asymptomatic; history of recurrent lower respiratory tract infections during childhood
- chronic cough, wheezing, dyspnea on exertion, hemoptysis
- obstructive lung disease pattern at pulmonary function test

Location: one / both lungs (usually entire lung, occasionally lobar / subsegmental)
√ hyperlucency of one lung ← air trapping ← bronchiolar obstruction
√ diminished number + size of pulmonary vessels:
  √ small ipsilateral hilum ← diminuted hilar vessels + attenuated arteries)
√ small hemithorax with decreased volume
√ normal hyperexpanded hemithorax ← collateral air drift
√ air trapping during expiration
  DDx: no air trapping with proximal interruption of pulmonary artery (no hilum), hypogenetic lung syndrome, pulmonary embolus
√ mild cylindrical bronchiectasis with paucity of bronchial subdivisions (cutoff at 4th–5th generation = "pruned tree" bronchogram)

HRCT (most useful modality):
  √ bilateral areas of decreased attenuation:
    √ areas of normal lung attenuation within hypoattenuating lung
    √ air trapping within hypoattenuating lung
    √ ipsilateral bronchiectasis
  √ diminished size of pulmonary vessels in hyperlucent areas

Angio:
  √ "pruned tree" appearance

NUC (V/Q scan):
  √ matched defects of perfusion + ventilation (with delayed washout) in hyperlucent regions

Bronchography:
  √ incomplete filling of ipsilateral peripheral bronchioles
  √ dilated bronchi with sharply terminating segments

DDx: pulmonary artery atresia (uncommon in adults), localized bullous emphysema (deviation of vessels), bronchial obstruction

SYSTEMIC LUPUS ERYTHEMATOSUS

= SLE = most prevalent of the potentially grave connective tissue diseases characterized by involvement of vascular system, skin, serous + synovial membranes

Incidence: 1–10 ÷ 100,000 persons per year; Blacks÷Caucasians = 3÷1; increased risk in relatives

Cause: complex systemic autoimmune disease including complement system, T suppressor cells, and cytokine production with deposition of antigen-antibody complexes / autoantibodies inducing necrotizing vasculitis (type III immune complex phenomenon) of arterioles + capillaries ← dysfunctional suppressive controls on immune system

Age: 16–41 years; <u>in adults</u> M÷F = 1÷11 (in ≥ 90% in women of childbearing age); <u>in children</u> M÷F = 2÷1

Diagnostic criteria (≥ 4 criteria = 98% specific, 97% sensitive):

(1) Malar rash

(2) Discoid lesions
(3) Photosensitivity
(4) Oral ulcers
(5) Nonerosive arthritis
(6) Serositis (pleuritis or pericarditis)
(7) Positive antinuclear antibody test
(8) Renal disease
(9) Neurologic disease: seizures / psychosis
(10) Hematologic abnormalities
(11) Immunologic disorder

Disease severity: defined by number of organ systems involved

- fatigue, malaise, anorexia, fever, weight loss
- clinically heterogeneous ← different types of serum antibodies
- antinuclear DNA antibodies (87%)
- hypergammaglobulinemia (77%); Sjögren syndrome (frequent)
- LE cells (= antigen-antibody complexes engulfed by PMNs) in 78%
- chronic false-positive Wassermann test for syphilis (24%)
- anemia (78%), leukopenia (66%), thrombocytopenia (19%)

Cx: deep venous thrombosis (9–35%) + thromboembolism with antiphospholipid antibodies in serum; ↑ prevalence of lymphoreticular malignancies; frequent infections

Prognosis: 60–90% 10-year survival; death from renal failure / sepsis / CNS involvement / myocardial infarction

Rx: nonsteroidal antiinflammatory drugs / oral steroids

Antiphospholipid Antibody Syndrome

= (aPL-ab syndrome) characterized by arterial + veno-occlusive disease, thrombocytopenia, recurrent vascular thromboses + miscarriages

Path: antibodies target cell surface molecules on vascular endothelium and platelets; acquired free protein S deficiency

- recurrent strokes + pulmonary embolism, Budd-Chiari syndrome, dural venous sinus thrombosis, ischemic bowel
- lupus anticoagulant serves as marker of functional activity

Dx: ≥ 1 clinical criterion: deep venous thrombosis, arterial thrombosis, pregnancy loss, thrombocytopenia AND
≥ 1 laboratory criterion: lupus anticoagulant, immunoglobulins [IgG, IgM, IgA] against cardiolipin

Minor criteria: heart valve abnormality, livedo reticularis, migraine, pulmonary hypertension, AVN, myelopathy, chorea

Cx: pulmonary arterial hypertension (25%) ← recurrent pulmonary thromboembolism

Rx: anticoagulants (for vascular occlusion)

Cardiovascular SLE

@ Cardiac valves (18–74%)
more often seen in patients with antiphospholipid antibody (aPL-ab) syndrome
√ valve leaflet thickening

√ **Libman-Sacks endocarditis**:
= small granular vegetations on mitral / aortic valve
√ 1–4 mm single / multiple verrucous vegetations
Cx: valve destruction

@ Pericardium (17–50%)
√ exudative pericardial effusion = serositis of pericardium
√ abnormal thickening + enhancement of pericardium

@ Myocardium
• clinically silent (in up to 50%)
√ global left ventricular dysfunction (uncommon)
√ cardiomegaly = primary lupus cardiomyopathy
Histo: myositis (myocarditis) with perivascular infiltration by lymphocytes and neutrophils

@ Vasculature
√ coronary atherosclerosis
Mortality rate: 9 x that of general population
√ marked arterial wall thickening < 100 μm in diameter
Histo: vasculitis with fibrinoid necrosis and minimal infiltration by inflammatory cells
Cx: ischemia / hemorrhage into bowel wall → perforation → peritonitis
√ aortitis (uncommon) → dissection, aneurysm

Drug-induced Lupus Erythematosus (DIL)

• temporary phenomenon
Agents: procainamide, hydralazine, isoniazid, phenytoin account for 90%
√ pulmonary + pleural disease more common than in SLE

Gastrointestinal SLE (in up to 50%)

• nonspecific vague abdominal pain (10–37%)
• buccal erosions / ulcerations; GI tract bleeding

@ Esophagus
• dysphagia, gastroesophageal reflux, atypical chest pain
√ hypomotility of distal ⅓ (13–32%) similar to scleroderma
√ mucosal granularity ± ulceration ← reflux esophagitis
Cx: reflux esophagitis

@ Pancreas
√ peripancreatic mesenteric fatty infiltration, phlegmon formation ± glandular enlargement = acute focal / diffuse pancreatitis (in 8–28%)
√ calcium deposition within ductal system + organ atrophy = chronic pancreatitis

@ Liver, spleen
√ hepatomegaly, hepatitis, cirrhosis, splenomegaly
√ "painful" ascites

@ Bowel
√ features of gastritis
√ features of bowel ischemia with ← small vessel vasculitis

Cx: pneumatosis intestinalis, perforation

√ mesenteric ischemia: colitis, pseudoobstruction, ileus, thumbprinting, luminal narrowing

Musculoskeletal SLE

@ Joints

• arthralgia (95%)

Location: small joints of hand, wrist, knee, shoulder

√ CHARACTERISTIC symmetric nonerosive nondeforming polyarthritis of hands

√ Jaccoud arthropathy (10%)

√ tumoral calcinosis

@ Ligaments

√ deformities in initially reversible SLE ← ligamentous instability and laxity

@ Bone

√ osteonecrosis / AVN (5–50%) of weight-bearing joints:

Location: femoral head > humeral head > femoral condyle > tibial plateau

√ insufficiency fracture

Cause: deconditioning, accelerated bone loss ← steroid therapy

√ septic arthritis and osteomyelitis

Organism: S aureus, Gram-negative bacilli, M. tuberculosis

Renal SLE

Prevalence: kidneys involved in 100% with renal disease developing in 30–50%

Histo: focal membranoproliferative glomerulonephritis = immune complex deposition in subepithelial and subendothelial layers of glomeruli (**SLE nephritis**)

• renal failure ← fibrinoid thickening of basement membrane

√ aneurysms in interlobular + arcuate arteries (similar to but less frequent than polyarteritis nodosa)

√ normal / decreased renal size

√ hydronephrosis ← detrusor muscle spasm with vesicoureteral reflux / fibrosis of ureterovesical junction

US:

√ kidney enlarged (early) / diminutive (late stage)

√ increased parenchymal echogenicity

CT:

√ multiple linear hypoattenuating bands ← vasculitis

Cx: (1) Nephrotic syndrome (common)

(2) Renal vein thrombosis (in 33%) ← nephrotic syndrome induces hypercoagulability

Prognosis: end-stage renal disease is common cause of death

Skin SLE (81%)

• "**butterfly rash**" (= facial erythema), discoid lupus erythematosus, alopecia, photosensitivity

• Raynaud phenomenon (15%)

Thoracic SLE (30–70%)

◊ Affects respiratory system more commonly than any other connective tissue disease

- pleuritic chest pain (35%); fever, cough, dyspnea (40–57%)
- respiratory dysfunction (> 50%): single-breath diffusing capacity for carbon monoxide most sensitive indicator

@ Pleura (50%)

√ recurrent small uni- / bilateral (½) pleural effusions (in 30–50% during course of disease) ← pleuritis

√ pleural thickening / fibrosis (50–83%)

Dx: pleural fluid analysis (exudate positive for lupus erythematosus cells, immune complexes, anti-DNA antibodies)

@ Lung (> 50%)

Cause: chronic antibody damage to alveolar-capillary membrane

√ parenchymal opacification:

√ <u>pneumonia</u> (most common) ← bacteria / opportunistic organism

Risk: 3 x higher than in general population ← ⇓ phagocytic activity + ⇓ natural killer cell activity against pathogens + poor clearance of secretions + immunosuppressive therapy

√ <u>diffuse alveolar hemorrhage</u> (2–5%):

√ bilateral areas of consolidation + ground-glass opacities + septal thickening in lower lungs

Prognosis: 80% mortality ← extensive blood loss

√ pulmonary edema

√ **acute lupus pneumonitis** (10–14%):

Histo: diffuse alveolar damage + necrosis with cellular infiltrates + hyaline membranes

Rx: responsive to corticosteroids

√ uni- / bilateral poorly defined patchy areas of increased density peripherally at lung bases (alveolar pattern)

√ ground-glass opacity on CT

√ cavitating nodules (vasculitis)

√ pulmonary fibrosis (< 3%):

Pattern: nonspecific interstitial pneumonia (NSIP)

√ architectural distortion, honeycombing

√ subpleural interstitial reticulations in lower lung fields (chronic form) in 3%

√ fleeting platelike atelectasis in both bases (? infarction due to vasculitis)

√ hilar + mediastinal lymphadenopathy (extremely rare)

@ Diaphragm

Path: respiratory muscle dysfunction (25%) ← primary myopathy + phrenic neuropathy + pleural inflammation

- dyspnea out of proportion to severity of chest radiographic abnormalities
- ↓ static lung volumes + vital capacity ← restrictive process with normal diffusing capacity

√ linear atelectasis + ill-defined juxtadiaphragmatic areas of increased opacity

√ **shrinking lung syndrome** (0.6%):
√ progressive loss of lung volume
√ elevated diaphragms
√ sluggish diaphragmatic excursions

Cx: (1) Community-acquired pneumonia (14%)
(2) Pulmonary arterial hypertension (14%) ← chronic interstitial disease, vasculopathy, recurrent pulmonary embolism

Neuropsychiatric SLE / CNS Lupus

Prevalence: 30–40%; 19% of lupus-related deaths

• psychosis, stroke, epilepsy, headache, cognitive defects

√ cerebral ischemia + infarction:

Cause: (a) coagulopathy ← aPL-ab syndrome
(b) accelerated atherosclerosis ← steroids
(c) vasculitis,
(d) thromboemboli ← Libman-Sacks disease

Average age: 35 years

Distribution:
(a) clearly defined arterial territory of large-vessel disease
(b) small cortical / deep gray matter infarcts ← lupus angiitis / vasculitis

√ reduced diameter / occlusion of ICA
√ intracranial venous occlusion (in 29%)
√ intracranial hemorrhage (in up to 42%) = parenchymal / subarachnoid hemorrhage, subdural hematoma, petechial hemorrhage, hemorrhagic infarcts
√ cerebral white matter lesions in subcortical and periventricular regions at FLAIR + T2WI (in 60–86%)
√ cerebral atrophy (in about 43%)
√ myelopathy (in 1–3%)
√ optic neuritis (in 21–48%)

TALCOSIS

= prolonged inhalation of talc (= hydrated magnesium silicate)

Occupational exposure: manufacture of leather, rubber, paper, textiles, ceramic tiles

Often associated with: quartz, mica, kaolin, asbestos (amphibole fibers of tremolite and anthophyllite)

Different forms of disease depending on composition:

(1) Pure talcosis

CXR:

√ generalized haziness, nodulation, reticulation

√ large opacities resembling progressive massive fibrosis

HRCT:

√ small centrilobular + subpleural nodules

√ conglomerate masses + internal foci of high attenuation

(2) Talcosilicosis

√ small rounded + large opacities

√ fibrogenic process (NO regression after removal of patient from exposure)

(3) Talcoasbestosis

√ massive and bizarre pleural plaques

√ may encase lung with calcification

(4) Recreational IV drug use

√ diffuse small nodules, perihilar conglomerate masses, ground-glass opacities, emphysema

Location: typically sparing of apices + costophrenic sulci

TERATOID TUMOR OF MEDIASTINUM

= MEDIASTINAL GERM CELL TUMOR = [= TERATOMA]

Pathogenesis: "misplaced" multipotential primitive germ cells during migration from yolk endoderm to gonad

Frequency:

› adult: 15% of anterior mediastinal tumors

› child: 24% of anterior mediastinal tumors

› fetus: 10% of all fetal teratomas

◊ 16–28% of all mediastinal cysts!

◊ Occurs in same frequency as the usually larger thymoma!

◊ ⅓ of primary neoplasms in this area are in children

Classes: (1) Mature teratoma (solid)

(2) Cystic teratoma (dermoid cyst)

(3) Immature teratoma

(4) Malignant teratoma (teratocarcinoma)

(5) Mixed teratoma

Gonzalez-Crussi Grading System of Teratomas	
Grade	*Classification*
0	mature
1	immature / probably benign
2	immature / possibly malignant
3	frankly malignant

Location: mediastinum is 3rd most common site for teratoid lesions (after gonadal + sacrococcygeal location); 5% of all teratomas occur in mediastinum, mostly anterosuperiorly (in only 1% posteriorly)

◊ The anterior mediastinum is the most common extragonadal site of primary germ cell tumors (1–3% of all germ cell tumors)!

CXR:
- √ usually incidental large round lobulated mediastinal mass
- √ DIAGNOSTIC teeth / bone / fat / amorphous peripheral wall calcifications (in 20%)
- √ frontal CXR:
  - √ silhouetting of heart
  - √ obtuse angle to mediastinum + lung
  - √ disruption of azygoesophageal recess / anterior junction line
  - √ "hilum overlay" sign (= not of hilar origin!)

lateral CXR:
- √ obliteration of retrosternal clear space

MR:
- √ variable appearance depending on components of teratoma:
  - √ areas of high signal intensity on T1WI ← fat
  - √ areas of low SI on T1WI + high SI on T2WI ← fluid

Cx:
(1) Hemorrhage
(2) Pneumothorax ← bronchial obstruction with air trapping + alveolar rupture
(3) Respiratory distress ← rapid increase in size from fluid production with compression of trachea / SVC (SVC syndrome)
(4) Fistula formation to aorta, SVC, esophagus
(5) Rupture into bronchus → expectoration of oily substance / trichoptysis in 5–14%, lipoid pneumonia)
(6) Rupture into pericardium (pericardial effusion), pleural cavity (pleural effusion)

DDx: thymoma

Benign Teratoid Tumor (75–86%)

= MATURE (CYSTIC) TERATOMA = BENIGN TERATOMA

◊ Most common histologic type

1. Epidermoid (52%) = ectodermal derivatives
2. Dermoid (27%) = ecto- + mesodermal derivatives
3. Teratoma (21%) = ecto- + meso- + endodermal derivatives

Path: spherical lobulated well-encapsulated tumor; typically multi- / unilocular cystic cavities with clear / yellow / brown liquid

Histo:
(a) ectoderm: skin, sebaceous material, hair, cysts lined by squamous epithelium
(b) mesoderm: bone, cartilage, muscle
(c) endoderm: GI + respiratory tissue, mucus glands
◊ Tumor capsule commonly has remnants of thymic tissue!
◊ Cyst formation is typical (usually lined by mucus-secreting tall epithelial cells)!
Age: young adults / children; M = F
- asymptomatic (in up to 53%)
- cough, dyspnea, chest pain, pulmonary infection, respiratory distress ← compression by large tumor

Location:
(a) anterior superior mediastinum near thymus / within thymic parenchyma
(b) posterior mediastinum (rare, 3–8%)

CT:
√ smooth round mass bulging into right / left hemithorax
√ mass sharply demarcated by well-encapsulated wall
√ multicystic mass of internal heterogeneity with densities varying from -100 to +300 HU (that may all be present):
√ water density (85–90%), fat density (65–75%)
√ DIAGNOSTIC fat-fluid level (in 10%)
√ proteinaceous / hemorrhagic fluid component
√ homogeneous soft-tissue density (indistinguishable from lymphoma / thymoma)
√ curvilinear peripheral / central calcification (20–53%, 4 x more common in benign lesions) in tumor wall / substance, ossification in mature bone
√ PATHOGNOMONIC visualization of tooth
√ often inseparable from thymic gland
√ enhancement of rim / tissue septa

MR:
√ fat, fluid, soft-tissue signal intensities on T1WI + T2WI
√ macroscopic fat on fat-suppressed imaging
√ intracellular lipid on in- and out-of-phase imaging

Prognosis: ~ 100% 5-year survival rate
Rx: complete surgical excision

Malignant Teratoid Tumor (14–20%)

= TERATOCARCINOMA = MALIGNANT TERATOMA
Peak prevalence: 3rd decade; M > F
Histo: similar to mature teratoma but with primitive / immature tissue elements; commonly neural tissue arranged in rosettes / primitive tubules
√ features of malignancy:
√ nodular poorly defined mass with more solid components
√ areas of necrosis or hemorrhage; fat density in 40%
√ thick enhancing capsule
√ compression of adjacent structures

1. **Seminoma** = germinoma = dysgerminoma

◊ 2nd most common mediastinal germ cell tumor!
◊ Most common primary malignant germ cell tumor of mediastinum!
Frequency: 2–6% of all mediastinal tumors; 5–13% of all malignant mediastinal tumors
Age: 3rd–4th decade; M >> F; white
Histo: uniform polyhedral / round cells arranged in sheets or forming small lobules separated by fibrous septa; varying amounts of mature lymphocytes
Path: large unencapsulated well-circumscribed mass
• asymptomatic (20–30%); SVC obstruction (10%)
• chest pain / pressure, shortness of breath, weight loss, hoarseness, dysphagia, fever
• ↑ serum levels of hCG (7–18%)
• ↑ serum levels of LDH (80%) correlate with tumor burden + rate of tumor growth
Metastases: to regional lymph nodes, lung, bone, liver
√ large bulky well-marginated lobulated mass
√ usually NO calcification
√ homogeneous soft-tissue density with slight enhancement
Prognosis: 75–100% 5-year survival rate; death from distant metastases
Rx: surgery + radiation therapy (very radiosensitive) ± cisplatin

2. **Nonseminomatous malignant germ cell tumor**
(a) embryonic tissue
(1) Embryonal carcinoma
(b) extraembryonic tissue
(2) Yolk sac = endodermal sinus tumor
(3) Choriocarcinoma (least frequent)
(c) combination = mixed germ cell tumor
Path: large unencapsulated heterogeneous soft-tissue mass with tendency for invasion of adjacent structures
Age: during 2nd–4th decade: M÷F = 9÷1;
in children M = F
Associated with: Klinefelter syndrome (in 20%), hematologic malignancy
• chest pain, dyspnea, cough, weight loss, fever, SVC syndrome (90–100%)
• ↑ serum level of α-fetoprotein (80%) for endodermal sinus tumor / embryonal carcinoma
• ↑ serum level of LDH (60%)
• ↑ serum level of hCG (30%) (DDx: lung cancer; hepatocellular carcinoma; adenocarcinoma of pancreas, colon, stomach)
Metastases to: lung, liver
√ large tumor of heterogeneous texture with central hemorrhage / necrosis
√ well circumscribed / with irregular margins
√ enhancement of tumor periphery
√ lobulation suggests malignancy
√ invasion of mediastinal structures (SVC obstruction is ominous)
√ ± pleural / pericardial effusion (from local invasion)

◊ The absence of a primary testicular tumor / retroperitoneal mass proves a primary malignant germ cell tumor!

Rx: cisplatin-based chemotherapy + tumor resection

Prognosis: 50% long-term survivors

THORACIC DUCT CYST

= exceedingly rare benign mass of posterior mediastinum

Origin: congenital / degenerative weakening of thoracic duct wall

Histo: cystic space lined by hyalinized fibrous connective tissue surrounded by patchy collections of lymphocytes

Location: anywhere along thoracic duct

Size: 3–22 cm

- asymptomatic (up to 50%)
- dysphagia, chest pain / pressure, dyspnea, dysphonia

√ well-circumscribed posterior mediastinal mass

√ contiguity with cisterna chyli

√ enhancement of a smooth thin wall

CT:

√ homogeneous well-defined mass of water attenuation

MRI:

√ variable SI on T1WI; mildly hyperintense ← increased lipids + proteins

√ variously heterogeneous hyperintense mass on T2WI

Cx: rapid enlargement / spontaneous rupture after high-fat meal

Rx: resection under preservation of thoracic duct pedicles to avoid postoperative chylothorax

DDx: bronchogenic cyst (located adjacent to carina / in pulmonary parenchyma), esophageal duplication cyst (thick wall, young patient), pericardial cyst (located anteriorly at pericardiophrenic angle), hiatal hernia

THORACIC PARAGANGLIOMA

= CHEMODECTOMA

= rare neural tumor arising from paraganglionic tissue

Age: 3rd–5th decade; M÷F = 1÷1

Path: extremely vascular well-marginated / irregular mass that may adhere to / envelop / invade adjacent mediastinal structures (bronchus, spinal canal)

Histo: anastomosing cords of granule-storing chief cells arranged in a trabecular pattern; identical appearance for benign and malignant tumors

May be associated with:

syn- / metachronous adrenal / extrathoracic paragangliomas; multiple endocrine neoplasia type 2; bronchial carcinoid tumor

- asymptomatic; dyspnea, cough, chest pain, hemoptysis, neurologic deficits, SVC syndrome (if tumor large)
- signs of excessive catecholamine production: hypertension, headache, tachycardia, palpitations, tremor

Location: base of heart + great vessels (adjacent to pericardium / heart, within interatrial septum / left atrial wall); paravertebral sulci

CT:

√ sharply marginated 5–7-cm middle / posterior mediastinal mass

√ hypodense areas ← extensive cystic degeneration / hemorrhage
√ exuberant enhancement

MR:
√ heterogeneous intermediate SI with areas of signal void from flowing blood on T1WI
√ high signal intensity on T2WI

NUC (123I / 131I metaiodobenzylguanidine):
√ useful and relatively specific for localization purposes

Angio:
√ marked hypervascularity, multiple feeding vessels
√ homogeneous capillary blush

Cave: Angio may precipitate cardiovascular crisis!

Rx: surgical excision with preoperative administration of α- or β-blockers (hypertensive crisis, tachycardia, dysrhythmia during manipulation)

THORACIC SPLENOSIS

= autotransplantation of splenic tissue to pleural space following thoracoabdominal trauma; discovered 10–30 years later

Pathophysiology: splenic tissue parasitizes blood supply from pleura / chest wall / diaphragm

Frequency: 18% with injury of spleen and diaphragm by blunt trauma; more common in penetrating injury

M÷F = 3÷1 (higher rate of trauma in young men)

• usually asymptomatic / RARELY recurrent hemoptysis

√ one or several nodules in left pleura / fissures measuring several mm to 6 cm

√ splenectomy / splenules in left upper quadrant

√ positive ^{99m}Tc–labeled heat-damaged RBCs (most sensitive), ^{99m}Tc–sulfur colloid scan / 111Indium-labeled platelets

THYMIC CYST

Pathogenesis:

(1) Congenital cyst = persistent embryonic remnant of 3rd pharyngeal pouch (= tubular thymopharyngeal duct), develops during 5th–8th week of gestation)

(2) Acquired reactive multilocular cyst = progressive cystic degeneration of thymic (Hassall) corpuscles + thymic epithelial reticulum induced by an inflammatory process: eg, HIV, before + after chemotherapy for NHL / Hodgkin disease

(3) Neoplastic cyst (cystic teratoma, cystic degeneration within thymoma), thymic carcinoma, Hodgkin disease + NHL, germ cell tumor

◊ No association with myasthenia gravis / neoplasia!

Frequency: very uncommon lesion; 1–2% of mediastinal masses

Age: ⅔ in 1st decade; ⅓ in 2nd + 3rd decades; M > F

Path: unilocular thin-walled cyst with thymic tissue

Histo: squamous / cuboidal / respiratory epithelium in cyst wall; lobulated lymphoid tissue in cyst wall containing Hassall corpuscles; cholesterol crystals; small foci of thyroid / parathyroid tissue

• commonly asymptomatic slowly enlarging painless mass

• hoarseness, dysphagia, stridor, respiratory distress in newborns
• sudden symptomatic enlargement with Valsalva maneuver / hemorrhage / recent viral infection

Location:

(a) adjacent to carotid sheath from angle of mandible to thoracic inlet (along path of thymopharyngeal duct) parallel to sternocleidomastoid muscle; L > R

(b) anterior mediastinum

√ unilocular cyst with thin walls containing clear fluid / multilocular cyst with thick walls containing turbid fluid or gelatinous material

√ direct extension / fibrous cord along migratory tract of thymic tissue into mediastinum in 50%: through thyrohyoid membrane into pyriform sinus

√ may show partial wall calcification (rare)

√ low-density fluid (0–10 HU), may be higher depending on cyst contents

US:

√ typically anechoic

DDx: branchial cleft cyst (no thymic tissue), benign thymoma, teratoma, dermoid cyst, Hodgkin disease, non-Hodgkin lymphoma, pleural fibroma

THYMIC HYPERPLASIA

◊ Most common anterior mediastinal mass in pediatric age group through puberty

DDx: thymoma (focal mass, loss of normal fatty infiltration)

True Thymic Hyperplasia

= increase in size + weight of thymus with preservation of its organized microscopic features ← rebound hyperplasia after recovery from recent stress

Age: commonly in child, also in adult

Stress events: systemic infection (eg, pneumonia); surgery, burns; neoplasm; corticosteroid / radiation / chemotherapy (10–25%)

◊ Thymus atrophies under bodily stress to as little as 40% of its original volume ← endogenous steroids

Timing: rebound within 2 years of initiation of chemotherapy

√ size:

√ diffuse enlargement

√ > 50% transient overgrowth (reducible with steroids)

√ after recovery regrowth to original size within 9 months

√ shape:

√ smooth contour, normal vessels

√ normal / oval shape with loss of its distinct bilobed appearance

√ fine mixture of fat and lymphoid tissue

MR:

√ homogeneously decreased signal on out-of-phase images ← fatty infiltration of normal / hyperplastic thymus (unlike thymoma)

PET/CT:

√ may take up FDG mimicking thymoma

Thymic Lymphoid Hyperplasia

= increase in number of active lymphoid germinal centers in thymic medulla associated with lymphocytic and plasma cell infiltration

Associated with autoimmune disease:

WHO Classification of Thymic Epithelial Tumors
(poorly reproducible and without clinical implications)

Tumor Type	*Description*
A	medullary (epithelial cells: oval / fusiform shape)
AB	mixed
B	(epithelial cells: epitheloid shape)
B1	lymphocyte rich, predominantly cortical
B2	cortical
B3	epithelial = well-differentiated thymic carcinoma
C	thymic carcinoma

hyperthyroidism (most common), Graves disease, idiopathic thyromegaly, thyrotoxicosis, myasthenia gravis (65%), connective tissue disease (SLE, rheumatoid arthritis, scleroderma, vasculitis), sarcoidosis, red blood cell aplasia, acromegaly, Addison disease

√ diffuse symmetric enlargement / normal size

THYMOLIPOMA

Frequency: 2–9% of thymic tumors

Age: 3–60 years (mean age of 22 years); M÷F = 1÷1

Path: lobulated pliable encapsulated tumor capable of growing to large size (in 68% > 500 g, in 20% > 2,000 g, the largest > 16 kg)

Histo: benign adult adipose tissue interspersed with areas of normal / hyperplastic / atrophic thymus tissue (thymic tissue < 33% of tumor mass)

• usually asymptomatic; chest pain, dyspnea, cough (in 50%)

√ fatty mass with fibrous septa

√ large lesions slump inferiorly from anterior mediastinum toward diaphragm enlarging the cardiophrenic space

√ may drape around heart enlarging cardiac silhouette on frontal view

√ apparent elevation of diaphragm on lateral view

√ NO compression / invasion of adjacent structures

DDx: mediastinal lipoma (most common of intrathoracic fatty tumors), liposarcoma, teratoma (cystic changes, no connection to thymic bed)

THYMOMA

= THYMIC EPITHELIAL TUMOR

= slow growing neoplasm potentially exhibiting aggressive behavior (invasion of adjacent structures + involvement of pleura and pericardium), but rarely distant metastases

◊ Most common primary neoplasm of anterior mediastinum

Incidence: 1–5 ÷ 1,000,000 per year; 1% of all adult malignancies; 20% of all mediastinal neoplasms in adults; < 5% of mediastinal tumors in children

Age peak: 5th–6th decade (70%); almost all > 25 years of age; less frequent in young adults,

rare in children; M÷F = 1÷1

Associated with: parathymic (paraneoplastic) systemic syndromes (40%) such as

1. **Myasthenia gravis** (30–50%)
   = autoimmune disorder characterized by antibodies against nicotinic acetylcholine receptors of the postjunctional muscle membrane (M < F)
   • fatigability of skeletal muscles innervated by cranial nerves, eg, ptosis, diplopia, dysphagia, dysarthria, drooling, difficulty with chewing, progressive weakness, fatigue
   • ↑ serum level of anti-acetylcholine receptor antibodies
   ◊ 30–50% of thymoma patients have myasthenia gravis; removal of thymic tumor often results in symptomatic improvement; myasthenia gravis may develop after surgical thymoma excision
   ◊ 10–15% of myasthenia gravis patients have a thymoma (in 65% thymic hyperplasia)
   Rx: edrophonium chloride (cholinesterase inhibitor)
2. **Pure red cell aplasia** (5%)
   = aregenerative anemia
   = almost total absence of marrow erythroblasts + blood reticulocytes → severe normochromic normocytic anemia
   ◊ 5% of thymoma patients develop red cell aplasia
   ◊ 50% of patients with red cell aplasia have thymoma
3. Acquired hypogammaglobulinemia (6%)
   ◊ 6% of thymoma patients have hypogammaglobulinemia
   ◊ 10% of hypogammaglobulinemia patients have thymoma
4. Autoimmune disorders:
   Dermatomyositis; SLE; Rheumatoid arthritis; Cushing syndrome (ACTH production); Myocarditis; Syndrome of inappropriate antidiuretic hormone secretion (SIADH)
5. Nonthymic cancers: NHL, GI cancer, sarcoma, multiple myeloma

◊ Thymic carcinomas rarely cause paraneoplastic syndromes

Path: round / ovoid slow-growing primary epithelial neoplasm with smooth / lobulated surface divided into lobules by fibrous septa; areas of hemorrhage / necrosis / cystic component (⅓)

(a) encapsulated (⅔) = thick fibrous capsule ± calcifications
(b) locally invasive = microscopic foci outside capsule (⅓)
(c) metastasizing = benign cytologic appearance with pleural + pulmonary parenchymal seeding
(d) thymic carcinoma

Histo:

(a) biphasic thymoma (most common)
= epithelial + lymphoid elements in equal amounts
(b) predominantly lymphocytic thymoma
= > ⅔ of cells are lymphocytic
(c) predominantly epithelial thymoma
= > ⅔ of cells are epithelial

◊ Prognosis unrelated to cell type!

Classification: (1) Thymoma

(2) Thymic carcinoma

- asymptomatic (50% discovered incidentally)
- signs of mediastinal compression (25–30%):
  - cough, dyspnea, chest pain (in up to ⅓)
  - respiratory infection, hoarseness (recurrent laryngeal nerve), diaphragmatic paralysis, dysphagia
- signs of tumor invasion (rare): SVC syndrome
- systemic complaints ← paraneoplastic syndromes ← secretion of hormones, antibodies, cytokines by tumor

Location: any anterior mediastinal location between thoracic inlet and cardiophrenic angle; rare in neck, other mediastinal compartments, lung parenchyma, or tracheobronchial tree

Mean size: 5 (range, 1–10) cm; maximum 34 cm

CXR:

√ abnormally wide mediastinum + nodule / mass in retrosternal region
√ mass usually on one side of midline obscuring heart border
√ displacement of heart + great vessels posteriorly
√ thickening of anterior junction line
√ irregular borders with adjacent lung ← advanced disease
√ elevation of hemidiaphragm ← phrenic nerve involvement
√ pleural nodularity ← pleural metastases (stage IVa)

CT:

√ oval / round well-marginated unilateral asymmetric homogeneous mass of soft-tissue density (equal to muscle)
√ smooth / lobulated border partially / completely outlined by fat
√ soft-tissue nodules in a cystic anterior mediastinal lesion = cystic thymoma
√ ± intratumoral punctate / amorphous coarse flocculent / curvilinear capsular calcifications (5–25%)
√ homogeneous enhancement (CHARACTERISTIC)
√ areas of decreased attenuation + heterogeneous enhancement (⅓) ← necrosis / cystic change / hemorrhage

Signs of invasion:

Masaoka-Koga Staging System for Thymoma *(as a good predictor of survival)*	
Stage	*Description*
I	intact capsule
II	pericapsular growth into mediastinal fat
IIA	microscopic pericapsular growth
IIB	macroscopic growth into surrounding fat
III	invasion of neighboring organs such as lung, pericardium, SVC, aorta
IV	metastatic
IVA	within thoracic cavity (metastases to pleura + lung in 6%, pericardium)
IVB	extrathoracic metastases (liver, bone, lymph nodes, kidneys, brain)

› signs of Masaoka stage II–IV thymoma:
√ lobulated / irregular contours
√ cystic / necrotic regions within the tumor
√ multifocal calcifications
› signs of Masaoka stage III–IV thymoma:
√ primary tumor ≥ 7 cm
√ fat infiltration surrounding tumor
√ lobulated tumor contours
› signs of vascular invasion:
√ irregular contour of vessel lumen
√ vascular encasement / obliteration
√ endoluminal soft tissue ± extension into heart chambers
› pleural drop metastases:
√ smooth nodular / diffuse pleural nodules / masses, almost always ipsilateral to anterior mediastinal tumor
√ pleural effusion uncommon with pleural metastases

MR:
√ low to intermediate signal intensity = isointense to skeletal muscle on T1WI
√ high signal intensity approaching fat on T2WI
√ heterogeneous signal intensity:
√ low T1 + high T2 SI ← tumor necrosis / cystic change
√ low-signal-intensity regions ← fibrous tumor septa and nodularity / hemosiderin deposition

Rx: surgical resection for stage I; radiation therapy
◊ Completeness of resection is a major prognostic factor

DDx: ◊ Thymoma rarely manifests with lymphadenopathy /pleural effusions / extrathoracic metastases
(1) Thymic hyperplasia (young child, smooth borders, preserved normal thymic shape)
(2) Primary thymic malignancy: thymic carcinoma, thymic carcinoid
(3) Nonthymic tumor: lymphoma, germ cell tumor, small-cell lung cancer (mediastinal

lymphadenopathy, pleural effusions, pulmonary metastases)

Noninvasive [Benign] Thymoma

Terminology: "benign" not acceptable ← all thymomas are malignant tumors with potential to metastasize

Thymic Carcinoma

= INVASIVE [MALIGNANT] THYMOMA

◊ Malignancy defined according to extent of invasion into adjacent mediastinal fat + fascia!

Frequency: 20–35% of thymic epithelial tumors

Mean age: 50 years; uncommon in adults, rare in children

Path: thymic carcinomas usually lack well-defined capsule

Distant metastases at diagnosis:

› 50–65% of patients with thymic carcinomas

› 5% of patients with invasive thymomas

CT:

√ large multilobulated mass with irregular contour:

√ heterogeneous attenuation

√ invasion of mediastinal fat

√ spread by contiguity along pleural reflections, extension along aorta reaching posterior mediastinum / crus of diaphragm / retroperitoneum (transdiaphragmatic tumor extension):

√ unilateral diffuse nodular pleural thickening / pleural masses encasing lung circumferentially

√ vascular encroachment

√ pleural effusion UNCOMMON

√ distant metastases + regional lymphadenopathy

MR:

√ high signal intensity on both T1WI and T2WI

√ heterogeneous signal intensity ← hemorrhage / necrosis

DDx: malignant mesothelioma, lymphoma, thymic carcinoma / malignant germ cell tumor (older male, no diffuse pleural seeding), peripheral lung carcinoma (no dominant mediastinal mass), metastatic disease (not unilateral)

Rx: radical excision ± adjuvant radiation therapy

Prognosis: 5-year survival of 93% for stage I, 86% for stage II, 70% for stage III, 50% for stage IV; 2–12% recurrence rate for resected encapsulated thymoma

TORSION OF LUNG

= rare complication of severe chest trauma

Frequency: rare (< 30 cases)

Age: almost invariably in children

Cause: compression of lower thorax, tear on inferior pulmonary ligament, completeness of fissures

Mechanism: compression of lower thorax with lung twisted through 180°; usually in presence of a large amount of pleural air / fluid

Associated with:

surgery (lobectomy), trauma, diaphragmatic hernia, pneumonia, pneumothorax, bronchus-obstructing tumor

Histo: ± hemorrhagic infarction + excessive air trapping

√ collapsed / consolidated lobe in unusual position + configuration:

√ hilar displacement of atelectatic-appearing lobe in an inappropriate direction

√ change in position of opacified lobe on sequential radiographs

√ alteration in normal course of pulmonary vasculature:

√ main lower lobe artery sweeping upward toward apex

√ rapid opacification of an ipsilateral lobe from edema + hemorrhage into airspaces ← infarction (DDx: pleural effusion)

√ bronchial cutoff / distortion

√ lobar air trapping

√ lower lung vessels diminutive

TRACHEOBRONCHOMEGALY

= MOUNIER-KUHN SYNDROME

= primary atrophy / dysplasia of supporting structures of trachea + major bronchi with abrupt transition to normal bronchi at 4th–5th division

Frequency: 0.5–1.5%

Age: discovered in 3rd–5th decade

• cough with copious sputum, shortness of breath on exertion

• long history of recurrent pneumonias

May be associated with: Ehlers-Danlos syndrome

√ marked dilatation of trachea (> 29 mm), right (> 20 mm) + left (> 15 mm) mainstem bronchi

√ sacculated outline / diverticulosis of trachea on lateral CXR (= protrusion of mucous membrane between rings of trachea)

√ may have emphysema / bullae in perihilar region

TRACHEOBRONCHOPATHIA OSTEOCHONDROPLASTICA

= rare benign disease characterized by multiple submucosal cartilaginous / osseous nodules projecting into tracheobronchial lumen

Cause: unknown; may be due to chronic inflammation, degenerative process, irritation by oxygen / chemical, metabolic disturbance, amyloidosis, tuberculosis, syphilis, heredity (high prevalence in Finland)

Pathogenetic theories:

(1) Ecchondrosis / exostosis of cartilage rings

(2) Cartilaginous / osseous metaplasia of internal elastic fibrous membrane of trachea

Path: foci of submucosal hyaline cartilage with areas of lamellar bone

Histo: adipose tissue + calcified areas with foci of bone marrow; thinned normal overlying mucosa with inflammation + hemorrhage

Average age: 50 (range, 11–78) years; M÷F = 3÷1

• usually asymptomatic (incidentally diagnosed)

• dyspnea, productive cough, hoarseness, hemoptysis, fever, recurrent pneumonia

Location: distal ⅔ of trachea, larynx, lobar / segmental bronchi, entire length of trachea; spares

posterior membrane of trachea

CXR:

√ scalloped / linear opacities surrounding + narrowing trachea (best on lateral view)

CT:

√ deformed thickened narrowed tracheal wall

√ irregularly spaced 1–3-mm calcific submucosal nodules of trachea + bronchi (similar to plaques)

Dx: bronchoscopy

DDx: relapsing polychondritis, tracheobronchial amyloidosis (does not spare posterior membranous wall of trachea), sarcoidosis, papillomatosis, tracheobronchomalacia

TUBERCULOSIS

Prevalence: 10 million people worldwide; active TB develops in 5–10% of those exposed; 3÷100,00 in USA (2014)

Organism: Mycobacterium = acid-fast aerobic rods staining red with carbol-fuchsin: M. tuberculosis (95%), atypical types increasing: M. avium-intracellulare, M. kansasii, M. fortuitum

Susceptible: infants, pubertal adolescents, elderly, alcoholics, Blacks, diabetics, silicosis, measles, AIDS (30–40% infected with HIV), sarcoidosis (in up to 13%)

At risk: immunocompromised, minorities, poor, alcoholics, immigrants from 3rd world countries, prisoners, the aged, nursing home residents, homeless

Pathologic phases:

(a) exudative reaction (initial reaction, present for 1 month)
(b) caseous necrosis (after 2–10 weeks with onset of hypersensitivity)
(c) hyalinization = invasion of fibroblasts → granuloma formation in 1–3 weeks
(d) calcification / ossification
(e) chronic destructive form in 10% (< 1 year of age, adolescents, young adults)

Spread: regional lymph nodes, hematogenous dissemination, pleura, pericardium, CNS, head & neck, spondylitis, osteomyelitis, arthritis, peritonitis, GI & GU tract

- Positive PPD tuberculin test: 3 weeks after infection
- Negative PPD test: overwhelming tuberculous infection (miliary TB); sarcoidosis; corticosteroid therapy; pregnancy; infection with atypical Mycobacterium

Former Rx: plombage with insertion of plastic packs, Lucite™ balls, polythene spheres; oleothorax (= injection of oil / paraffin)

Mortality: 1÷100,000

Tuberculoma

= manifestation of primary / postprimary TB

√ round / oval smooth sharply defined mass

√ 0.5–4 cm in diameter remaining stable for a long time

√ lobulated mass (25%)

√ satellite lesions (80%)

√ may calcify

Cavitary Tuberculosis

= hallmark of reactivation tuberculosis
= semisolid caseous material is expelled into bronchial tree after lysis
√ moderately thick-walled cavity with smooth inner surface
Cx:
(1) Dissemination to other bronchial segments
√ multiple small acinar shadows remote from massive consolidation
(2) Colonization with Aspergillus
√ aspergilloma

Rasmussen, Fritz Valdemar (1837–1877), chair of pathology at University of Copenhagen, Denmark

(3) **Rasmussen aneurysm** = fragile aneurysm of terminal branches of pulmonary artery within wall of TB cavity ← inflammatory necrosis of the vessel wall (4% at autopsies of cavitary TB):
[Fritz Valdemar Rasmussen (1837–1877), chair of pathology at University of Copenhagen, Denmark]
• sentinel hemoptysis prior to catastrophic hemorrhage
√ central cavity near hilum:
√ enlargement of intracavitary solid protrusion
√ replacement of cavity by a nodule
√ rapidly growing mass
√ opacification of pseudoaneurysm on CT / angio

Endobronchial (Acinar) Tuberculosis
◊ Most common complication of tuberculous cavitation with active organisms spreading via airways following caseous necrosis of bronchial wall
Path: ulceration of bronchial mucosa → fibrosis →
(a) bronchial stenosis → lobar consolidation
(b) bronchiectasis
(c) acinar nodules reflecting airway spread
HRCT:
√ clustered centrilobular nodules
√ "tree-in-bud" appearance = small poorly defined centrilobular nodules + branching centrilobular areas of increased opacity (= severe bronchiolar impaction with clubbing of distal bronchioles) occurring at multiple contiguous branching sites
√ masslike areas of consolidation
√ cavitation in larger nodules / masses
√ bronchiectasis

Primary Pulmonary Tuberculosis
= self-limiting disease in patients not previously exposed
Mode of infection: inhalation of infected airborne droplets ← coughing expels and aerosolizes organism in 1–5-μm particles remaining suspended in air for several hours
Age: most common form in infants + childhood (highest prevalence in children < 5 years of age); increasingly encountered in adults (23–34%)

• asymptomatic (91%); symptomatic (5–10%)

@ Parenchymal disease

Location: middle lobe, lower lobes, anterior segment of upper lobes

√ normal radiograph (in up to 15%)

√ one / more areas of homogeneously dense well-defined airspace consolidation of 1–7 cm in diameter in 25–78%:

√ absent response to antibiotic Rx for "pneumonia"

DDx: bacterial pneumonia

√ fine discrete nodular areas of increased opacity

DDx: varicella pneumonia, histoplasmosis, metastases, sarcoidosis, pneumoconiosis, hemosiderosis

√ lobar / segmental atelectasis (in 8–18%)

Location: anterior segment of upper lobe / medial segment of middle lobe

Age: in children < 2 years of age

Cause: (a) endobronchial tuberculosis

(b) bronchial / tracheal compression by enlarged lymph nodes (68%)

@ Lymphadenopathy (up to 96% of children, 43% of adults)

◊ may be the sole radiographic manifestation

Location: typically right unilateral (hilum + paratracheal region); bilateral in ⅓

√ <u>in children</u>: massive hilar (60%) / paratracheal (40%) / subcarinal lymphadenopathy

<u>in adults</u>: mediastinal lymphadenopathy in 5–35–48%

DDx of Lnn: metastases, histoplasmosis

√ nodes > 2 cm with low-attenuation center ← necrosis = highly suggestive of active disease

√ lymph node calcification (36%) in hilum / mediastinum usually > 6 months after initial infection

@ Pleural effusion

◊ Often sole manifestation of TB

Onset: 3–7 months after initial exposure ← subpleural foci rupturing into pleural space

Frequency: 10% in childhood, 23–38% in adulthood

US:

√ usually unilateral often complex septated effusion

√ may result in pleural thickening + calcification

Cx (rare): empyema, fistulization, bone erosion

Outcome of Primary Infection:

1. Restitutio ad integrum (in ⅔)

= resolution of primary focus without sequelae

√ **Simon focus** = healed site of primary infection in lung apex; may take up to 2 years

2. Immunity prevents multiplication of organism

= containment of initial infection by delayed hyper-sensitivity response + granuloma formation in 1–3 weeks

√ calcified lung lesion (in up to 17%) / parenchymal scar < 5 mm = **Ghon focus (lesion)**

√ **Ranke complex** = Ghon lesion + calcified lymph node (22%)

DDx: histoplasmosis

3. Progressive primary TB
   = inadequate immune mechanism → local progression in 10%, most common in older children / teenagers
   √ persistent masslike opacity = tuberculoma (9%) ± cavitation
4. Miliary tuberculosis (uncontrolled massive hematogenous dissemination overwhelming host defense system)
5. Postprimary TB = reactivation TB (= reactivation of dormant organisms after asymptomatic years)

Prognosis: 3.6% mortality rate; usually self-limiting

Cx: (1) Bronchopleural fistula + empyema
(2) Fibrosing mediastinitis

DDx: postprimary tuberculosis (predilection for upper lobes, cavitation, absence of lymphadenopathy

MILIARY PULMONARY TUBERCULOSIS

= massive hematogenous dissemination of organisms within 6 months of initial exposure

Cause:
(1) severe immunodepression during postprimary state of infection
(2) impaired defenses during primary infection in elderly / infants = PROGRESSIVE PRIMARY TB

Frequency: 1–3.5–7% of all forms of TB

Onset: radiographically recognizable after 6 weeks post hematogenous dissemination

√ CXR initially normal / with signs of hyperinflation
√ chronic focus often not identifiable
√ generalized evenly distributed small interstitial granulomatous foci of pinpoint to 2–3 mm size with slight lower lobe predominance (in 85%)
√ ± coalescence into focal / diffuse consolidation
√ resolution with appropriate therapy within 2–6 months

HRCT (earlier detection than CXR):
√ diffusely scattered discrete 1–2-mm nodules in random distribution

Cx: dissemination via bloodstream affecting lymph nodes, liver, spleen, skeleton, kidneys, adrenals, prostate, seminal vesicles, epididymis, fallopian tubes, endometrium, meninges

Resolution: within 2–6 months under treatment
√ NO scarring / calcification
√ may coalesce into focal / diffuse consolidation

Postprimary Pulmonary Tuberculosis

= REACTIVATION TB = RECRUDESCENT TB
= progressive infection under the influence of acquired hypersensitivity and immunity ← longevity of bacillus + impairment of cellular immunity

Frequency: 1% per year with normal immunity, in up to 10% with deficient T-cell immunity

Age: primarily in adolescents + adults

Etiology:

(a) reinfection
(b) reactivation of focus acquired in childhood (90%)
(c) continuation of initial infection = progressive primary tuberculosis (rare)
(d) initial infection in individual vaccinated with BCG

Path: foci of caseous necrosis with surrounding edema, hemorrhage, mononuclear cell infiltration; formation of tubercles = accumulation of epithelioid cells + Langhans giant cells; bronchial perforation leads to intrabronchial dissemination (19–21%)

Site: 85% in apical + posterior segments of upper lobe, 10% in superior segment of lower lobe, 5% in mixed locations (anterior + contiguous segments of upper lobe); R > L (DDx: histoplasmosis tends to affect anterior segment)

• hemoptysis (most common cause worldwide)
Rx: bronchial artery embolization

Prognosis: progressive

The features of primary and postprimary tuberculosis may overlap. The distinguishing features of postprimary tuberculosis include cavitation, a predilection for the upper lobes, and the absence of lymphadenopathy.

Local Exudative Tuberculosis

√ patchy / confluent ill-defined areas of acinar consolidation (87–91%), commonly involving two / more segments (earliest finding)
√ thin-walled cavitation with smooth inner surface (present in more advanced disease):
  √ cavity under tension (air influx + obstructed efflux)
  √ air-fluid level = strong evidence for superimposed bacterial / fungal infection
  √ "air-crescent" sign = mobile intracavitary mycetoma
√ accentuated drainage markings toward ipsilateral hilum
√ acinar nodular pattern (20%) ← bronchogenic spread
√ pleural effusion (18%)
CT:
  √ micronodules in centrilobular location (62%) = solid caseation material in / surrounding the terminal / respiratory bronchioles
  √ interlobular septal thickening (34–54%) = increase in lymphatic flow as inflammatory response / impaired lymphatic drainage ← hilar lymphadenopathy

Local Fibroproductive Tuberculosis

@ Parenchymal disease:
  √ sharply circumscribed irregular + angular masslike fibrotic lesion (in up to 7%)
  √ cavitation (HALLMARK) ← expulsion of caseous necrosis into airways; rare in children, in up to 45–51% in adults; often multiple suggesting high likelihood of active TB:
    Site: apical / posterior segments of upper lobes
    √ cavity forms within areas of consolidation
    √ thick irregular cavity wall → smooth thin cavity wall with successful treatment
    √ ± air-fluid level (rare) may indicate superinfection
  √ reticular pulmonary scars
  √ cicatrization atelectasis = volume loss in affected lobe

- √ peripheral tree-in-bud opacities (indicative of active disease)
- √ pneumothorax (5%)

@ Airway involvement
- √ long-segment bronchial stenosis (in 10–40%) with irregular wall thickening, luminal obstruction, and extrinsic compression:
  - √ persistent segmental / lobar collapse
  - √ lobar hyperinflation
  - √ obstructive pneumonia
  - √ mucoid impaction
- √ traction bronchiectasis in apical / posterior segments of upper lobes
- √ tree-in-bud opacities in lung periphery ← endobronchial spread of active infection

@ Pleural extension:
- √ small septated pleural effusions remaining stable for years (in 18%):
  - √ air-fluid level in pleural space = bronchopleural fistula
- √ pleural thickening:
  - √ apical cap = pleural rind = thickening of layer of extrapleural fat (3–25 mm) + pleural thickening (1–3 mm)
  - √ rim-enhancing / calcified soft-tissue mass of chest wall
- √ destruction of bone / costal cartilage
- √ fistulization to skin

@ Lymphadenopathy (in 5%):
- √ tuberculous lymphadenitis = enlarged nodes with central areas of low attenuation
- √ calcified hilar / mediastinal nodes:
  - broncholithiasis = erosion into adjacent airway

Extrapulmonary Tuberculosis

In order of frequency: kidney, liver, spleen, bone, adrenal

@ Genitourinary

@ Hepatosplenic

@ Musculoskeletal system (1–3%): spine (5%)

@ Lymph nodes, peritoneum, GI tract

@ Head & neck (15%)

@ CNS (5%)

@ Heart (0.5%)
- √ > 3 mm irregular pericardial thickening (in adults)
- √ IVC distention to > 3 cm in diameter
- √ pericardial effusion / localized pericardial calcification (< 20%)
- √ miliary lesions / tuberculomas of myocardium
- √ typically bilateral pleural effusions
- √ deformities of intraventricular septum

Extrarenal Signs of TB on Abdominal Plain Film
- √ osseous / paraspinous changes of TB (= diskitis + psoas abscess)
- √ calcified granulomas in liver, spleen, lymph nodes, adrenals

UNILATERAL PULMONARY AGENESIS

= one-sided lack of primitive mesenchyme

Cause: ? abnormal blood flow in dorsal aortic arch during 4th week of gestation

Associated with:

anomalies in 60% (higher if right lung involved): PDA, anomalies of great vessels, pulmonary sling, tetralogy of Fallot (left-sided pulmonary agenesis), bronchogenic cyst, congenital diaphragmatic hernia, complete tracheal rings, bone anomalies

• may be asymptomatic versus respiratory infections

Location: R (worse prognosis) > L (better prognosis)

√ completely opaque hemithorax

√ ipsilateral absence of pulmonary vessels (arteries + veins)

√ absent ipsilateral mainstem bronchus + airways

√ symmetrical chest cage with approximation of ribs

√ marked contralateral lung hyperexpansion + hyperlucency

√ ipsilateral shift of mediastinum + diaphragm

VARICELLA-ZOSTER PNEUMONIA

Frequency: 14% overall; 50% in hospitalized adults

Age: > 19 years (90%); 3rd–5th decade (75%); contrasts with low incidence of varicella in this age group

• vesicular rash

√ patchy diffuse airspace consolidation

√ tendency for coalescence near hila + lung bases

√ widespread nodules (30%) representing scarring

√ tiny 2–3-mm calcifications widespread throughout both lungs (2%)

Cx: unilateral diaphragmatic paralysis

Prognosis: 11% mortality rate

WILLIAMS-CAMPBELL SYNDROME

= congenital bronchial cartilage deficiency in the 4th–6th bronchial generation either diffuse or restricted to focal area

HRCT:

√ cystic bronchiectasis distal to 3rd bronchial generation

√ emphysematous lung distal to bronchiectasis

√ inspiratory ballooning + expiratory collapse of dilated segments

WILSON-MIKITY SYNDROME

= PULMONARY DYSMATURITY

= similarity to bronchopulmonary dysplasia in normal preterm infants breathing room air; rarely encountered anymore due to mechanical assisted ventilation

Predisposed: premature infants < 1,500 g who are initially well

• gradual onset of respiratory distress between 10 and 14 days

√ hyperinflation

√ reticular pattern radiating from both hila

√ small bubbly lucencies throughout both lungs (identical to bronchopulmonary dysplasia)
Prognosis: resolution over 12 months
DDx: perinatally-acquired infection (especially CMV)

ZYGOMYCOSIS

= PHYCOMYCOSIS
= group of severe opportunistic sinonasal + pulmonary disease caused by a variety of Phycomycetes (soil fungi)
Organism: ubiquitous Mucor (most common), Rhizopus, Absidia with broad nonseptated hyphae of irregular branching pattern
At risk: immunoincompetent host with
(1) Lymphoproliferative malignancies and leukemia
(2) Acidotic diabetes mellitus
(3) Immunosuppression through steroids, antibiotics, immunosuppressive drugs (rare)
Entry: inhalation / aspiration from sinonasal colonization
Path: angioinvasive behavior similar to aspergillosis
A. RHINOCEREBRAL FORM
= involvement of paranasal sinuses (frontal sinus usually spared) with extension into:
(a) orbit = orbital cellulitis
(b) base of skull = meningoencephalitis + cerebritis
B. PULMONARY FORM
√ segmental homogeneous consolidation
√ cavitary consolidation + "air-crescent" sign
√ nodules (from arterial thrombi + infarction)
√ rapidly progressive (often fatal) pneumonia
Dx: culture of fungus from biopsy specimen / demonstration within pathologic material
DDx: aspergillosis

BREAST

DIFFERENTIAL DIAGNOSIS OF BREAST DISORDERS

VARIATIONS IN BREAST DEVELOPMENT

Unilateral Breast Development

may exist 2 years before other breast becomes palpable

Premature Thelarche

= breast development < 7 years of age (in African American girls) and < 8 years of age (in white girls)

Cause:

(1) isolated idiopathic = mostly subtle hyperfunction of pituitary-ovarian axis

Age: 1–3 years

- NO growth spurt / advanced bone age / menses

(2) central precocious puberty

√ enlargement of uterus + ovaries

√ advanced bone age

√ uni- / bilateral normal breast tissue

Congenital Anomalies

1. Polythelia = more than normal number of nipples
2. Polymastia = more than normal number of breasts
3. Amastia = absence of mammary glands

BREAST DENSITY

= relative amount of radiopaque epithelial + stromal elements compared with amount of radiolucent fat on mammography

The masking effect of dense breasts on cancer detection is greatly reduced by digital over film-screen mammography.

Inter- and intraobserver variability on breast density:

- low reliability of interreader density agreement ($\kappa = 0.59$)
- imperfect intrareader agreement ($\kappa = 0.72$)

Factors affecting breast density between mammograms:

body mass index, weight changes, age, HRT, dietary intake

Breast density may vary over time through variability of interpretation, physiologic changes and breast positioning.

Mammographic sensitivity vs. breast density:

Mammographic sensitivity plummets from 80–98% in women with entirely fatty breasts to 30–64% in women with extremely dense breasts.

Asymmetric Breast Density

A. BENIGN
   1. Postsurgical scarring
   2. Noniatrogenic trauma
   3. Postinflammatory fibrosis
   4. Radial scar
   5. Ectopic / accessory breast tissue (in axillary tail / close to abdomen)
   6. Asymmetric breast development / asymmetric involution
   7. Simple cyst
   8. Fibrocystic conditions: fibrosis / sclerosing adenosis
   9. Hormonal therapy: replacement, contraceptives

B. MALIGNANT
   1. Invasive ductal carcinoma: desmoplastic reaction
   2. Invasive lobular carcinoma
   3. Tubular carcinoma
   4. Primary lymphoma of breast

C. IMAGING PROBLEMS
   1. Superimposed normal fibroglandular tissue
   2. Lesion obscured by overlapping dense parenchyma
   3. Lesion outside field of view

Diffuse Increase in Breast Density

◊ Increased breast density masks breast cancer detection and is also a primary risk factor for breast cancer!

The relative risk for cancer in women with heterogeneously dense breasts compared with the average woman is ~ 1.2.

The relative risk for cancer in women with extremely dense breasts compared with the average woman is ~ 2.1.

√ generalized increased density
√ skin thickening
√ reticular pattern in subcutis

A. CANCER
   1. “Inflammatory” breast cancer
   2. Diffuse primary noninflammatory breast cancer
   3. Diffuse metastatic breast cancer
   4. Lymphoma / leukemia ← obstructive lymphedema of breast

B. INFECTIOUS mastitis
   usually in lactating breast

C. RADIATION
   (a) diffuse exudative edema within weeks after beginning of radiation therapy
   (b) indurational fibrosis months after radiation therapy

D. EDEMA
E. HEMORRHAGE
   1. Posttraumatic
   2. Anticoagulation therapy
   3. Bleeding diathesis
F. ACCIDENTAL INFUSION OF FLUID
   into subcutaneous tissue

Breast Edema

1. Lymphatic obstruction: extensive axillary / intrathoracic lymphadenopathy, mediastinal / anterior chest wall tumor, axillary surgery, SVC syndrome, filariasis, intestinal lymphangiectasia
2. Skin disorder: psoriasis, burns
3. Generalized body edema: congestive heart failure (breast edema may be unilateral if patient in lateral decubitus position), hypoalbuminemia (renal disease, liver cirrhosis), fluid overload

Abnormal Uptake of Bone Agents within Breast

1. Breast carcinoma
2. Prosthesis
3. Drug-induced

MAMMOGRAPHIC RISK ASSESSMENT

for invasive breast carcinoma

A. NO INCREASED RISK
   1. Nonproliferative lesions: adenosis, florid adenosis, apocrine metaplasia without atypia, macro- / microcysts, duct ectasia, fibrosis, mild hyperplasia (more than 2 but not more than 4 epithelial cells deep), mastitis, periductal mastitis, squamous metaplasia
   2. Fibroadenoma

B. PROLIFERATIVE LESIONS WITHOUT ATYPIA
   Relative risk increase: 1.5–2.0
   1. Columnar cell change / hyperplasia = blunt duct adenosis
   2. Moderate + florid solid / papillary hyperplasia without atypia
   3. Sclerosing adenosis
   4. Intraductal papilloma with fibrovascular core
   5. Pseudoangiomatous stromal hyperplasia (PASH)
   6. Radial sclerosing lesion

C. PROLIFERATIVE LESIONS WITH ATYPIA
   Relative risk increase: 4–5
   1. Atypical ductal hyperplasia (ADH)
   2. Lobular neoplasia: separation based on degree of distension of affected terminal ductules:
      (a) Atypical lobular hyperplasia (ALH)
      (b) Lobular carcinoma in situ (LCIS)

BREAST LESION

Mammographic Evaluation of Breast Masses

True mass or pseudomass?

A. SIZE
   - › well-defined nodules < 1.0 cm are of low risk for cancer
   - › "most likely benign" nodules approaching 1 cm should be considered for ultrasound / aspiration / biopsy

B. SHAPE
   - › increase in probability of malignancy: architectural distortion > irregular > lobulated > oval > round

C. MARGIN / CONTOUR (<u>most important factor</u>)
   - › well-circumscribed mass with sharp abrupt transition from surrounding tissue is almost always benign
   - › "halo" sign of apparent lucency = optical illusion of Mach effect + true radiolucent halo is almost always (92%) benign but NOT pathognomonic for benignity
   - › microlobulated margin worrisome for cancer
   - › obscured margin may represent infiltrative cancer
   - › irregular ill-defined margin has a high probability of malignancy
   - › spiculated margin due to
     - (a) fibrous projections extending from main cancer mass
     - (b) previous surgery
     - (c) sclerosing duct hyperplasia (radial scar)

D. LOCATION
   - › intramammary lymph node typically in upper outer quadrant (in 5% of all mammograms)
   - › large hamartoma + abscess common in retro- / periareolar location
   - › sebaceous cyst in subcutaneous tissue

E. X-RAY ATTENUATION = DENSITY
   - › fat-containing lesions are never malignant
   - › high-density mass suspicious for carcinoma (density higher than for equal volume of fibroglandular tissue ← fibrosis)

F. NUMBER
   - › multiplicity of identical lesions decreases risk

G. INTERVAL CHANGE
   - › enlarging mass needs biopsy

H. PATIENT RISK FACTORS
   - › increasing age increases risk for malignancy
   - › positive family history
   - › history of previous abnormal breast biopsy
   - › history of extramammary malignancy

Focal Asymmetry

Definition:

= asymmetry confined to less than a quadrant
  (a) lesion with definable borders only seen on 1 view

(b) lesion of similar shape on 2 orthogonal views lacking convex margins + conspicuity of a true mass

A real lesion may not be included in the field of view of the orthogonal view!

Cause:

1. Pseudolesion (in 2% of screening mammograms)
   = **summation artifact** of overlapping breast tissue
2. Breast cancer
   ◊ A focal asymmetry is a malignancy in only 1–3%
   ◊ A developing / new focal asymmetry represents a malignancy in 6–27%
   ◊ In 9–38% missed cancers were retrospectively visible as a focal asymmetry
   A 1-view lesion is of concern if associated with: outward convex margins / straight lines of architectural distortion or spiculation / microcalcifications / palpability

Dense fibroglandular tissue may obscure a real lesion on the orthogonal view!

Histo: invasive lobular carcinoma (in 33%), invasive ductal carcinoma

Well-circumscribed Breast Mass

◊ Well-defined nonpalpable lesions have a 4% risk of malignancy!

A. BENIGN
   1. Cyst (45%)
   2. Fibroadenoma
   3. Sclerosing adenoma
   4. Intraductal papilloma (intracystic / solid)
   5. Galactocele
   6. Sebaceous cyst
   7. Pseudoangiomatous stromal hyperplasia

B. MALIGNANT
   1. Medullary carcinoma
   2. Mucinous carcinoma
   3. Intracystic papillary carcinoma
   4. Invasive ductal cancer not otherwise specified (rare)
   5. Pathologic intramammary lymph node
   6. Metastases to breast: melanoma, lymphoma / leukemia, lung cancer, hypernephroma

De Novo Mass in Woman > 40 Years of Age

1. Cyst
2. Papilloma
3. Carcinoma (10–20%)
   (a) Invasive ductal carcinoma (not otherwise specified)
   (b) Mucinous carcinoma
   (c) Medullary carcinoma
   (d) Intracystic papillary carcinoma
   (e) Invasive papillary carcinoma
   (f) Metaplastic carcinoma
   (g) Malignant phyllodes tumor

(h) Adenoid cystic carcinoma

4. Sarcoma (rare)
5. Fibroadenoma (exceedingly rare)
6. Metastasis (extremely rare)

Fibrous Breast Lesion

1. Fibroadenoma
2. Phyllodes tumor
3. Sclerosing lobular hyperplasia
4. Pseudoangiomatous stromal hyperplasia
5. Diabetic mastopathy
6. Focal fibrosis
7. Fibromatosis

Fat-containing Breast Lesion

◊ Fat contained within a lesion usually proves benignity!

1. Lipoma
2. Galactocele
   = fluid with high lipid content (last phase)
   • during / shortly after lactation
3. Oil cyst= traumatic lipid cyst = fat necrosis
   • site of prior surgery / trauma
4. Focal collection of normal breast fat

Mixed Fat- and Water-density Lesion

1. Fibroadenolipoma / hamartoma
2. Intramammary lymph node
3. Galactocele
4. Hamartoma = lipofibroadenoma = fibroadenolipoma
5. Small superficial hematoma
6. Cancer engulfing fat
   √ irregular / spiculated margins]

Secretory Disease

1. Retained lactiferous secretions
   = incomplete / prolonged involution of lactiferous ducts
   √ branching pattern of fat density in dense breast (high lipid content)
2. Prolonged inspissation of secretion + intraductal debris
   = **Mammary duct ectasia**
3. Galactocele
4. Plasma cell mastitis

Breast Lesion with Halo Sign

A. HIGH-DENSITY LESION
   = vessels + parenchymal elements not visible in superimposed lesion
   1. Cyst

2. Sebaceous cyst
3. Wart

B. LOW-DENSITY LESION
= vessels + parenchyma seen superimposed on lesion
1. Fibroadenoma
2. Galactocele
3. Cystosarcoma phylloides

Stellate / Spiculated Breast Lesion

= mass / architectural distortion characterized by thin lines radiating from its margins
› The majority of invasive breast cancers are stellate (stellate÷circular = 65÷35)
› 93% of all stellate lesions are malignant
Risk of malignancy:
› 75% for nonpalpable spiculated masses
› 32% for nonpalpable irregular masses

A. PSEUDOSTELLATE STRUCTURE
= SUMMATION SHADOW / ARTIFACT
caused by fortuitous superimposition of normal fibrous + glandular structures; unveiled by rolled views, spot compression views ± microfocus magnification technique

B. "BLACK STAR"
√ groups of fine straight / curvilinear fibrous strands bunched together like a broom
√ circular / oval lucencies within center
√ change in appearance from view to view
1. Radial scar = sclerosing duct hyperplasia (86%)
2. Sclerosing adenosis
3. Posttraumatic fat necrosis (11%)

C. "WHITE STAR"
√ individual straight dense spicules
√ central solid tumor mass
√ little change in different views
(a) malignant lesions
1. Invasive ductal carcinoma (65%) = **scirrhous carcinoma**
= desmoplastic reaction + secondary retraction of surrounding structures
• clinical dimensions > mammographic size
√ distinct central tumor mass with irregular margins
√ length of spicules increase with tumor size
√ localized skin thickening / retraction when spiculae extend to skin
√ commonly associated with malignant-type calcifications
2. Invasive lobular carcinoma (21%)
• palpable mass
√ lack of central tumor mass
3. Tubular carcinoma (9%)
4. Other (5%)
(b) benign lesions
1. Postoperative scar

• correlation with history + site of biopsy
√ scar diminishes in size + density over time

2. Postoperative hematoma
   • clinical information
   √ short-term mammographic follow-up confirms complete resolution
3. Breast abscess
   • clinical information
   √ high-density lesion with flamelike contour
4. Hyalinized fibroadenoma with fibrosis
   √ changing pattern with different projections
   √ may be accompanied by typical coarse calcifications of fibroadenomas
5. Granular cell myoblastoma
6. Fibromatosis
7. Extra-abdominal desmoid

mnemonic: STARFASH

Summation shadow
Tumor (malignant)
Abscess
Radial scar
Fibroadenoma (hyalinized), **F**at necrosis
Adenosis (sclerosing)
Scar (postoperative)
Hematoma (postoperative)

Tumor-mimicking Lesions

1. "Phantom breast tumor" = simulated mass
   (a) asymmetric density
   √ scalloped concave breast contour
   √ interspersed fatty elements
   (b) summation artifact = chance overlap of normal glandular breast structures
   √ failure to visualize "tumor" on more than one view
2. Silicone injections
3. Skin lesions
   (a) Dermal nevus
   √ sharp halo / fissured appearance
   (b) Skin calcifications
   √ lucent center (= clue)
   √ superficial location (tangential views)
   (c) Sebaceous / epithelial inclusion cyst
   (d) Neurofibromatosis
   (e) Biopsy scar
4. Lymphedema
5. Lymph nodes
   Frequency: 5.4% for intramammary nodes
   Location: axilla, subcutaneous tissue of axillary tail, lateral portion of pectoralis muscle,

intramammary (typically in upper outer quadrant)

√ ovoid / bean-shaped mass(es) with fatty notch representing hilum

√ central zone of radiolucency (fatty replacement of center) surrounded by "crescent" rim of cortex

√ usually < 1.5 cm (up to 4 cm) in size

√ well-circumscribed with slightly lobulated margin

US:

√ reniform hypoechoic rim with echogenic center

√ echogenic hilum for entry and exit of vessels

6. Hemangioma

Solid Breast Lesion by Ultrasound

Morphologic Descriptors of Solid Benign Breast Mass

1.	Shape	oval (84% NPV), round, irregular (62% PPV)
2.	Orientation	parallel (78% NPV), nonparallel (69% PPV) to chest wall ("taller-than-wide" / "vertical")
3.	Margin	circumscribed (90% NPV), microlobulated, indistinct, angular, spiculated (86% PPV)
4.	Lesion boundary	abrupt, echogenic halo
5.	Internal echo pattern	anechoic, hyperechoic, complex, hypoechoic, isoechoic *(in reference to SQ fat)*
6.	Posterior acoustic feature	shadowing, enhancement

Posterior Acoustic Shadowing

1. Invasive carcinoma
2. Postoperative scar
3. Complex sclerosing lesion
4. Microcalcifications
5. Dense breast tissue

Posterior Acoustic Enhancement

1. Normal anatomic structure
2. Cyst: simple / complicated
3. Fibroadenoma
4. Nodular sclerosing adenosis
5. Papilloma
6. Complex cystic mass
7. Invasive ductal carcinoma
8. Lymphoma

Echogenic Breast Lesion

Incidence: 0.6–5.6% of breast masses

◊ Hyperechogenicity alone does not allow exclusion of malignancy!

A. Benign

1. Lipoma
2. Angiolipoma
3. Hematoma
4. Seroma
5. Fat necrosis
6. Silicone granuloma
7. Sebaceous / epidermal inclusion cyst
8. Abscess
9. PASH
10. Galactocele / lactating adenoma
11. Ductal ectasia
12. Apocrine metaplasia

An echogenic mass that correlates with a well-delineated radiolucent mass at mammo is benign!

B. Malignant

1. Invasive ductal carcinoma
2. Invasive lobular carcinoma
3. Metastasis
4. Lymphoma
5. Angiosarcoma

Breast carcinoma is RARELY purely echogenic!

Malignant Sonographic Characteristics

◊ Approximately 5 malignant features are found per cancer. The combination of 5 findings increases the sensitivity to 98.4%!

√ spiculation = straight lines radiating perpendicularly from surface of tumor:
- √ coarse spiculation (less common) = hypoechoic lines (= fingers of invasive tumor / DCIS) alternating with hyperechoic lines (= interface between tumor and surrounding tissue)
- √ fine spiculation (more common):
  - √ hyperechoic spicules in fatty tissue
  - √ hypoechoic spicules in fibrous tissue
- √ thick echogenic halo = spicules too small to resolve

√ angular margins = contour of junction between hypo- or isoechoic solid nodule and surrounding tissue at acute / obtuse / 90° angles

√ acoustic shadowing behind all / part of nodule (= desmoplastic reaction as host response to tumor)

√ taller-than-wide lesion (feature of small lesions)
= AP dimension greater than craniocaudal / transverse dimension

√ microlobulations = many small lobulations at surface of solid nodule (= duct distended with DCIS / cancerized lobule)

√ duct extension (= intraductal growth of breast cancer in single large duct extending toward nipple)
√ branch pattern (= intraductal growth of breast cancer in multiple small ducts extending away from nipple)
√ hypoechoic texture = central part of solid lesion markedly hypoechoic with respect to fat ← invasive tumor mass / fluid within tumor / acoustic shadow
√ punctate echogenic calcifications within hypoechoic duct extension / branch pattern / microlobulations (acoustic shadowing commonly not present)

Sonographic Findings of Malignancy
(according to data from A.T. Stavros)

Certainty	*US Finding*
Hard = invasive carcinoma	Spiculation, thick echogenic halo
	Angular margins
	Acoustic shadowing
Indeterminate	Hypoechoic texture
	Taller-than-wide orientation
Soft = DCIS component	Microlobulation
	Duct extension
	Branch pattern
	Calcifications

Benign Sonographic Characteristics

√ absence of any malignant characteristics
◊ A single malignant feature prohibits classification of a nodule as benign!
√ marked hyperechogenic well-circumscribed nodule compared with fat = normal stromal fibrous tissue (may represent a palpable pseudomass / fibrous ridge)
√ smooth well-circumscribed ellipsoid shape
√ 2–3 smooth well-circumscribed gentle lobulations
√ thin echogenic capsule
√ kidney-shaped lesion = intramammary lymph node
◊ If specific benign features are not found the lesion is classified as indeterminate!

Complex Cystic Breast Mass

= cyst with thick wall, thick septa, intracystic discrete solid components

Classification:

Type 1 thick outer wall ± thick internal septa
Type 2 one / more intracystic masses
Type 3 mixed cystic (> 50%) and solid components
Type 4 predominantly solid + eccentric cystic foci

(a) benign breast lesion
1. Fibrocystic changes: adenosis, sclerosing adenosis, apocrine metaplasia, cyst formation ± rupture, ductal ectasia
2. Intraductal / intracystic papilloma
3. Fibroadenoma

4. Breast varix

(b) atypical (high-risk) breast lesion
1. Atypical ductal hyperplasia
2. Atypical papilloma
3. Lobular neoplasia

(c) malignant breast lesion
1. DCIS
2. Infiltrating ductal carcinoma
3. Infiltrating lobular carcinoma

Benign Sonographic Characteristics
(according to data from A.T. Stavros)

US Characteristic	*Sens.*	*Specif.*	*NPV*	*Rel. risk*
Hyperechoic	100.0	7.4	100.0	0.00
≤ 3 lobulations	99.2	19.4	99.2	0.05
Ellipsoid shape	97.6	51.2	99.1	0.05
Thin echogenic capsule	95.2	76.0	98.8	0.07

MALE BREAST DISEASE

Benign Male Breast Disease

1. Gynecomastia
2. Lipoma
3. Pseudoangiomatous stromal hyperplasia
4. Granular cell tumor
5. Fibromatosis / desmoid tumor
6. Myofibroblastoma
7. Schwannoma
8. Hemangioma

Malignant Male Breast Disease

A. CARCINOMA
1. Invasive ductal carcinoma
   Incidence: 0.17% of all male breast cancers
   Mean age: 59 years
   √ microcalcifications in only 13–30%
2. Papillary carcinoma
3. Invasive lobular carcinoma
4. Adenoid cystic carcinoma

B. SARCOMA
1. Liposarcoma
2. Dermatofibrosarcoma
3. Pleomorphic hyalinizing angiectatic tumor

C. OTHERS
1. Basal cell carcinoma of nipple

2. Lymphoma / leukemia
   = most common hematopoietic disease of the breast
   √ axillary lymphadenopathy: unilateral in primary / bilateral in secondary breast lymphoma
3. Metastasis

BREAST CALCIFICATIONS

= deposits of calcium salts
(a) precipitated salts in accumulated fluid secreted by epithelial cells
b) in / on necrotic cells
(c) fibrous capsule of foreign object

Indicative of focally active process; often requiring biopsy
◊ 75–80% of biopsied clusters of calcifications represent a benign process
◊ 10–30% of microcalcifications in asymptomatic patients are associated with cancers

Composition: hydroxyapatite / tricalcium phosphate / calcium oxalate

Results of breast biopsies for microcalcifications:
(without any other mammographic findings)
(a) benign lesions (80%)
1. Mastopathy without proliferation 44%
2. Mastopathy with proliferation 28%
3. Fibroadenoma 4%
4. Solitary papilloma 2%
5. Miscellaneous 2%

(b) malignant lesions (20%)
1. Lobular carcinoma in situ 10% in 8% no spatial relationship to LCIS
2. Infiltrating carcinoma 6%
3. Ductal carcinoma in situ 4%

◊ A positive biopsy rate of > 35% is desirable goal!

A. LOCATION
(a) intramammary
1. **Ductal microcalcifications**
   √ 0.1–0.3 mm in size, irregular, sometimes mixed linear + punctate
   Occurrence: secretory disease, epithelial hyperplasia, atypical ductal hyperplasia, intraductal carcinoma
2. Lobular microcalcifications
   √ smooth round, similar in size + density
   Occurrence:
   cystic hyperplasia, adenosis, sclerosing adenosis, atypical lobular hyperplasia, lobular carcinoma in situ, cancerization of lobules (= retrograde migration of ductal carcinoma to involve lobules), ductal carcinoma obstructing egress of lobular contents
   N.B.: lobular and ductal microcalcifications occur frequently in fibrocystic disease + breast cancer!

(b) extramammary: arterial wall, duct wall, fibroadenoma, oil cyst, skin, etc.

B. SIZE
◊ Mammography detects calcifications > 100 µg; down to ~ 75 µg for spot magnification views
√ malignant calcifications usually < 0.5 mm; rarely > 1.0 mm

C. NUMBER
√ < 4–5 calcifications per 1 cm^2 have a low probability for malignancy

D. MORPHOLOGY
(a) benign
1. Smooth round calcifications: formed in dilated acini of lobules
2. Solid / lucent-centered spheres: usually ← fat necrosis
3. Crescent-shaped calcifications that are concave on horizontal beam lateral projection = sedimented milk of calcium at bottom of cyst
4. Lucent-centered calcifications: around accumulated debris within ducts / in skin
5. Solid rod-shaped calcifications / lucent-centered tubular calcifications: formed within / around normal / ectatic ducts
6. Rimlike / eggshell calcifications in rim of breast cyst, fibrous wall of fat necrosis ("oil cyst"), pseudocapsule of fibroadenoma
7. Calcifications with parallel track appearance = vascular calcifications

(b) malignant
= calcified cellular secretions / necrotic cancer cells within ducts
√ calcifications of vermicular form, varying in size, of linear / branching shape

E. DISTRIBUTION
1. Clustered heterogeneous calcifications: adenosis, peripheral duct papilloma, hyperplasia, cancer
2. Segmental calcifications within single duct network: suspect for multifocal cancer within lobe
3. Regional / diffusely scattered calcifications with random distribution throughout large volumes of breast: almost always benign

F. TIME COURSE
malignant calcifications can remain stable for > 5 years!

G. DENSITY

Malignant Calcifications

1. **Granular calcifications** = resembling fine grains of salt
√ amorphous, dotlike / elongated, fragmented
√ grouped very closely together
√ irregular in form, size, and density
2. **Casting calcifications** = fragmented cast of calcifications within ducts
√ variable in size + length
√ great variation in density within individual particles + among adjacent particles
√ jagged irregular contour
√ ± Y-shaped branching pattern
√ clustered (> 5 per focus within an area of 1 cm^2)

Benign Calcifications

1. **Lobular calcifications** = arise within a spherical cavity of cystic hyperplasia, sclerosing adenosis, atypical lobular hyperplasia
   √ sharply outlined homogeneous solid spherical "pearl-like"
   √ little variation in size
   √ numerous + scattered
   √ associated with considerable fibrosis
   (a) adenosis
      √ diffuse calcifications involving both breasts symmetrically
   (b) periductal fibrosis
      √ diffuse / grouped calcifications + irregular borders, simulating malignant process
2. Sedimented milk of calcium
   Frequency: 4%
   √ multiple bilateral scattered / occasionally clustered calcifications within microcysts
   √ smudge-like particles ("cotton balls") at bottom of cyst on vertical beam (CC image)
   √ crescent-shaped on horizontal projection = "teacup-like" (ML / MLO image)
3. Plasma cell mastitis = periductal mastitis
   √ sharply marginated calcifications of uniform density = intraductal form
   √ sharply marginated hollow calcifications = periductal form
4. Peripheral eggshell calcifications
   (a) with radiolucent lesion
      › liponecrosis micro- / macrocystica calcificans (= fatty acids precipitate as calcium soaps at capsular surface) as calcified fat necrosis / calcified hematoma
      ◊ May mimic malignant calcifications!
   (b) with radiopaque lesion
      › degenerated fibroadenoma
      › macrocyst
      √ high uniform density in periphery
      √ usually subcutaneous
      √ no associated fibrosis
5. Papilloma
   √ solitary raspberry configuration in size of duct
   √ central / retroareolar
6. Degenerated fibroadenoma
   √ bizarre, coarse, sharply outlined, "popcornlike" very dense calcification within dense mass (= central myxoid degeneration)
   √ eggshell type calcification (= subcapsular myxoid degeneration)
   √ heterogeneously grouped macrocalcifications with circumferential nature in postmenopausal woman
7. Arterial calcifications
   √ parallel lines of calcifications
8. Metastatic calcifications
   Cause: 2° hyperparathyroidism (in up to 68%)

Dermal Calcifications

Site: hair follicle, nevus, sebaceous cyst, lupus erythematosus, dermatomyositis, scar

Cause: inspissated material in sebaceous glands, secondary to chronic folliculitis
Location: most commonly visible in lower inner breast
Site: near periphery of skin surface (may project deep within breast even on 2 views at 90° angles)
Size: same size as skin pores
√ round lucent centered calcifications:
  √ hollow radiolucent center (hair follicle)
√ linear orientation when caught in tangent
√ polygonal shape
Proof: superficial marking technique (= skin localization work-up)

Dystrophic Calcifications

= calcium deposits on / in necrotic material, cellular debris, devitalized tissue
(a) skin: lupus erythematosus, dermatomyositis, scar, parasite, breast implant
(b) foreign body: suture, parasite, breast implant
√ larger coarser calcifications than with DCIS

Calcifications in Branching Tubular Opacity

1. Ductal carcinoma in situ
2. Atypical ductal hyperplasia
3. Secretory disease
4. Peripheral papillomatosis
5. Vascular: calcified artery; Mondor disease (= thrombophlebitis of superficial vein)
6. Fat necrosis
7. S/P Galactography

NIPPLE & AREOLA

Nipple-Areolar Complex

(a) benign process
  1. Nipple inversion
     Cause: mammary duct ectasia, postsurgical changes, fat necrosis, fibrocystic changes, Mondor disease
     √ uni- / bilateral
     DDx: malignancy (developing over a few months)
  2. Inflammation / abscess
  3. Mammary duct ectasia
  4. Calcifications
     √ spherical with central area of lucency (associated with glands + hair follicles)
     √ nonspecific in association with sutures, fat necrosis, intraductal papilloma, Paget disease, intraductal ca.
  5. Cutaneous horn
     = conical projection of keratin above skin surface that may grow rapidly
     • vulnerable to trauma
     DDx: squamous cell carcinoma, Paget disease, sebaceous adenoma, granular cell

tumor
6. Nipple adenoma

(B) MALIGNANT PROCESS
1. Paget disease
2. Subareolar carcinoma
3. Lymphoma

Benign Mass of the Nipple
1. Papilloma
2. Fibroadenoma
3. Nipple adenoma

Nipple Retraction
1. Positional
2. Relative to inflammation / edema of periareolar tissue
3. Congenital
4. Acquired (carcinoma, ductal ectasia)

Nipple Discharge
Prevalence: 7.4 % of breast surgeries
◊ 3rd most common breast complaint

Classification:

A. Provoked
postovulatory state, duct ectasia, medication, stimulation by exercise, breast self-examination, sexual manipulation

B. Spontaneous
(a) physiologic: pregnancy; lactation; galactorrhea, duct ectasia; duct stricture; communicating cysts
(b) pathologic: benign / malignant neoplasm; galactorrhea ← hyperprolactinemia from a pituitary adenoma

C. Unilateral
◊ Unilateral spontaneous discharge is significant + requires investigation!
(a) benign (50%): duct ectasia; intraductal papilloma
(b) malignant (15%): papillary carcinoma; ductal carcinoma in situ (DCIS); invasive ductal carcinoma

D. Bilateral
◊ Expressed bilateral multipore blood-negative discharge is physiologic and benign!

Type of discharge:

A. Lactating breast: galactorrhea

B. Nonlactating breast:
(a) normal:
› milky
› multicolored sticky (blue, green, gray, brown, black)
(b) abnormal:
› purulent: antibiotics, incision, drainage

(c) surgically significant (in 14.3% cancerous)
› clear / watery: cancer in 33%
› bloody / sanguineous: cancer in 28%,
› pink / serosanguinous: cancer in 13%
› yellow / serous: cancer in 6%
› cheesy: chronic duct ectasia with chronic periductal mastitis / comedo-DCIS

◊ Intraductal papilloma is the most common cause of bloody and serosanguinous discharge (in 40%)!

◊ Exfoliative cytology not helpful (TP in only 11%, FN in 18%)

Site of origin:

A. Lobules + terminal duct lobular unit:
1. Galactorrhea
2. Fibrocystic changes

B. Larger lactiferous ducts (collecting duct, segmental duct, subsegmental duct)
1. Solitary papilloma
2. Papillary carcinoma
3. Duct ectasia

High-risk nipple discharge:

= discharge likely caused by carcinoma / papilloma
(1) Spontaneous
(2) Unilateral
(3) Single duct orifice
(4) Clear / serous / serosanguinous / frankly bloody

Low-risk nipple discharge:

= discharge likely caused by hyperprolactinemia, duct ectasia, fibrocystic change
(1) Expressible only
(2) Bilateral
(3) Multiple duct orifices
(4) Greenish / milky

Galactography / Ductography

= diagnostic procedure of choice for spontaneous ± guaiac-positive unilateral nipple discharge

» injection of 0.2–0.3 mL of water-soluble contrast material (Conray 60 ®, Isovue ®) through straight blunt 27-gauge pediatric sialography cannula (0.4–0.6 mm outer diameter) / 30-gauge cannula (Ranfac Corp, Avon, MA) / Jabczenski cannula (tip bent 90°)

Timing: within 24 hours of noticing discharge (without squeezing nipple / breast)

Results of positive galactography:
papilloma (48%), benign conditions (42%), intraductal carcinoma (10%)

Contraindications to ductography:
history of severe allergy to iodinated contrast material; inability of patient to cooperate (debilitating anxiety, mental disorder); history of prior nipple surgery; abscess; diffuse mastitis

DDx of dilated ducts:

(1) Duct ectasia
(2) Blocked duct (during lactation)
(3) Inflammatory infiltrates
(4) Periductal mastitis
(5) Apocrine metaplasia

DDx of intraductal defects:

(1) Papilloma
(2) Gas bubble, clot, inspissated secretions, infection
(3) Epithelial hyperplastic lesion
(4) Duct carcinoma

Galactographic Filling Defect		
Type of Tumor	*Single*	*Multiple*
Multiple papilloma	5.60%	14.0%
Cancer	0.05%	9.7%

BREAST SKIN

Skin (Dermal) Lesions of Breast

A. DERMAL
   1. Sebaceous cyst
   2. Epidermal inclusion cyst
   3. Dermal calcifications

B. HYPODERMAL = subcutaneous fat
   (a) fat-containing lesions
      1. Lipoma
      2. Fat necrosis
   (b) vascular lesions
      1. Hemangioma
      2. Angiolipoma
      3. Thrombosed vessel
   (c) neurogenic
      1. Granular cell tumor
   (d) lymphatic

C. SUPERFICIAL MAMMARY TISSUE = anterior TDLU

   N.B.: TDLUs may be located within anterior Cooper ligament extensions into subcutaneous fat

   1. Superficial breast cancer
   2. Peripheral papilloma
   3. Fibroadenoma
   4. Adenosis

Lesions of Nipple-Areolar Complex

1. Epidermal inclusion cyst

2. Sebaceous cysts / obstructed Montgomery gland
3. Breast cancer arising from anterior TDLUs / large lactiferous ducts / central papillomas
4. Nipple adenoma
5. Paget disease of nipple

NIPPLE CHANGES

(a) benign: eczema, psoriasis, allergic contact dermatitis , irritant dermatitis, lichen simplex chronicus
(b) malignant: Paget disease, Bowen disease (squamous cell carcinoma in situ)

Skin Thickening of Breast

Normal skin thickness: 0.8–3 mm; 0.5–2 mm at MRI; may exceed 3 mm in inframammary region

◊ Epidermis is indistinguishable as a separate layer from the dermis at imaging!

A. LOCALIZED SKIN THICKENING
1. Trauma prior biopsy, burns
2. Carcinoma
3. Abscess
4. Nonsuppurative mastitis
5. Dermatologic conditions: psoriasis

B. GENERALIZED SKIN THICKENING

Skin Thickening on MR		
Mild	Moderate	Severe
< 3 mm	3–5 mm	> 5 mm

◊ Skin is thickened initially and to the greatest extent in the lower dependent portion of the breast!

√ overall increased density with coarse reticular pattern ← dilated lymph vessels + interstitial fluid triggering fibrosis

(a) axillary lymphatic obstruction
1. Primary breast cancer
› advanced breast cancer
› invasive comedocarcinoma in large area
◊ Primary breast cancer not necessarily seen due to small size / hidden location (axillary tail, behind nipple)!
2. Primary malignant lymphatic disease (eg, lymphoma)

(b) intradermal + intramammary obstruction of lymph channels
1. Lymphatic spread of breast cancer from contralateral side
2. Inflammatory breast carcinoma = diffusely invasive ductal carcinoma

(c) mediastinal lymphatic blockage
1. Sarcoidosis
2. Hodgkin disease
3. Advanced bronchial / esophageal carcinoma
4. Actinomycosis

(d) advanced gynecologic malignancies

via thoracoepigastric collaterals
1. Ovarian cancer
2. Uterine cancer

(e) inflammation
1. Acute mastitis
2. Retromamillary abscess
3. Fat necrosis
4. Radiation therapy
5. Reduction mammoplasty

(f) right heart failure
may be unilateral (R > L) / migrating with change in patient position (to avoid decubitus ulcer)

(g) nephrotic syndrome, anasarca
1. Dialysis
2. Renal transplant

(h) subcutaneous extravasation of pleural fluid following thoracentesis

LYMPHADENOPATHY

Terminology for microscopic metastatic deposits:

› "isolated tumor cells": < 0.2 mm
› "micrometastasis": 0.2 – 2.0 mm

N.B.: Metastases < 2 mm are NOT identifiable at imaging!

Imaging of Normal Lymph Nodes

• nonpalpable

Mammo:
√ well-circumscribed mass of low to moderate density:
√ round to oval / bean-shaped
√ slightly lobulated margin
√ radiolucent fatty notch / hilum (visible in 78%)
√ central zone of radiolucency (= fatty replacement of center) surrounded by "crescent" rim of cortex
√ usually < 1.5 cm (up to 4 cm) in size:
√ < 1 cm within breast tissue, < 1.5 cm within axilla
◊ Normal axillary nodes may be larger than 5 cm!

US:
√ reniform hypoechoic rim + hyperechoic center
√ echogenic hilum for entry and exit of vessels
√ bidirectional hilar blood flow

MR:
√ smooth cortex + axillary symmetry → high NPV for exclusion of metastasis
√ cortical thickness of < 3 mm (91% NPV)
› T1WI
√ lymph nodes not recognizable within parenchyma

√ recognizable in extraparenchymal location as oval well-circumscribed hypointense lesion with central hyperintense area

› enhanced T1WI:

√ no / slight enhancement of bland lymph nodes

√ strong enhancement of cortex + type III wash-out kinetic pattern

› T2WI / STIR:

√ intermediate to increased signal intensity

Intramammary Lymphadenopathy

= adenopathy > 1 cm surrounded by breast tissue

Frequency: 5.4%

Location: axilla, subcutaneous tissue of axillary tail, lateral portion of pectoralis muscle, intramammary (typically in upper outer quadrant)

N.B.: nodes located high within axillary tail (= tail of Spence) are mammographically difficult to differentiate from inferior axillary lymph nodes

[James Spence (1812–1882), chair of systematic surgery at Edinburgh University in Scotland]

Axillary Lymphadenopathy

= solid node > 1.5 cm in size without fatty hilum

N.B.: lymph nodes of up to 3 cm may be normal if largely replaced by fat

A. MALIGNANT

1. Metastasis from breast cancer in 26%

◊ Primary breast lesion may not be found in 33%!

Currently, axillary surgery is considered the only definitive test to determine the absence of axillary metastases.

The main goal of preoperative imaging of the axilla is to identify metastases with a high-enough PPV to proceed directly to axillary lymph node dissection.

2. Metastases from non-breast primary (lung, melanoma, thyroid, GI tract, ovary)
3. Lymphoproliferative disease: lymphoma / chronic lymphocytic leukemia (17%)

B. BENIGN

1. Nonspecific benign lymphadenopathy (29%)
2. Reactive nodal hyperplasia (breast infection / abscess / biopsy)
3. Collagen vascular disease: rheumatoid arthritis, SLE
4. Granulomatous disease: sarcoidosis
5. Psoriasis
6. HIV-related adenopathy
7. Silicone-related adenopathy

Bilateral Axillary Lymphadenopathy

A. NEOPLASM

1. Secondary breast lymphoma

◊ Bilateral axillary lymphadenopathy is suggestive of lymphoproliferative disease!

2. Other neoplasms
3. Metastases

B. BENIGN

1. Collagen vascular disease
2. Granulomatous disease
3. HIV
4. Silicone-related adenopathy

Lymph Node Features Suspicious For Malignancy

√ size increase of > 100% over baseline:
  √ size > 3.3 cm
    ◊ Size of node usually NOT useful criterion (although small nodes have high NPV)
√ change in shape:
  √round shape / long-to-short axis ratio of < 2
  √ focal bulge / eccentric cortical thickening
√ spiculation of margins
√ intranodal microcalcifications (without history of gold Rx)
√ loss of radiolucent fatty center / hilar notch
√ increase in density

Ultrasound of Malignant Lymph Nodes

Ultrasound is the primary nonsurgical method for evaluating axillary nodes!

Value: 62–92% sensitive, 75–91% specific
Path: metastases embed subcortically in end vasculature
√ loss of reniform shape
√ bulbous contour with cortical thickening:
  √ focal eccentric cortical thickening
  √ symmetric diffuse cortical thickening > 3–5 mm
    (a) adjacent to several normal nodes
    (b) while contralateral nodes are normal
  ◊ Cortical thickening is the target for biopsy!
√ loss of normal central fatty hilum / hilar indentation
√ severely flattened / compressed node with loss of echogenic center
√ more than 1 feeding vessel:
  √ hyperemic hilar blood flow
  √ nonhilar cortical blood vessel (= entering capsule rather than lymph node mediastinum)
√ high-impedance waveform with sharp systolic high-velocity peak
DDx: reactive node (symmetric cortical thickening, adjacent nodes with similar morphology, often bilateral, no capsular vessels, low-impedance pattern with round low-velocity systolic peak)

MR of Malignant Axillary Lymph Nodes

◊ Axilla may be obscured by pulsation artifact from heart
Advantage: more global view of axillae compared to US allowing side-to-side comparison

MRI findings highly suggestive of metastatic lymph nodes (similar to other modalities):
  √ markedly enlarged lymph node

√ morphologically grossly abnormal (= distinctly different from other visible axillary nodes)

√ perifocal edema (100% PPV)

Dynamic CEMR:

√ strong heterogeneous enhancement (DDx: reactive inflammatory node)

√rim enhancement = higher SI in node periphery than center at 11 min after contrast infusion (100% PPV)

VASCULAR BREAST DISEASE

Venous Disorders of Breast

1. Collateral flow ← venous blockage / occlusion
   - √ unilateral dilatation of breast veins ← axillary or subclavian vein blockage
   - √ bilaterally enlarged breast veins ← occlusion of SVC
2. Congestive heart failure
   - √ bilateral breast venous congestion
   - √ bilateral skin thickening
   - √ interstitial breast edema

Benign Vascular Breast Mass

1. Hemangioma
2. **Lymphangioma**

   = extremely rare mass in child / young adult

   Histo: dilated lymphatic channels filled with lymphatic fluid + lined with endothelial cells

   Location: axilla / axillary tail of breast

   √ solitary lobulated mass with single cystic space (lymphangioma circumscriptum) / multicystic mass
3. Angiolipoma

Malignant Vascular Breast Mass

1. Angiosarcoma
2. Hemangiopericytoma

Devascularized Breast Mass

= loss of normal blood supply → infarction of breast tissue most commonly associated with fat necrosis

Cause: trauma, radiation therapy, spontaneous infarction of breast mass (hamartoma)

1. Infarcted lactating adenoma
2. Infarcted giant juvenile fibroadenoma

T2-HYPERINTENSE BREAST TUMOR

(in order of descending frequency)

A. EPITHELIAL TUMOR
   1. Mucinous carcinoma
   2. Invasive ductal carcinoma

3. Metaplastic carcinoma
4. Papillary carcinoma
5. Invasive lobular carcinoma
6. Adenoid cystic carcinoma
7. Sebaceous carcinoma
8. Intraductal papilloma

B. MESENCHYMAL TUMOR
1. Fibrosarcoma
2. Myofibroblastoma
3. Cavernous hemangioma

C. FIBROEPITHELIAL TUMOR
1. Myxoid fibroadenoma
2. Phyllodes tumor: benign / borderline / malignant

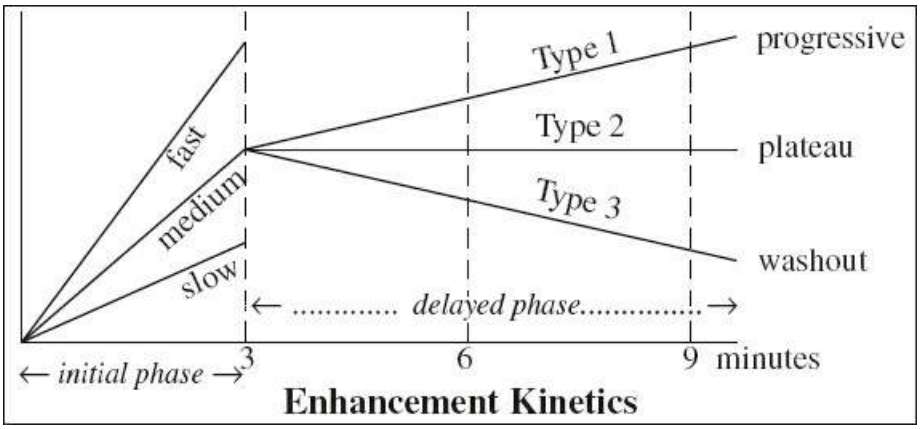
T2-hyperintensity is seen with extensive tumor necrosis, cystic + microcystic components, fatty (sebaceous) components, mucinous stroma, loose myxoid stroma, stromal edema, hemorrhagic changes!

MR ENHANCEMENT PATTERNS

Enhancement Kinetics

◊ Best performed on days 7–12 (= 2nd week of menstrual cycle) to minimize hormonal effect!

◊ Considerable overlap in enhancement characteristics between benign and malignant lesions!



◊ Nonmass-like lesion (invasive lobular carcinoma) may exhibit low-magnitude and persistent-enhancement kinetics (? due to weak angiogenic activity)

Malignant: plateau or washout pattern (63% sensitive, 65% specific)

INITIAL PHASE

= initial peak SI within first 2–3 min after contrast administration relative to SI of unenhanced image

or when shape of kinetic curve begins to change

Categories: < 50% (slow); ≥ 50% and < 100% (medium); ≥ 100% (fast)
Intensity threshold (color): 2 minutes > 50–100%
DCIS: 70% exhibit fast, initial enhancement, with variable delayed-phase enhancement patterns

DELAYED PHASE

= enhancement curve that develops after 2–3 minutes or after kinetic curve changes ($SI_{postinitial}$ = postinitial intensity during 4th, 5th, 6th minute + SI at 6 minutes by comparison with the initial peak obtained during 1st, 2nd and 3rd minute)

Type 1 = Persistent / Progressive / Continuous Pattern

= continuous increase in $SI_{postinitial}$ > **10%**

• usually benign
Distribution: 83% benign, 9% malignant
Benign lesion: 52% sensitive, 71% specific
◊ 45% PPV for malignancy

Type 2 = Plateau Pattern

= $SI_{postinitial}$ change of ±**10%**

• occasionally malignant
Malignant lesion: 43% sensitive, 75% specific

Type 3 = Washout Pattern

= progressive decrease of $SI_{postinitial}$ < **10%**

• highly suspicious
Malignant lesion: 21% sensitive, 90% specific
◊ 76% PPV for malignancy

Quantitative Kinetic Parameters

1. Initial enhancement percentage (E_1)
2. Peak enhancement percentage (E_{peak})
3. Time to peak enhancement (T_{peak})

Lack of Enhancement

• palpable lesion
• mammographically visible abnormality
NPV: 88–96%
FN: DCIS (48%), small invasive carcinoma / small invasive component (52%)
√ nonenhancing architectural distortion suggests a radial scar

Unilateral Diffuse Enhancement on MR

› Common
1. Parenchymal asymmetry
2. Fibrocystic changes
3. Adenosis
4. Unilateral implant

› Rare
5. Normal: unfavorable cycle phase, HRT
6. Mastitis
7. Inflammatory breast cancer
8. Extensive carcinoma: diffuse lobular carcinoma, lymphangiosis, extensive DCIS
9. Prior ipsilateral radiotherapy within last few months

Background Parenchymal Enhancement (BPE)

= additional tool for risk stratification in high-risk women

◊ ↑ odds of breast cancer with moderate / marked BPE

1. False-positive interpretation ← focal / regional /asymmetric BPE
2. False-negative interpretation ← moderate / marked BPE

ENHANCING LESIONS ON BREAST MR

Homogeneously Enhancing Well-Demarcated Round Lesion

◊ Homogeneous enhancement suggests benign disease!

› Common
1. Fibroadenoma: endotumoral septa
2. Adenoma
3. Papilloma
4. Carcinoma

› Rare
5. Intramammary node:
   √ lipomatous hilum
6. Fat necrosis:
   √ macrocalcifications on mammogram
7. Granuloma
8. Carcinoma: esp. medullary form
9. Phylloides tumor
10. Metastasis

Rim-Enhancing Lesion

› Common
1. Complicated cyst / postoperative seroma:
   √ narrow hyperintense ring on T2
2. Invasive carcinoma:
   √ broad hypo- / isointense ring on T2WI ← vital tumor
   √ thick irregular shaggy rim
3. Fat necrosis:
   √ centrally low signal of fat content
   √ confirmatory low-density lesion on mammogram
4. Superimposition of blood vessels: tubular structures on MIP

› Rare
5. Adenosis

6. Abscess
7. Lymphadenitis

Multiple Homogeneously Enhancing Lesions with Well-defined Borders

› Common
1. Fibrocystic changes
2. Fibroadenomas
3. Adenoma
4. Papilloma

› Rare
5. Multicentric carcinoma
6. Metastases

Dendritic Enhancement

› Common
1. Adenosis
2. Fibrocystic change
3. DCIS
4. Motion artifacts on subtraction image
5. Superposition of intramammary veins

› Rare
6. Previous galactography: history
7. Chronic mastitis

Lesion-in-Lesion Morphology

1. Giant juvenile fibroadenoma
2. Phyllodes tumor
3. Papilloma
4. Papillary carcinoma
5. Hemorrhage

Enhancing Lesion

Benign Enhancing Lesion

1. Nonproliferative lesion: mild hyperplasia, fibroadenoma
2. Proliferative lesion without atypia: sclerosing adenosis, radial and complexing sclerosing lesion, moderate hyperplasia, intraductal papilloma
3. Atypical lobular and ductal hyperplasia
4. Normal breast parenchyma in premenopausal woman

Morphologic Criteria for Benignity

√ smooth margin (95% NPV)
√ low-signal-intensity internal septa (98% NPV)
√lobulated margin + minimal / no enhancement (100% NPV)
√ enhanced portion on T1WI shows hyperintensity on T2WI

Morphologic Criteria for Malignancy

√ regional enhancement with a mass (81% PPV)
√ segmental distribution (78% PPV)
√ irregular / spiculated margin (84–91% PPV)
√ rimlike enhancement (84% PPV)
√ heterogeneous internal enhancement
√ enhancing internal septa
√ linear / branching ductal distribution (24–85% PPV)
√ regional enhancement WITHOUT a mass:
  √ homogeneous enhancement (67% PPV)
  √ clumped enhancement (60% PPV)
  √ heterogeneous enhancement (53% PPV)
  √ stippled enhancement (25% PPV)

Ancillary Features of Enhancing Lesions

√ hyperintense T2 signals in enhancing portion suggests benignity (eg, myxoid fibroadenoma of younger woman):
  √ not reliable for any irregular / spiculated mass
  Exception: medullary cancer
√ iso- / hypointense T2 signal suggests malignancy
√ focal perilesional edema highly suggestive of malignancy

MRI Differentiation of Benign from Malignant Lesion

	Benign	*Malignant*
Morphology	smooth	irregular
Kinetics	continuous rise	rapid rise
Enhancement	homogeneous	heterogeneous
T2 signal	high	variable (usually low)
T1 signal	high (protein, blood, melanin)	variable (usually low)
internal septa	nonenhancing	enhancing

√ enhancing architectural distortion highly suggestive of malignancy

POSTLUMPECTOMY BREAST MRI

Benign Postlumpectomy Changes

1. Skin thickening
2. Architectural distortion
3. Edema
   • may never resolve entirely
   √ persists in 25% at 6 years after breast conservation Rx
4. Signal voids / flare from surgical / biopsy clips
5. Fluid cavity filled with blood / seroma
6. Bleeding / hemosiderin

Probably Benign Postlumpectomy Changes

1. Small focal / thin linear non-masslike enhancement
   - √ seen for up to 18 months
   - √ slow initial + persistent delayed enhancement
2. Fat necrosis
   - √ persists up to 5 years

Suspicious Postlumpectomy Changes

- √ nodular non-masslike enhancement (NMLE) > 5 mm around a seroma cavity
- √ segmental / ductal / clumped NMLE
- √ masslike enhancement
- √ rapid initial + washout kinetics NOT consistent with fat necrosis
- √ increasing size of formerly "probably benign" lesion

Highly Suspicious Postlumpectomy Changes

- √ focal / multifocal masses with rapid initial + delayed washout kinetics
- √ irregular / spiculated margins (84–91% PPV)
- √ rim enhancement

MAMMOGRAPHIC FILM READING TECHNIQUE

1. Confirm patient identifiers are correct
2. Ensure images are of adequate quality:
   - › good contrast
   - › good compression
   - › adequate positioning (nipple in profile)
   - › lack of blur
   - › lack of artifacts
3. Compare with earlier films (preferably ≥ 2 years) whether finding is new / growing / stable
   - ◊ Beware of stability = breast cancer may grow slowly

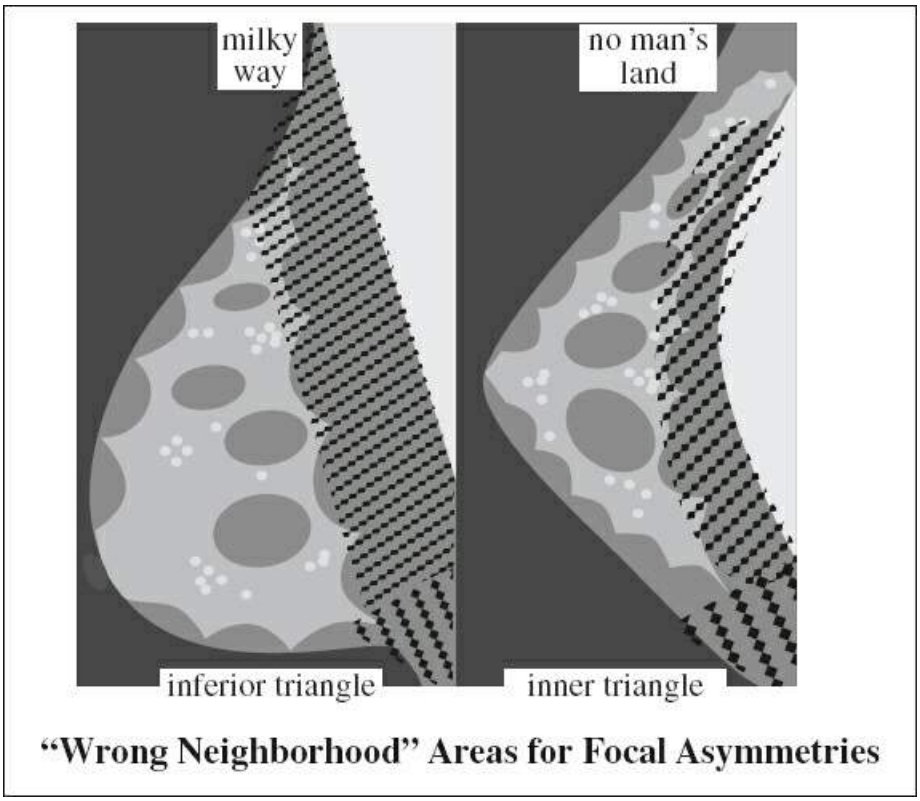
> Lesion morphology takes precedence over stability!

4. Compare left with right side
5. Scan "forbidden / living in the wrong neighborhood" areas
   - › MLO-view
     - (a) "Milky Way" = 2–3 cm wide area parallel to the edge of the pectoral muscle
     - (b) inferior triangle
   - › CC-view
     - (c) "No man's land" = retromammary fat between posterior border of parenchyma + chest wall
     - (d) Medial / inner triangle of breast

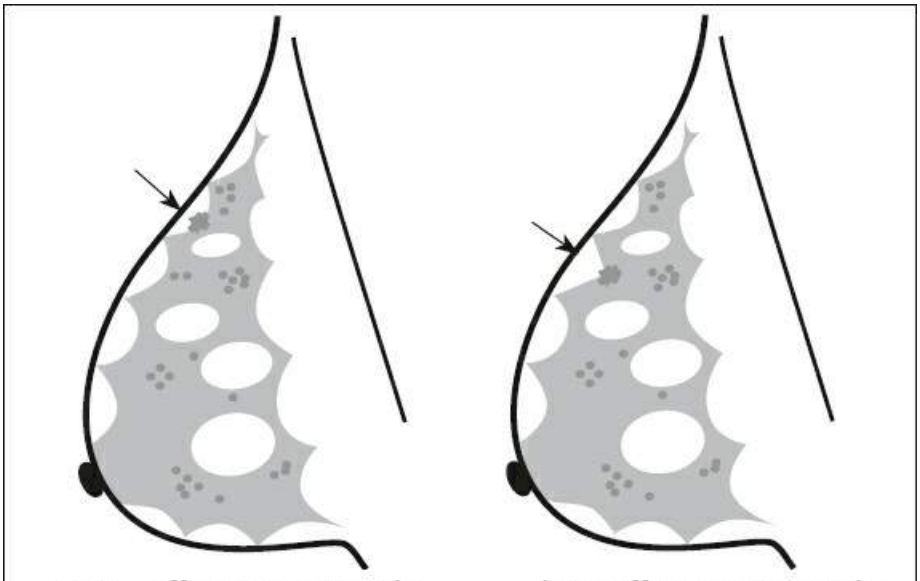
> Almost ¾ of breast cancers in women < 50 years occur in a 1-cm wide zone <u>beneath</u> the SQ fat!

6. Look for:
   - › global / focal asymmetry in breast parenchymal pattern disrespecting normal breast architecture + boundaries

› increased retroareolar density
› contour deformity at interface with fat



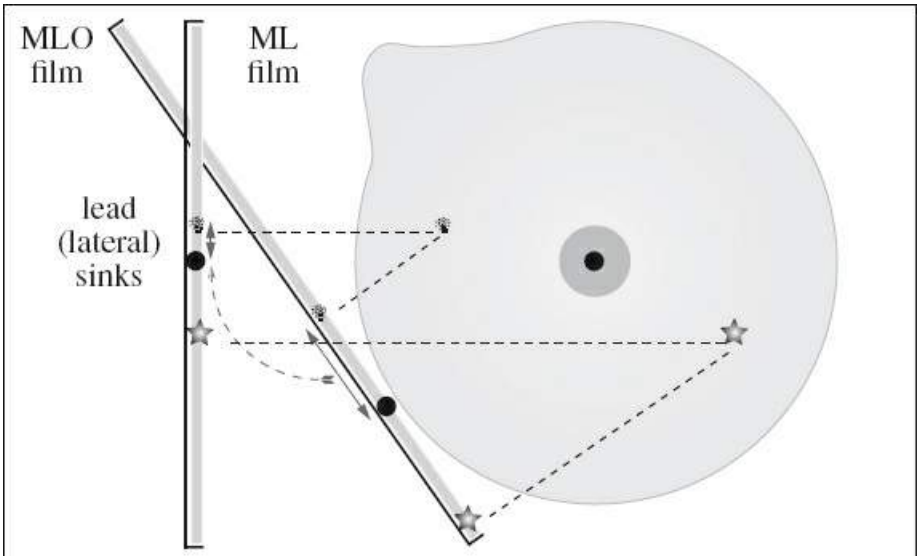
"Wrong Neighborhood" Areas for Focal Asymmetries



outwardly convex margin
"Slow down for the speed bump"

inwardly convex margin
"Look for the hook"

Breast Contour Deformity 2° to Cancer in Dense Breast



Shift in Position from MLO to ML View *(right breast)*
medial (stellate) lesion projects lower on MLO and wanders higher on ML view;
lateral lesion (calcifications) projects higher on MLO view and wanders lower on ML view
mnemonic: **"Lead (lateral) sinks, muffins (medial) rise"**;
◊ Central lesion shifts little, far lateral or medial lesions substantially!

(a) inwardly convex angulated margin
mnemonic: "Look for the hook"
(b) outwardly convex margin (= loss of scalloped margin)
mnemonic: "Slow down for the speed bump"

› straight lines superimposed on normal scalloped contour
› architectural distortion (magnification views!)
› calcifications (magnification views!)

7. DON'T STOP looking after one lesion is found

Diagnostic Evaluation of a Mass / Focal Asymmetry

Never recommend a biopsy based on screening alone!

Purpose of diagnostic workup:

1. Locate mass / focal asymmetry with additional views
   (a) mandatory additional views to characterize a lesion:
   › true LM / ML view depending on lesion location
   › spot compression in CC and MLO projections to reduce geometric unsharpness + blur
   Note: magnification (requires ↑ in exposure time → ↑ likelihood of motion-related blurring)
   ◊ Magnify microcalcifications NOT soft-tissue abnormalities

(b) optional additional views to localize a lesion:
› exaggerated CC lateral view
› cleavage view
› step-oblique views @ 15° intervals between true lateral and CC views
› medially / laterally rolled CC views
◊ Roll breast on the view that reveals the abnormality!
◊ Roll focal asymmetry toward fat!

2. Characterization of mass / focal asymmetry to develop a level of suspicion → for equivocal findings supplement with targeted US
3. Extent of disease
4. Multifocality
   Rule of multiples = the likelihood of malignancy decreases if multiple similar findings are present, especially if bilateral
   ◊ All lesions must have exclusively benign features!
5. Staging of axilla with ultrasound
   ◊ The most predictive sign of axillary metastasis is a lymph node with a cortex > 2 mm thick
6. Discuss findings with patient, answer questions
7. Arrange for biopsy

Skin Localization Work-up

» Use mammographic paddle with alphanumeric grid

(1) Compress breast with grid opening along surface Ca^{2+}
(2) Place metallic skin marker directly over calcification cluster at appropriate alphanumeric location
(3) Repeat image to confirm accurate skin marker placement
(4) Obtain magnification view in orthogonal plane with skin marker tangential to x-ray beam

Interpretation:
→ calcifications in skin project into dermis
→ superficial parenchymal calcifications project into breast tissue

Surveillance

(1) Only for lesion that satisfies benign criteria = BI-RADS ® category 3
(2) Obtain reproducible mammographic image (CC views are more consistent compared with MLO)
(3) Change
◊ Stability for several years does not guarantee benignity (eg, tubular carcinoma)
◊ Any new mass requires workup
◊ A 3-mm change represents a doubling of volume in a 1-cm lesion
If lesion acquires certain benign features change to BI-RADS ® category 2
(4) Requires a compliant patient following recommended intervals
N.B.: ~ 40% of patients are not compliant (numbers are different for US, mammography and MRI)!

False negative rate: < 2% if done appropriately

Receptor Status Correlated with Histopathology	
Receptor Status	*Histopathology*
ER–	Nonmass-like enhancement (in <20% of lesions)
ER+	Nonmass-like enhancement (in 0% of lesions)
ER+ or ER–	equal incidence of multiple masses
HER2+	multicentric masses (in 60%)
triple negative	masses
ER = estrogen receptor; HER2 = human epidermal growth factor	

MAMMOGRAPHY REPORT

based on BI-RADS® (**B**reast **I**maging **R**eporting and **D**ata **S**ystem) published by the ACR (American College of Radiology)

Report Contents

1. Indication for exam
2. Comparison to previous studies
3. Breast Composition
4. Findings
5. Overall Assessment
6. Communication of result (as IMPORTANT as the diagnosis)

A. ASYMMETRY

= planar density seen only in a <u>single projection</u> WITHOUT convex margins / suspicious calcifications / architectural distortion ± interspersed fat

1. **Global asymmetry** (= asymmetric breast tissue)
   = parenchymal volume greater in one breast compared to the other involving <u>at least one quadrant</u>
   = common and usually normal variant
   Of concern if associated with:
   architectural distortion / decrease in breast size ("shrinking breast") / skin thickening / axillary adenopathy / clinical findings
2. **Focal asymmetry**
   = asymmetry confined to less than a quadrant

B. MASS (challenge of perception)

= 3-dimensional space occupying lesion with convex margins seen in <u>two different projections</u>

size	measurements
shape	round, oval, lobulated, irregular
margins	circumscribed, lobulated, obscured, indistinct, spiculated
density	relative to an equal volume of breast tissue: high, equal, low, fat
location	based on face of clock; depth (anterior, middle, posterior); subareolar; central; axillary
posterior extent	pectoralis muscle / chest wall

C. ARCHITECTURAL DISTORTION
= straight lines in a radial arrangement

D. CALCIFICATIONS (challenge of disposition)

benign	skin, vascular, coarse popcorn-like, large rodlike (secretory), round, punctate, lucent center, eggshell / rim, milk of calcium, suture, dystrophic
indeterminate	amorphous / indistinct
probably malignant	pleomorphic (coarse heterogeneous / fine pleomorphic), fine linear / fine linear branching
number	
size	
distribution	grouped / clustered, linear, segmental, regional (within large volume of breast tissue), scattered / diffuse, multiple groups
stability	increasing, stable

E. Associated Findings

skin invasion	thickening (diffuse, focal), retraction
nipple involvement	retraction, inversion
trabeculae	thickening, architectural distortion
axilla	adenopathy

F. MULTIPLE MASSES = multicentricity / multifocality
number > 1 distance between 2 masses (outer edge to outer edge)

Breast Imaging Reporting and Data System (BI-RADS®)

◊ Additional image evaluation may be necessary: off-angle / spot compression mammographic views; ultrasound
◊ Unexplained abnormalities warrant biopsy

ASYMMETRIC BREAST TISSUE
= greater volume / density in one breast compared with corresponding area in contralateral breast

DENSITY IN ONE PROJECTION
= density seen on only one standard mammographic view

ARCHITECTURAL DISTORTION
= focal area of distorted breast tissue (spiculations with common focal point / focal retraction / tethering) without definable central mass

FOCAL ASYMMETRIC DENSITY
= focal asymmetric density seen on two mammographic views but not identified as a true mass

Lexicon Descriptors for Breast MR Reports

suspicious areas are described as (<u>underlined</u> signs suggest malignancy)

A. **Focus / foci** area < 5 mm in diameter
shape (= mini-mass: round / oval, <u>spiculated /</u>

	irregular
margin	smooth, not smooth
T2	bright, not bright
hilum	with fat, without fat
curve	persistent, washout
priors	stable, new / increasing)

B. **Mass** 3-D space-occupying lesion ≥ 5 mm with a convex margin

shape	round, oval, lobulated, irregular
margin	smooth, irregular, spiculated
internal enhancement	homogeneous, dark internal septations, heterogeneous, rimlike, enhancing internal septations, central

C. **Nonmass-like Enhancement** (NMLE)

distribution	focal area (< 25% of quadrant), linear (not ductal, sheetlike), diffuse, ductal, segmental, regional, multiregional (not ductal)
internal enhancement	homogeneous, heterogeneous, stippled / punctate, clumped, reticular / dendritic symmetry symmetrical, asymmetrical

◊ Biopsy if associated with microcalcifications / if segmentally distributed / if asymmetric / if patient > 45 years

D. **Associated findings**

edema
adenopathy
cysts
skin involvement
chest wall involvement

E. **Kinetic curve assessment** *(if morphology is probably benign)*

initial phase	slow, medium, rapid
delayed phase	persistent / plateau (→ follow up), washout (→ biopsy)

REPORT NOTICE ON BREAST DENSITY

"If your mammogram demonstrates that you have dense breast tissue, which could hide small abnormalities, you might benefit from supplementary screening tests, which can include a breast ultrasound screening or a breast MRI examination, or both, depending on your individual risk factors. A report of your mammography results, which contains information about your breast density, has been sent to your physician's office and you should contact your physician if you have any questions or concerns about this report."

BI-RADS® Categories (American College of Radiology)				
Cat.	*Mammography*	*Ultrasound*	*MR*	*Malignancy Likelihood*
0	**Need additional imaging** evaluation or prior mammogram for comparison: eg, spot compression, magnification, special views, ultrasound	**Need additional imaging**: eg, an MR for (1) palpable confirmed mass (2) recurrence versus scar after lumpectomy	**Need additional imaging** evaluation: eg, (1) technically unsatisfactory scan (2) screening MR without kinetic imaging (3) incomplete information	---
1	**Negative**: symmetric breasts, no masses, architectural distortion, suspicious calcifications	**Negative**: no mass, architectural distortion, skin thickening, microcalcifications	**Negative**: symmetric breasts; no architectural distortion, abnormal enhancement, or mass	0%
2	**Benign** findings: eg, involuting calcified fibroadenoma, multiple secretory calcifications, oil cyst, lipoma, galactocele, hamartoma, intramammary node, vascular calcifications, implants, architectural distortion related to prior surgery	**Benign** findings: eg, simple cyst, intramammary lymph node, breast implant, stable postsurgical changes, probable fibroadenoma	**Benign** findings: hyalinized nonenhancing fibroadenoma, cyst, scar, fat-containing lesion (oil cyst, lipoma, galactocele, mixed-density hamartoma), breast implant	0%
3	**Probably benign** (< 2% risk of malignancy) – initial short-interval follow-up suggested (in 6 months), not expected to change (over > 2 years) after complete diagnostic work-up: eg, noncalcified circumscribed solid mass, focal asymmetry, cluster of round punctate calcifications	**Probably benign** – short-interval follow-up suggested (< 2% risk of malignancy): eg, classic findings of a fibroadenoma, nonpalpable complicated cyst, clustered microcysts	**Probably benign** – short-interval follow-up suggested: a malignancy is highly unlikely	2% *(only 71% comply!)*
4	**Suspicious** abnormality – biopsy should be considered: not classic appearance of malignancy	**Suspicious** abnormality – biopsy should be considered: intermediate (3–94%) probability of malignancy: eg, solid mass without all criteria of a fibroadenoma	**Suspicious** abnormality – biopsy should be considered: lesion morphology not characteristic of breast cancer but of concern	3–90%
4a	Low probability	Low suspicion		3–50%
4b	Intermediate probability / suspicion	Intermediate suspicion		50–80%
4c	Moderate probability / suspicion	Moderate suspicion		80–90%
5	**Highly suggestive of malignancy** (≥ 95% probability of cancer) – appropriate action should be taken: eg, lesion could be considered for one-stage surgical treatment, however, biopsy usually required	**Highly suggestive of malignancy** (> 95% probability) – appropriate action should be taken: image-guided core needle biopsy	**Highly suggestive of malignancy** – appropriate action should be taken: almost certainly malignant	>90%
6	Known **biopsy-proven malignancy** eg, mammogram during neoadjuvant chemotherapy comparing it to pre-therapy mammogram	Known **biopsy-proven malignancy** eg, prior to chemotherapy, lumpectomy, mastectomy	Known **biopsy-proven malignancy** corresponding to the lesion imaged with MR	100%

BREAST ANATOMY AND MAMMOGRAPHIC TECHNIQUE

BREAST DEVELOPMENT

Embryology

6th week GA	"milk line" develops from ectodermal elements on ventral surface of embryo extending from axilla to medial thigh
12th week	nipple-areolar complex in 4th intercostal space develops with differentiation of mesenchymal cells into smooth muscle
16th week	special apocrine glands form Montgomery glands consisting of 8–12 mammary ducts associated with sebaceous glands near epidermis
32nd week	differentiation into breast parenchyma + pigmentation of nipple-areolar complex

Nipple-Areolar Complex

› composed of pigmented squamous epithelium
› contains sebaceous Montgomery glands
› contains many sensory nerve endings
› contains layer of circumferential smooth muscle
› contains abundant lymphatic system (= subareolar lymphatic plexus = Sappey plexus)
› hair follicles around areola may contain calcifications
› overlies area between 2nd and 6th rib at full development

[Marie Philibert Constant Sappey (1810–1896), professor of anatomy and president of Académie Nationale de Médecine, Paris, France]

MONTGOMERY GLAND

= large type of sebaceous gland of areola transitional between sweat glands + mammary gland

[William Fetherstone Montgomery (1797–1859), professor of midwifery at College of Physicians in Dublin, Ireland]

› capable of secreting milk
› openings at 1–2-mm small raised papules in periphery of areola (= Morgagni tubercles)

Variant Anatomy

Polythelia	=	supernumerary accessory nipple(s); usually unilateral; most inferior location = proximal medial thigh; may be mistaken for moles
Polymastia	=	true accessory mammary gland; most often in axilla
Hypoplasia	=	underdevelopment of breast
Amazia	=	lack of breast tissue + proper nipple; usually due to surgery / irradiation
Amastia	=	lack of breast tissue + lack of nipple; associated with aplasia of pectoral

muscle (Poland syndrome)

Tuberous breast = reduced parenchymal volume + herniation of breast parenchyma through nipple-areolar complex

Tanner Stages

= scale of physical development

Stage I (prepubertal)

Histo: epithelial-lined ducts surrounded by connective tissue stroma

- nipple elevates
- palpable subareolar nodules for first 6–12 months

√ ill-defined mildly heterogeneous hyperechoic retroareolar tissue

√ ducts often enlarged in full-term infants ← effect of maternal hormones

Stage II (formation of breast bud)

Cause F: estrogen for ductal proliferation and branching + progesterone for terminal ductal-lobular units

M: transient proliferation with spontaneous resolution ← 30-fold increase in testosterone

- palpable subareolar bud = **thelarche** begins with onset of puberty (at < 13 years of age; mean age: 9.8 years)
  - ◊ may be asymmetric / unilateral
- breast tissue + nipple arise as a single mound of tissue

√ hyperechoic retroareolar nodule

√ central star-shaped / linear hypoechoic area (= simple branched ducts)

Stage III (breast extension beyond areolar margin)

- enlargement + elevation of single mound

√ hyperechoic glandular tissue extending away from retroareolar area

√ central spider-shaped hypoechoic area

Stage IV (mounding of areola + papilla)

- secondary mound develops (very transient) with nipple + areolar complex projecting above the breast tissue

√ hyperechoic periareolar fibroglandular tissue

√ prominent central hypoechoic nodule

Stage V (mature breast)

- regression of areola forming a smooth contour with the rest of the breast tissue

√ hyperechoic glandular tissue

√ increased subcutaneous adipose tissue anteriorly

√ NO hypoechoic central nodule

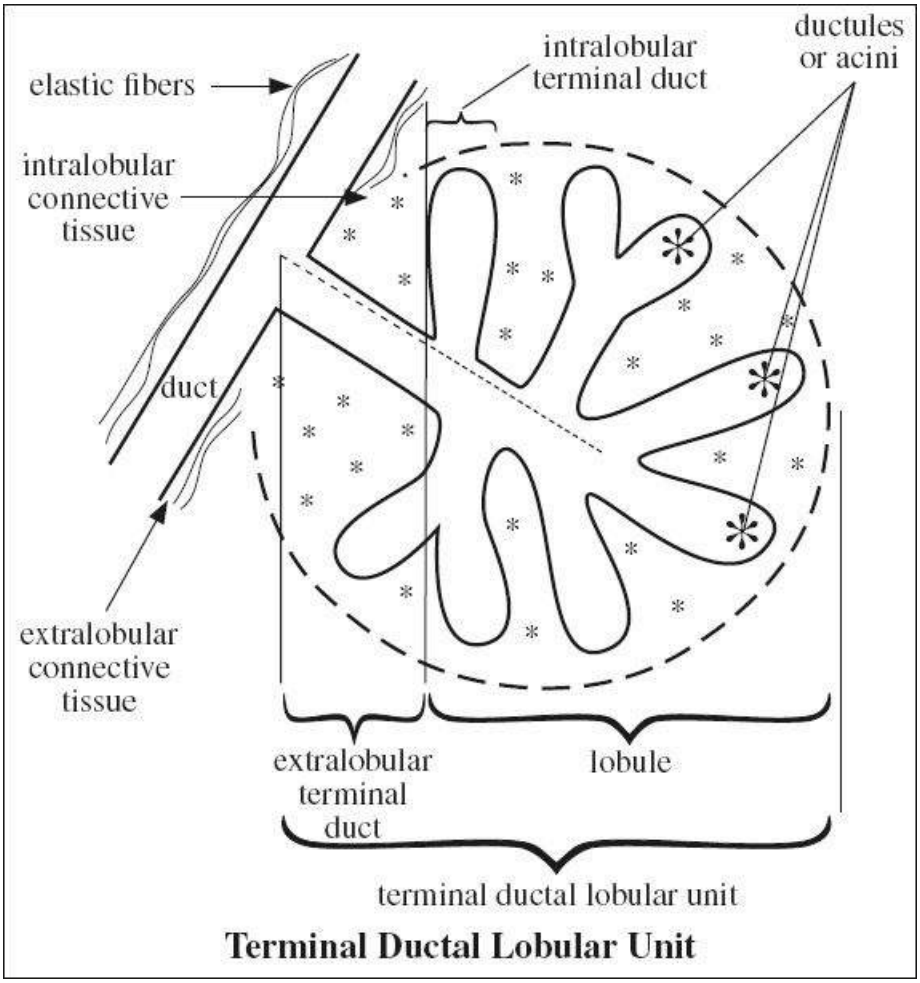
BREAST ANATOMY

Lobes

15–20 lobes disposed radially around nipple; each lobe has a main lactiferous duct of 2 mm in diameter

Nipple

(a) 5–20 duct openings on nipple surface: immediately deep to orifices are areas of dilatation (= milk sinuses) ← storage function during lactation



◊ >90% of nipples contain 5–9 ductal orifices

(b) multiple other blind-ending orifices: connected to sebaceous glands of 1–4 cm in length

√ bilateral symmetric enhancement pattern of normal nipple:

√ 1–2 mm superficial layer of intense linear enhancement

√ underlying region of nonenhancement deep to dermis

Ducts

lactiferous ducts coalesce in subareolar region into 5–8 mm wide lactiferous sinuses exiting in the central portion of nipple; organized into

(a) central ducts: extending to chest wall

(b) peripheral ducts: arranged in a radial fashion

Main lactiferous duct → branches dichotomously into segmental duct → subsegmental duct → terminal duct → blunt-ending acinus

Terminal Duct Lobular Unit (TDLU)

(1) Extralobular terminal duct
Histo: lined by columnar cells + prominent coat of elastic fibers + outer layer of myoepithelium

(2) Lobule
(a) intralobular terminal duct
Histo: lined by 2 layers of cuboidal cells + outer layer of myoepithelium (for milk propulsion)
Significance: invasive ductal, papillary, mucinous, medullary adenoid cystic cancers arise from ductal epithelium in TDLU and most commonly appear as spiculated irregular masses ± calcifications / developing asymmetries
(b) ductules / acini
(c) intralobular connective tissue

Size: 1–2 (range, 1–8) mm in diameter

Change:
(a) reproductive age: cyclic proliferation (up to time of ovulation) + cyclic involution (during menstruation)
(b) post menopause: regression with fatty replacement

Significance:
TDLU is the site of fibroadenoma, epithelial cyst, apocrine metaplasia, adenosis (= proliferation of ductules + lobules), epitheliosis (= proliferation of mammary epithelial cells within preexisting ducts + lobules), ductal + lobular carcinoma in situ, infiltrating ductal + lobular carcinoma

Components of Normal Breast Parenchyma

1. Nodular densities surrounded by fat
   (a) 1–2 mm = normal lobules
   (b) 3–9 mm = adenosis
2. Linear densities
   = ducts and their branches + surrounding elastic tissue
3. Structureless ground-glass density
   = stroma / fibrosis with concave contours

Parenchymal Breast Pattern (László Tabár)

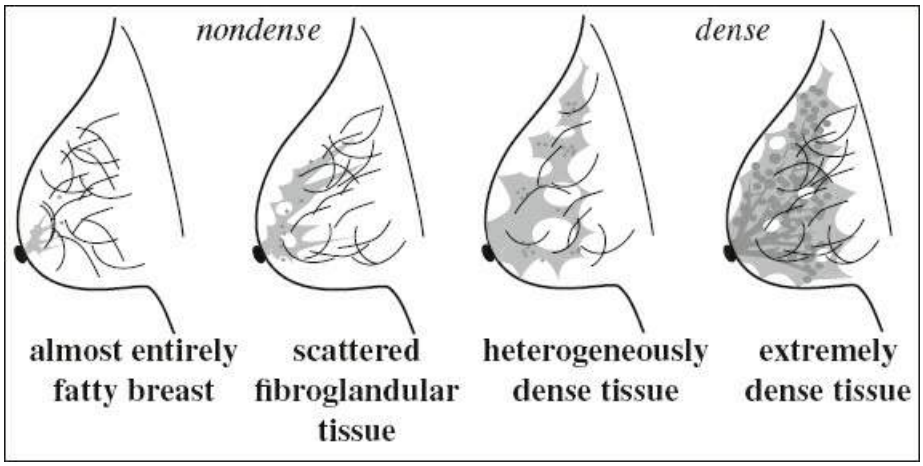
Effect of breast density on sensitivity:
women in their 40s have a 68% higher risk of a FN screening mammogram compared to older women

Recommendation: perform mammography during 1st week of menstrual cycle

Inter- and intraobserver variability on breast density:
› low reliability of interreader density agreement ($\kappa = 0.59$)
› imperfect intrareader agreement ($\kappa = 0.72$)

Factors affecting breast density between mammograms:
body mass index, weight changes, age, HRT, dietary intake

Breast Composition (*BI-RADS®*)			
Breast Density	*Population [%]*	*Descriptor*	*Glandular tissue [%]*
1	9	Almost entirely fatty breast	< 25
2	44	Scattered fibroglandular tissue that could obscure a lesion	25–50
3	38	Heterogeneously dense tissue that may lower mammographic sensitivity	51–75
4	9	Extremely dense breast tissue that lowers mammographic sensitivity	> 75



Overall odds ratio of breast cancer for > 75% tissue density:
- › compared to 10% density 4.74
- › with interval cancer developed in 1 year 17.81

Relative risk of cancer associated with breast density:
- › breast tissue density of 50–74% 2.92
- › breast tissue density of > 75% 4.64

Pattern I

named QDY = quasi dysplasia (for Wolfe classification)
- √ concave contour from Cooper's ligaments
- √ evenly scattered 1–2 mm nodular densities (= normal terminal ductal lobular units)
- √ oval-shaped / circular lucent areas (= fatty replacement)

Pattern II

similar to N1 (Wolfe)
- √ total fatty replacement
- √ NO nodular densities

Pattern III

similar to P1 (Wolfe)
- √ normal parenchyma occupying < 25% of breast volume in retroareolar location

Pattern IV = adenosis pattern

similar to P2 (Wolfe)
Cause: hypertrophy + hyperplasia of acini within lobules
Histo: small ovoid proliferating cells with rare mitoses
√ scattered 3–7 mm nodular densities (= enlarged terminal ductal lobular units) = adenosis
√ thick linear densities (= periductal elastic tissue proliferation with fibrosis) = fibroadenosis
√ no change with increasing age (genetically determined)

Pattern V
similar to DY (Wolfe)
√ uniformly dense parenchyma with smooth contour (= extensive fibrosis)

Enhancement of Normal Parenchyma on MR

= Background Parenchymal Enhancement (BPE)
◊ Breast enhancement does NOT correlate with breast density
• varies among women + within same woman over time

Proper enhancement present if:
› veins contrasted on MIP
› both internal mammary arteries depicted
› nipple enhances

Common pattern of enhancement:
√ bilateral symmetric diffuse enhancement:
√ slow minimal / early enhancement
√ persistent delayed enhancement
√ linear patchy enhancement
√ confluent enhancement on late dynamic scan

Distribution of enhancement:
√ bilateral symmetric enhancement with
(a) moderate / marked degree of BPE
(b) diffuse / regional distribution
(c) homogeneous / internally stippled
√ "picture framing" of vascular inflow = enhancement commonly begins in periphery + gradually becomes apparent in more central breast tissue
√ scattered innumerable 9–10 mm foci of enhancement
√ geographic areas of symmetric regional enhancement
√ multiple larger symmetric areas of enhancement (DDx: asymmetry suggest malignancy)

BPE Effect on Interpretation of MR Images:
1. Falsely positive ← focal / regional / asymmetric background parenchymal enhancement
2. Falsely negative ← moderate / marked BPE

Classification of Background Parenchymal Enhancement:

Minimal	< 25% of glandular tissue
Mild	25–50%
Moderate	50–75%
Marked	> 75%

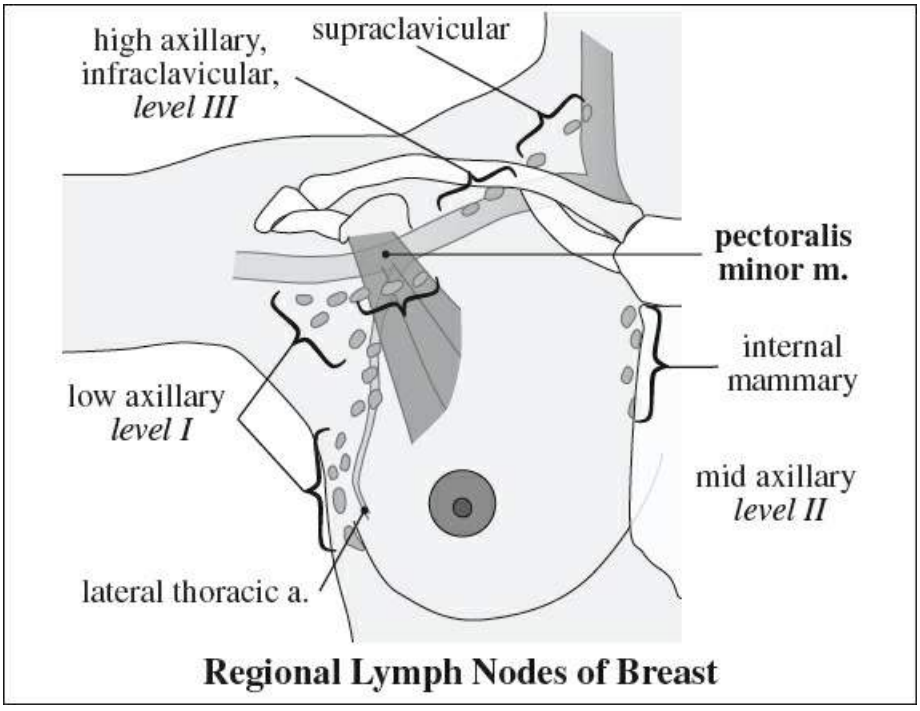
Hormonal Influence on BPE

1. Menstruation
   √ enhancement high during days 21–28 and days 1–6 after menstruation + low during days 7–20
2. Lactation
   ◊ Breast involution after lactation takes 3 months
   Note: NO impairment in cancer detection in lactating patients!
   Breast-feeding: **safe** after contrast-enhanced MRI ← minute amounts of Gd in breast milk
3. Postmenopausal period without HRT
   √ decrease in fibroglandular tissue → degree of BPE typically less than that in premenopausal women
4. Hormone replacement therapy (HRT)
   √ increase in BPE in amount + degree + distribution with great interindividual variations:
   ◊ Hormonal effect reverses after 30–60 days
5. Endocrine antihormonal therapy
   Antiestrogenic agents: selective estrogen receptor modulators, aromatase inhibitors
   √ significant decrease in amount of fibroglandular tissue + cysts + BPE
   √ effect on BPE evident early in treatment (< 90 days)
   √ tamoxifen rebound after medication discontinued:
   √ global / focal increase in BPE
6. Oophorectomy → decrease in BPE

MRI preferably performed during 2nd week of menstrual cycle!

Lymphatic Drainage

1. Axillary nodes
   = 5 groups of lymph nodes in axilla divided into 3 levels by pectoralis minor muscle



Regional Lymph Nodes of Breast

Cancerous involvement: 97%

(a) **Inferior group** = Berg I level

Location: inferior to inferolateral border of pectoralis minor muscle

Divided into:

› lateral group (deep)

Landmark: 3rd segment of axillary a. + v.; subscapular artery (arising from inferior surface of axillary artery)

› subscapular group (posterolateral)

Landmark: along course of hook-shaped thoracodorsal artery

› pectoral group (anteromedial)

Landmark: lateral thoracic artery parallel and <u>posterior</u> to lateral margin of pectoralis minor muscle arising from terminal portion of 2nd segment of axillary artery

Most sentinel nodes are inferior level I axillary nodes!

(b) **Central group** = Berg II level

Location: posterior to and between lateral and medial borders of pectoralis minor muscle + between pectoralis minor muscle and pectoralis major m. (= Rotter space nodes)

Lymphatic route: received from level I nodes

Staging: N1 = < 4 nonmatted movable nodes N2 = > 4 / matted nonmovable nodes

(c) **Apical group** = Berg III level

Location: medial to superior border of pectoralis minor muscle (+ infraclavicular nodes)

Lymphatic route: received from level II nodes → subclavian lymphatic trunk and supraclavicular nodes → (left-sided) thoracic duct + right

lymphatic duct

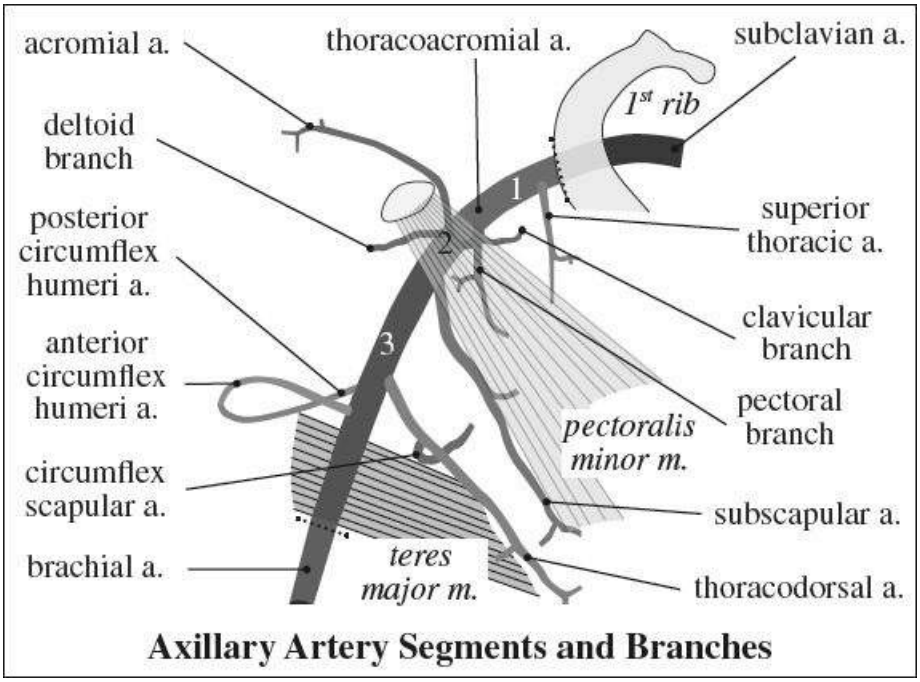
Staging: N3 = stage IIIC disease

2. Internal mammary nodes (3%)

The presence of internal mammary nodal metastasis changes stage, prognosis and radiation therapy field!

Location: follow internal mammary artery and vein between pleura / endothoracic fascia and chest wall near margin of sternum in 1st – 6th intercostal spaces

Lymphatic route: from level of diaphragm (= anterior phrenic nodes) to termination in thoracic venous system on right and thoracic duct on left



Axillary Artery Segments and Branches

Normal size: < 6 mm

Cancerous involvement: isolated in 3% originating from deep / medial lesion

Staging: (a) without axillary met = N2

(b) with axillary met = N3b / stage IIIC disease

Metastases to internal mammary nodes usually occur after a tumor has metastasized to the axilla!

Axillary Artery

Origin: lateral margin of 1st rib (out of subclavian artery)

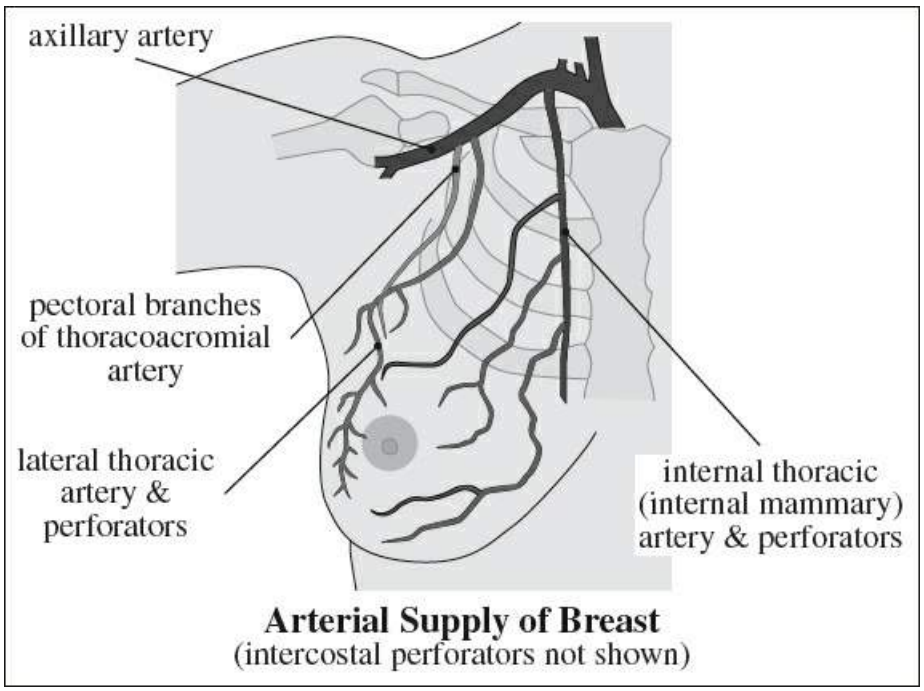
Segments & Branches:

mnemonic: "**S**crew **T**he **L**awyers **S**ave **A** **P**atient"

1. Segment: medial to pectoralis minor m.
   Superior thoracic a.
2. Segment: posterior to pectoralis minor m.
   Thoracoacromial a.
   Lateral thoracic a.

3. Segment: lateral to pectoralis minor m.
   Subscapular a.
   Anterior humeral circumflex a.
   Posterior humeral circumflex a.

Terminus: lower margin of teres major m. (into brachial a.)



Arterial Supply of Breast
(intercostal perforators not shown)

Arterial Supply of Breast

1. Branches of **internal thoracic artery** (= dominant vessel)
   Supply: medial + central breast parenchyma
2. Branches of **lateral thoracic artery**
   Supply: superolateral breast parenchyma
3. Branches of **subclavian + axillary arteries** (including thoracoacromial + subscapular + thoracodorsal arteries)
   Supply: portion of superior breast parenchyma
4. Branches of **musculophrenic artery** (= continuation of internal thoracic artery)
   Supply: variable portion of inferior breast
5. Perforating branches of anterior + posterior **intercostal arteries** perforate chest wall musculature
   Supply: deep central breast parenchyma

BREAST DURING PREGNANCY & LACTATION

Cause: increase in estrogen, progesterone, prolactin
Onset: early in 2nd month of 1st trimester
Histo:

1st trimester:

(a) marked ductular sprouting with some branching + discrete lobular growth

(b) involution of fibrofatty stroma

Breast Changes during Pregnancy & Lactation		
Period	*Histo*	*Hormone*
2nd month of 1st trimester	marked ductular sprouting → some branching + discrete lobular growth; simultaneous involution of fibrofatty stroma; increase in glandular vascularity;	estrogen
2nd + 3rd trimester	marked lobular growth with great epithelial proliferation; relative decrease of stromal components; alveolar cells of TDLU differentiate into colostrum-cell epithelium;	progesterone
	initiation of protein synthesis (lactogenesis I)	prolactin opposed by progesterone
Lactation (= secretory state)	cytoplasm of lobular cells becomes vacuolated; secretion progressively accumulates in distended lobular glands: hyperchromatic nuclei often with small nucleoli + flattening of myoepithelial cells	high prolactin level after rapid withdrawal of progesterone
	marked distention of lobular glands + accumulation of secretion of fat, lactose, and proteins (lactogenesis II) as basic nutrients of milk	in conjunction with insulin, corticosteroids, thyroid hormone, growth hormones
Milk ejection	maintenance of milk production (lactogenesis III) regulated by autocrine system (= neuroendocrine mechanism in the posterior pituitary gland)	release of oxytocin stimulated by breast-feeding
Breast involution	characterized by marked lobular atrophy that occurs over a period of about 3 months after lactation ceases	

(c) increase in glandular vascularity

<u>2nd + 3rd trimester:</u>

(a) marked lobular growth
(b) stromal decrease
(c) epithelial proliferation with cellular enlargement
(d) differentiation of alveolar cells into colostrum-cell epithelium

<u>lactation:</u>

= formation + secretion of milk (= fat + lactose + proteins)

• high levels of prolactin + rapid withdrawal of progesterone

(a) cytoplasmic vacuolation of lobular cells with hyperchromatic nuclei + small nucleoli
(b) distension of lobular glands ← accumulating secretions
(c) flattening + attenuation of myoepithelial cells

Mammography (low sensitivity):

◊ To be performed immediately after breast-feeding in case of a suspected malignancy
◊ Effective in detecting microcalcifications / subtle areas of distortion
√ diffuse, markedly dense, heterogeneously coarse, confluent nodular breast parenchyma (NOT in all patients)
√ marked decrease in adipose tissue

US (method of choice):

◊ identifies a palpable area as a true mass / normal parenchyma

(a) during pregnancy
√ slight diffuse hypoechogenicity of enlarged nonfatty fibroglandular component

(b) during lactation
√ diffuse hyperechogenicity of breast parenchyma
√ prominent ductal system + increased vascularity

MR (routine use is inappropriate + interpretation difficult):

√ diffuse high SI on T2WI ← ↑ fraction of mobile water

√ rapid enhancement + early plateau

Lactogenesis

Lactogenesis I
= formation of colostrum around 16 weeks EGA
Lactogenesis II
= secretion of copious milk around day 4 postpartum
Lactogenesis III
= maintenance of milk supply around day 10 postpartum via autocrine control
• release of oxytocin in posterior pituitary gland stimulated by breast feeding → milk ejection
Lactogenesis IV
= decreased milk production ← epithelial apoptosis
• gradual breast involution completed by 3 months

MAMMOGRAPHIC TECHNIQUE

BEAM QUALITY
Molybdenum target material with characteristic emission peaks of 17.9 + 19.5 keV (lower average energy than tungsten)
FOCAL SPOT
0.1–0.4 mm (0.1 mm for magnification views)
TUBE OUTPUT
80–100 mA
EXPOSURE
(a) without grid: 25 kV (optimum between contrast + penetration), exposure time of 1.0 sec
(b) with grid: 26–27 kV; exposure time of 2.3 sec
(c) microfocus magnification: 26–27 kV; 1.5–2.0 times magnification with 16–30 cm air gap
(d) specimen radiography: 22–24 kV
FILTER
(a) beryllium window (absorbs less radiation than glass tube)
(b) molybdenum filter (0.03 mm): allows more of lower energy radiation to reach breast
REDUCTION OF SCATTER RADIATION
(1) adequate compression (also improves contrast + decreases radiation dose)
(2) beam collimation to < 8–10 cm
(3) air gap with microfocus magnification
(greater spatial resolution, 2–3-fold increase in radiation exposure)
(4) Moving grid
grid if compressed breast > 5 cm / very dense breast (facilitates perception, 2–3-fold increase in radiation exposure)
SCREEN-FILM COMBINATION
(1) Intensifying screen phosphor
single screen systems
(2) Film-screen contact
(3) Mammography film with minimal base fog, sufficient maximum density + contrast
FILM PROCESSING

(1) Processing time of 3 min (42–45 sec in developing fluid) superior to 90-sec processor for double-emulsion film (which creates underdevelopment + compensatory higher radiation exposure)
(2) Developing temperature of 35°C (95°F)
(3) Developing fluid replenishment rate:
450–500 mL replenisher per square meter of film

QUALITY CONTROL
(1) Processor (daily)
with sensito- / densitometric measurements
(a) base fog < 0.16–0.17
(b) maximum density > 3.50
(c) contrast > 1.9–2.0
(2) X-ray unit (semiannually)
(a) beam quality
(b) phototimer

Average glandular dose:
< 0.6 mGy per breast for nonmagnification film-screen mammogram (ACR accreditation requirement)
Screen/film technique (molybdenum target; 0.03 mm molybdenum filter, 28 kVp):
mean absorbed dose: 0.05 rad for CC view 0.06 rad for LAT view

Effective dose equivalent HE:
screen-film mammography 0.11 mSv
xeroradiographic mammography 0.78 mSv
chest 0.05 mSv
skull 0.15 mSv
abdomen 1.40 mSv
lumbar spine 2.20 mSv

Advantages of magnification mammography:
1. Sharpness effect = increased resolution
2. Noise effect = noise reduced by a factor equal to the degree of magnification
3. Air-gap effect = increased contrast by reduction in scattered radiation
4. Visual effect = improved perception and analysis of small detail

Computer-Aided Detection (CAD)

Utility of Computer-Aided Detection (CAD):
(a) significant
1. Clustered microcalcifications
2. Spiculated lesion
(b) moderate
3. Poorly defined mass / asymmetry
(c) low
4. Focal asymmetry
5. Architectural distortion (1–2% detected)
(d) none
6. Developing asymmetry (no comparison with prior)

Cancers missed by Computer-Aided Detection (CAD):

(1) Microcalcifications few
(2) Nonspiculated mass 20%
(3) Architectural distortion 50%
(4) Focal asymmetry 99%
(5) Developing asymmetry 100%

Factors Affecting Mammographic Image Quality

Radiographic Sharpness

= subjective impression of distinctness / perceptibility of structure boundary / edge

1. **Radiographic contrast**

= magnitude of optical density difference between structure of interest + surroundings influenced by

(a) <u>subject contrast</u>

= ratio of x-ray intensity transmitted through one part of the breast to that transmitted through a more absorbing adjacent part; affected by

› absorption differences in the breast (thickness, density, atomic number)
› radiation quality (target material, kilovoltage, filtration)
› scattered radiation (beam limitation, grid, compression)

(b) <u>receptor contrast</u>

= component of radiographic contrast that determines how the x-ray intensity pattern will be related to the optical density pattern in the mammogram

affected by analog factors

› film type
› processing (chemicals, temperature, time, agitation)
› photographic density
› fog (storage, safelight, light leaks)

Causes of poor contrast:

underexposure, inadequate compression, high kV, target material selection (tungsten vs. molybdenum), look-up table selection (altered by engineer)

2. **Radiographic blurring**

= lateral spreading of a structural boundary (= distance over which the optical density between the structure and its surroundings changes)

(a) <u>motion</u>

reduced by compression + short exposure time

(b) <u>geometric blurring</u>

affected by

› focal spot: size, shape, intensity distribution

for analog only:

› focus-object distance (= cone length)
› object-image distance

(c) <u>receptor blurring</u>

= light diffusion (= spreading of the light emitted by the screen) affected by

› phosphor thickness + particle size

› light-absorbing dyes + pigments
› screen-film contact

Causes of image blur:
large focal spot size, damaged anode, patient motion (inadequate compression, poor patient cooperation, long exposure time)

Causes of long exposure:
inadequate compression, kV too low, low mAs output, dense breast, large breast, magnification

Radiographic Noise

= unwanted fluctuation in optical density

1. **Radiographic mottle**
   = optical density variations consist of
   (a) receptor graininess
      = optical density variation from random distribution of finite number of silver halide grains
   (b) quantum mottle (principal contributor to mottle)
      = variation in optical density from random spatial distribution of x-ray quanta absorbed in image receptor

   affected by
   › film speed + contrast
   › screen absorption + conversion efficiency
   › light diffusion
   › radiation quality

   (c) structure mottle
      = optical density fluctuation from nonuniformity in the structure of the image receptor (eg, phosphor layer of intensifying screen)
2. **Artifacts**
   = unwanted optical density variations in the form of blemishes on the mammogram
   (a) improper film handling (static, crimp marks, fingerprints, scratches)
   (b) improper exposure (fog)
   (c) improper processing (streaks, spots, scratches)
   (d) dirt + stains

   Artifacts in digital mammography:
   (a) transmission
   (b) data loss
   › processing artifact (edge artifact): raw data not affected
   › horizontal line artifact due to failure of detector element
   (c) decompression artifact
   (d) gain calibration

ABSCESS OF BREAST

= complication of mastitis

Organism:

(a) aerobes: Staphylococcus aureus, Staphylococcus epidermidis, Streptococcus pyogenes
(b) anaerobes: Peptostreptococcus, Bacteroides
(c) others: TB, other mycobacteria, fungi, parasites
(d) sterile culture (21–45%)

• palpable mass, pain (80%), redness (71%), heat, fever (5–47%):
◊ Clinical signs same as for mastitis!

US:

√ ill-defined area of altered echotexture:
√ hypoechoic often multiloculated fluid collection with acoustic enhancement + surrounding increased flow
√ adjacent hypoechoic glandular parenchyma
√ increased echogenicity of surrounding inflamed fat lobules
√ mild skin thickening ← distended lymphatics
√ mild to moderate cortical thickening of axillary lymph nodes + increased flow on Doppler

Mammo (to exclude malignancy):

Indication: in women > 30 years of age; prolonged course during breast-feeding period
N.B.: delay until after acute episode if possible

√ asymmetric density / mass / distortion
√ skin thickening

DDx: inflammatory breast carcinoma (< 1%)

Rx: percutaneous drainage + antibiotics

Rarely a malignant breast abscess can occur in inflammatory breast cancer!

Puerperal / Chronic Abscess of Breast (14–59%)

= Lactational ABSCESS = COLD ABSCESS

Frequency: 5–11% of cases of mastitis during lactation; most common in primiparous mothers (65%)

Cause: complication of mastitis (in 5–11%) developing in 1–24% of primiparous breast-feeding women

Time of onset: within 12 weeks after birth / weaning

Organism: penicillinase-producing Staphylococcus aureus

Route of infection: small skin laceration

• fever, leukocytosis, breast erythema, induration, pain
• rapid response to antibiotics

Location: most commonly in central / subareolar area

√ ill-defined / circumscribed mass of increased density with flamelike contour

√ secondary changes common: architectural distortion, nipple + areolar retraction, lymphedema, skin thickening, pathologic axillary nodes
√ liquefied center can be aspirated
US:
√ nearly anechoic / mixed / echogenic area with posterior enhancement
MR (reserved for typical situation):
› T1WI:
√ hyperintense round / ovoid lesion (high protein content)
› enhanced T1WI:
√ no contrast uptake centrally
√ strong enhancement of abscess wall
› T2WI:
√ hyperintense round / oval lesion
DDx: seroma, inflammatory breast cancer
Rx: antibiotics, repeated aspirations, percutaneous drainage > surgery; continue breast feeding to disengorge ducts; cessation of breast feeding with antibiotics (contraindicated for newborn / with surgical drainage)

Nonpuerperal Abscess (41–86%)

= abscess occurring outside breast-feeding period
Risk factors: black race, obesity, tobacco smoking, diabetes
Organism: mixed flora (Staphylococcus, Streptococcus); greater risk of anaerobes

Central / Periareolar Nonpuerperal Abscess

= complication of periductal mastitis

Most common form of abscess that develops outside of the breast-feeding period in young smoking woman!

Frequency: 34–94% of all breast abscesses
Pathophysiology:
squamous metaplasia of cuboidal epithelium → keratin plug + acute infiltrate + cellular debris → distension of obstructed lactiferous duct → secondary infection with abscess formation + cutaneous fistula
Zuska disease = recurring central nonpuerperal abscesses associated with lactiferous fistulas
Prognosis: difficult to treat; 25–40% recurrence rate
Rx: percutaneous drainage + antibiotics; cessation of smoking; diagnostic mammogram if > 35 years of age to rule out malignancy

Peripheral Nonpuerperal Abscess

Cause: underlying chronic medical condition (diabetes, rheumatoid arthritis), on steroids, recent breast intervention (postoperative / postradiation Rx)
Age: older age group
Prognosis: good response to therapy; rare recurrences

BREAST CANCER

Epidemiology of Breast Cancer

Incidence: 1.5–4.5 cases per 1,000 women per year in USA; 246,660 new cases of invasive breast cancer + 61,000 new cases of carcinoma in situ (2016) M÷F = 100÷1, whites÷blacks = 70÷1

- ◊ 2nd most common cancer among women (after lung cancer)!
- ◊ 2nd leading cause of death by cancer in women (after lung cancer)!
- ◊ 12.5% lifetime risk of breast cancer = 1 in 8 women will develop breast cancer!

Age: 0.3–2% in women < 30 years of age;
15% in women < 40 years of age;
85% in women > 30 years of age

Mortality: about 40,450 deaths in USA per year (2016)

Risk Factors (increasing risk):

Demographic Factors in Breast Cancer

- increasing age (66% of cancers in women > 50 years):

Age	*Prevalence of Breast Cancer*	
25	5÷100,000	1÷19,608
40	80÷100,000	1÷1,250
45	1075÷100,000	1÷93
50	180÷100,000	1÷555
55	3030÷100,000	1÷33
60	240÷100,000	1÷416

Relative Risk Compared with Woman of Age 60			
30 years of age	0.07	60 years of age	1.00
35 years of age	0.19	70 years of age	1.27
40 years of age	0.35	80 years of age	1.45
50 years of age	0.71		

- Ashkenazi Jewish women + nuns
- upper > lower social class
- unmarried > married women
- Whites > Blacks after age 40

Reproductive Variables in Breast Cancer

- nulliparous > parous:

Relative Risk Compared with Nulliparous:		
age at 1st pregnancy	< 19 years	0.5
age at 1st pregnancy	20–30 years	—
age at 1st pregnancy	30–34 years	1.0
age at 1st pregnancy	> 35 years	> 1.0

- first full-term pregnancy after age 35: 2 x risk
- low parity > high parity

- early age at menarche (< 12 years):
  relative risk compared with onset of regular ovulatory cycle:

	Menarche < 12	*Menarche > 12*
immediately	3.7	1.6
1–4 years	2.3	1.6

- late age at menopause:
  relative risk compared with menopause before age 44:
  natural menopause > 55 years of age 2.00
- early bilateral oophorectomy:
  relative risk compared with menopause between ages 45–49 years:
  artificial menopause at 50–54 years 1.34
  artificial menopause before age 45 0.77

MULTIPLE PRIMARY CANCERS in BREAST CANCER

- 4–5 x increase in risk for cancer in contralateral breast
- increased risk after ovarian + endometrial cancer

BRCA (breast cancer)

= mutation of tumor suppressor gene accounts for 50% of hereditary breast cancers

5–10% of all breast cancers are hereditary!

- BRCA1 on long arm of chromosome 17
- BRCA2 on chromosome 13

Carrier: group of women at high risk for breast cancer
◊ Strict surveillance mandatory!

1% of women are at very high risk for developing breast cancer due to a genetic disposition!

FAMILY HISTORY of BREAST CANCER

- breast cancer in first-degree relative:
  Relative risk compared with negative family Hx:
  (+) for mother 1.8
  (+) for sister 2.5
  (+) for mother + sister 5.6
- 25% of patients with carcinoma have a positive family history
- carcinoma tends to affect successive generations ~ 10 years earlier

BENIGN BREAST DISEASE AND BREAST CANCER

- 2–4 x increased risk with atypical hyperplasia relative risk compared with no biopsy:
  benign breast disease in all patients 1.5
  nonproliferative disease 0.9
  proliferative disease without atypia 1.6
  fibroadenoma + hyperplasia 3.5
  atypical duct hyperplasia (ADH):
  no family history of breast cancer 4.4
  family history of breast cancer 8.9

PARENCHYMAL BREAST PATTERN AND BREAST CANCER

- prominent duct pattern + extremely dense breasts according to Wolfe classification
  N1 (0.14%), P1 (0.52%), P2 (1.95%), DY (5.22%)

RADIATION EXPOSURE and BREAST CANCER

excess risk of 3.5–6 cases per 1,000,000 women per year per rad after a minimum latent period of 10 years (atomic bomb, fluoroscopy during treatment of tuberculosis, irradiation for postpartum mastitis, Hodgkin disease)

GEOGRAPHY

- Western + industrialized nations (highest incidence)
- Asia, Latin America, Africa (decreased risk)

Breast Cancer Evaluation

	MRI	*Mammo*	*US*	*Physical*	*all 4*
Sensitivity [%]	77–100	25–40	33–40	9	95
Specificity [%]	81–97	93–99	91–96		
Recall [%]	10.8	3.9–5.4			
FN [%]	0.2–0.4	0.4–1.5			

Localizing Signs of Breast Cancer

= PRIMARY SIGNS OF BREAST CANCER

1. Dominant mass seen on two views with
   (a) **Spiculation** = stellate / star-burst appearance (= fine linear strands of tumor extension + desmoplastic response); "scirrhus" caused by:
      (1) infiltrating ductal carcinoma (75% of all invasive cancers)
      (2) invasive lobular carcinoma (occasionally)
      √ mass feels larger than its mammographic / sonographic size
      DDx: prior biopsy / trauma / infection
   (b) **Smooth border**
      (1) intracystic carcinoma (rare): subareolar area; bloody aspiration
      (2) medullary carcinoma: soft tumor
      (3) mucinous / colloid carcinoma: soft tumor
      (4) papillary carcinoma
      √ "telltale" signs: lobulation, small comet tail, flattening of one side of the lesion, slight irregularity
      √ "halo" sign (= Mach band) may be present
      DDx: cyst (sonographic evaluation)
   (c) **Lobulation**
      appearance similar to fibroadenoma (only characteristic calcifications may exclude malignancy)
      ◊ The likelihood of malignancy increases with number of lobulations
      • clinical size of mass > radiographic size (1951) (**Leborgne's law**)
        [Raul Alfredo Leborgne Fossemale (1907–1986), Uruguayan radiologist created the mammograph, discovered radiological signs and developed the first method of radiologically guided mammary biopsy]

2. **Asymmetric density** = star-shaped lesion
   √ distinct central tumor mass with volumetric rather than planar appearance → additional coned compression view
   √ denser relative to other areas (= vessels + trabeculae cannot be seen within high-density lesion)
   √ fat does not traverse density
   √ corona of spicules
   √ in any quadrant → but fatty replacement occurs last in upper outer quadrant
   DDx: postsurgical fibrosis, traumatic fat necrosis, sclerosing duct hyperplasia
3. **Microcalcifications**
   associated with malignant mass by mammogram in 40%, pathologically with special stains in 60%, on specimen radiography in 86%

   ◊ 20% of clustered microcalcifications represent a malignant process!

   (a) shape: fragmented, irregular contour, polymorphic, casting rod-shaped without polarity, Y-shaped branching pattern, granular "salt and pepper" pattern, reticular pattern
   (b) density: various densities
   (c) size: 100–300 µm (usually); rarely up to 2 mm
   (d) distribution: tight cluster over an area of 1 cm^2 or less is most suggestive; coursing along ductal system seen in ductal carcinoma with comedo elements
4. **Architectural distortion**
   Cause: desmoplastic reaction
   √ ragged irregular borders
   DDx: postsurgical fibrosis
5. **Interval change**
   (a) neodensity = de novo developing density → in 6% malignant
   (b) enlarging mass → in 10–15% malignant
6. **Enlarged single duct**
   = low probability for cancer in asymptomatic woman with normal breast palpation
   √ solitary dilated duct > 3 cm long
   DDx: inspissated debris / blood / papilloma
7. **Diffuse increase in density** (late finding)
   Cause: (1) plugging of dermal lymphatics with tumor cells
   (2) less flattening of sclerotic + fibrous elements of neoplasm in comparison with more compressible fibroglandular breast tissue

Nonlocalizing Signs of Breast Cancer

= SECONDARY SIGNS OF BREAST CANCER

1. Asymmetric thickening
2. Asymmetric ducts especially if discontinuous with subareolar area
3. Skin changes
   (a) **skin retraction** = dimpling of skin
   Cause: desmoplastic reaction → shortening of Cooper ligaments / direct extension of tumor to skin

DDx: trauma, biopsy, abscess, burns

(b) **skin thickening** ← blocked lymphatic drainage / tumor in lymphatics
- peau d'orange

DDx: normal in inframammary region

4. Nipple / areolar abnormalities
   (a) **retraction / flattening of nipple**
   DDx: normal variant
   (b) **Paget disease** = eczematoid appearance of nipple + areola in ductal carcinoma
   √ associated with ductal calcifications toward nipple
   DDx: nipple eczema
   (c) **nipple discharge**
   - spontaneous persistent discharge
   - need not be bloody

   DDx: lactational discharge
5. **Axillary nodes** (sign of advanced / occult cancer)
   √ > 1.5 cm without fatty center
   DDx: reactive hyperplasia
6. Abnormal veins
   √ venous diameter ratio of > 1.4÷1 in 75% of cancers (= late sign + thus not very important)

Location of Breast Masses

benign + malignant masses are of similar distribution

@ upper outer quadrant 54%
@ upper inner quadrant 14%
@ lower outer quadrant 10%
@ lower inner quadrant 7%
@ retroareolar 15%

◊ Mediolateral oblique view is important part of screening because it includes largest portion of breast tissue + considers most common location of cancers!

Metastatic Breast Cancer

@ Axillary lymph adenopathy
Prevalence: 40–74%
Risk for positive nodes: 30% if primary > 1 cm, 15% if primary < 1 cm

@ Bone

@ Liver
Prevalence: 48–60%
US:
√ hypoechoic (83%) / hyperechoic (17%) mass

Screening of Asymptomatic Patients

Definition of screening (World Health Organization):

A screening test must
(a) be adequately sensitive and specific

(b) be reproducible in its results
(c) identify previously undiagnosed disease
(d) be affordable
(e) be acceptable to the public
(f) include follow-up services

Guidelines of American Cancer Society, American College of Radiology, American Medical Association, National Cancer Institute:

1. Breast self-examination to begin at age 20
2. Breast examination by physician every 3 years between 20–40 years, in yearly intervals after age 40
3. Baseline mammogram between age 35–40; follow-up screening based upon parenchymal pattern + family Hx
4. Initial screening at 30 years if patient has first-degree relative with breast cancer in premenopausal years; follow-up screening based upon parenchymal pattern
5. Mammography at yearly intervals after age 40
6. All women who have had prior breast cancer require annual follow-up

Additional recommendations:

7. Screening at 2-year intervals for women > 70 years
8. Baseline mammogram 10 years earlier than age of mother / sister when their cancer was diagnosed

Rate of detected abnormalities:

30 abnormalities in 1,000 screening mammograms:
20–23 benign lesions
7–10 cancers

Acceptable recall rate for screening examination:

10% for initial prevalence screening;
5% for subsequent incidence screening

Interval cancers: 10–20% of cancers surface between annual screenings

Predictive Value of Radiographic Signs of Malignancy Related to Clinical Findings		
Mammographic Sign	*Palpable*	*PPV (%)*
Classic for malignancy	+	100
Classic for malignancy	–	74
Microcalcifications*	+	25
Microcalcifications*	–	21
Indeterminate mammogram	+	11
Indeterminate mass	–	5
Benign mass	+	2
Asymmetric density (? mass)	+	4
Asymmetric density (? mass)	–	0
Dilated vein		0
Skin thickening		0
Dilated duct		0
* (>3 punctate irregular microcalcifications in area <1 cm^2)		

Role of Mammography

Overall detection rate:

58–69%; 8% if < 1 cm in size

Mammographic accuracy:

88% correctly diagnosed by radiologist

27% detected only by mammography

8% misinterpretations

4% not detected

15–30% positive predictive value (national average):
25% PPV for women in 5th decade
50% PPV for women in 8th decade

Value of Screening Mammography

Indication:

decrease in cancer mortality through earlier detection + intervention when tumor size is small + lymph nodes negative; tumor grade of no prognostic significance in tumors < 10 mm in size

1. **Health Insurance Plan** (HIP) 1963–1969
   randomized controlled study of 62,000 women aged 40–64
   - 25–30% reduction in mortality in women > 50 years (followed for 18 years)
   - 25% reduction in mortality in women 40–49 years (followed for 18 years); no significant effect at 5- and 10-year follow-up
   - 19% of cancers found by mammography alone
   - 61% of cancers found at physical examination
   - effectiveness of screening < 50 years of age is uncertain
2. **Breast Cancer Detection Demonstration Project** (BCDDP) 1973–1980

4,443 cancers found in 283,000 asymptomatic volunteers
› 41.6% of cancers found by mammography alone (77% with negative nodes)
› 8.7% of cancers found by physical examination alone
› 59% of noninfiltrating cancers found by mammography alone
› 25% of cancers were intraductal (versus 5% in previous series)
› 21% of cancers found in women aged 40–49 years (mammography alone detected 35.4%)
› 51% of cancers found with both mammography + physical examination

3. **Swedish Two-county Trial** 1977–1990
randomized controlled study of 78,000 women in study group + 56,700 in control group aged 40–74 years with screening phase lasting 7 years
(a) single MLO mammogram at 2-year intervals for women < 50 years of age
(b) single MLO mammogram at 3-year intervals for women ≥ 50 years of age
› 40% reduction in mortality at 7 years in women 50–74 years
› 0% reduction in mortality at 7 years in women 40–49 years
› At 29-year follow-up 34 years of life per 1000 women were saved screened over a 7-year period
› At 29-year follow-up 1 breast cancer was prevented for each 519 women screened for 7 years
4. **Meta-analysis** of combined results of 5 Swedish trials for women aged 39–49
• 29% reduction in breast cancer mortality with screening mammograms offered at intervals from 18 to 28 months

OCCULT VERSUS PALPABLE BREAST CANCER

◊ 27% are occult cancers (NO age difference)
Positive axillary nodes:
occult cancers (19%); palpable cancers (44%)
10-year survival:
occult cancers (65%); palpable cancers (25%)

Mammographically Missed Cancers

False-negative screening mammogram:
= pathologic diagnosis of breast cancer within 1 year after negative mammogram with the following types of misses:
(a) lesion could not be seen in retrospect (25–33%) = "acute cancer" = cancer surfacing in screening interval
(b) cancer undetected by first reader but correctly identified by second reader (14%)
(c) cancer visible in retrospect on prior mammogram (61%)
Prevalence: ~ 4–15–34% of all cancers; ~ 3 cancers ÷ 2,000 mammograms; 5–15–22% of palpable breast cancers

◊ A second reader will detect an additional 5–15% of cancers!

Cause:
1. Logistical error
(a) prior films not made available
(a) prior films not back far enough

◊ For comparison use a mammographic interval of 3 years to detect slowly developing asymmetries (tumor doubling time ~150 days)

2. Interpretation error (52%):
   (a) benign appearance (18%): medullary carcinoma, colloid carcinoma, intracystic papillary carcinoma, some infiltrating ductal carcinomas
   (b) present on previous mammogram (17%)
   (c) seen on one view only (9%)
   (d) site of previous biopsy (8%)
   (e) calcifications assumed to be benign
3. Observer error (30–43%):
   (a) overlooked: one lesion / group of calcifications doesn't fit the rule of multiplicity
   (b) intrinsic distraction = presence of an obvious finding leads to overlooking of a more subtle lesion = "satisfied search" phenomenon
   (c) no knowledge of clinical finding
   (d) rushed interpretation
   (e) heavy caseload
   (f) extraneous distraction
   (g) eye fatigue
   (h) inexperience
4. Wrong assumption
   (a) misleading long history of a lump results in screening rather than diagnostic mammogram
   (b) acceptance of irreconcilable size discrepancy / lesion location between sonogram and mammogram
   (c) suspicious findings remain suspicious!
4. Technical error (5%):
   (a) inadequate radiographic technique: improper positioning, inadequate compression, under- / overexposed image, poor screen-film contact, geometric motion blurring
   (b) misapplied workup = failure to image region of interest: spot compression magnification view may displace lesion out of field of view
   (c) suboptimal viewing conditions: inadequate luminance of view boxes, extraneous view box light, high ambient room light
5. Tumor biology:
   (a) small tumor size
   (b) failure to incite desmoplastic reaction (eg, invasive lobular carcinoma)
   (c) limitations of screen-film mammography in physically dense breasts
   (d) no associated microcalcifications (~ 50% of cancers)
   (e) developing soft-tissue density
      ◊ A developing density that cannot be reconciled with a history of trauma, inflammation or hormones and does not represent a cyst or lymph node requires a biopsy!
   (f) stability of mammographic findings
      ◊ Malignant calcifications may be stable for up to 63 months

◊ A mass may not change for up to 4.5 years

6. Difficult location:
   (a) axillary tail
   (b) inframammary fold
   (c) busy subareolar region

   Location of missed cancers:
   retroglandular area (33%), lateral parenchyma (31%), central (18%), medial (13%), subareolar (4%)

DISCLOSING UNANTICIPATED OUTCOMES

(a) Content to be disclosed to patient:
   1. Provide facts about events = presence of error / system failure if known
   2. Express regret = apology

(b) Institutional requirements:
   1. Integrate disclosure, patient safety and risk management
   2. Establish disclosure support system
   3. Use performance improvement tools to track and enhance disclosure

Radiation-induced Breast Carcinoma

◊ Lifetime risk with cumulative carcinogenic effect related to age!

(a) women age < 35: 7.5 additional cancers per 1 million irradiated women per year per rad

(b) women age > 35: 3.5 additional cancers per 1 million irradiated women per year per rad

Role of Breast Ultrasound in Breast Cancer

Indications:

◊ Ultrasound is no screening tool!

A. TARGETED EXAM
   (1) Initial study of palpable lump in patient < 30 years of age / pregnant / lactating
      ◊ Ultrasound will not add useful information in an area that contains only fatty tissue on a mammogram!
   (2) Characterization of mammographic / palpable mass as fluid-filled / solid
      ◊ Ultrasound will add useful information if there is water-density tissue in the area of palpable abnormality!
      ◊ Differentiation of cystic from solid lesion is the principal role of ultrasound!
   (3) Additional evaluation of nonpalpable abnormality with uncertain mammographic diagnosis
   (4) Search for focal lesion as cause for mammographic asymmetric density
   (5) Confirmation of lesion seen in one mammographic projection only

B. WHOLE-BREAST EXAM
   (1) Breast secretions
   (2) Suspected leaks from silicone implant
   (3) Follow-up of multiple known mammographic / sonographic lesions
   (4) Radiographically dense breast with strong family history of breast cancer

(5) Metastases thought to be of breast origin, but with negative clinical + mammographic exam
(6) Mammography not possible: "radiophobic" patient, bedridden patient, after mastectomy

C. INTERVENTIONAL PROCEDURE
(1) Ultrasound-guided cyst aspiration
(2) Ultrasound-guided core biopsy
(3) Ultrasound-guided ductography, if
(a) secretions cannot be expressed
(b) duct cannot be cannulated

Accuracy: 98% accuracy for cysts; 99% accuracy for solid masses; small carcinomas have the least characteristic features

Role of Breast MR in Breast Cancer

◊ Impact of routine breast MRI on survival still unknown → use of MRI for preoperative staging controversial!

Pathophysiology of tumor detection:
growth of tumor vessels (= neoangiogenesis) with abnormal leaky capillaries (= increased permeability) → rapid uptake (= early enhancement) and rapid washout of intravenous contrast material in cancerous lesions

Indications:
(1) Improve detection + characterization of primary
• palpable mass + negative mammogram + sonogram
• status post lumpectomy with positive resection margins
◊ Helps to reduce the rate of re-excision (4–43%)
• repeated indeterminate mammogram
• staging:
› tumor size: MR more accurate in estimate of tumor size than mammography / ultrasound
› detection of extensive intraductal component: MR superior to mammography
› multifocality (16–50%): in 70% detected by MR only
› multicentricity(15–30%): in 50% detected by MR only
◊ Reduces rate of "recurrence" / preoperatively undetected foci of cancer from 6.8% to 1.2%
◊ May change accelerated partial breast irradiation to whole-breast irradiation
› before + after 2nd cycle of neoadjuvant chemotherapy to separate responders from nonresponders
› chest wall invasion

(2) "Clearing" (= screening) of contralateral breast:
bilaterality (3–5%) in 75% detected by MR only
◊ Increases detection of contralateral breast cancer from 4% to 17% (of which 35% are DCIS)

(3) Screening of high-risk groups
• young patient with positive BRCA1 gene
• dense breast + high-risk lesion of LCIS

- status post mastectomy + breast reconstruction with implant (yearly screening)

(4) Improve detection of recurrent breast cancer
- planning for biopsy to determine scar versus recurrent tumor after breast-conserving therapy

(5) Evaluate response to neoadjuvant chemotherapy

(6) Examine breasts in patient with metastatic breast cancer but unknown origin of primary (2–7%)
- axillary node malignancy + negative mammogram

(7) Implant imaging

Sensitivity: 72–**90**–100% (for DCIS 40–**73**–100%, for invasive cancer 91%)

Specificity: 37–**70**–100%

◊ A normal MR mammogram
› correctly rules out malignancy in > 96%
› means no invasive cancer > 3 mm
› means no further exam for 2 years (for 1 year if BRCA positive)
› FN: DCIS, LCIS, lobular cancer, tubular cancer

Optimal timing of MR: 7–20 days after beginning of cycle; 6 months after open biopsy; 12 months after radiation therapy

MR:

Malignant morphology always trumps kinetics!

√ reduced signal on T2WI
√ irregular morphology
√ lymphangitic bridges / streaks
√ contrast enhancement:
√ rapid ⇑ in SI after contrast injection = rapid wash-in
◊ **90/90 rule** = cancers show an SI increase of > 90% in the first 90 sec!
√ markedly ⇑ amplitude than normal parenchymal tissue

Indication for Screening Breast MR
(if score > 2.0)

History	*Score*
BRCA 1 or 2	2.0
Personal history of breast / ovarian cancer	2.0
Breast cancer in mother < 60 years	1.0
Breast cancer in sibling < 60 years	0.5
Menstruation > 35 years	0.5
Nulliparous	0.5
First pregnancy > 30 years	0.5
Breast cancer in first-degree relative (nonsibling)	0.5
Ashkenazi Jew	0.5
Dense breast	0.5

BI-RADS® Score & Interpretation of Breast MR	
Descriptor	*Score*
Major feature	
Peak enhancement in 90 sec	2.0
Centripetal wash-in	2.0
Spiculated lesion	2.0
Rapid wash-out	2.0
T2 isointense mass	1.0
Initial contrast uptake >100%	1.0
Minor feature	
Perilesional edema (T2 / STIR)	1.0
Branching lesion	1.0
Dendritic configuration adjacent to primary	1.0
Heterogeneous lesion on T2	1.0
Size of lesion >10 mm	0.5
Lobulated margins of lesion	0.5
Interpretation	
Compatible with malignancy	> 7
Probably malignant	> 5
Indeterminate	3–5
Probably benign	< 3
Compatible with benignity	< 1

√ plateau / fast wash-out in postinitial phase
√ "arterial feeder" sign
√ intense early rim / peripheral enhancement (± central necrosis)
√ centripetal progression of enhancement
√ malignant mass margination

Slowly / Nonenhancing Breast Cancer on MR

1. Lobular carcinoma
2. Tubular carcinoma
3. Mucinous carcinoma
4. Grade I invasive ductal carcinoma

Role of PET/CT in Breast Cancer

PET-CT useful ONLY in

(a) inflammatory breast cancer
(b) > 3 cm large breast cancer
(c) stage II/III breast cancer

Staging of Breast Cancer

(1) Initial staging
◊ PET/CT is efficient for locally advanced + inflammatory breast cancer

√ 40% of breast primaries NOT visualized
√ 61% sensitive + 80% specific for axillary nodes
√ unsuspected disease detected in mediastinal / internal mammary lymph nodes in 30%

(2) Restaging
◊ PET/CT performs better than all other imaging
√ 92–100% sensitive for recurrence, 72–82% specific (changes with time interval since therapy)
√ PET/CT may change clinical management in 36%

High SUV Values in Breast Cancer

(1) Ranking: infiltrating ductal carcinoma > infiltrating lobular carcinoma > ductal carcinoma in situ
(2) Estrogen receptor-negative tumor
(3) Cancer with poor prognosis: triple negative breast tumor (negative for estrogen + progesterone receptors + HER2/neu overexpression)

Distant Metastases in Breast Cancer

Soft-tissue lesion: mediastinal nodes (24%), liver (15%), supracentimetric lung nodules
Bone lesion:
(a) osteosclerotic: PET lacks sensitivity; downstaging with no FDG uptake (in 12%)
(b) osteolytic / mixed lesions: PET more efficient than CT / bone scintigraphy
◊ Bone scintigraphy may no longer be necessary!

Role of Stereotactic Biopsy

Indications: obviously malignant nonpalpable lesion, indeterminate likely benign lesion, anxiety over lesion
Targets: well-defined solid mass, indistinct / spiculated mass, clustered microcalcifications
Advantage: single-stage surgical procedure
Problematic: 3–5-mm small lesion, fine scattered microcalcifications, indistinct density, area of architectural distortion
Sensitivity: 85–99% with core needle biopsy (100% specific), 68–93% with fine-needle aspiration (88–100% specific)
Indication for excision:
(a) anatomic reason: lesion close to chest wall, lesion in axillary tail, very superficial lesion
(b) pathologic reason:
1. Radial scar suspected (in up to 28% associated with tubular carcinoma)
2. Atypia / atypical hyperplasia (in 49–61% associated with malignancy)
3. Carcinoma in situ (in 9–20% associated with invasion)
4. Branching microcalcifications suggestive of DCIS with comedo necrosis

Miss rate: 3–8% for stereotactic biopsy, 3% for surgery

Incidental Breast Cancer Detection by CT

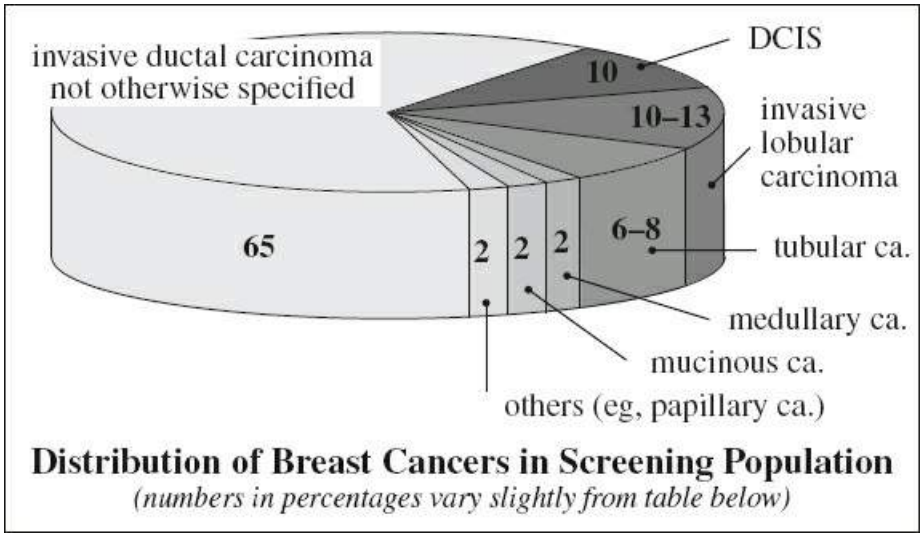
› highly predictive features:
√ irregular margins, irregular shape, rim enhancement

√ washout pattern on postcontrast images
√ diffuse regional enhancement

› most accurate sign:
√ spiculated + irregular margin

Categories of Breast Cancer

A. Invasive ductal carcinoma (NOS) + DCIS 85%
B. Other types of malignancy 15%
(a) Invasive lobular carcinoma (ILC)



Distribution of Breast Cancers in Screening Population
(numbers in percentages vary slightly from table below)

(b) Well-differentiated subtypes of IDC
1. Tubular carcinoma
2. Mucinous carcinoma
3. Medullary carcinoma
4. Papillary carcinoma

(c) Cancers of stromal origin
1. Phyllodes tumor
2. Angiosarcoma
3. Osteosarcoma
4. Adenoid cystic carcinoma

(d) Metastatic disease (0.5–2.0%)
1. NHL
2. Malignant melanoma
3. Metastatic carcinoma
4. Rhabdomyosarcoma
5. Leukemia

Origin: terminal ductal lobular unit (TDLU);
terminal duct → ductal carcinoma (85%)
acinus → lobular carcinoma (10–12%)
stroma → fibrosarcoma, liposarcoma, angiosarcoma, phylloides sarcoma

Staging of Breast Cancer

(a) primary tumor

(b) lymph nodes:

› anatomy

› signs of malignancy

Internal mammary node metastases usually occur after axillary involvement indicating stage N3b / IIIC.

Isolated internal mammary node metastases occur in 1–5% of breast cancers usually from a deep / medial lesion indicating N2b disease.

(c) distant metastasis = stage IV disease

◊ 4% of patients present with distant metastases and of those 10% have lesions at multiple sites

Location: bone, lung, brain, liver

Prognosis: 22% 5-year survival rate

(c) AJCC stage (American Joint Committee on Cancer)

Stage 0	TisN0M0
Stage IA	T1N0M0
Stage IB	T0–T1 with N^{1mi} and M0
Stage IIA	T0–T1 with N1M0 / T2N0M0
Stage IIB	T2N1M0 / T3N0M0.
Stage IIIA	T0–T2 with N2M0 / T3 with N1–N2 + M0
Stage IIIB	T4 with N0–N2 and M0
Stage IIIC	any T with N3M0.
Stage IV	M1 with any T + any N

NONINVASIVE BREAST CANCER (15 %)

= malignant transformation of epithelial cells lining mammary ducts + lobules confined within boundaries of basement membrane

Rx: few data are available to provide insight into proper treatment

Ductal Carcinoma In Situ (DCIS)

= highly heterogeneous group of intraductal carcinomas (“cancer waiting to become malignant”)

= nonobligate precursor to invasive cancer

◊ 30% become invasive over 10 years

Incidence: 20–25% of all cancers in screening population; 70% of noninvasive carcinomas

T Descriptors in TNM Staging of Breast Cancer	
Descriptor	*Definition (= tumor size + locoregional invasion)*
Tis	Carcinoma in situ: DCIS, LCIS, Paget disease of nipple (not associated with invasive carcinoma / carcinoma in situ in underlying breast parenchyma)
T1	all invasive tumors ≤ 20 mm
T1mi	Tumor ≤ 1 mm
T1a	Tumor > 1 mm but ≤ 5 mm
T1b	Tumor > 5 mm but ≤ 10 mm
T1c	Tumor > 10 mm but ≤ 20 mm
T2	Tumor > 20 mm but ≤ 50 mm *mnemonic:* "**T2 over 2** cm"
T3	Tumor > 50 mm
T4	Any tumor size with extension to chest wall / skin (invasion of dermis alone does not qualify)
T4a	extension to chest wall = involvement of ribs /serratus anterior muscle / intercostal muscles (pectoralis muscle invasion alone does not qualify)
T4b	ulceration, ipsilateral satellite skin nodules ± skin edema (= peau d'orange without meeting classic criteria for inflammatory breast cancer)
T4c	T4a + T4b
T4d	inflammatory carcinoma (IBC)
Size of largest tumor determines stage, if > 1 malignancy in same breast. Tumor size is most accurately measured by MRI (size is underestimated by 14% on mammo and by 18% on US)	

N Descriptors in TNM Staging of Breast Cancer	
Descriptor	*Definition (metastases to ...)*
N1	ipsilateral level I–II axillary lymph nodes
N2	
N2a	clinically "fixed" / matted N1
N2b	ipsilateral internal mammary lymph nodes in the absence of axillary nodes
N3	
N3a	ipsilateral infraclavicular (level III) lymph nodes
N3b	ipsilateral level I–II axillary + internal mammary nodes
N3c	ipsilateral supraclavicular nodes
Biopsy the most suspicious lymph node! √ lymph node anatomy √ imaging criteria of malignancy	

Age-adjusted prevalence: 32.5÷100,000 women (2005); 88÷100,000 women 50–64 years
Age: most > 55 (40–60) years
Path: heterogeneous group of malignancies with proliferation of malignant cells lining

TDLU + duct

Histo: proliferation of malignant epithelial cells that line a TDLU without invasion through basement membrane → duct diameter increases from 90 µm to 360 µm

Subgroups: comedonecrosis (often); non-comedocarcinomas (solid, papillary, micropapillary, cribriform)

Nuclear grade: low, intermediate, high

Van Nuys Classification (most reproducible):

Group 1: low / intermediate grade <u>without</u> necrosis

Group 2: low / intermediate nuclear grade <u>with</u> necrosis

Group 3: <u>high nuclear grade</u>

Van Nuys group 1 lesions more likely manifest as noncalcified abnormalities than higher-grade lesions!

Associated with: ADH + invasive ductal carcinoma

N.B.: by definition not capable of metastasizing to regional lymph nodes, HOWEVER axillary metastases in 1.3–13%

Risk factors: increasing age, family history, high breast density, postmenopausal hormone use

- may persist for years without palpable abnormality (in screening population)
- palpable mass (12%) / Paget disease of nipple / nipple discharge (in 12% of symptomatic patients)

◊ 50% of DCIS are > 5 cm in size

◊ Histologic size of DCIS is independent of histologic subgroup

◊ Almost all "comedo" type DCIS contain significant microcalcifications

◊ DCIS often involves the nipple + subareolar ducts

◊ Calcifications in ductal orientation like "string of beads"

Multicentricity: in 8–47% (increasing with tumor size)

Multifocality: in 27%

Multicentricity	Multifocality
> 1 focus in <u>different breast quadrants</u> with a minimum distance of 2 cm → mastectomy	> 2 foci in <u>same breast quadrant</u> → breast conservation therapy
mnemonic: "**C** before **D**" = Centricity for Different quadrants	

Average size: 10–15 mm

Mammo (27–95% sensitive):

√ microcalcifications (in 90%):

› in 75% sole finding

› in 15% associated with soft-tissue component

Shape: amorphous; coarse; heterogeneous; fine pleomorphic (most common)

Distribution: clustered / linear / segmental

√ fine linear / fine linear branching (high-grade DCIS)

√ amorphous microcalcifications (low-grade DCIS)

√ soft-tissue mass / asymmetry (10%):

◊ more frequently associated with low-grade DCIS

√ dominant mass with well-defined margin (14%)
√ ill-defined indistinct obscured mass (2%)
√ architectural distortion (7–13%)
√ soft-tissue abnormality + calcifications (14%)
√ invisible (6%)

US:
√ microcalcifications:
√ associated with ductal changes (most common)
√ echogenic regions without duct changes / mass
√ intraductal mass ± multiple punctate echogenic foci within dilated duct
√ solid mildly hypoechoic irregularly shaped intraparenchymal mass with indistinct / microlobulated margins + normal acoustic transmission
√ pseudomicrocystic appearance

MR (60–100% sensitive, 18–100% FN [!]):

DCIS Grade	*MR Sensitivity*
high	98%
intermediate	91%
low	80%

Sensitivity for DCIS is much higher for MRI (92%) than for mammography (56%)!

◊ Preoperative MR evaluation is utilized in women with newly developed breast cancer to discover:
(a) extent of disease and tumor margins
(b) ipsilateral multicentric involvement
(c) contralateral disease (in 3.3%)

√ hypo- to isointense to surrounding parenchyma on T1WI + fatsat T2WI
◊ Not helpful in decision whether to biopsy clustered microcalcifications or not!

CEMR:

Morphology of DCIS on Enhanced MRI

Type	*Definition*	*Frequency*
NME	nonmass-like enhancement of an area that is not a mass	60–81%
mass	3-dimensional space-occupying lesion of enhancement	14–41%
focus	< 5 mm region of enhancement	1–12%

High likelihood of cancer:
√ clumped linear (beady, string of pearls) ductal / segmental enhancement (HALLMARK)
√ linear enhancement adjacent to synchronous malignant mass

Enhancement pattern of DCIS:

The internal enhancement pattern of nonmass-like DCIS is commonly clumped or heterogeneous (50% vs. 20%)

√ nonmass-like (60–81%) enhancement (NME) pattern:
√ clumped (41–64%)

√ internally heterogeneous (16–29%) / homogeneous (16%)
√ reticular / dendritic (9%), stippled (8%), punctate (3%)
√ oval / round masslike (14–41%) enhancement pattern:
√ irregular (14–83%) / spiculated (0–92%) / smooth (4–8%) mass margins

DCIS most frequently manifests as an irregular mass!

√ homogeneous (9–25%) / heterogeneous (9–67%) internal enhancement / rim enhancement (0–8%)
√ focal (1–12%) enhancement pattern
√ no enhancement (in 5–10%)

Enhancement distribution of DCIS:
√ segmental (42%), focal (33%), diffuse (9%), linear-ductal (9%), regional (6%)

A segmental distribution is the most common pattern accounting for 33–77% of all DCIS!

Enhancement kinetics of DCIS:
√ initial period: fast (49–68%), medium (20%), slow (20%)
√ delayed period: plateau (20–52%), washout (28–44%), persistent (20–30%)
◊ There is no pathognomonic kinetic pattern:
› lower-grade lesions tend to show steep initial period + washout
› higher-grade lesions tend to show persistent increase

The most common enhancement kinetics for DCIS are a fast initial phase with a delayed-phase plateau!

Prognosis: 96–98% 10-year survival rate

Rx: (1) Simple / modified mastectomy: cure rate of 98%; reserved for tumor > 5 cm or multicentric / diffuse disease
(2) Local excision alone (breast-conserving Rx): local recurrence in 4 years:
› 19% for poorly differentiated
› 10% for moderately differentiated
› 0% for well differentiated
(3) Lumpectomy + radiotherapy: 7% rate of recurrence

Treatment problems:
◊ Underestimation of extent of disease in 30% for mammography and in 19% for MRI!

MRI provides an accurate assessment of the extent of DCIS (89%) compared to mammo (55%) and US (47%) OR an overestimation!

1. Occult invasion in 5–20% of patients
2. Multifocality in 30%
3. Multicentricity in 14% of lesions < 25 mm, in 100% of lesions > 50 mm
4. Axillary metastases in 1–2%

Increased risk of recurrent DCIS:
(1) Positive margins after surgery
(2) Residual synchronous foci of DCIS

Presentation: 50% as invasive cancer; 20% as distant metastases in 10 years

High Nuclear Grade DCIS ("comedo type")

Prevalence: 60% of all DCIS
Precursor: none; one stage de novo development
Path: "comedo" = pluglike appearance of necrotic material that can be expressed from the cut surface
[*comedo* , Latin = worm of waxy material that can be squeezed from a blackhead believed to feed (*edere* = to eat) on the body]
Characteristics:
› nuclear grade: large / intermediate nuclei, numerous mitoses, aneuploidy
› growth pattern: predominantly solid cell proliferation; atypically papillary / micropapillary / cribriform
[*cribriform*, Latin = small holes or open spaces like a sieve)
› necrosis: extensive (HALLMARK) ← rapid growth
› calcifications (90%): dystrophic / amorphous within necrosis in center of dilated ductal system outlining most of the lobe in classic solid growth pattern
• estrogen-receptor + progesterone-receptor negative
• overexpression of ErbB-2 oncogene product and P53 suppressor gene mutation
• often symptomatic lesion with nipple discharge
√ ductal system enlarged to 300–350 µm
√ linear / branching pattern of calcifications scattered in a large part of lobe / whole lobe
√ large solid high-density casting calcifications (fragmented, coalesced, irregular) in solid growth pattern
√ "snake skin–like" / "birch tree flowerlike" dotted casting calcifications within necrosis of micropapillary / cribriform growth pattern
√ palpable dominant mass without calcifications (very unusual)
√ nipple discharge (rare)
Prognosis: higher recurrence rate than noncomedo-group

Low Nuclear Grade DCIS ("noncomedo type")
Prevalence: 40% of all DCIS
Precursor lesion: atypical ductal hyperplasia (ADH) with slight / moderate / severe atypia
◊ 52–56% of ADH at core biopsy are associated with malignancy at excision!
Characteristics:
› nuclear grade: monomorphic small round nuclei, few / no mitoses
› growth pattern: predominantly micropapillary / cribriform; atypically solid cell proliferation (often coexist)
› necrosis: not present in classic micropapillary / cribriform growth pattern
› calcifications (50%): laminated / psammoma-like ← active secretion by malignant cells into duct lumen
√ fine granular "cotton ball" calcifications in cribriform growth pattern
√ coarse granular "crushed stone" / "broken needle tip" / "arrowhead" calcifications in less common solid growth pattern
◊ Size of "noncomedo" DCIS often underestimated mammographically (? ← lower density of calcifications at periphery of lesion)!

√ powdery calcifications (45%)
√ palpable dominant mass without calcifications (intracystic papillary carcinoma, multifocal papillary carcinoma in situ)
√ nonpalpable asymmetric density with architectural distortion
√ occasionally serous / bloody nipple discharge + ductal filling defects on galactography

Risk of recurrence: 2%

Prognosis: 30% eventually develop into invasive cancer

Dx: surgical biopsy

◊ Core needle biopsy could result in diagnosis of only proliferative breast disease that is usually intermixed!

Lobular Carcinoma In Situ (LCIS)

= arises in epithelium of blunt ducts of mammary lobules

◊ NOT a precancerous lesion – BUT a marker for an increased risk of subsequent invasive cancer in either breast! ("Risk factor waiting to become malignant")

Prevalence: 0.8–3.6% in screening population; 3–6 % of all breast malignancies; 25% of all noninvasive carcinomas; high incidence during reproductive age → decreasing with age

Age: most 40–54 years (earlier than DCIS / invasive tumors)

Histo: monomorphous small cell population filling + expanding ductules of the lobule

◊ Synchronous invasive cancer in 5%!

• not palpable
√ mammographically occult
√ may atypically present as a noncalcified mass (in 7%), calcifications + mass (in 10%), asymmetric opacity (2%)

MR:

› T1WI:
√ isointense to breast parenchyma
› enhanced T1WI:
√ ill-defined enhancement with nonspecific intensity curves

◊ High frequency of multicentricity (50–70%) + bilaterality (30%)!

Dx: incidental microscopic finding depending on accident of biopsy (performed for unrelated reasons + findings)

Prognosis:

◊ LCIS serves as a marker of increased risk for developing invasive carcinoma in <u>either</u> breast!

◊ 20–30% develop invasive ductal > lobular carcinoma within 20 years after initial diagnosis
◊ 1% per year lifetime risk for invasive malignancy

Rx: recommendations range from observation (with follow-up examinations every 3–6 months + annual mammograms) to uni- / bilateral simple mastectomy

Intracystic Papillary Carcinoma In Situ (0.5–2%)

= rare variant of noncomedo DCIS

Age: usually older postmenopausal woman; peak 34–52 years
Histo: papillary fronds within the wall of a cystically dilated duct; (partial) absence immunohistochemical marker p63 for myoepithelial cell layer
- well-circumscribed + freely movable
- aspiration yields straw-colored / dark red / brown fluid ← ruptured capillaries in cyst wall / necrosis of tumor cells; reaccumulation of fluid within 3–4 weeks
- fluid cytology negative for cancer in 80%

Size: 1.9 (range, 0.4–7.5) cm
√ solid intracystic mass on US
√ round benign appearing mass with sharply circumscribed lobulated borders on mammography
√ intracystic mass on pneumocystography
√ fast growth ← accumulation of fluid + proliferation of neoplastic cells
Rx: lumpectomy
Prognosis: 10-year disease-free survival rate of 91%
DDx on mammogram: mucinous / medullary carcinoma, hematoma, metastasis

INVASIVE BREAST CANCER (85%)

= cancer cells outside mammary ducts / TDLUs after penetrating basement membrane
Pathophysiology:
malignant cells of ~ 1 billion cells = 1 cm^3 (= critical mass) outgrow their nutrient supply inside confines of basement membrane → tumor elaborates
(1) angiogenic factor stimulating growth of new arterial channels (neovascularity) and
(2) proteolytic enzyme weakening / dissolving basement membrane
Subtypes: estrogen receptor, progesterone receptor, Her2 (= **H**uman **e**g**fr 2**), CK5/6 (= CytoKeratin 5/6), EGFR (= **E**pidermal **G**rowth **F**actor **R**eceptor)
Growth rate: average doubling time of 110–150 (range, 25–1000) days
√ **mass** = 3-dimensional lesion apparent on 2 views:
√± spicules = extension of malignant cells
√ focal **asymmetry** = confined parenchymal area of similar shape
› without identifiable borders in 2 views
› with definable border on 1 view
√ architectural **distortion** = alteration of anticipated normal orderly undulating curvilinear breast parenchyma into straight or converging lines / a convexity / acute angle:
√ surrounding corona of radiolucency
√ nipple retraction / skin retraction
√ tenting / flattening / shrinking
√ bulging contour
√ edema (lymphatic obstruction) + skin thickening
√ adenopathy
MR:
√ peripheral / rim enhancement
Prognosis:

Tumor size	Survival at 10 years after diagnosis
< 1 cm	95% (independent on tumor grade)
1–2 cm	85%
2–5 cm	60% (dependent on tumor grade)

A reduction of breast cancer mortality is possible through detection of small invasive cancers!

Infiltrating / Invasive Ductal Carcinoma (65%)

= NO SPECIAL TYPE / NOT OTHERWISE SPECIFIED (NOS)

◊ Most frequently encountered breast malignancy

◊ 10% false-negative ratio

Age: any age; peaks between 50 and 60 years

Histo:

grade I = well-differentiated

grade II = moderately differentiated

grade III = poorly differentiated

◊ Strong fibrotic component!

- palpable: 70% are first palpated by the patient
- larger by palpation than on mammogram (Leborgne's law)
- often poorly movable + indolent

Location: multifocal in 15%; bilateral in 5%

Mammo:

√ spiculated (36%) / irregular mass = PRINCIPAL FINDING

√ developing asymmetry

√ lobulated / round / oval mass

√ increased central density

√ ± malignant calcifications (45–60%)

US:

√ ill-defined hypoechoic mass with intermediate hyperechoic margins

√ central / peripheral acoustic shadowing

√ ductal extension (HIGHLY SPECIFIC)

√ perilesional hypervascularity

<u>less common:</u>

√ irregular cystic lesion with surrounding round / tubular hypoechoic areas (= ductal extension)

√ intraductal mass

√ ill-defined spiculated hyperechoic mass with acoustic shadowing

CT:

√ dense spiculated mass

√ marked early and / or peripheral enhancement

MR (88–98% sensitive)

› T1WI:

√ isointense to parenchyma; hypointense to fat

› enhanced T1WI:

√ round / ovoid / spiculated lesion with ill-defined margins
√ ring enhancement in up to 50% with centripetal progression
√ strong (60%) / moderate (35%) / mild (5%) contrast uptake
√ plateau (most frequent) / wash-out (often) / continuous increase (rare) on postinitial phase
√ dilated veins draining the tumor

› T2WI:
√ moderately hyperintense ← viable tumor cells in tumor periphery
√ hyperintense ← central area of necrosis / infarction

On T2WI areas of tumor infarction + necrosis exhibit high SI, viable tumor cells show moderately high SI!

Infiltrating / Invasive Lobular Carcinoma (10–15%)

= neoplasm arising from terminal ductules of breast lobules
= ILC
◊ 2nd most common form of invasive breast cancer
◊ 30–50% of patients will develop a second primary in same / opposite breast within 20 years

Median age: 45–56 years; 2% of breast cancers in women < 35 years; 11% of breast cancers in women > 75 years

Multiplicity: multicentric (30%) + bilateral (6–28%)
◊ Relatively high frequency of bilaterality!

Histo: straight single file of uniform small cells with round oval nuclei + scanty cytoplasm growing around ducts, vessels, and lobules with lack of cohesiveness + without destruction of anatomic structures ("Indian files, targetoid growth pattern) like a spiderweb resulting in subtle changes in architecture; little desmoplastic stromal reaction

Grade: 20% grade I, 64% grade II, 16% grade III

Spread: by diffuse infiltration with little disruption of underlying anatomy

Metastases: peritoneum, retroperitoneum, gynecologic organs, GI tract, carcinomatous meningitis
◊ Consider ILC in women presenting with ascites, hydronephrosis, pelvic masses!

- palpable in 69%:
  - area of subtle thickening / induration
  - skin / nipple retraction
  - large rubbery / indiscrete firm mass / fine nodularity
- decreasing breast size; aching / pulling sensation

Mammo (57–81% sensitive):

◊ Mammogram often underestimates tumor size relative to physical finding + histology; highest FN rate of all invasive breast cancers (up to 19%)

√ solitary inhomogeneous mass (44–65%):
√ with spiculated / ill defined margins (40%)
√ round well-circumscribed (1–3–11%)

√ opacity equal to / lower than normal fibroglandular tissue
√ architectural distortion (= retraction of normal glandular tissue with thickening + disturbance of fibrous septa) in 10–15–34%
√ focal asymmetry (= ill-defined area of increased density without central tumor nidus) in 8–16–19%
◊ May be evident on ONLY one standard view: CC (typically better compressed) > ML > MLO!
√ global asymmetry with unilateral increase in parenchymal volume (1–11–14%)
√ "shrinking breast" = in large tumor breast size appears mammographically smaller compared to contralateral side due to decreased compliance + compressibility
• physical size at inspection symmetric + unchanged
√ microcalcifications (0–24%)
√ retraction of skin (25%) + nipple (26%)
√ skin thickening
√ normal / benign finding (8–16%)
US (68–98% sensitive):
√ irregular / angular hypoechoic mass with heterogeneous internal echoes + ill-defined / spiculated margins + posterior acoustic shadowing (54–61%):
√ circumscribed shadowing mass (pleomorphic ILC)
√ focal shadowing without a discrete mass (classic ILC)
√ rarely hyperechoic mass
MR (83–100% sensitive):
◊ Additional unexpected ipsilateral lesions (in 32%) + contralateral lesion (in 7%):
√ dominant lesion surrounded by multiple small enhancing foci
› T1WI:
√ isointense to parenchyma
› enhanced T1WI:
√ moderate / strong initial enhancement
√ postinitial plateau (frequently) / wash-out (rare) / delayed maximum enhancement (typical)
√ lack of mass effect + amorphous asymmetry
√ ring enhancement of nodular tumor form (in up to 50%)
√ enhancing solitary irregular / angular mass with spiculated / ill-defined margins (31–43%)
√ multiple small enhancing foci with interconnected enhancing strands
√ enhancing septa
› T2WI:
√ iso- to hypointense to breast parenchyma
Dx: core biopsy (controversial) may help in surgical planning prior to surgical excision
Rx: frequently associated with positive margins at excision
Prognosis: survival rate slightly higher than for usual type of invasive ductal carcinomas
DDx: radial sclerosing lesion

Adenoid Cystic Carcinoma (0.1–0.4%)
Histo: mixed glandular + stromal material with predominantly basaloid cells in a variable

architectural pattern (solid, cribriform, tubular, trabecular); microcystic areas formed by coalescent spaces in dilated glands (in 25%)

√ well-defined irregular mass with parallel growth
√ smooth macrolobulated / indistinct margins
√ architectural distortion
√ asymmetric density

US:
√ heterogeneous hypoechoic irregular mass

MR:
√ variable signal intensity on T2WI
√ predominantly persistent enhancement kinetics

Prognosis: excellent

Tubular Carcinoma (< 2%)

= well-differentiated low nuclear-grade ductal carcinoma

Multiplicity: multicentric (28%), bilateral (12–38%)
(a) low grade: bilateral in 1÷3
(b) high grade: bilateral in 1÷300

Associated with: lobular carcinoma in situ in 40%

Median age: 44–49 years

• positive family history in up to 40%; nonpalpable

Mean size: 8 mm (up to 17 mm in diameter)

√ high-opacity nodule with spiculated margins:
√ spicules often longer than central mass
√ may be stable for years
√ associated microcalcifications (50%)
√ multicentric (28%), bilateral (12–38%)

US:
√ hypoechoic solid mass + ill-defined margins + posterior acoustic shadowing

MR:
› T1WI:
√ stellate hypointense lesion well seen in fat
› enhanced T1WI:
√ stellate tumor with moderate / strong initial uptake
√ ring enhancement rare
√ postinitial plateau (frequent) / wash-out (rare) / continuous increase (very rare)
› T2WI:
√ iso- / slightly hypointense to parenchyma
√ occasional peritumoral edematous zone

Prognosis: 97% 10-year survival

DDx: radial scar (histologically α-smooth muscle / maspin staining of myoepithelial cells)

Medullary Carcinoma (2%)

= SOLID CIRCUMSCRIBED CARCINOMA

◊ Fastest growing breast cancer!

◊ Often associated with BRCA gene!
Prevalence: < 5% of all breast carcinomas; 11% of breast cancers in women < 35 years
Path: well-circumscribed mass with nodular architecture + lobulated contour; central necrosis is common in larger tumors; reminiscent of medullary cavity of bone
Histo: poorly differentiated cells with scant stroma + intense lymphoplasmacytic infiltration (reflecting host resistance); propensity for syncytial growth; no glands
Mean age: 46–54 years
• softer than average breast cancer
• often palpable tumor ← rapid growth
Mean size: 2–3 cm
√ well-defined round / oval noncalcified uniformly dense mass (← hemorrhage) with lobulated margin
√ may have partial / complete "halo" sign
US:
√ hypoechoic homogeneous / mildly heterogeneous mass with some degree of through transmission
√ distinct / indistinct margins
√ large central cystic component
MR:
√ irregular internal architecture (no septa!)
› T1WI:
√ well-circumscribed hypointense lesion difficult to detect in parenchyma
› enhanced T1WI:
√ moderately / strongly enhancing round / ovoid lesion with smooth edge
√ homogeneous internal enhancement (← high cellularity) / (occasionally) ring enhancement
√ postinitial type II plateau pattern (frequent) / wash-out (occasionally) / continuous increase (rare)
› T2WI:
√ iso- or mildly hypointense to parenchyma
DDx: myxoid fibroadenoma
Prognosis: 92% 10-year survival rate

Metaplastic Carcinoma (< 1%)
= metaplastic conversion of ductal carcinoma into nonglandular growth pattern of squamous / spindle / heterogeneous mesenchymal cells
Prevalence: < 1% of all newly diagnosed breast cancers; < 5% of invasive breast cancers
Histo: spectrum from poorly differentiated ductal to keratinizing squamous cell carcinoma
Age: > 50 years
• rapidly growing palpable mass
√ predominantly circumscribed noncalcified mass of high density
US:
√ round lobular mass with well-circumscribed microlobulated margin
√ ± complex internal echogenicity with solid + cystic components ← necrosis / cystic degeneration

MR:
› enhanced T1WI:
√ rimlike enhancement
√ postinitial type III wash-out pattern in enhancing peripheral portion
› T2WI:
√ high signal intensity ← necrosis, cystic degeneration, myxoid matrix, intratumoral hemorrhage, loose edematous stroma

Mucinous / Colloid Carcinoma (1–7%)

= well-differentiated low nuclear-grade ductal carcinoma with large amount of extracellular epithelial mucus

Prevalence: 1–7% of all invasive breast cancers

Histo:

(a) pure form: aggregates of tumor cells floating in abundant pools of extracellular mucin (gelatinous / colloid fluid) → less aggressive slow growth

(b) mixed form: contains areas of infiltrating ductal carcinoma not surrounded by mucin

Age: 7% of all carcinomas in women > 75 years; 1% of breast cancers in women < 35 years

• "swish" / "crush" sensation during palpation
• 60% estrogen-receptor positive
√ well-circumscribed usually lobulated round / ovoid mass of low density:
√ poorly defined margins on spot compression
√ pleomorphic clustered / clumped amorphous / punctate calcifications (rare)
√ may enlarge fast (through mucin production)

US:
√ heterogeneous mass with mixture of solid + cystic components
√ posterior acoustic enhancement (common)
√ posterior acoustic shadowing (uncommon)

MR:
› T1WI:
√ well-circumscribed lobulated lesion of variable intensity ← differences in protein concentration
› enhanced T1WI:
√ typically type I persistent enhancement pattern
√ very strong (usually) / moderate (occasionally) / slight (rare) initial uptake
√ postinitial plateau (frequent) / wash-out (occasionally) / continuous increase (very rare)
√ rarely ring enhancement
› T2WI:
√ homo- / heterogeneously hyperintense mass ← predominant mucin component

Prognosis: excellent (unless of mixed form)

Papillary Carcinoma (1–2%)

= rare ductal carcinoma arising from benign papilloma

N.B.: Do not confuse with micropapillary / cribriform growth pattern of ductal carcinoma

Histo: multilayered papillary projections extending from vascularized stalks; no myoepithelial layer (as in benign lesions); neurosecretory granules + positive CEA-reactivity in 85% (absent in benign lesions)

Types:

(a) intraductal papillary carcinoma (often multiple)

(b) intracystic papillary carcinoma = in situ malignancy

(c) invasive carcinoma with papillary growth pattern (microscopic frond formation)

Mean age: 63–67 (range, 25–89) years; peak of 40–75 years

- slow growing palpable central mass (67%)
- nipple discharge (22–34%) often tinged with blood
- rich in estrogen and progesterone receptors

Location: single nodule in central portion of breast; multiple nodules extending from subareolar area to periphery of breast

Size: average diameter of 2–3 cm

√ multinodular pattern (55%) = lobulated mass / cluster of well-defined contiguous nodules

√ solitary well-circumscribed round / ovoid mass of equal or high density ← hemorrhage into cystic space

√ usually confined to single quadrant

√ associated microcalcifications in 60%

√ multiple filling defects / disruption of an irregular duct segment / complete obstruction of duct system at galactography

US:

√ cyst with an intracystic mass of lobulated smooth margins + acoustic enhancement

√ complex mass

√ ± blood flow on color Doppler

MR:

› T1WI:

√ well-circumscribed hypointense retroareolar lesion

› enhanced T1WI:

√ strong initial enhancement + postinitial wash-out (type II washout pattern) / (less often) plateau

√ ring enhancement possible

› T2WI:

√ well-circumscribed lesion of intermediate intensity in signal-intense cyst

Prognosis: 90% 5-year survival after simple mastectomy + axillary node dissection

DDx: solitary central duct papilloma; multiple peripheral benign papillomas

Intraductal Papillary Carcinoma

Path: growth within dilated ducts surrounded by zone of fibrosis without cystic component

√ single / multiple clusters of microcalcifications (most common feature)

MR:

√ clumped areas of enhancement

Distribution: focal / ductal / segmental / regional

√ intratumoral high T2 signal ← microcystic components

Intracystic Papillary Carcinoma

Prevalence: 2–5% of all breast cancers
Origin: dilated duct
Path: friable bosselated well-circumscribed mass within a cystic space (0.3–2.0%) / without a cyst as solid variant
Histo: epithelial frond-forming growth pattern supported by a fibrovascular core lined by ≥ 1 layer of epithelial malignant cells; incomplete / absent myoepithelial cell layer identified by immunohistochemical marker p63
Average age: 70 (range, 27–99) years

- asymptomatic; slowly enlarging palpable mass
- bloody nipple discharge (22–34%)

Location: retroareolar; multifocal
√ round / oval well-circumscribed mass
√ spiculation
√ nipple retraction
US / MR:
√ cystic mass ± septa
√ intracystic solid papillary mass with peripheral fronds projecting from cyst wall into lumen
√ thick fibrotic cyst wall
√ fluid-debris level ← spontaneous hemorrhage
√ positive color Doppler flow
√ posterior acoustic enhancement ← fluid component
√ fluid component serous (low signal on T1WI + high signal on T2WI) / frequently hemorrhagic (high signal on T1WI + T2WI)
√ marked enhancement of mural nodule + cyst wall + septa
Dx: surgical excision to document invasion at tumor periphery
Prognosis: 10-year survival rate approaches 100%
DDx: cyst, mucinous / medullary carcinoma, hematoma, metastasis

Paget Disease of the Nipple (5%)

[Paget, Sir James Paget, 1st Baronet (1814–1899), English surgeon at St. Bartholomew's Hospital, London, England and one of the founders of scientific medical pathology; first described in 1874]
= uncommon manifestation of breast cancer characterized by infiltration of the nipple epidermis by adenocarcinoma
◊ NEARLY ALWAYS a sign of underlying breast malignancy!
Origin: likely from preexisting DCIS / invasive ductal cancer
Prevalence: 1–3% of all breast cancers
Age: all ages; peak between 40 and 60 years

- nipple changes (32%): eczema, erythema of nipple + areola, scaly / flaky skin, nipple erosion, nipple ulceration, nipple inversion, retraction of nipple and areola, bloody discharge:
  ◊ Median delay of correct diagnosis by 6–11 months as features suggest a benign diagnosis of eczema!

- nipple changes + palpable mass / thickening of breast (45%)
- palpable mass / thickening of breast only (14%)
- nipple itching, ± serous / sanguineous nipple discharge

Histo: Paget cell = large round cell with pale clear abundant cytoplasm + enlarged pleomorphic nucleus invading epidermis; histologically and biologically similar to comedocarcinoma

Histogenesis:

(1) Epidermotropic theory = subareolar cancer cells break away from malignancy → migrate through milk ducts along basal membrane → enter nipple and areola

(2) Intraepidermal transformation theory = in situ malignant transformation / degeneration of existing cells

Associated with:

extensive invasive (30%) / in situ ductal carcinoma (60%) limited to one duct in subareolar area / remote + multicentric

Staging: Paget disease associated with breast carcinoma should be categorized on the basis of parenchymal disease!

The mammographic appearance is normal in 22–50%!

@ nipple-areolar complex
- √ nipple / areolar / skin thickening
- √ nipple retraction
- √ dilated duct
- √ linearly distributed subareolar malignant microcalcifications
- √ discrete retroareolar soft-tissue mass / masses

@ breast parenchyma
- √ discrete mass(es) > 2 cm from nipple-areolar complex elsewhere in breast with asymmetry, architectural distortion, diffuse malignant calcifications

MR:

› T1WI:
- √ flattening / thickening of mamillary region

› enhanced T1WI:
- √ variable initial uptake: absent / mild / intense
- √ postinitial plateau / wash-out
- √ asymmetric enhancement of nipple
- √ retroareolar lymphatic enhancement

› T2WI:
- √ rarely asymmetric areolar hyperintensity

Dx: full-thickness biopsy of nipple + areola → followed by radiologic evaluation to detect an underlying malignancy;

cytologic smear of a weeping nipple secretion

Prognosis: survival rate with palpable mass similar to infiltrating duct carcinoma; 85–90% 10-year survival rate without palpable mass; positive axillary nodes in 0–13%

Inflammatory Breast Carcinoma (IBC)

= clinical entity with diffuse erythema + edema involving > ⅓ of breast skin ± angiolymphatic

tumor emboli
Prevalence: 2–5% of breast cancers
Average age: 52 years
Histo: no specific type
◊ Tumor invasion of dermal lymphatics demonstrated in only 60% of specimens!
Staging: T4d (T4b if < ⅓ of breast skin involved)
◊ 20–40% risk of distant metastases at time of Dx
N.B.: dermal lymphatic invasion alone is NOT necessary / sufficient for a diagnosis of IBC
Location: L > R breast; bilaterality in 30–55%
◊ Metastatic at time of presentation in 20%!
Site: often dorsal + central within breast
• rapid symptomatic development > ⅓ of breast surface:
  • palpable tumor (63%); nipple retraction (13%)
  • diffuse erythema + edema of skin (13–64%)
  • erysipeloid edge = peau d'orange edema of skin (13%)
• palpable axillary adenopathy (in up to 91%)
√ NO fluid collection (DDx to abscess)
√ tumor mass ± malignant-type calcifications
√ dense edematous breast
√ stromal coarsening (50%)
√ thickening of Cooper ligaments
√ extensive skin thickening (71%)
CT:
√ marked skin thickening + peripheral enhancement
PET/CT (superior in staging + restaging of IBC):
√ detection of primary breast lesion, skin involvement
√ extent of lymph node metastases for radiation therapy planning: ipsilateral axillary, subpectoral, infra- and supraclavicular, internal mammary (25%)
√ detection of unexpected distant metastases
MR (most accurate modality):
› T1WI:
√ unilateral breast enlargement
√ skin thickening
› enhanced T1WI:
√ patchy asymmetric enhancement of parenchyma + Cooper ligaments
√ strong increased uptake in thickened skin:
√ "punched-out" sign = patchy nodular enhancement of skin at different points in time + different locations
√ strong increased uptake in tumor infiltrated parenchyma:
√ occasionally delineation of primary tumor
› T2WI:
√ diffuse increase in intensity compared to contralateral breast (= prepectoral edema)
√ sometimes hypovascular tumor surrounded by nontumoral edema

Dx: skin punch biopsy

◊ MRI can help identify a biopsy target to confirm Dx.
Both tissue diagnosis & clinical evidence of inflammatory disease are required for a diagnosis of IBC.

Rx: multimodal: neoadjuvant chemotherapy + surgery (ie, modified radical mastectomy) + radiation therapy ± further adjuvant medical therapy with anti-HER antibody / hormonal therapy

Prognosis: 25–50% 5-year survival; median survival time of 7 months (untreated) + 18 months (after radical mastectomy)

DDx:

1. Mastitis
   √ often arises in subareolar area
   (a) infectious mastitis (test treatment for 2–3 weeks with macrolide antibiotic azithromycin, eg, Zithromax Z-pak®)
   (b) inflammatory mastitis (connective tissue disease, SLE, psoriasis)
   (c) granulomatous mastitis
2. Breast abscess
3. Edema (lymphedema, venous obstruction from cardiac pacemakers / dialysis catheters, vascular stenosis / malformation, nephrogenic systemic fibrosis)
4. Ruptured epidermal inclusion / sebaceous cyst associated with skin trauma / follicular inflammation
5. Iatrogenic (prior radiation Rx)
   • localized scleroderma-type skin reaction (rare) = radiation-induced morphea [*morpheus*, Greek = God of dreams or maker of shapes]
   √ skin thickening + fat necrosis
6. Recurrent breast cancer
7. Noninflammatory locally advanced breast cancer (LABC)

   • onset of symptoms usually longer than 3 months with slow progression

   ◊ 10% risk of distant metastases at time of Dx
   Average age: 66 years
8. Metastasis: melanoma, GI cancer, ovarian cancer, lymphoma / leukemia

Pregnancy-Associated Breast Cancer

= PABC = breast cancer that occurs during pregnancy / within 1 year of delivery
Frequency: 1÷3,000–10,000 pregnancies; 3% of all breast malignancies
Path: high rates of inflammatory tumor; lymph node involvement (in > 50%)
Histo: high-grade tumor (in > 50%); high prevalence of hormone-receptor–negative and HER2/neu–positive tumors ← aggressive biologic growth pattern
• palpable mass, swelling, erythema, diffuse breast enlargement
√ same radiologic features as for non-PABC
Mammo:
√ required to detect malignant microcalcifications, multifocality, multicentricity, bilaterality
Sensitivity: lower in pregnant / lactating patients ← increased glandular density

Recommendation: Try to avoid mammography during 1st trimester – evaluate breast disease with US instead!

Risk to fetus: malformations may occur with exposure to > 0.05 Gy of radiation

Dose: standard 2-view mammography of each breast performed with abdominal shielding subjects fetus to only 0.004 Gy of radiation

◊ Abdominal shielding can be performed during pregnancy with minimal / NO risk to fetus!

MR: MRI should be avoided during pregnancy!

Breast biopsy: cytologic diagnosis of breast lesions during pregnancy and lactation should be avoided – use core biopsy instead!

Prognosis: tendency for larger more advanced neoplasms at diagnosis → poorer outcome ← delayed diagnosis + aggressive growth pattern; recurrence common within 2–3 years

BREAST CYST

Frequency: most common single cause of breast lumps between 35 and 55 years of age

Age: any; most common in later reproductive years + around menopause

Histo: cyst wall lined by single layer of

(a) flattened epithelial cells
- cyst fluid with Na+/ K+ ratio ≥ 3

(b) epithelial cells with apocrine metaplasia → secretory function
- cyst fluid with Na+/K+ ratio < 3

Cause: fluid cannot be absorbed ← obstruction of extralobular terminal duct by fibrosis / intraductal epithelial proliferation

- size changes over time

◊ A simple cyst in a male is suspicious because benign cystic disease typically does not occur in men!

Simple Breast Cyst

√ well-defined flattened oval / round (if under pressure) mammographic mass + surrounding halo (DDx: well-defined solid mass)

√ solitary / multiple

√ needle aspiration of fluid (proof) + postaspiration mammogram as new baseline

US (98–100% accuracy):

◊ Correlate with palpation / mammogram as to size, shape, location, surrounding tissue density!

√ spherical / ovoid lesion with anechoic center

√ well-circumscribed thin echogenic capsule

√ posterior acoustic enhancement (may be difficult to demonstrate in small / deeply situated cysts)

√ thin edge shadows

√ occasionally multilocular ± thin septations / cluster of cysts

MR:

› T1WI:

√ well-circumscribed hypointense lesion without discernible cyst wall; well seen within adipose parenchyma; poorly seen in normal parenchyma

› enhanced T1WI:

√ no change in SI; improved demarcation ← enhancement of surrounding parenchyma

› T2WI:

√ well-circumscribed hyperintense lesion with homogeneous internal texture (detectable at a diameter of ~ 2 mm)

Pneumocystogram (for symptomatic cysts)

√ air remains mammographically detectable for up to 3 weeks

√ therapeutic effect of air insufflation (equal to 60–70% of aspirated fluid volume): no cyst recurrence in 85–94% (40–45% cyst recurrence without air insufflation)

Complex / Complicated Breast Cyst

= any cyst that does not meet criteria of simple cyst

Cause: fibrocystic changes (vast majority), infection, malignancy (extremely rare)

◊ 0.3% of all breast cancers are intracystic

◊ A complex cystic mass in a male should prompt Bx!

◊ Patients with apocrine cysts are at greater risk to develop breast cancer!

√ uniformly thick wall + tenderness = inflammation / infection

√ diffuse low-level internal echoes (= "foam" cyst):

(a) with mobility upon increase in power output

= subcellular material like protein globs, floating cholesterol crystals, cellular debris

(b) without mobility upon increase in power output

= cells like foamy macrophages, apocrine metaplasia, epithelial cells, pus, blood

√ fluid-debris level

Rx: aspiration to rule out blood / pus

√ thick septation / eccentric wall thickening further characterized by:

› protruding ill-defined outer margin

› convex microlobulated inner margin ("mural nodule")

› nonmobile mass with coarse heterogeneous echotexture

› color Doppler flow within thickening

Rx: treated like solid nodule

√ spongelike cluster of microcysts

Rx: treated like solid nodule

MR:

› T1WI:

√ hyper- / isointense cyst content (hemorrhage) ± sign of sedimentation

› enhanced T1WI:

√ thick ring-enhancing cyst wall (inflammation)

√ slight contrast uptake in surrounding tissue (= reactive hyperemia)

Rx: complete aspiration (assures benign cause), core needle biopsy (if partially / nonaspiratable)

DDx: artifactual scatter in superficial / deep small cysts, fibroadenoma, papilloma, carcinoma

Cyst Aspiration

- inspection of cyst fluid:
  (a) normal: turbid greenish / grayish / black fluid
  (b) abnormal: straw-colored clear fluid / dark blood

√ needle moves within nonaspiratable complex cyst

Processing of fluid:

(1) Fluid without blood should be discarded
(2) Bloody fluid should be examined cytologically

CARCINOMA OF MALE BREAST

Incidence: 1.3÷100,000 per year (in 2000); 2,600 new cases / year with 440 deaths (in 2016); 1% of all breast cancers; 0.17% of all male cancers

◊ 3.7% of male breast carcinomas occur in men with Klinefelter syndrome!

Peak age: 60–69 (mean, 59) years

At risk: males with chronically increased estrogen levels

1. Advanced age
2. Klinefelter syndrome (20- to 50-fold risk over normals): XXY chromosomes
3. Liver dysfunction: cirrhosis, schistosomiasis, malnutrition
4. Genetic predisposition: BRCA2 > BRCA1 mutation, family history in 1st-degree male / female relative (in up to 30%)
5. Testicular atrophy: injury, mumps orchitis, undescended testes
6. Radiation therapy to chest (latent period of 12–35 years)
7. Occupational heat exposure (diminished testicular function)
8. Jewish background

◊ Gynecomastia is NOT a risk factor!

Histo: same as in females; invasive ductal carcinoma NOS (80–85%), associated DCIS (35–50%), infiltrating mammary carcinoma with mixed features, invasive papillary carcinoma (2 x more than in women); invasive lobular carcinoma distinctly uncommon (tubular structures usually not found in male breast)

- breast swelling, bloody nipple discharge (25%)
- firm painless irregular mass ± associated gynecomastia
- nipple retraction, skin ulceration / thickening

Location: L > R breast; bilateral in < 1%

Site: retroareolar / upper-outer-quadrant

Mammo (screening not feasible ← low incidence):

√ high-density irregular mass:
  √ spiculated / lobulated / microlobulated margin resembling scirrhous carcinoma of female breast
  √ usually located eccentrically

√ microcalcifications (in only 13–30%): fewer + less linear (= more scattered) + more round + coarser than in female

√ solid nodules / papillary projections arising along a cyst wall (= papillary carcinoma)

√ enlarged axillary nodes (in 50% at time of presentation)

US:

√ invasive ductal carcinoma appears as a solid hypoechoic subareolar mass of irregular shape with spiculated / microlobulated margins, eccentric to the nipple!

√ metastases to pleura, lung, bone, liver

Delay in diagnosis from onset of symptoms: 6–18 months

Rx: simple / modified radical mastectomy + sentinel node biopsy, hormonal manipulation (85% estrogen receptor and 75% progesterone receptor positive)

Prognosis: 5-year survival rate for stage 1 = 82–100%, for stage 2 = 44–77%, for stage 3 = 16–45%, for stage 4 = 4–8% (same as for women!)

DDx: breast abscess, gynecomastia, epidermal inclusion cyst

DERMATOPATHIC LYMPHADENOPATHY

= benign reactive lymphadenopathy within breast associated with cutaneous rashes

Cause: exfoliative dermatitis, erythroderma, psoriasis, atopic dermatitis, skin infection)

Histo: follicular pattern retained, germinal centers enlarged, enlarged paracortical area with pale-staining cells (lymphocytes, Langerhans cells, interdigitating reticulum cells)

• mobile nontender firm subcutaneous nodules

Location: often bilateral

Site: predominantly upper outer quadrant

√ regional subcentimeter masses with central / peripheral radiolucent notches

DESMOID TUMOR (MAMMARY FIBROMATOSIS)

= LOW-GRADE FIBROSARCOMA = AGGRESSIVE FIBROMATOSIS

= rare tumor without metastatic potential

Incidence: over 100 isolated cases reported

Histo: spindled fibroblasts + myofibroblasts forming interlacing fascicles entrapping ducts + lobules; actin positive, variably positive for desmin + S-100; nuclear expression of β-catenin

May be associated with: trauma, surgery, Gardner syndrome, familial adenomatous polyposis, familial multicentric fibromatosis

M÷F = 3÷1

• painless firm mobile mass

• ± skin retraction, dimpling, nipple retraction

Size: 0.5–10 cm

√ spiculated mass without calcifications

√ hypoechoic mass with spiculated / irregular / microlobulated margins

√ low to intermediate SI on T1WI + variable SI on T2WI

√ benign progressive kinetic enhancement pattern (common)

MRI is the optimal modality for assessment of chest wall involvement, given its superior soft-tissue resolution and the locally aggressive nature of fibromatosis!

Prognosis: 27–29% recurrence rate

DIABETIC (FIBROUS) MASTOPATHY

= rare fibroinflammatory breast disease
Cause: long-standing type 1 diabetes → increased resistance of collagen to normal degradation
Histo: stromal sclerosis with an increased number of spindle cells, scattered epithelial cells and perivascular dense lymphocytic infiltrate
Age: young woman, 20 years after onset of diabetes
• firm to hard nontender breast mass
√ nonspecific discrete mass / regional asymmetry of dense tissue
US:
√ single / multiple bilateral masses hypoechoic to SQ fat
√ hypovascular / avascular on color flow imaging
√ posterior acoustic shadowing
Dx: (frequently required) core biopsy
DDx: breast cancer

DUCT ECTASIA

= nonspecific dilatation of one / more ducts > 2 mm / of ampullary duct segment > 3 mm
Cause: ?; periductal inflammation; malignancy
• occasionally nipple discharge / retraction
• palpable mass, pain / tenderness
(a) benign
Location: central
√ retroareolar serpentine radiodense structures converging on the nipple-areolar complex
√ anechoic smooth-walled branching structures tapering toward the periphery
√ filled with fluid / thick inspissated secretions or cellular debris ± movement of particulate matter
√ ± coarse smooth-bordered rod-/ cigar-shaped calcifications pointing toward the nipple
(b) malignant features
Location: peripheral
√ irregularity of duct margin
√ focal thickening of duct wall
√ adjacent hypoechoic tissue

An echogenic intraductal mass within an ectatic duct warrants biopsy to exclude malignancy!

DDx: blocked duct (during lactation); inflammatory infiltrate (masslike intraductal lesions); periductal mastitis (premenopausal, periductal enhancement)

EPIDERMAL INCLUSION CYST

= most common benign cutaneous / subcutaneous lesion

Origin: infundibulum (uppermost portion) of hair follicle

Cause: ?

(a) spontaneous: congenital, ? squamous metaplasia of ductal epithelium

(b) trauma (breast core biopsy, reduction mammoplasty → displacement of epidermis during surgery

Path: cyst filled with keratin

Histo: wall lined by stratified squamous epithelium

- palpable skin cyst with tiny visible skin opening:
  - smooth round nodule attached to skin with "blackhead" (= blackened pore = clogged hair follicle), movable against underlying tissue
- occasional whitish discharge from opening + subsequent decompression of palpable mass

√ circumscribed isodense or high-density mass

√ contiguous with dermis (tangential view)

√ ± calcifications

US:

√ hypoechoic well-circumscribed solid / cystic lesion

√ heterogeneous content ← variable amounts of internal keratinous debris and granulation tissue:

√ ± internal whorled / onion-ring appearance (= lamellated keratinous material)

√ ill-defined margins + peripheral vascularity if inflamed

Dx: CHARACTERISTIC imaging findings

◊ NO biopsy ← increased risk of inflammatory response

DDx: sebaceous cyst (indistinguishable)

FAT NECROSIS OF BREAST

= TRAUMATIC LIPID CYST = OIL CYST

= nonsuppurative saponification of fat by tissue lipase ← local destruction of fat cells with release of lipids + hemorrhage + fibrotic proliferation

Etiology: direct external trauma (seat belt injury), lumpectomy, reduction mammoplasty, implant removal, breast reconstruction, irradiation, nodular panniculitis (Weber-Christian disease), ductal ectasia of chronic mastitis, foreign body reaction (to silicone / paraffin injection)

Prevalence: 0.5% of breast biopsies

At risk: middle-aged obese women with fatty pendulous breasts

Histo: cavity with oily material surrounded by "foam cells" (= lipid-laden macrophages)

- history of trauma in 40% (eg, prior surgery, radiation > 6 months ago, reduction mammoplasty, lumpectomy)
- usually clinically occult
- firm, slightly fixed tender / painless mass
- skin retraction (50%); yellowish fatty fluid on aspiration

Location: anywhere; more common in superficial periareolar region; near biopsy site / surgical

scar
√ early: ill-defined irregular spiculated dense mass
√ later: well-circumscribed mass with translucent areas at center (= homogeneous fat density of oil cyst) surrounded by thin pseudocapsule (in old lesion)
√ calcifies in 4–7% (= liponecrosis macrocystica calcificans):
√ occasionally curvilinear / eggshell calcification in wall
√ fine spicules of low density vary with projection
√ localized skin thickening / retraction possible
US:
√ hypo- / anechoic mass with ill- / well-defined margins ± acoustic shadowing
√ occasionally echogenic ± acoustic shadowing
√ complex cyst with mural nodules / echogenic bands
MR:
› T1WI:
√ signal intensity nearly isointense to fat
√ round lesion with hyperintense fat signal (oil cyst)
√ signal loss with macrocalcifications
› enhanced T1WI:
√ localized ill-defined area of moderate enhancement + continuous postinitial increase (= granulation tissue) within 6 months after trauma
√ rim-enhancement / no enhancement in late lesion / oil cyst
› T2WI:
√ ill-defined hyperintense area (= reactive edema of fresh lesion)
√ round lesion with central SI of fat (in oil cyst)
DDx: breast cancer (indistinguishable from carcinoma if associated with distortion, skin thickening, retraction), breast abscess

Weber-Christian Disease

= nonsuppurative panniculitis with recurrent bouts of inflammation = areas of fat necrosis, involving subcutaneous fat + fat within internal organs
• accompanied by fever + nodules over trunk and limbs

FIBROADENOMA

= ADULT-TYPE FIBROADENOMA
= estrogen-induced benign fibroepithelial tumor originating from TDLU; forms during adolescence; pregnancy and lactation are growth stimulants; regression after menopause (mucoid degeneration, hyalinization, involution of epithelial components, calcification)
Frequency: 3rd most common type of breast lesion after fibrocystic disease + carcinoma; most common benign solid tumor in women of childbearing age (~ 10%)
Mean age: 30 (range, 13–80) years; most common breast tumor under age 25 years
Hormonal influence:
slight enlargement at end of menstrual cycle + during pregnancy; regresses after menopause; may occur in postmenopausal women receiving estrogen replacement therapy
Path: well-circumscribed smooth / mildly lobulated mass with well-demarcated interface

between stroma + uninvolved parenchyma (NO capsule)

Histo: concurrent proliferation of fibrous stroma + glandular epithelium

(a) intracanalicular fibroadenoma: dense stroma compressing ducts into slitlike space

(b) pericanalicular fibroadenoma: NO duct compression

(c) combination

◊ Cellular FA = highly cellular predominantly epithelial elements in younger woman

◊ Fibrous FA = acellular predominantly fibrotic elements in older postmenopausal woman

- slowly enlarging firm rubbery, smooth, sometimes lobulated, freely movable mass
- in 35% not palpable; NO skin fixation
- rarely tender / painful; clinical size = radiographic size

Size: 1–5 cm (in 60%)

Location: multifocal in 15–25%; bilateral in 4%; often located in upper outer quadrant

√ circular / oval-shaped lesion of low density

√ nodular / lobulated contour when larger (= areas with different growth rates)

√ well-defined smooth discrete margins (indistinguishable from cysts when small)

√ often with "halo" sign

√ smoothly contoured calcifications of high + fairly equal density in 3% ← necrosis from regressive changes in older women:

(a) peripheral subcapsular myxoid degeneration

√ peripheral marginal ring- / dotlike calcifications that coalesce over time

(b) central myxoid degeneration

√ "popcorn" type of calcification (PATHOGNOMONIC)

(c) small calcifications within ductal elements

√ pleomorphic / dystrophic linear ± branching pattern

Dx: biopsy may be necessary

◊ Calcifications enlarge as soft-tissue component regresses!

US:

√ round (3%) / oval (96%) mass with long axis parallel to chest wall with length-to-depth ratio of > 1.4 (in carcinomas usually < 1.4)

√ hypoechoic similar to fat lobules (80–96%) / hyperechoic / mixed pattern / anechoic / isoechoic compared with adjacent fibroglandular tissue

√ homogeneous (48–89%) / inhomogeneous (12–52%) texture

√ regular (57%) / lobulated (15–31%) / irregular (6–58%) contour

√ "hump and dip" sign = small focal contour bulge immediately contiguous with a small sulcus (57%)

√ intratumoral bright echoes (10%) = macrocalcifications

√ posterior acoustic enhancement (17–25%) / acoustic shadow without calcifications (9–11%)

√ echogenic halo (capsule) with lateral shadowing

√ slight compressibility of tumor

√ avascular / some central vascularity on color flow imaging

MR:

› T1WI:

√ iso- / mildly hypointense compared to parenchyma
√ more obvious in fatty tissue
√ endotumoral signal loss ← macrocalcifications
› enhanced T1WI:
√ very strong enhancement (with proportionately larger epithelial component)
√ postinitial continuous increase / plateau
√ endotumoral septa with mild contrast uptake
› T2WI:
√ high SI (for tumor with proportionately larger epithelial component) in 50%
√ occasionally endotumoral septations ← fibrotic component
√ iso- / slightly hypointense compared to breast parenchyma (for predominantly fibrotic tumor) in 50%

Management: follow-up in 6 month to assess interval growth
Cx: spontaneous infarction (esp. during 3rd trimester of pregnancy / after delivery) ← intravascular thrombosis
DDx: phyllodes tumor (rapid growth, recurrence of fibroadenoma, cellular fibroadenoma in postmenopausal patient); adenosis tumor / florid adenosis

Juvenile / Giant / Cellular Fibroadenoma

= fibroadenoma > 5 cm in diameter / weighing > 500 g
Frequency: 7–8% of all fibroadenomas; multiple / bilateral in 10–25%
Cause: hyperplasia + distortion of normal breast lobules ← hormonal imbalances between estradiol + progesterone levels
Age: any (mostly in adolescent girls); most often in African-American girls
Histo: more glandular + more stromal cellularity than adult type of fibroadenoma; ductal epithelial hyperplasia
• rapidly enlarging well-circumscribed nontender mass
• dilated superficial veins, stretched skin ± ulceration
√ discrete mass with rounded borders
√ ± cleftlike depressions and tiny cysts (similar to phyllodes tumor)
MR:
› T1WI:
√ iso- to slightly hypointense round / oval mass difficult to separate from normal breast parenchyma
› enhanced T1WI:
√ strong enhancement with sharp demarcation from surrounding tissue + endotumoral septations
› T2WI:
√ typically hyperintense
Cx: infarction → edema, hemorrhage
DDx: medullary / mucinous / papillary carcinoma / carcinoma within fibroadenoma

Tubular Adenoma

= variant of pericanalicular fibroadenoma with florid epithelium like in adenosis

FIBROCYSTIC CHANGES

= MAZOPLASIA = MASTITIS FIBROSA CYSTICA = CHRONIC CYSTIC MASTITIS = CYSTIC DISEASE = GENERALIZED BREAST HYPERPLASIA = DESQUAMATED EPITHELIAL HYPERPLASIA = FIBROADENOMATOSIS = MAMMARY DYSPLASIA = SCHIMMELBUSCH DISEASE = FIBROUS MASTITIS = MAMMARY PROLIFERATIVE DISEASE

◊ Not a disease since it is found in 72% of screening population > 55 years of age

◊ The College of American Pathologists suggests use of the term "fibrocystic changes / condition" in mammography reports!

Prevalence: most common diffuse breast disorder; in 51% of 3,000 autopsies

Age: 35–55 years

Etiology: exaggeration of normal cyclical proliferation + involution of the breast with production + incomplete absorption of fluid by apocrine cells ← hormonal imbalance

Histo:

(1) overgrowth of fibrous connective tissue = stromal fibrosis, fibroadenoma
(2) cystic dilatation of ducts + cyst formation (in 100% microscopic, in 20% macroscopic)
(3) hyperplasia of ducts + lobules + acini = adenosis; ductal papillomatosis

• asymptomatic with macrocystic disease
• fullness, tenderness, pain in microcystic disease
• palpable nodules + thickening
• symptoms occur with ovulation
• regression with pregnancy + menopause

√ individual round / ovoid cysts with discrete smooth margins
√ lobulated multilocular cyst
√ enlarged nodular pattern (= fluid-distended lobules + extensive extralobular fibrous connective tissue overgrowth)
√ "teacup-like" curvilinear thin calcifications with horizontal beam + low-density round calcifications in craniocaudal projection = milk of calcium (4%)
√ "oyster pearl–like" / psammoma-like calcifications
√ "involutional type" calcifications = very fine punctate calcifications evenly distributed within one / more lobes against a fatty background ← mild degree of hyperplasia in subsequently atrophied glandular tissue

US:

√ ductal pattern, ductectasia, multiple cysts of varying size, ill-defined focal echogenic lesions with / without posterior sound attenuation

MR:

› T1WI:
√ hypointense compared to intramammary adipose tissue
√ interspersed hypointense cysts of varying sizes

› enhanced T1WI:
√ patchy to diffuse increased enhancement (correlating with degree of adenosis)
◊ Avoid scheduling patient during 1st and 4th week of menstrual cycle / under HRT
√ continuous rise after postinitial phase

› T2WI:
√ occasionally diffusely increased SI (in 2nd half of menstrual cycle / under HRT)

√ interspersed hyperintense cysts of varying sizes

Risk for invasive breast carcinoma:

A. NO INCREASED RISK (70%)
   1. Nonproliferative lesions: adenosis, florid adenosis, apocrine metaplasia without atypia, macro- / microcysts, duct ectasia, fibrosis, mild hyperplasia (more than 2 but not more than 4 epithelial cells deep), mastitis, periductal mastitis, squamous metaplasia
   2. Fibroadenoma

B. SLIGHTLY INCREASED RISK (1.5–2 times):
   1. Moderate + florid solid / papillary hyperplasia
   2. Papilloma with fibrovascular core
   3. Sclerosing adenosis

C. MODERATELY INCREASED RISK (5 times):
   Ductal / lobular atypical hyperplasia (= borderline lesion with some features of carcinoma in situ)

D. HIGH RISK (8–11 times):
   1. Atypical hyperplasia + family history of breast cancer
   2. Ductal / lobular carcinoma in situ

Classification of Fibrocystic Changes

Grade	*Frequency*	*Histological Category*	*Breast Cancer Risk*
I	70%	Nonproliferative lesion	0
II	25%	Proliferative lesion without atypia	2x
III	5%	Proliferative lesion with atypia	4–5x

Adenosis

Age: all

Path: lobulocentric lesion derived from TDLU with distortion and effacement of underlying lobules

Histo: epithelial and myoepithelial proliferation of ductules + lobules with nuclear pleomorphism + increase in cell size

√ increase in size of TDLUs to 3–7 mm

√ "snowflake pattern" of widespread ill-defined nodular densities

√ often round intralobular microcalcifications / milk of calcium (less common + less extensive than in sclerosing adenosis)

US:

√ adenosis lobules are sonographically iso- to mildly hypoechoic compared with fat

MR:

√ no abnormalities on T1WI / T2WI

√ usually strong, occasionally branching contrast uptake in focal areas of adenosis

DDx: malignancy

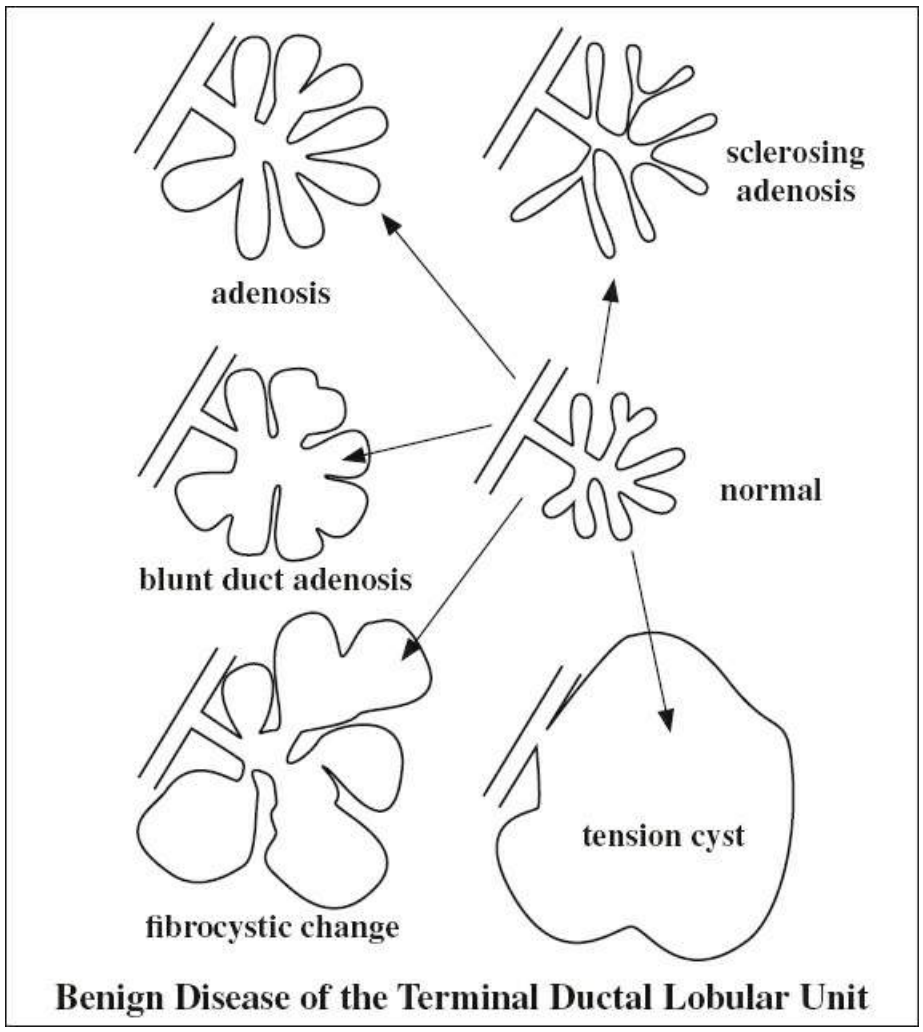
Sclerosing Adenosis

Path: myoepithelial proliferation + reactive stromal fibrosis
Histo: stromal sclerosis involving > 50% of all TDLUs, which become elongated + distorted + compressed by sclerosis
DDx: tubular carcinoma (absence of basement membrane + myoepithelial cells); radial scar (more extensive fibrosis + central fibrocollagenous scar)

- palpable mass (rare) = "adenosis tumor"

Rarely associated with: lobular carcinoma in situ > ductal carcinoma in situ

◊ Sclerosing adenosis is not a risk factor / precursor of breast cancer!



Benign Disease of the Terminal Ductal Lobular Unit

√ punctate calcifications of calcium oxalate casts forming in obstructed acini in 50%

(a) focal form
- √ "rosettes" = focal cluster of microcalcifications occupying all acini of one / several TDLUs
- √ architectural distortion
- √ focally dense breast → as a nodule / spiculated lesion

(b) diffuse form
- √ adenosis + diffusely scattered "starry night" calcifications

√ diffusely dense breast

DDx: other spiculated lesions

Adenosis Tumor = Florid Adenosis

Average age: 30 years

Histo: focal proliferation of ductules and lobular glands with hyperplasia of epithelial + myoepithelial cells

• firm clinically discrete / ill-defined mass

√ nodular mass usually < 2 cm in diameter

√ ± microcalcifications

DDx: fibroadenoma

Gestational & Secretory Hyperplasia

(a) gestational (= related to pregnancy):

Histo: calcifications in lobular acini

√ round microcalcifications in a diffuse / focal distribution (most commonly)

(b) secretory (= related to lactation)

Histo: ductal hyperplasia

√ irregular microcalcifications in a linear distribution + branching pattern closely resembling malignancy (less commonly)

(c) coexistence of both types of microcalcifications

DDx: pseudolactational hyperplasia (same radiologic-pathologic findings in nonpregnant nonlactating women)

Fibrosis

√ round / oval clustered microcalcifications with smooth contours + associated fine granular calcifications filling lobules

Atypical Lobular Hyperplasia

= proliferation of round cells of LCIS type growing along terminal ducts in permeative fashion (pagetoid growth) between benign epithelium + basal myoepithelium BUT NOT completely obliterating terminal ductal lumina / distending lobules (as in lobular carcinoma in situ)

√ no mammographic correlate

Atypical Ductal Hyperplasia

= low-grade intraductal proliferation with partial / incompletely developed features of noncomedo DCIS

√ frequent calcifications

Sclerosing Lobular Hyperplasia

= FIBROADENOMATOID MASTOPATHY

= benign proliferative lesion

Path: enlarged lobules, increased number of intralobular ductules, sclerosis of intralobular septa

Mean age: 32 years; black woman
• palpable circumscribed mass
√ resembles noncalcified fibroadenoma

FIBROUS NODULE OF BREAST

= FIBROUS DISEASE OF THE BREAST = FIBROUS DISEASE = FOCAL FIBROSIS OF THE BREAST = FIBROUS MASTOPATHY = FIBROUS TUMOR OF THE BREAST
Frequency: 3–4% of benign masses; 8% of surgical breast specimens
Histo: focally dense collagenous stroma surrounding atrophic epithelium; NONSPECIFIC
Age: 20–50 years; only 8% postmenopausal
• palpable / nonpalpable mass: edge merges into surrounding dense tissue
Location: unilateral (80–85%) / bilateral (15–20%)
√ circumscribed (55%) / indistinct (32%) margin
√ suggestive of malignancy (11%): irregular shape, spiculated margin, posterior acoustic shadowing
DDx: fibroadenoma, malignancy

GALACTOCELE

= retention cyst of fatty material in areas of cystic duct dilatation appearing during / (more commonly) shortly after lactation
◊ Most common benign breast lesion in lactating women!
Cause: ? abrupt suppression of lactation / obstructed milk duct
Path: smooth-walled cyst lined by simple cuboidal to columnar apocrine-type epithelium filled with milky fluid; often accompanied by inflammatory / necrotic debris ← leakage of cyst fluid
Age: occurs during / shortly after lactation; may occur in children of either gender
• enlarging painless mass; thick inspissated milky fluid (colostrum)
Location: retroareolar area; uni- / bilateral
√ large radiopaque lesion of water density (1st phase)
√ smaller lesion of mixed density + SPECIFIC fat-water level with horizontal beam (2nd phase)
√ pseudohamartoma = NO physical separation of fat + water ← high viscosity of milk
√ pseudolipoma = small radiolucent lesion resembling lipoma
√ ± fluid-calcium level
US:
√ heterogeneous complex mass / cyst with a mixture of low + high internal echogenicity ← hypoechoic water component + hyperechoic fat component
√ hyperechoic-hypoechoic fat-fluid level ← fresh milk
√ well-defined solid-appearing mass with posterior acoustic enhancement + highly echogenic material
MR:
√ enhancement of wall + septations
Cx: infection (relatively common)
Dx: diagnostic + therapeutic aspiration of milky fluid

GIGANTOMASTIA

= very rare condition characterized by massive enlargement of both breasts

Incidence: 1÷100,000 pregnancies

Etiology: ? abnormal response to hormonal stimulation during pregnancy

• dramatic growth of breasts up to 4–6 kg per breast → dyspnea

√ radiologic studies NOT required

Cx: tissue necrosis, ulceration, infection, hemorrhage

Rx: bromocriptine administration; surgical intervention (reduction mammoplasty / simple mastectomy with posterior reconstruction) if disorder progresses

GYNECOMASTIA

= benign usually reversible excessive development of male breast

◊ NOT a risk factor for development of breast cancer!

◊ Most common disease in males

Cause:

(1) Hormonal stimulation by excess estrogens or decreased androgens
   (a) neonate: influence from maternal estrogens crossing placenta
   (b) puberty: high estradiol levels
      Prevalence: in up to 60–75% of healthy adolescents
      Age: 1 year after onset of puberty (13–14 years)
      Prognosis: subsides within 1–2 years
   (c) senescence: decline in serum testosterone levels of elderly
   (d) hypogonadism (Klinefelter syndrome, anorchism, acquired testicular failure (eg, testicular neoplasm), pituitary hormone deficiency

(2) Other hormonal disorders obesity (increased conversion of testosterone to estrogen), hyperthyroidism

(3) Neoplasm: hepatoma (with estrogen production), feminizing adrenocortical tumor, gonadotropin-secreting tumor (hepatoblastoma, fibrolamellar carcinoma, choriocarcinoma), pituitary tumor (prolactinoma), estrogen-producing testicular tumor (Sertoli / Leydig cell tumor), hyperthyroidism, testicular feminization syndrome, neurofibromatosis I

(4) Systemic disorders
advanced alcoholic cirrhosis, hemodialysis in chronic renal failure, chronic pulmonary disease (emphysema, TB), malnutrition

Gynecomastia versus Male Breast Cancer		
Feature	*Gynecomastia*	*Breast Cancer*
Age	peripubertal + > 50 years	> 60 years
Clinical	soft tender; mobile mass	soft / firm nontender / nonmobile mass
Site	central	eccentric
Location	(commonly) bilateral	(usually) unilateral
Mammo	fan- / flame-shaped density	discrete mass, calcifications, skin thickening, nipple retraction, axillary adenopathy

(5) Drug-induced
marijuana, anabolic steroids, corticosteroids, leuprolide acetate (Lupron Depot®), estrogen treatment for prostate cancer, thiazide diuretics, cimetidine, omeprazole, digitalis, spironolactone, reserpine, isoniazid, ergotamine, diazepam, tricyclic antidepressants

(6) Idiopathic

mnemonic: CODES
Cirrhosis
Obesity
Digitalis
Estrogen
Spironolactone

Frequency: 85% of all male breast masses
Age: neonatal period; adolescent boys (40%); men > 50 years (32%)
Histo: hyperplasia (= increased number) of ducts, proliferation of duct epithelium, periductal edema, fibroplastic stroma, adipose tissue

- breast enlargement
- (usually) uni- (less common) bilateral breast tenderness, subjective burning sensation
- palpable firm nodules > 2 cm in subareolar region

Location: bilateral (63%), left-sided (27%), right-sided (10%)
Site: concentric to the nipple-areola complex
Pattern:

Gynecomastia has 3 radiographic patterns: nodular, dendritic, diffuse, which reflect the underlying pathologic changes.

(a) nodular gynecomastia: in early florid phase
- symptoms for less than 1 year

Histo: hyperplasia of intraductal epithelium + periductal inflammation + stromal edema
√ hypoechoic subareolar nodule of disk / fan shape ± hypervascularity
√ indistinct borders
Prognosis: reversible if stimulus eliminated

(b) dendritic gynecomastia: during quiescent fibrotic phase
- symptoms for more than 1 year

Histo: fibrous gynecomastia with more hyalinized fibrous stroma + dilated ducts

√ flame-shaped subareolar density with linear projections interdigitating into deeper adipose tissue
√ fingerlike projections extending into retroareolar breast
Prognosis: irreversible ← fibrosis

(c) diffuse glandular gynecomastia
• often 2° to exposure to high-dose exogenous estrogen
√ heterogeneously dense breasts
√ combination of nodular + dendritic gynecomastia

US:
√ hypoechoic echotexture
√ absence of posterior acoustic enhancement
√ mild prominence of subareolar ducts in nodular / poorly defined / flame-shaped distribution (focal type)
√ homogeneously dense breast (diffuse type)

MR:
√ hypointense retromamillary area
√ no / slight contrast enhancement

Rx: surgical removal; discontinuation of offending drug

DDx: **pseudogynecomastia** (= fatty proliferation without glandular elements in obese males); breast cancer (hard / firm to palpation, usually unilateral, frequently not central to nipple-areola complex)

HAMARTOMA OF BREAST

= FIBROADENOLIPOMA = LIPOFIBROADENOMA = ADENOLIPOMA

Prevalence: 2 –16 ÷ 10,000 mammograms

Mean age: 45 (range, 27–88) years

Histo: normal / dysplastic mammary tissue composed of dense fibrous tissue + variable amount of fat, delineated from surrounding tissue without a true capsule

• soft, often nonpalpable (60%)

Location: retroareolar (30%), upper outer quadrant (35%)

√ round / ovoid well-circumscribed mass usually > 3 cm
√ mixed density with mottled center (2° to fat) = "slice of sausage" pattern
√ thin smooth pseudocapsule (= thin layer of surrounding fibrous tissue)
√ "halo" sign = peripheral radiolucent zone ← compression of surrounding tissue
√ may contain calcifications

MR:
› T1WI:
√ well-circumscribed round / oval / lobulated lesion with pseudocapsular demarcation:
√ intermediate intensity for parenchymal component
√ high intensity for lipomatous component
√ low intensity for cystic component
› enhanced T1WI:
√ no / strong enhancement in parenchymal component with continuous postinitial increase (dependent on vascularization)

› T2WI:
√ intermediate intensity for parenchymal + lipomatous components
√ high intensity for cystic component

DDx: liposarcoma, Cowden disease

HEMANGIOMA OF BREAST

= rare tumor in breast

Incidence: up to 11% at autopsies

Histo: dilated endothelium-lined vascular channels filled with erythrocytes; negative for S-phase kinase-associated protein 2; low value for Ki-67

Classification: capillary / cavernous

• may be palpable

Location: within superficial tissue; parallel to chest wall

√ circumscribed oval / macrolobulated mass ± calcifications

US:

√ well-defined hypoechoic / ill-defined hyperechoic mass (DDx: fibroadenoma; complex cyst)

MR:

√ ovoid mass with intermediate SI on T1WI (similar to fibroglandular tissue) ± peripheral areas of ↑ signal ← fat
√ hyperintense on T2WI ← cavernous / cystic spaces with slow-flowing blood
√ low–signal-intensity foci ← calcification / flow void / fibrosis / thrombosis
√ early diffuse enhancement (DDx: angiosarcoma)
√ delayed central fill-in enhancement

Clue: excessive bleeding during core biopsy

DDx: low-grade angiosarcoma (skin discoloration, large palpable lesion, positive for S-phase kinase-associated protein 2, value for Ki-67 > 175 on pathology)

HEMATOMA OF BREAST

= area of localized hemorrhage

Cause: (1) Surgery / biopsy (most common)
(2) Blunt trauma
(3) Coagulopathy: leukemia, thrombocytopenia
(4) Anticoagulant therapy

√ well-defined ovoid mass (= hemorrhagic cyst)
√ ill-defined mass with diffuse increased density ← edema + hemorrhage)
√ adjacent skin thickening / prominence of reticular structures
√ regression within several weeks leaving
(a) no trace
(b) architectural distortion
(c) incomplete resolution
√ calcifications (occasionally)

US:

√ complex hypoechoic mass with internal echoes dependent on age of hematoma:

√ hyperechoic (in acute stage + occasionally before resolution)
√ hypoechoic to anechoic (= hematoma progression)

MR:

› T1WI:
√ homogeneous high signal ± sedimentation (fresh)
√ low SI + peripheral ring of high signal (deoxyhemoglobin of subacute hematoma)

› enhanced T1WI:
√ no uptake within hematoma
√ moderate diffuse reactive enhancement surrounding hematoma + continuous postinitial increase

› T2WI:
√ homogeneous low signal intensity (fresh)
√ low SI + peripheral ring of low SI

Dx: resolution on short-term follow-up; biopsy

JUVENILE PAPILLOMATOSIS

= distinctive rare benign clinical-pathologic entity that characteristically involves young patients

Frequency: low but increasing

Path: 1–8 cm tumor composed of many aggregated cysts of < 2 cm with interspersed dense stroma ("swiss cheese disease"); calcifications common

Histo: multiple macrocysts lined by flat duct epithelium / epithelium with apocrine metaplasia, sclerosing adenosis, ductectasia; marked papillary hyperplasia of duct epithelium with often extreme atypia

Mean age: 23 (range, 12–48) years

• localized palpable firm tumor; no nipple discharge
• family history of breast cancer in 28–58% (affected first-degree relative in 8%; in one / more relatives in 28–53%)

√ usually negative mammogram / asymmetric density
√ ± microcalcifications
√ marked enhancement with benign enhancement profile on MR

US:

√ ill-defined hypoechoic masses filled with multiple cysts of variable size clearly demarcated from surrounding normal parenchyma

Prognosis: development of synchronous (4%) / metachronous (5–15%) breast cancer after 8–9 years

Recommendation: follow-up of female relatives ← development of carcinomas in nearly 50%

Dx: may be suspected with core biopsy

Rx: complete surgical excision requiring negative margins

DDx: fibroadenoma

LACTATING ADENOMA

= newly discovered painless benign breast mass during pregnancy / lactation

Etiology: ?

(a) adenomatous / lactational transformation of preexisting fibroadenoma / tubular adenoma / lobular hyperplasia
(b) de novo neoplasm unique to pregnancy

Path: well-circumscribed yellow spherical mass with lobulated surface + rubbery firm texture and without capsule

Histo: pure adenoma composed of secretory lobules lined by granular and foamy to vacuolated cytoplasm separated by scant stromal components of connective tissue

• firm rubbery smooth slightly lobulated freely movable mass
• may enlarge rapidly during first 2 trimesters
• usually painless unless infarction has occurred

Size: typically < 3 cm

Mammo (insensitive ← increased breast density during pregnancy):
√ mass of equal / slightly decreased density = fat content of milk ← lactational hyperplasia
√ punctate calcifications may be present

US:
√ usually benign features:
√ homogeneously hypoechoic / isoechoic mass
√ smooth lobulations + well-defined margins
√ long axis parallel to chest wall
√ posterior acoustic enhancement
√ occasionally malignant features:
√ irregular angulated margins
√ posterior acoustic shadowing
√ fibrous septa may be present
√ ± small central hyperechoic foci (= fat within milk)
√ increased vascularity by Doppler

Dx: biopsy

Cx: infarction → painful breast mass

Prognosis: regression after completion of breast feeding

Rx: excision if without spontaneous resolution / with pain

DDx: fibroadenoma; complex cyst; tubular adenoma (rare, typically in young woman); galactocele (after cessation of breast feeding); phyllodes tumor; lymphoma; breast carcinoma (1÷1,300–1÷6,200 pregnancies)

LIPOMA OF BREAST

= usually solitary unilateral asymptomatic slow-growing lesion
◊ Most common benign tumor of male breast

Prevalence: extremely rare

Histo: encapsulated tumor containing mature fat cells

Mean age: 45 years + post menopause

• clinically often occult; soft, freely movable, well delineated
√ usually > 2 cm
√ radiolucent tumor easily seen in dense breast; almost invisible in fatty breast
√ discrete thin radiopaque line (= capsule), seen in most of its circumference

√ displacement of adjacent breast parenchyma
√ calcification with fat necrosis (extremely rare)
√ may enlarge in response to hormonal stimulation
US:
√ homogeneously hypo-, iso- or mildly hyperechoic lesion
√ posterior acoustic enhancement possible
√ ± encapsulated margin
√ no internal / peripheral vascularity
MR:
› T1WI:
√ well-circumscribed hyperintense lesion
√ ± thin hypointense capsule
√ no contrast enhancement
› T2WI:
√ signal intensity equivalent to subcutaneous fat
DDx: fat lobule surrounded by trabeculae / suspensory ligaments; fat necrosis

Angiolipoma of Breast

= rare fat-containing tumor
Frequency: 5–17% of all benign fatty tumors
Path: mature adipocytes intermixed with vascular proliferation; NO malignant potential
(a) infiltrative type
(b) noninfiltrative type: in breast
Histo: vascular lesion with cellular atypia + mitotic activity; HALLMARK of scattered microthrombi in small blood vessels
Location: back, neck, shoulder, rare in breast
• faint skin discoloration
√ solid circumscribed mass without characteristic imaging finding
√ asymmetry with mixed density (= soft-tissue density interspersed with fat density)
US:
√ iso- to hyperechoic / hypoechoic mass with internal vascularity
Dx: biopsy required to make diagnosis
DDx: lipoma; fibroadenolipoma (hamartoma)

LYMPHOMA OF BREAST

A. PRIMARY LYMPHOMA
= extranodal lymphoma of the breast without prior history of lymphoma / leukemia
Prevalence: 0.12–0.53% of all breast malignancies; 2.2% of all extranodal lymphomas
• asymptomatic
B. SECONDARY LYMPHOMA
◊ One of the most common metastatic lesion in the breast!
• fever, pain
Histo: B-cell NHL (majority), Hodgkin disease, leukemia (CLL), plasmacytoma
Age: 50–60 years; M < F

Location: right-sided predominance; 13% bilateral
√ well / incompletely circumscribed round / oval lobulated mass / masses
√ infiltrative with poorly defined borders
√ NO calcifications / spiculations
√ skin thickening + trabecular edema
√ bilateral axillary adenopathy in 30–50%
US:
√ oval / round homo- / heterogeneously hypoechoic mass(es)
√ sharply defined / poorly defined borders
√ posterior acoustic shadowing / enhancement
Prognosis: 3.4% 5-year disease-free survival for all stages; 50% remission rate with aggressive chemotherapy
Recurrence: mostly in contralateral breast / other distant sites
DDx: circumscribed breast carcinoma, fibroadenoma, phylloides tumor, metastatic disease

Pseudolymphoma
= lymphoreticular lesion as an overwhelming response to trauma

MAMMARY DUCT ECTASIA

= PLASMA CELL MASTITIS = VARICOCELE TUMOR OF BREAST = MASTITIS OBLITERANS = COMEDOMASTITIS = PERIDUCTAL MASTITIS = SECRETORY DISEASE OF BREAST
= rare aseptic inflammation of subareolar area
Pathogenesis (speculative):
(1) Stasis of intraductal secretion → duct dilatation + leakage of inspissated material into parenchyma → aseptic chemical mastitis (periductal mastitis); the extravasated material is rich in fatty acids → nontraumatic fat necrosis
(2) Periductal inflammation → damage to elastic lamina of duct wall → duct dilatation
Histo: ductal ectasia, heavily calcified ductal secretions; infiltration of plasma cells + giant cells + eosinophils
Mean age: 54 years; may develop in young children
• often asymptomatic; bloody nipple discharge in children
• breast pain, nipple retraction, mamillary fistula, subareolar breast mass
Location: subareolar, often bilateral + symmetric; may be unilateral + focal
√ dense triangular mass with apex toward nipple
√ duct dilatation = distended ducts connecting to nipple
√ periphery blending with normal tissue
√ multiple often bilateral dense round / oval a few mm long calcifications with lucent center + polarity (= linear orientation toward subareolar area / nipple)
(a) periductal
√ oval / elongated calcified ring around dilated ducts with very dense periphery (= surrounding deposits of fibrosis + fat necrosis)
(b) intraductal
√ fairly uniform linear, often rod-shaped / sausage-shaped / needle-shaped calcifications of wide caliber, occasionally branching (within ducts / confined to duct walls)

√ nipple retraction / skin thickening may occur
Sequelae: cholesterol granuloma
DDx: breast cancer

MAMMOPLASTY

= COSMETIC BREAST SURGERY

Augmentation Mammoplasty

◊ Most frequently performed plastic surgery in USA
Frequency: 307,180 procedures in 2011 (70% for cosmetic reasons, 30% for reconstruction); 5,083,717 American women have breast implants (estimate for 2010) = 4.9% (census data)
Methods:

1. Injection augmentation (no longer practiced): paraffin, silicone, fat from liposuction
   Cx: tissue necrosis resulting in dense, hard, tender breast masses; lymphadenopathy; infection; granuloma formation (= siliconoma)
2. Implants (prepectoral / subpectoral)
   (a) spongelike masses of Ivalon®, Etheron®, Teflon®
   (b) Silicone elastomer (silastic) smooth / textured shell containing silicone oil / saline: > 100 varieties of dimethylpolysiloxane
   › single lumen of polymerized methyl polysiloxane with smooth / textured outer silicone shell / polyurethane coating
   › double lumen with inner core of silicone + outer chamber of saline
   › "reverse double-lumen" = inner saline-filled lumen surrounded by silicone-filled envelope
   › triple lumen

Silicone breast implants were FDA-approved for primary breast augmentation in 2006.

   (c) expandable implant ± intraluminal valves = saline injection into port with gradual tissue expansion for breast reconstruction
   Location: retroglandular / subpectoral
3. Autogenous tissue transplantation
   (for breast reconstruction) with musculocutaneous flap: transverse rectus abdominis muscle (TRAM), latissimus dorsi, tensor fasciae latae, gluteus maximus

Mammographic technique for implants:

1. Two standard views (CC and MLO views) for most posterior breast tissue
   ◊ 22–83% of fibroglandular breast tissue obscured on standard views by implant depending on size of breast + location of implant + degree of capsular contraction!
   ◊ The false-negative rate of mammography increases from 10–20% to 41% in patients with implants!
2. Two Eklund (= implant displacement) views (CC and 90° LAT views) for compression views of anterior breast tissue = "push-back" view = breast tissue pulled anteriorly in front of implant while implant is pushed posteriorly + superiorly thus excluding most of the implant

Mammographic sensitivity for breast cancer detection: 45% with augmentation versus 67% without

augmentation

MR technique for implants:

Physical principle: resonant frequencies of water, fat (~ 220 Hz lower than water) and silicone (~ 100 Hz lower than fat) differ

Most effective sequence: inversion recovery (IR), which suppresses fat

(a) with additional suppression of water = pure depiction of silicone

(b) with additional suppression of silicone = pure depiction of saline component

Orientation: axial + sagittal (2 angulations mandatory)

Cx of silicone-gel–filled implant:

Screening MRI for asymptomatic implant rupture at 3 years after implantation followed by 2-year intervals!

◊ Increase of complication rate with **augmentation** (desire for a larger breast) > **reconstruction** (after mastectomy) > **revision** (subsequent surgery in 15–25%)

1. **Capsular fibrosis** (100%)
   = normal host response to wall off foreign body
   √ low-intensity implant shell + fibrous capsule cannot be differentiated on MR
   √ physiologic fluid may occupy space between implant shell + fibrous capsule
   √ radial folds (normal) = hypointense lines emanating from the fibrous capsule-shell junction as a wrinkle
   √ gently undulating circumferential contour (normal)
2. **Contracture** (12–20%): more frequent with retroglandular implants → increasing with time
   • distortion of breast contour, hardening of breast
   • tightness, pain
   √ crenulated contour (US helpful)
   √ capsular calcifications at periphery of prosthesis
   √ focal bulge = herniation of a locally weakened fibrous capsule
   √ fibrous capsule delineated by US (unleaked silicone is echolucent)
   √ extensive periprosthetic calcifications

   MR (low specificity):
   √ rounded implants with transverse diameter < 2x the anteroposterior diameter
   √ marked thickening of fibrous capsule
   √ signal-free periprosthetic zone of macrocalcifications
   √ complete absence of radial folds
   √ contrast enhancement ← granulomatous inflammation

   Rx: not health hazard; capsulotomy (release); capsulectomy (removal of scar tissue)
2. **Implant migration**
   Cause: overdistension of implant pocket at surgery
3. **Rupture of prosthesis**
   = hole / tear in implant shell observed at surgery
   Implant failure: 11% after 5 years, 49% after 12 years, 95% after 20 years
   Cause: violation of elastomer shell during surgery (years 1–5); mechanical / fatigue (years 5–10)
   Result: total / partial / no collapse of shell

- change in contour / location of implant
- flattening of implant, breast pain

4. **"Gel bleed" = silicone leaching** (100% = normal condition as all implants bleed)
   = leakage of microscopic quantities of silicone oil through semiporous but intact barrier shell made of silicone elastomer
   √ silicone-equivalent signal within keyhole-shaped terminal bend of radial folds + between capsule and implant shell
   Dx: microscope
5. Infection / hematoma formation
6. Localized pain / paresthesia

N.B.: NO association between silicone breast implants and connective tissue disease / malignancy

Intracapsular Rupture

= broken implant casing, which swims within silicone gel contained by intact fibrous capsule

Frequency: 80–90% of all ruptures

Mammo (11–23% sensitive, 89–98% specific):
√ bulging / peaking of implant contour (DDx: herniation through locally weakened capsule)

US (59–70% sensitive, 57–92% specific, 49% accurate):
√ "stepladder" sign = series of parallel horizontal echogenic straight / curvilinear lines inside implant (= collapsed implant shell floating within silicone gel)
√ heterogeneous aggregates of low- to medium-level echogenicity (65% sensitive, 57% specific)

N.B.: visualization of internal lumen within anechoic space in double-lumen implants can be confused on US with intracapsular rupture

MR (81–94% sensitive, 93–97% specific, 84% accurate):
√ multiple curvilinear low–signal-intensity lines often parallel to fibrous capsule (corresponding to collapsed prosthesis shell inside the silicone-filled fibrous capsule):
  √ "linguine" sign = multiple hypointense wavy lines within implant (= pieces of free-floating collapsed envelope), 100% PPV
  √ in incomplete rupture "inverted teardrop" / "noose" / "keyhole" / "lariat (= lasso)" sign = loop-shaped hypointense structure contiguous with implant envelope (= small focal invagination / fold of shell with silicone on either side)
  [*la reata*, Spanish = lasso]
  DDx: radial fold (extending from periphery perpendicular to surface directed toward center of implant)
√ "water droplet" / "salad-oil" sign = appearance of multiple droplets of fluid of extracapsular origin / saline-containing envelope within lumen of silicone implant (DDx: 1–2 droplets may be normal; after injection of saline / Betadine® / antibiotics / steroids)

Extracapsular Rupture

= extrusion + migration of silicone droplets through tear in both implant shell + fibrous capsule

Frequency: up to 20% of all ruptures

• palpable breast masses

US:

√ "snowstorm" / "echogenic noise" pattern = markedly hyperechoic nodule with well-defined anterior + indistinct echogenic noise posteriorly (= free silicone droplets mixed with breast tissue)

√ highly echogenic area with acoustic shadowing

√ hypoechoic masses almost indistinguishable from cysts + usually surrounded by echogenic noise (= large to medium-sized collections of free silicone) with low-level internal echoes

MR:

√ discrete hypointense foci on fat-suppressed T1WI + hyperintense signal on water-suppressed T2WI in continuity with / separate from implant

√ "linguine" sign = sign of associated intracapsular rupture

Mammography:

√ lobular / spherical dense area of opacities adjacent to / separate from silicone implant

√ rim calcifications

EXTRACAPSULAR SPREAD OF SILICONE

Source: gel bleed, implant rupture (11–23%) more common with thinner shell + older implants

• silicone lymphadenopathy

• paresthesia of arm ← nerve impingement ← fibrosis surrounding silicone migrated to axilla / brachial plexus

• silicone nipple discharge (rare)

• migration to arm (→ constrictive neuropathy of radial nerve), subcutaneous tissue of lower abdominal wall, inguinal canal

√ migration to ipsilateral chest wall + axillary nodes

√ silicone droplets in breast in 11–23% (97% specific, 5% sensitive)

Siliconoma = Silicone Granuloma

= collection of silicone within breast parenchyma surrounded by a foreign-body granulomatous reaction

Histo: granuloma formation + fibrosis

Location: typically at edge of breast implant

√ hyperechoic mass with fine internal echoes

√ "dirty" posterior acoustic shadowing / "snowstorm" pattern of acoustic scattering

Reduction Mammoplasty

= removal of excess fat + glandular tissue + skin

Purpose:

(1) Aesthetics to achieve desired breast size

(2) Relief of back pain
(3) Restore chest symmetry after contralateral lumpectomy
√ swirled architectural distortion (in inferior breast best seen on mediolateral view)
√ postsurgical distortion
√ residual isolated islands of breast tissue
√ fat necrosis
√ dystrophic calcifications
√ asymmetric tissue oriented in nonanatomic distribution

MASTITIS

Acute Mastitis

= infection of the breast with primary ascending canalicular + secondary interstitial spread
Cause: mammary duct obstruction / ectasia; cellulitis; immunocompromised state; nipple injury
Pathogen: S. aureus (most commonly)
Histo: acute + chronic inflammatory infiltration, fibrosis, occasional multinucleated giant cells
Age: any; most commonly in lactating woman
• tender swollen erythematous breast (DDx: inflammatory ca.)
• enlarged painful axillary lymph nodes
• fever (5–12–47%), elevated ESR, leukocytosis
√ diffuse increased density
√ diffuse skin thickening
√ swelling of breast
√ enlarged axillary lymph nodes
√ rapid resolution under antibiotic therapy
US:
√ increased echogenicity in fat lobules
√ hypoechoic thick-walled complex multiloculated collection + acoustic enhancement = abscess
√ increased peripheral color Doppler flow
MR:
√ circumscribed area of low signal intensity on T1WI
√ strong initial enhancement + postinitial plateau
Cx: abscess, fistula

Puerperal Mastitis (14–59%)

= LACTATIONAL MASTITIS
= usually interstitial infection during lactational period
(a) through infected nipple crack / skin abrasion
(b) hematogenous
(c) ascending via ducts = galactophoritis
Prevalence: 1–24% of breast-feeding women
At risk: primipara (65% of cases)

Risk factor: milk stasis = excellent culture medium
Organism: S. aureus > Streptococcus (from nose + throat of nursing infant)
√ imaging NOT required
√ skin and trabecular thickening from breast edema
Cx: abscess (in 5–11%) in first 12 weeks after birth / at time of weaning
Rx: continue breast feeding under conservative therapy to disengorge ducts (unless contraindicated by type of antibiotic!); amoxicillin-clavulanate / cloxacillin; incision + drainage

Nonpuerperal Mastitis (41–86%)
= outside breast-feeding period
Organism: Streptococcus, E. coli
1. Infected cyst
2. Purulent mastitis with abscess formation
3. Plasma cell mastitis
4. Nonspecific mastitis

CENTRAL NONPUERPERAL MASTITIS
= PERIAREOLAR MASTITIS (most common)
Cause: complication of periductal mastitis
Pathophysiology:
squamous metaplasia of cuboidal epithelium → keratin plugs → central acute inflammatory infiltrate → obstruction of lactiferous ducts → secondary infection → cutaneous fistula
At risk: smoker
Prognosis: recurrence in 25–40%

PERIPHERAL NONPUERPERAL MASTITIS
At risk: diabetes, rheumatoid arthritis, steroid medication, recent breast intervention

Granulomatous Mastitis
= very rare chronic inflammatory process
Median age: 41 years (most commonly during post partum / post lactation period)
Histo: noncaseating nonvasculitic granulomatous inflammatory reaction centered on lobules
under exclusion of:
TB, fungal infection, sarcoidosis, Wegener granulomatosis, granulomatous reaction associated with carcinomas
Organism: Corynebacterium (in up to 75%)
• acute onset of a distinct firm / hard tender painful mass sparing subareolar region; nipple retraction
√ focal asymmetric density (most frequently)
√ dense breast tissue / mass with benign / malignant features
√ reactive enlargement of axillary nodes (in up to 15%)
US:
√ multiple clustered contiguous tubular hypoechoic lesions
√ ± large hypoechoic mass

Prognosis: spontaneous healing over time; corticotherapy

METASTASIS TO BREAST

Prevalence: 0.5–3% of all malignant breast tumors; 5% of all male breast cancers
Mean age: 43 years
Intramammary primary:
commonly located in contralateral breast
Extramammary primary:
malignant melanoma > NHL > lung cancer (small- and large-cell types) > sarcoma > carcinoma of ovary, stomach, kidney, prostate
◊ In up to 40% no known history of primary cancer!
in children: rhabdomyosarcoma, acute leukemia, NHL
Location: subcutaneous fat rather than glandular tissue; bilaterality in up to 30%
√ round homogeneous mass with smooth margin
√ solitary mass, esp. in upper outer quadrant
√ usually multiple masses
√ skin adherence (25%) ± skin thickening
√ axillary node involvement (40%)
√ NO calcifications
US:
√ hypervascularity in a predominantly echogenic mass (in 64% of breast lymphoma, in 99% of melanoma)

Hemorrhagic Metastasis to Breast

1. Malignant melanoma
2. RCC
3. Choriocarcinoma
4. Kaposi sarcoma

MONDOR DISEASE

= rare usually self-limited thrombophlebitis of subcutaneous veins (mostly thoracoepigastric v.) of the breast / anterior chest wall
Cause: unknown; trauma, physical exertion, surgery, breast cancer, inflammation, dehydration
May be associated with: carcinoma (in up to 12%), DVT
• painful tender palpable cordlike structure
• skin dimpling, erythema
Location: usually lateral aspect of breast
√ linear ropelike tubular superficial structure ± beading
√ rarely calcification of vein
US:
√ superficial hypoechoic tubular structure containing low-level internal echoes (= thrombus)
Prognosis: resolves spontaneously in 2–4 weeks

MYOFIBROBLASTOMA

= SPINDLE CELL TUMOR OF BREAST = SPINDLE CELL LIPOMA = FIBROMA = MYOGENIC STROMAL TUMOR = SOLITARY FIBROUS TUMOR = ATYPICAL VARIANT OF LEIOMYOMA
= rare benign stromal tumor
Age: 6th–7th decade
May be associated with: gynecomastia
• slow growing unilateral painless mobile mass
Path: bands of hyalinized collagen separating short fascicles of bland spindle cell with pseudoencapsulation of peripherally compressed fibrous tissue; positive for muscle-specific actin + α-smooth muscle actin + desmin
Size: 1–4 cm
√ well-defined round / ovoid dense mass
US:
√ solid well-circumscribed homogeneously hypoechoic mass
√ occasionally ill-defined with posterior acoustic shadowing
MR:
√ homogeneous enhancement (similar to fibroadenoma) with nonenhancing internal septations on T2WI

NIPPLE ADENOMA

= FLORID PAPILLOMATOSIS = EROSIVE ADENOMATOSIS = SUPERFICIAL PAPILLARY ADENOMATOSIS
= uncommon variant of intraductal papilloma involving nipple
• bloody discharge, crusting, nodularity
• tenderness, swelling, erythema (resembling Paget disease)
Rx: complete local excision

PAPILLOMA OF BREAST

= proliferation of ductal epithelial tissue on a fibrovascular stalk within a duct
Prevalence: rare; 1–2% of all benign tumors
Age: 30–77 years (juvenile papillomatosis = 20–26 years); may occur in men
Histo: hyperplastic proliferation of ductal epithelium; lesion may be pedunculated / broad-based; connective tissue stalk covered by epithelial cells proliferating in the form of apocrine metaplasia / solid hyperplasia → may cause duct obstruction + distension to form an intracystic papilloma; immunohistochemical marker p63 for myoepithelial cell layer present in a complete layer
Mammo:
√ negative mammogram / intraductal nodules in subareolar area
√ may be associated with coarse microcalcifications
Galactography:
√ dilated duct with distorting intraluminal filling defect / complete duct obstruction
US:
√ solid round / oval / slightly lobulated well-circumscribed hypoechoic mass in dilated duct
√ ± hypervascularity on color Doppler
MR:
› T1WI:

√ round / oval tumor with signal isointense to parenchyma (usually not detectable on precontrast T1WI)
√ homo- / heterogeneous contrast enhancement stronger than surrounding parenchyma
√ continuous postinitial increase / occasionally plateau

Cx: invasive papillary carcinoma / DCIS (lesion > 1 cm, location > 3 cm from nipple, patient age > 50 years)

Rx: surgical excision (because of low risk of upgrade to DCIS)

Prognosis: in 24% recurrence after surgical treatment

Central Solitary Papilloma

= NOT premalignant

Location: major subareolar duct; bilateral in 25%

- asymptomatic
- spontaneous usually bloody / serous (9–48%) / clear nipple discharge (52–88–100%):

◊ Most common cause of serous / serosanguinous nipple discharge!

- "trigger point" = nipple discharge produced upon compression of area with papilloma
- intermittent mass disappearing with discharge

√ asymmetrically dilated single duct

Peripheral Multiple Papillomas

= INTRADUCTAL PAPILLOMATOSIS

Age: perimenopausal

Location: within terminal ductal lobular unit; bilateral in up to 14%

In 10–38% associated with:
atypical ductal hyperplasia, lobular carcinoma in situ, DCIS (papillary + cribriform intraductal cancers), invasive cancer, sclerosing adenosis, radial scar

√ segmental distribution with dilated duct extending from beneath the nipple (20%)

PHYLLODES TUMOR

[*phyllon*, Greek = leaf → phyllodes = leaflike]

Prevalence: 1÷6,300 examinations; 0.3–1.5% of all breast neoplasms; 3% of all fibroadenomas

Mean age: 45 years (5th–6th decade); occasionally in women < 20 years of age

Histo: similar to fibroadenoma but with increased cellularity + pleomorphism of its stromal elements (wide variations in size, shape, differentiation); fibroepithelial tumor with leaflike growth pattern = branching projections of tissue within cleftlike spaces lined with layers of myoepithelial and ductal epithelium; cavernous structures contain mucus, cystic degeneration + hemorrhage
Subtypes: (a) benign (b) borderline (c) malignant

- sense of fullness
- rapidly enlarging breast mass; periods of remission
- huge, firm rubbery, mobile, discrete, lobulated, smooth mass
- thinning + livid discoloration of skin, wide veins, shining skin → skin ulceration / invasion of chest wall

Size: 1–20 cm

Mammo:
- √ large homogeneous noncalcified isodense mass with smooth polylobulated margins mimicking fibroadenoma
- √ rapid growth to large size (> 6–10 cm), may fill entire breast
- √ occasional "halo" sign ← compression of surrounding tissue

US:
- √ round / lobulated hypoechoic mass with smooth margins
- √ heterogeneous internal echoes without acoustic shadowing
- √ anechoic fluid-filled clefts in large tumors (DDx from fibroadenoma)

MR:
- › T1WI:
  - √ hypo- / isointense to parenchyma
  - √ hypointense regions of cystic / necrotic changes (occasionally)
- › enhanced T1WI:
  - √ strong initial uptake in solid tumor component
  - √ continuous increase / plateau in postinitial phase
  - √ increasing demarcation of nonenhancing cystic components (mass-in-mass morphology)
- › T2WI:
  - √ iso - to hyperintense to breast parenchyma
  - √ hyperintense regions of cystic / necrotic changes (occasionally) = "slit-like" cystic channels

Dx: excisional biopsy ← histopathology of core biopsy may mimic hypercellular fibroadenoma

Cx: malignant degeneration (25%)

DDx: fibroadenoma (uncommon in postmenopausal woman)

Benign Phyllodes Tumor

= FIBROADENOMA PHYLLODES = GIANT FIBROADENOMA

= benign giant form of intracanalicular fibroadenoma

Histo: low mitotic activity (0–4 mitoses / 10 HPF)

Cx: in 5–10% degeneration into malignant fibrous histiocytoma / fibro- / lipo- / leiomyo- / chondro- / osteosarcoma with local invasion + hematogenous metastases to lung, pleura, bone (axillary metastases quite rare)

Prognosis: 15–20% recurrence rate after excision

Malignant Phyllodes Tumor (16–30%)

= PHYLLODES SARCOMA = CYSTOSARCOMA PHYLLODES = ADENOSARCOMA

= rare fibroepithelial neoplasia

Histo: high mitotic activity (> 5 mitoses / 10 HPF) in a predominantly sarcomatous differentiation (angio-, chondro-, myo-, osteo-, liposarcoma); rare transformation into metaplastic breast cancer (squamous cell carcinoma in 1%)

√ ± coarse / eggshell calcifications

√ type III washout pattern in solid tumor portion

Prognosis: hematogenous spread in 20% (lung > bone > heart > liver) as late as 12 years after initial Rx; 20% local relapse rate; 65% 5-year survival; death in 30%

Rx: wide excision (without axillary node dissection); radiation + chemotherapy not useful

PSEUDOANGIOMATOUS STROMAL HYPERPLASIA

= PASH = benign hormonally stimulated mesenchymal myofibroblastic proliferation of mammary stroma

Spectrum: from focal incidental findings to clinically and mammographically evident breast masses

Histo: (a) incidental focal microscopic finding in 23% of all breast specimens
(b) tumoral form (rare)

Tumoral Form of PASH

Age: 4th–5th decade (range, 14–67 years); frequently in pre- and perimenopausal women

Associated with: gynecomastia in men (in 20–47%); immunosuppressive condition (eg, HIV); neurofibromatosis type 1

Path: well-defined mass with pseudocapsule

Histo: proliferating myofibroblasts creating slit-like anastomosing spaces positive for vimentin + CD34 (+ muscle actin + desmin); ER + PR positive in 95%; similar in appearance to low-grade angiosarcoma

Pathogenesis: high density of progesterone receptors

- single palpable movable painless firm rubbery mass
- may grow rapidly

Mean size: 4.2 (range, 1–12) cm

Mammo:

√ dense well / partially circumscribed noncalcified mass
√ rarely indistinct / spiculated border

US:

√ hypoechoic solid ovoid mass with long axis parallel to chest wall:
  √ slightly heterogeneous texture ± echogenic component
  √ rarely predominantly hyperechoic
√ ± circumscribed margins
√ ± small cystic component
√ usually no posterior phenomena

MR:

√ commonly persistent (type 1) or less frequently plateau (type 2) / washout (type 3) enhancement

Rx: excision for symptomatic / growing mass

Prognosis: recurrence after excisional biopsy (in 5–18%) requires 1–2 cm excisional margins; concurrent DCIS / invasive carcinoma in surrounding tissue (in 4–10%)

DDx: fibroadenoma; phyllodes tumor; angiosarcoma (slitlike spaces with atypical cell nuclei containing erythrocytes, positive for CD31 + factor VIII)

RADIAL SCAR

= SCLEROSING DUCT HYPERPLASIA = INDURATIVE MASTOPATHY = FOCAL FIBROUS DISEASE = BENIGN SCLEROSING DUCTAL PROLIFERATION = INFILTRATING EPITHELIOSIS = NONENCAPSULATED

SCLEROSING LESION

= benign proliferative breast lesion (malignant potential is controversial) unrelated to prior surgery / trauma

Prevalence: 0.1–2.0÷1,000 screening mammograms; in 2–16% of mastectomy specimens

Cause: ? localized inflammatory reaction, ? chronic ischemia with slow infarction

Path: "scar" = sclerotic center composed of acellular connective tissue (= fibrosis) and elastin deposits (= elastosis); entrapped ductules with intact myoepithelial layer in sclerotic core; corona of distorted ducts + lobules composed of benign proliferations (sclerosing adenosis, ductal hyperplasia, cyst formation, papillomatosis)

In up to 50% associated with:

tubular carcinoma, comedo carcinoma, invasive lobular carcinoma + contralateral breast cancer

◊ Avoid frozen section, fine-needle aspiration, core needle biopsy (controversial)!

• rarely palpable

√ mean diameter of 0.33 cm (range, 0.1–0.6 cm)

√ typically no central mass (BUT: irregular noncalcified mass often with architectural distortion)

√ variable appearance in different projections (= radial scars are typically planar in configuration)

√ oval / circular translucent areas at center

√ very thin long spicules, clumped together centrally

√ radiolucent linear structures (= fat) paralleling spicules ("black star" appearance)

√ no skin thickening / retraction

MR:

› T1WI:

√ stellate lesion with SI equal to parenchyma (difficult / impossible to visualize within parenchyma; good in adipose tissue)

› enhanced T1WI:

√ slight to moderate uptake with nonspecific curve

› T2WI:

√ no characteristic finding

Rx: surgical excision required for definitive diagnosis

DDx: carcinoma, postsurgical scar, fat necrosis, fibromatosis, granular cell myoblastoma

SARCOMA OF BREAST

Frequency: < 1% of malignant mammary lesions

Age: 45–55 years

Histo: fibrosarcoma, rhabdomyosarcoma, osteogenic sarcoma, mixed malignant tumor of the breast, malignant fibrosarcoma and carcinoma, liposarcoma

• rapid growth (4–6 cm at time of detection)

√ smooth / lobulated large dense mass

√ well-defined outline

√ palpated size similar to mammographic size

Angiosarcoma of Breast

= rare highly malignant endovascular breast tumor

Prevalence: 200 cases in world literature; 0.05% of all malignant breast tumors; 8% of all breast sarcomas

Age: 3rd–4th decade of life

Histo: hyperchromatic neoplastic endothelial cells; network of communicating vascular spaces

stage I: cells with large nucleoli

stage II: endothelial lining displaying tufting + intraluminal papillary projections

stage III: mitoses, necrosis, marked hemorrhage (= "blood lakes")

Immunohisto: factor VIII-related antigen, CD34, ulex-lectin antigen, desmin, vimentin, S-phase kinase-associated protein 2

Metastasis: hematogenous spread to lung, skin, SQ tissue, bone, liver, spleen, omentum, adrenal, gland, psoas muscle, brain, ovary; NO lymphatic spread

• rapidly enlarging painless immobile breast mass

Laterality: bilateral angiosarcoma (often in pregnancy)

Mammo:

√ normal (in 33%)

√ ill-defined / circumscribed lobulated round / oval mass

√ ± coarse calcifications

US:

√ skin thickening + nipple retraction

√ large solitary hypo- / hyperechoic heterogeneous mass

√ diffuse mixed echotexture without definable mass (38%)

√ well- / ill-defined multilobulated nonspiculated border

√ hyperechoic areas (← hemorrhage) ± acoustic shadowing

√ hypervascularity on color Doppler

MR:

√ heterogeneous mass with low SI on T1WI + intermediate to high SI on T2WI

√ pronounced early arterial enhancement with higher pathologic tumor grade

√ prolonged enhancement ← blood-filled vascular spaces

√ small focus of enhancement in irradiated thickened skin

PET/CT (useful for initial staging + surveillance):

√ FDG-avid

Biopsy: fine-needle aspiration / punch biopsies not diagnostic or misleading → excisional biopsy

Prognosis: dismal with 1.2–3.1 years median survival; 15% overall 5-year survival rate

Rx: simple mastectomy without axillary lymph node dissection

DDx: phylloides tumor, lactating breast, juvenile hypertrophy

◊ Frequently misdiagnosed as lymph- / hemangioma (negative for S-phase kinase-associated protein 2)

Secondary Angiosarcoma of Breast

Prevalence: 0.9–1.6÷1000 after radiation therapy

Risk factor: breast-conserving therapy accompanied by radiation therapy
Cause: radiogenic DNA mutations, genetic predisposition, congenital, idiopathic, traumatic factors; **Stewart-Treves syndrome** = angiosarcoma arising in region of chronic lymphedema
Age: > 65 years
Types:
(a) postradiation angiosarcoma (more common)
(b) lymphedema-associated cutaneous angiosarcoma (less common)
Criteria for radiation-associated neoplasm:
(a) site of origin within / adjacent to field of prior irradiation
(b) significant amount of radiation (25–80 Gy)
(c) interval of > 3–4 years since time of irradiation
(d) secondary sarcoma histologically different from primary neoplasm
Mean age: 65 years
• palpable mass
• skin macules / papules / vesicles → ulceration + edema
• change in skin color → blue, red, purple discoloration often accompanied by ecchymotic / telangiectatic /erythematous / eczematous component

Dermatofibrosarcoma Protuberans

= uncommon locally aggressive mesenchymal tumor; rarely in breast
Incidence: 5÷1,000,000 persons annually
Origin: dermis
Age: early / middle adulthood
Histo: CD34-positive spindle cell malignancy of typically storiform arrangement containing short fascicles within myxoid + hyalinized stromal background
• slow growing erythematous indurated subcutaneous nodule
√ hyperdense mass; NO calcifications; NO fat
US:
√ heterogeneously hypoechoic ovoid mass
√ parallel orientation
√ predominantly circumscribed microlobulated margins
√ scattered areas of internal vascularity
MR:
√ homogeneous mass T1-isointense to breast parenchyma
√ hyperintense mass on T2WI
√ intense enhancement
Prognosis: 20–50% recurrence rate
Rx: surgical excision with 2–3 cm wide margin

Liposarcoma of Breast

Prevalence: 0.7% of all breast cancers; 15% of all sarcomas
• slowly enlarging painful unilateral mass
• NO axillary lymphadenopathy; NO skin change
Median size: 8 cm

Histo: lipoblasts with scalloped irregular hyperchromatic nuclei + intracytoplasmic vacuoles indenting the nucleus confirm diagnosis
√ large encapsulated circumscribed hyperdense mass ± irregular margins
US:
√ heterogeneous hyperechoic echotexture
Rx: wide surgical excision

Pleomorphic Hyalinizing Angiectatic Tumor of Breast

= PHAT
= rare low-grade mesenchymal tumor of uncertain lineage
Histo: nonencapsulated mass with sheets of spindle + pleomorphic cells alternating with clusters of thin-walled ectatic vasculature surrounded by fibrin + collagen; positive for vimentin; variably positive for CD34, CD99, factor XIIIa and vascular endothelial growth factor
Location: lower extremity; breast
• slow-growing painless subcutaneous mass
√ large well-circumscribed retroareolar mass
√ NO calcifications
US:
√ ill-defined heterogeneous mass + flow on color Doppler
MR:
√ large solid + complex cystic mass:
√ hypointense SI on T1WI
√ hyperintense SI on T2WI
√ homogeneous enhancement
DDx: hematoma, Kaposi sarcoma

SEBACEOUS CYST

= epithelial cyst ← obstructed sebaceous gland arising from outer root sheath of hair follicle
Prevalence: less common dermal lesion than epidermal inclusion cyst
Location: dermis ± expansion into subcutaneous fat;
axilla / sternum (= **steatocystoma**) with flattened sebaceous gland lobules in relation to cyst wall
◊ NOT readily distinguishable from epidermal inclusion cyst by imaging / clinical features
Size: 0.8–10.0 cm in diameter
√ circumscribed round / oval mass of low (fatty) to variable density
US:
√ circumscribed mixed (commonly) / hyperechoic (occasionally) solid mass
√ cystic / solid depending on the internal contents
√ contiguous with dermis on tangential view
√ exiting hypoechoic track toward skin surface
DDx: epidermal inclusion cyst (indistinguishable)

SEROMA OF BREAST

= localized postoperative fluid collection of wound serum
Average size: 3.9 (range, 0.7–8.3) cm
√ oval / round mass with convex (outward-bulging) margins
√ slowly diminishes in size (= contraction)
√ evolution into scar by 1 year after surgery
√ occasionally reaccumulates / persists
US:
√ fluid collection ± solid echogenic component
CT:
√ hypo- / isodense lesion
MR:
› T1WI:
√ circumscribed area of mildly hypointense signal
› enhanced T1WI:
√ smooth ≤ 5 mm thin rim enhancement of surrounding parenchyma
› T2WI:
√ hyperintense area of fluid retention
Dx: gradual resolution / persistence on follow-up
DDx: indistinguishable from hematoma

HEART AND GREAT VESSELS

DIFFERENTIAL DIAGNOSIS OF CARDIOVASCULAR DISORDERS

Approach to Congenital Heart Disease		
	Acyanotic	*Cyanotic*
	√ enlarged main pulmonary artery	√ concave main pulmonary artery
Increased Pulmonary BF	L-R shunts	Admixture lesions = bidirectional shunts = T-lesions
+ increased C/T ratio	VSD	Transposition
	ASD	Truncus arteriosus
	PDA	TAPVR
	ECD	Tricuspid atresia (without RVOT obstruction)
	PAPVR	"Tingles" (single ventricle / atrium)
Normal Pulmonary Blood Flow	LV outflow obstruction	
+ normal C/T ratio	AS	
+ pulmonary venous HTN	Coarctation	
	Interrupted aortic arch	
	Hypoplastic left heart	
	LV inflow obstruction	
	Obstructed TAPVR	
	Cor triatriatum	
	Pulmonary vein atresia	
	Congenital MV stenosis	
	Muscle disease	
	Cardiomyopathy	
	Myocarditis	
	Anomalous LCA	
Decreased Pulmonary BF		R-to-L shunts
+ normal C/T ratio		+ nonrestrictive intracardiac shunt
		Tetralogy of Fallot
		Tricuspid atresia (with PS + nonrestrictive ASD)
		Pulmonary atresia + nonrestrictive VSD
+ increased C/T ratio		+ restrictive intracardiac shunt
		Pulmonary atresia + ASD without VSD
		PS with ASD / patent foramen ovale
		Tricuspid atresia + PS + restrictive ASD
		Trilogy of Fallot
		Ebstein anomaly
		Congenital tricuspid insufficiency

CONGENITAL HEART DISEASE

Incidence of CHD in Liveborn Infants

Overall incidence: 8–9÷1000 livebirths

◊ Most common CHD: bicuspid aortic valve (2%) [usually not recognized before late infancy / childhood]

◊ ASD + VSD + PDA account for 45% of all CHD
◊ 12 lesions account for 89% of all CHD:
Ventricular septal defect 30.3%
Patent ductus arteriosus 8.6%
Pulmonic stenosis 7.4%
Ostium secundum defect 6.7%
Coarctation of aorta 5.7%
Aortic stenosis 5.2%
Tetralogy of Fallot 5.1%
Transposition 4.7%
Endocardial cushion defect 3.2%
Hypoplastic right ventricle 2.2%
Hypoplastic left heart syndrome 1.3%
TAPVR 1.1%
Truncus arteriosus 1.0%
Single ventricle 0.3%
Double outlet right ventricle 0.2%

High-risk pregnancy:
(1) Previous sibling with CHD: 2–5%
(2) Previous 2 siblings with CHD: 10–15%
(3) One parent with CHD: 2–10%

Congenital Abnormality of Aortic Valve

1. **Bicuspid aortic valve**
   ◊ Most common congenital cardiac anomaly!
2. Unicuspid / unicomissural aortic valve
   = single commissure in (commonly) L posterior position
   Incidence: 0.02%
   Cx: early aortic stenosis, aneurysmal dilatation of ascending aorta
3. Quadricuspid aortic valve
   Incidence: 200 cases reported
   Cx: regurgitation
4. Aneurysmal dilatation of sinus of Valsalva
   Cause: (a) congenital: connective tissue disorder (Marfan), aortic insufficiency, bicuspid aortic valve, VSD
   (b) acquired: infection (endocarditis, syphilis, TB), medial degeneration, trauma, hypertension

Congenital Abnormality of Mitral Valve

1. Endocardial cushion defect
2. Parachute mitral valve (Shone syndrome)

CHD Presenting in 1st Year of Life

1. VSD

2. d-Transposition of great vessels
3. Tetralogy of Fallot
4. Isolated coarctation
5. Patent ductus arteriosus
6. Hypoplastic left heart syndrome

Most common causes for CHF + PVH in neonate:

1. Left ventricular failure ← outflow obstruction
2. Obstruction of pulmonary venous return

Presenting Age in CHD		
Age	*Severe PVH*	*PVH + Shunt Vascularity*
0–2 d	Hypoplastic left heart	Hypoplastic left heart
	Aortic atresia	TAPVR above diaphragm
	TAPVR below diaphragm	Complete transposition
	Myocardiopathy in IDM	
3–7 d	PDA in preterm infant	
7–14 d	CoA + VSD / PDA	Coarctation of aorta
	Aortic valve stenosis	Peripheral AVM
	Peripheral AVM	
	Endocardial fibroelastosis	
	Anomalous LCA	

CHD Compatible with Relatively Long Life

1. Mild tetralogy: mild pulmonic stenosis + small VSD
2. Valvular pulmonic stenosis: with relatively normal pulmonary circulation
3. Transposition of great vessels: some degree of pulmonic stenosis + large VSD
4. Truncus arteriosus: delicate balance between systemic + pulmonary circulation
5. Truncus arteriosus type IV: large systemic collaterals
6. Tricuspid atresia + transposition + pulmonic stenosis
7. Eisenmenger complex
8. Ebstein anomaly
9. Corrected transposition without intracardiac shunt

Classic Signs of Congenital Cardiovascular Anomalies

1. “Boot-shaped” heart
2. “Box-shaped” cardiomegaly
3. “Egg-on-a-string” sign
4. “Figure-of-3” and reverse “figure-of-3” sign
5. “Gooseneck” sign
6. “Scimitar” sign
7. “Snowman” sign

Juxtaposition of Atrial Appendages

1. Tricuspid atresia with transposition

2. Complete transposition
3. Corrected transposition of great arteries
4. DORV

Continuous Heart Murmur

1. PDA
2. AP window
3. Ruptured sinus of Valsalva aneurysm
4. Hemitruncus
5. Coronary arteriovenous fistula

Syndromes with CHD

5 p – (Cri-du-chat) Syndrome

Incidence of CHD: 20%

DiGeorge Syndrome

= congenital absence of thymus + parathyroid glands

1. Conotruncal malformation
2. Interrupted aortic arch

Down Syndrome

= MONGOLISM = TRISOMY 21

1. Endocardial cushion defect (25%)
2. Membranous VSD
3. Ostium primum ASD
4. AV communis
5. Cleft mitral valve
6. PDA
7. 11 rib pairs (25%)
8. Hypersegmented manubrium (90%)

Ellis-van Creveld Syndrome

Incidence of CHD: 50%

• polydactyly

√ single atrium

Holt-Oram Syndrome

= UPPER LIMB-CARDIAC SYNDROME

Incidence of CHD: 50%

1. ASD
2. VSD
3. Valvular pulmonary stenosis
4. Radial dysplasia

Hurler Syndrome

Cardiomyopathy

Ivemark Syndrome

Incidence of CHD: 100%

• asplenia

√ complex cardiac anomalies

Klippel-Feil Syndrome

Incidence of CHD: 5%

1. Atrial septal defect
2. Coarctation

Marfan Syndrome

= ARACHNODACTYLY

1. Annuloaortic ectasia
2. Aortic aneurysm
3. Aortic regurgitation
4. Pulmonary aneurysm

Noonan Syndrome

1. Pulmonary stenosis
2. ASD
3. Hypertrophic cardiomyopathy

Osteogenesis Imperfecta

1. Aortic valve insufficiency
2. Mitral valve insufficiency
3. Pulmonic valve insufficiency

Postrubella Syndrome

• low birth weight, deafness, cataracts, mental retardation

1. Peripheral pulmonic stenosis
2. Valvular pulmonic stenosis
3. Supravalvular aortic stenosis
4. PDA

Trisomy 13–15

VSD, tetralogy of Fallot, DORV

Trisomy 16–18

VSD, PDA, DORV

Turner Syndrome (XO)

= OVARIAN DYSGENESIS

Incidence of CHD: 35%

1. Coarctation of the aorta (in 15%)
2. Bicuspid aortic valve
3. Dissecting aneurysm of aorta

Williams Syndrome

= IDIOPATHIC HYPERCALCEMIA

- peculiar elfinlike facies, mental + physical retardation
- hypercalcemia (not in all patients)

1. Supravalvular aortic stenosis (33%)
2. ASD, VSD
3. Valvular + peripheral pulmonary artery stenosis
4. Aortic hypoplasia, stenoses of more peripheral arteries

SHUNT EVALUATION

Evaluation of L-to-R Shunts

A. AGE

› Infants:

(1) Isolated VSD
(2) VSD with CoA / PDA / AV canal
(3) PDA
(4) Ostium primum

› Children / adults:

(1) ASD
(2) Partial AV canal with competent mitral valve
(3) VSD / PDA with high pulmonary resistance
(4) PDA without murmur

B. SEX

99% chance for ASD / PDA in female patient

C. CHEST WALL ANALYSIS

√ 11 pair of ribs + hypersegmented manubrium → Down syndrome
√ pectus excavatum + straight back syndrome + funnel chest → prolapsing mitral valve
√ rib notching

D. CARDIAC SILHOUETTE

√ absent pulmonary trunk:
corrected transposition with VSD; pink tetralogy
√ left-sided ascending aorta:
corrected transposition with VSD
√ tortuous descending aorta:
aortic valve incompetence + ASD
√ huge heart:
persistent complete AV canal (PCAVC); VSD + PDA; VSD + mitral valve incompetence
√ enlarged left atrium:
intact atrial septum; mitral regurgitation (endocardial cushion defect, prolapsing mitral valve + ASD)

Differential Diagnosis of L-R Shunts						
	RA	*RV*	*PA*	*LA*	*LV*	*Prox. Ao*
ASD	↑	↑	↑	↔	↔	↔
VSD	↔	↑	↑	↑	↑	↔
PDA	↔	↔	↑	↑	↑	often ↑

Shunt with Normal Left Atrium

A. Precardiac shunt
   1. Anomalous pulmonary venous connection

B. Intracardiac shunt
   1. ASD (8%)
   2. VSD (25%)

C. Postcardiac shunt
   1. PDA (12%)

Aortic Size in Shunts

A. Extracardiac shunts
   √ aorta enlarged + hyperpulsatile
   1. PDA

B. Pre- and intracardiac shunts
   √ aorta small but not hypoplastic
   1. Anomalous pulmonary venous return
   2. ASD
   3. VSD
   4. Common AV canal

Left-to-Right Shunts Missed on Echocardiography

1. Sinus venosus defect
2. Patent ductus arteriosus
3. Anomalous pulmonary venous return

SITUS

= "position / site / location" referring to the position of the atria and viscera relative to the midline

Segmental Analysis of CHD

= 3-part **Van Praagh notation** of congenital heart disease corresponding to atria & ventricles & great vessels

◊ Only one type of situs anomaly is possible in any patient!

Step 1. **Visceroatrial situs** {X,_,_}:

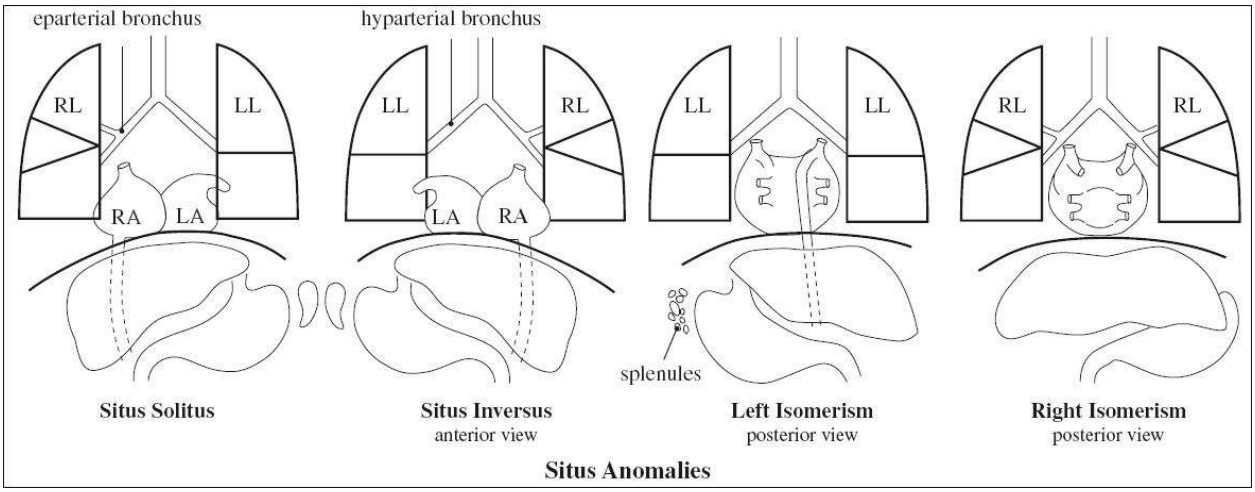
solitus ={S}, inversus = {I}, ambiguus = {A}

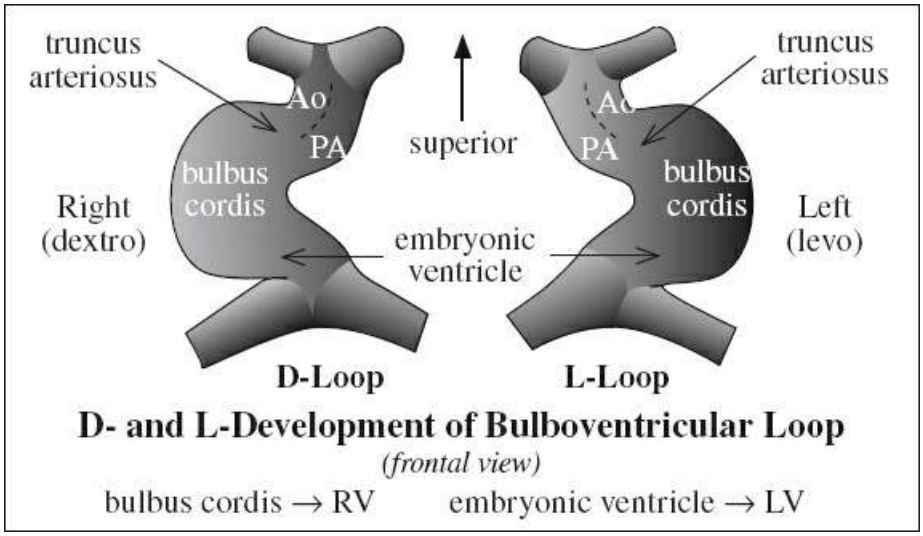
(a) establish <u>atrial situs</u> by morphology of atrial appendages
   √ broad blunt (triangular) appendage = RA
   √ narrow pointed tubular (fingerlike) appendage = LA
   ◊ Morphologic RA is on patient's right side

(b) establish atrial situs by lung morphology:
› morphologic RT lung
√ main RT lung bronchus is eparterial
› morphologic LT lung
√ main LT bronchus is hyparterial

The relationship between main RT + LT bronchi and pulmonary arteries is a reliable indicator of atrial arrangement.

(c) establish <u>visceral situs:</u>
√ largest lobe of liver on RT; stomach + spleen on LT
(b) establish <u>thoracoabdominal situs:</u>
√ supradiaphragmatic IVC connects to anatomic RA





√ RT lung + largest lobe of liver on right side

Supradiaphragmatic IVC / coronary sinus usually drain into anatomic RA (= rule of venoatrial concordance)

◊ Atrial + thoracoabdominal situs are usually concordant!

Step 2. **Ventricular loop orientation** {_,X,_}:

Embryology:

components of craniocaudal tube are truncus arteriosus (future great vessels), bulbus cordis (future right ventricle), embryonic LV, primitive atria, sinus venosus; tube curves toward right (D-loop) placing RV to right of LV

(a) identify morphologic RV and LV

(b) determine location of RV relative to LV

Hand rule: approaching heart from anteriorly place right / left hand in RV with palm against IVS. If right thumb is in inflow tract + right fingers in outflow tract = D-loop

Step 3. **Position of great vessels** {_,_,X}:

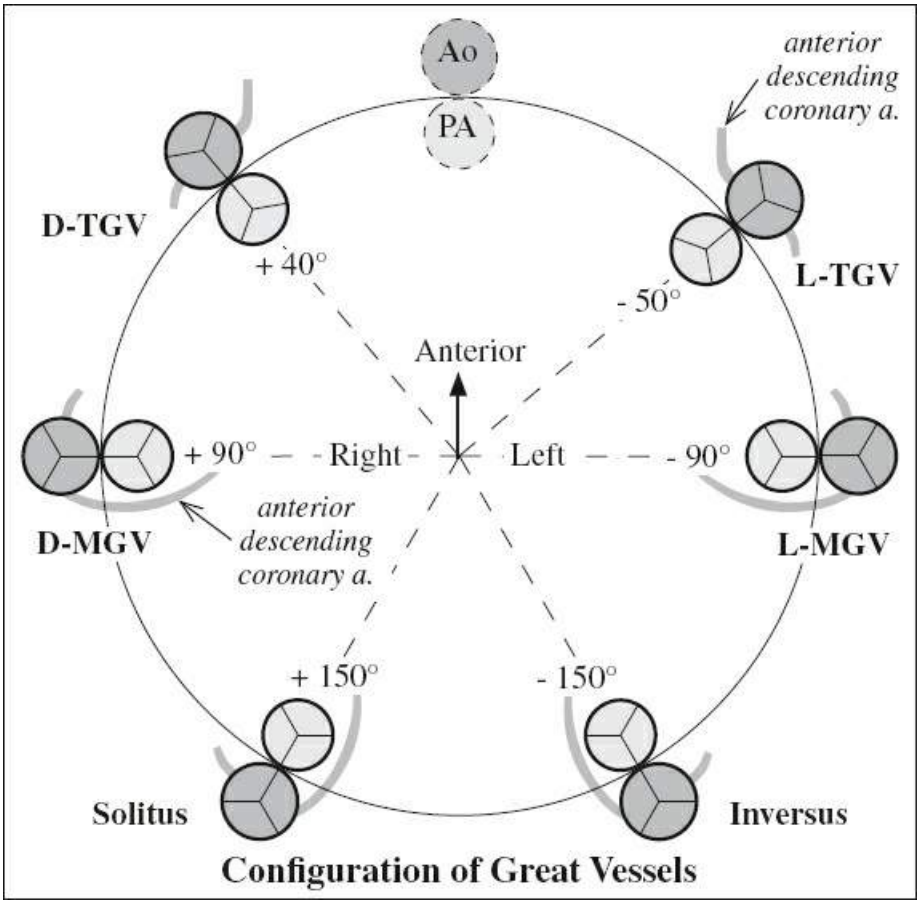
(a) identify morphologic aorta (Ao supplies at least 1 coronary artery + most systemic arteries) and main pulmonary artery (MPA supplies right + left pulmonary artery)

(a) designate position of Ao relative to MPA at level of aortic + pulmonic valves:

› normal or inverse position: solitus ={S}, inversus = {I}

› transposition of great arteries: dextrotransposition = {D-TGV}, levotransposition = {L-TGV}

› malposition if both arteries override / originate from same ventricle: Ao rightward from MPA = {D-MGV}, Ao leftward from MPA = {L-MGV}



Configuration of Great Vessels

Situs Solitus = Normal / Usual Situs

Right side	*Left side*
√ systemic atrium	√ pulmonary atrium
√ trilobed lung	√ bilobed lung
√ liver	√ stomach
√ gallbladder	√ single spleen
√ IVC	√ aorta

Associated with:

(a) levocardia : 0.6–0.8% chance for CHD

(b) dextrocardia : 95% chance for CHD

SITUS ANOMALY

Associated with: CHD, primary ciliary dyskinesia, abdominal anomalies (eg, intestinal malrotation)

Situs Inversus

= mirror-image arrangement of situs solitus

Frequency: 0.01%Associated with:

(a) dextrocardia = situs inversus totalis (usual variant): 3–5% chance for CHD (eg, Kartagener syndrome in 20%)

(b) levocardia (extremely rare): 95% chance for CHD

Left side	*Right side*
√ systemic atrium	√ pulmonary atrium
√ trilobed lung	√ bilobed lung
√ liver	√ stomach
√ gallbladder	√ single spleen
√ IVC	√ aorta

Situs Ambiguus = Heterotaxy

[*heteros*, Greek = other / different; *taxis*, Greek = arrangement]

= visceral malposition + dysmorphism associated with indeterminate atrial arrangement

Associated with: CHD in 50–100%

Subclassification:

1. Asplenia syndrome = double / bilateral right-sidedness
2. Polysplenia syndrome = double / bilateral left-sidedness

Bronchial Situs

Classification:

1. Right bronchial isomerism
   √ bilateral eparterial upper lobe bronchi = morphologically right lung
2. Left bronchial isomerism
   √ bilateral hyparterial upper lobe bronchi = morphologically left lung

The relationship of the upper lobe bronchus to the ipsilateral pulmonary artery is the most

reliable marker of bronchial situs at CT *for details see Anatomy and Function of Lung*

Less reliable: number of lobes, ratio of left to right main bronchial lengths, bronchial branching pattern

Cardiac Malposition

= location of heart other than within left hemothorax in situs solitus or within left hemithorax when other organs are ambiguous

◊ Determined by base-apex axis; no assumption is made regarding cardiac chamber / vessel arrangement

In general, cardiac and situs anomalies are less frequently found with a concordant position of the cardiac apex, stomach, and aortic arch.

A. POSITION OF CARDIAC APEX
   1. Levocardia = apex directed leftward
   2. Dextrocardia = apex directed rightward
   3. Mesocardia = vertical / midline heart (usually with situs solitus)

   √ atrial septum characteristically bowed into LA in cardiac situs solitus with dextrocardia + cardiac situs inversus with levocardia (DDx: juxtapositioned atrial appendages)

Cardiac Position as Predictor of CHD	
Visceroatrial Situs	*Frequency of CHD*
Situs solitus	
with levocardia	< 1%
with dextrocardia	**95%**
Situs inversus	
with dextrocardia	3–5%
with levocardia	**100%**
Situs ambiguus	
with left isomerism (polysplenia)	90%
with right isomerism (asplenia)	99–100%

   ◊ Does not imply a particular internal structure / specific location of other thoracoabdominal organs!

B. CARDIAC DISPLACEMENT
   by extracardiac factors (eg, lung hypoplasia, pulmonary mass)
   1. Dextroposition
      suggests hypoplasia of ipsilateral pulmonary artery (PAPVR implies scimitar syndrome)
   2. Levoposition
   3. Mesoposition

C. CARDIAC INVERSION
   = alteration of normal relationship of chambers
   1. D-bulboventricular loop
   2. L-bulboventricular loop

D. TRANSPOSITION
= alteration of anterior-posterior relationship of great vessels

CYANOTIC HEART DISEASE

Chemical cyanosis = $PaO_2 \leq 94\%$

Clinical cyanosis = $PaO_2 \leq 85\%$

◊ Decrease in hemoglobin delays detectability!

Most common cause of cyanosis:

› in newborn: transposition of great vessels

› in child: tetralogy of Fallot!

N.B.: tricuspid atresia = the great mimicker

Increased Pulmonary Blood Flow with Cyanosis

= ADMIXTURE LESIONS

= bidirectional shunt with 2 components:

(a) mixing of saturated blood (L-R shunt) and unsaturated blood (R-L shunt)

(b) NO obstruction to pulmonary blood flow

Evaluation process:

√ cardiomegaly

√ increased pulmonary blood flow

√ concave main pulmonary artery:

√ PA segment absent = transposition

√ PA segment present:

(a) L atrium normal (= extracardiac shunt) = TAPVR

(b) L atrium enlarged (= intracardiac shunt) = truncus arteriosus

N.B.: Overcirculation + cyanosis = complete transposition until proven otherwise!

Admixture Lesions = T-lesions

mnemonic: 5 T's + CAD

Transposition of great vessels = complete TGV ± VSD

◊ Most common cause for cyanosis in neonate

Tricuspid atresia with or without transposition + VSD

◊ 2nd most common cause for cyanosis in neonate

Truncus arteriosus

Total anomalous pulmonary venous return (TAPVR) above diaphragm:

(a) supracardiac

(b) cardiac (coronary sinus / right atrium)

"**T**ingle" = single ventricle

Common atrium

Aortic atresia

Double-outlet right ventricle (DORV type I) / Taussig-Bing anomaly (DORV type II)

Clues:

√ skeletal anomalies: Ellis-van Creveld syndrome (truncus / common atrium)

√ polysplenia: common atrium

√ R aortic arch: persistent truncus arteriosus
√ ductus infundibulum: aortic atresia
√ pulmonary trunk seen: supracardiac TAPVR; DORV; tricuspid atresia; common atrium
√ ascending aorta with leftward convexity: single ventricle
√ dilated azygos vein: common atrium + polysplenia + interrupted IVC; TAPVR to azygos vein
√ left-sided SVC: vertical vein of TAPVR
√ "waterfall" right hilum: single ventricle + transposition
√ large left atrium (rules out TAPVR)
√ prominent L heart border: single ventricle with inverted rudimentary RV; levoposition of appendage of RA (tricuspid atresia + transposition)
√ age of onset ≤ 2 days: aortic atresia

Decreased Pulmonary Blood Flow with Cyanosis

= two components of
(a) impedance of blood flow through right heart ← obstruction / atresia at pulmonary valve / infundibulum
(b) R-to-L shunt

• pulmonary circulation maintained through systemic arteries / PDA
√ normal / decreased pulmonary blood flow
√ concave main pulmonary artery
√ cardiomegaly
√ restrictive intracardiac R-to-L shunt

mnemonic: P2 TETT
Pulmonic stenosis with ASD
Pulmonic atresia
Tetralogy of Fallot
Ebstein anomaly
Tricuspid atresia with pulmonic stenosis
Transposition of great vessels with pulmonic stenosis

A. SHUNT AT VENTRICULAR LEVEL
1. Tetralogy of Fallot
2. Tetralogy physiology (associated with pulmonary obstruction):
› complete / corrected transposition
› single ventricle
› DORV
› tricuspid atresia (PS in 75%)
› asplenia syndrome

√ prominent aorta with L / R aortic arch; inapparent pulmonary trunk
√ normal RA (without tricuspid regurgitation)
√ normal-sized heart ← escape mechanism into aorta

Clues:
1. Skeletal anomaly (eg, scoliosis): tetralogy (90%)
2. Hepatic symmetry: asplenia
3. Right aortic arch: tetralogy, complete transposition, tricuspid atresia

4. Aberrant right subclavian artery: tetralogy
5. Leftward convexity of ascending aorta: single ventricle with inverted right rudimentary ventricle, corrected transposition, asplenia, JAA (tricuspid valve atresia)

B. SHUNT AT ATRIAL LEVEL

mnemonic: PET

1. **P**ulmonary stenosis / atresia with intact ventricular septum
2. **E**bstein malformation + Uhl anomaly
3. **T**ricuspid atresia (ASD in 100%)

√ moderate to severe cardiomegaly
√ RA dilatation
√ RV enlargement ← massive tricuspid incompetence
√ inapparent aorta
√ left aortic arch

Pulmonary Venous Hypertension with Cyanosis

(a) during 1st week of life

1. Hypoplastic left heart syndrome
   √ marked cardiomegaly
2. TAPVR below diaphragm
   √ normal cardiac size

(b) during 2nd week of life

3. Aortic coarctation
4. Aortic atresia

(c) during 4th–6th week of life

5. Critical aortic stenosis
6. Endocardial fibroelastosis
7. Anomalous origin of LCA
8. Atresia of common pulmonary vein

ACYANOTIC HEART DISEASE

Increased Pulmonary Blood Flow without Cyanosis

= indicates L-R shunt with increased pulmonary blood flow (shunt volume > 40%)

A. WITH LEFT ATRIAL ENLARGEMENT
indicates shunt distal to mitral valve = increased volume without escape defect

1. VSD (25%): small aorta in intracardiac shunt
2. PDA (12%): aorta + pulmonary artery of equal size in extracardiac shunt
3. Ruptured sinus of Valsalva aneurysm (rare)
4. Coronary arteriovenous fistula (very rare)
5. Aortopulmonary window (extremely rare)

B. WITH NORMAL LEFT ATRIUM indicates shunt proximal to mitral valve = volume increased with escape mechanism through defect

1. ASD (8%)
2. Partial anomalous pulmonary venous return (PAPVR) + sinus venosus ASD

3. Endocardial cushion defect (ECD) (4%)

Normal Pulmonary Blood Flow without Cyanosis

A. OBSTRUCTIVE LESION
   1. Right ventricular outflow obstruction
      (a) at level of pulmonary valve: subvalvular / valvular / supravalvular pulmonic stenosis
      (b) at level of peripheral pulmonary arteries:
          peripheral pulmonary stenosis
   2. Left ventricular inflow obstruction
      (a) at level of peripheral pulmonary veins:
          pulmonary vein stenosis / atresia
      (b) at level of left atrium: cor triatriatum
      (c) at level of mitral valve:
          supravalvular mitral stenosis, congenital mitral stenosis / atresia, "parachute" mitral valve
   3. Left ventricular outflow obstruction
      (a) at level of aortic valve:
          anatomic subaortic stenosis, functional subaortic stenosis (IHSS), valvular aortic stenosis, hypoplastic left heart, supravalvular aortic stenosis
      (b) at level of aorta:
          interruption of aortic arch, coarctation of aorta

B. CARDIOMYOPATHY
   1. Endocardial fibroelastosis
   2. Hypertrophic cardiomyopathy
   3. Glycogen storage disease

C. HYPERDYNAMIC STATE
   1. Noncardiac AVM: cerebral AVM, vein of Galen aneurysm, large pulmonary AVM, hemangioendothelioma of liver
   2. Thyrotoxicosis
   3. Anemia
   4. Pregnancy

D. MYOCARDIAL ISCHEMIA
   1. Anomalous left coronary artery
   2. Coronary artery disease (CAD)

ACQUIRED HEART DISEASE

√ LA enlargement = MV disease
√ dilated ascending aorta = aortic valve disease
√ RA enlargement = tricuspid valve disease

Pressure Overload

1. Systemic hypertension
2. Aortic stenosis
3. Mitral stenosis

Decreased Compliance

1. Myocardial infarction
2. Hypertrophic cardiomyopathy
3. Restrictive cardiomyopathy

Volume Overload

1. Aortic insufficiency
2. Mitral insufficiency
3. Tricuspid insufficiency

Systolic Anterior Motion of Mitral Valve

1. Hypertrophic Cardiomyopathy
2. Hypertensive heart
3. Diabetes mellitus
4. Acute myocardial infarction
5. Mitral valve dysfunction / repair

Concentric Left Ventricular Hypertrophy

1. Symmetric hypertrophic cardiomyopathy

Approach to Acquired Heart Disease

Criteria	*Mild–Moderate Cardiomegaly*	*Moderate–Severe Cardiomegaly*
C/T ratio	0.45–0.55	> 0.55
LA enlargement	pressure overload	volume overload
	mitral stenosis	mitral insufficiency
	decreased LV compliance	
	hypertrophic cardiomyopathy	
	restrictive cardiomyopathy	
Enlarged ascending aorta	pressure overload	volume overload
	aortic stenosis	aortic insufficiency
Normal LA + aorta	myocardial	myocardial
	acute infarction	dilated cardiomyopathy
	hypertrophic cardiomyopathy	ischemic cardiomyopathy
	restrictive cardiomyopathy	
	pericardial	pericardial
	constrictive pericarditis	pericardial effusion

2. Amyloidosis
3. Cardiac sarcoidosis
4. **Athlete's heart**
   √ ↑ LV mass, ↑ LV diastolic cavity dimension, ↑ LV wall thickness
   √ lack of areas of delayed myocardial hyperenhancement
   Dx (80% sensitive, 99% specific):
   LV Thicknessdiastole ÷ Volumeend-diastole (corrected to body surface area) < 0.15 mm/m2/mL
5. **Fabry disease**
   = rare X-linked autosomal recessive metabolic storage disorder caused by lysosomal a-galactosidase
   √ concentric thickening of LV wall
   √ delayed hyperenhancement of LV midwall on CEMR
6. Adaptive LV hypertrophy: hypertension, aortic stenosis

CARDIOMEGALY

1. CHF
2. Multivalvular disease
3. Pericardial effusion
   √ absence of pulmonary venous hypertension + hydrostatic edema

Cardiothoracic Ratio

= widest transverse cardiac diameter ÷ widest inside thoracic diameter
= primarily a measure of LV dilatation

< 0.45	normal
0.45–0.55	mild cardiomegaly
> 0.55	moderate / severe cardiomegaly

Falsely normal: with LV enlargement in up to 66%, moderate enlargement of LA + RV
Falsely elevated: in expiration, in recumbent position

Vascular Pedicle Width

= distance on a horizontal line between (1) point where right mainstem bronchus + SVC cross and (2) point where left subclavian artery crosses horizontal line

48 ± 5 mm	normal
> 53 mm	in 60% of cardiogenic edema, in 85% of volume overload

Cardiomegaly in Newborn

A. NONCARDIOGENIC
   (a) metabolic:
      1. Ion imbalance in serum levels of sodium, potassium, and calcium
      2. Hypoglycemia
   (b) decreased ventilation
      1. Asphyxia
      2. Transient tachypnea
      3. Perinatal brain damage

(c) erythrocyte function
    1. Anemia
    2. Erythrocythemia
(d) endocrine
    1. Glycogen storage disease
    2. Thyroid disease: hypo- / hyperthyroidism
(e) infant of diabetic mother
(f) arteriovenous fistula
    1. Vein of Galen aneurysm
    2. Hepatic angioma
    3. Chorioangioma

B. CARDIOGENIC
    1. Arrhythmia
    2. Myo- / pericarditis
    3. Cardiac tumor
    4. Myocardial infarction
    5. Congenital heart disease

Abnormal Heart Chamber Dimensions

A. LEFT VENTRICULAR VOLUME OVERLOAD
    1. VSD
    2. PDA
    3. Mitral incompetence
    4. Aortic incompetence
B. LEFT VENTRICULAR HYPERTROPHY
    1. Coarctation
    2. Aortic stenosis
C. RIGHT VENTRICULAR VOLUME OVERLOAD
    1. ASD
    2. Partial APVR / total APVR
    3. Tricuspid insufficiency
    4. Pulmonary insufficiency
    5. Congenital / acquired absence of pericardium
    [6. Ebstein anomaly] – not truly RV
D. RIGHT VENTRICULAR HYPERTROPHY
    1. Pulmonary valve stenosis
    2. Pulmonary hypertension
    3. Tetralogy of Fallot
    4. VSD
E. Fixed subvalvular aortic stenosis
F. Hypoplastic left / right ventricle, common ventricle
G. Congestive cardiomyopathy

Right Atrial Enlargement

Cause: tricuspid stenosis / regurgitation, ASD, atrial fibrillation, dilated

cardiomyopathy, Ebstein anomaly, pulmonary atresia

◊ RA enlarges in rightward + posterior direction

PA CXR:

√ prominent round superior border at junction with SVC

√ > 5.5 cm from midline to most lateral RA margin

√ > 2.5 cm from right vertebral margin

√ > 50% vertical height of RA compared with cardiovascular mediastinal height (from top of aortic arch to base of heart)

LAT CXR:

√ sharp horizontal interface with lung above RV

√ displacement of heart posterior to IVC mimicking LV enlargement

Right Ventricular Enlargement

Cause: pulmonary valve stenosis, cor pulmonale, ASD, tricuspid regurgitation, dilated cardiomyopathy, secondary to LV failure

◊ RV enlarges in anterior, superior + leftward direction causing levorotation of heart

PA CXR:

◊ Only extreme dilatation causes recognizable signs on frontal view!

√ straightening / convexity of left upper cardiac contour

√ upturned cardiac apex

√ left upper cardiac margin parallels left mainstem bronchus as a long convex curvature

√ increased distance between left upper cardiac margin + left mainstem bronchus

√ small appearance of rotated aortic arch + SVC

√ large appearance of main pulmonary artery

LAT CXR (most sensitive view):

√ filling of retrosternal air space by prominent convexity of anterior heart border > ⅓ of distance from sternodiaphragmatic angle to the point where trachea meets sternum

Left Atrial Enlargement

Cause:

(a) acquired: mitral stenosis / regurgitation, LV failure, LA myxoma

(b) congenital: VSD, PDA, hypoplastic left heart

◊ LA enlarges in multiple directions

PA CXR:

√ right retrocardiac double density with inferomedial curvature (earliest sign)

√ > 7.0 (female) / 7.5 (male) cm distance between midpoint of undersurface of left mainstem bronchus + right lateral LA shadow

√ left retrocardiac double density

√ > 75° splaying of carina with horizontal orientation of distal left mainstem bronchus

√ enlarged left-convex left atrial appendage ± calcifications (← rheumatic heart disease in 90%)

LAT CXR:

√ increased convexity of posterosuperior cardiac margin

√ posterosuperior atrial convexity crosses vertical plane formed by tracheal midline + upper lobe bronchus

√ posterior displacement of barium-filled esophagus
√ posterior displacement of LUL bronchus

Left Ventricular Enlargement

Cause:

(a) pressure overload: hypertension, aortic stenosis
(b) volume overload: aortic or mitral regurgitation, VSD
(c) wall abnormalities: LV aneurysm, hypertrophic cardiomyopathy

◊ LV enlarges in posterior, inferior + leftward direction

PA CXR:

√ leftward displacement of downturned cardiac apex = left ventricular configuration
√ depression of left hemidiaphragm + gastric bubble (with diaphragmatic inversion)

LAT CXR:

√ increased convexity of posteroinferior cardiac margin
√ posterior cardiac margin projects > 1.8 cm posterior to IVC measured at a point 2 cm above intersection of IVC with right hemidiaphragm (Hofman-Rigler rule)

Flattening / Inversion of Interventricular Septum

= position determined by pressure difference between RV + LV
√ normally convex shape with slight right-sided bulge during ventricular filling (LV diastolic pressure > RV pressure)

(a) RV volume / pressure overload:
1. ASD
2. Acute / chronic cor pulmonale

(b) pericardial abnormality:
1. Cardiac tamponade (↑ pericardial pressure)
2. Constrictive pericarditis (↓ pericardial compliance)

Enlargement of Coronary Sinus

Conditions Causing RA Dilatation

1. Tricuspid stenosis / regurgitation
2. Right ventricular dysfunction (failure): CHF, cardiomyopathy, atrial fibrillation, atrioventricular node reentrant tachycardia
3. Severe pulmonary hypertension
4. Right atrial hypertension
5. Cardiac tamponade

Congenital Structural Anomaly

(a) increased volume of systemic venous blood
(1) persistent left SVC draining into coronary sinus
(2) interrupted IVC with hemiazygos continuation to a left SVC / hepatic veins connecting directly into coronary sinus

The coronary sinus dilates most commonly due to a left SVC draining into the coronary sinus!

(b) L-to-R shunt: oxygenated blood

› low-pressure shunt:
1. Interatrial shunt (= coronary sinus-ASD) LA → unroofed coronary sinus

An unroofed coronary sinus is a complete / partial wall defect partitioning the coronary sinus from the left atrium!

2. TAPVR

› high-pressure shunt:
3. Coronary arteriovenous fistula

Small Coronary Sinus

A. ACQUIRED
1. Atrial systole
2. Lipomatosis
3. Small heart
4. Stenosis

B. CONGENITAL
1. Atresia
2. Hypoplasia: corrected TGA
3. Unroofed coronary sinus
4. CHD: corrected TGA, tetralogy of Fallot, Ebstein

Neonatal Cardiac Failure

A. LEFT-SIDED OBSTRUCTIVE LESIONS
1. Segmental hypoplasia of aorta
2. Critical coarctation of the aorta
3. Aortic valve stenosis
4. Asymmetrical septal hypertrophy / hypertrophic obstructive cardiomyopathy
5. Mitral valve stenosis
6. Cor triatriatum

B. VOLUME OVERLOAD
1. Congenital mitral valve incompetence
2. Corrected transposition with left (= tricuspid) AV valve incompetence
3. Congenital tricuspid insufficiency
4. Ostium primum ASD

C. MYOCARDIAL DYSFUNCTION / ISCHEMIA
1. Nonobstructive cardiomyopathy
2. Anomalous origin of LCA from pulmonary trunk
3. Primary endocardial fibroelastosis
4. Glycogen storage disease (Pompe disease)
5. Myocarditis

D. NONCARDIAC LESIONS
1. AV fistulas: hemangioendothelioma of liver, AV fistula of brain, vein of Galen aneurysm, large pulmonary AV fistula
2. Transient tachypnea of the newborn
3. Intraventricular / subarachnoid hemorrhage

4. Neonatal hypoglycemia (low birth weight, infants of diabetic mothers)
5. Thyrotoxicosis (transplacental passage of LATS hormone)

Congestive Heart Failure & Cardiomegaly

mnemonic: Ma McCae & Co.

Myocardial infarction
anemia
Malformation
cardiomyopathy
Coronary artery disease
aortic insufficiency
effusion
Coarctation

Congenital Cardiomyopathy

mnemonic: CAVE GI

Cystic medial necrosis of coronary arteries
Aberrant left coronary artery / Absent coronary artery
Viral myocarditis
Endocardial fibroelastosis
Glycogen storage disease (Pompe)
Infant of diabetic mother / Ischemia

Delayed Myocardial Hyperenhancement on MRI

A. Ischemic heart disease (MI)
B. Nonischemic
    1. Dilated / hypertrophic cardiomyopathy
    2. Myocarditis
    3. Sarcoidosis
    4. Systemic sclerosis
    5. Endocardial fibroelastosis
    6. Fabry disease
    7. Chagas disease
    8. RV pressure overload
    9. Amyloidosis
    10. Cardiac transplantation
    11. Uremia

Subendocardial Enhancement

1. Ischemic heart disease
2. Amyloidosis
3. Löffler endocarditis (hypereosinophilic syndrome)

Transmural Enhancement

1. Ischemic heart disease
2. Myocarditis

Subepicardial Enhancement

1. Myocarditis

Mesocardial Enhancement

= delayed enhancement in midinterventricular septum

1. Hypertrophic cardiomyopathy
2. Dilated cardiomyopathy

Nodular Patchy Enhancement

1. Amyloidosis
2. Myocarditis
3. Cardiac sarcoidosis

Cardiac Accumulation of FDG

Myocardial Uptake

1. Physiologic FDG uptake ← depending on levels of blood glucose and free fatty acids
   √ none / diffuse / focal uptake in walls of ventricles
   Remedy: uptake suppressed by low-carbohydrate dinner followed by 12-hour fast
2. Drug interaction
   (a) lowering uptake:
   › Bezafibrate for treating hyperlipidemia
   › Levothyroxine (thyroid hormone)
   (b) increasing uptake:
   › benzodiazepines: Diazepam
3. Sarcoidosis
   √ hypermetabolic myocardial foci in nonperivascular distribution
4. Biventricular chemotherapy-induced cardiomyopathy
   √ increased metabolic activity in ventricular myocardium
5. Ventricular enlargement associated with systemic + pulmonary hypertension and valvular heart disease
   √ diffuse uniform increase in myocardial activity
6. Inflammatory myocarditis
7. Endocarditis ← infected valve
8. Neoplasia: sarcoma, metastasis (breast, lung, melanoma, lymphoma), myxoma
9. Coronary artery disease ← shift from fatty acid metabolism to glucose utilization ← ischemia

ATRIAL UPTAKE

1. Atrial fibrillation
2. Radiofrequency ablation for atrial fibrillation
3. Crista terminalis: ? physiologic

Pericardial Uptake

1. Post–radiation pericarditis
2. Malignant pericardial effusion

3. Epipericarditis
4. Lipomatous hypertrophy interatrial septum

CARDIAC TUMOR

◊ Extremely rare; often asymptomatic until very large!

- symptoms of cardiopulmonary diseases:
  - congestive heart failure: dyspnea, orthopnea, peripheral edema, paroxysmal nocturnal dyspnea
  - palpitations, heart murmur, cough, chest pain
- symptoms caused by peripheral emboli to cerebral / systemic / coronary circulation: syncope
- weight loss, fever, malaise

Location: intracavitary (obstruction, emboli), intramural (arrhythmia), pericardial (tamponade)

CXR:

√ cardiomegaly, pericardial effusion
√ signs of CHF
√ abnormal cardiac contour
√ pleural effusion

DDx: thrombus, pericardial and bronchogenic cyst, intrathoracic neoplasm, gastrointestinal hernia

Primary Heart Tumor

Prevalence: 0.002–0.250%; 0.001–0.030% (autopsy series)

Benign Heart Tumor in Adults (75%)

◊ More common than malignant neoplasms

1. Myxoma (with almost 50% the most common primary cardiac tumor; 25% of all cardiac tumors)
2. Papillary fibroelastoma (10% of all primary cardiac tumors; with 75% most common valvular tumor)
3. Lipoma (10% of all cardiac tumors)
4. Hydatid cyst (uncommon):
   √ localized bulge of left cardiac contour
   √ curvilinear / spotty calcifications (resembling myocardial aneurysm)

Cx: may rupture into cardiac chamber / pericardium

Malignant Heart Tumors (25%)

Prevalence: 25% of all cardiac tumors in adults;
10% of all cardiac tumors in children

1. Sarcomas
2. Rhabdomyosarcoma
3. Lymphoma (rare)
4. Pericardial mesothelioma
5. Malignant teratoma
6. Multiple cardiac myxomas

Secondary (Metastatic) Heart Tumor

◊ Most common cause of a neoplastic cardiac mass!

Age: typically > 60 years with disseminated tumor

Prevalence: metastatic÷primary disease = 30÷1; 10–12% of cancer patients develop metastases to the heart (autopsy)

Origin: lung, breast, esophagus, melanoma, lymphoma, leukemia

◊ Melanoma has the highest prevalence of cardiac seeding of any neoplasm!

- asymptomatic (frequently)
- arrhythmia (most common clinical sign)
- chest wall pain ← transient ischemic attack
- CHF (shortness of breath, fatigue, peripheral edema)

Site:

(a) peri- / epicardium (most common): lung > breast > lymphoma > leukemia > breast > esophagus

(b) myocardium: malignant melanoma; secondary extension to myocardium from epicardium

◊ Most common sites for myocardial lesions are LV free wall + interventricular septum (= greatest myocardial mass)

(c) endocardial / intracavitary (in only 5%)

(d) transvenous extension: RCC, hepatoma, adrenal adenocarcinoma

√ nonspecific imaging features

ECHO: iso- / hyperechoic

US/CT/MR: enhancement

MR: T1-hypointense + T2-hyperintense

Exception: T1-hyperintensity of melanoma, hemorrhagic lesion

Prognosis: death (⅓) ← cardiac tamponade / CHF / coronary artery invasion, sinoatrial node invasion

Cavoatrial Tumor Extension

= neoplasm arising in infradiaphragmatic sites

1. Hepatocellular carcinoma
   extension into hepatic veins / IVC (7.5%), into RA (4%)
2. RCC
   invasion of renal vein / IVC (5–15%), into RA (1%)
4. Wilms tumor
   into renal veins / IVC (4–10%), into RA (1%)
5. Adrenocortical carcinoma
6. Uterine leiomyoma
7. Leiomyosarcoma of IVC
8. Osteogenic sarcoma of pelvis

N.B.: sudden death may occur when tumor in RA intermittently obstructs tricuspid valve leading to low cardiac output

Congenital Cardiac Tumor

The majority of primary cardiac tumors in children are benign, rhabdomyoma and fibroma accounting

for 70%!

Prevalence: 1÷10,000

1. Rhabdomyoma (58%): usually multiple masses
2. Teratoma (20%): intrapericardiac, extracardiac
   √ multicystic mass
3. Cardiac fibroma (12%)
4. Cardiac hemangioma

Cardiac Tumor by Location

A thrombus is the most common cause of a cardiac mass!

A. ENDOCARDIAL / INTRACAVITARY
   1. Myxoma
   2. Thrombus
   3. Myofibroblastic sarcomas (MFH, leiomyo- sarcoma, fibrosarcoma, myxosarcoma)

B. VALVULAR
   1. Papillary fibroelastoma
   2. Valve vegetations
   3. Thrombus
   4. Myxoma

C. MYOCARDIAL / INTRAMURAL
   1. Rhabdomyoma of heart
   2. Cardiac fibroma

D. ENDO- / MYO- / EPICARDIAL
   1. Cardiac lipoma
   2. Cardiac sarcoma
   3. Lymphoma of heart

Left Atrial Mass

1. Myxoma
2. Thrombus
3. Septal lipoma

Right Atrial Mass

1. Thrombus
2. Myxoma
3. Hypernephroma
4. Eustachian valve
5. Chiari network
6. Angiosarcoma

Left Ventricular Mass

1. Thrombus
2. Papillary muscle
3. Rhabdomyoma
4. Metastasis

5. Fibroma

Right Ventricular Mass

1. Thrombus
2. Rhabdomyoma
3. Secondary deposit
4. Angiosarcoma

Mitral Valve Mass

(a) frequent

1. **Idiopathic mitral annular calcification** (most common)
   Cx: caseous degeneration of annulus
   CT:
   √ well-defined peripherally calcified mass
   √ central region of variable attenuation
   MR:
   √ hypointense mass on all sequences
2. Vegetation, usually infective (2nd most common) ← rheumatic disease / mitral valve prolapse / mitral valve prosthesis
3. Thrombus
4. Papillary fibroelastoma

(b) rare:

1. Myxoma
2. Lymphoma
3. Sarcoma
4. Metastasis

Myocardial Fat

= focal area of attenuation < 20 HU / fat-suppression on MR

1. Physiologic fat: ↑ in degree with age
   Prevalence: 16–43% on CT; 85% on autopsy; ↑ with age
   Location: anterolateral free wall + RVOT
   Site: outer half of RV wall → extension toward endocardium sparing subendocardium
   √ increase of total myocardial thickness: RV > LV

Physiologic RV myocardial fat is most frequent on anterolateral free wall, i.e. basal superior wall > middle superior wall > RVOT!

2. Healed myocardial infarct
   = replacement of scar by fat; usually > 6 months after MI
   Prevalence: 22–62% with history of MI
   Location: subendocardial region of culprit coronary a.
   √ thin linear / curvilinear configuration
3. Arrhythmogenic RV cardiomyopathy
4. Cardiac lipoma
5. Lipomatous hypertrophy of interatrial septum
6. Tuberous sclerosis complex

7. Dilated cardiomyopathy

CARDIAC CALCIFICATIONS

Detected by:

fluoroscopy (at low-beam energies ≤ 75 kVp is 57% sensitive) < digital subtraction fluoroscopy < conventional CT < ultrafast CT (96% sensitive)

@ Coronary arteries

@ Cardiac valves

◊ Valvar calcification means stenosis — its amount is proportionate to degree and duration of stenosis!

1. **Aortic valve**

◊ Valve calcium best seen on lateral view!

◊ Good correlation between amount of calcium and degree of stenosis:

› heavy calcification = significant stenosis

› no calcification = aortic stenosis unlikely

Cause: congenital bicuspid valve (70–85%) > atherosclerotic degeneration > rheumatic aortic stenosis (rare), syphilis, ankylosing spondylitis

Location: above + anterior to a line connecting carina + anterior costophrenic angle (lateral view)

(a) **Congenital bicuspid aortic valvular stenosis**

• calcium first detected at an average age of 28 years

◊ In patients < 30 years aortic valve calcifications are mostly due to a bicuspid aortic valve!

√ usually extensive cluster of heavy densely calcific deposits:

√ nearly circular calcification with interior linear bar (DIAGNOSTIC)

√ poststenotic dilatation of ascending aorta

(b) **Isolated rheumatic aortic stenosis**

• calcium first detected at an average age of 47 years

◊ In patients 30–60 years of age aortic valve calcification suggests rheumatic valve disease!

√ cluster of heavy dense calcific deposits without bicuspid contour

(c) **Degenerative aortic stenosis**

• calcium first detected at an average age of 54 years

◊ In patients > 65 years aortic valve calcification in 90% due to atherosclerosis!

√ curvilinear shape of calcium outlining tricuspid leaflets

√ diffuse dilatation + tortuosity of aorta (NO poststenotic dilatation)

2. **Mitral valve** (MV)

Cause: rheumatic heart disease (virtually always), infected endocarditis, tumor attached to mitral valve, mitral valve prolapse

Location: inferior to a line connecting carina + anterior costophrenic angle (on lateral view)

• calcium first detected in early 30s when patients become overtly symptomatic

◊ a severely calcified MV is usually stenotic, but MV stenosis frequently exists without

calcium
√ delicate calcification similar to coronary arteries (DDx: calcium in RCA / LCX)
√ superior-to-inferior motion

3. **Pulmonic valve**
Cause: tetralogy of Fallot, pulmonary stenosis, atrial septal defect
√ calcific pattern similar to calcified mitral valve

4. **Tricuspid valve** (extremely rare)
Cause: rheumatic heart disease, septal defect, tricuspid valve defect, infective endocarditis

@ Annulus
= valve rings serve as fibrous skeleton of the heart for attachment of myocardial fibers + cardiac valves

1. **Mitral annulus**
Cause: degenerative (physiologic in elderly)
Age: > 65 years; M÷F = 1÷4
May be associated with: mitral valve prolapse
Commonly associated with:
aortic valve calcium (= aortic stenosis), hypertension, hypertrophic cardiomyopathy; NOT MV dysfunction
√ dense bandlike calcification starting at posterior aspect + progressing laterally frequently forming a "reversed C" / "O" / "U" / "J"
Cx: mitral insufficiency (← impaired anterior mitral leaflet); atrial fibrillation; heart block (← infiltration into posterior wall conduction pathway)
Prognosis: doubles risk of stroke

2. **Aortic annulus**
√ usually in combination with degenerative aortic valve calcification → NO effect on valve function

3. **Tricuspid annulus**
Associated with: long-standing RV hypertension
Location: right AV groove
√ bandlike C-shaped configuration

@ **Pericardium**
Cause: idiopathic pericarditis, rheumatic fever (5%), TB, viruses, uremia, trauma, radiotherapy to mediastinum
Location: calcification over less pulsatile right-sided chambers along diaphragmatic surface, atrioventricular grooves, pulmonary trunk
√ clumpy amorphous calcium deposits, frequently in atrioventricular groove
√ diffuse eggshell calcification sparing LA (not covered by pericardium)
Cx: constrictive pericarditis
◊ 50% of patients with constrictive pericarditis show pericardial calcifications!

@ **Myocardium**
Cause: infarction, aneurysm, rheumatic fever, myocarditis
Frequency: in 8% post myocardial infarction; M > F
Location: apex / anterolateral wall of LV (coincides with LAD vascular distribution +

typical location of LV aneurysms)

√ thin curvilinear contour outlining the aneurysm

√ shaggy laminated calcification suggests calcification of associated mural thrombus

√ coarse amorphous calcifications caused by trauma, cardioversion, infection, endocardial fibrosis

@ **Interventricular septum**

Location: triangular fibrous area between mitral + tricuspid annuli (= trigona fibrosa) representing the basal segment of interventricular septum, closely related to bundle of His

Always associated with:

heavy calcification of mitral annulus / aortic valve

Cx: heart block

@ **Left atrial wall**

Cause: rheumatic endocarditis

(a) diffuse sheetlike form

• patient usually in CHF + atrial fibrillation

√ curvilinear calcification sparing interatrial septum + posterolateral wall on right side

√ shaggy nodular deposits in atrial appendage

Cx: mural thrombus formation + emboli

◊ LA wall calcification indicates atrial fibrillation!

(b) localized form

√ nodular calcific scar in posterior wall (= MacCallum patch) ← injury from a forceful jet in mitral valve insufficiency

[William George MacCallum (1874–1944), one of the first graduates of the Johns Hopkins Medical School in 1897, professor of pathology at Columbia University and Johns Hopkins University]

@ **Cardiac tumor**

atrial myxoma (in 5–10% calcified), rhabdomyoma, fibroma, angioma, osteosarcoma, osteoclastoma

@ **Endocardium**

Cause: cardiac aneurysm, thrombus, endocardial fibroelastosis

@ **Pulmonary artery**

Cause: severe precapillary arterial pulmonary hypertension (pHTN), syphilis

@ **Ductus arteriosus**

(a) in adults: indicates patency of ductus with associated long-standing precapillary arterial pHTN

(b) in children: ductus likely closed

√ calcium deposition in ligament of Botallo

[Leonardo Botallo (1530–1600), Italian surgeon and anatomist in the French royal medical service in Paris]

Coronary Artery Calcification

◊ The amount of coronary calcification correlates with the extent of atherosclerosis!

◊ The absence of coronary calcifications implies the absence of angiographically significant coronary vessel stenosis!

Cause: (1) Arteriosclerosis of intima
(2) Mönckeberg medial sclerosis (exceedingly rare)

Histo: calcified subintimal plaques

Pathophysiology:
injury to endothelium → allows circulating histiocytes to lodge in vessel wall → transformation into macrophages; these accumulate lipids ("fatty streaks" beneath surface endothelium); lipids calcify; the thin fibrous cap overlying lipid deposits may rupture allowing circulating blood to mount a thrombogenic reaction resulting in narrowing of lumen

◊ Calcium is deposited as calcium hydroxyapatite in hemorrhagic areas within atheromatous plaques!

Location: **"coronary artery calcification triangle"**
= triangular area along mid left heart border, spine, and shoulder of LV containing calcifications of left main coronary artery + proximal portions of LAD + LCX

Frequency (autoptic): LAD (93%), LCX (77%), main LCA (70%), RCA (69%)

CXR (detection rate up to 42%):
√ parallel calcified lines (lateral view)
◊ Indicates more severe coronary artery disease

Fluoroscopy: (promoted as inexpensive screening test)
(a) asymptomatic population
› calcifications in 34% in asymptomatic male individuals
› in 35% of patients with calcifications exercise test will be positive (without calcifications only in 4% positive)
› calcifications indicate > 50% stenosis (72–76% sensitive, 78% specific); frequency of coronary artery calcifications with normal angiogram increases with age; predictive value in population < 50 years as good as exercise stress test
(b) symptomatic population
› in 54% of symptomatic patients with ischemic heart disease
◊ In symptomatic patients 94% specificity for obstructive disease (> 75% stenosis) of at least one of the three major vessels!

CT:
(a) electron beam: threshold of +130 HU
(b) spiral CT: threshold of +90 HU

Clinical outcome:
(a) for coronary calcifications detected at fluoroscopy: 5.4% event risk at 1 year (vs. 2.1% without calcification)
(b) for electron beam CT a calcification score of ≥ 100 is highly predictive in identifying patients with events

Prognosis: 58% (87%) 5-year survival rate with (without) calcifications

PERICARDIUM

Pericardial Compressive Syndromes

1. Cardiac tamponade
2. Constrictive pericarditis ← loss of elasticity ← scarring
3. Concomitant effusive-constrictive pericarditis
   = constrictive physiology + coexisting pericardial effusion
   • central venous pressure remains elevated after drainage of pericardial effusion

Pericardial Thickening

= pericardial thickness ≥ 4 mm

◊ Pericardial thickening / calcifications are NOT DIAGNOSTIC of constrictive pericarditis! It requires symptoms of physiologic constriction / restriction.

A. PERICARDITIS WITH RESTRICTION
   • clinical findings of heart failure
   1. Constrictive pericarditis

B. PERICARDITIS WITHOUT RESTRICTION
   • NO clinical findings of heart failure
   √ enhancement of thickened pericardium indicates inflammation
   1. Acute pericarditis
   2. Uremia
   3. Rheumatic heart disease
   4. Rheumatoid arthritis
   5. Sarcoidosis
   6. Mediastinal irradiation

Pericardial Effusion

= pericardial fluid > 50 mL

• dyspnea, fatigue, symptoms of cardiac tamponade (50%)

Etiology:

A. SEROUS FLUID = transudate
   congestive heart failure, hypoalbuminemia (liver insufficiency), renal failure, irradiation, Dressler syndrome, postpericardiotomy syndrome, myxedema, drug-induced pericarditis

B. BLOOD = hemopericardium
   (a) iatrogenic: cardiac surgery / catheterization, anticoagulants, chemotherapy, radiation
   (b) trauma: penetrating / nonpenetrating
   (c) acute myocardial infarction / rupture of free wall
   (d) aneurysm rupture of left ventricle / coronary artery
   (e) rupture of ascending aorta / pulmonary trunk / ruptured aortic dissection
   (f) coagulopathy
   (g) neoplasm (30%): mesothelioma, sarcoma, teratoma, fibroma, angioma, metastasis (lung, breast, lymphoma, leukemia, melanoma)

C. LYMPH
   neoplasm, congenital, cardiothoracic surgery, obstruction of hilum / SVC

D. FIBRIN = exudate
(a) infection: viral, pyogenic, tuberculous
(b) renal insufficiency: 18% in acute uremia; 51% in chronic uremia; dialysis patient
(c) collagen vascular disease: SLE, rheumatoid arthritis, acute rheumatic fever
(d) hypersensitivity: Dressler syndrome

mnemonic: CUM TAPPIT RV
Collagen vascular disease
Uremia
Metastasis
Trauma
Acute myocardial infarction
Purulent infection
Post MI syndrome
Idiopathic
Tuberculosis
Rheumatoid arthritis
Virus

CXR:
√ normal with fluid < 250 mL / in acute pericarditis
√ "water bottle configuration" = symmetrically enlarged cardiac silhouette
√ loss of retrosternal clear space
√ "fat-pad" sign = separation of retrosternal from epicardial fat line > 2 mm (in 15%) by water density
√ rapidly appearing cardiomegaly + normal pulmonary vascularity
√ "differential density" sign = increase in lucency at heart margin ← slight difference in contrast between pericardial fluid + heart muscle
√ diminished cardiac pulsations

CT:
√ effusion of greater than water density = hemopericardium, malignancy, purulent effusion, hypothyroid state
√ effusion of low attenuation = chylopericardium
√ pericardial thickening > 4 mm suggests pericarditis

MR:
√ effusion hypointense on T1WI + hyperintense on T2WI = simple transudate
√ effusion hyperintense on T1WI + hypointense on T2WI = proteinaceous / hemorrhagic fluid
√ septations + debris + pericardial thickening = complex effusion as in inflammatory pericarditis of uremia / TB

ECHO:
√ separation of epi- and pericardial echoes extending into diastole (rarely behind LA)
√ volume estimates by M-mode:
(a) separation only posteriorly = < 300 mL
(b) separation throughout cardiac cycle = 300–500 mL
(c) plus anterior separation = > 1000 mL

Pneumopericardium

Etiology: shearing mechanism of injury of the heart during blunt trauma

Path: tear in fibrous pericardium, usually along course of phrenic nerve, allows pneumomediastinal air to enter

√ thick shaggy soft-tissue density of fibrous pericardium separated by air from cardiac density

√ air limited to distribution of pericardial reflection

Tension Pneumopericardium

= intrapericardial pressure > 265 mm H_2O (normal intrapericardial pressure = 50–100 mm H_2O)

◊ MEDICAL EMERGENCY!

Cause: blunt / penetrating trauma, iatrogenic, positive pressure ventilation (barotrauma), pericarditis with gas-forming organisms, direct extension of inflammatory process from adjacent structures, fistulous communication with air-containing structures, extension of pneumomediastinum

- chest pain, dyspnea, cyanosis, hypotension, tachycardia
- cardiac tamponade + hemodynamic compromise

CXR:

√ "halo" sign = continuous rim of air outlining the heart borders

√ "small heart" sign = sudden substantial decrease in size of cardiac silhouette

CT:

√ substantial amount of air in pericardial cavity

√ compression + displacement of heart:

√ collapse of heart chambers

√ flattening of anterior heart border

√ distension of IVC

Rx: needle pericardiocentesis / placement of drain

Pericardial disease

A. CONGENITAL
   1. Pericardial cyst / diverticulum
   2. Pericardial defect

B. ACQUIRED
   1. Pericardial effusion
   2. Cardiac tamponade
   3. Inflammatory pericarditis
   4. Constrictive pericarditis

C. PERICARDIAL PSEUDOMASS

cystic lesion, hematoma, gossypiboma (= foreign body granuloma around surgical sponge), complex organized effusion, abundant epicardial fat, epicardial fat necrosis

D. TRUE PERICARDIAL MASS

Pericardial neoplasms are rarely asymptomatic usually presenting with nonspecific diverse symptoms:

- exertional dyspnea, chest pain, cough, palpitations

- fatigue, night sweats, fever
- facial / lower-extremity edema

due to: pericarditis, pericardial effusion, invasion of adjacent structures

(a) **Primary pericardial tumor** (extremely rare)
1. Pericardial mesothelioma
2. Pericardial sarcoma: angio-, lipo-, rhabdomyo-, synovial sarcoma, undifferentiated sarcoma
3. Pericardial lymphoma
4. Pericardial teratoma
5. Pericardial fibroma, hemangioma, lipoma

(b) Secondary pericardial tumor (in 10–12%):
› direct invasion by neoplasm of lung, mediastinum (lymphoma), heart (angiosarcoma)
› hematologic spread from malignant melanoma, lymphoma, breast cancer
› venous extension from renal cell carcinoma, HCC

Cx: (1) invasion of mediastinal structures
(2) regional / distant metastases
(3) pericardial effusion
(4) cardiac tamponade
(5) compression of vascular structures / cardiac chambers
(6) encasement of vital structures
(7) involvement of coronary arteries
(8) myocardial infarction
(9) diastolic dysfunction
(10) constrictive physiology

PULMONARY VASCULARITY

Normal Pulmonary Vasculature

A. VASCULAR DISTRIBUTION
√ pulmonary vessels within upper perihilum approximate ⅓ of total vascularity
√ pulmonary vessels within lower perihilum approximate ⅔ of total vascularity

B. VASCULAR TAPERING
√ pulmonary vessels taper near transition of middle ⅓ to outer ⅓ of lung

C. VASCULAR CALIBER
√ straight / slightly concave main pulmonary artery contour (mild convexity is normal in young females)
√ pulmonary trunk measures < 4.5 cm (leftward distance from vertical line at carina to most lateral aspect of main pulmonary artery contour)
√ right interlobar / intermediate pulmonary artery measures 10–15 (9–14) mm in males (females) on PA radiographs
√ pulmonary vessel size < 1–2 mm in extreme lung periphery
√ artery within 1st anterior intercostal space measure ≤ 3 mm

CT:

√ upper limits of normal for main pulmonary artery = 3 cm

Normal Pulmonary Vascularity & Normal-sized Heart

mnemonic: MAN

Myocardial ischemia
Afterload (= pressure overload problems)
Normal

Increased Pulmonary Vasculature

A. OVERCIRCULATION

= shunt vascularity = arterial + venous overcirculation

(a) congenital heart disease (most common)
  (1) L-R shunts
  (2) Admixture cyanotic lesions

(b) high-flow syndromes
  (1) Thyrotoxicosis
  (2) Anemia
  (3) Pregnancy
  (4) Peripheral arteriovenous fistula

√ diameter of right descending pulmonary artery larger than trachea just above aortic knob

√ increased size of vessels (veins + arteries) larger than accompanying bronchus (= "kissing cousin" sign), best seen just above hila on AP view

Evaluation of Pulmonary Vasculature on ERECT Chest Film

	Normal	*PAH*	*PVH*	*Overload*
Distribution (UL÷LL)	1÷2	1÷2	1÷1 or 1÷2	1÷1
Vessel tapering	middle–outer 1/3	variably pruned	outer third	outer third
Vascular caliber		increased	increased	increased
Artery-to-bronchus ratio:				
upper lung	0.85 ± 0.15		1.50 ± 0.25	1.62 ± 0.31
lower lung	1.34 ± 0.25		0.87 ± 0.20	1.56 ± 0.28
Vessel margins (edema)	sharp	sharp	obscured	obscured

√ enlarged hilar vessels (lateral view)

√ visualization of vessels below 10th posterior rib

B. PULMONARY VENOUS HYPERTENSION

√ redistribution of flow (not seen in younger children)

√ indistinctness of vessels with Kerley lines (= interstitial edema)

√ fine reticulated pattern

√ alveolar edema

C. PRECAPILLARY HYPERTENSION
- √ enlarged main + right and left pulmonary arteries
- √ abrupt tapering of pulmonary arteries

D. PROMINENT SYSTEMIC / AORTOPULMONARY COLLATERALS
1. Tetralogy of Fallot with pulmonary atresia (= pseudotruncus)
2. VSD + pulmonary atresia (single ventricle, complete transposition, corrected transposition)
3. Pulmonary-systemic collaterals
   - √ coarse vascular pattern with irregular branching arteries (from aorta / subclavian arteries)
   - √ small central vessels despite apparent ↑ in vascularity

Decreased Pulmonary Vascularity
= obstruction to pulmonary flow
- √ vessels reduced in size and number
- √ hyperlucent lungs
- √ small pulmonary artery segment + hilar vessels

PULMONARY ARTERY

Invisible Main Pulmonary Artery
A. UNDERDEVELOPED = RVOT obstruction
1. Tetralogy of Fallot
2. Hypoplastic right heart syndrome (tricuspid / pulmonary atresia)

B. MISPLACED PULMONARY ARTERY
1. Complete transposition of great vessels
2. Persistent truncus arteriosus

Major Aortopulmonary Collateral Arteries
= systemic pulmonary supply via aortic branches
1. Pulmonary atresia with VSD = severe form of tetralogy of Fallot
2. Tetralogy of Fallot
3. Transposition of great arteries
4. Double-outlet right ventricle
5. Truncus arteriosus

Decreased Diameter of Pulmonary Artery
1. Lung cancer
   - ◊ Tumor extending > 180° of arterial circumference of main pulmonary artery indicates unresectability!
2. Mediastinal fibrosis
3. Takayasu arteritis
4. Chronic thromboembolic disease

Unequal Pulmonary Blood Flow

1. Tetralogy of Fallot
   √ diminished flow on left side (hypoplastic / stenotic pulmonary artery in 40%)
2. Persistent truncus arteriosus (esp. type IV)
   √ diminished / increased blood flow to either lung
3. Pulmonary valvular stenosis
   √ increased flow to left lung ← jet phenomenon

Dilatation of Pulmonary Artery

1. Idiopathic dilatation of pulmonary trunk
2. Pulmonic valve stenosis
   √ poststenotic dilatation of trunk + left pulmonary artery
3. Pulmonary regurgitation
   (a) severe pulmonic valve insufficiency
   (b) absence of pulmonic valve (may be associated with tetralogy)
4. Congenital L-to-R shunts
5. Pulmonary arterial hypertension
6. Aneurysm: mycotic / traumatic
7. Intravascular pulmonary metastases

Filling Defect in Pulmonary Artery

1. Thromboembolism (99%)
2. Nonthrombotic embolus: fat droplets, bubbles of air / nitrogen, tumor, foreign bodies (talc, polymethylmethacrylate particles)
   ◊ Particles mostly too small to be visualized
3. Primary sarcoma

PULMONARY VEIN

Congenital Anomalies of Pulmonary Veins

A. ANOMALIES IN NUMBER
   1. Anomalous unilateral single pulmonary vein = **meandering pulmonary vein**
      √ serpentine tubular opacity adjacent to lung hilum
      DDx: scimitar syndrome, AVM, lung nodule

B. ANOMALIES IN DIAMETER
   2. Congenital unilateral pulmonary vein stenosis / atresia
      √ small lung with ipsilateral mediastinal deviation
      √ reticular opacities with Kerley B lines
      DDx: pulmonary neoplasm, fibrosing mediastinitis
   3. Pulmonary vein varix

C. ANOMALIES IN DRAINAGE
   4. TAPVR
   5. PAPVR
   6. Scimitar syndrome
   7. Sinus venosus defect
   8. Malposition of septum primum

9. Cor triatriatum

Pulmonary Vein Stenosis / Obstruction

Mechanism: extrinsic compression / invasion

1. Radiofrequency ablation for atrial fibrillation (1–10%)
2. Surgery: heart surgery, correction of APVR, lung transplantation
3. Neoplastic infiltration: lung primary, atrial tumor, primary sarcoma
4. Fibrosing mediastinitis
5. Benign inflammatory process: sarcoidosis, tuberculosis

Pulmonary Vein Calcification

1. Rheumatic mitral valve disease (long-term): associated with atrial fibrillation, considerable LA dilatation, high prevalence of dyspnea, female predominance
2. Chronic renal failure: (= deposits of extraskeletal metastatic calcium) associated with cardiac arrhythmia

PULMONARY HYPERTENSION (pHTN)

= sustained mean pulmonary arterial pressure of ≥ 25 mmHg at rest / > 30 mmHg with exercise
= pulmonary capillary wedge pressure ≤ 15 mmHg determined by right heart catheterization

Right heart catheterization is the reference standard for pulmonary HTN because it enables direct measurement of pulmonary pressure, resistance, and cardiac output!

Normal: resting mean pulmonary artery pressure ≤ 20 mmHg

Cause: elevated precapillary pulmonary resistance + normal pulmonary venous pressure (= pulmonary wedge pressure ≤ 15 mmHg)

Pathophysiology:

reduction in cross-sectional area of the pulmonary vascular bed → chronic elevation in pulmonary arterial pressure → RV hypertrophy → RA dilatation → abnormal septal motion impairing LV function → RV dilatation → tricuspid regurgitation → decreased cardiac output → right heart failure

In severe pulmonary hypertension the hypertrophied RV is of spherical shape with a greater cross-sectional area than the LV resulting in abnormal septal motion that impairs left ventricular function.

◊ The most useful noninvasive parameters to assess RV function: RV volume + RV ejection fraction measured at cardiac MR imaging!

Histo: intimal cellular proliferation + medial hypertrophy in walls of muscular arteries

Classification by anatomic level:

A. PRECAPILLARY CAUSE

= changes limited to pulmonary arterial circulation @ level of muscular arteries

1. Chronic thromboembolic pulmonary disease as a complication of single or multiple undiagnosed (? %) / diagnosed (4%) acute symptomatic pulmonary thromboembolic events
2. In-situ pulmonary arterial thrombotic disease (polycythemia, sickle-cell disease)
3. Widespread pulmonary embolism by intravascular
   (a) malignant cells (= tumor emboli) in cancer of kidney, liver, stomach, breast,

prostate, ovary, malignant melanoma, choriocarcinoma, right atrial myxoma

(b) parasites (= parasitic emboli), commonly of Schistosoma mansoni

(b) foreign material, eg. talcosis of IV drugs

◊ Fat, amniotic fluid, septic emboli rarely produce clinically significant PAH!

4. Pulmonary vasculitis: eg, collagen vascular disease (especially scleroderma), CREST, HIV
5. Longstanding cardiac L-to-R shunt = Eisenmenger syndrome with reversal into R-to-L shunt: VSD (in 10%), ASD (in 5%), PDA, TGV
6. Alveolar hypoventilation syndromes
7. Primary pHTN (idiopathic)

B. PULMONARY PARENCHYMAL DISEASE

= mechanical interference with small pulmonary arteries (classified under precapillary cause)

(a) hypoxic lung disease:

1. Chronic obstructive pulmonary disease
2. Interstitial pulmonary fibrosis (in 46% PAH)
3. Ventilatory failure ← thoracic cage deformity (kyphoscoliosis, thoracoplasty, restrictive pleural disease), diaphragmatic disorder, neuromuscular disease, spinal cord injury

(b) connective tissue disorder:

1. Scleroderma (PAH in 12%)
2. CREST variant of scleroderma (calcinosis, Raynaud phenomenon, esophageal motility disorder, sclerodactyly, telangiectasia)
3. Polymyositis, dermatomyositis, systemic lupus erythematosus, rheumatoid arthritis

(c) infection:

1. HIV (6–12 x compared to general population)
2. Sarcoidosis
3. Tuberculosis

C. **P**OSTCAPILLARY CAUSE

= PULMONARY VENOUS HYPERTENSION

= findings located in pulmonary venous circulation + between capillary bed and left atrium

1. Elevated left atrial pressure: usually MV disease, chronic left heart failure, left atrial tumor / thrombus
2. Fibrosing mediastinitis → narrowing of pulmonary veins, which may also affect precapillary vessels
3. Pulmonary venoocclusive disease: idiopathic
4. Pulmonary capillary hemangiomatosis

• often not clinically recognized until advanced stage
• nonspecific symptoms: exertional dyspnea, fatigue, syncope

ECG with Doppler (79–100% sensitive, 68–98% specific):

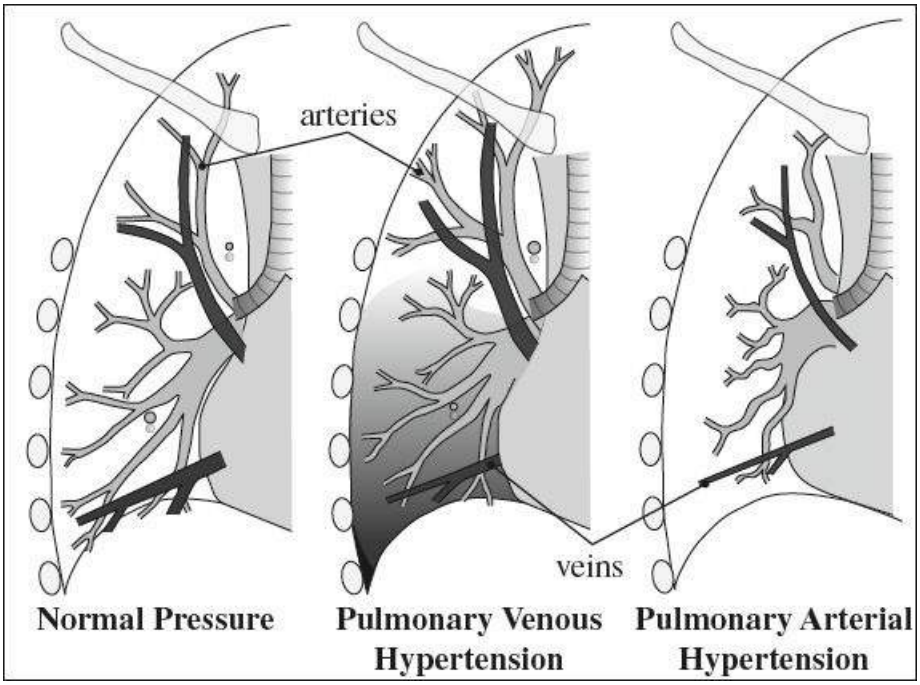
√ systolic pulmonary artery pressure
√ tricuspid regurgitant jet velocity

CXR:

√ may be normal in early stage
√ central pulmonary arterial dilatation
√ pruning of peripheral arteries
√ ↑ diameter of right interlobar artery: > 16 (> 15) mm in men (women) measured from its lateral margin to interlobar bronchus
√ ↓ retrosternal air space (LAT view) by RV enlargement

NUC (V/Q scan):

◊ A normal V/Q scan rules out chronic thromboembolic disease (modality of choice)!



√ normal / diffuse patchy perfusion defects in severe pHTN

CT pulmonary angiogram:

√ <u>vascular signs:</u>
- √ widest short-axis diameter of pulmonary trunk ≥ 29 mm (87% sensitive, 89% specific, 97% PPV) measured on transverse sections at level of PA bifurcation
  CAVE: in pulmonary fibrosis PA dilatation occurs without pHTN
- √ diameter ratio of distal pulmonary trunk to ascending aorta (measured at same level) > 1 (96% PPV, 92% specific) independent of systolic-diastolic variations with strong correlation in patients < 50 years
- √ diameter of main left + right pulmonary artery > 16 mm (= poor indicator of pulmonary arterial hypertension)
- √ segmental artery-to-bronchus ratio > 1 in 3 of 4 lobes (100% specific)
- √ "pruning" / tapering of peripheral pulmonary arteries
  = ↓ in caliber of smaller muscular arteries (← vasocon-striction) + disproportionate increase in caliber of central fibrous arteries (← sustained increase in flow by a factor of > 2)
- √ pulmonary veins

(a) small: ← precapillary pulmonary HTN
(b) enlarged: ← left-sided heart disease

√ enlargement of bronchial systemic arteries to > 1.5 mm: chronic thromboembolic pHTN (73%) > primary pHTN (14%)

√ vascular complications:

√ subpleural pulmonary infarcts (with elevated pulmonary venous pressure / underlying malignancy)

√ calcified plaques of central pulmonary arteries (PATHOGNOMONIC)

√ dissection / massive apposition thrombus of central pulmonary arteries

√ <u>lung parenchymal signs</u> (HRCT):

√ centrilobular ground-glass nodules (common in idiopathic pHTN)

Histo: cholesterol granulomas ← ingestion of RBCs by macrophages following repeated episodes of pulmonary hemorrhage

√ ***geographic mosaic pattern*** of lung attenuation ← regional variations in lung perfusion without dilatation of bronchi:

√ hyperdense areas containing large caliber vessels (= ↑ vessel diameter in areas of hyperattenuation)

N.B.: increase in density = increase in vessel caliber

√ hypodense areas containing small caliber vessels ← tapering of peripheral vessels in areas of hypoattenuation

◊ MOST COMMON + SPECIFIC SIGN of chronic pulmonary thromboembolism!

√ <u>mediastinal & cardiac signs:</u>

√ right heart hypertrophy + dilatation:

√ RV myocardial thickness > 4 mm

√ straightening / leftward bowing of interventricular septum

√ right heart dilatation = ratio of RV÷LV > 1÷1 at midventricular level on axial image

√ RA enlargement

√ dilatation of tricuspid valve annulus

√ dilatation of IVC + coronary sinus

√ reflux of contrast medium into IVC + hepatic veins (usefulness diminishes with injection rate > 3 mL/sec)

√ mild pericardial thickening + pericardial effusion

√ adenopathy + septal lines + ground-glass opacities suggestive of pulmonary venoocclusive disease

√ NO increase of pulsations in middle third of lung

Dana Point Classification of Pulmonary Hypertension (2008) *(based on similar pathophysiologic traits)*	
Group	*Description*
1	*Pulmonary arterial hypertension* (paHTN)
1.1	Idiopathic pulmonary arterial hypertension
1.2	Heritable
1.3	Drug / toxin induced
1.4	Associated with connective tissue disease, HIV infection, portopulmonary hypertension, CHD, schistosomiasis, chronic hemolytic anemia
1.5	Persistent pulmonary hypertension in newborn
1'	Pulmonary veno-occlusive disease / pulmonary capillary hemangiomatosis
2	pHTN due to *left heart failure*: systolic / diastolic dysfunction, valvular disease
3	pHTN due to *lung disease / hypoxia*: chronic obstructive pulmonary disease, interstitial lung disease, mixed restrictive + obstructive disease, sleep-disordered breathing, alveolar hypoventilation disorder, chronic high altitude exposure
4	pHTN due to *chronic thromboembolic disease*
5	pHTN with unclear *multifactorial* mechanisms: hematologic disorders (myeloproliferative disorder, splenectomy); systemic disorder (sarcoidosis, Langerhans cell histiocytosis, lymphangioleiomyomatosis, neurofibromatosis, vasculitis); metabolic disorder (glycogen storage disease, Gaucher disease, thyroid disorder); others (tumoral obstruction, fibrosing mediastinitis, chronic renal failure on dialysis)
': distinct category not completely separated from PAH but difficult to categorize	

√ functional parameter:
- √ reduced right pulmonary artery distensibility (= change in cross-sectional area between systole and diastole) of < 16.5% (86% sensitive, 96% specific) measured as (Areamax – Areamin) ÷ Area max • 100
  - ◊ Strong correlation with mean pulmonary artery pressure!
- √ decrease in RV ejection fraction

MR (steady-state free precession cine):
- √ RV hypertrophy (in almost 100% if RV systolic pressure exceeds 70 mmHg):
  - √ mean thickness of RV wall = 6 mm
  - √ ventricular mass index (= RV mass ÷ LV mass) > 0.6
- √ RV dilatation:
  - √ mean RV end-diastolic volume = 80 mL
  - √ tricuspid regurgitation ← dilatation of tricuspid valve annulus
- √ enlargement of RA + IVC + SVC
- √ septum straight / bowed leftward
- √ diminished RV ejection fraction (mean of 45%)

√ reduced distensibility of main pulmonary artery (mean of 8%)
√ systolic intraluminal signals in pulmonary arteries ← slow flow correlating with severity of PAH:
√ mean average velocity < 11.7 cm/sec (93% sensitive, 82% specific) on phase-contrast imaging

Angio (reference standard):
◊ Right heart catheterization = the only test that confirms pHTN!
√ direct measurement pulmonary pressure + resistance + cardiac output

Cx: central arterial thrombosis, premature atherosclerosis of central elastic + muscular pulmonary arteries, aneurysmal dissection of pulmonary arteries, hypertrophy + dilatation of right side of heart

Dx: clinical assessment of hemodynamic parameters, medical history, histologic findings

Pulmonary Arterial Hypertension (PAH)

= precapillary pHTN

Pathogenesis:

A. HYPERKINETIC CAUSES
1. L-to-R shunt
2. High cardiac output states: thyrotoxicosis, chronic anemia
3. Diffuse pulmonary arteriovenous shunts: hereditary hemorrhagic telangiectasia (Osler-Weber-Rendu), pregnancy, polysplenia syndrome, liver cirrhosis, complex cardiac malformations

B. OBLITERATIVE CAUSES
(a) vascular = precapillary pHTN:
1. Primary plexogenic pulmonary arteriopathy = Primary pHTN
2. Arteritis (eg, Takayasu)
3. Embolization
› chronic thromboembolic disease
› tumor
√ lymphangitic carcinomatosis
› parasites, eg, schistosomiasis
√ hepatosplenomegaly
› talc crystals
√ micronodular opacities
√ perihilar fibrotic masses
4. Persistent fetal circulation
5. Pulmonary capillary hemangiomatosis

(b) pleuropulmonic disease
1. Chronic interstitial lung disease = cor pulmonale:
COPD, emphysema, chronic bronchitis, asthma, bronchiectasis, malignant infiltrate, granulomatous disease, cystic fibrosis, end-stage fibrotic lung, S/P lung resection, idiopathic hemosiderosis, alveolar proteinosis, alveolar microlithiasis
2. Pleural disease + chest deformity: fibrothorax, thoracoplasty, kyphoscoliosis

(c) vasoconstriction

1. Chronic alveolar hypoxia
   = hypoxic pulmonary arterial hyperperfusion:
   chronic high altitude; sleep apnea; chronic hypercapnea ← hypoventilation ← neuromuscular disease / obesity
3. Portopulmonary hypertension (in 5% of patients with liver cirrhosis and portal hypertension)

(c) vasodilatation
1. Hepatopulmonary syndrome (in 20% of patients with liver cirrhosis) ← excessive vascular production of vasodilator nitric oxide

C. CHRONIC PULMONARY VENOUS HYPERTENSION

Cor Pulmonale

mnemonic: TICCS BEV

Thoracic deformity
Idiopathic: primary pulmonary hypertension (1%)
Chronic pulmonary embolism
COPD
Shunt: ASD, VSD, etc
Bronchiectasis
Emphysema
Vasculitis

Pulmonary Venous Hypertension (PVH)

= INCREASED VENOUS PULMONARY PRESSURE = VENOUS CONGESTION
= postcapillary pHTN = primary findings located within pulmonary venous circulation between capillary bed + LA

Dx: uniform / widely variable elevation of pulmonary capillary wedge pressure (PCWP) > 15 mmHg

Cause:

A. LV INFLOW TRACT OBSTRUCTION
√ normal-sized heart with right ventricular hypertrophy
√ prominent pulmonary trunk
@ proximal to mitral valve:
√ normal-sized left atrium
› pulmonary veins
1. TAPVR below the diaphragm
2. Pulmonary venoocclusive disease
3. Stenosis of individual pulmonary veins
4. Atresia of common pulmonary vein

› mediastinum
1. Fibrosing mediastinitis (may also affect precapillary vessels)
2. Constrictive pericarditis

› left atrium
1. Cor triatriatum
2. Left atrial mass: thrombus, myxoma, sarcoma, metastasis

3. Supravalvular ring of left atrium

@ at mitral valve level = mitral valve stenosis

√ enlarged left atrium

1. Rheumatic mitral valve stenosis ± regurgitation (99%)

√ enlarged left atrial appendage

2. Congenital mitral valve stenosis
3. Parachute mitral valve (= single bulky papillary muscle)

B. LEFT VENTRICULAR FAILURE (more common)

(a) ABNORMAL PRELOAD with secondary mitral valve incompetence (= volume overload)

1. Aortic valve regurgitation
2. Eisenmenger syndrome (= R-to-L shunt in VSD)
3. High-output failure:
   noncardiac AVM (cerebral AVM, vein of Galen aneurysm, large pulmonary AVM, hemangioendothelioma of liver, iatrogenic), thyrotoxicosis, anemia, pregnancy

(b) ABNORMAL afterload (= pressure overload)
= LV outflow tract obstruction

1. Hypoplastic left heart syndrome
2. Aortic stenosis (supravalvular, valvular, anatomic subaortic)
3. Interrupted aortic arch
4. Coarctation of the aorta

(c) DISORDERS OF CONTRACTION AND RELAXATION

1. Endocardial fibroelastosis
2. Glycogen storage disease (Pompe disease)
3. Cardiac aneurysm
4. Cardiomyopathy
   › congestive (alcohol)
   › hypertrophic obstructive cardiomyopathy, particularly in IDM
   (1) Asymmetric septal hypertrophy
   (2) Idiopathic hypertrophic subaortic stenosis

(d) MYOCARDIAL ISCHEMIA

1. Anomalous left coronary artery
2. Coronary artery disease

Histo:

(a) primary changes: venous medial hypertrophy + intimal proliferation, marked thickening of venous internal elastic lamina

(b) secondary changes: capillary bed congestion with adjacent vascular proliferation, interlobular septal and pleural edema + fibrosis, lymphatic dilatation, alveolar hemosiderosis, paraseptal venous infarcts adjacent to complete venous occlusion

Cx: secondary pulmonary arterial hypertension

CT:

√ interlobular septal thickening

√ pleural effusion

√ pulmonary edema
√ vascular redistribution (on coronal reformatted images!)
√ dilated left atrium (with left-sided heart disease)

CXR:
√ equalization of pulmonary vascularity: PCWP 13–15 mmHg
√ cephalization of pulmonary vascularity: PCWP 16–18 mmHg
√ interstitial pulmonary edema (PCWP 19–24 mmHg)
= fluid within peribronchovascular connective tissue:
√ peribronchial thickening / cuffing
√ indistinct vessel margins
√ Kerley B lines = short horizontal reticulations within lateral subpleural lung bases
√ Kerley A lines = 3–4-cm-long lines of interlobular septal thickening radiating from hila to mid and upper lung zones
√ perihilar haze = hilar interstitial edema
√ thickened pleural fissures / pseudoeffusion = fluid within subpleural connective tissue
√ small pleural effusions
√ alveolar pulmonary edema (PCWP ≥ 25 mmHg)
= bilateral perihilar and basilar airspace opacification

HEART VALVES

Pathology of Cardiac Valves

1. Degenerative disease
2. Inherited cause
3. Postrheumatic heart disease

AORTA

Enlarged Aorta

Definition: diameter > 50% above high end of normal range (depending on age + sex + body size + segment)

PA CXR:
√ aortic knob > 4.0 cm measured from indented trachea to most lateral margin of aorta
√ right convex contour above RA margin + lateral displacement of SVC (= dilatation of ascending aorta)

A. INCREASED VOLUME LOAD
1. Aortic insufficiency
2. PDA

B. POSTSTENOTIC DILATATION
1. Valvular aortic stenosis

C. INCREASED INTRALUMINAL PRESSURE
1. Coarctation
2. Systemic hypertension

D. MURAL WEAKNESS / INFECTION
1. Cystic media necrosis: Marfan / Ehlers-Danlos syndrome

2. Congenital aneurysm
3. Syphilitic aortitis
4. Mycotic aneurysm
5. Atherosclerotic aneurysm (compromised vasa vasorum)

E. LACERATION OF AORTIC WALL
1. Traumatic aneurysm
2. Dissecting hematoma

Enlarged Aortic Root

A. COMMON CAUSES
1. Connective tissue disorder: eg, Marfan syndrome, Ehlers-Danlos syndrome
2. Bicuspid aortic valve
3. **Loeys-Dietz syndrome:**
inherited autosomal dominant disorder with typically severe + widespread arterial disease
Cx: aortic dissection at small aortic diameter
4. Hypertension
5. Atherosclerosis: aneurysm typically diffuse + fusiform; descending > ascending aorta; root typically spared

B. LESS COMMON CAUSES
1. Infection: eg, syphilis
2. Vasculitis: eg, Takayasu arteritis, giant cell arteritis
3. Trauma
4. **Familial thoracic aneurysm disease:**
mostly autosomal dominant of variable expression + penetrance → aneurysm at significantly younger age
5. Turner syndrome

Aortic Wall Thickening

1. Intramural hematoma
= aortic dissection without intimal tear
2. Aortitis segments of aortic arch + branch vessels
3. Atherosclerotic plaque
√ irregular narrowing of aortic lumen
4. Adherent thrombus

Aortitis

A. Infectious aortitis

B. Idiopathic conditions
1. Idiopathic aortitis (pathologic diagnosis only)
2. Idiopathic inflammatory aortic aneurysm
3. Idiopathic retroperitoneal fibrosis

C. Noninfectious aortitis = vasculitis
Segment: mostly affecting ascending aorta
(a) rheumatic diseases commonly causing aortitis

1. Takayasu arteritis
2. Ankylosing spondylitis
3. Giant cell arteritis (GCA)
4. Cogan syndrome
5. Relapsing polychondritis

(b) rheumatic diseases uncommonly causing aortitis
1. Rheumatoid arthritis
2. Seronegative spondyloarthropathies
3. Behçet disease
4. SLE

(c) rheumatic diseases rarely causing aortitis
1. Sarcoidosis
2. Antineutrophil cytoplasmic antibody–associated aortitis: Wegener granulomatosis, polyarteritis nodosa
3. Juvenile rheumatoid arthritis

Rheumatic diseases with an > 10% prevalence of aortitis include Takayasu arteritis, GCA, long-standing ankylosing spondylitis, Cogan syndrome, relapsing polychondritis.

Acute Aortic Syndrome

1. Intramural hematoma
2. Penetrating atherosclerotic ulcer
3. Aortic dissection with overt false lumen

Narrowing of Abdominal Aorta in Childhood

1. Takayasu arteritis
2. Fibromuscular dysplasia
3. Prior radiation therapy
4. Neurofibromatosis-1
5. Williams syndrome
6. Midaortic syndrome

Aortic Calcifications

Intimal Calcification

Cause: part of atherosclerotic plaque
Associated with: inflammatory cells, lipid, vascular smooth muscle cells
Site: within perimeter of internal elastic lamina
√ discrete punctate lesion on radiograph

Medial Calcification

Cause: aging, diabetes, end-stage renal disease, neuropathy, genetic syndromes
Associated with: elastin + vascular smooth muscle cells
√ linear deposit along elastic lamellae resembling railroad tracks (when severe)

Vascular Rings

= anomaly characterized by encirclement of trachea + esophagus by aortic arch + branches

Prevalence: < 1% of all congenital cardiac defects

Cause: abnormal persistence / regression of 1 of 6 embryonic aortic arches

A. Usually symptomatic vascular ring
   - chronic stridor, wheezing, recurrent pneumonia
   - dysphagia, failure to thrive

   1. Double aortic arch with R descending aorta + L ductus arteriosus
   2. R aortic arch with R descending aorta + aberrant L subclavian artery + persistent L ductus / ligamentum arteriosum

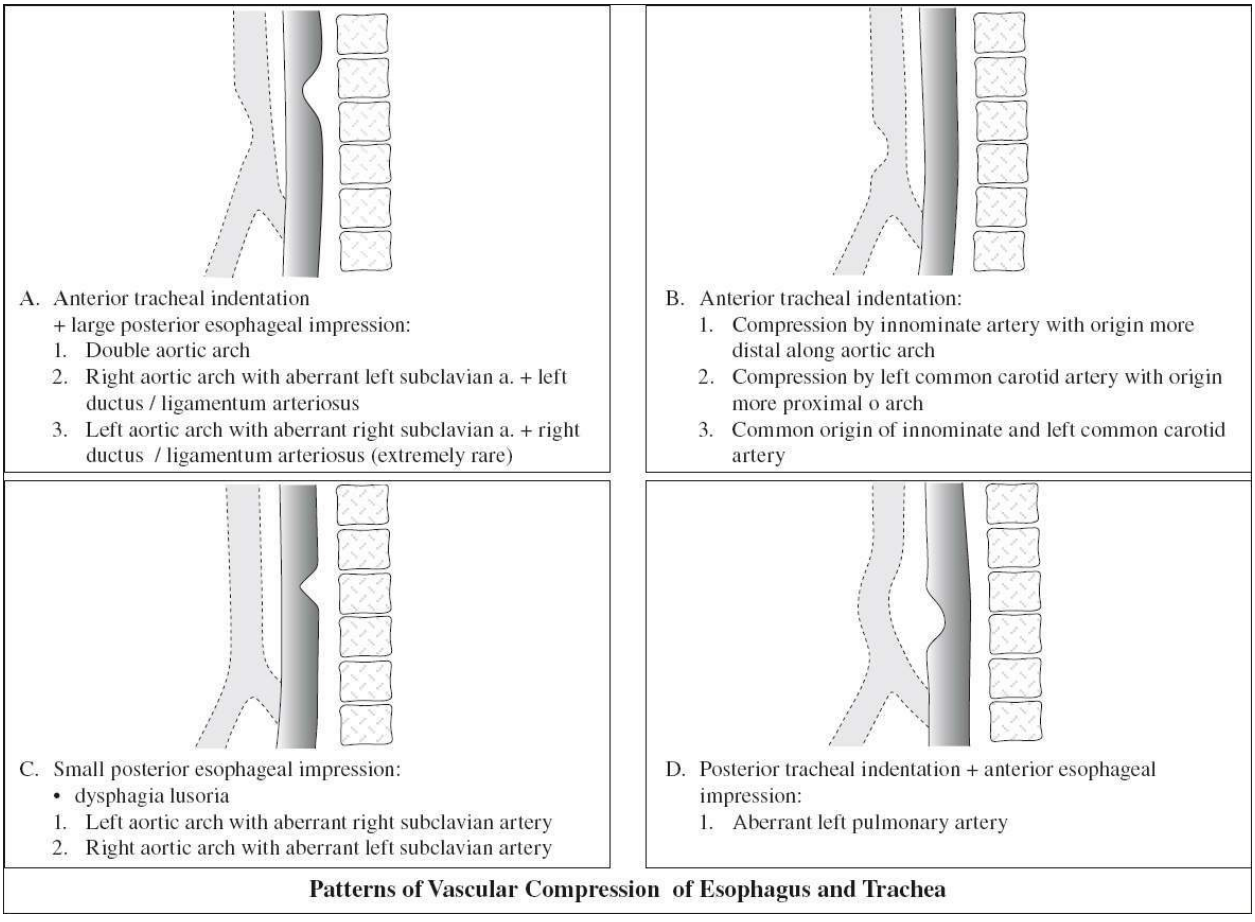
      N.B.: left obliterated ductus arteriosus (= **ligament of Botallo**) passes from L pulmonary artery to descending aorta / L subclavian artery

      - symptoms + radiographic findings identical to double aortic arch

      √ indentation on right lateral esophageal wall (by aortic arch)
      √ impression on the anterolateral esophageal wall (by ligament of Botallo)
      √ origin of L subclavian artery frequently dilated

   3. L arch with L descending aorta + R ductus / ligamentum
   4. Aberrant L pulmonary artery = "pulmonary sling"

Frequency of CXR findings:



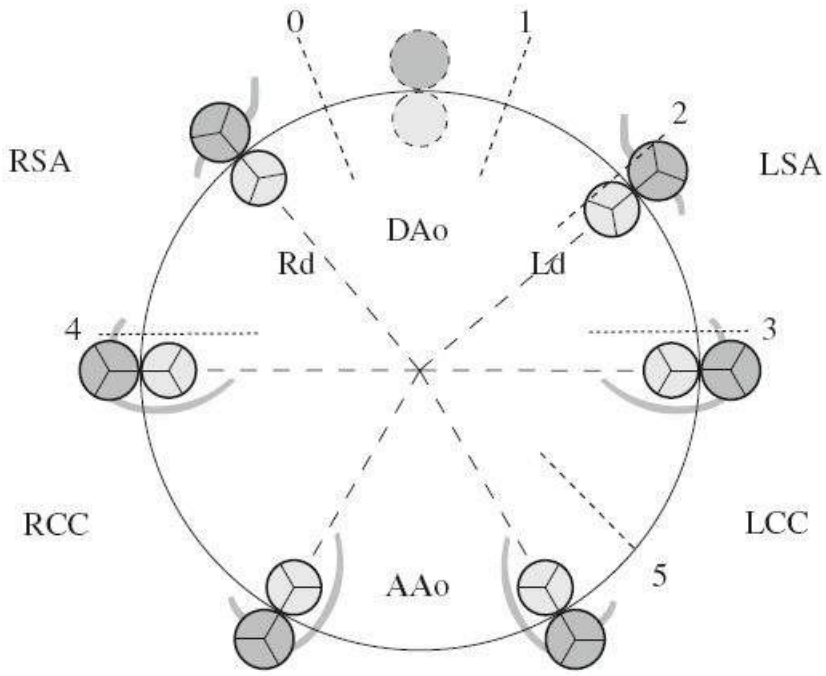
Patterns of Vascular Compression of Esophagus and Trachea

- › frontal CXR:
  - √ right aortic arch (85%)
  - √ focal indentation of distal trachea (73%)
- › lateral CXR:
  - √ anterior tracheal bowing (92%)
  - √ increased retrotracheal opacity (79%)
  - √ focal tracheal narrowing (77%)

B. Occasionally symptomatic lesions
   1. Anomalous R innominate artery
   2. Anomalous L common carotid artery / common trunk
   3. R aortic arch with L descending aorta + L ductus / ligamentum

C. Usually asymptomatic lesions
   1. L aortic arch + aberrant R subclavian artery
   2. L aortic arch with R descending aorta
   3. R aortic arch with R descending aorta + mirror-image branching
   4. R aortic arch with R descending aorta + aberrant L subclavian artery
   5. R aortic arch with R descending aorta + isolation of L subclavian artery
   6. R aortic arch with L descending aorta + L ductus / ligamentum

Complete Vascular Rings



Edwards' Hypothetical Aortic Arch Development

RSA	= right subclavian a.	AAo	= ascending aorta
LSA	= left subclavian a.	DAo	= descending aorta
RCC	= right common carotid a.	Rd	= right ductus
LCC	= left common carotid a.	Ld	= left ductus

0 = normal left aortic arch

1 = right aortic arch with mirror-image branching; ductus from pulmonary a. to left brachiocephalic / subclavian a. = no vascular ring

2 = right aortic arch with mirror-image branching; ductus from pulmonary a. to descending aorta = complete vascular ring

3 = right aortic arch with aberrant left subclavian a.; ductus from pulmonary a. to descending aorta (most common complete vascular ring)

4 = left aortic arch with aberrant right subclavian a.

5 = right aortic arch with aberrant left brachiocephalic artery; ductus from pulmonary a. to descending aorta (very uncommon)

2 + 3 = right aortic arch with isolated left subclavian a. (very uncommon)

1. Double aortic arch (55%)
2. R aortic arch + aberrant L subclavian a. + L ligamentum arteriosum (12–25%)
3. R aortic arch with mirror-image branching + retroesophageal L ligamentum arteriosum

4. L aortic arch + R descending aorta, R subclavian artery + R ligamentum arteriosum

Abnormal Left Ventricular Outflow Tract

LVOT = area between IVS + aML from aortic valve cusps to mitral valve leaflets

1. Membranous subaortic stenosis
   = crescent-shaped fibrous membrane extending across LVOT + inserting at aML
   √ diffuse narrowing of LVOT
   √ abnormal linear echoes in LVOT space (occasionally)
2. Prolapsing aortic valve vegetation
3. Narrowed LVOT (< 20 mm)
   (a) Long-segment subaortic stenosis
      √ aortic valve closure in early systole with coarse fluttering
      √ high-frequency flutter of mitral valve in diastole (aortic regurgitation)
      √ symmetric LV hypertrophy
   (b) ASH / IHSS
      √ asymmetrically thickened septum bulging into LV + LVOT
      √ systolic anterior motion of aML (SAM)
   (c) Mitral stenosis
   (d) Endocardial cushion defect

Obstruction of Left Ventricular Outflow Tract

1. Bicuspid aortic valve
2. Coarctation of aorta
3. Subvalvular aortic stenosis
4. Supravalvular aortic stenosis

VENA CAVA

Vena cava anomalies

Persistent Left SVC

= BILATERAL SVCS

Prevalence: 0.3–0.5% of general population; 3–11% of patients with CHD
◊ Most common congenital thoracic venous anomaly

Etiology: failure of involution of left anterior + left common cardinal veins + left horn of sinus venosus

Origin: confluence of left IJV + subclavian vein

Course: lateral to aortic arch, anterior to left hilum

Terminus: drains into enlarged coronary sinus (in 92%) / into LA (in 8%) creating a R-to-L shunt (increased prevalence of CHD)

Associated with:

(a) Right SVC (82–90%) normal / small = SVC duplication
(b) Bridging vein connecting right + left SVC (35–55%)
(c) Absence of right SVC (in 10–18%): → increased incidence of CHD (ASD, VSD, tetralogy of Fallot, bicuspid aortic valve, aortic coarctation, mitral atresia, cor

triatriatum, azygos continuation of IVC)

√ persistent left SVC should be suspected when a dilated coronary sinus is seen at cross-sectional imaging

√ left SVC arises from confluence of left subclavian and jugular veins + traverses caudally lateral to aortic arch
√ left SVC lies anterior to left hilum → traverses along ligament of Marshall → drains into RA via dilated coronary sinus
√ CVC placement into left SVC may be mistaken for arterial / mediastinal / pleural placement (frontal CXR)
√ hemiazygos arch formed by left superior intercostal vein + persistent left SVC (20%)
√ left brachiocephalic vein: present in 25–35%; absent / small in 65%

Circumaortic Left Renal Vein

Prevalence: 1.5–8.7%
Etiology: persistence of anterior intersubcardinal + posterior intersupracardinal anastomosis
√ venous collar encircling aorta
√ superior left renal vein crosses aorta anteriorly
√ inferior left renal vein receives left gonadal vein + crosses aorta posteriorly 1–2 cm below the superior left renal vein
Significance: preoperative plan for nephrectomy

Duplicated IVC

= DOUBLE IVC
Prevalence: 0.2–3%
Etiology: persistence of both supracardinal veins
√ small / equal-sized left IVC formed by left iliac vein
√ crossover to right IVC via left renal vein / or more inferiorly
√ crossover usually anterior / rarely posterior to aorta
Significance: recurrent pulmonary embolism after IVC filter placement
DDx: left gonadal v./ a., inferior mesenteric v.

DOUBLE IVC WITH RETROAORTIC RIGHT RENAL VEIN AND AZYGOS CONTINUATION OF IVC

Etiology: persistence of left supracardinal v. and dorsal limb of renal collar + regression of ventral limb + failure of formation of right subcardinal-hepatic anastomosis

DOUBLE IVC WITH RETROAORTIC RIGHT RENAL VEIN AND HEMIAZYGOS CONTINUATION OF IVC

Etiology: persistence of left lumbar + thoracic supracardinal v. + left suprasubcardinal anastomosis + failure of formation of right subcardinal-hepatic anastomosis
√ right IVC and right renal vein join the left IVC and continue cephalad as the hemiazygos vein
√ hemiazygos vein follows alternative pathways:
(a) crosses posterior to aorta at T8-9 and joins the rudimentary azygos vein
(b) continues cephalad + joins coronary vein via persistent left SVC
(c) accessory hemiazygos continuation to left brachiocephalic vein

√ hepatic segment of IVC drains into right atrium

Left IVC

= TRANSPOSITION OF IVC = SOLITARY LEFT IVC

Prevalence: 0.2–0.5%

Etiology: persistence of left + regression of right supracardinal vein

√ left IVC usually joins left renal vein

√ crossover as left renal vein usually anterior / rarely posterior to aorta

DDx: left-sided paraaortic adenopathy

Significance: difficult transjugular access to infrarenal IVC filter placement

Retroaortic Left Renal Vein

Prevalence: 1.8–2.1%

Etiology: persistence of posterior intersupracardinal anastomosis + regression of anterior intersubcardinal anastomosis

√ crossover usually below / occasionally at level of right renal vein

SVC Obstruction / Stricture

- SVC syndrome

A. INTRINSIC CAUSE long-standing CVCs, transvenous pacemaker, postoperative / postradiation effects, fibrin sheath, bland / tumor thrombus

B. EXTRINSIC CAUSE
compression from malignancy (small cell + non–small cell lung cancer, lymphoma, metastatic lymphadenopathy, tracheal malignancy), mediastinal mass, fibrosing mediastinitis, lymphadenopathy, ascending aortic aneurysm

IVC Obstruction

A. INTRINSIC OBSTRUCTION
   (a) neoplastic (most frequent)
      1. Renal cell carcinoma (in 10%), Wilms tumor
      2. Adrenal carcinoma, pheochromocytoma
      3. Pancreatic carcinoma, hepatic adenocarcinoma
      4. Metastatic disease to retroperitoneal lymph nodes (carcinoma of ovary, cervix, prostate)
   (b) nonneoplastic
      1. Idiopathic
      2. Proximally extending thrombus from femoroiliac veins
      3. Systemic disorders: coagulopathy, Budd-Chiari syndrome, dehydration, infection (pelvic inflammatory disease), sepsis, CHF
      4. Postoperative / traumatic phlebitis, ligation, plication, clip, cava filter, severe exertion

B. INTRINSIC CAVAL DISEASE
   (a) neoplastic
      1. Leiomyoma, leiomyosarcoma, endothelioma
   (b) nonneoplastic

1. Congenital membrane

C. EXTRINSIC COMPRESSION
   (a) neoplastic
      1. Retroperitoneal lymphadenopathy (adults) ← metastatic disease, lymphoma, granulomatous disease (TB)
      2. Renal + adrenal tumors (children)
      3. Hepatic masses
      4. Pancreatic tumor
      5. Tumor-induced desmoplastic reaction (eg, metastatic carcinoid)
   (b) nonneoplastic
      1. Hepatomegaly
      2. Tortuous aorta / aortic aneurysm
      3. Retroperitoneal hematoma
      4. Massive ascites
      5. Retroperitoneal fibrosis

D. FUNCTIONAL OBSTRUCTION
   1. Pregnant uterus
   2. Valsalva maneuver
   3. Straining / crying (in children)
   4. Supine position with large abdominal mass

E. COLLATERAL PATHWAYS
   1. Deep pathway: ascending lumbar veins to azygos vein (right) + hemiazygos vein (left) + intravertebral, paraspinal, extravertebral plexus (Batson plexus)
   2. Intermediate pathway: via periureteric plexus + left gonadal vein to renal vein
   3. Superficial pathway: external iliac vein to inferior epigastric vein + superior epigastric vein + internal mammary vein into subclavian vein
   4. Portal pathway: retrograde flow through internal iliac vein + hemorrhoidal plexus into inferior mesenteric vein + splenic vein into portal vein

Reflux of Contrast Media

IVC Reflux

1. Cardiac tamponade
2. Tricuspid regurgitation
3. Hypovolemic / cardiogenic shock
4. Pulmonary embolism

Azygos Vein Reflux

= sign of raised central venous pressure

1. Pulmonary arterial hypertension
2. Massive pulmonary embolism
3. Cor pulmonale
4. Ischemic right heart failure
5. Cardiac tamponade
5. Tumoral obstruction of main pulmonary artery

6. Bilateral pneumothoraces
7. Positive pressure ventilation for ARDS

INFLAMMATORY CARDIOVASCULAR DISEASE

@ Myocardium
   1. Cardiac sarcoidosis
   2. Myocarditis

@ Peri- & Epicardium
   1. Pericarditis
   2. Epipericarditis

@ Vessels
   1. Atherosclerosis
   2. Vasculitis

Eosinophilic Diseases with Cardiac Involvement

1. Eosinophilic heart disease
2. Churg-Strauss syndrome
3. Early giant cell myocarditis
4. Drug-induced hypersensitivity reaction
5. Parasitic infection
6. Tropical endomyocardial fibrosis
7. Malignancy

Vasculitis

= inflammation and necrosis of vessel wall

A. LARGE-VESSEL VASCULITIS
   1. Giant cell arteritis (= temporal arteritis)
   2. Takayasu arteritis
   5. Ankylosing spondylitis
   6. Reiter syndrome

B. MEDIUM-SIZED–VESSEL VASCULITIS
   1. Polyarteritis nodosa
   2. Kawasaki disease
   3. Relapsing polychondritis
   4. Drug-induced vasculitis:
      › methamphetamine
      › cocaine: neurovascular, cardiovascular complications, aortic dissection, venous thrombosis, mesenteric artery thrombosis, renal infarction

C. SMALL-VESSEL VASCULITIS
   (a) ANCA-associated small-vessel vasculitis (= antineutrophil cytoplasmic autoantibodies)
      1. Granulomatosis with polyangiitis = Wegener granulomatosis
      2. Eosinophilic granulomatosis with polyangiitis = Churg-Strauss syndrome
      3. Microscopic polyangiitis
   (b) immune-complex small-vessel vasculitis

1. IgA vasculitis = Henoch-Schönlein purpura
2. Essential cryoglobulinemic vasculitis
3. Cutaneous leukocytoclastic angiitis

others: lupus, rheumatoid, Sjögren, Behçet, Goodpasture, serum sickness, drug-induced, hypocomplementemic urticaria

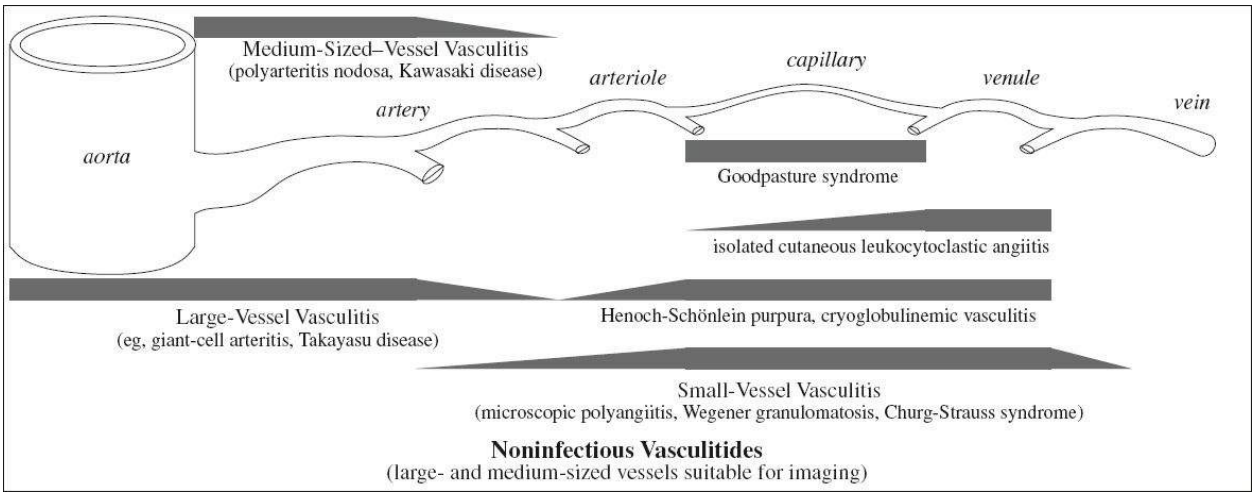
(c) inflammatory bowel disease vasculitis

D. VARIABLE-SIZED–VESSEL VASCULITIS
1. Behçet disease
2. Cogan syndrome

E. SINGLE-ORGAN VASCULITIS
1. Primary angiitis of CNS (PACNS)

F. VASCULITIS OF A SYSTEMIC DISEASE
1. Systemic lupus erythematosus (SLE)
2. Sjögren syndrome
3. Rheumatoid arthritis
4. APLA (antiphospholipid antibody) syndrome
5. Scleroderma

G. VASCULITIS WITH PROBABLE ETIOLOGY
1. Infection-induced vasculitis
2. Acute septic meningitis
3. Mycobacterium tuberculosis
4. Neurosyphilis
5. Viral: HIV-related vasculitis, varicella-zoster vasculopathy



Major Pediatric Vasculitides with Major Sites of Involvement		
Type	*Predilection Site*	*EULAR-PRES Criteria (European League Against Rheumatism - Paediatric Rheumatology European Society)*
Takayasu arteritis	aortic arch & branches, pulmonary arteries	Angio: characteristic abnormalities + absent peripheral pulses / claudication, blood pressure discrepancy in any limb, bruits, HTN, elevated acute phase reactants
Kawasaki disease	coronary arteries	fever > 5 days + bilateral conjunctival injection, changes of lips & oral cavity, cervical lymphadenopathy, polymorphous exanthem, changes in peripheral extremities / perineal area
Polyarteritis nodosa	GI tract, kidneys	Angio: abnormalities of medium to small-sized arteries with systemic necrotizing vasculitis + skin involvement, myalgia, HTN, peripheral neuropathy, renal involvement (proteinuria, hematuria, impaired function)
Granulomatosis with polyangiitis	upper + lower respiratory tract, kidneys	upper airway involvement + laryngotracheobronchial stenosis + pulmonary & renal involvement, histopathologic granulomatous inflammation, ANCA positivity
Henoch-Schönlein purpura	gut, skin , kidneys	purpura / petechiae with lower limb predominance + arthritis / arthralgia, abdominal pain, renal involvement (hematuria, proteinuria), IgA deposition

6. Fungal: mucormycosis aspergillosis
7. Parasitic: cysticercosis
8. Malignancy-induced vasculitis
9. Drug-induced vasculitis
10. Radiation-induced vasculitis

Classification of Childhood Vasculitis

European League against Rheumatism (EULAR) & Paediatric Rheumatology European Society (PRES)

Incidence: 23÷100,000 annually

The 2 most common types of primary pediatric vasculitis are Henoch-Schönlein purpura (49%) and Kawasaki disease (23%).

A. LARGE VESSEL
   1. Takayasu Arteritis
B. MEDIUM VESSEL
   1. Kawasaki disease
   2. Polyarteritis nodosa
   3. Cutaneous polyarteritis
C. SMALL-VESSEL GRANULOMATOUS
   1. Wegener granulomatosis
   2. Eosinophilic granulomatosis with polyangiitis
D. SMALL-VESSEL NONGRANULOMATOUS
   1. Henoch-Schönlein purpura
   2. Microscopic polyangiitis
   3. Isolated cutaneous leukocytoclastic vasculitis
   4. Hypocomplementemic urticarial vasculitis
E. OTHERS
   1. Behçet disease
   2. Vasculitis associated with connective tissue disease
   3. Secondary to infection, malignancy, drugs
   4. Isolated vasculitis of CNS
   5. Cogan syndrome

Multiple Aneurysms

1. Polyarteritis nodosa
   - fever, malaise, weight loss, myalgia
   - proteinuria, hematuria
2. Rheumatoid vasculitis
   - advanced rheumatoid arthropathy
3. Systemic lupus erythematosus
   - arthritis, photosensitivity
   - malar rash, discoid rash, oral ulcers
4. Churg-Strauss syndrome
5. Heroin / methamphetamine abuse
6. Wegener granulomatosis
7. Scleroderma
   - skin thickening, induration and tightness
8. Diabetes
9. Giant cell temporal arthritis (rare)

VASCULAR TUMORS & MALFORMATIONS

Classification of International Society for the Study of Vascular Anomalies (ISSVA)

Vascular Tumors

= true neoplastic lesion with cellular proliferation and hyperplasia characterized by rapid early proliferative stage and later involuting stage

1. Infantile hemangioma
2. Congenital hemangioma
3. Kaposiform hemangioendothelioma
4. Tufted angioma
5. Hemangiopericytoma
6. Pyogenic granuloma
7. Spindle cell hemangioendothelioma

Developmental Vascular Malformations

= error of vascular morphogenesis → collection of dysplastic abnormally dilated arteries, veins, capillaries, lymphatics characterized by

- greater conspicuity with age ← steady growth commensurate with patient growth (puberty, pregnancy, trauma, surgery may cause growth spurts)
- NO spontaneous involution / regression

1. **Slow-flow** vascular malformation
   √ absence of flow voids on SE images
   DDx: low-signal-intensity striations, septa, thrombosed vessels, phleboliths
   (a) Venous malformation
   (b) Lymphatic malformation
   (c) Capillary malformation
2. **High-flow** vascular malformation
   Frequency: 10% of malformations in extremities

√ presence of signal voids demonstrating enhancement and high-signal-intensity foci on GRE images

(a) Arteriovenous malformation

(b) Congenital arteriovenous fistula

Characterization:

√ NO blood flow = lymphatic malformation

√ venous flow ONLY:

√ WITH phlebolith = venous malformation

√ NO phlebolith = low-flow vascular malformation

Rx: sclerotherapy

1. Klippel-Trénaunay syndrome
2. Sturge-Weber syndrome
3. Blue rubber bleb nevus
4. Proteus syndrome
5. Gorham-Stout syndrome
6. Maffucci syndrome

√ arterial flow:

(a) WITH mass = vascular tumor

1. PHACE syndrome
2. Kasabach-Merritt syndrome

(b) NO mass = high-flow vascular malformation

Rx: arterial embolization

1. Parkes Weber syndrome
2. Hereditary hemorrhagic telangiectasia
3. Vascular metameric syndrome
   (a) Wyburn-Mason syndrome
   (b) Cobb syndrome

Serpentine High-Flow Vascular Channels on MRI

1. Hemangioendothelioma
2. Hemangiopericytoma
3 Angiosarcoma
4. Rhabdomyosarcoma
5. Synovial sarcoma
6. Alveolar soft-part sarcoma
7. Extraskeletal Ewing sarcoma

LYMPH FLOW DISORDERS

1. Lymphatic dysplasia
2. Lymphedema

PRIMARY HYPERCOAGULABLE STATES

= THROMBOPHILIA

• DVT of extremities / pulmonary embolism

(a) Qualitative defect / quantitative ↓ in an antithrombotic protein:
› antithrombin III
› protein C
› protein S
› Trousseau phenomenon in cancer: HCC, pancreatic ca.
(b) Increased level of a prothrombotic protein
› activated protein C resistance (Factor V Leiden)
› G20210A prothrombin gene mutation

SUDDEN CARDIAC DEATH IN YOUNG ADULTS

= death from unexpected circulatory arrest within 1 hour of onset of symptoms ← usually a result of cardiac arrhythmia

Incidence: 1–2÷1000

Age range: 18–35 years

- precipitated by:
  - ventricular tachycardia / fibrillation (75–80%)
  - bradyarrhythmia (15–20%) = AV block, asystole

Cause:

A. ANOMALOUS CORONARY ARTERY
   1. Interarterial / intramural course
   2. LCA arising from pulmonary artery
   3. Coronary artery fistula

B. PRIMARY CARDIOMYOPATHY
   1. Hypertrophic / dilated / noncompaction cardiomyopathy
   2. Lysosomal / glycogen storage disease
   3. Arrhythmogenic right ventricular hypertrophy

C. INHERITED ARRHYTHMIA SYNDROME
   1. Long / short QT syndrome
   2. Brugada syndrome
   3. Catecholaminergic polymorphic ventricular tachycardia

D. VALVULAR DISEASE
   1. Mitral valve prolapse
   2. Aortic stenosis

E. CONGENITAL HEART DISEASE
   1. L- and D-transposition of great vessels
   2. Tetralogy of Fallot
   3. Single left ventricle

In order of frequency:

hypertrophic cardiomyopathy > anomalous coronary artery with an interarterial / intramural course > arrhythmogenic right ventricular cardiomyopathy (ARVC)

CARDIAC SURGERY

Surgical Procedures

A. AORTICOPULMONARY WINDOW SHUNT
= side-to-side anastomosis between ascending aorta and left pulmonary artery (reversible procedure)
→ tetralogy of Fallot

B. BLALOCK-HANLON PROCEDURE
= surgical creation of ASD
→ complete transposition

C. BLALOCK-TAUSSIG SHUNT
= end-to-side anastomosis of subclavian artery to pulmonary artery, performed ipsilateral to innominate artery / opposite to aortic arch
MODIFIED BLALOCK-TAUSSIG SHUNT uses synthetic graft material such as polytetrafluoroethylene (Gore-Tex®) in an end-to-side anastomosis between subclavian artery + ipsilateral branch of pulmonary artery
→ tetralogy of Fallot, tricuspid atresia with pulmonic stenosis

D. FONTAN PROCEDURE
= systemic flow of venous blood to lungs without passing through any ventricle
(1) External conduit from right atrium to pulmonary trunk (= venous return enters pulmonary artery directly)
(2) Closure of ASD: floor constructed from flap of atrial wall and roof from piece of prosthetic material
→ tricuspid atresia

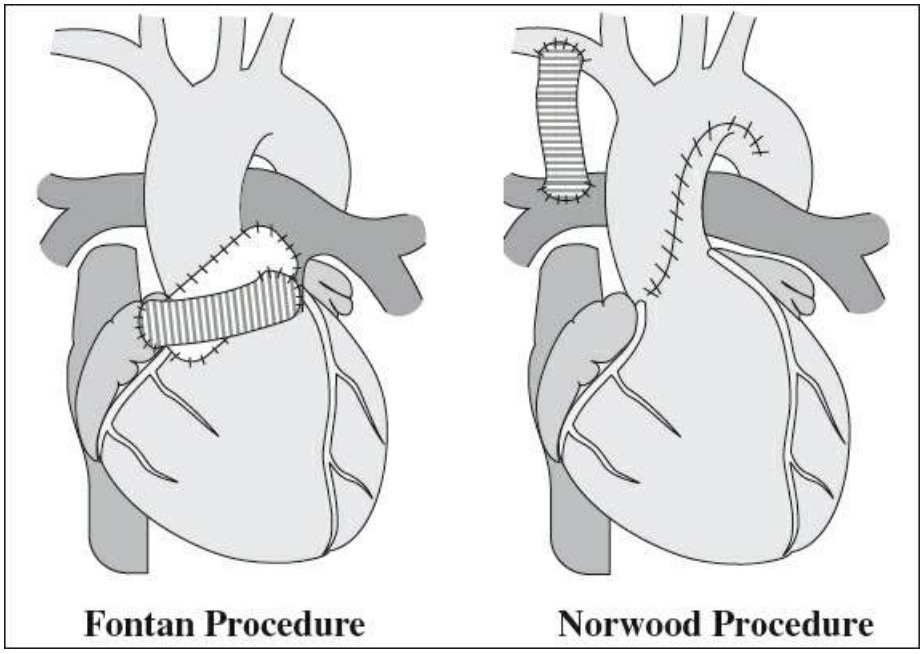
E. GLENN SHUNT
= end-to-side shunt between distal end of right pulmonary artery and SVC; reserved for patients with cardiac defects in which total correction is not anticipated
→ tricuspid atresia

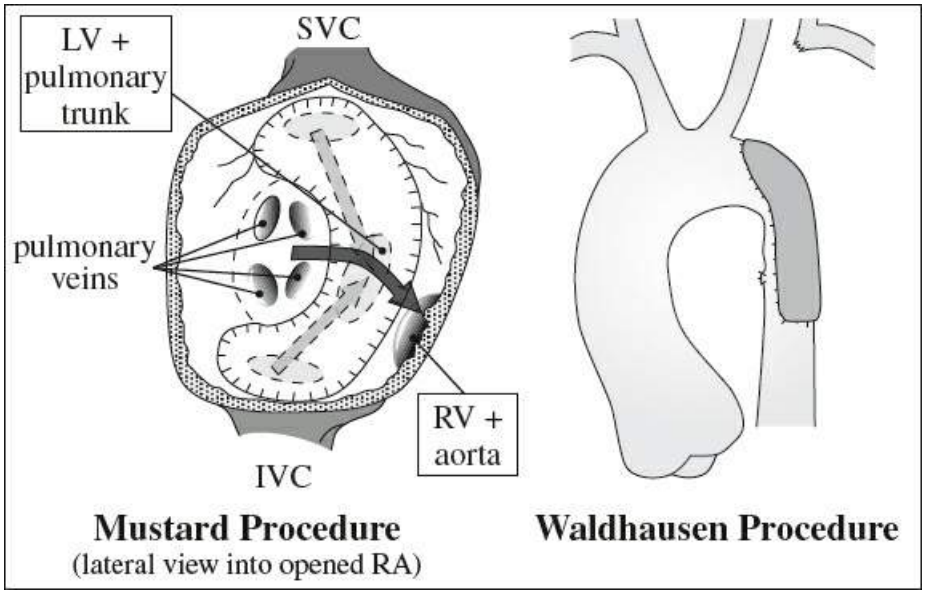
F. NORWOOD PROCEDURE
(1) Construction of "neoaorta" from aortic arch + descending aorta + main pulmonary artery supplying coronary and systemic circulation
(2) Communication between RV as systemic ventricle and systemic circulation
(3) Shunt between innominate artery + main pulmonary artery to control pulmonary arterial blood flow
(4) Excision of distal ductus arteriosus + atrial septum to prevent pulmonary venous hypertension
→ hypoplastic left heart syndrome

G. POTT SHUNT
= side-to-side anastomosis between descending aorta + left pulmonary artery
→ tetralogy of Fallot

H. MUSTARD PROCEDURE
(a) removal of atrial septum
(b) pericardial baffle placed into common atrium such that systemic venous blood is rerouted into LV and pulmonary venous return into right ventricle and aorta
→ complete transposition

I. RASHKIND PROCEDURE
= balloon atrial septostomy





→ complete transposition

J. RASTELLI PROCEDURE
external conduit (Dacron) with porcine valve connecting RV to pulmonary trunk
→ transposition

K. WALDHAUSEN PROCEDURE
= subclavian artery used to augment aortic lumen
= SUBCLAVIAN FLAP ANGIOPLASTY
(a) ligation of left subclavian artery at origin of left vertebral artery ± ligation of vertebral artery
(b) lateral incision of subclavian artery with extension into aortic isthmus
(c) excision of diaphragm of coarctation

(d) subclavian artery flap folded down into incision
→ coarctation

L. WATERSTON-COOLEY SHUNT
= side-to-side anastomosis between ascending aorta and right pulmonary artery;
(a) extrapericardial (WATERSTON)
(b) intrapericardial (COOLEY)
→ tetralogy of Fallot

Heart Valve Prosthesis

(a) mechanical valve requiring long-term anticoagulation
1. Starr-Edwards
√ caged ball
◊ Predictable performance from large long-term experience
2. Björk-Shiley / Lillehei-Kaster / St. Jude
√ tilting disk
◊ Excellent hemodynamics, very low profile, durable

(b) tissue (biologic) valve of limited durability
3. Hancock / Carpentier-Edwards (= porcine xenograft) Ionescu-Shiley (= bovine xenograft)
◊ Low incidence of thromboembolism, no hemolysis, central flow, inaudible

Postoperative Thoracic Deformity

A. ON RIGHT SIDE
1. Systemic-PA shunt: Blalock-Taussig shunt, Waterston-Cooley shunt, Glenn shunt, central conduit shunt
2. Atrial septectomy: Blalock-Hanlon procedure
3. VSD repair: through RA
4. Mitral valve commissurotomy

B. ON LEFT SIDE
1. PDA
2. Coarctation
3. PA banding
4. Mitral valve commissurotomy
5. Systemic-PA shunt: Blalock-Taussig shunt, Pott shunt

Postoperative Complications of Mitral Valve Surgery

1. Paravalvular abscess
2. Valvular vegetation
3. Pseudoaneurysm
4. Restricted leaflet excursion
5. Dehiscence of valve prosthesis / annuloplasty band
6. LCx artery injury

PULSUS ALTERNANS

= alternating arterial pulse height with regular cardiac rhythm

1. Intrinsic myocardial abnormality
   severe left ventricular dysfunction (CHF, aortic valvular disease, hypothermia, hypocalcemia, hyperbaric stress, ischemia)
2. Alternating end-diastolic volumes abnormalities in venous filling + return (obstructed venous return, IVC balloon

CARDIAC CONDUCTION DEVICES (CCD)

Components of CCD

A. Pulse generator hardware, programmable software, lithium iodide battery (5–10-year lifespan)
B. Leads for pacemaker / ICD
   1. Conductor
   2. Insulation: silicone rubber / polyurethane
   3. Electrode(s): uni- / bipolar
   4. Lead tip fixation in cardiac trabeculae:
      (a) passive: prongs, tines, fins, helix, cone
      (b) active: helical screw
   5. Proximal terminal connector pin → well seated in connector block

Cardiac Pacemaker

= electronic device providing small electrical stimuli for cardiac contraction as substitute for sinoatrial node activity in wall of RA near junction with SVC

Indication: periods of bradycardia / arrhythmia caused by disruption of electric conduction pathway (degenerative aging of SA node / AV node / conduction tissue, myocardial infarction)

A. Temporary epicardial electrode
B. **Single-chamber pacemaker** = 1 lead pacing RV / RA
   Placement:
   1. Apex of RV
      = single-lead intramyocardial electrode
      Indication: problematic conduction pathway
   2. Into RA (uncommon)
      Indication: SA node dysfunction, aberrant SA focus
B. **Dual-chamber pacemaker** = 2 leads pacing RV + RA
   Placement:
   1. 1 lead in RA
   2. 1 lead into apex of RV
   Indication: coordination of signals to atria + ventricles
C. **Biventricular pacemaker** = 3 leads pacing RV + LV ± RA
   Purpose: more efficient pumping action with simultaneous contraction of LV + RV
   Indication: moderate to severe drug-refractory CHF associated with inter- / intraventricular dyssynchrony; weakened enlarged heart
   Placement:
   1. 1 lead into apex of RV

2. 1 lead through coronary sinus into a posterior / lateral cardiac vein for LV
3. 1 lead into RA

= right atrial-biventricular synchronous pervenous device

Rx: cardiac resynchronization therapy (CRT) in combination with implantable defibrillator into appendage of RA

Implantable Cardioverter-Defibrillator (ICD)

= AUTOMATIC IMPLANTABLE CARDIOVERTER-DEFIBRILLATOR (AICD)

= electronic device generating a large amount of electrical energy to defibrillate the heart back into a normal rhythm

Indication: tachydysrhymthia (ventricular tachycardia / ventricular fibrillation) to prevent cardiac arrest

√ single lead with 2 shock coils

Placement:

1. 1 shock coil at junction of brachiocephalic vein + SVC
2. 1 shock coil into RV

Preferred Lead Implant Sites

1. Right atrial pacemaker lead

   Location: electrode tip in right atrial appendage

   √ electrode tip pointing upward + anteriorly

   √ electrode tip may be shaped into a preformed "J loop"

   √ slight redundancy of lead desirable to avoid tension during deep inspiration / arm movement

2. Right ventricular pacemaker / ICD lead

   Location: electrode tip in apex of RV

   √ electrode tip to left of spine (frontal view)

   √ electrode tip pointing anteriorly (lateral view)

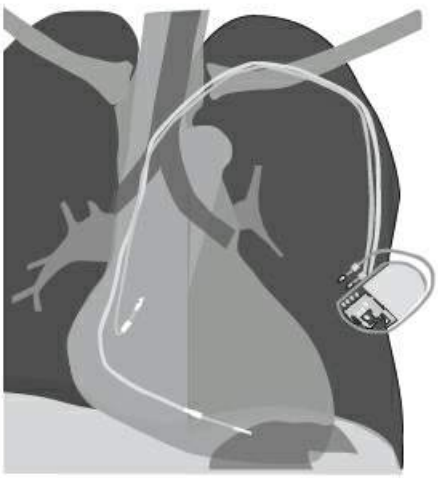
   √ (rarely) electrode tip intended for RVOT

3. Left ventricular pacemaker lead

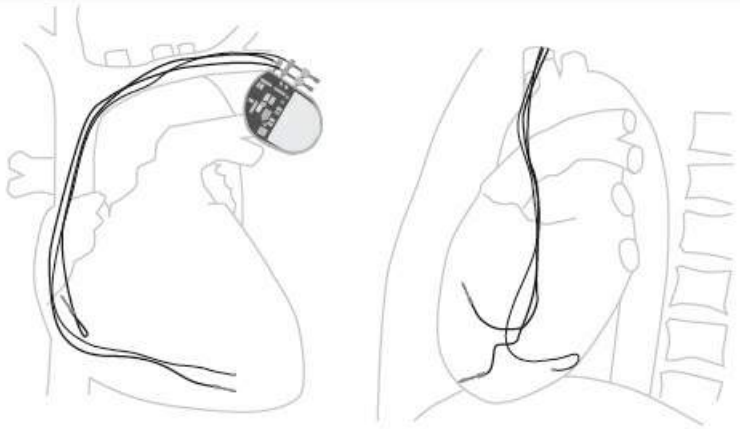
   Location: electrode tip in cardiac vein along lateral / posterior free wall of LV

   √ electrode tip posteriorly (lateral view)

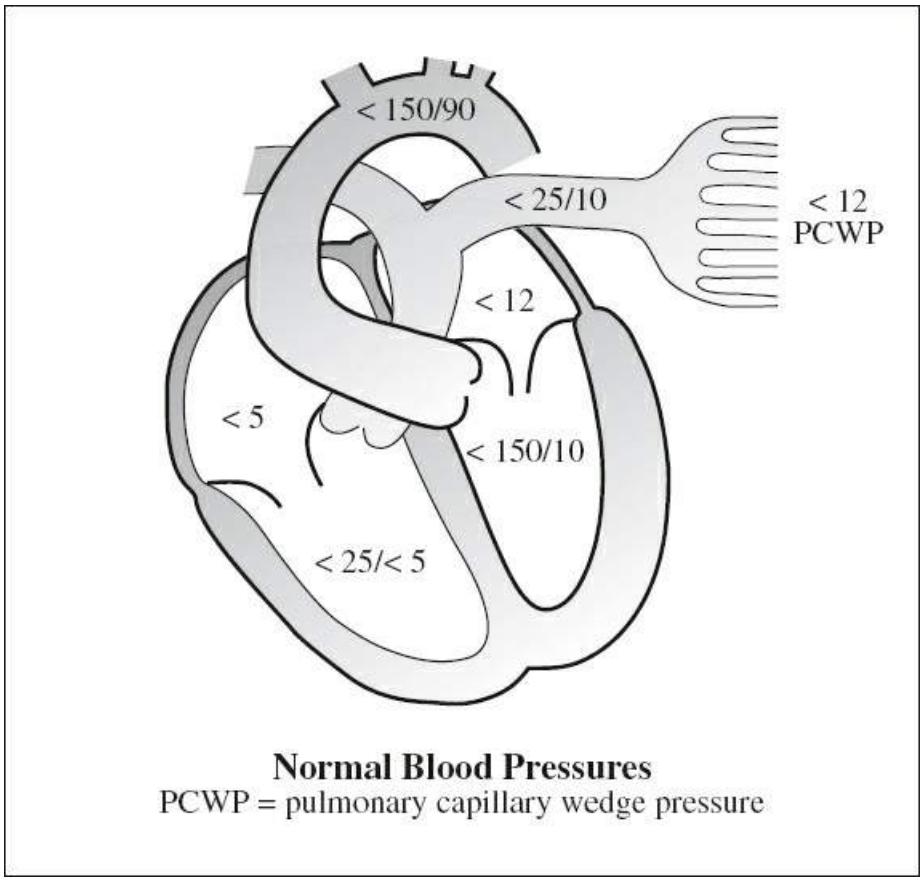
   √ inferiorly + laterally (frontal view)



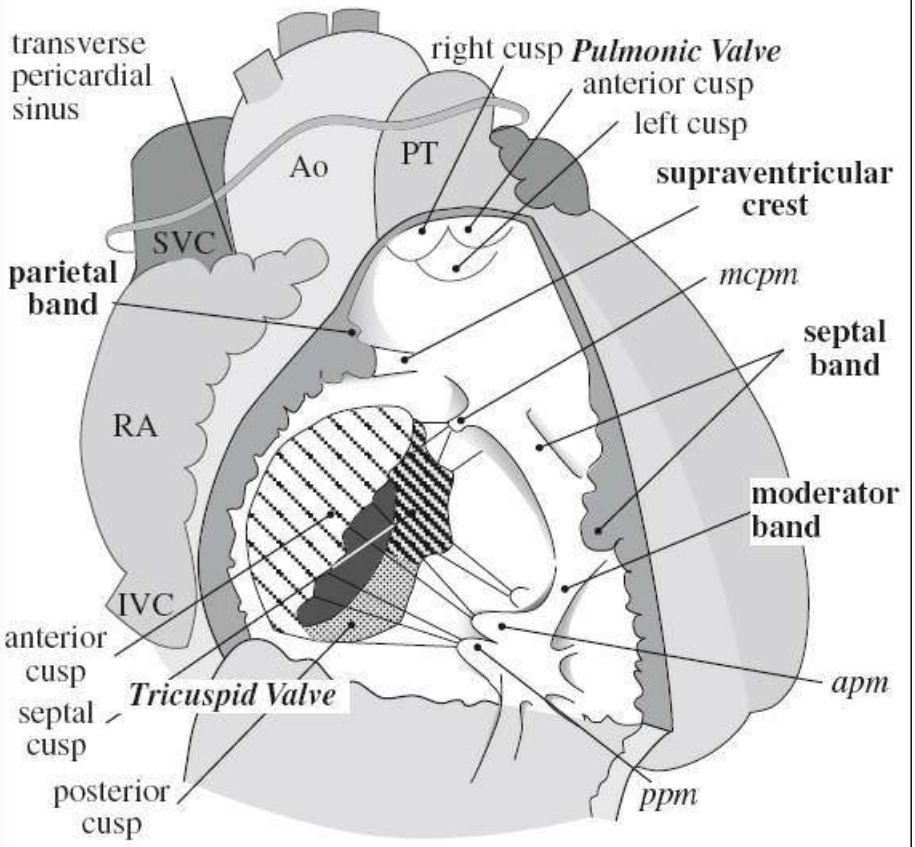
Dual-Chamber Cardiac Pacemaker



Biventricular Pacemaker
(dual chamber pacemaker with leads in RV + LV + RA)



Normal Blood Pressures
PCWP = pulmonary capillary wedge pressure



Right Ventricle Viewed from Front

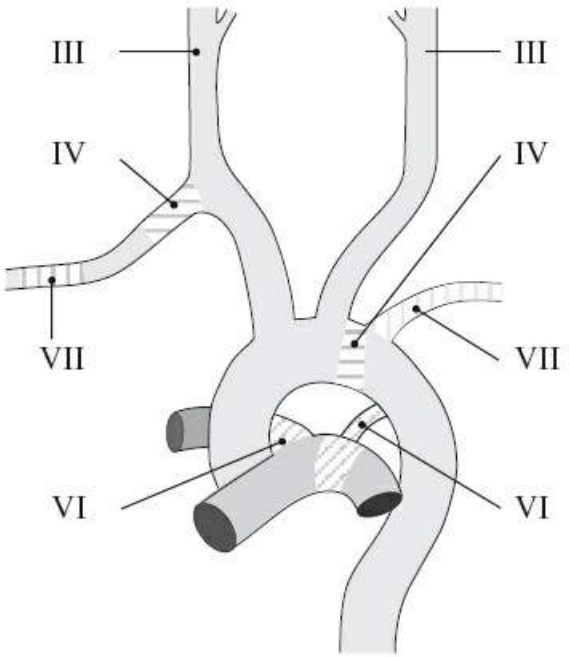
Demarcation between posteroinferior inflow portion and anterosuperior outflow portion by prominent muscular bands forming an almost circular orifice (parietal band, crista supraventricularis, septomarginal trabeculae (= septal band and moderator band)

apm = anterior papillary muscle attaches near apex of RV with chordae tendineae for anterior & posterior cusps
Anterior papillary muscle originates from moderator band!

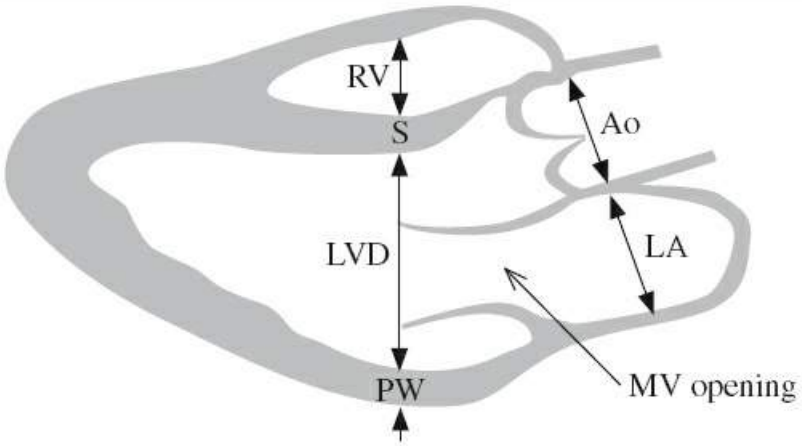
mcpm = medial supracristal (conal) papillary muscle arises from septal band with chordae tendineae for anterior & medial cusps

ppm = posterior *papillary muscle* attaches near apex of RV with chordae tendineae for posterior & medial cusps

Ao = aorta IVC = inferior vena cava PT = pulmonic trunk
RA = right atrium SVC = superior vena cava

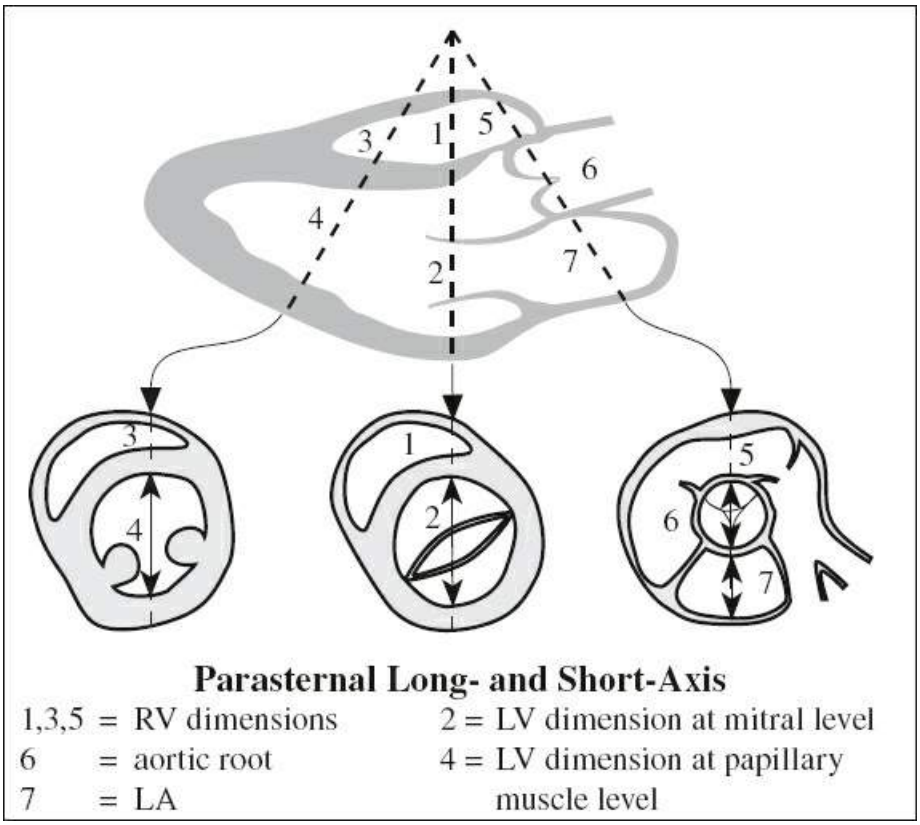


Development of Major Blood Vessels
numbers refer to embryologic aortic arches
(most portions of aortic arches I, II and V regress)
mnemonic: **Aor** from **Four**



Parasternal Long-Axis View

Ao = aorta	PW = posterior wall
LA = left atrium	RV = right ventricle
LVD = left ventricular diameter	S = septum



Parasternal Long- and Short-Axis

1,3,5 = RV dimensions
6 = aortic root
7 = LA
2 = LV dimension at mitral level
4 = LV dimension at papillary muscle level

HEART SIZE

Cardiothoracic Ratio

= CT ratio = widest transverse cardiac diameter ÷ widest inside thoracic diameter

< 0.5 = normal in > 1 month old (45% sensitive, 85% specific, 59% accurate)

< 0.6 = normal in < 1 month old

Purpose: measurement of LV dilatation

Dependent on:

- lung volume: CT ratio enlarges in expiration
- patient position: CT ratio increases on supine film

Pitfalls:

› no change unless LV volume increases by > ²/₃

› no change in moderate enlargement of LA / RV

CARDIAC IMAGING PLANES

Vertical Long Axis

= parasagittal plane along long axis of LV

Best assessment of:

1. LA and LV (relationship)
2. Inferior + anterior walls of LV myocardium
3. Bicuspid MV (structure & function) versus LV

4. LV (structure & function)
4. LA appendage and coronary sinus

Horizontal Long Axis / 4-Chamber View

= horizontal plane bisecting all 4 chambers

Best assessment of:

1. Chamber size and valve position
2. Septal + apical + lateral LV walls
3. AV valve (subjective assessment in cine mode)
4. Ventricular function (subjective assessment)
5. LA size (quick measurement)

Three-Chamber View

= oblique long-axis view optimizing visualization of LV, LA, aortic root, MV, aortic valve

Best assessment of:

1. LV outflow tract, aortic valve, aortic root, proximal ascending thoracic aorta
2. Posteromedial papillary muscles arising from LV free (lateral) wall
3. Chordae tendineae of MV

Short Axis View

= oblique coronal plane across barrel of LV lumen

1. Basal, middle, apical portions of LV myocardium
2. LV size (easy assessment)
3. LV myocardial contractility (easy assessment)

CARDIAC REPORTING

1. Coronary arteries: origin, course, segmental anatomy
2. Dominance and size of LAD artery, LCx artery, and RCA
3. Number of diagonal + marginal branches
4. Size of heart + cardiac chambers
5. LV function with ejection fraction and wall motion
6. End-diastolic + end-systolic LV volume
7. LV myocardial mass + thickness

HEART VALVES

Embryology:

semilunar valves develop simultaneously with formation of RV + right ventricular outflow tract (RVOT) from conotruncal endocardial cushions around distal part of conus

Heart Valve Positions

PA CXR:

reference line = oblique line drawn from distal left mainstem bronchus to right cardiophrenic angle

√ aortic valve resides in profile superior to this line overlying the thoracic spine

√ pulmonic valve just inferior to left mainstem bronchus

√ mitral valve resides inferior to this line centrally located within cardiac silhouette
√ tricuspid valve inferior to this line more basilar and midline

LAT CXR:

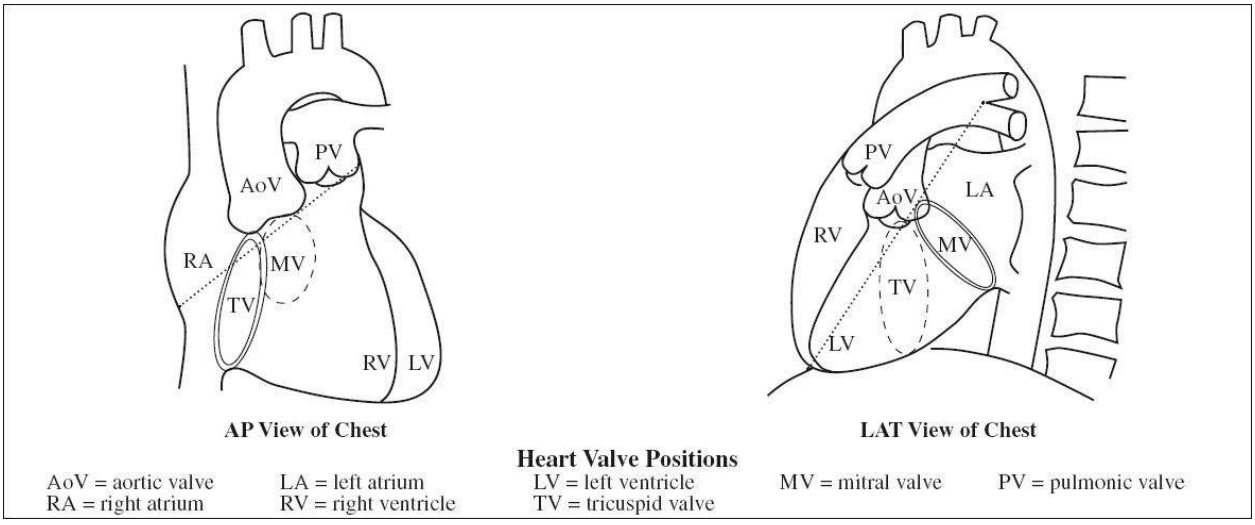
reference line = oblique line drawn from carina / right pulmonary artery shadow to anterior cardiophrenic sulcus

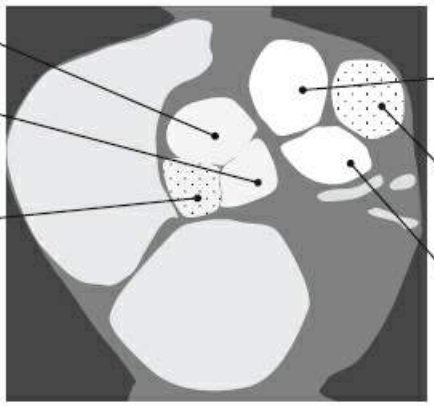
√ aortic valve resides superior to this line
√ pulmonic valve anterior + superior to aortic valve
√ mitral valve resides inferoposteriorly to this line
√ tricuspid valve inferior to this line anteriorly

Aortic Valve

= separates LV outflow tract from ascending aorta by a valve composed of annulus, commissures and usually 3 (range, 1 – 4) thin semilunar valve leaflets / cusps

(a) right cusp: inferior to right coronary sinus + origin of RCA
(b) left cusp: inferior to left coronary sinus + origin of LCA





Attitudinal CT of Semilunar Valves & Cusps

intrathoracic attitudinal view versus *heart-centric short-axis view*

left-facing sinus	= left anterolateral	= *anterior*
right-facing sinus	= right anterolateral	= *right posterior*
nonfacing sinus	= posterior	= *left posterior*

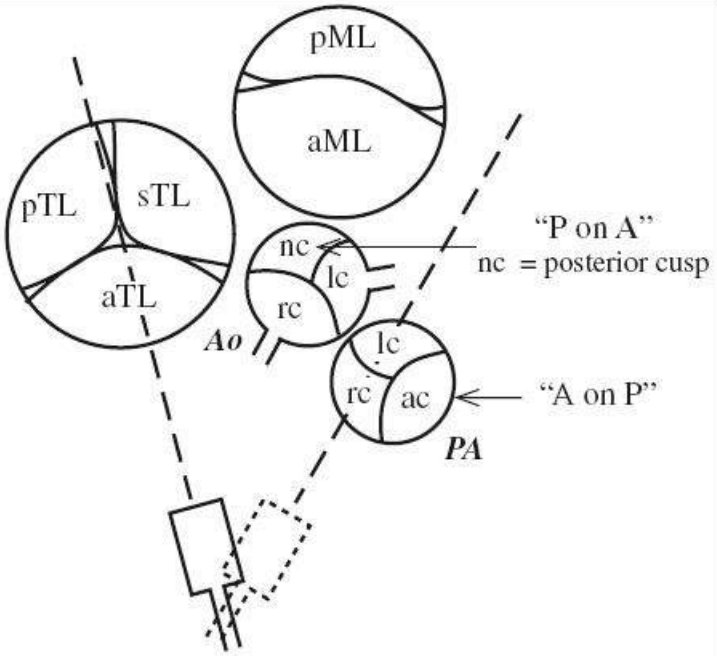


Diagram of the Relationship of the Four Cardiac Valves in Cross Section

aTL, pTL, sTL = anterior, posterior, septal (medial) tricuspid valve leaflets

Attachment of chordae tendineae:

- anterior papillary muscle attach to aTL + pTL
- posterior papillary muscle attach to pTL + sTL
- medial (conal) papillary muscle attach to aTL + sTL

aML, pML = anterior, posterior mitral valve leaflet

Attachment of chordae tendineae:

- anterior + posterior papillary mm. both attach to aML + pML

rc, lc, nc (Ao) = right, let, noncoronary cusps of aortic valve

rc, lc, ac (PA) = right, left, anterior cusps of pulmonary artery

Echocardiogram of Aortic Root		
Aortic root dimension	measured at end-diastole at R-wave of ECG	2.1–4.3 cm
increased in:	aneurysm of aorta, aortic insufficiency	
Aortic cusp separation		1.7–2.5 cm
decreased in:	aortic stenosis, low stroke volume	
increased in:	aortic insufficiency	
Left atrial diameter	measured at moment of mitral valve opening	2.3–4.4 cm
Eccentricity index of aortic valve cusps	ratio of anterior to posterior dimension (rarely used)	<1.3
Ratio of LA-to-aortic root dimension		0.87–1.11

(c) posterior / noncoronary cusp

Nodules of Arantius = thickened fibrous bulge at center of each free cusp margin forming central coaptation area

Commissures = junctions of cusps at attachment to aortic wall at level of sinotubular junction

Area: 2.5 –4.0 cm^2

Aortic valve planimetry is optimal during midsystole = 20% of R-R interval or 50–100 msec from R-wave peak!

Mitral Valve

= bicuspid valve (= 2 leaflets) anchored on mitral valve annulus + connected to LV papillary muscles by chordae tendineae; MV and aortic valve share fibrous continuity

Area: 4–6 cm^2

Circumference: 10 cm

Embryology: develops during 5th–15th week of gestation

Papillary Muscles of Mitral Valve

Origin: lateral wall of LV

(a) anterolateral papillary muscle

(b) posteromedial papillary muscle (single blood supply)

Prognosis: vulnerable to ischemia + rupture

Mitral Valve Annulus

= D-shaped ring within L atrioventricular groove; imbedded within myocardium as part of cardiac skeleton

(a) straight border = anterior portion of annulus; in fibrous continuity with aortic valve + heart skeleton

(b) curved border = posterior portion of annulus: attached to pliant endocardium

Function: site of valve leaflet attachment

Border: LCx artery + coronary sinus

Mitral Valve Leaflets

Normal thickness: < 5 mm

(a) semicircular anterior leaflet attaches to ⅓ of annulus + forms part of LVOT
Segments: lateral A1, middle A2, medial A3

(b) crescentic posterior leaflet
Segments: lateral P1, middle P2, medial P3

Mitral valve components are best evaluated on reformatted 2-chamber long-axis images perpendicular to the valve during middiastole = 65% of R-R interval for open mitral valve and 5% of R-R for closed mitral valve!

Pulmonic / Pulmonary Valve

= separates RV outflow tract from main pulmonary artery by a semilunar valve composed of 3 cusps (similar to aortic valve although separate from atrioventricular valve)

mnemonic: A cusp on P and P cusp on A anterior cusp (short-axis view) ← pulmonic valve posterior (noncoronary) cusp ← aortic valve

(a) anterior cusp
(b) right cusp
(b) left cusp

Area: 2.0 cm^2 / m2 of body surface area

Tricuspid Valve

= right atrioventricular valve separating RA from RV; anchored on tricuspid valve annulus + connected to RV papillary muscles by chordae tendineae; composed of 3 (range, 2 to 4) leaflets

Crista supraventricularis: muscular ridge that separates TV from pulmonary valve

(a) septal leaflet
(b) anterior leaflet
(b) posterior leaflet

VENTRICLES

Right Ventricle

Trabeculae: coarse

Papillary muscles: attached to interventricular septum + free wall; apical moderator band

Differentiating features of RV (from LV):

1. Heavily trabeculated apex
2. Well-developed infundibulum
3. Septal papillary muscles
4. Lack of fibrous continuity of AV valve + outflow tract

Moderator Band

= muscular band extending from interventricular septum to base of anterior papillary muscle

Function: part of right bundle branch conduction system

Right Ventricular Outflow Tract (RVOT)

= smooth muscular infundibulum / conus inferior to PV

In the right ventricle, trabeculae are coarse, and presence of an apical moderator band is CHARACTERISTIC!

Left Ventricle

Trabeculae: thin, delicate, smooth septal surface
Papillary muscles: attached to free wall only

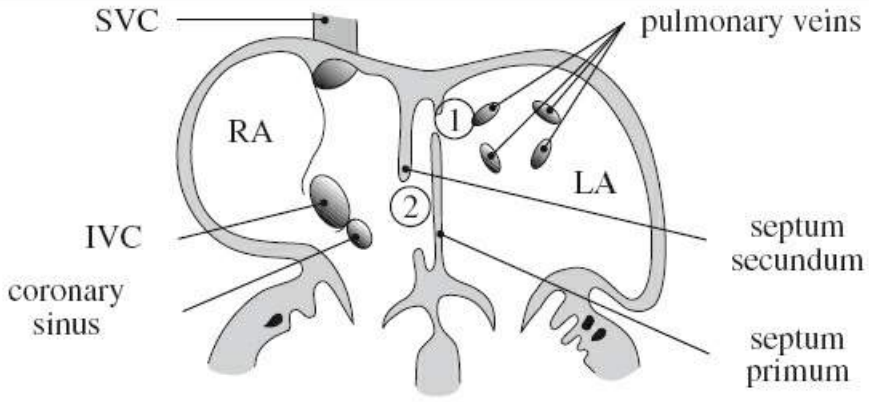
ATRIA

Embryology of Atrial Septa

1. **Septum primum** = thin partition dividing primitive atrium into right and left atria at 4th week; membrane grows from dorsal atrial wall toward endocardial cushion → ultimately forms thin flap valve of fossa ovalis
2. **Ostium primum** = temporary orifice between septum primum + endocardial cushions close to AV valves; it becomes obliterated by 5th week
3. **Ostium secundum** = multiple small coalescing fenestrations in center of septum primum
4. **Septum secundum** = stiff membrane developing on right side of septum primum growing from right atrial roof → ultimately forms thicker limbus of fossa ovalis
5. **Foramen ovale** = orifice limited by septum secundum + septum primum
6. **Foramen ovale flap** = lower edge of septum primum (patent in 6%, probe-patent in 25%); not considered an ASD

Right Atrium (RA)

Components:



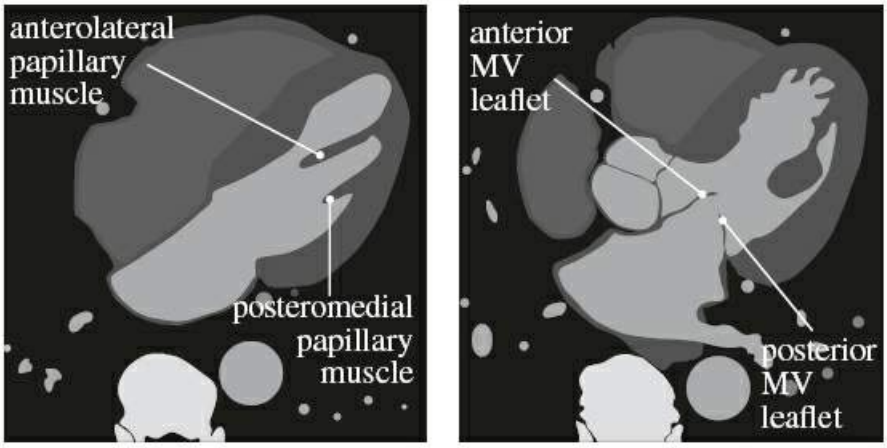
Normal Newborn Heart

Atrial septum consists of two components

(a) right side: septum secundum (muscular, firm) with posterior opening = foramen ovale

(b) left side: septum primum (fibrous, thin) with anterior opening = ostium secundum

1 = ostium primum 2 = ostium secundum



Papillary Muscles of MV **LV Outflow Tract**

Axial Diastolic Images of Left Ventricle

(Contrast-enhanced ECG-gated)

Echocardiogram of Right and Left Ventricle		
RV end-diastolic dimension	at R-wave of ECG	0.7–2.3 cm
increased in:	RV volume overload	
Septal thickness	end-diastolic thickness at R-wave of ECG	0.9 ± 0.06 cm
decreased in:	CAD	
increased in:	asymmetric septal hypertrophy, IHSS	
LV end-diastolic dimension	at R-wave of ECG	4.6 ± 0.54 cm
LVPW thickness	end-diastolic thickness at peak of R-wave	0.94 ± 0.09 cm
increased in:	LV hypertrophy	
LV end-systolic dimension		2.9 ± 0.5 cm
IVS÷LVPW thickness		<1.3
Fractional shortening	(EDD - ESD)/EDD x 100	
for LV		25–42%
for IVS		28–62%
for LVPW		36–70%

Morphologic Characteristics of Cardiac Ventricles		
Feature	*Right ventricle*	*Left ventricle*
Septum	moderator, septal and parietal bands	smooth septal surface
Trabeculae	coarse	thin and fine
Papillary muscles	attach to free wall and IVS	attach to free wall only
AV valve	tricuspid	bicuspid

Morphologic Characteristics of Cardiac Atria		
Feature	*Right Atrium*	*Left Atrium*
Appendage	blunt with broad connection to RA trapezoidal shape	small with narrow connection to RA fingerlike tubular shape
Blood from	coronary sinus and IVC	pulmonary veins
Pectinate muscle	extends outward toward AV canal	within tubular appendage
Myocardial component	crista terminalis and tenia sagittalis	none

(1) appendage
(2) venous part
(3) vestibule

Embryology: originates from primitive trabeculated RA (persists as RA appendage) + from sinus venosus forming smooth-walled portion of RA

Right Atrial Appendage

= triangular superior extension of RA that wraps around aortic root

√ pyramidal shape with narrow base

Rx: right atrial lead tip is typically placed at right atrial appendage for pacemaker / internal cardiac defibrillator

Sinus Venosus

› located in posterolateral wall of RA between orifices of SVC and IVC

(a) right horn: gives rise to crista terminalis, eustachian ridge, thebesian valve

(b) left horn: gives rise to coronary sinus

Vestibule of Right Atrium

= smooth muscular rim surrounding tricuspid orifice

Crista Terminalis

= prominent fibromuscular ridge separating smooth-walled venous part of posterior RA (= sinus venosus) from trabeculated muscle fibers of appendage anteriorly

Variations: in size + extent among individuals

Location: junction of sinus venosus and primitive RA

Clinical significance:

thickening of crista terminalis → development of atrial flutter + focal right tachycardias (⅔ arise in crista terminalis) → target for catheter RF ablation

√ vertically oriented smooth muscular ridge varying in size + thickness amongst individuals:

√ small thin valvelike / broad-based structure

√ may be large ← fatty infiltration of crista terminalis in lipomatous hypertrophy of the atrial septum

√ superiorly arches anterior to the orifice of the SVC

√ extends to area of anterior interatrial groove

√ merges with interatrial bundle (= Bachmann bundle)

√ indistinct inferior border located near IVC orifice merging with small trabeculations of inferior portion of cavotricuspid isthmus

› gives rise to thick muscle bundles

(a) anterior pectinate muscles fanning out anteriorly

(b) septum spurium = most prominent anterior pectinate muscle (in 80%) arising from crista terminalis

Mean thickness: 4.5 mm

Sinoatrial Node

= subepicardial spindle-shaped structure as source of cardiac impulse (= dominant pacemaker)

Length: 20 ± 3 mm

Location: in myocardium at superior cavoatrial junction between crista terminalis and

SVC

√ surrounds sinoatrial nodal artery, which may course centrally (70%) / eccentrically within node

Koch Triangle

Location: at orifice of coronary sinus

Borders:

› posteriorly: fibrous extension from eustachian valve (tendon of Todaro) = Todaro-eustachian ridge

› anteriorly: attachment of septal leaflet of tricuspid valve

› inferiorly: coronary sinus

› at apex: central fibrous body of heart (= site of penetration of His bundle)

› midportion: contains compact AV node (fast pathway)

› base: bordered by coronary sinus ostium + septal isthmus (= area between edge of coronary sinus ostium + septal tricuspid valve); contains slow pathway

◊ Septal isthmus = frequently target for ablation of slow pathway in AV node reentrant tachycardia!

AV Node

Location: within Koch triangle

Borders:

› coronary sinus ostium

› septal leaflet of tricuspid valve

› tendon of Todaro = fibrous band connecting eustachian and thebesian valves

[Francesco Todaro (1839–1918), Italian professor of anatomy at the Universities of Messina and Rome]

Importance: electrophysiologists frequently modify this node in dual atrioventricular nodal pathways → AV nodal reentrant tachycardia

Terminal Groove / Sulcus Terminalis

= fat-filled groove on epicardial side corresponding internally to crista terminalis close to cavoatrial junction

› location of sinus node + terminal segment of sinoatrial nodal artery

Eustachian Valve

[Bartolomeo Eustachi (1500 or 1514–1574), one of the founders of the science of human anatomy in Rome, Italy]

= valve of inferior vena cava (guarding entrance into IVC)

Function: directs flow toward foramen ovale

Location: junction of RA and IVC; inserts medially onto eustachian ridge (= border between oval fossa + coronary sinus)

› directs blood from IVC to foramen ovale in fetus

› free border continues as tendon of Todaro

√ thin linear structure, not routinely imaged

◊ Rarely an unusually large muscular valve may pose an obstacle to passage of a catheter!

Cavotricuspid Isthmus

= area between IVC + tricuspid valve of highly variable isthmian anatomy

◊ Target of catheter ablation as treatment of choice for isthmus-dependent atrial flutter!

N.B.: obstacles to successful ablation may be a large eustachian ridge, aneurysmal pouches, or a concave deformation of the entire isthmus

Thebesian Valve

= valve of coronary sinus

[Adam Christian Thebesius (1686–1732), anatomist and municipal physician in Hirschberg, Silesia]

Prevalence: in 80% of cadaveric specimens

Function: prevents reflux from RA into coronary sinus

Location: entry of coronary sinus into RA

Morphology: complete circular (30%), crescentic (35%), absent (20%), threadlike (2%), fenestrated (10%)

√ thin semilunar fold at anteroinferior rim of coronary sinus ostium

Mechanical barrier: large eustachian valve / ridge (25%), > 5 mm deep subthebesian recess (45%), hypoplastic coronary sinus ostium, large thebesian valve

Subthebesian Pouch

= subeustachian sinus = sinus of Keith

= pouchlike atrial wall inferior to orifice of coronary sinus

Depth: 4.3 ± 2.1 (range, 1.5–9.4) mm

◊ Substrate for reentrant circuit during atrial flutter

N.B.: main source of RF procedural difficulty

Interatrial Septum

Septum = wall that can be removed without exposing heart cavity to extracardiac structures

Parts: flap valve of foramen ovale (septum primum) + part of its anteroinferior margin

◊ Superior rim of fossa (septum secundum = infolded wall between SVC and right pulmonary veins) is not a true septum!

√ thin septum that is difficult to image

√ may contain small amount of fat sparing fossa ovalis

DDx: Lipomatous hypertrophy of interatrial septum

√ characteristic dumbbell shape ← sparing of fossa ovalis

√ abnormal amount of fat in older / obese adults

Fossa Ovalis

= circular indentation in interatrial septum

Variant: patent fossa ovalis / foramen ovale

PATENT FORAMEN OVALE

= PATENT FOSSA OVALIS

Prevalence: 15%

Function: can result in R-to-L shunt

Associated with:
paradoxical emboli, cryptogenic stroke, hypoxemia in patients with obstructive sleep apnea, increased risk for decompression sickness, increased risk for atrial fibrillation after cardiac surgery
√ demonstrated by contrast-enhanced echocardiography

Left Atrium (LA)

Components: venous component, vestibule, appendage
Embryology: originates from primitive trabeculated LA (persists as LA appendage) + from pulmonary veins forming smooth-walled portion of LA
√ smooth walled venous + septal component + vestibule
√ ridge of smooth muscle (± bulbous tip) at junction of LA appendage and entrance of left superior pulmonary vein

Venous Component of Left Atrium
= located posteriorly → pulmonary vein orifices at each corner

Left Atrial Vestibule
= surrounds the mitral orifice

Left Atrial Appendage
= arises from superolateral aspect of LA
√ rough trabeculated surface of tubular shape
√ projects anteriorly over proximal LCx artery
√ 3.5–6.5 mm thick superior wall / dome
Cx: narrow neck predisposes to thrombus deposition

Atrial Appendages

√ linear filling defects (R > L) = pectinate muscles fibers running parallel to each other measuring > 1 mm (in 97%)
DDx: thrombus in LA

CORONARY ARTERIES

Anatomy of Left Coronary Artery (LCA)

arises from left (posterior) coronary sinus (= left sinus of Valsalva) near sinotubular ridge; passes to left and posterior to pulmonary trunk

1. **Left main coronary artery** (LM)
   Segments: ostium to bifurcation = 5–20 mm short stem
   › bifurcates into LAD + LCx
   › trifurcates (in 15%) = ramus intermedius (RI) branch coursing laterally toward LV free wall similar to D1
2. **Left anterior descending** (LAD)
   Course: within anterior interventricular groove toward apex
   Supply: majority of LV + anterolateral papillary muscle ± small branches to anterior RV wall

Segments:
- › proximal: from left main bifurcation to origin of 1st septal branch
- › midportion: from 1st septal branch to an acute angle (may coincide with origin of 2nd septal perforator)
  - – otherwise split halfway between 1st septal perforator and apex into:
    - › middle LAD
    - › distal LAD
- › apical segment = termination of LAD

(a) **Diagonal** perforating branches (D1, D2, etc) arise from LAD, course over anterolateral wall of LV
Supply: LV free wall
mnemonic: **D**iagonals course **d**ownward from LA**D**

(b) **Septal** perforating branches (S) course medially toward anterior interventricular septum
Supply: majority of interventricular septum + AV bundle + proximal bundle branch

3. **Left circumflex artery** (LCx) travels within left atrioventricular sulcus (groove); terminates at obtuse (blunt / round) margin of heart

(a) **Obtuse marginal** (lateral) branches (OM1, OM2, etc) for lateral wall of LV

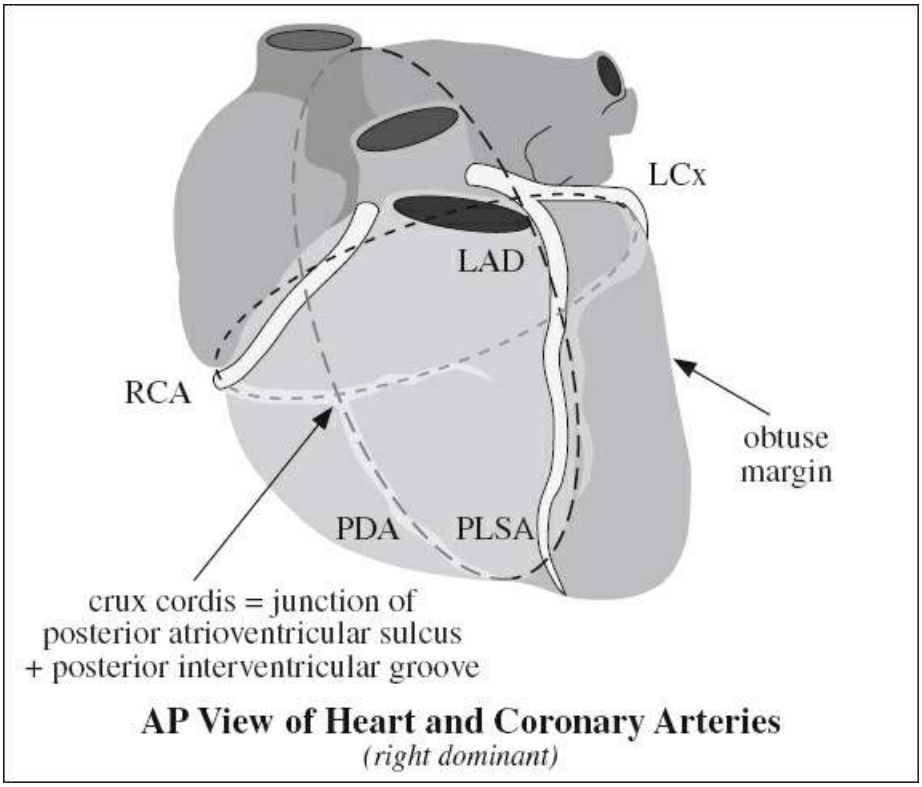
(b) Left atrial circumflex artery (LACX) for atrium

(c) variably: branches to posterolateral + posterior descending artery supplying diaphragmatic portion of LV (= left dominance)

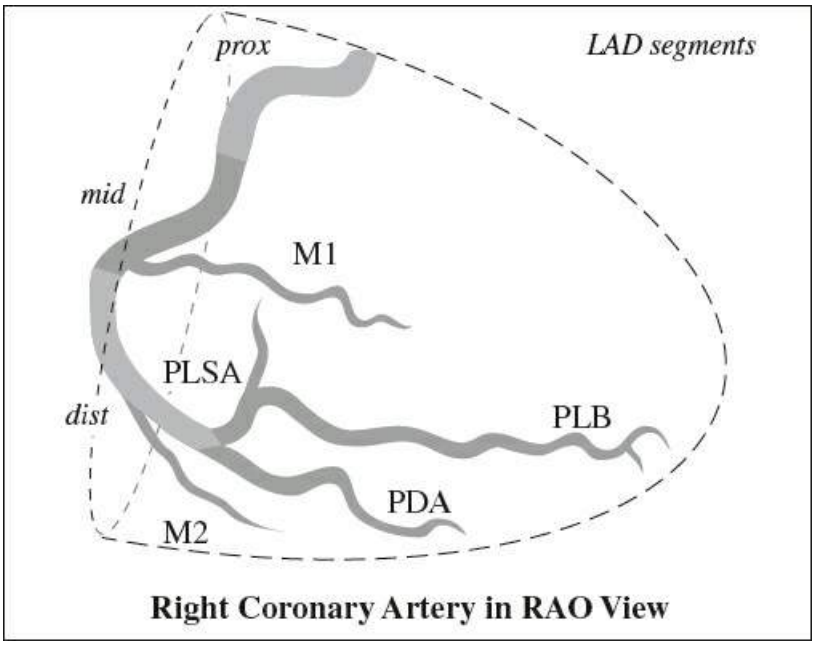
Supply: LV free wall + variable portion of anterolateral papillary muscle

Terminology from surface perspective of apical view:
- › rounded obtuse margin of heart formed mainly by LV
- › sharp angle = acute margin of heart formed mainly by RV

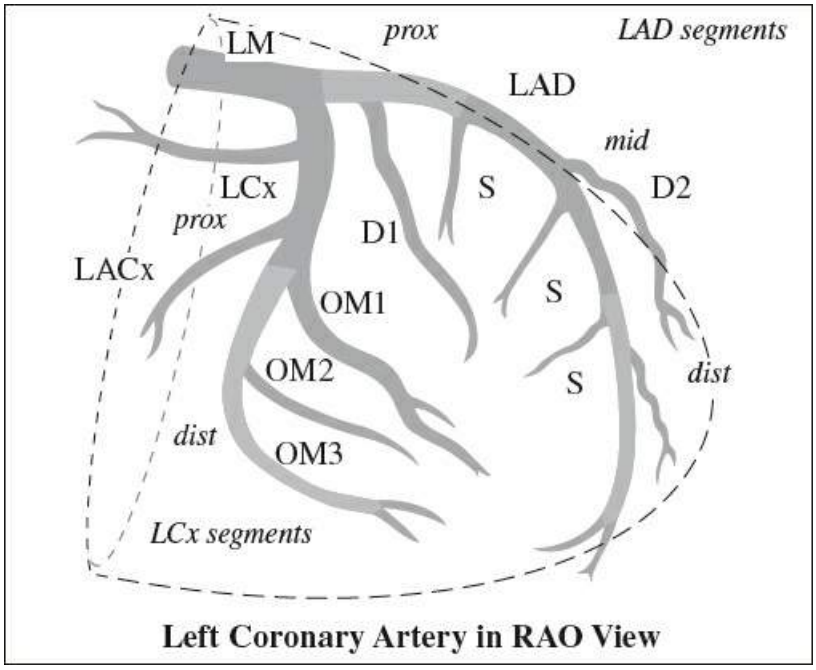
Segments: proximal + distal (based on origin of large obtuse marginal branches)



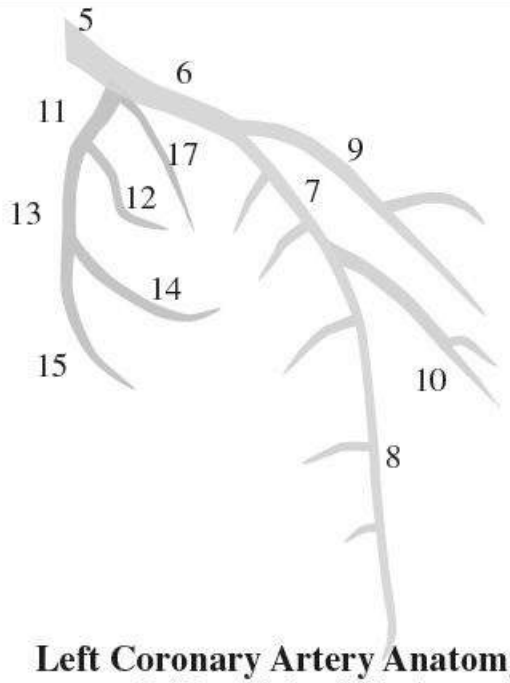
AP View of Heart and Coronary Arteries
(right dominant)



Right Coronary Artery in RAO View



Left Coronary Artery in RAO View

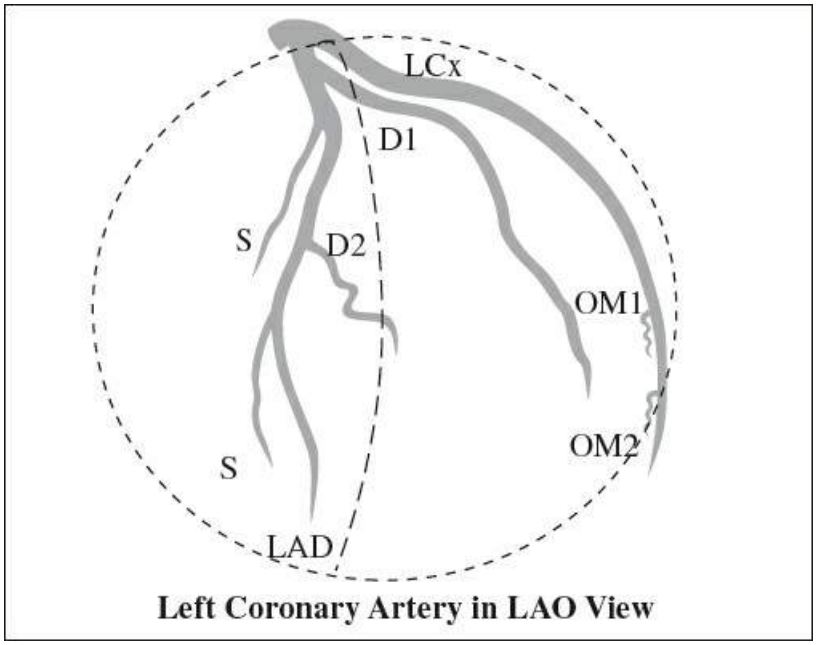


Left Coronary Artery Anatomy

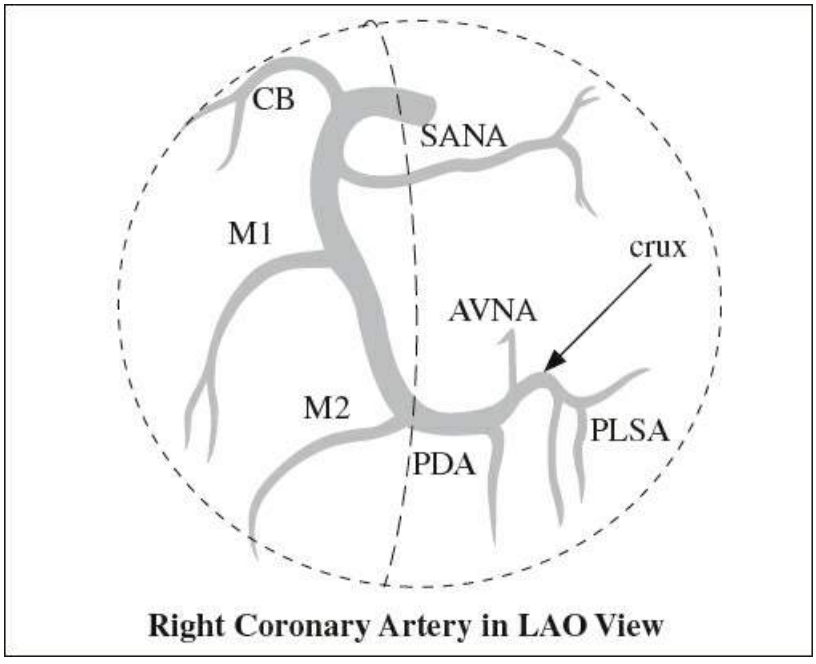
(LAO cranial projection)

17-Segment Classification by American Heart Association

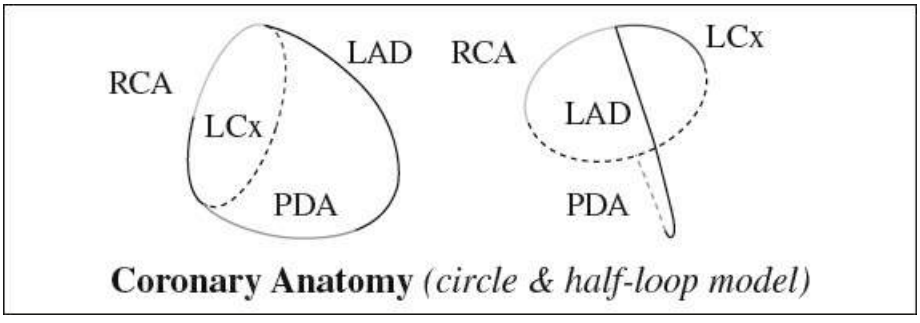
5 = main artery
6 = proximal segment of LAD branch
7 = middle segment of LAD branch
8 = distal segment of LAD branch
9 = first diagonal branch
10 = second diagonal branch
12 = proximal segment of LCx artery
13 = middle segment of LCx artery
14 = second obtuse marginal branch of LCx
15 = distal segment of LCx artery
17 = intermediate branch



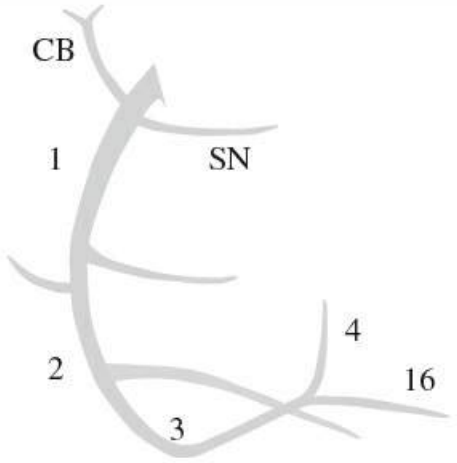
Left Coronary Artery in LAO View



Right Coronary Artery in LAO View



Coronary Anatomy *(circle & half-loop model)*

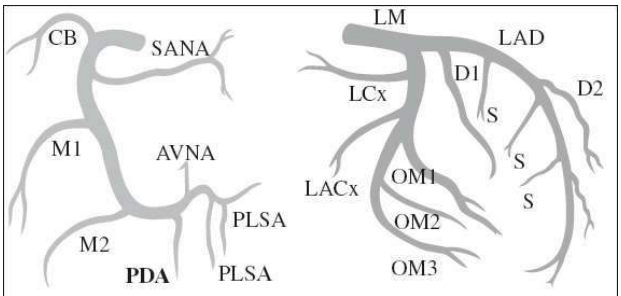


Right Coronary Artery Anatomy

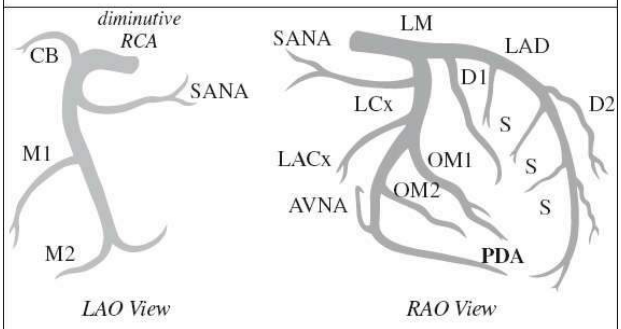
(RAO cranial projection)

17-Segment Classification by American Heart Association

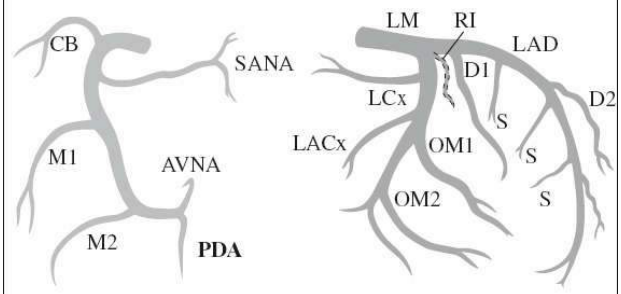
1	=	proximal segment of main artery
2	=	middle segment of main artery
3	=	distal segment of main artery
4	=	posterior descending branch
16	=	posterior left ventricular branch
SN	=	sinonodal branch
CB	=	conal branch



Right Dominant Circulation



Left Dominant Circulation



Balanced Circulation

Coronary Artery Angiograms of Varying Dominance

AVNA = atrioventricular node artery
CB = conus branch artery
D1 = 1st diagonal artery
D2 = 2nd diagonal artery
LACx = left atrial circumflex artery
LAD = left anterior descending artery
LCx = left circumflex artery
LM = left main coronary artery
M1 = 1st acute marginal branch artery
M2 = 2nd acute marginal branch artery
OM1 = 1st obtuse marginal artery
OM2 = 2nd obtuse marginal artery
PDA = posterior descending artery
PLB = posterolateral branch
PLSA = posterolateral segment artery
R = ramus intermedius (in 15%)
S = septal branch
SANA = sinoatrial node artery

Anatomy of Right Coronary Artery (RCA)

arises from right (anterior) coronary sinus → passes to right + posteriorly to pulmonary artery → travels downward within right atrioventricular sulcus (groove) → rounds the acute margin of the heart toward crux

Terminology based on posterior surface view of heart:

crux cordis = cross formed by
› AV groove (transecting a line formed by)
› posterior interventricular + interatrial sulci
[*crux*, Latin = cross, junction]

Segments:

› proximal: ostium to halfway to acute margin of heart
› mid:
› distal: acute angle of heart to origin of PDA

1. **Conus artery** (CB)
   = 1st branch of RCA (in 50–60% of patients); may originate directly from coronary sinus of aorta (in 30–35%)
   √ forms circle of Vieussens = anastomosis with LAD
   Supply: RVOT = conus arteriosus
2. **Sinoatrial node artery** (SANA)
   = 2nd branch of RCA (in 60%) / from LCx (in 40%)
   √ courses along anterior interatrial groove toward superior cavoatrial junction
   √ at cavoatrial junction circling either anteriorly (precaval) / posteriorly (retrocaval) to enter node
3. **Marginal branches** (M1, M2, etc) have an anterior course
   › **acute marginal branch** = at junction of middle + distal RCA
   Supply: RV
4. **Posterior descending artery** (PDA)
   = origin of PDA determines coronary artery dominance
   Origin: usually RCA near crux (in 70%) / distal acute marginal branch (= right dominance)
   Supply: posterior third of ventricular septum + diaphragmatic segment of LV + posteromedial papillary muscle
5. **Atrioventricular node artery** (AVNA)
   = small branch to AV node
   Origin: apex of U-turn of distal RCA (80–87%) / terminal portion of LCx (8–13%) / both RCA and LCx (2–10%)
   Supply: posterior interventricular septum, interatrial septum, AV node, His bundle
   √ penetrates base of posterior interatrial septum at crux
   √ may course beneath endocardium near ostium of coronary sinus + septal isthmus
   ◊ High risk for AV nodal artery coagulation during RF ablation!
6. **Posterolateral segment arteries** (PLSA)
   supplies posterolateral wall of LV

Coronary Artery Territory

septum	=	LAD
anterior wall	=	LAD
lateral wall	=	LCx
posterior wall	=	RCA
inferior / diaphragmatic wall	=	RCA
apex + inferolateral wall	=	watershed areas

Coronary Artery Dominance

Whichever artery crosses the crux of the heart and gives off the posterior descending artery (PDA) is considered the dominant coronary artery!

= artery that supplies the inferior portion of LV
- › RCA in 70–85% (= right dominance)
- › LCx in 7–10% (= left dominance)
- › RCA + LCx = codominance / balanced supply (7–8%)

Coronary Arteriography

◊ Average coronary artery diameter: 4 mm (M); 3 mm (F)

Contrast agents:

1. Monomeric ionic contrast material:
   (a) negative inotropic = depression of myocardial contractility ← hyperosmolality of sodium + decrease in total calcium
   (b) peripheral vasodilatation
2. Meglumine diatrizoate (contains small quantities of sodium citrate + EDTA)
3. Nonionic contrast material = slight increase in LV contractility

Dose: 3–10 mL

Mortality: 0.05%

Risk factors associated with death:

1. Multiple ventricular premature contractions
2. Congestive heart failure
3. Systemic hypertension
4. Severe triple-vessel coronary artery disease (highest risk)
5. LV ejection fraction < 30%
6. Left main coronary artery stenosis

Clues for projection:

45–70° LAO:
- √ ribs slanting to left side of image
- √ catheter in descending aorta on right side of image

15–30° RAO:
- √ ribs slanting to right side of image
- √ catheter in descending aorta on left side of image

Technique:

◊ 20–30° of cranial / caudal angulation variably used

Catheter in left coronary orifice:

(a) LAO + caudocranial angulation:

proximal ⅓ of LAD + origin of first diagonal branch

(b) LAO + craniocaudal angulation = "spider view":
LCA, proximal LCx, first marginal / diagonal branches

(c) RAO + craniocaudal angulation:
proximal third of LCx + origin of its branches

(d) RAO + caudocranial angulation:
separation of LAD from diagonal branches

Catheter in right coronary artery orifice: LAO ± RAO

False-negative interpretation:

(1) Eccentric lesion in 75%
(2) Foreshortening of vessel
(3) Overlap of other vessels remedied by angulated projections: improved diagnosis (50%), upgrade to more significant stenosis (30%), lesion unmasked (20%)

Coronary Artery Collaterals

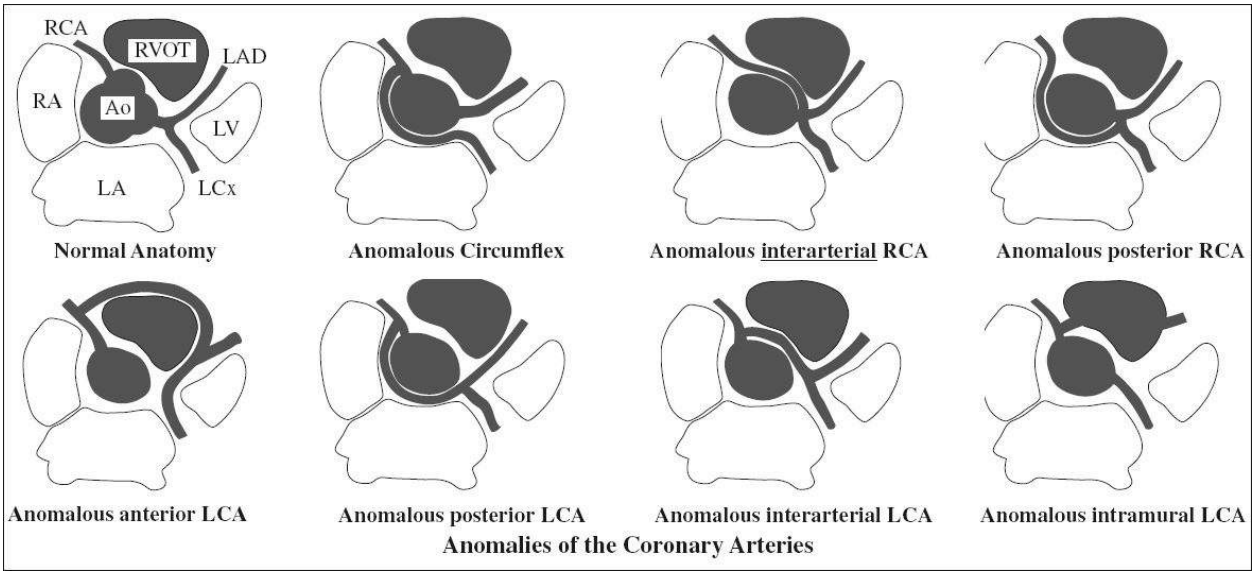
A. INTRACORONARY COLLATERALS
= filling of a distal portion of an occluded vessel from the proximal portion
√ tortuous course outside the normal path

B. INTERCORONARY COLLATERALS
= between different coronary arteries / between branches of the same artery
Location: on epicardial surface, in atrial / ventricular septum, in myocardium

1. Proximal RCA to distal RCA
   (a) by way of acute marginal branches
   (b) from sinoatrial node artery (SANA) to atrio-ventricular node artery (AVNA) = Kugel collateral
2. RCA to LAD
   (a) between PDA and LAD through ventricular septum / around apex
   (b) conus artery (1st branch of RCA) to proximal part of LAD
   (c) acute marginals of RCA to right ventricular branches of LAD
3. Distal RCA to distal LCx
   (a) posterolateral segment artery of RCA to distal LCx (in AV groove)
   (b) AVNA of RCA to LCx (through atrial wall)
   (c) posterolateral branch of RCA to obtuse marginal branches of LCx (over left posterolateral ventricular wall)
4. Proximal LAD to distal LAD
   (a) proximal diagonal to distal diagonal artery of LAD
   (b) proximal diagonal to LAD directly
5. LAD to obtuse marginal of LCx

Coronary Artery Anomalies

Prevalence: 0.3–1.3%; in 4–25% responsible for nontraumatic sudden death in young adults



Coronary Artery Anomaly of Hemodynamic Significance

= 2nd most common cause of sudden cardiac death among young adults

1. ALCAPA = most serious anomaly
2. Origin from opposite sinus of Valsalva / opposite coronary artery + interarterial / intramural course
3. Congenital coronary artery fistula

Coronary Artery Atresia

1. Congenital atresia of left main coronary artery
   √ fibrous connection between LAD-LCx junction + left coronary cusp
2. Atresia of right coronary artery
3. Atresia of left circumflex coronary artery

Anomaly of Coronary Artery Origin

1. High takeoff point from aorta (6%)
   = origin of RCA / LCA above the junctional zone between sinus + tubular part
   ◊ May be difficult to cannulate!
2. Multiple ostia
   (a) RCA + conus branch arise separately
   (b) LAD + LCx arise separately without LCA (0.41%)
3. Single coronary artery (0.0024–0.0440%)
4. Anomalous origin from pulmonary artery
5. Origin of coronary artery from opposite sinus / noncoronary sinus
   (a) RCA arising from left coronary sinus (0.03–0.17%)
   (b) LCA arising from right coronary sinus (0.09–0.11%)
   (c) LCx / LAD arising from right coronary sinus (0.32–0.67%)
   (d) LCA / RCA arising from noncoronary sinus
   may take the following course:
   › <u>interarterial</u> "malignant" course (between aorta + pulmonary trunk) just above pulmonary valve

◊ Most common clinically significant coronary artery anomaly → compression of coronary artery between aorta and PA → acute ischemia / arrhythmia → sudden cardiac death

√ anomalous artery surrounded by epicardial fat

› trans-septal: subpulmonic / beneath RVOT

› prepulmonic: anterior to RVOT

› retroaortic: posterior to aorta

› intramural: LCA within aortic wall → compression throughout cardiac cycle

√ slitlike coronary artery lumen

√ impaired coronary artery blood flow

Among 6.3 million military recruits 64 patients died from a cardiac cause: 54% had a left main coronary artery arising from the right sinus of Valsalva with an interarterial course!

Anomaly of Coronary Artery Course

1. Myocardial bridging
   = band of myocardial muscle overlying a segment of a coronary artery
2. Duplication of arteries: eg, LAD

Anomaly of Termination of Coronary Artery

1. Coronary artery fistula
2. Coronary arcade
   = angiographically demonstrable communication between RCA and LCA in the absence of a coronary artery stenosis
   √ prominent straight connection near crux
   DDx: tortuous collateral vessel
3. Extracardiac termination
   Cause: atherosclerotic CAD
   Receiver: bronchial, internal mammary, pericardial, anterior mediastinal, superior / inferior phrenic, intercostal arteries

EMBRYOGENESIS OF VEINS

Time of development: 6th–8th week of embryonic life

Origin: 3 main paired venous systems drain into sinus venosus

A. Vitelline (omphalomesenteric) venous system:
   blood from yolk sac to sinus venosus invagination separates left horn of sinus venous from LA

B. Umbilical venous system blood from chorionic villi to sinus venosus via ductus venosus

C. Intraembryonic cardinal venous system
   = continuous appearance + regression of 3 paired embryonic veins

(1) Cardinal veins

(a) <u>anterior</u> cardinal vein drains the cranial (cephalic) region

› part of left anterior cardinal vein→ left superior intercostal vein + adjacent left brachiocephalic vein

(b) <u>posterior</u> cardinal vein drains caudal portion of embryo (body of embryo +

mesonephros + anterior extremities)

Location: dorsolateral part of urogenital fold

› right posterior cardinal vein→ part of azygos vein

(c) right + left <u>common</u> cardinal veins (= ducts of Cuvier) formed by confluence of anterior + posterior cardinal veins

› right common cardinal vein→ superior vena cava

› right horn of sinus venosus → posterior wall of RA

› left horn of sinus venosus → coronary sinus

› regressing left common cardinal vein → ligament / vein of left atrium (vein of Marshall)

(d) vessel connecting right + left superior cardinal veins → left brachiocephalic vein

(2) Subcardinal veins drain urogenital system of metanephros + suprarenal glands

Location: ventromedial to posterior cardinal veins + ventrolateral to aorta

› intersubcardinal anastomoses form anterior to aorta below superior mesenteric artery and connect left + right subcardinal veins

(3) Supracardinal veins

drain body wall via intercostal veins

Location: dorsomedial to posterior cardinal vein + dorsolateral to aorta

› CRANIAL

(a) azygos vein on the right
drains 4–11 right intercostal veins

(b) portion of superior intercostal vein drains 2–3 left intercostal veins

(c) accessory hemiazygos drains 4–7 left intercostal veins

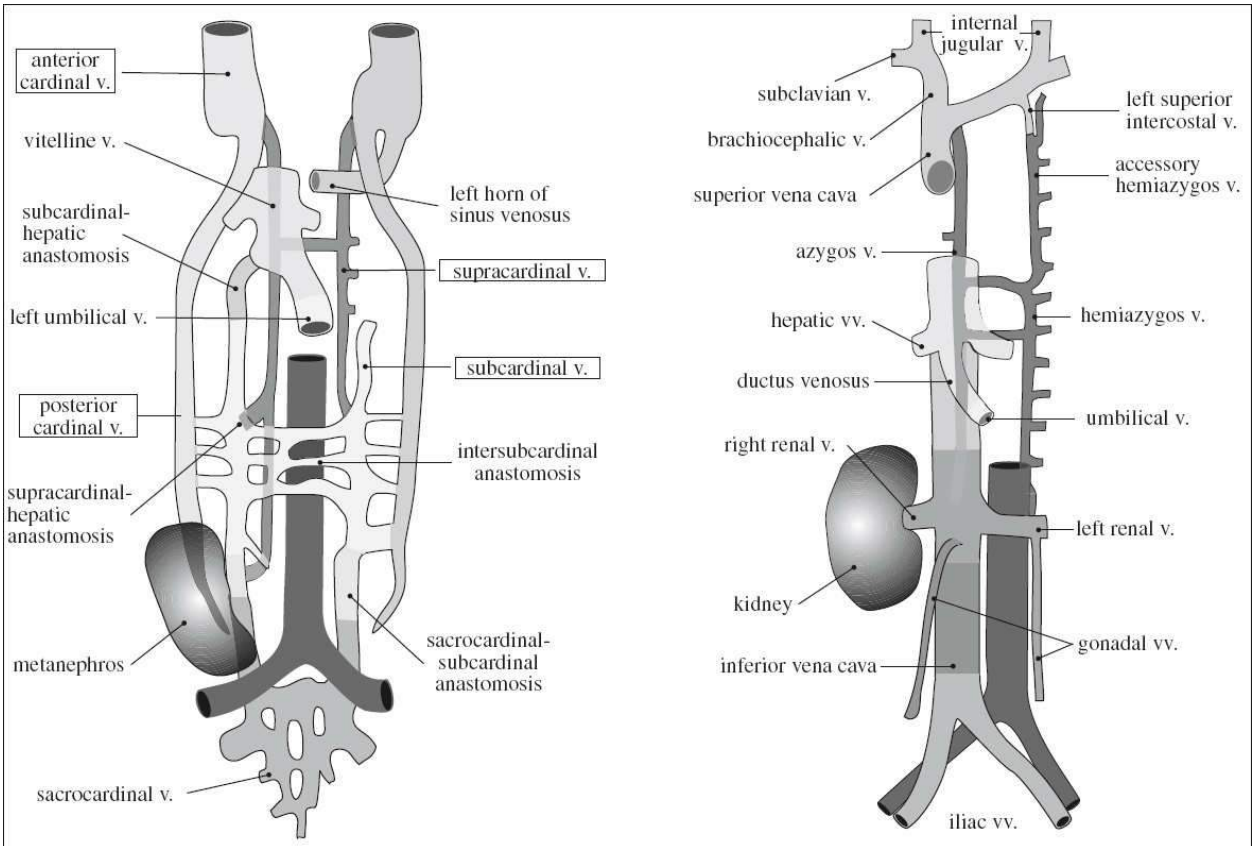
(d) hemiazygos vein drains left 8–11 intercostal veins

› CAUDAL: lumbar veins

Superior Vena Cava

Embryology: right common cardinal vein + proximal aspect of right anterior cardinal vein + right horn of sinus venosus form right superior vena cava

› Left common cardinal vein + proximal part of left anterior cardinal vein form left superior vena cava



Development of the Major Venous System
vitelline vein ⇒ hepatic segment of IVC; right subcardinal-hepatic anastomosis ⇒ suprarenal segment of IVC
right supracardinal-subcardinal anastomosis ⇒ renal segment of IVC; right abdominal supracardinal vein ⇒ infrarenal segment of IVC
thoracic supracardinal vein ⇒ azygos and hemiazygos veins

› Left superior vena cava involutes with development of innominate vein → ligament of Marshall

Origin: formed by confluence of right + left brachiocephalic vv.
Mean length: 7.1 ± 1.4 cm
Diameter: 2.1 ± 0.7 cm (in adults)
Shape on cross-section: major axis (1.5–2.8 cm), minor axis (1–2.4 cm)
Area threshold: < 1.07 cm^2 → obstruction / compression
CECT:
√ excellent uniform enhancement of SVC 60–75 seconds after injection of contrast agent into a peripheral vein
√ nonenhanced blood from contralateral veins and azygos vein can mimic a thrombus

Congenital Anomalies of SVC

1. Persistent left SVC

Inferior Vena Cava

1. Hepatic = posthepatic segment
   Origin: terminal part of right vitelline vein
2. Suprarenal segment

Origin: subcardinal-hepatic anastomosis

3. Renal segment
   Origin: part of right subcardinal vein + supracardinal-subcardinal anastomoses
4. Infrarenal segment
   Origin: right supracardinal / sacrocardinal vein

Congenital Anomalies of the IVC

1. Absence of hepatic segment of IVC with azygos continuation
2. Absence of infrarenal IVC with azygos / hemiazygos continuation
3. Duplication of IVC with azygos / hemiazygos continuation

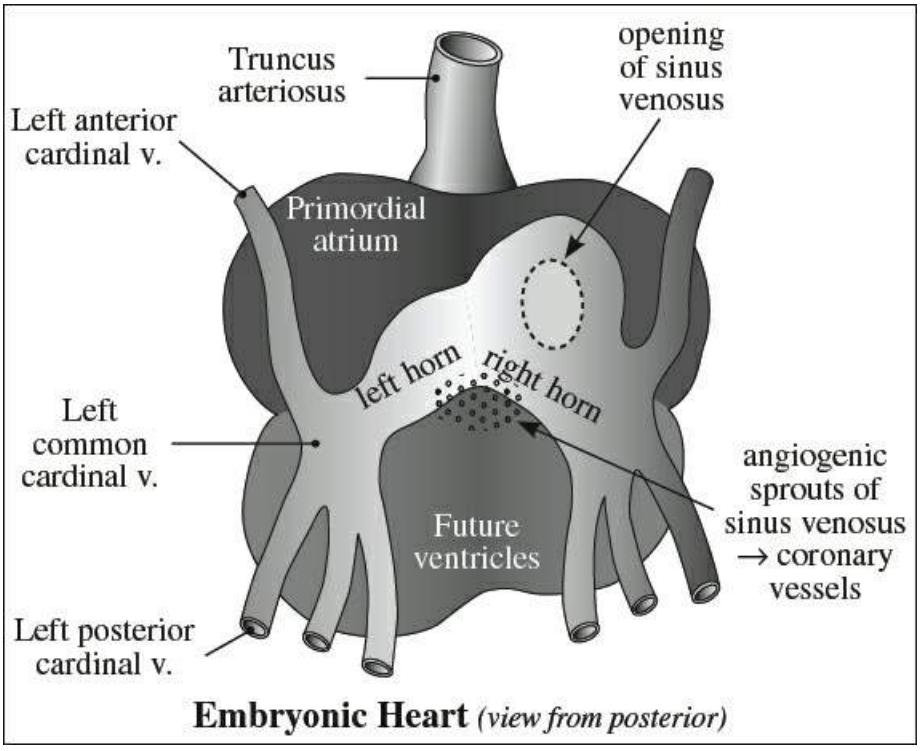
CARDIAC VEINS

Classification:

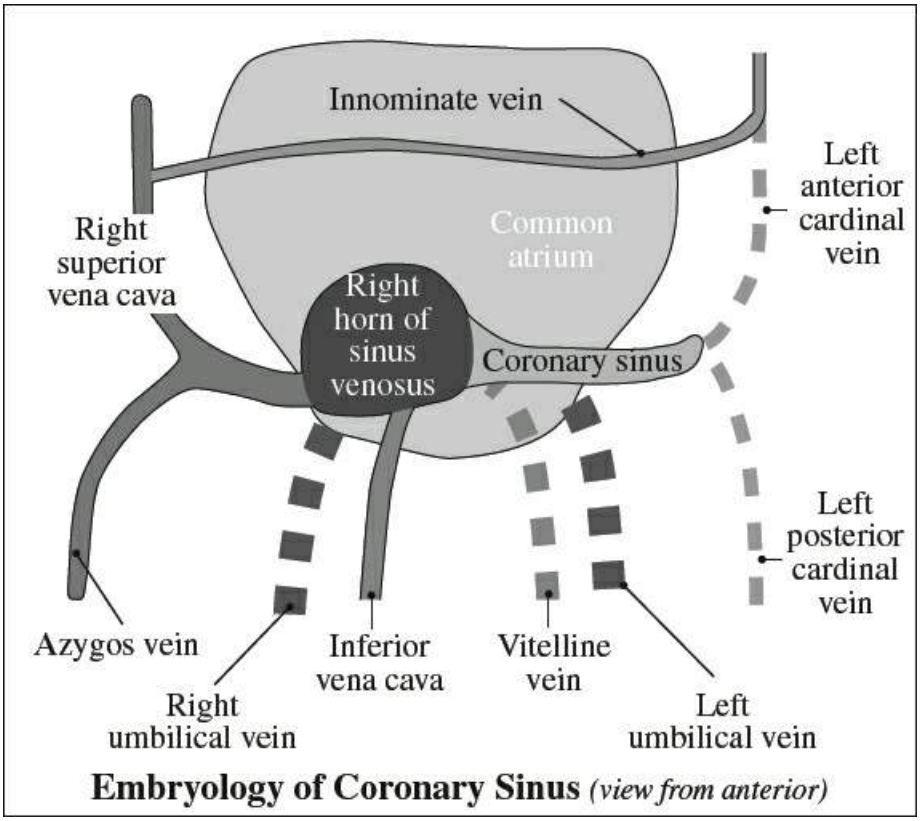
A. Greater cardiac (epicardial) venous system 70%
   › coronary sinus tributaries: 50% coronary sinus, anterior + posterior interventricular v., great cardiac v., small cardiac v., oblique vein of Marshall, atrial + septal vv.
   › noncoronary sinus tributaries: 20% anterior RV v., LA + RA vv., superior septal vv.

B. Smaller cardiac (intramural) venous system: 30% venoluminal, arterioluminal, venosinusoidal, arteriosinusoidal (= thebesian vessels 2 ° to arterial component)

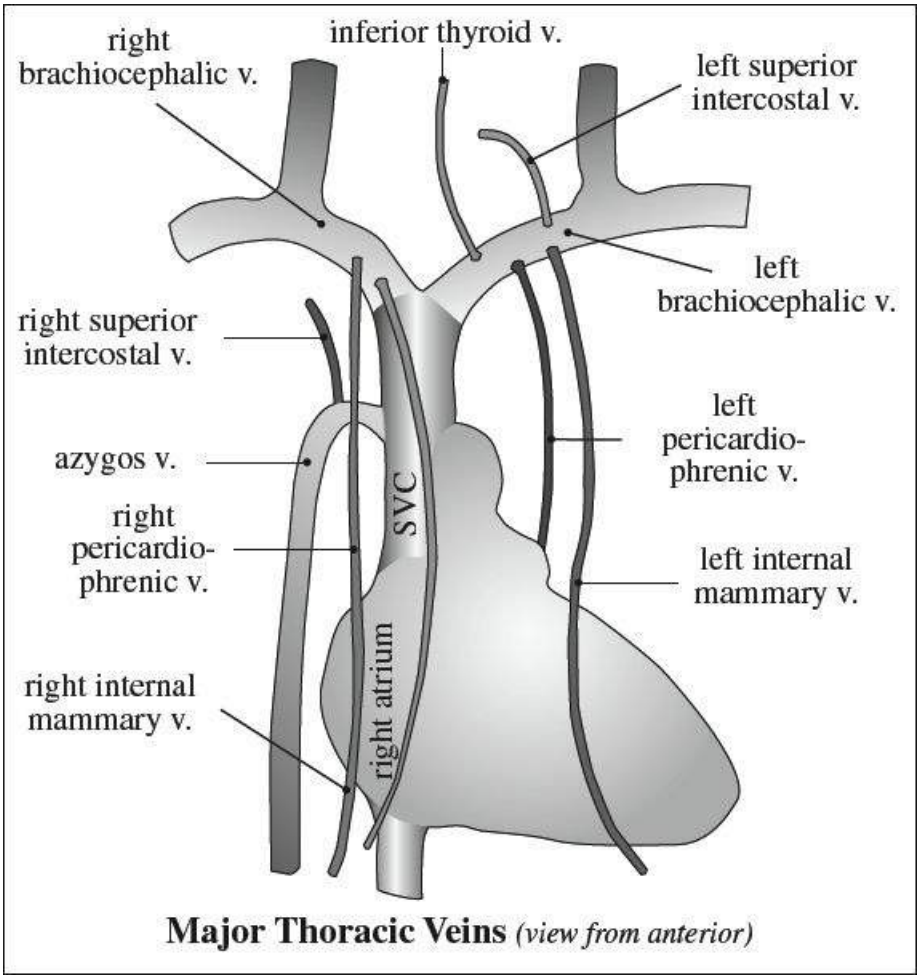
C. Compound cardiac venous system: venous tunnels of RA, sinoatrial node v., atrioventricular node v., RA wall v., ventricular septal v.



Embryonic Heart *(view from posterior)*



Embryology of Coronary Sinus *(view from anterior)*



Major Thoracic Veins *(view from anterior)*

Coronary Sinus

= distal portion of great cardiac vein

Origin: left horn of sinus venosus + adjacent left common cardinal vein receiving cardiac veins

› right horn of sinus venosus persists as venous portion of right atrium

Ostium: in RA medial to IVC + just superior to septal leaflet of tricuspid valve; guarded by thebesian valve

Length: 30–50 mm (in 75%)

Function: collects blood from left marginal vein; left posterior ventricular vein; small, middle, great, oblique cardiac veins

Clinical significance:

(1) Catheterization easiest via SVC ← sharp angle between coronary sinus and LA

(2) For cardiac resynchronization therapy (= implantation of automatic cardioverter-defibrillator for treatment of heart failure) a LV pacer lead is usually placed into posterior vein of LV / left marginal vein

(3) Conduit for catheter treatment of arrhythmias

Congenital Anomalies of Coronary Sinus

(a) variations

› in morphology: diverticulum (common at inferior aspect at junction with middle cardiac vein)
› in shape: wind sock (40%), tubular (50%), filiform (10%), varicoid, bifid
› in course: straight (16%), gently curved (62%), high-riding (22%)

Significance: difficult cannulation for mapping, ablation, left ventricular pacing; rarely of hemodynamic consequence

(b) enlargement
(c) absence / atresia: associated with heterotaxy syndromes + complex CHD
(d) atretic coronary sinus ostium
› with persistent left SVC
› with communication to LA

Coronary Sinus-Great Cardiac Vein Junction

Location: within 10 mm of each other
(1) Valve of Vieussens (in 65–85%) located 32 ± 5 mm from coronary sinus ostium
(2) Annular narrowing of external surface (20%) ← sphincterlike thickening of myocardial sleeve of coronary sinus
(3) Proximal / adjacent to oblique vein of Marshall

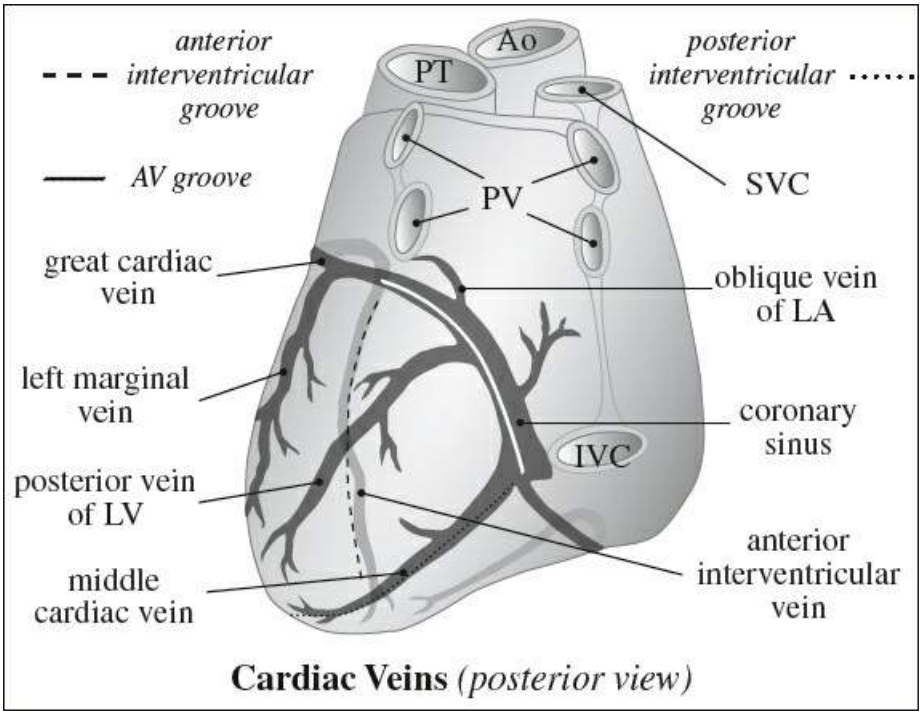
Valve of Vieussens: bi- / unicuspid (65%) or incomplete valve; present in 80%; cause of obstruction to cannulation

[Raymond Vieussens (1635–1715), French anatomist and pioneer in cardiology, head physician at Hôtel Dieu Saint-Éloi in Montpellier]

The 3 most constant anatomic landmarks of GCV-CS junction:
(1) orifice of the oblique vein of Marshall,
(2) valve of Vieussens,
(3) left margin of myocardial sleeve of coronary sinus

Great Cardiac Vein (GCV)

Location: inferior aspect of the heart in AV groove before emptying into RA
Course: crosses LAD + LCx
Drains: anterior interventricular septum, anterior surfaces of both ventricles, part of LA, cardiac apical region
Size: 45 mm long; 10–12 mm in diameter
Ostium: valve of Vieussens
Branches:



(1) Inferior interventricular (IIV) / posterior interventricular / middle cardiac vein
Location: posterior interventricular sulcus from apex to base of heart
Terminus: coronary sinus 1 cm from ostium
Drains: inferior walls of ventricles + cardiac apex + posterior $^{2}/_{3}$ of septum

(2) Left posterior / posterolateral vein of LV
Prevalence: 95%; single v. (60%), up to 3 veins
Terminus: coronary sinus (75%), GCV (25%)

(3) Left (obtuse) marginal vein
Prevalence: 70–95%
Terminus: GCV (80%), coronary sinus (20%)
Drains: much of LV myocardium

(4) Great cardiac vein
Location: left AV groove with LCx artery

(5) Anterior interventricular vein
Location: anterior interventricular groove from base of heart toward apex adjacent to LAD

Variability in Cardiac Veins

1. Absence of left marginal vein (15%)
2. Absence of posterior vein of LV (45%)

Variability in Great Cardiac Vein

@ beginning of coronary sinus
1. Oblique vein of Marshall = outer constriction
2. Vieussens valve = internal constriction

@ crossing of muscular LCx

√ kink in vein → luminal obstruction of great cardiac v.

PERICARDIUM

= double-walled sac (2-layered membrane) that envelops all cardiac chambers + origin of great vessels without direct attachment to heart

Pericardial thickness: 0.4–1.0 mm (1.2–1.7 mm by MRI; 0.7–2.0 mm by CT)

Function: regulates normal ventricular compliance by minimizing dilatation of RV + RA; physically protects heart by production of fluid + surfactants; limits displacement of heart within mediastinum; acts as pressure transducer between pleural space + cardiac chambers (augments systemic venous return + RV filling during inspiration)

A. FIBROUS / PARIETAL PERICARDIUM = FIBROSA
   = tough outer parietal layer that is mildly stretched
   √ attaches to sternum + proximal great vessels
   √ intrapericardial location of ascending aorta, main pulmonary artery, portions of venae cavae, most of PVs

B. SEROUS / VISCERAL PERICARDIUM = serosa
   = **epicardium**
   = delicate inner visceral layer forming a completely closed sac around the pericardial cavity; consists of a single layer of mesothelial cells
   • intimately connected to heart + epicardial fat

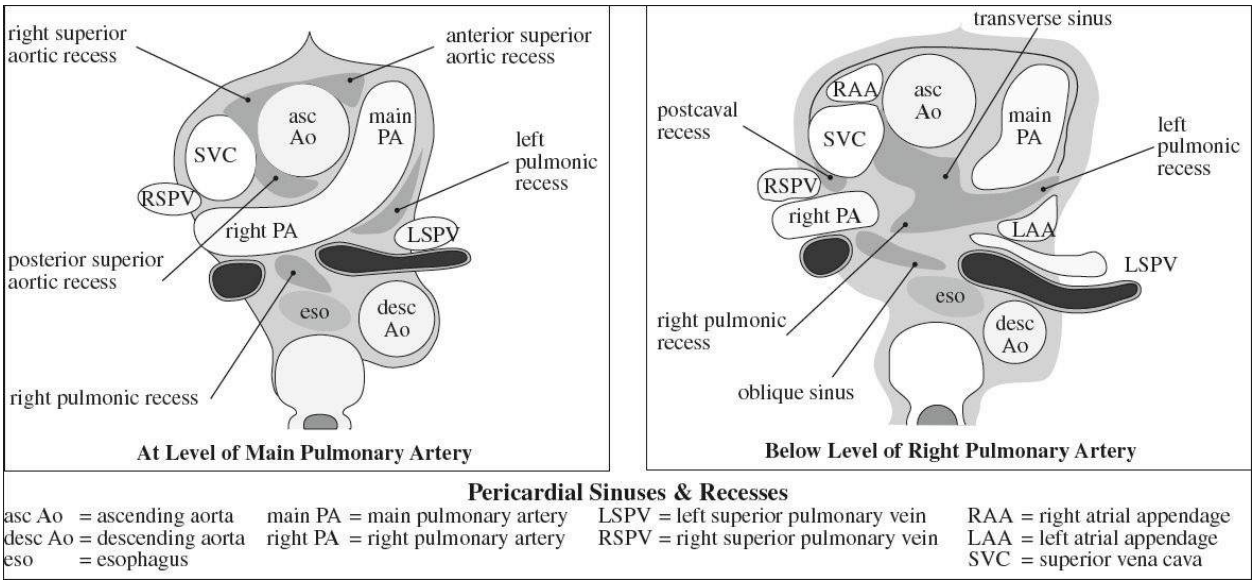
C. PERICARDIAL CAVITY
   = space between visceral and parietal pericardium
   √ sac contains 15–50 mL of serous fluid produced by mesothelial cells that line serosa
   √ normal intrapericardial pressure = 50–100 mm H_2O

Pericardial Sinuses and Recesses

= extensions of pericardial cavity

* = percentages give depiction on HRCT

A. Recesses of pericardial cavity proper
   1. Postcaval recess 23%*



√ behind and right lateral to SVC

2. Right pulmonic vein recess 29%*
   √ behind and right lateral to SVC
3. Left pulmonic vein recess 60%*
   √ behind and right lateral to SVC

B. Transverse sinus
   √ posterior to ascending aorta and pulmonary trunk + above left atrium 95%*
   1. Superior (aortic) recess
      √ along ascending aorta; may be divided into anterior, posterior, right lateral portion
      DDx: aortic dissection on NECT
   2. Left pulmonic recess
      √ below left pulmonary artery + posterolateral to proximal right pulmonary artery
   3. Right pulmonic recess
      √ below right pulmonary artery + above left atrium
   4. Inferior aortic recess
      √ between ascending aorta + inferior SVC / right atrium
      √ extending down to level of aortic valve

C. Oblique sinus 89%*
   √ behind left atrium + anterior to esophagus
   √ separated from transverse sinus by double reflection of pericardium (and fat) between right + left superior pulmonic veins
   1. Posterior pericardial recess 67%*
      √ behind distal right pulmonary artery + medial to bronchus intermedius

DDx: lymph nodes, esophageal / thymic process, vascular abnormality, pericardial cyst / tumor

Epicardial Fat

Thickness: increased in obesity

Asymmetric distribution: 3–4 x more along RV compared to left heart

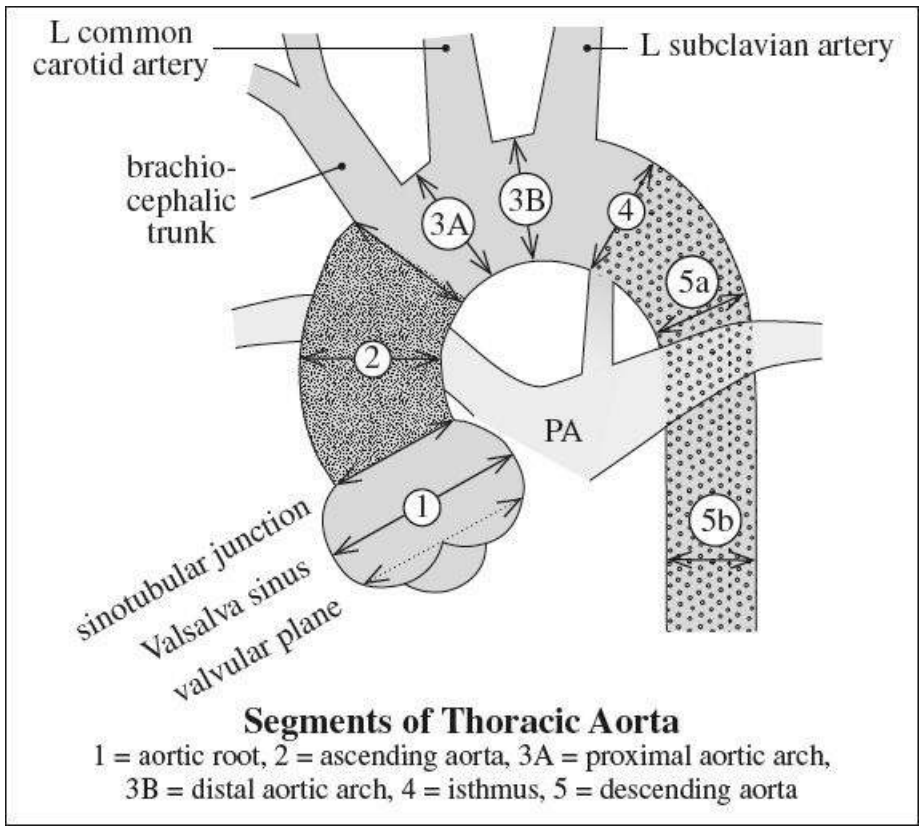
- can directly influence atherogenesis by free diffusion of fatty acids + adipokines into wall of coronary arteries

ANATOMY OF AORTA

Segments: Aortic root → Ascending aorta → Transverse aortic arch → Isthmus → Descending aorta

Aortic Root

(a) **Aortic annulus** = aortic valvular plane



Segments of Thoracic Aorta
1 = aortic root, 2 = ascending aorta, 3A = proximal aortic arch, 3B = distal aortic arch, 4 = isthmus, 5 = descending aorta

[*anulus* (diminutive of anus), Latin = small ring]
= firm fibrous band at aortoventricular junction surrounding and supporting aorta + valve leaflets

(b) **Aortic valve sinus** = Valsalva sinus
= 3 subtle dilatations of aortic root between aortic valve annulus + sinotubular ridge; associated with right + left + noncoronary cusp

(c) **Sinotubular junction** = landmark between aortic root and tubular portion of ascending aorta

Sinus of Valsalva

[Antonio Valsalva (1666 – 1723), professor of anatomy in Bologna, Italy and president of the Academy of the Sciences]
= 3 subtle outward bulges of aortic root wall between aortic valve annulus + sinotubular

ridge, each associated with corresponding right, left, noncoronary aortic valve cusp

Embryology: left + right truncoconal swellings develop along inferior end of truncus arteriosus during 5th week of embryogenesis → septation of truncus into anterior pulmonary + posterior aortic channels → each ventricular outflow tract contains 3 tubercles → form cusps of aortic and main pulmonary artery → formation of Valsalva sinuses + aortic valve leaflets (5th–9th weeks)

Aortic Diameter

Measurements are to be taken orthogonally to aortic lumen ← off-axis measurements overestimate the true diameter

(average diameter increases with age) underlined are points of standard aortic measurements (represented by thick arrows in drawing)

1. Sinotubular junction 36 mm
2. Ascending aorta (1 cm proximal to arch)
   Location: aortic root → origin of right brachiocephalic a.
   Diameter: always < 4 cm at any age
   › Midascending aorta = midpoint between 35 mm sinoaortic junction + proximal aortic arch
3. **Aortic arch**
   Location: right brachiocephalic artery → attachment of ligamentum arteriosum
   › aorta @ origin of brachiocephalic trunk 29 mm
   (A) proximal aortic arch:
   = immediately distal to innominate artery from right brachiocephalic artery → left subclavian artery
   (B) distal (mid)aortic arch:
   = immediately distal to left common carotid a.
4. Aortic isthmus = left subclavian artery → attachment of ligamentum arteriosum
5. Descending thoracic aorta
   Location: attachment of ligamentum arteriosum → aortic hiatus at diaphragm
   Diameter: always < 3 cm at any age
   (a) proximal descending aorta: 26 mm
   2 cm distal to left subclavian artery
   (b) middescending aorta: 25 mm
   (c) distal descending aorta: 24 mm
   @ diaphragm = 2 cm above celiac axis origin
6. Abdominal aorta @ celiac axis origin
7. Abdominal aorta @ most cephalic renal artery
8. Abdominal aorta @ most caudal renal artery
9. Infrarenal abdominal aorta
   (a) 15 mm below caudal renal artery
   (b) aorta just above bifurcation

Aortic Arch Branching Patterns

1. "Standard" branching pattern (65–75%) brachiocephalic trunk, left CCA, left subclavian

artery
2. Common origin of brachiocephalic trunk + left CCA (13%)
3. Bovine aortic arch (9%)
   = origin of left CCA from brachiocephalic trunk
4. Vertebral artery (usually left) arising from aortic arch (3%)
5. Left and right brachiocephalic trunks (1%)
6. Aberrant right subclavian artery as the last branch of the aortic arch (< 1%)

Cervical Aortic Arch

Associated with: right aortic arch (in ²/₃)

• pulsatile neck mass, upper airway obstruction, dysphagia
√ mediastinal widening
√ absence of normal aortic knob
√ aortic arch near lung apex
√ tracheal displacement to opposite side + anteriorly
√ apparent cutoff of tracheal air column ← crossing of descending aorta to side opposite of arch

DDx: carotid aneurysm

Aortic Isthmus Variants

Aortic Isthmus

= narrowing of the aorta in newborn between left subclavian artery and ductus arteriosus

Age: up to 2 months of age

Prognosis: aortic isthmus disappears ← cessation of flow through ductus arteriosus + increased flow through narrowed region

Aortic Spindle *(16%)*

= congenital narrowing of the aorta at the ligamentum arteriosum with distal fusiform dilatation
√ smooth circumferential bulge below isthmus in first portion of descending aorta

Ductus Diverticulum

= convex focal bulge along anterior undersurface of aortic isthmus

Origin: remnant of enlarged mouth of ductus arteriosus / result of traction from ligamentum arteriosum

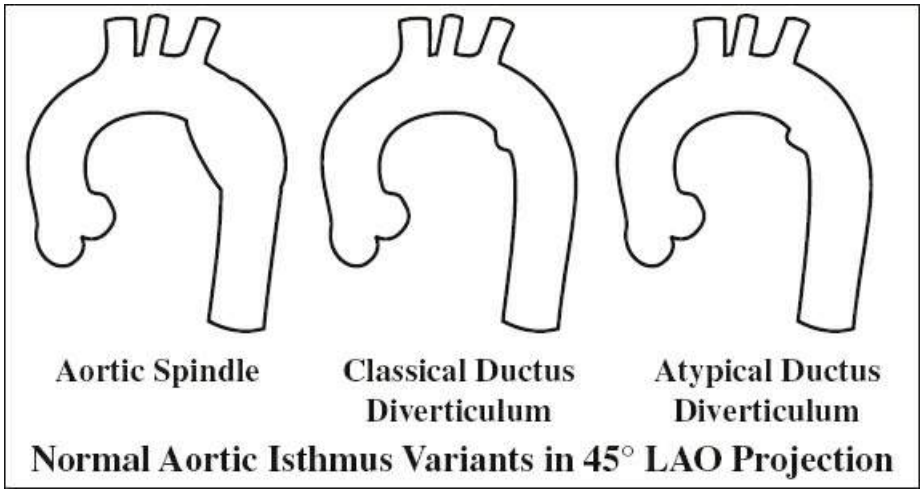
Frequency: in 33% of infants, in 9% of adults

√ focal bulge with smooth uninterrupted margin and obtuse angle with aortic wall:
  √ gently sloping symmetric shoulders (classic ductus diverticulum)
  √ shorter steeper slope superiorly + more gentle slope inferiorly (atypical ductus diverticulum)

DDx: posttraumatic pseudoaneurysm

Ductus Arteriosus

Origin: left 6th aortic arch



Normal Aortic Isthmus Variants in 45° LAO Projection

Location: connects proximal descending aorta (immediately distal to origin of left subclavian artery) with left pulmonary artery (at level of junction with main pulmonary artery)

Function: shunting of blood away from lungs (during fetal life)

Normal ductus physiology in mature infant:

↑ arterial oxygen pressure → constriction + closure of duct

◊ Functional closure ← muscular contraction within 10–18–48 hours after birth

◊ Anatomic closure ← subintimal fibrosis + thrombosis: in 35% by 2 wks; in 90% by 2 mo; in 99% by 1 year

Cx: premature closure → heart failure, fetal hydrops

PULMONARY VESSELS

Pulmonary Artery

1. Diameter of root: < 35 mm
2. Diameter at level of bifurcation: < 28 mm

Location: near bronchus

Pulmonary Veins

= 2 (superior + inferior) veins from R and L lung drain into either side of LA with separate ostia

Embryology: during first 2 months of fetal life lungs drain into systemic veins; these obliterate when common primitive pulmonary vein (developed from primitive LA) fuses with primitive lung

Pulmonary venous trunk:

= - distance from ostium to 1st-order branch:

Length: (a) superior pulmonary vein: 21.6 ± 7.5 mm

(b) inferior pulmonary vein: 14.0 ± 6.2 mm

Pulmonary vein ostium:

(a) superior pulmonary vein: 19–20 mm

(b) inferior pulmonary vein: 16–17 mm

Drainage:
RUL + RML → right superior pulmonary v.
LUL + lingula → left superior pulmonary v.
RLL / LLL → right / left inferior pulmonary v.

Variations of Pulmonary Vein Anatomy (in 38%)

1. Conjoined (common) left / right pulmonary vein (25%)
2. Supernumerary vein
   › separate right middle pulmonary vein draining RML:
   √ aberrant insertion with perpendicular orientation to posterior left atrial wall
   Mean size of ostium: 9.9 ± 1.9 mm
   Strong association with: atrial fibrillation
3. Early branching of pulmonary vein (< 1 cm)

Clinical significance:
LA muscle (as a focus of ectopic electrical activity) can extend into venous ostia → atrial fibrillation → treatment with radiofrequency catheter ablation

Pulmonary veins contribute to the origination and maintenance of atrial fibrillation, most commonly with a focus in the left superior pulmonary vein!

◊ Alert cardiologist about variant anatomy of additional pulmonary veins prior to RF ablation!

COLLATERAL CIRCULATION OF HAND

Vascular supply to hand is predominantly through ulnar a. with connections to radial artery via superficial + deep palmar arches

Blood supply: (1) Radial a. (2) Ulnar a. ± (3) Median a. (4) Interosseous a.

Circuits:

› at level of carpus
(1) Anterior carpal arch
(2) Posterior carpal arch

› at midcarpal level (with blood supply to fingers)
(3) Superficial palmar arch (larger)
= anastomosis between termination of ulnar a. + palmar branch of radial a.
√ origin to 3 common palmar digital arteries
(4) Deep palmar arch (smaller)
= anastomosis between termination of radial a. + palmar branch of ulnar a.
√ proximal to superficial arch
√ crosses bases of metacarpal bones
√ origin to 3 palmar metacarpal branches

Variations of arterial termination:

(1) Complete superficial palmar arch (66–96%)
= supplies all fingers + ulnar side of thumb
(2) Incomplete superficial palmar arch (4–7%)
= supplies all fingers + NO supply of thumb
(3) Distal end of superficial palmar arch of ulnar artery communicates with radial artery

(34%)
(4) Complete palmar arch + anastomosis to superficial palmar branch of radial artery (10%)
(5) Complete deep palmar arch (77–97%)
(6) Radial artery dominance
(7) Malformations of ulnar artery

Allen Test

= good clinical indicator of relative contribution of radial + ulnar arteries to circulation of hand

Purpose:
(1) Continuity assessment of palmar arch
(2) Test for arterial disease: thrombangiitis obliterans, scleroderma, occupational vasospastic disease
(3) Radial artery harvest of the nondominant arm for coronary artery bypass grafting (CABG)
(4) Prior to puncture / insertion of monitoring catheters into radial artery (19–92% incidence of occlusion after cannulation)

Pathophysiology: obliteration of one circulation → distal hypoperfusion + ↓ pressure + ↓ resistance → augmented flow in the opposite artery

Clinical Allen Test

Requirement: conscious cooperative patient

Technique: assessment of capillary refilling after active "exsanguination" of hand (= repetitive clenching into fist) under simultaneous compression of both radial and ulnar arteries followed by relaxed extension of fingers and release of one artery (more common)

N.B.: AVOID hyperextension of wrist or hand!

Results:
(1) Normal = complete capillary refilling and blush of entire hand within 6 sec. following release of arterial compression of one artery
(2) Incomplete continuity of palmar arch = any portion of hand without capillary refilling
(3) Occlusion of released artery = no capillary refilling of entire hand

◊ Considerable rate of false-positive and false-negative results!

Doppler Allen Test

◊ Independent of patient cooperation!

Technique: Doppler velocity detector placed on radial / ulnar artery at wrist before and during a period of compression of the opposite artery

Results:

Normal: arterial velocity increases in response to compression of opposite artery

Abnormal: absence of velocity increase indicates a lack of continuity between radial + ulnar circulation (= interruption of palmar arch)

Modified Allen Test For Radial Artery Harvest

Technique:

Doppler examination with recording of PSV (peak systolic velocity) + EDV (end diastolic velocity) of

(a) subclavian a., axillary a., brachial a., radial a. (at wrist), ulnar a. (at wrist)
(b) superficial palmar arch of radial a. (at imaginary line following proximal segment of 2nd metacarpal bone)
(c) princeps pollicis a. (medial aspect of base of thumb)
(d) 2nd common palmar digital a. (between heads of 2nd + 3rd metacarpal bones)
(i) 3rd common palmar digital a. (between heads of 3rd + 4th metacarpal bones)

Patient position: supine after a 10-min rest at standard room temperature

Criteria for safe radial artery harvest:

(1) Over 20% increase in systolic-diastolic flow rate in ulnar artery (suggests good arterial compliance to receive the entire flow from the brachial artery)
(2) Flow reversal in superficial palmar arch (indicates anatomic continuity of superficial palmar arch)
(3) Stable flow in 3rd common palmar digital a. (good palmar circulation)
(4) Up to 70% flow reduction in 2nd common palmar digital a.
(5) Up to 30% flow reduction in 1st common palmar digital a.

Contraindication to removal (6%):

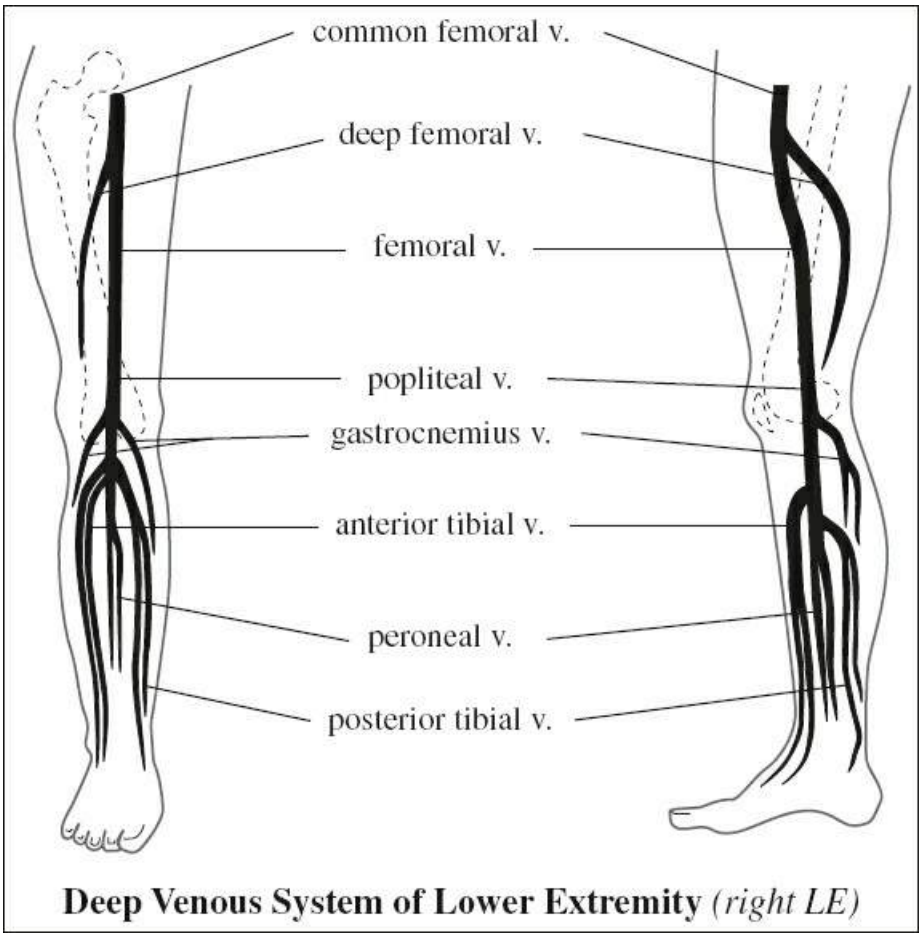
(1) Absence of expected increases in PSV and EDV in ulnar artery (MAIN CONTRAINDICATION)
(2) Atherosclerosis of upper limb arteries (1.6%)
◊ Patients are susceptible to catastrophic embolic episodes with a single artery supplying the forearm!
(3) Raynaud disease
(4) Disappearance of flow in superficial palmar arch

VENOUS SYSTEM OF LOWER EXTREMITY

Deep Veins of Lower Extremity

3 paired stem veins of the calf accompany the arteries as venae commitantes + anastomose freely with each other:

1. **Anterior tibial veins**
   draining blood from dorsum of foot, running within extensor compartment of lower leg close to interosseous membrane
2. **Posterior tibial veins**
   formed by confluence of superficial + deep plantar veins behind ankle joint
3. **Peroneal veins**
   directly behind + medial to fibula
4. Calf veins
   (a) **Soleus muscle veins**
   baggy valveless veins in soleus muscle (= sinusoidal veins); draining into posterior tibial + peroneal veins or lower part of popliteal vein
   (b) **Gastrocnemius veins**
   thin straight veins with valves; draining into lower + upper parts of popliteal vein



Deep Venous System of Lower Extremity *(right LE)*

5. **Popliteal vein**
   formed by stem veins of lower leg
6. **Femoral / superficial femoral vein**
   continuation of popliteal vein; receives deep femoral vein about 9 cm below inguinal ligament
7. **Deep femoral vein**
   draining together with superficial femoral vein into common femoral vein; may connect to popliteal vein (38%)
8. **Common femoral vein**
   formed by confluence of deep + superficial femoral vein; becomes external iliac vein as it passes beneath inguinal ligament

Superficial Veins of Lower Extremity

1. **Great (greater) saphenous vein** (GSV)
   formed by union of veins from medial side of sole of foot with medial dorsal veins; ascends in front of medial malleolus; passes behind medial condyles of tibia + femur
   (a) **Posterior arch vein**
   connected to deep venous system by communicating veins
   (b) **Anterior superficial tibial vein** = Anterior arch vein from lateral malleolus along lateral edge of tibia across tibia to join greater saphenous vein at upper ⅓ of calf

(c) **Posteromedial superficial thigh vein**
often connects with upper part of lesser saphenous vein
(d) **Anterolateral superficial thigh vein**
(e) Tributaries in fossa ovalis
› superficial inferior epigastric vein
› superficial external pudendal vein
› superficial circumflex iliac vein

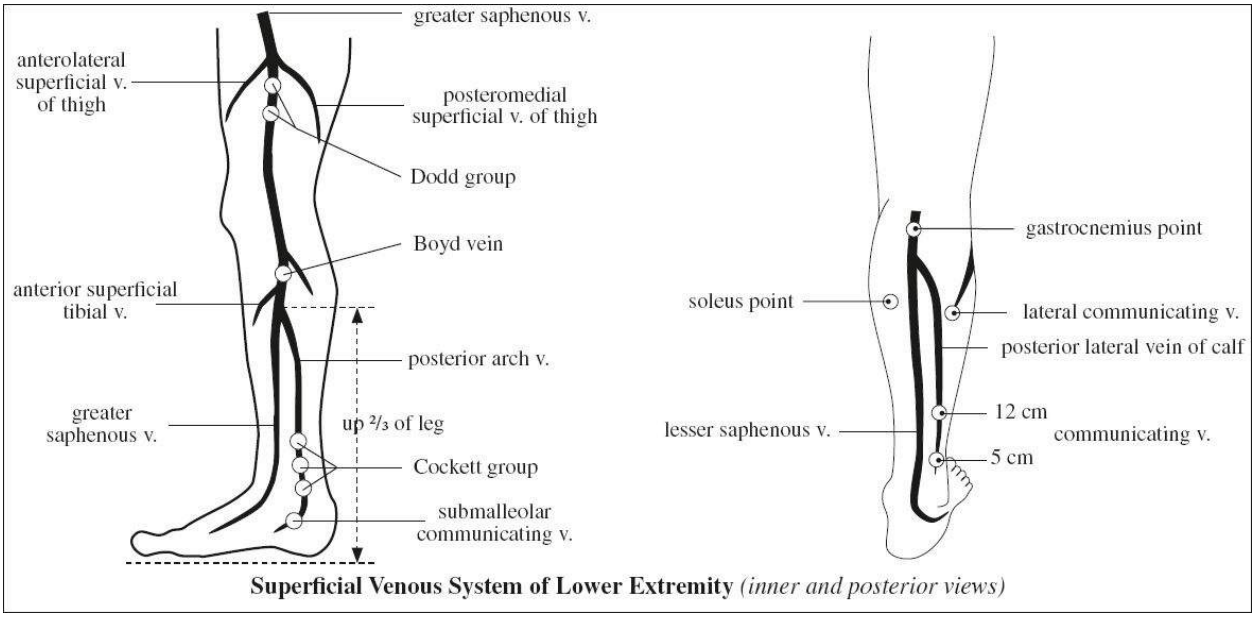
2. **Small (lesser) saphenous vein** (SSV)
originates at outer border of foot behind lateral malleolus as continuation of dorsal venous arch; enters popliteal vein between heads of gastrocnemius in popliteal fossa within 8 cm of knee joint (60%) or joins with greater saphenous vein via posteromedial / anterolateral superficial thigh vein (20%)

Communicating = Perforating Veins

> 100 veins in each leg

A. MEDIAL
1. Submalleolar communicating vein
2. **Cockett group**
group of 3 veins located 7, 12, 18 cm above the tip of medial malleolus connecting posterior arch vein with posterior tibial vein
3. **Boyd vein**
located 10 cm below knee joint connecting main trunk of greater saphenous vein to posterior tibial veins
4. **Dodd group**
group of 1 or 2 veins passing through Hunter canal (= subsartorial canal) to join greater saphenous vein with superficial femoral vein

B. LATERAL
1. **Lateral communicating vein**
located from just above lateral malleolus to junction of lower-to-mid thirds of calf connecting lesser saphenous vein with peroneal veins



Superficial Venous System of Lower Extremity *(inner and posterior views)*

2. **Posterior mid-calf communicating veins**
   located posteriorly 5 + 12 cm above os calcis joining lesser saphenous vein to peroneal veins
3. **Soleal + gastrocnemius points**
   joining short saphenous vein to soleal / gastrocnemius veins

PHASICITY

[*phasis* , Greek = speech]

= description of fluctuating / undulating cyclic (phasic) flow events (= velocity changes of acceleration, deceleration, direction) in a vessel audible by Doppler / graphically depicted as a Doppler waveform

Cause: pressure gradients generated by cardiac ± respiratory activity and exerted on the "column" of blood within the interrogated vessel segment

Origin: audible Doppler sounds created by changes in flow acceleration

Antegrade flow may be either toward or away from the transducer, depending on the spatial relationship of the transducer to the vessel. Therefore, antegrade flow may be displayed above or below the baseline.

Ambiguous terminology:

1. Flow direction: above / below baseline (favored)
2. Points of inflection = modulation of pitch (original)

PULSATILITY

= assessment of vascular resistance (increased resistance reduces diastolic flow)

◊ Can be assessed in vessels too small / tortuous to be imaged (Doppler angle unnecessary)!

◊ Index should be calculated for each of several cardiac cycles (5 heartbeats adequate) an average value taken

S = A = maximal systolic shift

D = B = end-diastolic frequency shift

1. Full pulsatility index of Gosling (PIF) = $1/A0_2\ SAi_2$
2. Simplified pulsatility index (PI) = (S - D)/mean
3. Resistance index (RI) = Pourcelot index
   = (S - D)/S or 1 - (D/S)
4. Stuart index = A/B ratio = S/D ratio
5. B/A ratio = B(100%)/A

High-Resistance Arteries

1. External carotid arteries
2. Extremity arteries
3. Fasting mesenteric arteries

Low-Resistance Arteries

1. Internal carotid arteries
2. Hepatic arteries
3. Renal arteries
4. Testicular arteries

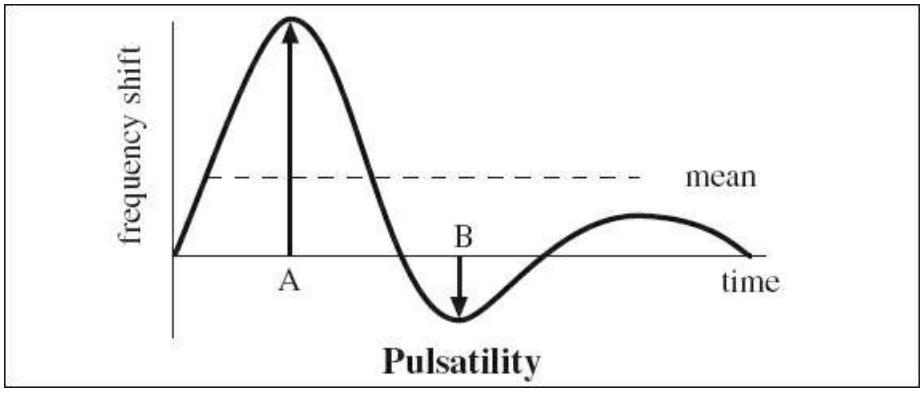
HEMOGLOBIN

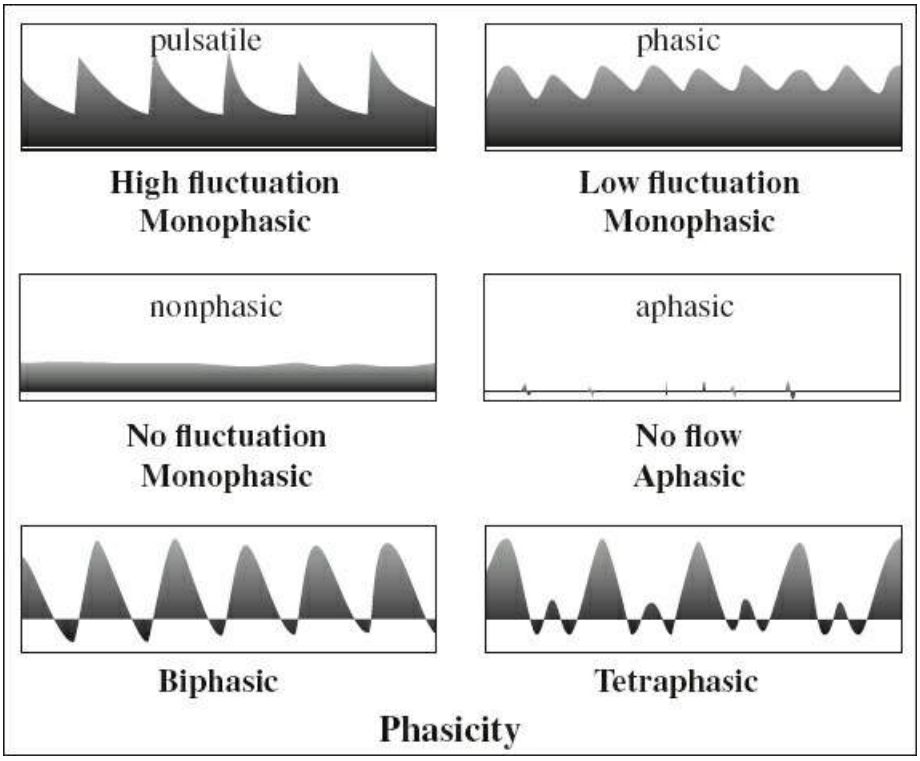
composed of 4 globular protein subunits + porphyrin ring holding an Fe2+ ion

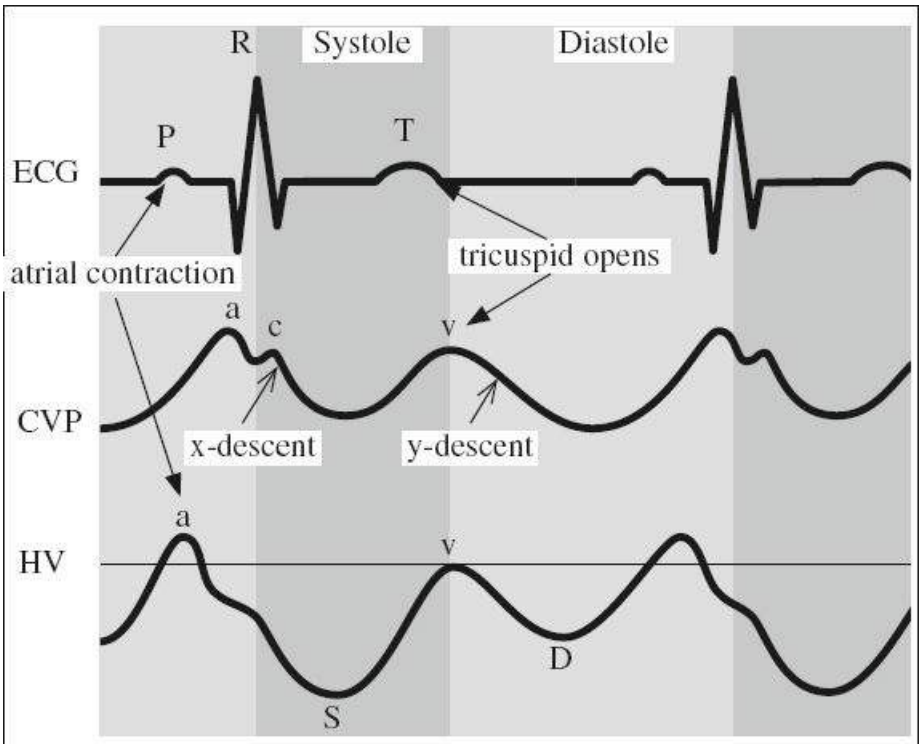
in fetus: Hb F

in adult: Hb A, Hb A2, Hb F

Variants: Hb H (β4).
Hb S (α2βS2)
Hb C (α2βC2)
Hb SA
Hb SC




pulsatile
phasic
High fluctuation
Monophasic
Low fluctuation
Monophasic
nonphasic
aphasic
No fluctuation
Monophasic
No flow
Aphasic
Biphasic
Tetraphasic
Phasicity



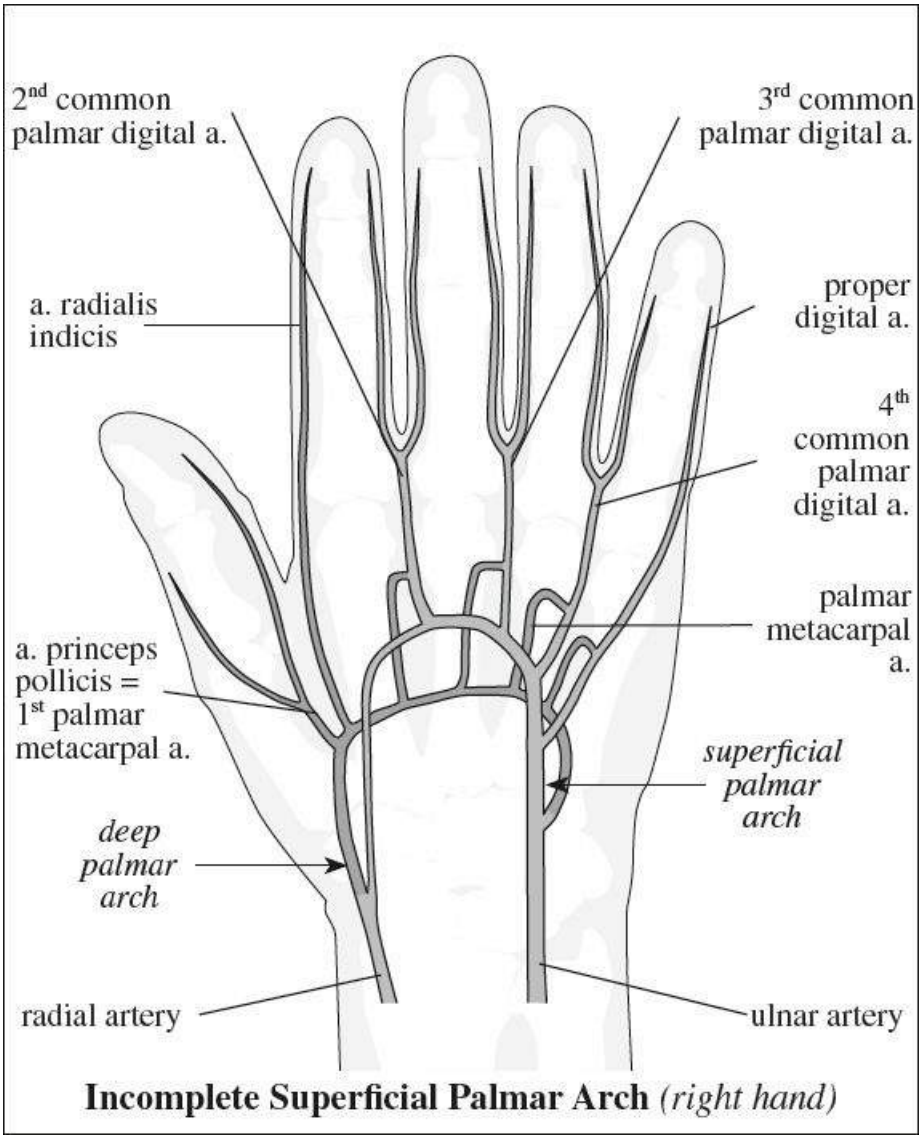
Time-correlated electrocardiographic (ECG), central venous pressure (CVP) and hepatic venous (HV) Waveform

S wave = trough correlates with peak negative pressure created by downward motion of AV annulus toward cardiac apex during midsystole

v wave = peak correlates with opening of tricuspid valve as the point of transition from systole to diastole; caused by RA overfilling against a closed tricuspid valve; occurs in <50% of patient

D wave = trough correlates with rapid early diastolic RV filling caused by opening of the tricuspid valve + blood flow from RA into RV; equal to / smaller than *S* wave

a wave = retrograde *a* wave at end-diastole caused by contraction of RA; in 66% of patients



Incomplete Superficial Palmar Arch *(right hand)*

Hb A (96–98%)

= in **A**dult composed of 4 subunits of polypeptides Hb α1, Hb α2, Hb β, Hb β

Genes & Locus:

HBA1 on chromosome 16p13.3

HBA2 on chromosome 16p13.3

HBB on chromosome 11p15.5

tetramer α2β2 composed of

- 2 α globin chains (141 amino acids)
- 2 β globin chains (146 amino acids)

Hb A_2 (1.5–3.5%)

tetramer α2δ2 composed of

- 2 α globin chains
- 2 δ globin chains

Hb F

in **F**etus + in F-cells of the adult

tetramer α2γ2 composed of

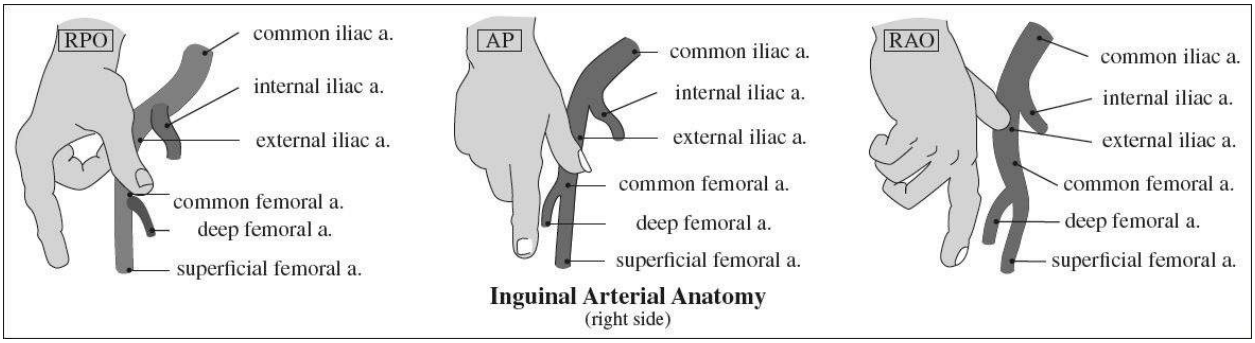
- 2 α globin chains
- 2 γ globin chains

• greater affinity to oxygen than Hb A

CONTENTS OF FEMORAL TRIANGLE

mnemonic: NAVEL (from lateral to medial)

Nerve
Artery
Vein
Empty space
Lymphatics



Inguinal Arterial Anatomy
(right side)

CARDIOVASCULAR DISORDERS

ABERRANT LEFT PULMONARY ARTERY

= LEFT PULMONARY ARTERY SLING = ANOMALOUS ORIGIN OF LEFT PULMONARY ARTERY

Embryology: failure of development / obliteration of left 6th aortic arch (= vascular pedicle for left lung); left lung parenchyma maintains a connection with right lung leading to development of a collateral branch of the right pulmonary artery to supply the left lung

Site: left PA passes above right mainstem bronchus + between trachea and esophagus on its way to left lung (= sling around proximal right main bronchus + distal trachea)

Age at presentation: neonate to adulthood

Classification:

(1) Normal bronchial pattern

(2) Malformation of bronchotracheal tree

Associated with:

(a) "napkin-ring trachea" = absent pars membranacea (50%)

(b) stenosis of long tracheal segment

(c) PDA (most common), ASD, persistent left SVC

- stridor (most common), wheezing, apneic spells, cyanosis
- respiratory infection, feeding problems

√ deviation of trachea to left

√ "inverted-T" appearance of mainstem bronchi = horizontal course ← lower origin of right mainstem bronchus

√ anterior bowing of right mainstem bronchus

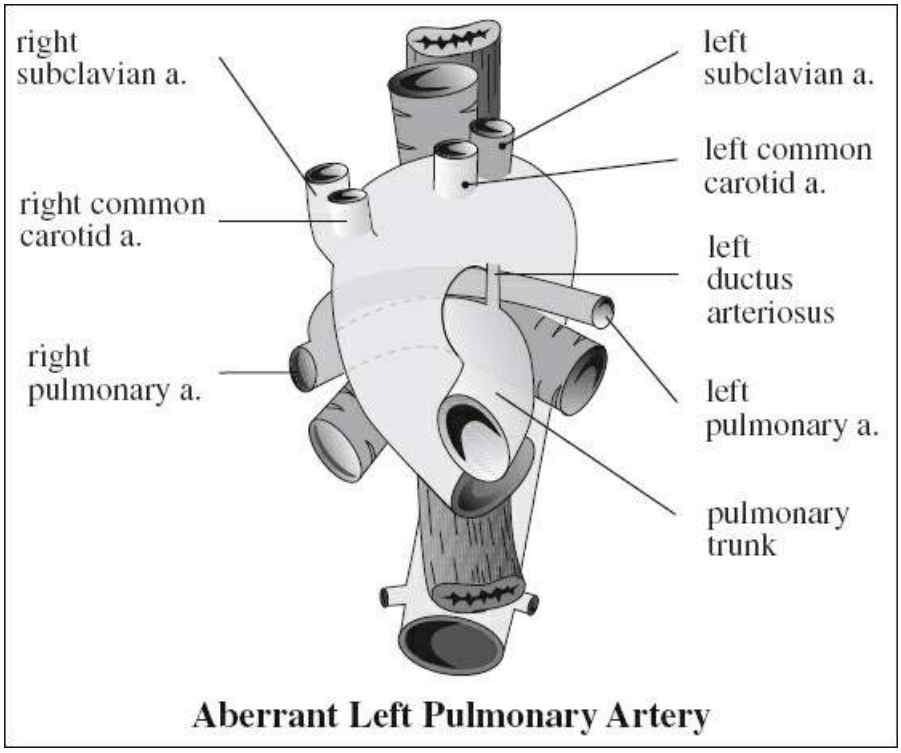
√ "carrot-shaped trachea" = narrowing of tracheal diameter in caudad direction resulting in functional tracheal stenosis

√ obstructive emphysema / atelectasis of RUL + LUL

√ low left hilum

√ separation of trachea + esophagus at hilum by soft-tissue mass

√ anterior indentation on esophagram



Aberrant Left Pulmonary Artery

AMYLOIDOSIS

= extracellular deposits of insoluble fibrillar protein (most commonly amyloid AL = light chain) in myocardial interstitium

Incidence: AL amyloidosis (50%); AA amyloidosis (2%);
isolated myocardial amyloid deposition (in 25% of autopsied patients > 85 years of age)

Path: commonly involvement of all 4 chambers

- asymptomatic / fatigue, weakness
- angina, CHF (diastolic dysfunction ⇉ restrictive cardiomyopathy), arrhythmia

CXR:
- √ normal / generalized cardiomegaly
- √ pulmonary congestion
- √ pulmonary deposits of amyloid

NUC:
- √ striking uptake of ^{99m}Tc-pyrophosphate greater than bone (50–90%)

ECHO:
- √ granular sparkling appearance of myocardium
- √ LV wall thickening
- √ decreased LV systolic + diastolic function

MR:
- √ diffuse decrease in SI on T1WI
- √ diffuse pattern of ventricular myocardial hypertrophy
- √ increase in thickness of interatrial septum + right atrial free wall > 6 mm (SPECIFIC)
  [DDx: ischemic heart disease thins myocardium]

CEMR:
√ predominant late enhancement of entire subendocardial circumference (HIGHLY SPECIFIC + SENSITIVE)

Dx: endomyocardial Bx with potential for severe complications

ANOMALOUS (INNOMINATE) BRACHIOCEPHALIC ARTERY COMPRESSION SYNDROME

= origin of R innominate (brachiocephalic) artery to the left of trachea coursing to the right
√ anterior tracheal compression
• ablation of right radial pulse by rigid endoscopic pressure
√ posterior tracheal displacement
√ focal collapse of trachea at fluoroscopy
√ pulsatile indentation of anterior tracheal wall by innominate artery on MR
Rx: surgical attachment of innominate artery to manubrium

ANOMALOUS LEFT CORONARY ARTERY

= **A** NOMALOUS ORIGIN OF **L** EFT **C** ORONARY **A** RTERY FROM **P** ULMONARY **A** RTERY SYNDROME = ALCAPA = BLAND-WHITE-GARLAND SYNDROME

Prevalence: 1÷300,000 live births; 0.25–0.50% of congenital heart defects

◊ One of the most common causes of myocardial ischemia + infarction in children!

Age: infancy / early childhood; adulthood (rare)
In 5% associated with: ASD, VSD, aortic coarctation
Location: LCA arises from left inferolateral aspect of main pulmonary artery just beyond pulmonary valve
Hemodynamics:
postnatal fall in pulmonary arterial pressure → perfusion of LCA drops (= "coronary steal") → L-to-R shunt (= collateral circulation from RCA with flow reversal in LCA)
› adequate collateral circulation = lifesaving
› inadequate collateral circulation = myocardial infarction
› large collateral circulation = volume overload of heart
• ECG: anterolateral infarction
√ LCA arising from the main pulmonary artery (HALLMARK) along its left inferolateral aspect just beyond pulmonic valve
√ coronary steal into PA
√ left ventricular wall motion abnormalities, mostly global hypokinesis
Rx: (1) Ligation of LCA at its origin from pulmonary trunk
(2) Ligation of LCA + graft of left subclavian artery to LCA
(3) Creation of an AP window + baffle from AP window to ostium of LCA
DDx: endocardial fibroelastosis; dilated cardiomyopathy; viral cardiomyopathy (NO shocklike symptoms)

A. INFANT TYPE
• symptomatic about 8 weeks after birth:
• failure to thrive, profuse sweating, dyspnea, pallor
• atypical chest pain while eating / crying
√ massive cardiomegaly during newborn period:

√ dilatation of LV ← chronic myocardial ischemia
√ enlargement of LA
√ congestive heart failure
√ mitral insufficiency ← myocardial infarction
√ normal pulmonary vascularity / redistribution
Prognosis: if untreated death within 1st year (in up to 90%)

B. ADULT TYPE (rare)
= sufficient right-to-left coronary artery collaterals
• asymptomatic, continuous murmur (if collaterals large)
• ischemic cardiomyopathy, malignant dysrhythmia
√ massively enlarged and tortuous collateral circulation from RCA to LCA ← increased flow:
√ abundant intercoronary collaterals on epicardial surface
√ development of dilated bronchial artery collaterals
Cx: chronic left ventricular subendocardial ischemia → malignant ventricular dysrhythmia
Prognosis: sudden cardiac death (in 80–90%)

ANOMALOUS PULMONARY VENOUS RETURN

= complete / partial failure of developing lung to connect with primitive common pulmonary vein retaining connections to primitive splanchnic system of cardinal veins (L-to-R shunt)

Total Anomalous Pulmonary Venous Return

= TAPVR = entire pulmonary venous return directed to RA = admixture lesion because of the combination of cyanosis + increased pulmonary vascularity (L-to-R and R-to-L shunt) = absent connection of pulmonary veins with LA

Embryology: persistence of primitive splanchnic pulmonary veins connecting to fetal cardinal systemic veins + failure of primitive common pulmonary vein to develop from posterior LA wall

◊ Usually isolated defect!

May be associated with:
asplenia; ASD / patent foramen ovale (necessary for survival); bronchopulmonary sequestration; pulmonary arteriovenous malformation; cystic adenomatoid malformation

Types: according to termination of anomalous pulmonary veins

I	supracardiac level	55%
II	cardiac level	30%
III	infracardiac / infradiaphragmatic level	13%
IV	termination at ≥ 2 levels (= mixed type)	2%

Prevalence: 2% of CHD

Age: symptomatic in 1st year of life

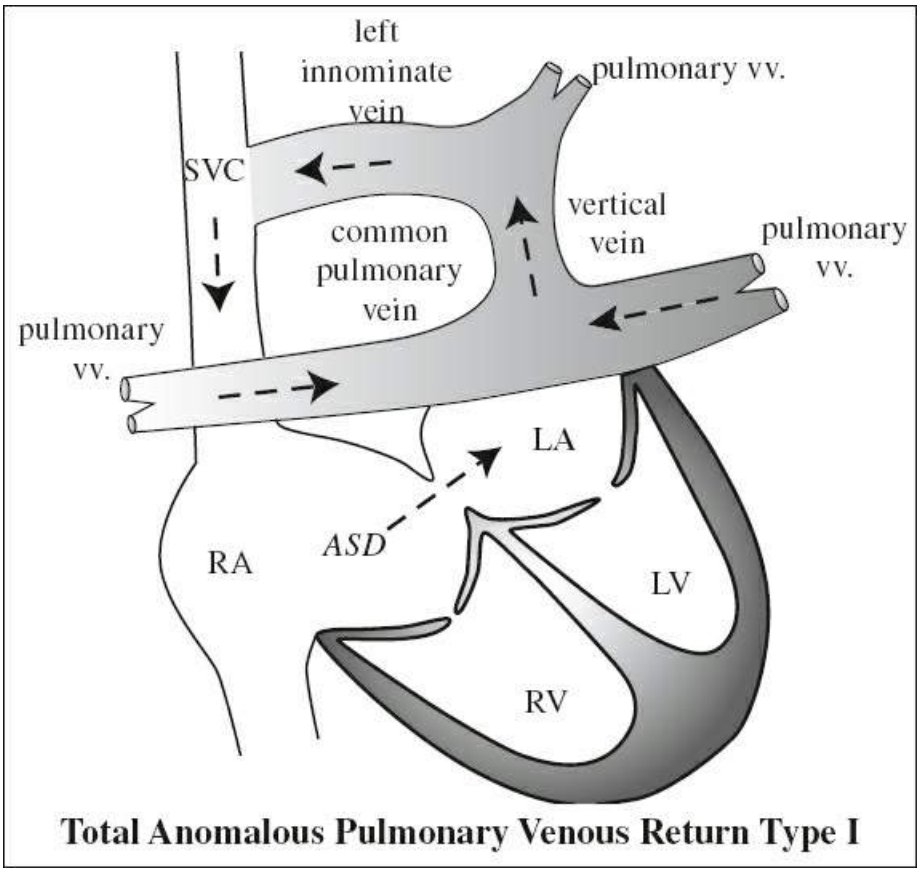
• cyanosis and congestive heart failure typically develop in the early neonatal period

Hemodynamics:
obstruction along the pulmonary venous pathway

RA ↔	RV ↔	Main PA ↔
Pulm vessels ↑		
LA ↔	LV ↔	Ao ↔

MR:

√ "retroatrial" sign = presence of veins posterior to LA
√ small LA without pulmonary venous connections
√ patent foramen ovale / ASD



Total Anomalous Pulmonary Venous Return Type I

√ anomalous vein with variable location

In most potentially clinically unstable neonates with TAPVR, complete anatomic delineation of the defect is possible with echocardiography alone!

Overall prognosis: 75% mortality rate within 1 year of birth if untreated

Supradiaphragmatic TAPVR *(85%)*

Hemodynamics:

› functional L-to-R shunt from pulmonary veins to RA
› increased pulmonary blood flow (= overcirculation)
› obligatory R-to-L shunt via usually patent foramen ovale / ASD → restores oxygenated blood to left side
› normal systemic venous pressure with increased flow through widened SVC

› after birth CHF secondary to
(a) mixture of systemic + pulmonary venous blood in RA
(b) volume overload of RV

Age: presentation < 1 years of age

In 30% associated with: other cardiac lesions, asplenia

• cyanosis, neck veins undistended (shunt level distally)
• R ventricular heave (= increased contact of enlarged RV with sternum)
• systolic ejection murmur (large shunt volume)

√ overall heart size notably normal:
√ slightly enlarged RV (= volume overload with time)
√ normal / enlarged RA
√ normal LA (= ASD acts as escape valve)

√ increased pulmonary blood flow (= overcirculation)

SUPRACARDIAC TAPVR (55%)

= drainage of pulmonary veins into a horizontally oriented confluence posterior to LA → ascending vertical vein posterior to left atrial appendage + usually anterior to left pulmonary a. → left brachiocephalic (innominate) vein / right or left persistent SVC / azygos vein

√ "figure of 8" / "snowman" configuration of cardiac silhouette:
√ "head of snowman" = dilated vertical vein on left + innominate vein on top + SVC on right
√ "body of snowman" = heart with enlarged RA

√ pretracheal density on lateral film (= left vertical vein)

= 4 anomalous pulmonary veins converge behind LA forming a common vertical vein, which passes anterior to left PA + left main bronchus to join
(a) innominate vein (most commonly)
(b) left brachiocephalic vein
(c) right SVC
(d) azygos vein

√ extrinsic venous obstruction if vertical vein courses between left PA anteriorly + left main bronchus posteriorly (10%)

CARDIAC TAPVR (30%)

= drainage of pulmonary veins into coronary sinus (80%) / RA / SVC / (often obstructed) azygos vein

ECHO:
√ "whale's tail" appearance ← dilated pulmonary veins and coronary sinus

Sub- / Infradiaphragmatic / Infracardiac TAPVR *(13%)*

= drainage of pulmonary veins into vertically oriented confluence posterior to LA → portal vein / ductus venosus / IVC / hepatic veins / left gastric vein; R-to-L shunt through ASD

Age: presentation in neonatal period with severe CHF

• intense cyanosis + respiratory distress

Hemodynamics: constriction of descending pulmonary vein by diaphragm en route through

esophageal hiatus → (in > 90%) pulmonary venous hypertension + RV pressure overload

Associated with: asplenia syndrome (80%), polysplenia

√ pulmonary veins join to form a common vertical descending vein ("inverted fir tree") posterior to LA:

√ vertical vein lies anterior to esophagus + descends through esophageal hiatus

√ low anterior indentation on barium-filled esophagus

√ connects (most commonly) to portal vein at confluence of splenic v. + superior mesenteric v.

√ unique appearance of pulmonary edema + pulmonary venous congestion with normal-sized heart (DDx: hyaline membrane disease)

√ thymic atrophy + depression of diaphragm

Cx: obstruction of pulmonary venous return in > 90%

Prognosis: death within a few days of life

Mixed Type of TAPVR *(2%)*

= with various connections to R side of heart (6%) at ≥ 2 levels, most commonly (a) vertical vein drains into left innominate (brachiocephalic) vein (b) anomalous vein(s) from right lung drain into RA / coronary sinus

Partial Anomalous Pulmonary Venous Return

= PAPVR = ≥ 1 pulmonary veins drain into systemic venous system / RA rather than LA (= L-to-R shunt)

Embryology: early atresia / malposition of central pulmonary v.

Prevalence: 0.3–0.7% of patients with CHD

Age: presentation later in life than TAPVR

N.B.: venous return almost never obstructed!

May be associated with: may occur in isolation

(1) Atrial septal defect (25%)

(a) RUL pulmonary vein (66%) enters SVC, RA, azygos vein, coronary sinus, IVC

Age: more common in children

◊ in 90% of patients with sinus venosus type ASD

◊ 50% of patients with PAPVR have a high sinus venosus type ASD near orifice of SVC

√ RUL vein courses in a horizontal direction

(b) LUL pulmonary vein (33%) enters brachiocephalic vein / coronary sinus

Age: more common in adults as incidental finding

Frequently associated with: ostium secundum type ASD (10–15%)

√ vertical mediastinal density lateral to aortic knob extending upward and medially with smooth curvilinear border (DDx: persistent left SVC)

(2) Hypogenetic lung as a component of congenital pulmonary venolobar / scimitar syndrome

• acyanotic and often asymptomatic

• ASD symptomatology (if ≥ 50% of pulmonary venous flow)

√ radiographic findings similar to ASD

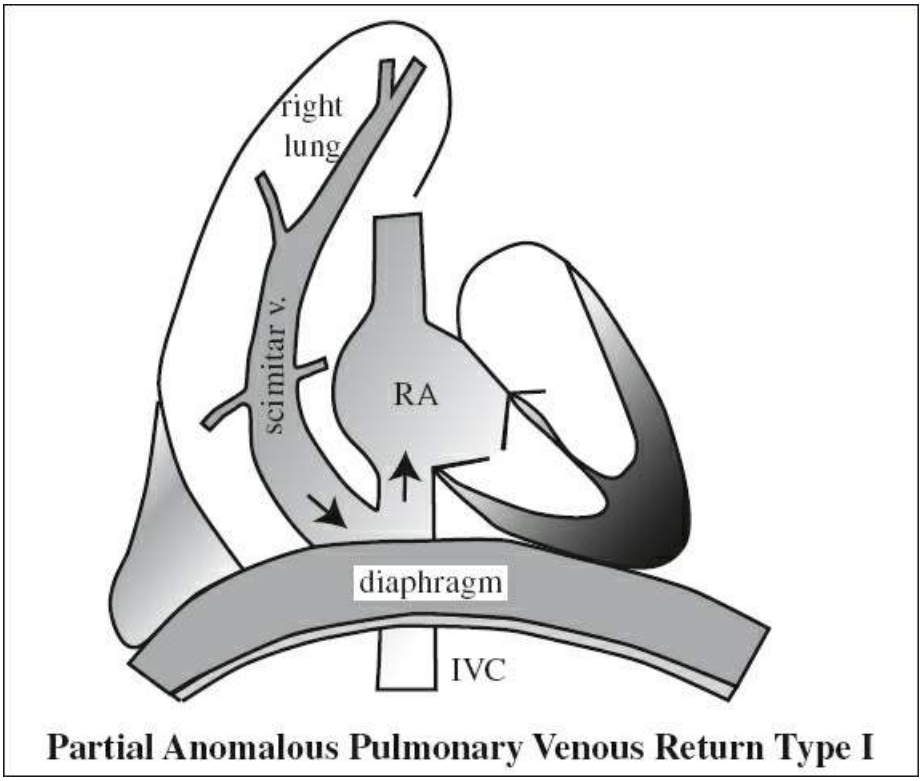
√ anomalous course of draining vein
√ enlargement of draining site: SVC, IVC, azygos vein
CECT:
√ nodular / tubular opacity (= anomalous vein), which opacifies in phase with pulmonary vein
Prognosis: near normal life expectancy

Scimitar Syndrome

= HYPOGENETIC LUNG SYNDROME = CONGENITAL PULMONARY VENOLOBAR SYNDROME
[*scimitar* = Persian or Turkish sword with curved blade]
= lower part / all of the hypogenetic lung is drained by an anomalous vein → L-to-R shunt
Hemodynamics: insignificant L-to-R shunt
Components: systemic supply + drainage of RLL
(1) Anomalous arterial supply of right lower lobe from abdominal aorta = systemic arterialization of the lung <u>without sequestration</u> (= pseudosequestration)
(2) Scimitar vein
(3) Hyopoplasia of right lung with dextroposition of heart:
(4) → Hypo- / aplasia of right pulmonary artery
Associated with: CHD (47–90%, most commonly ASD), extralobar sequestration, horseshoe lung, pulmonary AVM, bronchogenic cyst, accessory diaphragm
◊ High incidence of sinus venosus ASD with right upper lobe PAPVR

- asymptomatic (for shunt of < 50% of pulmonary flow) / pulmonary to systemic blood flow (Qp÷Qs) ≥ 1.5÷1
- acyanotic (until pulmonary arterial HTN occurs)
- heart murmur, fatigue, dyspnea

Location: almost exclusively on right side (1 case on left)



Partial Anomalous Pulmonary Venous Return Type I

CXR:

√ tubular structure paralleling the right heart border in an outward curved configuration of a Turkish sword increasing in diameter as the vein descends (PA view)

Site: middle of right lung to cardiophrenic angle

√ hypoplastic ipsilateral lung

√ small ipsilateral pulmonary hilum ← hypoplasia / aplasia of pulmonary artery

√ shift of heart + mediastinum into right chest

√ hyperinflated and hyperlucent contralateral lung

MR/CT:

The amount of L-to-R shunting is quantifiable by MR with cine phase-contrast flow analysis of the aorta and main pulmonary artery to estimate the Qp/Qs ratio!

√ systemic arterialization of right lung (without sequestration) ← anomalous artery from abdominal aorta / visceral artery

√ scimitar vein drains any / all lobes of right lung and connects to:

› infradiaphragmatic IVC (33%)

› suprahepatic IVC (22%)

› hepatic veins

› portal vein (11%)

› azygos vein

› coronary sinus

› right atrium (22%)

› left atrium = "meandering pulmonary vein"

◊ Drainage into suprahepatic portion of IVC / right atrium may be a clue for

interruption of intrahepatic portion of IVC!

Prognosis: normal / near-normal life span

Rx: anomalous vein / veins anastomosed to LA + repair of ASD

Sinus Venosus Defect

= SINUS VENOSUS–TYPE ATRIAL SEPTAL DEFECT

= unroofing of right pulmonary veins into SVC / IVC

N.B.: sinus venosus atrial septal defect is a misnomer since the true atrial septum is not involved

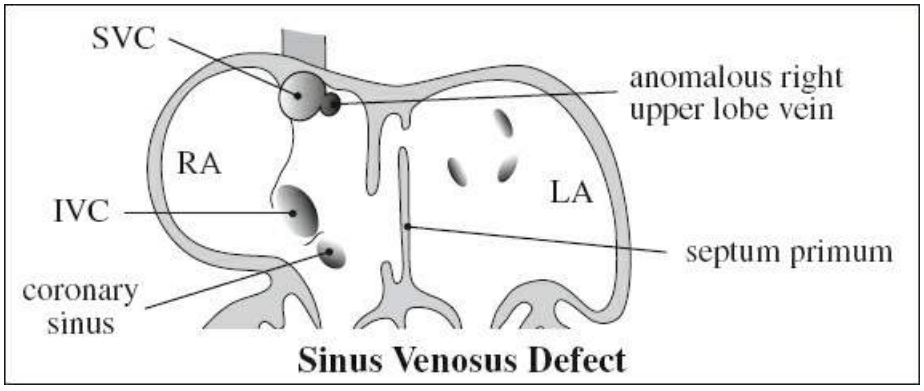
Types:

1. Sinus venosus defect of the SVC type
   = unroofing of the right <u>upper</u> pulmonary vein (RUPV) into SVC = defect of the superior inlet portion of extraseptal atrial wall separating SVC–right atrial junction from posterosuperior aspect of LA = drainage of RUPV into SVC
   Location: superior to fossa ovalis near entrance of superior vena cava (SVC straddles ASD)
2. Sinus venosus defect of the IVC type
   = unroofing of the right <u>lower</u> pulmonary vein (RLPV) into IVC

<u>variable:</u> involvement of the right middle pulmonary vein (RMPV) can occur with either type

Function: R-to-L shunt similar to large ASD

- symptoms of right ventricular volume overload:



Sinus Venosus Defect

- fatigue, dyspnea, arrhythmia, heart murmur

Associated with:

partial anomalous pulmonary venous return in 90% (RUL pulmonary veins connect to SVC / right atrium), Holt-Oram syndrome, Ellis-van Creveld syndrome

AORTIC ANEURYSM

An aneurysm is defined as a vessel segment with a diameter of > 150% of the diameter of a normal adjacent segment + involving < 50% of the total vessel length!

Cause:

1. Aortic dissection (53%)

2. Atherosclerosis (29–80%): descending aorta; usually multiple
3. Traumatic (15–20%): descending aorta; ← transection
4. Congenital (2%): aortic sinus, post coarctation, ductus diverticulum
5. Syphilis (4%): ascending aorta + arch
6. Mycotic infection = bacterial dissection; anywhere
7. Cystic media necrosis (Marfan / Ehlers-Danlos syndrome, annuloaortic ectasia): ascending aorta
8. Aortitis = inflammation of media + adventitia: Takayasu arteritis, giant cell arteritis, relapsing polychondritis, rheumatic fever, rheumatoid arthritis, ankylosing spondylitis, Reiter syndrome, psoriasis, ulcerative colitis, systemic lupus erythematosus, scleroderma, Behçet disease, ulcerative colitis, radiation
9. Increased pressure: systemic hypertension, aortic valve stenosis
10. Abnormal volume load: severe aortic regurgitation

Pathophysiology:
intimal injury of aortic wall → lipid-laden macrophage + lymphocyte infiltration → inflammatory cells secrete cytokines → activation of multiple proteolytic cascades → degradation of collagen + elastin within tunica media → weakening + dilatation of aortic wall

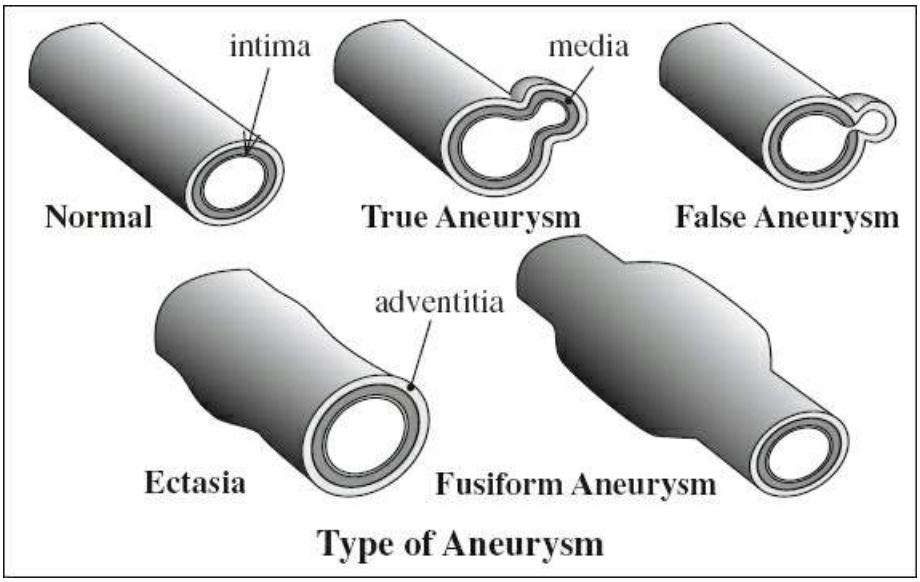
Location: abdominal aorta (31%), ascending aorta (22%), arch (12%), descending thoracic aorta (8%), thoracoabdominal (3%)

TRUE ANEURYSM

= permanent dilatation of all 3 layers (intima + media + adventitia) of weakened but intact wall

Fusiform Aneurysm (80%)

[*fusus* , Latin = spindle (tapered at each end)]
= longitudinal measurement > transverse diameter
Cause: atherosclerotic degeneration
√ circumferential involvement of wall over longer arterial segment
√ NO definable neck



√ NO relation to proximal stenosis

Saccular Aneurysm (20%)

[*saccus*, Latin = sack, pouch]

= transverse diameter > longitudinal measurement

Cause: penetrating ulcer / inflammation / infection

√ berry-like outpouching of portion of wall

√ frequently distal to area of proximal stenosis

√ often multisegmental

Cx: prone to thrombosis and rupture

FALSE ANEURYSM = PSEUDOANEURYSM

= loss of wall integrity with transition from 3-layered wall to an outwardly single/double layer

Cause: trauma, penetrating atheroclerotic ulcer, infection (= "mycotic" aneurysm)

Pathophysiology: escaped blood contained by adventitia / perivascular connective tissue + organized blood

Histo: disruption of the external elastic membrane

√ saccular dilatation with a narrow neck

ARTERIAL ECTASIA

= diffuse dilatation

Type I diffuse dilatation of 2–3 vessels

Type II ectasia of 1 vessel + aneurysm in another

Type III solitary ectatic vessel

Abdominal Aortic Aneurysm (AAA)

= focal widening > 3 cm (ultrasound literature); twice the size of normal aorta / > 4 cm [Bergan, Ann Surg 1984]

Normal size of abdominal aorta > 50 years of age:

14–21 [12–19] mm in men [women]

Prevalence: 1.4–8.2% in unselected population; in 6% > 80 years of age; in 6–20% of patients with signs of atherosclerotic disease; M > F; Whites÷Blacks = 3÷1

Cause: structural defect; ? genetic (10-fold ↑ in risk as 1st- degree relative of patient with AAA); copper deficiency

Risk factors: male sex, age > 75 years, white race, prior vascular disease, hypertension, cigarette smoking, family history, hypercholesterolemia

Age: > 60 years; M÷F = 5–9÷1

Associated with:

(a) visceral + renal artery aneurysm (2%)
(b) isolated iliac + femoral artery aneurysm (16%):
common iliac (89%), internal iliac (10%), external iliac (1%)
(c) stenosis / occlusion of celiac trunk / SMA (22%)
(d) stenosis of renal artery (22–30%)
(e) occlusion of inferior mesenteric artery (80%)
(f) occlusion of lumbar arteries (78%)

Growth rate of aneurysm of 3–6 cm in diameter:
0.39 cm annually

• asymptomatic (30%), abdominal mass (26%) / pain (37%)

◊ Imaging should provide information about:

(a) anatomic considerations of aneurysm:
» size
» proximal extent, which determines the site of clamping of the aorta (eg, origin of renal arteries)
» course of the left renal vein (retroaortic?)
(b) aneurysm growth rate
(c) findings of aneurysm instability

Location: infrarenal (91–95%) with extension into iliac arteries (66–70%)

◊ The infrarenal abdominal aorta has a lower concentration of elastin + vasa vasorum making it vulnerable to aneurysm formation!

Plain film:
√ mural calcification (75–86%)

US:
√ > 98% accuracy in size measurement

NCCT:
√ perianeurysmal fibrosis (10%) → ± ureteral obstruction

CECT:

(a) ruptured aneurysm
√ anterior displacement of kidney
√ extravasation of contrast material
√ fluid collection / hematoma within posterior pararenal + perirenal spaces
√ free intraperitoneal fluid
√ perirenal "cobwebs"
(b) contained leak
√ laminated mural calcification

√ periaortic mass of mixed / soft-tissue density
√ lateral "draping" of aneurysm around vertebral body
√ indistinct aortic wall (unreliable)
√ focal discontinuity of calcifications (unreliable)

A patchy discontinuous intimal calcification is common in stable and unstable aneurysms.

Angio (AP + LAT filming):
√ focally widened aortic lumen > 3 cm
√ apparent normal size of lumen ← mural thrombus (11%)
√ mural clot (80%)
√ slow antegrade flow of contrast medium

Cx:
(1) Aortic rupture (25%)
(2) Peripheral embolization
(3) Infection
(4) Spontaneous occlusion of aorta

Prognosis: 17% 5-year survival without surgery, 50–60% 5-year survival with surgery

Rx: (1) Excision of aneurysm + aortic interposition graft (4–5% surgical mortality for nonruptured, 30–80% for ruptured aneurysm)
(2) Endovascular aneurysm repair (70%) with post-repair complications of graft migration > 5 mm, graft kinking / fracture, persistent endoleak

Postoperative Cx:
(1) Left colonic ischemia (1.6%) with 10% mortality
(2) Renal failure (14%)
(3) 0–8% mortality rate for elective surgery

Acute Aortic Aneurysm Rupture

◊ Leading cause of death (4,500 annually) in USA in 1.3% of men > 65 years

Risk factors: female sex (M÷F = 1÷4), larger baseline aneurysm diameter, hypertension, continued tobacco use, low 1-second forced expiratory volume, history of cardiac / renal transplant

Risk for aneurysm rupture:
directly related to aneurysm size + rate of enlargement

Increased risk of aneurysm rupture: size > 6 cm

Aneurysm Size vs. Likelihood of Rupture

< 4 cm	10%	5–7 cm	25%
4–5 cm	23%	7–10 cm	46%
		> 10 cm	60%

› growth > 5 mm / 6 months

The most accurate + reproducible bidimensional aneurysm measurements are those that are orthogonal to a center line through the aorta.

• pain + tenderness
◊ The exact moment of rupture is unpredictable
• sudden severe abdominal pain ± radiating into back

• faintness, syncope, hypotension

Site:

(1) into retroperitoneum: commonly on left
(2) into GI tract: massive GI hemorrhage
(3) into IVC: rapid cardiac decompensation

CT:

√ high-attenuation crescent within mural thrombus = acute contained rupture / impending rupture
√ retroperitoneal hematoma ± extension into perirenal space / pararenal space / psoas muscle / peritoneum

CECT:

√ active extravasation into thrombosed portion

Prognosis: 64–94% die before reaching hospital

Rx: most vascular surgeons electively repair a typical fusiform abdominal aortic aneurysm if > 5.4 cm

Chronic Contained Aortic Aneurysm Rupture

= aortic wall no longer fully intact with hemorrhage enclosed by a thrombus and/or retroperitoneal soft tissues

• hemodynamically stable
• ± previous episode of abdominal pain

Angio:

√ absent parenchymal stain = avascular halo
√ displacement + stretching of aortic branches

CT:

√ loss of periaortic fat planes:
  √ commonly posterolateral focal area of soft-tissue attenuation intimately associated with aorta
√ "draped aorta" sign = posterior aortic wall not identifiable as distinct from adjacent structures / closely apposed to adjacent vertebral body contour
√ new saccular outpouching (= focal breach) of aneurysm wall in the region that appears draped on AXIAL view
√ anterior vertebral body scalloping ← chronic repetitive aortic pulsations and pressure

N.B.: contained rupture is unrelated to aneurysm size

Impending Aortic Aneurysm Rupture

A focal discontinuity of a circumferential calcified intimal plaque and outward displacement may indicate a contained rupture at NECT. A contained rupture is definite if the finding is new.

√ increasing size of aneurysm

Laplace law:

T (circumferential wall tension) = P (transmural pressure) • r (vessel radius)

√ thinning of thrombus = decreasing thrombus volume with progressive enlargement of flow lumen ← lysis of thrombus (thrombus protects against rupture)

√ focal discontinuity in circumferential wall calcifications ← focal plaque erosion = unstable aneurysm
√ "crescent" sign = periluminal curvilinear area of hyperattenuation in aneurysm wall / thrombus (= acute intramural hematoma) is 93% specific:
  √ attenuation higher than intraluminal blood on NECT
  √ attenuation higher than psoas muscle on CECT
√ ± perianeurysmal fat stranding

With bolus tracking a large aneurysm may not fully opacify, which can result in suboptimal enhancement of the aortic branches.

Extravasation indicative of active hemorrhage may not be apparent in a large rupturing aneurysm during the early arterial phase but rather during the late arterial / venous phase after the aneurysm has filled with contrast.

Indication for surgical repair:
√ diameter of > 5–6–7 cm
√ enlargement rate of ≥ 10 mm annually

Atherosclerotic Aneurysm of Abdominal Aorta

◊ There is no consensus regarding the definition of an atherosclerotic AAA!

Frequency: most common cause of aortic aneurysms; leading cause of thoracic aortic aneurysm

Histo: diseased intima with secondary degeneration + fibrous replacement of media → ultimately wall of aneurysm composed of acellular + avascular connective tissue

Pathophysiology:
progressive weakening of media → vessel dilatation + increased tension of vessel wall (law of Laplace = tensile stress varies with product of blood pressure and radius of vessel); compromise of mural vascular nutrition (vasa vasorum) → further degeneration + progressive dilatation

Age: elderly; M > F

- asymptomatic (most)
- chest pain; symptoms related to compression of adjacent structures (dysphagia, hoarseness, lobar atelectasis, pneumonia, parenchymal hemorrhage, superior vena cava syndrome)

Location: distal abdominal aorta (66%) > iliac a. > popliteal a. > common femoral a. > aortic + descending thoracic aorta > carotid a. > ascending aorta

Site:
(1) Infrarenal aorta (associated with thoracic aneurysm in 29%)
(2) Descending thoracic aorta distal to left subclavian artery
(3) Thoracoabdominal aorta

√ fusiform (80%), saccular (20%)
√ frequently contain calcified thrombus with irregular inner contour

Cx: rupture (cause of death in 50%): usually unrestrained + fatal in thoracic location

Degenerative Aneurysm

= medial degeneration

Most common cause of aneurysm in ascending aorta

Cause:
(1) Genetically transmitted metabolic disorder: Marfan syndrome, Ehlers-Danlos syndrome
(2) Acquired: result of repetitive aortic injury + repair associated with aging

Idiopathic Inflammatory Aortic Aneurysm

= defined as triad of
(1) thickened wall of aneurysm
(2) extensive perianeurysmal + retroperitoneal fibrosis
(3) dense adhesions of adjacent abdominal organs

Cause: slow leakage from aneurysm related to periaortic retroperitoneal fibrosis and autoimmune diseases (rheumatoid arthritis, systemic lupus erythematosus, giant cell arteritis)

Frequency: 5–25% of all AAAs; rare in ascending aorta + aortic arch

Mean age: 62–68 years; M÷F = 6÷1 to 30÷1

- abdominal / back pain; weight loss + anorexia (20–41%)
- elevated ESR (40–88%), fever
- tender pulsatile abdominal mass (15–30%)

Comorbidities: arterial hypertension (34–69%), arterial occlusive disease (10–47%), diabetes mellitus (3–13%), coronary artery disease (33–55%)

Size: usually small at presentation because of early symptomatology

CECT (83% sensitive, 99% specific):
√ rind of homogeneous soft-tissue density surrounding aorta anteriorly + laterally sparing posterior wall
√ delayed contrast enhancement of soft-tissue component (DDx from hematoma)

MR:
√ periaortic inflammation and adventitial fibrosis
√ turbulent intraluminal flow

US:
√ sonolucent halo around aorta

PET:
√ grading extent of inflammation

Cx: (1) Entrapment of ureters (10–21%) + hydronephrosis
(2) Aortic-sigmoid colon fistula + bleeding
(3) Secondary bacterial infection (eg, Salmonella)
(4) Enlargement + rupture irrespective of size (lower rate than in noninflammatory aneurysm)

Prognosis: 23% mortality during surgical repair

Leaking Aortic Aneurysm

- acute chest pain

At risk for rupture: symptomatic > asymptomatic aneurysm; mycotic aneurysm; thoracic aortic aneurysm > 6 cm

MR:

√ irregular aneurysm wall
√ extra-aortic blood
√ pleural effusion containing high SI on T1WI (methemoglobin)
√ admixture of lower-intensity blood products + fat in mediastinum

Cx: rupture into left pleural space (descending thoracic aorta); rupture into pericardium/mediastinum (ascending thoracic aorta)

Mycotic (Infected) Aneurysm

[mycotic = misnomer used by Osler in 1885 describing a mushroom-shaped aneurysm associated with endocarditis]

= false (majority) / true aneurysm that is prone to rupture

Frequency: 0.7–2.6% of all aortic aneurysms

Age: > 5th decade; M > F

Location: (a) aorta: suprarenal (70%) > infrarenal > descending thoracic > thoracoabdominal > juxtarenal > ascending aorta near sinus of Valsalva
(b) other arteries: abdominal visceral artery > intracranial artery > lower / upper extremity a.

A mycotic aneurysm of the aortic root and sinus of Valsalva may be associated with infectious endocarditis, uni- / bicuspid aortic valve, and infected prosthetic aortic valve!

A. PRIMARY MYCOTIC ANEURYSM (rare) unassociated with any demonstrable intravascular inflammatory process

B. SECONDARY MYCOTIC ANEURYSM
= aneurysm due to nonsyphilitic infection

Predisposing factors:
(1) Atherosclerosis
(2) Aortic trauma ← accidents, aortic valve surgery, arterial graft, coronary artery bypass surgery, intravascular catheter, arterial catheterization, joint prosthesis

Risk factors:
(1) IV drug abuse
(2) Sepsis
(3) Bacterial endocarditis (12%)
(4) Immunocompromise (malignancy, alcoholism, corticosteroid therapy, chemotherapy, autoimmune disease, diabetes)

Mechanism:
(a) hematogenous:
› septicemia with abscess formation via vasa vasorum
› septicemia with abscess formation via vessel lumen
(b) direct extension from adjacent infection: osteomyelitis of sternum or spine, renal or psoas abscess → weakening + destruction part of the aortic wall
(c) traumatic / iatrogenic: intima laceration (trauma, atherosclerosis, coarctation)

Organism: S. aureus (53%) > E. coli > Salmonella (33-50%) > nonhemolytic Streptococcus > Listeria > Haemophilus, Pneumococcus, Gonococcus, Mycobacterium (contiguous spread from spine / lymph nodes)

Histo: loss of intima + destruction of internal elastic lamella; varying degrees of destruction

of muscularis of media + adventitia
- frequently insidious → late-stage septic shock
- persistent fever, leukocytosis ← bacteremia (positive blood culture in only 53%); NO acute chest pain

Size: 1–11 cm

√ CHARACTERISTIC saccular formation (> 90%) with lobular contour arising eccentrically from aortic wall

√ rapid enlargement (faster expansion rate compared with atherosclerotic aneurysm as short as 7 days)

√ interrupted ring of aortic wall calcification

√ periaortic fat stranding / fluid / gas collection

√ adjacent vertebral / sternal osteomyelitis (rare)

√ periaortic / psoas abscess

√ adjacent reactive lymph node enlargement

Cx: (1) Life-threatening rupture + hemorrhage (50–75%)
(2) Uncontrolled sepsis if untreated

Rx: prompt surgery

Prognosis: 67% overall mortality

Syphilitic Aneurysm

= sexually transmitted chronic systemic infection caused by spirochete Treponema pallidum

= tertiary stage of syphilis consisting of neurosyphilis, gumma, cardiovascular involvement

Spectrum:

1. Uncomplicated syphilitic aortitis
2. Syphilitic aortic aneurysm (mostly saccular)
3. Syphilitic aortic valvulitis (aortic regurgitation)
4. Syphilitic coronary ostial stenosis

N.B.: dissection (uncommon) ← scarring of media

Frequency: 12% of patients with untreated syphilis

Onset: 5–30 years after initial spirochete infection

Histo: chronic inflammation of vasa vasorum → obstruction of vasa vasorum → nutritional impairment of aortic media → focal destruction of aortic media with loss of elastic + smooth muscle fibers replaced by scar

- positive venereal disease research laboratory (VDRL) test
- positive microhemagglutination assay - Treponema pallidum (MHA-TP) test

Location: ascending aorta (36–60%), aortic arch (34%), proximal descending aorta (25%), distal descending aorta (5%), aortic sinuses (< 1%)

√ asymmetric enlargement of aortic sinuses (DDx to annuloaortic ectasia with symmetric enlargement)

√ saccular (75%) / fusiform (25%) aneurysm

√ TYPICAL pencil-thin dystrophic aortic wall calcification (up to 40%) most severe in ascending aorta, frequently obscured by thick coarse irregular calcifications of secondary atherosclerosis

√ early sternal erosion affecting mainly right side of manubrium + medial end of right

clavicle
√ narrowing of coronary ostia (subintimal scarring)
Prognosis: death ← aortic rupture in 40%; death ← myocardial infarction within 6–8 months of onset of symptoms if untreated
Rx: penicillin

Thoracic Aortic Aneurysm

Most common vascular cause of mediastinal mass!
◊ 10% of mediastinal masses are of vascular origin!
Definitions:
diameter of 4 – 5 cm = **aortic ectasia**
diameter of > 5 cm = **aortic aneurysm**
Frequency: 25% of all aneurysms
Cause: atherosclerosis (29%), aortic dissection (53%), aortitis (8%), cystic medial necrosis (6%), syphilis (4%)
◊ Bicuspid aortic valve = independent risk factor!
Associated with: hypertension, coronary artery disease, abdominal aneurysm (30%)
Mean age: 65 years; M÷F = 3÷1
• substernal / back / shoulder pain (26%)
• SVC syndrome ← venous compression)
• dysphagia ← esophageal compression)
• stridor, dyspnea ← tracheobronchial compression)
• hoarseness ← recurrent laryngeal nerve compression)
Location: arch > descending aorta
√ mediastinal mass with proximity to aorta
√ wide tortuous aorta:
√ annual growth rate of 0.07–0.42 cm
√ curvilinear peripheral calcifications (75%)
√ circumferential / crescentic mural thrombus
N.B.: Angio may show normal caliber ← mural thrombus!
Cx:
(1) Rupture into mediastinum, pericardium, either pleural cavity, airway, esophagus
Median size at rupture-dissection:
5.9 cm for ascending aorta,
7.2 cm for descending aorta
√ high-attenuation fluid
(2) Aortobronchopulmonary fistula
√ consolidation of lung adjacent to aneurysm
◊ Most aneurysms rupture when > 10 cm in size
Prognosis: 1-year survival 57%; 3-year survival 26%; 5-year survival 19% (60% die from ruptured aneurysm, 40% die from other causes)
Rx: operative repair should be considered
for ascending aorta at > 5.5 cm
for descending aorta at > 6.5 cm
for Marfan syndrome > 5.0 cm

at annual growth rate > 1.0 cm

Surgical mortality: 9% for elective + 22% for emergent surgery

Annuloaortic Ectasia

= dilated sinuses of Valsalva with effacement of sinotubular junction

Cause: Marfan syndrome, idiopathic (30%), homocystinuria, Ehlers-Danlos syndrome, osteogenesis imperfecta

√ pear-shaped aorta

Valsalva Sinus Aneurysm

= aneurysm originating from a coronary sinus above aortic annulus

Prevalence: in 0.09% of autopsies; in 0.15%–3.50% of heart surgeries

Types:

(a) congenital: localized weakness of elastic lamina at junction of aortic media and annulus fibrosus in Marfan and Ehlers-Danlos syndrome

(b) acquired: infectious disease (bacterial endocarditis, syphilis, tuberculosis); degenerative (atherosclerosis, cystic medial necrosis); deceleration injury; aortic valve replacement

Associated with: supracristal VSD (30%–60% of patients), aortic insufficiency (20%–30%), bicuspid aortic valve (10%), coronary anomalies

Age: 35.4 (range, 4 days–96) years; M÷F = 2÷1 to 4÷1; Eastern/Asian÷Western countries = 5÷1

- asymptomatic (14%)
- cardiac murmur (57%), dyspnea (56%), chest pain
- insidiously progressive heart failure ← volume overload

Location: (a) right coronary sinus (72%)
(b) noncoronary sinus (22%
(c) coronary sinus (6%)

ECHO: diagnostic in 90%

Imaging criteria for a Valsalva sinus aneurysm include
(1) origin above aortic annulus
(2) saccular shape
(3) normal dimensions of adjacent aortic root and ascending aorta!

Cx:

(a) rupture (66%):
1. Aortic regurgitation (in 30–50%)
2. Aortocardiac shunt with RV (56%), RA (30%), RVOT (9%), LV (2%), interventricular septum (2%), LA (1%), extracardiac space (rare)

(b) mass effect:
1. Aortic regurgitation
2. Impaired function of tricuspid / mitral valve
3. Occluded / partially obstructed RVOT
4. Dissection into interventricular septum
5. Compression / occlusion of a coronary artery → myocardial ischemia

Surgery is indicated for asymptomatic patients without another underlying cardiovascular condition or disease, when aortic root measures ≥ 5.5 cm

DDx: prolapsing aortic cusp (below annulus)

Traumatic Aortic Pseudoaneurysm

= CHRONIC AORTIC PSEUDOANEURYSM

◊ 2nd most common form of thoracic aortic aneurysm

◊ Most common type occurring in young patients

Frequency: 2.5% of patients who survive initial trauma of acute aortic transection

√ usually calcified

√ may contain thrombus

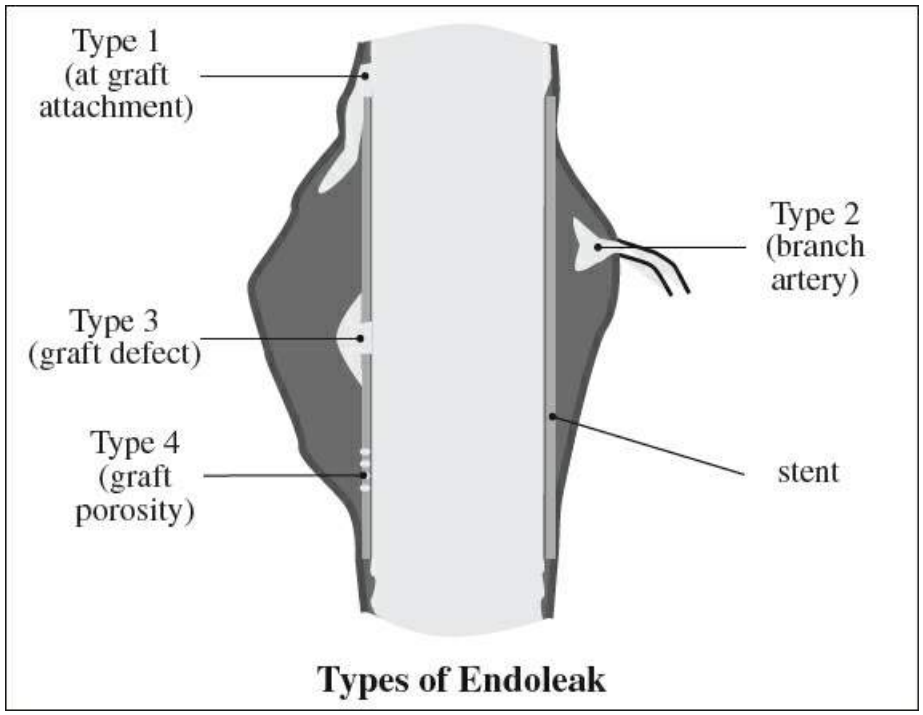
Cx: (1) Progressive enlargement

(2) Rupture (even years after insult)

Complications of Endovascular Stent-Graft Repair

1. **Endoleak** (2–45%)

   = leakage into the aneurysm outside stent-graft



Types of Endoleak

Type 1 = incomplete fixation of stent-graft to aortic wall at the proximal / distal attachment site

Type 2 = retrograde flow via parent artery (eg, lumbar / inferior mesenteric artery) in up to 24%

◊ High rate of spontaneous resolution if aneurysmal sac size remains stable

Type 3 = endograft defect with disruption of either metallic support / fabric

Type 4 = porous graft (uncommon)

Type 5 = endotension = aneurysm expansion > 5 mm without demonstrable endoleak (← nonvisualized endoleak, ultrafiltration of blood across graft membrane, thrombus as ineffective barrier)

2. Graft kinking
   Cause: diminishing diameter of aneurysm after stent-graft implantation also decreases length of aneurysm
   Associated with: distal migration of stent-graft
3. Graft infection
   √ interval development of perigraft soft-tissue attenuation / air
   Rx: antibiotics + total excision of infected graft
4. Graft thrombosis (3–19%)
   = intraluminal circular / semicircular thrombus
   Prognosis: spontaneous shrinkage, development of complete thrombosis
5. Graft occlusion
6. Shower embolism (4–17%)
   Cause: mural thrombus dispersed by delivery system
   Prognosis: perioperative death
7. Colon necrosis
   Cause: occlusion of inferior mesenteric a. by stent-graft
8. Aortic dissection
   Cause: retrograde injury by delivery system

AORTIC DISSECTION

= spontaneous longitudinal separation of aortic intima and adventitia by circulating blood having gained access to and splitting the media of the aortic wall

◊ Most common ACUTE EMERGENCY condition of the aorta!

Incidence: 3÷1,000 (more common than all ruptures of thoracic + abdominal aorta combined); 1÷205 autopsies; 2,000 cases annually in USA

Peak age: 60 years (range 13–87 years); M÷F = 3÷1

Predisposed: cystic medial necrosis / disease of aortic wall

◊ Starts in fusiform aneurysms in 28%

◊ Does not occur in aneurysms < 5 cm in diameter

1. Hypertension (60–90%)
2. Marfan syndrome (5–16%)
3. Ehlers-Danlos syndrome
4. Turner syndrome
5. Noonan syndrome
6. Polycystic kidney disease
7. Osteogenesis imperfecta
8. Valvular aortic stenosis
9. Coarctation
10. Bicuspid aortic valve
11. S/P prosthetic valve / other cardiovascular procedure
12. Blunt trauma (rare)

13. Inflammatory collagen vascular disease
14. Relapsing polychondritis
15. Aortitis (eg, Takayasu disease, SLE)
16. Behçet disease
17. Patient on corticosteroids
18. Cocaine abuse
19. Family history of dissection
20. Personal history of aortic aneurysm (2–12%)
21. Atherosclerosis of aorta (24–42%)
22. Pregnancy
    ◊ In women 50% of dissections occur during pregnancy!

N.B.: NOT syphilis

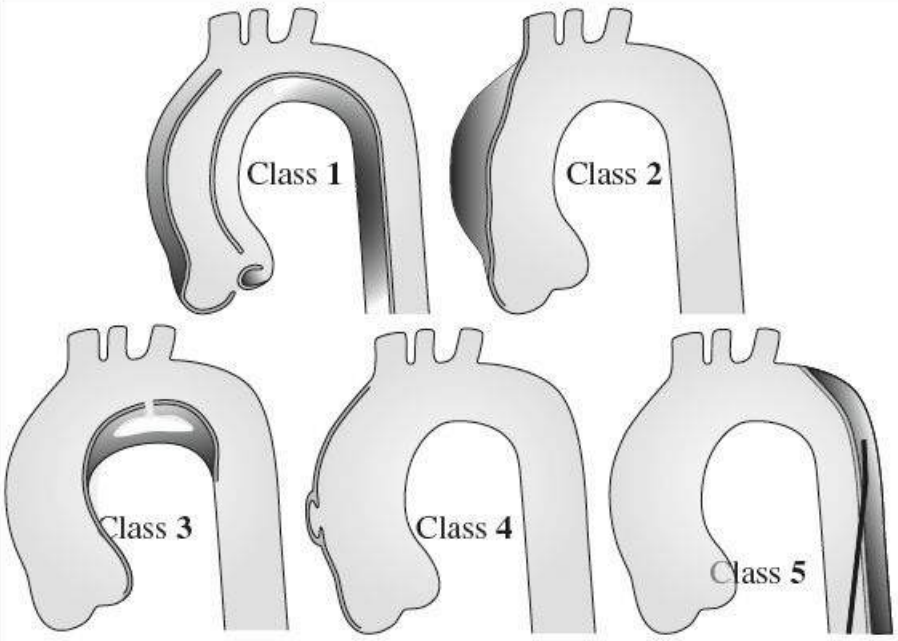
Path: destruction of media leads to formation of a false channel:

(1) Transverse tear in weakened intima (95–97%)
    ◊ The diagnosis relies primarily on visualization of an intimal flap + blood flow within a false lumen
(2) Primary hemorrhage into aortic wall WITHOUT intimal tear (3–5–13%) = atypical noncommunicating aortic dissection

Pathogenesis:

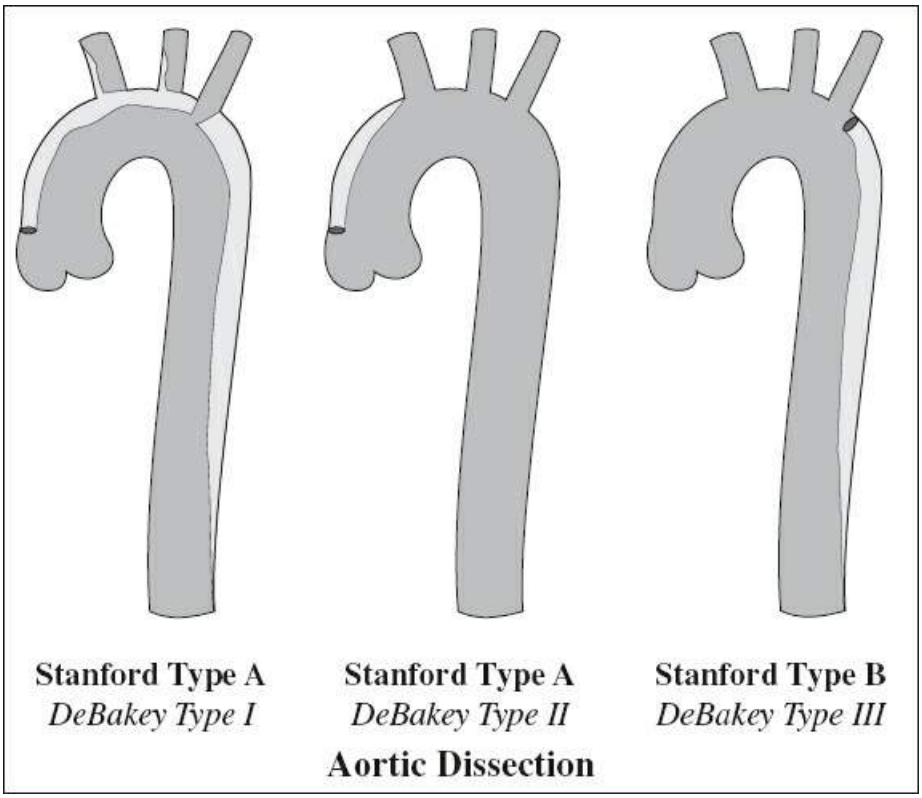
intimal tear results from combination of the following factors:

(a) media degeneration decreases cohesiveness of aortic wall
(b) persistent motion ← beating heart stresses aortic wall



Variants of Aortic Dissection *(Svensson LG)*

Class	*Description*
1	Separation of intima/media; dual lumina (classic)
2	Intramural hematoma separation of intima/media; angiographically no intraluminal tear or flap
3	Intimal tear without hematoma (limited dissection) and eccentric bulge
4	Atherosclerotic penetrating ulcer; ulcer usually penetrating to adventitia with localized hematoma
5	Iatrogenic/traumatic dissection



(c) hypertension accentuates hydrodynamic forces

The classic intimal flap is seen in ~ 70% of aortic dissections.

Pathophysiology:

luminal pressures:

intimal tear allows blood to enter media (= false lumen) with pressure in false lumen ≥ pressure in true lumen → collapse of true lumen + expansion of false lumen → possible compression + obstruction of true lumen;

degree of dilatation of false lumen depends on

(a) blood pressure
(b) depth of medial dissection plane,
(c) percentage of involved wall circumference;

flow direction in false lumen: antegrade / retrograde

effect on branch vessel:

(a) static obstruction = intimal flap enters branch-vessel origin without reentry point
(b) dynamic obstruction = intimal flap prolapses into / covers branch vessel like a curtain

fate of false lumen:

may remain patent / thrombose / recommunicate with true lumen through fenestrations / rupture into potential spaces (pericardial, pleural, peritoneal)

Definition of acute versus chronic dissection:

(a) acute aortic dissection = symptoms present for < 14 days
(b) chronic aortic dissection = symptoms present for ≥ 14 days

- sharp tearing intractable anterior / posterior chest pain (75–95%) radiating to jaw, neck, low back (DDx: myocardial infarction)

- murmur ± bruit (65%) from aortic regurgitation
- malperfusion symptoms:
  - asymmetric peripheral pulses + blood pressures (59%)
  - absent femoral pulses (25%), reappearing after reentry
  - pulse deficit: in up to 50% of type A dissection, in 16% of type B dissection; persistent oliguria, anuria
  - neurologic deficits (5–25%): hemiplegia, paraparesis ← compromise of anterior spinal artery of Adamkiewicz
- hemodynamic shock (25%)
- congestive heart failure (rare) ← acute aortic insufficiency:
  - diastolic murmur (40–50%)
- recurrent arrhythmias / right bundle branch block
- signs of pericardial tamponade: clouded sensorium, extreme restlessness, dyspnea, distended neck veins

Types:

DeBakey Classification:

Type I (29–34%) = ascending aorta + portion distal to arch
Type II (12–21%) = ascending aorta only
Type III (50%) = descending aorta only
subtype III A = up to diaphragm
subtype III B = below diaphragm

Stanford Classification: based on need for surgical therapy

Type A (60–70%) = ascending aorta ± arch in first 4 cm
Type B (30–40%) = descending aorta only

mnemonic: **A a**ffects **a**scending **a**orta and **a**rch; **B b**egins **b**eyond **b**rachiocephalic vessels; I = II + III

Flow velocities (average):

- 13.4 cm/second in true lumen
- 3.1 cm/second in false lumen
- retrograde flow more common in false lumen

Location of dissection flap (following helical flow pattern):

› on right anterolateral wall of ascending aorta just distal to aortic valve (65%)
› on posterosuperior wall of transverse aortic arch (10%)
› on left posterolateral wall of upper descending aorta distal to left subclavian artery (20%)
› more distal aorta (5%) usually terminating in left iliac artery (80%) / right iliac artery (10%) [involvement of left renal artery in 50%]
◊ An exit / distal tear / reentry occurs in 10%!

Imaging characteristics of true lumen:

√ usually smaller and oval / semiround
√ in continuity with undissected portion of aorta
√ higher concentration of contrast
√ ribbonlike

Imaging characteristics of false lumen:

√ SPECIFIC "cobweb" sign = slender linear areas of low attenuation ← residual ribbons of

media
√ "beak" sign at cross-sectional imaging = wedge of hematoma creating space for propagation of false lumen
√ rewinding around true lumen on axial plane
√ may become thrombosed

Atypical configurations of intimal flap:
√ circumferential intimal flap ← dissection of entire intima
√ filiform intimal flap creating an extremely narrow true lumen ± ischemic complications
√ mural calcification of false lumen (in chronic dissection)
√ three-channel aorta (= "Mercedes-Benz" sign) ← two false channels ← secondary dissection of one channel
◊ Multibarreled aortic dissections (9% of all aortic dissections) have a significantly poorer survival!
√ intimointimal intussusception → "windsock" appearance

Secondary signs of aortic dissection:
√ internal displacement of intimal calcification
√ delayed enhancement of false lumen
√ widening of aorta and mediastinum
√ pleural / pericardial hematoma

CXR (best assessment by comparison with serial films):
√ normal CXR in 10–25–40%
√ "calcification" sign = inward displacement of atherosclerotic plaque by > 4–10 mm from outer aortic contour (7%)
N.B.: can only be applied to contour of descending aorta due to projection; may be misleading in presence of periaortic soft-tissue mass / hematoma
√ disparity in size between ascending + descending aorta
√ irregular wavy contour / indistinct outline of aorta
√ widening of superior mediastinum to > 8 cm ← hemorrhage / enlarging false channel (40–80%)
√ cardiac enlargement ← LV hypertrophy / hemopericardium
√ left pleural effusion (27%)
√ atelectasis of lower lobe
√ rightward displacement of trachea / endotracheal tube

ECHO:
(a) transesophageal echocardiography (TEE): 95–100% sensitive + 77–97% specific
◊ Ultrasound can be performed at bedside!
False-positive (33%): reverberation artifacts from calcified aortic wall
(b) transthoracic US: 59–85% sensitive + 63–96% specific for type A dissection; poorer for type B
(c) intravascular US (in conjunction with aortography) to differentiate true from false lumen
√ intimal flap (seen in more than one view)
√ pericardial fluid
√ aortic insufficiency
False-positives: reverberation echoes from aneurysmal ascending aorta / calcified atheromatous plaque, postoperative periaortic hematoma

Angio (86–88% sensitive, 75–94% specific):

◊ Largely replaced by noninvasive cross-sectional imaging techniques

Superior to any other technique in demonstrating

› entry + reentry points (in 50%)

› branch vessel involvement + coronary arteries

› aortic insufficiency

√ visualization of intimal / medial flap (75–79%) = linear radiolucency within opacified aorta

√ "double barrel aorta" (87%) = opacification of two aortic lumens

√ abnormal catheter position outside anticipated aortic course

√ compression of true lumen by false channel (72–85%)

√ aortic valvular regurgitation (30%)

√ increase in aortic wall thickness > 6–10 mm

√ obstruction of aortic branches: left renal artery (25–30%)

√ ulcerlike projections caused by truncated branches

√ slower blood flow in false lumen

False-negative: complete thrombosis / very slow blood flow of false channel (10%), intimal flap not tangential to x-ray beam

False-positive: thickening of aortic wall due to aneurysm, aortitis, adjacent neoplasm / hemorrhage

NECT:

√ high attenuation within aortic wall 2° to:

(a) high-attenuation of false lumen (slow flow / thrombosis)

(b) presence of intramural hematoma

√ intimal flap separating two aortic channels (may be seen without contrast in anemic patients)

CECT (87–100% sensitive, 87–100% specific):

within 4 hours (if patient responds rapidly to medical Rx); detection as accurate as angio with single-level dynamic scanning (cardiac gating desirable to avoid overdiagnosis)

√ intimal flap separating two aortic channels

√ crescentic high-attenuation clot within false lumen

√ internally displaced intimal calcification (DDx: calcification of thrombus on luminal surface or within)

√ entry tear = most proximal split / discontinuity in intimal flap

False-negative: inadequate contrast opacification, thrombosed lumen misinterpreted as aortic aneurysm with mural thrombus

False-positive: perivenous streaks ← beam hardening + motion, cardiac / aortic motion artifacts; opacified normal sinus of Valsalva; normal pericardial recess mistaken for thrombus; mural thrombus in a fusiform aortic aneurysm; periaortic fibrosis; anemia with apparent high attenuation of aortic wall

MR (95–100% sensitive, 90–100% specific):

Advantage: large field of view in any plane; contrast material NOT necessary

Disadvantage: longer imaging time; difficulty monitoring acutely ill patients; image degradation from motion (uncooperative patient, atrial fibrillation)

SE images:

√ intimal flap of medium intensity outlined by signal voids of rapidly flowing blood in true + false lumen

√ intimal flap more difficult to detect in the presence of slow flow / thrombus ← false lumen has intermediate intensity instead of flow void

√ "cobwebs" (25%) traversing the corners of the false lumen = bands of medial elastic lamellae spanning the junction of the dissecting septum with outer wall of false lumen

GRE images:

√ lower-intensity intimal flap between high-intensity channels of flowing blood

√ intermediate signal from thrombosed lumen

√ aortic valve insufficiency = conical area of signal loss from aortic valve into LV during systole ← intravoxel dephasing caused by turbulence

Cx:

(1) Retrograde dissection (in Stanford type A)
  (a) aortic insufficiency
  (b) occlusion of coronary artery (8%)
  (c) internal rupture into RV, LA, vena cava, pulmonary artery producing a large L-to-R shunt

(2) Occlusion / transient obstruction of major aortic branches (in up to 27%)
  (a) static obstruction
    √ flap enters branch-vessel origin
  (b) dynamic obstruction = flap spares branch-vessel origin but covers it like a curtain
    √ collapsed true lumen outlined by a C-shaped flap envelope which is concave toward false lumen (= ischemic configuration)

(3) External rupture of aorta into mediastinum, pleural cavity / pericardial sac (75%), right ventricle, left atrium, vena cava, pulmonary artery: 70% mortality (= most common cause of death within 24 hours)
  NECT: √ hyperattenuating mediastinal / pericardial / pleural fluid collection
  CECT: √ extravasation of vascular contrast material

(4) Development of aneurysm (15%) of the true / false lumen

◊ Organs may receive their blood supply through either the true or false lumen or both!

Rx:

(1) Reducing peak systolic pressure to 120–70 mmHg (adequate ONLY for type III = B, which rarely progresses proximally):
  Cx: death from rupture of aortic aneurysm in 46% of hypertensive + 17% of normotensive patients
  Survival rate: 40–70% with medical / surgical management

(2) Immediate surgical graft reinforcement of aortic wall (Type I, II = A) preventing rupture + extension into aortic root → progressive aortic valve insufficiency
  Nonsurgical survival rate: < 10%
  Postsurgical mortality: 10–35%
  Cx: myocardial infarction, stroke, respiratory insufficiency, pulmonary embolism, aortic rupture, pseudoaneurysm, graft infection

Prognosis without Rx:

immediate death (3%); death within: 1 day (20–30%), 1 week (50–62%), 3 weeks (60%), 1 month (75%), 3 months (80%), 1 year (80–95%)

Prognosis with Rx:

5–10% mortality rate following timely surgery;
40% 10-year survival rate after leaving hospital

Death from thoracic aortic dissection may occur ← acute aortic regurgitation; ← major aortic branch obstruction; ← pericardial tamponade; ← aortic rupture into pericardium / left pleural cavity / mediastinum.

DDx: penetrating ulcer of thoracic aorta (= atherosclerotic lesion of mid-descending aorta with ulceration extending through intima into aortic media)

AORTIC HYPOPLASIA

Prevalence: 5–10% of congenital cardiac lesions

Cause: fibrous ridge deformity of aortic media + intima protruding into aortic lumen → prominent posterior infolding of aortic lumen that may extend laterally → eccentric narrowing of aortic lumen

Genetics: usually sporadic; increased frequency among patients with Turner syndrome (13–15%)

• CHF in neonatal period (in 50%) = 2nd most common cause of heart failure in newborns

Definition:

(a) external diameter of proximal arch segment < 60%
(b) external diameter of distal arch segment < 50%
(c) external diameter of isthmic segment < 40% compared to external diameter of ascending aorta

√ patent ductus arteriosus

Hemodynamics:

fetus : no significant change because only 10% of cardiac output flows through aortic isthmus
neonate : determined by how rapidly the ductus closes; without concurrent VSD overload of LV leads to CHF in 2nd / 3rd week of life

Prognosis: 11% mortality prior to 6 months of age

Rx: ages 3–5 years are ideal time for operation (late enough to avoid restenosis + early enough before irreversible hypertension occurs); surgical correction past 1 year of age decreases operative mortality drastically

Risk of surgery: 3–11% perioperative mortality

Procedures:

1. Resection + end-to-end anastomosis
2. Patch angioplasty
3. Subclavian artery used as flap (Waldhausen procedure)

Postsurgical Cx:

1. Residual coarctation (in 32%)
2. Subsequent obstruction (rare)
3. Mesenteric arteritis: 2–3 days after surgery ← paradoxical hypertension from increased plasma renin
   • abdominal pain, loss of bowel control

4. Chronic persistent hypertension

DDx: Normal (gradual tapering of distal aortic arch + isthmus during first 3 months of life)

Tubular Aortic Hypoplasia

= combination of abnormally small diameter + increased length (> 5 mm in infants) between aortic arch segments

AORTIC PROSTHETIC GRAFT INFECTION

Frequency: 1.3–6% of prosthetic graft procedures

Classification:

(1) PERIGRAFT INFECTION (2–6%)
- groin swelling, heat, tenderness, pulsatile mass, draining sinus tract; fever, chills, leukocytosis

(2) AORTOENTERIC FISTULA (0.6–2%)
- acute / chronic GI bleeding (may be occult), sepsis

- may be temporally remote (up to 10 years): median time of 3 years to manifestation (70% occur > 1st year)
- intracavitary signs: malaise, back pain, fever, elevated sedimentation rate, hydronephrosis, ischemia from clotted graft

Normal postoperative course:

√ ring of fat attenuation in early postoperative period < 5 mm between aneurysm wall and graft

◊ Complete resolution of hematoma by 3 months

◊ Disappearance of ectopic gas complete by 4–7 weeks

CT (94% sensitive, 85% specific, 91% accurate):

√ perigraft fluid

√ perigraft soft-tissue attenuation with indistinctness of graft margins

√ ectopic gas ← fistulous communication with bowel / gas-producing organism

√ pseudoaneurysm (25%)

√ focal bowel wall thickening → indicates fistula

√ > 5 mm soft tissue between graft + surrounding wrap (beyond 7th postoperative week)

√ focal discontinuity of calcified aneurysmal wrap

False positives:

perigraft hematoma in early postoperative period, pseudoaneurysm (in 15–20%)

NUC:

√ uptake of ^{99m}Tc-hexametazine labeled leukocytes (drawbacks: not performed quickly, hepatobiliary excretion)

Prognosis: 17–75% mortality; 30–50% morbidity

Dx: positive culture from needle aspirate (incubation period must be up to 14 days as organisms may be slow-growing)

AORTIC REGURGITATION / INSUFFICIENCY

Cause:

A. PRIMARY DISEASE OF ASCENDING AORTA distorting aortic root (more common)

(a) dilatation of aortic annulus
1. Idiopathic dilatation (most common cause)
2. Atherosclerosis ← systemic hypertension
3. Aortic aneurysm
4. Rheumatoid arthritis and variants:
   › Ankylosing spondylitis (5–10%)
   › Reiter disease
   › Psoriatic arthritis
5. Familial connective tissue disease:
   mnemonic: HOME
   › Homocystinuria
   › Osteogenesis imperfecta
   › Marfan syndrome (most common cause < 40 years of age)
   › Ehlers-Danlos syndrome
6. Relapsing polychondritis
7. Seronegative spondyloarthropathy: eg, Behçet
8. Syphilitic aortitis

(b) laceration of aorta

Classification of Aortic Regurgitation in Adults			
Classification	*Regurgitant Volume (mL/beat)*	*Regurgitant Fraction (%)*	*Valve Orifice Area (cm2)*
Mild	< 30	< 30	< 0.10
Moderate	30–59	30–49	0.10–0.29
Severe	≥ 60	≥ 50	> 0.30

1. Deceleration trauma → aortic dissection
2. Prosthetic valve: mechanical break, thrombosis, paravalvular leak

B. INTRINSIC AORTIC VALVE DISEASE impairing leaflet function (less common)
1. Congenital bicuspid valve
   N.B.: Most common cause in developed nations
2. Rheumatic endocarditis
   N.B.: Most common cause in developing world
3. Bacterial endocarditis (perforation / prolapse of cusp)
4. Rupture of congenitally fenestrated cusp
5. Myxomatous valve associated with cystic medial necrosis
6. Atherosclerotic degeneration
   ◊ Severely calcified aortic valves are often regurgitant
7. Connective tissue disorder: Marfan syndrome
8. Ergot toxicity, anorectic drugs
9. Systemic inflammation: lupus erythematosus, Crohn disease, Takayasu arteritis, giant cell arteritis
10. Aortic valve prolapse

Pathogenesis: LV volume overload → progressive enlargement of diastolic + systolic LV dimensions → increase in myocardial fiber length + increase in stroke volume;

decompensation occurs if critical limit of fiber length is reached

- "water-hammer pulse" = twin-peaked pulse
- systolic ejection murmur + high-pitched diastolic murmur
- Austin Flint murmur = soft mid-diastolic or presystolic bruit

√ LV enlargement (cardiothoracic ratio > 0.55) + initially normal pulmonary vascularity (DDx: congestive cardiomyopathy, pericardial effusion):
  √ LV wall may appear thin even with ventricular hypertrophy
√ normal aorta (in intrinsic valve disease)
√ dilatation of aorta (in systemic disease):
  √ ± calcification of ascending aorta (in aortic wall disease)
  √ ± enlarged aortic arch + tortuous descending aorta
√ increased pulsations along entire aorta

ECHO:
  √ aortic root dilatation
  √ CHARACTERISTIC high frequency flutter of aML (occasionally pML) during first $^{2}/_{3}$ of diastole
  √ high frequency diastolic flutter of IVS (uncommon)
  √ diastolic flutter of aortic valve (SPECIFIC, but rare)
  √ premature aortic valve opening (high diastolic LV pressure)
  √ decreased MV opening (aML pushed posteriorly by regurgitant aortic jet)
  √ premature closure of mitral valve (high diastolic LV pressure produces MV closure before beginning of systole in severe acute aortic insufficiency)
  √ LV dilatation + large amplitude of LV wall motion (volume overload, increased ejection fraction):

End-systolic LV diameter	Action
< 50 mm	yearly follow-up
50–54 mm	4- to 6-month follow-up
> 55 mm	valve replacement

Doppler:
  √ decrease of slope of peak diastolic to end-diastolic velocity > 3 m/sec2 in severe aortic regurgitation
  √ area of regurgitant flow visible by color Doppler
  √ ratio of width of regurgitant beam to width of aortic root is good predictor of severity (on color Doppler)

AORTIC RUPTURE

= blood leakage through aortic wall

1. Spontaneous rupture of aortic aneurysm
   Pathogenesis: small clefts occur at a fragile site within inner thrombus gradually expanding to outer layer of thrombus with gradual seepage of flowing blood into mural thrombus + aneurysmal wall

   CT:
     √ high-attenuation "crescent" sign (71%)
2. Spontaneous rupture of descending thoracic aorta

Predisposed: hypertension and atherosclerosis, NO preformed aneurysm!
Pathogenesis: pressure atrophy of media ← overlying intimal atheromatous plaque causing localized ballooning of aortic wall prior to perforation

3. Traumatic rupture / transection of thoracic aorta
   Cause: blunt trauma to thoracic aorta

AORTIC STENOSIS

Aortic valve area decreased to < 0.8 cm^2 = 0.4 $cm^2/m2$ BSA (normal 2.5–4.0 cm^2)

A. ACQUIRED AORTIC STENOSIS
   1. Rheumatic valvulitis: from postinflammatory fusion (almost invariably associated with mitral valve disease)
      N.B.: Most common cause worldwide
   2. Fibrocalcific senile aortic stenosis (degenerative)
      N.B.: Most common cause in developed countries
   3. Takayasu aortitis
   4. Radiation aortitis
   5. Aortic dissection
   6. Infected aortic aneurysm with abscess
   7. Pseudoaneurysm from laceration
   8. Atherosclerosis (rare)
   9. Syphilitic aortitis (rare)

B. CONGENITAL AORTIC STENOSIS (most common)
   = most frequent CHD associated with IUGR
   Location:
   1. Subvalvular AS (15–30%)
   2. Valvular AS (60–70%)
   3. Supravalvular AS (rare)
   Cause:
   1. Bicuspid aortic valve → predisposed to early stenosis
   2. Williams syndrome
   3. Neurofibromatosis
   4. Rubella
   5. Mucopolysaccharidosis
   6. Hypoplastic left heart syndrome

Pathogenesis:
gradual decrease in valve area → ↑ gradient across valve → ↑ LV afterload LV → hypertrophy and diminished LV compliance; ↑ muscle mass may outstrip coronary blood supply (subendocardial myocardial ischemia with angina → fibrosis); LV decompensation with impaired contractility + compliance → LV dilatation + pulmonary venous congestion

Aortic stenosis increases afterload on LV → compensatory LV hypertrophy, which initially minimizes wall stress and maintains cardiac output!

- asymptomatic for many years (until valve area 1 cm^2)

Severity of Aortic Stenosis in Adults			
Classification	*Aortic Jet velocity (m/sec)*	*Mean Pressure Gradient (mmHg)*	*Valve Orifice Area (cm^2)*
Normal	≤ 2.0	< 5	3.0–4.0
Mild	< 3.0	< 25	> 1.5
Moderate	3.0–4.0	25–40	1.0–1.5
Severe	> 4.0	> 40	< 1.0

- angina, dyspnea, syncope, heart failure, systolic murmur
- diminished aortic component of 2nd heart sound
- sudden death in severe stenosis (20%) after exercise (diminished flow in coronary arteries causes ventricular dysrhythmias + fibrillation); carotid pulsus parvus et tardus

√ poststenotic dilatation of ascending aorta (in 90% of acquired, in 70% of congenital AS)
√ normal-sized / enlarged LV (small LV chamber with thick walls)
@ in adults > 30 years
  √ calcification of aortic valve (best seen on RAO); indicates gradient > 50 mmHg:
    √ severe aortic calcifications = "porcelain aorta" → technically difficult / impossible valve replacement
  √ ectasia / aneurysmal dilatation of ascending aorta (NO correlation with severity of stenosis)
  √ calcification of mitral annulus
  √ "left ventricular configuration" = concavity along mid left lateral heart border + increased convexity along lower left lateral heart border
@ in children / young adults
  √ prominent ascending aorta
  √ left ventricular heart configuration
@ in infancy:
  √ left ventricular stress syndrome

CT:
  √ thickening + calcification of cusps
  √ reduction of aortic valve area

ECHO:
  √ thickened + calcified aortic valve with multiple dense cusp echoes throughout cardiac cycle (right > noncoronary > left coronary cusp)
  √ decreased separation of leaflets in systole with ↓ opening orifice: 13–14 mm = mild AS; 8–12 mm = moderate AS; < 8 mm = severe AS
  √ ± doming in systole
  √ dilated aortic root
  √ increased thickness of LV wall ← concentric LV hypertrophy
  √ hyperdynamic contraction of LV (in compensated state)
  √ decreased mitral EF slope ← reduced LV compliance
  √ LA enlargement
  √ increased aortic valve gradient (Doppler)
  √ decreased aortic valve area (unreliable)

DDx: calcification of aortic annulus in elderly / calcified coronary artery ostium (thickened cusp echoes only in diastole)

Prognosis: depends on symptomatology (angina, syncope, CHF → 2–3 years average survival w/o surgery)

Cx: aortic valve replacement (for symptomatic patient with substantial ventricular dysfunction)

Subvalvular Aortic Stenosis

= SUBAORTIC STENOSIS

A. ANATOMIC / FIXED SUBAORTIC STENOSIS

Associated with: cardiac defects in 50% (usually VSD)

Type I : thin 1–2-mm membranous diaphragmatic stenosis, usually located within 2 cm or less of valve annulus

Type II : thick collarlike stenosis

Type III : irregular fibromuscular stenosis

Type IV : "tunnel subaortic stenosis" = fixed tunnel-like narrowing of LVOT = excessive thickening of only upper ventricular septum with normal mitral valve motion

B. FUNCTIONAL / DYNAMIC SUBAORTIC STENOSIS

1. Asymmetric septal hypertrophy (ASH)
2. Idiopathic hypertrophic subaortic stenosis (IHSS)
3. Hypertrophic obstructive cardiomyopathy (HOCM) may occur in infants of diabetic mothers

√ no dilatation of ascending aorta

√ asymmetrically thicker ventricular septum than free wall of LV (95%)

√ normal / small left + right ventricular cavities (95%)

√ lucent subaortic filling defect in systole

√ focal convexity of left upper-mid cardiac margin = anterior aspect of ventricular septum (rare)

ECHO:

√ coarse systolic flutter of valve cusps

√ opening of leaflets followed by rapid inward move in mid systole, leaflets may remain in partially closed position through latter portion of systole (to appose borders of the flow jet)

√ systolic anterior motion of mitral valve

Cx: mitral regurgitation ← abnormal position of anterolateral papillary muscle preventing complete closure of MV in systole

Valvular Aortic Stenosis

= fusion of commissures between cusps

Degree: mild: > 0.7 cm^2; moderate: 0.5–0.7 cm^2; severe: < 0.5 cm^2

Congenital types:

(1) Bicuspid / unicuspid (in 95%): in 0.7–2.0% of population; M > F; commonly associated with aortic coarctation

◊ Valve degenerates a decade earlier compared with tricuspid configuration!

◊ Aortic ectasia ← marfanoid-type wall weakness + eccentric poststenotic jet

(2) Tricuspid (5%)

(3) Dysplastic thickened aortic cusps

@ IN INFANT with critical aortic stenosis:

- intractable CHF in first days / weeks of life with severe dyspnea; may simulate neonatal sepsis

Associated with: L-to-R shunts (ASD, VSD)

√ marked cardiomegaly ← thickened wall of LV
√ pulmonary venous hypertension
√ decreased ejection fraction
√ doming of thickened valve cusps
√ dilated ascending aorta

Rx: emergency surgical dilatation

@ IN CHILD:

- asymptomatic until late in life

√ normal pulmonary vascularity
√ LV configuration with normal size of heart
√ large posterior noncoronary cusp, smaller fused right + left cusps
√ doming of thickened valve cusps
√ eccentric jet of contrast

DDx of Valvular Aortic Stenoses

	Congenital	*Rheumatic*	*Degenerative*
Clinically apparent	< 30 years	30–60 years	> 65 years
Valve calcifications			
1st appearance	25 years	47 years	54 years
Ca^{2+} pattern	nodular / bicuspid	nodular	nodular / tricuspid
on CXR	> 90% (40–65 y)	< 10%	> 90% (> 65 y)
Aortic ectasia	ascending Ao	ascending Ao	entire Ao

√ poststenotic dilatation of ascending aorta

@ IN ADULT

√ valvular calcifications (in 60% of > 24 years of age)

ECHO:

√ increase in echoes from thickened deformed leaflets (maximal during diastole)
√ decrease in leaflet separation

Supravalvular Aortic Stenosis

= focal / diffuse narrowing of aorta starting at sinotubular junction + often involving entire ascending aorta (15%)

Types:

(a) localized hourglass narrowing just above aortic sinuses
(b) discrete fibrous membrane above sinuses of Valsalva
(c) diffuse tubular hypoplasia of ascending aorta + branching arteries

Genetics: (rare) sporadic form / autosomal inherited: mutation of elastin gene on

chromosome 7q11.23

Path: reduction + disorganization of elastin fibers within aortic media accompanied by hypertrophied smooth muscle cells and increased collagen content → reduced elasticity + increased shear stress

Associated with:

› peripheral PS
› valvular AS (in 50%): commonly bicuspid aortic valve
› discrete subvalvular aortic stenosis (in 16%)
› Williams-Beuren syndrome
› Marfan syndrome
› infantile hypercalcemia syndrome

√ small ascending thoracic aorta
√ dilatation + tortuosity of coronary arteries (may undergo early atherosclerotic degeneration 2° to high pressure)

ECHO:

√ narrowing of supravalvular aortic area (normal root diameter: 20–37 mm)
√ normal movement of cusps
√ left ventricular myocardial hypertrophy
√ bicuspid aortic valve

AORTOENTERIC FISTULA

= life-threatening condition

Mortality: approaches 100% without prompt surgery

Primary Aortoenteric Fistula (rare)

= complication of atherosclerotic aortic aneurysms WITHOUT previous aortic surgery / trauma

Incidence: 0.007÷1,000,000 annually

Predisposed: syphilis, TB, mycotic infection, collagen vascular disease

√ ectopic gas adjacent to / within aorta (KEY FINDING)
√ obliteration of fat plane between aorta and bowel
√ ± hematoma in retroperitoneum / bowel wall or lumen

Secondary Aortoenteric Fistula (more frequent)

= complication of aortic reconstructive surgery / stent graft

Incidence: 0.6%–2.0% annually

Time interval since surgery: 2 weeks to 10 years

Cause: complication of advanced perigraft infection

• GI bleeding (80%) preceded by "herald bleeds"
• abdominal pain (30%), back pain (15%), sepsis (44%)
• groin mass (12%), abdominal pulsatile mass (6%)

Location: horizontal + ascending duodenum (80%)

√ loss of fat plane between aorta and adjacent bowel, pseudoaneurysm, disruption of aortic wall:
  √ tethering / puckering of bowel wall toward aorta
√ perigraft soft-tissue edema, fluid / hematoma:

N.B.: resolution within 2–3 months after surgery

√ hyperattenuating fluid collection / mass acute = hematoma / partially thrombosed pseudoaneurysm

Strongly suggestive CT findings:

√ ectopic gas

N.B.: may be normal immediately after surgery

Cave: abnormal 3–4 weeks after surgery = sign of perigraft infection / fistulization

√ focal bowel wall thickening (challenging if involved bowel loop not distended)

√ breach of the aortic wall

√ extravasation of contrast material into bowel lumen (extremely rare but most SPECIFIC)

√ leakage of enteric contrast into periaortic space (rare)

CT features of perigraft infection should raise concern about the possibility of a secondary aortoenteric fistula.

Angio: usually no vascular abnormality

DDx: (1) Perigraft infection without fistulization

(2) Retroperitoneal fibrosis

(3) Infected (mycotic) aortic aneurysm

(4) Infectious aortitis

Aortoesophageal Fistula

= rare life-threatening subtype of intramural hematoma

Frequency: 3.5% of all deaths ← upper esophageal bleeding

Cause:

(a) aortic condition (75%): ruptured aneurysm, ruptured atheromatous plaque, penetrating ulcer, prosthetic grafting / reconstructive surgery

(b) esophageal condition: foreign body ingestion, malignancy, corrosive esophagitis

CT:

√ enhancing subepithelial esophageal mass with fistulous tract between aorta + esophagus

AORTOPULMONIC WINDOW

= AORTOPULMONARY WINDOW

= large round / oval communication between left wall of ascending aorta + right wall of pulmonary trunk / right pulmonary artery

Aortopulmonic window has well-defined separate aortic and pulmonary valve apparatuses unlike in truncus arteriosus!

Prevalence: 0.1% of all CHD

Cause: defect in septation process with incomplete fusion / malformation of right / left conotruncal rings

• clinically resembles PDA with frequent CHF

Mori classification:

Type I = proximal communication near semilunar valves (70–96%)

Type II = distal communication near pulmonary bifurcation at level of right pulmonary artery (14–25%); associated with type A of interrupted aortic arch

Type III = total absence of aortopulmonary septum (5%)

Associated with: other congenital cardiac anomalies (in up to 44%)

CXR:

√ shunt vascularity
√ cardiomegaly ← LA + LV enlarged
√ diminutive aortic knob
√ prominent pulmonary trunk ← arterial pHTN

Angio (left ventriculogram / aortogram in AP / LAO projection):

√ defect several mm above aortic valve
√ pulmonary valve identified (DDx to truncus arteriosus)

Rx: surgery (pulmonary artery flap, pericardial patch); nonsurgical (Amplatzer device implantation)

ARTERIOSCLEROSIS OBLITERANS

= ASO = HARDENING OF THE ARTERIES

Prevalence: 2.7% (in 1.0% of < 60 years of age, in 3.4% of ≥ 65 years of age); 2.4 million people in USA; in 1978 12% of autopsies had ASO as leading cause of death (excluding MI)

Etiology: unknown

Contributing factors: aging, diabetes (16–44%), hypertension, atherosclerosis

Effect of hyperlipidemia:

(a) high-density lipoproteins (HDL) have a protective effect: carry 25% of blood cholesterol
(b) low-density lipoproteins (LDL): carry 60% of cholesterol

Histo: deposition of lipids, blood products, carbohydrates, begins as disruption of intimal surface; fatty streaks (as early as childhood); fibrous plaques (as early as 3rd decade); thrombosis, ulceration, calcification, aneurysm

Age: 50–70 years; M > F (after menopause)

Clinical classification:

(1) Intermittent claudication = ischemic symptoms with exercise: in calf, thigh, hip, buttock
(2) Ischemic symptoms at rest (indicative of multisegment dz)

- cramping / burning / aching pain; cold extremity; paresthesia
- trophic changes: hair loss, thickened nails
- ulcer, gangrene; decreased / absent pulses

Location: medium + large arteries; frequently at bifurcations; most frequently affected sites are:

› superficial femoral artery within adductor canal (diabetics + nondiabetics)
› aortoiliac segment (nondiabetics)
› tibioperoneal trunk (diabetics)

Prognosis:

ASO accelerated by diabetes (34% will require amputation), hypertension, lipoprotein abnormalities, heart disease (= ↓ cardiac output → polycythemia → ↑ blood viscosity), chronic addiction to tobacco (11.4% will require amputation), intermittent claudication (5–

7% require amputation if nondiabetic = 1–2% annually), ischemic ulcer / rest pain (19.6% require amputation)

ATRIAL SEPTAL DEFECT

◊ Most common congenital cardiac defect after bicuspid aortic valve!

Frequency: 8–10–14% of all CHD; M÷F = 1÷3

Age: presentation frequently > age 40 secondary to benign course

(a) mildly symptomatic (60%): dyspnea, fatigue, palpitations

(b) severely symptomatic (30%): cyanosis, heart failure

Hemodynamics:

no hemodynamic perturbance in fetus; after birth physiologic ↑ in LA pressure + greater compliance of RA and RV create L-to-R shunt (shunt volume ~ 3–4 times that of systemic blood flow); volume overload of RV is well tolerated in childhood, → leads to RV dilatation, right heart failure; diastolic pressure differences in atria determine direction of shunt; pulmonary pressure remains normal for decades; after 40 years of age onset of pulmonary hypertension → increased R-to-L shunting (Eisenmenger syndrome); pulmonary hypertension in young adulthood (6%)

RA	↑	RV	↑	Main PA	↑
Pulm. vessels	↑				
LA	↔	LV	↔	Ao	↓/↔

- repeated respiratory infections; feeding difficulties
- atrial arrhythmias: atrial flutter + atrial fibrillation increases with age; thromboembolism
- asymptomatic; occasionally discovered by routine CXR
- fixed splitting of second heart sound with accentuation of pulmonary component (ejection murmur grade II/VI) heard at 2nd left intercostal space along PA
- ECG: right axis deviation + some right bundle branch block
- exertional dyspnea after development of pulmonary arterial hypertension (= Eisenmenger syndrome)
- cyanosis may occur (shunt reversal to R-to-L shunt), typically during 3rd–4th decade
- right heart failure in patients > 40 years; right ventricular heave

Types of ASD: ostium secundum > ostium primum > sinus venosus > unroofed coronary sinus

CXR:

√ normal (if shunt < 2 x systemic blood flow)

√ overcirculation = increase in pulmonary blood flow (if pulmonary-to-systemic blood flow ≥ 2÷1)

√ cardiomegaly:

√ heart small compared with pulmonary vascularity = closing shunt

√ heart large compared with pulmonary vascularity = intercurrent myocardial / aortic disease

√ loss of visualization of SVC ← clockwise rotation of heart ← RV hypertrophy

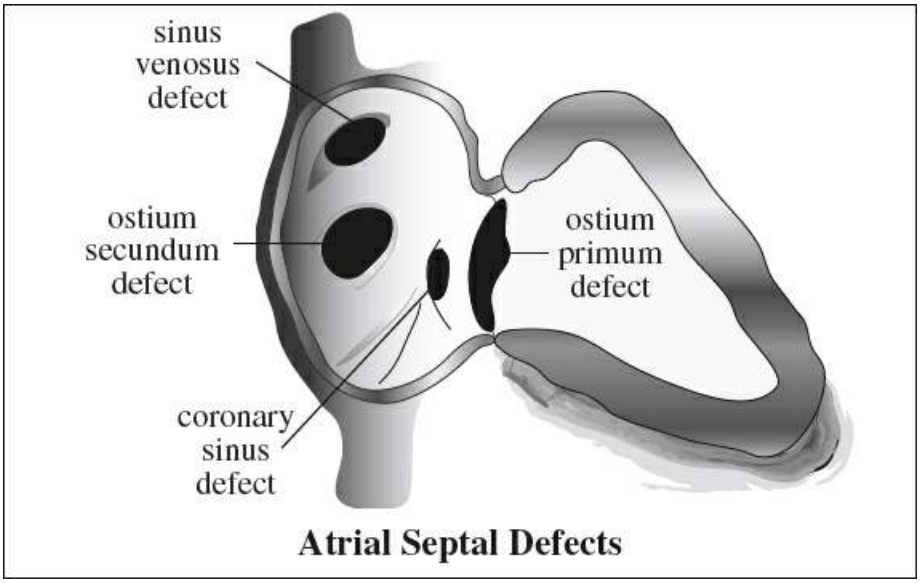
√ small appearing aorta with normal aortic knob

√ normal size of LA after shunt reversal ← immediate decompression into RA (in Eisenmenger syndrome):

√ enlargement of PA + central pulmonary arteries
√ RV enlargement
√ "hilar dance" = increased pulsations of central pulmonary arteries (DDx: other L-to-R shunts)

ECHO:
√ paradoxical interventricular septal motion ← RV volume overload
√ direct visualization of ASD (= lack of echoes of atrial septum) in subcostal view
√ diastolic blood flow from interatrial septum crossing RA + tricuspid valve directly observed by color Doppler

MR:
√ discrete area of interruption of the normal intermediate-intensity interatrial septum
CAVE: normal thinning of fossa ovalis can cause drop-out of atrial signal
√ area of signal loss from atrial septum into RA ← turbulent jet on GRE
√ ratio of stroke volumes in aorta to PA (measurement of flow volume on cine phase-contrast images)



Angio:
√ RA fills with contrast shortly after LA is opacified (on levophase of pulmonary angio in AP or LAO projection)
√ injection into RUL pulmonary vein to visualize exact size + location of ASD (LAO 45° + C-C 45°)

Prognosis:
(1) Mortality: 0.6% in 1st decade; 0.7% in 2nd decade; 2.7% in 3rd decade; 4.5% in 4th decade; 5.4% in 5th decade; 7.5% in 6th decade; median age of death is 37 years
(2) Spontaneous closure: 22% in infants < 1 year; 33% between ages 1 and 2 years; 3% in children > 4 years

Cx: (1) Tricuspid insufficiency ← dilatation of AV ring
(2) Mitral valve prolapse

(3) Atrial fibrillation (in 20% 1st presenting symptom in patients > age 40)

Rx: (if vascular changes still reversible = resistance of pulmonary-to-systemic system ≤ 0.7)

1. Surgical patch closure
2. Rashkind foam + stainless steel prosthesis

Indication for surgery (1% surgical mortality):

1. RA and RV enlargement ± symptoms
2. Paradoxical emboli
3. Pulmonary-to-systemic flow ratio > 1.5

Beneficial ASD

= secundum type ASD serves essential compensatory function in:

1. Tricuspid atresia
   RA blood reaches pulmonary vessels via ASD + PDA; improvement through Rashkind procedure
2. TAPVR
   significant shunt volume only available through ASD (VSD / PDA much less reliable)
3. Hypoplastic left heart
   systemic circulation maintained via RV with oxygenated blood from LA through ASD into RA

Ostium Secundum Defect

= persistent opening at site of foramen ovale

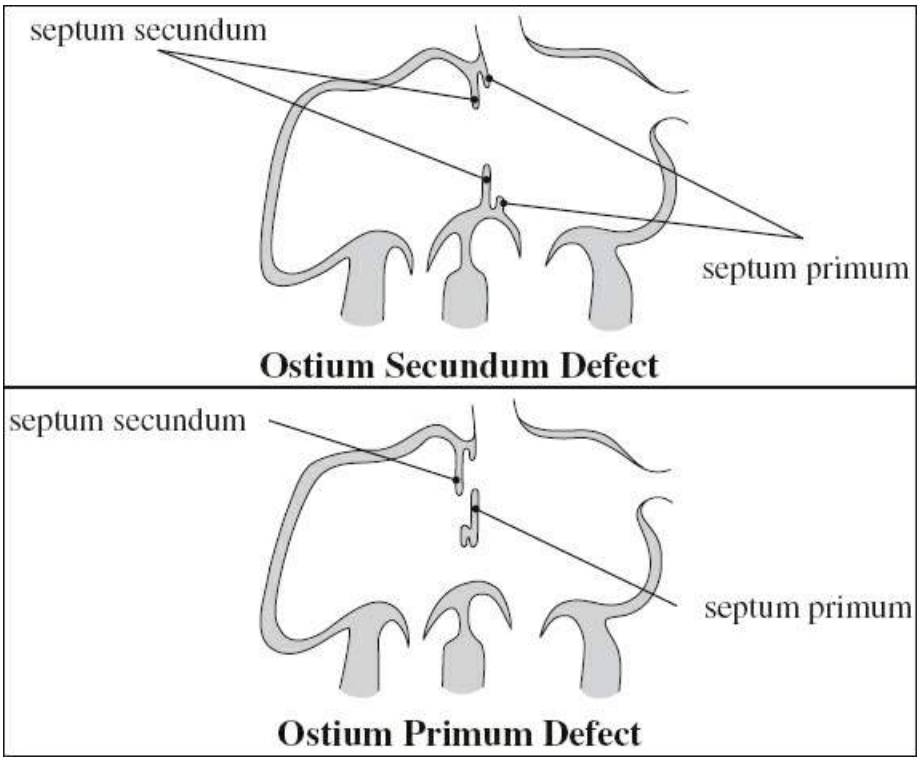
Cause: exaggerated resorptive process of septum primum → absence / fenestration of foramen ovale flap (Chiari network)

Location: in the center of the atrial chamber at fossa ovalis

Size: large defect of 1–3 cm in diameter

May be associated with:

prolapsing mitral valve (20–30%), pulmonary valve stenosis, tricuspid atresia, TAPVR, hypoplastic left heart, interrupted aortic arch



√ large direct communication between atria

Prognosis: often spontaneous closure by 2 years of age if diameter < 6 mm and if discovered in neonate

DDx: patent foramen ovale (interatrial connection of variable width + length)

Ostium Primum Defect

= defect of atrioventricular endocardial cushion

Location: lower end of septum inferior to fossa ovalis (at outlet portion of atrial septum) adjacent to atrioventricular valves

Almost always associated with:

Down syndrome, cleft mitral valve, common atrioventricular canal complex, anterior fascicular block

√ cardiomegaly + pulmonary vascular congestion

ECHO:

- √ direct visualization of abnormality
- √ measurement of flow and shunt size
- √ evaluation for valvular regurgitation
- √ both AV valves at same level (tricuspid valve usually more apically located than mitral valve)
- √ enlargement RA + RV + PA ← secondary pulmonary arterial hypertension

Unroofed Coronary Sinus

= CORONARY SINUS DEFECT

Cause: lack of septation between left atrium and coronary sinus → left-to-right shunt

Spectrum: multiple fenestrations in coronary sinus to complete atresia of thebesian valve
√ normal coronary sinus typically absent (unroofed)
√ dilated coronary sinus
√ connection between coronary sinus and left atrium
√ persistent SVC drains directly into LA

Malposition of Septum Primum

= anomalous drainage of right pulmonary vein into RA (= to right of leftward deviated septum primum)
Pathophysiology: lack of left heart filling → left heart hypoplasia
Associated with: heterotaxy, polysplenia, complex CHDs

Lutembacher Syndrome

= ASD + mitral stenosis

AZYGOS CONTINUATION OF IVC

= INTERRUPTED IVC WITH AZYGOS / HEMIAZYGOS CONTINUATION = ABSENCE OF THE HEPATIC SEGMENT OF THE IVC WITH AZYGOS CONTINUATION
Prevalence: 0.6%
Etiology: formation failure of right subcardinal-hepatic venous anastomosis → atrophy of right subcardinal vein → shunting of blood from supracardinal-subcardinal anastomosis to cranial portion of supracardinal vein (= retrocrural azygos vein)
May be associated with:
polysplenia syndrome (common), asplenia syndrome (rare), indeterminate situs (= situs ambiguus), persistent left SVC, dextrocardia, transposed abdominal viscera, duplicated IVC, retroaortic left renal vein, congenital pulmonary venolobar syndrome
√ absence of hepatic ± infrahepatic IVC:
  √ drainage of hepatic veins into RA via supra- / posthepatic segment of IVC (N.B.: IVC shadow present on LAT CXR!)
√ drainage of iliac + renal veins via azygos / hemiazygos vein:
  √ right renal artery crosses anterior to "IVC" on US
√ both gonadal veins drain into ipsilateral renal vein (since postcardinal-subcardinal anastomosis does not contribute to formation of IVC)
CXR:
  √ enlargement of azygos arch to > 7 mm
  √ widening of right paraspinal stripe contiguous with azygos arch (= enlarged paraspinal + retrocrural azygos veins)
  √ widening of left paraspinal stripe (= enlarged hemiazygos v.)
CT / MR:
  √ intensely enhancing well-defined tubular structure behind diaphragmatic crura paralleling aorta
DDx: right-sided paratracheal mass with retrocrural adenopathy

BACTERIAL ENDOCARDITIS

Incidence: 1.7–6.2÷100,000 annually in developed countries

Predisposed:

1. Native valve disease:
   (a) bicuspid aortic valve:
   responsible for 50% of aortic valvular bacterial endocarditis
   (b) rheumatic valve disease
   (c) mitral valve prolapse with mitral regurgitation
2. Prosthetic valve:
   4% incidence of bacterial endocarditis; mitral valve > aortic valve
   √ exaggerated valve motion (= disintegration of suture line + regurgitation)
3. Most CHD (VSD, TOF) except ostium secundum ASD
4. Previous endocarditis
5. Intravenous drug use:
   endocarditis of tricuspid valve → multiple septic pulmonary emboli
6. Central venous catheter
7. Other sources of infection: poor dentition, long-term hemodialysis, diabetes mellitus, HIV infection

Major criteria:

1. Oscillating valvular mass
2. Abscess
3. Dehiscent prosthetic valve

Minor criteria:

1. Pseudoaneurysm
2. Septic infarction

Valve Vegetations

Manifestations:
(1) Embolic phenomena
(2) Valvular regurgitation

CT:
√ peripheral cavitary (septic) lung nodules → assess for right-sided valvular vegetations

ECHO:
√ usually discrete focal echodensities with sharp edges; may show fuzzy / shaggy nonuniform thickening of cusps (vegetations) in systole + diastole
√ may appear as shaggy echoes that prolapse when the valve is closed (DDx to mitral valve prolapse)

ECG-gated CT (97% sensitive, 88% specific):
√ routinely depicts vegetations > 1 cm in diameter
√ depicts perivalvular abscess + pseudoaneurysm
√ septic + peripheral emboli

Cx: bundle-branch block, fistulation, refractory sepsis
(a) left: peripheral embolism, stroke, brain abscess
(b) right: septic pulmonary embolism, infarction

BEHÇET DISEASE

[Hulusi Behçet (1889–1948), dermatologist in Istanbul, Turkey]
= rare multisystemic chronic relapsing inflammatory vasculitis of variable-sized vessels in multiple organs of unknown origin

Countries: worldwide, most common in eastern Mediterranean countries, eastern rim of Asia; highest prevalence in Turkey with 80–370÷100,000

Histo: nonspecific necrotizing vasculitis with deposition of immune complexes in walls of small blood vessels

Associated with: human leukocyte antigen HLA-B51; genetic mutations including factor V Leiden → hyper-coagulability; triggered by microbial antigens

Age at onset: 3rd decade; M÷F = 2÷1

TRIAD of

1. Orogenital ulcers
2. Ocular inflammatory disease
3. Cutaneous lesions

Diagnostic criteria:

(1) Recurrent oral ulcers = aphthous stomatitis (95–100%)

plus 2 major criteria

(2) Recurrent genital ulcers (65–90%): ulcers on penis + scrotum / vulva + vagina

(3) Ocular inflammation (35–70%): anterior + posterior uveitis, relapsing iridocyclitis, hypopyon, choroiditis, papillitis, retinal vasculitis

(4) Skin lesion (40–50%):

› erythema nodosum, pseudofolliculitis, papulopustular lesions, acneiform nodules

› positive pathergy test (10–50%): pustule formation 24–48 hours after skin prick

Major criteria: buccal + genital ulceration, ocular inflammation, skin lesions

Minor criteria: thrombophlebitis, GI + CNS lesions, arthritis, family history

@ Joints

• arthritis (30–80%)

√ mild nondestructive arthritis

Rx: systemic corticosteroids for disease exacerbation

DDx: Reiter syndrome, Stevens-Johnson syndrome, SLE, ulcerative colitis, ankylosing spondylitis

Gastrointestinal Behçet Disease (5–42–60%)

Path: lymphocytic vasculitis of venules of bowel wall → chronic inflammation + intestinal ulceration

• abdominal pain + diarrhea (50%)

@ Esophagus (rarely involved)

√ single / multiple erosions / ulcerations

√ diffuse esophagitis, esophageal stenosis

√ mucosal dissection, intramural hematoma

√ downhill esophageal varices ← thrombotic occlusion of SVC → fibrosing mediastinitis → mediastinal collateral vessels draining into esophageal, coronary, hepatic veins + IVC

• hematemesis, SVC syndrome

@ Small bowel

Location: terminal ileum (most common), often together with proximal cecum
√ geographic large collar-button–shaped deep ulcer
√ aneurysmal dilatation of terminal ileum
√ cecal mass
Cx: perforation, fistula, hemorrhage

@ Large intestine
Location: ascending colon (most common)
√ multiple discrete punched-out ulcers throughout colon mimicking Crohn disease

Neurologic Behçet Disease (5–21–50%)
= develops > 10 years after onset of Behçet disease
Path: inflammatory cellular infiltrate around peripheral small venules + arterioles ← demyelination + edema

@ Parenchymal Neurobehçet (80%)
Location: brainstem (cerebral peduncles, pons) > thalamus > basal ganglia > centrum semiovale > peri-ventricular region, spinal cord, cranial nerve
√ isolated / confluent irregular T2 hyperintense foci of circular / linear / crescent shape that are iso- or hypointense relative to brain parenchyma on T1WI
DDx: multiple sclerosis (smaller + less extensive lesions), brainstem infarction, dilated perivenular spaces
√ atypically space-occupying lesion masquerading as unilateral brain tumor
DDx: lymphoma, other malignant tumor, abscess
√ leptomeningeal enhancement ← cranial nerve palsy /meningoencephalitis
Cx: small / (occasionally) large infarction

@ Nonparenchymal Neurobehçet (20%)
√ cerebrovascular disorders:
√ dural sinus thrombosis (5–25%) → raised intracranial pressure
√ multiple arterial aneurysm
√ arterial dissection / occlusion (rare)
√ aseptic meningitis (0.05–8.00%)

Cardiac Behçet Disease (1–16%)
= develops within 10 years after onset of Behçet disease
√ endocarditis, myocarditis, pericarditis
√ endomyocardial fibrosis
√ coronary artery disease, myocardial infarction
√ intracardiac thrombosis
√ aneurysm of sinus of Valsalva, periaortic pseudoaneurysm
√ valve dysfunction, conduction system disturbances

Vascular Behçet Disease (5–30–45%)
@ Veins (25%): migratory thrombophlebitis
√ subcutaneous / superficial venous thrombophlebitis
√ mediastinal widening ← edema ← thrombosis of SVC
√ thrombosis of IVC, veins in upper extremities

√ deep vein thrombosis in lower extremities
√ Budd-Chiari syndrome (3%)
√ portal vein thrombosis (9%)

@ Systemic arteries (3%)
√ saccular arterial aneurysm formation (⅓)
Histo: perivascular inflammatory cell infiltration → occlusion of vasa vasorum → transmural necrosis of wall → severe destruction of elastic fibers in media → perforation of vessel wall
Location: ascending thoracic aorta > aortic arch > abdominal aorta > pulmonary > femoral > coronary > subclavian > popliteal arteries
√ arterial occlusion/ pulseless disease (⅔)

@ Pulmonary artery
√ increased perihilar radiopacity ← pulmonary artery aneurysm
Location: artery to RLL > RPA > LPA
◊ Most common cause of pulmonary artery aneurysm!
√ in situ pulmonary artery thrombosis
√ pulmonary artery thromboembolism ← DVT ← hypercoagulable state

Thoracic Behçet Disease (1–8%)

@ Lung
√ multiple subpleural wedge-shaped / ill-defined increased opacities ← areas of pulmonary infarction ← hemorrhage / parenchymal necrosis
√ ill-defined ground-glass opacities with consolidation = hemorrhage ← ruptured pulmonary artery aneurysm
√ pleural effusion

BICUSPID AORTIC VALVE

= single fused commissure at birth resulting in 2 separate cusps of unequal size (usually fused L + R coronary cusps)

Sievers classification: based on
(a) number of raphes
(b) position of cusps and raphes

Prevalence: 1–2% in general population
◊ Most common congenital cardiac anomaly!

Genetics: autosomal dominant with incomplete penetrance

Histo: cystic medial degeneration; ↑ levels of matrix metalloproteinases; ↓ levels of fibrillin-1 in aortic wall

Bicuspid aortic valve patients have an aortopathy similar to Marfan syndrome with an increased propensity for aortic dilatation, aneurysm, dissection, and rupture!

Associated with: dilatation of aortic root (50%) + ascending aorta + transverse arch aortic; CoA

Cx: stenosis, regurgitation, endocarditis, aneurysmal dilatation of ascending aorta, aortic dissection

Recommendation: monitoring of aortic size with echocardiography / CT / MRI

BUERGER DISEASE

= THROMBANGIITIS OBLITERANS

[Leo Buerger (1879–1943), Austrian-American pathologist, surgeon and urologist at Mount Sinai Hospital, Beth David Hospital, Bronx Hospital, and Wyckoff Heights Hospital, Brooklyn, New York]

= idiopathic recurrent segmental obliterative vasculitis of small + medium-sized peripheral arteries + veins (panangiitis)

Frequency: < 1% of all chronic vascular diseases; more common in Israel, Orient, India

Etiology: unknown

Histo:

(a) acute stage: multiple microabscesses within fresh / organizing thrombus; all layers of vessel wall inflamed but intact; internal elastic lamina may be damaged; multinucleated giant cells within microabscesses (PATHOGNOMONIC)

(b) subacute stage: thrombus organization with little residual inflammation

(c) chronic stage: lumen filled with organized recanalized thrombus, fibrosis of adventitia binds together artery, vein, and nerve

Associated with: cigarette smoking (95%)

- instep claudication ± distal ulceration (symptoms abate on cessation of smoking + return on its resumption)
- Raynaud phenomenon (33%)

Location: legs (80%), arms (10–20%)

Site: starts in palmar + plantar vessels with proximal progression

√ superficial + deep migratory thrombophlebitis (20–33%)
√ arterial occlusions, tapered narrowing of arteries
√ abundant corkscrew-shaped collaterals
√ direct collateral following the path of the original artery (Martorell sign) in 80%
√ skip lesions = multiple segments involved with portions of arterial wall remaining unaffected
√ absence of generalized arteriosclerosis / arterial calcifications (90%)

CARDIAC ARREST

= sudden cessation of cardiac pump function

CT:

√ layering of static blood within heart + great vessels
√ hematocrit effect ← sedimentation of RBCs
√ good depiction of cardiac anatomy ← NO cardiac motion

CECT:

√ contrast pooling in dependent portion of venous system (right atrium, hepatic veins)
√ no contrast in pulmonary artery + left heart structures

Rx: prompt cardiopulmonary resuscitation

CARDIAC FIBROMA

= FIBROMATOSIS = FIBROUS HAMARTOMA = FIBROELASTIC HAMARTOMA

= congenital neoplasm / hamartoma of the heart

Prevalence: 100 cases reported; 2nd most common benign cardiac neoplasm of childhood (after

rhabdomyoma)

Mean age: 13 (range, 0–56) years; 33% in children < 1 year of age / in utero; 15% in adolescents + adults

Increased prevalence in: Gorlin (basal cell nevus) syndrome

- heart failure, cardiac murmur (⅓), ventricular arrhythmia
- NO embolism; asymptomatic (⅓)

Path: 2–10-cm large <u>single</u> round bulging well-circumscribed tumor within ventricular myocardium; foci of calcification / ossification (50%)

Histo: collection of fibroblasts interspersed among large amounts of collagen; numerous elastic fibers (> 50%); NO foci of cystic change / hemorrhage / necrosis

Location: ventricular septum > left ventricular free wall

√ cardiomegaly
√ focal cardiac bulge ← tumor in free ventricular wall
√ may be pedunculated
√ centrally cystic degeneration (rare)
√ ± pericardial effusion

ECHO:

√ noncontractile echogenic heterogeneous solid mass:
√ mean diameter > 5 cm; may obliterate cardiac chamber
√ multifocal dystrophic central tumor calcifications
√ affected myocardium hypokinetic

DDx: focal hypertrophic cardiomyopathy, hypertrophy of ventricular septum

CT:

√ homogeneous mural mass of soft-issue attenuation
√ sharply marginated / infiltrative
√ calcifications (25%)
√ variable enhancement

MR:

√ iso- / hypointense homogeneous discrete mural mass / myocardial thickening on T1WI
√ homogeneously hypointense on T2WI
√ no / little hetero- or homogeneous enhancement

Prognosis:

(1) Sudden death ← arrhythmia ← invasion / compression of cardiac conduction system
◊ 2nd most common primary cardiac tumor associated with sudden death (after endodermal heterotopia of AV node)
(2) May remain stable in size for years

Fibromas often are single lesions that do not regress, unlike rhabdomyomas!

Cx: fetal hydrops ← obstruction, pericardial effusion, fetal arrhythmia, fetal death

Rx: surgical excision / partial resection

DDx in infants: rhabdomyoma (multiple masses)

DDx in children: rhabdomyosarcoma (no calcification, cystic or necrotic tumor, invasion of pulmonary veins or pericardial space)

CARDIAC HEMANGIOMA

= rare benign vascular tumor of the heart
Prevalence: 5–10% of benign cardiac tumors
Association: Kasabach-Merritt syndrome (multiple systemic hemangiomas, recurrent thrombocytopenia, consumptive coagulopathy)
Path: predominantly intramural spongy mass / well-circumscribed endocardial-based soft mass growing into pericardial space; may contain fat
Histo: capillary (= small capillary-like vessels); cavernous (= multiple thin-walled dilated vessels); arteriovenous (= thick-walled dysplastic arteries + veins + capillaries)
• asymptomatic; dyspnea on exertion, chest pain, right-sided CHF
• arrhythmia, syncope, pericarditis, sudden death
Location: any chamber
√ mass-occupying lesion impinging upon cardiac cavities
√ ± pericardial effusion
US:
√ hyperechoic mass
CT:
√ heterogeneous intensely enhancing mass
MR:
√ heterogeneously iso- / hypointense on T1WI
√ hyperintense / occasionally hypointense on T2WI
√ inhomogeneous hyperintense enhancement pattern
Angio:
√ vascular blush in capillary + arteriovenous type
√ no enhancement for cavernous type
Prognosis: spontaneous regression possible
Rx: surgical resection (for symptomatic lesion)

CARDIAC INJURY

Frequency: 25% of traumatic deaths related to heart injury
◊ Congestive heart failure, pulmonary edema, cardiogenic shock, new cardiac murmur, pericardial friction should prompt evaluation for cardiac injury!

In blunt trauma, a triad of hyperdense pericardial effusion + distention of IVC and renal vv. + hypodense periportal fluid suggests cardiac tamponade!

Blunt Cardiac Injury

= most common type of cardiac injury after blunt thoracic trauma, but difficult to diagnose
Cause: MVC, fall, explosion, work-related accident, recreational activity, CPR
Location: RV (35%), LV (25%), RA atrium (33%), LA (14%), aorta (14%)
Associated with: rib fracture (83%), pneumothorax (39%), hemothorax (31%), lung contusion (13%), fracture of clavicle (13%), sternum (10%)

Myocardial Concussion

= mildest form of cardiac injury without proved myocardial cell damage / morphologic injury = myocardial stunning

- NO chemical abnormalities; NO elevated enzymes
- ± arrhythmia

ECHO:

√ segmental wall motion abnormalities

Myocardial Contusion

Frequency: 10–75%

Site: anterior surface of heart (RV > LV)

- precordial pain and dyspnea with varying ECG changes
- elevated cardiac enzymes:
  - › creatine kinase (> 90% sensitive, < 6% specific)
  - › serum cardiac troponin (> 90% sensitive + specific): level proportional to extent of myocardial damage

√ distinct boundary between normal + contused tissue

√ patchy necrosis + hemorrhage → eventually heal to form patchy and irregular fibrosis

ECHO:

√ increased myocardial echogenicity

√ focal systolic hypokinesis

NUC: not found to be helpful

Cx: arrhythmia, low cardiac output, ventricular septal defect, ventricular rupture, valvular dysfunction

◊ Extensive myocardial contusion + hemopericardium may be present without external signs of thoracic trauma

Myocardial Rupture

Frequency: 0.3–1.1% (in ER), 36–65% (in autopsy)

Site: right side of heart

- refractory hypotension + tachycardia

√ pericardial effusion → tamponade → cardiac arrest

√ myocardial disruption:

√ traumatic VSD typically occurs in the apical interventricular septum ← anteroposterior cardiac compression between sternum and thoracic spine.

√ extravasation of IV contrast into pericardial space

Prognosis: 33% surgical mortality, excellent long-term prognosis in survivors

Pericardial Injury / Rupture

Location of tear: longitudinal path along phrenic nerve

√ pericardial effusion

√ pneumopericardium ← pericardial tear (in 0.3–0.5%)

√ delayed traumatic diaphragmatic hernia

√ focal pericardial dimpling + discontinuity

√ lung interposition between aorta + pulmonary artery / heart + diaphragm / RA + RVOT

Cx: partial / complete trans-defect cardiac herniation

CARDIAC HERNIATION

N.B.: life-threatening condition (33–47% survival rate)

Prevalence: in 64% of pericardial ruptures
√ contour abnormality of heart = deformed ventricular silhouette
√ cardiac displacement into either hemithoracic cavity
√ pericardial sac "empty" = delineated by air / filled with loops of gas-containing bowel
Cx: strangulation of cardiac structures ← constrictive pericardial defect

CARDIAC LUXATION

= cardiac herniation and volvulus
Frequency: in 28% of pericardial ruptures
• change in electrical axis of heart
√ cardiac displacement:
√ leftward deviation of the myocardial septum
√ torsion along IVC + great vessels = strangulation of entire heart
√ entrapment of LA + LV
√ cardiac herniation through pericardial defect
√ pneumopericardium, esp. if associated with pneumothorax
Cx: SVC obstruction, right heart strain
Mortality rate: up to 67%

Coronary Artery Injury

Frequency: < 2% of blunt chest trauma
Site: LAD > RCA >> left circumflex artery
Path: intimal tear → dissection → thrombosis
• hypotension, ventricular arrhythmias
• acute myocardial infarction + ST-segment elevation
Rx: percutaneous transluminal angioplasty + stenting
Cx: rapid tamponade

Traumatic Valvular Dysfunction

Site: aortic > mitral > tricuspid valve
Pathophysiology:
(1) direct blunt cardiac trauma → abrupt increase in intracardiac chamber pressure against closed valve → maximal transvalvular gradient
(2) sudden rise in intraabdominal pressure → waterhammer effect to L > R heart
√ pulmonary edema ← new onset heart failure
@ Aortic valve
√ tear / avulsion from annulus of aortic valve cusp (esp. noncoronary cusp)
@ Mitral valve
Site: rupture of papillary muscle > chordae tendineae > tear of leaflet
@ Tricuspid valve (rare)
Site: rupture of chordae tendineae > tear of anterior papillary muscle > tear of leaflet

Penetrating Cardiac Injury

Cause: stabbing (knives), gunshot (handgun)
Location: RV (62%), LV (38%)

In penetrating chest trauma, CT is useful for depicting hemopericardium (100% sensitive, > 96% specific), pneumopericardium, intrapericardial hernia, and cardiac compression by a mediastinal hematoma.

Mortality: prehospital (94%), in-hospital (50%), gunshot (81–90%), stabbing (16–67%)
Cause of death: hemorrhagic shock (78%), cardiac tamponade (22%)

CARDIAC LIPOMA

= very rare benign neoplasm; 2nd most common cardiac tumor
Prevalence: 60 reported cases
Age: wide range; typically in adults
Path: encapsulated spherical / elliptical solitary mass, often very large (up to 4,800 g) by the time they come to clinical attention; multiple lipomas in CHD, tuberous sclerosis
Histo: mature adipocytes surrounded by capsule
Associated with: tuberous sclerosis (with multiple lipomas)
• mostly asymptomatic
• dyspnea (in intracavitary lipoma ← blood flow obstruction, in pericardial lipoma ← displacement of lung)
• arrhythmia ← involvement of conduction system
• right heart failure ← direct obstruction of tricuspid valve / vena cava with large lipoma
Location: broad-based from
(a) epicardial surface growing into pericardial space
(b) endocardial surface growing into cardiac chamber
(c) interatrial septum (atrioventricular grooves)
√ cardiomegaly, globular-shaped heart
√ echogenic / hypoechoic broad-based nonmobile mass
√ round mass with smooth contour
CT:
√ homogeneous mass of ≤ −50 HU in cardiac chamber / pericardial space
MR:
√ mass similar to adjacent subcutaneous / mediastinal fat:
√ homogeneously hyperintense on T1WI
√ intermediate to high signal intensity on T2WI
√ ± few thin septations
√ uniform drop in signal intensity with fat saturation
√ NO contrast enhancement
PET:
√ NO FDG activity
Rx: surgical resection

CARDIAC PARAGANGLIOMA

= extremely rare, usually benign sporadic neoplasm arising from intrinsic cardiac sympathetic paraganglial (chromaffin) cells
Prevalence: < 50 cases
Mean age: 40 (range, 18–85) years

- catecholamine-producing tumor (in the majority):
  - headache, arterial hypertension, palpitations, flushing
  - elevated levels of urinary norepinephrine, vanillylmandelic acid, total metanephrine, plasma norepinephrine, epinephrine

Associated with:

(a) additional paragangliomas (in 20%) in carotid body, adrenal gland, bladder, paraaortic

(b) metastases to bone (in 5%)

Path: 2–14 cm large encapsulated / poorly circumscribed and infiltrative highly vascular mass; necrotic in 60%

Histo: monomorphic tumor composed of nests of paraganglial cells (= "Zellballen") surrounded by sustentacular cells

Location: posterior wall of left atrium > roof of left atrium > atrial cavity > interatrial septum > ventricle

Site : epicardial surface of the base of the heart with tendency to involve coronary arteries

CXR:

√ middle mediastinal mass splaying carina simulating left atrial enlargement (for typically located tumor)

ECHO:

√ large echogenic left atrial mass

√ compression of SVC, encasement of coronary arteries

DDx: myxoma (broad base of attachment, softer)

NUC (^{131}I- or ^{123}I-MIBG):

√ for total body imaging with a sensitivity of 90%

NECT:

√ circumscribed / ill-defined heterogeneous mass:

√ hypoattenuating

√ isoattenuating to cardiac structures (may be missed)

√ ± tumor calcifications

√ ± extracardiac extension

CECT:

Cave: Premedicate patient with alpha- and beta-blockers as contrast material can trigger a hypertensive crisis!

√ markedly enhancing mass adherent to / involving left atrium / anterior to aortic root

√ central area of low attenuation (in 50%) from necrosis

MR:

√ mass iso- / hypointense to myocardium on T1WI

√ very hyperintense mass on T2WI

√ intense often heterogeneous enhancement

CARDIAC SARCOMA

◊ Most common primary malignant tumor of the heart!

Mean age: 41 years; extremely rare in infants + children

(a) right-sided heart inflow obstruction (tumor in right atrium)

1. Angiosarcoma (37–80%)

(b) mitral valve obstruction (tumor in left atrium)

2. Undifferentiated sarcoma (24–37%)
3. Malignant fibrous histiocytoma (11–24%)
4. Leiomyosarcoma (1–9%): predilection for left atrium; tends to invade pulmonary veins + mitral valve

Age: 5–10 years earlier than other sarcomas

5. Primary cardiac osteogenic sarcoma (3–9%)

DDx: myxoma (at fossa ovalis)

• dyspnea, pericardial tamponade, arrhythmia, syncope, peripheral edema, sudden death
• embolic phenomena, chest pain, pneumonia, fever
√ contrast enhancement, areas of hemorrhage, central necrosis

CXR:

√ cardiomegaly, RA enlargement
√ CHF
√ pleural effusion, pericardial effusion
√ focal cardiac mass
√ pulmonary consolidation

PET:

√ difficult identification of sarcoma if myocardial FDG activity is high

Metastatic to: lung, lymph nodes, bone, liver, brain, bowel, spleen, adrenal gland, pleura, diaphragm, kidney, thyroid, skin

Prognosis: mean survival of 3 month to 1 year

Dx: invasion of adjacent cardiac chambers + pericardium (DDx: benign mass)

Clue for subtypes:

√ macroscopic fat favors liposarcoma
√ calcifications favor fibrosarcoma
√ right atrial location favors angiosarcoma

Angiosarcoma (37–80%)

Frequency: most common cardiac malignancy of adulthood

Age: typically in middle-aged men

Path: frequently hemorrhagic + necrotic mass, often adherent to pericardium → pericardial effusion

Histo: mesenchymal cells characterized by ill-defined vascular spaces lined by atypical endothelial cells

• chest pain, right heart failure, supraventricular arrhythmia
• fever, weight loss; pericardial tamponade = bloody fluid on pericardiocentesis (rarely with malignant cells)

Spread to: right ventricle, lung, vena cava, liver (in 66–89% at presentation)

Location: right atrial free wall + involvement of pericardium (80%)

(a) well-defined large mass protruding into a cardiac chamber

√ usually originating from RA with sparing of atrial septum
√ areas of central necrosis communicating with cardiac chamber
√ disruption of fat planes, pericardial thickening / nodularity
√ low-attenuation mass on CT

√ heterogeneous contrast enhancement
√ heterogeneous MR signal:
√ "cauliflower appearance" = local nodular predominantly hyperintense areas interspersed within areas of intermediate SI on T2WI
√ central areas of necrosis

(b) diffusely infiltrative mass extending along epicardial surface
√ obliterated pericardial space (hemorrhage + necrotic tumor debris)
√ "sunray appearance" = linear contrast enhancement along vascular lakes on MR

Prognosis: poor (← late patient presentation); median survival of 6 months

Leiomyosarcoma of Heart (1–9%)

Location: predilection for left atrium; multiple (in 30%); tends to invade pulmonary veins + mitral valve
Age: 5–10 years earlier than other sarcomas
• dyspnea, CHF ← mitral valve obstruction
√ iso- to hypointense on T1WI + hyperintense on T2WI
√ marked contrast enhancement

Primary Osteogenic Sarcoma of Heart (3–9%)

= OSTEOSARCOMA OF HEART = CARDIAC OSTEOSARCOMA
Frequency: rare; 3–9% of primary cardiac sarcomas
Histo: osteo- / chondro- / fibroblastic differentiation
Location: left atrium sparing fossa ovalis
√ broad base of attachment with invasive behavior
√ dense calcifications (frequent) on CT
√ heterogeneously hypointense on T1WI
√ hyperintense on T2WI
DDx: metastatic osteosarcoma, myxoma

Rhabdomyosarcoma of Heart

Frequency: most common primary cardiac malignancy of childhood
Histo: embryonal type (in children + adults); pleomorphic type (in adults)
Location: no specific chamber with tendency to involve valves; multiple sites
• CHF (common)
MR:
√ isointense to myocardium on T1WI
√ central areas of low SI ← tumor necrosis
√ homogeneous enhancement

Undifferentiated Sarcoma (24–37%)

= PLEOMORPHIC SARCOMA = ROUND CELL SARCOMA = SPINDLE CELL SARCOMA
Frequency: 2nd most common cardiac malignancy
Age: 45 years (range, neonates to elderly)
• pulmonary congestion
Location: left atrium

√ large irregular hypodense intracavitary mass
√ polypoid mass isointense to myocardium
√ thickening / irregularity of myocardium ← tumor infiltration
√ tendency to involve valves
√ hemorrhagic mass replacing the pericardium (similar to angiosarcoma)

CARDIAC TAMPONADE

= PERICARDIAL TAMPONADE
◊ Cardiac tamponade is a clinical diagnosis!
= significant compression of heart by fluid / blood / pus / gas / tissue (= benign or malignant neoplasia) contained within pericardial sac → impaired diastolic filling of ventricles

In blunt trauma, the triad of hyperdense pericardial effusion + distention of IVC and renal veins + hypodense periportal fluid suggests cardiac tamponade!

Hemodynamics:
incremental ↑ in intrapericardial volume exceeds limit of pericardial stretch → ↑ intrapericardial pressure → compression of heart → ↑ diastolic filling pressures + ↓ volumes of cardiac chambers → severe hemodynamic impairment (= ↓ stroke volume) → reduced cardiac output → ↓ arterial blood pressure + ↓ coronary blood flow

Intrapericardial pressure: normally equals intrapleural pressure; pathologically equals cardiac chamber pressure
◊ With rapid fluid accumulation as little as 200 mL of fluid can cause cardiac tamponade!

Dx: clinical suspicion confirmed by echocardiography

Rate of accumulation versus pericardial volume:
(a) rapid / acute: 100–200 mL
(b) slow / gradual: up to 1,000–1,500 mL

- Beck triad:
  - muffled "distant" heart sounds
  - jugular venous distention ← ↑ central venous pressure
  - falling blood pressure / hypotension
- compensatory mechanisms:
  - tachycardia, increased contractility
  - vasoconstriction: cool legs, arms, ears, nose, peripheral cyanosis
- pulsus paradoxus = exaggerated drop in systolic arterial pressure > 10 mmHg during inspiration (← ↑ in right heart filling during inspiration at the expense of left heart filling)
  DDx: massive pulmonary thromboembolism, obstructive lung disease, profound hemorrhagic shock / other forms of severe hypotension
- shortness of breath
- ECG: reduced voltage, ST elevation, PR depression, nonspecific T-wave abnormalities

CXR:
√ normal lung fields + normal pulmonary vascularity
√ rapid enlargement of heart size (requires > 200 mL of pericardial effusion):
  √ global cardiomegaly with "water bottle" cardiac silhouette
  √ mediastinal widening

- √ hilar mass
- √ ± epicardial "fat pad" sign:
  - √ curvilinear fat density displaced posteriorly from sternum by pericardial effusion on LAT view
- √ ± tension pneumopericardium:
  - √ "small heart" sign = substantial decrease in size of cardiac silhouette

ECHO (imaging method of choice):

- √ cardiac chamber compression:
  - √ RV collapse during early diastole ← pericardial pressure exceeds RV pressure (38–48% sensitive, 84–100% specific)
  - √ inward movement of RA wall during late diastole + early systole lasting for > 30% of cardiac cycle (55–60% sensitive, 50–68% specific)
  - √ highly specific collapse of LA during late diastole (late sign in 25%)
- √ exaggerated respiratory variation in mitral + tricuspid inflow ← increased ventricular coupling
- √ distended inferior vena cava (IVC plethora) → NO decrease in diameter of proximal IVC by > 50% after deep inspiration / sniff
- √ Doppler flow velocity paradoxus = exaggerated paradoxical increase of right versus decrease of left transvalvular inflow velocities during early diastole
- √ compression of intrapericardial pulmonary trunk + thoracic IVC → indentation of RA at level of IVC junction anteriorly
- √ paradoxical motion of the interventricular septum → during inspiration sharply toward left, during expiration to right
- √ swinging motion of heart inside pericardial sac

Limitations of ECHO:

1. High rate of false-positive findings ← adjacent pathologic conditions simulating pericardial effusions: pleural effusion, lower lobe atelectasis, pericardial + intracardiac mass, other mediastinal lesions
2. Difficulty in identifying blood clot within pericardium
3. Differentiation of small fluid collections from pericardial thickening
4. Differentiation of fluid in the anterior and posterior spaces around the heart from epicardial fat
5. Identification of loculations in complex pericardial collections

CT:

- √ various attenuation values:
  - √ fat (chylopericardium)
  - √ simple serous fluid (underlying heart failure, renal failure, nonhemorrhagic carcinomatous involvement)
  - √ greater than water (hemopericardium, malignancy, purulent exudates, myxedematous effusion associated with hypothyroidism)
- √ signs of pericardial thickening:
  - √ presence of nodular areas
  - √ typically anterior location
  - √ lack of change at decubitus positioning

- √ pericardial contrast enhancement
- √ extrapericardial venous changes:
  - √ SVC enlargement: SVC diameter ≥ adjacent thoracic aorta
  - √ IVC enlargement: diameter > twice that of adjacent aorta
  - √ distension of hepatic + renal veins
  - √ reflux of contrast medium into azygos vein + IVC
  - √ periportal lymphedema
  - √ hepatomegaly
- √ intrapericardial venous changes:
  - √ compression of coronary sinus
  - √ compression of pulmonary trunk
  - √ compression of short intrathoracic segment of IVC (extrapericardial posteriorly, but covered by pericardium anteriorly)
- √ "flattened heart" sign ← pericardial fluid / tissue (↑ intrapericardial pressure → transient reversal of transmural left ventricular pressure during diastole):
  - √ flattening of anterior heart surface with ↓ in AP diameter
  - √ straightening of the right cardiac contour
  - √ inversion of wall with concave deformity of RA / RV
- √ RV + LV of equal size ← equalization of ventricular pressures
- √ angulation / bowing / inversion of interventricular septum

MR:

- ◊ Limited role due to emergent life-threatening disease!
- √ detection of pericardial effusions as small as 30 mL
- √ swinging heart and paradoxical septal bounce (cine MR)

Doppler-US:

- √ distension of IVC + hepatic veins with diastolic flow reversal (= hepatopetal flow)
- √ episodes of high-velocity hepatopetal flow separated by long intervals of minimal flow

Rx: needle pericardiocentesis (95% success with anterior effusion > 10 mm) / surgical pericardial drainage (intrapericardial bleeding, purulent effusion, clotted hemopericardium)

DDx: effusive-constrictive pericarditis

Malignant Pericardial Disease

- √ mass arising from / contiguous with pericardium
- √ obliteration of normal tissue planes between paracardiac mass and heart / pericardium
- √ compression + narrowing of cardiac chambers by pericardial effusion / mass
- √ hyperattenuating pericardial effusion ← hemorrhage / debris with fluid usually > 20 HU
- √ irregular enhancing nodular pericardial thickening
- √ signs of right-sided heart failure
- √ often evidence of primary malignancy of breast / lung

Rx: emergent pericardiocentesis ± drain placement

CARDIAC THROMBUS

A thrombus is the most common cause of a cardiac mass!

Cardiac thrombi in children are more commonly associated with indwelling central venous catheters, less likely with congenital heart disease or dilated cardiomyopathy.

A. Left atrial thrombus
Associated with: mitral valve disease
• atrial fibrillation
Site: atrial appendage
√ atrial dilatation
√ irregular / lobulated border
√ microcavitations
√ laminated appearance

B. Right atrial thrombus

Cause: underlying coagulation disorders / atrial arrhythmias / central venous catheters / pacemaker leads / mechanical tricuspid valve

Incidence: 4–7% with suspected pulmonary embolism
√ hyperechoic mass (DDx: crista terminalis, myxoma)
√ absence of mobility
√ multiple lesions favor thrombus
Prognosis: 80–100% mortality in untreated patients
◊ Large right atrial mobile thrombi are life-threatening!
Rx: anticoagulation, thrombectomy, thrombolysis, surgical resection
DDx: cardiac myxoma

C. Left ventricular thrombus
Site: region of ventricular dyskinesia / aneurysm ← prior myocardial infarction
√ usually NO enhancement:
√ peripheral enhancement ← neovascularization in chronic thrombus
√ homogeneous attenuation on CT
√ heterogeneous signal on SE MR images
√ low-signal intensity on GRE MR images
DDx: myxoma (heterogeneous texture on CT)

CARDIOMYOPATHY

= mechanical / electrical dysfunction of myocardium exhibiting inappropriate ventricular hypertrophy + dilatation
Prevalence: 1÷5439 in USA
Cause:

A. PRIMARY / INTRINSIC CARDIOMYOPATHY
(a) genetic
1. Hypertrophic cardiomyopathy
2. Arrhythmogenic RV dysplasia
3. Noncompaction cardiomyopathy
4. Glycogen storage disease
5. Conduction defects
6. Mitochondrial myopathy
7. Ion channel disorders

(b) acquired
1. Inflammatory (myocarditis)
2. Stress provoked
3. Peripartum
4. Tachycardia induced
5. Infants of diabetic mothers

(c) mixed
1. Dilated cardiomyopathy
2. Restrictive cardiomyopathy

B. SECONDARY CARDIOMYOPATHY (majority of cases)
= characterized by multiorgan involvement
(a) infiltrative: amyloidosis, Gaucher disease, Hurler disease, Hunter disease
(b) storage: hemochromatosis, Fabry disease, glycogen-storage disease type II, Niemann-Pick disease
(c) toxicity: drugs, heavy metals, chemical agents
(d) endomyocardial: endomyocardial fibrosis, hypereosinophilic syndrome (Löffler endocarditis)
(e) inflammatory: sarcoidosis
(f) endocrine: diabetes mellitus, hyperparathyroidism, hyper- / hypothyroidism, pheochromocytoma, acromegaly
(g) neurologic: Friedreich ataxia, Duchenne-Becker muscular dystrophy, myotonic dystrophy, neurofibromatosis, tuberous sclerosis
(h) autoimmune: SLE, dermatomyositis, rheumatoid arthritis, scleroderma, polyarteritis nodosa
(i) electrolyte imbalance: deficiencies of potassium, phosphate, magnesium; anorexia nervosa; laxative abuse
(j) cancer therapy: anthracyclines (doxorubicin), cyclophosphamide, radiation

Dilated and Ischemic Cardiomyopathy

= CONGESTIVE CARDIOMYOPATHY

Etiology:

1. Idiopathic
2. Myocarditis: viruses, bacteria
3. Alcoholism
4. Pregnancy / post partum
5. Endocardial fibroelastosis = thickened endocardium + reduced contractility
6. Infants of diabetic mothers
7. Inborn error of metabolism: glycogenosis, mucolipidosis, mucopolysaccharidosis
8. Coronary artery disease: myocardial infarction, anomalous origin of L coronary artery, coronary calcinosis
9. Muscular dystrophies

• tendency for CHF when EF < 40%
√ global 4-chamber enlargement
√ poor ventricular contractility (= reduced EF)
√ LA enlargement without enlargement of LA appendage

√ bilateral atrioventricular valve insufficiency

ECHO:

√ enlarged LV with global hypokinesis

√ IVS + LVPW of equal thickness with ↓ motion amplitude

√ low-profile / "miniaturized" mitral valve

√ mildly enlarged LA ← elevated end-diastolic LV pressure

√ enlarged hypokinetic right ventricle

Dilated Cardiomyopathy

= dilatation + impaired contraction of LV or LV + RV

Prevalence: 36÷100,000 in USA

Cause:

1. Idiopathic (50%)
   (a) familial (20–35%): autosomal dominant / recessive, maternal, X chromosome–linked trait
3. Injury: coronary artery disease, systemic disease, nutritional deficiency, excessive consumption of alcohol, anthracyclines, catecholamines
4. Infection: viral, bacterial, fungal, rickettsial
5. Neuromuscular syndromes: Duchenne muscular dystrophy, Friedreich ataxia

Histo: patchy loss of myocytes with progressive replacement by interstitial fibrosis + eccentric hypertrophy of adjacent uninvolved cells

Hemodynamics: ↑ diastolic volume, ↑ systolic volumes, ↓ ejection fraction

• congestive heart failure, progressive dyspnea, orthopnea

◊ 3rd most common cause of heart failure after ischemia + valvular disease

◊ Most common cause of heart failure in the young

• arrhythmias, thromboembolism

√ biventricular dilatation

√ global ventricular hypokinesia

√ myocardial wall thinning (= diastolic wall thickness < 5.5.mm)

√ increase in myocardial mass

√ mitral / tricuspid regurgitation, atrial enlargement

√ intracardiac thrombus

Risk factor of sudden death: LV ejection fraction < 35%

Rx: ICD placement (for LV ejection fraction of ≤ 35%)

DDx: CAD, myocarditis, cardiac sarcoidosis

Hypertrophic Cardiomyopathy (10%)

= genetic disorder of cardiac muscle characterized by hypertrophy of LV in the absence of cardiac / systemic disease with subsequently decreasing size of LV cavity

Phenotypes (variable penetrance + expression):

1. Asymmetric (septal) HCM 60–70%
2. Apical HCM 2–25%
3. Symmetric (concentric) HCM in up to 42%
4. Midventricular HCM
5. Masslike HCM

Prevalence: 2÷1,000 (one of the most common genetic disorders)

Etiology: mutation in one of sarcomeric genes with autosomal dominant transmission (> 60%); sporadic form

Histo: myocyte disarray + interstitial fibrosis; dysplasia of small intramural coronary arterioles ← increased pressure from adjacent hypertrophic myocytes

Age: 3rd–5th decade; occasionally infants + elderly

- asymptomatic, fatigue, systolic murmur
- dyspnea on exertion (75%) ← impaired diastolic function ← impaired LV filling + preserved systolic function:
  - elevated LV diastolic pressure
- angina (66%) ← LV outflow obstruction + decreased flow through intramural coronary arteries
- syncope ← arrhythmia / decreased cardiac output during exercise because of LV outflow obstruction
- high voltage + inverted T waves at ECG
- sudden cardiac death in children (5% risk annually)

Risk factors of sudden cardiac death:

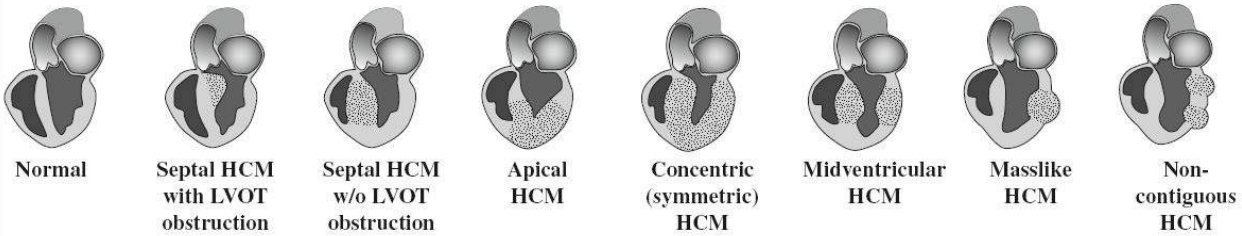
(1) Family history of sudden cardiac death
(2) Unexplained syncope
(3) Nonsustained ventricular tachycardia = greater than 3 beats at ≥ 120 bpm
(4) Hypotensive / blunted blood pressure response to exercise = rise of systolic pressure < 20 mmHg

Risk factors identified on cardiac imaging:

(1) LV wall thickness of ≥ 30 mm
(2) LVOT obstruction with gradient of ≥ 30 mmHg at rest or ≥ 50 mmHg with provocation
(3) LV dilatation with depressed ejection fraction
(4) Fibrosis
(5) Perfusion defect
(6) Reduced functional reserve flow

Role of imaging:

(1) Establish diagnosis
(2) Monitor gene carriers without phenotypic hypertrophic cardiomyopathy for development of the disease
(3) Screen family members of affected individuals
(4) Help stratify risk for sudden cardiac death
(5) Evaluate for complications



Phenotypes of Hypertrophic Cardiomyopathy (HCM)

There is a linear relationship between maximal myocardial thickness + risk for sudden cardiac death: maximal myocardial thickness of > 30 mm → indication for ICD placement!

Location:

› asymmetric septal hypertrophy = ratio of septal to inferolateral wall thickness of ≥ 1.3
› apical / midventricular hypertrophy
› focal masslike hypertrophy
› right ventricular hypertrophy

√ LV wall hypertrophy > 15 mm at end-diastole; often asymmetric / segmental / discontinuous
√ NO dilatation of LV cavity → decreasing in size
√ normal heart size
√ diastolic dysfunction:
  √ reduced LV compliance with relatively preserved systolic function and normal LV ejection fraction
√ LA enlargement ← mitral insufficiency ← abnormal mitral valve apparatus (in 30%) / diastolic dysfunction
√ prominent left midheart border (septal hypertrophy)
√ ± mild pulmonary venous hypertension

MR:

Cardiac MR imaging is a powerful imaging modality for differentiating HCM from other cardiomyopathies!

√ marked thickening of LV wall + small LV cavity
√ myocardial crypts at base of LV
√ average end-diastolic thickness of septal + posterolateral wall = 23.5 mm + 11.4 mm; ratio 2.1
√ increased LV mass (estimated by cine MR)
√ large + prolonged signal void from site of obstruction toward aortic valve within normally high-intensity flowing blood ← turbulent flow during systole
√ substantially elevated ejection fraction
√ prolonged systolic contact of the anterior mitral valve leaflet with septum ← elongation of anterior MV leaflet
√ systolic flow void from mitral valve into left atrium ← mitral valve regurgitation (on cine MR)
√ impairment of LV relaxation (= abnormal LV stiffness) → poor early diastolic filling

CEMR:

√ delayed hyperenhancement of hypertrophic myocardium (in 80%), on average 10% of

overall LV myocardial volume

ECHO (modality of choice):

√ IVS ≥ 15 mm thick; posterolateral wall > 11 mm thick; IVS÷LVPW thickness > 1.3÷1

√ systolic anterior motion of mitral valve (SAM) → narrowed LVOT during systole

√ dynamic LVOT obstruction ← hypertrophy of basal septum + SAM:

√ increased LVOT gradient with late systolic peaking on Doppler

√ midsystolic closure of aortic valve

√ hyperdynamic ventricular contraction → high LV ejection fraction

√ impaired myocardial relaxation

Dx: LV wall thickness ≥ 15 mm at end-diastole (without explanation); 12–14 mm = borderline values of mild dz

Prognosis: 1–6% annual mortality rate (sudden death in young patients); progressive LV dilatation, atrial arrhythmia, intractable CHF

Hypertrophic cardiomyopathy is the most common cause of sudden cardiac death in young adults and athletes!

Rx: beta-blockers, calcium antagonists, myomectomy of hypertrophied septum, septal alcohol ablation, cardiac transplantation, ICD (effective prevention of cardiac death)

DDx: athlete's heart

Apical Hypertrophic Cardiomyopathy

= myocardial wall thickening confined to apical portion of LV with sparing of septum

Age: middle-aged men

- usually clinically benign (no obstruction to LV flow), rarely associated with sudden cardiac death
- frequently complicated by hypertension
- giant (negative) inverted T-wave

Dx: (1) Absolute apical wall thickness > 15 mm (typically most evident in anteroseptal myocardium) *or*

(2) $\text{Thickness}_{\text{apical wall}} \div \text{Thickness}_{\text{basal LV wall}} = 1.3–1.5$

√ spade-like deformity of LV cavity at end-diastole (best seen on vertical long axis view)

Specific Cx: apical infarction resulting in aneurysm formation (= burned-out apex)

At risk for: thrombus formation, thromboembolism

Prediction of adverse outcome:

√ significant amount of delayed enhancement (> 5%)

Arrhythmogenic Right Ventricular Cardiomyopathy

= ARRHYTHMOGENIC RV DYSPLASIA

= heritable genetic progressive replacement of RV myocardium by fibrofatty tissue

- palpitations, fatigue, heart failure syncope, chest pain
- sustained monomorphic ventricular tachycardia with left bundle-branch block during exercise
- sudden cardiac death with physical exertion (rare)

Prevalence: 1÷1,000–1÷5,000; increase during 15–20 years of age; familial in up to 50%

Age: adolescence to middle-aged; M÷F = 3÷1
Location: triangle of dysplasia = between RV outflow tract + RV apex + diaphragmatic aspect of RV beneath posterior leaflet of tricuspid valve
Site: progression from epicardium to endocardium
Path: segmental / diffuse transmural loss of (RV >> LV > interventricular septum) myocardium with replacement by fibrofatty tissue; saccular aneurysm in triangle of dysplasia (in up to 50%)
√ almost imperceptibly thin free wall of RV
√ dilatation of RV (body + RVOT)
√ regional RV akinesia / dyskinesia / dyssynchrony
ECHO:
√ RVOT ≥ 29 mm on parasternal long axis view
√ RVOT ≥ 32 mm on parasternal short axis view
√ reduction of RV ejection fraction to ≤ 45%
√ increased RV end-diastolic volume index
CT:
√ myocardial fat in RV trabeculae + moderator band (difficult DDx: abundant epicardial fat)
√ conspicuous trabeculae
√ scalloped / bulging appearance of RV free wall

Functional and structural assessment of the RV is more reliable than fibrofatty changes!

MR:
√ fatty infiltration of RV / (rarely) epicardial LV free wall
√ aneurysm formation of RV
√ ratio of RV end-diastolic volume to body surface area ≥ 100 (90) mL/m2 for male (female) on parasternal long axis view
√ reduction of RV ejection fraction to ≤ 45%
√ "accordion" sign = corrugated pattern to RV wall ← RV akinesia / dyskinesia / dyssynchronous contraction

A diagnosis of ARVC requires these RV findings: dilatation, wall motion abnormalities, scalloped / bulging free wall, and myocardial fat in free wall, trabeculae, moderator band, interventricular septum!

Rx: avoidance of strenuous exercise, β blocker, ICD placement, antiarrhythmic Rx, catheter ablation
DDx: (1) Physiologic myocardial fat (normal myocardial thickness + size of RV)
(2) Healed MI (coronary artery territory, subendocardial location)
(3) Cardiac sarcoidosis (left / biventricular enlargement)
(4) Unrecognized shunt lesion: ASD, PAPVR
(5) Pectus excavatum (restricted motion of basolateral + inferolateral RV wall, narrowing of RV base with relative enlargement of RV apex + RVOT)

Asymmetric Septal Hypertrophy (ASH)

= IDIOPATHIC HYPERTROPHIC SUBAORTIC STENOSIS (IHSS) = SUBAORTIC STENOSIS

Asymmetric septal hypertrophy is the most common morphologic variant of HCM (60–70%). The ventricular septum is disproportionately enlarged, most commonly involving the anteroseptal myocardium. Septal hypertrophy can be limited to subaortic / midventricular / apical regions.

◊ Most common + clinically significant form!

Dx: The normal thickness of the LV is ≤ 11 mm measured during diastole.
(1) Septal thickness ≥ 15 mm (typically most evident in anteroseptal myocardium) *or*
(2) Thickness $_{\text{septum}}$ ÷ Thickness $_{\text{inferior LV wall}}$ > 1.5 at midventricular level

Clinical distinction:

1. Hypertrophic obstructive cardiomyopathy
   = gradient between LV outflow tract + aorta at rest and/or with provocation
   Cause: systolic anterior motion of MV leaflets + midsystolic contact of MV leaflets with IVS
   √ peak systolic pressure gradient at rest ≥ 50 mmHg
2. Nonobstructive cardiomyopathy
   = no systolic obstruction of LV outflow tract

Hemodynamics:

› LV hypertrophy → subaortic stenosis → abnormal diastolic function → myocardial ischemia
› rapid blood flow through narrow outflow tract → anterior leaflet of mitral valve displaced anteriorly toward septum during systole (**Venturi effect**)
› concomitant mitral regurgitation ← displaced MV leaflets with incomplete leaflet apposition

• mitral regurgitation
√ basal / upper part of LV septum disproportionately thickened
√ anterolateral wall of LV often also abnormally thick

CEMR:
√ midwall patchy or punctate midwall hyperenhancement in thickened myocardium in a noncoronary distribution

Rx: septal myomectomy / alcohol ablation

MIDVENTRICULAR CARDIOMYOPATHY

= rare variant of asymmetric HCM
• ventricular arrhythmia, myocardial necrosis
• systemic embolism
√ hypertrophy of middle ⅓ of LV wall
√ apposition of midventricular wall → obstruction
May be associated with: apical aneurysm ← increased systolic pressure in apex

Symmetric / Concentric Hypertrophic Cardiomyopathy

= HYPERTENSIVE HYPERTROPHIC CARDIOMYOPATHY
= concentric LV hypertrophy with a small cavity WITHOUT evidence of secondary causes
• commonly in older women
(a) midventricular
(b) diffuse

(c) apical
√ marked concentric LV hypertrophy
√ small LV cavity
DDx: Concentric LV hypertrophy

Masslike Hypertrophic Cardiomyopathy
= focal segmental hypertrophic cardiomyopathy
√ parallels homogeneous SI + perfusion of normal myocardium
DDx: neoplasm

Noncompaction Cardiomyopathy

= sponge myocardium
= rare congenital myocardial disorder caused by intrauterine arrest of endomyocardial compaction → persistence of embryonic myocardium
Prevalence: in 0.05% of adult echocardiograms
Path: noncompacted subendocardial myocardium comprises numerous prominent trabeculations; deep intertrabecular recesses extend into compacted myocardial layer
• asymptomatic; supraventricular / ventricular arrhythmia
• congestive heart failure, embolic event, sudden cardiac death
Location: primarily LV + concomitant RV involvement (41%)
Site: from apex along lateral + inferior wall to mid portion of left ventricle
MR:
√ overall increased myocardial thickness:
√ 2-layers of thin compacted subepicardial layer (C) + thick noncompacted subendocardial layer (NC)
√ NC÷C ratio of > 2.3 in end-diastole (on 2D Steady State Free Precession imaging)
ECHO:
√ maximal end-systolic NC÷C ratio of > 2 (short-axis view)

Restrictive Cardiomyopathy

= intrinsic myocardial disease that impairs the myocardial ability to relax normally + impairs ventricular filling
Etiology: (a) idiopathic: endomyocardial fibroelastosis, drugs, anthracyclines, carcinoid
(b) infiltrative disease: amyloidosis, sarcoidosis, hemochromatosis, Fabry disease, glycogen storage disease, Löffler's hypereosinophilic endocarditis, Gaucher disease
Hemodynamics: reduced myocardial compliance → ↑ ventricular pressure with small increases in volume → ↓ diastolic ventricular filling → diastolic heart failure with preservation of systolic function
• increasing dyspnea + exercise intolerance
• palpitations, syncopal attacks, conduction disturbances
√ varying degrees of pulmonary venous hypertension
√ dilatation of RA + IVC reflecting high RV filling pressure (DDx: constrictive pericarditis)
√ ± LA enlargement
ECHO:

√ reduced early + late diastolic annular velocities

Diagnostic key imaging features:
√ left ventricular hypertrophy
√ delayed enhancement of myocardium at MRI
√ normal pericardium

Prognosis: 70% 5-year mortality rate after initial manifestation of symptoms
DDx: constrictive pericarditis

CHRONIC VENOUS STASIS DISEASE

= CHRONIC VENOUS INSUFFICIENCY

= insufficiency / incompetence of venous valves in deep venous system of lower extremity

Cause:

(a) postphlebitic valvular incompetence: short thickened valves ← scar formation ← destruction of valve apparatus

(b) primary valvular incompetence: shallow elongated redundant valve cusps prevent effective closure

Associated with: incompetent venous valves in calf ← pressure dilatation from stasis in deep venous system leading to superficial vein varicosities

- edema (= fluid exudation from increased capillary pressure), induration; aching pain
- ulceration ← minor trauma + decreased diffusion of oxygen ← fibrin deposits around capillaries
- skin hyperpigmentation (= breakdown products of exudated RBCs)

√ venous reflux on descending venography with Valsalva:

(a) 82% in deep venous system alone

(b) 2% in saphenous vein alone

(c) 16% in both

bilateral in 75%

Grade:

1 = minimal incompetence = to level of upper thigh

2 = mild incompetence = to level of lower thigh

3 = moderate incompetence = to level of knee

4 = severe incompetence = to level of calf veins

CHURG-STRAUSS SYNDROME

= ALLERGIC ANGIITIS AND GRANULOMATOSIS = EOSINOPHILIC GRANULOMATOSIS WITH POLYANGIITIS

= rare multisystemic disorder with necrotizing vasculitis of small vessels associated with extravascular eosinophilic granulomas occurring exclusively in patients with asthma + peripheral eosinophilia = variant of polyarteritis nodosa

Etiology: ? hypersensitivity response to an inhaled agent

Incidence: 1–7÷1,000,000 annually

Mean age: 28 (range, 20–40) years; M÷F = 1÷1

Clinical phases (CLASSIC TRIAD):

(1) Prodromal: asthma, allergic rhinitis, sinus pain, headaches

(2) Eosinophilic: peripheral blood (> 30%) and tissue hypereosinophilia with Löffler syndrome (almost in 100%)

(3) Systemic small-vessel granulomatous vasculitis: usually developing within 3 years of onset of asthma

Path: (1) Necrotizing vasculitis

(2) Eosinophilic tissue infiltration

(a) eosinophilic pneumonia
(b) eosinophilic gastroenteritis

(3) Extravascular "allergic" granulomas / eosinophilic abscesses

Diagnostic criteria of American College of Rheumatology (at least 4 must be present):
(1) Asthma (in older patient)
(2) Eosinophilia > 10% of WBC differential count
(3) Polyneuropathy
(4) Migratory / transient pulmonary opacities
(5) Paranasal sinus abnormalities
(6) Extravascular eosinophils at biopsy

- fever, malaise, gastrointestinal symptoms, arthralgias
- p-ANCA (perinuclear antineutrophil cytoplasmic autoantibodies) in 40–70%
- elevated rheumatoid factor in 52%

√ vascular aneurysms + thrombosis

@ Lung (most frequent): intraalveolar hemorrhage
- √ normal CXR (25%)
- √ often transient peripheral widespread nonsegmental air-space opacities without zonal predominance
- √ diffuse miliary nodules:
  - √ nodules may coalesce up to 2 cm (rare)
  - √ cavitation is atypical (and suggests infection)
- √ eosinophilic pleural effusions (29%)

HRCT:
- √ subpleural consolidation / ground-glass attenuation in a lobular distribution (59%)
- √ bilateral centrilobular nodules
- √ diffuse interstitial reticular / reticulonodular opacities
- √ interlobular septal thickening
- √ bronchial wall thickening
- √ uni- / bilateral pleural (30%)

<u>less common:</u>
- √ hyperinflation
- √ mediastinal / hilar lymphadenopathy
- √ pericardial effusion

@ Skin (2nd most frequent): palpable purpura, macular / papular erythematous rash, subcutaneous nodules

@ GI tract (20%): ulceration, hemorrhage, perforation
- diarrhea, bleeding, obstruction
- √ mesenteric vasculitis (= polyarteritis nodosa)
- √ eosinophilic gastroenteritis (= bowel wall infiltration by eosinophils)

@ Heart (up to 47%): coronary vasculitis with myocardial infarction, myocarditis, acute pericarditis with pericardial tamponade (accounting for 50% of deaths)

◊ Higher frequency of cardiac involvement than in Wegener granulomatosis

@ CNS (commonly involved)
- diffuse peripheral neuritis, mononeuritis multiplex
- cranial nerve palsy (frequent): ischemic optic neuropathy

• confusion, seizures, coma (in severe cases)
√ micro- or macrohemorrhages of cerebral ischemia

@ Kidney:
• renal artery-induced hypertension, hematuria
√ focal segmental glomerulonephritis
◊ Less frequent + less severe renal disease compared with Wegener granulomatosis + microscopic polyangiitis

@ Muscles & joints: myalgia, joint pain

Prognosis: 85% 5-year survival; death from intraabdominal /cardiac complications, cerebral hemorrhage, renal failure, status asthmaticus

Rx: corticosteroids, cyclophosphamide

DDx: (1) Chronic eosinophilic pneumonia (no granulomatous arteritis, no extrapulmonary lesions, homogeneous peripheral airspace consolidation)
(2) Wegener granulomatosis (solitary / multiple nodules with cavitation)
(3) Hypereosinophilic syndrome

COARCTATION OF AORTA

= CoA = JUXTADUCTAL COARCTATION
= short aortic narrowing at level of ligamentum arteriosum

Former Classification:
(a) adult / postductal / localized type of aortic coarctation
(b) infantile / preductal / diffuse type of aortic coarctation

Prevalence: 7% of congenital heart disease; M÷F = 1.5÷1; rare in Blacks

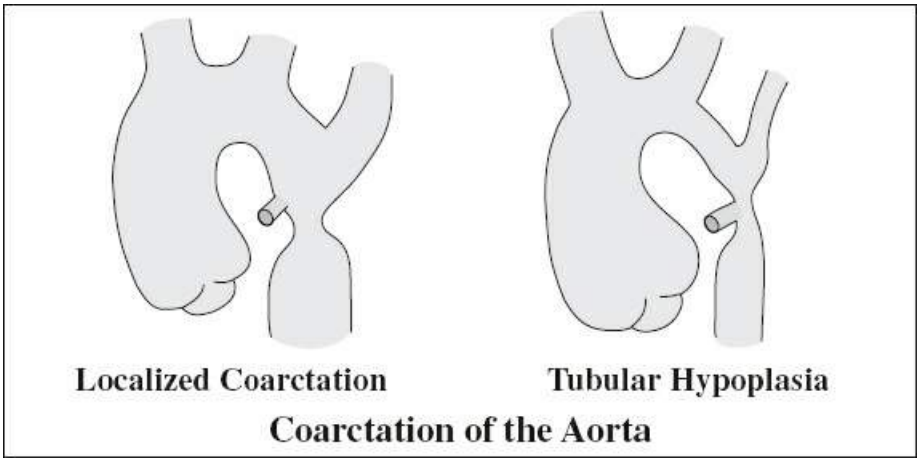
Cause: hemodynamic hypothesis (= abnormal preductal flow); ductal hypothesis (= ectopic ductal tissue extending into aorta)

◊ Usually solitary lesion (in 82%)!

May be associated with:
1. Bicuspid aortic valve (22–42%), which may result in calcific aortic valve stenosis (after 25 years of age) + bacterial endocarditis
2. Intracardiac malformations:
   › PDA (33%), VSD (15%), ASD, TGV
   › aortic stenosis / insufficiency
   › ostium primum defect
   › truncus arteriosus, double-outlet right ventricle
   › Shone complex = LVOT obstruction + parachute mitral valve
   › aortic hypoplasia: isolated isthmic hypoplasia, isolated aortic arch hypoplasia, isthmic + aortic arch hypoplasia
3. Noncardiac malformations (13–15%): Turner syndrome
4. Intracranial berry aneurysms (10%)
5. Mycotic aneurysm distal to CoA

Path: juxta- / periductal narrowing ± extension into aortic arch and isthmus

Histo: cystic medial necrosis (common), intimal thickening with fragmentation of elastin and increased collagen deposition → gradually thickening of media and ↓ luminal diameter



Coarctation of the Aorta

Location: most frequent in juxtaductal portion of arch
• systemic arterial hypertension in upper extremities
• incidental finding late in life with differential pressures between upper + lower extremities
• systolic murmur; ductus usually closed
√ shelflike lesion at any point along the aortic arch
√ poststenotic aortic dilatation
√ juxtaductal aortic narrowing
√ collateral circulation via subclavian artery and its branches:
› thoracoacromial trunk › thyrocervical trunk
› anterior spinal artery › descending scapular artery
› lateral thoracic artery › transverse cervical artery
› internal mammary artery
→ draining into external iliac + intercostal arteries
Cx: wall changes predispose to infective endarteritis, intimal dissection, aortic aneurysm
Prognosis: 75% mortality by 46 years of age
Cause of death: CHF (26%), aortic rupture (21%), complications of endocarditis (18%), intracranial hemorrhage (12%)
Rx: prosthetic overlay, tube graft, aortoplasty, percutaneous balloon angioplasty ± stent placement
DDx: pseudocoarctation

Symptomatic CoA

◊ Second most common cause of CHF in neonate (after hypoplastic left heart)
Onset:
(a) toward the end of 1st week of life in "critical stenosis"
(b) more commonly presents in older child
• lower extremity cyanosis (in tubular hypoplasia)
• left ventricular failure (usually toward end of 1st week of life)
CXR:
√ generalized cardiomegaly
√ increased pulmonary vascularity (L-to-R shunt through PDA / VSD)
√ pulmonary venous hypertension / edema

√ "figure-of-3" sign hidden by thymus

Asymptomatic CoA

• headaches ← hypertension; claudication ← hypoperfusion
√ "figure-of-3" sign (in 50–66% of adults)
= indentation of left lateral margin of aortic arch in the region of aortic-pulmonic window resembling the number 3 on frontal CXR view:
√ dilatation of left subclavian artery + prestenotic aorta
√ indentation at site of aortic stenosis
√ dilatation of poststenotic aorta
√ "reverse figure-of-3" sign = indentation of esophageal contour during barium esophagram on LAO view
√ elevated left ventricular apex ← LV hypertrophy
√ collateral vessels bypassing coarctation:
√ dilatation of brachiocephalic vessels + aorta proximal to stenosis
√ obscuration of superior margin of aortic arch
@ superior epigastric arteries
@ internal mammary arteries
√ scalloped contouring of soft-tissues posterior to sternum (= dilated tortuous internal mammary arteries) on LAT CXR (in 28%)
@ intercostal arteries
√ inferior rib notching (in 75%; mostly in adults over age 20; unusual before age 6)
Location: ribs 3–8 (most pronounced in 3rd + 4th ribs, less pronounced in lower ribs); 1st + 2nd rib do not participate because they have arteries originating from the costocervical trunk
Site: central + lateral thirds of posterior ribs
(a) bilateral
(b) unilateral on left side: left aortic arch with aberrant right subclavian artery below CoA
(c) unilateral on right side: right aortic arch and anomalous left subclavian artery below CoA

CONGENITAL ABSENCE OF PULMONARY VALVE

= massive regurgitation between pulmonary artery and RV
In 90% associated with: VSD, tetralogy of Fallot (50%)
• cyanosis (not in immediate newborn period)
• repeated episodes of respiratory distress; continuous murmur
• ECG: right ventricular hypertrophy
√ prominent main, right, and left pulmonary artery
√ RV dilatation (increased stroke volume)
√ partial obstruction of right / left mainstem bronchus ← compression by vessel
√ right-sided aorta (33%)

CONGESTIVE HEART FAILURE

Congestive Left Heart Failure

= increase in circulating blood volume with diminishing cardiac function → elevation of microvascular pressure of lung

Frequency: most common cause of interstitial + airspace edema of lungs

Cause:

(a) back pressure from LV: long-standing systemic hypertension, aortic valve disease, coronary artery disease, cardiomyopathy, myocardial infarction

(b) obstruction proximal to LV: mitral valve disease, LA myxoma, cor triatriatum

Histo:

(1) Interstitial phase: fluid in loose connective tissue around conducting airways and vessels + engorgement of lymphatics

(2) Alveolar phase: increase in alveolar wall thickness

(3) Alveolar airspace phase: alveoli filled with fluid with loss of alveolar volume; pulmonary fibrosis upon organization of intraalveolar fibrin (if chronic)

• LA pressure / pulmonary venous pressure > 12 mmHg (measured by wedging a pulmonary artery catheter [PAWP])

√ enlarged heart:

√ enlargement of LA (mitral stenosis)

√ enlargement of LA + LV (mitral regurgitation)

√ enlargement of LV (aortic valve disease)

1. **Flow inversion = cephalization of pulmonary vessels**

Cause: chronic elevation of LA pressure (as in left heart failure / mitral valve disease)

Pathophysiology:

long-standing ↑ of LA pressure → ↑ in atriovenous reflux; initially ↑ LA pressure is met with an ↑ tonus of LA wall (= absence of atrial enlargement in acute left heart failure); → eventually LA enlarges → inciting a protective atrial-pulmonary-vascular reflex vasospasm → narrowing of lower lobe vessels and ↓ atriovenous reflux

• pulmonary artery wedge pressure 13–17 mmHg

√ basal oligemia (= arterial + venous constriction)

√ hyperemia of upper lobes:

√ vessel diameter equal to / greater than comparable lower zone vessels

√ upper zone arteries wider than accompanying bronchus

√ vessel diameter in 1st anterior intercostal space > 3 mm

N.B.: flow inversion is never seen in pulmonary edema of renal failure / overhydration / low oncotic pressure

2. **Interstitial pulmonary edema** (invariably precedes alveolar edema) = engorgement of interstitium

• NO abnormal physical finding

• hypoxemia (ventilation-perfusion inequality)

• pulmonary artery wedge pressure > 17 mmHg

√ perihilar haze = loss of sharp definition of vascular markings in large perihilar interstitium

√ thickening of interlobular septa (Kerley lines)

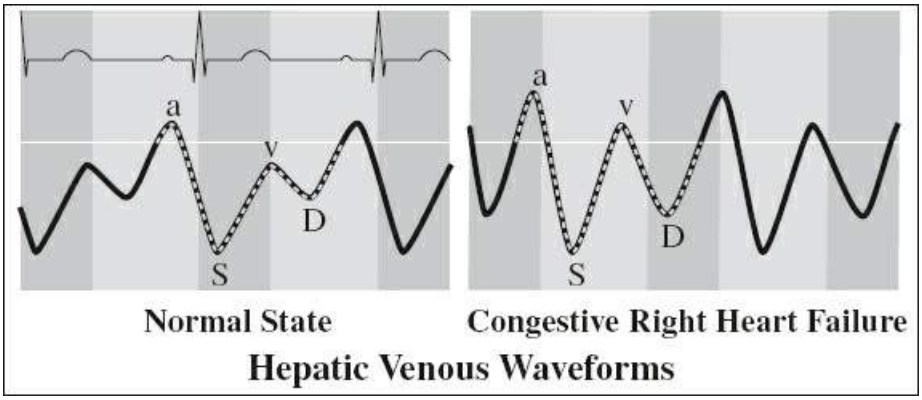
√ peribronchial cuffing = poorly defined increased bronchial wall thickness

√ thickening of interlobar fissures ← fluid accumulation in subpleural connective tissue layer
√ usually right pleural effusion (if PAWP > 20 mmHg)

3. **Alveolar pulmonary edema = airspace edema**
   Cause: acute LA pressure elevation → volume of capillary filtration exceeds that of lymphatic drainage
   • severe dyspnea / orthopnea; tachypnea + cyanosis
   • dry cough / copious frothy sputum
   • hypoxemia ← vascular shunting
   √ pulmonary venous pressure > 20 mmHg
   √ poorly defined patchy acinar opacities
   √ coalescence of acinar consolidation, particularly in medial ⅓ of lung
   √ air bronchograms
   √ butterfly / bat-wing distribution of consolidation (= consolidated hilum + uninvolved lung cortex)
   √ always coexists with interstitial pulmonary edema
4. **Generalized oligemia**
   Cause: aortic valvular disease

Congestive Right Heart Failure

• pitting edema of lower extremities
√ abnormal hepatic vein Doppler spectrum:
  √ abnormally tall *a* wave (increased right atrial pressure + volume toward end-diastole)
  √ abnormally tall *v* wave (increased right atrial pressure + volume toward end systole) of hepatic vein waveform
  √ normal relationship between *S* and *D* waves



Extrathoracic Manifestations of CHF

@ Hepatobiliary
  √ GB wall edema
  √ periportal edema
  √ enlarged IVC

CORONARY ARTERY FISTULA

= direct precapillary connection between branch of coronary a. + lumen of heart chamber / systemic or pulmonary circulation

Prevalence: 0.05–0.25% of coronary angiographies; 0.002% of general population

Cause: congenital (most), posttraumatic, iatrogenic

Hemodynamics: L-to-R shunt; pulmonary÷systemic blood flow = < 1.5÷1 (usually)

Involved coronary artery:

RCA (in 50–60%), LCA (in 40–42%), both (in < 5%)

Drain into:

RV (in 41–45%), RA (in 26%), pulmonary artery (in 15–17%), coronary sinus (7%), SVC

- asymptomatic (commonly LCA, small fistula)
- audible continuous heart murmur

√ may have normal CXR (in small shunts)

√ cardiomegaly + shunt vascularity (in large shunts)

Angio:

√ dilated tortuous coronary artery with anomalous connection

√ single (most) / multiple communications / network of fine vessels

Cx: myocardial ischemia / sudden cardiac death (in large shunt), CHF, endocarditis, arrhythmia, rupture, embolization

Rx: observation, surgical ligation, transcatheter embolization

COR TRIATRIATUM

= rare congenital anomaly in which a fibromuscular septum with a single stenotic / fenestrated / large opening separates the embryologic common pulmonary vein from the LA:

(1) proximal / accessory chamber lies posteriorly receiving pulmonary veins (= primitive common pulmonary vein)

(2) distal / true atrial chamber lies anteriorly connected to left atrial appendage + emptying into LV through mitral valve

Embryology: failure of common pulmonary vein to incorporate normally into left atrium → persistence of primitive splanchnic connections

Associated with: ASD, PDA, anomalous pulmonary venous drainage, left SVC, VSD, tetralogy of Fallot, atrioventricular canal

- symptoms of pulmonary venous obstruction clinically similar to mitral valve stenosis:
  - pulmonary hypertension, heart failure with pulmonary edema
  - dyspnea, hemoptysis, failure to thrive
  - frequent pulmonary infections

√ pulmonary venous distention + interstitial edema + dilatation of pulmonary trunk + pulmonary arteries (in severe obstruction)

√ enlarged RA + RV

√ mild enlargement of LA

Angio:

√ dividing membrane on levophase of pulmonary arteriogram

MR:

√ accessory chamber (representing the common pulmonary vein) communicates with LA through a stenosed opening

√ accessory chamber lies always above level of LA appendage

Prognosis (if untreated):

usually fatal within first 2 years of life; 50% 2-year survival; 20% 20-year survival

Flow gradient across stenosis + RV pressures are the most important pieces of information to assess the degree of pulmonary venous obstruction!

Rx: surgical excision of obstructing membrane

DEEP VEIN THROMBOSIS (DVT)

Incidence: ~ 600,000 new cases annually in USA; 1÷100 patients with DVT dies (= 15% of in-hospital deaths); 6–7 million stasis skin changes; in 0.5% cause of skin ulcers

Pathogenetic factors:

1. Hypercoagulability
2. Decreased blood flow / stasis
3. Intimal injury
4. Decreased fibrinolytic potential of veins
5. Platelet aggregation

Risk factors:

1. Surgery, esp. on legs / pelvis: orthopedic (45–50%) especially total hip replacement > 50%), gynecologic (7–35%), neurosurgery (18–20%), urologic (15–35%), general surgery (20–25%)
2. Severe trauma
3. Prolonged immobilization: hemiplegic extremity, paraplegia + quadriplegia, casting / orthopedic appliances
4. Malignancy (risk factor 2.5) = Trousseau phenomenon
5. Obesity (risk factor 1.5)
6. Diabetes
7. Pregnancy (risk factor 5.5) with peak at 36 weeks and for 8–12 weeks post partum
   Cause: progesterone-induced venodilation, pelvic venous compression by gravid uterus
8. Medication: birth control pills, estrogen replacement, tamoxifen (risk factor 3.2)
9. Decreased cardiac function: congestive heart failure, myocardial infarction (20–50%; risk factor 3.5)
10. Inflammatory bowel disease
11. Age > 40 years (risk factor 2.2)
12. Varicose veins
13. Previous DVT (risk factor 2.5)
14. Patients with blood group A > blood group 0
15. Polycythemia
16. Smoking

Pathologic terminology:

"***organized thrombus***" = transition to a vascularized lesion of connective tissue adherent to vessel wall

"***recanalized thrombus***" = vascular channel network within an organized clot reducing it to septations of collagen and elastic fibers often lined by endothelium

Location:

1. Dorsal veins of calf (± ascending thrombosis)
2. Iliofemoral veins (± descending thrombosis)
3. Peripheral + iliofemoral veins simultaneously
4. rare: internal iliac, ovarian, ascending lumbar veins

Side: L÷R = 7÷3 ← compression of left common iliac vein by left common iliac artery (arterial pulsations lead to chronic endothelial injury with formation of intraluminal spur (in 22% of autopsies + in 90% of patients with DVT)

- Local symptoms ← obstruction / phlebitis usually only when (a) thrombus occlusive, (b) clot extends into popliteal / more proximal vein (14–78% sensitivity, 4–21% specificity):
  - warmth, swelling (measurement of circumference)
  - deep crampy pain in affected extremity: worse in erect position, improved while walking
  - tenderness along course of affected vein
  - Homans sign = calf pain with dorsal flexion of foot
  - Payr sign = pain upon compression of sole of foot
  - ◊ ⅔ of deep vein thromboses are clinically silent:
    - ◊ DVT diagnosed ante mortem in < 30%
    - ◊ Only 10–33% of patients with fatal PE are symptomatic for DVT
  - ◊ Clinically suspected DVT accurate in only 26–45%:
    - ◊ DVT symptomatology due to other causes in 15–35%
    - ◊ Negative bilateral venograms in 30% of patients with angiographically detected pulmonary emboli (**big bang** theory = clot embolizes in toto to the lung leaving no residual in vein)

Venography (89% sensitive, 97% specific, 11% FN, 5% FP):

◊ venography aborted / nondiagnostic in 5%

Risk: postvenography phlebitis (1–2%), contrast reaction, contrast material-induced skin slough, nephropathy

√ intraluminal filling defect constant on all images

√ nonfilling of calf veins

√ inadequate filling of common femoral vein and external + common iliac veins

B-Mode US (88–100% sensitive, 92–100% specific, > 90% accurate for DVT in thigh and popliteal veins):

A. ACUTE DEEP VEIN THROMBOSIS
   - √ NO complete luminal collapse with venous compression (DDx: deformity + scarring from prior DVT; technical difficulties in adductor canal + distal deep femoral vein)
   - √ visualization of clot within vein (DDx: slow flowing blood; machine noise):
     - √ homogeneous poorly echogenic / anechoic substance within venous lumen
     - √ smooth border of thrombus
   - √ < 75% increase in diameter of common femoral vein during Valsalva
   - √ venous diameter at least twice that of adjacent artery suggests thrombus < 10 days old

B. SUBACUTE / CHRONIC DEEP VEIN THROMBOSIS
   - √ echogenic material within venous lumen
   - √ irregular surface of thrombus
   - √ incomplete compressibility of vein

Doppler US:

√ absence of spontaneity (= any waveform recording): NOT RELIABLE in peripheral veins

√ continuous venous signal = absence of phasicity (= no cyclic variation in flow velocity with respiration, ie, ↓ in expiration and ↑ in inspiration) is SUSPICIOUS for proximal obstruction

√ attenuation / absence of augmentation (= no increase in flow velocity with distal compression) indicates venous occlusion / compression in intervening venous segments

√ pulsatile venous flow is a sign of congestive heart failure / pericardial effusion / cardiac tamponade / pulmonary embolism with pulmonary hypertension

NEMR:

N.B.: limited by flow signal artifacts

√ high SI / absence of low SI flow within vein on true FISP sequence

√ low-signal–intensity filling defect in a high-signal-intensity patent vein on true FISP sequence

√ absence of normal low-signal–intensity flow void in a patent vessel on T2WI

√ variable signal intensity on T1WI depending on age of luminal blood products

Venous Occlusion Plethysmography:

= temporary obstruction of venous outflow by pneumatic cuff around mid-thigh inflated above venous pressure → progressive increase in blood volume in lower leg; upon release of cuff → limb quickly returns to resting volume with prompt venous runoff; limb blood volume changes are measured by impedance plethysmography in which a weak alternating current is passed through the leg; the electrical resistance varies inversely with blood volume; current strength is held constant so that voltage changes directly reflect blood volume changes

› 87–95–100% sensitive, 92–100% specific for above-knee DVT

› 17–33% sensitive for below-knee DVT

√ ↓ initial rise in venous capacitance (= venous volume)

√ delay in venous outflow (= "fall" of curve) measured at 3 sec

False positives (6%): severe cardiopulmonary disease, pelvic mass, reduced arterial inflow

False negatives: calf vein thrombosis, small thrombus

^{125}I-Labeled Fibrinogen:

› 90% sensitive for calf vein thrombus

› 60–80% sensitive for femoral vein thrombus

› insensitive for thrombus in upper thigh / pelvis

Risk: results not available for several days, possible virus transmission

False positives: hematoma, inflammation, wound, old small thrombus isolated in common femoral / iliac v.

Cx:

(1) **Pulmonary embolism** (50%): in 90% from lower extremity / pelvis; in 60% with proximal "free-floating" / "widow-maker" thrombus; occurs usually between 2nd to 4th (7th) day of thrombosis

Source of pulmonary emboli:

multiple sites (⅓), cryptogenic in 50%;

(a) lower extremity (46%)
(b) inferior vena cava (19%)
(c) pelvic veins (16%)
(d) mural heart thrombus (4.5%)
(e) upper extremity (2%)

Likelihood of pulmonary embolism:
77% for iliac veins, 35–67% for femoropopliteal vein, 0–46% for calf veins

(2) **Postphlebitic syndrome** in 20% of cases with DVT ← valvular incompetence ← recanalization to a smaller lumen with focal wall changes

(3) **Phlegmasia** [*phlegma* , Greek = inflammation; *dolens* , Latin = painful] = blanching of skin (phlegmasia **alba dolens**) / blue leg (phlegmasia **cerulea dolens**) → severely impaired venous drainage → acute limb ischemia → gangrene

Prognosis: tibial / peroneal venous thrombi resolve spontaneously in 40%, stabilize in 40%, propagate into popliteal vein in 20%

Prophylaxis: intermittent compression of legs, heparin, warfarin

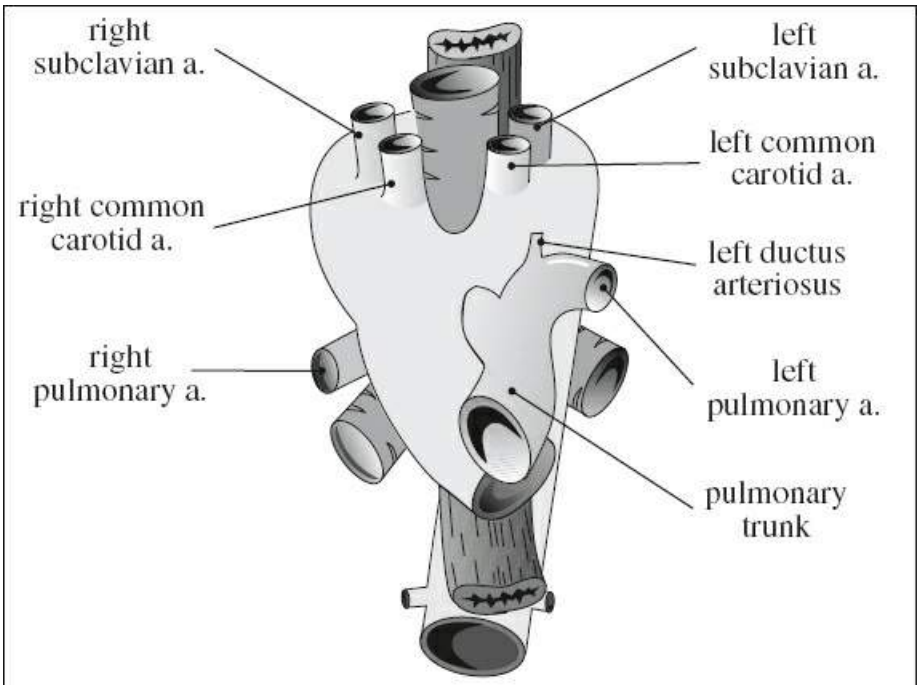
Rx:

(1) Heparin IV

(2) Systemic anticoagulation (warfarin) for ≥ 3 months decreases risk of recurrent DVT in initial 3 months from 50% to 3% + fatal pulmonary embolism from 30% to 8%; necessity for anticoagulation in DVT of calf veins is CONTROVERSIAL

(3) Caval filter (10–15%) in patients with contraindication / complication from anticoagulation or progression of DVT / PE despite adequate anticoagulation

DDx: pseudothrombophlebitis (= signs + symptoms of DVT produced by popliteal cyst / traumatic hematoma)



Double Aortic Arch

DOUBLE AORTIC ARCH

◊ Most common + serious type of a complete vascular ring; usually isolated condition

Embryology: failure of regression of both right + left embryonic 4th arches, joined to form dorsal aorta

Types:

1. Dominant right (posterior) arch (75%)
2. Dominant left (anterior) arch (20%)
3. Symmetric arches of same size (5%)

The less dominant arch is atretic in ⅓ !

Frequency: 55% of all vascular rings

Age: usually detected in infancy

- usually asymptomatic; stridor, dyspnea, recurrent pneumonia
- dysphagia (less common than respiratory symptoms, more common after starting baby on solids)

Location: descending aorta in 75% on left, in 25% on right side; smaller arch anterior in 80%; right arch larger + more cephalad than left in 80%

√ two separate arches arise from single ascending aorta

√ each arch joins to form a common descending aorta

√ trachea in midline:

- √ impressions may be present on both sides of trachea: usually R > L (in older children)
- √ trachea narrowed and displaced posteriorly with small anterior impression

Esophagram:

- √ broad horizontal posterior indentation at the level of 3rd / 4th thoracic vertebra ← right arch crossing obliquely to join left
- √ bilateral esophageal indentations with a reversed S-shaped configuration (= right indentation higher than left)

CT:

- √ "four-artery" sign = each arch gives rise to 2 dorsal subclavian + 2 ventral carotid arteries evenly spaced around trachea on section cephalad to aortic arch

DDx: right arch with aberrant left subclavian artery (when dominant arch on right indistinguishable by esophagram)

DOUBLE-OUTLET RIGHT VENTRICLE

= DORV = TAUSSIG-BING HEART

= most of the aorta + pulmonary artery arise from the RV ← maldevelopment of conotruncus

Prevalence: 127÷1,000,000 live births

Hemodynamics:

similar to: VSD, tetralogy of Fallot, transposition of great arteries, single ventricle, atrioventricular atresia

fetus: NO CHF in utero (in absence of other obstructing anomalies)

neonate: ventricular work overload → CHF

Associated with: VSD (100%), pulmonary stenosis / atresia (75%), mitral stenosis / atresia, PDA

◊ location of VSD affects physiologic function and classification relative to semilunar valves into subaortic (50%), subpulmonic (30%), uncommitted, doubly committed

√ NO continuity between mitral valve + adjacent semilunar valve (PATHOGNOMONIC)

√ aorta posterior / parallel / anterior to pulmonary artery:

√ aorta and pulmonary artery side by side with aorta in D-malposition on the right (most frequent)

√ aorta overriding the interventricular septum with predominant connection to RV

√ normal / hypoplastic / absent LV

DUCTUS ARTERIOSUS ANEURYSM

= fusiform aneurysm of ductus arteriosus, usually patent toward aorta + completely / incompletely occluded toward pulmonary a.

Prevalence: < 100 cases

Classification:

(a) according to age: infantile, childhood, adult type

(b) according to cause: congenital, infectious, traumatic

Pathogenesis: ? delay in closure, ? myxoid degeneration of ductus wall, ? abnormal elastic fibers

Age: most < 2 months of age

• dyspnea, tachypnea, hoarseness

√ pulmonary artery displaced anteromedially

√ distal aortic arch displaced laterally

CXR:

√ left upper mediastinal mass in aorticopulmonary window

√ tracheal displacement to right + anteriorly / posteriorly

√ consolidation of adjacent lung (compression, fibrosis, hemorrhage)

CT:

√ contrast-enhancing mass in classic location

ECHO:

√ cystic mass with pulsatile flow

Cx: rupture, dissection, infection, thromboembolic disease, phrenic nerve compression

Prognosis: usually fatal (without prompt surgery)

EBSTEIN ANOMALY

[Wilhelm Ebstein (1836–1912), internist in Breslau, Germany]

◊ Most common cause of congenital tricuspid regurgitation.
=atrialization of RV (HALLMARK) = apical / downward displacement of septal + posterior leaflets of dysplastic tricuspid valve into inflow portion of RV

RV is divided into:

(a) a large superior atrialized inflow portion with thin ventricular wall (incorporating part of the RV into the RA), and

(b) a small inferior functional chamber with shortened chordae tendineae

Valve morphology:

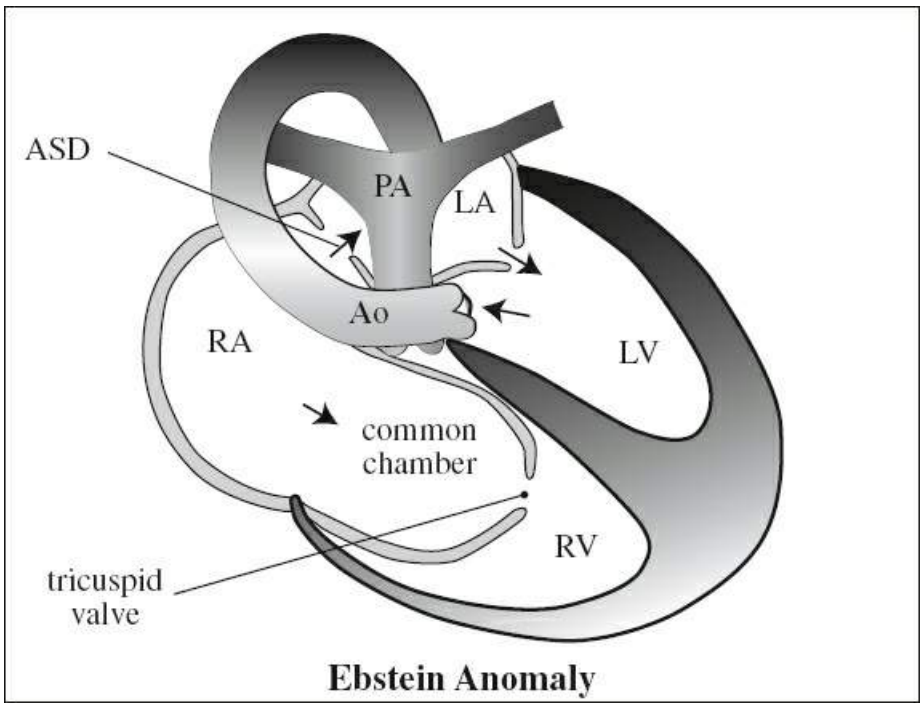
inappropriately low attachment of posterior ± septal malformed defective tricuspid valve leaflets; only anterior leaflet attaches normally to tricuspid annulus, but may be dysplastic / sail-like

Etiology: oral lithium therapy during pregnancy (10%)

◊ 0.5–0.7% of all CHD!

Hemodynamics:

tricuspid valve insufficiency → tricuspid regurgitation ("ping-pong" volume) + severely dilated RA; RA dilatation stretches interatrial septum → incompetence of foramen ovale (R-to-L shunt) in 75%



Ebstein Anomaly

RA	↑	RV	↓	Main PA	↔
Pulm. vessels	↔/↓				
LA	↔	LV	↔	Ao	↔

Associated with: ostium-secundum–type ASD / patent foramen ovale (R-to-L shunt), VSD, PDA, pulmonary atresia

- symptoms and prognosis depend on amount of tricuspid regurgitation, right ventricular function, and cyanosis:

- ± cyanosis in neonatal period (depending on degree of R-to-L shunt): may improve / disappear postnatally with decrease in pulmonary arterial pressure
- CHF in utero / in neonate (in 50%)
- systolic murmur (tricuspid insufficiency)
- **Wolff-Parkinson-White syndrome** (10%) = paroxysmal supraventricular tachycardia / right bundle branch block (responsible for sudden death)
  Cause: conduction system develops during formation of tricuspid valve adjacent to it

Ebstein anomaly is the ONLY cyanotic CHD in which aorta and pulmonary trunk are hypoplastic (= smaller than normal)!

√ "box-shaped / funnel-like" cardiomegaly:
  √ extreme RA enlargement ← insufficient tricuspid valve forming a common right ventriculoatrial chamber
  √ dilated right ventricular outflow tract
√ IVC + azygos dilatation ← tricuspid regurgitation
√ normal LA
√ calcification of tricuspid valve may occur
√ distance of septal leaflet to anterior mitral valve leaflet:
  √ > 15 mm in child < 14 years of age
  √ > 20 mm in adult
  √ > 0.8 mm/cm^2 of body surface area = DIAGNOSTIC

MR:
  √ marked right atrial enlargement
  √ small right ventricle ± dilatation of RV infundibulum

ECHO:
  √ large "sail-like" tricuspid valve structure within dilated right heart
  √ tricuspid regurgitation identified by Doppler ultrasound

Prognosis: sudden death ← fatal atrial arrhythmia; 50% infant mortality; 13% operative mortality

Survival rate: 70% at 2 years, 50% at 13 years; survival into adulthood if valve functions normally

Rx: 1. Digitalis + diuretics
2. Tricuspid valve prosthesis

EISENMENGER COMPLEX

= EISENMENGER DEFECT
= (1) high VSD ± overriding aorta with hypoplastic crista supraventricularis
  (2) RV hypertrophy
  and as consequence of increased pulmonary blood flow:
  (3) → dilatation of pulmonary artery + branches
  (4) → intimal thickening + sclerosis of small pulmonary arteries + arterioles
• cyanosis appears in 2nd + 3rd decade with shunt reversal

EISENMENGER SYNDROME

= EISENMENGER REACTION
= development of high pulmonary vascular resistance after many years of L-to-R shunt (ASD, PDA, VSD) → ↑ pulmonary blood flow → bidirectional (= balanced) shunt and ultimately → shunt reversal (R-to-L shunt)

Etiology:
pulmonary microscopic vessels undergo reactive muscular hypertrophy, endothelial thickening, in situ thrombosis, tortuosity + obliteration; once initiated, pulmonary hypertension accelerates vascular reaction → increasing pulmonary hypertension in a vicious cycle

with RV failure + death

Path: adaptive anastomotic pathways connect plexiform lesions of pulmonary arterial vessels to bronchial arteries supplying terminal bronchioles + vasa vasorum of pulmonary arteries

Pathologic classification of severity (Heath & Edwards):

Grade I = medial hypertrophy of muscular pulmonary arteries and arterioles
- potentially reversible

Grade II = grade I + intimal proliferation in small muscular arteries and arterioles
- potentially reversible

Grade III = grade II + intimal laminar fibrosis + progressive vessel obliteration
- borderline for reversibility

Grade IV = occlusion of vessels with progressive aneurysmal dilatation of small arteries nearby
- irreversible

Grade V = tortuous "glomeruloid" channels within proliferation of endothelial cells (= plexiform + angiomatoid lesions)
- irreversible

Grade VI = thrombosis + necrotizing arteritis
- irreversible

CXR:
- √ pronounced dilatation of central pulmonary arteries (pulmonary trunk, main pulmonary a., intermediate branches)
- √ pruning of peripheral pulmonary arteries
- √ enlargement of RV + RA (proportionate to volume overload)
- √ LA + LV return to normal size (with decrease of L-to-R shunt ← markedly elevated pulmonary vascular resistance)
- √ normal pulmonary veins (unless superimposed cardiac volume overload):
  - √ pulmonary veins NOT distended ← NO increase in pulmonary blood flow)
  - √ NO redistribution of pulmonary veins (normal venous pressure)

CT:
- √ massive aneurysmal dilatation of pulmonary trunk
- √ linear calcification + thrombus in central pulmonary arteries
- √ atheromatous calcification of pulmonary arteries
- √ mural calcification / aneurysmal dilatation of ductus arteriosus (in case of patent ductus arteriosus)

Dx: measurement of pulmonary artery pressure + flow via catheter

Rx: heart-lung transplant

ENDOCARDIAL CUSHION DEFECT

= ECD = ATRIOVENTRICULAR SEPTAL DEFECT
= PERSISTENT OSTIUM ATRIOVENTRICULARE COMMUNE
= PERSISTENT COMMON ATRIOVENTRICULAR CANAL

= persistence of primitive atrioventricular canal + anomalies of AV valves ← interruption of normal development of endocardial tissues

Frequency: 4% of all cases of CHD

Endocardial cushion = forms lower portion of atrial septum, upper portion of interventricular septum + septal leaflets of MV and TV

Cause: deficiency of conus + sinus portions of interventricular septum → narrowing of left ventricular outflow tract

A. INCOMPLETE / PARTIAL ECD

= (1) Ostium primum ASD
(2) Separate tricuspid + mitral valves with cleft in anterior mitral valve leaflet / trileaflet
(3) Accessory short chordae tendineae arising from anterior MV leaflet insert directly into crest of deficient ventricular septum

√ left atrioventricular valve usually has 3 leaflets with a wide cleft between anterior + septal leaflet

√ **"gooseneck"** deformity on LV angiography = concavity of IVS below MV + elongation and narrowing of LVOT ← downward attachment of anterior MV leaflet close to interventricular septum by accessory chordae tendineae

√ communication between LA–RA or LV–RA, occasionally LV–RV

√ right atrioventricular valve usually normal

B. TRANSITIONAL / INTERMEDIATE ATRIOVENTRICULAR CANAL (uncommon)

= (1) Ostium primum ASD
(2) High membranous VSD
(3) Wide clefts in septal leaflets of both AV valves
(4) Bridging tissue between anterior + posterior common leaflet of both AV valves

C. COMPLETE ECD = AV COMMUNIS = COMMON AV CANAL

= (1) Ostium primum ASD above
(2) Posterior inlet membranous VSD below
(3) One AV valve common to RV + LV with 5–6 leaflets
(a) anterior common "bridging" leaflet
(b) two lateral leaflets
(c) posterior common "bridging" leaflet

Type 1 = chordae tendineae of anterior bridging leaflet attached to both sides of ventricular septum

Type 2 = chordae tendineae of anterior leaflet attached medially to anomalous papillary muscle within RV, but unattached to septum

Type 3 = free-floating anterior leaflet with chordae attachments to septum; only type becoming symptomatic in infancy!

Associated with:

(1) Down syndrome:
in 25% of trisomy 21 an ECD is present;
in 45% of ECD trisomy 21 is present
(2) Asplenia, polysplenia

√ common atrioventricular orifice

√ oval septal defect consisting of a low ASD + high VSD

√ atrial septum secundum usually spared ("common atrium" if absent)

√ frequently associated with mesocardia / dextrocardia

Hemodynamics:

fetus: atrioventricular valves frequently incompetent leading to regurgitation + CHF

neonate: L-to-R shunt after decrease of pulmonary vascular resistance resulting in pulmonary hypertension

• incomplete right bundle branch block (distortion of conduction tissue); left-anterior hemiblock

CXR:

◊ Radiographic findings similar to ASD, but more marked

√ increased pulmonary vascularity (= shunt vascularity)

√ redistribution of pulmonary blood flow (mitral regurgitation)

√ enlarged pulmonary artery

√ diminutive aorta ← L-to-R shunt

√ cardiac enlargement out of proportion to pulmonary vascularity ← L-to-R shunt + mitral insufficiency

√ enlarged RV + LV

√ enlarged RA ← LV blood shunted to RA

√ normal-sized LA ← ASD

ECHO:

√ visualization of ASD + VSD + valve + site of insertion of chordae tendineae

√ paradoxical anterior septal motion ← ASD

√ atrioventricular insufficiency + shunts identified by Doppler ultrasound

Angio:

AP projection:

√ "gooseneck deformity" (in diastole) ← deficiency of conus and sinus portion of interventricular septum below mitral valve with narrowing of LVOT

√ cleft in anterior leaflet of mitral valve (in systole)

√ mitral regurgitation

Hepatoclavicular projection in 45° LAO + C-C 45° (= 4-chamber view):

√ best view to demonstrate LV-RA shunt

√ best view to demonstrate VSD (inflow tract + posterior portion of interventricular septum in profile)

LAT projection:

√ irregular appearance of superior segment of anterior mitral valve leaflet over LVOT

Prognosis: 54% survival rate at 6 months, 35% at 12 months, 15% at 24 months, 4% at 5 years; 91% long-term survival with primary intracardiac repair, 4–17% operative mortality

ENDOCARDIAL FIBROELASTOSIS

= diffuse endocardial thickening of LV + LA ← deposition of collagen + elastic tissue

Etiology:

(1) ? Viral infection

(2) Secondary endocardial fibroelastosis
= subendocardial ischemia in critical LVOT obstruction: aortic stenosis, coarctation, hypoplastic left heart syndrome

• sudden onset of CHF during first 6 months of life
√ mitral insufficiency:
  (a) involvement of valve leaflets
  (b) shortening + thickening of chordae tendineae
  (c) distortion + fixation of papillary muscles
√ enlarged LV (= dilatation of hypertrophied LV) ← mitral regurgitation
√ restricted LV motion
√ enlarged LA
√ pulmonary venous congestion + pulmonary edema
√ LLL atelectasis ← compression of left lower lobe bronchus by enlarged LA
Prognosis: mortality almost 100% by 2 years of age

Carcinoid Heart Disease

Etiology: secretion of 5-hydroxytryptamine by tumor cells metastatic to liver → deposition of fibrous tissue on endocardial surfaces of right heart
Prevalence: in up to 60% of patients with carcinoid syndrome
Location: both tricuspid and pulmonary valve leaflets + corresponding subvalvular apparatus
√ thickening of valve leaflets and cusps → eventually retracted + shortened + immobile
√ thickening + fusion of chordae
Cx: valvular regurgitation, valvular stenosis

EOSINOPHILIC HEART DISEASE

= manifestation of hypereosinophilic syndrome
Cause: active damage of endomyocardium by toxic cationic proteins released after degranulation of infiltrated eosinophils
Pathophysiology: Fibrous tissue deposition within endocardium + adjacent myocardium along inflow tracts and apices of one / both ventricles → rigidity of ventricular walls, papillary muscles, atrioventricular valves
Phases:
(1) Acute necrosis
  • palpitations, dyspnea, fever, malaise
(2) Mural thrombosis
  • infarction ← thromboembolism
  • DVT ← hypercoagulable state
(3) Fibrosis
  • right / left ventricular dysfunction, valvular incompetence, thromboembolic episodes, organ dysfunction

MR:
√ ventricular wall thickening
√ regional wall motion abnormalities
√ extensive myocardial hyperintensity on T2WI
CEMR (10-min delay):
√ CHARACTERISTIC 3-layered appearance of ventricular wall:
√ outer normal nulled (black) myocardium

√ adjacent enhancing hyperintense subendocardium ← fibrosis
√ innermost nonenhancing mural thrombus

√ pericardial effusion with variable degree of pericardial enhancement ← pericarditis (rare)

ECHO / CT:

√ endocardial thickening, cardiac mural thrombus
√ restrictive ventricular diastolic (filling) dysfunction ← reduced size, atrial enlargement, atrioventricular valve incompetence
√ nonenhancing intracardiac mural thrombus
√ fibrotic endocardial thickening

FIBROMUSCULAR DYSPLASIA

= nonatherosclerotic noninflammatory angiopathy of unknown pathogenesis caused by proliferation of muscular + fibrous elements in middle- and small-caliber arteries

Prevalence: 0.6–1.1%; < 1% of cerebral angiographies

Age: children + young adults < 30–40 years; ²/₃ > 50 years; M÷F = 1÷3 to 1÷4

• hypertension, progressive renal insufficiency, neurologic deficits
• decreased peripheral pulses, bruit, asymmetric limb pressures

Location:

@ Craniovertebral arteries (25–30%):
cervical + intracranial ICA (85%), extracranial carotid artery (30%), vertebral artery (7–10%); both anterior + posterior circulations (8%); bilateral (60–65%)
Site: adjacent to C1-C2
Associated with: brain ischemia (up to 50%), intracranial aneurysms (up to 30%), intracranial tumors (30%), bruits, trauma

@ Abdominal aorta:
renal artery (60–75%), other aortic branches (in 1–2%: celiac a., hepatic a., splenic a., mesenteric a., iliac artery)
◊ Simultaneous involvement of renal / muscular arteries in 3%

1. **Intimal Fibroplasia** (1–2%)
= INTIMAL HYPERPLASIA
• progressive
Path: circumferential / eccentric fibrous tissue between intima + internal elastic lamina
Age: children + young adults; M÷F = 1÷1
Site: main renal artery + major segmental branches; often bilateral
√ focal narrow annular radiolucent band
√ smooth tubular stenosis
√ poststenotic fusiform dilatation
Cx: spontaneous dissection
DDx: atherosclerosis, Takayasu arteritis

2. **Medial Fibroplasia** (60–85%)
= fibromuscular hyperplasia = medial fibroplasia with microaneurysms
Age: 20–50 years; typically affects women; common cause of renal artery stenosis in children
Path: multiple fibromuscular ridges + severe mural thinning with loss of smooth muscle

+ internal elastic lamina

Site: mid + distal renal artery + branches; bilateral in 50%

√ "string-of-beads" sign = alternating areas of weblike stenoses + aneurysms (which exceed the normal diameter of the artery)

√ single tubular focal stenosis

Cx: dissection

3. **Perimedial Fibroplasia** (rare)

= SUBADVENTITIAL FIBROPLASIA

Age: young females

Path: fibroplasia of outer 1/2 of media replacing external elastic lamina

Site: distal (mostly right) main renal artery

√ long irregular stenosis

√ beading = NO aneurysm formation (diameter of beads not wider than normal diameter of artery)

4. **Medial Hyperplasia** (5–15%)

= FIBROMUSCULAR HYPERPLASIA

Path: smooth muscle + fibrous tissue hyperplasia within arterial media

Site: main renal artery and branches

√ long smooth concentric tubular narrowing

DDx: Takayasu arteritis, sclerosing arteritis, vessel spasm, arterial hypoplasia

5. **Adventitial Fibroplasia** (< 1%)

= SUBADVENTITIAL / PERIADVENTITIAL HYPERPLASIA

Path: adventitial + periarterial proliferation in fibrofatty tissue

Site: main renal artery, large branches

√ long segmental stenosis

<u>added to original 5 types:</u>

6. **Medial Dissection** (5–10%)

Path: new channel in outer ⅓ of media within external elastic lamina

Site: main renal artery + branches

√ false channel, aneurysm

7. **Atypical Fibromuscular Dysplasia**

(= ? variant of intimal fibroplasia)

√ web = smooth / corrugated mass involving only one wall of vessel + projecting into lumen

DDx: atherosclerotic disease, posttraumatic aneurysm

VARIANT: **Segmental mediolytic arteriopathy**

= rare noninflammatory disease of small + medium arteries

Histo: focal segmental disruption of medial smooth muscle cells with mediolysis

√ string-of-beads appearance

√ irregular stenoses + aneurysms

Cx: dissection (in 3%), macroaneurysm formation, intramural hemorrhage, subarachnoid hemorrhage

Prognosis: tends to remain stable / minimal progression of lesions in 20% causing decline in renal function

Rx: (1) Resection of diseased segment with end-to-end anastomosis
(2) Replacement by autogenous vein graft, excision + repair by patch angioplasty
(3) Transluminal balloon angioplasty (90% success rate with very low restenosis rate)

FLAIL MITRAL VALVE

Cause:
(1) Ruptured chordae tendineae in rheumatic heart disease, ischemic heart disease, bacterial endocarditis
(2) Ruptured head of papillary muscle in acute myocardial infarction, chest trauma

Location: chordae to leaflet from posteromedial papillary muscle (single vessel blood supply)
√ deep holosystolic posterior movement of leaflet
√ random anarchic motion pattern of flail parts in diastole
√ excessively large amplitude of opening of aML

HENOCH-SCHÖNLEIN PURPURA

[Eduard Heinrich Henoch (1820–1910, pediatrician in Berlin and director of the first children's hospital in Germany]
[Johann Lukas Schönlein (1793–1864), German physician in Bamberg, the cradle of German hospital medicine, and at the University of Würzburg, where he introduced bedside teaching]
= I G A VASCULITIS
= most common systemic allergic hypersensitivity-related acute small-vessel vasculitis in children

Incidence: 20÷100,000 annually; mostly occurring in winter
Precipitated by: bacterial (b-hemolytic Streptococcus) / viral infection (URI in 50%), allergies, insect sting, drugs (eg, penicillin, sulfonamides, aspirin), certain foods
Cause: deposition of IgA-dominant immune complexes in vessel walls (venules, capillaries, arterioles)
Peak age: 7 (range, 3–15) years + adults > 20 years (in up to 30%); M÷F = 1.5÷1.0
◊ Most common vasculitis 4–7 years of age
Path: acute leukocytoclastic small-vessel vasculitis with IgA deposits at dermoepidermoid junction and renal mesangium

- often begins as an upper respiratory tract infection
- 3–4 weeks mean duration of symptoms; at least 1 recurrence (⅓)

@ Skin disease
- nonthrombocytopenic petechial / maculopapular skin rash
- palpable purpura concentrated in dependent / pressure-bearing regions of lower extremities + buttocks + extensor surfaces of arms (95–100%)

@ Joint disease (60–84%)
- arthralgias / arthritis of large joints

@ GI tract involvement (57–65–76%)
- may precede skin rash / within 1 week of onset of rash
- colicky abdominal pain ± diarrhea, nausea, vomiting
- GI bleeding ± melena

√ multifocal short-segment (< 15 cm) small bowel wall thickening of 7–12 mm (← intramural hemorrhage + edema) with skipped areas (DDx from other types of vasculitis)
√ "comb" sign = hypervascular engorged vasa recta
√ intestinal dilatation
√ ± bowel ulceration
√ mesenteric fat stranding + adenopathy of < 1.5 cm

@ Renal disease (20–100%)
- microscopic hematuria + proteinuria in 50%
- nephrotic syndrome in 10%
- proliferative glomerulonephritis with IgA deposits demonstrated by immunofluorescence (in up to ⅓)

√ normal / bilaterally enlarged kidneys
√ increased echogenicity of renal cortex
√ ± intramural hematoma of urinary bladder / ureter

@ Scrotal disease (15–37%)
√ mostly bilateral scrotal wall thickening
√ epididymal enlargement, reactive hydrocele
√ ± orchitis

@ CNS (rare)
√ hypertensive / uremic encephalopathy
√ focal ischemic / hemorrhagic lesions

Cx: (1) Bowel infarct / perforation / irreducible ileocecal intussusception (1–3–5%)
(2) Renal insufficiency (10–20%), end-stage renal disease (5%)

Dx: 4 diagnostic criteria:
(1) Age < 20 years at onset
(2) Palpable purpura
(3) Gastrointestinal bleeding
(4) Biopsy evidence of granulocytes around small arteriolar + venular walls (skin biopsy)

Rx: supportive; high doses of corticosteroids and azathioprine; IV immunoglobulin therapy
◊ Radiologic diagnosis avoids unnecessary surgery!

Prognosis: self-limiting without requiring treatment in 37% of adults + 60% of children

Mortality: 60% during 1st year of life

DDx: SLE (multiple segments of symmetric bowel thickening in jejunum + ileum, bowel dilatation, increased attenuation of mesentery, ascites); Yersinia enterocolitis (terminal ileum involved); Crohn disease (erythema nodosum + pyoderma gangrenosum)

HEMANGIOMA

= true neoplasm with vascular channels lined by proliferating endothelial cells

Infantile Hemangioma

= CAPILLARY HEMANGIOMA

Prevalence: 2–3% in all children; higher in prematurity
◊ Most common vascular tumor of infancy

Age: normally not visible at birth; manifest during first few weeks after birth; often evident by 3 months of age; M÷F = 1÷3 to 1÷5

Histo:

(a) proliferating phase = hyperplastic proliferating endothelial cells forming syncytial masses with ↑ metabolic turnover and ↑ number of mast cell
- strawberry-like pulsatile warm mass
- in first few weeks of life
- rapid growth with subsequent regression

(b) involuting phase = thinning of endothelial lining with progressive perivascular deposition of fibrofatty tissue
- slow constant regression into grayish dark red mass
- regression completed by age 7–10 years

Location: face and neck (60%), trunk (25%), extremity (15%)

- subcutaneous strawberry-like bluish-red mass with bruit, pulsatility and warmth
- rapid growth during first few months (= proliferating phase)

MR:

√ well-defined lobulated mass with high SI on T2WI
√ intermediate SI on T1WI
√ flow voids within high-flow feeding arteries and draining veins on SE images
√ high signal intensity on GRE images
√ NO perilesional edema
√ early intense uniform enhancement without AV shunting
√ heterogeneous lesion with foci of increased SI intensity on T1WI (= fatty replacement) + less avid enhancement during involuting phase

Rx: usually none; needed when symptomatic / in region with possible secondary loss of function or lifetime aesthetic impairment: propranolol / embolization / surgery

Congenital Hemangioma

Age: present at birth (fully grown); M÷F = 1÷1

(a) rapidly involuting congenital hemangioma
- complete regression during first 2 years of life

(b) noninvoluting congenital hemangioma
- growth proportional to that of child without regression

MR:

√ similar to infantile hemangioma

HETEROTAXY SYNDROME

[*hetero*, Greek = different; *taxis*, Greek = arrangement]

= CARDIOSPLENIC SYNDROMES

= situs ambiguus with a spectrum of various congenital truncal abnormalities + frequently cardiac malformations from asplenia to polysplenia

Embryology:

primary defect in lateralization with disruption of complete separation of cardiac chambers during 20–30 days of gestation

Inheritance: multifactorial (autosomal dominant, autosomal recessive, X-linked recessive)
Individualized approach of classification:
describes all critical structures by analyzing
(a) position of atria
(b) position of venous drainage below diaphragm relative to midline
(c) position of aorta relative to midline
(d) position of the stomach + presence of malrotation
(e) position of liver + gallbladder
(f) position of cardiac apex
(g) presence, appearance, and number of spleens
(h) presence of bi- / trilobed lungs

Asplenia Syndrome

= BILATERAL RIGHT-SIDEDNESS = RIGHT ISOMERISM
= IVEMARK SYNDROME

Prevalence: 1÷1,750–1÷40,000 livebirths; M > F
Associated with:
(a) CHD (in 50%):
TAPVR (almost 100%), endocardial cushion defect (85%), single ventricle (51%), TGA (58%), pulmonary stenosis / atresia (70%), dextrocardia (42%), mesocardia, VSD, ASD, absent coronary sinus, common atrium, common hepatic vein
(b) GI anomalies:
Partial / total situs inversus, annular pancreas, agenesis of gallbladder, ectopic liver, esophageal varices, duplication + hypoplasia of stomach, Hirschsprüng disease, hindgut duplication, imperforate anus
(c) GU anomalies (15%):
Horseshoe kidney, double collecting system, hydroureter, cystic kidney, fused / horseshoe adrenal, absent left adrenal, bilobed urinary bladder, bicornuate uterus
(d) Cleft lip / palate, scoliosis, single umbilical artery, lumbar myelomeningocele

- cyanosis in neonatal period / infancy (if severe cyanotic CHD)
- severe respiratory distress; Howell-Jolly bodies = RBC inclusions in patients with absent spleen

@ Lung
√ right bronchial isomerism:
√ bilateral trilobed lungs = bilateral minor fissures (SPECIFIC)

Heterotaxy Syndromes		
	Asplenia = bilateral right-sidedness	*Polysplenia = bilateral left-sidedness*
Clinical		
Presenting age	newborn / infant	infant / adult
Sex predominance	male	female
Cyanosis	severe	usually absent
Heart disease	severe	moderate / none (5–10%)
Howell-Jolly / Heinz bodies	present	absent
Spleen scan	no spleen	multiple small spleens
Characteristic ECG	none	abnormal P-wave vector
Prognosis	poor	good
Mortality	high	low
Plain radiograph		
Lung vascularity	decreased	normal / increased
Aortic arch	right / left	right / left
Cardiac apex	right / left / midline	right / left
Bronchi	bilateral eparterial	bilateral hyparterial
Minor fissure	possibly bilateral	none / normal
Stomach	midline / right / left	right / left
Liver	symmetrical / R / L	in various positions
Malrotation of bowel	yes (microgastria)	yes
Cardiography		
Coronary sinus	usually absent	sometimes absent
Atrial septum	common atrium (100%)	ASD (84%)
AV valve	atresia / common valve	normal / abnormal MV
Single ventricle	44%	infrequent
IVS	VSD	VSD common
Great vessels	d- / l-transposition (72%)	normal relationship
Pulmonary stenosis	the rule	frequent
Pulmonary veins	TAPVR	PAPVR (42%) TAPVR (6%)
Single coronary a.	19%	
SVC	bilateral (53%)	bilateral (33%)
IVC-aorta relationship	same side of spine	normal
IVC	normal	interrupted (84%) / normal
Azygos vein	inapparent	continuation R / L

√ bilateral eparterial bronchi (MR / tomogram):
√ main bronchus passes superior to ipsilateral main pulmonary artery
√ pulmonary arteries inferior to bronchi (on PA view) + projecting anterior to trachea (on LAT view)
√ diminished pulmonary vascularity / pulmonary venous hypertension (TAPVR below diaphragm)

@ Heart & great vessels
√ bilateral systemic / right morphologic atria with broad-based appendages
√ ipsilaterality of abdominal aorta + IVC
= juxtaposed "piggybacked" IVC (aorta usually posterior) (MOST RELIABLE INDICATOR)
√ bilateral SVC

@ Abdomen
√ asplenia = absent spleen (risk of sepsis)
√ midline liver = centrally located "bridging" liver = hepatic symmetry
√ variably located stomach (on right / left side / in central position) and small (microgastria)
√ cardiac apex discordant from stomach + liver

Prognosis: up to 90% mortality by end of 1st year of life

Polysplenia Syndrome

= BILATERAL LEFT-SIDEDNESS = LEFT ISOMERISM

Age: presentation in infancy / adulthood; M < F

Associated with:

(a) CHD (> 50%):
APVR (70%), dextrocardia (37%), ASD (37%), ECD (43–65%), pulmonic valvular stenosis (23%), TGA (13–17%), DORV (13–20%)
• no / mild CHD in most patients

(b) GI abnormalities:
esophageal atresia, tracheoesophageal fistula, gastric duplication, preduodenal portal vein, duodenal webs + atresia, short bowel, mobile cecum, malrotation, semiannular pancreas, biliary atresia, absent GB

(c) GU anomalies (15%):
renal agenesis, renal cysts, ovarian cysts

(d) Vertebral anomalies, common celiac trunk–SMA

• CHF ← L-to-R shunt; heart murmur, occasional cyanosis
• leftward / superiorly directed P-wave vector
• heart block ← endocardial cushion defect
• extrahepatic biliary obstruction
√ absence of IVC (on LAT CXR)
√ large azygos vein (on AP CXR) may mimic aortic arch

@ Lung
√ left bronchial isomerism:
√ bilateral morphologic left lungs with 2 lobes (55–68%), normal (18%), bilateral R-sided lungs (7%)

√ bilateral hyparterial bronchi = main bronchus passes inferior to ipsilateral main pulmonary artery:
√ arteries projecting superior to bronchi (on PA view) + posterior to tracheobronchial tree (on LAT view)
√ normal / increased pulmonary vascularity
√ absence of middle lobe fissure

@ Heart & great vessels
√ bilateral pulmonary / left morphologic atrium with pointed tubular narrow-based appendages
√ cardiac apex on right / in midline
√ bilateral SVC (50%)
√ interruption of hepatic segment of IVC with azygos / hemiazygos continuation in 65–70% (MOST CONSISTENT FINDING)

@ Abdominal heterotaxy (56%)
√ polysplenia = presence of ≥ 2 spleens (usually two major + indefinite number of splenules) located on both sides of the mesogastrium (esp. greater curvature of stomach)
√ midline centrally located liver = hepatic symmetry
√ absence of gallbladder (50%)
√ variably located stomach → always on same side of spleen(s)
√ malrotation of bowel (80%)
√ preduodenal portal vein

OB-US:
√ absence of intrahepatic IVC
√ aorta anterior to spine in midline
√ "double vessel" sign = 2 vessels of similar size in paraspinous location posterior to heart = aorta + azygos vein on left / right side of spine

Prognosis: 50% mortality by 4 months; 75% mortality by 5 years; 90% mortality by midadolescence

HYPOPLASTIC LEFT HEART SYNDROME

= SHONE SYNDROME = AORTIC ATRESIA
= underdevelopment of left side of heart characterized by
(a) hypoplastic / atretic aortic valve
√ subvalvar aortic stenosis
(b) hypoplastic / atretic mitral valve
√ parachute mitral valve = all chordae tendineae arise from single fused papillary muscle
√ supravalvar mitral ring
(c) hypoplastic LV ← endocardial fibroelastosis
(d) hypoplastic ascending aorta
√ aortic coarctation
(e) normally related great vessels

Prevalence: 0.2÷1,000 live births; M÷F = 2÷1
◊ 4th most common cardiac malformation manifesting in 1st year of life (after VSD, TGV,

tetralogy of Fallot)
◊ Most common cause of CHF in neonate
◊ Responsible for 25% of all cardiac deaths in 1st week of life

Hemodynamics:
pulmonary venous blood in LA faces an atretic / stenotic MV (= pulmonary venous outflow obstruction) → flow diverted to RA through herniated foramen ovale / ASD (L-to-R shunt); RV supplies (a) pulmonary artery, (b) ductus arteriosus, (c) descending aorta (antegrade flow), (d) aortic arch + ascending aorta + coronary circulation (retrograde flow) → RV work overload + CHF

Associated malformations:
coarctation of aorta, PDA, patent foramen ovale, dilated pulmonary artery, VSD, dilated RA, enlarged RV, double-outlet right ventricle, endocardial fibroelastosis

- severe CHF ← RV volume + pressure overload:
  - characteristically presents within first few hours of life
- ashen gray color / dusky complexion ← systemic underperfusion ← inadequate atrial L-to-R shunt
- myocardial ischemia ← decreased perfusion of aorta [= "common coronary artery"] + coronary arteries):
  - cardiogenic shock, metabolic acidosis (when ductus arteriosus closes)

CXR:
√ hypoplastic / normal / enlarged cardiac silhouette:
√ prominent right atrial border
√ ± absence of left ventricular silhouette
√ ± thymic atrophy
√ interstitial + alveolar pulmonary edema ← pulmonary venous hypertension with severely restrictive interatrial communication in 80%
√ normal pulmonary vasculature (with wide nonrestrictive interatrial communication in 20%)

OB-US (may be missed < 22 weeks GA):
√ small left ventricular cavity (apex of LV and RV should be at same level)
√ hypoplastic ascending aorta
√ aortic coarctation (in 80%)
√ diastolic flow reversal in narrow ascending aorta is DIAGNOSTIC

ECHO:
√ normal / enlarged LA
√ slitlike / small / normal LV
√ enlarged RA
√ herniation + prolapse of foramen ovale flap into RA
√ hypoplastic ascending aorta (< 5 mm = aortic atresia)
√ absent / grossly distorted mitral valve echoes

Angio:
√ retrograde flow in ascending aorta + aortic arch + coronary arteries via PDA
√ stringlike ascending aorta < 6 mm in diameter
√ massive enlargement of RV + RVOT

Prognosis: almost 100% fatal by 6 weeks

Time of diagnosis: 32% pre-, 65% 1–4 days postnatally

Rx: (1) Prostaglandin E1 → patency of ductus arteriosus

(2) Hypoventilation (increase in CO_2 maintains high pulmonary vascular resistance)

(3) Nitroprusside IV (decreases systemic vascular resistance)

(4) Norwood procedure = palliative attempt

(5) Cardiac transplant

HYPOPLASTIC RIGHT VENTRICLE

= PULMONARY ATRESIA WITH INTACT VENTRICULAR SEPTUM

= underdeveloped right ventricle ← pulmonary atresia in the presence of an intact interventricular septum

Type I = small RV ← competent tricuspid valve (more common)

Type II = normal / large RV ← incompetent tricuspid valve

Hemodynamics:

fetus: L-to-R atrial shunt through foramen ovale; retrograde flow through ductus arteriosus into pulmonary vascular bed

neonate: closure of ductus → cyanosis, acidosis, death

√ small right ventricular cavity (apex of RV + LV should be at same level)

√ atresia of pulmonary valve

√ hypoplastic proximal pulmonary artery

√ secundum atrial septal defect (frequently associated)

Rx: prostaglandin E1 infusion + valvotomy + systemic-pulmonary artery shunt

IDIOPATHIC DILATATION OF PULMONARY TRUNK

= CONGENITAL ANEURYSM OF PULMONARY ARTERY

Age: adolescence; M < F

• asymptomatic; systolic ejection murmur (in most cases)

√ dilated main pulmonary artery causes a round bulge at the mediastinal border simulating a mass

√ normal peripheral pulmonary vascularity

√ normal pulmonary arterial pulsations

√ NO lateralization of pulmonary flow

Dx per exclusion:

1. Absence of shunts, CHD, acquired disease
2. Normal RV pressure
3. No significant pressure gradient across pulmonic valve

Prognosis: nonprogressive

DDx: (1) Marfan syndrome

(2) Takayasu arteritis

INFECTIOUS AORTITIS

= inflammation of aorta caused by bacterium / virus / fungus

The aorta is normally very resistant to infection. However, an abnormal aortic wall as occurs with atherosclerotic disease, preexisting aneurysm, cystic medial necrosis, diabetes, vascular malformation, medical devices, or surgery, makes it susceptible to infection!

Organism:

1. Bacterial: Staphylococcus > Streptococcus > Salmonella, Clostridium septicum (exceedingly rare, but strongly associated with GI / hematologic malignancy)
2. Luetic = syphilis
3. Mycobacterial = Mycobacterium tuberculosis
4. Viral: eg, HIV infection / AIDS

√ thickening of aortic wall + intramural gas (KEY FEATURE)

N.B.: aorta may appear normal on imaging

Rx: empiric antibiotic therapy against S. aureus and gram-negative rods

DDx: infected aortic aneurysm (dilated aorta prone to rupture)

Syphilitic Aortitis

= LUETIC AORTITIS

Prevalence: in 10–15% of untreated patients (accounts for death in ⅓)

Path: periaortitis (via lymphatics), mesaortitis (via vasa vasorum) = primarily disease of media leading to secondary injury of intima, which predisposes the intima to premature calcific atherosclerosis

Age: 40–65 years

Site: ascending aorta (36%), aortic arch (24%), descending aorta (5%), sinus of Valsalva (1%), pulmonary artery

√ thick aortic wall ← fibrous + inflammatory tissue

√ saccular (75%) / fusiform (25%) dilatation of ascending aorta:

√ small saccular aneurysm often protrudes from fusiform aneurysm

√ fine pencil-like calcifications of intima (15–20%) in ascending aorta, late in disease

Cx: (1) Stenosis of coronary ostia ← intimal thickening

(2) Aortic regurgitation (syphilitic valvulitis), rare

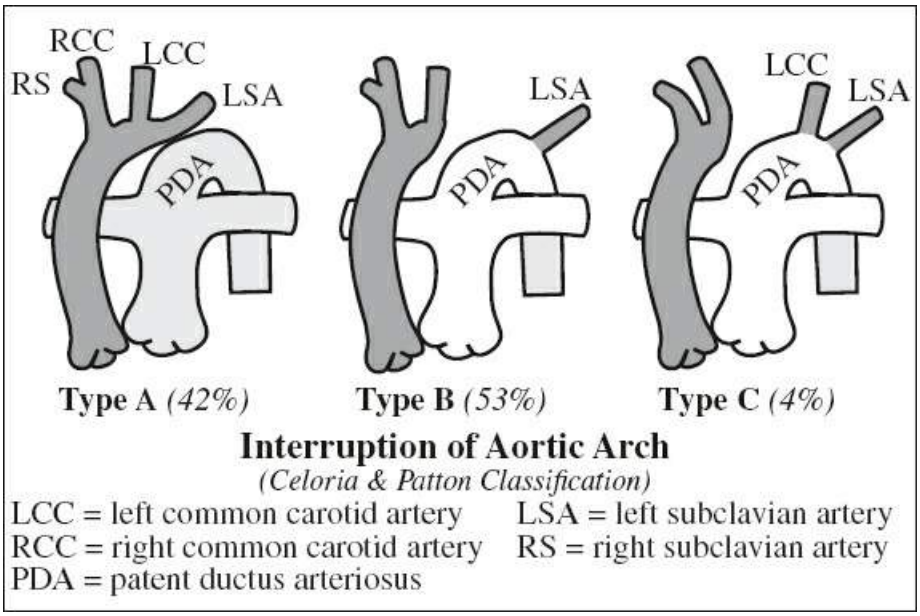
DDx: Degenerative calcification of ascending aorta (older population, no aneurysm, no aortic regurgitation)

INTERRUPTION OF AORTIC ARCH

= IAA = rare congenital anomaly with complete luminal and anatomic discontinuity between ascending + descending aorta

Prevalence: 1% of CHD

◊ Common cause of death in neonatal period after physiologic closure of PDA (4–10 days)



Trilogy: (1) Luminal discontinuity between ascending + descending thoracic aorta
(2) VSD (in 90%)
(3) PDA (pulmonary blood supplies lower part of body) in nearly 100%

Cause: ? altered hemodynamics through 4th aortic arch / teratogenic exposure

Genetics: chromosome 22q11.2 deletion (50%), DiGeorge syndrome (= hypocalcemia and T-cell defects ← thymic hypoplasia in 42%)

Forms: (a) Simple IAA

(b) Complex IAA (in ⅓) associated with:

1. Bicuspid aortic valve
2. Muscular subaortic stenosis
3. Truncus arteriosus
4. Aortopulmonary window
5. ASD
6. Transposition of great arteries
7. Double-outlet right ventricle
8. Functional single ventricle
9. Complete anomalous pulmonary venous return

• presents with CHF

Location:

Type A: distal to left subclavian artery (13–42%)
Type B: between left CCA and subclavian artery (53–84%)
Type C: between innominate and left CCA (3–4%)

√ dilatation of right atrium + ventricle
√ dilatation of pulmonary artery
√ ascending aorta much smaller than pulmonary artery
√ arch formed by pulmonary artery + ductus arteriosus gives the appearance of a low aortic arch
√ aortic knob absent

√ trachea in midline
√ NO esophageal impression
√ retrosternal clear space increased (small size of ascending aorta)
√ increased pulmonary vascularity ← L-to-R shunt
√ aberrant right subclavian artery arising from right side of proximal descending thoracic aorta
Cx: hypoperfusion with acute renal failure + metabolic acidosis
Prognosis: 59–70% overall survival rate by 16 years of age
Rx: prostaglandin E1 in neonatal period (to keep the ductus arteriosus open); cardiac surgery during 1st year of life (with 15–20% mortality)

INTERRUPTION OF PULMONARY ARTERY

= pulmonary trunk continues only as one large artery to one lung while systemic aortic collaterals supply the other side
Cause: abnormal development of 6th aortic arch in utero
Associated with: CHD (particularly if interruption on left side):
1. Tetralogy of Fallot
2. Scimitar syndrome = congenital pulmonary venolobar syndrome
3. PDA, VSD
4. Pulmonary hypertension

Collateral supply:
1. Arteries arising from arch + ascending aorta
2. Bronchial vessels
3. Intercostal vessels
4. Branches from subclavian artery (internal mammary artery)

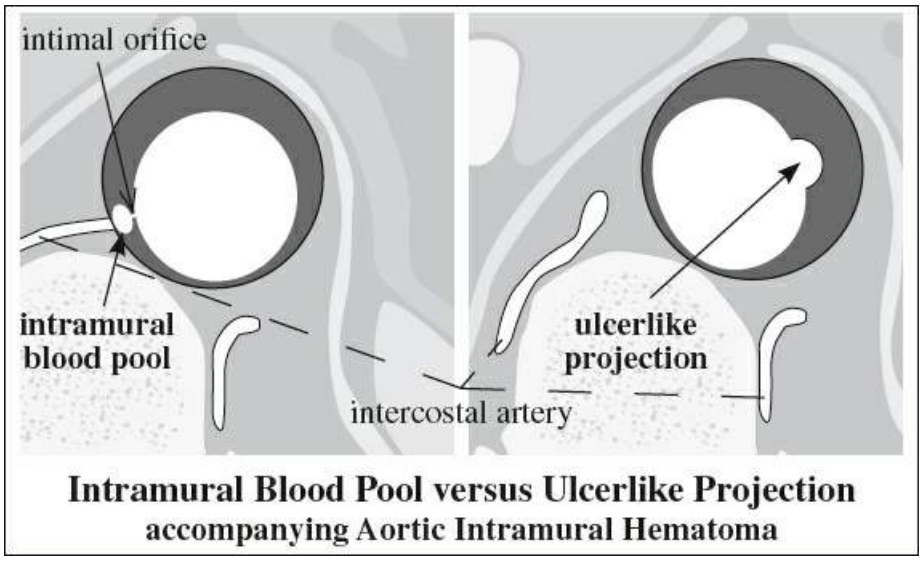
Location: usually opposite from aortic arch; R > L pulmonary artery
CXR:
√ hypoplastic ipsilateral lung
√ lung opacity similar to normal lung / slightly increased
√ volume loss of affected hemithorax:
  √ small ipsilateral chest
  √ mediastinal shift toward involved lung
  √ ipsilateral shift of anterior junction line
  √ ± elevation of ipsilateral hemidiaphragm
  √ ipsilateral narrowed intercostal spaces
  √ absent / diminutive appearance of pulmonary hilum with "comma-shaped" small distorted hilar shadow
  √ occasionally rib notching
√ hyperexpanded + hyperlucent contralateral lung with herniation into smaller hemithorax
√ asymmetry of pulmonary vascularity
√ normal respiratory motion (normal aeration of hypoplastic lung)

CECT:
√ affected pulmonary artery completely absent / terminates within 1 cm of its origin
√ reconstitution of more peripheral pulmonary arteries ← collateral vessels
√ multiple linear opacities perpendicular to pleural surface (= transpleural systemic

collateral vessels)
√ serrated pleural thickening (= enlarged intercostal + transpleural arteries)
NUC:
√ absent perfusion with normal aeration
Angio:
√ absent pulmonary artery
Cx: recurrent pulmonary infection, hemorrhage, hemoptysis (10%), mild exertional dyspnea, pulmonary hypertension (19–25%)
Rx: Surgical anastomosis between proximal + distal pulmonary artery (to prevent progressive pulmonary hypertension with dyspnea, cyanosis, hemoptysis, death)
DDx: (1) Hemitruncus
(2) Swyer-James syndrome (ipsilateral air trapping, reduced ventilation + perfusion)
(3) Chronic thromboembolic occlusion
(4) Takayasu arteritis
(5) Mediastinal fibrosis
(6) Hypogenetic lung syndrome (abnormal bronchial branching pattern)

INTRAMURAL AORTIC HEMATOMA (3–13%)

= ATYPICAL AORTIC DISSECTION = IMH
= aortic dissection without demonstrable intimal flap / penetrating aortic ulcer
Cause: rupture of vasa vasorum; in 94% spontaneous; in 6% traumatic (? early stage of limited dissection or thrombosis of false lumen)
Pathophysiology:
rupture of vasa vasorum → hemorrhage into aortic media → intramural blood clot → weakening of aortic wall; no detectable flow within the "false channel"
Median age: 68 years
Risk: hypertension (53%)
• signs + symptoms + classification identical to classic aortic dissection:
• chest pain / back pain or both (in 80%)
◊ IMH detected in 5–20% of patients presenting with signs of classic aortic dissection
Stanford classification: in 57% type A; in 43% type B
May be associated with: pericardial / pleural effusion, mediastinal hematoma
√ NO intimal tear / flap at initial imaging
√ NO penetrating atherosclerotic ulcer
NECT (necessary):



Intramural Blood Pool versus Ulcerlike Projection accompanying Aortic Intramural Hematoma

√ DIAGNOSTIC eccentric cuff / crescent of aortic wall > 7 mm thick with a density of 60–70 HU:
- √ attenuation identical to intraluminal blood after 1 week
- √ decreased thickness within a few weeks
- √ complete resolution within 1 year

√ displacement of intimal calcifications maintaining a semicircular / circular curvilinear configuration

CECT:

√ nonenhancing mural region of low attenuation with smooth border maintaining a constant circumferential relationship with aortic wall

√ predictors of outcome:
- (a) maximal aortic diameter,
- (b) maximal axial thickness of hematoma,
- (c) minimum + maximum transverse aortic diameter at level of maximal thickness of intramural hematoma

MR:

◊ Review source images!

√ crescent-shaped eccentric wall thickening

√ T2 white blood imaging:
- √ hyperintense signal (< 7 days of age)
- √ intermediate signal intensity (≥ 7 days)

√ subacute / chronic hematoma on T1 black blood imaging:
- √ subacute isointense (= oxyhemoglobin)
- √ hyperintense hematoma (= methemoglobin)

Aortography: not useful!

Cx: (1) Ulcerlike projection with progression to open dissection
(2) Saccular or fusiform aneurysmal dilatation
(3) Rupture

Rx: (1) Emergency surgical repair for type A hematoma (probably represents early stage

with development of classic aortic dissection)

(2) Observation for type B hematoma (may heal completely)

Mortality: 21% (similar to classic aortic dissection)

DDx:

(1) Acutely thrombosed false lumen of dissection (opacification of true + false lumina; intimal flap; multilayered pattern of increasing attenuation; linear configuration of intimal calcifications; tendency to spiral longitudinally around aorta)

(2) Aortitis (segmental mural thickening of aorta + branch vessels interspersed with normal segments)

(3) Acute aortic hematoma of fusiform aortic aneurysm with hyperattenuating crescent (= sign of impending rupture)

(4) Atheromatous mural thrombus (irregular intraluminal surface in segment of dilated aorta, abdominal location, multiple sites)

(5) Penetrating atherosclerotic ulcer (small focal contrast-enhanced outpouching of intima + adjacent subintimal hematoma, located in abdominal / descending thoracic aorta, associated with extensive atherosclerosis)

(6) Intramural blood pool

= intramural contrast-medium filled pool

√ tiny intimal orifice ± connection with intercostal / lumbar artery

Prognosis: good

(7) Focal periaortic soft-tissue mass (circumferential involvement with irregular external border)

(a) Idiopathic retroperitoneal fibrosis

(b) Periaortic lymphoma

(8) Aortic motion artifact simulating type A IMH

ISCHEMIC HEART DISEASE

= CORONARY ARTERY DISEASE (CAD)

Incidence: 1.5 million annually; leading cause of death in industrial nations

Prognosis: 28.7÷1,000 men annually; 3.1÷1,000 deaths annually

• **Acute Coronary Syndrome**

(a) transmural myocardial infarction

(b) subendocardial myocardial infarction

(c) unstable angina

Likelihood of Myocardial Ischemia	*Preferred Imaging Modality*
high	Catheter angiography
moderate	ECG-gated SPECT
low	Coronary CT angiography

CXR:

√ often normal

√ coronary artery calcification

√ pulmonary venous hypertension following acute infarction (40%)

√ LV aneurysm

A. NONINVASIVE TESTING
   1. Noninvasive testing is of marginal benefit when disease prevalence is < 0.2 / > 0.7
   2. Concordant ^{201}Thallium and stress ECG are greater predictors of disease probability than either one used alone and/or when discordant
   3. Sequential ^{201}Thallium and stress ECG are most useful to establish the diagnosis of CAD when pretest prevalence is intermediate + test results are concordant

B. INVASIVE TESTING
   1. Nonstress Myocardial Perfusion Study (^{99m}Tc-Sestamibi) administered during acute chest pain: 99% NPV, 92% sensitive for early diagnosis

Coronary CTA / Triple CTA		
Risk category	*CT Interpretation*	*Clinical Guideline*
High	Coronary calcium score > 400 > 70% stenosis in any vessel > 50% stenosis in left main	Admission
Medium	Coronary calcium score 100–400 30–70% stenosis in any vessel	Cardiology consultation
Low	Coronary calcium score < 100	Follow-up with cardiology
Negative	Normal scan	Follow-up with regular MD
Results are negative / in low risk category in 75%!		

Pitfalls: breast attenuation, diaphragmatic attenuation (repeat study in prone position)

   2. ECHO (90% sensitive, 53–78% specific for infarction)
      √ region of dilatation with disturbance of wall motion:
      (1) Akinesis = no wall motion
      (2) Hypokinesis = reduced wall motion
      (3) Dyskinesis = paradoxical systolic expansion
      (4) Asynchrony = disturbed temporal sequence of contraction
   3. Coronary angiography: 1.2 million procedures annually
   4. Coronary CTA
   5. Cardiac PET/CT

Imaging of Coronary Artery Disease

(1) DIRECTLY with <u>myocardial perfusion imaging</u> providing a pictorial representation of the relative perfusion of viable myocardial tissue using exercise + rest physiology images
   (a) ^{201}Tl chloride SPECT imaging (92% sensitive, 68% specific)
   (b) ^{99m}Tc-sestamibi / tetrofosmin SPECT imaging (89% sensitive, 90% specific)
   (c) PET

(2) INDIRECTLY with <u>imaging of ventricular function</u>,
i.e., evaluation of wall motion + ejection fraction
   (a) multigated acquisition studies (MUGA)
      › ^{99m}Tc-labeled RBCs

› ^{99m}Tc-human serum albumin

(b) first-pass radionuclide angiography

› sodium pertechnetate

› diethylenetriamine pentaacetic acid (DTPA)

› sulfur colloid

› ^{195m}Au (gold)

› ^{191m}Ir (iridium)

(3) SIMULTANEOUS assessment of myocardial perfusion + ventricular function
= first-pass radionuclide angiography + gated SPECT perfusion imaging

Interpretation:

A. NORMAL MYOCARDIUM

√ homogeneous perfusion

√ similar appearance at rest + with exercise

B. ISCHEMIC VIABLE MYOCARDIUM

√ normal perfusion at rest

√ relative hypoperfusion with exercise (= reversible defect)

DDx:

(1) Reversible septal defect in left bundle branch block

(2) Differing soft-tissue attenuation artifact

C. MYOCARDIAL INFARCTION

√ reduced muscle mass

√ absent / reduced uptake at rest + with exercise (= fixed defect)

DDx: (1) "**Hibernating myocardium**" = chronic myocardial hypoperfusion producing abnormal regional ventricular function

(2) Soft-tissue attenuation artifacts

√ marked variability in LV tracer uptake of inferior wall (diaphragmatic attenuation) + anterior wall (breast attenuation)

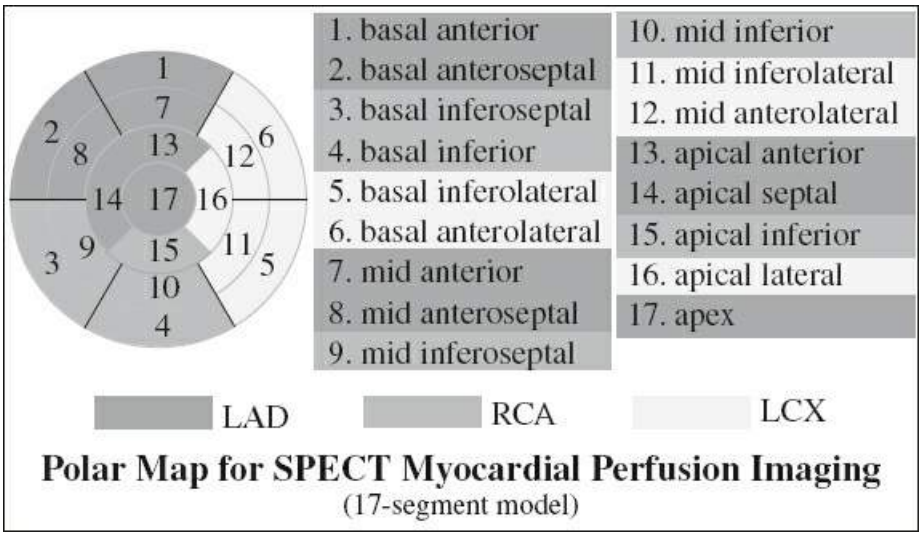
(3) Infiltrative disorders

DDx of a mild fixed defect:

1. Scar
2. Hibernating myocardium
3. Attenuation artifact

Myocardial Viability Assessment

1. Perfusion



» ^{201}Tl rest injection with redistribution images preferable to sestamibi
√ uptake > 50% of maximum

2. Metabolic activity
» FDG may provide best assessment (normal myocardium uses fatty acids as chief metabolic substrate, but can switch to glucose metabolism)
√ enhanced glucose uptake by ischemic but viable myocardium

Analysis of Perfusion Defect

Report must address: location, size, severity, reversibility of a perfusion defect

(1) TYPE OF PERFUSION ABNORMALITY
√ fixed defect
= myocardial scar / severe myocardial ischemia
√ reversible defect
= perfusion abnormality on poststress images normalizes on resting images
√ partially reversible defect
= 20–30% improvement in regional activity

(2) LOCATION OF PERFUSION ABNORMALITY described with regard to
(a) LV wall
→ anterior, septal, inferior, lateral, apical
◊ Avoid "posterior" as it has been variably assigned to the lateral wall (LCX) or basal inferior wall (RCA)
(b) expected coronary vascular territory involvement

(3) DEGREE OF REVERSIBILITY OF PERFUSION DEFECT
√ cross-hatching of perfusion defect on stress image-based polar map
√ improvement by ≥ 2 points in SSS / absolute SSS of 0 or 1 on rest images

◊ If an area of infarcted myocardium with a fixed defect has perfusion of greater than 50% of the database norm, it is considered to be at least partially viable

(4) SIZE / EXTENT OF PERFUSION DEFECT

Size of Myocardial Perfusion Defect	
Description	*Size of Total LV Volume*
small	5–10%
medium	15–20%
large	20–40%
extensive	> 40%

(5) SEVERITY OF PERFUSION DEFECT

» Qualitative

- mild = 10% reduction of peak tracer activity, of unknown clinical significance
- moderate
- severe

» Semiquantitative Segmental Scoring for more accurate + more consistent reporting

- Summed rest score (SRS)
- Summed stress score (SSS

Semiquantitative Segmental Scoring		
Score	*Reduction in Perfusion*	*Decrease from Norm*
0	normal / no difference	0%
1	equivocal / mild	< 40%
2	moderate	40–60%
3	severe	> 60%
4	absent perfusion	no activity

Myocardial Perfusion SPECT for Detection and Management of CAD			
	Normal	*Mildly Abnormal*	*Moderately Severely Abnormal*
Summed Stress Score	< 4	4–8	> 8
Likelihood of Coronary Artery Disease	low	high	high
Risk of Myocardial Infarction	low	intermediate	intermediate
Risk of Cardiac Death	low	low	intermediate

Risk for Future Hard Cardiac Events	
Risk	*Summed Stress Score*
Normal	0–3
Low risk	4–7
Intermediate risk	8–12
High risk	> 12

- Summed difference score (SDS) = SRS - SSS

= measure of reversibility (≥ 2-grade improvement represents substantial ischemia)

(a) no / mild ischemia = SDS ≤ 4
(b) determines risk for future hard cardiac even

QUANTITATIVE ANALYSIS
= using a reference profile (= database normalized to specific gender, radiopharmaceutical, and population) perfusion data is displayed as a polar map / bull's-eye projection / circumferential profile serving as a "second observer"
√ blackout map (most popular) = perfusion values below a threshold (usually of 2.5 SD below mean) displayed in black
√ cross-hatched areas = area above threshold value but with abnormal perfusion during stress indicating reversible defect

Common Artifacts in Myocardial Perfusion Imaging

1. Patient motion artifact
   ◊ Motion ≥ 2 pixels is unacceptable!
   (a) superior → inferior
   (b) laterally
   (c) "upward creep" ← increase of respiratory excursion after strenuous exercise
   √ heart in different locations on adjacent SPECT projection images
   √ "apical flame / hurricane" sign = artifactual perfusion defect in apical septum + mild offset of septal aspect of LV relative to lateral aspect + tail of activity extending superiorly from distal LV on short-axis views resembling depiction of a hurricane on weather maps
   Remedy: (1) repeat imaging without delay / reinjection → ^{99m}Tc-labeled radiotracers remains relatively fixed for as long as 2 hours
   (2) use of motion correction software → eliminates misregistration due to slight / moderate motion
2. Misregistration artifact
   = patient motion between sequential acquisition of low-dose CT data obtained for attenuation correction and SPECT image
   Remedy: use of coregistration software for precise superimposition of CT + SPECT
3. Left bundle branch block artifact
   Effect: decrease in septal blood flow at higher heart rate ← asynchronous septal contraction ← perturbed activation sequence + incomplete relaxation of septum during diastole
   √ apparent septal defect typically sparing apex and anterior wall (often more pronounced during stress induced by exercise / dobutamine instead of vasodilators that have a limited effect on heart rate)
   √ asynchronous / hypokinetic / paradoxical septal wall motion with preserved septal wall thickness
4. Normal prominent apical thinning
   √ apparent perfusion defect with matching stress and rest perfusion pattern
   ◊ Best seen on vertical and horizontal long-axis images + polar map display
   √ normal wall motion + normal wall thickness
5. Lung activity increased ← severe left ventricular dysfunction

6. RV uptake usually RV intensity 50% of peak LV intensity; ↑ in
   (a) RV hypertrophy ← pulmonary HTN
   (b) globally reduced LV uptake
7. Extracardiac activity
   › skin / clothing contamination
   › intense subdiaphragmatic activity from liver / GI tract ← hepatobiliary excretion of ^{99m}Tc-labeled radiotracers

   Effect: (1) Scatter radiation → apparent increased perfusion in inferior myocardial wall masking true perfusion defect
   (2) Normalized to highest count activity apparent LV activity relatively low → simulating extensive perfusion defect

   √ ramp artifact
   = band of pixels with negative counts around hot objects during SPECT reconstruction

   Remedy: (1) Repeat acquisition after delay → clearance of radiotracer superimposed on heart
   (2) Repeat imaging in prone position
   (3) Combination of vasodilator administration with low-level exercise protocol → reduction of splanchnic blood flow may prevent subdiaphragmatic activity
   (4) Patient drinks water to clear stomach

   › neoplastic lesion lung, breast, sarcoma, lymphoma, thymoma, parathyroid tumor, thyroid abnormality, kidney tumor, liver tumor
8. Attenuation (in up to 40% of all studies)
   › overlapping breast tissue (women)
   › diaphragm (men) → affects inferior myocardial wall

   Effect: artifactual activity decrease in anterior myocardial wall ± septal and lateral walls

   Clue: (1) Apparent perfusion defect present on stress-rest set of images (without change in position)
   (2) Normal LV wall motion and wall thickness
   (3) Noncoronary distribution of abnormality
   (4) Large dense breasts at cinematic review of raw images

   Remedy: (1) Attenuation correction method: like low-dose breath-hold CT on hybrid SPECT/CT
   (2) Repeat imaging in prone position

KAPOSIFORM HEMANGIOENDOTHELIOMA

= vascular neoplasm of borderline malignancy + intermediate aggressiveness
Associated with: Kasabach-Merritt syndrome
Location: extremity, trunk, head and neck
Spread: to regional lymph nodes (rare)
MR:
√ ill-defined margins with involvement of multiple tissue planes + destructive changes

√ small feeding + draining vessels
√ hemosiderin deposits
DDx: infantile hemangioma

KAWASAKI DISEASE

= MUCOCUTANEOUS LYMPH NODE SYNDROME
= acute febrile generalized multisystem vasculitis of unknown cause involving medium-sized (large + small) arteries with a HALLMARK predilection for coronary arteries
◊ Leading cause of acquired pediatric heart disease in developed countries; 2nd most common pediatric vasculitis
Incidence: 20.8÷100,000 annually in children < 5 years of age; highest in Asian countries (Japan, Korea)
Cause: unknown; probable activation of immune system by an infectious trigger in a genetically susceptible host
Histo: necrotizing panvasculitis
Age: < 5 years of age (in 85%); peak age of 2–3 years; M÷F = 1.6÷1.0
Associated with: polyarthritis (30–50%), aseptic meningitis (25%), hepatitis (5–10%), pneumonitis (5–10%)
Seasonal variation: peaks in winter
Clinical phases:
(1) Acute phase (lasts 11 days): fever, nonexudative bulbar conjunctivitis, erythema of lips + oral mucosa, rash; ± pericarditis, myocarditis, abdominal pain, ascites, GB hydrops
(2) Subacute phase (lasts 2 weeks): resolution of fever, coronary artery aneurysms may develop; highest risk of sudden cardiac death
(3) Convalescent phase: 4–8 weeks after onset

- abrupt onset of high fever > 5 days
- mucosal reddening: injected fissured lips, injected pharynx, strawberry tongue in 99%
- maculopapular rash on extensor surfaces (99%)
- bilateral nonpurulent conjunctivitis (96%)
- erythema of palms + soles with desquamation (88%)

@ Cardiovascular system (⅓)
1. Coronary artery abnormality (15–25%)
◊ Perform cardiac ECHO at diagnosis, at 2 weeks, and at 6–8 weeks after onset of illness!
√ mild coronary artery dilatation (in up to 50%)
√ **coronary artery aneurysm**: LCA (⅔), RCA (⅓); proximal segment in 70%; as early as 3 days after onset of illness; 48% regress, 37% diminish in size
Risk factors: male sex, extremes of age, prolonged fever, delay in diagnosis, persistent fever after treatment
√ coronary artery stenosis (39%) ← thrombus formation in aneurysm with intimal thickening
√ coronary artery occlusion (8%) in aneurysms > 9 mm
2. Myocarditis (25%)

3. Pericarditis
4. Valvulitis
5. Atrioventricular conduction disturbance

Coronary artery involvement is the most characteristic manifestation of Kawasaki disease. Other medium-sized muscular arteries may also be involved.

@ CNS
√ subdural effusion
√ cerebral infarction, atrophy
√ lesion with reversible T2 hyperintensity in splenium of corpus callosum + subcortically
√ posterior reversible encephalopathy syndrome

@ Neck
• firm nonfluctuant cervical lymphadenopathy (82%), unresponsive to antibiotics
√ typically unilaterally enlarged nonsuppurative lymph nodes

@ Abdomen
√ intestinal pseudoobstruction
√ focal colitis
√ bowel infarction → ischemic stricture
√ transient gallbladder hydrops (15%)

Prognosis: 0.4–3.0% mortality (from myocardial infarction / myocarditis with congestive heart failure / rupture of coronary artery aneurysm)

Rx: aspirin (100 mg/kg per day) + gamma globulin

DDx: infantile polyarteritis

LEFT AORTIC ARCH WITH ABERRANT RIGHT SUBCLAVIAN ARTERY

= right subclavian artery arises as 4th branch from proximal descending aorta = arteria lusoria

Prevalence: 0.4–2.3% of population; in 37% of Down syndrome children with CHD;

◊ Most common congenital aortic arch anomaly!

Associated with: (1) Absent recurrent pharyngeal nerve (2) CHD in 10–15%

• asymptomatic / **dysphagia lusoria** (rare)
[*lusoria* = *lusus naturae,* Latin = freak / mutant / monster of nature]

Course: (a) behind esophagus (80%)
(b) between esophagus + trachea (15%)
(c) anterior to trachea (5%)

√ soft-tissue opacity crossing the esophagus obliquely upward toward the right shoulder (PATHOGNOMONIC)
√ masslike opacity in right paratracheal region
√ rounded opacity arising from superior aortic margin posterior to trachea + esophagus on LAT CXR
√ dilated origin of aberrant right subclavian artery (in up to 60%) = **diverticulum of Kommerell** = remnant of embryonic right arch
√ unilateral L-sided rib notching (if aberrant right subclavian artery arises distal to

coarctation)

LIPOMATOUS HYPERTROPHY OF INTERATRIAL SEPTUM

= LHIAS = excessive deposition of brown fat in interatrial septum

Prevalence: 3%; ↑ with older age

Associated with: obesity, pulmonary emphysema

Dx: thickening of interatrial septum > 2 cm (transverse diameter)

Histo: unencapsulated infiltration of adipocytes (brown fat) between atrial muscle cells, NOT true neoplasm

Brown fat: increased vascularity + high density of mitochondria → generation of heat

- commonly asymptomatic, more commonly female

Site: at level of fossa ovalis BUT with sparing of fossa ovalis

√ fatty mass of dumbbell shape ← sparing of fossa ovalis

√ no contrast enhancement

√ increase in mediastinal and epicardial fat

√ ± focally increased FDG activity = mean SUV of 1.84 (range, 0.48–3.48) ← metabolically active brown fat

DDx: potential imaging pitfall suggesting infectious /inflammatory / neoplastic lesion

Cx: supraventricular arrhythmias, vena caval obstruction

LEIOMYOSARCOMA OF IVC

= rare slow growing neoplasm; < 300 patients in literature

◊ Most common primary tumor of the IVC

◊ 2nd most frequent retroperitoneal neoplasm in adults

Age: 5th–6th decade; M÷F = 1÷2 to 1÷3

Growth patterns: extraluminal (62%), intraluminal (5%), combined extra- and intraluminal (33%)

Histo: atypical interlaced pattern with sweeping bundles of spindle-shaped cells with elongated / occasionally truncated blunt-ended nuclei

- most common:
  - exhaustion, abdominal pain, weight loss
  - abdominal mass / swelling, nausea, vomiting
- late stage:
  - abdominal distention, changes in defecation habits
  - shortness of breath ← decreased cardiac return
  - leg edema, back / radicular pain, frequent urination
  - elevated liver functions, jaundice

Location:

(a) upper IVC = hepatic vein to right atrium (24%) → Budd-Chiari syndrome from sudden / gradual occlusion of hepatic veins / IVC / both

(b) middle IVC = hepatic to renal veins (42%) → nephrotic syndrome

(c) lower IVC = infrarenal area (34%) → lower extremity edema

(d) entire length of IVC (10–17%)

Spread to: liver, lung, lymph nodes, brain, peritoneum; skin, soft tissue, bone, kidney, omentum

(less common)
◊ Distant seeding in 40% at presentation!

√ lobulated well-defined heterogeneous tumor exhibiting signs of hemorrhage
√ rarely necrotic predominantly cystic mass
√ venous dilatation + total / near-complete vessel obstruction
√ calcification unusual
√ collateral pathways bypassing IVC: hemiazygos, azygos
√ tumor extension from IVC into right atrium / pulmonary artery

US:
√ blood flow in IVC / hepatic veins may be absent / reversed / turbulent (depending on degree of obstruction)
√ tumor vascularity (DDx from bland thrombus)

CT:
√ irregular contrast enhancement of tumor
√ mass of intermediate attenuation mass

Prognosis: local recurrence (40–77%)

DDx: retroperitoneal tumor compressing / invading IVC; bland thrombus

DDx of tumor extension into right atrium:
renal cell carcinoma, hepatocellular carcinoma

LYMPHATIC DYSPLASIA

Primary Lymphatic Dysplasia

• uni- / bilateral swelling of lower / upper extremities
› resembles other angiodysplastic syndromes:
1. Klippel-Trénaunay-Servelle syndrome
= venous + lymphatic abnormalities
2. Klippel-Trénaunay-Weber syndrome
= venous + lymphatic + arterial disturbances
3. Milroy disease
= inherited autosomal disorder with high penetrance characterized by lymphedema of one / both lower /upper extremities, face, other body parts

Secondary Lymphatic Dysplasia

= obstruction of lymph flow from an acquired cause

Cause:
1. Treatment of cancer: obliteration of lymph nodes by excision or irradiation
◊ Lymphedema may appear months to years after treatment ← gradual deterioration in intrinsic contractile force of lymphatic wall / valve incompetence
2. Filariasis
= nematode (Wuchereria bancrofti, Brugia malayi) resides within peripheral lymphatic vessels + nodes + obstructs lymph flow
• elephantine / pachydermatous extremities / genitalia
• chyluria, hydrocele, chylous reflux (chylometrorrhagia, chylous vesicles), genital edema, massive breast engorgement

3. Long-standing venous disease / following venous stripping
4. Lymphatic obstruction by cancer, Kaposi sarcoma
5. Lymphatic inflammation: topical use of Cantharone ® (for eradication of plantar warts); injection treatment of varicosities
6. Minor trauma to soft tissue / bone
7. Sedentary condition: eg, confinement to wheelchair
8. Morbid obesity
9. Lymphedema tarda
   = congenital lymphedema with delayed manifestation secondary to superimposed secondary cause

LYMPHEDEMA

Primary Lymphedema

• no history of cancer chemotherapy, nodal extirpation / irradiation, severe trauma

Age: birth to > 25 years

Cause: primary / acquired lymphatic disorder

√ complete absence / delay of radiotracer transport

√ absence / paucity of lymphatic collectors (truncal flow)

√ intense dermal dispersion / backflow

• chylous skin vesicles; external leakage of milky lymph

√ lymphatic dysplasia may involve viscera

Pitfall: subcutaneous injection leads to factitious failure of radiotracer movement

Congenital Lymphedema

Age: birth to 5 years

Lymphedema Precox

Age: puberty to 25 years

(a) congenital

√ lack of lymph collectors, dermal diffusion, delayed transport

(b) acquired

√ intact collectors, rapid regional transport, delayed dermal diffusion

Secondary Lymphedema

√ prominent lymphatic trunks:

√ long-standing lymphatic obstruction leads to "die-back" (obliteration) of lymphatics ← intraluminal coagulum-gel deposition / reactive inflammation

√ dermal diffusion (backflow) of variable intensity

√ delayed radiotracer transport

√ faintly visualized regional lymph nodes

LYMPHOMA OF HEART

PET:

√ difficult to differentiate from normal myocardial uptake

DDx: (1) Metastasis: lung cancer, malignant melanoma

(2) Cardiac angiosarcoma (involving large areas of heart, more aggressive with penetration of valves + great vessels, central necrosis, prominent enhancement)

Secondary Cardiac Lymphoma

Prevalence: in 16–28% on autopsy for NHL; pericardial involvement more frequent than for primary; more common in immunocompromised patients

Secondary cardiac involvement by lymphoma, either through direct extension or via hematogenous spread, is more common than primary cardiac lymphoma.

Primary Cardiac Lymphoma

= lymphoma that involves only heart ± pericardium at time of diagnosis (extremely rare)

Mean age: 60 (range, 13–90) years

Predisposed: immunocompromised patients, esp. AIDS

Path: multiple firm nodules; contiguous invasion of pericardium

Histo: typically NHL: well-differentiated B-cell lymphoma, follicular center cell lymphoma, diffuse large cell lymphoma, undifferentiated Burkitt-like lymphoma

The most common symptoms of cardiac lymphoma are dyspnea, congestive heart failure, pericardial effusion, hemopericardium, arrhythmias and nonspecific EKG abnormalities (AV block).

- chest pain; unresponsive rapidly progressive heart failure
- cardiac tamponade, SVC syndrome

Location: RA > RV > LV > LA > atrial septum > ventricular septum; > 1 chamber (75%)

When infiltration beyond the myocardium occurs, the right atrium is most commonly involved, with subsequent venous extension leading to SVC / IVC thrombosis.

A curious feature of cardiac lymphoma:

√ tendency of tumor to extend along epicardial surfaces → primarily encasing adjacent structures like coronary arteries and aortic root!

√ massive pericardial effusion

CXR:

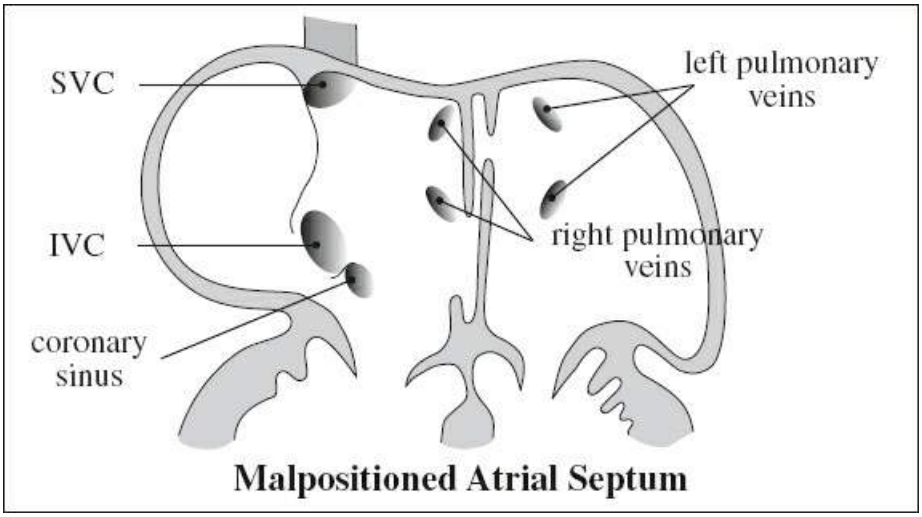
√ cardiomegaly

√ signs of CHF

√ massive pericardial effusion

ECHO:

√ hypoechoic myocardial masses in RA / RV



√ pericardial effusion

CT:

√ hypo- / isoattenuating masses relative to myocardium

√ heterogeneous enhancement of masses

MR:

√ poorly marginated heterogeneous lesions of iso- to hypointensity relative to myocardium on T1WI

√ heterogeneously hyperintense to myocardium on T2WI

√ heterogeneous enhancement with gadolinium with areas of low enhancement in center of lesion

Dx: positive cytology in pericardial fluid (in 67%); exploratory thoracotomy with biopsy of cardiac tissue

Prognosis: invariably very poor

Primary Effusion Lymphoma

= PEL = BODY CAVITY LYMPHOMA

Prevalence: 4% of all HIV-associated NHL

Associated with: concomitant diagnosis of Kaposi sarcoma

Histo: unique subgroup of B-cell lymphoma with features of both high-grade anaplastic and B-cell immunoblastic lymphoma

CXR: √ cardiomegaly

CT: √ massive pericardial effusion

MALPOSITION OF SEPTUM PRIMUM

= anomalous drainage of normally connected pulmonary veins ← leftward deviation / curvature of septum primum

Associated with: complex congenital heart defects, heterotaxy, polysplenia

√ leftward curvature of atrial septum

√ anomalous drainage of right upper pulmonary vein into RA

Variations: ± right lower pulmonary vein ± left pulmonary veins (in extreme degrees of

malposition)
√ ± left heart hypoplasia ← lack of left heart filling
Rx: resection + repositioning of atrial septum in a more normal position

MAY-THURNER SYNDROME

= ILIAC VEIN COMPRESSION SYNDROME = ILEOCAVAL COMPRESSION SYNDROME = COCKETT SYNDROME
[Robert May (1912–1984), surgeon in Innsbruck, Austria]
[Josef Thurner (1927–????), pathologist in Salzburg, Austria]
= obstruction of left common iliac vein caused by crossing of right common iliac artery
Pathophysiology:
(a) extrinsic : physical entrapment with compression of left common iliac vein (CIV) by right common iliac artery against underlying vertebral body → chronic venous stagnation → chronic left lower extremity swelling ± thrombosis of left iliac vein + femoral vein
(b) intrinsic: chronic repetitive pulsatile force of the right common iliac artery → intimal hypertrophy → formation of endovascular spur (= intravenous web / band) in left CIV
Path: spurlike projection in proximal left CIV in 22% (autopsy), in 49–62% of left iliofemoral thrombosis
Risk factors: surgery, injury, pregnancy, oral contraceptive use
Incidence: 0.2% annually in patients evaluated for venous thrombosis of left lower extremity
Age: 2nd–4th decade; M < F
• persistent left lower extremity swelling without obvious cause
• exertional pain
• varicose veins, venous eczema, hyperpigmentation
√ compression of left common iliac vein on CT / venography
√ tortuous pelvic venous collaterals joining contralateral veins
Prognosis: 60% of individuals with May-Thurner syndrome develop postthrombotic syndrome at some time during their lives
Cx: deep vein thrombosis (L÷R = 5÷1), chronic venous stasis ulcer; pulmonary embolism; phlegmasia cerulea dolens
Rx: (1) Endovascular stent after catheter-directed thrombolysis (95% success rate)
(2) Surgery: vein-patch angioplasty, relocation of right common iliac artery behind vein / IVC, contralateral saphenous vein bypass graft to ipsilateral common femoral vein with creation of a temporary AV fistula (Palma crossover)

MEDIAN ARCUATE LIGAMENT COMPRESSION

= MALS = CELIAC AXIS COMPRESSION SYNDROME = DUNBAR SYNDROME
= dynamic compression of celiac artery (± superior mesenteric artery) by median arcuate ligament → relieved by caudal movement of celiac artery with inspiration
Cause: abnormally cephalad origin of celiac artery / abnormally low median arcuate ligament
Median arcuate ligament:
archlike fibrous band connecting diaphragmatic crura on both sides of aortic hiatus passing
(a) usually superior to celiac axis at L1
(b) low anteriorly over celiac axis (in 10–24%)

Age: 30–84 years; M÷F=2÷3; especially young thin women
Incidence: 50–60% stenosis in 5–12% of healthy adults during inspiration / in 16% during expiration
• often postprandial epigastric pain, weight loss
• abdominal bruit with expiration
◊ Isolated compression of celiac axis during expiration may not be clinically significant!
CTA, DSA, MRA:
√ focal narrowing in proximal celiac axis (more prominent in expiration → superior movement of aorta + celiac artery
◊ Narrowing observed during inspiration → likely clinically significant!
√ superior indentation of proximal celiac a. creating a CHARACTERISTIC "hooked" appearance (SAG plane!)
√ direct visualization of median arcuate ligament
√ poststenotic dilatation of celiac a.
√ collateral filling via SMA + pancreaticoduodenal arcades
√ absence of atherosclerotic changes in adjacent aorta and proximal celiac segment
US:
√ peak systolic velocity in celiac artery ≥ 250 cm/s (70–99% stenosis) or in SMA ≥ 275 cm/s (70–99% stenosis)
√ normalization of elevated velocity during deep inspiration / standing upright position
Dx: lateral aortography / reformatted MDCT
Rx: surgical division of median arcuate lig. (50% long-term cure) ± celiac artery stenting (does not always relieve symptoms)
DDx: fixed celiac stenosis (atherosclerosis, vasculitis)

MICROSCOPIC POLYANGIITIS

= MICROSCOPIC POLYARTERITIS = HYPERSENSITIVITY VASCULITIS = LEUKOCYTOCLASTIC VASCULITIS
= pauci-immune necrotizing small-vessel angiitis without granulomatous inflammation
Path: necrotizing arteritis identical to polyarteritis nodosa but in vessels smaller than arteries (= arterioles, venules and capillaries)
Trigger: drugs (eg, penicillin), microorganisms, heterologous proteins, tumor antigens
• hemoptysis, hematuria, proteinuria
• abdominal pain, GI bleeding, muscle pain + weakness
• ANCA (antineutrophil cytoplasmic autoantibodies) in > 80%
• negative serologic tests for hepatitis B
Location: skin, mucous membranes, lung, brain, heart, GI tract, kidney, muscle
◊ Most common cause of pulmonary-renal syndrome!
@ Kidney
√ glomerulonephritis (90%)
@ Lung
√ pulmonary infiltrates ← capillaritis
@ CNS (involved in 37–72%)
√ mononeuritis multiplex

√ cerebral hemorrhage, nonhemorrhagic cerebral infarction
√ pachymeningitis
√ variable degrees of small-vessel disease involving white and gray matter

Rx: removal of offending agent

MITRAL REGURGITATION

= MITRAL INSUFFICIENCY

= most common manifestation of mitral valve dysfunction of any component (mitral valve annulus, leaflets, chordae tendineae, papillary muscle)

Hemodynamics:

during LV systole → backward flow of blood from LV into LA → ⇑ volume of blood under elevated pressure → dilatation of LA; ⇑ increase in LV diastolic volume with little increase in LV diastolic pressure (= increase in preload without increase in afterload = ↑ ejection fraction + ↑ LV stroke volume)

Quantification of Severity of Mitral Regurgitation:

Degree	*Regurgitant Volume [mL/beat]*	*Regurgitant Fraction [$Vol_{regurge}$ / Vol_{stroke}]*
Mild	< 30	< 30%
Moderate	30–59	30–49%
Severe	> 60	> 50%

The severity of mitral regurgitation can be quantified with CT / MRI by calculating the regurgitant volume and regurgitant fraction!

ECHO:

√ left ventricular volume overload:
  √ normal-sized / enlarged LV
  √ increased septal + posterior wall motion
√ increased EF slope
√ early closure of aortic valve (LV stroke volume partially lost to LA)
√ left atrial enlargement (in chronic MV insufficiency)
√ bulging of interatrial septum to the right during systole

Rx: surgical valve repair / replacement (if LV ejection fraction < 60% / LV end-systolic diameter > 40 mm)

Acute Mitral Regurgitation

Cause:

1. Spontaneous rupture of chordae tendineae
2. Myocardial infarction → rupture / dysfunction of papillary muscle (posteromedial > anterolateral papillary muscle)
3. Bacterial (= infectious) endocarditis with rupture of chordae tendineae / leaflet perforation
4. Periprosthetic valve leak

• markedly elevated LA pressure

√ pulmonary venous hypertension with engorged pulmonary vessels and cephalization (less

than with mitral stenosis)
√ symmetric interstitial / alveolar pulmonary edema:
√ asymmetric right upper lobe edema (9%) ← preferential flow of regurgitant jet into pulmonary vein of RUL (PATHOGNOMONIC)
√ limited cardiac enlargement

Chronic Mitral Regurgitation

Cause:

1. Rheumatic heart disease ← acute rheumatic fever
   (a) isolated: frequently seen in children
   (b) uncommon in adults (mostly combined with stenosis)
2. Mitral valve prolapse syndrome
3. Atrial myxoma
4. Coronary artery disease = ischemic cardiomyopathy → regional wall motion abnormality, LV / annular dilatation → functional mitral regurgitation
5. Idiopathic hypertrophic subaortic stenosis (IHSS)
6. Myxomatous degeneration of mitral valve: eg, Marfan syndrome, SLE
7. Mitral annulus calcification
8. Dilated / hypertrophic obstructive / amyloid cardiomyopathy → severe dilatation of LV → dilatation of mitral ring
9. Congenital heart disease: short / abnormally inserted chordae tendineae; persistent ostium primum ASD with cleft mitral valve; corrected transposition with Ebstein-like anomaly

√ massively dilated left atrium:
√ posterior LA wall calcification (McCallum patch)
√ enlarged LA appendage (with history of previous rheumatic heart disease)
√ elevation of left mainstem bronchus
√ enlarged pulmonary arteries ← venous hypertension
√ marked LV enlargement (cardiothoracic ratio > 0.55)
√ left heart failure
√ mitral annular calcification (frequent)

MITRAL STENOSIS

= characterized by fusion of edges of anterior + posterior leaflets along commissure

Cause: rheumatic heart disease (5–15 years after initial episode of rheumatic fever); carcinoid syndrome; eosinophilic endocarditis; rheumatoid arthritis; SLE; mass obstructing LV inflow (tumor, atrial myxoma, thrombus); congenital (parachute MV, double-orifice MV)

Mitral stenosis caused by rheumatic disease may have distinctive morphologic features unlike those of mitral stenosis produced by other causes!

M÷F = 1÷8

Hemodynamics:

increasing transvalvular pressure gradient (with mitral valve area of < 2.5 cm^2) → rise in LA + pulmonary vascular pressure throughout systole and into diastole → compensatory dilation of LA + pulmonary venous hypertension; development of medial hypertrophy + intimal

sclerosis in pulmonary arterioles → postcapillary pulmonary arterial hypertension; RV hypertrophy; tricuspid regurgitation; RV dilatation; right heart failure

May be associated with: ASD = Lutembacher syndrome (in 0.6%) causing L-to-R shunt

- history of rheumatic fever (in 50%)
- dyspnea on exertion, orthopnea, paroxysmal nocturnal dyspnea ← pulmonary hypertension; atrial fibrillation
- systemic embolization from thrombosis of atrial appendage

Stages (according to degree of pulmonary venous hypertension):

Stage 1 : loss of hilar angle, redistribution
Stage 2 : interstitial edema
Stage 3 : alveolar edema
Stage 4 : hemosiderin deposits + ossification

Quantification of Severity of Mitral Stenosis:

Degree	*Valve Area in Diastole [cm^2]*	*Mean Diastolic Gradient [mmHg]*
Normal	4.0–6.0	0
Mild	1.6–3.9	< 5
Moderate	1.0–1.5	5–10
Severe	< 1.0	> 10

Quantifiable parameters of severity of mitral stenosis are planimetric valve area + mean diastolic gradient across the valve on velocity-encoded phase-contrast cine images!

@ Left heart
√ enlarged LA ± wall calcification:
√ "double density" seen through right upper cardiac border (AP view)
√ bulge of superior posterior cardiac border below carina (lateral view)
√ splaying of mainstem bronchi
√ esophagus displaced toward right + posteriorly
√ dilated left atrial appendage (not present with retracting clot), in 90% associated with rheumatic heart disease

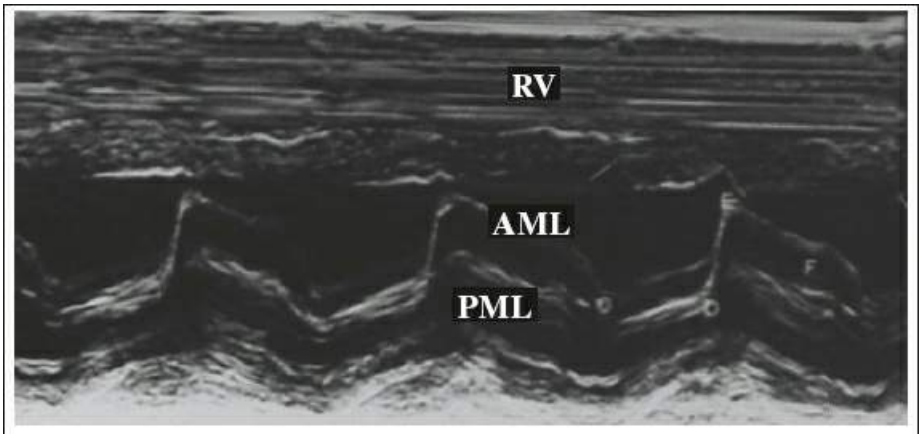
◊ Dilatation of left atrial appendage + calcification = rheumatic heart disease!

√ calcification of valve leaflets in 60% of severe mitral stenosis, usually > 50 years of age (DDx: calcification of mitral annulus, calcified chronic LA thrombus)
√ normal / undersized LV ← LV hypertrophy
√ small aorta ← decrease of forward cardiac output

@ Right heart
√ prominent pulmonary artery segment ← precapillary pulmonary hypertension
√ RV hypertrophy
√ dilatation of RV ← tricuspid insufficiency / pulmonary hypertension
√ increase in cardiothoracic ratio
√ diminution of retrosternal clear space
√ IVC pushed backward (lateral view)

@ Lung
√ pulmonary arterial enlargement ← pulmonary hypertension

√ pulmonary vascular cephalization = redistribution of pulmonary blood flow to upper lobes (= postcapillary pressure 16–19 mmHg):
  √ diameter of pulmonary artery > corresponding bronchus
  √ diameter of upper lobe vessels > lower lobe vessels
√ interstitial pulmonary edema (= postcapillary pressure 20–25 mmHg)
  DDx: interstitial fibrosis / deposition of hemosiderin-laden macrophages (= "brown induration") of chronic mitral valve stenosis
√ alveolar edema (= postcapillary pressure 25–30 mmHg)



M-mode Echogram in Mitral Valve Stenosis
anterior tracking of posterior mitral valve leaflet (pML)

DDx: diffuse alveolar hemorrhage = diffuse confluent acinar / ground-glass areas of increased opacity sparing the lung periphery (= "window frame" effect)
√ pulmonary hemosiderosis:
  √ 1–3 mm ill-defined nodules
  √ fine / coarse reticular areas of increased opacity with bias for middle and lower lungs
√ pulmonary ossification (3–13%) = densely calcified 1–3–5 mm nodules (± trabeculae) mainly in middle and lower lungs

ECHO:
√ thickening of leaflets toward free edge (fibrosis, calcification)
√ flattening of EF slope = MV remains open throughout diastole ← persistently high LA pressure (crude index of severity of MV stenosis)
√ diastolic anterior tracking of pML in 80% ← diastolic anterior pull by larger + more mobile aML
√ diastolic doming of MV leaflets
√ commissure fusion = increased echodensity + decreased leaflet motion at level of commissure
√ <u>area reduction of MV orifice:</u> *(see under Quantification)* (reproducible to within 0.3 cm^2)
√ shortening + fibrosis of chordae tendineae
√ abnormal septal motion = early diastolic dip of IVS due to rapid filling of RV (in severe MV stenosis)
√ slowed LV filling pattern of small LV

√ dilatation of LA (> 5 cm increases risk of atrial fibrillation + left atrial thrombus)
√ DE opening amplitude reduced to < 20 mm indicating loss of valve pliability (DDx: low cardiac output state)
√ absent A-wave common (atrial fibrillation)
√ increase in valve gradient + pressure halftime on Doppler

Rheumatic Mitral Stenosis

√ "fish-mouth" appearance of thickened valve with commissural fusion on short-axis images
√ "hockey-stick" appearance of bowed thickened fibrotic anterior leaflet during diastole on 2- / 4-chamber images

Rx: (1) Commissurotomy / balloon valvuloplasty if valves pliable + calcium absent + MV regurgitation absent
(2) Valve replacement for symptomatic patients with severely stenotic valves

DDx: (1) Pseudomitral stenosis in decreased LV compliance (decreased EF slope, normal leaflet thickness + motion)
(2) Rheumatic mitral insufficiency (indistinguishable findings + evidence of LV volume overload)
(3) LA myxoma (mass behind MV + in LA)
(4) Low cardiac output (apparent small valve orifice)

Lutembacher Syndrome

= rheumatic mitral valve stenosis + ASD

MITRAL VALVE PROLAPSE

= MVP = systolic bowing of mitral leaflet ≥ 2 mm beyond annular plane into atrium
◊ Most common cause of nonischemic mitral regurgitation
At increased risk for: ventricular arrhythmia, sudden death
Prevalence: 2–6% of general population; 5–20% of young women; ? autosomal dominant inheritance
Age: commonly 14–30 years
Terminology:
(1) **billowing** leaflet = bowing of leaflet body
(2) **flail** leaflet = prolapse of free leaflet edge
Classification:
(1) **MVP syndrome** = systolic click + mid- to late-systolic murmur and classic echocardiographic criteria
Age: young woman
• benign clinical course
(2) **Myxomatous mitral valve disease** = thickened redundant valve leaflets (most common cause of MVP and mitral valve surgery)
= "Floppy mitral valve" = elongation of cusps + chordae tendineae → redundant valve tissue → prolapse into LA during systole
Age: older man
• higher risk for complications, frequently needing repair

Path: myxomatous proliferation of middle layer of MV leaflets, surface fibrosis of MV leaflets, thinning of chordae tendineae, myxomatous annulus

Associated with: Barlow syndrome = straight back syndrome

(3) **Secondary MVP**:

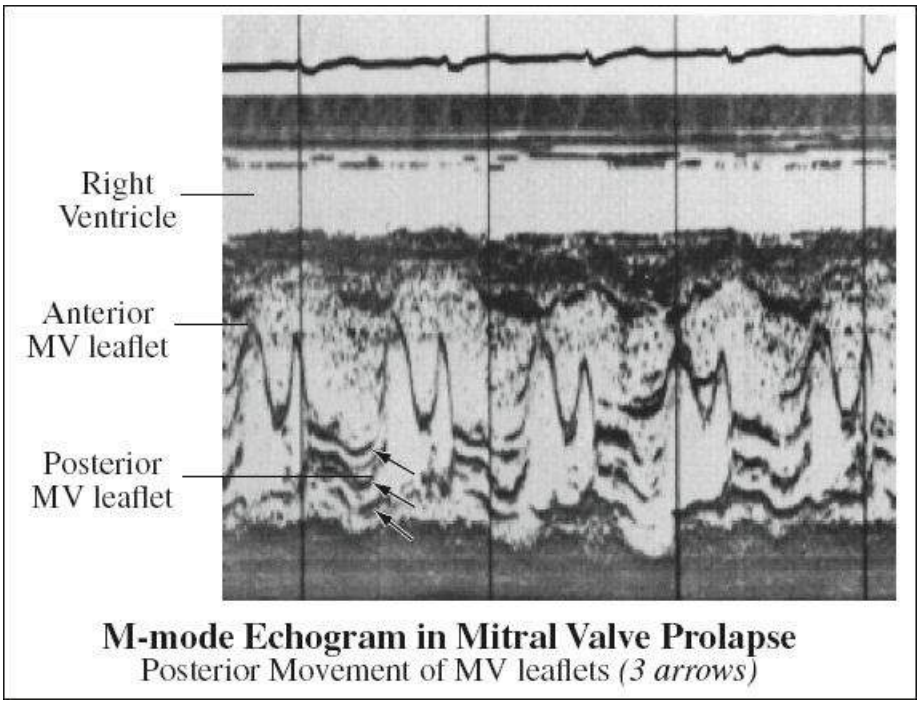
Associated with:

(a) Connective tissue disease: Marfan syndrome (MVP in 91%), Ehlers-Danlos syndrome (in 6%)

(b) CHD: ASD (MVP in 10%), coarctation of aorta (MVP in 2%)

(c) Skeletal abnormalities: scoliosis, straightening of thoracic spine, narrow anteroposterior chest dimension, pectus excavatum deformity of sternum

(d) ischemia / infarction with papillary muscle dysfunction / rupture or rupture of chordae tendineae, rheumatic mitral insufficiency, infective endocarditis, hypertrophic cardiomyopathy, primary pulmonary hypertension, tricuspid valve prolapse, ADPKD



M-mode Echogram in Mitral Valve Prolapse
Posterior Movement of MV leaflets *(3 arrows)*

To decrease mortality preoperative detection of coexisting coarctation of the aorta is important in patients with mitral regurgitation!

- arrhythmia, palpitation, chest pain, light-headedness, syncope
- responsible for midsystolic click + late systolic murmur (when associated with mitral regurgitation)

Location: middle scallop of posterior leaflet (P2 segment)

√ LA NOT enlarged (unless associated with significant mitral regurgitation)

ECHO:

√ interruption of CD line with bulge toward left atrium:

√ abrupt midsystolic posterior buckling of both leaflets (classic pattern)

√ "hammocklike" pansystolic posterior bowing of both leaflets
√ multiple scallops on mitral valve leaflets (short-axis parasternal view)
√ valve leaflets may appear > 5 mm thick (myxomatous degeneration + valve redundancy)
√ ± flail leaflet = eversion of mitral leaflet tip into atrium during systole (← rupture of chordae tendineae)
√ mitral valve leaflets passing > 2 mm posterior to plane of mitral annulus (apical 4-chamber view)
√ hyperactive atrioventricular groove
√ mitral annulus may be dilated > 4.7 cm^2

CT / MR:
√ leaflet thickness > 5 mm + flail leaflet

2- and 3-chamber views are preferred when assessing mitral valve prolapse!

DDx: (1) Pericardial effusion (systolic posterior displacement of MV leaflets + entire heart)
(2) Bacterial endocarditis (mimicked by locally thickened + redundant leaflets)

MYOCARDIAL INFARCTION

= MI = myocardial cell death ← prolonged ischemia overwhelming cellular repair mechanisms

Cause: luminal thrombosis (frequent) superimposed on coronary atherosclerosis, coronary spasm, embolism, > arteritis, dissection, congenital abnormalities, hypercoagulable states, cocaine

Pathophysiology:
↓ perfusion → ↓ tissue oxygenation → ↓ phosphocreatine → repolarization abnormalities → diastolic dysfunction → systolic dysfunction → ↓ adenosine triphosphate → edema → tissue necrosis

Time of dysfunction: loss of contractility (at 60 sec): loss of viability (at 20–40 min)

Wavefront phenomenon:
myocardial ischemia → zone of subendocardial infarction → extension to midmyocardial zone → transmural infarction (from subendocardial to subepicardial layers)

Size of infarct: microscopic < 10% of myocardium
moderate 10–30% of myocardium
large > 30% of myocardium

Incidence: 1,500,000 annually in USA resulting in 500,000 deaths (50% occur in asymptomatic individuals)

Peak age: 40–65 years; more severe + lethal in women

• ST-segment elevation MI (STEMI)
• atrioventricular block (common with inferior wall infarction as AV nodal branch originates from RCA); complete heart block has worse prognosis because it indicates a large area of infarction

CXR:
√ normal-sized heart (84–95%) in acute phase, if previously normal
√ cardiomegaly: high incidence of congestive heart failure with anterior wall infarction, multiple myocardial infarctions, double- and triple-vessel CAD, LV aneurysm

CECT:

√ perfusion defect within 60–90 sec after bolus injection
√ delayed enhancement of infarcted tissue peaking at 10–15 min (← accumulation of iodine in ischemic cells), size of enhanced area correlates well with size of infarct

MR:
√ no change / mildly decreased SI of myocardium on T1WI (= edema of myocardium)
√ high-intensity focus + wall thickening in region of acute infarction on T2WI ← myocardial edema
√ LV wall thinning + decreased SI on T2WI (in remote infarction)
√ increased intracavitary signal ← slow flow caused by stasis of blood adjacent to infarcted myocardium
√ regional wall-motion abnormalities on cine images
√ pericardial effusion (25%), possibly hemorrhagic

CEMR:
√ hyperenhancement = pooling of gadolinium within region of infarction on delayed images 20–30 min post injection:
  √ higher volume of distribution ← increased extracellular space ← myocyte death with membrane disintegration / cell rupture
  √ increased intracellular entry of gadolinium
  √ slow wash-in and washout ← capillary plugging
√ highlighting of infarcted tissue with contrast using magnetic susceptibility to selectively suppress signals from normal myocardium

Delayed-enhancement imaging is the most important technique + most accurate method for diagnosing MI or nonischemic cardiomyopathies, quantifying scar, assessing viability, and evaluating thrombus!

Cx: myocardium is prone to rupture during 3rd–14th day post infarction
Prognosis: 90–95% survival for hospital admissions

Left Ventricular Failure (60–70%)
• "cardiac shock" = systolic pressure < 90 mmHg
◊ Signs of pulmonary venous hypertension are a good predictor of mortality (> 30% if present, < 10% if absent)
√ progressive enlargement of heart
√ haziness + indistinctness of pulmonary arteries
√ ↑ size of right descending pulmonary artery > 17 mm
√ pleural effusion
√ septal lines
√ perihilar ± peripheral parenchymal clouding
√ alveolar pulmonary edema
Mortality: 30–50% with mild LV failure; 44% with pulmonary edema; 80–100% with cardiogenic shock; 8% in absence of LV failure

Ventricular Aneurysm (in 12–15% of survivors of MI)
= saccular protrusion of LV wall of mechanically weak necrotic / scarred fibrotic wall
Location: anterior + apical walls (70–85%)
√ wide-mouthed protrusion with thrombus (in 50%)

√ calcification of wall and thrombus
√ akinetic / dyskinetic wall section during systole
√ delayed hyperenhancement ← scarring
Cx: heart failure, ventricular arrhythmia, thromboembolism

Myocardial Rupture (in 3–20% of infarcts)

At increased risk: first MI, female, ≥ 60 years, multivessel disease, transmural MI involving 20% of wall, poor collateral supply, absence of ventricular hypertrophy, delayed initiation of thrombolytics

Path: myocardial rupture contained by parietal pericardium + thrombus + scar tissue = pseudoaneurysm (mouth smaller than actual size of aneurysmal segment) → high risk of expansion + rupture (30–45%)

• occurs usually on 3rd–5th day post MI

Location: free wall > septum; LV > RV; commonly at apex

√ enlargement of heart (slow leakage of blood into pericardium)

CEMR (delayed-enhancement MRI):

√ loss of continuity of myocardium with irregular margins
√ pericardial enhancement
√ dyskinetic section during systole + diastole

Prognosis: cause of death in 13% of all infarctions; mortality almost 100%

DDx: true aneurysm (mouth larger than size of aneurysmal segment; dyskinetic wall section during systole only)

Rupture of Papillary Muscle (1%)

Cause: infarction of posteromedial papillary muscle in inferior MI (common) / anterolateral papillary muscle in anterolateral MI (uncommon)

• sudden onset of massive mitral insufficiency
• unresponsive to medical management
√ abrupt onset of severe persistent pulmonary edema
√ asymmetric PVH in right upper lobe
√ minimal LV enlargement / normal-sized heart
√ NO dilatation of LA ← immediate decompression into pulmonary veins

Prognosis: 70% (80–90%) mortality within 24 hours (2 weeks)

Rupture of Interventricular Septum (0.5–2%)

= VENTRICULAR SEPTAL RUPTURE

• occurs usually within 2–21 days with rapid onset of L-to-R shunt
• Swan-Ganz catheterization: increase in oxygen content of RV, capillary wedge pressure may be within normal limits

Location: typically at apex

√ right-sided cardiac enlargement
√ engorgement of pulmonary vasculature:
√ asymmetric PVH of right upper lobe
√ NO pulmonary edema (DDx to ruptured papillary muscle)

Prognosis: 24% mortality within 24 hours; 87% mortality (> 90%) within 2 months (1 year)

Rx: emergency surgery (VSD patch repair + coronary artery bypass grafting)

Dressler Syndrome (3–4%)

= POSTMYOCARDIAL INFARCTION SYNDROME = LATE PERICARDITIS

Etiology: autoimmune reaction to myocardial infarction

Onset: 2–3 weeks (range 1 week–several months) following infarction

- relapses occur as late as 2 years after initial episode
- pleuritic chest pain, fever

√ thickening of pericardium
√ pericardial effusion
√ pleural effusion
√ pneumonitis

Right Ventricular Infarction

◊ RV involved in 33% of left inferior myocardial infarction
√ decreased RV ejection fraction
√ accumulation of ^{99m}Tc-pyrophosphate

Prognosis: in 50% RV ejection fraction returns to normal within 10 days

Cx: (1) Cardiogenic shock (unusual)
(2) Elevation of RA pressure
(3) Decrease of pulmonary artery pressure

MYOCARDITIS

= acute / chronic inflammation of the myocardium

Cause:

1. Infection: viral (Coxsackie B, other enteroviruses, herpesvirus, adenovirus, parvovirus B19, Epstein-Barr virus); bacterial (diphtheria, Streptococcus); parasitic (Trypanosoma cruzi)
2. Autoimmune process
3. Cardiotoxic drugs: anthracyclines, trastuzumab, catecholamines, chemotherapy
4. Hypersensitivity reaction
5. Myocardial infarction / mechanical injury / radiation Rx

Histo: lymphocytic infiltration associated with myocyte injury in the absence of ischemia

- usually asymptomatic; acute chest pain
- atrial / ventricular arrhythmias
- rapid recent onset of heart failure
- cardiogenic shock, sudden cardiac death (12%)
- CK-MB (creatine kinase - myocardial b fraction specific for heart muscle) with high specificity but limited sensitivity
- troponin I more often elevated than CK-MB

Sequela: dilated cardiomyopathy (in up to 10%)

Echocardiography (low sensitivity):

√ normal heart function or global / regional LV hypokinesis

MR:

√ patchy diffuse / nodular hyperenhancement in nonvascular distribution up to 4 weeks after infection ← inflammation and cell necrosis

Location: inferior and inferolateral myocardial segments

Site: subepicardial / midmyocardial

√ increased T2 signal

√ wall motion abnormalities in affected regions

Benefit: biopsy guidance to areas of higher pathologic yield

PET/CT:

√ increased metabolic activity in myocardium ← microvascular + myocyte damage + changes in fatty-acid metabolism

Dx: endomyocardial biopsy

MYXOMA

= most common benign primary cardiac tumor (true neoplasm) in adults; 40–50% of all cardiac tumors

Mean age: 50 (range, 11–82) years; 90% of patients are between ages 30 and 60 years; M÷F = 1÷1.7 to 1÷4

Etiology: ? overgrowth of trapped embryologic rest

Classification: sporadic type (most frequent); familial type (mean age of 24 years); complex type = Carney syndrome

Path: (a) papillary / villous pedunculated friable gelatinous tumor

(b) round / ovoid lobular smooth sessile tumor (25%) with firm surface
◊ No infiltration of underlying tissues!

Histo: composed of myxoma cells (= ovoid nucleus with large / inconspicuous nucleoli + abundant eosinophilic cytoplasm) forming rings / syncytia / cords; hypocellular amorphous acid mucopolysaccharide matrix in areas without fibrosis; hemorrhage and hemosiderin; fibrosis, calcifications (56%); covered by a mono-layer of endothelial cells (= endocardial tumor)

Mean size: 5.7 (range, 0.6–12.0) cm

- short history + rapid progression; dyspnea, chest pain
- constitutional symptoms (30%):
  - fever, malaise, weight loss, myalgia, arthralgia, lethargy
  - leukocytosis, anemia, elevated ESR, petechiae
  - hypergammaglobulinemia

  Cause: ? autoimmune phenomenon
- positional symptoms (ie, change with position) due to hemodynamic obstruction:
  - arrhythmia (20%), heart murmur
  - congestive heart failure (valve obstruction); syncope
- embolization (30–40%) to CNS, coronary artery, aorta, kidney, spleen, extremities, pulmonary artery ← tumor fragments / accumulated thrombus

Location: LA (75–80%); RA (10–20%); ventricle (5%); biatrial ← growth through fossa ovalis

Site: attached to interatrial septum by small stalk adjacent to or in fossa ovalis (75%) / to wall of cardiac chambers / to valve surfaces; may protrude into ventricle causing partial obstruction of atrioventricular valve

√ small myxomas produce no CXR findings
√ cardiomegaly
√ atrial obstruction (mimicking valvular stenosis)
√ persistent defect in atrium / diastolic defect in ventricle

A. LEFT ATRIAL MYXOMA (75–80%) with obstruction of mitral valve:
   √ pulmonary venous hypertension:
      √ pulmonary vascular redistribution
      √ interstitial pulmonary edema
   √ enlargement of LA
   √ NO enlargement of atrial appendage
   √ ossific lung nodules

   Cx: systemic emboli (27%) in 50% to CNS (= stroke / "mycotic" aneurysm) ← thrombotic nature of mass

B. RIGHT ATRIAL MYXOMA (10–20%) with obstruction of tricuspid valve:
   - peripheral edema, hepatic congestion, ascites ← potential obstruction of systemic venous return

   √ tumor calcification: R > L
   √ enlargement of RA
   √ prominent SVC, IVC, azygos vein
   √ decreased pulmonary vascularity
   √ pleural effusion (occasionally)

Cx: pulmonary emboli ← thrombotic nature of mass

ECHO: (2D-ECHO is study of choice)
- √ tumor attached by narrow stalk → transvalvular prolapse (DDx to thrombus)
- √ tumor mobility:
  - √ prolapse across AV valve during diastole
- √ tumor distensibility
- √ hyperechoic spherical mass:
  - √ internal hypoechoic areas (= hemorrhage, necrosis)
  - √ speckled echogenic foci (= calcifications)
  - √ frondlike surface projections

Doppler:
- √ valvular regurgitation

M-mode findings of only historical interest:
- √ dense echoes appearing posterior to aML soon after onset of diastole
- √ pML obscured
- √ tumor echoes can be traced into LA
- √ dilated LA
- √ reduced E-F slope

CT:
- √ well-defined spherical / ovoid intraluminal filling defect
- √ lobular / smooth surface contour
- √ tumor attenuation lower than unopacified blood ← gelatinous component
- √ heterogeneous texture ← hemorrhage, necrosis, cyst formation, fibrosis, calcification (16%), ossification

MR:
- √ heterogeneous signal intensity:
  - √ iso- / hypointense on T1WI relative to myocardium
  - √ hyperintense areas on T1WI ← older hemorrhage
  - √ (nearly always) markedly hyperintense on T2WI ← myxomatous tissue
  - √ areas of decreased SI ← calcifications, hemosiderin deposits, fibrous tissue
- √ heterogeneous contrast enhancement:
  - √ increased SI ← vascularity and inflammation
  - √ decreased SI ← necrotic areas
- √ CHARACTERISTIC mobility ± prolapse through AV valve (best seen on 4-chamber horizontal long-axis cine MRI) ← suspended by narrow stalk

PET:
- √ very low-grade / no significant FDG activity

Rx: urgent surgical excision ± valvuloplasty / valve replacement

Cx: malignant transformation (exceedingly rare)

Prognosis: 5–14% recurrence rate (multifocal myxomas); isolated cases of metastatic disease

DDx: (1) Thrombus (more likely in posterior location in LA and LV, NO contrast enhancement, NO transvalvular prolapse)

(2) Papillary fibroelastoma (also arises from narrow stalk, much smaller, different SI characteristics)

(3) Other cardiac tumors: sarcoma, malignant mesenchymoma, metastasis

Carney Complex

= CARNEY SYNDROME = COMPLEX MYOMA

[J. Aidan Carney (–), pathologist at Mayo Clinic, Rochester, Minnesota]

= autosomal-dominant inherited syndromic disorder

Prevalence: 7% of all myxomas; 150 patients identified since 1985 worldwide

Age: younger than patients with sporadic myxoma

- endocrine overactivity:
  - Cushing syndrome; sexual precocity; acromegaly

(a) Cardiac myxomas: multifocal (66%), outside left atrium, recurring at an increased rate after resection

(b) Hyperpigmented skin lesions: lentigines, ephelides, blue nevi

(c) Extracardiac tumors:

1. Pituitary adenoma
2. Myxoid fibroadenoma of the breast
3. Psammomatous melanotic schwannoma
4. Testicular tumor: large-cell calcifying Sertoli cell tumor
5. Primary pigmented nodular adrenocortical hyperplasia

N.B.: not related to Carney triad (pulmonary hamartomas, extraadrenal paragangliomas, gastric leiomyosarcoma)

NUTCRACKER PHENOMENON

= RENAL VEIN ENTRAPMENT SYNDROME

= entrapment of left renal vein (LRV) between SMA and aorta (= anterior nutcracker) / between aorta and underlying vertebral body in retroaortic LRV (*posterior* nutcracker)

Anterior nutcracker syndrome may occur simultaneously with SMA syndrome. Both are associated with a thin / asthenic body habitus, rapid weight loss, and loss of retroperitoneal fat.

Prevalence: rare (unknown);

◊ Insignificant anatomic compression is present in 72% of the general population!

Normal anatomy:

SMA arises from aorta at L1-2 forming an aortomesenteric angle (AMA) of 28–65°; duodenum is cushioned by retroperitoneal fat in mesenteric root maintaining an aortomesenteric space / diameter (AMD) of 10–34 mm

Pathophysiology:

squeezed left renal vein → increased venous pressure → intra- and extrarenal hypertensive valveless venous collaterals

(a) → increased capillary pressure → hematuria

(b) → reflux into left gonadal vein

» female: ovarian vein → congestion in ovarian and parametrial venous plexus = **pelvic congestion syndrome** (vulvar + pelvic + thigh varices, postcoital ache, pelvic pain, dysmenorrhea, dyspareunia)

» male: testicular vein → left-sided **varicocele**

Pathogenesis: steep angulation of SMA relative to aorta can predispose to nutcracker

syndrome → simultaneous SMA syndrome

Age: 3rd–4th decade; M < F

• intermittent asymptomatic mild microhematuria
• severe gross hematuria → passage of ureteral blood clots → left flank pain
• mild to severe orthostatic proteinuria

√ compression of left renal vein + prestenotic dilatation
√ reflux into dilated adrenal + gonadal veins
√ hilar + periureteric + perirenal + pelvic venous collaterals
√ decreased aortomesenteric space (AMD) of 3 mm
√ decreased aortomesenteric angle (AMA) of < 16°

US:
√ venous flow velocity of > 100 cm/s (78% sensitive, 100% specific)
√ peak systolic velocity ratio of > 4.7 at point of renal vein compression compared to hilar renal vein (100% sensitive, 90% specific)

IVP:
√ indentations / scalloping of renal pelvis / ureter ← enlarged retroperitoneal varices

Retrograde venography:
√ renal venous–caval pressure gradient > 3 mmHg (less than 1 mmHg in healthy subjects)

Rx: (1) Expectant: hyperalimentation in thin patient < 18 years
(2) Surgery (in severe cases): renal vein transposition, venous stent placement, left nephrectomy, renal autotransplantation to iliac fossa

PAPILLARY FIBROELASTOMA

= FIBROELASTIC PAPILLOMA = PAPILLOMA / MYXOMA / FIBROMA OF VALVES = GIANT LAMBL EXCRESCENCE
= MYXOFIBROMA = HYALINE FIBROMA
= rare benign excrescence predominantly affecting surface of cardiac valves

Prevalence: 25% of all cardiac valvular tumors (most common valvular tumor); 10% of all primary cardiac tumors (2nd most common primary benign cardiac neoplasm after myxoma + similar to lipoma)

Peak age: 7th and 8th decade; M÷F = 1÷1

Cause: ? reactive process, ? hamartoma

Path: gelatinous mass with "sea anemone" appearance ← multiple delicate branching papillary fronds attached to endocardium by short thin pedicle

Histo: avascular papilloma = avascular connective tissue composed of fibrous core + lined by a single layer of endothelium; scattered smooth muscle cells within papillary projections

• mostly asymptomatic (incidental finding at autopsy, surgery, echocardiography, cardiac catheterization)
• chest pain, dyspnea, embolic events (TIA / stroke from thrombi collecting on tumor)
• NO valvular dysfunction ← away from free edge of valve

Location: cardiac valves (> 90%): aortic (29%) > mitral (25%) > tricuspid (17%) > pulmonary valve (13%)

Site: NOT at free edge of valve
(a) AV valve: nonvalvular endocardial surface of atrium (frequently) / ventricle (16%)

(b) semilunar valve: nonvalvular endocardial surface of aorta

Size: usually < 1.0–1.5 cm in diameter (may be as large as 5 cm)

ECHO:

√ homogeneous mobile pedunculated mass:

√ elongated strandlike projection / well-defined head

√ CHARACTERISTIC stippled edge with a "shimmer / vibration" at interface between tumor and surrounding blood (DDx: amorphous thrombus)

√ flutters / prolapses with cardiac motion

√ turbulent blood flow

CT:

√ slightly hypoattenuating mass

MR: difficult to visualize on static fast SE images

√ intermediate SI / hypointense compared to myocardium

√ mobile mass (on cine gradient-echo images)

Rx: surgical excision ± leaflet repair / valve replacement

DDx: vegetation (destruction of valvular leaflets, valvular incompetence, fever, murmur, embolic events, small vessel vasculitis); thrombus; myxoma (slightly larger)

PATENT DUCTUS ARTERIOSUS

= PDA = persistence of left 6th aortic arch permeable ≥ 3 months after birth = L-to-R shunt

Prevalence: 9 (range, 5–10)% of all CHD; M÷F = 1÷2; in 1÷2,000 full-term infants, higher in prematurity

Cause: failure of immature ductus arteriosus to close ← persistent postnatal hypoxia + failure of ductus contraction

Associated with:

prematurity, birth asphyxia, high-altitude birth, maternal rubella syndrome, VSD, coarctation, trisomy 18 + 21, 4p syndrome, single gene mutation (Carpenter syndrome, Holt-Oram syndrome), X-linked mutations (incontinentia pigmenti)

Morphologic types (useful to select closure device):

A. (conical): √ ampulla at aortic end (most common type)

B. (window): √ ductus narrows at aortic end

C. (tubular): √ NO narrowing / constrictions

D. (complex): √ ductus with multiple constrictions

E. (elongated): √ bizarre configuration; constriction away from pulmonary artery end

Hemodynamics of PDA:

increased volume of blood flows from aorta → through PDA → pulmonary artery → lungs → left side of heart

→ pulmonary artery → lungs → left side of heart

RA	↔	RV	↔	Main PA	↑
Pulm. vessels	↑				
LA	↔/↑	LV	↔/↑	Ao	↑

- mostly asymptomatic; continuous murmur
- congestive heart failure (rare), usually by 3 months of age if L-to-R shunt large

• bounding peripheral pulses ← intraaortic pressure runoff through PDA

CXR (mimics VSD):

√ enlarged pulmonary artery segment
√ increase of pulmonary vasculature; less flow directed to LUL
√ ↑ ascending aorta + aortic arch (thymus may obscure this)
√ LA + LV enlargement
√ enlarged RV (only with pulmonary hypertension)
√ prominent ductus infundibulum (diverticulum)
= prominence between aortic knob + pulmonary a. segment
√ obscured aortopulmonary window
√ "railroad track" = calcified ductus arteriosus

ECHO:

√ LA÷Ao ratio ≥ 1.2÷1 (signalizes significant L-to-R shunt)

Angio:

√ catheter course from RA to RV, main pulmonary artery, PDA, descending aorta
√ communication from aorta (distal to left subclavian artery) → left pulmonary artery (on AP / LAT / LAO aortogram)

PDA in Premature Infant

premature infant not subject to medial muscular hypertrophy of small pulmonary artery branches (which occurs in normal infants subsequent to progressive hypoxia in 3rd trimester)

• CHF

Cause:

(a) pulmonary artery pressure remains low without opposing any L-to-R shunts (PDA / VSD)
(b) ductus arteriosus remains open ← hypoxia in RDS

√ recurrence of alveolar airspace filling after resolution of RDS
√ granular pattern of hyaline membrane disease becomes more opaque
√ enlargement of heart (masked by positive pressure ventilation)

Rx:

(a) Medical therapy:
(1) Supportive oxygen, diuretics, digitalis
(2) Avoid fluid overload (NOT to increase shunt volume)
(3) Antiprostaglandins = indomethacin opposes prostaglandins, which are potent duct dilators
(b) Surgical ligation

Beneficial PDA

= compensatory effect of PDA (= decreasing shunt volume) in:

1. Tetralogy of Fallot
cyanosis usually occurs during closure of duct shortly after birth
2. Eisenmenger pulmonary hypertension
PDA acts as escape valve shunting blood to descending aorta
3. Interrupted aortic arch
supply of lower extremity via PDA

Nonbeneficial PDA

in L-to-R shunts (VSD, aortopulmonic window) a PDA increases shunt volume

PENETRATING AORTIC ULCER

= PENETRATING ATHEROSCLEROTIC ULCER OF THE AORTA

= PAU = atherosclerotic ulcer that penetrates deep through intima and internal elastic lamina into media rendering the aortic wall unstable ← complication of aortic atherosclerosis

Prevalence: uncommon

Cause: new intimal disruption

Age: elderly with hypertension, hyperlipidemia and severe atherosclerosis; M÷F = 4÷1

- often asymptomatic
- chest pain that may radiate to back (29%) WITHOUT pulse difference, aortic regurgitation, CNS symptoms
- occasional distal ischemia ← embolic event

Location: middle / distal ⅓ of descending thoracic aorta (70%); abdominal aorta (30%)

√ localized contrast-medium filled pouch widely communicating with true lumen
√ extensive atherosclerotic disease + ectasia
√ lack of compression of the aortic lumen
√ intramural hematoma (thoracic >> abdominal aorta)
√ NO intimal flap

CECT:

√ focally ulcerated plaque
√ adjacent subintimal hematoma (DDx from intraluminal thrombus / atherosclerotic plaque not possible):
√ inward displacement of calcified intima (common)
√ thickening / enhancement of adjacent aortic wall

MR (valuable for patients in renal failure):

√ focal excavation of aortic wall
√ subacute hematoma in aortic wall of high SI on T1WI + T2WI (methemoglobin) either localized or mimicking type 3 dissection

Angio:

√ ulcerated atherosclerotic plaque
√ aortic wall thickening

Cx:

(1) Ulcer expansion
(2) Aortic dissection (7%) ← intramural hemorrhage:
  (a) localized / extensive
  (b) communicating "double-barreled" / thrombosed
(3) Saccular / fusiform aortic aneurysm (30%) ← stretching of aortic wall
(4) Aortic rupture (40%)

Prognosis: poor and negatively modified by diameter of abdominal aorta, bidimensional size of ulcer, severity of intimal calcification

Rx: (1) Antihypertensive medication, analgesics
(2) Excision of ulcer + aortic interposition graft (for recurrent symptoms /

pseudoaneurysm formation)

DDx: (1) Aortic dissection (intimal flap, patent false lumen)
(2) Atheroma / chronic intramural thrombus (low SI on T1WI + T2WI)
(3) Intramural blood pool

PERICARDIAL CYST

Etiology:
(a) defect in embryogenesis of celomic cavities
(b) sequelae of pericarditis

Frequency: 1÷100 000; 13–17% of all mediastinal cysts
◊ Most common congenital cystic mediastinal lesion

Histo: benign unilocular lesion composed of connective tissue + lined by single layer of mesothelial cells

Age: 30–40 years; M÷F = 3÷2

- asymptomatic (50%)
- chest pain (severe if torsed), dyspnea, cough (in < ⅓)

Location: 90% of pericardial cysts contact diaphragm ± extension into major fissure; R÷L = 3÷1 to 3÷2
(a) right cardiophrenic angle (65%)
(b) left cardiophrenic angle (25%)
(c) mediastinum (10%)

CT:
√ well-defined nonenhancing homogeneous lesion of water attenuation values (20–40 HU)
√ no internal septa / nodules
√ ± proteinaceous fluid of intermediate attenuation
√ ± hemorrhagic content of increased attenuation

√ encapsulated round / ovoid triangular mass usually 3–8 cm (range, 1–28 cm) in diameter:
√ change in location = pedunculated migrating cyst
√ change in shape with change in location ← compressible

MRI:
√ intermediate to low signal intensity on T1WI
√ high signal intensity on T2WI

√ proteinaceous cyst:
√ high SI on T1WI
√ intermediate to low signal intensity on T2WI
√ no restricted diffusion on DWI + high signal on ADC map
√ hemorrhagic cyst:
√ high SI on T1WI
√ susceptibility on GRE

Rx: surgical resection / percutaneous drainage if
(a) individual symptomatic (b) complication present
(c) diagnosis uncertain (d) pathology needed

DDx: congenital cyst (thymic, bronchogenic, neurenteric, duplication cyst); cystic tumor

Pericardial Diverticulum

= focal outpouching of pericardial sac
√ direct communication with pericardial cavity
√ change in size + shape with respiration / body position

PERICARDIAL DEFECT

= CONGENITAL ABSENCE OF PERICARDIUM
= failure of pericardial development ← premature atrophy of left duct of Cuvier (cardinal vein), which fails to nourish the left pleuropericardial membrane during embryogenesis

Frequency: 1÷13,000; M÷F = 3÷1
Mean age at detection: 21 years (range, newborn to 81 years)
Location:

A. PARTIAL ABSENCE (91%)
  (a) complete absence on left side 35%
  (b) foraminal defect on left side 35%
  (c) diaphragmatic pericardial aplasia 17%
  (d) foraminal defect on right side 4%
B. TOTAL BILATERAL ABSENCE (9%)

In 30% associated with:

(1) Bronchogenic cyst (30%)
(2) VSD, PDA, mitral stenosis
(3) Diaphragmatic hernia, sequestration

• mostly asymptomatic
• symptoms ← entrapment / incarceration of cardiac structures:
  • palpitations, tachycardia, dyspnea, dizziness, syncope
  • positional discomfort while lying on left side
  • nonspecific intermittent chest pain: lack of pericardial cushioning, torsion of great vessels, tension on pleuro-pericardial adhesions, pressure on coronary arteries by rim of pericardial defect
• ECG: right axis deviation, right bundle branch block
√ variations in size:
  › small foraminal defect = no abnormality
  › large defect = herniation of cardiac structures / lung
  › complete absence = levoposition of heart
√ absence of left pericardial fat-pad
√ levoposition of heart + aortic knob with lack of visualization of right heart border while trachea remains at midline
√ prominence / focal bulge in the area of RVOT, main pulmonary artery, left atrial appendage
√ sharp margination + elongation of left heart border
√ insinuation of lung between heart + left hemidiaphragm
√ insinuation of lung between aortic knob + pulmonary artery
√ increased distance between heart + sternum ← absence of sternopericardial ligament (cross-table lateral projection)
√ pneumopericardium following pneumothorax

√ NO tracheal deviation

CT + MR:

√ excessive levorotation + displacement of heart

√ cardiac indentation at location of defect

◊ Direct visualization of left pericardium NOT possible!

Cx: cardiac strangulation

Rx: foraminal defect requires surgery because of

(a) herniation + strangulation of left atrial appendage → infarction of appendage

(b) herniation of LA / LV

(c) compression of left coronary artery especially during exercise → cardiac ischemia

(1) Closure of defect with pleural flap

(2) Resection of pericardium

PERICARDIAL MESOTHELIOMA

= PRIMARY MALIGNANT PERICARDIAL MESOTHELIOMA

= malignant primary neoplasm arising from mesothelial cells of the pericardium

Prevalence: 0.0022% at autopsy; < 1% of all mesotheliomas; 50% of all primary pericardial tumors

◊ Most common primary malignancy of pericardium!

Mean age: 46 (range, 2–78) years; M÷F = 2÷1

Path: multiple coalescing pericardial masses with obliteration of pericardial space; myocardial invasion is rare

Histo: epithelial > biphasic (mixed) > fibrous (spindle cell); biphasic tumor composed of epithelial areas forming tubulopapillary structures (resembling carcinoma) and spindled areas (resembling sarcoma)

- chest pain, cough, dyspnea, palpitations
- signs of constrictive pericarditis, cardiac tamponade
- conduction abnormalities ← myocardial infiltration

CXR:

√ cardiac enlargement with irregular contour

√ diffuse mediastinal enlargement

CT / MR:

√ irregular diffuse pericardial thickening / cardiac encasement by soft-tissue masses

√ ± invasion of adjacent vascular + anatomic structures

√ pericardial effusion

√ heterogeneous enhancement with involvement of parietal + visceral layers of pericardium

PET:

√ hypermetabolic activity

Dx: pericardiocentesis → hemorrhagic fluid, malignant cells (in only 20%)

Rx: palliative surgery + radiation therapy

Prognosis: 6 weeks – 15 months survival, regardless of therapy

PERICARDIAL TERATOMA

= benign germ cell neoplasm

Age: infants + children
Histo: derivatives of all 3 germ cell layers (neuroglia, cartilage, skeletal muscle, liver, intestine, pancreas, glandular tissue)
Location: within pericardial sac connected to a great vessel via a pedicle; intramyocardial (rare)
• respiratory distress, cyanosis ← pericardial tamponade + compression of SVC, RA, aortic root, PA
CXR:
√ enlarged cardiomediastinal silhouette
√ formed calcified teeth
US:
√ intrapericardial heterogeneous complex multilocular cystic mass:
√ intrinsic echogenic foci (= calcifications)
√ pericardial effusion
√ fetal hydrops (ascites, pleural effusion, subcutaneous edema, polyhydramnios)
MR:
√ large mass of heterogeneous signal intensity
Rx: emergent pericardiocentesis (life-threatening lesion); urgent surgical excision
Prognosis: good

PERICARDITIS

Etiology:
A. IDIOPATHIC (85%, 2nd most common cause today)
B. NONIDIOPATHIC (15%)
(a) infectious / inflammatory
1. Virus (Coxsackie B, influenza)
2. Bacterium
3. Tuberculosis (formerly most common etiology)
◊ TB is major cause in developing countries + in HIV-immunocompromised patients
3. Fungus / parasite
4. Connective tissue disease: rheumatoid arthritis, lupus erythematosus
(b) traumatic
1. Cardiac surgery (most frequent today)
2. Radiotherapy to mediastinum: breast cancer, mediastinal tumor
3. Percutaneous coronary intervention, pacemaker insertion, catheter ablation
4. Acute myocardial infarction
› **Epistenocardiac pericarditis**
= inflammation in close temporal relationship to acute transmural infarction
Frequency: 10% of patients with acute MI
Cause: pericardial spread of infarct-related inflammation
› Dressler syndrome
(c) autoimmune disorder (5%)
(d) uremia = chronic renal failure

(e) neoplastic (5%) = tumor invasion by carcinoma of breast / lung, lymphoma / leukemia, sarcoma, mesothelioma

Constrictive Pericarditis

= PERICARDIAL CONSTRICTION
= fibrous thickening of pericardium interfering with filling of ventricular chambers via restriction of heart motion
Age: 30–50 years; M÷F = 3÷1
Etiology: infection, trauma, radiation, postoperative status
Hemodynamics of decreased compliance of pericardium:
(a) dissociation between intracardiac + intrathoracic pressure → isolates heart from normal respiratory changes
(b) increased ventricular coupling
(c) increased cardiac filling pressures with equalization of atrial + ventricular pressures

- dyspnea + weakness, peripheral edema, neck vein distension
- abdominal enlargement (ascites + hepatomegaly)
- pericardial knock sound = loud early-diastolic sound
- **Kussmaul sign** = failure of venous pressure to fall (= elevation of jugular venous pressure) with inspiration
- prominent X and Y descent on venous pressure curve

◊ Other causes of right heart failure must be excluded first, ie, pulmonary hypertension, severe tricuspid insufficiency, myocardial infarction

Diagnostic key imaging features):
√ pericardial thickening + enhancement + calcifications
√ biatrial enlargement + tubular ventricles

@ Pericardium
Location: most pronounced over RV + anterior AV groove + posterior surface of LV
√ irregular thickening of pericardium
√ linear / plaquelike pericardial calcifications (27%) as a nonspecific response to chronic inflammation

@ Heart
√ flattened tubular shape of cardiac cavities
√ uni- / bilateral atrial enlargement
√ small atria; occasionally compensatory dilatation of nonconstricted portions, eg, LA enlargement (20%)
√ normal / small-sized heart (enlargement only due to preexisting disease)
√ straightening of heart borders:
√ straight / concave on right side
√ squared on left side
√ pericardial tenting
√ increase in ejection fraction (small EDV)

@ Veins (↑ cardiac filling pressure)
√ dilatation of SVC (77%), IVC, azygos vein (69%), hepatic veins

@ Lung & abdomen

√ normal pulmonary vascularity / pulmonary venous hypertension (43%)
√ pleural effusion (34% bilateral, 26% right PE)
√ ascites

CT:
√ pericardial thickening to 4 mm ± 1 mm in reversible constrictive pericarditis
√ thinning of pericardium to 2 mm ± 1 mm in end-stage irreversible chronic fibrosing pericarditis
√ reflux of contrast into coronary sinus
√ flattening of RV with narrow tubular configuration
√ sigmoid-shaped curvature of interventricular septum toward left

MR:
√ pericardial thickening ≥ 4 mm (suggestive) and > 5–6 mm (highly specific)
◊ Maximal pericardial thickness in constrictive pericarditis has a wide range of 1–17 mm!
◊ Up to 20% of patients have normal thickness of ≤ 2 mm
◊ Degree of pericardial thickening is only weakly related to degree of cardiac constriction!
√ pericardium of intermediate SI similar to myocardium sandwiched between high-signal epicardial and mediastinal fat (on T1WI); most easily identified anterior to RV > RA > free wall of LV
√ often small LV + tubular appearing RV
√ dilatation of RA + IVC reflecting high RV filling pressure (DDx: restrictive cardiomyopathy)
√ flattened / sigmoid-shaped septum
√ NO pericardial enhancement in end stage of disease

Phase-contrast MRI:
√ tricuspid valve inflow: ↑ early filling + ↓ / absent late filling
√ IVC: ↓ / absent forward or reversed systolic flow; ↑ early diastolic flow; late reversed diastolic flow
√ RV filling ↑ on inspiration + LV filling ↑ on expiration
√ "**septal bounce**" = flattening / inversion of septum during early diastolic ventricular filling ← increased ventricular coupling:
√ most pronounced at onset of inspiration
√ right-sided septal shift at onset of expiration

ECHO (nonspecific features):
√ thickening of pericardium (not reliably demonstrated unless pericardial fluid present)
√ immobile pericardium
√ rapid early filling of LV
√ rapid early filling motion followed by flat posterior wall motion during diastasis period (= period between early rapid filling and atrial contraction)
√ premature opening of pulmonic valve

Cx: protein-losing enteropathy ← increased pressure in IVC + portal vein

Rx: antiinflammatory drugs; pericardiectomy = surgical stripping of pericardium

DDx: (a) restrictive physiology:

1. Cardiac tamponade
2. Restrictive cardiomyopathy: eg, amyloid

(b) nonrestrictive physiology:
1. S/P recent cardiac surgery
2. Organized intrapericardial hematoma

Epipericarditis

= EPIPERICARDIAL FAT NECROSIS
= uncommon benign condition of unknown cause that manifests with acute pleuritic chest pain and no prodrome
• focal chest pain varying with changes in patient's position
• normal levels of troponin
CT:
√ focally increased attenuation within epipericardial fat
PET/CT:
√ low-grade FDG uptake
Rx: antiinflammatory medication
Prognosis: symptoms and image findings resolve over time

Inflammatory Pericarditis

Prevalence: 1% of autopsies
Clinical course: acute / subacute / recurrent / chronic
√ pericardial thickening + enhancement + fluid
√ mild to moderate increase / NO increase in FDG uptake

Acute Pericarditis

Cause: mnemonic: MUSIC
Myocardial infarction (acute)
Uremia
Surgery (cardiac)
Infection
Cancer

Histo: inflamed pericardial layers composed of highly vascularized granulation tissue with fibrin deposition

• typical often severe chest pain
• pericardial friction rub (← pericarditis sicca)
• elevated serologic markers of inflammation (eg, C-reactive protein); widespread ST elevation

CT:
√ thickening of pericardial layers
√ diffuse enhancement of pericardium
√ pericardial effusion ± loculations

MR:
√ edema on STIR
√ enhancement of pericardium ± surrounding fat ± myocardium

Cx: (1) Progression to chronic sclerosing pericarditis (< 0.5% for viral pericarditis, relatively frequent for purulent + tuberculous pericarditis)

(2) Myocarditis = atypical ECG changes, transient regional / global wall motion abnormalities, increase in cardiac enzymes

Rx: NSAID

Chronic Pericarditis

Histo: fibroblasts + collagen deposition

Subtypes: (1) Chronic sclerosing pericarditis

(2) Chronic fibrosing pericarditis

√ irregularly thickened pericardial layers

√ loculated pericardial effusion

Cx: stiff pericardium → constrictive pericarditis

PERSISTENT DUCTUS VENOSUS (rare)

= portosystemic shunt ← failure of ductus closure during the 1st week of life (usually immediately after birth in full-term neonate)

Anatomy: ductus arises from posterior aspect of left PV (opposite umbilical vein opening) and drains into HV

Associated with: prematurity, CHD

PERSISTENT FETAL CIRCULATION

= PERSISTENT PULMONARY HYPERTENSION OF THE NEWBORN

= delay in transition from intra- to extrauterine pulmonary circulation

Cause: primary disorder related to birth asphyxia; concurrent parenchymal lung disease (meconium aspiration, pneumonia, pulmonary hemorrhage, hyaline membrane disease, pulmonary hypoplasia); concurrent cardiovascular disease; hypoxic myocardial injury; hyperviscosity syndromes)

• labile pO2

√ structurally normal heart

POLYARTERITIS NODOSA

= PERIARTERITIS NODOSA = PAN

= systemic necrotizing inflammation of medium-sized + small muscular arteries WITHOUT glomerulonephritis or vasculitis in arterioles, capillaries, venules

Frequency: 4–9÷1,000,000 annually(rare); 70÷1,000,000 annually in patients with hepatitis B

Etiology: ? deposition of immune complexes

Mean age: 55 (range, 8–81) years; M÷F = 2÷1 3% of childhood vasculitides in USA

Path: focal panmural necrotizing vasculitis with nodules along the vessel walls; mucoid degeneration + fibrinoid necrosis begins within media; multiple small aneurysms of small + medium-sized arteries; absence of vasculitis in vessels other than arteries (DDx: necrotizing angiitis, mycotic aneurysm)

Histo: polymorphonuclear cell infiltrate in all layers of arterial wall + perivascular tissue (acute phase), mononuclear cell infiltrate, intimal proliferation, thrombosis, perivascular

inflammation (chronic stage)

Associated with: hepatitis B + HIV antigenemia

- low-grade fever, malaise, abdominal pain, weight loss
- myalgia (over weeks), arthralgia, hypertension
- elevated ESR, thrombocytosis, anemia
- positive for hepatitis B surface antigen (up to 30%)
- positive perinuclear ANCA titers; mononeuritis multiplex

Location: all organs may be involved, kidney (70–90%), heart (65%), liver (50–60%), spleen (45%), pancreas (25–35%), GI tract, CNS (cerebrovascular accident, seizure), skin

@ Kidney (involved in 70–80–90%)

- painless hematuria, nephrotic syndrome (proteinuria)
- acute / chronic renal failure

√ irregular nephrogram
√ radiolucent cortical areas
√ prolonged washout of contrast material
√ multiple small intrarenal microaneurysms (at bifurcation of interlobar / arcuate arteries)
√ aneurysms may disappear (thrombosis) or appear in new locations
√ arterial narrowing + thrombosis (chronic / healing stage)
√ multiple small cortical infarcts

CECT:

√ lobulated renal contour + irregular thinning ← prior cortical infarcts
√ multiple hypoattenuating bands (arterial occlusion)

Cx: intrarenal / subcapsular / perinephric hemorrhage ← rupture of aneurysm

@ Chest (involved in 70%)

- CHF, myocardial infarction

√ cardiac enlargement / pericardial effusion (14%)
√ pleural effusion (14%)
√ pulmonary venous engorgement (21%)
√ massive pulmonary edema (4%)
√ linear densities / platelike atelectasis (10%)
√ wedge-shaped / round peripheral infiltrates of nonsegmental distribution (14%) simulating thromboembolic disease with infarction
√ cavitation may occur
√ interstitial pneumonitis in lower lung fields

@ Liver (involved in 50–66%)

√ prolonged washout of contrast material ← increase in peripheral hepatic arterial resistance + hepatic infarcts

@ GI tract (involved in 50–70%)

Location: small intestine > mesentery > colon

- abdominal pain, nausea, vomiting (66%)

√ ulcer formation, GI bleeding (6%)
√ bowel perforation (5%), intestinal infarction (1.4%)
√ pneumatosis intestinalis ± portal venous gas

@ Skeletal muscle (involved in 39%)

- myalgia, arthralgia (50%), limb claudication

√ aneurysms of lumbar + intercostal arteries (19%)
√ lower extremity ischemia (16%)
@ Skin (involved in 20%)
• palpable purpura, infection, ischemic ulcer
• tender subcutaneous nodules (15%)
• peripheral neuropathy (= mononeuritis multiplex)
@ CNS (involved in 10%)
√ sulci of high-signal-intensity on FLAIR image
√ leptomeningeal enhancement on T1WI
Angiography (61–89% sensitive, 90% specific, 55% PPV, 98% NPV, 80% true-positive rate):
√ multiple (> 10) aneurysms of small + medium-sized arteries typically at branching points as a result of pannecrosis of the internal elastic lamina in 50–60% (HALLMARK):
√ 1–5 mm saccular aneurysms in 60–75%
√ fusiform aneurysms / arterial ectasia
◊ Aneurysms are found in 12–94% of polyarteritis nodosa
√ luminal irregularities (in up to 90%)
√ stenoses of arteries
√ arterial occlusions + organ infarcts (98%)
DDx: rheumatoid vasculitis, drug abuse, systemic lupus erythematosus, Churg-Strauss syndrome
Dx: angiography, tissue biopsy
Cx: renin-mediated hypertension, renal failure, hemorrhage ← aneurysm rupture (9%), organ infarction ← vessel thrombosis: gangrene of fingers / toes
Prognosis: clinical course lasts several months to > 1 year; relapse in 40% with median interval of 33 months; 13% 5-year survival rate if untreated
Rx: immunosuppression with corticosteroids + cyclophosphamide (increases 5-year survival rate to 48–90%)

Polyarteritis Nodosa of Childhood

Frequency: 3% of childhood vasculitides in USA
Mean age: 9 years
• history of recent URI
May be associated with: familial Mediterranean fever
Types:
(1) Systemic polyarteritis nodosa (57%)
= malaise, fever, weight loss, myalgia, abdominal pain, arthralgia
Organs: skin, MSK, kidney, GI, heart, CNS, lung
• livido reticularis, subcutaneous nodules
• peripheral gangrene
Cx: visceral hemorrhage ← ruptured aneurysm, bowel infarction
(2) Cutaneous polyarteritis nodosa (30%)
= benign course
Involved organs: skin, MSK WITHOUT internal organs
(3) Hepatitis B-associated polyarteritis nodosa (< 5%) more typical for adults
Dx: CLASSIC angiographic findings of aneurysm, stenosis, occlusion of medium-sized to

small muscular arteries ← necrotizing vasculitis
Location: predominantly renal + mesenteric + hepatic arteries
Renal DSA (digital subtraction angiography):
√ aneurysms in small to medium-sized renal arteries (40%)
√ segmental narrowing
√ variations in arterial caliber
√ pruning of peripheral vascular tree
Mortality rate: 1–4%

POPLITEAL ARTERY ENTRAPMENT SYNDROME

= vascular compression syndrome of popliteal artery (PopA)
Prevalence: 0.165% of young males entering military service
Prevalence: 35 cases in American surgical literature; bilateral in 22–67%
Normal anatomy: PopA courses between the two heads of gastrocnemius muscle = lateral to medial head of gastrocnemius muscle (medGastroc)
Aberrant anatomy:
(1) medial course of PopA around medGastroc
(2) lateral insertion of medGastroc on distal femur
(3) accessory slip of gastrocnemius m. (30%; most common)
(4) hypertrophy / accessory slip of gastrocnemius muscle
(4) fibrous band of popliteus muscle
Pathophysiology:
flow unimpeded when muscle relaxed; increased arterial angulation with muscle contraction (early); progressive intimal hyperplasia ("atheroma" = misnomer) ← microtrauma in area of repeated arterial compression; ultimately occlusion / thrombosis within aneurysm (late)
Age peaks: 17 and 47 years; < 35 years in 68%; M÷F = 9÷1 to 15÷1
• unilateral claudication + exercise-induced leg pain (90%):
  • slowly progressive, esp. during periods of prolonged standing
• acute ischemia of leg with permanent occlusion of popliteal a. (late)
Pulse volume recording (PVR with 40% false-positive results):
√ posterior tibial pulse obliterated during active plantar flexion against resistance / dorsiflexion of foot
  ◊ 50% of general population has some narrowing of PopA!
√ ankle-arm index reduced during active muscle contraction
√ Doppler waveforms of posterior tibial artery diminished during muscle contractions
Angio (biplanar views with hyperextended knee):
√ medial deviation of artery (29%), popliteal stenosis (11%), poststenotic dilatation (8%)
Dx:
√ arteriography with typical medial deviation of popliteal artery before + after gastrocnemius contraction
√ popliteal artery thrombosis / occlusion
Cx: popliteal artery aneurysm
DDx: cystic adventitial disease of popliteal artery, arterial embolism, premature arteriosclerosis, popliteal aneurysm with thrombosis, popliteal artery trauma, popliteal

artery thrombosis, Buerger disease, spinal cord stenosis (= neurogenic claudication)

POSTRHEUMATIC HEART DISEASE

Cause: infection by group A streptococcus → acute rheumatic fever (= systemic inflammatory infection) involving heart, joints, skin, SQ tissue

Path: pancarditis with vegetations forming predominantly on mitral + aortic valve → scarring of chronic inflammation → valvular deformity

• manifestation after latency of 20–25 years

Location: mitral valve > aortic valve

Cx: valvular malfunction (stenosis / insufficiency) → volume overload of proximal cardiac chamber → ventricular damage + remodeling

PRIMARY PULMONARY HYPERTENSION

= PLEXOGENIC PULMONARY ARTERIOPATHY = ppHTN

= idiopathic precapillary cause of pulmonary hypertension (pHTN)

Diagnosis per exclusion:

NO identifiable cause; clinically unexplained progressive pulmonary arterial hypertension without evidence for thromboembolic disease / pulmonary venoocclusive disease

At risk: portal hypertension (with / without liver disease); autoimmune disorders (Raynaud disease, collagen vascular disease); pregnancy; HIV infection; aminorex fumarate (appetite suppressant) ingestion

Histo: plexogenic arteriopathy (HALLMARK) = intimal cell proliferation with focal disruption of internal elastic lamina and media by glomeruloid small vascular channels that ramify into alveolar septal capillaries (75%); acute + organizing intraluminal thrombi (50%)

Age: 3rd decade (range, 20–45 years); M÷F = 1÷3

• gradual onset of progressive dyspnea on exertion (60%)

• easy fatigability, syncope, angina, hyperventilation, hemoptysis

• Raynaud phenomenon, symptoms of cor pulmonale

√ right ventricular enlargement ← hypertrophy + dilatation

√ dilatation of central pulmonary arteries

CXR:

- √ prominent central pulmonary arteries:
  - √ enlarged pulmonary trunk
  - √ right descending pulmonary artery > 25 mm wide
- √ pulmonary vascularity:
  - √ oligemia + rapidly tapering vessels
  - √ overcirculation + vascular distension

CT:

- √ enlargement of central pulmonary arteries:
  - √ diameter of main pulmonary artery > 29 mm (87% sensitive, 89% specific) measured at scan plane of bifurcation at right angle to its long axis just lateral to ascending aorta
  - √ segmental artery-to-bronchus ratio > 1÷1
  - √ pulmonary artery-to-aorta ratio (rPA) > 1
- √ abrupt decrease in caliber of segmental + subsegmental arteries (at outer to medial ⅓ of

lung mantle)
√ small tortuous peripheral vessels = plexogenic arteriopathy
√ absence of detectable intraluminal thrombi
in severe cases:
√ wall-adherent apposition thrombus in central pulmonary aa.
√ pericardial effusion (worse prognosis)
√ focal perivascular groundglass opacities in peripheral / perihilar distribution

HRCT:
√ patchy mosaic pattern of lung attenuation ← regional variations in lung perfusion (rare):
√ hyperdense areas containing large caliber vessels
√ hypodense areas containing small caliber vessels

MR:
√ reversal of interventricular septal curvature
√ direct linear correlation between mean pulmonary artery pressure (PAP) and ratio of main pulmonary artery caliber to descending aorta (MPA/AO)
√ abnormal intravascular signal in 92% on gated T1WI ← slow arterial flow ← ↑ pulmonary vascular resistance

NUC:
√ normal / low-probability V/Q scans

Angio:
√ symmetrically enlarged central arteries
√ diffuse pattern of abruptly tapering + pruned subsegmental vessels
√ filamentous / "corkscrew" peripheral arteries
√ subpleural collaterals (occasionally)
√ bronchial artery dilatation is uncommon (14%) in primary pHTN for unknown reasons and is useful for differentiation from chronic thromboembolic disease.

Prognosis: death in 2–5 years; 34% 5-year survival
Rx: vasodilators, calcium channel blockers, diuretics, anticoagulants; lung / heart-lung transplantation

PSEUDOCOARCTATION

= AORTIC KINKING
= elongated redundant thoracic aorta with acute kink / anterior buckling just distal to origin of left subclavian artery at ligamentum arteriosum
= variant of coarctation without a pressure gradient
Age: 12–64 years
Associated with: hypertension, bicuspid aortic valve, PDA, VSD, aortic / subaortic stenosis, single ventricle, ASD, anomalies of aortic arch branches
• asymptomatic; ejection murmur
• NO pressure gradient across the buckled segment

CXR:
√ anteromedial deviation of aorta
√ "chimney-shaped" high aortic arch (in children)
√ rounded / oval soft-tissue mass in left paratracheal region + superior to presumed normally

positioned aortic arch ← elongation of ascending aorta + aortic arch (in adults)
√ anterior displacement of esophagus
√ NO rib notching / dilatation of brachiocephalic arteries / LV enlargement / poststenotic dilatation

CT/MR:
√ shelflike lesion at any point along the aortic arch
√ poststenotic aortic dilatation

Angio:
√ high position of aortic arch
√ "figure 3" sign = notch in descending aorta at attachment of short ligamentum arteriosum

DDx: true coarctation, aneurysm, mediastinal mass

PULMONARY ARTERY PSEUDOANEURYSM

= tear / disruption of layers of vessel wall with extravasation of blood contained by adventitia / clot / compressed surrounding tissue

Prevalence: rare

Cause:

A. TRAUMA
   1. Improper placement of Swan-Ganz catheter
   2. Penetrating / blunt (rare) trauma
B. INFECTION:
   1. Mycotic aneurysm ← endovascular seeding from endocarditis / direct extension from necrotizing pneumonia
   2. Mycobacterial aneurysm (= Rasmussen aneurysm)
   3. Syphilitic aneurysm
C. VASCULAR ABNORMALITY: cystic medial necrosis, Behçet disease, Marfan syndrome, Takayasu disease
D. OTHER: septic emboli, neoplasm

Associated with: patent ductus arteriosus

• hemoptysis ← leakage of blood into bronchial tree

CXR:
√ stable / increasing focal lung mass

CT:
√ enhancing round lung mass isointense to central pulmonary a.

Cx: 100% mortality with rupture

PULMONARY ATRESIA

= CONGENITAL ABSENCE OF PULMONARY ARTERY

= atretic pulmonary valve with underdeveloped pulmonary artery distally

May be associated with: hypogenetic lung

CXR:
√ small hemithorax of normal radiodensity
√ mediastinal shift to affected side
√ elevation of ipsilateral diaphragm

√ reticular network of vessels on affected side ← systemic collateral circulation from bronchial arteries
√ rib notching from prominence of intercostal arteries ← large transpleural collateral vessels

OB-US:
√ small / enlarged / normal right ventricle
√ progressive atrial enlargement ← tricuspid regurgitation
√ flow reversal in ductus arteriosus + main pulmonary artery (most reliable)

Proximal Interruption of Pulmonary Artery

= AGENESIS OF PULMONARY ARTERY
= atresia of mediastinal portion of right / left pulmonary artery (usually opposite the side of the aortic arch) with distal pulmonic circulation supplied by aortopulmonary collaterals / bronchial arteries
• recurrent infections, dyspnea, pulmonary hypertension
• hemoptysis (10%) ← ruptured systemic collateral vessels
(a) Interrupted left pulmonary artery
Associated with: right aortic arch + severe CHD (including tetralogy of Fallot)
(b) Interrupted right pulmonary artery (more common), generally as isolated finding

CT:
√ complete absence of mediastinal portion of affected pulmonary artery
√ short pulmonary a. terminating within 1 cm of its origin
√ hypoplastic ipsilateral lung + hyperinflated contralateral lung rotating across midline
√ abundant systemic collaterals to affected lung ← dilated bronchial arteries, subclavian artery, intercostal arteries
√ linear peripheral lung opacities = transpleural vascular collaterals

Pulmonary Atresia with Ventricular Septal Defect

= part of spectrum of tetralogy of Fallot (TOF)

Pulmonary Atresia with Intact Interventricular Septum

Associated with: ASD → R-to-L shunt
Type I : NO remaining RV, NO tricuspid regurgitation
√ moderately ↑ RA (depending on size of ASD)
Type II : normal RV with tricuspid regurgitation
√ massive enlargement of RA
√ cardiomegaly ← increase in size of LV + RA
√ concave / small pulmonary artery segment
√ diminished pulmonary vascularity
Rx: prolonged infusion of prostaglandin E, stent placement into ductus, modified Blalock-Taussig shunt, atrial septotomy, transpulmonary valvotomy

PULMONIC INSUFFICIENCY / REGURGITATION

Pathophysiology:
forward blood flow may be maintained ← contraction of RA + pumping of systemic venous return from left heart

Cause:

(a) normal (in 30%) if trivial / mild
(b) bi- and quadricuspid valve
(c) dilatation of valve: pulmonary hypertension, Marfan syndrome, syphilis
(d) damage of cusps: carcinoid heart disease, rheumatic heart disease, infectious endocarditis
(e) after surgical / percutaneous treatment for pulmonary stenosis and repair of TOF

CT:

√ inadequate apposition of cusp at end-diastole
√ dilatation of pulmonic ring + pulmonary artery
√ RV dilatation + hypertrophy

MR / ECHO:

√ ± late diastolic forward flow in pulmonary trunk with each atrial contraction → regurgitant flow usually < 50%

Measurement of pulmonary regurgitant fraction:

√ accurately quantified with through-plane (true transverse with < 15° angulation) velocity mapping
= $\text{Volume}_{\text{regurgitant}} \times 100 / \text{Volume}_{\text{forward}}$ [%]
◊ A regurgitant fraction of ≥ 40% is considered severe!

PULMONIC (PULMONARY) STENOSIS

Frequency: pulmonary artery stenosis without VSD in 8% of all CHD

Embryology: infundibulum formed from proximal portion of bulbis cordis; pulmonary valves develop in 6th–9th week from outgrowth of 3 tubercles

• mostly asymptomatic; cyanosis / heart failure
• loud systolic ejection murmur
√ systolic doming of pulmonary valve (= incomplete opening)
√ normal / diminished / increased pulmonary vascularity (depending on presence + nature of associated malformations)
√ enlarged pulmonary trunk + left pulmonary artery (= poststenotic dilatation)
√ prominent left pulmonary artery + normal right pulmonary a.
√ hypertrophy of RV with reduced size of RV chamber:
√ elevation of cardiac apex
√ increased convexity of anterior cardiac border on LAO
√ diminution of retrosternal clear space
√ cor pulmonale
√ mild enlargement of LA (reason unknown)
√ calcification of pulmonary valves in older adults (rare)

Prognosis: death at mean age of 21 years if untreated

Shape of pulmonary stenosis:

(1) Dome-shaped valve (40–60%) with normal leaflets
(2) Dysplastic thickened immobile cusps (20–30%)
(3) Supravalvular narrowing with deep bottle-shaped sinuses + hourglass deformity (16%)
(4) Bicuspid (0.1%) / quadricuspid (0.2%) pulmonary valve
(5) Dome-shaped valve with dysplastic leaflets

Subvalvular Pulmonic Stenosis

A. INFUNDIBULAR PULMONIC STENOSIS
typically in tetralogy of Fallot

B. SUBINFUNDIBULAR PULMONIC STENOSIS
= hypertrophied anomalous muscle bundles crossing portions of RV
Associated with: VSD (73–85%)
(a) low type: courses diagonally from low anterior septal side to crista posteriorly
(b) high type: horizontal defect across RV below infundibulum

√ late-peaking jet
√ no dilatation of PA because of dissipation of RV force through elongated area of obstruction

Valvular Pulmonic Stenosis / Pulmonary Valve Stenosis

Cause:
(a) congenital (95%):
› isolated (most often)
› associated with other congenital anomalies:
» tetralogy of Fallot (bicuspid pulmonary valve)
» Noonan syndrome (dysplastic pulmonary valve)
» LEOPARD syndrome (= **l**entigines, **e**lectrocardiographic anomalies, **o**cular hypertelorism, **p**ulmonary stenosis, **a**bnormalities of genitalia, **r**etardation of growth, **d**eafness)
(b) acquired: metastatic carcinoid, rheumatic fever, infective endocarditis, prosthetic valve, RVOT conduit

1. CLASSIC / TYPICAL PULMONIC VALVE STENOSIS (95%)
= commissural fusion of pulmonary cusps → funnel shape with small circular orifice
Age of presentation: childhood
• pulmonic click
• ECG: hypertrophy of RV
√ <u>dome-shaped</u> valve:
√ mobile valve with 2–4 raphes
√ incomplete separation of valve cusps
√ jet of contrast through small central orifice
√ dilated main + left pulmonary artery
Rx: balloon valvuloplasty (for peak instantaneous gradient above 50 mmHg)

2. DYSPLASTIC PULMONIC VALVE STENOSIS (5%)
= thickened redundant immobile distorted cusps ← myxomatous tissue
• NO click
√ cauliflower-like thickening at free margin of leaflets
√ NO poststenotic dilatation
Rx: surgical resection of redundant valve tissue
Hemodynamics: obstruction of RV systolic ejection with pressure burden on RV

RA	↔/↑	RV	↑	Main PA	↑
Pulm. vessels	↔			LPA	↑
LA	↔	LV	↔	Ao	↔

CXR:
√ normal pulmonary vascularity
√ normal-sized heart
√ enlargement of main + left pulmonary artery
CT:
√ poststenotic enlargement of main + left PA
√ normal size of right PA (not exposed to turbulent jet from stenotic valve due to 90° angle from main PA)
√ RV hypertrophy
√ bowing of interventricular septum to the left
√ decreased mobility of pliable + thin valve leaflets
Angio:
√ increase in trabecular pattern of RV
√ hypertrophied crista supraventricularis (lateral projection)

Supravalvular Pulmonic Stenosis

60% of all pulmonic valve stenoses
Site of narrowing: sinutubular junction, pulmonary trunk, pulmonary bifurcation, one / both main pulmonary arteries, lobar pulmonary artery, segmental pulmonary artery
Shape of narrowing:
(a) localized with poststenotic dilatation
(b) long tubular hypoplasia
May be associated with:
(1) Valvular pulmonic stenosis, supravalvular aortic stenosis, VSD, PDA, systemic arterial stenoses
(2) Familial peripheral pulmonic stenoses + supravalvular aortic stenosis
(3) **Williams-Beuren syndrome**: autosomal dominant multisystem disorder with supravalvular AS (in 71%), MV prolapse, PS, peculiar facies
(4) Ehlers-Danlos syndrome
(5) **Postrubella syndrome**: peripheral pulmonic stenoses, valvular pulmonic stenosis, PDA, low birth weight, deafness, cataract, mental retardation
(6) Tetralogy of Fallot / critical valvular pulmonic stenosis

Peripheral Pulmonary Artery Stenosis

Frequency: 5% of all pulmonary artery stenoses with an intact ventricular septum

RAYNAUD SYNDROME

= episodic digital ischemia in response to cold / emotional stimuli
Pathogenesis:
(1) Increase in vasoconstrictor tone
(2) Low blood pressure
(3) Slight increase in blood viscosity
(4) Immunologic factors (4–81%)
(5) Cold provocation

- exaggerated response of digit to cold / emotional stress:
  - numbness + loss of tactile perception
  - demarcated pallor / cyanosis
- hyperemic throbbing during rewarming
- sclerodactyly; small painful ulcers at tip of digit

Raynaud Disease

= PRIMARY VASOSPASM = SPASTIC FORM OF RAYNAUD SYNDROME

= exaggerated cold-induced constriction of smooth muscle cells in otherwise normal artery

Cause: ? acquired adrenoreceptor hypersensitivity

May be associated with: reflex sympathetic dystrophy, <u>early stages</u> of autoimmune disorders

Age: most common in young women

- usually affects all fingers of both hands equally

√ normal segmental arm + digit pressures at room temperature

√ peaked digit volume pulse = rapid rise in systole, anacrotic notch just before the peak, dicrotic notch high on the downslope

PPG:

√ flat-line tracing at low temperatures (10°–22°C) with sudden reappearance of normal waveform at 24–26°C = "threshold phenomenon"

Raynaud Phenomenon

= SECONDARY VASOSPASM WITH OBSTRUCTION

= OBSTRUCTIVE FORM OF RAYNAUD SYNDROME

= digital artery occlusion ← stenotic process in normally constricting artery / associated with an abnormally high blood viscosity

Cause:

1. Atherosclerosis (most frequent)
   (a) embolization from an upstream lesion
   (b) occlusion of major arteries supplying arm
2. Arterial trauma
3. <u>End stage</u> of many autoimmune disorders:
   eg, scleroderma, rheumatoid arthritis, systemic lupus erythematosus
4. Takayasu disease
5. Buerger disease
6. Drug intoxication: ergot, methysergide)
7. Dysproteinemia
8. Primary pulmonary hypertension
9. Myxedema

- normal vasoconstrictive response to cold

√ reduced segmental arm + digit pressures at room temperature

PPG (76% sensitivity, 92% specificity):

√ flat-line / barely detectable tracing at low temperature with gradual increase of amplitude upon rewarming

Hand magnification angiography:

1. Baseline angiogram with ambient temperature
2. Stress angiogram immediately following immersion of hand in ice water for 20 seconds

RECREATIONAL DRUG ABUSE

= INTRAVENOUS DRUG ABUSE

Incidence: 35,000,000 > 12 years of age admit to cocaine use at least once in their lifetime; 6,000,000 in a year, 2,300,000 in a month; 8,000,000 have used "crack"

◊ Cocaine is the most commonly used illicit drug + most frequent cause of drug-related deaths

Drugs:

nasal insufflation of cocaine, smoking of alkaloidal cocaine ("freebase", "crack"), amphetamines, amphetamine derivatives (3,4-methylenedioxymethamphetamine [MDMA] = "ecstacy"), opiates, cannabis, inhaled volatile agents (amyl and butyl nitrites = "poppers"), industrial solvents (toluene)

Complications secondary to:

(a) physical / mechanical effects of method of administration (eg, injection technique + choice of injection site [eg, "groin hit" into femoral vein; "pocket shot" into jugular, subclavian, brachiocephalic vein])
(b) chemical / pharmacologic effects of drug or combination of drugs (eg, heroin + cocaine / Talwin®)
(c) effects of adulterants / filler agents (eg, heroin is mixed ["cut"] with quinine, baking soda, sawdust)
(d) microbiologic sequelae (septic preparation)
(e) social + behavioral consequences

Cardiovascular Complications of Drug Abuse

A. Cardiac complications
   1. Acute myocardial ischemia + infarction
      Cause: intense coronary vasoconstriction, platelet activation (cocaine)
      Drug: amphetamines, cocaine
   2. Arrhythmia
   3. Dilated cardiomyopathy (often reversible)
      Cause: chronic drug abuse
   4. Endocarditis (esp. of tricuspid valve)
      Cause: bacteremia (most commonly S. aureus) with nonsterile IV administration

B. Arterial complications
   1. Aortic dissection
      Cause: systemic hypertension + positive inotropic + chronotropic cardiac effects of cocaine
   2. Arterial occlusion
      (a) at injection site ← intimal damage, thrombosis, spasm
      (b) distal to injection site ← embolization, spasm
   3. Pseudoaneurysm
   4. Mycotic aneurysm

5. Arteriovenous fistula
4. Embolization of infectious agent / foreign body / air through inadvertent arterial injection ("hit the pink")

C. Venous complications
1. Deep vein thrombosis (DVT) (after superficial veins have been exhausted)
"groin hit" into femoral vein; "pocket shot" into jugular, subclavian vein, brachiocephalic vein
2. Septic thrombophlebitis
3. Intravenous migration of needle to heart / lungs

Respiratory Complications of Drug Abuse

1. Bronchitis, epiglottitis, sinusitis
Drug: nasal insufflation of cocaine hydrochloride, smoking of alkaloidal cocaine (freebase, crack)
2. Nasal septal perforation = "cocaine nose"
Cause: ischemic necrosis from chronic cocaine use
3. Pneumonia
Cause: aspiration during altered consciousness, anesthetic effect of cocaine on pharynx
4. Pulmonary edema
Drug: opiate overdose, IV use of cocaine hydrochloride, smoking of crack cocaine, amphetamine, MDMA
Cause: cardiogenic, neurogenic pulmonary edema ← CNS effects of drug, direct toxic effect on alveolar-capillary membrane, immune response activation
5. Pulmonary hemorrhage
Drug: crack cocaine
6. Bland / septic pulmonary embolism
Cause: DVT, septic thrombophlebitis, tricuspid valve endocarditis
7. Pulmonary granulomatosis
Drug: insoluble filler agents in oral medications abused intravenously like talc (magnesium silicate), starch, cellulose
8. Emphysema
Drug: marijuana, IV abuse of methylphenidate (Ritalin)
9 Hemo- / pyo- / pneumothorax
Cause: attempted subclavian / jugular vein puncture ("pocket shot"), rupture of drug-related bulla, rupture of peripheral pulmonary abscess, inhalational maneuvers during crack / cannabis use

Neurologic Complications of Drug Abuse

1. Intracranial hemorrhage
Cause: sympathomimetic effect of → systemic vasoconstriction → increased cardiac output → severe acute hypertension
N.B.: in 50% underlying vascular lesion
Drug: esp. alkaloidal form of cocaine, amphetamine
2. Ischemic stroke
Cause: vasoconstrictive effects; platelet activation of cocaine; vasculitis in amphetamine

+ cocaine; embolic events in endocarditis / injection of particulate material

Drug: cocaine, MDMA, heroin

3. Posterior reversible encephalopathy syndrome (PRES)
   Drug: cocaine, amphetamine
4. Diffuse cerebral edema
   Cause: anoxic brain injury after drug-induced cardiac arrest, severe respiratory depression in opiate overdose, fulminant multiorgan failure in drug overdose
5. Toxic leukoencephalopathy
   Drug: inhalation of heroin vapor (pyrolysate) heated on tinfoil ("chasing the dragon"); inhalant abuse of industrial solvent toluene
6. Cerebral atrophy (esp. frontal lobes)
   Cause: chronic drug abuse
7. CNS infection
   Cause: left-sided endocarditis

Soft-tissue Complications of Drug Abuse

1. Cellulitis from subcutaneous injection ("skin popping") after exhausting all venous access
2. Pyomyositis
3. Necrotizing fasciitis
4. Abscess: esp. iliopsoas
5. Hematoma
6. Foreign bodies
7. Lymphadenopathy

Skeletal Complications of Drug Abuse

1. Osteomyelitis
   (a) direct contamination: eg, pubic bone ("groin hit") / clavicle ("pocket shot")
   (b) hematogenous: spine most commonly affected
2. Septic arthritis: sacroiliac, sternoclavicular, symphysis pubis, acromioclavicular, hip, knee, wrist
3. Diskitis

Cx: 1. Spinal epidural abscess in 5–18% ← vertebral osteomyelitis
2. Cord compression ← collapsed vertebral body

Visceral Complications of Drug Abuse

A. Gastrointestinal complications
   1. Severe colonic ileus resulting in chronic constipation + fecal impaction ← opiates
      Cx: stercoral colitis ← pressure necrosis; perforation of rectum / sigmoid colon
   2. Mesenteric ischemia / infarction (cocaine, amphetamines)
   3. Colonic pseudoobstruction
   4. Necrotizing enterocolitis
   5. Liver abscess

B. Genitourinary complications
   1. Acute renal toxicity
   2. Rhabdomyolysis

3. Renal infarction
4. Focal / segmental glomerulosclerosis ← heroin abuse
5. Distal tubular renal acidosis ← toluene abuse
6. Amyloidosis

C. Acquired viral infection
Cause: sharing of contaminated needles
1. HIV (in 5–10%)
2. Hepatitis B + C (20–59%)

RHABDOMYOMA OF HEART

= benign myocardial hamartoma
Prevalence: most common cardiac tumor in infancy + childhood (up to 90%)
Age: usually discovered < 1 year of age
Path: well-circumscribed intramural lobulated nodule / multiple < 1 mm nodules (= rhabdomyomatosis)
Histo: "spider cells" = enlarged vacuolated cells with high glycogen content + central nucleus surrounded by clear cytoplasm and radial extensions
Associated with: congenital heart disease

With cardiac rhabdomyomas tuberous sclerosis is found in 60–80%. With tuberous sclerosis > 50% have rhabdomyomas!

- asymptomatic (incidental detection at prenatal US)
- murmur, arrhythmia
- heart failure ← obstruction of left ventricular outflow tract / reduction of enddiastolic volume / decreased contractility
- supraventricular tachycardia ← accessory conductive pathways within tumor

Presentation: cardiac rhabdomyomas may precede skin lesions (hypopigmented "ash-leaf" macules) and neuroradiologic findings (subependymal nodules, cortical tubers) by months or years!

Location: multifocal (in up to 90%); ventricular wall with intramural growth + tendency to involve interventricular septum; atrial wall (rare)
Average size: 3–4 cm; up to 10 cm in diameter
US (good for small intramural lesions):
√ fetal nonimmune hydrops
√ solid echogenic sessile mass ± intracavitary component bulging into ventricular outflow tract / atrioventricular valve
√ diffuse myocardial thickening (with multiple small lesions)
MR (complimentary to US):
√ tumor iso- to marginally hyperintense on T1WI
√ hyperintense to myocardium on T2WI
√ hypointense to myocardium after contrast enhancement
Prognosis: may regress spontaneously in patients < 4 years old
Rx: surgical excision for life-threatening symptoms
DDx: fibroma (solitary centrally calcified + cystic tumor, in ventricular myocardium, associated with Gorlin syndrome); teratoma (single intrapericardial multicystic mass);

hemangioma (arise from right atrium, pericardial effusion, skin hemangiomas)

RIGHT AORTIC ARCH (RAA)

Prevalence: 1–2%

Embryology: persistence of right aortic arch and right descending aorta + regression of left aortic arch

Course: to right of trachea + esophagus, over right mainstem bronchus; crosses lower thoracic spine; passes through left hemidiaphragm

Incidence of right aortic arch in CHD:

1. Truncus arteriosus 35%
2. Pulmonary atresia 25%
3. Tetralogy of Fallot 25%
4. Tricuspid atresia 15%
5. DORV 12%
6. TGV 8%
7. Large VSD 2%

Rare anomalies:

1. Corrected transposition
2. Pseudotruncus
3. Asplenia
4. Pink tetralogy

RAA with Aberrant Left Subclavian Artery

= RAA with ALSA + left ligamentum arteriosum

Embryology: interruption of embryonic left arch between left CCA + left subclavian artery

◊ Most common type of right aortic arch anomaly

Prevalence: 1 ÷ 2,500; 35–72% of right aortic arch anomalies

◊ 2nd most common cause of vascular rings (12–25%) after double aortic arch

Associated with: congenital heart disease in 5–12%:

1. Tetralogy of Fallot (⅔ = 8%)
2. ASD ± VSD (¼ = 3%)
3. Coarctation (1/12 = 1%)

- usually asymptomatic (loose ring around trachea + esophagus)
- may be symptomatic in infancy / early childhood:
  - wheezing + stridor provoked by bronchitis + tracheal edema
  - dysphagia (50% of children and adults)
- may be symptomatic in adulthood provoked by torsion of aorta

√ left common carotid artery is first branch of ascending aorta

√ left subclavian artery arises from descending aorta via the remnant of the left dorsal aortic root (= lusorian artery)

√ bulbous configuration of origin of LSA (= remnant of embryonic left arch) = retroesophageal aortic diverticulum = **diverticulum of Kommerell** (N.B.: originally described as diverticular outpouching at origin of right subclavian artery with left aortic arch):

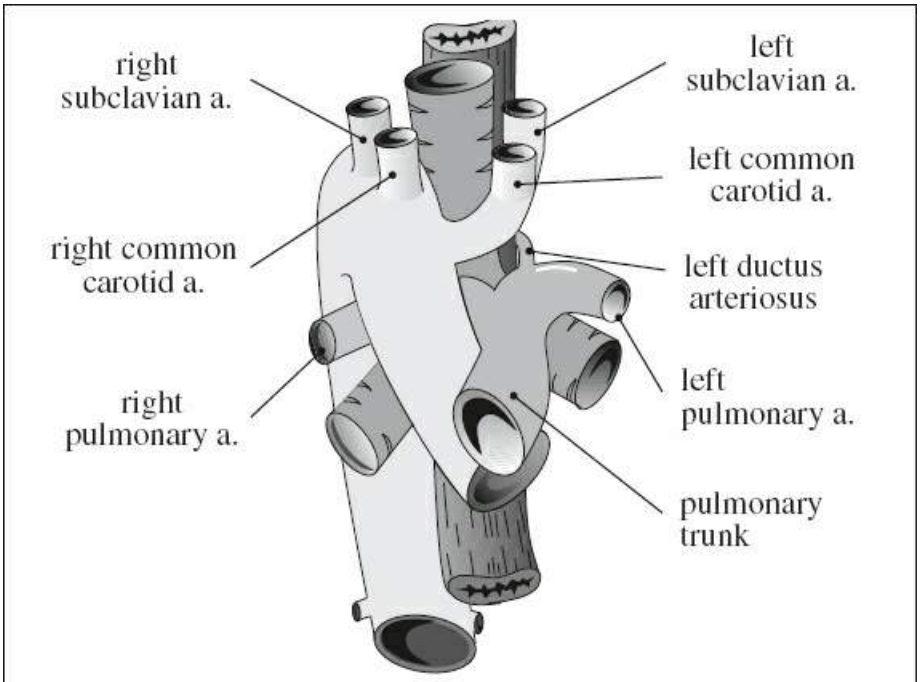
[Burckhard Friedrich Kommerell (1901-1990), chief of radiology at the Charité University Clinic in Berlin and radiologist in Heidelberg, Germany]

√ small rounded density left lateral to trachea

√ impression on left side of esophagus simulating a double aortic arch (by aortic diverticulum or ductus / ligamentum arteriosum)

√ vascular ring (= left ductus extends from aortic diverticulum to left pulmonary artery):

√ impression on tracheal air shadow (by right aortic arch)



Right Aortic Arch with Mirror-image Branching

√ right esophageal indentation (by right aortic arch)

√ masslike density silhouetting top of aortic arch just posterior to trachea on LAT CXR ← aberrant left subclavian artery

√ broad posterior impression on esophagus ← left subclavian artery / aortic diverticulum

√ small anterior impression on trachea ← left common carotid artery

√ descending aorta on right side

CT:

√ "four artery" sign = 2 dorsal subclavian arteries and 2 ventral carotid arteries evenly spaced around trachea

Right Aortic Arch with Mirror-image Branching

◊ 2nd most common aortic arch anomaly: 24–60%

= interruption of embryonic left arch between left subclavian artery and descending aorta; retroesophageal left ductus arteriosus / lig. arteriosum

Interruption of Left Aortic Arch Distal to Ductus Arteriosus = Type 1 (common)

Associated with: cyanotic CHD in 98%:

1. Tetralogy of Fallot (87%)
2. Multiple defects (7.5%)
3. Truncus arteriosus (2–6%)
4. Transposition (1–10%)
5. Tricuspid atresia (5%)
6. ASD ± VSD (0.5%)

◊ 25% (37%) of patients with tetralogy of Fallot (truncus arteriosus) have a right aortic arch!

√ NO vascular ring, NO retroesophageal component

√ NO structure posterior to trachea

√ R arch impression on tracheal air shadow

√ NORMAL barium swallow

Interruption of Left Aortic Arch Proximal to Ductus Arteriosus = Type 2 (rare)

= true vascular ring (if duct persists); rarely associated with CHD

RAA with Isolated Left Subclavian Artery

◊ 3rd most common right aortic arch anomaly: 2%

= interruption of embryonic left arch between
(a) left CCA and left subclavian artery and
(b) left ductus and descending aorta
resulting in a connection of left subclavian artery with left pulmonary artery

Associated with: tetralogy of Fallot

√ left common carotid artery arises as the first branch

√ left subclavian artery attaches to left pulmonary artery through PDA

√ NO vascular ring, NO retroesophageal component

• congenital subclavian steal syndrome

RAA with Aberrant Left Brachiocephalic Artery

Similar in appearance to R aortic arch + aberrant L subclavian artery

SINGLE VENTRICLE

= UNIVENTRICULAR HEART = DOUBLE INLET SINGLE VENTRICLE

= failure of development of interventricular septum ± absence of one atrioventricular valve (mitral / tricuspid atresia) ± aortic / pulmonic stenosis

Associated with: TGV or DORV

• conduction defect ← aberrant anatomy of conduction system

√ 2 atrioventricular valves connected to a main ventricular chamber

√ the single ventricle may be a LV (85%) / RV / undetermined

√ a second rudimentary ventricular chamber may be present, which is located anteriorly (in left univentricle) / posteriorly (in right univentricle):
√ rudimentary chamber ± connection to one great artery

√ may be associated with tricuspid / mitral atresia

SPLENIC ARTERY ANEURYSM

= most frequent of visceral artery aneurysms
Etiology: medial degeneration with superimposed atherosclerosis, congenital, mycotic, pancreatitis, trauma, portal hypertension (in 7–10% ← high flow rate)
Predisposed: women with ≥ 2 pregnancies (88%)
May be associated with: fibromuscular disease (in 20%)
M÷F = 1÷2
• usually asymptomatic / pain, GI bleeding
Location: intra- / extrasplenic
√ calcified wall of aneurysm (²/₃)
Cx: rupture of aneurysm (6–9%, higher during pregnancy) especially if > 1.5 cm in diameter
Mortality: up to 76%
DDx: renal artery aneurysm, tortuous splenic artery

SUBCLAVIAN STEAL SYNDROME

= stenosis / obstruction of subclavian artery near its origin with flow reversal in ipsilateral vertebral artery at the expense of the cerebral circulation
Frequency: 2.5% of all extracranial arterial occlusions
Etiology:
(a) congenital: interruption of aortic arch, preductal infantile coarctation, hypoplasia of left aortic arch, hypoplasia / atresia / stenosis of an anomalous left subclavian artery with right aortic arch, coarctation with aberrant subclavian artery arising distal to the coarctation
(b) acquired: atherosclerosis (94%), dissecting aneurysm, chest trauma, embolism, tumor thrombosis, inflammatory arteritis (Takayasu, syphilitic), ligation of subclavian artery in Blalock-Taussig shunt, complication of coarctation repair, radiation fibrosis
Average age: 59–61 years; M÷F = 3÷1; Whites÷Blacks = 8÷2
Associated with: additional lesions of extracranial arteries in 81%
• lower systolic blood pressure by > 20–40 mmHg on affected side
• delayed weak / absent pulse in ipsilateral extremity
• signs of vertebrobasilar insufficiency (40%):
  • syncopal episodes initiated by exercising the ischemic arm
  • headaches, nausea, vertigo, ataxia
  • mono-, hemi-, para-, quadriparesis, paralysis
  • diplopia, dysphagia, dysarthria, paresthesias around mouth
  • uni- / bilateral homonymous hemianopia
• signs of brachial insufficiency (3–10%):
  • intermittent / constant pain in affected arm precipitated by increased activity of that arm
  • paresthesia, weakness, coolness, numbness, burning in fingers + hand; fingertip necrosis
Location: L÷R = 3÷1
Color Doppler:
√ reversal of vertebral artery flow → augmented by arm exercise / reactive hyperemia (= blood pressure cuff inflated above systolic pressure for 5 min)
Angio:
√ subclavian stenosis / occlusion (aortic arch injection)
√ reversal of vertebral artery flow (selective injection of contralateral subclavian / vertebral

artery)

CAVE: "false steal" = transient retrograde flow in contralateral vertebral artery caused by high-pressure injection

Rx: bypass surgery, PTA (good long-term results)

Partial Subclavian Steal Syndrome

= retrograde flow in systole + antegrade flow in diastole

Occult Subclavian Steal Syndrome

= reverse flow seen only after provocative maneuvers, ie, ipsilateral arm exercise of 5 min / 5 min inflation of sphygmomanometer > systolic blood pressure levels

SUPERIOR MESENTERIC ARTERY SYNDROME

= ARTERIOMESENTERIC DUODENAL COMPRESSION SYNDROME = WILKIE SYNDROME = CHRONIC DUODENAL ILEUS = BODY CAST SYNDROME

= rare cause of duodenal obstruction ← compression of 3rd portion of duodenum between SMA and aorta; probably representing a functional reflex dilatation

Normal anatomy: see "nutcracker phenomenon"

Cause: congenital, weight loss, visceroptosis ← loss of abdominal muscle tone (as in pregnancy), asthenic build, exaggerated lumbar lordosis, prolonged bed rest in supine position

Pathophysiology:

(1) rapid severe weight loss ← cachexia (AIDS, malabsorption, cancer); catabolic condition (burns, major surgery); eating disorder (anorexia nervosa); drug abuse; post bariatric surgery → loss of retroperitoneal fat → decrease in angle (AMA) + space (AMD) → duodenal compression

(2) Post scoliosis surgery → lengthening of spine → increased tension on mesentery → decreased AMA and AMD

(3) Applied external abdominal pressure (body / hip spica cast)

(4) Anatomic variant: insertional variation of ligament of Treitz / low origin of SMA → more cranial disposition of duodenum → acute AMA

Frequency: 0.1–0.3% of barium studies

Age: 10–39 years; M÷F = 1÷2

- postprandial epigastric pain and fullness relieved by lying prone / in left lateral decubitus position
- nausea, repetitive vomiting, weight loss, anorexia
- severe esophagitis + gastritis ← stasis / chronic obstruction

Angio / sagittal MR / reformatted CT (test of choice):

√ narrowing of angle between SMA + aorta to 6–22° (AMA)

√ reduced distance between SMA + aorta to 2–8 mm (AMD)

Upper GI:

√ megaduodenum = pronounced dilatation of 1st + 2nd portion of duodenum + frequently dilated stomach (best seen in supine position)

√ vertical linear compression defect in transverse portion of duodenum overlying spine

√ abrupt change in caliber distal to compression defect

√ antiperistaltic waves proximal to obstruction
√ delayed gastroduodenal emptying
√ relief of obstruction by postural change into prone knee-elbow position

Rx: (1) conservative: fluid + electrolyte resuscitation, nasojejunal feeding, small liquid meals, prone / left lateral decubitus patient position, restoration of retroperitoneal fat through hyperalimentation)

(2) surgery: duodenojejunostomy, gastrojejunostomy, Strong procedure (= lysis of ligament of Treitz with derotation of bowel)

SUPERIOR VENA CAVA SYNDROME

= obstruction of SVC with development of collateral pathways

Etiology:

A. MALIGNANT LESION (78–97%)
   1. Bronchogenic carcinoma (50–80%)
   2. Lymphoma (2–20%)
   3. Metastatic mediastinal nodes (← commonly breast ca.)
   4. Mediastinal germ cell tumor
   5. Malignant thymoma

B. BENIGN LESION
   1. Granulomatous mediastinitis: usually histoplasmosis, sarcoidosis, TB
   2. Substernal goiter
   3. Ascending aortic aneurysm
   4. Pacer wires / central venous catheter (23%)
   5. Constrictive pericarditis

Collateral routes:

1. Esophageal venous plexus = "downhill varices" (predominantly upper $^{2}/_{3}$ of esophagus)
2. Azygos + hemiazygos veins
3. Accessory hemiazygos + superior intercostal veins = "aortic nipple" (visualization in normal population in 5%)
4. Lateral thoracic veins + umbilical vein
5. Vertebral veins

• head and neck edema (70%), headache, dizziness, syncope
• cutaneous enlarged venous collaterals, proptosis, tearing
• with benign etiology: slower onset + progression, both sexes at 25–40 years of age
• with malignancy: rapid progression within weeks, mostly males at 40–60 years of age
• dyspnea, cyanosis, chest pain, hematemesis (11%)

√ superior mediastinal widening (64%)
√ encasement / compression / occlusion of SVC
√ dilated cervical + superficial thoracic veins (80%)
√ SVC thrombus

NUC:

√ increased tracer uptake in quadrate lobe + posterior aspect of medial segment of left lobe ← umbilical pathway toward liver when injected in upper extremity

TAKAYASU ARTERITIS

= PULSELESS DISEASE = AORTITIS SYNDROME

= AORTOARTERITIS = IDIOPATHIC MEDIAL AORTOPATHY = AORTIC ARCH SYNDROME = MARTORELL SYNDROME

= idiopathic chronic relapsing necrotizing obliterative segmental large-vessel panarteritis affecting mainly elastic arteries (aorta > main aortic branches > pulmonary arteries) limited to persons usually < 50 years of age

◊ The only form of aortitis that produces stenosis / occlusion of the aorta!

Etiology: probably cell-mediated autoimmune process

Prevalence: 1÷1,000,000; 2.2% (at autopsy)

Incidence: 2.6÷1,000,000 annually (USA)

Geography: common in Asia, Mediterranean basin, South Africa, Latin America; rare in Europe + North America

Age: 12–66 years; M÷F = 1÷8; especially in Asians

◊ Primary large-vessel vasculitis in children and adults!

◊ 3rd most common form of childhood vasculitis!

Histo: (a) Acute stage: granulomatous infiltrative process focused on elastic fibers of media of arterial wall consisting of multinucleated giant cells, lymphocytes, histiocytes, plasma cells; perivascular cuffing of vasa vasorum

(b) Fibrotic stage (weeks to years): progressive fibrosis of vessel wall resulting in constriction from intimal proliferation / thrombotic occlusion / aneurysm formation (← extensive destruction of elastic fibers in media); → ultimately fibrosis of intima + adventitia

◊ Morphologically indistinguishable from temporal arteritis!

Clinical stages: often overlapping ← relapsing course

» prepulseless / systemic / early phase

Duration: few months – 1 year

- nonspecific systemic signs + symptoms: fever, night sweats, weakness, weight loss, myalgia, arthralgia

◊ Mean interval of 8 years between onset of symptoms + Dx

» vascular inflammatory phase

» pulseless / occlusive / late phase

- signs + symptoms of ischemia of limb (arm claudication, pulse deficit, bruits, discrepant blood pressures)
- renovascular hypertension, abdominal angina
- visual symptoms

- neurologic symptoms: transient ischemic attack, stroke, hypertensive encephalopathy
- erythrocyte sedimentation rate (ESR) > 20 mm/hour in 80%

The diagnosis of Takayasu arteritis is based on clinical information, laboratory evaluation, and diagnostic imaging, because a large-vessel biopsy cannot be performed.

Numano classification: involvement usually bilateral

Type I : branches of aortic arch = brachiocephalic trunk + carotid arteries + subclavian arteries

Type II : combination of type I + III
IIa : ascending aorta / aortic arch ± branches
IIb : descending thoracic aorta ± ascending aorta / aortic arch with its branches
Type III : entire descending aorta ± renal arteries
Type IV : abdominal aorta ± renal arteries
Type V : entire aorta with branches
C / P(+) = involvement of coronary / pulmonary arteries
Commonly involved: left subclavian artery (< 50%), left common carotid artery (20%), brachiocephalic trunk, renal arteries, celiac trunk, superior mesenteric a., pulmonary a.
Infrequently involved: axillary, brachial, vertebral, iliac arteries (usually bilaterally), coronary arteries

Angiography / DSA:
◊ Difficult catheterization / risk of ischemic complications ← increase in coagulation!
√ arterial wall thickening + contrast enhancement
√ full-thickness calcification (= chronic disease)
√ mural thrombi
Dx: involvement of > 2 medium-sized branch vessels

CXR:
√ widened supracardiac shadow > 3.0 cm
√ wavy / scalloped appearance of lateral margin of descending aorta
√ aortic calcifications (15%) commonly in aortic arch + descending aorta
√ focal decrease of pulmonary vascularity

NECT:
√ high-attenuation arterial walls of variable thickness
√ calcifications in aorta + its branches

CT angiography (95% sensitive, 100% specific):
√ concentric thickening of vessel wall > 3 mm:
√ "double ring" appearance = poorly enhanced internal ring (= swollen intima) + enhancing outer ring (= inflamed media and adventitia)
√ mural thrombus, stenosis, occlusion
√ vessel ectasia, aneurysm, ulcer
√ typically linear wall calcifications after > 5 years (usually sparing ascending aorta)

MR:
› acute / active inflammatory phase:
√ thickened enhancing arterial wall (on fat-suppressed T1)
√ mural edema of arterial wall (STIR) = measure of disease activity
√ bright T2 signal around inflamed vessel
√ mural thrombus, multilevel stenosis
√ thickening of aortic valve cusps
√ pericardial effusion
› late phase:
√ dilatation of ascending aorta

√ segmental dilatation with stenotic regions of CCA + subclavian artery
√ complete occlusion of supra-aortic arteries at their origin, + multiple collaterals
» luminal changes: multifocal stenoses, fusiform vascular dilatation, mural thrombi, collateral vessel formation

US:
√ "macaroni sign" long segment of smooth homogeneous concentric wall thickening
√ increased intimal-medial thickness = reliable marker for disease activity

@ Aorta (common involvement)
Location: abdominal aorta > descending thoracic > arch
√ long + diffuse / short + segmental irregular stenosis / occlusion of major branches of aorta near their origins
√ stenotic lesions of descending thoracic > abdominal aorta
√ frequent skipped lesions
√ abundant collateralization (late phase)
√ aneurysmal dilatation of ascending aorta + arch (= diffusely dilated lumen with irregular contours) → aortic insufficiency
√ fusiform / saccular aortic aneurysms (10–15%) (common in descending thoracic + abdominal aorta)
Cx: rapid aneurysm expansion → aortic rupture (33%)

@ Brachiocephalic arteries
√ multisegmented dilatation of carotid artery producing segmental septa
√ diffuse homogeneous circumferential thickening of vessel wall in proximal common carotid artery
√ increase in flow velocity + turbulence
√ distal CCA, ICA, ECA spared with dampened waveforms

@ Pulmonary arteries (50–80%)
Location: segmental + subsegmental (common); lobar + main pulmonary arteries (uncommon)
◊ often late manifestation of disease
√ dilatation of pulmonary trunk (19%)
√ nodular thrombi (3%)
√ "pruned tree" appearance / flame-shaped stenosis of pulmonary arteries (66%)
√ unilateral occlusion / aneurysm of pulmonary artery
√ systemic-pulmonary artery shunts
CT angio:
√ wall thickening with enhancement (acute)
√ luminal + mural calcium deposition (chronic)
√ pulmonary artery stenosis / occlusion (chronic)

@ Coronary arteries (in up to 20%)

Cx: (1) Cerebrovascular accidents (10–20%)
(2) Heart failure ← aortic regurgitation

DDx: atherosclerosis; temporal arteritis (CCA not involved); fibromuscular dysplasia (in ICA not CCA); idiopathic carotid dissection (ICA); syphilitic aortitis (calcification of ascending aorta)

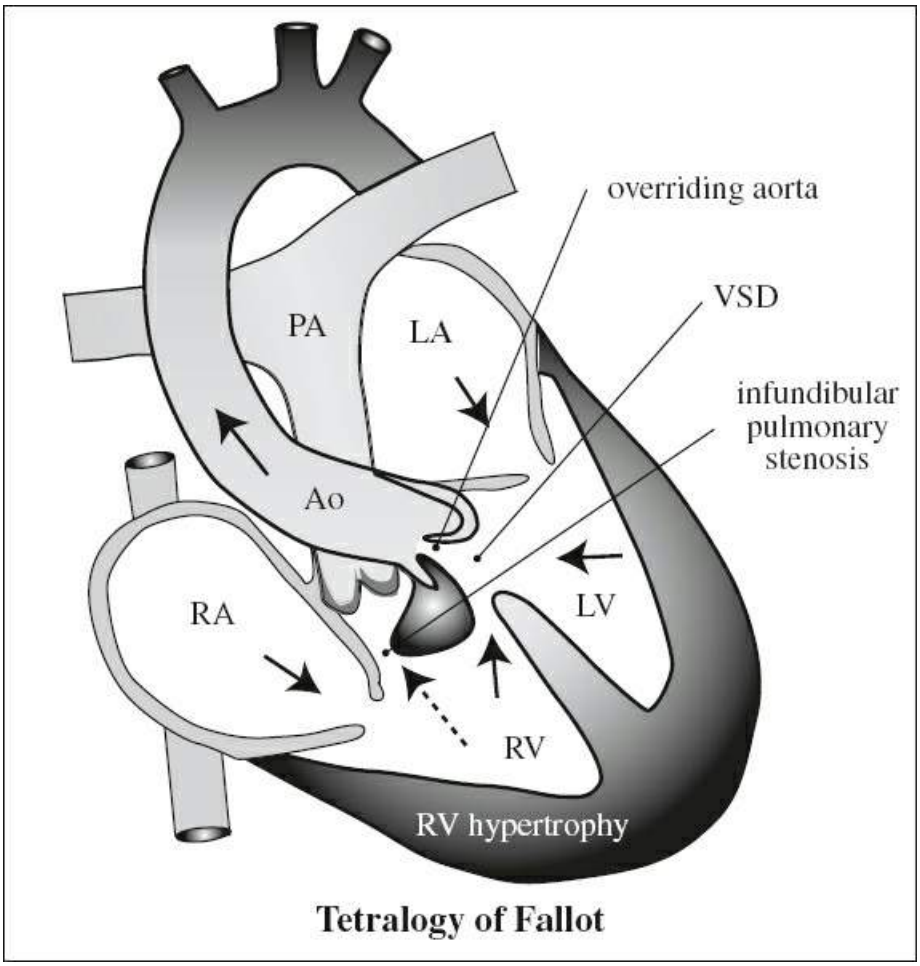
Rx: high-dose glucocorticoids, angioplasty after decline of active inflammation

TEMPORAL ARTERITIS

= CRANIAL / GRANULOMATOUS ARTERITIS
= POLYMYALGIA RHEUMATICA = GIANT CELL ARTERITIS (poor choice because Takayasu disease is also a giant cell arteritis)
= systemic chronic granulomatous vasculitis

Giant cell arteritis is a chronic vasculitis that affects large and medium-sized vessels, usually involving the superficial cranial arteries. It is closely related to polymyalgia rheumatica.

Incidence: 20÷100,000 annually;
◊ Most common form of aortitis in North America!
Age: usually limited to persons > 50 years of age
Histo: closely related to polymyalgia rheumatica
(a) acute stage: granulomatous infiltrative process focused on elastic fibers of arterial wall (internal elastic lamina) consisting of multinucleated giant cells, lymphocytes, histiocytes, plasma cells
(b) fibrotic stage (weeks to years): progressive fibrosis of vessel wall resulting in constriction from intimal proliferation / thrombotic occlusion / aneurysm formation
◊ Morphologically indistinguishable from Takayasu arteritis!
Age peak: 65–75 years; M÷F = 1÷3
› prodromal phase of flulike illness of 1–3 weeks:
• malaise, low-grade fever, weight loss, myalgia
• unilateral headache (50–90%), facial pain
› chronic stage:
• jaw claudication (while chewing + talking)
• neuroophthalmic manifestations: visual impairment /diplopia / blindness; palpable tender temporal artery
• polymyalgia rheumatica (50%) = intense myalgia of shoulder + hip girdles
• erythrocyte sedimentation rate (ESR) of 40–140 mm/hour (HALLMARK)
Location:
any artery of the body; mainly medium-sized branches of aortic arch (10%), external carotid artery branches (particularly superficial temporal / occipital artery); vertebral artery; coronary arteries; mesenteric arteries; extracranial arteries below neck (9%): subclavian > axillary > brachial > profunda femoris > forearm > calf



Note: intracranial ICA + intracranial vertebral artery are not involved as internal elastic lamina ceases to exist 5 mm distal to entry point through dura mater

Distribution: commonly bilateral + symmetric

√ long smooth stenotic arterial segments with skip areas

√ smooth tapered occlusions with abundance of collateral supply

√ absence of atherosclerotic changes

CT angiography:

√ luminal changes: stenosis, occlusion, dilatation

√ mural thrombus, aneurysm formation, mural calcifications

MR angiography:

√ edema of arterial wall (STIR) = measure of disease activity

√ smooth tapering proximal + distal to lesion

US:

√ "halo" sign = diffusely thickened hypoechoic arterial wall

√ ± turbulent flow + stenosis of affected vessel

PET (56% sensitive, 98% specific):

√ abnormal uptake in aortic arch + large thoracic arteries

@ Aorta

√ anuloaortic ectasia + ascending aortic aneurysm that may extend into aortic arch (late

complication)
√ aortic valve insufficiency, acute dissection
√ abdominal aortic aneurysm

Cx: stroke in vertebrobasilar territory (rare)

Dx: biopsy of palpable temporal artery

Prognosis: disease may be self-limiting (1–2 years); 10% mortality within 2–3 years

TETRALOGY OF FALLOT

[Etienne-Louis Arthur Fallot (1850–1911), physician of forensic medicine and hygiene in Marseille, France]

= underdevelopment of pulmonary infundibulum ← unequal partitioning of conotruncus = anterior malalignment of conal septum

Frequency: 8–11% of all CHD; most common cyanotic CHD

Prevalence: 3.3÷100,000 live births

TETRAD:

1. Large VSD immediately below aortic valve
2. Right ventricular hypertrophy (in long-standing untreated disease) ← elevated RV systolic pressure
3. Overriding aorta straddling VSD and receiving blood from both ventricles
4. Obstruction of right ventricular outflow tract: usually of pulmonary infundibulum, occasionally pulmonic valve atresia

mnemonic: Don't DROP the baby

Defect: VSD
Right ventricular hypertrophy
Overriding aorta
Pulmonary stenosis

Embryology:

abnormal spiraling caudad growth of truncoconal ridges in 3rd–4th week causes unequal partitioning of the conotruncus into a small underdeveloped anteromedial pulmonary infundibulum + large posterolateral LV outflow tract

Hemodynamics:

fetus: pulmonary blood flow supplied by retrograde flow through ductus arteriosus with absence of RV hypertrophy / IUGR

neonate: R-to-L shunt bypassing pulmonary circulation with decrease in systemic oxygen saturation (cyanosis); pressure overload + hypertrophy of RV ← pulmonic-infundibular stenosis

RA	↔/↑	RV	↑	Main PA	↓
Pulm. vessels	↓			LPA	↑
LA	↔	LV	↔	Ao	↑

Systemic pulmonary supply:

via major aortopulmonary (systemic-pulmonary) collaterals

Associated with:

1. Bicuspid pulmonic valve (40%)

2. Stenosis of left pulmonary artery (40%)
3. Right aortic arch (25%) with mirror-image branching
4. Tracheoesophageal fistula
5. Down syndrome
6. Forked ribs, scoliosis
7. Anomalies of coronary arteries in 10% (single RCA / LAD from RCA)

- cyanosis by 3–4 months of age (concealed at birth by PDA)
- dyspnea on exertion, clubbing of fingers and toes
- "squatting position" when fatigued → ↑ pulmonary blood flow
- "episodic spells" = loss of consciousness
- polycythemia, lowered pO2 values, systolic murmur in pulmonic area

CXR:

√ coeur en sabot (boot-shaped heart)
[*sabot* , French = wooden shoe / clog]
= uplifting of cardiac apex due to (1) right ventricular hypertrophy + (2) small / absent main pulmonary artery (in 65%) accentuated by large lung volume + small thymus + lordotic projection

√ pronounced concavity in region of pulmonary artery trunk ← small / absent PA

√ marked reduction in caliber + number of pulmonary arteries ← reduced blood flow to lungs:

√ asymmetric pulmonary vascularity

√ reticular pattern with horizontal course usually in periphery (= prominent collateral circulation of bronchial vessels + pleuropulmonary connections)

√ enlarged aorta

√ right-sided aortic arch in 25%

OB-US:

√ dilated aorta overriding the interventricular septum

√ usually perimembranous VSD

√ mildly stenotic RV outflow tract

√ NO RV hypertrophy in midtrimester

ECHO:

√ discontinuity between anterior aortic wall + interventricular septum (= overriding of the aorta)

√ small left atrium

√ RV hypertrophy with small right ventricular outflow tract

√ widening of the aorta

√ thickening of right ventricular wall + interventricular septum

Prognosis: spontaneous survival without surgical correction in 50% (10%) up to age 7 (21) years

Rx: surgery in early childhood

(a) palliative

1. Blalock-Taussig shunt = end-to-side anastomosis of subclavian to pulmonary artery opposite aortic arch [64% (55%) survival rate at 15 (20) years]
2. Pott operation on left = anastomosis of left PA with descending aorta

3. Waterston-Cooley procedure = anastomosis between ascending aorta + right pulmonary artery
4. Central shunt = Rastelli procedure = tubular synthetic graft between ascending aorta + pulmonary artery

(b) corrective open cardiac surgery = VSD-closure + reconstruction of RV outflow tract by excision of obstructing tissue (82% survival rate at 15 years)

Operative mortality: 3–10%

Pink Tetralogy

= infundibular hypertrophy → minimal RVOT obstruction + VSD (3%) with predominantly L-to-R-shunt → no cyanosis

Pentalogy of Fallot

= tetralogy + ASD

Trilogy of Fallot (infantile presentation)

(1) Severe pulmonic valvular stenosis
(2) Hypertrophy of RV
(3) ASD with R-to-L shunt (increased pressure in RA forces foramen ovale open)

THORACIC OUTLET SYNDROME

= neurovascular syndrome caused by compression of subclavian vessels + brachial plexus between chest and arm

Prevalence: 0.3–8.0%

Age: 20–40 years; M÷F = 1÷3 to 1÷4

Thoracic outlet: above 1st rib and behind clavicle

(a) interscalene triangle = most medial space
◊ In 50% responsible for neurologic compression!
Borders: anterior scalene muscle (anteriorly), middle scalene muscle (posteriorly), medial surface of 1st rib (inferiorly)
Content: subclavian artery, 3 divisions of brachial plexus

(b) costoclavicular space
◊ Most frequent site of vascular compression!
◊ In 50% responsible for neurologic compression!
Borders: middle ⅓ of clavicle (superiorly), subclavius muscle (anteriorly), 1st rib + middle scalene muscle (posteriorly)
Content: subclavian vein

(c) retropectoralis minor / subcoracoid space
◊ Rare site of compression!
Borders: pectoralis minor muscle (anteriorly), subscapularis muscle (posteriorly + superiorly), anterior chest wall (posteriorly + inferiorly)
Content: axillary vessels, 3 cords of brachial plexus

Arm abduction: → narrowing of thoracic inlet in costoclavicular + retropectoralis minor spaces

Cause:

A. CONGENITAL / ANATOMIC
   1. Cervical rib (< 1% of general population)
   2. Scalene muscle anomaly
      (a) hypertrophy of anterior scalene muscle = **scalenus anticus syndrome** (most common)
      (b) common origin of anterior + middle scalene mm.
      (c) passage of brachial plexus through substance of anterior scalene muscle
      (d) supernumerary scalenus minimus muscle (rare) extending from transverse process of 7th cervical vertebra to 1st rib with insertion between brachial plexus + subclavian artery
   4. Anomalous 1st rib = unusually straight course with narrowing of costoclavicular space
   5. Elongated transverse process of C7
   6. Congenital fibromuscular bands

B. ACQUIRED / POSTTRAUMATIC
   1. Fracture of clavicle / 1st rib (34%) with nonanatomic alignment / exuberant callus
   2. Posttraumatic fibrosis of scalene muscles
   3. Slender body habitus
      = long neck, sagging / drooping shoulders ← backpacking
   4. Muscular body habitus
      = arterial compression in pectoralis minor tunnel affecting weight lifter, swimmer, tennis player
   5. Supraclavicular tumor (lipoma, neurogenic tumor) / lymphadenopathy

Neurogenic Thoracic Outlet Syndrome (95%)

- pain in forearm + hand that increases upon elevation and abduction of arm (sustained reaching overhead)
- paresthesias of hand + fingers (C8 + T1) in ulnar nerve distribution with numbness, "pins and needles" in 95%
- arm pain in radial nerve distribution (C5-C7 roots) and pain in neck, ear, upper chest, upper back
- numbness, weakness, thenar wasting

Rx: physical therapy; NSAID; muscle relaxants

Venous Thoracic Outlet Syndrome (4%)

- arm swelling, distention of superficial veins, cyanosis, pain

Paget-von Schrötter Syndrome

[Leopold von Schrötter (1837–1908), director of the world's first laryngological clinic at Vienna General Hospital and head of the department of internal medicine]

= EFFORT THROMBOSIS

= primary thrombosis of subclavian vein at costoclavicular junction (= subtype of thoracic outlet syndrome)

Incidence: 1–2÷100,000 annually

Cause: repetitive / vigorous activity

Rx: catheter-mediated thrombolysis (initially) + surgical decompression of

costoclavicular junction

Arterial Thoracic Outlet Syndrome (1%)

- decreased skin temperature, discoloration of hand
- intermittent claudication of fingers (from ischemia)
- hyperabduction maneuver with obliteration of radial pulse (34%)
- Raynaud phenomenon (40%): episodic constriction of small vessels
- supraclavicular bruit (15–30%)
- **Roos test** = repeated clenching of fist with abducted + externally rotated arms
- Adson test = palpation of radial pulse with patient sitting upright, hands on thigh, neck hyperextended, head turned toward affected side
- **Wright test** = diminution of pulse during hyperabduction of arms

Bidirectional Doppler:

1. **Adson maneuver** (for scalenus anticus muscle)
   = hold deep inspiration while neck is fully extended + head turned toward ipsilateral and opposite side
2. Costoclavicular maneuver (compression between clavicle + 1st rib) = exaggerated military position with shoulders drawn back and downward
3. Hyperabduction maneuver (compression by humeral head / pectoralis minor muscle) = extremity monitored through range of 180° abduction

√ complete cessation of flow in one position

Photoplethysmography:

1. Photo pulse transducer secured to palmar surface of one fingertip of each hand
2. Arterial pulsations recorded with arm in
   (a) neutral position
   (b) extended 90° to side
   (c) 180° over the head
   (d) in "military" position with arms at 90° + shoulders pressed back

√ complete disappearance of pulse in one position

Angio:

√ abnormal course of distal subclavian artery
√ focal stenosis / occlusion
√ poststenotic dilatation of distal subclavian artery
√ aneurysm
√ stress test: bandlike / concentric constriction
√ mural thrombus ± distal embolization
√ venous thrombosis / obstruction

Positional CTA (with adducted + then hyperabducted arms):

√ vascular compression
√ collateral arterial circulation

MR:

√ denervation-related fatty atrophy of muscles
√ effacement of fat planes around compressed plexus
√ abnormal intramuscular course of brachial plexus components

Rx: thrombolytic therapy + concomitant anticoagulation (in acute thrombosis); NOT

endoluminal stent; surgery

DDx: Cervical disk disease, radiculopathy, spinal cord tumor, trauma to brachial plexus, arthritis, carpal tunnel syndrome, Pancoast tumor, peripheral arterial occlusive disease, aneurysm, causalgia, thromboembolism, Raynaud disease, vasculitis

TRANSPOSITION OF GREAT ARTERIES

Complete Transposition of Great Arteries

= TGA = D-TRANSPOSITION

= great vessels originate from inappropriate ventricle:

(1) Aorta originates from morphologic RV with an infundibulum

(2) Pulmonary artery originates from morphologic LV

(3) Normal position of atria + ventricles

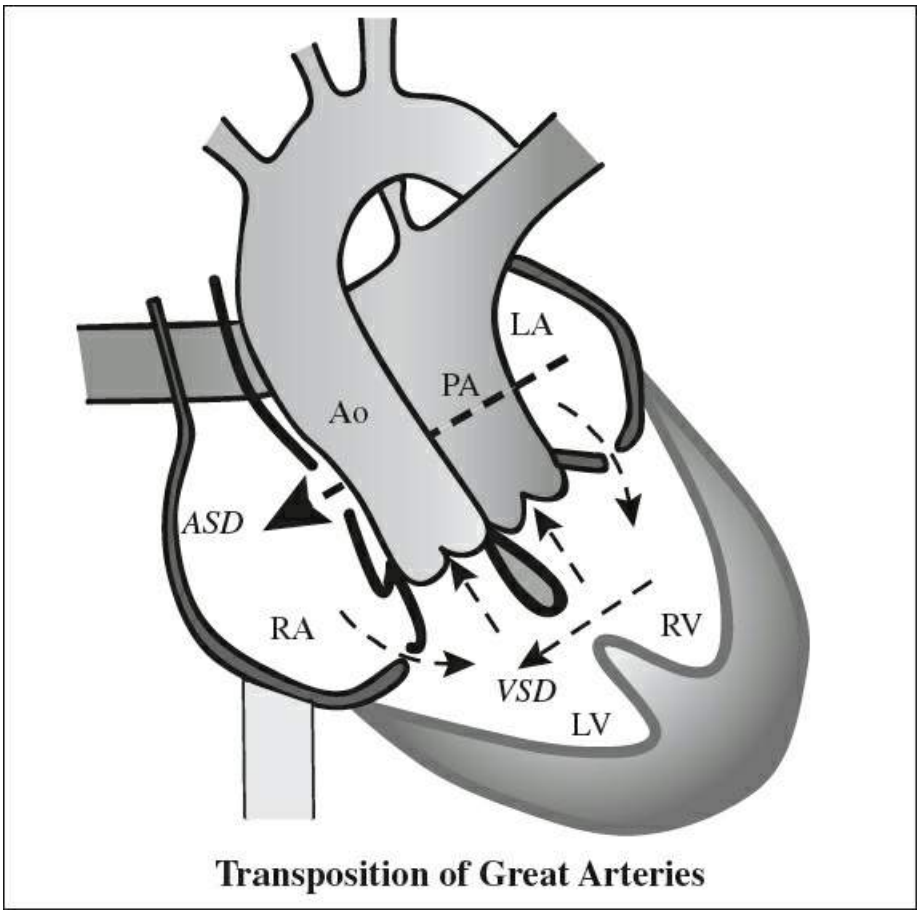
Embryology: failure of the aorticopulmonary septum (= truncoconal ridges) to follow a spiral course

Frequency: 5–7% of all CHD

In 10% associated with: a syndrome / extracardiac malformation; in 90% isolated

VARIATIONS:

1. Complete TGA + intact interventricular septum



Transposition of Great Arteries

2. Complete TGA + VSD: CHF due to VSD
3. Complete TGA + VSD + PS: PS prevents CHF = longest survival

Hemodynamics:

fetus : no hemodynamic compromise with normal birth weight

neonate : mixing of the 2 independent circulations necessary to sustain life

Admixture of blood from both circulations via:

(1) PDA (carries aortic blood into pulmonary artery)

Prognosis: worst when PDA closes → increase in volume of pulmonary blood flow

(2) ASD / patent foramen ovale (allows saturated blood to enter RA from LA)

(3) VSD (in 50%)

RA	↑	RV	↑	Main PA	↔
Pulm. vessels	↑				
LA	↔	LV	↔	Ao	↔

Associated with: diabetic mothers

- cyanosis: most common cause for cyanosis in neonate; 2nd most common cause of cyanosis after tetralogy of Fallot

- symptomatic 1–2 weeks following birth

CXR:

√ "egg-on-a-string" appearance of heart (on frontal CXR):

√ abnormal convexity of RA border (= "egg")

√ narrow superior mediastinum (= "string" = MOST CONSISTENT SIGN):

√ PA situated to the right of its normal location

√ PA obscured by aorta

√ stress-induced thymic atrophy

√ hyperaeration

√ cardiac enlargement beginning 2 weeks after birth (= "egg on its side") following closure of PDA:

√ enlargement of right heart

√ enlargement of LA (with VSD)

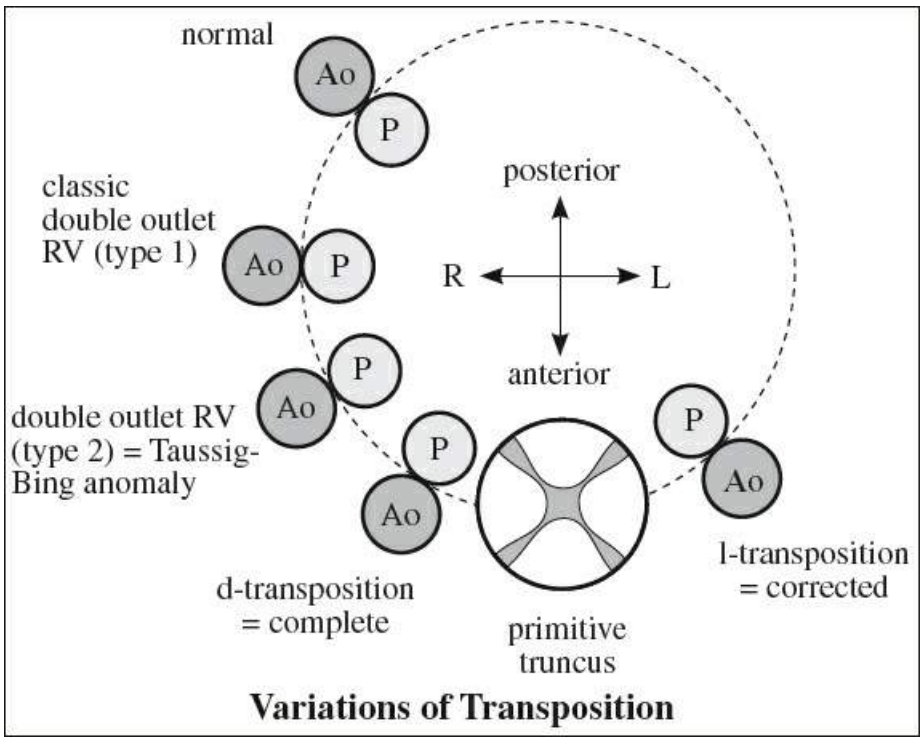
√ absent pulmonary trunk (99%) = PA located posteriorly in midline

√ increased pulmonary blood flow (if not associated with PS) → enlargement of LA

√ midline aorta (30%) / ascending aorta with convexity to the right

√ right aortic arch in 3% (difficult assessment due to midline position + small size)

OB-US:



Variations of Transposition

√ great arteries arise from ventricles in a parallel fashion
√ aorta anterior + to right of pulmonary artery (in 60%; rarely side by side)

Prognosis: overall 70% survival rate at 1 week, 50% at 1 month, 11% at 1 year by natural history

Rx:

(1) Prostaglandin E1 administration to maintain ductal patency
(2) Rashkind procedure = balloon septostomy to create ASD
(3) Blalock-Hanlon procedure = surgical creation of ASD
(4) Mustard operation (corrective) = removal of atrial septum + creation of intraatrial baffle directing the pulmonary venous return to RV + systemic venous return to LV; 79% 1-year survival rate; 64–89% 5-year survival

Corrected Transposition of Great Arteries

= CONGENITALLY CORRECTED TRANSPOSITION = L-TRANSPOSITION = VENTRICULAR INVERSION
= anomalous looping of the bulboventricular loop (= primordial ventricles) associated with lack of spiral rotation of conotruncal septum characterized by

(1) Transposition of great arteries (= aorta anterior + to right of PA)
(2) Inversion of ventricles (LV on right side, RV on left side):
  (a) RA connected to morphologic LV
  (b) LA connected to morphologic RV
(3) AV valves + coronary arteries follow their corresponding ventricles

Hemodynamics: functionally corrected abnormality

Associated with:

(1) Usually perimembranous VSD (in > 50%)
(2) Pulmonic stenosis (in 50%)

(3) Anomaly of left (= tricuspid) atrioventricular valves (Ebstein-like) → insufficiency
(4) Dextrocardia (high incidence)

• NO cyanosis, atrioventricular block (malalignment of atrial + ventricular septa)

CXR:
√ abnormal convexity / straightening in upper portion of left heart border (ascending aorta arising from inverted RV)
√ inapparent aortic knob + descending aorta (overlying spine)
√ inapparent pulmonary trunk (rightward posterior position) = PREMIER SIGN
√ humped contour of lower left heart border with elevation above diaphragm (anatomic RV)
√ apical notch (= septal notch)
√ increased pulmonary blood flow (if shunt present)
√ pulmonary venous hypertension (if left-sided AV valve incompetent)
√ LA enlargement

MR:
√ posterior cardiac chamber has moderator band + muscular infundibulum (morphologic RV)

Angio:
√ original LV on right side: smooth-walled, cylinder- / cone-shaped with high recess emptying into aorta (= venous ventricle)
√ original RV on left side: bulbous, triangular shape, trabeculated chamber with infundibular outflow tract into pulmonary trunk (= arterial ventricle)

OB-US:
√ great arteries arise from ventricles in a parallel fashion
√ aortic valve separated from tricuspid valve by a complete infundibulum
√ fibrous continuity between pulmonic valve + mitral valve

Prognosis: (unfavorable ← additional cardiac defects); 40% (30%) 1-year (10-year) survival rate

TRAUMATIC AORTIC INJURY

= AORTIC LACERATION = BLUNT TRAUMA TO THORACIC AORTA
= laceration that disrupts the physical integrity of > 1 structural layer of the aorta
Incidence: > 100,000 people in USA annually
Cause: rapid deceleration (high-speed MVA > 48 km/hour with unrestrained driver or ejected passenger, fall from height > 3 m) / crushing chest injury
Pathomechanism: horizontal / vertical deceleration with shear between fixed arch and mobile descending aorta, hydrostatic force, osseous pinch between spine and sternum

Extent of laceration:

1. Incomplete rupture (15%)
   ◊ Aorta goes on to rupture completely within 24 hours in 50% of patients!
   › INTIMA
   (a) intimal hemorrhage without tear
   (b) transverse laceration of intima with hemorrhage (= **intimal tear / flap = traumatic**

aortic dissection)
Minimal aortic injury (10%) = intimal flap of < 10 mm without significant periaortic hematoma

› MEDIA
tear into media with subadventitial hematoma (40–60%)

› ADVENTITIA
(a) periaortic hemorrhage (± aortic injury)
(b) **traumatic pseudoaneurysm** = laceration of intima + media + adventitia with locally contained periadventitial hematoma

2. Complete rupture (85%) = transmural extension of laceration = **aortic transection** = **traumatic aortic rupture**
• exsanguination before patient reaches a hospital

Length of tear: circumferential tear (in majority)
Site: at aortic attachment
(1) Aortic isthmus (88–95%): brachiocephalic arteries + ligamentum arteriosum fix aorta in this region
Site: within 2 cm of origin of left subclavian artery
(2) Aortic arch with avulsion of brachiocephalic trunk (4.5%)
(3) Aortic root immediately above aortic valve (5–9%)
Cx: aortic valve rupture, coronary artery laceration, hemopericardium + cardiac tamponade; NO mediastinal hematoma
(4) Aortic hiatus in diaphragm (1–3%)
◊ Most often posteriorly (in noncircumferential tear)

Acute Thoracic Aortic Injury

Prevalence: 10–16–20% of all fatalities in high-speed deceleration accidents
• severe chest pain: precordial (ascending aorta), neck-jaw (aortic arch), interscapular (descending thoracic aorta)
• anterior chest wall contusion, dyspnea, dysphagia
• blood pressure changes:
  • unexplained hypotension
  • scapulothoracic syndrome = decreased / absent upper extremity pulses
  • acute coarctation syndrome = decreased / absent lower extremity + normal upper extremity pulses with upper extremity hypertension + systolic murmur in 2nd left parasternal interspace

CXR (53–100% sensitive, 1–60% specific, 4–20% PPV):

◊ A normal anteroposterior upright CXR virtually excludes acute thoracic aortic injury (96–98% NPV)!

N.B.: There are no plain CXR findings of aortic injury (since aortic integrity is maintained by intact adventitia)! The sources of <u>mediastinal hematoma</u> are frequently the azygos, hemiazygos, internal thoracic, paraspinal and intercostal vessels!
◊ Aortic injury is the cause of mediastinal hematoma in only 12.5%!

√ normal admission CXR in 28% (radiographic signs may not develop until 6–36 hours): supine CXR is very INACCURATE for mediastinal widening

Most specific and valuable signs:
- √ deviation of nasogastric / endotracheal tube to the right of T3-T4 spinous process (12–100% sensitive, 80–95% specific)
- √ depression of left mainstem bronchus anteroinferiorly > 40° below the horizontal + toward right (in 53%)
- √ indistinct / blurred aortic contour at arch / descending aorta (53–100% sensitive, 21–55% specific)

√ mediastinal widening > 8 cm at level of origin of left subclavian artery (present in 75–92%; 90–95% sensitive, 5–10% specific):
- √ mediastinal width to chest width > 0.25

√ obscuration of aortopulmonary window (40–100% sensitive, 56–83% specific)
√ widened left paraspinal "stripe" > 5 mm (12–83% sensitive, 89–97% specific)
√ thickening of right paratracheal stripe > 4–5 mm ← hematoma between pleura + trachea
√ left / right "apical pleural cap" sign in 37%
← extrapleural hematoma along brachiocephalic vessels
√ tracheal compression + displacement toward right (61%)
√ rapidly accumulating commonly left-sided hemothorax without evident rib fracture ← break in mediastinal pleura
√ fractures of 1st + 2nd rib (17%)

mnemonic: BAD MEAT
Bronchus depression (left main)
Aortic silhouette shaggy
Death in 80–90%
Mediastinal widening
Enteric (nasogastric) tube displacement
Apical cap
Tracheal shift

NECT screening (90–100% sensitive, 19–45% specific, 0–50% PPV, 94–100% NPV):
√ mediastinal fluid often of high density
√ obliteration of aorta-fat interface with increased attenuation ← mediastinal / periaortic hematoma

Source of blood: small veins, vasa vasorum of aortic wall

◊ A negative CT examination for mediastinal hemorrhage has an almost 100% NPV for aortic injury!

False positive:
residual thymic tissue, periaortic atelectasis, pericardial recess, patient motion, streak artifacts, volume averaging of pulmonary artery, pleural effusion adjacent to descending aorta, sternal + spinal fracture

CECT (100% sensitive, 92–99% specific, 0–39% FP, 0.7% FN):
Multidetector CT: 100 mL at 4 mL/sec with bolus tracking; 1–2 mm collimation for 3D reconstruction with 50% overlap

Disadvantages: CT delays surgery
Advantages: unsuspected injuries are discovered (pulmonary contusion, pneumothorax, pericardial effusion, rib fracture)

√ intraluminal low-density filling defect:
  √ linear = intimal flap
  √ polypoid = clot
√ contour deformity of outer aortic wall = pseudoaneurysm
√ contour deformity of inner aortic wall:
  √ intramural hematoma
  √ pseudocoarctation = abrupt tapering of the diameter of descending aorta compared with ascending aorta
√ extravasation of contrast material (extremely rare)

False positive:
pulsation artifact (aortic valve leaflets, wall of ascending aorta, cardiac motion), streak artifact ← high-density contrast in brachiocephalic vein, volume averaging, prominent periaortic bronchial / mediastinal vessels, atherosclerotic pseudoaneurysm, small ductus diverticulum

Transesophageal echocardiography:
(in 2–15% technically unsuccessful, 57–63% sensitive, 84–91% specific):
√ intimal flap
√ intraluminal thick stripes
√ pseudoaneurysm
√ aortic occlusion (= pseudocoarctation)
√ fusiform aneurysm
√ aortic wall hematoma

Advantage: portable, relatively fast

Disadvantage: operator dependent with false negatives for ascending aorta + aortic arch

Aortography (92% sensitive, 98–100% specific):

Technique: LAO + RAO projection; high-flow pigtail catheter; 50 mL at 35 mL/sec

Morbidity: 1.7% (iatrogenic extension of flap, entry of guidewire into pseudoaneurysm)

Delay: 147 minutes between admission and angio

True positive: in 17–20% of mediastinal hematomas angio demonstrates acute traumatic aortic injury!

False negative: small transverse intimal tears may be missed!
√ resistance in advancing guide wire
√ intimal irregularity, linear defect, filling defect = intimal flap = posttraumatic dissection (5–10%)
√ intramural injury:
  √ thickening of aortic wall
  √ posttraumatic coarctation
√ transmural laceration:
  √ contained extravasation = traumatic false aneurysm
  √ free extravasation = aortic rupture

DDx: ductus diverticulum (in 10% of normals), aortic spindle, infundibula of brachiocephalic arterial branches; volume averaging with left brachiocephalic vein / left superior intercostal vein / right bronchial arteries (vs. intimal flap); artifact from physiologic streaming / mixing of contrast material; athero-sclerotic aortic ulceration; atheromatous plaque; syphilitic aortic aneurysm

Recommendations for work-up:
(1) Normal well-defined mediastinal + aortic contours on CXR: no further imaging
(2) Stable patient:
angio CT of chest + CT of head, abdomen, pelvis
(3) Unstable patient + unequivocally abnormal CXR / strong clinical evidence of aortic injury:
angio CT / emergency surgery

Rx: (1) Antihypertensive medication
(2) Stent graft for high-risk patients
(3) Surgical repair : 20–54% mortality, 5–10% morbidity ← paraplegia

Prognosis:
(1) 80–90% fatal at scene of accident
◊ Mortality rises rapidly within first 24 hours
(2) 10–20% reach hospital
← formation of periaortic hematoma + false aneurysm contained by adventitia ± surrounding connective tissue
(a) without intervention: 30% (40–50%) dead within 6 (24) hours; 90% dead within 4 months; chronic false aneurysm may develop in 2–5% at isthmus / descending aorta
(b) with surgical repair: 60–70% survive; surgical mortality rate of 9–44% varies with degree of hemodynamic instability + severity of associated injuries + magnitude of aortic laceration
Cx: postoperative paraplegia (9%) ← aortic cross clamping > 30 minutes
(3) Chronic pseudoaneurysm (1%): potentially unstable

Chronic Posttraumatic Aortic Pseudoaneurysm

= aneurysm that exists for > 3 months

Risk: amount of wall fibroplasia following rupture usually not sufficient to prevent subsequent rupture until at least 3 months after initial traumatic episode

Prevalence: 2–5% of patients surviving aortic transection > 24–48 hours

- symptom-free period of months to years (in 11% > 10 years)
- delayed clinical symptoms: 42% (85%) within 5 (20) years consisting of chest pain, back pain, dyspnea, cough, hoarseness, dysphagia, systolic murmur

Location: descending aorta at level of lig. arteriosum filling the aorticopulmonary window (most commonly)

√ well-defined rounded mass in left paramediastinal region
√ ± inferior displacement of left mainstem bronchus

Cx: CHF, partial obstruction of aortic lumen, bacterial endocarditis, aortoesophageal fistula, aortic dissection, obstruction of tracheobronchial tree, systemic emboli

Prognosis: enlargement + eventual rupture;
10-year survival rate: 85% with surgical repair, 66% without surgical repair

TRICUSPID ATRESIA

2nd most common cause of pronounced neonatal cyanosis (after transposition) characterized by
(1) Absent tricuspid valve
(2) ASD

(3) Small VSD (in most patients)

Frequency: 1.5% of all CHD

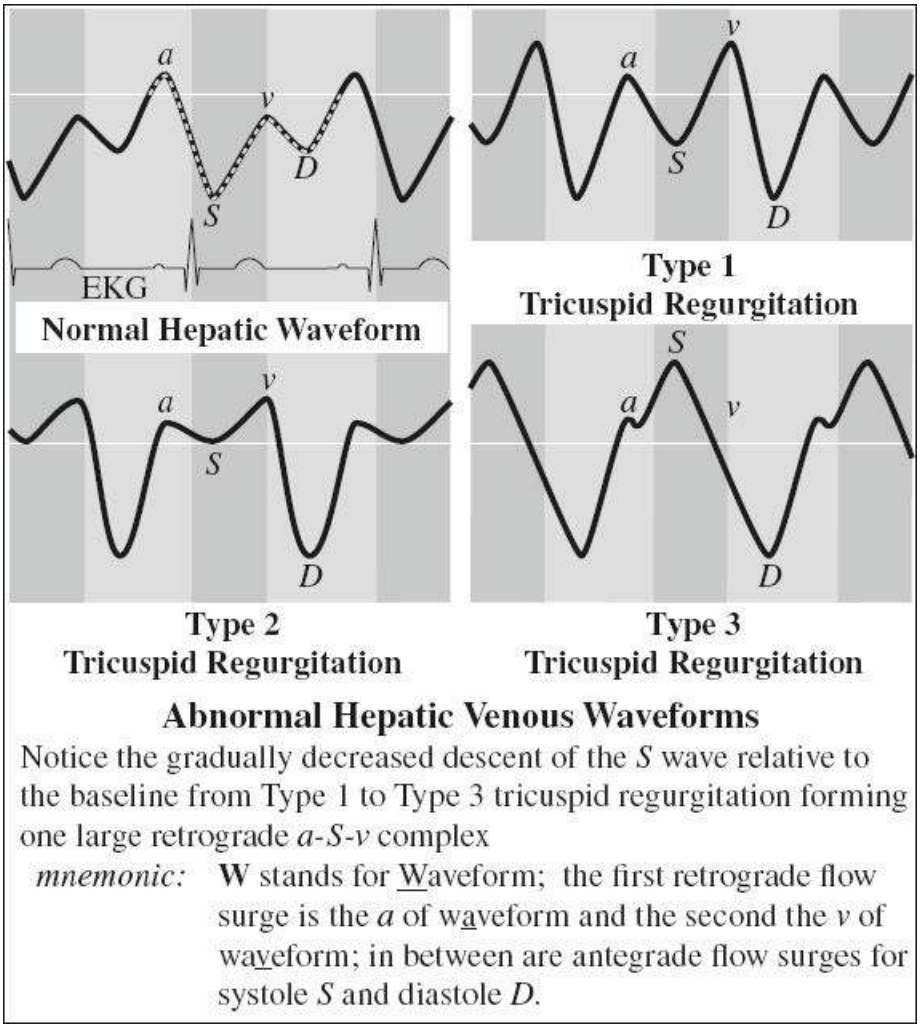
Embryology: imbalanced tissue proliferation + resorption results in absence of valvular tissue

1. TRICUSPID ATRESIA WITHOUT TRANSPOSITION (80%)
   (a) without PS, (b) with PS, (c) with pulmonary atresia
2. TRICUSPID ATRESIA WITH TRANSPOSITION
   (a) without PS, (b) with PS [most favorable combination], (c) with pulmonary atresia

◊ Usually small VSD + PS (75%) restrict pulmonary blood flow

Hemodynamics:

absent tricuspid valve forces blood from an enlarged RA through an ASD into LA (R-to-L shunt); pulmonary blood flow limited by pulmonary valvular stenosis



RA	↑	RV	↓	Main PA	↓
Pulm. vessels	↓				
LA	↑	LV	↑	Ao	↑

- progressive cyanosis from birth on, increasing with crying = OUTSTANDING FEATURE (inverse relationship between degree of cyanosis + volume of pulmonary blood flow)

• pansystolic murmur (VSD)
• ECG: left-axis deviation

CXR (typical cardiac contour):

√ heart size ranges from normal to moderately enlarged (depending on volume of pulmonary blood flow and size of RA)
√ left rounded contour = enlargement + hypertrophy of LV
√ right rounded contour = enlarged RA
√ flat / concave pulmonary segment
√ normal / decreased pulmonary vascularity
√ typical flattening of right heart border with transposition (in 15%)

Prognosis: may survive well into early adulthood

Rx:

(1) Blalock-Taussig procedure (if pulmonary blood flow decreased in infancy)
(2) Glenn procedure = shunt between IVC + right PA (if total correction not anticipated)
(3) Fontan procedure = external conduit from RA to pulmonary trunk + closure of ASD (if pulmonary vascular disease has not developed)

TRICUSPID REGURGITATION / INSUFFICIENCY

Cause:

RV dilatation is the most common cause of tricuspid regurgitation, with dilatation of the tricuspid annulus causing improper coaptation of the valve leaflets.

A. SECONDARY = dilatation of RV + annulus ← elevated pulmonary artery pressure
   1. Left heart failure
   2. Pulmonary vascular disease
   3. Chronic lung disease ← pulmonary hypertension
   4. Carcinoid syndrome
   ◊ Mild / trace of tricuspid regurgitation is normal!
B. PRIMARY = lesion of intrinsic valve apparatus (chordae tendineae / leaflets / annulus / papillary muscles)
   1. Rheumatic heart disease
   2. Bacterial endocarditis
   3. Tricuspid valve prolapse
   4. Papillary muscle dysfunction: myocardial infarction, trauma, (metastatic) carcinoid heart syndrome
   6. Connective tissue disorder: Marfan syndrome
   7. Congenital heart disease: Ebstein anomaly, atrioventricular cushion defect
   8. Pacemaker leads
   9. Radiation therapy, certain drug-based treatments

• exhaustion and fatigue
• symptoms of right heart failure: peripheral edema, ascites

√ normal / reduced pulmonary vascularity
√ cardiomegaly ← RA + RV hypertrophy and enlargement
√ distension of IVC > SVC

Doppler ECHO:

√ systolic reversal of hepatic vein flow with normal sinus rhythm
√ dilatation of RA
√ flattening / leftward bowing of interventricular septum during diastole
√ vena contracta (= smallest stream diameter) width > 0.7 cm
√ color flow jet area > 10 cm^2
√ proximal isovelocity surface area radius > 0.9 cm
√ decreased *S* wave = *S* wave no longer as deep as the *D* wave, gradually rising with degree of regurgitation
√ one large *a*-*S*-*v* complex in severe incompetence

CT:
√ RV displaced to the left
√ interventricular septum bowed to the left
√ hepatic venous congestion
√ emphysema, pulmonary hypertension, left heart disease

Prognosis: if untreated → RV dysfunction, congestive hepatopathy, cardiac cirrhosis

TRICUSPID STENOSIS

= thickening + fusion of tricuspid valve apparatus

Cause:
1. (Nearly always) rheumatic heart disease:
   √ often accompanied by mitral + aortic valve disease
   √ NO valve calcifications
2. Infectious endocarditis: IV drug users
3. Congenital abnormalities
4. Fabry disease
5. Whipple disease
6. Metastatic carcinoid syndrome
7. Pacemaker-related complications

• fatigue, dyspnea, congestion, right heart failure with elevated jugular pressure, hepatomegaly, ascites
• arrhythmias ← severe right atrial enlargement

CXR:
√ RA enlargement + dilatation of both venae cavae
√ normal pulmonary arteries

ECHO (findings of hemodynamic significance):
√ mean transvalvular pressure gradient of > 5 mmHg (clinically most relevant)
√ inflow time-velocity integral > 60 cm
√ pressure half-time > 190 msec
√ valve area by continuity equation of < 1 cm^2

CT:
√ thickened tricuspid valve leaflets: shortening of chordae tendineae + fusion of edges of leaflets
√ narrowed valve annulus
√ RA dilatation

√ enlargement of superior + inferior venae cavae
√ hepatic venous congestion
Cx: often coexisting tricuspid regurgitation exacerbating RA enlargement → increasing risk for arrhythmia

TROUSSEAU SYNDROME

= PARANEOPLASTIC THROMBOEMBOLISM

Prevalence: 1–11%; higher in terminally ill cancer patients

Tumors: mucin-secreting adenocarcinoma of GI tract and pancreas (most common), lung, breast, ovary, prostate

Pathogenesis: (?)

(a) tumors activate coagulation + depress anticoagulant function
(b) cancer cells cause injury to endothelial lining, activate platelets + coagulation

Type of lesion: (1) Venous thrombosis
(2) Arterial thromboembolism
(3) Nonbacterial thrombotic endocarditis

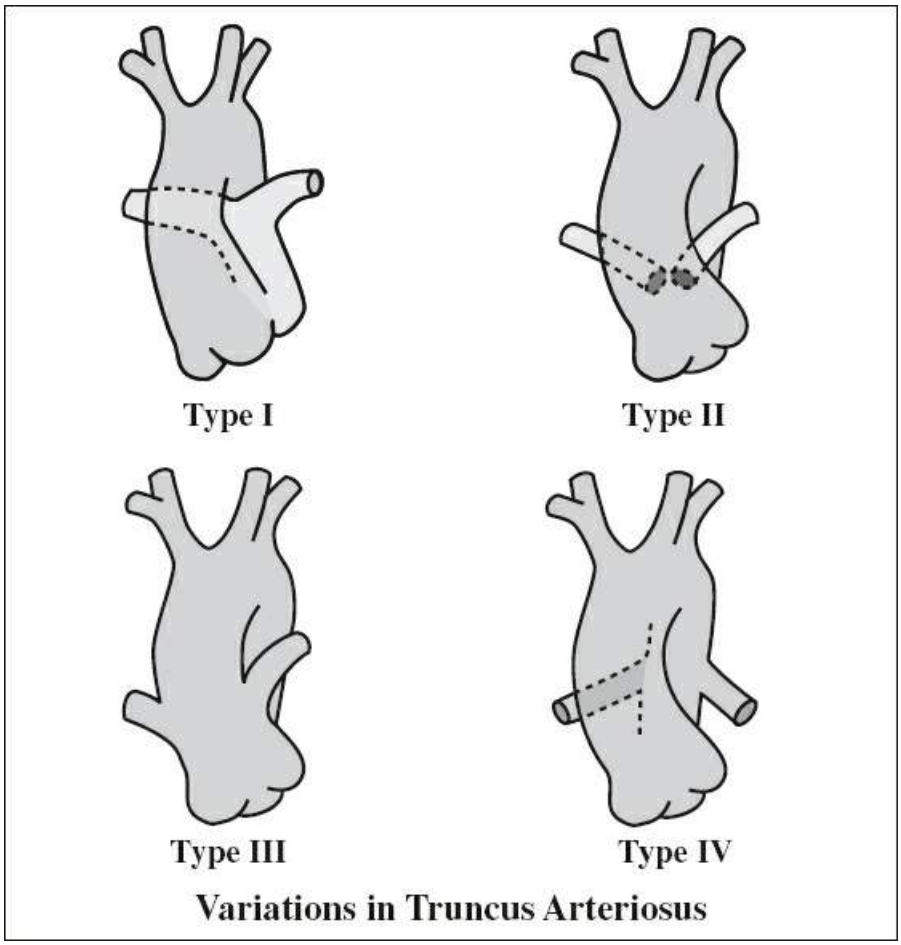
◊ Patients with thromboembolism have an increased incidence of occult malignancy!

Prevalent criteria:

› absence of apparent cause for thromboembolism
› age > 50 years
› multiple sites of venous thrombosis
› simultaneous venous + arterial thromboembolism
› resistance to oral anticoagulant therapy
› associated other paraneoplastic syndromes
› regression of thromboembolism with successful treatment of cancer

• disorders of consciousness ← cerebral emboli
• muscular pain + weakness ← emboli to skeletal muscle
• decompensated disseminated intravascular coagulation
√ deep vein thrombosis
√ pulmonary embolism
√ nonbacterial thrombotic endocarditis (echocardiography)

Rx: (1) Heparin (more successful than warfarin)
(2) Greenfield filter



Variations in Truncus Arteriosus

TRUNCUS ARTERIOSUS

= PERSISTENT TRUNCUS ARTERIOSUS = SINGLE OUTLET OF THE HEART = COMMON ARTERIAL TRUNK

= septation failure of the conotruncus characterized by

(1) Single great artery arising from the heart (larger than the aorta at a comparable age)
(2) Giving rise to coronary, pulmonary, and systemic arteries
(3) Overriding the ventricular septum
(4) Large VSD

Prevalence: 1% of CHD detected in fetus; 94÷1,000,000 live births

Collett & Edwards classification:

Type I	(50%)	=	both pulmonary arteries arise from a short pulmonary trunk distal to truncal valve
Type II	(25%)	=	separate origin of both pulmonary arteries from posterior aspect of truncus
Type III	(10%)	=	separate origin of both pulmonary arteries at lateral aspect of truncus
Type IV		=	pseudotruncus
Subtype A		=	infundibular VSD present
Subtype		=	VSD absent

B

Associated with:

(1) Right aortic arch (in 35%)
  ◊ Right aortic arch + cyanosis + shunt vascularity = TRUNCUS
(2) Genetic abnormality: chromosome 22q11 deletion, DiGeorge syndrome
(3) Interrupted aortic arch / coarctation (11–14%)
(4) Forked ribs

Hemodynamics:

admixture lesion (R-to-L and L-to-R shunt across VSD) with volume of pulmonary blood flow inversely related to degree of pulmonary vascular resistance

fetus : CHF only with incompetent valve ← massive regurgitation from truncus to ventricles

neonate : L-to-R shunt after decrease in pulmonary resistance (massive diversion of flow to pulmonary district) → CHF (ventricular overload) / pulmonary hypertension with time

RA	↔	RV	↑	Trunk	↑
Pulm. vessels	↑				
LA	↔	LV	↑		

- moderate cyanosis (degree inversely related to volume of pulmonary blood flow), apparent with crying
- severe CHF within first days / months of life (in large R-to-L shunt); wide pulse pressure
- systolic murmur (similar to VSD)
- early diastolic murmur (with truncal insufficiency)

CXR:

√ cardiomegaly:
  √ increased volume of both ventricles
  √ enlarged LA (50%) ← increased pulmonary blood flow
√ wide mediastinum ← large "aortic shadow" = truncus arteriosus
√ "waterfall / hilar comma" sign = elevated right hilum (30%); elevated left hilum (10%)
√ concave pulmonary segment (50%) = type I has left convex pulmonary segment
√ markedly ⇑ pulmonary blood flow, may be asymmetric

ECHO:

√ single arterial vessel overriding the interventricular septum (DDx: tetralogy of Fallot)
√ frequently dysplastic single semilunar valve with 3–6 leaflets (most commonly tricommissural = 3 leaflets)
  √ truncal valve may be stenotic
  √ truncal valve insufficiency with age (in 25%)

Dx: (often stenotic / insufficient) truncal valve with 2–5 cusps + atretic pulmonary valve + flow direction

Prognosis: 40% (20%) 6-month (1-year) survival rate

Rx: Rastelli procedure (30% no longer operable at 4 years of age) = (a) artificial valve placed high in RVOT and attached via a Dacron graft to main pulmonary artery (b) closure of VSD (5% mortality rate)

DDx: aortopulmonary window (2 separate valves)

Hemitruncus

= rare acyanotic anomaly characterized by
  (a) one pulmonary artery (commonly right PA) arises from truncus
  (b) one pulmonary artery arises from RV / supplied by systemic collaterals

Associated with: PDA (80%), VSD, tetralogy (usually isolated to left PA)

Pseudotruncus Arteriosus

= TRUNCUS TYPE IV

= severe form of tetralogy of Fallot with atresia of the pulmonary trunk; entire pulmonary circulation through bronchial collateral arteries (NOT a form of truncus arteriosus in its true sense); characterized by
  (1) Pulmonary atresia
  (2) VSD with R-to-L shunt
  (3) RV hypertrophy

Associated with: right aortic arch in 50%

• cyanosis
√ concavity in area of pulmonary segment
√ commalike abnormal appearance of pulmonary artery
√ absent normal right + left pulmonary artery (lateral chest film)
√ esophageal indentation posteriorly ← large systemic collaterals
√ prominent hilar + intrapulmonary vessels (= systemic collaterals)
√ "coeur en sabot" = RV enlargement
√ prominent ascending aorta with hyperpulsations

VASCULAR MALFORMATION

Arteriovenous Malformation

= nidus composed of multiple dysplastic vascular channels connecting feeding arteries with draining veins in the absence of a normal capillary bed

Age: present at birth in the early quiescent stage; not usually evident until childhood / adulthood

Growth: proportionate increase in size with child growth

Exacerbation: hormonal changes (puberty, pregnancy) / thrombosis, infection, trauma

• red pulsatile warm mass with thrill
• high-output congestive heart failure

MR:
  √ NO well-defined mass
  √ large serpentine flow voids on SE images / high-signal-intensity foci on GRE images = enlarged feeding arteries + draining veins
  √ decreased marrow signal intensity on T1WI ← intraosseous extension of lesion
  √ areas of high signal intensity on T1WI ← hemorrhage, intravascular thrombosis, flow-related enhancement

CEMR:
  √ contrast material rise time of 5–10 seconds
  √ early venous filling

Cx: bone overgrowth, arterial steal phenomenon, cutaneous ischemia

Congenital Arteriovenous Fistula

= single vascular channel between an artery and a vein
Cause: arrested vascular embryonic development
Location: extremity, neck, face
MR:
√ large signal voids on SE images or high-signal-intensity foci on GRE images without a well-defined mass ← arterial + venous components
DDx: chronic secondary AVF (with time enlarging supplying arteries + draining veins ← strong flow)

Capillary Malformation

= area of congenital ectasia of thin-walled small-caliber vessels of the skin (dermis / mucous membrane)
Age: present at birth in 0.3% of children
Associated with:
(1) Sturge-Weber syndrome
(2) Klippel-Trénaunay syndrome
(3) Parkes Weber syndrome
• cutaneous lesion of red discoloration
Location: predominantly in head & neck
MR (MRI not usually required ← clinical diagnosis):
√ subtle skin thickening ± occasional increased subcutaneous thickness

Lymphatic Malformation

Prevalence: 2nd most common type of vascular malformation after venous malformation
Cause: sequestered lymphatic sacs that fail to communicate with peripheral draining channels
Age: discovered in first 2 years of life
Path: infiltrative lesion permeating fat planes + involving multiple tissues consisting of chyle-filled cysts lined with endothelium
Commonly associated with: other vascular malformations
• smooth noncompressible soft-tissue mass with rubbery consistency:
A. MACROCYSTIC lymphatic malformation = cysts of variable size > 2 mm in diameter
• smooth translucent multiple masses beneath normal skin
√ rim + septal enhancement without central filling of cystic structures
B. MICROCYSTIC lymphatic malformation = cysts of < 2 mm in size on background of solid matrix
• permeation of skin
• diffuse soft-tissue thickening + surrounding lymphedema
√ NO significant enhancement
√ occasionally diffuse enhancement ← septal enhancement of small nonperceptible cysts / venous component in mixed venous-lymphatic malformation
Location: neck (70–80%); axillary region (20%); extremities (rare)
Site: posterior cervical triangle

MR:
√ lobulated septated mass with intermediate to decreased SI on T1WI + increased signal intensity on T2WI + STIR
√ internal fluid-fluid levels (common)

Venous Malformation

= simple slow-flow malformation + abnormal venous network
= "cavernous hemangioma" (misnomer)
Path: lesion may permeate across tissue planes and invade multiple adjacent tissues; connection to adjacent physiologic veins via narrow tributaries
Histo: small + large dysplastic postcapillary thin-walled vascular channels with sparse smooth muscle and variable amounts of hamartomatous stroma, thrombi, phleboliths
Age: childhood / early adulthood (present at birth)
• skin level: faint blue soft compressible nonpulsatile mass
  • enlarging with Valsalva maneuver + in dependent position
  • decreasing with elevation of extremity + local compression
• deep level: pain, impaired mobility, skeletal deformity
Location: head & neck (40%), extremities (40%), trunk (20%)
Associated with:
(1) Blue rubber bleb nevus syndrome
(2) Proteus syndrome
(3) Maffucci syndrome
√ absence of enlarged feeding vessels / arteriovenous shunting
√ lack of arterial + early venous enhancement
√ slow gradual filling with contrast material (contrast material rise time of about 90 seconds) + CHARACTERISTIC nodular enhancement of tortuous vessels during delayed venous phase
MR:
√ septated lesion of intermediate to decreased SI on T1WI:
  √ heterogeneous SI on T1 ← thrombosis / hemorrhage
√ increased signal intensity on T2WI and STIR
√ occasionally internal fluid-fluid levels ← hemorrhage / high protein content
√ small low-signal-intensity foci on all pulse sequences ← phleboliths
Dx: low-flow malformation based on absence of flow voids on SE images
Rx: sclerotherapy after lack of evident connection between malformation and deep venous system

VENTRICULAR ANEURYSM

A. CONGENITAL LEFT VENTRICULAR ANEURYSM
rare, young Black adult
(1) Submitral type:
  √ bulge at left middle / upper cardiac border
(2) Subaortic type:
  √ small + not visualized
  √ heart greatly enlarged (from aortic insufficiency)

B. ACQUIRED LEFT VENTRICULAR ANEURYSM

= complication of myocardial infarction, Chagas disease

- may be asymptomatic + well tolerated for years
- occasionally associated with persistent heart failure, arrhythmia, peripheral embolization

True Ventricular Aneurysm

= circumscribed noncontractile outpouching of ventricular cavity with broad mouth + localized dyskinesis

Cause: sequelae of transmural myocardial infarction

Location:

(a) left anterior + anteroapical: readily detected (anterior + LAO views)

(b) inferior + inferoposterior: less readily detected (steep LAO + LPO views)

Detection rate: 50% by fluoroscopy; 96% by radionuclide ventriculography; frequently not visible on CXR

√ localized bulge of heart contour = "squared-off" appearance of mid left lateral margin of heart border

√ localized paradoxical expansion during systole (CHARACTERISTIC)

√ rim of calcium in fibrotic wall (chronic), rare

√ akinetic / severely hypokinetic segment

√ left ventriculography in LAO, RAO is diagnostic

√ wide communication with heart chamber (NO neck)

Cx: wall thrombus with embolization

Prognosis: rarely ruptures

Pseudoaneurysm of Ventricle

= FALSE ANEURYSM

= left ventricular rupture contained by fused layers of visceral + parietal pericardium / extracardiac tissue

(a) cardiac rupture with localized hematoma contained by adherent pericardium; typically in the presence of pericarditis

(b) subacute rupture with gradual / episodic bleeding

Etiology: trauma, myocardial infarction

Location: typically at posterolateral / diaphragmatic wall of LV

√ left retrocardiac double density

√ diameter of mouth smaller than the largest diameter of the globular aneurysm

√ delayed filling

Cx: high risk of delayed rupture (infrequent in true aneurysms)

VENTRICULAR SEPTAL DEFECT

Most common CHD (25–30%):

(a) isolated in 20%

(b) with other cardiac anomalies in 5% (PDA, CoA)

◊ Acyanotic L-to-R shunt + right aortic arch (in 2–5%) = VSD

Embryology:

single ventricular chamber divides into two by fusion of membranous portion of ventricular

septum + endocardial cushions + bulbis cordis (= proximal part of truncus arteriosus) between 4th–8th week

1. MEMBRANOUS = PERIMEMBRANOUS VSD (75–80%)
   Location: posterior + inferior to crista supraventricularis near commissure between right and posterior (= noncoronary) aortic valve cusps
   May be associated with:
   small aneurysms of membranous septum commonly leading to decrease in size of membranous VSD (their presence does not necessarily predict eventual complete closure)
2. SUPRACRISTAL = CONAL VSD (5–8%)
   ◊ Crista supraventricularis = inverted U-shaped muscular ridge posterior + inferior to pulmonary valve
   (a) RV view = VSD just beneath pulmonary valve with valve forming part of superior margin of defect
   (b) LV view = VSD just below commissure between R + L aortic valve cusps
   Cx: right aortic valve cusp may herniate into VSD → aortic insufficiency
3. MUSCULAR VSD (5–10%)
   May consist of multiple VSDs; bordered entirely by myocardium
   Location: (a) inlet portion
   (b) trabecular portion
   (c) infundibular / outlet portion
4. ATRIOVENTRICULAR CANAL TYPE
   = ENDOCARDIAL CUSHION TYPE = POSTERIOR VSD (5–10%)
   Location: adjacent to septal + anterior leaflet of mitral valve; rare as isolated defect

Hemodynamics:
small bidirectional shunt during fetal life (similar pressures in RV + LV); after birth pulmonary arterial pressure ↓ and systemic arterial pressure ↑ with development of L-to-R shunt

Classification:

"Maladie de Roger"
= small restrictive VSD with defect < 1 cm; little / no hemodynamic significance with normal pulmonary artery pressure, normal pulmonary vascular resistance
- asymptomatic
- holosystolic heart murmur at 4th left rib interspace

√ normal plain film
Prognosis: spontaneous closure

Moderate Shunt
VSD defect < 75% of aortic diameter (1–1.5 cm); systolic LV pressure > systolic RV pressure; intermediate pulmonary artery pressure; normal pulmonary vascular resistance

Heart size	↑	Main PA	↔ to ↑
Pulm. vessels	↔ to ↑	LA	↑

- respiratory infections, mild dyspnea

√ slight prominence of pulmonary vessels (45% shunt)
√ slight enlargement of LA
Prognosis: spontaneous closure in large percentage

Nonrestrictive Large Shunt

VSD defect > 75% of aortic diameter; systolic LV pressure = systolic RV pressure (pulmonary vascular disease + hypertension increases RV pressure); pulmonary artery pressure approaching systemic levels; slightly increased pulmonary vascular resistance; pulmonary blood flow 2–4 times systemic flow

Heart size	↑	Main PA	↑
Pulm. vessels	↑	LA	↑

- bouts of respiratory infections
- feeding problems, failure to thrive
- CHF soon after birth ← RV overload

√ prominent pulmonary segment + vessels (= shunt vascularity)

√ calcification of pulmonary arteries
= PATHOGNOMONIC for pulmonary arterial hypertension

√ enlargement of LA + LV

√ normal / small thoracic aorta

Eisenmenger syndrome

large VSD eventually leads to shunt reversal (R-to-L shunt) ← irreversible increase in pulmonary vascular resistance (= intima + medial hyperplasia) when pulmonary vascular resistance > 0.75 of systemic vascular resistance

RA	↑	RV	↑	Main PA	↑
Pulm. vessels	↓/↑				
LA	↑ to ↔	LV	↑ to ↔	Ao	↑ to ↔

Frequency: 10% of large VSDs by 2 years of age

- cyanotic, but less symptomatic; CHF rare

√ eventual decrease of pulmonary vessel caliber

√ eventual decrease in size of LA + LV

NATURAL HISTORY OF VSD causing reduction in pulmonary blood flow:

1. Spontaneous closure
   in 40% within first 2 years of life; 60% by 5 years (65% with muscular VSD, 25% with membranous VSD); with small (large) VSD in 50% (10%)
2. RVOT obstruction
   infundibular hypertrophy in 3% = pink tetrad
3. Prolapse of right aortic valve cusp
   = aortic valve insufficiency

CXR (with increase in size of VSD):

√ variable appearance ← variations in defect size

√ enlargement of LA

√ enlargement of pulmonary artery segment

√ enlargement of LV

√ RV hypertrophy

√ increase in pulmonary blood flow (if > 45% of pulmonary blood flow from systemic circulation)

√ Eisenmenger reaction

ECHO:
√ prolapse of aortic valve cusp (in supracristal VSD)
√ deformity of aortic cusp (in membranous VSD)
√ lack of echoes in region of interventricular septum with sharp edges (DDx: artifactual dropout with sound beam parallel to septum); muscular VSD difficult to see
√ LA enlargement
Angio:
Projections:
(a) LAO 60° C-C 20° for membranous + anterior muscular VSD
(b) LAO 45° C-C 45° (hepatoclavicular) for posterior endocardial cushion + posterior muscular VSD
(c) RAO for supracristal VSD + assessment of RVOT
√ RVOT / pulmonary valve fill without filling of RV chamber (in supracristal VSD)
Rx:
(a) large VSD + left heart failure at 3 months of age: aim is to delay closure until child is 18 months of age; pulmonary-to-systemic blood flow > 2÷1 requires surgery before pulmonary hypertension becomes manifest
1. Digitalis + diuretics
2. Pulmonary artery banding
3. Patching of VSD: surgical approach through RA / through RV for supracristal VSD
(b) small VSDs without increase in pulmonary arterial pressure are followed

WEGENER GRANULOMATOSIS

[Friedrich Wegener (1907–1990), German pathologist in Berlin, Breslau and Lübeck describes rhinogenic granulomatosis in 1936]
= GRANULOMATOSIS WITH POLYANGIITIS
= ANCA-positive systemic vasculitis that affects small arteries characterized by systemic necrotizing granulomatous destructive angiitis
Incidence: 3÷100,000 annually in USA
Path: peribronchial necrotizing granulomas + vasculitis not intimately related to arteries with little / NO deposition of immunoglobulins / complement components (pauci-immune)
Mean age of onset: 40–50 years (range of all ages); M÷F = 2÷1; majority in Whites (90%)
Mean age in childhood: 14 (range 4–17) years; M < F
CLASSIC TRIAD:
(1) Upper airway granulomatous inflammation
◊ The most common presenting symptoms (in up to 67%): rhinitis, sinusitis, otitis media, nasal mucosa ulcer, bone deformity, subglottic stenosis
(2) Lower respiratory tract involvement
(3) Necrotizing glomerulonephritis
• circulating antineutrophil cytoplasmic antibodies (cANCA) directed against proteinase 3 + myeloperoxidase (found in neutrophils) in up to 90%
• rarely eosinophilia (DDx: Churg-Strauss syndrome)
• constitutional symptoms: fever, malaise, weight loss
Location: upper respiratory tract + sinuses in > 90%; kidneys in 85%

◊ Prone to venous thrombosis in lower extremities ← antiphospholipid antibodies

@ Pulmonary disease (94%)
- intractable cough (occasionally with hemoptysis)
- chest pain, dyspnea
- anemia, decrease in serum iron + ferritin levels (in diffuse alveolar hemorrhage)

Path: vasculitis of medium-sized and small pulmonary arteries + veins + capillaries, geographic necrosis, granulomatous inflammation

√ bilateral interstitial reticulonodular opacities, most prominent at lung bases (earliest stage)

√ randomly distributed irregular masses / nodules of varying sizes (5 mm to 10 cm), especially in lower lung fields (69%) usually sparing apices:
- √ usually < 10 masses, solitary in up to 25%
- √ cavitation of > 2-cm nodules with thick wall + irregular shaggy inner lining (25–50%)

√ bilateral multifocal patchy air-space opacities (in up to 50%):
- √ acute airspace pneumonia
- √ intraalveolar pulmonary hemorrhage

√ smooth / nodular thickening of subglottic / tracheal / bronchial wall producing stenosis with oligemia + emphysema + lobar / segmental atelectasis (60%)

√ uni- / bilateral pleural effusion (usually exudative) in 10–20%

√ focal pleural thickening = acute / chronic fibrinous pleuritis

√ reactive hilar / mediastinal lymphadenopathy (unusual)

√ interstitial pulmonary edema ± cardiomegaly (from renal / cardiac involvement)

CT:
- √ nodules in peribronchovascular distribution:
  - √ central cavitation in nodules > 2 cm in diameter
  - √ feeding vessels entering nodules (= angiocentric distribution)
- √ pleura-based wedge-shaped lesions (= infarcts)
- √ ground-glass opacity and consolidation (= pulmonary hemorrhage / infection) in up to 50%:
  - √ in a bilateral perihilar + peribronchovascular distribution
  - √ waxing and waning
  - √ air bronchogram in dense consolidation
  - √ CT "halo" sign (= rim of ground-glass attenuation surrounding a pulmonary lesion) due to adjacent parenchymal hemorrhage (in up to 15%)
  - √ CT "atoll" / "reverse halo" sign = central ground-glass opacity surrounded by a rim of opacified lung ← organizing pneumonia reaction in periphery of focal hemorrhage
- √ radiating linear scarring, spiculation + pleural tags of nodules and masses (prominent feature!)

Cx: (1) Dangerous airway stenosis (15% of adults, 50% of children)
(2) Massive life-threatening pulmonary hemorrhage
(3) Spontaneous pneumothorax (rare)

@ Tracheobronchial stenosis (16–23%)
- stridor ← tracheal inflammation + sclerosis

Location: subglottic portion of trachea (most often)

√ uni- / multifocal / segmental subglottic / tracheobronchial stenosis:
√ 2–4 cm long segment
√ smooth / nodular circumferential wall thickening of posterior membrane of trachea
√ ± intra- and extraluminal soft-tissue masses

@ Renal disease (85%) focal glomerulonephritis in 20–40% at presentation, as disease progresses in 80–90%
Histo: focal necrosis, crescent formation, paucity/ absence of immunoglobulin deposits
• may present as overt acute renal failure
√ large echogenic kidneys (early)
√ small shrunken echogenic kidney (late in renal failure)

@ Paranasal sinuses (91%)
Location: maxillary antra most frequently
• sinus pain, purulent sinus drainage, rhinorrhea
√ thickening of mucous membranes of paranasal sinuses
√ gradual reduction in sinus volume
√ residual lumen filled with material of ground-glass opacity
√ periantral soft-tissue infiltration
√ bone thickening + sclerosis of sinus walls ← chronic obstruction + inflammation
Cx: invasion of orbital fat + extraocular muscles + optic nerve ± local bone destruction

@ Nasopharynx (64%)
• chronic nasal obstruction (may be misdiagnosed as chronic sinusitis)
• epistaxis from nasal mucosal ulceration
• necrosis of nasal septum, saddle nose deformity
√ partial / complete erosion of nasal septum
√ truncated + shortened turbinates
√ progressive destruction of turbinates + lateral nasal wall (DDx: relapsing polychondritis)
√ destruction of hard palate with sinonasal-oral fistulas
√ granulomatous masses filling nasal cavity

@ CNS (involved late in 22–35%)
• central / peripheral neuritis
√ cerebral lesions ← intracranial extension of granulomas located in nasal cavity + paranasal sinuses
√ necrotizing cerebral vasculitis (nearly always with active sinusitis / otitis / lung disease)
√ leptomeningeal enhancement
√ nonspecific isolated enhancing intracranial / spinal lesions

@ Other organ involvement:
(a) Joints (67%): migratory polyarthropathy
(b) Ear (61%): otitis media
(c) Eye (58%): ocular inflammation, proptosis
(d) Skin + muscle (45%): inflammatory nodular skin lesions, cutaneous purpura
(e) Heart + pericardium (12–28%):
coronary vasculitis (rare), pancarditis, valvular lesions
Cx: acute pericarditis (6%), dilated congestive cardiomyopathy, acute valvular insufficiency with pulmonary edema, cardiac arrest ← ventricular arrhythmia, myocardial infarction

(f) Splenic disease
(g) GI tract (10%):
- abdominal pain, diarrhea, blood loss
√ ischemia, inflammation, ulceration, perforation

Cx: (1) Hypertension
(2) Uremia
(3) Facial nerve paralysis

Dx: (1) Lung / renal biopsy
(2) c-ANCA: 96% sensitive for generalized disease, 99% specific

Prognosis: death within 2 years from renal (83%) / respiratory failure; 90–95% mean 5-year survival under Rx

Rx: corticosteroids, cytotoxic drugs (cyclophosphamide), renal transplantation; 75–93% remission with therapy

DDx: Churg-Strauss (asthma, 47% cardiac involvement, less severe renal + sinus disease, p-ANCA); Goodpasture syndrome; SLE; mixed connective tissue disease; microscopic polyangiitis

Limited Wegener Granulomatosis

= Wegener granulomatosis largely confined to lung WITHOUT renal / upper airway involvement

Dx: c-ANCA (96% sensitive, 99% specific)

M < F

Prognosis: more favorable than classical Wegener's

Midline Granuloma

= mutilating granulomatous + neoplastic lesions limited to nose + paranasal sinuses with very poor prognosis; considered a variant of Wegener granulomatosis WITHOUT the typical granulomatous + cellular components

LIVER, BILE DUCTS, PANCREAS AND SPLEEN

DIFFERENTIAL DIAGNOSIS OF HEPATIC, BILIARY, PANCREATIC AND SPLENIC DISORDERS

RIGHT UPPER QUADRANT PAIN

A. BILE DUCTS
   1. Biliary colic / bile duct obstruction
   2. Acute cholecystitis / cholangitis

B. LIVER
   1. Acute hepatitis:
      (a) alcoholic, viral, drug-related, toxic
      (b) steatohepatitis
   2. Hepatic abscess
   3. Hepatic tumor: metastases, hepatocellular carcinoma, hemangioma, focal nodular hyperplasia, hepatic adenoma
   4. Hemorrhagic cyst
   5. Hepatic congestion: acute hepatic congestion, Budd-Chiari syndrome
   6. Perihepatitis = Fitz-Hugh-Curtis syndrome

C. PANCREAS
   1. Acute pancreatitis

D. INTESTINES
   1. Acute appendicitis
   2. Peripyloric ulcer
   3. Small bowel obstruction
   4. Irritable bowel
   5. Colitis / ileitis
   6. Intestinal tumor

E. LUNG
   1. Pneumonia
   2. Pulmonary infarction

F. KIDNEY
   1. Acute pyelonephritis
   2. Ureteral calculus
   3. Renal / perirenal abscess
   4. Renal infarction
   5. Renal tumor

G. OTHERS
   1. Costochondritis
   2. Herpes zoster

LIVER

Diffuse Liver Disease

A. Infectious
   1. Hepatitis
   2. Candidiasis
   3. Sarcoidosis
B. Reparative
   1. Cirrhosis
C. Infiltrative
   1. Iron deposition: hemochromatosis
   2. Fat deposition: fatty liver
   3. Glycogen storage disease
   4. Wilson disease
D. Vascular
   1. Intrahepatic shunts
   2. Budd-Chiari syndrome
   3. Right-sided CHF
   4. Portal vein thrombosis
   5. Venoocclusive disease
E. BILIARY
   1. Caroli disease
   2. Cholangitis: primary sclerosing cholangitis

Diffuse Hepatic Enlargement = Hepatomegaly

A. METABOLIC
   1. Fatty infiltration
   2. Amyloid
   3. Wilson disease
   4. Gaucher disease
   5. Von Gierke disease
   6. Niemann-Pick disease
   7. Weber-Christian disease
   8. Galactosemia
B. MALIGNANCY
   1. Lymphoma
   2. Diffuse metastases
   3. Diffuse HCC
   4. Angiosarcoma
C. INFLAMMATION / INFECTION
   1. Hepatitis
   2. Mononucleosis
   3. Miliary TB, histoplasmosis
   4. Malaria
   5. Syphilis

6. Leptospirosis
7. Chronic granulomatous disease of childhood
8. Sarcoidosis

D. VASCULAR
1. Passive congestion

E. OTHERS
1. Early cirrhosis
2. Polycystic liver disease

Hepatosplenomegaly

1. Disorders associated with extramedullary hematopoiesis + hemolytic anemia
2. Metabolic storage disease
3. Viral infection
4. Sarcoidosis
5. Leukemia, lymphoma, myeloproliferative disease

Hepatic Gas

Hepatic gas may be indicative of serious acute disease or simply an incidental finding of no clinical significance. Knowledge of the clinical history and clues on images may allow to determine its clinical relevance.

A. NONIATROGENIC
1. Liver abscess
2. Mesenteric infarction, necrotizing enterocolitis, colitis → portal venous gas
3. Hepatic artery thrombosis in liver transplant
4. Inflammatory bowel disease
5. Abdominal trauma
6. Emphysematous cholecystitis, ascending cholangitis

B. IATROGENIC

Hepatic gas is to be expected after therapeutic interventions like surgery, embolization, or tumor ablation.

1. Biliary gas: sphincterotomy / choledochojejunostomy
2. Colonoscopy, barium enema examination
3. Liver biopsy
4. Hepatic artery embolization: chemoembolization, brachytherapy, posttraumatic embolization
4. Percutaneous tumor ablation
5. Migration of hepatic venous gas: femoral venous / spinal / epidural catheter or lumbar puncture
6. Oxidized cellulose sponge (SURGICEL®)

Hepatic venous gas may be seen after placement of a femoral central venous catheter and aggressive fluid resuscitation.

Increased Liver Attenuation

= abnormal deposits of substances with high atomic numbers

√ normal liver density on NECT: 55–65 HU

A. IRON

√ density of iron-laden liver on NECT: > 72–80 HU

(a) diffuse iron deposition

› hepatocyte deposition

1. Genetic hemochromatosis
2. Erythropoietic hemochromatosis: intravascular hemolysis, paroxysmal nocturnal hemoglobulinuria
3. Bantu siderosis
4. Cirrhosis

› recticuloendothelial deposition

4. Transfusional iron overload

(b) focal iron accumulation

1. Hemorrhagic metastases: choriocarcinoma, melanoma
2. Hepatic adenoma
3. Siderotic regenerative nodules of cirrhosis
4. Focal hemochromatosis

B. COPPER

Wilson disease

C. IODINE

Amiodarone (= antiarrhythmic drug with 37% iodine by weight)

√ 95–145 HU (range of normal for liver 30–70 HU)

D. GOLD

Colloidal form of gold for therapy of rheumatoid arthritis

E. THOROTRAST

Alpha-emitter with atomic number of 90

F. THALLIUM

Accidental / suicidal ingestion of rodenticides (lethal dose is 0.2–1.0 gram)

G. ACUTE MASSIVE PROTEIN DEPOSITS

H. GLYCOGEN STORAGE DISEASE

mnemonic: GG CHAT

Gold therapy
Glycogen storage disease
Cyclophosphamide
Hemochromatosis / hemosiderosis
Amiodarone
Thorotrast

Generalized Increase in Liver Echogenicity

1. Fatty liver
2. Steatohepatitis
3. Cirrhosis (fibrosis + fatty liver)
4. Chronic hepatitis
5. Vacuolar degeneration

Marked Decrease in Hepatic T2 Signal Intensity

= paramagnetic effect of intracellular iron deposition (ferritin, hemosiderin)

◊ Signal intensity of pancreas does not help distinguish between primary + secondary hemochromatosis!

1. Primary / hereditary hemochromatosis (dietary iron)
2. Secondary hemochromatosis
   √ bone marrow of low SI (DDx: myelofibrosis)
3. Transfusional siderosis (RES)
   √ bone marrow of low signal intensity
   √ decreased T2 signal in spleen
4. Intravenous administration of ultrasmall superparamagnetic iron oxide

PERIHEPATIC SPACE

Perihepatic Fat Attenuation

1. Spontaneous rupture of cystic ovarian teratoma
2. Lipoma / liposarcoma
3. Pseudolipoma
   = detached degenerating epiploic appendage lodged between diaphragm and superior aspect of liver
3. Juxtacaval fat
   = medial to IVC near hepatic venous confluence
   Prevalence: 0.5% of CTs in adults
4. Omental infarction
5. Intrahepatic omental packing

Perihepatitis

= inflammation of peritoneal capsule of liver

√ hepatic capsular enhancement

A. Infection
   1. Fitz-Hugh-Curtis syndrome
   2. Perforated cholecystitis
   3. Perforated hepatic abscess
   4. Tuberculous peritonitis
B. Inflammation
   1. SLE
   2. Radiation therapy
C. Tumor = peritoneal carcinomatosis
D. Pseudoperihepatitis
   = low liver density simulates capsular enhancement
   1. Fatty liver

LIVER MASS

◊ Hepatic masses account only for 5–6% of all intraabdominal masses in children!

Primary Benign Liver Tumor

A. EPITHELIAL TUMORS
   (a) hepatocellular
      1. Hepatic adenoma
      2. Focal nodular hyperplasia
      3. Nodules in cirrhosis: regenerative nodule, dysplastic nodule
      2. Nodular regenerative hyperplasia
   (b) cholangiocellular
      1. Hepatic cyst
      2. Bile duct hamartoma
      3. Peribiliary cyst
      4. Biliary cystadenoma
      5. Caroli disease
      3. Biliary papillomatosis
B. MESENCHYMAL TUMORS
   (a) tumor of adipose tissue
      1. Hepatic lipoma
      2. Hepatic myelolipoma
      3. Hepatic angiomyolipoma
   (b) tumor of muscle tissue
      1. Leiomyoma
   (c) tumor of blood vessels
      1. Infantile hemangioendothelioma
      2. Hemangioma
      3. Peliosis hepatis
   (d) tumor of neural crest
      1. Hepatic paraganglioma
   (e) mesothelial tumor
      1. Benign mesothelioma
C. MIXED TISSUE TUMOR
   1. Mesenchymal hamartoma
   2. Hepatoblastoma
   3. Benign teratoma
D. MISCELLANEOUS
   1. Adrenal rest tumor
   2. Pancreatic rest
E. PSEUDOLESION
   1. Focal fatty infiltration
   2. Focal fat sparing
   3. Confluent hepatic fibrosis

Pediatric Benign Liver Mass

1. Infantile hemangioendothelioma
2. Mesenchymal hamartoma

infrequent:

3. Focal nodular hyperplasia
4. Hepatocellular adenoma
5. Nodular regenerative hyperplasia

Primary Malignant Liver Tumor

◊ Hepatic malignancies are the most common GI malignancy in children, but account for < 2% of all pediatric malignancies!

A. EPITHELIAL TUMOR
   (a) hepatocellular
      1. Hepatoblastoma (7%)
      2. Hepatocellular carcinoma (75%)
   (b) cholangiocellular (6%)
      1. Cholangiocarcinoma
      2. Biliary cystadenocarcinoma

B. MESENCHYMAL TUMOR
   (a) tumor of blood vessels
      1. Angiosarcoma
      2. Epithelioid hemangioendothelioma
      3. Kaposi sarcoma
   (b) other tumor
      1. Embryonal sarcoma
      2. Fibrosarcoma

C. TUMOR OF MUSCLE TISSUE
   1. Leiomyosarcoma
   2. Embryonal rhabdomyosarcoma of the biliary tree

D. MISCELLANEOUS
   1. Carcinosarcoma
   2. Teratoma
   3. Yolk sac tumor
   4. Carcinoid
   5. Squamous carcinoma
   6. Primary lymphoma

Pediatric Malignant Liver Mass

A. PRIMARY
   1. Hepatoblastoma
   2. Hepatocellular carcinoma
   3. Fibrolamellar carcinoma
   4. Undifferentiated (embryonal) sarcoma
   5. Epithelioid hemangioendothelioma
   6. Embryonal rhabdomyosarcoma

B. SECONDARY (metastasis)
   ◊ Most common neoplasm involving liver
   Origin: neuroblastoma, Wilms tumor, lymphoma

Solitary Liver Lesion

A. Benign tumor
   1. Cavernous hemangioma
   2. Adenoma
   3. Focal nodular hyperplasia
   4. Mesenchymal hamartoma

B. Infection
   1. **Pyogenic abscess**
   2. Echinococcal cyst
   3. Inflammatory pseudotumor

C. Trauma
   1. Hematoma
   2. Traumatic cyst

D. Malignant tumor
   1. Primary tumor
   2. Metastasis

E. Other
   1. Fatty change
   2. Simple cyst

Solitary Cystic Lesion

√ well-defined lesion with predominant near-water attenuation (0–30 HU) / signal intensity exhibiting negligible enhancement at dynamic imaging

√ variability of cystic component accounts for differences in attenuation / signal intensity:
   (a) liquids: serous, mucinous, bilious, hemorrhagic, proteinaceous, or mixed fluids
   (b) intratumoral necrosis
   (c) tissue with a high water content

√ septa may contain a range of tissues including epithelium, fibrotic tissue, stroma, neoplastic tissue, inflammatory cells.

1. Biliary cystadenoma / biliary carcinoma
2. Cystic degeneration of hepatocellular carcinoma
3. Bacterial / parasitic abscess
4. Metastatic disease
5. Posttraumatic resolving hematoma

Typical MR Characteristics of Benign Liver Tumors

Lesion	*T1WI*	*T2WI*	*Contrast Enhancement*		
	(relative to normal liver parenchyma)		*Arterial Phase*	*Portal Venous Phase*	*Delayed Phase*
Adenoma	hyper- to isointense	slightly hyperintense	hyperintense	isointense	
FNH	iso- to hypointense	hyper- to isointense (hyperintense central scar)	hyperintense (hypointense central scar)	hyper- to isointense	isointense (hyper- to isointense central scar)
Regenerative nodule	variable	hypointense	no enhancement	---------- variable ----------	
Dysplastic nodule	variable	variable – may have hyperintense foci	slight / no enhancement	---------- variable ----------	
Hepatic cyst	hypointense	hyperintense	no enhancement		
Hemangioma	hypointense	hyperintense	peripheral nodular enhancement	increasing peripheral enhancement	hyperintense

Multilocular Cystic Hepatic Lesions

A. CONGENITAL
    1. Polycystic liver disease
B. NEOPLASTIC
    1. Biliary cystadenoma / ~carcinoma
    2. Hepatocellular carcinoma
    3. Cystic metastasis: neuroendocrine tumor, melanoma, GIST, mucinous colorectal / mucinous ovarian carcinoma; treated metastasis
    4. Inflammatory myofibroblastic tumor
    5. Mesenchymal hamartoma
C. INFECTIOUS
    1. Pyogenic abscess
    2. Amebic abscess
    3. Echinococcal cyst
D. TRAUMATIC
    1. Intraparenchymal hematoma
    2. Biloma

Attenuation of Cystic Hepatic Lesions

1. Simple hepatic cyst -10 – 10 HU
2. Hematoma (acute) 40 – 60 HU
3. Clotted blood 45 – 70 HU
4. Biloma 0 – 15 HU
5. Pyogenic abscess 0 – 45 HU
6. Hydatid mother cyst 3 – 30 HU
7. Hydatid daughter cyst lower than mother cyst
6. Amebic abscess 10 – 20 HU

◊ Density measurements in general are of little help due to variability of cyst content and change over time!

Solitary Echogenic Liver Mass

mnemonic: **H**yperechoic **F**ocal **M**asses **A**ffecting the **L**iver
Hematoma, **H**epatoma, **H**emangioma, **H**emochromatosis, **H**epatoblastoma
Fatty infiltration, **F**ocal nodular hyperplasia, **F**ibrosis
Metastasis
Adenoma
Lipoma

Solid Liver Lesion with Cystic Degeneration

1. Hepatocellular carcinoma / adenoma
2. Fibrolamellar carcinoma
3. Intrahepatic cholangiocarcinoma
4. Angiosarcoma
5. Epithelioid hemangioendothelioma
6. Lymphoma
7. Metastatic disease

Liver Mass Surrounded by Echogenic Rim

1. Metastasis: esp., cystic pancreatic endocrine tumor
2. Adenoma
3. Hemangioma

Multiple Liver Lesions

A. BENIGN TUMOR
   1. Cavernous hemangioma
   2. Adenoma
   3. Regenerating hepatic nodules
   4. Biliary microhamartomas

B. INFECTION
   1. Multiple abscesses / microabscesses
   2. Mycobacterial + fungal infection
   3. Inflammatory pseudotumors

C. CONGENITAL
   1. Polycystic disease
   2. Caroli disease

D. MALIGNANCY
   1. Metastases (most common malignant liver tumor)
   2. Multifocal hepatoma
   3. Lymphoma

E. OTHER
   1. Sarcoidosis
   2. Simple cysts
   3. Langerhans cell histiocytosis (echogenic nodules)
   4. Multifocal fat deposition

Bull's-eye Lesions of Liver

1. Candidiasis (in immunocompromised)
2. Metastases
3. Lymphoma, leukemia
4. Sarcoidosis
5. Septic emboli
6. Other opportunistic infections
7. Kaposi sarcoma

Miliary Hepatosplenic Lesions

1. Tuberculosis
2. Metastases
3. Fungal infections
4. Sarcoidosis
5. Lymphoma

Fat- / Lipid containing Liver Mass

1. Lipoma

2. Angiolipoma
3. Angiomyolipoma: eg, tuberous sclerosis
4. Hepatocellular carcinoma
5. Hepatocellular adenoma
6. Liposarcoma metastasis
7. Malignant teratoma metastasis (+ calcifications)
8. Focal fatty change
9. Focal nodular hyperplasia (rare)
10. Regenerative & dysplastic nodules
11. Fat packing

Cystic Liver Lesion

A. NONNEOPLASTIC
   1. Congenital hepatic cyst
   2. Hematoma
   3. Echinococcal cyst
   4. Liver abscess
   5. Fibropolycystic liver disease
   6. Intrahepatic pseudocyst
   7. Biloma

B. NEOPLASTIC
   1. Mesenchymal hamartoma
   2. Undifferentiated (embryonal) sarcoma
   3. Malignant mesenchymoma
   4. Biliary cystadenoma / cystadenocarcinoma
      ◊ < 5% of intrahepatic cysts are of biliary origin!
   5. Lymphangioma
   6. Necrotic ischemic neoplasm: HCC, giant cavernous hemangioma
   7. Cystic metastasis: ovarian / gastric carcinoma

Fibropolycystic Liver Disease

= unique group of entities with derangement of embryonic biliary ductal plate development surrounding portal vein

◊ Coexistence of hepatic + renal anomalies

A. SMALL INTERLOBULAR BILE DUCTS
   1. Congenital hepatic fibrosis
   2. Biliary hamartomas

Associated with: autosomal recessive (juvenile) polycystic kidney disease

B. MEDIUM-SIZED BILE DUCTS
   1. Autosomal dominant polycystic disease

Associated with: autosomal dominant (adult) polycystic kidney disease

C. LARGE INTRAHEPATIC BILE DUCTS
   1. Caroli disease

D. LARGE EXTRAHEPATIC BILE DUCTS
   1. Choledochal cyst

Liver Mass with Capsule

1. Hepatocellular carcinoma
2. Hepatocellular adenoma
3. Focal nodular hyperplasia (thin incomplete capsule)

Liver Mass with Capsular Retraction

1. Cholangiocarcinoma
2. Fibrolamellar carcinoma
3. Epithelioid hemangioendothelioma
4. Confluent hepatic fibrosis

or any hepatic malignancy

Disease of Hepatic Capsular & Subcapsular Region

A. INFECTION / INFLAMMATION
   1. Perihepatitis
   2. Parasites: fascioliasis, paragonimiasis, sparganosis
      → penetration of intestinal wall → migration through peritoneal cavity → perforation of liver capsule with initially subcapsular infestation

B. METASTATIC DISEASE
   (a) seeded metastasis: ovarian cancer
   (b) invasion via perihepatic ligaments: cancer of stomach, duodenum, pancreas, colon, anterior abdominal wall
   (c) direct invasion from adjacent organ: cancer of stomach, gallbladder, adrenal gland, kidney

C. PSEUDOLESION OF ALTERED HEMODYNAMICS
   1. Third inflow
   2. Arterioportal shunt
   3. Compression of liver
   4. Portal vein obstruction
   5. Hepatic vein / IVC obstruction
   6. Hepatic infarction
   7. Intrahepatic vascular shunt: superior vein of Sappey, umbilical + paraumbilical veins, right posterior portal vein, venovenous surface collaterals

D. OTHERS
   1. Focal fat sparing / focal fat infiltration
   2. Confluent hepatic fibrosis

Hyperintense Liver Mass on T1WI

◊ Usually due to lipid, hemorrhage or melanin!

1. Hepatocellular adenoma
2. Hepatocellular carcinoma
3. Regenerative & dysplastic nodule
4. Melanoma
5. Hemorrhage (methemoglobin), hemorrhagic tumor
6. Focal fat deposit, lipoma

7. Cyst with high protein content
8. Thrombosed hemangioma (rare)
9. Paramagnetic contrast agents + iodized oil

Hypointense Liver Lesion on T2WI

A. ABSOLUTE
- › blood degradation products
  - » acute intracellular deoxyhemoglobin
  - » subacute intracellular methemoglobin
  - » chronic intracellular iron ferritin / hemosiderin
  1. Hepatocellular adenoma ← internal bleeding
  2. Hepatocellular carcinoma ← internal bleeding
  3. Metastasis
  4. Focal nodular hyperplasia ← intratumoral hemolysis
  5. Nodular regenerative hyperplasia
  6. Peliosis hepatis ← hemorrhage in large vascular spaces
  7. Hematoma
- › iron (intracellular paramagnetic Fe3+)
  1. Siderotic nodule
  2. Dysplastic nodule
  3. HCC
- › copper (= divalent paramagnetic copper)
  1. Wilson disease
  2. HCC
  3. Focal nodular hyperplasia
- › macromolecules ← restricted motion of water bound to protein
  - » smooth muscle
    1. Leiomyoma
    2. Angiomyolipoma
  - » fibrosis
    1. Fibrolamellar HCC
    2. Intrahepatic cholangiocarcinoma
    3. HCC
    4. Metastasis of adenocarcinoma
    5. Focal nodular hyperplasia
    6. HCA
  - » mucin (= desiccated mucinous secretions)
    1. Metastasis
  - » fibrinogen (intracytoplasmic inclusions = fibrinogen in dilated rough endoplasmic reticulum)
    1. HCC
  - » keratin
    1. Metastasis
  - » melanin ← presumably related to higher melanin levels or to old hemorrhage
    1. Malignant melanoma

2. Metastasis

› necrosis (coagulative = dehydrated necrosis)
1. Metastasis
2. Solitary necrotic nodule
3. HCC
4. HCA

› calcium
1. Granuloma
2. Healed inactive hydatid cyst
3. Fibrolamellar HCC
4. Metastasis: mucinous cancer of colon, stomach, breast, ovary / osteo- and chondrosarcoma
5. HCA
6. Teratoma

B. RELATIVE

› fat (= macroscopic intratumoral fat)
1. Hepatocellular adenoma
2. Hepatocellular carcinoma
3. Lipoma
4. Angiomyolipoma
5. Focal nodular hyperplasia

Liver Mass on Diffusion-Weighted Imaging

= quantification of water diffusion + microcapillary blood perfusion ← based on incoherent intravoxel motion

A. Tissue with restricted diffusion (↓ ADC)
1. Tumor: usually lower ADC for malignant lesion
2. Cytotoxic edema
3. Abscess

B. Tissue with less restricted diffusion (↑ ADC)
= tissue of low cellularity / with disrupted cell membranes
1. Cyst
2. Hemangioma
3. Treated nonviable / necrotic tumor

Uptake of Superparamagnetic Iron Oxide Particles

Action: preferential entrapment by Kupffer cells

1. Focal nodular hyperplasia
2. Well-differentiated HCC
3. Dysplastic nodule
4. Hepatic adenoma

Enhancement Characteristics of Liver Mass

Hypovascular Liver Lesion

= less dense than adjacent liver parenchyma during arterial + portal venous phase

Hypo- / Nonenhancing benign Liver Lesion

1. "To small to characterize" implies unreliable density measurement
   › small metastasis = low probability
   › microabscesses = clinically obvious
   › biliary hamartoma = usually multiple
2. Hepatic cyst
3. Caroli disease
4. ADPKD
5. Abscess
6. Hydatid cyst
7. Biliary cystadenoma
8. Regenerating / dysplastic nodule
9. Lipoma
10. Bile duct hamartoma
12. Sarcoidosis
13. Histoplasmosis

Hypoenhancing Malignant Liver Lesion

1. Metastasis to liver
2. Lymphoma
3. Cholangiocarcinoma

Low-density Hepatic Mass with Enhancement

1. Hepatocellular carcinoma
2. Hypervascular metastases
   = lesions that may be obscured after contrast injection: pheochromocytoma, carcinoid, melanoma
3. Cavernous hemangioma
4. Focal nodular hyperplasia with central fibrous scar
5. Hepatic adenoma

Ring-enhancing Targetlike Liver Mass

1. Metastasis
2. Abscess
3. Cholangiocarcinoma
4. Treated HCC
5. Epithelioid hemangioendothelioma
6. Confluent hepatic fibrosis
7. Giant atypical cavernous hemangioma

Rim Enhancement

1. Biliary cystadenoma / ~ adenocarcinoma
2. Hematoma (some)
   √ bright on T1WI ← subacute hematoma

√ dark on T2WI ← hemosiderin of chronic hematoma

Hypervascular Liver Mass

√ detected during hepatic arterial + portal venous phase

A. BENIGN
   1. Focal nodular hyperplasia
   2. Hepatocellular adenoma
   3. Hemangioma (Type 1)

B. MALIGNANT
   (a) Primary malignant liver tumor
      1. Hepatocellular carcinoma
      2. Hemangioendothelioma
      3. Angiosarcoma
   (b) Hypervascular liver metastases

HYPERVASCULAR MASS IN NORMAL LIVER

1. Small hemangioma (Type 1)
2. Focal nodular hyperplasia
3. Hepatocellular adenoma
4. Metastasis

HYPERVASCULAR MASS IN CHRONIC LIVER DISEASE

1. Hepatocellular carcinoma
2. Nodular regenerative hyperplasia
3. Mimickers:
   AVM, FNH, hemangioma, dysplastic nodule, transient hepatic intensity difference

HYPERVASCULAR MASS WITH CENTRAL SCAR

1. Focal nodular hyperplasia
2. Giant cavernous hemangioma
3. Fibrolamellar carcinoma of liver
4. Well-differentiated hepatocellular carcinoma
5. Hypervascular metastasis
6. Intrahepatic cholangiocarcinoma

NODULE-WITHIN-NODULE ENHANCEMENT

1. Focus of early HCC within dysplastic nodule
   √ moderately high SI on T2WI within nodule of generally low SI
   √ marked arterial enhancement on T1WI

PERIPHERAL WASHOUT SIGN

1. Metastasis: carcinoid, breast, colon, stomach
   √ hypointense peripheral rim relative to center (best seen 10 minutes after contrast administration)

DELAYED PHASE-ENHANCING LESION

1. Hemangioma

2. Intrahepatic cholangiocarcinoma
3. Peliosis hepatis

Hepatic Calcification

A. INFECTION (most common cause)
   1. Granulomatous disease: tuberculosis (48%), histoplasmosis, brucellosis, coccidioidomycosis
      √ calcium involves entire lesion
   2. Echinococcal cyst (in 10–20%)
      √ curvilinear / ring calcification
   3. CMV, toxoplasmosis, Pneumocystis carinii
   4. Chronic granulomatous disease of childhood
   5. Old pyogenic / amebic abscess
   6. Schistosomiasis
      √ turtleback / tortoise shell calcifications
   7. Cysticercosis, filariasis, paragonimiasis, Armillifer infection, dracunculiasis
   8. Syphilitic gumma
B. VASCULAR
   1. Hepatic artery aneurysm
   2. Portal vein thrombosis
   3. Hematoma
C. BILIARY
   1. Hepatolithiasis = intrahepatic calculi
   2. Recurrent pyogenic cholangitis
   3. Ascariasis
   4. Clonorchiasis
D. BENIGN TUMORS
   1. Congenital cyst
   2. Cavernous hemangioma
      √ large coarse centrally located calcification (in 10–20%)
   3. Hepatocellular adenoma
   4. Capsule of regenerating nodules
   5. Infantile hemangioendothelioma
E. PRIMARY MALIGNANT TUMOR
   1. Fibrolamellar carcinoma (calcified in 15–25%)
   2. Hepatocellular carcinoma
   3. Hepatoblastoma (10–20%)
   4. Intrahepatic cholangiocarcinoma (in 18%)
      √ calcification accompanied by desmoplastic reaction
   5. Epithelioid hemangioendothelioma
   6. Cystadenocarcinoma
F. METASTATIC TUMOR
   1. Mucin-producing neoplasm: carcinoma of colon, breast, stomach
   2. Ovarian carcinoma (psammomatous bodies)
   3. Melanoma, thyroid carcinoma, pleural mesothelioma, chondro- and osteosarcoma,

carcinoid, leiomyosarcoma, neuroblastoma

mnemonic: 4H TAG MAP

Hepatoma
Hemochromatosis
Hemangioma
Hydatid disease
Thorotrast
Abscess
Granulomas (healed)
Metastases
Absent mnemonic
Porcelain gallbladder

Spontaneous Hepatic Hemorrhage

A. RUPTURE OF PRIMARY HYPERVASCULAR NEOPLASM
   1. Hepatocellular carcinoma (86%)
   2. Hepatocellular adenoma (6%)
   3. Hepatic hemangioma (3%)
   4. Hepatic metastasis: lung, RCC, melanoma (1%)
   5. Focal nodular hyperplasia
   6. Amyloidosis
   7. Peliosis hepatis
   8. Angiomyolipoma

(b) COAGULATION DISORDER
   1. Cirrhosis (4%)

(c) SYNDROMIC HEMOLYSIS
   1. HELLP syndrome

Colloid Shift

= increased uptake of injected colloid by bone marrow

A. HEPATIC DYSFUNCTION
   1. Cirrhosis
   2. Hepatitis
   3. Chronic passive congestion

B. AUGMENTED PERFUSION of spleen + bone marrow
   1. Hematopoietic disorders
   2. Long-term corticosteroid therapy

Focal Hot Liver Lesion

1. IVC / SVC obstruction
   √ increased perfusion of quadrate lobe located at posterior aspect of medial segment left hepatic lobe (collateral pathway via umbilical vein)
2. Budd-Chiari syndrome
   √ "increased" perfusion of caudate lobe ← actually decrease of activity elsewhere in liver

3. FNH (varying amount of Kupffer cells)
   √ hot (DIAGNOSTIC) / cold / isoactive with surrounding parenchyma
4. Regenerating nodules of cirrhosis

Focal Liver Defects

A. NEOPLASTIC
   (a) primary liver tumor: hepatoma, hemangioma, hepatic adenoma, FNH
   (b) metastases: 85% sensitive, 75–80% specific for lesion > 1–2 cm
B. INFECTIOUS DISEASE / ABSCESS
C. BENIGN CYST
D. TRAUMA (= hematoma)
E. PSEUDOTUMOR = normal variant

mnemonic: L-CHAIM
Lymphoma
Cyst
Hematoma
Abscess
Infarct
Metastasis

Mottled Hepatic Uptake

1. Cirrhosis
2. Acute hepatitis
3. Lymphoma
4. Amyloidosis
5. Granulomatous disease: sarcoidosis, fungal, viral, parasitic
6. Chemo- / radiation therapy

PORTA HEPATIS

Spectrum of Disease of Porta Hepatis

A. VASCULAR
   1. Main portal vein (MPV): thrombosis, stenosis, aneurysm, gas
   2. Common hepatic artery (CHA): thrombosis, stenosis, aneurysm
B. BILE DUCTS
   1. Cholangiocarcinoma
   2. Intrabiliary metastasis
      Origin: lung, breast, gallbladder, colon, testis, prostate, pancreas, melanoma, lymphoma
   3. Benign biliary stricture
   4. Choledochal cyst
C. LYMPH NODES
   1. Benign reactive lymph nodes
   2. Noninfectious inflammatory disease
   3. Infectious disease

4. Metastasis
5. Lymphoma
6. Posttransplant proliferative disease

D. NERVES
1. Schwannoma = neurilemmoma
2. Neurofibroma
3. Neurofibrosarcoma

E. CONNECTIVE TISSUE
1. Rhabdomyosarcoma
2. Granulocytic sarcoma

F. MISCELLANEOUS
1. Periportal edema
2. Porta hepatis fluid collection see below
3. Periportal fat deposition

Low-density Mass in Porta Hepatis

1. Choledochal cyst
2. Hepatic cyst
3. Pancreatic pseudocyst
4. Enteric duplication
5. Hepatic artery aneurysm
6. Biloma
7. Embryonal rhabdomyosarcoma of biliary tree

Porta Hepatis Fluid Collection

Cause: orthotopic liver transplantation, trauma, cholecystectomy, other biliary injury

1. Biloma
2. Hematoma
3. Abscess
4. Seroma

Enlarged Lymph Nodes of Porta Hepatis

Location: along anterior and posterior to portal vein + hepatoduodenal ligament

Normal size: < 6 mm

A. LIVER DISEASE
1. Hepatitis B and C
2. Cirrhosis

B. INFECTION / INFLAMMATION
1. Tuberculosis
2. Autoimmune diseases
3. Sarcoidosis

C. MALIGNANCY
1. Metastasis: esophagus, stomach, pancreas, gallbladder, liver, biliary tree, breast, lung, kidney
   √ may be associated with hepatic metastasis

√ compression / thrombosis of portal vein

2. Lymphoma

Defects in Porta Hepatis on Liver Scintigram

1. Normal variant ← thinning of hepatic tissue overlying portal veins + gallbladder
2. Biliary causes: dilatation of bile ducts, gallbladder hydrops
3. Enlarged portal lymph nodes
4. Metastases
5. Hepatic cyst
6. Hepatic parenchymal disease (= pseudotumor)
7. Hepatic compression by adjacent extrinsic mass
8. Postsurgical changes following cholecystectomy

LIVER CIRCULATION

Liver perfusion

Dual blood supply: normally hepatic artery 25% + portal vein 75%

PV ↓ and HA ↑: cirrhosis & portal hypertension, portal vein thrombosis (bland, malignant), PV compression (adenopathy in porta hepatis)

PV ↑ and HA ↓: postprandial state, HA stenosis (orthotopic liver transplant) / thrombosis, HA encasement (pancreatic cancer)

Global Heterogeneous Hepatic Enhancement

1. Passive hepatic congestion
2. Budd-Chiari Syndrome
3. Hereditary hemorrhagic telangiectasia
4. Peliosis hepatis

Transient Hepatic Parenchymal Enhancement

= HYPERPERFUSION ABNORMALITIES OF LIVER

= TRANSIENT HEPATIC ATTENUATION DIFFERENCE (THAD LESION) = TRANSIENT HEPATIC INTENSITY DIFFERENCE (THID)

= attenuation difference of liver appearing during dynamic bolus-enhanced CT

√ patchy area of transient high attenuation during early arterial phase

√ fading with return to normal during portal venous phase

√ peripheral location, triangular shape, straight margins

√ presence of normal vessels coursing through lesion

Cause: imbalance between hepatic arterial + portal venous supply ← decreased portal blood flow, formation of intrahepatic arterioportal shunts, increased aberrant drainage through hepatic veins

A. LOBAR / SEGMENTAL
   1. Portal vein obstruction: portal vein thrombosis, tumor invasion, surgical ligation
   2. Cirrhosis with arterioportal shunt
   3. Hypervascular gallbladder disease

B. SUBSEGMENTAL

1. Obstruction of peripheral portal branches
2. Percutaneous needle biopsy + drainage procedure / ethanol ablation
3. Acute cholecystitis + cholangitis

C. SUBCAPSULAR
   (a) due to peripheral parenchymal compression
      1. Rib compression
      2. Perihepatic peritoneal implants
      3. Pseudomyxoma peritonei
      4. Perihepatic fluid collections
   (b) idiopathic (unexplained)

D. PSEUDOLESION
   = systemic venous blood flow draining into hepatic sinusoids = third hepatic inflow
   1. Accessory cystic vein of gallbladder fossa
   2. Aberrant right gastric vein
   3. Capsular veins
   4. Parabiliary venous system
   5. Epigastric-paraumbilical venous system

E. RETICULAR-MOSAIC PATTERN
   1. Cirrhosis
   2. Hereditary hemorrhagic telangiectasia
   3. Hepatic vein obstruction

Arterioportal Shunt

= organic / functional communication between high-pressure hepatic arterial branch + low-pressure portal venous system at level of trunk / sinusoids / peribiliary venules

√ small nodular peripheral nonspherical focus isoattenuating with aorta during arterial phase → isoattenuating to liver during portal phase

√ for peripheral arterioportal shunt transient wedge-shaped subsegmental area of enhancement during arterial phase → normal parenchymal attenuation during portal venous phase

Pathophysiology:
   (a) shunted contrast material enhances a focal area of liver parenchyma before adjacent parenchyma is enhanced via the usual splanchnic route
   (b) large shunt may cause arterialized hepatofugal flow in portal vein detectable by Doppler ultrasound

Cause:
   A. CONGENITAL
      1. Hereditary hemorrhagic telangiectasia
   B. ACQUIRED
      1. Cirrhosis
         √ normal SI on T1WI + T2WI
         √ pseudolesion = small peripheral subcapsular wedge-shaped area of transient homogeneous enhancement during arterial phase of CECT
         √ pseudolesion remains stable / resolves spontaneously over time
      2. Primary hepatic neoplasm: HCC (63%), hemangioma, cholangiocarcinoma

√ abnormal SI on T1WI + T2WI with growth on follow-up
√ transient wedge-shaped area of increased attenuation / intensity on arterial phase CECT / CEMR = Transient Hepatic Parenchymal Enhancement
√ enhancement of portal vein branch ± main portal vein from periphery without enhancement of splenic vein / superior mesenteric vein

3. Secondary hepatic neoplasm: metastasis
4. Hepatic trauma: blunt abdominal trauma, iatrogenic trauma (biopsy, percutaneous abscess drainage, transhepatic biliary drainage, ethanol injection)
5. Rupture of hepatic artery pseudoaneurysm into portal vein

Small arterioportal shunts 2° to cirrhosis either remain stable or resolve spontaneously, whereas those 2° to HCC generally demonstrate growth at follow-up.

Route of fistulous communication:

1. Macroscopic fistula
2. Transsinusoidal = between microscopic interlobular arteriole + portal venule
3. Transvasal = via tumor thrombus
4. Transtumoral = via draining vein from a hypervascular tumor
5. Transplexal / peribiliary = via capillary network surrounding bile ducts

DDx: HCC (hypoattenuated during portal venous and parenchymal phase; growth after repeat imaging in 6 months)

HEPATIC ARTERY

Hepatic Artery Enlargement

A high RI is not specific for liver disease; therefore, it is less meaningful as an isolated finding than is a low RI.

1. Cirrhosis → compensatory response to decreased portal venous flow
2. Intrahepatic arteriovenous shunting
   (a) vascular neoplasm
   (b) hepatic artery-portal vein fistula
   Cause: biopsy, trauma
   √ turbulent high-velocity low-resistance flow
   √ soft-tissue bruit (= random assignment of color in perivascular soft tissue due to tissue vibration)
   √ arterialized frequently retrograde flow in portal vein
3. Hereditary hemorrhagic telangiectasia
   √ large tortuous feeding arteries with high velocity + aliased flow
   √ multiple dilated vessels (representing AVMs)
   √ large draining veins
   √ areas of fatty change + fibrosis
4. Chronic active hepatitis

Elevated Hepatic Artery Resistance (RI > 0.7)

A. PHYSIOLOGIC
   1. Postprandial state

2. Advanced age of patient

B. PATHOLOGIC
   1. Chronic hepatocellular disease
   2. Hepatic venous congestion
      (a) acute: generalized peripheral vasoconstriction
      (b) chronic: cardiac cirrhosis
   3. Transplant rejection

An RI that is too high may be the result of a postprandial state, advanced patient age, or diffuse distal microvascular disease with a wide variety of causes including chronic liver disease due to cirrhosis or chronic hepatitis.

Decreased Hepatic Artery Resistance (RI < 0.55)

A. PROXIMAL ARTERIAL NARROWING
   1. Transplant stenosis
   2. Atherosclerotic disease
   3. Arcuate ligament syndrome

B. DISTAL VASCULAR SHUNT
   1. Cirrhosis with portal hypertension
   2. Posttraumatic / iatrogenic
   3. Hereditary hemorrhagic telangiectasia

An RI that is too low may be the result of
- proximal stenosis or
- distal vascular shunting (arteriovenous / arterioportal fistulas) as seen in severe cirrhosis;
- trauma (including iatrogenic injury); or
- Osler-Weber-Rendu syndrome.

Hepatic Artery Aneurysm

= 2nd most common type of splanchnic aneurysm = up to 20% of visceral aneurysms

Cause:

1. Atherosclerosis
2. Fibromuscular dysplasia
3. Collagen vascular disease
4. Trauma: penetrating, blunt, iatrogenic (liver transplant)
5. Mycotic aneurysm
6. Tumor-related aneurysm
7. Vasculitis (multiple aneurysms): polyarteritis nodosa

- abdominal pain (55%), gastrointestinal hemorrhage (46%)

Site: common hepatic artery (in up to 63%)
Cx: aneurysm rupture → hemobilia / hemoperitoneum (20–35% mortality rate)
Rx: endovascular stenting (89% success rate)

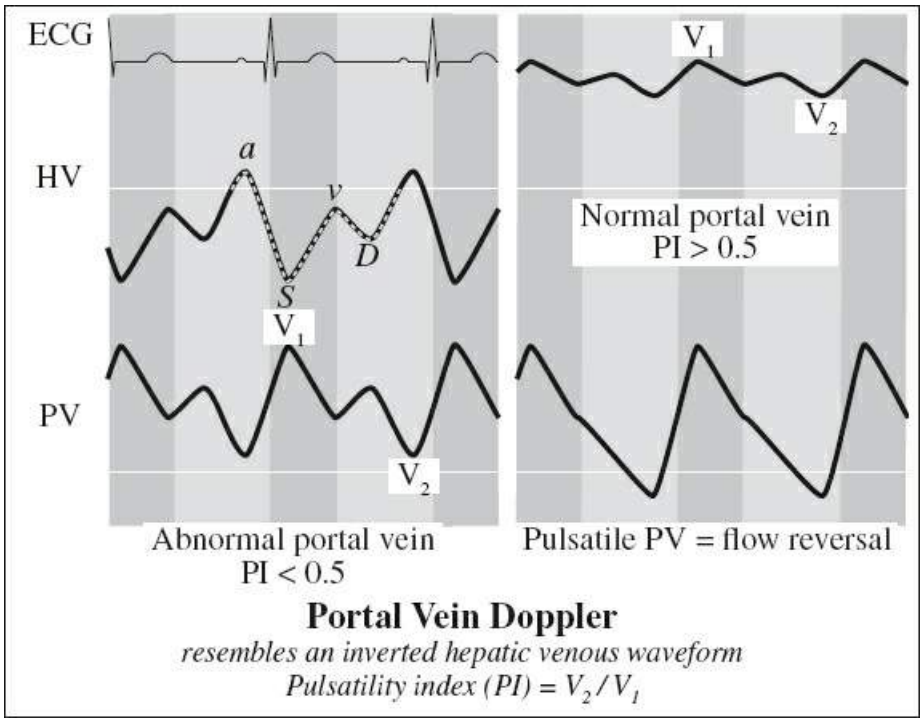
HEPATIC VEINS

Dampening of Hepatic Vein Doppler Waveform

= dampened oscillations of hepatic veins resembling portal vein flow ← "shielding" of hepatic veins from activity of right atrium = decreased phasicity
= "portalization" of hepatic vein flow pattern
√ drop of *a* wave of hepatic venous waveform below baseline

A. INCREASED LIVER TISSUE STIFFNESS
   1. Liver cirrhosis
   2. Various parenchymal abnormalities of liver: fatty liver, diffuse metastatic liver disease

B. INTRINSIC / EXTRINSIC VENOUS OBSTRUCTION
   1. Budd-Chiari syndrome intrahepatic / suprahepatic obstruction
   2. Hepatic venoocclusive disease
   3. Inferior vena cava obstruction
   4. Extrinsic compression of hepatic veins
   5. Right-sided CHF



Irregular Flow Pattern in Hepatic Veins

1. Arrhythmia
2. Turbulent blood flow
3. Technical / patient factors: sedated patient, mechanical ventilation, SOB

Pulsatile Hepatic Doppler

= *D* wave greater than S wave

1. Tricuspid regurgitation
2. Right heart failure

PORTAL VEIN

Abnormal Portal Venous Flow

Pulsatile Portal Vein

= waveform pulsatility with > 2/3 change from peak velocity to minimum velocity

Pathophysiology: transmission of abnormal pressure to sinusoids via hepatic veins / arteries

A. INCREASED VENOUS PRESSURE IN SINUSOIDS (sinusoids connect portal vein with hepatic arteries and hepatic veins)

√ dilated hepatic veins

1. Tricuspid regurgitation
   √ decreased *S* wave in hepatic venous Doppler
2. Right-sided CHF without tricuspid regurgitation
   √ tall *a* and *v* waves in hepatic venous Doppler

B. ARTERIOVENOUS SHUNT

1. Arteriovenous shunt in severe cirrhosis
   √ compressed hepatic veins
2. Hepatic artery-portal vein fistula
3. Portal-to-hepatic vein fistula
4. Hereditary hemorrhagic telangiectasia (rare) → arteriovenous fistulas

Slow Portal Venous Flow

Pathophysiology: back pressure limits forward velocity

Cause:

Portal hypertension: peak velocity < 16 cm/sec

(a) prehepatic: portal vein thrombosis
(b) intrahepatic: cirrhosis from any cause
(c) posthepatic: right-sided heart failure, tricuspid regurgitation, Budd-Chiari syndrome

Hepatofugal (Retrograde) Portal Venous Flow

= waveform below the baseline

Pathophysiology: back pressure exceeds forward pressure with flow subsequently reversing direction

Cause: severe portal hypertension from any cause

Absent / Aphasic Portal Venous Flow

A. STAGNANT PORTAL VENOUS FLOW

1. Severe portal hypertension with neither hepatopetal nor hepatofugal flow → at risk for portal vein thrombosis

B. OCCLUSION OF PORTAL VEIN

√ cavernous transformation = development of collateral vessels in / around occluded portal vein

1. Bland portal vein thrombus
2. Malignant invasion of portal vein (= tumor thrombus)
   √ "thread & streak" sign = color signal with arterial (pulsatile) waveform within thrombus

Periportal Hypoattenuating Halo

= accumulation of lymph around the portal tract

1. Edema: CHF, acute hepatitis, hepatic venoocclusive disease
2. Infiltration: lymphoma, extramedullary hematopoiesis
3. Lymphatic dilatation ← obstruction in porta hepatis by enlarged nodes / mass / in liver transplant
4. Hemorrhage (asymmetric involvement)
5. Fat accumulation

Periportal Lymphedema

= ill-defined hypodensity at porta hepatis / hypodensity parallel to portal vein

1. Acute hepatitis
2. Cirrhosis
3. Hepatic venoocclusive disease
4. Liver / bone marrow transplant
5. Overhydration
6. Blunt abdominal trauma ± liver injuries
7. Chronic congestive heart failure
8. Cardiac tamponade
9. Malignancy: hepatic / retroperitoneal

Portosystemic Shunt

A. EXTRAHEPATIC PORTOSYSTEMIC SHUNT
   (a) congenital (rare)
   (b) acquired (most common)
      Cause: portal venous hypertension
B. INTRAHEPATIC PORTOSYSTEMIC SHUNT (rare)
C. ARTERIOPORTAL SHUNT
D. PERSISTENT DUCTUS VENOSUS

Portal Venous Stenosis

Cause:

1. Tumor encasement: locally recurrent periampullary cancers = pancreatic carcinoma, hepatocellular carcinoma, cholangiocarcinoma, metastasis
2. Inflammation: acute pancreatitis
3. Surgical complication: liver transplantation (1%), partial hepatectomy, pancreaticoduodenectomy
4. Radiation therapy

√ focal segment of vessel narrowing ± poststenotic dilatation
√ inhomogeneous peripheral subcapsular increase in arterial inflow during hepatic arterial phase
√ secondary portal hypertension → increased number and size of collaterals

US:

√ focal color aliasing
√ accelerated flow across stenosis = 4-fold velocity gradient

√ spectral broadening of waveform (= poststenotic turbulence)

Cx: portal venous hypertension with massive intractable ascites + recurrent variceal bleeding

Rx: balloon angioplasty, stent placement

Portal Venous Gas

◊ Should be considered a life-threatening event and sign of bowel infarction + gangrene until proved otherwise!

Etiology:

A. INTESTINAL NECROSIS (in 74% of adults)
   1. Bowel infarction ← arterial and venous occlusions (vascular accidents, SMA syndrome)
   2. Ulcerative colitis
   3. Necrotizing enterocolitis associated with mesenteric arterial thrombosis
   4. Perforated gastric ulcer

B. GI OBSTRUCTION
   1. Small bowel obstruction: eg, duodenal atresia
   2. Imperforate anus
   3. Esophageal atresia

C. MISCELLANEOUS
   1. Hemorrhagic pancreatitis
   2. Sigmoid diverticulitis
   3. Intraabdominal abscess
   4. Pneumonia
   5. Iatrogenic injection of air during endoscopy / BE
   6. Dead fetus
   7. Diabetes
   8. Diarrhea

mnemonic: BE NICE

BE (air embolism during double contrast barium enema)
Necrotizing enterocolitis
Infarction (mesenteric)
Catheterization of umbilical vein
Erythroblastosis fetalis

Pathogenesis:

1. Intestinal wall alteration permitting passage of intraluminal air into intestinal venules:
   (a) ulceration of gastric, duodenal, bowel wall
   (b) sloughing of epithelial lining
   (c) enhanced mucosal permeability
   eg, intestinal ischemia with bowel necrosis (most common); perforated gastric carcinoma / ulcer; inflammatory bowel disease (Crohn disease, ulcerative colitis); ingestion of a caustic substance
   Prognosis: 75–90% mortality rate within 1 week of Dx
2. Bowel distension with elevated intraluminal pressure causes minimal mucosal

disruption + permits passage of intraluminal air into veins:
(a) iatrogenic dilatation of hollow viscus: gastrostomy, sclerotherapy, ERCP, colonoscopy, barium enema)
(b) spontaneous paralytic ileus, mechanical obstruction, acute gastric dilatation
(c) blunt trauma (< 1%) with acute pressure changes
(d) barotrauma

Prognosis: surgery often not indicated

3. Intraabdominal sepsis
   (a) ? gas from septicemia in branches of mesenteric veins / portal vein (= pylephlebitis)
   (b) ? increased intraluminal fermentation of carbohydrates ← bacterial overgrowth
   (c) ? mesocolic abscess → inframesocolic perforation dissecting between peritoneal leaflets, eg, diverticulitis, intra- or retroperitoneal abscess / gangrene, TB, inflammatory bowel disease, necrotizing pancreatitis
4. Idiopathic (15%)
   eg, organ transplantation (liver [18%], kidney, bone marrow), pulmonary disease (chronic obstructive pulmonary disease, bronchopneumonia, asthma), drugs (steroids, cytostatics), seizure

Composition of colonic gas:
methane, carbon dioxide, oxygen, nitrogen, hydrogen

Location: predominantly in left lobe = nondependent position when patient supine

Plain film:
◊ Substantial amount necessary for detection
√ branching linear gas densities:
  √ in periphery of liver extending to within 2 cm of liver capsule
  √ predominantly within more anteriorly located left lobe of liver
√ pneumatosis of intestinal wall

CT:
◊ Small amount of gas detectable
√ tubular branching areas of decreased attenuation (similar to air) in periphery 2 cm deep to liver capsule
√ gas in superior / inferior mesenteric veins
√ gas in small mesenteric veins at mesenteric border of bowel

MR:
√ susceptibility artifacts in portal vein

US:
◊ Small amount of gas detectable
√ intensely hyperechoic foci (= reverberation artifacts)within lumen of portal vein + intrahepatic portal radicles

Doppler:
√ sharp high-amplitude bidirectional spikes (overloading of Doppler receiver from strong reflection of gas bubble in bloodstream) superimposed on normal portal vein spectrum

Mortality rate: 29–43% for mesenteric ischemia with portal vein gas

Rx: (1) Surgery for mesenteric ischemia, diverticulitis, bowel obstruction

(2) Conservative management in trauma, colonoscopy, idiopathic causes

DDx: pneumobilia (located centrally within bile ducts close to liver hilum + within left lobe of liver)

Portal Vein Calcification

Location: portal vein > splenic vein > superior mesenteric vein > inferior mesenteric vein

Associated with: portal venous hypertension, congenital abnormalities, umbilical vein catheterization

- asymptomatic

Cx: biliary obstruction (if densely calcified)

GALLBLADDER

Nonvisualization of Gallbladder on US

1. Status post cholecystectomy
2. Obscured by costal margin
3. Anomalous position (intrahepatic, subphrenic)
4. Gallbladder carcinoma replacing gallbladder
5. Perforation of gallbladder
6. Congenital absence
7. Contracted gallbladder
   (a) nonfasting status without stones
   (b) in fasting status with stones
   √ wall-echo-shadow (WES triad) interfaces

Acoustic Shadowing in Gallbladder Fossa

1. WES (wall-echo-shadow) triad
2. Gas in duodenum / colon obscuring gallbladder
3. Porcelain gallbladder
4. Emphysematous cholecystitis
5. Cholecystoenteric fistula
6. Status post ERCP with retrograde air injection

Hyperattenuating Bile

1. Hemorrhagic cholecystitis
2. Hemobilia
3. Prior contrast administration
   (a) vicarious excretion of IV iodinated contrast agent
   (b) retained contrast agent from cholangiography
   (c) cholecystopaque
4. Milk of calcium bile
5. Biliary sludge, purulent bile
6. Aneurysm / pseudoaneurysm with active extravasation into biliary system
7. Malignancy

Displaced Gallbladder

A. NORMAL IMPRESSION
by duodenum / colon (positional change)

B. HEPATIC MASS
hepatoma, hemangioma, regenerating nodule, metastases, intrahepatic cyst, polycystic liver, hydatid disease, hepar lobatum (tertiary syphilis), granuloma, abscess

C. EXTRAHEPATIC MASS
1. Retroperitoneal tumor (renal, adrenal)
2. Polycystic kidney
3. Lymphoma
4. Lymph node metastasis to porta hepatis
5. Pancreatic pseudocyst

Alteration in Gallbladder Size

Enlarged Gallbladder

= CHOLECYSTOMEGALY = HYDROPS OF GALLBLADDER

Size:

(a) infants < 1 year: > 3 cm in length
(b) children: > 7 cm in length
(c) adults: > 10 x 4 cm (L x W)

A. OBSTRUCTION
1. Cystic duct obstruction (40%)
   (a) hydrops: chronic cystic duct obstruction + distension with clear sterile mucus (white bile)
   (b) empyema: acute / chronic obstruction with superinfection of bile
2. Cholelithiasis causing obstruction (37%)
3. Cholecystitis with cholelithiasis (11%)
4. **Courvoisier phenomenon** (10%)
   ← neoplastic process in pancreas / duodenal papilla / ampulla of Vater / common bile duct
5. Pancreatitis
6. Infection: leptospirosis, ascariasis, typhoid fever, scarlet fever, familial Mediterranean fever

B. UNOBSTRUCTED (mostly neuropathic)
1. S/P vagotomy
2. Diabetes mellitus
3. Alcoholism
4. Appendicitis (in children)
5. Narcotic analgesia
6. WDHA syndrome
7. Hyperalimentation
8. Acromegaly
9. Kawasaki syndrome
10. Anticholinergics

11. Bedridden patient with prolonged illness
12. AIDS (in 18%)
13. Dehydration
14. Prolonged fasting
15. Total parenteral nutrition
16. Sepsis

C. NORMAL (2%)

Small Gallbladder

1. Chronic cholecystitis
2. Cystic fibrosis: in 25% of patients
3. Congenital hypoplasia / multiseptated gallbladder
4. Postprandial
5. Intrahepatic cholestasis: viral, drug-related

Gallbladder Wall Thickening

Diffuse Gallbladder Wall Thickening

= anterior wall of gallbladder > 3 mm

A. INTRINSIC
   (a) infection
      1. Acute cholecystitis
      2. Chronic cholecystitis (10–25%)
      3. Xanthogranulomatous cholecystitis
      4. Gallbladder perforation
      5. Sepsis
      6. Brucellosis
   (b) inflammation
      1. AIDS cholangiopathy (average of 9 mm in up to 55%)
      2. Sclerosing cholangitis
      3. Eosinophilic cholecystitis
   (c) tumor infiltration
      1. Gallbladder carcinoma (in 41% diffuse)
      2. Leukemic infiltration (AML)
      3. Multiple myeloma
   (d) others
      1. Hyperplastic cholecystosis (in 91% diffuse)
      2. Gallbladder varices

B. EXTRINSIC
   (a) liver disease
      1. Hepatitis (in 80%)
      2. Cirrhosis
      3. Hepatic venous obstruction
      4. Fitz-Hugh–Curtis syndrome
   (b) fluid overload

1. Hypoalbuminemia
2. Renal failure
3. Right heart failure
4. Systemic venous hypertension
5. Ascites
6. Lymphatic obstruction (by portal nodes)

(c) others

2. Graft-versus-host disease
3. Pancreatitis

(d) drugs

1. Chemoinfusion of hepatic artery (ischemia)
2. Treatment with interleukin

C. PHYSIOLOGIC

= contracted gallbladder after eating

Focal Gallbladder Wall Thickening

A. METABOLIC
1. Metachromatic sulfatides
2. Hyperplastic cholecystoses

B. BENIGN TUMOR
1. Adenoma: glandular elements (0.2%)
2. Papilloma: fingerlike projections (0.2%)
3. Villous hyperplasia
4. Fibroadenoma
5. Cystadenoma: ? premalignant
6. Neurinoma, hemangioma
7. Carcinoid tumor

C. MALIGNANT TUMOR
1. Carcinoma of gallbladder: adenocarcinoma / squamous cell carcinoma (in 59% focal)
2. Leiomyosarcoma
3. Metastases: from malignant melanoma (15%), lung, kidney, esophagus, breast, carcinoid, Kaposi sarcoma, lymphoma, leukemia

D. INFLAMMATION / INFECTION
1. Inflammatory polyp: in chronic cholecystitis
2. Parasitic granuloma: Ascaris lumbricoides, Paragonimus westermani, Clonorchis, filariasis, Schistosoma, Fasciola
3. Intramural epithelial cyst / mucinous retention cyst
4. Xanthogranulomatous cholecystitis (in 9% focal)

E. WALL-ADHERENT GALLSTONE = embedded stone

F. HETEROTOPIC MUCOSA
1. Ectopic pancreatic tissue
2. Ectopic gastric glands
3. Ectopic intestinal glands
4. Ectopic hepatic tissue

5. Ectopic prostatic tissue

Filling Defects of Gallbladder

Fixed Filling Defects of Gallbladder

mnemonic: PANTS
Polyp
Adenomyomatosis
Neurinoma
Tumor, primary / secondary
Stone, wall-adherent

GALLBLADDER POLYP

= sessile projection of GB wall into GB lumen

Prevalence: 3-7% by ultrasound, 2–12% of cholecystectomy specimens

A. PSEUDOTUMOR
   1. Cholesterol polyp (63–74%): on average 8 polyps
   2. Adenomyoma (7%)
   3. Inflammatory polyp (4%)
   4. Others: heterotopic gastric glands

B. TUMOROUS POLYP (85%)
   (a) benign (85%)
      1. Adenoma (84%)
      2. Fibroma, leiomyoma, lipoma, neurofibroma, neuroendocrine tumor (1%)
   (b) malignant (15%)
      1. Adenocarcinoma (4%)
      2. Squamous cell carcinoma, carcinosarcoma, small cell carcinoma, lymphoma
      3. Metastasis: melanoma (60%), RCC

◊ 94% of benign lesions are < 10 mm; 88% of malignant lesions are > 10 mm

◊ Any polyp > 10 mm should be operated on
   › in a symptomatic patient
   › in a patient > 50 years of age
   › with coexisting gallstones
   or followed every 3–6 months for 1 year

DDx: (1) Adherent gallstone
(2) Adherent tumefactive sludge

Mobile Intraluminal Mass in Gallbladder

1. Tumefactive sludge
2. Blood clot
3. Nonshadowing stone

Comet-tail Artifact in Liver and Gallbladder

A. LIVER
   1. Foreign metallic body: eg, surgical clip
   2. Intrahepatic calcification

3. Pneumobilia
4. Multiple bile duct hamartoma = von Meyenburg complex

B. GALLBLADDER
1. Rokitansky-Aschoff sinus
2. Intramural stone
3. Cholesterolosis of gallbladder

Echogenic Fat in Hepatoduodenal Ligament

= sign of pericholecystic inflammation

1. Cholecystitis
2. Perforated duodenal ulcer
3. Pancreatitis
4. Diverticulitis

False-positive DISIDA Scan

mnemonic: F2C2 PAL

Food (meal within last 4 hours = GB empty)
Fasting / total parenteral nutrition (GB full)
Cystic duct cholangiocarcinoma
Chronic cholecystitis
Pancreatitis, acute
Alcoholism (= alcohol-toxic hepatitis)
Liver dysfunction (hepatitis)

False-negative DISIDA Scan

mnemonic: ADA

Acalculous cholecystitis
Duodenal diverticulum simulating GB
Accessory cystic duct

Rim Sign

= curvilinear pericholecystic rim of increased hepatic tracer activity adjacent to a photopenic gallbladder fossa

Cause: local hyperemia with increased perfusion + injury of hepatocytes with impaired excretion of radiotracer

1. Acute cholecystitis (34–61% sensitive)
2. Complicated acute cholecystitis
   √ nonvisualization of GB @ 1 hour (94–100% PPV, 95–100% specific)
3. Chronic cholecystitis

BILE DUCTS

Hemobilia

1. Iatrogenic trauma: liver biopsy, transhepatic cholangiography / percutaneous transhepatic biliary drainage (4–18%) / portography, sphincterotomy, endoscopic biliary stent

placement, radiofrequency ablation
2. Blunt / penetrating trauma
3. Rupture of hepatic artery aneurysm / pseudoaneurysm
4. Anticoagulation

Gas in Biliary Tree = Pneumobilia

mnemonic: I GET UP

Incompetent sphincter of Oddi (after sphincterotomy / passage of a gallstone)
Gallstone ileus
Emphysematous cholecystitis (actually in gallbladder)
Trauma
Ulcer (duodenal ulcer perforating into CBD)
Postoperative (eg, cholecystoenterostomy)

√ gas outlines choledochus ± gallbladder
√ peripheral branches of bile ducts not filled

Pneumobilia is a common finding with patent biliary stents. It may not be present when the stent is occluded ← no communication with the duodenum.

Obstructive Jaundice in Adult

Etiology:

A. BENIGN DISEASE (76%)
   1. Traumatic / postoperative stricture (44%): cholecystectomy (incidence of 0.2–0.7%), liver transplantation
   2. Calculi (21%)
   3. Chronic pancreatitis (8%)
   4. Sclerosing cholangitis (1%): primary sclerosing cholangitis, IgG4-related sclerosing disease
   5. Recurrent pyogenic cholangitis
   6. Parasitic disease: eg, ascariasis
   7. Liver cysts
   8. Aortic aneurysm
   9. Papillary stenosis

B. MALIGNANCY (24%)
   1. Pancreatic carcinoma (18%)
   2. Ampullary / duodenal carcinoma (8%)
   3. Cholangiocarcinoma (3%)
   4. Metastatic disease (2%): stomach, pancreas, lung, breast, colon, lymphoma

Level and cause of obstruction:

A. INTRAPANCREATIC
   1. Choledocholithiasis
      ◊ Most common cause of biliary obstruction (in 15% of patients with cholelithiasis)!
   2. Chronic pancreatitis
   3. Pancreatic carcinoma

B. SUPRAPANCREATIC (5%)

= between pancreas + porta hepatis
1. Cholangiocarcinoma
2. Metastatic adenopathy

C. PORTA HEPATIS (5%)
1. Klatskin tumor
2. Spread from adjacent tumor (GB, liver)
3. Surgical stricture

D. INTRAHEPATIC
1. Cystadenoma, cystadenocarcinoma
2. Mirizzi syndrome
3. Caroli disease
4. Cholangitis: recurrent pyogenic cholangitis, sclerosing cholangitis, AIDS cholangitis

Incidence of infected bile in bile duct obstruction:

(a) in 64% with incomplete / partial obstruction
(b) in 10 with complete obstruction

◊ Infection twice as high with biliary calculi than with malignant obstruction!

Organism: E. coli (21%), Klebsiella (21%), enterococci (18%), Proteus (15%)

Test sensitivity for common bile duct obstruction:

1. Intravenous cholangiography
depends on level of bilirubin: < 1 (2) mg/dL in 92%; < 2 mg/dL in 82%; < 3 mg/dL (> 4) in 40% (< 10%)
False-negative rate: 45%
Cx: adverse reactions in 4–10%
2. US
88–90% sensitivity for dilatation of CBD
◊ In 27–95% US gives correct level of obstruction
◊ In 23–81% US gives correct cause of obstruction
√ CBD > 4–6 mm / 10% of patient's age in years in mm
√ increase in CBD size after fatty meal
√ "Swiss cheese" sign = abundance of fluid-filled structures on liver sections ← dilated intrahepatic bile ducts
√ intrahepatic bile duct > 2 mm / > 40% of adjacent portal vein branch
√ intrahepatic "double channel" / "shotgun" sign = two parallel tubular structures composed of portal vein + dilated intrahepatic bile duct
False-negative (= obstruction without dilatation):
no dilatation in acute early obstruction (in 70%), sclerosing cholangitis, intermittent obstruction from choledocholithiasis
False-positive (= dilatation without obstruction):
post decompression of prior obstruction, dilated hepatic artery in cirrhosis / portal hypertension / hepatic neoplasm, in patients after cholecystectomy
3. CT
100% visualization in tumorous obstruction
60% visualization in nontumorous obstruction
4. CEMR cholangiopancreatography

= 1st imaging method of choice → most comprehensive evaluation of biliary stricture

Caveat: pseudostricture secondary to

(a) MRI technique / postprocessing
(b) incomplete volume acquisition
(c) blooming artifact ← cholecystectomy clips
(d) pulsation artifact from hepatic and gastroduodenal arteries

5. MRCP provides information about the biliary tree that cannot be obtained with more invasive methods:
   (a) delineates biliary-enteric anastomosis
   (b) detects complications: anastomotic biliary stricture, intraductal stones, biliary dilatation

6. NUC
   √ delayed / nonvisualization of biliary system (93% specific)
   √ vicarious excretion of tracer through kidneys

DDx: Hepatocellular dysfunction (delayed clearance of cardiac blood pool)

Hyperbilirubinemia in Infants

= UNCONJUGATED HYPERBILIRUBINEMIA

A. PHYSIOLOGIC

Frequency: in 60% of full-term infants, in 80% of preterm infants

Course: increase by day 2–3, peak by day 5–7 (up to 12 mg/dL in full-term babies, up to 14 mg/dL in premature infants)

◊ Breast-fed babies may have an elevated bilirubin level until the end of 2nd week of life!

B. NONPHYSIOLOGIC

- onset of jaundice within first 24 hours
- persistent / new-onset jaundice in infants 2 weeks of age
- rise of serum bilirubin > 5 mg/dL per 24 hours
- direct bilirubin level > 1 mg/dL

Neonatal Obstructive Jaundice

= severe persistent jaundice in a child beyond 3–4 weeks of age

Cause:

A. INFECTION
   (a) bacterial: E. coli, Listeria monocytogenes
   (b) viral: TORCH, coxsackie virus, ECHO virus, adenovirus

B. METABOLIC
   (a) inherited: alpha-1 antitrypsin deficiency, cystic fibrosis, galactosemia, hereditary tyrosinemia
   (b) acquired: inspissated bile syndrome = "bile plug" syndrome (= cholestasis ← erythroblastosis); cholestasis ← total parenteral nutrition; choledocholithiasis

C. BILIARY TRACT ABNORMALITIES
   (a) extrahepatic: biliary obstruction / hypoplasia / atresia, choledochal cyst, spontaneous perforation of bile duct
   (b) intrahepatic: ductular hypoplasia / atresia

D. IDIOPATHIC NEONATAL HEPATITIS

◊ The 3 most common causes of jaundice in neonates are hepatitis, biliary atresia, and

choledochal cyst!

mnemonic: CAN
Choledochal cyst
Atresia
Neonatal hepatitis

NUC–imaging regimen:
(1) Premedication with phenobarbital (5 mg/kg/d) over 5 days to induce hepatic microsomal enzymes→ enhancing uptake and excretion of certain compounds → increase of bile flow
(2) IDA scintigraphy (50 μCi/kg; minimum of 1 mCi)
(3) Imaging at 5-min intervals for 1 hr + at 2, 4, 6, 8, 24 hours

Jaundice in Older Children

A. DISEASE OF HEPATOCYTES
  (a) infection / inflammaton
    1. Acute hepatitis: infection, toxic agents, drugs
    2. Chronic hepatitis
  (b) metabolic
    1. Wilson disease
    2. Cystic fibrosis
    3. Glycogen storage disease
    4. Tyrosinemia
    5. Alpha-1 antitrypsin deficiency
B. OBSTRUCTION
  (a) malignant neoplasm
    1. Hepatoblastoma
    2. Hepatocellular carcinoma
    3. Sarcomas: angiosarcoma, lymphosarcoma, rhabdomyosarcoma of bile ducts, undifferentiated embryonal sarcoma
    4. Metastatic disease: neuroblastoma, Wilms tumor, leukemia/lymphoma
  (b) benign neoplasm
    1. Infantile hemangioendothelioma
    2. Mesenchymal hamartoma
  (c) benign stricture: congenital choledochal cyst
  (d) cholelithiasis / choledocholithiasis (uncommon)

Large Nonobstructed CBD

1. Passage of stone (return to normal after days to weeks)
2. Common bile duct surgery (return to normal in 30–50 days)
3. Postcholecystectomy dilatation (in up to 16%)
4. Intestinal hypomotility
5. Normal variant (aging)

Fatty-meal sonography (to differentiate from obstruction with 74% sensitivity, 100% specificity)
Method: peroral Lipomul® (1.5 mL/kg) followed by 100 mL of water [cholecystokinin

causes contraction of gallbladder, relaxation of sphincter of Oddi, increase in bile secretion], CBD measured before and 45 / 60 min after stimulation

√ little change / decrease in size = normal response
√ increase in size > 2 mm = partial obstruction

Filling Defect in Bile Ducts

A. ARTIFACT
   1. Pseudocalculus
      (a) contracted sphincter of Boyden + Oddi with smooth arcuate contour
      (b) bridge of tissue between cystic duct + CHD
      (c) underfilling of cystic duct during ERCP
      (d) admixture defect at cystic duct junction
   2. Air bubble: confirmed by positional changes
   3. Blood clot: spheroid configuration, spontaneous resolution with time
B. BILIARY CALCULI
C. MIRIZZI SYNDROME
D. NEOPLASM
   (a) malignant
      1. Cholangiocarcinoma: irregular stricture, intraluminal polypoid mass
      2. Metastatic tumor: colon, gallbladder, lung, breast, testis, prostate, pancreas, melanoma, lymphoma
      3. Others: ampullary carcinoma, hepatoma, hamartoma, carcinoid, embryonal rhabdomyosarcoma of biliary tree
   (b) benign
      1. Papilloma: most common benign neoplasm
         Histo: vascular connective tissue covered by single layer of columnar epithelium
      2. Adenoma
         Histo: epithelial glandular tissue surrounded by fibrous tissue
      3. Fibroma, lipoma, neuroma
      4. Granular cell myoblastoma (= Schwann-cell–derived biliary tumor) in young black woman
E. PARASITES
   1. Ascaris lumbricoides
   2. Clonorchis sinensis
   3. Fasciola hepatica
   3. Schistosoma japonicum
   4. Hydatid cyst

Echogenic Material in Bile Ducts

1. Calculi
2. Gas
3. Blood
4. Tumor
5. Parasites

Bile Duct Narrowing / Stricture

= fixed focal narrowing of bile duct

A stenosis caused by a malignant lesion usually manifests as an irregular stricture with shouldered margins, whereas a benign stenosis tends to have smooth borders with gradually tapered margins.

A. BENIGN STRICTURE (44%)

Cause: injury → inflammatory response → fibrosis

√ often short-segment involvement (not diagnostic!)

√ often smooth concentric narrowing (not diagnostic!)

(a) trauma

1. Postoperative stricture (95–99%):
   - › open cholecystectomy (0.2–0.7%)
   - › laparoscopic cholecystectomy (1.2%)
   - › cadaveric liver transplant (5–15%)
   - › living donor liver transplant (28–32%)
2. Blunt / penetrating trauma
3. Hepatic artery embolization

(b) inflammation

1. Sclerosing cholangitis:
   - › primary sclerosing cholangitis
   - › IgG4-related sclerosing disease
2. Eosinophilic portal cholangiopathy
3. Chronic pancreatitis
   - ◊ 10% of all benign biliary strictures
4. Acute pancreatitis (less common)
5. Pancreatic pseudocyst
6. Perforated duodenal ulcer
7. Erosion by biliary calculus
8. Mirizzi syndrome
9. Radiation therapy

(c) infection

1. Acute bacterial cholangitis
2. Recurrent pyogenic cholangitis
3. Chemotherapy-induced cholangitis
4. AIDS-related cholangitis
5. Abscess

(d) congenital

1. Choledochal cyst

B. MALIGNANT STRICTURE

1. Pancreatic adenocarcinoma
2. Ampullary cancer
3. Cholangiocarcinoma
4. Compression by enlarged lymph node
5. Metastasis

A narrowed segment with the following MRI features is more likely to be malignant:

√ hyperenhancement relative to liver during portal venous phase
√ length of > 12 mm
√ wall thickness > 3 mm
√ indistinct outer margin
√ luminal irregularity and asymmetry

Cause of Biliary Stricture by Location

@ distal CBD

Malignant vs. Benign CBD Stricture		
Criteria	*Malignant*	*Benign*
Borders	irregular	smooth
Luminal margin	shouldered	tapered
Stricture length (mm)	18 ± 7	9 ± 7
Duct diameter proximally (mm)	22 ± 5	18 ± 5
Duct wall thickness >1.5 mm	80%	15%
Enhancement, arterial phase	85%	10%
Enhancement, portal phase	95%	15%
Progression of stricture	rapid	gradual
Bilirubin > 8.4 mg/dL	+	-
CA 19-9 > 100 U/L	+	-

1. IgG4-related sclerosing cholangitis

@ junction of cystic duct + CHD
1. Cholecystectomy
2. Mirizzi syndrome

@ confluence of left + right hepatic ducts
1. Cholecystectomy
2. IgG4-related sclerosing cholangitis

@ intrapancreatic portion of CBD
1. Chronic pancreatitis

@ intra- and extrahepatic bile ducts
1. Primary sclerosing cholangitis
2. IgG4-related sclerosing cholangitis
3. Recurrent pyogenic cholangitis
4. AIDS cholangiopathy

Multifocal Intrahepatic Bile Duct Strictures

1. Primary sclerosing cholangitis
2. Ascending cholangitis ← stricture / stone / bile duct anomaly
3. Oriental cholangiohepatitis
4. AIDS-related cholangitis
5. Ischemia
   (a) floxuridine treatment
   (b) hepatic arterial thrombosis (in liver transplant)

6. NEOPLASM
   (a) cholangiocarcinoma
   (b) metastases: GI tract, lymphoma, breast, lung
7. Previous bile surgery
8. Congenital biliary anomalies

Congenital Biliary Cysts

(Todani classification)

I. Choledochal cyst (77–87%)
   Ia diffuse cystic dilatation of entire extrahepatic duct
   Ib focal segmental dilatation of extrahepatic duct
   Ic fusiform cystic dilatation of only CBD
   Cause: anomalous pancreaticobiliary union
II. Diverticulum of extrahepatic ducts (1.2–3%)
   originating from extrahepatic bile duct (CBD / CHD)
   √ neck of diverticulum open / closed
III. Choledochocele (1.4–6%)
IV. Multiple segmental bile duct cysts
   IVa multiple intra- and extrahepatic biliary cysts + saccular dilatation of CBD (19%)
   IVb multiple extrahepatic biliary cysts + normal intrahepatic bile ducts (rare)
V. Caroli disease = intrahepatic biliary cysts

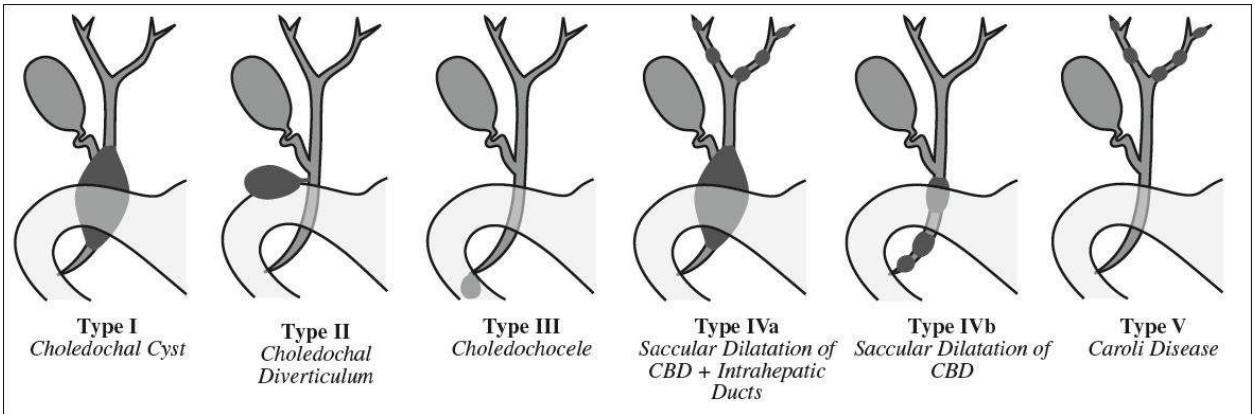
Papillary Stenosis

= blockage of bile / pancreatic fluid flow at sphincter of Oddi WITHOUT an ampullary mass / inflammatory lesion

Etiology:

A. PRIMARY PAPILLARY STENOSIS (10%)
   1. Congenital malformation of papilla
   2. Sequelae of acute / chronic inflammation
   3. Adenomyosis

B. SECONDARY PAPILLARY STENOSIS (90%)
   1. Sphincter of Oddi dysfunction
      Prevalence: 1.5% (most common cause)
      Associated with: pancreas divisum, history of pancreatitis
   2. Mechanical trauma of stone passage → papillitis
      › choledocholithiasis in 64%
      › cholecystolithiasis in 26%
   3. Reflex spasm = papillary dyskinesia
   4. Scar from previous surgical manipulation
   5. Periampullary neoplasm



Classification of Congenital Biliary Cysts

√ prestenotic dilatation of CBD
√ increase in pancreatic duct diameter (83%)
√ long smooth narrowing / beak ← fibrotic stenosis
√ prolonged bile-to-bowel transit time > 45 minutes on Tc-IDA scintigraphy
√ papillary size < 12.3 mm = the only independently reliable variable for differentiating benign from malignant causes

N.B.: for suspected ampullary stenosis employ secretin stimulation test with imaging 4–10 min post injection

Bulging Papilla

1. Papillitis: ← acute pancreatitis, acute cholangitis, passage of biliary stone, periampullary diverticulum, parasite, infection
2. Intraductal papillary mucinous neoplasm
3. Ampullary neoplasm
4. Periampullary neoplasm
5. Autoimmune pancreatitis
6. Choledochocele

Signs of malignant ampullary obstruction:
- √ identification of an ampullary mass
- √ papillary bulging
- √ irregular asymmetric luminal narrowing of distal CBD
- √ diffuse upstream intra- + extrahepatic biliary dilatation

Signs of a benign obstruction:
- √ smooth symmetric luminal narrowing of CBD
- √ central biliary dilatation without an ampullary mass or papillary bulging

Ampullary and Periampullary Lesions

A. NEOPLASM
   (a) related to ampulla
      1. Ampullary cancer (4%)
      2. Ampullary adenoma
      3. Periampullary lipoma
   (b) related to pancreas

1. Pancreatic adenocarcinoma (85%)
2. Pancreatic neuroendocrine tumor
3. Intraductal papillary mucinous neoplasm

(c) related to bile duct
1. Cholangiocarcinoma distal CBD (6%)

(d) related to duodenal wall
1. Duodenal adenocarcinoma
2. Duodenal adenoma
3. Duodenal carcinoid
4. GIST

B. NONNEOPLASTIC LESION

(a) related to hepatopancreatic duct
1. Papillary stenosis
2. Choledocholithiasis
3. Pancreas divisum
4. Santorinicele
5. Choledochocele

(b) related to pancreas
1. Groove pancreatitis
2. Autoimmune pancreatitis
3. Pancreaticoduodenal artery pseudoaneurysm

(c) related to duodenum
1. Brunner gland hyperplasia and hamartoma
2. Duodenitis
3. Duodenal Crohn disease
4. Duodenal diverticula
5. Duodenal perforation and transection

Periampullary Tumor

= tumor arising within 2 cm of major duodenal papilla including carcinoma of ampulla of Vater, distal CBD, head + uncinate process of pancreas, periampullary portion of duodenum

Double-Duct Sign

= dilatation of common bile duct + pancreatic duct

A. MALIGNANT
1. Ampullary tumor (most common)
2. Pancreatic ductal adenocarcinoma
3. Distal CBD cholangiocarcinoma
4. Duodenal carcinoma
5. Lymphoma

B. BENIGN
1. Stone impacted in ampulla of Vater
2. Papillary / ampullary stenosis
3. Chronic pancreatitis

PANCREAS

Congenital Pancreatic Anomalies

A. Fusion Anomaly
   1. Pancreas divisum
   2. Agenesis of dorsal pancreas

B. Migration Anomaly
   1. Annular pancreas
   2. Ectopic pancreas

C. Duplication Anomaly
   (a) variations in number
   (b) variations in form

D. Genetics
   1. Von Hippel-Lindau disease

E. Underdevelopment
   1. **Pancreatic Agenesis** (extremely rare)
      Cause: mutation of developmental protein IPF1
      Associated with: gallbladder aplasia, polysplenia, fetal growth retardation
      • incompatible with life
   2. Pancreatic hypoplasia / partial agenesis
      = absence of ventral / dorsal anlage
      (a) agenesis of dorsal pancreas
      (b) agenesis of ventral pancreas
      (c) isolated hypoplasia of uncinate process

Paraduodenal Pancreatitis

1. Groove pancreatitis
2. Cystic dystrophy of duodenal wall
3. Paraduodenal wall cysts

Location: in + around minor papilla

Common features:

√ dilated ducts and cysts in duodenal wall
√ Brunner gland hyperplasia
√ hamartomatous pancreatic tissue in pancreaticoduodenal groove

Pancreatic Calcifications

1. CHRONIC PANCREATITIS
   Numerous irregular stippled calcifications of varying size; predominantly intraductal
   (a) Alcoholic pancreatitis (in 20–50%):
      √ small speckled intraductal calculi limited to head / tail in 25%
   (b) Biliary pancreatitis (in 2%)
   (c) Hereditary pancreatitis (in 35–60%):
      √ round calcifications throughout gland
   (d) Idiopathic pancreatitis
   (e) Pancreatic pseudocyst

(f) Juvenile tropical pancreatitis
√ discrete dense up to 5 cm large calculi

2. NEOPLASM
   (a) Microcystic adenoma (in 33%):
   √ "sunburst" appearance of calcifications
   (b) Macrocystic cystadenoma In 15%):
   √ amorphous peripheral calcifications
   (c) Adenocarcinoma (in 2%): with "sunburst" pattern
   (d) Cavernous lymphangioma / hemangioma:
   √ multiple phleboliths
   (e) Metastases from colon cancer
3. INTRAPARENCHYMAL HEMORRHAGE
   (a) Old hematoma / abscess / infarction
   (b) Rupture of intrapancreatic aneurysm
4. HYPERPARATHYROIDISM (in 20%):
   ◊ 50% of patients develop chronic pancreatitis + concomitant nephrocalcinosis
   ◊ Indistinguishable from alcoholic pancreatitis
5. CYSTIC FIBROSIS
   Fine granular calcifications imply advanced pancreatic fibrosis
6. HEMOCHROMATOSIS

Chronic Calcifying Pancreatitis

1. Alcoholism (70–80%) in developed countries
2. Juvenile tropical pancreatitis
3. Hereditary pancreatitis
4. Inborn errors of metabolism
5. Hyperlipidemia
6. Hypercalcemia

Atrophy and Fatty Replacement of Pancreas

1. Main pancreatic duct obstruction
2. Cystic fibrosis
   ◊ Most common cause in childhood!
3. Shwachman-Diamond syndrome
4. **Johanson-Blizzard syndrome** (= pancreatic insufficiency, nasal alar hypoplasia, absence of permanent teeth, short stature, congenital deafness)
5. Hemochromatosis
6. Viral infection
7. Severe malnutrition
8. Cushing syndrome, steroid therapy, obesity, elderly
9. Diabetes mellitus

DDx of total fatty replacement of pancreas:
pancreatic agenesis → absence of ductal system

Uneven Pancreatic Lipomatosis

√ commonly focal sparing of peribiliary region
1 sparing of uncinate process + peribiliary region
1a replacement of head 35%
1b replacement of head, neck, body 36%
2 sparing of peribiliary region only
2a replacement of head + uncinate process 12%
2b total replacement of pancreas 18%

Diffusely Enlarged Pancreas

1. Malignant lymphoma
2. Plasmacytoma
3. Metastases
4. Diffuse infiltrative pancreatic carcinoma
5. Autoimmune pancreatitis

Pancreatic Neoplasm

Origin: › in 99% exocrine ductal epithelium
› in 1.0% acinar portion of pancreatic glands
› in 0.1% malignant ampullary tumor with better prognosis

A. EXOCRINE NEOPLASM
(a) Ductal cell origin
1. Ductal adenocarcinoma (90%)
2. Ductectatic mucinous tumor
= mucin-hypersecreting carcinoma
3. Cystic neoplasm (10–15%)
› serous microcystic neoplasm
› mucinous macrocystic neoplasm
› cystic PET
4. Solid pseudopapillary tumor (rare)
5. Von Hippel-Lindau disease
(b) Acinar cell origin
1. Acinar cell carcinoma (1%)
2. Adenoma
(c) Indeterminate origin
1. Pancreatoblastoma
2. Dermoid cyst (< 27 years of age, 8–12 cm in size)
3. Giant cell tumor

B. PANCREATIC ENDOCRINE TUMOR (PET in 5%)
(a) Nonfunctioning (nonsyndromic) PET
(b) Functioning (syndromic) PET
1. Insulinoma (β cells)
2. Glucagonoma
3. Gastrinoma (δ cells)
4. Somatostatinoma
5. VIPoma (WDHA syndrome)

6. "PPoma" = pancreatic polypeptide
7. Carcinoid

C. NONEPITHELIAL ORIGIN

(a) Primary tumor

1. Primary lymphoma
   < 1% of pancreatic neoplasms
2. Primitive neuroectodermal tumor (in children, part of Ewing sarcoma family of tumors)
3. Rhabdomyosarcoma

(b) Solid mesenchymal tumor (1%)

> Benign primary nonepithelial neoplasms of the pancreas are a rare group of usually sharply marginated solid and cystic tumors.

1. Schwannoma
2. Neurofibroma
3. Ganglioneuroma
4. Desmoid tumor
5. Leiomyoma
6. Lipoma
7. Perivascular epithelioid cell tumor: clear cell "sugar tumor", angiomyolipoma, lymphangiomyomatosis, clear cell tumor

(c) Cystic nonepithelial neoplasm

1. Mature cystic teratoma
2. Lymphangioma

(d) Metastases to pancreas

Pediatric Pancreatic Tumors

1. Pancreatoblastoma
2. Solid-pseudopapillary tumor
3. Islet cell tumor
4. Nesidioblastosis
5. Acinar cell carcinoma
6. Burkitt lymphoma
7. Lymphangioma
8. Primitive neuroectodermal tumor (PNET)
9. Neuroblastoma (secondary involvement)

Hypervascular Pancreatic Tumors

A. PRIMARY
islet cell tumor, microcystic adenoma, solid-pseudopapillary tumor of pancreas

B. METASTASES from
angiosarcoma, leiomyosarcoma, melanoma, carcinoid, RCC, adrenal carcinoma, thyroid carcinoma

Pancreatic Pseudotumor

1. Intrapancreatic accessory spleen

Location: pancreatic tail

2. Pancreatic lobulation
   Prevalence: 34% of general population
   Location: posterior (19%), anterior (10%), horizontal (5%)
3. Tuber omentale = focal prominence of anterior pancreatic surface to left of SMA
4. Pancreas bifidum = fish tail pancreas = bifid pancreatic tail
   √ pancreatic tail does not reach splenic hilum

Pancreatic Cyst

With clearer depiction of septa, cyst contents and pancreatic ductal system, MRI can often achieve a more specific diagnosis.

Incidence: 2.6% of consecutive CT scans, 13.5% at MRI

A. INFLAMMATORY / INFECTIOUS
   (a) pseudocyst (85%):
   (b) acquired cyst:
      1. Retention cyst (= exudate within bursa omentalis from acute pancreatitis)
      2. Parasitic cyst: Echinococcus multilocularis, amebiasis
      3. Pancreatic abscess
      4. Lymphoepithelial cyst: cysts are lined by squamous epithelium and surrounded by dense lymphoid tissue
      5. Mucinous non-neoplastic unilocular cyst

B. CONGENITAL (rare)
   (a) solitary true pancreatic cyst
   (b) systemic disease / syndromes with multiple true cysts
      Associated with: cystic disease of liver / other organs
      1. Autosomal dominant polycystic kidney disease (ADPKD); autoptic liver (pancreatic) cysts in 90% (9%)
         √ nearly always associated with renal cysts
      2. Von Hippel-Lindau disease
         pancreatic cysts in 72% (25%) at autopsy (CT)
         √ renal involvement in all cases
      3. Beckwith-Wiedemann syndrome
      4. Meckel-Gruber syndrome
      5. Cystic fibrosis

C. CYSTIC NEOPLASM
   Frequency: < 10% of all pancreatic neoplasms
   (a) common cystic pancreatic neoplasms (5–15%)
      1. Intraductal papillary mucinous tumor (36%)
      2. Serous cystadenoma (20%)
      3. Pseudocyst (14%)
      4. Cystadenocarcinoma (7%)
      5. Mucinous cystic neoplasm
   (b) rare cystic pancreatic neoplasms
      1. Solid pseudopapillary tumor

2. Acinar cell cystadenocarcinoma
3. Retroperitoneal lymphangioma
4. Retroperitoneal hemangioma
5. Cystic neuroendocrine tumor

(c) solid pancreatic neoplasms with cystic degeneration

1. Pancreatic ductal adenocarcinoma
2. Cystic pancreatic endocrine tumor (rare)
3. Cystic metastasis (3–12% at autopsy)
   RCC, melanoma, lung tumors, breast carcinoma, hepatocellular carcinoma, ovarian carcinoma
4. Cystic teratoma
5. Pancreatic sarcoma (extremely rare)

Features of malignancy:

√ > 10 mm main pancreatic duct dilatation
√ > 10 mm large mural node
√ > 3 cm large cyst
√ > 2.5 SUV positivity on FDG
√ irregular / septate features
√ calcification

Imaging performance for malignant cystic lesion:

FDG-PET: 56% sensitive, 83% specific
CT: 81% sensitive, 100% specific
PET/CT: 94%sensitive, 100% specific

MRCP can image the pancreatic duct after Whipple procedure, distal pancreatectomy, and central pancreatectomy with pancreaticojejunostomy.

Unilocular Pancreatic Cyst

◊ A cyst < 3 cm is almost always benign (97% PPV) + may be followed at 6-month intervals for 3 years!

1. Pseudocyst
   • history of pancreatitis
2. Intraductal papillary mucinous neoplasm (IPMN)
   √ narrow neck at cyst-duct junction
3. Benign unclassified cyst
4. Unilocular serous cystadenoma
5. Lymphoepithelial cyst

MULTIPLE UNILOCULAR PANCREATIC CYSTS

1. Pseudocysts
2. Von Hippel-Lindau disease
3. Intraductal papillary mucinous neoplasm (rarely)

Pancreatic Cyst with Solid Component

◊ All tumors are either malignant or have a high malignant potential!
› true cystic neoplasm

1. Mucinous cystic neoplasm
2. Intraductal papillary mucinous neoplasm (IPMN)

› cystically degenerated neoplasm

3. Pancreatic endocrine tumor
4. Solid pseudopapillary tumor
5. Pancreatic adenocarcinoma
6. Metastasis

Macrocystic Lesion of Pancreas

= multilocular cyst, each compartment > 2 cm in size

1. Mucinous cystic neoplasm
   √ in body + tail of pancreas
   √ peripheral eggshell calcification
2. Intraductal papillary mucinous neoplasm: side-branch / mixed
   √ septated cyst communicating with main duct
3. Nonfunctioning neuroendocrine tumor
4. Congenital lymphangioma

Microcystic Lesion of Pancreas

= pancreatic lesion with > 6 cysts each < 2 cm in size

1. Serous cystadenoma
   √ fibrous central scar ± stellate pattern (30%)
   √ growth rate of 4 mm/year at follow-up

Mucin-Containing Cyst of Pancreas

1. Mucinous nonneoplastic cysts
   = nonneoplastic mucinous differentiation of epithelial lining without soft-tissue component
2. Mucinous cystadenoma
3. Mucinous cystadenocarcinoma
4. Intraductal papillary mucinous neoplasm

Hyperamylasemia

A. PANCREATIC
   1. Acute / chronic pancreatitis
   2. Pancreatic trauma
   3. Pancreatic carcinoma

B. GASTROINTESTINAL
   1. Perforated peptic ulcer
   2. Intestinal obstruction
   3. Peritonitis
   4. Acute appendicitis
   5. Afferent loop syndrome
   6. Mesenteric ischemia / infarction
   7. Portal vein thrombosis

C. TRAUMA

1. Burns
2. Cerebral trauma
3. Postoperative

D. OBSTETRICAL
1. Pregnancy
2. Ruptured ectopic pregnancy

E. RENAL
1. Transplantation
2. Renal insufficiency

F. METABOLIC
1. Diabetic ketoacidosis
2. Drugs

G. PNEUMONIA

H. SALIVARY GLAND LESION
1. Facial trauma
2. Mumps

SPLEEN

Nonvisualization of Spleen

1. Asplenia syndrome
2. Polysplenia syndrome
3. Traumatic fragmentation of spleen
4. Wandering spleen

Small Spleen

1. Infarction
2. Celiac disease
3. Congenital / hereditary hypoplasia of spleen
   ◊ Associated with recurrent bacterial infections!
4. Fanconi anemia
5. Irradiation
6. Partial splenectomy
7. Polysplenia syndrome
8. Atrophy

Splenomegaly

√ inferior tip of spleen extends below tip of right lobe of liver
√ AP diameter of spleen > $^{2}/_{3}$ of abdominal diameter

A. CONGESTIVE SPLENOMEGALY heart failure, portal hypertension, cirrhosis, cystic fibrosis, portal / splenic vein thrombosis, acute splenic sequestration crisis of sickle cell anemia

B. NEOPLASM leukemia, lymphoma, lymphoproliferative disease, Langerhans cell histiocytosis, metastases, primary neoplasm

C. STORAGE DISEASE Gaucher disease, Niemann-Pick disease, mucopolysaccharidoses,

gargoylism, amyloidosis, diabetes mellitus, hemochromatosis

D. INFECTION
   (a) bacterial: TB, subacute bacterial endocarditis, typhoid fever, syphilis, brucellosis
   (b) viral: hepatitis, infectious mononucleosis
   (c) protozoal: echinococcosis, malaria, kala azar, American leishmaniasis
   (d) fungal: histoplasmosis

E. HEMOLYTIC ANEMIA hemoglobinopathy, hereditary spherocytosis, primary neutropenia, thrombotic thrombocytopenic purpura, extracorporeal membrane oxygenation (← RBC damage)

F. EXTRAMEDULLARY HEMATOPOIESIS osteopetrosis, myelofibrosis

G. COLLAGEN VASCULAR DISEASE SLE, rheumatoid arthritis, Felty syndrome

H. SPLENIC TRAUMA

I. OTHERS
   1. Sarcoidosis
      √ splenomegaly in up to 60%
      √ inhomogeneous enhancement after bolus injection (multiple 2–3-cm hypodense nodular lesions)
      √ necrotic mass with focal calcifications
   2. Hemodialysis
   3. Autoimmune lymphoproliferative syndrome

Solid Splenic Lesion

A. MALIGNANT TUMOR
   1. Lymphoma (Hodgkin disease, non-Hodgkin lymphoma, primary splenic lymphoma)
      ◊ Splenomegaly in non-Hodgkin lymphoma indicates involvement in most patients
      ◊ 30% of patients with splenomegaly have NO involvement from non-Hodgkin lymphoma
      ◊ 30% of patients with lymphoma of any kind have splenic involvement without splenomegaly
      √ homogeneous splenomegaly (from diffuse infiltration)
      √ miliary nodules
      √ large 2–10-cm nodules (10–25%)
      √ nodes in splenic hilum (50%) in NHL; uncommon in Hodgkin disease
   2. Metastasis (7%) melanoma (6–34%), breast carcinoma (12–21%), bronchogenic carcinoma (9–18%), colon carcinoma (4%), renal cell carcinoma (3%), ovary (8%), prostate (6%), stomach (7%), pancreas, endometrial cancer
   3. Angiosarcoma
   4. Malignant fibrous histiocytoma, leiomyo-, fibrosarcoma
   5. Langerhans cell histiocytosis
      √ splenomegaly
      √ multiple hypoechoic nodules (less often)

B. BENIGN TUMOR
   1. Hamartoma = splenoma
   2. Hemangioma
   3. Hematopoietic

4. Sarcoidosis
5. Gaucher disease (islands of RES cells laden with glucosylceramide)
6. Inflammatory pseudotumor
7. Lymphangioma

C. SPLENIC INFARCTION

Cystic Splenic Lesion

A. CONGENITAL
1. Epidermoid cyst = true cyst = congenital cyst

B. VASCULAR
1. Splenic laceration / fracture
2. Hematoma
3. **False cyst** = posttraumatic cyst = nonpancreatic pseudocyst of the spleen
◊ 80% of all splenic cysts are pseudocysts (= secondary cysts)
Cause: cystic end stage of trauma, infection, infarction
√ internal echoes from debris
√ calcifications within cyst wall may resemble eggshell
√ smaller size than true cyst
4. Cystic degeneration of infarct
(a) occlusion of splenic a. / branches (hemolytic anemia, endocarditis, SLE, arteritides, pancreatic cancer)
(b) venous thrombosis of splenic sinusoids (massive splenomegaly)
5. Peliosis

C. INFECTION / INFLAMMATION
1. **Pyogenic abscess**
Prevalence: 0.1–0.7%
Cause: hematogenous spread in sepsis (75%), penetrating trauma (15%), infarction (10%)
Predisposed: endocarditis, drug abuse, penetrating trauma, neoplasm, sickle cell disease
• fever, chills, LUQ pain (in < 50%)
√ irregular borders without capsule
√ gas bubbles within abscess
√ rim enhancement
Rx: 76% success rate for percutaneous drain
2. **Microabscesses**
Organism: fungus (especially Candida, Aspergillus, Cryptococcus)
Prevalence: 26% of splenic abscesses
Predisposed: immunocompromised patient
√ hepatosplenomegaly
√ multiple round hypoechoic / hypoattenuating "target" lesions of 5–10 mm often associated with hepatic + renal involvement
√ "wheel-in-wheel" appearance when central hyperechoic portion becomes necrotic + hypoechoic
3. Granulomatous infection

(a) Mycobacterium tuberculosis: miliary TB
√ mild splenomegaly (uncommon)
(b) M. avium-intracellulare
√ marked splenomegaly (in 20%)

4. Pneumocystis carinii infection
√ splenomegaly + multiple hypoattenuating foci
5. **Parasitic cyst** (Echinococcus)
Prevalence: in < 2% of patients with hydatid disease
Cause: systemic dissemination, intraperitoneal spread of ruptured liver cyst
√ solitary cyst ± subjacent daughter cysts
√ hydatid sand ± infolded membranes
√ ± linear calcification
6. Intrasplenic pancreatic pseudocyst
Prevalence: in 1–5% of patients with pancreatitis

D. CYSTIC NEOPLASM
1. Cavernous hemangioma
◊ Most common primary neoplasm of the spleen!
√ hyperdense lesion
2. Lymphoma (most common malignant neoplasm!)
√ splenomegaly
√ multiple small / large masses
3. Lymphangioma / lymphangiomatosis
√ multiple septated subcapsular cystic lesions
4. Necrotic metastasis:
malignant melanoma (in 50%), breast, lung, ovarian, pancreatic, endometrial, colonic, prostatic, carcinoma; chondrosarcoma
◊ In 7% of patients with widespread metastasis!

E. TRUE CYST (with epithelial lining)
1. Congenital cyst = epidermoid cyst
2. Parasitic cyst

F. FALSE CYST = PSEUDOCYST (lacking epithelial lining)
1. Traumatic cyst
2. Postinfarct cyst

Solitary Splenic Lesion

mnemonic: L'CHAIM
Lymphoma
Cyst
Hematoma, **H**emangioma, **H**amartoma
Abscess
Infarct
Metastasis

Multiple Splenic Nodules and Masses

1. Lymphoma, leukemia

2. Metastases
3. Inflammatory lesions
4. Benign tumors
5. Splenic cysts
6. Splenic infarcts
7. Gaucher cells

Increased Splenic Density

1. Sickle cell anemia (in 5% of sicklers)
2. Hemochromatosis
3. Thorotrast exposure
4. Lymphangiography

Splenic Calcifications

A. DISSEMINATED
   1. Phlebolith: visceral angiomatosis
   2. Granuloma (most common): histoplasmosis, TB, brucellosis

B. CAPSULAR & PARENCHYMAL
   1. Pyogenic / tuberculous abscess
   2. Pneumocystis carinii infection
   2. Infarction (multiple)
   3. Hematoma

C. VASCULAR
   1. Splenic artery calcification
   2. Splenic artery aneurysm
   3. Splenic infarct
   4. Autosplenectomy

D. CALCIFIED CYST WALL
   1. Congenital cyst
   2. Posttraumatic cyst
   3. Echinococcal cyst
   4. Cystic dermoid
   5. Epidermoid

mnemonic: HITCH

Histoplasmosis (most common)
Infarct (sickle cell disease)
Tuberculosis
Cyst (Echinococcus)
Hematoma

Iron Accumulation in Spleen

A. DIFFUSE
   1. Multiple blood transfusions
   2. Sickle cell anemia

B. FOCAL

1. Gamna-Gandy bodies
2. Angiosarcoma

Hyperechoic Splenic Spots

1. Granulomas: miliary tuberculosis, histoplasmosis
2. Phleboliths
3. Lymphoma / leukemia
4. Myelofibrosis
5. Gamna-Gandy nodules (in portal hypertension)

Spontaneous Splenic Rupture

1. Posttraumatic delayed rupture
2. Splenomegaly
3. Hemangioma
4. Epidermoid cyst
5. Peliosis
6. Previous splenic infarction

Hyposplenism

= no uptake of ^{99m}Tc-sulfur colloid

A. ANATOMIC ABSENCE OF SPLEEN
   1. Congenital asplenia = Ivemark syndrome
   2. Splenectomy

B. FUNCTIONAL ASPLENIA
   = marked decrease in splenic phagocytic function despite presence of splenic tissue within the body
   1. Circulatory disturbances: occlusion of splenic artery / vein, hemoglobinopathies (sickle cell disease, hemoglobin-SC disease, thalassemia), polycythemia vera, idiopathic thrombocytopenic purpura
   2. Altered RES activity: thorotrast, irradiation, combined splenic irradiation + chemotherapy, replacement of RES by tumor / infiltrate, splenic anoxia (cyanotic congenital heart disease), sprue
   3. Autoimmune disease

   Cx: children at risk for pneumococcal pneumonia (liver partially takes over immune response later in life)

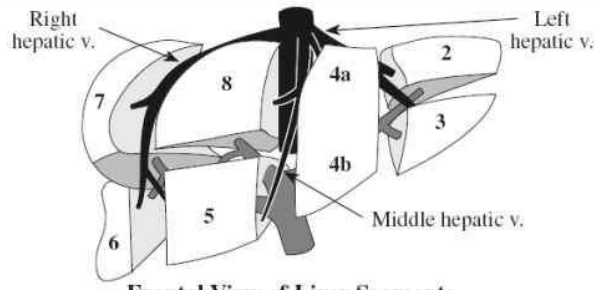
C. FUNCTIONAL ASPLENIA + SPLENIC ATROPHY
   ulcerative colitis, Crohn disease, celiac disease, tropical sprue, dermatitis herpetiformis, thyrotoxicosis, idiopathic thrombocytopenic purpura, thorotrast

D. FUNCTIONAL ASPLENIA + NORMAL / LARGE SPLEEN
   sarcoidosis, amyloidosis, sickle cell anemia (if not infarcted), after bone marrow transplantation

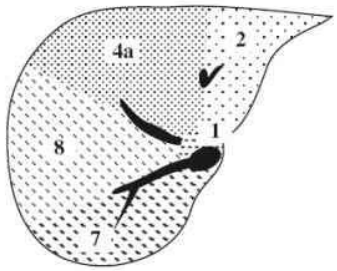
- RBC (acanthocytes, siderocytes)
- lymphocytosis, monocytosis
- Howell-Jolly bodies (intraerythrocytic inclusions)
- thrombocytosis

√ spleen not visualized on ^{99m}Tc-sulfur colloid
√ ^{99m}Tc-heat–damaged RBCs / ^{111}In-labeled platelets may demonstrate splenic tissue if ^{99m}Tc-sulfur colloid does not
Cx: increased risk of infection (pneumococcus, meningococcus, influenza)

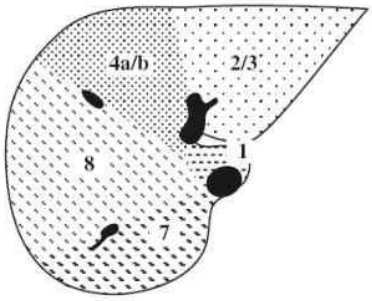
ANATOMY OF LIVER, BILE DUCTS, PANCREAS AND SPLEEN



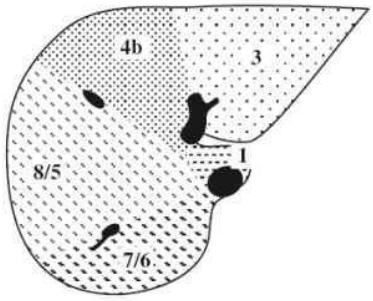
Frontal View of Liver Segments



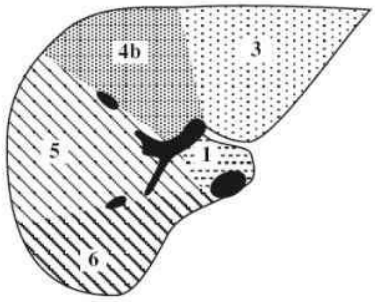
Level of Hepatic Vein Junction



Level of Left Portal Vein



Level of Right Portal Vein

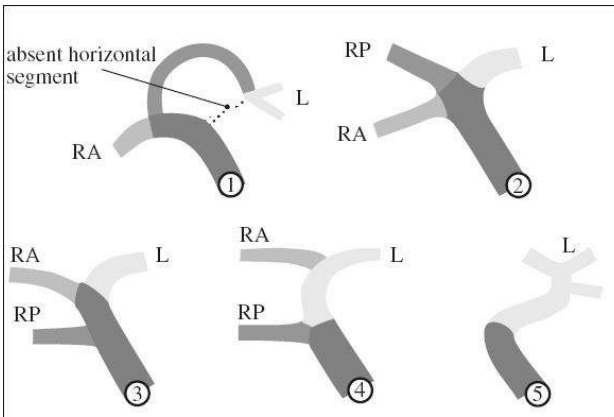


Level of Splenic Vein

Functional Segmental Liver Anatomy

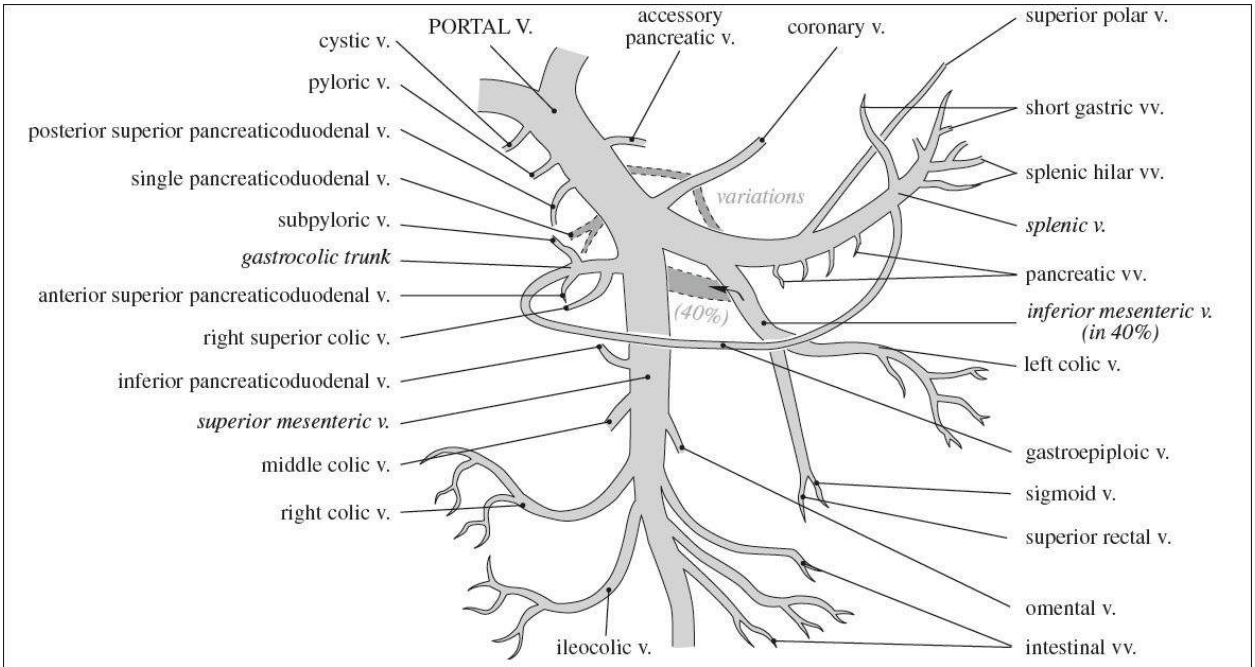
Federative Committee on Anatomical Terminology in Terminologia Anatomica (1998)

Goldsmith & Woodburne		*Couinaud & Bismuth (based on 3rd order portal branching)*		*Blood Supply*
CAUDATE LOBE		Caudate lobe	I	Left portal vein
LEFT LOBE	Left lateral segment	Left lateral superior subsegment	II	Left portal vein
		Left lateral inferior subsegment	III	Left portal vein
	Left medial segment	Left medial superior subsegment	IVa	Left portal vein
		Left medial inferior subsegment	IVb	Left portal vein
RIGHT LOBE	Right anterior segment	Right anterior inferior subsegment	V	Anterior RPV
		Right anterior superior subsegment	VIII	Anterior RPV
	Right posterior segment	Right posterior inferior subsegment	VI	Posterior RPV
		Right posterior superior subsegment	VII	Posterior RPV



A. LEFT PORTAL VEIN
1. Absence of horizontal segment (0.2%)
B. RIGHT PORTAL VEIN
2. Trifurcation of main portal vein (9–15%)
3. Origin of RP segment from main portal vein (5–13%)
◊ Unrecognized variant results in devascularization of segments V & VIII during left trisegmentectomy (resection of segments II & III & IV) / harvest of left lobe for transplantation!
4. Origin of RA segment from left portal vein (1–4%)
5. Absence of main right, RA, and RP portal segments
6. Separate RPI segment (VI) of RPV (6%)
7. Separate RPS segment (VII) of RPV (1%)

Variations of Intrahepatic Portal Venous System (35%)



Extrahepatic Portal Vein Tributaries

LIVER

Functional Segmental Liver Anatomy

based on distribution of 3 major hepatic veins:

(a) middle hepatic vein
divides liver into right and left lobe;
also separated by main portal vein scissura
(**Rex-Cantlie line** = extrapolated line from posthepatic IVC to long axis of gallbladder demarcating on liver surface anteriorly the right and left parts of liver)

(b) left hepatic vein
divides left lobe into medial + lateral sectors

(c) right hepatic vein

divides right lobe into anterior + posterior sectors

Each of the four sections is further divided:

by an imaginary transverse line drawn through the right + left portal vein into anterior + posterior segments; the segments are numbered counterclockwise from IVC

Portal Vein Anatomy (Akgul Classification)

Type A Normal anatomy: bifurcation of MPV and RPV (79–86%)

◊ Posterior branch of RPV as 1st portal vein branch (13%) = most common variant

N.B.: unintended devascularization of hepatic segments V + VIII during left trisegment-ectomy (resection of segments II, III, IV) / harvest of left lobe for liver transplantation if unrecognized

Type B Trifurcation of MPV (9–15%)

Type C Right anterior portal vein from LPV (1–4%)

Type D LPV from right anterior portal vein (0.3–1.2%)

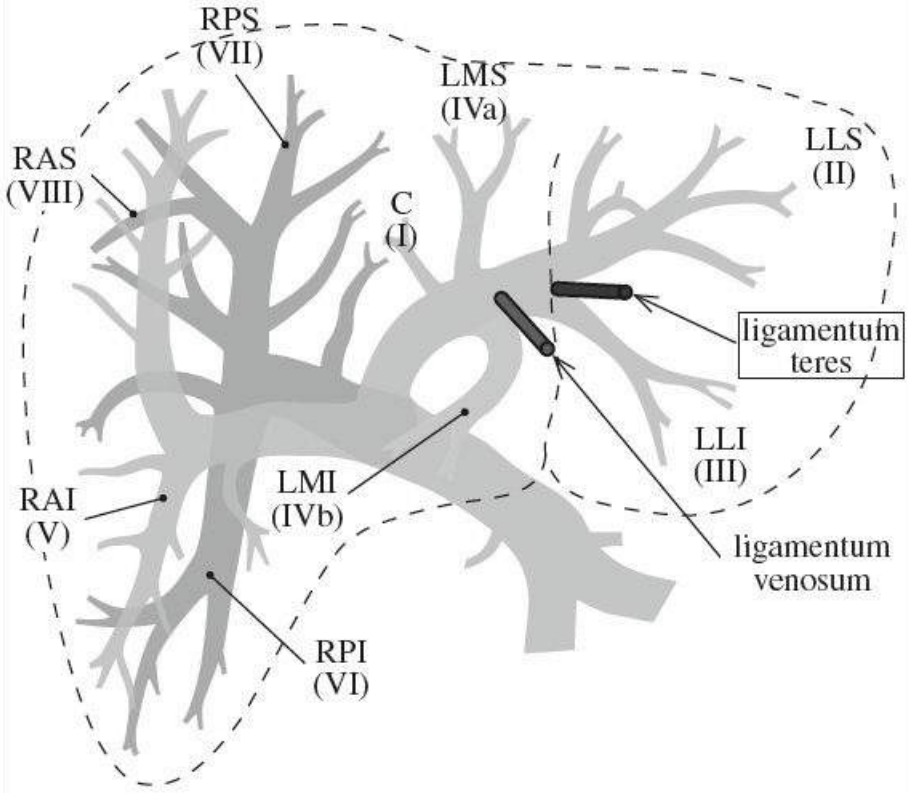
Type E Right anterior portal vein from MPV (1–3%)

Maximum Cross-sectional Diameter of Portal Vein

(a) child < 10 years of age: 8.5 mm

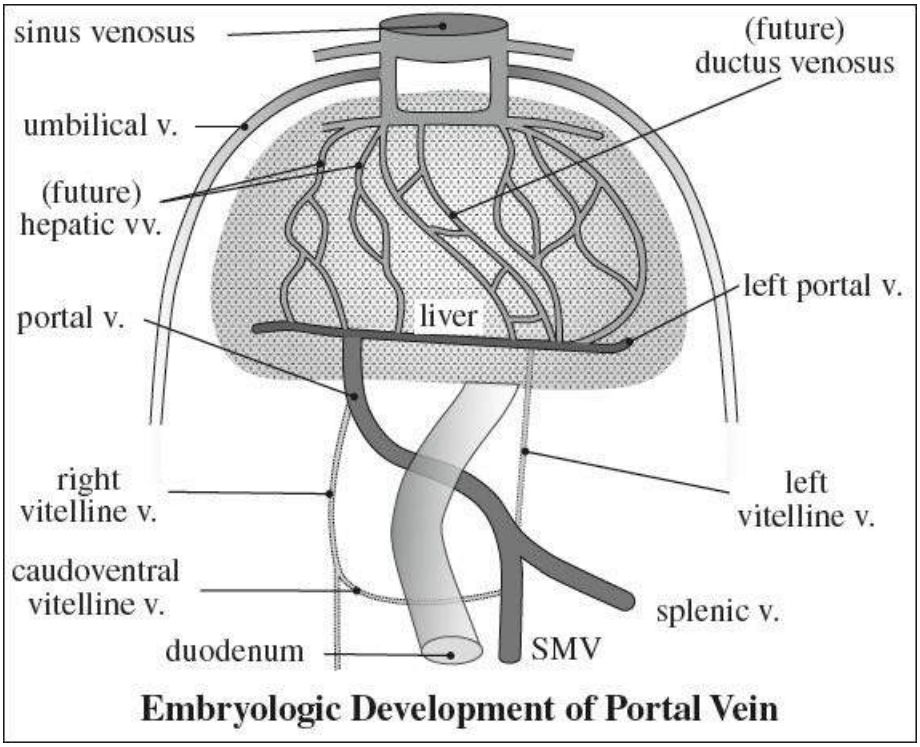
(b) 10–20 years of age: 10.0 mm

(c) adult: 13.0 mm



Intrahepatic Portal Vein Branches (in 65% of individuals)
(umbilical portion of L portal v. = segment between ligg. venosum + teres)

R			= right portal vein
	RA		= right anterior segment
		RAI	= right anterior inferior (V)
		RAS	= right anterior superior (VIII)
	RP		= right posterior segment
		RPI	= right posterior inferior (VI)
		RPS	= right posterior superior (VII)
C			= caudate lobe (I)
L			= left portal vein
		LMI	= left median inferior (IVb)
		LMS	= left median superior (IVa)
		LLI	= left lateral inferior (III)
		LLS	= left lateral superior (II)



Embryologic Development of Portal Vein

Embryology of Portal Vein

Time: 4th–12th week of GA

› paired vitelline veins around duodenum → form 3 major side-to-side anastomoses (cranioventral + caudoventral + dorsal) → pierce septum transversum (primitive liver) → broken up into sinusoids → drain into sinus venosus (of primitive heart)

› selective involution of caudal part of right vitelline vein + cranial part of left vitelline vein:

» regression of caudoventral anastomosis

» dorsal anastomosis → main portal vein

» cranioventral anastomosis → left portal vein

» caudal right vitelline vein → superior mesenteric vein

» caudal left vitelline vein → splenic vein

Major Anatomic Variants of Portal Vein *(rare)*

1. Duplication of portal vein
2. Congenital portosystemic shunt
3. Congenital absence of portal vein
4. Absent branching of portal vein
5. Preduodenal portal vein

Hepatic Artery Anatomy (Michels classification)

Type 1 (55–60%):

› celiac trunk trifurcates into common hepatic artery (CHA) + left gastric artery (LGA) + splenic artery (SpA)

› CHA divides into

Location: CHA courses to right along superior ridge of pancreas branching at lower end of epiploic foramen

(a) proper hepatic artery (PHA)

Location: PHA courses right + upward along anterior border of epiploic foramen

(b) gastroduodenal artery (GDA)

› right hepatic artery (RHA) + left hepatic artery (LHA) arise from PHA

› middle hepatic a. (supplying caudate lobe) arises from:

(a) LHA / RHA

(b) PHA (in 10%)

Type 2 (4–10%):

› CHA divides into RHA + GDA

› LHA replaced to LGA

› middle hepatic artery from RHA

Type 3 (8–11%):

› CHA divides into GDA + LHA

› RHA replaced to SMA

› middle hepatic artery from LHA

Type 4 (2–4%):

› CHA divides into middle hepatic artery + GDA

› RHA + LHA are both replaced

Type 5 (9–16%):

› accessory L hepatic a. arises from LGA

Type 6 (1–7%):

› accessory R hepatic artery arises from SMA

Type 7 (1%):

› accessory R + L hepatic arteries

Type 8 (2–3%):

› combinations of accessory + replaced hepatic arteries

Type 9 (1–3%):

› hepatic trunk replaced to SMA

Type 10 (0.5%):

› hepatic trunk replaced to LGA

The presence of a portal branch without corresponding artery indicates a replaced or accessory vascular anatomy or transhepatic hepatofugal collateral vessels.

Aberrant Hepatic Artery

= hepatic artery coursing between IVC + portal vein

1. Replaced right hepatic artery (50%)
2. Right hepatic artery with early bifurcation of common hepatic artery into right + left hepatic arteries (20%)
3. Accessory right hepatic artery (15%)
4. Replacement of entire hepatic trunk to SMA (15%)

Left Hepatic Artery

= usually arises from proper hepatic artery (PHA)

Location: from hepatic hilum to umbilical portion of left portal vein (usually to its right) coursing up- and leftward

Accessory LHAs: from LGA / celiac trunk / aorta

Division (arteriographic description):

after forming an arch overriding the portal vein

› A2 branches: course to left corner of liver, usually superior to A3

› A3 branches: course ventral + caudal along left side of umbilical portion of PV and then toward left

Right Hepatic Artery

= usually arises from PHA / SMA when replaced

Accessory RHAs: from SMA / celiac trunk / aorta

Division (arteriographic description):

› anterior branch: straight right + upward course

› posterior branch: proximally meandering course

A6: inferolateral course to lower corner of liver

A7: compact complex meandering course superiorly (on frontal projection)

The RHA forms anterior and posterior branches characterized by a straight right upward course and by a meandering proximal portion, respectively.

Caudate Lobe

= located behind liver hilum + wrapping around IVC, supplied by multiple small branches from LHA + RHA

Variations (arteriographic description):

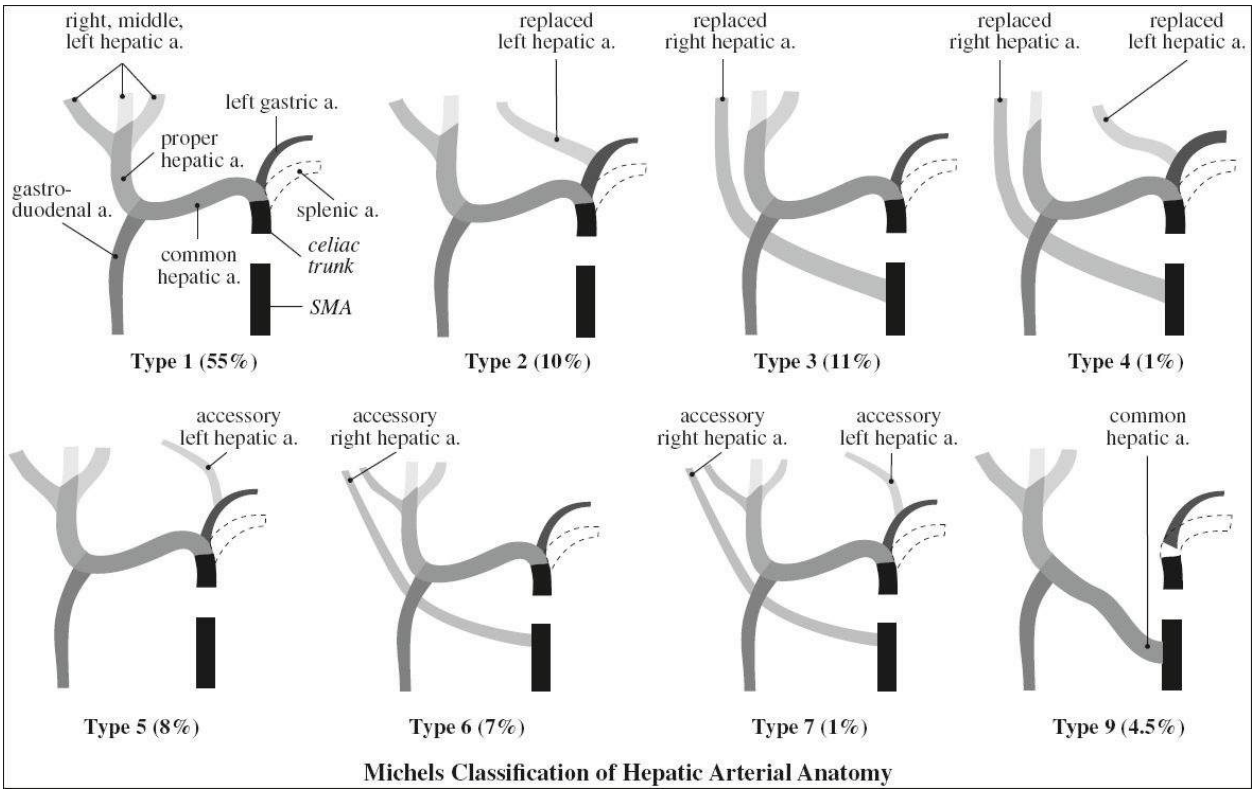
› RHA + LHA (53%)

› RHA only (35%)

Location: courses posteromedially mainly supplying the lateral (= paracaval portion and papillary process) of S1

› LHA only (12%)

Location: courses posteriorly mainly supplying medial portion (= caudate process, Spiegel lobe) of S1



Hepatic Vein Drainage Pattern of Right Hepatic Lobe (Nakamura Classification)

Type 1 Large right hepatic vein (RHV) drains extensive area of right lateral sector + part of right paramedian sector; small short hepatic vein drains small area of right lateral sector (occasionally absent) (39–57%)

Type 2 Right hepatic vein of medium size; one thick short hepatic vein of 5–10 mm in diameter (= middle / inferior hepatic vein) drains right lateral sector concomitantly directly into IVC (29–37%)

Type 3 Right lobe drainage allocated to a short RHV that drains superior part of right lateral sector and large middle hepatic vein (MHV) + inferior right hepatic vein that drains inferior part of right lateral sector (15–24%)

It is important to identify any variation in the middle hepatic vein because the hepatectomy plane in living donors is about 1 cm to the right of the middle hepatic vein along the gallbladder fossa.

Third Inflow to Liver

= aberrant veins supplying small areas of liver tissue + communicating with intrahepatic portal vein branches

Effect: focal decrease of portal vein perfusion resulting in areas of fat-sparing / fat accumulation

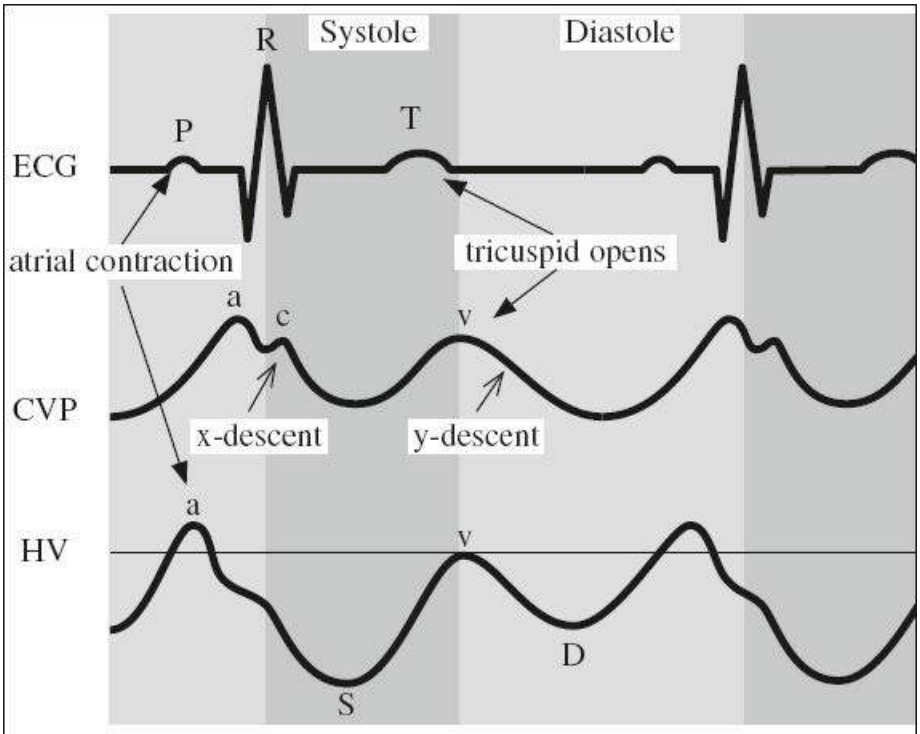
1. Cholecystic veins
   › directly entering liver segments 4 + 5
   › veins joining the parabiliary veins via triangle of Calot
2. Parabiliary venous system
   = venous network within hepatoduodenal ligament anterior to main portal vein

Tributaries:
› cholecystic vein through triangle of Calot
[Jean-François Calot (1861–1944), French surgeon]
› pancreaticoduodenal vein
› right gastric / pyloric vein
√ pseudolesion at dorsal aspect of segment 4

3. Epigastric-paraumbilical venous system
= small veins around falciform ligament draining anterior part of abdominal wall directly into liver
Subgroups:
(a) **superior vein of Sappey**
[Marie Philibert Constant Sappey (1810–1896), professor of anatomy and president of the Académie Nationale de Médecine, Paris, France]
› drains upper portion of falciform ligament + medial part of diaphragm
› enters peripheral left portal vein branches
› communicates with superior epigastric + internal thoracic veins
(b) **inferior vein of Sappey**
› drains lower portion of falciform ligament
› enters peripheral left portal vein branches
› communicates with branches of inferior epigastric vein around the umbilicus
(c) **vein of Burow**
› terminates in middle part of collapsed umbilical v.
› communicates with branches of inferior epigastric vein around the umbilicus
(d) **intercalary veins**
› interconnect vein of Burow + inferior vein of Sappey

Normal Hemodynamic Parameters of Liver

Portal vein velocity: > 11 (range, 16–40) cm/sec
Portal vein cross-section: 0.99 ± 0.28 cm^2
Congestion index: 0.070 ± 0.09 cm•sec
(= cross-sectional area of portal vein divided by average velocity)
Hepatic artery resistive index: 0.60–0.64 ± 0.06



Time-correlated electrocardiographic (ECG), central venous pressure (CVP) and hepatic venous (HV) waveform

S wave = trough correlates with peak negative pressure created by downward motion of AV annulus toward cardiac apex during midsystole = ventricular **S**ystole

v wave = transitional peak between systole + diastole correlates with return of tricuspid **v**alve toward cardiac apex; caused by RA overfilling against a closed tricuspid valve; occurs in < 50% of patient

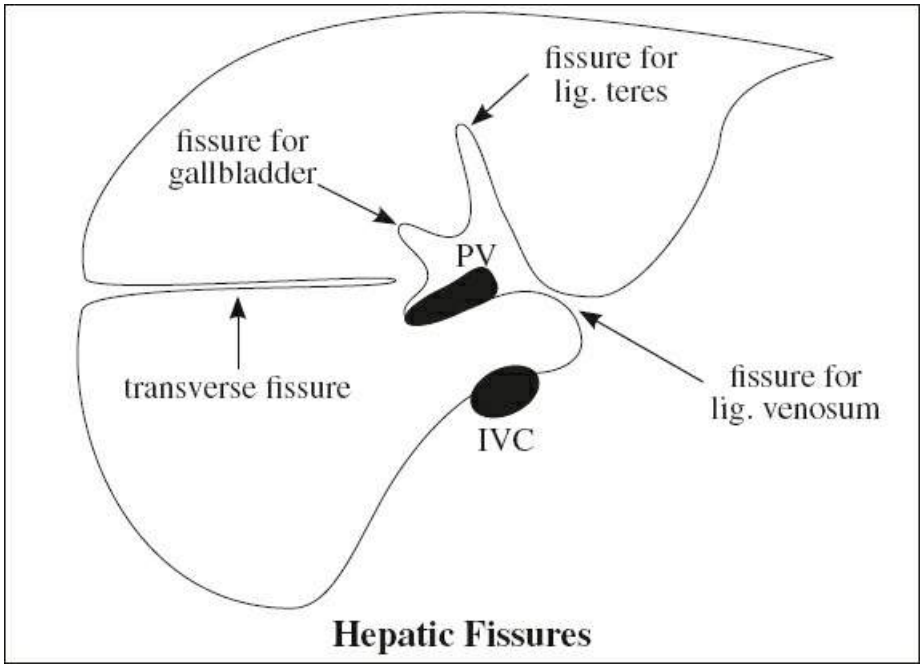
D wave = trough correlates with rapid early diastolic RV filling caused by opening of the tricuspid valve + blood flow from RA into RV during ventricular **D**iastole; equal to / smaller than *S* wave

a wave = retrograde *a* wave at end-diastole caused by contraction of RA = **a**trial systole; in 66% of patients

Hepatic Fissures

1. **Fissure for ligamentum teres** = umbilical fissure
   = invagination of ligamentum teres = embryologic remnant of obliterated umbilical vein connecting placental venous blood with left portal vein
   › located at dorsal free margin of falciform ligament
   › runs into liver with visceral peritoneum
   › divides left hepatic lobe into medial + lateral segments (divides subsegment 3 from 4)

2. **Fissure for ligamentum venosum**
   = invagination of obliterated ductus venosus
   = embryologic connection of left portal vein with left hepatic vein
   › separates caudate lobe from left lobe of liver
   › lesser omentum within fissure separates the greater sac anteriorly from lesser sac posteriorly
3. **Fissure for gallbladder** (GB)
   = shallow peritoneal invagination containing the GB
   › divides right from left lobe of liver
4. **Transverse fissure**
   = invagination of hepatic pedicle into liver
   › contains horizontal portion of left + right portal veins
5. **Accessory fissures**
   (a) Right inferior accessory fissure = from gallbladder fossa / just inferior to it → to lateroinferior margin of liver
   (b) Others (rare)



Hepatic Fissures

Size of Liver

A. YOUNG INFANT
   right hepatic lobe should not extend > 1 cm below right costal margin
B. CHILD
   right hepatic lobe should not extend below right costal margin
C. ADULT
   (a) midclavicular line (vertical / craniocaudad axis):
      < 13 cm = normal
      13.0–15.5 cm = indeterminate (in 25%)

> 15.5 cm = hepatomegaly (87% accuracy)

(b) preaortic line < 10 cm

(c) prerenal line < 14 cm

Liver Capsule

= 2 adherent layers:

(a) thick, fibrous inner layer = Glisson capsule

(b) outer serous layer derived from peritoneum excluding

› bare area near diaphragm

› porta hepatis

› gallbladder attachment

Liver Echogenicity & Attenuation

US: pancreatic > splenic ≥ hepatic > renal echogenicity

CT: 50–65 HU (precontrast)

CECT: early arterial phase (20 sec), late arterial phase (30–40 sec), portal venous phase (60–70 sec); maximal enhancement at 45–60 sec

Enzymatic Liver Tests

A. Alkaline phosphatase (AP)

Formation: bone, liver, intestine, placenta

High increase:

cholestasis with extrahepatic biliary obstruction (confirmed by rise in γGT), drugs, granulomatous disease (sarcoidosis), primary biliary cirrhosis, primary + secondary malignancy of liver

Mild increase: all forms of liver disease, heart failure

B. Gamma-glutamyl transpeptidase (γGT)

very sensitive in almost all forms of liver disease

Utility: confirms hepatic source of elevated AP, may indicate significant alcohol use

C. Transaminases

High increase: viral / toxin-induced acute hepatitis

(a) aspartate aminotransferase (AST; formerly serum glutamic oxaloacetic transaminase [SGOT])

Formation: liver, muscle, kidney, pancreas, RBCs

(b) alanine aminotransferase (ALT; formerly serum glutamic pyruvic transaminase [SGPT])

Formation: primarily in liver

• rather specific elevation in liver disease

D. Bilirubin

helps differentiate between various causes of jaundice

(a) unconjugated / indirect bilirubin = insoluble in water

Formation: breakdown of senescent RBCs

Metabolism: tightly bound to albumin in vessels, actively taken up by liver, cannot be excreted by kidneys

(b) conjugated / direct bilirubin = water-soluble

Formation: conjugation in liver cells
Metabolism: excretion into bile; NOT reabsorbed by intestinal mucosa; excreted in feces
Elevation:
› ↑ production: hemolytic anemia, resorption of hematoma, multiple transfusions
› ↓ hepatic uptake: drugs, sepsis
› ↓ conjugation: Gilbert syndrome, neonatal jaundice, hepatitis, cirrhosis, sepsis
› ↓ excretion into bile: hepatitis, cirrhosis, drug-induced cholestasis, sepsis, extrahepatic biliary obstruction

E. Lactic dehydrogenase (LDH)
nonspecific and therefore not helpful
high increase: primary or metastatic liver involvement

F. Alpha-fetoprotein (AFP)
> 400 ng/mL strongly suggests that a focal mass represents a hepatocellular carcinoma

PORTA HEPATIS

= LIVER HILUM
= deep short transverse fissure that passes across left posterior aspect of undersurface of right lobe of liver separating caudate lobe from quadrate lobe

Contents:
(a) **portal triad**:
1. Main portal vein (MPV)
2. Proper hepatic artery: left anterior to MPV
3. Common hepatic duct: right anterior to MPV

(b) nerves: left vagal trunk + sympathetic hepatic plexus
(c) lymphatics

Within the porta hepatis, the common bile duct and proper hepatic artery typically are located anterior to the portal vein, with the common bile duct to the right and the proper hepatic artery to the left.

Enveloped by:
(a) hepatoduodenal ligament
(b) lesser omentum
(c) loose areolar tissue
(d) fibrous capsule of Glisson

GALLBLADDER

Size & Capacity & Wall Thickness

Physiologic distension: optimal after 8–12 hours of fasting
GB function: concentration of bile through absorption of 90% of water
Wall layers: (a) mucosa
(b) lamina propria
(c) muscularis propria
(d) serosa

N.B.: The GB has NO muscularis mucosa / submucosa

Length:

(a) infant < 1 year old: 1.5–3.0 cm

(b) older child: 3–7 cm

(c) adult: 7–10 cm

Wall thickness: 2–3 mm

Width: 2.0–3.5 cm

Capacity: 30–50 mL

Bile volume: 250–1,000 mL/d secreted by hepatocytes

Gallbladder Function

= evaluation of volume and ejection fraction following ingestion of a fatty meal / infusion of cholecystokinin

Methods:

1. HIDA scintigraphy
2. MR cholangiography with mangafodipir trisodium = MnDPDP = manganese (II) DPDP [N,N′-**di**pyridoxylethylenediamine-N,N′-**di**acetate 5,5′-bis(**p**hosphate)]
   Dose: 0.5 mL/kg of MnDPDP up to 35–50 mL
   » slow IV injection for 1–2 minutes
   » followed by a 10-mL saline flush
   » scanned 15–30 minutes after injection
3. MR cholangiography with gadolinium BenzylOxyPropionicTetraAcetate (Gd-BOPTA) = MultiHance®)
   Dose: 0.05 mmol (0.1 mL)/kg up to 15 mL
   » IV injection with power injector at 2 mL/sec
   » followed by a 20-mL saline flush
   » T1WI at 30–60 minutes after injection to obtain gadolinium-enhanced MR cholangiopancreatograms

Gallbladder Ejection Fraction (GBEF)

$$GBEF = [GB_{initial} - GB_{post}] \div GB_{initial}$$

Indication:

(1) ↑ sensitivity of study for acute (acalculous) cholecystitis

(2) in patients with abdominal pain and no cholelithiasis

(3) to establish that gallstones are the primary cause of abdominal pain

Technique:

1. Discontinue opioids for > 24 hours
2. Select ROI over GB
3. Administer Sincalide 1 hour post HIDA in a dose of 0.02 µg/kg body weight IV over 30 minutes (with infusion pump)
4. Image acquisition for 20 more minutes post infusion to detect paradoxical filling of gallbladder in sphincter of Oddi dysfunction

Normal result: > 30% GBEF

LOW GALLBLADDER EJECTION FRACTION

Cause: CCK-induced cystic duct spasm in chronic calculous / acalculous cholecystitis, gallbladder dyskinesia, opioid intake

Reproducibility: a low GBEF does not recover (if opioid intake is ruled out) and further deteriorates over time

Frequency: ⅓ of all cholecystectomies are performed for chronic acalculous cholecystitis

Rx: cholecystectomy with pain relief in 89%

Differentiation of abdominal pain:

(a) **biliary pain** = low GBEF ± gallstones

Pathophysiology of biliary pain:

CCK-induced cystic duct spasm → reduction in GBEF → bile stasis → stretching of GB wall against impedance to bile flow → biliary pain

(b) **nonbiliary pain** = normal GBEF + gallstones

Cause of nonbiliary pain (?):

CCK-induced rapid bile transit ← increased peristalsis in small intestine + colon; others

Congenital Gallbladder Anomalies

Agenesis of Gallbladder

Prevalence: 0.04–0.07 % (autopsy)

Associated with:

common: rectovaginal fistula, imperforate anus, hypoplasia of scapula + radius, intracardiac shunt

rare: absence of corpus callosum, microcephaly, atresia of external auditory canal, tricuspid atresia, tracheoesophageal fistula, dextroposition of pancreas + esophagus, absent spleen, high position of cecum, polycystic kidney

Hypoplastic Gallbladder

(a) congenital

(b) associated with cystic fibrosis

Septations of Gallbladder

A. LONGITUDINAL SEPTA

1. **Bilobed gallbladder = duplication of gallbladder**
   = two separate lumina + two cystic ducts
   Prevalence: 1÷3,000 to 1÷12,000
2. **Bifid gallbladder = double gallbladder**
   = two separate lumina with one cystic duct
3. Triple gallbladder (extremely rare)

B. TRANSVERSE SEPTA OF GALLBLADDER

1. Isolated transverse septum
2. **Phrygian cap** (2–6% of population)
   = kinking / folding of fundus ± septum
3. Multiseptated gallbladder (rare)

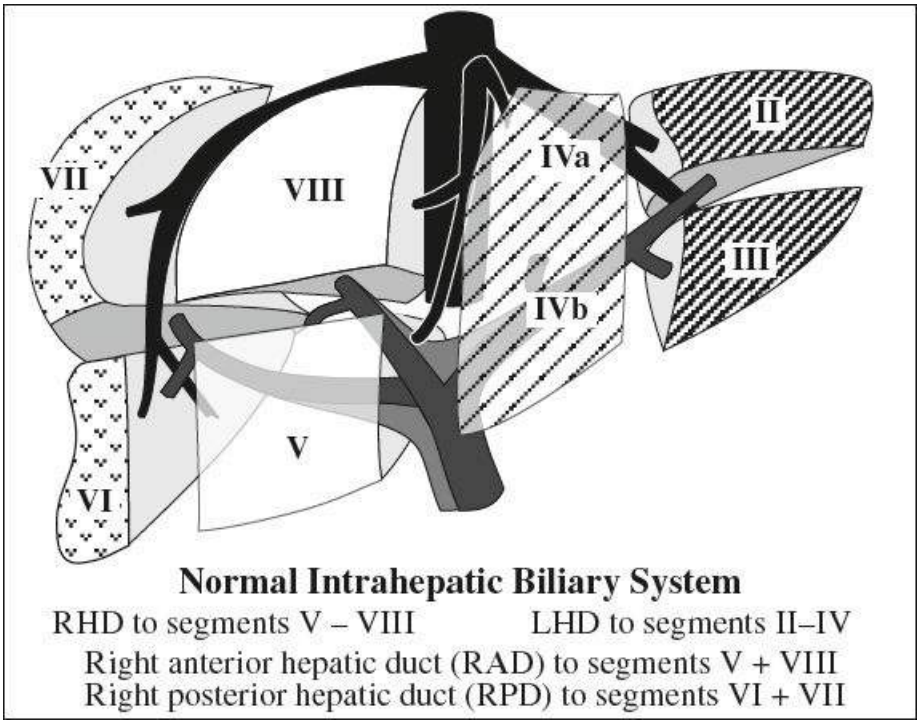
= multiple cystlike compartments connected by small pores
Cx: stasis + stone formation

C. GALLBLADDER DIVERTICULUM
= persistence of cystohepatic duct

Gallbladder Ectopia

most frequent locations:
(1) beneath the left lobe of the liver >
(2) intrahepatic >
(3) retrohepatic

rare locations:



Normal Intrahepatic Biliary System
RHD to segments V – VIII LHD to segments II–IV
Right anterior hepatic duct (RAD) to segments V + VIII
Right posterior hepatic duct (RPD) to segments VI + VII

(4) within falciform ligament, (5) within interlobar fissure, (6) suprahepatic (lodged between superior surface of right hepatic lobe + anterior chest wall), (7) within anterior abdominal wall, (8) transverse mesocolon, (9) retrorenal, (10) near posterior spine + IVC, (11) intrathoracic GB (← inversion of liver)

Associated with: eventration of diaphragm

"FLOATING GB"

= gallbladder with loose peritoneal reflections, may herniate through foramen of Winsløw into lesser sac

BILE DUCTS

Embryology of Bile Ducts

Ductal plate: hepatocyte cells form double-layer sleeve around central portal vein at 4

weeks GA → remodelling over next few weeks → into several normally connected bile ducts adjacent to portal tracts from hilum to periphery

Genetics: PKHD1 (polycystic kidney hepatic disease 1) gene codes for fibrocystin/polyductin protein that acts on primary cilia lining bile ducts

Pathology: mutation of PKHD1 gene → abnormal cilia → abnormal ductal plate formation → dilated abnormally branching irregular channels increased in number; intervening connective tissue over time becomes fibrotic

Normal Size of Bile Ducts

@ CBD at point of maximum diameter = free edge of gastrohepatic ligament (point of least constraint):
  (a) adolescents & adults
    ≤ 5 mm = normal; 6–7 mm = equivocal;
    ≥ 8 mm = dilated
    ◊ In patient > 60 years of age add 1 mm/decade = **presbyductectasia** (eg, 60 = 6 mm, 70 = 7 mm)
    ◊ Following cholecystectomy up to 8 mm
  (b) neonates: < 1 mm
  (c) infants up to 1 year of age: < 2 mm
  (d) older children: < 4 mm

@ CHD at porta hepatis + CBD in head of pancreas: 5 mm

@ right intrahepatic bile duct just proximal to CHD: 2–3 mm / < 40% of diameter of accompanying portal vein
  ♦ Right Hepatic Duct (RHD): ← segments V–VIII
    › Right Posterior Duct (RPD ← segments VI & VII
    › Right Anterior Duct (RAD) ← segments V & VIII
  ♦ Left Hepatic Duct (LHD): ← segments II–IV

@ Cystic duct
  Valves of Heister = normal mucosal folds
  Diameter: 1.8 mm
  Average length: 1–2 cm
  √ distal cystic duct posterior to CBD (in 95%), anterior to CBD (in 5%)

Bile Duct Anatomy (Couinaud Classification)

[Claude Couinaud (1922–2008), French surgeon and anatomist]
= intrahepatic biliary system runs parallel to portal venous supply of liver

(1) **Right hepatic duct** (RHD) drains segments V–VIII of right hepatic lobe with 2 major branches:
  (a) right posterior duct (RPD) drains posterior segments VI + VII
    √ almost horizontal course
  (b) right anterior duct (RAD) drains anterior segments V + VIII
    √ more vertical course

(2) **Left hepatic duct** (LHD) drains segments II–IV of left hepatic lobe

Variants of Bile Duct Confluence

N.B.: important for donor of right hepatic lobe transplant

◊ RPD has the most frequent anomalous insertions!

◊ Bile duct from caudate lobe joins origin of LHD / RHD

Type A Normal R posterior duct drains into R hepatic duct, which joins L hepatic duct to form CHD 54–61%

Type B "triple confluence" = trifurcation of RAD + RPD + LHD 11–16%

Type C RAD / RPD joins CHD separately 15–23%

Type D RPD empties into L hepatic duct 13–19%

Type ? RAD / RPD joins LHD separately 4–8%

Type E absence of defined upper biliary confluence with all sectorial ducts joining separately 3–4%

Type F RPD may join neck of GB / may be entered by cystic duct 1%

Bile Duct Aberrations

Prevalence: 2.4% of autopsies; 13–18.5% of operative cholangiograms

Significance: aberrant ducts near cystic duct / gallbladder have the greatest risk of iatrogenic injury at cholecystectomy

Cx: (1) postoperative bile leak if severed

(2) segmental biliary obstruction if ligated

A. **ABERRANT HEPATIC DUCT**

= direct drainage of RPD into the CHD (CBD, cystic duct, gallbladder): on right side (5%) / on left side (1%)

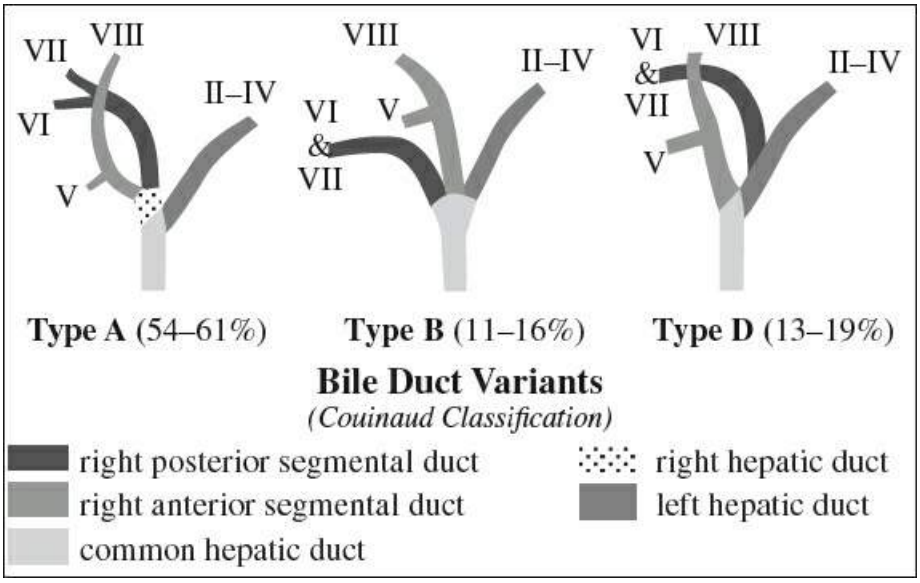
› RHD joins extrahepatic bile duct at / near cystic duct insertion (4–5%)

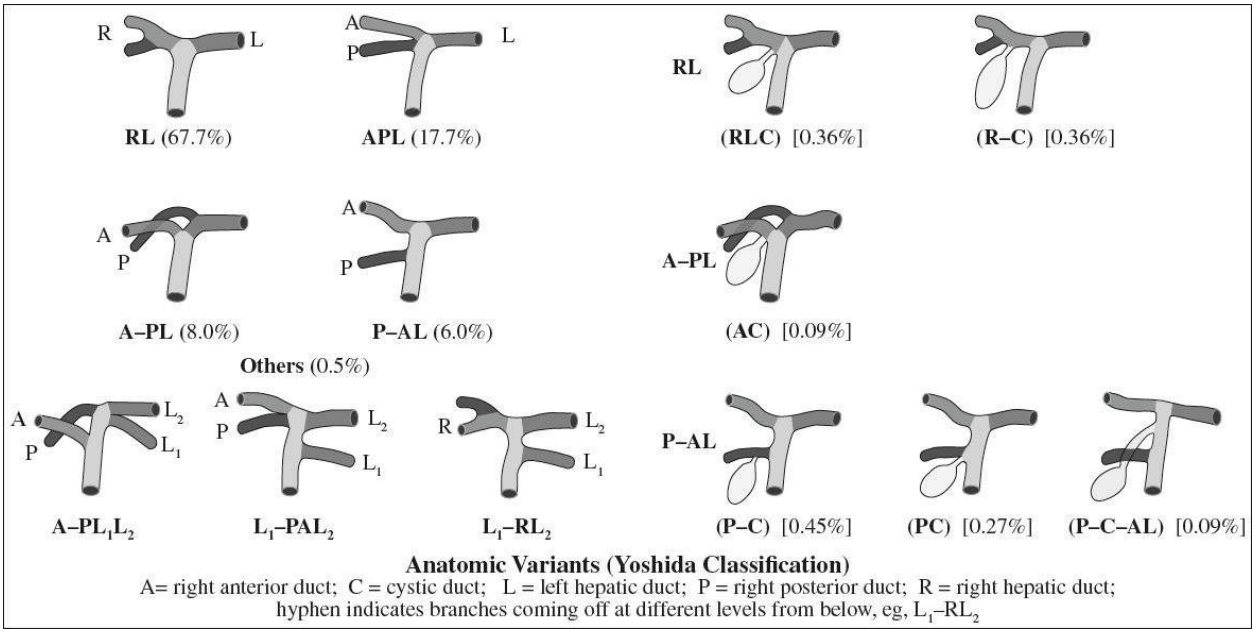
› cysticohepatic duct (1–2%) = anomalous RHD inserts into cystic duct

› anomalous LHD: not susceptible to injury and therefore of no clinical significance

B. CYSTIC DUCT ENTERING RHD

C. DUCTS OF LUSCHKA





[Hubert von Luschka (1820–1875), extraordinary ordinarius and director of the anatomical institute in Tübingen, Germany]

= SUBVESICAL / **ACCESSORY BILE DUCTS**

= small ducts from liver bed draining directly into GB

Incidence: 2%

Origin: right hepatic lobe; R/ L ductal system

Course: along gallbladder fossa

Drain: variably into gallbladder, intra- / extrahepatic bile ducts

Significance: may be injured during surgical dissection / cauterization → bile leak

D. DUPLICATION OF CYSTIC DUCT / CBD

± duplication of gallbladder

E. CONGENITAL TRACHEOBILIARY FISTULA

= fistulous communication between carina and LHD

- infants with respiratory distress
- productive cough with bilious sputum

√ pneumobilia

Variants of Cystic Duct Insertion

N.B.: important prior to laparoscopic cholecystectomy

Prevalence: variations occur in 18–23%

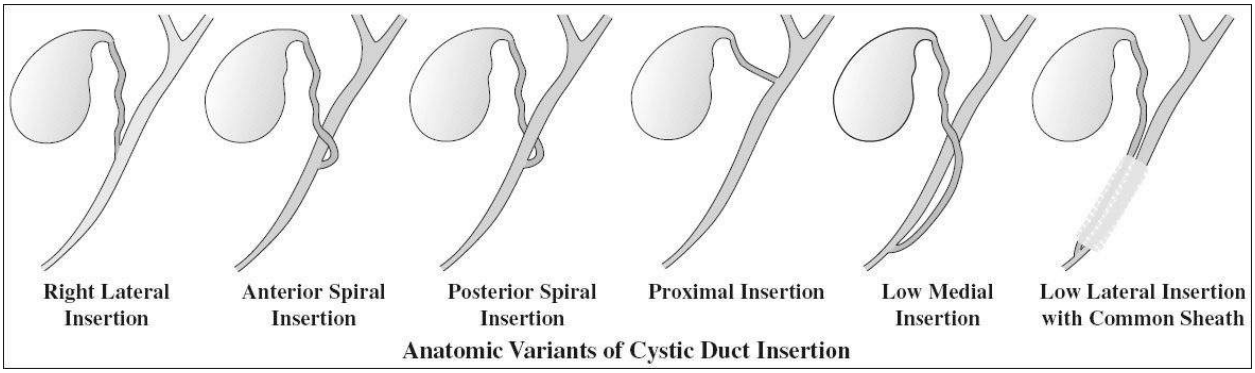
(a) craniocaudad insertion into extrahepatic bile duct

› proximal ⅓ = common hepatic duct high in porta hepatis

› middle ⅓ of extrahepatic bile duct 75%

› distal ⅓ of extrahepatic bile duct 10%

√ cystic duct parallels extrahepatic bile duct (implies common fibrous sheath)



Anatomic Variants of Cystic Duct Insertion

Cx: during cholecystectomy
(1) common hepatic duct stricture
(2) inadvertent ligation / transection of extrahepatic bile duct
(3) long cystic duct remnant

(b) mediolateral insertion into common hepatic duct
› left (medial) 10–17%
› right lateral
› anterior / posterior spiral
› parallel course for > 2 cm 1.5–25%
» low lateral (with common sheath)
» low medial (at / near ampulla of Vater)

(c) insertion into intrahepatic bile duct
› right hepatic duct (0.3%)
› left hepatic duct (rare)

(d) absence of cystic duct
√ gallbladder drains directly into common bile duct

Hepatobiliary Triangle
= TRIANGLE OF CALOT
= anatomic space bordered by CHD medially, cystic duct inferiorly, and cystic artery superiorly

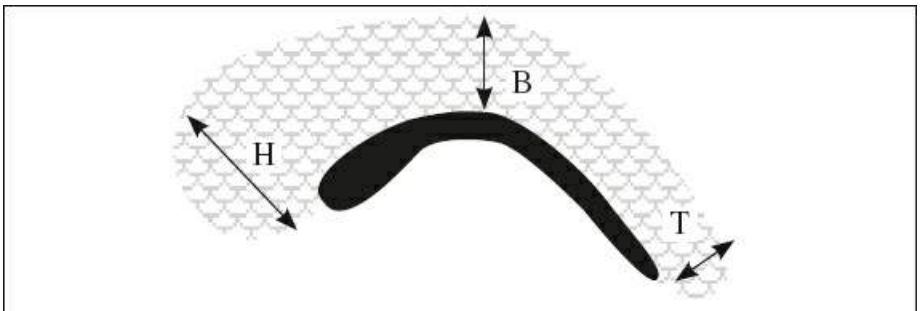
PANCREAS

Pancreatic Anatomy

Location: anterior pararenal space of retroperitoneum; crossing anterior to aorta, IVC, left kidney, renal veins, right renal artery

Parts:

1. **Head**: within curvature (C-loop) of duodenum, to right of SMV
Relationship to CBD: partially covered by pancreas posteriorly (53%), totally covered (30%), not at all covered (17%)
Posterior surface: separated from IVC by retroperitoneal fat



Age-dependent Pancreatic Diameters

(on TRV image)

H = head = 10–22 mm; 24 ± 3.6 mm (in 6th decade)
B = body = 4–10 mm; 16 ± 2.0 mm (in 6th decade)
T = tail = 8–22 mm; 15 ± 1.9 mm (in 6th decade)

Connection:

- › to liver + lesser gastric curvature via hepatoduodenal + gastrohepatic ligaments (= derivative of ventral mesogastrium)
- › to splenic hilum + greater gastric curvature via splenorenal + gastrosplenic ligaments (= derivative of dorsal mesogastrium)

2. **Uncinate process**: triangular leftward prolongation of caudal part of head with straight / concave anteromedial border curving behind SMA and SMV; variably drained by dorsal and ventral ducts
3. Neck: constricted portion of pancreas that lies anterior to SMA + SMV = beginning of portal vein
4. Body: behind lesser sac + stomach
5. Tail: begins about ½ of distance between neck + tip of tail (located in splenorenal ligament)

Weight: 90–100 g
Length: 15–20 cm
Width: 1.0–1.5 cm
Size: gradual decrease with age; pancreatic head & neck make up 60–70% of the pancreatic parenchyma
Blood supply: branches from celiac trunk and SMA

Physiology of Pancreas

Pancreatic islet cells = endocrine cells clustered in islets of Langerhans; 1–2% of total mass of pancreas receiving 10–15% of pancreatic blood flow; innervated by parasympathetic + sympathetic neurons modulating secretion of insulin + glucagon

Function: secretion of

- › insulin production in β-cells (B cells); most abundant in center of islet
- › glucagon in α-cells (A cells)
- › somatostatin in δ-cells (D cells)
- › VIP in δ1-cells (D1 cells)
- › serotonin in enterochromaffin cells
- › pancreatic polypeptide in PP cells → stimulate secretion of gastric and intestinal

enzymes + inhibit intestinal motility) in islets + scattered throughout exocrine pancreas

Pancreatic Development

during the 4th–5th week of gestation 2 endodermal diverticula form in the foregut near its junction with the yolk sac (= endodermal lining of duodenum)

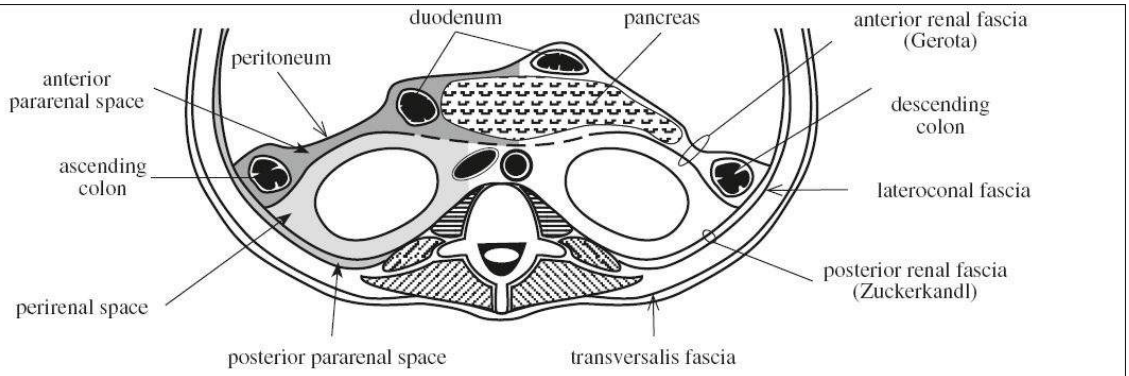
A. DORSAL ANLAGE (= single dorsal bud)

Origin: derives from dorsal wall of duodenum in dorsal mesoduodenum (mesogastrium) and is later displaced to the left

› forms cranial portion of head + isthmus + body + tail of pancreas

• prone to atrophy (poor in polypeptides)

√ drains to minor papilla through accessory duct of Santorini



Extraperitoneal Spaces

B. VENTRAL ANLAGE (= 2 ventral buds)

Origin: arises from ventral wall of duodenum ← hepatic diverticulum (below primordial liver bud)

(a) left ventral bud regresses completely

(b) right ventral bud rotates 180° clockwise posteriorly (viewed from top) and inferiorly (simultaneously with rotation of foregut); comes to lie to left and caudad of duodenum where it fuses with dorsal bud at 7th week EGA

› forms caudal portion of pancreatic head + pancreatic neck + uncinate process + CBD

• not prone to atrophy (rich in polypeptides)

√ ventral duct drains with CBD through ampulla of Vater + becomes the major drainage pathway for the entire pancreas after fusion with dorsal duct

Peritoneal Investment of Pancreas

◊ NO distinct capsule

√ appearance of fat clefts between glandular tissues at CT → surround areolar tissue + dip into pancreas

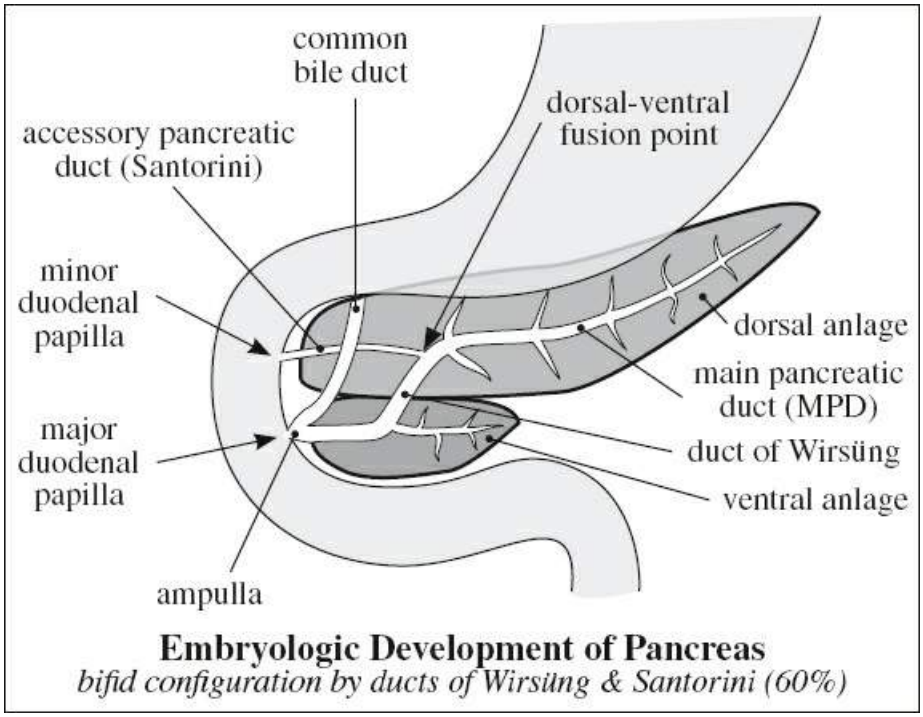
› during foregut rotation dorsal mesoduodenum + dorsal mesogastrium fuse with parietal layer of peritoneum
→ forms posterior wall of lesser sac

› dorsal mesogastrium pouches out
→ forms omentum

› posterior leaf of mesogastric outpouching fuses with mesentery of midgut

→ forms transverse mesocolon over pancreas

› most distal portion of pancreatic tail remains within dorsal mesogastrium
→ splenorenal ligament carrying splenic artery and vein



Embryologic Development of Pancreas
bifid configuration by ducts of Wirsüng & Santorini (60%)

Main Pancreatic Duct of Wirsüng

mnemonic: "upside down **M**(ain) reads W(irsüng)"

[Johann Wirsüng (1589–1643), German physician in Padua, Italy]

= term broadly used for duct traversing the entire length of pancreas (= combination of MPD + duct of Wirsüng)

= in restricted sense portion of ventral duct between dorsal-ventral fusion point and major papilla

› distal portion of dorsal duct connects with ventral duct

› proximal portion of dorsal duct may disappear

Origin: dorsal anlage (duct) → drains tail, body, and anterior portion of pancreatic head

Width: 3.5 mm in head, 2.5 mm in body, 1.5 mm in tail (gradual tapering)

Length: 9.5–25 cm

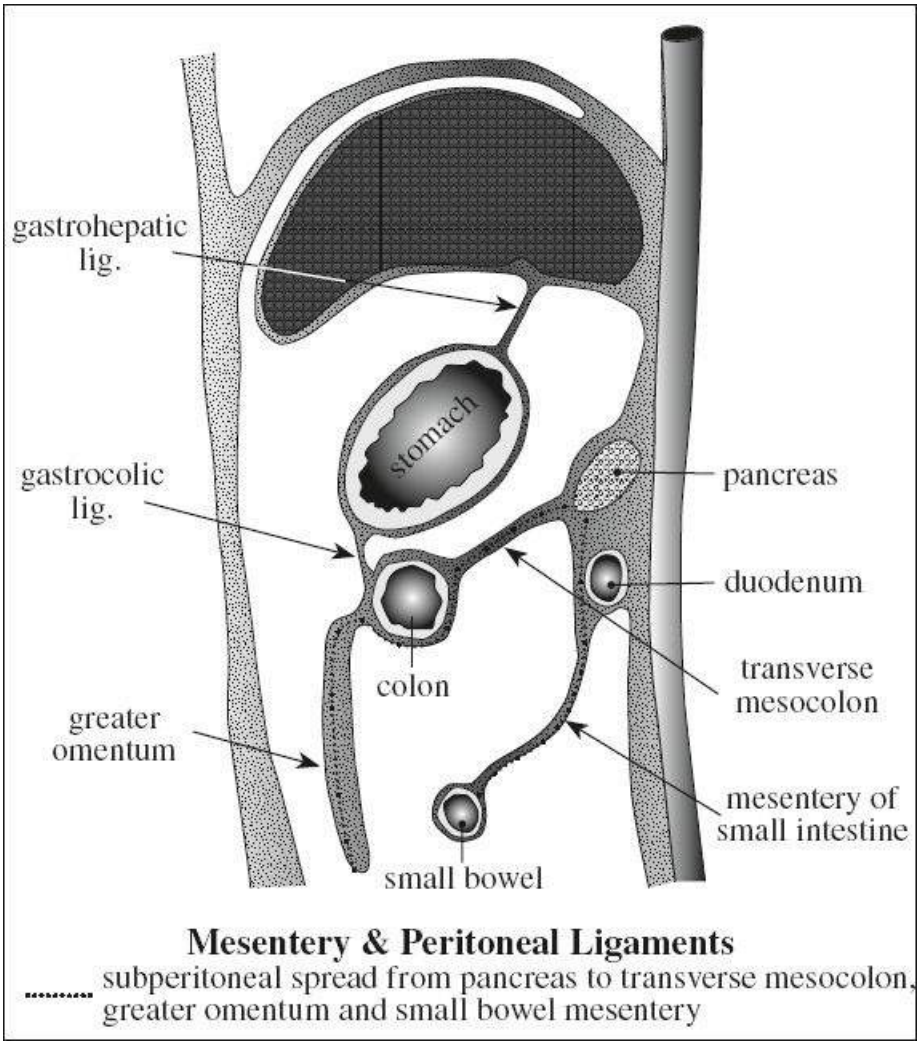
√ receives 20–35 tributaries / side branches that enter at right angles

√ usually drains through major papilla

√ unites with CBD within sphincteric segment (sphincter of Oddi) in 80–90%

√ focal saccular dilatation of terminal part of (ventral) MPD = **wirsüngocele** (incidental finding)

◊ Major drainage route for 91% of individuals



Accessory Pancreatic Duct of Santorini

[Giovanni Santorini (1681–1737), anatomist in Venice, Italy]

= proximal segment of dorsal duct distal to dorsal-ventral fusion point, which has not atrophied

◊ Present in 44% of individuals

√ drains anterosuperior portion of head into minor papilla

DOWNSTREAM VARIANTS OF PANCREATIC DUCTS

√ physiologic narrowing of duct caliber at "knee" of MPD = site of fusion of dorsal and ventral ducts

(1) Bifid duct system 60%

(2) Rudimentary duct of Santorini 30%

√ branch of MPD after loss of communication with minor papilla

(3) Dominant duct of Santorini 1%

(4) Ansa pancreatica rare

√ duct of Santorini forms sigmoid curve as it courses toward duct of Wirsüng

(5) Duplication anomaly of MPD common

(6) Duplication anomaly of dorsal anlage / ventral anlage (rare)

Ampulla of Vater

= slightly dilated conduit that results from the union of common bile duct + duct of Wirsüng

◊ Actual dilatation of common channel is unusual

Location: major duodenal papilla in medial wall of 2nd / 3rd portion of duodenum below surface of papilla of Vater

(a) common channel (74%):

» 2–10 (mean 5) mm short common channel (55–85%) with a diameter of 3–5 mm

√ V-type configuration

» 8–15 mm long common channel

√ Y-type configuration

(b) separate openings (19%)

» **1** orifice in papilla with 2 separate openings for each duct (= double-barrel configuration in 19–38%)

(c) interposed septum (7%)

» **2** orifices in papilla draining each duct separately

SPHINCTER OF ODDI

[Ruggero Oddi (1864–1913), physiologist in Genoa, Italy]

= SPHINCTER OF HEPATICOPANCREATIC AMPULLA

= 3 separate smooth muscles interspersed with glandular tissue encircling ampulla of Vater

(a) choledochal sphincter (Boyden) = encircles distal CBD

(b) pancreatic duct sphincter (in 33% separate)

(c) ampullary sphincter

Length: 10–15 mm

Function: regulates flow of bile + pancreatic juices into duodenum

Major Duodenal Papilla

= PAPILLA OF VATER

= conic / cylindric protuberance at medial aspect of duodenum

Location: middle ⅓ of descending duodenum (75%), horizontal portion of duodenum (25%)

◊ Drainage of common bile duct in 100%

◊ Drainage of main pancreatic duct of Wirsüng in 90%

√ oval protruding structure < 5–10 mm in diameter (seen on thin-section CT in 20%)

√ ± targetlike enhancement similar to that of adjacent duodenal mucosa

Minor Duodenal Papilla (present in 60%)

Location: 2 cm anterosuperior from major duodenal papilla

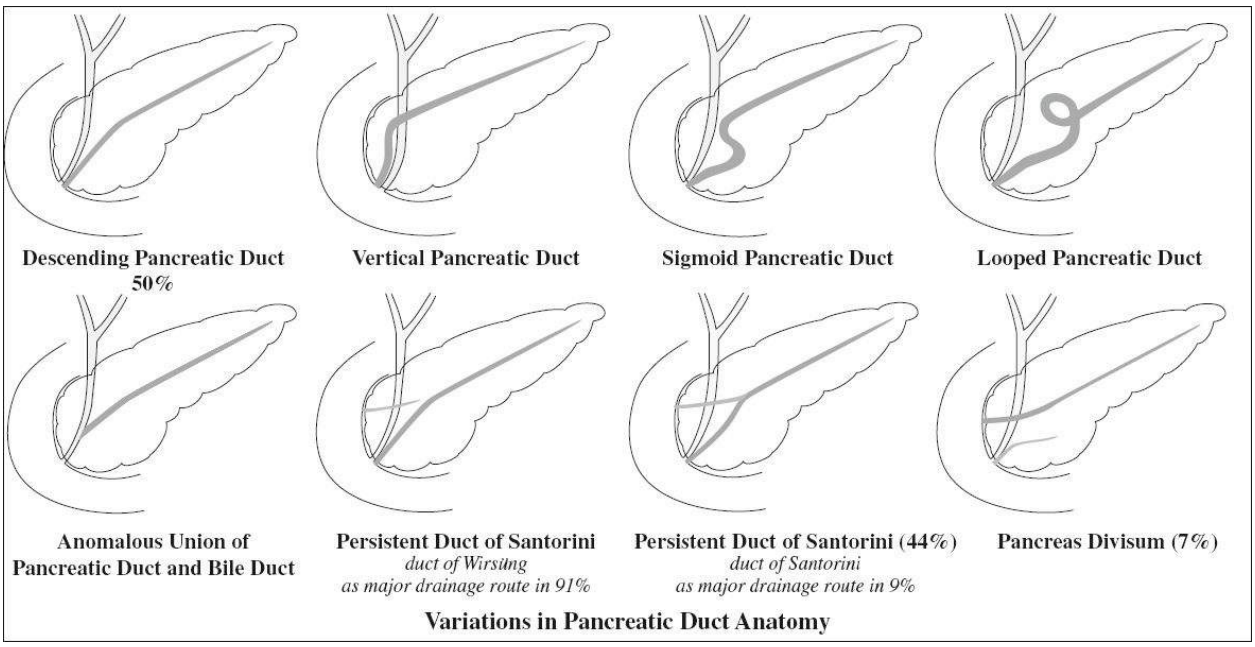
◊ Drainage of accessory pancreatic duct of Santorini

◊ Drainage of main pancreatic duct in 10%

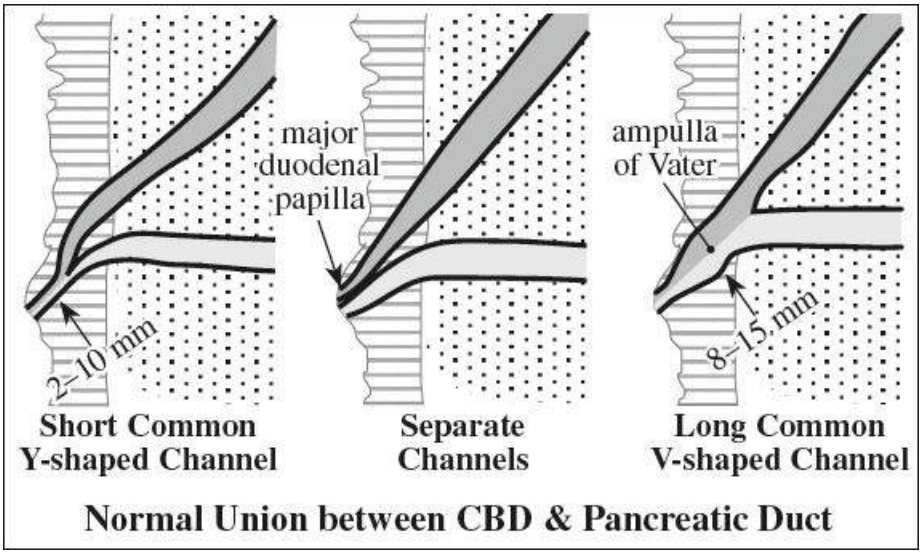
Pancreaticobiliary Junction Variants

A. Angle between CBD + pancreatic duct:
   (a) usually acute at 5°–30°
   (b) occasionally abnormal at up to 90°

B. **Anomalous pancreaticobiliary junction**



Variations in Pancreatic Duct Anatomy



Normal Union between CBD & Pancreatic Duct

= anomalous high junction outside duodenal wall beyond influence of sphincter of Boyden (1.5–3.2%)

(a) pancreatic duct inserting into CBD > 15 mm from entrance into duodenum
   › pancreaticobiliary reflux → choledochal web / cyst → gallbladder carcinoma
   › biliopancreatic reflux→ pancreatitis

(b) CBD inserting into pancreatic duct

Relationship of CBD to Pancreatic Head

1. CBD covered posteriorly by pancreatic tissue:
   (a) partially covered 51.5%
   (b) totally covered 30.0%
   (c) not covered at all 16.5%
2. CBD courses lateral to pancreatic head (occasionally)

SPLEEN

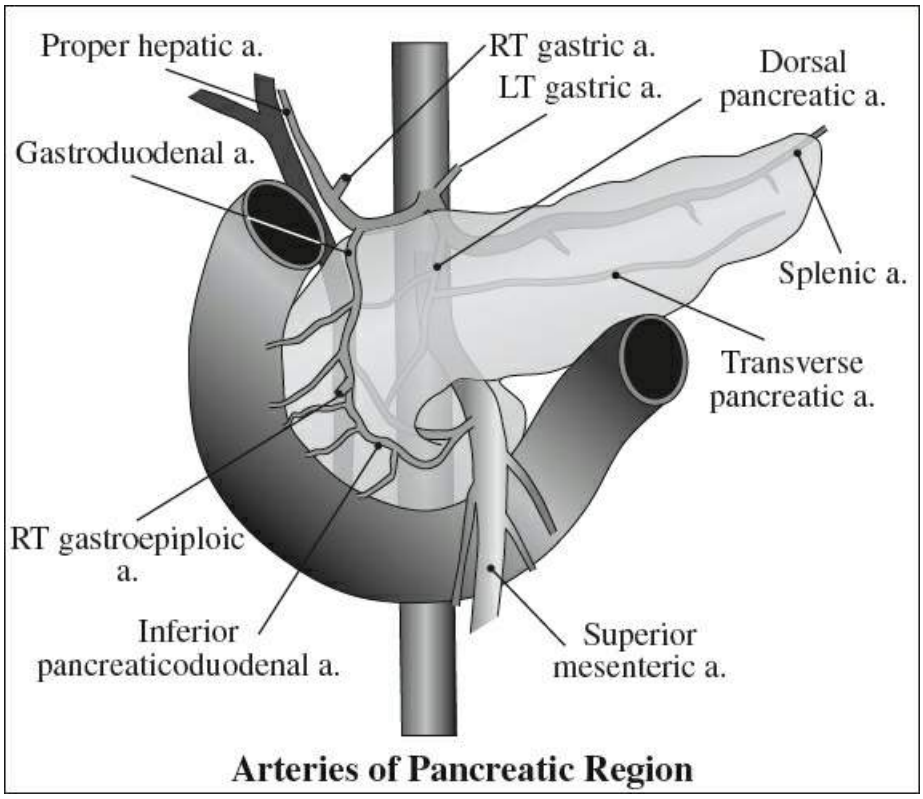
Size of Spleen

in adults: 12 cm length, 7–8 cm anteroposterior diameter, 3–4 cm thick; normal upper limit for splenic length correlates with height of individual (for men: 183 cm = 14.0 cm, 193 cm = 14.8 cm, 203 cm = 15.0 cm, 213 cm = 16.3 cm
for women; 173 cm = 12.6 cm, 183 cm = 13.2 cm; 188 cm = 13.4 cm, 198 cm = 14.0 cm)

in children: logarithmic increase in length with increasing age; formula for length = 5.7 + 0.31 x age (in years) cm

in infants (0–3 months of age): < 6.0 cm in length

Sonographic index: 0.524 x W x T x (ML + CCL)/2 normal range: 107–314/480 cm^3



Arteries of Pancreatic Region

W = width defined as greatest overall dimension from anterior to posterior on TRV image analog to CT

T = thickness as shortest distance between hilum and outer convex margin on same TRV image analog to CT

ML = maximum length from most medial to most lateral margin on LON/COR image

CCL = craniocaudal length from superior to inferior margin on same LON/COR image

Weight of Spleen

at birth: 15 g

in adults: 150 (range, 100–265) g

Estimated weight = splenic index = L × W × T × 0.55

Embryology of Spleen

› spleen arises from mesenchymal cells between layers of dorsal mesogastrium during 5th week GA

› splenic primordium differentiates→ forms capsule, connective tissue framework, splenic parenchyma

› major site of hematopoiesis until 28 weeks GA; retains capacity for extramedullary hematopoiesis well into adult life

√ spleen recognizable by 12th week GA ← as fusion of mesenchymal aggregates occurs

√ splenic clefts / notches / lobules may persist

√ accessory spleen (in up to 30% by autopsy)

Histology of Spleen

(a) RED PULP = numerous vascular sinuses

(b) WHITE PULP = lymphoid follicles + cells of RES

Development: ratio of white to red pulp increases with age + progressive antigenic stimulation

Imaging Characteristics of Spleen

A. CT ATTENUATION

(a) without enhancement:
40–60 HU (= 5–10 HU less than liver)

(b) with enhancement: normal heterogeneous enhancement during first minute after bolus injection ← different blood flow rates through the cords of the red + white pulp

√ arciform (alternating bands of high + low attenuation) / focal / diffuse heterogeneity

√ heterogeneity resolved in portal venous phase

B. MR SIGNAL INTENSITY directly related to ratio of white to red pulp

(a) neonate < 8 months of age:

√ T1WI- and T2WI-intensity: spleen < liver ← predominance of red pulp

DDx: hemochromatosis

(b) adult + older child:

√ T2WI-intensity: spleen > liver

√ T1WI-intensity: liver > spleen > muscle

IRON METABOLISM

Total body iron: 5 g

(a) functional iron: 4 g
Location: hemoglobin of RBCs, myoglobin of muscle, various enzymes (cytochromes)
(b) stored iron: 1 g
Location: hepatocytes, reticuloendothelial cells of liver (Kupffer cells) + spleen + bone marrow

Absorption: 1–2 mg/d via gut mucosa (10% of total amount ingested)
Recycling: through reuse of iron from senescent erythrocytes
Loss: 1–2 mg/d via epithelial desquamation, menstruation, other forms of blood loss
Excretion: none
Transport: bound to transferrin intravascularly
Deposition: stored as ferritin
(a) transferrin-transfer to:
hepatocytes, RBC precursors in erythron, parenchymal tissues (eg, muscle)
(b) phagocytosis by:
reticuloendothelial cells phagocytize senescent erythrocytes (= extravascular hemolysis); RBC iron stored as ferritin / released and bound to transferrin
◊ RES cells are incapable of storing excess iron!

Excess iron: leads to toxicity because it can catalyze the conversion of unstable hydrogen peroxide (H_2O_2) into free radicals hydroxyl (HO–) and superoxide O_2–) that cause damage to cell membranes, proteins, and DNA
Medullary erythropoiesis: requires about 20 mg/d of iron

ACCESSORY SPLEEN

= failure of coalescence of several small mesodermal buds in the dorsal mesogastrium that comprise the spleen

Prevalence: 10–30% of population; multiple (up to 6) in 10%

◊ Undergoes hypertrophy after splenectomy and is responsible for recurrence of hematologic disorders (idiopathic thrombocytopenic purpura, hereditary spherocytosis, acquired autoimmune hemolytic anemia, hypersplenism)

Location:

(a) near splenic hilum along the course of splenic vessels (most common)
(b) within layers of omentum (gastrosplenic ligament, other suspensory ligaments of spleen)
(c) anywhere in abdomen (eg, intrapancreatic, pelvis)
(d) attached to left ovary / testis = **splenogonadal fusion** ← close relationship between developing spleen + mesonephros + left gonadal anlage)

NUC (^{99m}Tc-sulfur colloid scan / spleen-specific ^{99m}Tc-denatured RBCs):

√ usually < 1 cm in diameter
√ < 10% identified when normal spleen present

Cx: disease recurrence ← hypertrophy of accessory spleen after splenectomy for hypersplenism

AMPULLARY TUMOR

= benign / malignant tumors arising from glandular epithelium of ampulla of Vater

Histo: (a) dysplastic epithelium in glandular / villous structures of tubular / villous adenoma
(b) carcinoma in situ
(c) invasive carcinoma often with desmoplastic reaction

Age: 6th–7th decade; M÷F = 2÷1

Path: average diameter of < 3 cm

- malaise, epigastric pain, weight loss
- intestinal bleeding (tumor ulceration)
- intermittent painless jaundice (ductal obstruction), pruritus
- gray "aluminum / silver-colored" stools (3%)
- chills, fever, RUQ pain (ascending cholangitis) in up to 20%
- endoscopy: tumor extending through orifice (63%), prominent papilla / submucosal mass (25%), not visualized (9%)

√ tumor often inapparent ← small size (more readily visualized with well-distended duodenum)

UGI:

√ indentation of duodenal lumen at papilla of Vater with filling defect > 1.5 cm
√ surface irregularity + deep barium-filled crevices in villous tumor

Biliary imaging:

√ dilatation of most distal segment of common bile duct
√ stenosis ← circumferential tumor growth around ampulla / desmoplastic reaction
√ irregular predominantly polypoid filling defect
√ ± pancreatic dilatation = "**double-duct" sign** (may be absent if tumor small / accessory pancreatic duct decompresses pancreatic system / main pancreatic duct drains into minor papilla)

DDx:

1. Periampullary duodenal adenoma / adenocarcinoma (usually larger lesion with significant intraduodenal extension)
2. Choledochocele (cystic lesion filling with biliary contrast)
3. Brunner gland tumor, pancreatic rest ("myoepithelial hamartoma"), leiomyoma, carcinoid (often production of somatostatin)
4. Duodenitis, pancreatitis
5. Stone impaction in ampulla

Ampullary Cancer

= AMPULLARY ADENOCARCINOMA
= rare malignancy arising in ampullary complex distal to confluence of the pancreatic duct and CBD

Incidence: 0.70÷100,000 men, 0.45÷100,000 women

TNM staging:

T1 : tumor confined to ampulla
T2 : tumor extending into duodenal wall
T3 : invasion of pancreas < 2 cm deep
T4 : invasion of pancreas > 2 cm deep

International Union Against Cancer Staging:

I = tumor confined to ampulla
II = tumor extension into duodenal wall / pancreas
III = regional lymph node involvement (Lnn stations around head + body of pancreas, anterior + posterior pancreaticoduodenal, pyloric, common bile duct, proximal mesenteric nodes)
IV = invasion of pancreas > 2 cm deep

• obstructive symptoms early in disease process

CT:
√ discrete nodular mass with irregular filling defect at distal margin of pancreaticobiliary junction (62%):
√ lobulated / infiltrating borders
√ hypoattenuating mass of ~ 40 HU
√ enhancement on arterial + portal venous phase

MR:
√ small nodular mass:
√ isointense relative to adjacent duodenal wall on T1WI
√ variable signal intensity on T2WI

√ hypointense relative to surrounding duodenum at arterial phase imaging
√ delayed contrast enhancement
√ irregular ductal wall thickening
√ bulging of duodenal papilla
√ intraductal polypoid mass
√ improved detection of ampullary carcinoma with DWI

MRCP:
√ filling defect / focal stricture at distal end of dilated CBD
√ "double-duct" sign = dilatation of biliary + pancreatic ducts (in 52%):
√ marked abrupt dilatation of distal CBD / pancreatic duct
√ NO signs of pancreatitis / pancreatic mass / stone
√ NO "double-duct" sign if separate duodenal openings for biliary and pancreatic ducts

Endoscopic US (most sensitive technique):
87% staging accuracy

Dx: papillotomy + deep biopsy (for duct dilatation WITHOUT visible mass)
Rx: Whipple procedure (= pancreaticoduodenectomy)
Prognosis: 28–70% 5-year survival for ampullary carcinomas (depending on stage)

Ampullary Adenoma

= uncommon premalignant lesion
Prevalence: 0.04–0.12% (at autopsy)
Associated with: familial adenomatous polyposis syndromes (eg, familial polyposis coli, Gardner syndrome) [100–200-fold risk], colon ca.
√ soft-tissue mass > 1 cm with irregular margin of ampulla
√ extrahepatic biliary duct + pancreatic duct dilatation
Cx: malignant transformation into adenocarcinoma

ANGIOSTRONGYLOSIS

= infection by nematode Angiostrongylus costaricensis
Countries: Central America, South America (sporadic cases)
Infection: ingestion of contaminated food
Cycle: parasite transmitted from snail to rat; ingestion of contaminated food by humans (= incidental host) → migration through lymphatic system → mesenteric veins + portal vein → liver
Histo: tissue eosinophilia, edema of intestinal wall, granulomas with eggs, larvae within blood vessels
• abdominal pain, anorexia, eosinophilia, fever
Location: terminal ileum, appendix, cecum

The adult worm resides inside mesenteric artery branches evoking an inflammatory response. Tissue samples show marked eosinophilic vasculitis.

√ nonspecific imaging findings:
√ bowel wall edema, occasionally, perforation
Dx: histopathologic findings

ANNULAR PANCREAS

= rare; 2nd most common congenital anomaly

Cause: failed / incomplete rotation of portion of ventral anlage → part of ventral pancreas passes posterior to descending duodenum → partial / complete encirclement of 2nd part of duodenum

Theory: (1) Adhesion of right anlage to duodenal wall (Lecco)
(2) Persistence of left ventral anlage (Baldwin)
(3) Tip of left ventral anlage adheres to duodenum

Types: (a) extramural = ventral pancreatic duct encircles duodenum and joins MPD
(b) intramural = pancreatic tissue intermingled with muscle fibers inside duodenal wall; small ducts drain directly into duodenum

Prevalence: 5–15÷100,000 (autoptic); 1÷250 (ERCP)

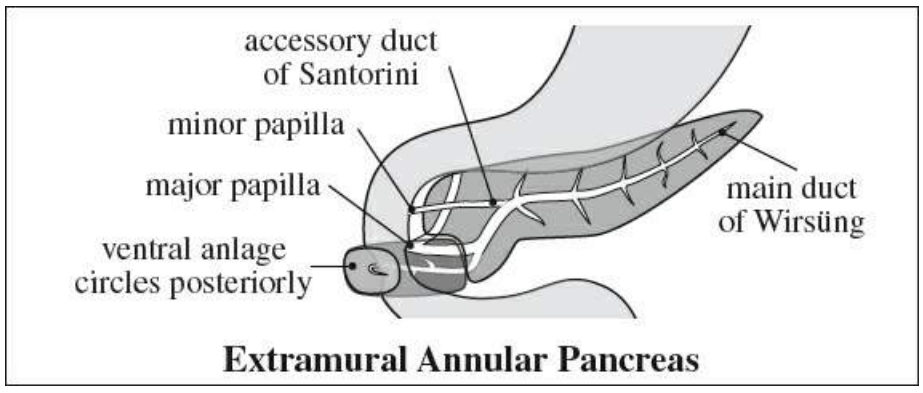
Age at discovery: during childhood (52%) + 4th–5th decade of adulthood (48%) = bimodal distribution

Associated with: other congenital anomalies (in 75%) like
esophageal atresia, tracheoesophageal fistula, duodenal atresia / stenosis, duodenal diaphragm, imperforate anus, malrotation, Down syndrome (in child);
pancreas divisum + bile duct carcinoma (in adult)

Location: 2nd portion of duodenum (85%);
1st / 3rd portion of duodenum (15%)

- mostly asymptomatic with incidental discovery
- neonate : persistent vomiting ← "gastric outlet" obstruction (in 10%)
- adult : nausea, vomiting (60%), abdominal pain (70%), jaundice (50%), hematemesis (10%); symptoms of peptic ulcer disease (25%) / acute pancreatitis (13%)

√ "double bubble" = dilated duodenal bulb (= smaller distal bubble) + distended stomach (= larger proximal bubble)
√ proximal duodenal dilatation
OB–US: √polyhydramnios



Extramural Annular Pancreas

UGI:
√ eccentric narrowing with lateral notching + medial retraction of 2nd part of duodenum
√ concentric ringlike narrowing of mid-descending duodenum between major and minor papilla

√ reverse peristalsis, pyloric incompetency

CT:

√ enlargement of pancreatic head

√ pancreatic tissue encircling descending duodenum

ERCP (most specific) / MR pancreatography (MRCP):

√ normally located main duct in pancreatic body + tail

√ small aberrant duct encircles duodenum (= originates anterior to + passes posterior to duodenum) communicating with:

› main duct of Wirsüng (in 85%)

› accessory duct of Santorini

› intrapancreatic common bile duct

Cx: in adults increased incidence of

(1) Periampullary peptic ulcers

(2) Pancreatitis (15–20%): usually confined to pancreatic head and annulus

(3) Duodenal obstruction (10%)

Rx: gastrojejunostomy / duodenojejunostomy

AGENESIS OF DORSAL PANCREAS

Variation: complete (extremely rare) / partial

May be associated with: heterotaxia (abnormal situs, polysplenia), intestinal malrotation

• nonspecific abdominal pain ← ? pancreatitis

• diabetes (in many)

√ short round pancreatic head adjacent to duodenum

√ absence of pancreatic neck, body, tail, duct of Santorini, minor duodenal papilla

DDx: pancreatic carcinoma with upstream pancreatic atrophy

ASCARIASIS

Organism: nematode (roundworm) Ascaris lumbricoides, 15–50 cm long + 3–6 mm thick adult worm; life span of 1 year

◊ 3rd most common helminthic infection (after hookworm + trichuriasis)

Endemic: in tropical + subtropical areas

(a) in parts of Africa (along Gulf Coast, Nigeria), Southeast Asia, China, South America: 90%

(b) in USA: 12% in blacks, 1% in whites; endemic in Appalachian range + Ozark Mountains

Prevalence: most common cosmopolitan parasitic infection (25% of world population infected); 1 billion humans harbor the roundworm [*cosmos* , Greek = world; *polites* , Greek = citizen]

Infection: fecal-oral route

Cycle:

contaminated water / soil / vegetable → ingestion of eggs; eggs hatch (= release larvae) in duodenum → larvae penetrate intestinal wall + migrate into mesenteric lymphatics and venules;→ carried to lungs via right heart + pulmonary artery; → mature in pulmonary capillary bed to 2–3 mm length → burrow into alveoli → ascend in bronchial tree; through

swallowing again reach small intestine → mature in jejunum into adult worms within 2.5 months (worms may migrate and settle in biliary + pancreatic ducts) → production of 200,000 eggs daily leave body by fecal route

Age: children 1–10 years of age

- pulmonary + intestinal symptoms:
  - fever, cough, expectoration (hematemesis / pneumonitis)
  - appendicitis
- biliary symptoms:
  - jaundice (if bile ducts infested); abnormal liver function tests
  - biliary colic ← Ascaris secretions induce spasm of sphincter of Oddi
- eosinophilia:
  - hypereosinophilia only present during acute stage of larval migration; Löffler syndrome = pulmonary eosinophilia

Pancreatic / biliary manifestations occur when the adult worm migrates from small bowel into the main pancreatic duct / biliary tree. Related complications are biliary colic, gallstone formation, cholecystitis, liver abscess, and pancreatitis.

Location: jejunum > ileum (99%), duodenum, stomach, CBD, pancreatic duct

Barium study:

√ 15–35 cm long elongated tubular filling defects
√ whirled appearance, occasionally in coiled clusters ("bolus of worms")
√ ± barium-opacification of enteric canal within nematode

CT:

√ worms are hyperattenuating relative to bile

MR:

√ worms exhibit low signal intensity on T2WI
√ fluid-filled GI tract of worms hyperintense on T2WI

CXR:

√ migratory patchy alveolar infiltrates that characteristically clear within 10 days
√ lobar consolidation + alveolar hemorrhage

Cx: (1) Intestinal obstruction ← massive infestation
(2) Bowel perforation
(3) Intermittent biliary obstruction with acute cholangitis, cholecystitis, pancreatitis
(4) Recurrent pyogenic cholangitis
(5) Liver abscess (rare)
(6) Granulomatous stricture of extrahepatic bile ducts (rare)

Dx: fecal examination (eggs in stool), larvae in sputum

Rx: mebendazole

Ascaris-induced Pancreatitis

= occasional migration of worm through ampulla of Vater into pancreaticobiliary tree via abnormally open ampullary orifice ← preexisting biliary tract disease / endoscopic sphincterotomy

◊ Most common parasitic cause of pancreatitis!

Mean age: 35–42 years; M÷F = 1÷3
US:
√ biliary / pancreatic ductal dilatation
√ pancreatic + peripancreatic inflammation
√ echogenic tubular structure without acoustic shadowing within bile / pancreatic duct with 2–4-mm wide central sonolucent line (= worm's digestive tract)
√ worm may slowly move at real-time imaging
Cx: biliary colic, cholangitis, acute cholecystitis, hepatic abscess, acute pancreatitis, septicemia

AUTOSOMAL DOMINANT POLYCYSTIC DISEASE

= POLYCYSTIC LIVER DISEASE
= part of spectrum of fibropolycystic liver disease
Etiology: biliary ductal plate malformation at the level of the small intrahepatic bile ducts with progressive dilation of the abnormal noncommunicating bile ducts of biliary hamartomas
M÷F = 1÷2
Associated with: polycystic kidney disease (in 50%)
• upper abdominal pain + distension from hepatomegaly
√ enlarged diffusely cystic liver: cysts of 1 mm – 12 cm in diameter
√ calcifications of cyst wall ← hemorrhage / infection
√ ± diffuse dilatation of intra- and extrahepatic bile ducts
Cx: infection, compression, bleeding, rupture of cysts

BANTI SYNDROME

= NONCIRRHOTIC IDIOPATHIC PORTAL HYPERTENSION = NONCIRRHOTIC PORTAL FIBROSIS = HEPATOPORTAL SCLEROSIS
= syndrome characterized by
(1) Splenomegaly
(2) Hypersplenism
(3) Portal hypertension
Etiology: increased portal vascular resistance possibly ← portal fibrosis + obliterative venopathy of intrahepatic portal branches
Histo: slight portal fibrosis, dilatation of sinusoids, intimal thickening with eccentric sclerosis of peripheral portal vein walls
Age: middle-aged women; rare in America + Europe; common in India + Japan
• elevated portal vein pressure (without cirrhosis, parasites, venous occlusion)
• normal liver function tests, cytopenia (← hypersplenism)
• normal / slightly elevated hepatic venous wedge pressure
√ esophageal varices
√ patent hepatic veins
√ patent extrahepatic portal vein + multiple collaterals
Prognosis: 90% 5-year survival; 55% 30-year survival

BILE LEAK

Posttraumatic bile leaks / biliary tract injuries related to recent surgery are easily overlooked due to
(a) nonspecific imaging findings, especially in the setting of multiorgan injury
(b) even less specific clinical findings
(c) difficulties to discern from other postoperative fluid collections.

Cause:
1. Post orthotopic liver transplantation
2. Pancreaticoduodenectomy
3. Hepatic or biliary surgery
4. Cholecystectomy (2%): laparoscopic > open
5. Radiofrequency ablation, percutaneous biliary drainage
6. Transcatheter arterial chemoembolization

Prevalence: 7% after laparoscopic cholecystectomy
Time of onset: during 1st postoperative week
• asymptomatic subclinical bile leak (7%)
• abdominal pain, fever, nausea, vomiting
Location: cystic duct stump / ducts of Luschka (= subvesical / accessory biliary ducts)
Cholescintigraphy:
√ DIAGNOSTIC but with poor anatomic definition and spatial resolution necessitating a secondary diagnostic evaluation (especially ERCP)
MRCP with hepatobiliary contrast medium:
Agents: gadoxetate disodium (Eovist®) with 50% liver excretion 20 minutes after administration; gadobenate dimeglumine (MultiHance®) with 5% liver excretion 60–120 minutes after administration
√ dynamic biliary imaging during hepatobiliary phase with improved characterization of biliary anatomy
ERCP:
√ depicts peripheral sites of leakage that may not be filled with retrograde injection
Cx: (1) Biloma= encapsulated extrabiliary bile collection
(2) Bile peritonitis (days to weeks after initial trauma)
Prognosis: high morbidity + mortality rates if undiagnosed
Rx: endoscopic / surgical management

BILIARY CYSTADENOCARCINOMA

= BILE DUCT CYSTADENOCARCINOMA
= rare malignant multilocular cystic tumor originating from biliary cystadenoma
Histo: (a) with ovarian stroma (good prognosis), in females only
(b) without ovarian stroma (poor prognosis)
• hemorrhagic internal fluid
√ nodularity with septations are suggestive of malignancy
√ coarse calcifications
DDx: NO image differentiation from biliary cystadenoma

BILIARY CYSTADENOMA

= BILE DUCT CYSTADENOMA

= very rare benign multilocular cystic tumor originating in bile ducts as premalignant form of biliary cystadenocarcinoma; probably deriving from ectopic nests of primitive biliary tissue

Frequency: 4.6% of all intrahepatic cysts of bile duct origin

Age: > 30 years (82%), peak incidence in 5th decade; M÷F = 1÷4; predominantly in Caucasians

Path: multilocular cystic tumor containing proteinaceous fluid with well-defined thick capsule

Histo: single layer of cuboidal / tall columnar mucin-secreting biliary-type epithelium with papillary projections, subepithelial stroma resembling that of the ovary

◊ Similar to mucinous cystic tumors of pancreas + ovary

Location: intrahepatic÷extrahepatic bile ducts = 85÷15; right lobe (48%); left lobe (20–35%); both lobes (15–30%); gallbladder (rare)

- chronic abdominal pain
- dyspepsia, anorexia, nausea + vomiting, jaundice
- abdominal swelling with palpable mass (90%)

Size: 1.5–35 cm (reportedly up to 11 liters of liquid content)

√ well-defined cystic mass containing clear / cloudy, serous / mucinous / gelatinous, purulent / hemorrhagic / bilious fluid with hemosiderin / cholesterol / necrosis

√ thick fibrous capsule

√ papillary excrescences + mural nodules

√ septations between cysts

US:

√ ovoid multiloculated anechoic mass with highly echogenic septations / papillary growths

√ may contain fluid-fluid levels

CT:

√ multiloculated mass of near water density

√ contrast enhancement in wall + internal septa

MR:

√ locules with variable SI on T1WI + T2WI depending on their protein content

Angio:

√ avascular mass with small clusters of peripheral abnormal vessels

√ stretching + displacement of vessels

√ thin subtle blush of neovascularity in septa + wall

Cx: (1) Malignant transformation into cystadenocarcinoma (indicated by invasion of capsule)

(2) Rupture into peritoneum / retroperitoneum

Rx: surgical resection (recurrence common)

DDx: biliary cystadenocarcinoma, liver abscess, echinococcal cyst, cystic mesenchymal hamartoma (children + young adults), undifferentiated sarcoma (children + young adults), necrotic hepatic metastasis, cystic primary hepatocellular carcinoma

BILIARY-ENTERIC FISTULA

Frequency: 5% at cholecystectomy; 0.5% at autopsy

Etiology: cholelithiasis (90%), acute / chronic cholecystitis, biliary tract carcinoma, regional invasive neoplasm, diverticulitis, inflammatory bowel disease, peptic ulcer disease, echinococcal cyst, trauma, congenital communication

Communication with:

duodenum (70%), colon (26%), stomach (4%), jejunum, ileum, hepatic artery, portal vein (caused death of Ignatius de Loyola), bronchial tree, pericardium, renal pelvis, ureter, urinary bladder, vagina, ovary

A. CHOLECYSTODUODENAL FISTULA (51–80%)
   1. Perforated gallstone (90%):
      associated with gallstone ileus in 20%
   2. Perforated duodenal ulcer (10%)
   3. Surgical anastomosis
   4. Gallbladder carcinoma

B. CHOLECYSTOCOLIC FISTULA (13–21%)

C. CHOLEDOCHODUODENAL FISTULA (13–19%)
   due to perforated duodenal ulcer disease

D. MULTIPLE FISTULAE (7%)

√ pneumobilia = branching tubular radiolucencies, more prominent centrally within the liver
√ barium filling of biliary tree
√ shrunken gallbladder mimicking pseudodiverticulum of duodenal bulb
√ multiple hyperechoic foci with dirty shadowing

DDx: patulous sphincter of Oddi, ascending cholangitis, surgery (choledochoduodenostomy, cholecystojejunostomy, sphincterotomy)

BUDD-CHIARI SYNDROME

= syndrome of global / segmental hepatic venous outflow obstruction at level of hepatic veins / IVC

Cause:

A. IDIOPATHIC (66%)

B. THROMBOSIS
   (a) myeloproliferative disorder:
   polycythemia rubra vera (⅓), essential thrombocytosis
   (b) hypercoagulable state:
   mnemonic: 6 P's
   Paroxysmal nocturnal hemoglobulinuria (12%)
   Platelets (thrombocytosis)
   Pill (birth control pills)
   Pregnancy + **P**ostpartum state
   Polycythemia rubra vera
   Protein C deficiency
   also: sickle cell disease
   (c) injury to vessel wall:
   phlebitis, trauma, hepatic radiation injury, chemotherapeutic + immunosuppressive drugs in patient with bone marrow transplant, venoocclusive disease from

pyrrolizidine alkaloids (Senecio) found in medicinal bush teas in Jamaica

C. NONTHROMBOTIC OBSTRUCTION
  (a) compression or invasion of IVC / hepatic veins:
    › benign: cirrhosis, hematoma, abscess
    › malignant: renal cell carcinoma, adrenal carcinoma, hepatoma, cholangiocarcinoma, metastasis, primary leiomyosarcoma of IVC, Hodgkin disease
  (b) membranous obstruction of suprahepatic IVC
    = IVC diaphragm (believed to be a congenital web / acquired lesion from long-standing IVC thrombosis); common in Oriental + Indian population (South Africa, India, Japan, Korea, Israel); very rare in Western countries
  (c) right atrial tumor: atrial myxoma
  (d) constrictive pericarditis
  (e) right heart failure

D. SYSTEMIC INFLAMMATION / INFECTION
  1. Inflammatory bowel disease
  2. Behçet syndrome

Pathophysiology:
hepatic venous thrombosis → elevation of sinusoidal pressure → diminished / reversed portal venous flow → centrilobular congestion → necrosis + atrophy
(a) acute form (= no time for development of collateral veins) → rapid development of hepatic necrosis
(b) subacute / chronic form (venous thrombosis incomplete) → peripheral atrophy + preservation of central region with caudate lobe hypertrophy (drained by accessory veins)

In 25% associated with: portal vein thrombosis
Age: all ages; M < F

- right upper quadrant pain, lower-extremity edema
- shortness of breath ← decreased cardiac return
- nonspecific elevated transaminases, jaundice

Location:

Type I	:	occlusion of IVC ± hepatic veins
Type II	:	occlusion of major hepatic veins ± IVC
Type III	:	occlusion of small centrilobar venules

√ gallbladder wall thickening > 6 mm
√ portal vein diameter > 12 mm (in adults), > 8 mm (in children)
MR:
√ reduction in caliber / complete absence of hepatic veins
√ "comma" sign = multiple comma-shaped intrahepatic flow voids ← intrahepatic collaterals
√ hyperintense thrombi
Doppler US (85–100% sensitive, 85% specific):
√ one / more major hepatic veins reduced in size to < 3 mm / filled with thrombus / not visualized
√ stenoses of hepatic veins
√ communicating intrahepatic venous collaterals

√ decreased / absent / reversed blood flow in hepatic veins
√ flat flow / loss of cardiac modulation in hepatic veins
√ demodulated portal venous flow = disappearance of portal vein velocity variations with breathing
√ slow flow of < 11 cm/sec / hepatofugal flow in portal vein
√ portal vein congestion index > 0.1 [cm • sec] (= ratio between cross-sectional area [cm^2] and blood flow velocity [cm/sec])
√ portal vein thrombosis (20%)
√ compression of IVC by enlarged liver / caudate lobe
√ sluggish / reversed / absent blood flow within IVC
√ hepatic artery resistive index > 0.75

NUC (^{99m}Tc-sulfur colloid):
√ central region of normal activity (= hot caudate lobe ← venous drainage of hypertrophied caudate lobe into IVC by separate vein) surrounded by greatly diminished activity
√ colloid shift to spleen + bone marrow
√ wedge-shaped focal peripheral defects

Angio (inferior venocavography, hepatic venography):
√ absence of main hepatic veins
√ spider web pattern of collateral + recanalized veins
√ high-pressure gradient between infra- and suprahepatic portion of IVC ← enlarged liver
√ stretching + draping of intrahepatic arteries with hepatomegaly
√ inhomogeneous prolonged intense hepatogram with fine mottling
√ large lakes of sinusoidal contrast accumulation

Portography:
√ central hepatic enhancement (normal hepatopetal flow)
√ reversed portal flow in liver periphery (supplied only by hepatic artery)
√ bidirectional / hepatofugal main portal vein flow

Dx: liver biopsy

Rx: control of ascites with diuretics + sodium restriction; anticoagulation, thrombolytic therapy, surgery / balloon dilatation (depending on etiology); transjugular portosystemic shunt (in preparation for) orthotopic liver transplantation (for advanced cases)

Acute Budd-Chiari Syndrome (⅓)

◊ Caudate lobe has not had time to hypertrophy!

• TRIAD:
  • rapid onset of abdominal pain (liver congestion)
  • insidious onset of intractable ascites
  • hepatomegaly without derangement of liver function
• jaundice

√ enlarged morphologically normal liver
√ splenomegaly
√ ascites (97%)

NECT:
√ diffusely hypoattenuating liver
√ IVC + hepatic veins:

√ narrowed lumina (without thrombus)
√ hyperattenuating lumina containing thrombus (in 18–53%)
√ enlarged inferior right hepatic vein (18%)

CECT:

√ normal early enhancement of caudate lobe and central portion around IVC + decreased enhancement of peripheral liver (← portal and sinusoidal stasis) during arterial phase
√ "flip-flop" pattern during portal venous phase:
√ decreased attenuation (washout) of enhancing central areas
√ increasing patchy inhomogeneous enhancement in liver periphery ← contrast inflow from capsular veins

MR:

√ peripheral liver parenchyma of moderately low SI on T1WI + moderately high SI on T2WI compared with central portion
√ diminished + mottled peripheral enhancement

Subacute Budd-Chiari Syndrome

• portal hypertension, varying degrees of liver decompensation
√ diffuse peripheral hypoattenuation ← hepatocellular necrosis + steatosis

Chronic Budd-Chiari Syndrome (²/₃)

• insidious onset of jaundice, intractable ascites
• portal hypertension, variceal bleeding
• renal impairment (in 50%)
√ dysmorphic liver:
√ nonsegmental / lobar atrophy of affected liver (← extensive fibrosis) with diminished attenuation before + after contrast administration
√ compensatory hypertrophy of caudate lobe (88%) + central parenchymal segments of right lobe + medial segment of left lobe:
√ width of caudate ÷ right lobe ≥ 0.55 (DDx: cirrhosis)
√ visualization of collateral pathways
(a) portosystemic: paraumbilical vein
(b) bypassing IVC: azygos, hemiazygos
(c) intrahepatic collateral veins (almost DIAGNOSTIC): right / middle hepatic vein → inferior right hepatic vein; hepatic vein → portal vein
√ development of 1–4 cm regenerative nodules (in areas of adequate blood supply)
√ ascites

CECT:

√ invisible IVC ± hepatic veins ← collapse / diminished flow rate:
√ nonvisualization of hepatic veins (75%) / vein diameter < 3 mm (measured 2 cm from IVC)
√ ± narrowing / obstruction of intrahepatic IVC
√ progressive heterogeneous patchy enhancement radiating outward from major portal vessels
√ "reticulated mosaic" enhancement = diffuse patchy lobular enhancement separated by irregular linear areas of low density in central area

√ delayed homogeneous enhancement of entire liver after several minutes
√ reversed portal venous blood flow ← increased postsinusoidal pressure produced by hepatic venous obstruction / rarely infarcts

Color Doppler:
√ PATHOGNOMONIC "bicolored" hepatic veins ← intrahepatic collateral pathways

MR:
√ absence of flow within hepatic veins
√ minimal differences in SI between central and peripheral portions of liver
√ intrahepatic collateral vessels

CANDIDIASIS OF LIVER

= almost exclusively seen in immunocompromised patients (acute leukemia, chronic granulomatous disease of childhood, renal transplant, chemotherapy for myeloproliferative disorders)

Prevalence: at time of autopsy in 50–70% of acute leukemia, in 50% of lymphoma patients
◊ Most common systemic fungal infection in immunocompromised patients!

• abdominal pain, elevated alkaline phosphatase
• persistent fever in neutropenic patient whose leukocyte count is returning to normal
√ hepatomegaly
√ "target" / "bull's-eye" sign = multiple small hypoechoic / hypoattenuating masses with centers of increased echogenicity / attenuation distributed throughout liver
◊ Bull's-eye lesion becomes visible only when neutropenia resolves!
√ hyperintense lesions on T2WI

NUC:
√ uniform uptake / focal photopenic areas
√ diminished ^{67}Ga uptake

Dx: biopsy evidence of yeast / pseudohyphae in central necrotic portion of lesion

DDx: metastases, lymphoma, leukemia, sarcoidosis, septic emboli, other infections (MAI, CMV), Kaposi sarcoma

CAROLI DISEASE

[Jacques Caroli (1902–1979), surgeon in Paris, France]

= COMMUNICATING CAVERNOUS ECTASIA OF INTRAHEPATIC BILE DUCTS

◊ Original classification as Type V choledochal cyst (Todani classification) is NO longer accepted!

= rare congenital autosomal recessive disorder characterized by multifocal segmental saccular cystic dilatation of large intrahepatic bile ducts

Etiology: (a) ductal plate malformation
(b) ? perinatal hepatic artery occlusion
(c) ? hypoplasia / aplasia of fibromuscular wall components

Path: communication with biliary tree

Age: childhood + 2nd–3rd decade, occasionally in infancy; M÷F = 1÷1

Associated with: benign renal tubular ectasia, medullary sponge kidney (in 80%), infantile polycystic kidney disease, choledochal cyst (rare), congenital hepatic

fibrosis, cholangiocarcinoma

- recurrent cramplike right upper quadrant pain
- bouts of fever ← cholangitis ← bile stasis
- transient jaundice ← bile stasis ← blocking stone / sludge
- cirrhosis / portal hypertension (very rare)

Location: diffuse / segmental or lobar

Types:

(1) pure form (type 1): attacks of cholangitis + intraductal stone formation

(2) complex form (type 2) – more common: associated with hepatic fibrosis / other ductal plate malformations

√ multiple small localized / diffusely scattered cysts converging toward porta hepatis communicating with bile ducts

√ beaded ducts with alternating dilated and strictured segments

√ sludge / pus / calculi in dilated ducts

CT / US/ MR:

√ **"central dot" sign** = enhancing fibrovascular bundle of portal vein radicles completely surrounded by cystically altered dilated intrahepatic bile ducts (IBD)

Cholangiography and MRCP (DIAGNOSTIC):

√ segmental saccular > fusiform beaded dilatation of intrahepatic bile ducts extending to periphery of liver up to 5 cm in diameter

√ ± filling defects ← intraductal calculi

√ bridge formation across dilated lumina

√ intraluminal bulbar protrusions

√ frequent ectasia of extrahepatic ducts + CBD

Dx: ERCP, direct cholangiography, MRCP

Cx: (1) Bile stasis → sludge + recurrent cholangitis

(2) Biliary calculi (predominantly bilirubin)

(3) Liver abscess

(4) Septicemia

(5) Increased risk of cholangiocarcinoma (7%)

DDx: (1) Primary sclerosing cholangitis (multiple irregular strictures of intra- and extrahepatic bile ducts, pseudotumoral enlargement of caudate lobe, lobulated liver contour)

(2) Recurrent pyogenic cholangitis (nonsaccular dilatation of central intra- and extrahepatic bile ducts, bile ducts tapered toward periphery)

(3) Autosomal dominant polycystic liver disease (no communication with bile ducts)

(4) Biliary hamartomas (no communication with bile ducts)

(5) Microabscesses

(6) Biliary papillomatosis

Caroli Syndrome

= both features of Caroli disease and congenital hepatic fibrosis

= arrest of bile duct remodeling during embryogenesis + during later development of more

peripheral biliary ramifications
- hematemesis ← ruptured esophageal varices ← portal hypertension

CHOLANGIOCARCINOMA

= primary malignancy arising from cholangiocyte of biliary tract

Frequency: 0.5–1.0% of all cancers;
10% of hepatic primary malignancies
◊ 2nd most common primary hepatobiliary cancer after HCC!

Anatomic classification:

A. INTRAHEPATIC (PERIPHERAL)
peripheral / distal to 2nd-order branches 8–13%

B. PERIHILAR (CENTRAL) = Klatskin tumor
at bifurcation / 1st-order branches
confluence of hepatic ducts 10–26%

C. EXTRAHEPATIC
common hepatic duct 14–37%
proximal CBD 15–30%
distal CBD 30–50%
cystic duct 6%

D. GALLBLADDER

Path (Japanese Liver Cancer Study Group):

(a) **mass-forming** (= nodular / exophytic) type:
commonly in peripheral cholangiocarcinoma
- homogeneous sclerotic mass typically without hemorrhage / necrosis
- central portion with variable degree of fibrosis + coagulative necrosis with scanty tumor cells

(b) **periductal infiltrating** / diffuse type:
commonly in hilar + extrahepatic cholangiocarcinoma
- elongated spiculated / branching growth along dilated / narrowed bile duct

(c) **intraductal tubular polypoid** / papillary type:
- infrequent slow growing tumor with relatively favorable prognosis
- frequently associated with marked mucin production

(d) **mixed** = combination of mass-forming + periductal

Histo: well / moderately / poorly differentiated ductal adenocarcinoma (most common) / papillary / mucinous / signet-ring cell / mucoepidermoid / adenosquamous adenocarcinoma with abundant fibrous stroma

Unusual manifestation:
1. Mucin-hypersecreting cholangiocarcinoma
   √ severe diffuse dilatation of intra- and extrahepatic bile ducts proximal + distal to tumor
2. Squamous cell carcinoma
   = metaplastic transformation of adenocarcinoma

Genetics: mutation in p53 tumor suppressor gene + k-ras gene

Peak prevalence: 7th decade; M > F

Predisposed: conditions causing chronic biliary inflammation

(1) Inflammatory bowel disease (10 x increased risk); incidence of 0.4–1.4% in ulcerative colitis; latent period of 15 years; tumors usually multicentric + predominantly in extrahepatic sites; GB involved in 15% (simultaneous presence of gallstones is rare)
(2) Biliary lithiasis: cholecystolithiasis (20–50%), hepatolithiasis (5–10%)
(3) Primary sclerosing cholangitis (10–15%)
(4) Infection with liver flukes: Opisthorchis viverrini and Clonorchis sinensis infestation (Far East)
    ◊ Most common cause worldwide!
(5) Recurrent pyogenic cholangitis = hepatolithiasis
(6) Viral infection: HIV, hepatitis B virus, hepatitis C virus, Epstein-Barr virus
(7) Congenital biliary cystic disease: choledochal cyst / congenital hepatic cyst / congenital biliary atresia
(8) Anomalous pancreaticobiliary junction
(9) Ductal plate malformation:
    › Biliary hamartoma
    › Autosomal dominant polycystic disease
    › Congenital hepatic fibrosis
    › Caroli disease ← chronic biliary stasis
(10) Papillomatosis of bile ducts
(11) Choledochoenteric anastomosis
(12) History of other malignancy (10%)
(13) Toxins: thorotrast exposure, polyvinyl chloride
(14) Heavy alcohol consumption
(15) Alpha−1 antitrypsin deficiency
(16) Familial polyposis

MR:

√ moderate peripheral enhancement followed by progressive centripetal enhancement
√ single / multifocal biliary strictures
√ focal / diffuse ductal thickening ± contrast enhancement
√ intraductal polypoid growth

Prognosis: median survival of 7 months, 0–10% 5-year survival

Extrahepatic Cholangiocarcinoma

= BILE DUCT CARCINOMA

Age peak: 6th–7th decade; M÷F = 3÷2

Incidence: 1÷100,000; < 0.5% of autopsies; 90% of all cholangiocarcinomas; more frequent in Far East

Histo: well-differentiated sclerosing adenocarcinoma (2/3), anaplastic carcinoma (11%), cystadenocarcinoma, adenoacanthoma, malignant adenoma, squamous cell carcinoma, epidermoid carcinoma, leiomyosarcoma

- gradual onset of fluctuating painless jaundice
- cholangitis (10%), weight loss, fatigability
- intermittent epigastric pain, enlarged tender liver
- elevated bilirubin + alkaline phosphatase

Growth pattern:

(1) Infiltrating / sclerosing type (94%)
  √ ductal wall thickening + sudden luminal obliteration

(2) Papillary / tubular polypoid type (5–6%)
  √ intraductal polypoid mass with irregular margin ± diffuse marked duct ectasia (mucin production)

Spread: (a) lymphatic spread: cystic + CBD nodes (> 32%), celiac nodes (> 16%), peripancreatic nodes, superior mesenteric nodes

(b) infiltration of liver (23%)

(c) peritoneal seeding (9%)

(d) hematogenous (extremely rare): liver, peritoneum, lung

UGI:

√ infiltration / indentation of stomach / duodenum

Cholangiography (PTC or ERC best modality to depict bile duct neoplasm):

√ prestenotic diffuse / focal biliary dilatation (100%)

√ progression of ductal stricture (100%)

√ frequently long / rarely short concentric focal stricture with irregular margins (in infiltrating type):
  √ nipple / rattail termination

√ exophytic intraductal tumor mass (46%), 2–5 mm in diameter

US / CT:

√ mural thickening / small encircling mass of bile duct at point of obstruction (in 21% visible on US, in 40% visible on CT):
  √ focal or diffuse stricture / complete obstruction of bile ducts
  √ dilatation of intrahepatic ducts without extrahepatic duct dilatation

√ infiltrating tumor visible in 22% on CT as highly attenuating lesion, in 13% on US

√ exophytic tumor: visible on CT as hypoattenuating mass in 100%, in 29% on US

√ polypoid intraluminal tumor: visible on US as isoechoic mass within surrounding bile in 100%, in 25% on CT

√ regional lymph node enlargement

CECT:

√ hyperattenuating lesion at delayed imaging ← delayed accumulation + washout of fibrous center

MR:

√ hypointense relative to liver parenchyma on T1WI

√ hyperintense relative to liver parenchyma on T2WI

√ more conspicuous on fat-suppressed MR

Angiography:

√ hypervascular tumor with neovascularity (50%)

√ arterioarterial collaterals along the course of bile ducts associated with arterial obstruction

√ poor / absent tumor stain

√ displacement / encasement / occlusion of hepatic artery + portal vein

Cx: (1) Obstruction leading to biliary cirrhosis

(2) Hepatomegaly
(3) Intrahepatic (subdiaphragmatic, perihepatic) abscess → septicemia
(4) Biliary peritonitis
(5) Portal vein invasion

Dx: endoscopic brush biopsy (30–85% sensitive)

Prognosis: median survival of 5 months; 1.6% 5-year survival; 39% 5-year survival for carcinoma of papilla of Vater

DDx: periportal lymphangitic metastasis (no ductal dilatation, diffuse involvement of both sides of liver); sclerosing cholangitis, AIDS cholangitis, benign stricture, chronic pancreatitis, edematous papilla, idiopathic inflammation of CBD

Intrahepatic Cholangiocarcinoma

= CHOLANGIOCELLULAR CARCINOMA

Frequency: 2nd most common primary hepatic tumor after hepatoma; ⅓ of all malignancies originating in the liver; 8–13% of all cholangiocarcinomas

Histo: adenocarcinoma arising from the epithelium of a small intrahepatic bile duct with prominent desmoplastic reaction (fibrosis); ± mucin and calcifications

Average age: 50–60 years; M > F

- abdominal pain (47%); painless jaundice (12%)
- palpable mass (18%), weight loss (18%)

Spread: (a) local extension along duct
(b) local infiltration of liver substance
(c) metastatic spread to regional lymph nodes (in 15%)
◊ Biliary + vascular obstruction is typical!

√ ill-defined mass of 5–20 cm in diameter
√ satellite nodules in 65%
√ punctate / chunky calcifications in 18%
√ calculi in biliary tree
√ liver atrophy is suggestive although not specific
√ fibrotic pseudocapsule + secondary capsular retraction

US:
√ dilated biliary tree
√ predominantly solitary homo- / heterogeneous mass
√ hyperechoic (75%) mass for tumors > 3 cm
√ iso- / hypoechoic (14%) mass for tumor < 3 cm
√ mural thickening
√ peripheral hypoechoic tumor rim (35%) of compressed liver parenchyma

NECT:
√ single large predominantly homogeneous round / oval hypo- to isoattenuating dense mass with irregular margin
√ capsular retraction
√ stippled / punctate hyperattenuating foci (= hepatolithiasis)
√ dilatation of biliary tree peripheral to tumor

CECT:

√ hypoattenuating mass during arterial + portal venous phase
√ marked homogeneous delayed enhancement at 15 minutes (36–74%):
√ progressive concentric filling in of contrast medium (late) ← slow diffusion into interstitial tumor spaces within fibrous stroma
√ "peripheral washout" sign = (early) minimal to moderate thin rimlike / thick bandlike ragged enhancement around tumor:
√ clearing of contrast material in rim of lesion on delayed images
√ obliteration of portal vein + atrophy of involved segment
√ satellite nodules

MR:
√ large central heterogeneously hypo- to isointense mass on T1WI
√ variably hyperintense mass on T2WI depending on amount of mucinous material, fibrous tissue, hemorrhage, tumor necrosis:
√ hyperintense periphery (viable tumor) with irregular margin
√ large central hypointensity (fibrosis) on T2WI
√ hyperintense lesion on DWI ← suppression of high signal from vessels + bile ducts
√ ± DWI for small lesion

CEMR:
√ minimal / incomplete enhancement at tumor periphery on early images ← areas of early enhancement + rapid washout indicate active neoplastic growth
√ concentric centripetal internal fill-in = prominent progressive central enhancement on equilibrium / delayed phase ← vascular fibrotic stroma in tumor center
√ intense homogeneous enhancement during arterial phase + prolonged enhancement during delayed phase in smaller lesions with less fibrosis
√ satellite nodules in 10–20%

MR cholangiography:
√ localizing site of obstruction (100% accurate)
√ determining cause of obstruction (95% accurate)

Angiography:
√ avascular / hypo- / hypervascular mass
√ stretched / encased arteries (frequent)
√ neovascularity in 50%
√ lack of venous invasion

NUC:
√ cold lesion on sulfur colloid / IDA scans
√ segmental biliary obstruction
√ may show uptake on gallium scan

PET:
√ ring-shaped uptake ← excessive desmoplastic response of tumor center + neovascularity at tumor periphery
√ metastases to lymph nodes, liver, and distant sites

ERCP:
√ diagnostic bile sampling with cytologic analysis
√ biliary stent placement to relieve obstruction

Prognosis: < 20% resectable; 30% 5-year survival

DDx: (1) Metastatic adenocarcinoma (central necrosis = strongly T2-hyperintense + T1-hypointense)
(2) Hemangioma (strong globular enhancement, NO ragged rim)
(3) Sclerosing / cirrhotic HCC (NO distinguishing features)
(4) Organizing abscess (thick enhancing wall with central cystic change)
(5) Tuberculosis (multilayered appearance)

Intrahepatic Peripheral Cholangiocarcinoma

• NO jaundice
Location: right lobe predilection
√ solitary mass (nodular form) without hypoechoic halo
√ diffusely abnormal liver texture (infiltrative form):
  √ tumor more hypoechoic if < 3 cm
  √ tumor more hyperechoic if > 3 cm
√ well-marginated cystic mass (papillary mucin-producing tumor) ± diffuse hyperechoic flecks of tumor calcification
√ capsular retraction
√ delayed enhancement at 10 minutes
√ dilatation of bile ducts peripheral to tumor (31%)
√ tumor fingers in bile duct
DDx: metastatic adenocarcinoma / leiomyosarcoma; sclerosing hepatocellular carcinoma

Klatskin Tumor

[Gerald Klatskin (1910–1986), pathologist in Yale, USA]
= INTRAHEPATIC CENTRAL CHOLANGIOCARCINOMA = HILAR CHOLANGIOCARCINOMA
= tumor at confluence of hepatic ducts (up to 50–70% of all cholangiocarcinomas)
Age: > 65 years at presentation
Path growth pattern: infiltrating (70%) / intraluminal polypoidal / mass-forming
• abdominal pain, discomfort, anorexia, weight loss
• pruritus, jaundice (late symptom)
√ direct signs of Klatskin tumor:
  √ failure to demonstrate confluence of L + R hepatic ducts
  √ iso- to hyperechoic central porta hepatis mass / focal irregularity of ducts (for infiltrating cholangiocarcinoma)
  √ polypoid / smooth nodular intraluminal mass (for papillary + nodular types of cholangiocarcinoma) with associated mural thickening
√ indirect signs of Klatskin tumor:
  √ segmental dilatation with nonunion of right + left ducts at porta hepatis + normal caliber of extrahepatic ducts
  √ pressure effect / encasement / invasion / obliteration of portal vein and hepatic artery
√ lobar atrophy (14%) = dilated crowded ducts extending to liver surface ± geographic fatty change in one lobe
Rx: > 50% inoperable at diagnosis ← advanced stage

Inoperability (CT and MR 75–93% accurate):

(1) Invasion of right / left hepatic duct with extension to 2nd-order biliary radicles
(2) Atrophy of 1 hepatic lobe + involvement of contra- lateral portal vein branch / 2nd-order biliary radicle
(3) Vascular encasement / invasion of main portal vein or main hepatic artery
(4) Metastatic disease: lymph node / distant

CHOLANGITIS

Acute Obstructive / Ascending Cholangitis

= biliary duct obstruction associated with bacterial overgrowth

Cause:

(a) benign disease:
1. Stricture from prior surgery (36%) after bile duct exploration / bilioenteric anastomosis
2. Calculi (30%)
3. Sclerosing cholangitis
4. Obstructed drainage catheter
5. Parasitic infestation (liver fluke)

(b) malignant disease:
1. Ampullary carcinoma

Types:

(a) **Acute nonsuppurative ascending cholangitis**
- bile remains clear, patient nontoxic

(b) **Subacute nonsuppurative cholangitis**
= Cholangitis lenta = nonacute response of liver to systemic bacterial / fungal infection
◊ Important cause of liver failure + mortality with OLT

(c) **Acute suppurative ascending cholangitis** (14%)
Associated with: obstructing biliary stone or malignancy
- biliary sepsis, CNS depression, lethargy, mental confusion, shock (50%)

√ purulent material fills biliary ducts
√ marked inhomogeneous hepatic parenchymal enhancement during arterial phase (60%)

Prognosis: 100% mortality if not decompressed; 40–60% mortality with treatment; 13–16% overall mortality rate

Organism: E coli (31%), Klebsiella pneumoniae (17%), Enterococcus faecalis (17%), Streptococcus (17%)

- recurrent episodes of sepsis + RUQ pain
- Charcot triad (70%): fever + chills + jaundice
- bile cultures in 90% positive for infection

√ may have gas in biliary tree

CECT:

√ nodular / patchy / wedge-shaped / geographic inhomogeneous transient hepatic parenchymal enhancement in periportal location on hepatic arterial phase (= hyperemic changes around bile ducts)

√ diffuse concentric thickening of extrahepatic bile ducts, often with enhancement

Cx: miliary pyogenic hepatic abscesses; portal vein thrombosis; biliary peritonitis; secondary sclerosing cholangitis

Acute Bacterial Cholangitis

= potentially life-threatening disease induced by acute biliary infection

Cause: obstruction of CBD by stones (in up to 80%), malignancy (10–30%), sclerosing cholangitis, instrumentation of biliary tree (in 18% of transhepatic percutaneous biliary drainage catheter placement)

◊ Acute cholangitis occurs in 6–9% of patients admitted for gallstone disease

Pathophysiology: increased intrabiliary pressure (≥ 20 cm H_2O) → stagnant bile → biliary bacterial contamination

Risk factors: advanced age >70 years, neurologic disease, periampullary diverticulum

Organism: polymicrobial (30–80%); gram-negative rods (88%)

- Charcot triad (75%) = fever, pain, jaundice
- Reynolds pentad = fever, pain, jaundice, shock, lethargy
- positive culture: bile (50%), blood (20–30%)

@ CBD:

√ diffuse concentric wall thickening + enhancement

√ frequently dilatation of CBD

@ Intrahepatic bile ducts:

√ central (38%), diffuse (16%), segmental (46%) dilatation

√ wall thickening + enhancement (in up to 92% during delayed-phase of fat-suppressed MRI)

√ ± pneumobilia

@ Liver parenchyma

Distribution: wedge-shaped (72%) / peripheral patchy (14%) / peribiliary (14%)

√ increased SI on T2WI (69%) ← extension of inflammation into periportal + liver tissues

√ hepatic contrast enhancement: arterial only (58%), delayed only (16%), arterial and delayed (26%) phase

Cx: sepsis, hepatic abscess, portal vein thrombosis, bile peritonitis

Mortality: 4–65%

Rx: emergent endoscopic / percutaneous decompression of biliary tree; antibiotic therapy alone inadequate

AIDS-related Cholangitis

= AIDS CHOLANGIOPATHY= HIV-RELATED CHOLANGITIS

= infectious cholangitis characterized by opportunistic organisms in advanced AIDS patient with markedly depressed CD4 count of < 100/mm3

Organism: NO definite pathogen identified in 50%

(a) opportunistic: Cryptosporidium parvum (protozoan parasite typically infecting GI tract epithelium), CMV, Microsporidium, Mycobacterium avium complex

- opportunistic organism isolated from bile (in 50%)

(b) direct invasion of epithelium: Herpes simplex virus

Histo: marked periductal inflammatory response with interstitial edema + interstitial inflammatory cell infiltrates + necrotic biliary epithelium

- RUQ pain, fever, nausea; jaundice (rare)
- abnormal LFTs (esp. serum alkaline phosphatase; normal / mildly elevated bilirubin); elevated WBC count

Location: preferentially large intrahepatic bile ducts

Pattern: (1) combination of sclerosing cholangitis appearance + papillary stenosis (50%)
(2) isolated intrahepatic sclerosing cholangitis–like appearance (20%)
(3) isolated papillary stenosis (15%)
(4) long-segment extrahepatic duct stricture in isolation / with intrahepatic disease (15%)

√ irregular mild dilatation of intra- and extrahepatic bile ducts resembling sclerosing cholangitis

US:
√ stricture of distal CBD / papillary stenosis ← papillitis
√ echogenic nodule at the distal end of the CBD
√ mural thickening of gallbladder + bile ducts
√ saccular dilatations, debris, pruning of bile ducts
√ periductal echogenicity
√ ± pericholecystic fluid

CT:
√ "pseudogallstone" appearance = marked circumferential edema of gallbladder wall + mucosal enhancement
√ periportal edema

MR: resembling primary sclerosing cholangitis
√ multiple intra- and extrahepatic biliary strictures, saccular dilatations + ductal pruning
√ enhancing wall thickening of bile ducts
√ isolated 1–2-cm long extrahepatic bile duct stricture
√ irregular wall thickening of dilated CBD ← papillary stenosis
√ thickened gallbladder wall ← acalculous cholecystitis

Cholangiography:
√ strictures + beading of central intrahepatic bile ducts
√ pruning of peripheral bile ducts

DDx: acalculous cholecystitis, papillary stenosis, sclerosing cholangitis

Dx: inflammatory changes + associated pathogens in duodenal / papillary biopsy

Chemotherapy-induced Cholangitis

= inflammatory fibrosing process about the portal triads simulating primary sclerosing cholangitis

Predisposed: patients with liver metastases from colon cancer

Cause: direct effect of hepatic arterial infusion with chemotherapeutic agents (eg, floxuridine) / ischemia ← thrombosis of intrahepatic arterial branches

√ bile duct strictures as early as 2 months after therapy (in up to 15%)
√ stricture of common hepatic duct + sparing of distal CBD

IgG4-related Sclerosing Cholangitis

= biliary manifestation of IgG4 sclerosing disease

Histo: infiltration by abundant IgG4-positive plasma cells

Associated with: IgG4-involvement of pancreas, kidneys, thyroid gland, salivary glands

Age: older patient

Accompanied by: extra- / intrapancreatic lesions (frequent)

- ± obstructive jaundice

Rx: resolution under steroid therapy (often)

- elevated serum IgG4 level

√ patterns of biliary strictures:

(a) distal intrapancreatic CBD stricture (most common)

(b) diffuse intra- and extrahepatic bile duct strictures

(c) hilar + distal CBD stricture

(d) isolated hilar stricture

√ long continuous multifocal strictures + prestenotic dilatation

√ duct wall thickening = thick symmetric circumferential rind of enhancing tissue surrounding stricture

DDx: (1) Primary sclerosing cholangitis (multifocal + short intrahepatic biliary strictures with beaded / "pruned-tree" lesions)

(2) Cholangiocarcinoma (confined to bile ducts, not affecting pancreatic duct, hepatic capsular retraction)

(3) Pancreatic adenocarcinoma

(4) Ischemic biliary strictures

(5) AIDS cholangiopathy

Primary Sclerosing Cholangitis

= PSC = FIBROSING CHOLANGITIS = STENOSING CHOLANGITIS = CHRONIC OBLITERATIVE CHOLANGITIS

= insidious progressive obliterative fibrosing inflammation of the biliary tree leading to multifocal strictures, bile duct obliteration, cholestasis, and biliary cirrhosis

Etiology: idiopathic, ? autoimmune process (speculative); altered bile acid metabolism with increase in lithocholic acid by bacterial overgrowth

Prevalence: 1% as common as alcoholic liver disease

Mean age: 39 (range, 21–67) years; < 45 years (⅔); M÷F = 7÷3

Classification:

(a) large-duct PSC

(b) small duct PSC = clinical + biochemical + histologic features of PSC BUT normal appearance on cholangiography

Histo:

Stage 1: degeneration of epithelial bile duct cells + infiltration with lymphocytes ± neutrophils; inflammation + scarring + enlargement of periportal triads (pericholangitis)

Stage 2: fibrosis + inflammation infiltrating periportal parenchyma with piecemeal necrosis of hepatocytes; enlargement of portal triads; bile ductopenia

Stage 3: portal-to-portal fibrous septa; severe degenerative changes + disappearance of bile ducts; cholestasis in periportal + paraseptal hepatocytes
Stage 4: frank cirrhosis

Associated with:

(1) Inflammatory bowel disease (ulcerative colitis in 50–74%, Crohn disease in 13%)
  ◊ 1–4% of patients with inflammatory bowel disease develop primary sclerosing cholangitis!
  ◊ 10% of patients with PSC have Crohn disease
(2) Cirrhosis, chronic active hepatitis, pericholangitis, fatty degeneration
(3) Peyronie disease
(4) Sjögren syndrome
(5) Systemic lupus erythematosus
(6) Rheumatoid arthritis

- abnormal liver function tests: serum bilirubin, serum alkaline phosphatase, γ-glutamyltransferase
- progressive chronic / intermittent obstructive jaundice (75%)
- fever, night sweats, chills, RUQ pain, pruritus (10–15%)
- ANCA and antinuclear antibodies(low titers with low specificity)
- history of previous biliary surgery (53%) + chronic / recurrent pancreatitis (14%)

Location:

1. CBD almost always involved
2. Intra- and extrahepatic ducts (68–89%)
3. Cystic duct (15–18%)
4. Intrahepatic ducts only (1–11–25%)
5. Extrahepatic ducts only (2–3%)

Dx: PSC is diagnosed in patients with clinical + biochemical signs of cholestasis, typical cholangiographic imaging findings and after exclusion of secondary causes of sclerosing cholangitis.

√ intrahepatic bile duct calculi (8–30%): soft black crushable stones / sandlike grit

US:

√ brightly echogenic portal triads
√ echogenic biliary casts / punctate coarse calcifications along portal vein branches
√ extrahepatic ductal dilatation + choledocholithiasis
√ ± gallbladder wall thickening

√ gallbladder polyps (in 60% malignant)

Cholangiography:

√ <u>multifocal strictures</u> with predilection for bifurcations + skip lesions (= uninvolved duct segments of normal caliber) involving intra- and extrahepatic bile ducts:
  √ CLASSIC "string-of-beads" appearance (= alternating segments of dilatation and focal annular stenoses)
  √ "pruned tree" appearance (= opacification of central ducts + nonvisualization of peripheral smaller radicles ← diffuse obstruction)
  √ "cobblestone" appearance (= coarse nodular mural irregularities) in 50%
  √ new strictures + lengthening of strictures between 6 months and 6 years (< 20%)
  √ minimal duct dilatation ← periductal inflammation + fibrosis

√ marked ductal dilatation (24%)
DDx: ascending cholangitis, cholangiocarcinoma
√ diverticula / pseudodiverticula (PATHOGNOMONIC) = small eccentric saccular outpouchings (up to 27%)
√ ductal webs = focal 1–2 mm thick areas of incomplete circumferential narrowing
√ angles formed between central and peripheral ducts change from acute to obtuse
√ polypoid mass (7%)
√ gallbladder irregularities uncommon
√ cholestasis-related choledocholithiasis

CT:
√ dilatation, stenosis, pruning (decreased arborization), beading of tortuous intrahepatic bile ducts = "tree-in-winter" / "pruned tree" appearance (80%)
√ wall nodularity, duct wall thickening, mural contrast enhancement of extrahepatic bile ducts (100%)
◊ Periductal soft-tissue > 1.5 cm thick with delayed enhancement is worrisome for cholangiocarcinoma!
√ hepatic metastases + lymph nodes in porta hepatis
√ subtle foci of high attenuation in intrahepatic bile ducts
√ lobar atrophy in preferentially affected portions

MR:
√ enlarged central liver from macroregenerative nodules
√ atrophied periphery with hyperintense wedge-shaped areas on T2WI
√ dilated isolated "floating" bile ducts in periphery
√ periportal intensity intermediate on T1WI + hyperintense on T2WI ← inflammation

MRCP:
@ Bile ducts
√ "beaded" bile ducts = multifocal short-segment strictures of intra- + extrahepatic bile ducts alternating with normal bile ducts / mildly dilated duct ectasias
√ peripheral pruning of intrahepatic ducts
√ multifocal enhancing ductal wall thickening
√ ± intrahepatic duct stones
@ Liver
√ peripheral wedge-shaped / reticular T2-hyperintense abnormalities
√ hypertrophy of caudate lobe + medial segment of left lobe with atrophy of lateral + posterior segments
√ large regenerating nodules
√ multiple areas of enhancing fibrosis in liver periphery
√ ± periportal lymph nodes

NUC (^{99m}Tc-IDA):
√ multiple persistent focal areas of retention in distribution of intrahepatic biliary tree
√ marked prolongation of hepatic clearance
√ gallbladder visualized in only 70%

Cx: (1) Biliary cirrhosis (up to 49%) after > 10 years
(2) Portal hypertension

(3) Malignancy (10–15%):
  (a) cholangiocarcinoma (in 5–36% at autopsy / liver transplantation):
    • screening with tumor marker CA-19.9 > 129 U/mL (79% sensitive, 99% specific)
  (b) colorectal cancer (10- to 14-fold increased risk compared to general population)
  (c) pancreatic cancer
(4) Secondary recurrent bacterial cholangitis

Rx: (1) Palliative: ursodeoxycholic acid, dilatation of dominant strictures
(2) Curative: liver transplantation (4th leading indication)

DDx:
(1) IgG4-related sclerosing cholangitis

Primary sclerosing cholangitis occurs in younger patients, is associated with inflammatory bowel disease, and is less acute with longer duration of symptoms compared to IgG4-related sclerosing cholangitis.

(2) Sclerosing cholangiocarcinoma (progressive cholangiographic changes within 0.5–1.5 years of initial diagnosis, marked ductal dilatation upstream from a dominant stricture, intraductal mass > 1 cm in diameter)
(3) Acute ascending cholangitis (history)
(4) Recurrent pyogenic cholangitis
(5) Primary biliary cirrhosis (disease limited to intrahepatic ducts, strictures less pronounced, pruning + crowding of bile ducts, normal AMA titer)
(6) AIDS cholangiopathy (same cholangiographic findings)
(7) Ischemic strictures

Recurrent Pyogenic Cholangitis

= PRIMARY CHOLANGITIS = RECURRENT PYOGENIC HEPATITIS = ORIENTAL CHOLANGIOHEPATITIS = ORIENTAL CHOLANGITIS = ORIENTAL INFESTATIONAL CHOLANGITIS = HONG KONG DISEASE = INTRAHEPATIC PIGMENTed STONE DISEASE

= progressive biliary disease characterized by recurrent episodes of bacterial cholangitis ← biliary obstruction by pigmented stones + biliary strictures + bile duct ectasia

Etiology: ? Clonorchis sinensis infestation, coliform infection of bile, portal bacteremia, malnutrition

Prevalence: 3rd most common cause of an acute abdomen in Hong Kong after appendicitis and perforated ulcer; uncommon in USA

Epidemiology: endemic to Southeast Asia (South China, Indochina, Taiwan, Japan, Korea); Asian immigrants in USA

Strongly associated intrabiliary infestation:
Ascaris lumbricoides, Clonorchis sinensis, Opisthorchis viverrini / felineus, Fasciola hepatica, E coli

Pathophysiology: chronic recurrent infections → developing pigmented calculi → cholangitic abscesses + inflammatory strictures

Path: pericholangitis, periductal abscesses, fibrosis of bile duct walls, heavy infiltration of portal tracts by PMNs, intraductal bile pigment calculi

Age: 20–50 years; M÷F = 1÷1

- poor nutritional + low socioeconomic status of patient
- recurrent attacks of fever, chills, abdominal pain, jaundice

Location: particularly in lateral segment of L lobe + posterior segment of R lobe + extrahepatic duct

Associated findings:

√ gallstones
√ splenomegaly
√ portal vein obstruction, varices
√ markedly dilated (3–4 mm) proximal intrahepatic (1st- & 2nd-order) bile ducts (in 100%):
  √ decreased arborization (branching) of intrahepatic radicles with abrupt tapering = "arrowhead appearance"
√ multifocal < 1 cm long bile duct strictures (22%)
√ pneumobilia (3–52%)
√ intra- and extrahepatic bile ducts filled with nonshadowing soft mudlike pigment (= calcium bilirubinate) stones (74%):
  √ stones hyperattenuating compared to unenhanced liver parenchyma (in 90%)
  √ stones T1-hyperintense + T2-hypointense to liver
  √ disproportionate diffuse dilatation of central bile ducts involving stone-bearing and stone-free ducts (68%)
  √ thickened periportal space ← periductal inflammation + fibrosis
√ biloma
√ segmental hepatic atrophy (36%): left lobe / right posterior segments
√ hepatic abscesses

CT:

√ abrupt nonvisualization of peripheral branches
√ enhancement of thickened bile duct wall

ERCP:

◊ Worsening of cholangitis / sepsis if patients do not receive antibiotics!
√ acute tapering + straightening + rigidity of bile ducts
√ decreased arborization + increased branching angle of bile ducts

MRCP:

√ intra- / extrahepatic bile duct stones
√ multiple intrahepatic biliary strictures
√ short-segment focal extrahepatic bile duct stricture
√ localized dilatation of lobar / segmental bile ducts with predilection for lateral segment of left lobe + posterior segment of right lobe
√ wall thickening, abrupt tapering, ↓ arborization of intrahepatic bile ducts

Cx: liver abscess (18%), splenomegaly (14%), biloma (4%), pancreatitis (4%), cholangiocarcinoma (2–6%): [peripheral (80%) or hilar / extrahepatic (20%)]

Prognosis: progressive destructive cholangiopathy + liver failure

Rx: endoscopic sphincterotomy, choledochoduodenostomy, surgical resection (if disease in single segment / lobe)

DDx: (1) Caroli disease (saccular dilatation of intrahepatic bile ducts)

(2) Primary sclerosing cholangitis (focal discontinuous bile duct dilatation)
(3) Clonorchiasis (biliary ductal dilatation limited to intrahepatic bile ducts)

Secondary Sclerosing Cholangitis

= heterogeneous group of chronic cholestatic disorders morphologically similar to PSC

Cause:

(1) Intraductal stone disease / choledocholithiasis → bile duct stricture → recurrent pyogenic cholangitis
(2) Ischemic cholangiopathy from treatment with intraarterial chemotherapy / floxuridine
(3) Autoimmune pancreatitis
(4) AIDS-asscociated cholangiopathy
(5) Eosinophilic cholangitis
(6) Previous biliary tract surgery / blunt trauma
(7) Hepatic inflammatory pseudotumor
(8) Congenital biliary tree anomalies
(9) Bile duct neoplasm

CHOLECYSTITIS

Etiology: (a) in 80–95% cystic duct obstruction by impacted calculus; 85% disimpact spontaneously if stone < 3 mm
(b) in 10% acalculous cholecystitis

Acute Calculous Cholecystitis

Pathogenesis: chemical irritation from concentrated bile, bacterial infection, reflux of pancreatic secretions

Age peak: 5th–6th decade; M÷F = 1÷3

Associated with: choledocholithiasis (15–25%)

◊ 5% of patients presenting to ED have acute cholecystitis!

- persisting (> 6 hr) RUQ pain radiating to right shoulder / scapula / interscapular area (DDx: biliary colic usually < 6 hours)
- nausea, vomiting, chills, fever, RUQ tenderness + guarding
- Murphy sign = inspiratory arrest upon palpation of GB area (falsely positive in 6% of patients with cholelithiasis)
- ± leukocytosis, elevated levels of alkaline phosphatase and transaminase and amylase
- mild hyperbilirubinemia (20%)

US (40–97% sensitive, 64–100% specific, 92% PPV, 95% NPV):

√ ± GB wall thickening > 3 mm (45–72% sensitive, 76–88% specific):
  √ hazy delineation of GB wall
  √ "halo" sign = GB wall lucency (in 8%) = 3-layered configuration with sonolucent middle layer (edema)
  √ striated wall thickening (62%) = several alternating irregular discontinuous lucent + echogenic bands within GB wall (100% PPV)
√ GB hydrops = distension with AP diameter > 5 cm or enlargement of greater than 4 x 10 cm

√ positive **sonographic Murphy sign** (in 85–88%)
= maximum tenderness during compression with transducer directly over gallbladder (63–94% sensitive, 85–93% specific, 72% NPV)
False-negative sonographic Murphy sign:
lack of patient responsiveness, pain medication, inability to press directly on GB (position deep to liver / protected by ribs), GB wall necrosis
√ crescent-shaped / loculated pericholecystic fluid (in 20%) = inflammatory intraperitoneal exudate / abscess
√ gallstones (83–98% sensitive, 52–77% specific):
√ impacted gallstone in GB neck / cystic duct
√ echogenic shadowing fat within hepatoduodenal ligament ± conspicuous color Doppler flow ← inflammation
DDx: bowel gas
√ sludge

Color Doppler US:
√ visualization of cystic artery > 50% of the length of the gallbladder (30% sensitive, 98% specific)

CT (* = signs with highest sensitivity+ specificity):
Dose: on average 11 mSv

The negative predictive value of CT for acute cholecystitis is 89%. While this is lower than for US, CT can exclude acute cholecystitis when clinical suspicion for gallbladder disease is low and clinical symptoms are nonspecific.

@ GB size
√ distended gallbladder > 8 cm long / > 4 cm in diameter
@ GB wall
√ irregular gallbladder wall
√ gallbladder wall thickness ≥ 7 mm*
√ gallbladder wall thickness < 2 mm
√ increased gallbladder wall attenuation
√ air in gallbladder wall
√ local / widespread absence of GB wall enhancement* = gangrenous acute cholecystitis
@ GB content
√ gallstone in infundibulum
√ increased attenuation of bile
√ intraluminal membranes
@ Hepatic pedicle (= vessels and ducts of porta hepatis)
√ hyperdense areas in fatty tissue around hepatic pedicle = haziness of pericholecystic fat
√ pericholecystic fluid / effusion*
@ Hepatic parenchyma
√ pericholecystic abscess
√ transient focal increased attenuation of liver parenchyma around gallbladder fossa on hepatic arterial phase ← hepatic arterial hyperemia + early venous drainage

@ Adjacent organs
√ contact between GB wall and wall of duodenum / colon

MR:
√ T2-hyperintense thickened wall > 3 mm (best seen on fat-suppressed T2WI)
√ increased signal intensity within + surrounding GB on T2WI ← pericholecystic fluid
√ signal void in cystic duct / gallbladder neck ← obstructing stone
√ marked enhancement of gallbladder wall
√ transient enhancement of pericholecystic hepatic parenchyma in 70% (HIGHLY SPECIFIC)

MRCP = MR cholangiopancreatogram (high sensitivity):
√ low-signal–intensity defect surrounded by high-signal–intensity bile on T2WI

Cholangiography:
√ sharply defined filling defect in contrast-material filled lumen of cystic duct

NUC (98% sensitive, 100% specific, 95–98% accurate):
= functional information about cystic duct patency
Dose: on average 3.7 mSv
◊ Tracer uptake hinges on adequate hepatic function + fasting status
√ nonvisualization of normal biliary anatomy:
√ nonvisualization of GB during 1st hour (in 83%)
√ nonvisualization of GB by 4 hours (99% specific)
√ nonvisualization of GB + CBD (in 13%)
√ "dilated cystic duct" sign (= radiotracer activity in a short segment of cystic duct proximal to obstructing stone) that may be mistaken for gallbladder
√ "pericholecystic rim" sign (34% sensitive) on initial images = increased hepatic activity adjacent to GB fossa: 94% PPV for acute cholecystitis + 57% PPV for gangrenous cholecystitis
Cause: local hepatocyte inflammation + hyperemia in transmural process → increased perfusion to GB fossa during "arterial phase"

Endpoint of imaging:
» when tracer fills GB
» 4 hours of delayed imaging after tracer injection
» 45 minutes after morphine injection

False-positive scans (10–12%)
= nonvisualization of GB without acute cholecystitis:
(a) absent gallbladder: congenital absence of GB, post cholecystectomy
(b) recent feeding < 4–6 hours prior to study
(c) sludge preventing filling of gallbladder: prolonged fasting, total parenteral nutrition, hyperalimentation
(d) other hepatobiliary disease: chronic cholecystitis, CBD obstruction, carcinoma of GB
(e) hepatocellular dysfunction: alcoholic liver disease, acute pancreatitis

Reduction to 2% false-positive scans through:
(1) delayed images up to 4 hours
(2) cholecystokinin (Sincalide®) injection 15 minutes prior to study
(3) morphine IV (0.04 mg/kg) at 40 minutes with reimaging after 20 minutes →

contraction of sphincter of Oddi → rise in intrabiliary pressure

False-negative scans (4.8%):

(a) acute cholecystitis without cystic duct obstruction: acalculous / rare calculous cholecystitis

(b) extrahepatic radiotracer accumulation mistaken for gallbladder activity: duodenal diverticulum, biliary duplication cyst, gangrenous cholecystitis with accumulation in gallbladder bed, "dilated cystic duct" sign

Cx:

mnemonic: GAME BEG

Gangrene
Abscess (pericholecystic)
Mirizzi syndrome
Emphysematous cholecystitis
Bouveret syndrome (= gallstone erodes into duodenum leading to duodenal obstruction)
Empyema
Gallstone ileus

Gangrene of Gallbladder = Gangrenous Cholecystitis

= common severe complication of acute cholecystitis

Frequency: 26% of patients with acute cholecystitis

• positive Murphy sign (33%)

US:

√ irregular / absent gallbladder wall
√ shaggy, irregular, asymmetric wall (mucosal ulcers, intraluminal hemorrhage, necrosis)
√ hyperechoic foci within GB wall (microabscesses in Rokitansky-Aschoff sinuses)
√ intraluminal pseudomembranes (gangrene)
√ coarse nonshadowing nondependent echodensities (= sloughed necrotic mucosa / sludge / pus / clotted blood within gallbladder)

CT (insensitive but highly specific):

√ intramural / intraluminal gas
√ intraluminal membranes
√ irregular / absent GB wall, lack of wall enhancement
√ pericholecystic abscess formation.

MR:

√ interrupted "rim" sign = patchy enhancement of mucosa on contrast-enhanced fat-suppressed MR

NUC:

√ radiotracer accumulation in gallbladder fossa

Rx: laparoscopic cholecystectomy (frequently converted to open surgery)

Pericholecystic Abscess

Cause: subacute perforation of gallbladder wall subsequent to gangrene + infarction ← acute cholecystitis

Prevalence: 2–20%

Location:
(a) gallbladder bed (most common)
√ area of low-level echoes in liver adjacent to GB
(b) intramural
√ small area of low-level echoes within thickened gallbladder wall
(c) intraperitoneal
√ area of low-level echoes within peritoneal cavity adjacent to gallbladder

Rx: (1) Emergency operation
(2) Antibiotic treatment + elective operation
(3) Percutaneous abscess drainage

Perforation of Gallbladder *(in 2–20%)*

Average age: 60 years; M>F

Types:
(1) Acute free perforation with peritonitis → pericholecystic abscess in 33%
(2) Subacute localized perforation → pericholecystic abscess in 48%
(3) Chronic perforation → internal biliary fistula → pericholecystic abscess in 18%

Location: most commonly at fundus ← poor blood supply

√ gallstone lying free in peritoneal cavity = SPECIFIC

US:
√ sonolucent / complex collection surrounding GB
√ collection in liver adjacent to gallbladder

CT:
√ "hole" sign = focal gallbladder wall defect

NUC:
√ extrabiliary radiotracer activity (that may be mistaken for activity within gallbladder) best appreciated with delayed imaging

Mortality: up to 15% (attributed to delayed diagnosis)

Cx: free intraperitoneal air; bile leak; abscess formation in liver / GB fossa / peritoneum; SBO

Empyema of Gallbladder

√ multiple medium / coarse highly reflective intraluminal echoes without shadowing / layering / gravity dependence (purulent exudate / debris)

Acute Acalculous Cholecystitis

Frequency: 5–15% of all acute cholecystitis cases

Associated with: recent surgery in 50%

Etiology: probably decreased blood flow within cystic artery

(1) Debilitated patients: depressed motility / starvation in trauma, burns, surgery, total parenteral nutrition, anesthesia, positive pressure ventilation, narcotics, shock, vasoactive amines, congestive heart failure, arterio-sclerosis, polyarteritis nodosa, SLE, diabetes mellitus
◊ Diagnosis in the ICU patient sonographically difficult due to fasting state, medications, CHF, etc.

(2) Obstruction of cystic duct by extrinsic inflammation, lymphadenopathy, metastases
(3) Infection (only in 50%): Salmonella, Helicobacter, cholera, Kawasaki syndrome, cytomegalovirus, cryptosporidiosis

√ thickened gallbladder wall > 4–5 mm
√ echogenic bile / sludge
√ gallbladder distension
√ pericholecystic fluid in absence of ascites
√ striated subserosal edema
√ sloughed mucosal membrane
√ Murphy sign = pain + tenderness with transducer pressure over the gallbladder (difficult to assess in ICU patient with altered mental status)
√ decreased response to cholecystokinin
√ intramural gas

CT:
√ pericholecystic stranding (= edema)
√ decreased attenuation in adjacent liver (= perihepatitis)

NUC: same criteria as for calculous cholecystitis
Cx: gallbladder perforation, gangrene, pericholecystic abscess
Rx: percutaneous cholecystostomy trial (low threshold for ICU patients)
Prognosis: 6.5% mortality rate

Chronic Cholecystitis

◊ Most common form of gallbladder inflammation
√ gallstones
√ smooth / irregular GB wall thickening (mean of 5 mm)
√ mean volume of 42 mL

NUC:
√ normal GB visualization in majority of patients
√ delayed GB visualization (1–4 hours)
√ visualization of bowel prior to gallbladder (45% sensitive, 90% specific)
√ noncontractility / decreased response after CCK injection (decreased GB ejection fraction)

Emphysematous Cholecystitis

= variant of acute cholecystitis ← ischemia of gallbladder wall + infection with gas-producing organisms
Frequency: 1% of all acute cholecystitis cases
Etiology: small-vessel disease with cystic artery occlusion, complication of acute cholecystitis
Organism: Clostridium perfringens, Clostridium welchii, E. coli, Bacillus fragilis
Age: > 50 years; M÷F = 2÷1 to 5÷1
Predisposed: diabetics (20–50%), debilitating diseases; calculous (70–80%) / acalculous cystic duct obstruction
Pathophysiology: obstructive endarteritis → ischemia → secondary infection with anaerobes

- WBC count may be normal (⅓)
- point tenderness rare (diabetic neuropathy)

Plain film:
- √ gas appears 24–48 hours after onset of symptoms
- √ air-fluid level in GB lumen, air in GB wall within 24–48 hours after acute episode
- √ pneumobilia (rare)

US:
- √ arclike high-level echoes outlining GB wall mimicking porcelain gallbladder / multiple stones in contracted GB
- √ cholecystolithiasis (50%)

CT (most sensitive and specific imaging modality):
- √ identification of gas in gallbladder lumen / wall
- √ irregularity / discontinuity of gallbladder wall
- √ pneumobilia, pericholecystic fluid, abscess formation

Cx: gangrene (75%); gallbladder perforation (20%)

Mortality: 15%

Rx: urgent cholecystectomy; temporizing percutaneous cholecystostomy + antibiotics

DDx: (1) Enteric fistula
(2) Incompetent sphincter of Oddi
(3) Air-containing periduodenal abscess
(4) Periappendiceal abscess in malpositioned appendix
(5) Lipomatosis of gallbladder

Xanthogranulomatous Cholecystitis

= FIBROXANTHOGRANULOMATOUS INFLAMMATION = CEROID GRANULOMAS OF THE GALLBLADDER

= uncommon severe inflammatory disease of gallbladder characterized by presence of multiple intramural nodules

Prevalence: 1–2%

Predisposition: gallstones, obesity, diabetes mellitus

Pathophysiology:
cystic duct obstruction or rupture of occluded Rokitansky-Aschoff sinuses → mucosal / mural injury → extravasation of inspissated bile + mucin attracting histiocytes → phagocytosis of insoluble bile lipids and cholesterol → lipogranuloma formation → fibrosis

Age: 5th + 6th decade

Histo: mixture of xanthoma cells with foamy histiocytes + fibroblasts + multinucleated foreign body giant cells + lymphocytes containing areas of necrosis

May be associated with: gallbladder carcinoma (11%)

√ preservation of 2–3-mm thick mucosal lining (in 82%)
√ thickened gallbladder wall: 91% diffuse, 9% focal
√ infiltration of pericholecystic fat: in 45% focal, in 54% diffuse
√ hepatic extension (45%)
√ biliary obstruction (36%)

√ lymphadenopathy (36%)
US:
√ intramural hypoechoic nodules
CT:
√ 5–20-mm small intramural hypoattenuating nodules
√ poor / heterogeneous contrast enhancement
MR:
√ areas of marked T2-hyperintensity ← necrosis / abscess
√ xanthogranulomas show delayed strong enhancement
DDx: gallbladder carcinoma with local spread (in 59% focal, in 41% diffuse thickening of gallbladder wall, multiple masses within liver)

CHOLEDOCHAL CYST

= CYSTIC DILATATION OF EXTRAHEPATIC BILE DUCT
= rare congenital biliary tract anomaly characterized by dilatation of all / part of the extra- / intrahepatic bile ducts without involvement of gallbladder / cystic duct
◊ Most common congenital lesion of bile ducts
Etiology: ?
(a) biliary ductal plate malformation of extrahepatic bile ducts as part of congenital fibrocystic disease
(b) anomalous junction of pancreatic duct and CBD proximal to duodenal papilla → higher pressure in pancreatic duct with absence of ductal sphincter → allows free reflux of enzymes into CBD → chemical + inflammatory changes → weakening of CBD wall + dilatation of CBD

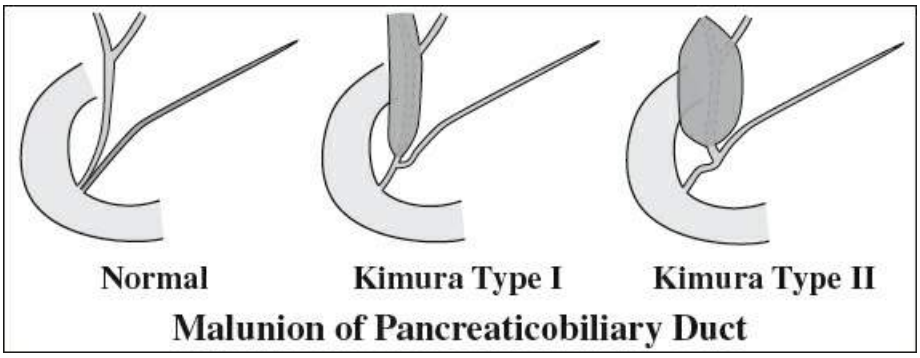
Classification of malunion of pancreaticobiliary duct

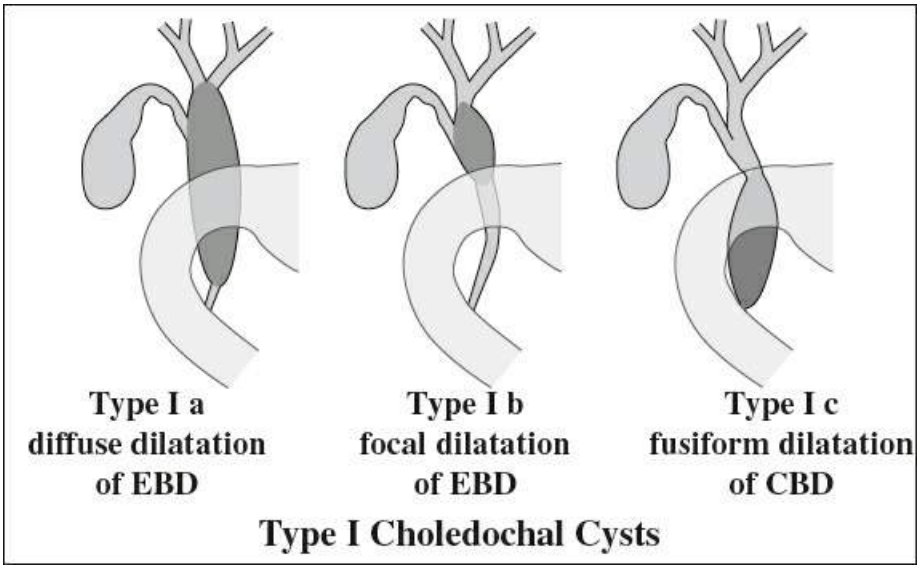
Kimura type I	=	pancreatic duct enters the proximal / mid CBD (10–58%) at right angle
Kimura type II	=	CBD drains into pancreatic duct

Classification by 5 subtypes (Todani): according to common cystic changes but probably different pathophysiologic features
(1) Todani type I choledochal cyst
confined to extrahepatic bile duct (EBD)
Cause: anomalous pancreaticobiliary union → formation of a long frequently ectatic common channel
(a) Todani type Ia = <u>diffuse</u> EBD cyst
(b) Todani type Ib = <u>focal</u> segmental EBD cyst
(c) Todani type Ic = <u>fusiform</u> CBD cyst
(2) Todani type II choledochal cyst = true diverticulum
(3) Todani type III choledochal cyst = choledochocele
= focal dilatation of intraduodenal segment of distal CBD
(4) Todani type IV choledochal cyst = multiple cysts
(a) Todani type IVa multiple choledochal cysts
= multiple cysts of both EBD + IBD
(b) Todani type IVb multiple choledochal cysts

= multiple saccular dilatations of EBD only

(5) Todani type V choledochal cyst = Caroli disease





Prevalence: 1÷13,000 admissions; high prevalence in Japanese / Asian infants

Age: < 10 years (60%) + young adulthood; 80% diagnosed in childhood; 7% during pregnancy; occasionally detected up to 8th decade; M÷F = 1÷4

Histo: fibrous cyst wall without epithelial lining

Associated with:

(1) Dilatation / stenosis / atresia of other segments of the biliary tree (2%)
(2) Gallbladder anomaly: aplasia, double GB
(3) Failure of union of left + right hepatic ducts
(4) Pancreatic duct + accessory hepatic bile ducts may drain into cyst
(5) Polycystic liver disease

- Classic triad in 2–38% (20–30%) of all (adult) patients:
  (1) Intermittent obstructive jaundice (33–50%)
    ◊ Uncommon cause of obstructive jaundice!
  (2) Recurrent RUQ colicky pain (> 75–90%), back pain
  (3) Intermittent palpable RUQ abdominal mass (< 25%)
- recurrent fever, chills, weight loss, pruritus

Types:
(a) marked cystic dilatation of CBD + CHD
(b) focal segmental dilatation of CBD distally
(c) cylindric dilatation of CBD + CHD

Size: CBD diameter of 2–15 cm
◊ The largest choledochal cyst contained 13 liters

√ NO / mild peripheral intrahepatic bile duct dilatation
√ may contain stones / sludge

UGI:
√ soft-tissue mass in RUQ
√ anterior displacement of 2nd portion of duodenum + distal portion of stomach (on LAT view)
√ widening of C-loop with inferior displacement of duodenum (on AP view)

US:
√ ballooned / fusiform cyst beneath porta hepatis separate from gallbladder
◊ Communication with common hepatic / intrahepatic ducts needs to be demonstrated!
√ abrupt change of caliber at junction of dilated segment to normal duct
√ intrahepatic bile duct dilatation (16%) ← stenosis

OB-US (earliest diagnosis at 25 weeks MA):
√ right-sided cyst in fetal abdomen + adjacent dilated hepatic ducts
DDx: duodenal atresia; cyst of ovary, mesentery, omentum, pancreas, liver

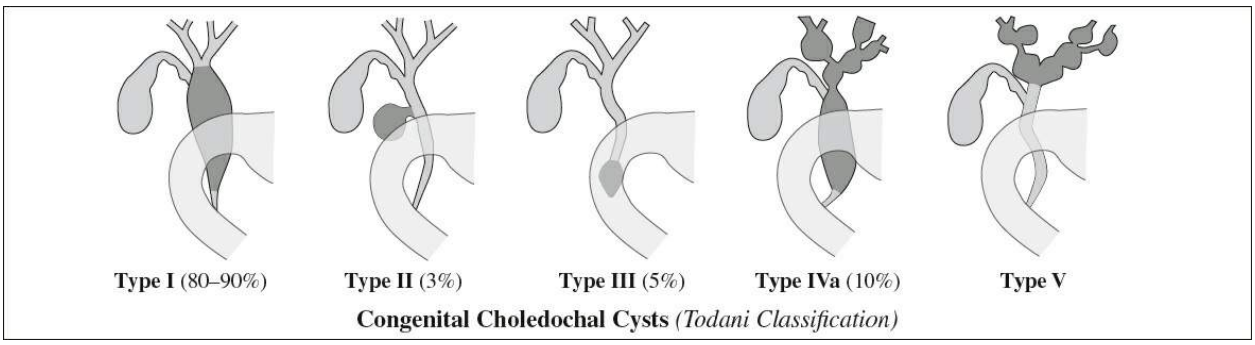
NUC with HIDA:
◊ At times the choledochal cyst does not fill with radionuclide!
√ photopenic area within liver that fills within 60 min + stasis of tracer within cyst
√ lack of tracer passage into small intestine
√ prominent hepatic ductal activity ← dilatation of ducts
DDx: often excludes hepatic cyst, pancreatic pseudocyst, enteric duplication, spontaneous loculated biloma

Cholangiography / MRCP (confirms diagnosis):
√ anomalous pancreaticobiliary junction with long common channel
√ dilated intrahepatic bile ducts
√ intraductal calculi

Cx: (1) Stones (8–50%) in gallbladder, in CBD, within cyst, in intrahepatic biliary tree, in pancreatic duct
(2) Malignant transformation into bile duct carcinoma + gallbladder carcinoma (increasing with age, < 1% in 1st decade, 7–14% > age 20)
(3) Recurrent acute pancreatitis (33%)
(4) Recurrent cholangitis / cholecystitis (20%)
(5) Cyst rupture with bile peritonitis (1.8%)
(6) Bleeding
(7) Biliary cirrhosis + portal hypertension
(8) Portal vein thrombosis
(9) Hepatic abscess

Rx: excision of cyst + Roux-en-Y hepaticojejunostomy

DDx: mesenteric, omental, ovarian, renal, adrenal, hepatic, enteric duplication cyst, pancreatic pseudocyst, hydronephrotic kidney, hepatic artery aneurysm, biloma (← spontaneous perforation of CBD)



Congenital Choledochal Cysts *(Todani Classification)*

CHOLEDOCHOCELE

= DUODENAL DUPLICATION CYST = ENTEROGENOUS CYST OF AMPULLA OF VATER / DUODENUM = INTRADUODENAL CHOLEDOCHAL CYST = TYPE III CHOLEDOCHAL CYST = DIVERTICULUM OF COMMON BILE DUCT

= cystic dilatation of distal / intramural duodenal portion of CBD with herniation of CBD into duodenum (similar to ureterocele)

Etiology:

(1) congenital:

(a) originates from tiny bud / diverticulum of distal CBD (found in 5.7% of normal population)

(b) stenosis of ductal orifice / weakness of ductal wall

(2) acquired:

stone passage followed by stenosis + inflammation

Age: 33 years (manifestation usually in adulthood)

Types: (a) CBD terminates in cyst, cyst drains into duodenum (common)

(b) cyst drains into adjacent intramural portion of CBD (less common)

- biliary colic, episodic jaundice, nausea, vomiting
- bulging papilla; high amylase level within bile

Associated with: stones / sludge (frequent)

UGI:

√ smooth well-defined intraluminal duodenal filling defect in region of papilla

√ change in shape with compression / peristalsis

Cholangiography (diagnostic):

√ opacified smooth clublike / saclike dilatation of intramural segment of CBD prolapsed into duodenum

CT:

√ spheric dilatation of terminal bile duct protruding into duodenal lumen

Cx: pancreatitis, duodenal obstruction, cholecystitis

Rx: sphincterotomy / sphincteroplasty

DDx: choledochal cyst (involves more than only terminal portion of CBD)

CHOLELITHIASIS

Prevalence:
25,000,000 adults in USA;
10–15% of population + 2% of children

Age: increasing with age (40% of women in 9th decade);
M÷F = 2%÷4% (10%÷25%) in 3rd (7th) decade

Predisposing factors: "female, forty, fair, fat, fertile, flatulent"

Pathogenesis: supersaturation of bile constituents, most notably cholesterol ← defects in biliary lipid metabolism; biliary dysmotility; prolonged intestinal transit; aggravated by sedentary lifestyle + diet

(1) Hemolytic disease:
sickle cell disease (7–37%), hereditary spherocytosis (43–85%), thalassemia, pernicious anemia (16–20%), prosthetic cardiac valves + mitral stenosis (hemolysis), cirrhosis (hemolysis ← hypersplenism), Rhesus / ABO blood group incompatibility (perinatal period)

(2) Metabolic disorder = disruption of biliary lithogenic index: diabetes mellitus, obesity, pancreatic disease, cystic fibrosis, hypercholesterolemia, type 4 hyperlipidemia, hemosiderosis (20%), hyperparathyroidism, hypothyroidism, prolonged use of estrogens / progesterone, pregnancy

(3) Cholestasis
› hepatic dysfunction: hepatitis, neonatal sepsis
› biliary tree malformation: Caroli disease
› biliary obstruction: parasitic infection, benign / malignant strictures, foreign bodies (sutures, ascariasis)
› prolonged fasting (total parenteral nutrition)
› methadone intake

(d) Intestinal malabsorption
→ 10 x increased risk of stone formation
› inflammatory bowel disease: Crohn disease (28–34%)
› ileal resection
› bypass surgery

(e) Genetic predisposition = familial:
Navaho, Pima, Chippewa Indians

(f) Others
muscular dystrophy

Composition:

A. CHOLESTEROL STONE (70%)
= main component of most calculi
√ lucent (93%), calcified (7%)
√ slightly hypodense compared with bile
(a) pure cholesterol stones (10%): yellowish, soft
√ buoyancy in contrast-enhanced bile

√ density of < 100 HU

(b) mixture of cholesterol + calcium carbonate / bilirubinate (70%)

√ laminated appearance

√ radiopaque on plain film (15–20%)

MR:

√ hypointense on T2WI + T1WI

√ occasionally hyperintense center on T2WI + T1WI (protein molecules)

B. PIGMENT STONE (30%)

• brown (common) = granular precipitate of calcium bilirubinate containing < 25% cholesterol (by definition)

Cause: inflammation / infection of gallbladder, status post cholecystectomy

• black (less common) = compact "lacquer" of bilirubin derivatives with a high affinity for calcium carbonate

√ multiple tiny faceted / spiculated homogeneously radiopaque stones

CT:

√ usually denser than bile

MR:

√ hypointense on T2WI + hyperintense on T1WI (related to degree of hydration)

C. GAS-CONTAINING GALLSTONE

Mechanism: dehydration of older stones leads to internal shrinkage + dendritic cracks + subsequent nitrogen gas–filling from negative internal pressure

√ "crow-foot" = "Mercedes-Benz" sign = radiating streaklike lucencies within stone, also responsible for buoyancy

D. FLOATING GALLSTONE (20–25%)

(a) relatively pure cholesterol stones

(b) gas-containing stones

(c) rise in specific gravity of bile (= 1.03) from oral cholecystopaques (specific gravity of 1.06) causing stones with a specific gravity of 1.05 to float

E. GALLBLADDER SLUDGE

= calcium-bilirubinate granules + cholesterol crystals associated with biliary stasis

Cause: prolonged fasting, parenteral nutrition, hyperalimentation, hemolysis, extrahepatic bile duct obstruction, cystic duct obstruction, acute + chronic cholecystitis

√ nonshadowing homogeneously echogenic material:

√ fluid-sludge level

√ "sludge ball" = tumefactive sludge:

√ slowly shifting with repositioning of patient

DDx: gallbladder cancer

Prognosis: may cause acute cholecystitis

DDx: hemobilia with blood clot, parasitic infestation, mucus

Radiopacity:

√ lucent stones (84%): cholesterol (85%), pigment (15%)

√ calcified stones (15–20% on plain film, 60% on CT): cholesterol (33%), pigment (67%)

◊ CT sensitivity highest at 140 kVp

Location of calcium:

√ <u>calcium phosphate</u> deposited centrally within cholesterol stones

√ calcium carbonate deposited radially within aging cholesterol / peripherally around cholesterol + pigmented stones

Gallstones in Fetus

EGA: > 28 weeks EGA
Cause: hemolytic disease, cholestasis, maternal drug use
Prognosis: usually resolve before / after delivery

Gallstones in Neonate

◊ Rare without predisposing factors
Associated with: obstructive congenital biliary anomaly, total parenteral nutrition, furosemide, GI dysfunction (short-gut syndrome), prolonged fasting, phototherapy, dehydration, infection, hemolytic anemia

Gallstones in Older Children

Associated with: sickle cell disease, cystic fibrosis, malabsorption, total parenteral nutrition, Crohn disease, intestinal resection, hemolytic anemia, choledochal cyst

Gallstones in Pregnancy

Prevalence: 2–4% of pregnant patients have gallstones, 5% develop symptoms
Acute cholecystitis:
» NO increased risk during pregnancy
» 2nd most common condition requiring surgery (in 1÷1600–10,000 pregnancies)!

Cholecystolithiasis

- asymptomatic (60–65%); become symptomatic at a rate of 1–2–4% per year
- biliary colic (misnomer) ← transient obstruction of cystic duct / common bile duct develops in 33% (18% overall risk in 20 years):
  = acute RUQ / epigastric / LUQ / precordial / lower abdominal pain increasing over seconds / minutes + remaining fairly steady for 1–3(–6) hours associated with nausea + vomiting
  - no tenderness upon palpation

Abdominal plain film (10–16% sensitive):
√ calcified gallstones
CT (80% sensitive):
√ hyperdense calcified gallstones in 60%
√ hypodense cholesterol stones ≤ 140 HU = pure cholesterol stone (= ≥ 80% cholesterol content):
◊ Inverse relationship between CT attenuation number + cholesterol content
√ gallstones isointense to bile (< 30 HU) in 21–24% and thus undetectable by CT
US (91–98% sensitive; in 5% falsely negative):
√ bright (= highly reflective) echo from anterior surface of gallstone within gallbladder:
√ marked posterior acoustic shadowing
√ mobile upon repositioning of patient (may infrequently be adherent to wall)
√ reverberation artifact

◊ Small calcifications < 2 mm may not shadow

√ nonvisualization of GB + collection of echogenic echoes with acoustic shadowing (15–25%):

√ "wall-echo-shadow" = "double-arc shadow" sign

= 2 echogenic curvilinear parallel lines separated by sonolucent line (ie, anterior GB wall + bile + stone with acoustic shadowing)

√ focal nonshadowing opacities < 5 mm in diameter (in 70% gallstones)

False-negative US (5%):

contracted GB, GB in anomalous / unusual location, small gallstone, gallstone impacted in GB neck / cystic duct, immobile patient, obese patient, extensive RUQ bowel gas

Prognosis: stones < 3 mm may pass through cystic duct

Cx: acute cholecystitis (in 30%), choledocholithiasis, cholangitis, pancreatitis, duodenitis, biliary fistula, gallstone ileus, Mirizzi syndrome; cancer of GB + bile ducts (2–3 x more frequent)

Cholangiolithiasis

Choledocholithiasis

◊ Most common cause of bile duct obstruction!

Etiology: (a) passed stones originating in GB

(b) primary development in intra- / extrahepatic ducts (rare)

Frequency: in 12–15% of cholecystectomy patients; in 3–4% of postcholecystectomy patients; in 75% of patients with chronic bile duct obstruction

Risk indicators for CBD stone:

(1) Recent history of jaundice
(2) Recent history of pancreatitis
(3) Elevated serum bilirubin > 17 µmol/L
(4) Elevated serum amylase > 120 IU/L
(5) Dilated CBD > 6 mm (16%)
(6) Obscured bile duct

- asymptomatic: 10% of patients treated with cholecystectomy have unsuspected CBD calculi
- recurrent episodes of right upper quadrant pain, jaundice, chills, fever (25–50%)
- elevated serum bilirubin + alkaline phosphate levels
- elevated transaminase (75%)
- spontaneous passage with stones < 6 mm size

Location: dependently in duct

Cholangiography (most specific technique):

√ stone visualization in 92%

√ dependent round filling defects

DDx: air bubbles, neoplasm, concentrated bile

Peroperative cholangiography:

prolongs operation by 30 min;

4% false-negatives; 4–10% false-positives

US (22–82% sensitive):

√ stone visualization in 13–75% (more readily with CBD dilatation + good visibility of pancreatic head)
√ dilated ducts in 64–77% / duct < 8 mm in diameter in 24–36%
√ increased dilatation of CBD with administration of fatty meal / cholecystokinin
√ no stone in gallbladder (1.2–11%)

CT (25–90% sensitive, 97% specific, 94% accurate):
◊ No IV / enteric contrast + thin collimation at 140 kVp improves rate of detection
√ hyperattenuating stone surrounded by hypoattenuating bile + ampullary soft tissue = visualized in 75–88%
√ isoattenuating to surrounding bile (in 12–25%)
√ often angulated + geometric with a rim of bile along stone's anterior margin
√ "target" sign = intraluminal mass with crescentic ring (= stone of soft-tissue density) in 85%
√ subtle alternating low- and high-attenuation rings (= mixed cholesterol-calcium stones)

MRCP (pooled 95% sensitive, 95–99% specific):
◊ Thinner sections without intersection gaps provided by 3D isotropic MRCP
√ signal void (= dark filling defect) within high SI of static fluid on moderately T2WI (TE of 100 msec) (DDx: tumor, edematous papilla of Vater)
√ no enhancement of calculus
√ papillitis ← stone:
√ bile duct obstruction at papilla
√ smooth symmetric papillary edema
√ increased enhancement of papilla
√ obscured / missed calculi:
√ visible SI on T1WI ← sufficient water content
√ isointensity relative to bile
√ stones < 2–3 mm in diameter (< 50% sensitive)

MRCP is highly sensitive and specific for the detection of biliary filling defects and of stones in particular. It can identify choledocholithiasis as the cause of acute pancreatitis and thus direct interventional care.

NUC:
√ delayed bowel activity beyond 2 hours
√ persistent hepatic + common bile duct activity to 24 hr
√ prominent ductal activity beyond 90 minutes with visualization of secondary ducts

Cx: acute cholangitis, gallstone pancreatitis

Stone in Cystic Duct Remnant

retained in 0.4% after surgery for choledocholithiasis

CHRONIC GRANULOMATOUS DISEASE OF CHILDHOOD

= X-linked recessive (60%) / autosomal (40%) immunodeficiency disorder characterized by neutrophil dysfunction resulting in purulent infections + granuloma formation primarily involving lymph nodes, skin, lung

Prevalence: 1÷200,000 to 1÷250,000 in USA

Normal leukocyte function:

phagocytosis → activation of NADPH (nicotinamide adenine dinucleotide phosphate) oxidase → "respiratory burst" = electron transfer to molecular oxygen → formation of microbicidal free radical superoxide in phagocytic vacuole

Pathogenesis:

dysfunctional NADPH oxidase in polymorphonuclear (PMN) leukocyte → inability to generate hydrogen peroxide → prolonged intracellular survival of phagocytized catalase-positive bacteria → dissemination in reticuloendothelial system → chronic struggle of immune system → granuloma formation

Catalase-positive organisms:

most commonly Staphylococcus, Burkholderia cepacia, Nocardia, Mycobacteria, Serratia marcescens, Klebsiella, Pseudomonas, fungi (Aspergillus, Candida)

Path: recurrent and chronic infection → lymphadenitis / granuloma formation / caseation / suppuration

Age: onset within first 2 years;
M÷F = 6÷1 (more severe in boys)

- recurrent chronic infections: lung (most common)
- nitroblue tetrazolium test (NBT): low percentage of WBCs that reduce the yellow NBT dye to dark blue formazan after stimulation by phagocytosis / contact with endotoxin (normally > 90%)

@ Bone
√ osteomyelitis (⅓) commonly of spine, ribs, metatarsals

@ Chest
√ recurrent pneumonia (80%)
√ lung abscess / empyema (in up to 20%)
√ hilar lymphadenopathy
√ pleural + pericardial effusions (in up to ⅓)

@ Liver
√ hepatosplenomegaly (in up to 90%)
√ hepatic abscess (most common abdominal process)
√ liver calcifications

@ GI tract
- chronic diarrhea with malabsorption
- vomiting, anorexia, heartburn, weight loss

Histo: inflammation with granulomas and lipid-laden histiocytes of lamina propria, smooth muscle, serosa

Location: esophagus to rectum
√ esophageal dysmotility, esophagitis, stricture
√ gastric antral narrowing ± gastric outlet obstruction (16%)
√ segmental bowel wall thickening
√ enlarged mesenteric lymph nodes ± calcifications
√ perianal fistula + abscess

@ GU tract
- dysuria, UTI (5–15%)

√ cystitis
√ obstruction of urethra + ureters
@ Lymph nodes: cervical > femoral > inguinal
√ suppurative lymphadenitis
@ Skin
• pyoderma
Rx: prophylactic long-term trimethoprim-sulfamethoxazole + interferon gamma therapy
Prognosis: 2–5% mortality per year; death by pneumonia / sepsis due to Aspergillus / Burkholderia cepacia

CIRRHOSIS

= chronic liver disease characterized by diffuse parenchymal necrosis, regeneration and scarring with abnormal reconstruction of preexisting lobular architecture

Pathophysiology:
single insult / repetitive liver injury → hepatocyte death → macromolecules in extracellular matrix → activation of hepatic stellate (collagen-producing) cells by fibrogenic cytokines → nodular regeneration + fibrotic scarring

Liver fibrosis: = excess deposition of collagen, proteoglycans, and other macromolecules in extracellular matrix in response to repetitive liver injury

Etiology:
A. TOXIC / CHEMICAL
(1) Ethanol in 75%
(2) Aflatoxin = product of fungus Aspergillus flavus in improperly stored grain and nuts
(3) Drug-induced: prolonged methotrexate, oxyphenisatin, alpha-methyldopa, nitrofurantoin, isoniazid
(4) Iron overload: hemochromatosis, hemosiderosis
B. INFECTION / INFLAMMATION
(1) Chronic viral hepatitis B
(2) Chronic viral hepatitis C ← silent epidemic in USA in 1960s to 1980s with 4 million chronically infected
(3) Schistosomiasis
C. BILIARY OBSTRUCTION
(1) Cystic fibrosis
(2) Inflammatory bowel disease
(3) Primary biliary cirrhosis
(4) Obstructive infantile cholangiopathy
D. CARDIAC / VASCULAR
(1) Prolonged CHF = cardiac cirrhosis
(2) Hepatic venoocclusive disease
(3) Budd-Chiari syndrome
E. NUTRITIONAL
(1) Intestinal bypass
(2) Severe nonalcoholic steatosis + steatohepatitis ← obesity epidemic in USA (40 million adults, 6 million children) with 10–20% expected to develop cirrhosis

(3) Abetalipoproteinemia

F. HEREDITARY

(1) Wilson disease
(2) Alpha-1 antitrypsin deficiency
(3) Juvenile polycystic kidney disease
(4) Galactosemia
(5) Type IV glycogen storage disease
(6) Hereditary fructose intolerance
(7) Tyrosinemia
(8) Hereditary tetany
(9) Osler-Weber-Rendu syndrome
(10) Familial cirrhosis

G. IDIOPATHIC / CRYPTOGENIC (15%)
probably due to nonalcoholic steatohepatitis

Cirrhosis in children:
chronic hepatitis, congenital hepatic fibrosis, cystic fibrosis, biliary atresia, alpha-1 antitrypsin deficiency, tyrosinemia, galactosemia, hemochromatosis, Wilson disease, schistosomiasis, total parenteral nutrition

Associated with: anemia, coagulopathy, hypoalbuminemia, cholelithiasis, pancreatitis, peptic ulcer disease, diarrhea, hypogonadism

Path:

Semispecific Liver Patterns in Cirrhosis	
Differentiating Findings	*Cause*
Micronodules (≤ 3 mm)	Ethanol, hemochromatosis, nonalcoholic steatohepatitis
Macronodules (3–15 mm)	chronic viral hepatitis B, autoimmmune hepatitis
Enlargement of central liver + atrophy of periphery	Primary sclerosing cholangitis
Diffuse hypertrophy + periportal halo sign	Primary biliary cirrhosis

Histo: fibrotic bridges carving liver into regenerative nodules = HALLMARK of cirrhosis

Path:

The cirrhotic liver develops characteristic morphologic alterations such as (1) surface nodularity, (2) widening of fissures, (3) expansion of gallbladder fossa, (4) notching and atrophy of right lobe, (5) relative enlargement of lateral segments of left and caudate lobe.

- anorexia, weakness, fatigue, weight loss, ascites
- jaundice, continuous low-grade fever
- bleeding from esophageal varices, hepatic encephalopathy

Early hepatic findings:

√ enlarged (very early stage) / normal / shrunken liver:
√ atrophy (= shrinkage) of right lobe (segments 5–8) and medial segment of left lobe (segments 4a + 4b)

- √ concomitant hypertrophy of lateral segment of left lobe (segments 2 + 3) and caudate lobe (segment 1):
  - √ ratio of width of caudate to right lobe > 0.65 on transverse images [100% specific; 26% sensitive; 84–96% accurate; least sensitive in alcoholic cirrhosis, most sensitive in cirrhosis caused by hepatitis B] (DDx: Budd-Chiari syndrome)
  - √ diameter of quadrate lobe (segment 4) < 30 mm (= distance between left wall of gallbladder and ascending portion of left portal vein) ← selective atrophy (95% specific)
- √ enlargement of hilar periportal space
- √ "gallbladder fossa" sign = expansion of interlobar fissure

√ associated with fatty infiltration (in early cirrhosis)

Late hepatic changes:

√ surface nodularity + indentations (regenerating nodules)
- √ right posterior hepatic "notch" sign = indentation between hypertrophied caudate + atrophied right lobe of liver (PPV 99%; in 2% of normal population)

√ fibrous septa / bands

√ distorted hepatic architecture

√ confluent hepatic fibrosis

Extrahepatic findings:

√ signs of portal hypertension: portosystemic varices, portal vein thrombosis

√ splenomegaly

√ ascites ← failure of albumin synthesis, overproduction of lymph due to increased hydrostatic pressure in sinusoids / decreased splanchnic output due to portal hypertension)

√ mesenteric edema

√ bowel wall thickening ← edema

√ lymph nodes:
- › few and small in alcoholic cirrhosis
- › large and numerous in viral hepatitis
- › numerous in primary biliary cirrhosis

US (65–80% sensitive; DDx: chronic hepatitis, fatty infiltration):

Hepatic signs:
- √ surface nodularity (54% sensitive, 95% specific)
- √ caudate lobe hypertrophy (41% sensitive, 91% specific)
- √ "portalization" of hepatic vein waveform = dampened oscillations of hepatic veins resembling portal vein flow (57% sensitive, 76% specific)
- √ hepatomegaly (in 63%)
- √ increased hepatic parenchymal echogenicity in 66% (as a sign of superimposed fatty infiltration):
  - √ increased sound attenuation (9%)
  - √ decreased / normal definition of walls of portal venules (sign of associated fatty infiltration NOT of fibrosis)
- √ heterogeneous coarse (usually) / fine echotexture (in 7%)
- √ occasional depiction of isoechoic regenerative nodules
- √ dilatation of hepatic arteries ← increased arterial flow with demonstration of

intrahepatic arterial branches (DDx: dilated biliary radicals)
√ increase in hepatic artery resistance (mean RI of 0.58–0.66 in normals to 0.63–0.85 in cirrhotics):
√ blunted increase in RI after meal ingestion (from 42% in normals to 7% in cirrhotics)

Extrahepatic signs:
√ splenomegaly
√ ascites
√ signs of portal hypertension

US Elastography:
= US-based transient elastography = pulse-echo US acquisition following the wave propagation and velocity measurement of a probe-generated vibration of mild amplitude and low frequency (directly related to Young elastic modulus)

CT:
√ native + enhanced parenchymal inhomogeneity:
√ bridging bands of fibrous scarring
√ wedge-shaped / stellate confluent fibrosis in segments IV, V and VIII with capsular retraction (78%)
Confluent fibrosis: broad fibrotic scar up to several cm thick with a masslike appearance
√ decreased attenuation (steatosis) in early cirrhosis
√ isodense / hyperdense (siderotic) regenerative nodules
√ nodular / lobulated liver contour
√ predominantly portal venous supply to dysplastic nodules
√ hypodense area adjacent to portal vein (= peribiliary cysts from obstructed extramural peribiliary glands)
√ rapid tapering of intrahepatic portal + hepatic venous branches

CECT:
√ enlarged tortuous hepatic artery ← compensatory increase in arterial blood flow
√ arterioportal shunts (= trans-sinusoidal shunts in liver periphery + transplexal shunts with hypertrophy of peribiliary plexus) in hepatic arterial phase:
√ poorly demarcated transient peripheral wedge-shaped hepatic parenchymal enhancement
DDx: hepatocellular carcinoma (growth in 3- to 6-month intervals, defect on portal venous phase)
√ early retrograde enhancement of portal vein branches
√ hepatofugal flow
Cause: with occlusion of small hepatic venules, portal vein turns from a supplying vein into a draining vein

NEMR (problem-solving tool):
√ no alteration of liver parenchyma
√ extensive parenchymal heterogeneity ← fibrosis + cirrhotic nodules + perfusion abnormalities + fat and iron deposition
√ fibrotic septa / bridges / confluent fibrosis = devoid of iron and fat even with hepatic iron overload / fat deposition:
√ hypointense reticulations on T1WI
√ T2-hyperintense ← large water content of advanced fibrosis

√ NOT hypointense on T2* (= NO iron)
√ no signal loss on out-of-phase images (= NO fat)

√ generalized decrease in hepatic SI on T2WI ← mild iron deposition for unknown reasons
√ reticulations surround regenerative nodules typically of:
√ intermediate to high SI on unenhanced T1WI
√ intermediate to low SI on unenhanced T2WI

CEMR:
√ enhancement of liver fibrosis on T1WI ← Gd-contrast accumulation ← large extracellular component
√ progressive enhancement on delayed images with peak during late venous + equilibrium phases
√ occasional arterial hypervascularity within focal fibrosis (DDx to HCC: wedge-shaped configuration and persistence of enhancement into late venous phase)
√ enhancement of usually ill-defined arterioportal shunts:
√ visible only during arterial phase
√ fading to isointensity in late venous phase
√ areas of patchy hyperenhancement at arterial phase ← active inflammation

MR Elastography:
= observing the effect of 40–120 Hz shear waves generated by a mechanical device placed in contact with body → increase in velocity and wavelength proportionate with greater tissue stiffness
√ color-encoded quantitative liver stiffness maps of ROIs ← phase shifts in MR signal accumulate at tissue locations where gradient cycling is exactly in phase with generated mechanical wave

MR with Superparamagnetic Iron Oxide (SPIO):
Mechanism: RES–specific contrast agent = iron oxide particles → cleared from blood through phagocytosis → accumulate in RES cells of liver (80% uptake), spleen, bone marrow
√ reticulations of hepatic fibrosis with high SI on SPIO ← less iron oxide accumulation ← ↓ Kupffer cell density
√ pronounced T2* shortening + signal loss greatest on GRE ← local magnetic field inhomogeneities

Angio:
√ stretched hepatic artery branches (early finding)
√ enlarged tortuous hepatic arteries = "corkscrewing" ← increase in hepatic arterial flow
√ shunting between hepatic artery and portal vein
√ mottled parenchymal phase
√ delayed emptying into venous phase
√ pruning of hepatic vein branches (normally depiction of 5th order branches) ← postsinusoidal compression by developing nodules

NUC (^{99m}Tc–labeled sulfur colloid):
√ high blood pool activity ← slow clearance
√ colloid shift to bone marrow + spleen + lung
√ shrunken liver with little or no activity + splenomegaly
√ mottled hepatic uptake (pseudotumors) on colloid scan (normal activity on IDA scans!)
√ displacement of liver + spleen from abdominal wall by ascites

Cx: (1) Ascites: cause / contributor to death in 50%
(2) Portal hypertension → bland portal vein thrombosis (in 11–16%)
(3) Hepatocellular carcinoma (in 7–12%)
(4) Cholangiocarcinoma

Fatality from:
esophageal variceal bleeding (in 25%), hepatorenal syndrome (10%), spontaneous bacterial peritonitis (5–10%), complications from treatment of ascites (10%)

Dx: liver biopsy (0.03% fatality rate); poor underdiagnosed Bx (in 32%): specimen should be at least 2 cm long + contain at least 11 portal triads

DDx:
(1) Pseudocirrhosis
(2) Diffuse metastatic disease with desmoplastic reaction: breast, melanoma
(3) Fulminant hepatic necrosis ± regeneration
(4) Noncirrhotic intrahepatic portal hypertension: nodular regenerative hyperplasia, periportal fibrosis, hepatoportal sclerosis

Nodular Lesions in Liver Cirrhosis

Concept: gradual progression of regenerating (regenerative) nodule to → low-grade dysplastic nodule → high-grade dysplastic nodule → dysplastic nodule with subfocus of HCC → early HCC → progressed HCC

Radiologic diagnosis of HCC can be made with multiphasic CECT / CEMR

Pathophysiology:

As nodules dedifferentiate → progressive decrease in portal vascularization + ↑ blood supply via nontriadal arteries:
1. Hypoenhancement during portal phase
2. Increased number of nontriadal arteries during arterial phase (= hypervascularity)

MR visibility vs nodule size: > 2 cm (100%), 1–2-cm (52%), < 1 cm (4%)
Sensitivity of modality: MR (70–85%), CT (50–68%)
Recommendation: US surveillance at 6-month intervals

Nodule suspicious for HCC by US requires further investigation with CECT / CEMR if:
√ nodule > 1 cm is new
√ nodule enlarges over time

Challenges for imaging:
√ nodule visualization ↓ due to heterogeneity of fibrosis
√ heterogeneous enhancement may be mistaken for tumor
√ small nodules may demonstrate typical findings of HCC

The continuous histologic changes that nodules undergo result in significant overlap of enhancement patterns and findings on T1- and T2WI, complicating their imaging and histopathologic differential diagnosis.

Management protocol for small nodules < 2 cm:

The likelihood of a nodule to be HCC increases with size:
< 1 cm (indeterminate) = unlikely malignant → watch for interval growth
1–2 cm = close monitoring with imaging + biopsies

> 2 cm = likely malignant

(a) nodule < 1 cm:
re-examine after 3 months with same imaging technique used to depict lesion initially
› stable: return to routine screening
› growth: evaluation with 4-phase CT / MR

(b) nodule ≥ 1 cm:
evaluation with 4-phase CT / MR (unenhanced, arterial, portal, and equilibrium phases)
› typical for HCC: diagnosis confirmed
› atypical for HCC: biopsy

Regenerative (Cirrhotic) Nodule *(vast majority)*

= heterogeneous regeneration = localized proliferation of normal hepatocytes + supporting stroma with normal blood supply (25% hepatic arterial + 75% portal venous)

Morphology:

(a) **micronodular cirrhosis** (≤ 3 mm): usually due to alcoholism, biliary obstruction, hemochromatosis, venous outflow obstruction, previous small-bowel bypass surgery, Indian childhood fibrosis

(b) **macronodular cirrhosis** (3–15 mm, up to several cm): usually due to chronic viral hepatitis B, Wilson disease, alpha-1 antitrypsin deficiency

(c) mixed cirrhosis

CT:

√ iso- to hyperdense on hepatic arterial phase
√ iso- to hypodense on portal venous phase

MR:

√ variably SI relative to liver on T1WI:
√ hyperintense with lipid / protein / copper contents
√ iso- to hypointense relative to liver on T2WI
√ **siderotic nodules** (in 25%) with variable iron content:
√ hypointense on T1WI ← magnetic susceptibility
√ markedly hypointense on T2- / T2*WI
√ blooming on GRE

DDx of Liver Nodules in Cirrhosis

Features	*Regenerative nodule / low-grade dysplasia*	*High-grade dysplasia / HCC*
Blood supply	portal venous	nontriadal arteries (loss of portal supply)
Vascularity	like normal liver	hypovascular (if small) hypervascular (if large)
Enhancement	like normal liver	in arterial phase

√ signal loss on in-phase images
◊ An iron-poor focus within a siderotic nodule on T2WI suggests HCC!
√ **steatotic nodules** (usually multifocal):
√ hyperintense on in-phase gradient images

√ signal loss on out-of-phase images

CEMR:

√ Gd-enhancement similar to liver / slightly less

√ NO Gd-enhancement on arterial phase images

√ similar to liver on hepatobiliary specific imaging

√ similar to liver on superparamagnetic iron oxide

Lesions that exhibit enhancement similar to that of adjacent liver are likely regenerative and low-grade dysplastic nodules.

Dysplastic Nodule *(15–28%)*

= regenerative nodule with atypical cells

Histo: cluster of hepatocytes > 1 mm in diameter with evidence of (nuclear + cytoplasmic) dysplasia

Cause: common in hepatitis B and C, alpha-1 antitrypsin deficiency, tyrosinemia

Frequency: in 15–28% of explanted cirrhotic livers

LOW-GRADE DYSPLASTIC NODULE

= macroregenerative nodule, type I / ordinary adenomatous hyperplasia

Histo: preserved hepatic architecture, low-grade cytologic atypia, varying numbers of portal tracts, inconstant increase in number of unpaired arterioles

Prognosis: low malignant potential

√ variable SI on T1WI, iso- / hypointense on T2WI

√ enhancement similar to liver ← main blood supply from portal venous system

DDx: regenerative nodule (similar imaging features)

◊ No practical consequence of inability to differentiate between the two diagnoses!

HIGH-GRADE DYSPLASTIC NODULE

= macroregenerative nodule type II / adenomatous hyperplasia with atypia

Histo: moderate cytologic + architectural atypia, reduced number of portal tracts, progressive sinusoidal capillarization, ↑ number of unpaired arterioles

Prognosis: premalignant

√ variable SI on T1WI (depending on content)

√ usually iso- / hypointense on T2WI

√ mostly hypovascular ± arterial enhancement

◊ Nodules with loss of portal supply and development of insufficient number of nontriadal arteries to produce hypervascularity are difficult to diagnose and responsible for the high rate of false-negative imaging results.

Dysplastic Nodule with Subfocus of HCC

= adenomatous hyperplasia with microscopic HCC

Frequency: 6% of patients with dysplastic nodules

√ SI as any dysplastic nodule

√ "n**odule-in-nodule**" appearance = focus of high SI during arterial enhancement within dysplastic nodule

Small Hepatocellular Carcinoma

= adenomatous hyperplasia with macroscopic HCC < 2 cm

Prevalence: 27% for hepatitis B, 22% for hepatitis C

Sensitivity: 80–100% for lesion > 2 cm; 50% for lesion 1–2 cm; 5–33% for lesion < 1 cm in diameter

Histo: abnormally high number of muscularized unpaired arterioles + capillarized vessels

EARLY SMALL HEPATOCELLULAR CARCINOMA

Histo: well-differentiated with invasion of portal tracts; neoplastic cells replace normal cells; ± portal tracts; fatty change in 40%

Prognosis: 89% 5-year survival; 8% recurrence rate within 3 years of resection

√ high SI on T1WI

√ hypo- / isointense on T2WI

CEMR:

√ hypo- / isointense during arterial phase ← insufficient development of unpaired arteries

√ hypointense during portal phase of enhancement ← loss of portal vascularization

◊ Early HCC has mostly hypovascular or equivocal findings and thus is difficult to differentiate from a high-grade dysplastic nodule. Progressed small HCC has characteristics similar to classic HCC.

DDx: high-grade dysplastic nodule (requires biopsy)

PROGRESSED SMALL HEPATOCELLULAR CARCINOMA

Histo: no portal tracts; numerous nontriadal arteries + well-developed sinusoidal capillarization; microscopic vessel invasion in 27%

Prognosis: 48% 5-year survival

√ well-defined homogeneous round / oval lesion

√ variable SI on T1WI

√ moderately hyperintense on T2WI

CEMR:

√ enhancement = hyperintense during arterial phase ← main blood supply from hepatic arterial system

√ washout during portal / delayed phase

◊ A > 1 cm nodule with arterial phase hyperenhancement and portal venous / delayed phase washout may be diagnosed as HCC by either (CECT / CEMR).

Primary Biliary Cirrhosis

= CHRONIC NONSUPPURATIVE DESTRUCTIVE CHOLANGITIS

Histo: idiopathic progressive destructive cholangitis of interlobar and septal bile ducts, portal fibrosis, nodular regeneration, shrinkage of hepatic parenchyma

Age: 35–55 years; M÷F = 1÷9

Associated autoimmune disorders:

rheumatoid arthritis, Hashimoto thyroiditis, Sjögren syndrome, scleroderma, sarcoidosis

◊ 66–100% of patients with primary biliary cirrhosis have sicca-complex signs of the

Sjögren syndrome
- fatigue, insidious onset of pruritus (60%)
- xanthelasma / xanthoma (25%); hyperpigmentation (50%)
- IgM increased (95%)
- positive antimitochondrial antibodies (AMA) in 85–100%

√ normal extrahepatic ducts
√ cholelithiasis in 35–39%
CT:
√ scattered dilated intrahepatic ducts with no apparent connection to main bile ducts
√ periportal "halo" sign = perivascular cuffing
√ smooth capsule
√ caudate lobe hypertrophy (in 98%):
√ hypertrophied hyperattenuating caudate lobe surrounded by hypoattenuating rindlike right lobe (pseudotumor)
√ atrophy of lateral segment of left hepatic lobe
√ intrahepatic biliary calculi (20%)F
MR:
√ periportal "halo" sign (in 40%, SPECIFIC)
√ lymphadenopathy (in 62%)
NUC:
√ marked prolongation of hepatic ^{99m}Tc-IDA clearance
√ uniform hepatic isotope retention
√ normal visualization of GB and major bile ducts in 100%

Cx: hepatocellular carcinoma (in 5%)

DDx: (1) Sclerosing cholangitis (young men)
(2) CBD obstruction

Prognosis: mean survival 6 (range, 3–11) years after onset of cholestatic symptoms

Complications of End-Stage Liver Disease

Acute Respiratory Distress Syndrome

Pathophysiology: compromised liver function → systemic spillover of proinflammatory substances (cytokines)
√ patchy lung opacities (early)
√ diffuse bilateral dependent lung consolidation (late)
Prognosis: poor

Hepatopulmonary Syndrome

Dx: (1) Chronic liver disease
(2) Increased alveolar-arterial oxygen gradient
(3) Intrapulmonary vascular dilatation

Prevalence: 15–20% of cirrhotic patients
- hypoxemia with progressive dyspnea, cyanosis, clubbing

Typical MR Characteristics of Cirrhotic Liver Nodules					
Lesion	*T1WI*	*T2WI*	*Contrast Enhancement*		
	(relative to normal liver parenchyma)		*Gadolinium CM*	*Hepatobiliary CM*	*SPIO CM*
Regenerative nodule	variable, hyperintense with lipid / protein / copper contents	iso- to hypointense	similar to liver parenchyma	similar to liver parenchyma	similar to liver parenchyma
Low-grade dysplastic nodule	variable, often hyperintense	iso- or hypointense	similar to liver parenchyma	similar to liver parenchyma	similar to liver parenchyma
High-grade dysplastic nodule	variable, often hyperintense	iso- or hypointense	usually hypovascular ± arterial phase ↑	similar to liver parenchyma	similar to liver parenchyma
Early HCC	variable, often hyperintense	iso- or hypointense	usually hypovascular ± arterial phase ↑	± enhancement	± enhancement
Progressed HCC	variable, often iso- / hyperintense	moderately hyperintense	arterial-phase ↑, portal-phase washout	± enhancement	± enhancement
Large HCC	heterogeneous, predominantly hypointense	heterogeneous, predominantly hyperintense	arterial-phase ↑ in 80–90%, portal-phase washout	no enhancement	no enhancement

Pathomechanism:
elevation of unknown vasoactive substances in cirrhotic patient → pulmonary vascular dilatation (from 8–15 μm to 15–500 μm) → excess perfusion for a given ventilation (= diffusion-perfusion mismatch)

√ increased number of dilated arterioles + nontapering terminal branches extending to pleura (86%)

√ intrapulmonary arteriovenous shunts (14%):

√ nodular dilatation of peripheral pulmonary vessels

√ ^{99m}Tc activity in brain, liver, spleen on macroaggregated albumin imaging

√ bubbles in LA on microbubble echocardiography

CXR:

√ basilar nodular / reticulonodular areas of increased opacity (in 46–100%)

Hepatic Hydrothorax

= large pleural effusion in cirrhotic patient without primary pulmonary / cardiac disease

Prevalence: 5–10%

Mechanism: pressure gradient favors fluid movement from peritoneal to pleural cavity through small diaphragmatic defects; may occur in the absence of ascites

• dyspnea, nonproductive cough, pleural chest pain, hypoxemia

√ pleural fluid: right in 67–85%, left in 13–17%, bilateral in 2–17%

Portopulmonary Hypertension

Prevalence: 2–5% in patients with liver cirrhosis

Cause:

(a) thromboembolic: portal venous thrombus reaches lung through spontaneous / surgically created portosystemic shunts

(b) plexogenic: vasoconstriction from vasoactive substances (serotonin, thromboxane, interleukin I, endothelin I) that bypass the liver through portosystemic shunts

(c) cardiogenic: high cardiac output associated with cirrhosis → increased shear stress on pulmonary endothelial cells → endothelial hyperplasia

Dx: mean pulmonary artery pressure > 25 mmHg; pulmonary capillary wedge pressure < 15 mmHg

Prognosis: mean survival of 15 months

Pseudocirrhosis

= retracted tumor tissue + scarring between areas of regenerative liver parenchyma resembling macronodular cirrhosis

Cause: (1) Liver metastases treated with chemotherapy
(2) Hepatotoxic effect of chemotherapy

Time: within a few weeks or months after chemotherapy

Histo: macronodular regenerative hyperplasia; no bridging portal fibrosis

√ lobular liver margin
√ volume loss
√ caudate hypertrophy
√ portal hypertension

Confluent Hepatic Fibrosis

= geographic pattern of fibrosis involving an entire segment

Predisposed: liver cirrhosis

Location: mostly medial segment of left lobe + anterior segment of right lobe / both

Site: (a) wedge-shaped at subcapsular portion (b) radiating from porta hepatis

CT:
√ hypoattenuating lesion with volume loss:
√ overlying retraction of liver capsule

CECT:
√ vessel crowding
√ isoattenuating / minimally hypoattenuating on arterial phase + delayed enhancement
√ delayed contrast enhancement ← pooling of contrast material within edema / nonarterial vascular channels

MR:
√ low SI on T1WI + mildly high SI on T2WI ← edema and numerous vascular spaces
√ hypointensity during hepatobiliary phase (70%)

DDx: HCC (mass effect on liver contour and adjacent blood vessels, more nodular appearance, no retraction of liver capsule, not typically geographic pattern)

CLONORCHIASIS

Rarely of clinical significance

Country: endemic to Southeast Asia: Japan, Korea, Central + South China, Taiwan, Indochina; Eastern Europe

Organism: Chinese liver fluke = Clonorchis sinensis

Closely related: Opisthorchis viverrini (Thailand and Laos); Opisthorchis felineus (Siberia)

Cycle: parasite cysts digested by gastric juice → larvae migrate up the bile ducts → remain in small intrahepatic ducts until maturity (10–30 mm in length) → travel to larger ducts to deposit eggs

Infection: snail + freshwater fish serve as intermediate hosts; infection occurs by eating raw fish; hog, dog, cat, man are definite hosts

Path: (a) desquamation of epithelial bile duct lining with adenomatous proliferation of ducts + thickening of duct walls (inflammation, necrosis, fibrosis)
(b) bacterial superinfection with formation of liver abscess

• remittent incomplete obstruction + bacterial superinfection

Location: medium-sized + small intrahepatic bile ducts, primarily in subcapsular region

√ diffuse uniform dilatation of small intrahepatic bile ducts + NO dilatation of extrahepatic bile ducts + NO focal obstructing lesion

√ diffusely thickened bile duct walls

√ multiple crescent- / stiletto-shaped filling defects within bile ducts:
√ echogenic focus / cast on US

Cx: (1) Bile duct obstruction ← conglomerate of worms / adenomatous proliferation of ducts
(2) Calculus formation ← stasis / dead worms / epithelial debris
(3) Jaundice in 8% ← stone / stricture / tumor
(4) Generalized dilatation of bile ducts (2%)

CONGENITAL BILIARY ATRESIA

Etiology: ? variation of same infectious process as in neonatal hepatitis with additional component of sclerosing cholangitis or vascular injury

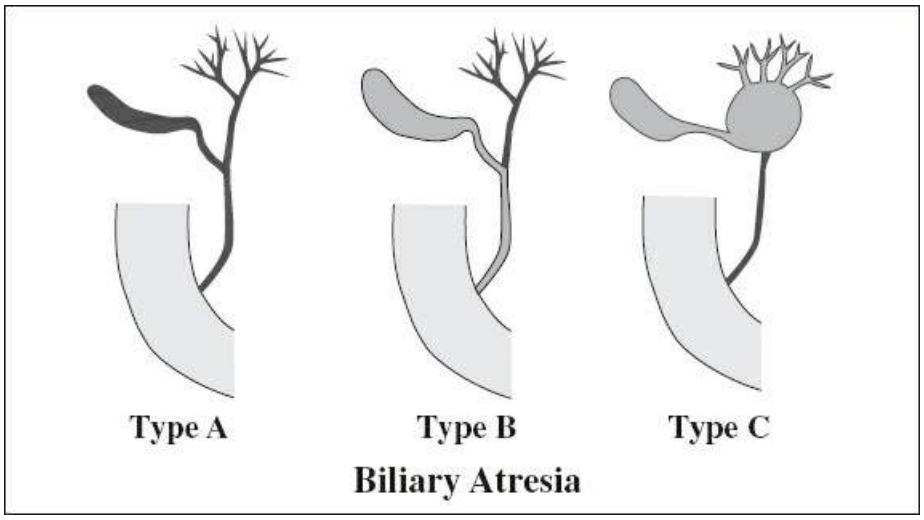
Prevalence: < 10÷100,000 live births

Age: neonate; M÷F = 2÷1

Histo: periportal fibrosis, proliferation of small intrahepatic bile ducts, mixed inflammatory infiltrates

In 15% associated with: polysplenia, trisomy 18

Types:
I Focal = intrauterine vascular insult (extremely rare)
II Intrahepatic biliary atresia = paucity of intrahepatic bile ducts (uncommon)
III Extrahepatic biliary atresia = atresia of CBD + patent intrahepatic bile ducts



Subtype 1 = perinatal type (66%)
• jaundice develops after regression of physiologic jaundice

√ bile duct remnant in porta hepatis

Subtype 2 = embryonic / fetal type (34%)

- normal decline in bilirubin does not occur

√ NO bile duct remnant in porta hepatis

Associated with:

polysplenia (10–12%), intestinal malrotation, azygos continuation of IVC, symmetric bilobed liver, situs inversus, preduodenal portal vein, anomalous hepatic arteries, bilobed right lung, complex CHD

US:

@ Liver:

√ normal / increased size of liver

√ normal / increased liver echogenicity

√ ↓ visualization of peripheral portal veins ← fibrosis

√ "triangular cord" / tubular echogenic structure in porta hepatis ← fibrous tissue = PATHOGNOMONIC

@ Gallbladder:

√ nonvisualization of gallbladder

√ small gallbladder < 1.5 cm in length + varying degrees of luminal compromise (DDx: hepatitis)

√ normal gallbladder > 1.5 cm in length (19%) with atresia of CBD distal to insertion of cystic duct

@ Bile ducts:

√ NO dilatation of intrahepatic bile ducts ← panductal sclerosis

√ ± visualization of bile duct remnant in porta hepatis (depending on type of biliary atresia)

√ small focal cystic dilatation of extrahepatic bile duct (= choledochal cyst) = patent segment of CBD with other parts being occluded ← fibrosis ± communication with gallbladder / intrahepatic bile ducts

NUC [phenobarbital-augmented cholescintigraphy] (90–97% sensitive, 60–94% specific, 75–90% accurate):

» preparation of patient with 5 ng/kg/d phenobarbital twice a day for 3–7 days to stimulate biliary secretion (via induction of hepatic enzymes + increase in conjugation + excretion of bilirubin)

√ good hepatic activity within 5 minutes (infants of < 3 months of age have a normal hepatic extraction fraction)

√ NO biliary excretion:

√ NO visualization of bowel on delayed images at 6 and 24 hr

√ delayed clearance from cardiac blood pool

√ increased renal excretion + bladder activity

DDx: severe hepatocellular dysfunction (DDx from neonatal hepatitis impossible in the absence of small bowel activity) requires liver biopsy

MR cholangiography:

√ nonvisualization of extrahepatic bile ducts

√ atrophic gallbladder

√ periportal thickening

Cholangiography (percutaneous / endoscopic / intraoperative)

Liver Biopsy (60–97% accurate)

Rx: (1) Roux-en-Y choledochojejunostomy (20%);

(2) Kasai procedure = portoenterostomy (80%)

(a) child < 60 days of age: 91% success rate

(b) child between 60 and 90 days of age: 50% success rate ← developing cirrhosis

(c) child > 90 days of age: 17% success rate

(3) Liver transplant

DDx:

(1) Neonatal hepatitis

(2) Sclerosing cholangitis

(3) **Alagille syndrome** = arteriohepatic dysplasia (abnormal facies, butterfly vertebra, pulmonic stenosis, complex CHD)

CONGENITAL HEPATIC FIBROSIS

= congenital cirrhosis with rapid + fatal progression

Histo: fibrous tissue within hepatic parenchyma with excess numbers of distorted terminal interlobular bile ducts + cysts that rarely communicate with bile ducts = extensive fibrosis WITHOUT regenerative nodules

Age: early childhood – 6th decade;
majority diagnosed in adolescence / early adulthood

Associated with:

autosomal recessive polycystic kidney disease (invariably), Meckel-Gruber syndrome, vaginal atresia, tuberous sclerosis, nephronophthisis, medullary sponge kidney (80%), autosomal dominant polycystic kidney disease (rare)

- liver function tests normal / mildly elevated
- portal hypertension; predisposed to cholangitis + calculi

√ "lollipop-tree" = ectasia of peripheral biliary radicles

√ atrophy of right lobe + normal / enlarged medial segment of left lobe + hypertrophy of left lateral segment and caudate lobe

√ splenomegaly

√ portosystemic varices

√ enlarged hepatic artery associated with large multiacinar regenerative nodules

Cx: cirrhosis, portal hypertension, hepatocellular carcinoma, cholangiocellular carcinoma

CONGENITAL TRUE PANCREATIC CYST

= very rare entity

Cause: sequestration of primitive pancreatic duct

Age: mostly in children < 2 years; M < F

Histo: cuboidal epithelium

- usually asymptomatic palpable mass, abdominal distention
- epigastric pain, vomiting, jaundice ← compression by cyst

May be associated with: Von Hippel-Lindau disease, Beckwith-Wiedemann syndrome,

hepatorenal polycystic disease

Location: pancreatic body / tail

√ uniform thin-walled single / multiple cysts

ECHINOCOCCAL DISEASE

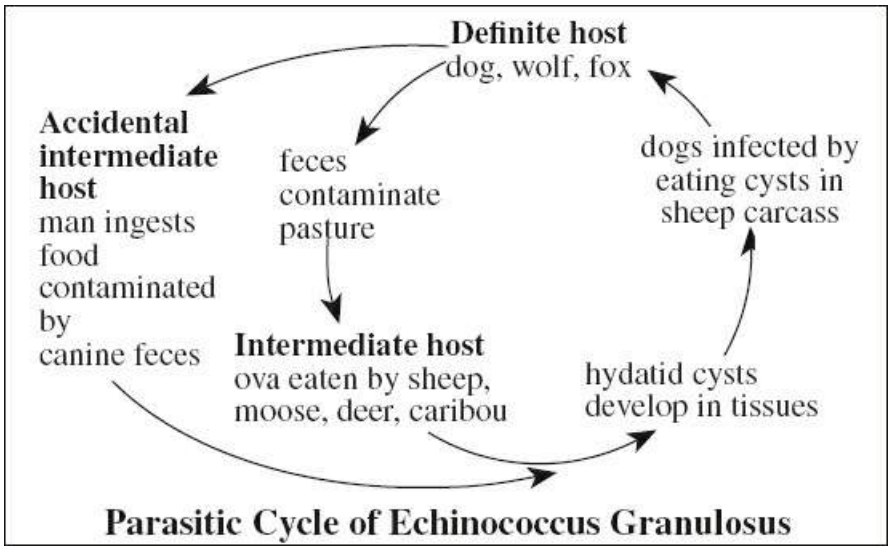
= zoonotic parasitic disease endemic in pastoral regions

Anatomy of cestode (tapeworm) in primary host:

3–6 mm adult sexually mature flatworm attaches to small intestines of canine with hooks on rostellum (tubular beak) + 4 suckers on its scolex (head); strobila (body) is composed of a colony of proglottids (segments) resembling a strip of tape; new segments are continuously produced by the proliferative neck piece pushing older segments towards tail; each segment has its own digestive tract + female and male reproductive structures (hermaphrodite); uterus of last segment filled with about 500 eggs drops off; lifespan of adult worm is 5–12 months

Life cycle relying on carnivores eating infected herbivores:

eggs excreted fecally by definite host (dog / fox / other carnivore) + intermediate host (sheep / rodents, other ruminants) into environment → grazing intermediate host ingests ova → ovum loses protective layer during digestion in duodenum → freed embryo (oncosphere armed with 6 hooks = hexacanth) attaches to + penetrates intestinal mucosa → migrates to liver by way of portal / lymphatic system → oncospheres are filtered by capillaries of liver (first line of defense) >> lung > other organs → intrahepatic development of oncosphere into metacestode = unilocular cyst (E. cysticus) / multiple cysts (E. multilocularis) that have brood capsules attached to inside of germinal layer and produce protoscolices → cycle completes when definitive host ingests infected viscera from intermediate host



Parasitic Cycle of Echinococcus Granulosus

Echinococcus Granulosus (E. cysticus)

= HYDATID DISEASE (= more common unilocular form compared to E. multilocularis)

= canine tapeworm in sheep-and cattle-grazing areas= zoonosis with worldwide distribution caused by larvae of echinococcus tapeworm, primarily E. granulosus

Endemic to certain regions of the world where livestock + dogs are raised together:

Australia, New Zealand, Africa (Kenya, Uganda, Sudan, Ethiopia), Eastern Europe, Russia, Mediterranean countries (Israel, Tunisia, Turkey, Italy, Spain, Croatia), China,

Japan, South America (Uruguay, Peru, Chile, Argentina), Middle East
◊ Reported on all continents except Antarctica!

Prevalence: 1 million persons infected worldwide

Primary / definitive host (harbors adult tapeworm):
(a) sylvatic life cycle: wolf, red fox, jackal, coyote
(b) domestic life cycle: dog, cat

Secondary / intermediate host (harbors larva stage):
(a) sylvatic life cycle: wild ungulate (deer, moose), kangaroo, wallaby, other grazing ruminants
(b) domestic life cycle: ungulates (= hoofed animals) like sheep, goat, swine, cattle, horse, camel

Accidental intermediate host: human ingesting eggs

Histo of 3-layered hydatid cyst:
A. CYST FLUID = antigenic clear / pale yellow transudate with neutral pH containing sodium chloride, proteins, glucose, ions, lipids, polysaccharides → may cause eosinophilia / anaphylaxis
B. TRUE WALL OF PARASITE
1. ENDOCYST = thin translucent inner **germinal layer** (resembling wet tissue paper) gives rise to brood capsules (daughter vesicles), which may
(a) harbor up to 400,000 protoscolices
(b) break up into numerous self-contained daughter cysts remaining attached to cyst wall by small pedicle (brood capsule)
(c) detach + form sediment in cyst fluid = "hydatid sand"
2. ECTOCYST = **cyst membrane** = thin acellular laminated membrane of chitinlike substance secreted by parasite; allows passage of nutrients
C. PERICYST (host response) = rigid outermost layer of protective zone of dense fibrous granulation tissue (fibroblasts, giant cells, eosinophils) replacing tissue necrosis ← compression by the expanding cyst; marginal vascular rim of 0.5–4 mm

N.B.: The hydatid cyst consists of the endocyst, where the scolices are produced, and the pericyst, which is composed of host cells that form a peripheral layer of reactive fibrous tissue.

• Tests:
1. Casoni intradermal test (60% sensitivity; may be falsely positive)
2. Complement fixation double diffusion (65% sensitivity)
3. Enzyme-Linked ImmunoSorbent Assay (ELISA) (90% sensitive in hydatid liver disease)
4. Indirect hemagglutination (85% sensitivity)

Time to diagnosis: 51 (range, 11–81) years; chronic disease with latent stage that may last years

Affected organs:
liver (50–75%); <u>widespread dissemination uncommon</u>: lung (14–43%); peritoneum (12%); kidney (2–6%); spleen (0.9–8%); CNS (1–4%); orbit (1%); bone (0.5–4%); bladder; thyroid; prostate; heart

Types of cysts (corresponding to stages of cyst growth):
(1) Unilocular cyst (initially):
√ simple on CT

√ laminated wall (double line sign) / free-floating scolices (snowflakes sign) on US
√ fibrous persistently hypointense rim on MR

(2) Cyst with daughter vesicles / daughter cysts = spoke-wheel appearance
√ daughter cysts of lower attenuation and less T1-hypointense compared to mother cyst ← free-floating scolices

(3) Partially / completely calcified
◊ Only complete calcification of all layers implies death of parasite!

Rx: (1) Surgery (in 10% recurrence)
(2) Antihelmintics (benzimidazoles)
(3) PAIR technique
= Puncture, Aspiration, Injection, Reaspiration
Dx: fluid analysis positive for hydatid disease in 70% (fragments of laminated membrane in 54%; scolices in 15%; hooklets in 15%)
Rx: injection of scolecidal agent (silver nitrate; 20 to 30% hypertonic saline solution; 0.5% cetrimide solution; 10% povidone iodine; 95% ethanol) with reaspiration
Cx: risk of anaphylactic shock (0.5%), asthma (3%), implantation of spilled protoscoleces (after rupture / following diagnostic puncture)

Hydatid Disease of Bone *(1%)*

Epidemiology: occurs occasionally in USA; usually in foreign-born individuals\
Path: no connective tissue barrier; daughter cysts extend directly into bone

@ Pelvis, sacrum, rarely long tubular bones
√ round / irregular regions of rarefaction
√ multiloculated lesion (bunch of grapes)
√ no sharp demarcation (DDx: chondroma, giant cell tumor) with secondary infection:
√ thickening of trabeculae with generalized perifocal condensation
√ cortical breakthrough with soft-tissue mass

@ Vertebra
√ sclerosis without pathologic fracture
√ intervertebral disks not affected
√ vertebral lamina often involved
√ frequently involvement of adjacent ribs

Hydatid Disease of CNS *(1–2–4%)*

• increased intracranial pressure and seizure

Location: subcortical parietal lobe; (rarely) dura, subarachnoid space, ventricular system, brainstem, spinal canal

√ usually single large well-defined oval / round cyst in brain parenchyma similar to CSF attenuation + intensity
√ occasional CHARACTERISTIC hypointense nonenhancing rim on T2WI
√ multiple cysts suggest rupture of preexisting single cyst
√ occasionally faint surrounding T2 hyperintense halo ← pericyst composed of inflammatory cells + fibrous tissue
√ NO significant surrounding edema; NO rim enhancement

√ heterogeneous predominantly cystic mass + fluid-debris level ← hydatid sand

Hydatid Disease of Kidney

- asymptomatic for many years until cyst size > 10 cm
- flank mass + pain; dysuria
- acute renal colic + hydatiduria from cyst rupture into collecting system (18%)

Site: cortex of upper / lower pole; typically unilateral + solitary

Plain film:
- √ abdominal mass
- √ curvilinear calcifications of pericyst (20–30%)

IVP:
- √ infundibular + calyceal distortion
- √ obstruction; renal dysfunction

US:
- √ unilocular cyst (DDx: simple renal cyst)
- √ multiseptated daughter cysts (DDx: polycystic kidney disease)
- √ thick bilayered cyst wall
- √ PATHOGNOMONIC "falling snowflake" or "snowstorm" sign = multiple echogenic foci from hydatid sand dispersed with repositioning of patient
- √ "floating membranes" = detachment of parasite wall from pericyst
- √ "wheel-spoke" pattern = mixture of membranes + broken daughter vesicles + scolices + hydatid sand

CT:
- √ unilocular type 1 cyst (initial stage)
- √ multilocular type 2 cyst (intermediate stage):
  - √ mixed internal attenuation
  - √ daughter cysts with lower attenuation
  - √ enhancing thick wall + internal septa
- √ completely calcified type 3 cyst

MRI:
- √ hypointense rim on T2WI = dense fibrous pericyst
- √ fluid hypointense on T1WI + markedly hyperintense on T2WI
- √ linear intracystic structures in type 2 cyst = collapsed membranes of daughter cysts:
  - √ hypointense on all sequences ± contrast enhancement
- √ low SI on all pulse sequences for type 3 cyst

Rx: total or partial nephrectomy / enucleation / marsupialization / cystectomy

Cx: cyst rupture → severe antigenic immune response

Hydatid Disease of Liver *(60%)*

Location: right > left lobe of liver; multiple cysts in 20%

Average size: 5 (up to 50) cm; up to 16 liters of fluid

- pain / asymptomatic (for years); incidental discovery in ⅓
- recurrent jaundice + biliary colic ← transient obstruction by membrane fragments + daughter cysts expelled into biliary tree; blood eosinophilia (20–50%)
- urticaria + anaphylaxis ← following cyst rupture

Spread: usually disruption of hepatic cysts during invasive treatment / spontaneous rupture / traumatic rupture
Growth: 2–3 cm annually
Plain film:
- √ peripheral crescentic / curvilinear / polycyclic calcifications (10–20–33%), located in pericyst
- √ pneumohydrocyst (infection / communication with bronchial tree)

US:
- ◊ Look for membranes / peripheral daughter vesicles
- √ well-defined anechoic cyst (common):
  - √ cyst wall of double echogenic lines separated by hypoechoic layer
  - √ "snowstorm" sign = multiple internal echogenic foci settling to most dependent portion of cyst (= hydatid sand)
  - √ multivesicular cyst of "racemose" / honeycomb appearance = multiple septa between daughter cysts inside mother cyst, CHARACTERISTIC but rare:
    - √ "wheel spoke" pattern = daughter cysts separated by echogenic material of hydatid matrix composed of broken daughter vesicles + scolices + hydatid sand
  - √ HIGHLY SPECIFIC serpentine linear structures within hydatid matrix
- √ partial / complete detachment of endocyst from pericyst ← decreasing intracystic pressure = sign of degeneration / trauma / host response / response to therapy:
  - √ localized split in wall with floating undulating membrane, CHARACTERISTIC but rare
  - √ "water lily" sign = complete detachment of membrane
  - ◊ Floating membrane does not indicate death of parasite!
- √ eggshell calcification in cyst wall (least common)

CT:
- √ well-demarcated round low-density mass of fluid attenuation of 3–30 HU (= mother cyst containing debris of hydatid sand + detached cyst walls):
  - √ round peripheral fluid collections of lower attenuation (= daughter cysts) arranged in CHARACTERISTIC wheel-spoke pattern
  - √ linear areas of increased attenuation = detached laminated floating membrane (after rupture of daughter cyst)
  - √ cyst wall of high attenuation on NECT
- √ enhancement of cyst wall + septations
- √ calcification of cyst wall / internal septa

MR:
- √ cyst with hypointense rim (= dense collagenous pericyst) on T1WI + T2WI
- √ peripheral cysts within cyst hypointense on T1WI + hyperintense on T2WI (= daughter cysts)
- √ twisted linear structures within cyst = collapsed parasitic membrane

Angio:
- √ avascular area with splaying of arteries
- √ halo of increased density around cyst (inflammation / compressed liver)

Cholangiography:
- √ cyst may communicate with bile ducts: right hepatic duct (55%), left hepatic duct

(29%), CHD (9%), gallbladder (6%), CBD (1%)

Local Cx:

(1) Rupture (50–90%)
  (a) contained = rupture of laminated membrane of endocyst, pericyst remains intact
    √ floating membranes
  (b) communicating = cyst contents escapes through biliary (5–15%) / bronchial tree
  (c) direct = tear of endocyst + ectocyst + pericyst with cyst contents spilling into pleural / peritoneal cavity → anaphylaxis, metastatic hydatidosis
(2) Infection (5–8%) following rupture
(3) Transdiaphragmatic growth (0.6–16%) through bare area of liver
  (a) rupture into pleural cavity
  (b) seeding in pulmonary parenchyma
  (c) chronic bronchial fistula
(4) Perforation into hollow viscus (0.5%)
(5) Peritoneal seeding (13%) = encysted peritoneal hydatidosis
(6) Compression of vital structures (bile ducts, portal vein)

Prognosis: usually favorable (but fatal if untreated); death from cholangitis / hepatobiliary septicemia (biliary obstruction with bacterial + fungal superinfection)

Hydatid Disease of Lung *(25%)*

= LUNG ECHINOCOCCOSIS

Source: (a) hematogenous spread from liver lesion
(b) transdiaphragmatic route (1–16% of hepatic disease) = migration of parasite from liver to pleural cavity

Frequency: 10–30% of hydatid disease
◊ Most common site of secondary involvement in children + 2nd most frequent site in adults
◊ Coexistence of liver + lung disease in 6%

- asymptomatic for months to years; eosinophilia (< 25%)
- fever, chest pain, sudden cough attacks:
  - hemoptysis, bilioptysis
  - expectoration of cyst fluid / membranes / scolices
- hypersensitivity reaction (if cyst rupture occurs)

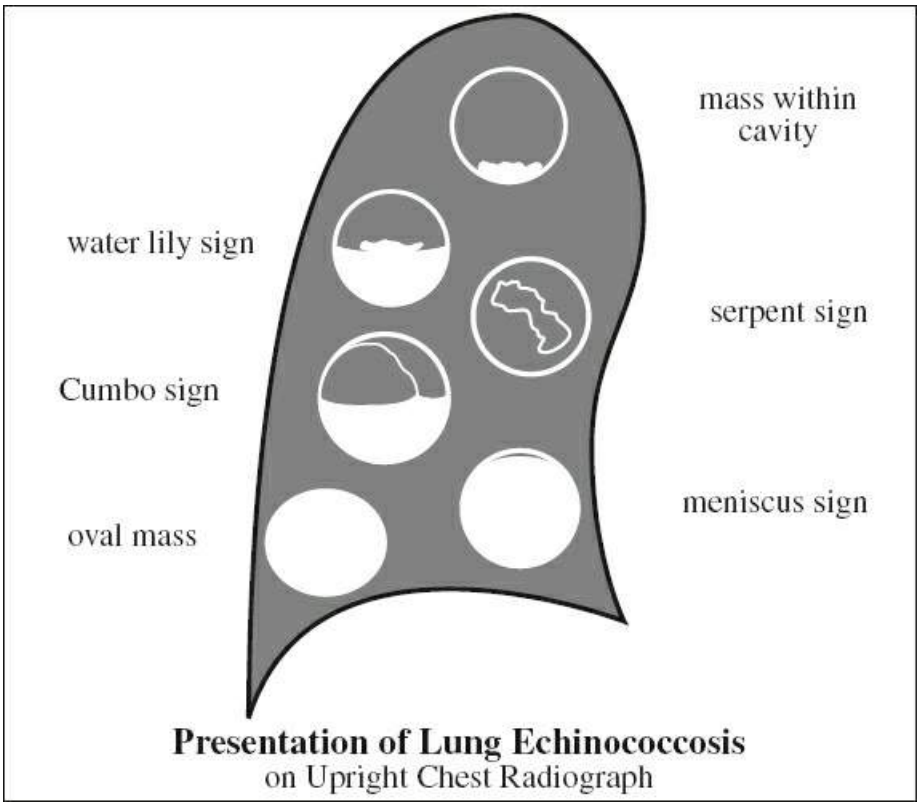
Location: lower lobes in 60%; bilateral in 20–50%

√ solitary (60–75%) / multiple (25–30%) spherical / ovoid masses with well-defined borders
√ size of 1–20 cm in diameter (16–20 weeks doubling time)
√ cyst communication with bronchial tree (= chronic bronchial fistula):
  √ "meniscus sign", "double arch" sign, "moon" sign, "crescent" sign (5%) = thin radiolucent crescent in uppermost part of cyst ← cyst erosion into adjacent bronchioles with air dissecting between pericyst and laminated membrane
  √ air-fluid level = rupture of all cyst walls with air entering the endocyst
  √ Cumbo / "onion peel" sign = air-fluid level inside endocyst + air between pericyst

and endocyst
√ "serpent" sign = collapsed membranes inside cyst outlined by air (after expectoration of cyst contents)
√ "water lily" sign, "sign of the camalote" = completely collapsed crumpled cyst membrane floating on cyst fluid
√ mass within cavity = crumpled membranes fall to most dependent portion of cavity after complete expectoration of cyst fluid
√ hydropneumothorax
√ calcification of cyst wall (0.7%)
√ rib + vertebral erosion (rare)
√ mediastinal cyst: posterior (65%), anterior (26%), middle (9%) mediastinum
Cx: pleuritis, lung abscess, parasitic pulmonary embolism, anaphylaxis ← cyst rupture, bacterial cyst superinfection (after cyst rupture)
DDx: metastasis, Wegener granulomatosis, other granulomatous diseases

Echinococcus Multilocularis

= E. ALVEOLARIS = ALVEOLAR ECHINOCOCCOSIS
= less common but more aggressive form of echinococcal dz.
Endemic to:
limited to Northern Hemisphere; western and central Europe (central + eastern France, southern Germany, western Austria, Switzerland), much of former Soviet Union, Iran, Iraq, some areas in Turkey, predominance in western and central China, northern Japan (Hokkaido Island), Midwestern USA, Arctic (Alaska, Canada, entire tundra)
Primary / definite host: (harbors 3–6 mm adult tapeworm)
(a) sylvatic life cycle (predominant): red fox, wolf, coyote
(b) domestic life cycle: dog; cat
Secondary / intermediate host: (harbors larva stage)
› sylvatic life cycle (predominant): small wild rodents (moles, lemmings, mice)
Accidental intermediate host:
human ingesting wild fruits, vegetable, water contaminated with fox / wolf feces; direct contact with fox /wolf; contact with dogs / cats that have ingested infested rodents



Path: diffuse infiltrative multivesicular mass (= persistence of larval forms without cyst maturation) resembling malignancy composed of many cysts of irregular shape + size (< 1 mm – 30 mm) associated with host reaction of fibrosis (chronic granuloma) + frequent central necrosis, cavitation, calcification; absence of clear margin between parasitic tissue + adjacent normal liver parenchyma

Histo: daughter cysts with thick lamellar wall arising on outer surface of original cyst rarely contain scolices; cyst has darkly staining thin outer laminar membrane and nonstaining delicate inner germinal layer; surrounded by inner zone of necrosis + outer layer of histiocytes and lymphocytes

Location: liver (access via portal vein / lymphatics); other organs in < 1% (lung, brain, bone)

- clinical manifestation 5–20 years after infection
- epigastric pain, jaundice, hepatomegaly, eosinophilia
- hemoptysis, chest pain, cough with expectoration, exertional dyspnea (with lung involvement)
- positive immunoserology for Em2 (E. multilocularis-specific native antigen isolated from metacestodes)

√ aggressive rapid growth pattern:
  √ geographic infiltrating lesion with ill-defined margins
  √ displacement of hepatic veins, portal vein, biliary tree
  √ regional atrophy of liver with capsular retraction ← biliary / vascular invasion

√ faint / dense amorphous coalescent nodular / flame-shaped calcifications = dystrophic central calcifications scattered throughout necrotic + granulomatous tissue (33–100%)

√ metastases to lung, heart, brain (in 10%)

Spread: widespread dissemination (2%)

› hematogenous: lung (7–20%), brain (1–3%)

› lymphatic: abdominal lymph nodes

› direct extension to / invasion of IVC, hepatic vein, diaphragm, trachea, lung, pericardium, esophagus, GI tract, retroperitoneum, perirenal space, peritoneum, gallbladder, pancreas, peripancreatic space, spleen, parietal wall (muscle, skin, bone [1%])

US (initially):

√ complex large heterogeneous mass mimicking a solid mass (70%):

√ juxtaposed areas of internal hyper- and hypoechogenicity with irregular margins

√ scattered foci of calcifications

√ pseudocyst with large area of central necrosis surrounded by an irregular ringlike region of hyperechogenicity (fibrous tissue)

√ "hailstorm pattern" = echogenic geographic ill-defined single / multiple hemangioma-like solid masses

√ pseudocyst with massive necrosis

DDx: benign liver cyst, cystadenoma, cystadenocarcinoma, hydatid disease

√ small calcified lesion

√ ± irregular cystic areas

√ distortion and displacement of hepatic + portal veins + biliary tree; invasion of IVC (on color Doppler)

√ propensity of spread to liver hilum:

√ dilatation of intrahepatic bile ducts

CT (morphologic assessment):

√ heterogeneous hypodense poorly marginated infiltrating masses

√ pseudocystic necrotic regions of near water density surrounded by hyperdense solid component

√ irregular ringlike region of often partly calcified fibrous tissue

√ little / no enhancement

MR (characterization of components):

√ fibrosis + parasitic tissue hypointense on T1WI

√ small cystic peripheral extensions + central necrosis hyperintense on T2WI

√ fibrotic collagenous components hypointense on T2WI

√ multivesicular structure resembling bunch of grapes / honeycomb

√ lesions hypointense on DWI (DDx to malignancy)

Kodama classification:

Type 1 (4%): multiple small cysts w/o solid component
Type 2(40%): multiple small cysts + solid component
Type 3 (46%): irregular large cysts + solid component
Type 4 (4%): solid without cysts
Type 5 (6%): single large cyst w/o solid component

Angio:

√ intrahepatic arterial tapering + obstruction

Cx: liver abscess (← superinfection by bacteria + fungi); secondary biliary cirrhosis;

portal hypertension (→ bleeding esophageal / duodenal varices); Budd-Chiari syndrome; obstruction of IVC; heart, lung, brain involvement

Prognosis: 50–75% mortality rate (higher for older age and poor local health care); death within 10–15 years if treatment not curative

Rx: radical surgery, liver transplantation, mandatory long-term benzimidazoles (antihelmintic drugs)

Dx: immunohistochemical + histologic analysis, serologic tests

DDx: cholangiocarcinoma, biliary cystadenoma + cystadeno- carcinoma, hepatocellular carcinoma (biopsy!), large hemangioma (characteristic enhancement pattern), metastasis, epithelial hemangioendothelioma

Alveolar Echinococcosis of CNS

Associated with: multicystic liver disease

√ heterogeneous solid / partially solid / cystic masses:

√ prominent surrounding edema (common)

√ heterogeneous ringlike / nodular cauliflower-like enhancement (typical)

√ calcifications

DDx: cerebral neoplasm

ECTOPIC PANCREAS

= PANCREATIC REST / CHORISTOMA = HETEROTOPIC PANCREAS = MYOEPITHELIAL HAMARTOMA

= presence of abnormally located pancreatic tissue with its own ductal system and NO vascular / neural / anatomic contact with normal pancreas

Frequency: 1–14% of population; M÷F = 2÷1

◊ Most common heterotopia within GI system!

- usually asymptomatic in GI tract (although stenosis, ulceration, bleeding, intussusception may develop)
- abdominal pain similar to peptic ulcer disease (77%)
- abdominal fullness (30%), melena (24%)
- functional: subject to usual pancreatic inflammatory + neoplastic disorders

Pathogenesis: metaplasia of multipotent endodermal cells; displacement and transplantation of pancreatic cells during embryonic development

Site: submucosa (in ½) / muscularis propria

Location: lesions may be multiple

(a) proximal portion of duodenum (30%): pylorus, duodenal bulb

(b) 2nd–4th portion of duodenum (20%)

(c) greater curvature of antrum 1–6 cm from pylorus (26%)

Prevalence: 1%–2%: in ¾ submucosal

(d) other small bowel (16%): proximal jejunum, ileum, Meckel diverticulum

(e) rarely in: colon, esophagus, gallbladder, bile ducts, liver, spleen, umbilicus, mesentery, mesocolon, omentum, fallopian tubes

Size: usually 0.5–2.0 (up to 5.0 cm in its largest diameter)

√ smooth cone- / nipple-shaped submucosal nodule 1–5 cm (rarely > 3–4 cm) in size

√ central umbilication representing orifice of filiform duct

CT:

√ flat / ovoid irregularly marginated intramural mass
√ homogeneously enhancing with intraluminal extension (= enhancement pattern similar to pancreatic tissue)
√ 5–20 mm small cystic change in markedly thickened wall of 2nd part of duodenum ← pseudocysts of groove pancreatitis / cystic dystrophy of duodenum / paraduodenal wall cysts

MR:
√ area with SI similar to native pancreas
√ ± surrounding inflammatory changes
√ PATHOGNOMONIC presence of ducts on MRCP

Endoscopic US:
√ solid mass of intermediate echogenicity

Cx: biliary + intestinal obstruction, massive GI bleeding, pancreatitis, paraduodenal pancreatitis, pseudocyst, insulinoma, malignant transformation

DDx of submucosal mass without umbilication:
Brunner gland adenoma, leiomyoma, lymphoma

EMBRYONAL RHABDOMYOSARCOMA OF BILIARY TREE

= rare tumor most commonly arising from CBD

Frequency: 1% of liver tumors in children

Median age: 3 years; < 5 years in 75%; M > F

Path: intraluminal biliary mass / cluster of grapelike masses (similar to rhabdomyosarcoma of bladder / vagina)

Histo: same as sarcoma botryoides; positive reactions for muscle markers

- jaundice (in 60–80%), abdominal distension, fever
- hepatomegaly, malaise, nausea, vomiting
- ↑levels of conjugated bilirubin + alkaline phosphatase

Metastases (in up to 30%):
retroperitoneal + mesenteric lymph nodes, lung

Location: common bile duct (most frequently) and intrahepatic bile ducts → invasion of liver

Size: 8–20-cm

√ bulky heterogeneous mass in porta hepatis
√ intrahepatic bile duct dilatation
√ regional lymphadenopathy
√ displacement / invasion of duodenum, stomach, pancreas

Cholangiography:
√ large bulky intraluminal mass / grapelike cluster of intraluminal masses → focally distending common bile duct + obstructing proximal bile ducts

US:
√ solitary heterogeneous hypoechoic mass
√ multiple hypoechoic nodules separated by septa
√ portal vein displacement without thrombosis
√ multiple tumor arteries with low-resistance spectrum

CT:

√ homo- / heterogeneous hypo- / hyperattenuating mass
√ ± prominent fluid component
√ NO / intense heterogeneous globular enhancement

MR:
√ T1 hypointense + T2 hyperintense / predominantly fluid-intensity mass in CBD or biliary radicals
√ heterogeneous intrahepatic mass with large areas of fluid

MRCP:
√ partially cystic mass within / adjacent to CBD causing mural irregularity of duct

Prognosis: 78% survival with local disease after multimodal therapy; total resection possible in 20–40%

DDx: choledochal cyst, infantile hemangioendothelioma, (intense peripheral nodular enhancement with centripetal fill-in), mesenchymal hamartoma of liver (predominantly cystic), hepatoblastoma (elevated AFP)

EPIDERMOID CYST OF SPLEEN

= EPITHELIAL CYST = PRIMARY CYST OF SPLEEN

Frequency: 10% of all benign nonparasitic cysts

Cause: infolding of peritoneal mesothelium / collection of peritoneal mesothelial cells trapped within splenic sulci

Histo:
(1) Mesothelial lining
(2) Squamous epithelial lining = epidermoid cyst
= squamous metaplasia from embryonic inclusions within preexisting mesothelial surface epithelium

Age: 2nd–3rd decade (average age of 18 years)

May be associated with: polycystic kidney disease

A. Unilocular + solitary (80%)
B. Multiple + multilocular (20%)

Average size: 10 cm

√ well-defined thin-walled anechoic lesion of water density
√ peripheral septations / cyst wall trabeculations (in 86%)
√ curvilinear calcification in wall (9–25%)
√ may contain cholesterol crystals, fat, blood

Cx: trauma, rupture, infection

EOSINOPHILIC CHOLANGIOPATHY

= rare benign cause of biliary obstruction

Prevalence: 15 cases in literature

Cause: unknown

Histo: transmural eosinophilic infiltration of biliary tract

A. Eosinophilic cholecystitis
B Eosinophilic cholangitis
C. Both

May be associated with: multiple organ involvement (in 50%) of GI tract, urinary tract, bone marrow, pancreas, lymph nodes

• jaundice ± peripheral eosinophilia

√ thickened bile duct wall ± biliary dilatation

√ wall irregularities in beaded pattern

Rx: steroids

DDx: lymphoma, AIDS cholangiopathy, collagen vascular disease, cholangiocarcinoma, amyloidosis

EPITHELIOID HEMANGIOENDOTHELIOMA

= rare primary low-grade malignant vascular tumor of liver (soft tissue, skin, bone, lung)

Incidence: 0.1÷100,000 annually

Average age: 44 (range, 25–58) years; M÷F = 2÷3

May be associated with: oral contraceptives, exposure to vinyl chloride

Path: multifocal nodules varying in size from a few mm to several cm involving both lobes of the liver ← rapid perivascular extension along hepatic + portal veins); nodules may coalesce in liver periphery

Histo: dendritic spindle-shaped cells + epithelioid round cells in a matrix of myxoid + fibrous stroma; neoplastic endothelial cells invade sinusoids + terminal hepatic + portal veins cutting off the tumor's blood supply; immunohistochemical stain with antibodies to factor VIII (von Willebrand factor), CD31 / CD34

• in 80%: RUQ abdominal pain, weakness, anorexia, jaundice

• hepatomegaly, weight loss

In 27–40% metastases to: lung, peritoneum, lymph nodes, bone, spleen, mesentery

Growth pattern:

(a) multifocal nodular form of early stage:

√ multiple predominantly peripheral nodules

(b) diffuse form of advanced stage:

√ coalescence of nodules into confluent masses

√ peripheral subcapsular growth (in 75%) without capsular bulge

√ capsular retraction (in 25–69%) ← fibrotic reaction

√ increased tumor vascularity

√ hypertrophy of uninvolved liver

Plain film:

√ hepatic calcifications within myxoid stroma (in 15%)

US:

√ individual / confluent nodules or diffusely heterogeneous echotexture

√ nodules with echogenicity unrelated to size:

√ hypoechoic ← central core of myxoid stroma

√ hyperechoic ± hypoechoic rim

√ isoechoic with hypoechoic halo

√ no blood flow

CT:

√ homogeneously ↓ attenuation ← myxoid + hyalinized stroma

√ capsular retraction in peripheral lesion

CECT:

√ target / halo pattern = nonenhanced outer rim of avascular tissue + enhanced inner peripheral rim

√ peripheral + progressive centripetal enhancement with incomplete fill-in on delayed phase

√ enhanced / nonenhanced tumor center on delayed imaging

MR:

√ central hypointensity on T1WI

√ "target" sign / concentric zones = alternating high- and low-signal–intensity rings on T2WI:

√ central zone of fibrosis / hemorrhage / necrosis

√ rim of cellular proliferation + edema

√ hyperintense center + thin rim of hypointensity on T2WI

CEMR:

√ multilayered targetlike appearance with prominent rimlike enhancement

√ central nodular enhancement (38%)

√ "lollipop" sign = synchronous targetlike enhancement of tumor mass + along hepatic / portal veins terminating at / near periphery

Angio:

√ hyper- and hypovascularity (dependent upon degree of sclerosis + hyalinization)

√ invasion ± occlusion of portal + hepatic veins

NUC:

√ decreased perfusion to central myxoid tumor portion + increased perfusion to cellular areas on sulfur colloid scan

√ photopenic defect on static sulfur colloid scan

√ NOT gallium avid

√ moderate to intense uptake on PET

Prognosis: 20% die within 2 years, 20% survive for 5–28 years ± treatment

Rx: liver transplantation (without spread); radical resection; transarterial chemoembolization

DDx of single nodule: cholangiocarcinoma; confluent hepatic fibrosis in advanced cirrhosis; treated HCC, large atypical cavernous hemangioma

DDx of multiple nodules: metastatic disease, angiosarcoma

DDx of diffuse form: sclerosing carcinoma; vasoocclusive disease

FASCIOLIASIS

= infection by trematode Fasciola hepatica (liver fluke)

Life cycle:

miracidia infests freshwater snails → multiply + excreted as cercariae → ingested as contaminated water by sheep / cattle / human → metacercariae encyst in stomach → perforate duodenal wall → migrate into peritoneal cavity → perforation of liver capsule by fluke (= hepatic phase) digesting hepatocytes forming clusters of small peripheral sterile necrotic cavities + tunnel-shaped microabscesses → parasites become established in biliary ducts (= biliary phase), mature and release eggs into bile ducts → move into central + extrahepatic bile ducts + gallbladder to accommodate increasing size of parasite

Endemic to: South America, Asia, Africa, Europe, USA

• fever, abdominal pain, hepatomegaly, eosinophilia, biliary colic

CT:

√ multiple serpentine branching hypoattenuating subcapsular lesions pointing toward central liver

√ "tunnels and caves" sign = multiple clustered hypoattenuating nodules

US:

√ intrabiliary filling defects + biliary dilatation

√ wall thickening of extrahepatic ducts and gallbladder

FATTY LIVER

= FATTY INFILTRATION OF THE LIVER = HEPATIC STEATOSIS

= accumulation of triglyceride droplets in hepatocytes

N.B.: no fatty infiltration of liver parenchyma

Prevalence: 15–35% in general population; > 60 g alcohol daily (45%); hyperlipidemia (50%); obesity with body mass index > 30 kg/m² (75%); obesity coupled with high alcohol consumption (95%)

Mechanism: injury to mitochondrial structure / processes (β-oxidation, energy depletion) of hepatocytes

Cause:

A. METABOLIC DERANGEMENT

metabolic syndrome (= obesity, insulin resistance, hypertriglyceridemia), acute fatty liver of pregnancy, protein malnutrition (kwashiorkor, marasmus), starvation, total parenteral hyperalimentation / nutrition (TPN), malabsorption (jejunoileal bypass), glycogen storage disease, Wilson disease, glycogen synthetase deficiency, cystic fibrosis, Reye syndrome, corticosteroids, severe hepatitis, trauma, chronic illness (TB, CHF), chemotherapy

B. HEPATOTOXINS

alcohol, carbon tetrachloride, arsenic, phosphorus

Common drugs: 5-fluorouracil, irinotecan, methotrexate, amiodarone, tamoxifen, corticosteroids, antipsychotics

C. INFLAMMATION

chronic viral hepatitis C > B, chronic autoimmune hepatitis

Path: > 5% fat of total liver weight

Histo: hepatocytes with large cytoplasmic fat vacuoles containing triglycerides (= steatosis) ← defects in free fatty acid metabolic pathways

Location: most pronounced + earliest around central vein

Histopathologic analysis of biopsy specimens allows:

(1) Grading of severity of steatosis
(2) DDx between steatosis and steatohepatitis
(3) Confirmation of nonalcoholic fatty liver disease / nonalcoholic steatohepatitis
(4) Detection of unsuspected coexisting disease like viral hepatitis.

• most common cause of elevated liver function tests

Pattern of fat deposition: diffuse (most common), focal, multifocal, perivascular, subcapsular

√ rapid change with time (few days to > 10 months) depending on clinical improvement (abstinence from alcohol, improved nutrition) + degree of severity + early stage

Cx: steatohepatitis (inflammatory cell injury), cirrhosis

Acute Fatty Liver of Pregnancy

Time: during late 3rd trimester

- slowly evolving right upper quadrant / epigastric pain
- jaundice
- symptoms of preeclampsia: HTN, edema, proteinuria

√ hepatomegaly + diffuse fatty change of liver

Diffuse Fat Deposition in the Liver

◊ Most frequently encountered pattern

√ hepatomegaly (75–80%) / normal sized liver

Plain film:

√ "radiolucent liver" sign = enlarged radiolucent liver

US (60–100% sensitive, 77–95% specific, 85–97% accurate):

√ liver echogenicity exceeds that of renal cortex / spleen:

√ fine (more typical) / coarse hyperechogenicity

√ increased sound attenuation:

◊ Attenuation of sound beam (= scattering of sound beam) is a feature of fat, NOT fibrosis

√ poor definition of posterior aspect of liver / diaphragm

√ decreased visibility of portal triads

√ poor delineation of intrahepatic architecture

√ impaired visualization of borders of hepatic vessels

NECT (43–95% sensitive, 90% specific):

An increase in fat content leads to a decrease in CT numbers at low energy. With higher energy levels the fat attenuation values are higher as well.

› relative criteria with internal control:

√ attenuation of liver less than that of intrahepatic vessels (= marked steatosis)

√ density of liver at least 10 HU less than that of spleen

√ hepatosplenic attenuation difference (Δ = L – S)

The spleen serves as a good internal control for comparison with the liver because:

› splenic attenuation is unaffected by various diffuse pathologic processes

› spleen is located at the same cross section as liver

At NECT, a normal liver has higher attenuation than a normal spleen. A lower liver attenuation suggests a diagnosis of hepatic steatosis.

Δ > 5 HU no macrovesicular steatosis (0–5%)

Δ -10 to 5 HU mild to moderate steatosis (6–30%)

Δ < -10 HU steatosis of > 30%

√ ratio of liver÷spleen < 1

◊ A hepatic attenuation index of < 0.8 is 100% specific for > 30% macrovesicular steatosis

The hepatic attenuation index is an objective measure of fatty liver disease.

› absolute criteria:

√ liver attenuation of < 48 HU; of < 40 HU = 30% fat

64.4 ± 3.1 HU	0% fat	41.9 ± 6.7 HU	26–50%
59.1 ± 7.3 HU	1–25%	25.0 ± 15.5 HU	> 50%

CECT:
- √ absolute liver attenuation < 40 HU (limited sensitivity)
- √ liver attenuation < musculature (marked steatosis)

Dual-energy CT (scans at 140 + 80 kVp):
- √ hepatic steatotic attenuation changes more marked with a change in tube potential compared to normal liver
- ◊ Tube current variation (from 200 to 50 mAs) does not affect the mean tissue attenuation values!

NUC:

^{99m}Tc-sulfur colloid scan:
- √ diffuse heterogeneous uptake (68%)
- √ reversal of liver-spleen uptake (41%)
- √ increased bone marrow uptake (41%)

^{133}Xe ventilation scan:
- √ increased activity during washout phase (38%)

MR (81% sensitive, 100% specific):
- √ slightly higher signal intensity on T1WI + T2WI; relatively insensitive (10% fat by weight will alter SE signal intensities by only 5–15%)
- √ signal loss on out-of-phase (= opposed-phase) compared to in-phase images / fat turns black with Dixon technique (chemical shift imaging):
  Explanation: difference in precession frequencies for protons in fat ($–CH_2$) and water (–OH)
  - √ estimation of liver fat content by comparing liver tissue to spleen and muscle as internal references
  - √ quantifiable by degree of SI loss
- √ chemical fat saturation sequence (usually less sensitive but superior in the presence of cirrhosis)
- √ MR spectroscopy (most accurate noninvasive method)

The advantage of MR spectroscopy is its ability to determine the absolute liver fat concentration. It has a high sensitivity for detecting small amounts of hepatic triglycerides.

Focal Fat-Sparing in Diffuse Fatty Liver

Cause: disturbance in portal venous flow / direct drainage of systemic blood into liver

Characteristic locations:
(a) in porta hepatis = posterior edge of segment 4 anterior to portal vein bifurcation ← drainage of aberrant gastric vein
(b) next to gallbladder bed (drainage of cystic vein)
(c) adjacent to falciform ligament / ligamentum venosum
(d) subcapsular skip areas

- √ geographic configuration

√ poorly delineated margins
√ contrast enhancement similar to normal liver
√ pseudolesion = NO mass effect (= undisplaced course of intrahepatic vessels)

US:

Relative Frequency of Causes of Fatty Liver

Most common	*Common*	*Rare*	*Congenital*
Alcohol overuse	Viral infection	Nutritional / dietary	Storage disorders
Insulin resistance	Hepatitis C	TPN	Glycogen storage disease
Obesity	Hepatitis B	Rapid weight loss	a_1-Antitrypsin deficiency
Hyperlipidemia	Drug use	Starvation	Wilson disease
	Steroids	Jejunoileal bypass	Hemochromatosis
	Chemotherapy	Irradiation	Cystic fibrosis
	Amiodarone		Others:
	Valproic acid		Prader-Willi syndrome, Bardet-Biedl syndrome, Metabolic disorders

√ hypoechoic ovoid / spherical / sheetlike mass

CT:

√ hyperattenuating relative to surrounding liver

MR:

√ hyperintense on T1WI
√ lack of decrease in SI on opposed-phase gradient-echo T1WI

DDx: mass (round / ovoid shape, well-demarcated margins, no fat content, random location, mass effect + displacement of vessels, contrast uptake above that of normal liver)

Focal Fat Deposition in the Liver

Etiology: (?) relative ischemia due to ↓ portal venous flow / ↓ delivery of unknown substances via portal vein

Key factor: ↑ levels of insulin in portal venous blood

Distribution:
(a) lobar / segmental uniform lesions
(b) lobar / segmental nodular lesions
(c) perihilar lesions
(d) diffuse nodular lesions = multifocal
(e) diffuse patchy lesions

Location:

› periligamentous: along falciform ligament and fissure for ligamentum teres, and medial aspect of left lobe ← aberrant internal mammary + paraumbilical veins
› perihilar: within anterior aspect of segment IV adjacent to porta hepatis ← aberrant right / left gastric veins
› pericholecystic: ← aberrant cholecystic vein
› subcapsular: around perforating capsular vessels
› perivascular: predominantly in centrilobar + periportal regions ← variants of blood supply = "third inflow" from connections between peripheral portal radicles + systemic veins

√ fan-shaped lobar / segmental distribution with angulated / interdigitating geographic

margins
√ lesions extend to liver capsule
√ pseudolesion = NO mass effect ← undisplaced course of vessels, no bulging of liver contour
√ perivenous halo of fat (= tram- / ring-like configuration on cross sections) around hepatic veins / portal veins / both

US:
√ hyperechoic area with poorly defined / sharp margins
√ multiple / rarely single echogenic nodules simulating metastases (rare)

CT:
√ patchy areas of decreased attenuation ranging from –40 to +10 HU (DDx: liver tumor)
√ NO contrast enhancement

MR:
√ high signal on T1WI + low / isointense signal on T2WI
√ decreased SI on opposed-phase gradient-echo T1WI relative to in-phase imaging

NUC with colloid:
√ no significant changes on sulfur colloid images (SPECT imaging may detect focal fatty infiltration)

DDx: primary / secondary hepatic tumor; fat-containing regenerative nodules of liver cirrhosis

Hepatic Subcapsular Steatosis

= in patients with renal failure and insulin-dependent diabetes, insulin can be delivered in peritoneal dialysate

Pathophysiology:
intraperitoneal insulin → subcapsular hepatocytes exposed to higher concentration of insulin → blocks oxidation of free
fatty acids within hepatocytes → preferential esterification into triglycerides → accumulation of intracellular fat

√ unique subcapsular pattern of fatty infiltration

FOCAL NODULAR HYPERPLASIA

= FNH = 2nd most common benign tumor of liver after hemangioma

Prevalence: 0.9%; 3–8% of all primary hepatic tumors in adult population, 2–4% in pediatric population (typically between 2 and 5 years); twice as common as hepatocellular adenoma

Cause: (?) circulatory disturbance or reparative process in areas of focal injury → triggers focal hepatocellular hyperplasia owing to a regional increase in blood flow
◊ Oral contraceptives DO NOT cause FNH, but exert a trophic effect on its growth!

Path: localized well-delineated usually solitary (80–95%) subcapsular mass composed of numerous small nodules within an otherwise normal liver; NO true capsule; frequently central fibrous scar in area of interconnection of fibrous bands (HALLMARK); angioarchitecture typically has one / more thick-walled arteries within fibrous septa radiating from the center toward the periphery → dividing into numerous capillaries

connected to sinusoids → drained by large hepatic veins (NO portal veins!)

Histo: composed of multiple spherical aggregates of hyperplastic hepatocytes often containing increased amounts of fat (in 50%) + triglycerides + glycogen; high number of Kupffer cells line sinusoids; proliferation of small bile ducts within fibrous septa without connection to biliary tree; difficult differentiation from regenerative nodules of cirrhosis + hepatocellular adenoma

Pathologic classification:

A. Classic FNH (80%):
abnormal nodular architecture, malformed vessels, cholangiolar proliferation

B. Nonclassic FNH (20%) without septa / central scar:
◊ Difficult to differentiate from other liver masses by imaging
(a) telangiectatic FNH (15%)
(b) FNH with cytologic atypia (3%)
(c) mixed hyperplastic + adenomatous FNH (2%)
√ globally resembling hepatic adenoma
√ no prominent septa
√ vaguely lobulated contours
√ central scar (in only 4%)

Age peak: 3rd–4th decade (range, 7 months to 75 years); M÷F = 1÷2 to 1÷8

Associated with: hepatic hemangioma (in 23%), meningioma, astrocytoma, arterial dysplasia of other organs in case of multiple FNH

- initially often asymptomatic (in 50–90% incidental discovery)
- vague abdominal pain (10–15%) ← liver capsule distention / mass effect on adjacent organs / blood flow variations
- normal liver function + normal AFP
- hepatomegaly / abdominal mass

Location: right lobe÷left lobe = 2÷1; multiple in 5–20%

Mean size: 4 cm in diameter; < 5 cm (in 85%)

√ well-circumscribed nonencapsulated nodular cirrhotic-like mass in an otherwise normal liver:
√ often near liver surface
√ pedunculated mass (in 5–20%)
√ multiple masses (in 20%)

√ central stellate scar = central fibrous core (NOT true scar) with radiating fibrous septa containing congeries of arteriovenous malformation [*congerere*, Latin = to collect, heap up]
√ spoke-wheel pattern (in 50% on average, in 80% if > 3 cm) (DDx: fibrolamellar HCC)

√ highly vascular tumor:
√ supplied by enlarged anomalous hepatic artery
√ venous drainage always into hepatic veins (DDx: HCC drains into portal venous system in 98%)
√ hemorrhage is unlikely

√ pseudocapsule of a few mm in thickness ← surrounding compressed hepatic parenchyma, perilesional vessels, inflammatory reaction:
√ fuzzy margins

√ calcifications EXTREMELY rare
NECT:
√ iso- / slightly hyperattenuating homogeneous mass
CECT (3 phases necessary!):
› arterial phase (30–60 sec after bolus injection):
√ transient intense hyperdensity of most of the lesion except for central scar
√ hypodense central scar (15–33%)
› portal venous phase:
√ early washout into hyperdense draining vein
√ lesion becomes isodense
› delayed / equilibrium phase:
√ lesion remains isodense
√ hyperdense central scar ← delayed washout of contrast from myxomatous scar tissue
US:
√ iso- / mildly hypo- / mildly hyperechoic (33%) homogeneous mass
√ hypoechoic halo (of compressed liver parenchyma / displaced hepatic vessels)
√ hyperechoic central scar in 18%
Doppler:
√ enlarged afferent blood vessel with central arterial hypervascularity + centrifugal filling to the periphery in a "spoke-wheel" pattern
√ large draining veins at tumor margins
√ may show high-velocity Doppler signals with arterial pulsatility from arteriovenous shunts (DDx: hepatocellular adenoma has intratumoral venous flow)
MR (70% sensitive, 98% specific, requires 3 phases):
√ usually homogeneous signal intensity of lesion
› T1WI:
√ iso- to mildly hypointense (94%)
√ atypically hyperintense lesion in 6%
√ T2WI: isointense / mildly hyperintense (94–100%)
√ central scar (more often detected than on US / CT)
√ hypointense on T1WI
√ hyperintense on T2WI in 75–84% ← edema within myxomatous tissue + vascular channels + bile ductules
√ hypointense on T2WI in 25% ← absent / minimal edema
CEMR (2-D / 3-D GRE):
√ marked homogeneous enhancement in arterial phase fading to isointensity on delayed image
√ iso- to slightly hyperintense during portal venous / delayed phase relative to liver
√ occasionally slightly hyperenhancing in equilibrium phase ← entrapment of Gd-DTPA by functioning hepatocytes inside tumor followed by 1% excretion into biliary tree
√ central scar after Gd-chelate administration:
√ low SI on early phase of enhancement
√ late + prolonged enhancement of central scar ← enlarged interstitial space with increased fluid content (gradually taking up contrast material)
√ enhancement of pseudocapsule on delayed images

√ homogeneously iso- to hyperintense (in 96%) / peripheral ring enhancement on 1-hour delayed images with hepatocyte-specific contrast agent (eg, gadobenate dimeglumine [Gd-**B**enzyl**O**xy**P**ropionic**T**etra**A**cetate]) (DDx: adenomas never enhance)

√ less uptake of IV superparamagnetic iron oxide (ferucarbotran, mangafodipir trisodium) than surrounding liver (= uptake mechanism similar to that of sulfur colloid)

◊ Use iron oxide in lesions with atypical features!

NUC:

Sulfur colloid scan:

◊ Only FNH contains sufficient Kupffer cells to cause uptake:

√ normal uptake (60–75%)

√ increased uptake = virtually DIAGNOSTIC

√ cold spot (33%) ← less Kupffer cells (DDx: hepatic adenoma, hemangioma, hepatoblastoma, liver herniation, hepatocellular carcinoma)

Tc-HIDA:

√ increased uptake (90%), normal uptake, cold spot (10%) with delayed excretion ← biliary ductules in FNH not communicating with biliary tree

^{99m}Tc-tagged RBCs:

√ increased uptake during early phase

√ defect relative to liver on delayed images

Angio:

√ discretely marginated hypervascular mass (90%) with intense capillary blush / hypovascular (10%)

√ enlargement of main feeding artery with central blood supply (= "spoke-wheel" pattern in 33%)

√ homogeneous parenchymal stain

√ decreased vascularity in central stellate fibrous scar

Rx: (1) Discontinuation of oral contraceptives
(2) Resection of pedunculated mass
(3) Diagnostic excisional biopsy for extensive tumor (FNH seldom requires surgery)
(4) Conservative in asymptomatic patient

Cx: rarely rupture with hemoperitoneum (increased incidence in patients on oral contraceptives – 14%)

DDx:

(1) Fibrolamellar carcinoma (metastases, retroperitoneal adenopathy, tumor hemorrhage + necrosis causing pain, collagenous calcified hypointense scar on T2WI)
(2) Hepatic adenoma (10 cm large tumor, symptomatic due to propensity for hemorrhage in 50%, central scar atypical, use of oral contraceptives)
(3) Well-differentiated hepatocellular carcinoma (internal necrosis + hemorrhage, vascular invasion, metastases, persistent rim-enhancement of tumor capsule)
(4) Giant cavernous hemangioma (larger tumor, may calcify, globular peripheral enhancement followed by centripetal filling, retention of contrast on delayed images, central scar with CSF-like behavior on MR)
(5) Hypervascular metastasis (hypovascular during portal venous phase, in older patient)
(6) Intrahepatic cholangiocarcinoma (less vascular, dominant large central scar, metastases)

Multiple Focal Nodular Hyperplasia Syndrome

(1) Liver hemangioma
(2) Berry aneurysm
(3) Meningioma, astrocytoma
(4) Systemic arterial dysplasia & portal vein atresia

Telangiectatic Focal Nodular Hyperplasia

Frequency: 10% of all FNH
Mean age: 38 years; women
Associated with: oral contraceptives (mean time, 15 years)
Mean size: 7 cm
√ multiple lesions in 20–50%
√ strong arterial enhancement
√ persistent lesion enhancement (61%) ← sinusoidal dilatation
√ absence of a central scar (92%)
√ heterogeneous pattern (43%) ← necrosis, sinusoidal dilatation, hemorrhagic foci
MR:
√ hyperintensity on T1WI (53%) ← intrasinusoidal dilatation
√ strong hyperintensity on T2WI (44%)
DDx: hepatic adenoma

GALLBLADDER ADENOMA

Incidence: 0.15% of cholecystectomy specimens, 4–7% of all gallbladder polyps
• usually incidental finding, rarely symptomatic
May be associated with: primary sclerosing cholangitis, gastrointestinal polyposis syndromes (Peutz-Jeghers, Gardner syndrome)
√ sessile / pedunculated mass:
√ solitary (in ⅔); 2–5 in number (in ⅓)
√ up to 20 mm in size
√ internal vascularity at color Doppler interrogation
√ typically enhancing (DDx adenocarcinoma)
Prognosis: dysplasia-to-carcinoma sequence
◊ Adenomas >12 mm in diameter may exhibit malignancy
DDx: polypoid gallbladder adenocarcinoma (NO reliable differentiation)

GALLBLADDER CARCINOMA

Incidence: 0.4–4.6% of biliary tract operations; 5th most common gastrointestinal malignancy worldwide (after colon, pancreas, stomach, liver, esophagus); 3% of all intestinal neoplasms; 7,000 new cases annually in USA
◊ Most common biliary cancer (9 x more common than extrahepatic bile duct cancer)
Prevalence: 3÷100,000 (USA)
Demographics: most common in Israel, Bolivia, Chile, northern Japan, New Mexico
Ethnicity: Native Americans + Hispanic Americans (with increased prevalence of gallstones)

Median age: 72 years; M÷F = 1÷3 to 1÷4; whites > blacks
◊ 85% occur in 6th decade or later!

Risk factors: gallstones; increased body mass; female gender; postmenopausal status; cigarette smoking; exposure to chemicals (rubber, automobile, wood finishing, metal fabricating industries); chronic Salmonella typhi infection

Associated with:

(1) Disorder of gallbladder:
  (a) Cholelithiasis in 74–92%
    ◊ Gallbladder carcinoma occurs in only 1% of all patients with gallstones!
  (b) Porcelain gallbladder (in 4–60%): prevalence of gallbladder carcinoma in 10–25% of autopsies
  (c) Chronic cholecystitis
  (d) Gallbladder polyp: a polyp > 2 cm is likely malignant!
(2) Disorder of bile ducts:
  (a) Primary sclerosing cholangitis (PSC)

In patients with primary sclerosing cholangitis 60% of gallbladder polyps are malignant.

  (b) Congenital biliary anomalies: most types of choledochal cyst, cystic dilatation of biliary tree, anomalous junction of pancreaticobiliary ductal union, low insertion of cystic duct
(3) Inflammatory bowel disease (predominantly ulcerative colitis, less common in Crohn disease)
(4) Familial polyposis coli

Path: diffusely infiltrating lesion (68%), intraluminal polypoid growth (32%)

Histo:

(a) adenocarcinoma (90%):
  › papillary (6%): densely cellular papillary fronds protruding into GB lumen with dysplasia and increased mitoses
  › intestinal type (= variant of well-differentiated adenocarcinoma with intestinal glands)
  › mucinous (5%, with > 50% extracellular mucin)
  › signet-ring cell (abundant intracytoplasmic mucin)
  › clear cell (well-defined cytoplasmic borders)
(b) rare epithelial cell types (10%): poorer prognosis
  › adenosquamous carcinoma (3%)
  › squamous cell carcinoma (1%)
  › small (oat) cell carcinoma (0.5%, highly aggressive, ± paraneoplastic Cushing syndrome)
  › undifferentiated carcinoma
(c) nonepithelial cell types (2%):
  carcinoid, carcinosarcoma, basal cell carcinoma, lymphoma

Modified Nevin Stage:

I mucosa only (in situ carcinoma)
II mucosa + muscularis invasion
III mucosa + muscularis + serosa
IV gallbladder wall + lymph nodes

V hepatic / distant metastases

- Early diagnosis usually unsuspected ← lack of specific signs + symptoms:
  - history of past GB disease (50%)
  - malaise, vomiting, weight loss; chronic RUQ pain (54–76%)
  - obstructive jaundice (35–74%)
  - abnormal liver function tests (20–75%)
  - ± elevated α-fetoprotein and CEA

Location: fundus (60%), body (30%), neck (10%)

Growth types:

√ mass replacing the gallbladder (37–70%) with engulfed gallstones

√ irregular eccentric thickening of GB wall (20–30%) ← submucosal spread:

√ focal (59%) / diffuse (41%) wall thickening

DDx: acute / chronic inflammation (usually < 10 mm)

√ intraluminal polypoid / fungating "cauliflower-like" mass with wide base (15–25%)

√ pericholecystic infiltration: in 76% focal, in 24% diffuse

√ dilatation of biliary tree (38–70%):

√ infiltrative tumor growth along cystic duct

√ lymph node enlargement causing biliary obstruction

√ intraductal tumor spread

√ fine granular / punctate flecks of calcification (= mucinous adenocarcinoma)

√ lymph node enlargement in porta hepatis

N.B.: misdiagnosis by US / CT in 50%, especially in the presence of gallstones

Abdominal radiograph:

√ calcified gallstones

√ porcelain gallbladder

√ RUQ gas collection (after invasion of adjacent bowel)

Cholangiography:

√ malignant stricture / obstruction of extrahepatic bile ducts / right + left bile duct confluence, intrahepatic duct of right lobe

√ intraluminal GB filling defect (= tumor / stones)

√ mass displacing / invading gallbladder

√ intraductal filling defects (= tumor / stones)

US:

√ gallbladder replaced by mass with irregular margins + heterogeneous echotexture (= tumor necrosis)

√ immobile intraluminal well-defined round / oval polypoid mass (15–25%) hypoechoic relative to liver

DDx: tumefactive sludge

Clues to polypoid malignancy:

√ solitary polyp > 10 mm

√ wide polyp base

√ focal wall thickening > 3 mm

√ coexisting gallstones

√ focal / diffuse thickening of gallbladder wall (20–30%)

√ echogenic foci = coexisting gallstones / wall calcifications / tumoral calcification

√ tumor inseparable from liver
√ hypovascular on color Doppler

CT:
√ hypo- / isoattenuating mass in gallbladder fossa:
√ low-attenuation areas of necrosis
√ areas of enhancement (= viable tumor)
√ subtle extension beyond wall of GB
√ invasion of liver (40–65%) with protrusion of anterior surface of medial segment of left lobe

MR:
√ hypointense mass on T1WI relative to liver
√ ill-defined early contrast enhancement
√ hyperintense mass on T2WI
√ lower apparent diffusion coefficient than for benign lesion

PET:
√ FDG uptake within GB polyp greater than liver background

Metastases: in 75–77% at time of diagnosis

(a) direct extension (most common mode): invasion of liver (34–65–89%), duodenum (12–15%), colon (9–15%), pancreas (6%), stomach, bile duct, right kidney, abdominal wall
Cause: thin GB wall with only a single muscle layer + no substantial lamina propria + perimuscular connective tissue continuous with interlobular connective tissue of liver

(b) lymphatic spread (26–41–75%):
cystic, pericholedochal, celiac, superior mesenteric, foramen of Winsløw, paraaortic nodes, superior + posterior pancreaticoduodenal

(c) intraperitoneal seeding (common)

(d) hematogenous spread (less common): stomach, duodenum, liver, lung, bones, heart, pancreas, kidney, adrenal, brain

(e) neural spread (frequent): associated with more aggressive tumors

(f) intraductal spread (least common): particularly in papillary adenocarcinoma

Cx: perforation of gallbladder → abscess formation
√ gallstones located within abscess

Prognosis: 75% unresectable at presentation; average survival is 6 months; 5% (< 5%) 1-year (5-year) survival rate

DDx: (1) Xanthogranulomatous cholecystitis (lobulated mass filling gallbladder + stones)
(2) Acute / chronic cholecystitis (generalized gallbladder wall thickening < 10 mm)
(3) Liver tumor invading gallbladder fossa
(4) Tumors from adjacent organs: pancreas, duodenum
(5) Metastases: melanoma, leukemia, lymphoma
(6) Polyps: cholesterol ~, hyperplastic ~, granulation polyp
(7) Adenomyomatosis

GALLBLADDER TORSION

= rare cause of abdominal pain (1÷365,520 hospital admissions)
At risk: generalized loss of elastic + adipose tissue, kyphoscoliosis, calcification of cystic artery
Cause: abnormal / absent mesenteric fixation of GB to inferior margin of liver ("floating GB")
Age: elderly; M÷F=16%÷84%
A. INCOMPLETE torsion = rotation < 180°
- mimics biliary colic with recurrent episodes of pain

B. COMPLETE torsion = rotation > 180°
- acute RUQ pain, nausea, vomiting, ± palpable mass

√ gallbladder wall thickening + adjacent free fluid
√ gallbladder hydrops ← cystic duct obstruction
√ ectopic anterior / inferior GB location
√ cystic duct to right of GB + tapering / twisting of cystic duct
Cx: perforation ← necrosis ← impaired venous drainage

GLYCOGEN STORAGE DISEASE

= autosomal recessive diseases with varying severity and clinical syndromes (13 different types, 8 affect the liver)
◊ Type Ia and Ib are associated with hepatocellular carcinoma!
◊ Type III and IV progress to cirrhosis!
◊ Type I and III are associated with hepatic adenomas!
◊ Hepatomegaly + hypoglycemia + growth retardation + disproportional distribution of body fat in children consider glycogen storage disease!

Von Gierke Disease (Type Ia)

Etiology: defect in glucose-6-phosphatase with excess deposition of glycogen in liver, kidney, intestines
Dx: failure of rise in blood glucose after glucagon administration
Age at presentation: infancy
@ Liver
√ hepatomegaly
US:
√ increased liver echogenicity (glycogen / fat)
√ nephromegaly
CT:
√ increased (glycogen) / normal / decreased (fat) parenchymal attenuation

@ Kidney
- proximal + distal tubular dysfunction; hyperuricosuria
- focal segmental glomerulosclerosis
- Fanconi-like syndrome

√ nephromegaly
√ increased cortical + medullary echogenicity ← nephrocalcinosis, nephrolithiasis
√ amyloidosis
√ high renal blood flow
Prognosis: death in infancy, may survive into adulthood with early therapy

Cx: (1) Hepatic adenoma (in 22–75% of adults)
(2) Hepatocellular carcinoma (10% risk)

Pompe Disease (Type II)

= abnormal metabolism with enlargement of myocardial cells ← glycogen deposition; similar to endocardial fibroelastosis
Etiology: defect in lysosomal glucosidase
√ massive cardiomegaly with CHF
√ hepatomegaly
Prognosis: sudden death in 1st year of life ← conduction abnormalities; survival rarely beyond infancy

Forbes / Cori Disease (Type III)

Cx: hepatic adenoma, cirrhosis

Anderson Disease (Type IV)

Cx: cirrhosis

McArdle Disease (Type V)

Hers Disease (Type VI)

HEMOCHROMATOSIS

= pathologic state of intracellular iron accumulation / excess iron deposition in various parenchymal organs (liver, pancreas, spleen, kidneys, heart) leading to cirrhosis with portal hypertension
• Lab tests (of low sensitivity + specificity):
  • ↑ ferritin level; ↑ transferrin saturation index
Role of imaging:
(1) Clinically silent disease often first uncovered by imaging
(2) Monitor effectiveness of clinical treatment noninvasively
NECT (63% sensitive + 96% specific in iron overload):
√ diffuse / rarely focal increase in liver density (> 72 HU)
√ depiction of portal + hepatic veins against background of hyperattenuating liver
√ dual energy CT (at 80 + 120 kVp) can quantitate amount of iron deposition
◊ Superimposed steatosis reduces sensitivity!
◊ Wilson disease, colloidal gold treatment, long-term amiodarone treatment decreases specificity!
MR: (skeletal muscle = good SI reference)
◊ Effect proportional to field strength!
@ Liver

MRI is the best noninvasive method for measuring the level of iron in the liver with high sensitivity, specificity, positive and negative predictive values to:
› confirm the diagnosis
› determine severity

› monitor therapy.

The liver parenchyma demonstrates higher SI than the paraspinal musculature on all sequences. Slight to moderate iron overload is better identified on GRE images → decreased SI of the liver parenchyma.

√ T1 + T2 + T2* shortening proportional to iron deposition

Physics: paramagnetic susceptibility of ferritin and ferric ions leads to profound shortening of longitudinal relaxation time T1 + transverse relaxation time T2, particularly T2*, of adjacent protons; ↓ SI in affected organs is proportional to iron deposition

√ decreased SI on in-phase compared with out-of-phase images (opposite to steatosis)

√ quantification of amount of iron overload on GRE sequences with T2* weighting + progressively longer echo times

Dx: liver biopsy (= standard method for diagnosis) to

› quantify iron overload
› determine prognosis based on level of hepatopathy
› monitor evolution of disease
› monitor effects of treatment

Genetic Hemochromatosis

= IDIOPATHIC / PRIMARY / HEREDITARY HEMOCHROMATOSIS

= genetic defect in iron transport with excessive duodenal absorption + parenchymal retention of normal intake of dietary iron favoring accumulation within non-RES organs

◊ Clinically more severe than transfusional hemosiderosis!

Cause: autosomal recessive disorder (abnormal HFE gene located near human-leukocyte antigen [HLA] on short arm of chromosome 6) → excessive absorption of intestinal iron (2–3 x of normal population)

Prevalence: 1÷220 whites of northern European ancestry; homozygote frequency of 0.25–0.50%; heterozygote carriers in 10%

◊ Most common genetic disease in Caucasians in USA

Pathophysiology:

absorbed iron is selectively bound to transferrin; increased transferrin saturation in portal circulation favors selective iron uptake initially by periportal hepatocytes → excess iron stored as crystalline iron oxide (= ferric oxyhydroxide [Fe_2O_3]) within cytoplasmic ferritin + lysosomal hemosiderin; → spread to rest of liver, pancreas, thyroid → cellular damage, organ dysfunction, malignancy (→ if untreated), progression to cirrhosis, HCC, diabetes, cardiac dysfunction

N.B.: iron overload affects parenchymal cells, NOT the reticuloendothelial system (Kupffer cells + RES cells of bone marrow + spleen)!

Organ distribution: liver, pancreas, heart, anterior pituitary, thyroid, synovium, skin

◊ RES cells are incapable of storing excess iron!

Age: after middle age; female iron loss during menses and pregnancy provides some protection

- asymptomatic during 1st decade of disease
- symptomatic in 80–90% if iron deposits > 10 g
- hyperpigmentation = bronzing of skin (90%)

- hepatomegaly (90%); arthralgias (50%)
- diabetes mellitus (30%); CHF + arrhythmia (15%)
- low serum testosterone → decreased libido, impotence
- fatigue, amenorrhea, loss of body hair, testicular atrophy
- liver iron index > 2 (= liver iron concentration [μmol per gram of dry weight] per patient's age)
- serum Fe > 300 mg/dL; serum transferrin saturation > 50%

MR:

@ Liver
√ significantly hypointense T2 signals = SI equal to background noise
√ hepatomegaly, fibrosis, HCC (in advanced disease)

@ Pancreas
√ normal pancreatic signal intensity in noncirrhotics
√ pancreatic SI equal to / less than muscle (in 90% of cirrhotic patients)

@ Spleen
√ normal SI of spleen (in 86%) + bone marrow ← abnormal RES function

@ Pituitary (in advanced disease)
- hypopituitarism, hypogonadism ← gonadotroph malfunction

√ profound T2 hypointensity of adenohypophysis (anterior pituitary) similar to ICA flow void
√ decreased parenchymal enhancement on T1WI
√ diminutive pituitary height (< 4.89 ± 0.87 mm)

@ Heart (in advanced disease)
- arrhythmia

√ congestive cardiomyopathy (15%)
√ pericarditis

Cx: (1) Periportal fibrosis resulting in micronodular cirrhosis (if iron concentration > 22,000 μg/g of liver tissue)
√ low signal intensity on long TE GRE
(2) Hepatocellular carcinoma (14–36%)
√ HCC does not contain iron
(3) Insulin-dependent diabetes mellitus (30–60%) ← insulin resistance by hepatocytes + damage of pancreatic β-cell ← iron deposition
(4) Hypoparathyroidism

Rx: phlebotomies in precirrhotic stage

Prognosis: normal life expectancy with early diagnosis and treatment

Secondary Hemochromatosis

= any nongenetic cause of iron accumulation in RES organs of liver + spleen + bone marrow
[*Hemosiderosis* = increased iron deposition without organ damage]

Cause: acquired

(a) Chronic hemolytic anemia ± multiple transfusions
= erythrogenic hemochromatosis
= increased duodenal absorption of iron ← erythroid hyperplasia with ineffective erythropoiesis

1. Thalassemia
2. Congenital dyserythropoietic anemia
3. Sideroblastic anemia ← impaired protoporphyrin production

◊ NOT in sickle cell anemia

Path: no excess Kupffer cell iron

Some types of anemia like Fanconi anemia benefit from treatment with steroids (oxymetholone, danazol, methyltestosterone) to stimulate erythropoietin production. These drugs can induce hepatocellular adenoma, HCC, and peliosis hepatis.

(b) Myelodysplastic syndrome

(c) Exogenous increase of iron

› parenteral infusion

1. Transfusional siderosis (*see below*)
2. Iron overload siderosis

› secondary to ↑ in iron absorption

1. Alcoholic hepatitis
2. Hepatitis C
3. Cirrhosis

› excessive ingestion

1. **Bantu siderosis** = excessive dietary iron from food preparation in iron containers (Kaffir beer)

Organ distribution: RES of liver + spleen + bone marrow

Path: iron deposition initially in RES (phagocytosis of intact RBCs) with sparing of parenchymal cells of pancreas; <u>after</u> saturation of RES storage capacity parenchymal cells of other organs accumulate iron

Age: 4th–5th decade; M÷F = 10÷1

MR:

@ Liver

√ signal loss in liver on T2WI

= SI <u>greater than background noise</u> ← iron in Kupffer cells with <u>sparing of parenchymal liver cells</u>)

@ Spleen

√ splenic signal intensity less than muscle

@ Bone marrow

√ low SI of bone marrow (= siderotic marrow)

Transfusional Siderosis

= iron deposited in reticuloendothelial system in patients receiving > 40 units of blood (iron storage capacity of RES = 10 g of iron)

Organ distribution:

› common: liver, spleen, bone marrow, lymph nodes

› less common: adrenals, pancreas, GI tract

mnemonic: **S**iderosis affects the **S**pleen!

• abnormal iron deposition in RES is clinically of little significance (NO damage of affected organs)

MR:
√ low SI of bone marrow (= siderotic marrow) + spleen
√ ± low signal intensity of liver
√ normal SI of pancreas (except when storage capacity of RES exceeded)
DDx: diffuse calcification ← autosplenectomy of sickle cell anemia
Risk: parenchymal iron deposition occurs when storage capacity of RES is exhausted
◊ Parenchymal iron deposition can cause organ dysfunction
Rx: iron chelation therapy to remove excess iron

HEPATIC (LIVER) ABSCESS

= localized collection of pus in the liver ← any infectious process with destruction of the hepatic parenchyma + stroma
Types: pyogenic (85%), fungal (9%), amebic (6%)
Location: multiple in 50%
◊ A pyogenic abscess tends to be centrally located, an amebic abscess peripherally!
√ hepatomegaly
√ elevation of right hemidiaphragm
√ pleural effusion
√ right lower lobe atelectasis / infiltration
√ gas within abscess: esp. Klebsiella
MR:
√ hypointense on T1WI + hyperintense on T2WI (72%)
√ perilesional edema (35%)
√ "double target" sign on T2WI = hyperintense center (fluid) + hypointense sharply marginated inner ring (abscess wall) + hyperintense poorly marginated ring (perilesional edema)
√ rim enhancement (86%)

Amebic Abscess

Organism: trophozoite Entamoeba histolytica
Etiology: spread of viable amebae from colon → portal system → liver
Frequency: in 1–25% of intestinal amebiasis
Age: 3rd–5th decade; M÷F = 4÷1
• amebic dysentery; amebic hepatitis (15%)
Location: liver abscess (right lobe) in 2–25%; multiple liver abscesses in 25%; systemic dissemination by invasion of lymphatics / portal system (rare); liver÷lung÷brain = 100÷10÷1
Size: 2–12 cm
√ nonspecific variable appearance indistinct from subacute pyogenic abscess
√ nodularity of abscess wall (60%)
√ internal septations (30%)
√ NOT gas-containing (unless hepatobronchial / hepatoenteric fistula present)
√ ± disruption of diaphragm

CT:
√ nonspecific hypoattenuating area
√ enhancing wall
US:
√ homogeneous hypoechoic area
√ posterior acoustic enhancement
√ well-defined smooth thin wall
NUC:
√ 98% sensitivity of sulfur colloid scan
√ photon-deficient area surrounded by rim of uptake on ^{67}Ga scan
Aspiration:
typically opaque reddish / dirty brown / pink material ("anchovy paste" / "chocolate sauce"), usually sterile, parasite confined to margin of abscess

Cx: (1) Diaphragmatic disruption (rare) is strongly suggestive of amebic abscess
(2) Fistulization into colon, right adrenal gland, bile ducts, pericardium

Rx: conservative treatment with chloroquine / metronidazole (Flagyl®); percutaneous drainage (for left hepatic abscess spontaneous rupture into pericardium with tamponade possible)

Prognosis: resolution under therapy may take from 1 month to 2 years; permanent cysts may remain behind

Pyogenic Liver Abscess

◊ Most common type of liver abscess

Organism: E. coli, aerobic streptococci, Enterococcus, S. aureus, anaerobic bacteria, Klebsiella (45%); polymicrobial (> 50%)

Prevalence: 0.016%

Predisposed: steroids, immunosuppressed state, excessive antibiotics usage

Etiology:

(1) Cholangitic (biliary disease in 60%):
ascending cholangitis ← obstructive biliary tract disease (malignant / benign stricture), Crohn disease (sclerosing cholangitis, gallstones), cholecystitis

(2) Pylephlebitic(= portal phlebitis = portal pyemia): spread of intraabdominal sepsis ← suppurative appendicitis, colitis, diverticular disease

(3) Disseminated sepsis via hepatic artery:
infarction from sickle cell disease / embolism / postembolization for primary and metastatic cancer / septicemia; indwelling arterial catheters

(4) Contiguous spread from a local infection:
cholecystitis, peptic ulcer, subphrenic abscess

(5) Blunt / penetrating trauma:
rupture, penetrating wounds, biopsy, surgery, liver transplantation, previous biliary instrumentation / stent placement, radiofrequency ablation (1.4%)

(6) Cryptogenic in 20–45%:
invasion of cysts; superinfection of dead tissue (eg, primary / secondary hepatic tumor) by pyogenic intestinal flora

Path: liquefaction necrosis of liver parenchyma (→ central fluid collections of pus) + septa of fibrotic tissue (with inflammatory infiltrates of epitheloid macrophages, lymphocytes, eosinophils, neutrophils)

Classification by size: macroabscess (≥ 2 cm in diameter) microabscess (< 2 cm in diameter)

Mean age: 56–64 years; M > F

- pyrexia (79%), abdominal pain (68%), jaundice (0–20%)
- vomiting / weight loss, malaise (39%)
- nocturnal sweating (43%); positive blood culture (50%)
- ↑ WBCs, ↑ alkaline phosphatase

Location: solitary abscess in right lobe (40–75%), in left lobe (2–10%); multiple abscesses in 10–34–73% (more often of biliary than hematogenous origin)

√ honeycomb pattern of cluster of small abscesses at early stage

√ "cluster" sign = coalescence of several microabscesses each < 2 cm within the same anatomic area into single multiseptated larger cavity at later stage (suggests biliary origin)

US:

√ hypoechoic round lesion with well-defined mildly echogenic rim
√ posterior acoustic enhancement
√ coarse clumpy debris / low-level echoes / fluid-debris level with internal movement
√ intensely echogenic reflections with reverberations (from gas) in 20–30%

CT (95% sensitive):

√ inhomogeneous hypoattenuating (0–45 HU) single / multiloculated (multiseptated) cavity

√ "single target" sign = hypoattenuating mass surrounded by single enhancing rim ← after cluster of small abscesses aggregate + coalesce into single larger cavity
√ "double target" sign(6–30%):
  √ hypoattenuating pus centrally surrounded by
  √ inner hyperattenuating ring ← granulation tissue
  √ outer hypoattenuating zone ← inflammatory edema
√ air density
√ segmental / wedge-shaped transient hepatic enhancement surrounding abscess ← reduced portal venous flow ← inflammation and stenosis + compensatory increase in hepatic arterial flow

MR:

√ very low SI on T1WI + very high SI on T2WI (varies with protein content)
√ intense peripheral rim enhancement of capsule of variable thickness + septa

NUC:

√ photon-deficient area on sulfur colloid + IDA scan
√ ^{67}Ga citrate uptake in 80%
√ ^{111}In-tagged WBC uptake is highly specific (since WBCs normally go to liver, may need sulfur colloid test for correlation)

Cx: (1) Septicemia
(2) Rupture into right subphrenic space
(3) Rupture into abdominal cavity
(4) Rupture into pericardium

(5) Empyema
(6) Common hepatic duct obstruction

Mortality: 2–10%; 100% if unrecognized / untreated

Rx: percutaneous catheter drainage for multilocular abscesses + abscesses > 5 cm in diameter; surgical drainage (lower failure rate)

Patterns of Iron Deposition Related to Possible Causes of Hemochromatosis

Deposition Pattern	*Liver*	*Spleen*	*Bone Marrow*	*Pancreas*	*Kidney*	*Cause*
RES	Yes	**Yes**	**Yes**	No	No	**multiple transfusions**
Parenchymal	**Yes**	No	No	Yes	No	**increased iron absorption**: primary hemochromatosis, chronic anemia with inefficient erythropoiesis (thalassemia, congenital dyserythropoietic anemia, sideroblastic anemia)
Renal	No	No	No	No	**Yes**	intravascular hemolysis (artificial heart valve), paroxysmal nocturnal hemoglobinuria, hemolytic crisis of sickle cell disease
Mixed	Yes	Possible	Possible	Possible	Possible	chronic anemia due to ineffective erythropoiesis requiring multiple transfusions

Microabscesses

Predisposed: immunocompromised after neutrophil recovery
√ "cluster" sign = multiple microabscesses in geographic proximity (= early stage of abscess in evolution)
√ heterogeneous enhancement ← clustered coalescing abscesses
√ peripheral / septal enhancement
US (79% sensitive):
√ multiple small hypoechoic nodules in liver ± spleen
CT (97% sensitive):
√ multiple well-circumscribed hepatic / splenic lesions
MR (may be more sensitive than CT):
√ T2 hyperintensity + faint restricted diffusion ← necrosis + purulent debris
√ perilesional T2 hyperintensity ← edema
√ dynamic gadolinium-enhanced MR may show more lesions than CT
DDx: HCC (sepsis, no peripheral / septal enhancement)

HEPATIC ADENOMA

= HEPATOCELLULAR ADENOMA = LIVER CELL ADENOMA
= epithelial neoplasm composed of normal hepatocytes
◊ The most frequent hepatic tumor in young women after > 2-year use of oral contraceptives (4÷100,000 women annually)!

Prevalence: half as common as FNH; increasing with duration of oral contraceptive use + size of estrogen dose

Path: spherical benign growth with high incidence of hemorrhage + necrosis + fatty change; pseudocapsule ← compression of liver tissue containing multiple large vessels; NO scar

Histo: hepatocytes arranged in sheets without acinar structure (no portal or central vein), separated by thin-walled sinusoids fed by large peritumoral arteries, containing increased amounts of glycogen ± fat; few abnormally functioning Kupffer cells; NO connection with bile ducts (DDx to FNH)

Peak age: 40 years; young women in childbearing age (90%); not seen in males unless on anabolic steroids; rare in children (girls > 10 years)

Categories: 3 distinct genetic and pathologic subtypes
(a) inflammatory hepatocellular adenoma (most common)
- frequently in obese patients + in young women with a history of oral contraceptive

Risk of: hemorrhage, malignancy(10%)

(b) hepatocyte nuclear factor 1 alpha (HNF-1 α)–mutated hepatocellular adenoma (2nd most common)
- woman with a history of oral contraceptive use

(c) β-catenin–mutated hepatocellular adenoma
- more common in men with a history of anabolic steroid use / glycogen storage disease

Risk of: malignant transformation (highest rate)

Associated with:
› oral contraceptives (2.5 x risk after 5-year use, 7.5 x risk after 9-year use, 25 x risk > 9-year use); pregnancy
› anabolic steroids; familial diabetes mellitus; galactosemia
› type IA (von Gierke) glycogen storage disease (adenomas in 22–60–75% at an early age), also in type III (Cori)
› androgenic steroid therapy in Fanconi anemia

◊ Pregnancy may increase tumor growth rate + lead to tumor rupture!
◊ Tumor regression may occur with dietary therapy leading to normal insulin, glucagon, and serum glucose levels
• RUQ pain as sign of mass effect (40%) / intratumoral (10%) or intraperitoneal hemorrhage → hypovolemic shock
• asymptomatic (20%), ↑ liver function tests, normal AFP
• hepatomegaly

Mean size: 3–5 (range, 1–15–30 cm) in diameter
Location: right lobe of liver in subcapsular location (75%); multiple in up to 21%
Multiplicity: associated with glycogen storage disease / use of anabolic steroids; solitary lesion (in 70–80%); hepatic adenomatosis (see below)
√ spherical / ovoid well-circumscribed mass
√ frequently heterogeneous ← dilated sinusoids, blood-filled (pelioid) spaces, focal necrosis, infarction, hemorrhage, myxoid stroma, fatty change, calcifications
√ pseudocapsule (17–31%)
√ intraparenchymal / pedunculated (in 10%)
√ unusual "**nodule-in-nodule**" appearance in large tumors (DDx: hepatocellular carcinoma)
√ eccentric dystrophic calcifications (5–15%)

CT:
√ round usually isoattenuating mass (without hemorrhage)
√ mass of decreased density ← gross fat (7–10%) + areas of necrosis (30–40%)
√ hyperdense areas of fresh intratumoral hemorrhage (15–50%)

CECT:
√ transient avid homogeneous enhancement on arterial-phase images in small adenomas (90%) / initial peripheral enhancement with centripetal filling in larger adenomas (← supply by hepatic artery)

- √ iso- / hypoattenuating on portal venous + delayed-phase images

US:
- √ usually small well-demarcated nonlobulated solid heterogeneous mass of variable echogenicity:
  - √ hyperechoic lesion with well-defined hypoechoic rim in normal surrounding liver
  - √ echogenic in areas of fat or hemorrhage
  - √ hypoechoic in background of diffuse fatty infiltration
  - √ anechoic cystic areas if large

Color Doppler:
- √ central vessels with triphasic pattern / continuous flat venous waveform
- √ peripheral peritumoral arterial + venous flow

MR:
- √ heterogeneous on all pulse sequences in 88% (indistinguishable from HCC):
  - ◊ Small homogeneous adenomas (uncomplicated by hemorrhage / intracellular lipid in 4%) mimick FNH!
- √ variable intensity on T1WI:
  - √ mildly hypointense on T1WI
  - √ often hyperintense areas ← hemorrhage / presence of intralesional lipid-laden hepatocyte (in 35–77%)
  - √ signal loss with out-of-phase / fat-suppressed imaging ← intracellular lipid (DDx to FNH)
- √ variable heterogeneous intensity on T2WI:
  - √ isointense / mildly hyperintense sheets of hepatocytes
  - √ hyperintense areas of necrosis / hemorrhage in 47–77%
- √ pseudocapsule hypointense on T1WI, variointense on T2WI ± delayed enhancement
- √ variable intensity (commonly increased) on DWI
- √ enhancement characteristics:
  - √ heterogeneous hypervascularity during arterial phase (less vascular than FNH)
  - √ iso- or hypointense on portal venous + delayed phase
  - √ delayed washout = delayed enhancing pseudocapsule
  - √ hypointense on 1-hour delayed imaging with gadobenate dimeglumine (Gd-**B**enzyl**O**xy**P**ropionic**T**etra**A**cetate)

NUC:
- √ photopenic lesion on sulfur colloid scan (← lesion composed of hepatocytes + nonfunctioning Kupffer cells) surrounded by rim of increased uptake (← compression of adjacent normal liver containing Kupffer cells); may show uptake equal to / slightly less than liver (23%)
- √ usually increased uptake / retention on HIDA scan
- √ NO gallium uptake

Angio:
- √ usually hypervascular mass
- √ homogeneous but not intense stain in capillary phase
- √ enlarged hepatic artery with feeders at tumor periphery (50%)
- √ hypo- / avascular regions ← hemorrhage / necrosis

√ neovascularity

CAVE: percutaneous biopsy carries high risk of bleeding!

Cx: (1) Spontaneous intratumoral hemorrhage (likely related to infarction as tumor outgrows blood supply) with subcapsular hematoma

(2) Hepatic rupture + hemoperitoneum (41%) in lesions > 5 cm

(3) Malignant transformation (rare) ← contiguous development of hepatocellular carcinoma

(4) Recurrence after resection

Rx: discontinuation of hormone therapy; screening for malignant degeneration with α-fetoprotein; surgical resection (to prevent rupture)

◊ Hepatocellular adenomas > 5 cm in maximum dimension in males with glycogen storage disease should be surgically resected followed by detailed histopathologic review for tumor geno- and phenotypic characterization.

DDx: (1) Hepatocellular carcinoma (presence of cirrhosis / hepatitis B / hemochromatosis, positive for α- fetoprotein, peripheral rim of high attenuation on delayed phase, vascular invasion)

(2) Fibrolamellar carcinoma (eccentric scar with calcification, adenopathy)

(3) FNH (stellate scar, homogeneous mass, NO intralesional fat / glycogen, arterial flow in spoke-wheel pattern, normal / increased uptake of ^{99m}Tc sulfur colloid)

Inflammatory Hepatocellular Adenoma *40–50%*

= TELANGIECTATIC FOCAL NODULAR HYPERPLASIA = TELANGIECTATIC ADENOMA

Age: young woman with a history of oral contraceptive usage; obese patient

- systemic inflammatory syndrome: fever, leukocytosis, elevated serum levels of C-reactive protein
- ↑ serum levels of transaminase, alkaline phosphatase, γ-glutamyl transferase; chronic anemia

Genetics: somatic gain-of-function mutation of interleukin-6 signal transducer gene (IL6ST) located at chromosome 5q11

Path: heterogeneous in appearance, with areas of congestion and frank hemorrhage; sinusoidal dilatation, peliotic areas, abnormal arteries

Histo: intense polymorphous inflammatory infiltrates, marked sinusoidal dilatation / congestion, thick-walled arteries; tumor cells show immunoreactivity to acute phase inflammatory markers like serum amyloid A and C-reactive protein

√ delayed persistent enhancement (85% sensitive, 87% specific)

US:

√ arterial vascularity with centripetal filling + peripheral rim of sustained enhancement + central washout during late venous phase

NECT:

√ heterogeneously hyperattenuating mass

MR:

√ isointense / mildly hyperintense on T1WI with minimal / no signal drop-off on chemical shift sequences

√ intense enhancement during arterial phase persisting into portal venous + delayed phase

√ marked diffuse T2-hyperintensity:
√ higher signal intensity in periphery of lesion ← dilated sinusoids

Cx: (1) intratumoral bleeding (20–30%), esp. for tumors > 5 cm in maximum diameter; subcapsular tumor with greater tendency for bleeding + rupture
(2) 10% risk of malignancy

HNF-1α–mutated Hepatocellular Adenoma 30–35%

= usually incidentally discovered tumor (multiple in about 50%) occurring exclusively in female with history of oral contraceptive use in > 90%

Genetics: nonfunctioning tumor suppressor gene located on chromosome 12q24 ← biallelic inactivating mutation of the hepatocyte nuclear factor-1α (HNF1A) gene that produces a transcription protein involved in hepatocyte differentiation

Histo: excessive lipid accumulation in tumor hepatocytes

√ diffuse intratumoral steatosis

√ diffuse fatty infiltration of liver ← associated with **m**aturity-**o**nset **d**iabetes of the **y**oung (MODY)

√ moderate tumor enhancement during arterial phase

US:
√ iso- to moderately increased vascularity + mixed filling during arterial phase + isoechogenicity during portal venous + delayed phases (after contrast material)

CT:
√ macroscopic fat in tumor (7%)

MR:
√ iso- to slightly hyperintense tumor on T2WI
√ predominantly T1-hyper- / isointense
√ chemical shift imaging:
√ homogeneous signal drop-off (86% sensitive, 100% specific) ← intracellular steatosis
√ macroscopic fat in tumor (in 35–77%)

Prognosis: risk of bleeding / malignancy is minimal

β-Catenin–mutated Hepatocellular Adenoma 10–15%

Genetics: activating mutation of β-catenin gene encoded by catenin β 1 gene (CTNNB1) located at chromosome 3p21 → uncontrolled hepatocyte proliferation

Associated with: male hormone administration, glycogen storage disease, familial adenomatous polyposis

Histo: high nuclear-cytoplasmic ratio, nuclear atypia, formation of acini; strong diffuse positivity to glutamine synthase

√ strong arterial enhancement

MR:
√ homo- / heterogeneous hyperintense T1 + T2 signal depending on presence of hemorrhage ± necrosis

Prognosis: 5–10% risk of HCC

Risk factors: male sex, glycogen storage disease, anabolic steroid usage, β-catenin–mutated subtype, tumor >5 cm in maximum dimension

Hepatic Adenomatosis

= rare condition with > 10 adenomas in both hepatic lobes without history of steroid therapy / glycogen storage disease

Cause: nonalcoholic liver disease, HNF-1α gene mutation

Age: 4th–5th decade; female

HEPATIC ANGIOMYOLIPOMA

= rare benign mesenchymal tumor

Associated with: tuberous sclerosis

Histo: smooth muscle cells, fat, proliferating blood vessels

• asymptomatic

√ intratumoral fat is DIAGNOSTIC

√ soft-tissue component may enhance

US:

√ circumscribed hyperechoic mass (DDx: hemangioma)

√ sound attenuation + subtle acoustic shadowing

√ relative hypervascularity

CT:

√ areas of macroscopic fat

√ marked enhancement with visualization of large central vessels during arterial phase

MR:

√ hyperintense areas of macroscopic fat on T1WI

√ marked decrease in SI with T1 fat suppression technique

√ intense enhancement during arterial phase with dark areas of macroscopic fat on fat-suppressed T1WI

Cx: intratumoral hemorrhage

HEPATIC ANGIOSARCOMA

= HEMANGIOENDOTHELIAL SARCOMA = KUPFFER CELL SARCOMA = HEMANGIOSARCOMA

Prevalence: 0.14–0.25÷1,000,000; < 2% of all primary liver neoplasms; most common sarcoma of liver (followed by fibrosarcoma > malignant fibrohistiocytoma > leiomyosarcoma)

Etiology:

(a) thorotrast = thorium dioxide (7–10%) with latent period of 15–24 years

(b) arsenic compounds

(c) polyvinyl chloride (latent period of 4–28 years)

Associated with: hemochromatosis, anabolic steroids, cirrhosis, von Recklinghausen disease

Path:

(a) multifocal / multinodular lesions (71%) of up to > 5 cm in size

(b) large solitary mass with hemorrhage + necrosis

Histo: vascular derivation confirmed by reactivity to factor VIII-related antigen, CD31 and CD34

(a) vessels lined with malignant endothelial cells (eg, sinusoids) causing atrophy of surrounding liver

(b) vasoformative → forming poorly organized vessels (responsible for RBC trauma + platelet trapping)
(c) forming solid nodules of malignant spindle cells

Age: 6th–7th decade; M÷F = 4÷1

- abdominal pain, weakness, fatigue, weight loss, jaundice
- spontaneous hemoperitoneum (15–27%)
- microangiopathic hemolytic anemia (23%), thrombocytopenia (54%), DIC (31%); NO elevation of α-fetoprotein

Early metastases to:

lung (23%), spleen (16–46%), porta hepatis nodes, portal vein, thyroid, peritoneal cavity, bone marrow (rapid metastatic spread)

◊ Predilection for splenic metastases!

√ portal vein invasion
√ hemorrhagic ascites
√ unifocal / multifocal / infiltrative lesion

Plain film:
√ circumferential displacement of residual thorotrast

NUC:
√ single / multiple photopenic areas on sulfur colloid scan
√ increased gallium uptake
√ perfusion blood pool mismatch (initial decrease followed by slow increase in RBC concentration) as in hemangioma on 3-phase red blood cell scan

US:
√ solid / mixed mass with anechoic areas (hemorrhage / necrosis)
√ multiple nodules
√ diffuse heterogeneous echotexture of entire liver

CT:
√ hypodense masses with high-density regions (hemorrhage) / low-attenuation regions (old hemorrhage / necrosis)
√ focal areas of peripheral enhancement with fill-in on dynamic CT as in large hemangioma (uncommon)

MR:
√ hypointense on T1WI with irregular areas of high signal (hemorrhage)
√ heterogeneously hyperintense on T2WI + fluid-fluid levels

CEMR:
√ markedly heterogeneous enhancement: predominantly peripheral, progressive on delayed phase, lack of central filling

Angio:
√ hypervascular stain around tumor periphery in late arterial phase with puddling; NO arterial encasement

PET:
√ may demonstrate marked uptake in liver tumor
√ localization of extrahepatic disease

CAVE: Biopsy may lead to massive bleeding in 16%! Have surgical backup available!

Prognosis: rapid deterioration with median survival of 6 months (13 months under chemotherapy)
DDx for multiple lesions: hypervascular metastases
DDx for single lesion: cavernous hemangioma, HCC (no splenic metastases)

HEPATIC CYST

◊ Second most common benign hepatic lesion after hemangioma
Prevalence: 2–7–14%; increasing with age; M < F
A. ACQUIRED HEPATIC CYST
Cause: trauma, inflammation, parasitic infestation, neoplasia
B. CONGENITAL HEPATIC CYST
Cause: defective development of aberrant / obstructed intrahepatic bile ducts; ? derived from bile duct hamartoma
Frequency: liver cysts detected at autopsy in 50%; in 22% detected during life
Age of detection: 5th–8th decade
Path: no communication with biliary tree
Histo: cyst surrounded by fibrous capsule + lined by columnar epithelium, related to bile ducts within portal triads; NO communication with bile duct
Associated with:
(1) Tuberous sclerosis
(2) Polycystic kidney disease (25–33% have liver cysts)
(3) Polycystic liver disease: autosomal dominant
• simple cyst: almost always asymptomatic
• hepatomegaly (40%); pain (33%); jaundice (9%)
Size of cyst: range from microscopic to huge (average 1.2 cm; in 25% (40%) largest cyst < 1 (> 4) cm; maximal size of 20 cm)
Number of cysts: multiple cysts spread throughout liver (in 60%) / solitary cyst
◊ Consider polycystic liver disease if > 10 cysts
√ well-circumscribed round / ovoid unilocular lesion:
√ imperceptible wall ± rim calcification
√ anechoic with posterior acoustic enhancement
√ very bright on T2WI
√ water attenuation (-20 to +20 HU)
√ no enhancement
√ hypointense on T1WI, hyperintense on T2WI
√ "cold spot" on IDA, Ga-68, ^{99m}Tc-sulfur colloid scans
Pitfall:
(1) Metastatic neuroendocrine tumor (can be very cystic ± very bright on T2WI)
(2) Cystic metastasis (in cystic primary tumor)
Rare Cx: infection, rupture, torsion, hemorrhage, malignant transformation into adenocarcinoma
√ fluid-fluid interface
√ wall thickening
√ intracystic debris ± septations

Rx: sclerosing therapy with minocycline hydrochloride (Dose: 1 mg per 1-mL cyst content up to 500 mg in 10 mL of 0.9% saline + 10 mL 1% lidocaine) following contrast opacification of cyst to confirm absence of communication with biliary tree / leakage into peritoneal cavity

HEPATIC HEMANGIOMA

Cavernous Hemangioma of Liver

= most common solid benign liver tumor (78%); 2nd most common liver tumor after metastases

Prevalence: 1–4%; autopsy incidence 0.4–7.3%; increased with multiparity

Cause: ? enlarging hamartoma present since birth, ? true vascular neoplasm

Age: rarely seen in young children; M÷F = 1÷2–5

Path: large vascular channels filled with slowly circulating blood; lined by single layer of mature flattened endothelial cells separated by thin fibrous septa; NO bile ducts; thrombosis of vascular channels commonly results in fibrosis + hemorrhage + myxomatous degeneration + calcifications

Pathophysiology: large blood volume with low blood flow

Associated with:
(1) Hemangiomas in other organs
(2) Focal nodular hyperplasia
(3) Rendu-Osler-Weber disease
(4) Klippel-Trénaunay-Weber syndrome
(5) Von Hippel-Lindau disease

- asymptomatic if tumor small (50–70%)
- may enlarge during pregnancy

Location: frequently peripheral / subcapsular in posterior right lobe of liver; 20% are pedunculated; multiple in 10–20%

Size: < 4 cm (90%)

◊ Very small + very big lesions have the most atypical imaging features ← calcifications, fibrosis, thrombosis of tumor portions, cystic / necrotic areas within tumor!

√ well-circumscribed lobulated mass

√ blood supply from hepatic artery with arterial enhancement characteristics

√ may have central area of fibrosis = areas of nonenhancement / nonfilling / cystic space (occurrence increases with age and size)

√ central septal calcifications within areas of fibrosis / phleboliths (5–20%)

US:

√ uniformly hyperechoic (60–70%) mass ← multiple interfaces created by blood-filled spaces separated by fibrous septa

√ hypoechoic mass (up to 40%) in larger hemangiomas / on background of fatty infiltration or liver fibrosis

√ well-defined thick / thin echogenic lobulated border

√ homogenous (58–73%) / heterogeneous ← hemorrhagic necrosis, thrombosis, scarring, myxomatous change, central fibrosis

√ ± hypoechoic center
√ may show acoustic enhancement (37–77%)
√ unchanged size / appearance (82%) on 1–6-year follow-up
√ no Doppler signals / signals with peak velocity of < 50 cm/sec
√ contrast enhancement

CT (combination of precontrast images, good bolus, dynamic scanning, 88% sensitive, 84–100% specific):

√ well-circumscribed spherical / ovoid low-density mass:
  √ may have areas of higher / lower density within mass
√ enhancement patterns:
  Type 1 = immediate uniform enhancement (**"flash filling"**); in 42% of hemangiomas < 1 cm
    DDx: hypervascular tumor (does not remain hyperattenuated on delayed phase)
  Type 2 = peripheral nodular enhancement + complete fill-in on delayed images 3–30 min post IV bolus (in 55–89%):
    DDx: metastasis (nodular / rim enhancement ± centripetal fill-in possible)
  Type 3 = peripheral nodular enhancement + partial (24%) / no (2%) fill-in to isodensity on delayed phase in giant hemangioma > 5 cm ← thrombosis
  √ central scar in large lesion may not enhance at any time

MR (98–100% sensitive, 92–98% specific, 90–95% accurate):

√ spheroid / ovoid (87%) mass with smooth well-defined lobulated margins (87%); NO capsule
√ homogeneous internal architecture if < 4 cm, hypointense internal inhomogeneities if > 4 cm ← fibrosis
√ hypo- / isointense mass relative to liver on T1WI
√ markedly hyperintense **"light bulb"** appearance (← slow flowing blood) increasing with echo time on heavily T2WI; more intense than spleen (92% accurate)
  (DDx: hepatic cyst, hypervascular tumor, necrotic tumor, cystic neoplasm)
√ for hyalinized hemangioma: only mildly hyperintense on T2WI + lack of enhancement in early phase + slight peripheral enhancement in late phase (DDx: malignant hepatic tumor)
√ hyperintense on DWI ← T2 shine-through
√ enhancement pattern as on CT with gadolinium-DTPA:
  Type 1 = immediate uniform enhancement at 1 sec in 40% of small hemangiomas < 1.5 cm
  Type 2 = peripheral nodular + interrupted enhancement (77%) equal to blood pool progressing centri-petally with centrally uniform enhancement
  Type 3 = peripheral nodular enhancement with centripetal progression but persistent hypointensity for giant hemangioma > 5 cm
  DDx: hypervascular metastasis (contrast washout on > 5 min delayed images)

Angio (historical gold standard):

√ dense opacification of well-circumscribed, dilated, irregular, punctate vascular lakes / puddles ("cotton wool / snowy tree" appearance) in late arterial + capillary phase

starting at periphery in ring- / C-shaped configuration
√ normal-sized feeders; AV shunting (very rare)
√ contrast persistence late into venous phase

NUC (95% accuracy with SPECT):

Indication: lesions > 2 cm (detectable in 70–90%) with atypical imaging characteristics on cross-sectional imaging

√ initially cold lesion on ^{99m}Tc-labeled RBC scans (dose of 15–20 mCi) with increased activity on delayed images at 1–2 hours
√ cold defect on sulfur colloid scans

Bx: may be biopsied safely provided normal liver is present between tumor + liver capsule

√ nonpulsatile blood (73%)
√ endothelial cells without malignancy (27%)

Prognosis: no growth when < 4 cm in diameter; giant cavernous hemangiomas may enlarge; may involute into hyalinized hemangioma

Cx (rare): (1) Spontaneous rupture (4.5%)
(2) Abscess formation
(3) Kasabach-Merritt syndrome (platelet sequestration)

Mimics:

(1) Angiosarcoma
(2) Epitheloid hemangioendothelioma
(3) Treated metastasis
(4) Neuroendocrine metastasis (bright on T2WI)

DDx: hypervascular malignant neoplasm / metastasis

Giant Hepatic Cavernous Hemangioma

= hemangioma > 5 cm / at least one dimension exceeding 8–10 cm (in literature no agreement on size)

Associated with: coexistent smaller < 5 cm hemangioma in 13%

Histo: hemorrhage, thrombosis, extensive hyalinization, liquefaction, fibrosis; central cleft due to cystic degeneration / liquefaction

- may present with spontaneous life-threatening hemorrhage (5%); hepatomegaly; abdominal mass
- RUQ fullness + pain ← thrombosis in large hemangioma
- Kasabach-Merritt syndrome (rare)

US:

√ heterogeneous mass

NECT:

√ heterogeneous hypoattenuating mass with marked central areas of low attenuation
√ ± coarse central calcification

CECT:

√ early peripheral globular enhancement
√ incomplete filling of central portions

MR:

√ sharply marginated hypointense mass with cleftlike area of lower intensity on T1WI
√ large markedly hyperintense cleftlike area (← cystic degeneration / liquefaction) with some hypointense internal septa inside a hyperintense mass on T2WI

CEMR:
√ peripheral nodular enhancement
√ central cleftlike area remains hypointense

Cx: inflammatory changes; intralesional hemorrhage; intraperitoneal hemorrhage; torsion of pedunculated lesion; Kasabach-Merritt syndrome

DDx: metastasis, HCC, cholangiocarcinoma, hepatic adenoma, FNH (smaller and less hyperintense central scar on T2WI), focal fatty infiltration

Infantile Hemangioendothelioma of Liver

= INFANTILE HEPATIC HEMANGIOMA = CAPILLARY / CAVERNOUS HEMANGIOMA

◊ Most common benign hepatic tumor during first 6 months of life!

Histo: multiple anastomosing thick-walled vascular spaces similar to cavernous hemangioma lined by plump immature endothelial cells in single or (less often) multiple cell layers; areas of thrombi / extramedullary hematopoiesis; scattered bile ducts; involutional changes (infarction, hemorrhage, necrosis, scarring)

Classification based on immunoreactivity to glucose transporter protein 1 (GLUT1):

(1) Multifocal lesions staining positive for GLUT1 ± associated arteriovenous shunts / cutaneous hemangiomas, absence of central necrosis
Prognosis: proliferation followed by involution

(2) Focal lesion WITHOUT staining for GLUT1 variably demonstrating arteriovenous shunts; often containing central areas of hemorrhage / necrosis / thrombosis
Prognosis: complete involution by age 12–14 months

(3) Diffuse disease with liver largely replaced by growing tumors causing massive hepatomegaly, secondary respiratory distress, inferior vena cava compression, abdominal compartment syndrome

Age at presentation: < 6 months in 85%, during 1st month in 33%, > 1 year in 5%; M÷F = 1÷1.4–1÷2

Associated with: hemangiomas in other organs + skin in 10–15%

Prevalence: increased with hemihypertrophy + Beckwith-Wiedemann syndrome

- abdominal mass ← hepatomegaly; hemangiomas of skin
- may present with high-output CHF 2° to AV shunts within tumor (8 –15–25%)
- hemolytic anemia; Kasabach-Merritt syndrome
- cardiac dysfunction + mental retardation ← severe hypothyroidism ← tumor produces high levels of type 3 iodothyronine deiodinase activity

Location in other sites:
skin, trachea, thorax, adrenal gland, dura mater (10–70%); especially with multifocal liver tumors → chest x-ray, brain imaging

Average size: 3.0 (range, 0.5–20.0) cm; multifocal lesions around 1 cm in diameter

√ diffuse involvement of entire liver → hepatomegaly
√ focal single mass (50%) / multifocal masses (50%)
√ enlargement of celiac + hepatic arteries + proximal aorta
√ rapid decrease in aortic caliber below celiac trunk

√ enlarged hepatic veins (increased venous flow)

Plain film:

√ fine speckled / fibrillary calcifications in 16–25% (DDx: hepatoblastoma, hamartoma, metastatic neuroblastoma)

√ cardiomegaly + pulmonary edema with CHF

US:

√ predominantly hypoechoic / mixed (uncommonly hyperechoic) lesion

√ heterogeneous echotexture in large lesion ← central hemorrhage, necrosis + fibrosis

√ multiple sonolucent areas = enlarging vascular channels ← initial rapid growth (DDx: mesenchymal hamartoma):

√ vascular components demonstrated by color Duplex

√ tiny echogenic foci + posterior acoustic shadowing = calcifications (in 36–50%)

Color Doppler:

√ artery with little systolic-diastolic variation (= AV shunt)

√ artery + vein with high- / low-frequency shifts

√ large feeding + draining vessels within and surrounding tumor

√ direct visualization of arteriovenous / portovenous shunts

OB-US:

Time of detection: as early as 16 weeks GA

√ anasarca, ascites, pleural effusion, cardiomegaly

Cx:

(1) Kasabach-Merritt sequence (hemolytic anemia, thrombocytopenia, and consumptive coagulopathy) in fetus

(2) fetal hydrops → anasarca, ascites, pleural effusion, cardiomegaly

(3) polyhydramnios

NECT:

√ large well-defined hypoattenuating mass(es)

√ hemorrhage (not uncommon)

√ speckled calcifications (in 16–50%)

CECT (similar to cavernous hemangioma):

√ early peripheral nodular / corrugated enhancement (72%)

√ progressive centripetal fill-in + variable delayed central enhancement

√ intense uniform enhancement in small multifocal tumors

MR:

√ heterogeneous hypointense multinodular lesion on T1WI ± hyperintense areas of hemorrhage

√ varying degrees of hyperintensity on T2WI (resembling adult hemangioma)

√ decreasing SI with fibrotic replacement on T2WI

√ flow voids in / adjacent to some lesions

NUC (sulfur colloid, tagged RBC):

√ increased flow in viable portions of lesion during angiographic phase

√ increased activity mixed with central photopenic areas (hemorrhage, necrosis, fibrosis) on delayed tagged RBC images

√ photopenic defect on delayed sulfur colloid images

Angio (if use of embolotherapy is contemplated):

√ enlarged, tortuous feeding arteries and stretched intrahepatic vessels
√ hypervascular tumor with inhomogeneous stain; clusters of small abnormal vessels
√ pooling of contrast material in sinusoidal lakes with rapid clearing through early draining veins (AV shunting)

Prognosis: rapid growth in first 6 months followed by regression + involution within 6–8 months; 32–90% survival rate in complicated cases

Cx: (1) Congestive heart failure
(2) Hemorrhagic diathesis
(3) Obstructive jaundice
(4) Hemoperitoneum ← rupture of tumor
(5) Malignant transformation into angiosarcoma (rare)

Rx: (1) No treatment if asymptomatic
(2) Reduction in size with steroids / radiotherapy / chemotherapy (interferon-α-2a, vincristine)

Differentiation of Hemangioma from Hemangioendothelioma

Findings	*Hemangioma*	*Hemangioendothelioma*
Presenting age	older children	< 6 months of age
Lesion size	usually < 2 cm	2–15 cm
Location	R lobe	L + R lobe
Multiple lesions	in 10–20%	single / multiple
Signs	symptomatic	hepatomegaly, CHF
US	well-defined, hyperechoic	varied
Malignant	never	rarely

(3) Embolization
(4) Surgical resection / liver transplantation

DDx: (1) Hepatoblastoma (> 1 year of age, markedly elevated α-fetoprotein in 90%, more heterogeneous enhancement pattern)
(2) Mesenchymal hamartoma (usually multicystic multilocular mass, hypovascular mass with enhancement of septa + solid tumor portions)
(3) Metastatic neuroblastoma (elevated urinary catecholamines, adrenal / retroperitoneal / posterior mediastinal masses, nonenhancing multiple liver masses)
(4) Angiosarcoma (heterogeneous SI in multifocal lesions on T2WI, lack of flow voids, central / mild peripheral enhancement)

Kasabach-Merritt syndrome *(in 11%)*

[Haig Haigouni Kasabach (1898–1943) American radiologist]
[Katharine Krom Merritt (1886–1986) American pediatrician]
= HEMANGIOMA THROMBOCYTOPENIA SYNDROME
= consumptive thrombocytopenia with hemorrhagic diathesis ← disseminated intravascular coagulation

• low platelets; hemolytic anemia

- hemangioma / hemangioendothelioma / angiosarcoma → platelet sequestration by tumor → thrombocytopenic purpura → increased systemic fibrinolysis
- disseminated intravascular coagulopathy → hemorrhage, infection, multiple organ failure

Prognosis: fatal outcome in 12–24%

Rx: tumor extirpation, steroid, vincristine, interferon, radiation therapy

HEPATIC VENO-OCCLUSIVE DISEASE

= occlusion of small centrilobular veins without involvement of major hepatic veins

Etiology: radiation and chemotherapy in bone-marrow transplant patients; bush tea (alkaloid) consumption in Jamaica

√ main hepatic veins + IVC normal

√ bidirectional / reversed portal venous flow

√ gallbladder wall thickening

HEPATITIS

Cause: alcohol, medication, viral infection, NASH (nonalcoholic steatohepatitis)

Acute Hepatitis

= process present for < 6 months

- markedly elevated AST + ALT
- increase in serum-conjugated bilirubin

√ hepatomegaly / normal size of liver

√ gallbladder wall thickening

√ lymphadenopathy

CT:

√ periportal low attenuation (lymph edema)

US:

√ diffuse decrease in liver echogenicity

√ increased brightness of portal triads (**"starry sky"** pattern) = centrilobular pattern ← edema in hepatocytes (DDx: leukemic infiltrate, diffuse lymphomatous involvement, toxic shock syndrome)

√ edema of gallbladder fossa + gallbladder wall thickening

√ thickening + increase in echogenicity of fat within falciform ligament, ligamentum venosum, porta hepatis, periportal connective tissue

Drugs Associated with Cholestatic Liver Injury	
Drug Class	*Common Agents*
Antibiotics	
Penicillins	amoxicillin-clavulanate
Sulfonamides	trimethoprim-sulfamethoxazole
Macrolides	erythromycin
Tetracyclines	doxycycline
Antifungals	ketoconazole
Antiretrovirals	
Anti-inflammatories	diclofenac, ibuprofen
Psychotropes	chlorpromazine, tricyclic antidepressants
Immunosuppressives	cyclosporine, azathioprine
Other	oral contraceptives, estrogens, anabolic steroids

CEMR:
√ heterogeneous enhancement during arterial phase
√ elevated T2 signal ← edema + inflammation in more severe disease

Drug-induced Acute Hepatitis

Drug-induced injury is the number-one cause of acute liver failure (10% of all cases of acute hepatitis).

◊ Most common cause of postmarketing drug withdrawals and warnings
Implicated drugs: > 900; especially antibiotics + analgesics
Mechanism: direct toxic effects of a drug or its metabolites

Histo: categorized according to predominant histopathologic and biochemical features; grouped as hepatocellular / cholestatic / mixed patterns of liver injury.

Classification: according to clinical phenotype + course
(1) Acute hepatitis
(2) Cholestatic hepatitis
(3) Bland cholestasis
(4) Sinusoidal obstructive syndrome
(5) Steatosis (= nonalcoholic fatty liver)

Cholestatic Hepatitis

Mechanism: compromised perfusion of bile ducts
Common drugs: cyclosporine, trimethoprim-sulfamethoxazole, chlorpromazine
√ often NO radiologic findings
√ small bile ducts diminished in number
√ hepatomegaly
√ heterogeneously enhancing parenchyma
DDx: primary sclerosing cholangitis, primary biliary cirrhosis, biliary obstruction (eg, cholelithiasis, choledocholithiasis), primary sclerosing cholangitis, primary biliary cirrhosis, bile duct tumor, pancreatitis, pancreatic tumor

Chronic Hepatitis

= process present for at least 6 months

Cause: autoimmune hepatitis; hepatitis B, C, D; cryptic hepatitis; chronic drug hepatitis; primary biliary cirrhosis; primary sclerosing cholangitis; Wilson disease; alpha-1 antitrypsin deficiency

US:

√ increased liver echogenicity
√ coarsening of hepatic echotexture
√ silhouetting / loss of definition of portal venules = decreased visualization of walls of peripheral portal veins
√ NO sound attenuation

Cx: cirrhosis (10% for hepatitis B; 20–50% for hepatitis C)

Neonatal Hepatitis

Cause:

A. INFECTION: virus, protozoa, spirochete, toxoplasmosis, rubella, CMV, herpes, hepatitis A/B, syphilis
B. METABOLIC: alpha-1 antitrypsin deficiency, familial recurrent cholestasis, errors of metabolism → nesidioblastosis (= acquired hyperinsulinism with beta cell hyperplasia)
C. IDIOPATHIC

Age: 1–4 weeks of age; M > F

Histo: multinucleated giant cells with hepatic parenchymal disruption, relatively little bile within bile duct canaliculi

US:

√ normal-sized / enlarged liver
√ increase in parenchymal echogenicity
√ decreased visualization of peripheral portal veins
√ normal bile duct system
√ gallbladder of normal size / small ← decrease in bile volume in severe hepatocellular dysfunction
√ decrease in gallbladder size after milk feeding (DDx: congenital biliary atresia)

NUC:

Technique: often performed after pretreatment with phenobarbital (5 mg/kg x 5 days) to maximize hepatic function

Viral Markers of Hepatitis		
Virus	*Tests*	*Interpretation*
HAV	Anti-HAV IgM	acute hepatitis (can remain positive for >1 year) due to picorna virus
	Anti-HAV IgG	past hepatitis, lifelong immunity
HBV	HBsAg	acute / chronic disease due to hepadnavirus
	Anti-HBc IgM	acute infection (if titer high); chronic infection (if titer low)
	Anti-HBc IgG	past / recent HBV contact (may be only serum indicator of past infection)
	HBe	active viral replication
	Anti-HBe	low / absent replicative state (typically present in long-standing HBV carriers)
	Anti-HBs	immunity after vaccination
	HBV-DNA	active viral replication
HCV	Anti-HCV	past silent (1960s–1980s) / current infection due to flavivirus
	RIBA	test for various viral components
	HCV-RNA	active viral replication
HDV	Anti-HDV IgM	acute / chronic infection
	Anti-HDV IgG	chronic infection (if titer high + IgM positive); past infection if titer low + IgM negative)
	HDV-RNA	active viral replication
HEV	Anti-HEV IgM	acute hepatitis due to hepatitis E virus
	Anti-HEV IgG	past hepatitis
	HEV-RNA	viral replication
HFV		due to togavirus
HGV		due to GB virus

√ normal / decreased hepatic tracer accumulation
√ prolonged clearance of tracer from blood pool
√ bowel activity faint / delayed usually by 24 hours (best seen on lateral view; covering liver activity with lead shielding is helpful)
√ gallbladder may not be visualized

Prognosis: spontaneous remission
DDx: biliary atresia (NO small bowel activity)

Radiation Hepatitis

Acute Radiation-induced Hepatitis

Time of onset: 2–6 weeks after completion of radiation therapy with dose > 3,500 rad (35 Gy)

• abnormal liver function tests; RUQ discomfort
√ hepatomegaly
√ ascites
Prognosis: complete recovery in majority

Chronic Radiation-induced Hepatitis
√ increased attenuation in irradiated parenchyma (no fatty infiltration)
√ geographic areas of hypointensity on T1WI + hyperintensity on T2WI ← increased water content

HEPATOBLASTOMA

Frequency: 3rd most common abdominal tumor in children; most common congenital hepatic malignancy in children < 3 years of age
Incidence increased with: hemihypertrophy, Beckwith-Wiedemann syndrome
Associated with: Gardner syndrome, familial adenomatous polyposis, type 1A glycogen storage disease, trisomy 18; other congenital GI + GU anomalies in 5%
Histo:
(a) epithelial type = small cells resembling embryonal / fetal liver
(b) mixed type = epithelial cells + mesenchymal cells (of osteoid, cartilaginous, fibrous tissue)
Peak age: 18–24 months (range, newborn to 15 years); congenital in 4%; in 50% < 18 months; 90% by 5 years of age; M÷F = 1.5÷1 to 2÷1
◊ Strong inverse association with birthweight
• upper abdominal mass; jaundice (5%), pain
• weight loss, anorexia (= loss of appetite), nausea, vomiting
• precocious puberty in boys (production of hCG)
• persistently + markedly elevated α-fetoprotein (90%): AFP is normally elevated at birth until 6 months of age
Metastases to: lung (10–20%), bone, brain, lymph nodes, eye, ovary
Location: right lobe of the liver
Average size: 10–12 cm
√ usually solitary mass (80%), multifocal (20%)
√ well-circumscribed + lobulated with septa
√ coarse chunky calcifications / osseous matrix (12–30%)
√ ± invasion / compression of portal vein + hepatic veins + IVC
Abdominal X-ray:
√ hepatomegaly / mass ± coarse / dense calcifications
US:
√ large heterogeneous solid mostly hyperechoic mass:
√ often with echogenic shadowing calcifications
√ hypoechoic fibrotic septa in spoke-wheel configuration
√ occasionally cystic areas ← necrosis / extramedullary hematopoiesis
√ well-demarcated appearance ← pseudocapsule
Common Cx: intrapartum rupture + hemorrhage, hydrops, metastases
CT:

√ sharply circumscribed hypoattenuating mass with peripheral rim enhancement
√ speckled / amorphous calcifications (in > 50%)
√ slight enhancement of tumor but less than liver:
√ lobulated / septated (in 50%)

MR:
√ inhomogeneously hypointense on T1WI with hyperintense foci (= hemorrhage)
√ inhomogeneously hyperintense with hypointense bands (= fibrous septa) on T2WI

NUC:
√ photopenic defect

Angio:
√ hypervascular mass with dense stain
√ marked neovascularity; NO AV-shunting
√ vascular lakes may be present
√ avascular areas ← tumor necrosis
√ may show caval involvement (= unresectable)

Prognosis: 40–60% resectable (in 85% following neoadjuvant chemotherapy); 30–75% mortality; better prognosis than hepatoma; better prognosis for epithelial type than mixed type

DDx: (1) Infantile hemangioendothelioma (fine granular calcifications, < 1 year of age, rare AFP elevation, intense nodular / corrugated peripheral enhancement + centripetal fill-in on delayed images)

(2) Mesenchymal hamartoma (predominantly cystic tumor, normal serum AFP)

(3) Hepatocellular carcinoma (> 5 years of age, no calcifications, elevated serum AFP)

(4) Metastatic neuroblastoma

HEPATOCELLULAR CARCINOMA

= HEPATOMA

= most common (90%) primary malignancy of the liver; most frequent primary visceral malignancy in the world; 2nd most frequent malignant hepatic tumor in children (39%) after hepatoblastoma

◊ Worldwide 3rd most common cause of death from cancer (2nd [6th] most common for men [women])!

Prevalence: (a) in industrialized world: 0.2–0.8%

(b) in sub-Saharan Africa, Southeast Asia, Japan, Greece, Italy: 5.5–20%

Age-adjusted prevalence: 2.2 (women) – 6.8 (men) ÷ 100,000 in North America

Peak age:

(a) industrialized world: 6th–7th decade; M÷F = 2.5÷1; fibrolamellar subtype (in 3–10%) below age 40 years

(b) high incidence areas: 30–40 years; M÷F = 5÷1

(c) in children: > 5 years of age (peak at 12–14 years); M÷F = 1.8÷1 to 2.2÷1

Etiology:

1. Cirrhosis (60–90%)

› toxic (alcohol), cardiac, biliary atresia

Latent period: 8 months – 14 years from onset of cirrhosis

Incidence of HCC with underlying cirrhosis:

2–7% per year

› 44% in macronodular (= postnecrotic) cirrhosis ← hepatitis B virus, alcoholism, hemochromatosis

› 6% in micronodular cirrhosis ← alcoholism

2. Hepatitis C virus infection (50–60%)
3. Chronic hepatitis B (20%)
4. Nonalcoholic steatohepatitis ← obesity
5. Carcinogens: aflatoxin, siderosis, thorotrast, oral contraceptives / anabolic androgens
6. Inborn errors of metabolism: hemochromatosis, Wilson disease, alpha-1 antitrypsin deficiency, galactosemia, type I glycogen storage disease (von Gierke), hereditary tyrosinemia

Prevalence of HCC in Underlying Cirrhosis

Prevalence	*Cause of Cirrhosis*
17–30%	Hepatitis C infection
21%	Hereditary hemochromatosis
10–15%	Hepatitis B virus infection
5–8%	Alcoholic cirrhosis
4%	Advanced biliary cirrhosis

mnemonic: WHAT causes HCC?

Wilson disease
Hemochromatosis
Alpha-1-antitrypsin deficiency
Tyrosinosis
Hepatitis
Cirrhosis (alcoholic, biliary, cardiac)
Carcinogens (aflatoxin, sex hormones, thorotrast)

Path: soft tumor due to lack of stroma, often hemorrhagic + necrotic

Histo: HCC cells resemble hepatocytes in appearance + structural pattern (trabecular, pseudoglandular = acinar, compact, scirrhous)

(a) expansive encapsulated HCC: collapsed portal vein branches at capsule

(b) infiltrative nonencapsulated HCC: commonly intrasinusoidal + intravascular growth (portal venules communicate with tumoral sinusoids) → often invasion of portal ± hepatic veins

Grading system (Edmondson):

I cells similar in size to normal hepatocytes, arranged in relatively thin trabeculae; rarely acini containing bile (DDx: hepatocellular adenoma)

II cells larger than normal hepatocytes, hyperchromatic nuclei in a greater proportion of cells; thicker trabeculae; commonly acini containing bile

III cells with large nuclei occupying > 50% of cytoplasm; dominant trabeculae with solid areas ± isolated giant and bizarre cells; bile rarely present

IV cell nuclei occupying most of the cytoplasm; mostly solid areas with little / no bile (DDx: tumor of nonhepatocellular origin)

Vascular supply: hepatic artery (94%), portal vein (6%); HCC is directly supplied by (newly formed) "unpaired" or "nontriadal" arteries (= not part of portal tracts)

Natural history of HCC (suggests 3 stages):
(1) Molecular stage consisting of sequential changes leading to cell transformation
(2) Preclinical stage when HCC is too small to be detectable at imaging
(3) Clinical / symptomatic stage when the tumor has reached a diameter of 4.5–8 cm and develops symptoms

- fever, weight loss, anorexia
- persistent RUQ pain, hepatomegaly, ascites
- α-fetoprotein elevated in 75–90% (DDx: negative α-fetoprotein in cholangiocarcinoma)
- elevated liver function tests (not helpful for diagnosis)
- Paraneoplastic syndromes:
  (a) sexual precocity / gynecomastia
  (b) hypercholesterolemia
  (c) erythrocytosis ← tumor produces erythropoietin
  (d) hypoglycemia
  (e) hypercalcemia
  (f) carcinoid syndrome

Metastases to: lung (most common = 8%), adrenal, lymph nodes, bone

Growth pattern (Eggle classification):
(a) <u>massive</u> solitary pattern (27–50–59%):
√ large tumor bulk in one (most often right) lobe with an unclear boundary + satellite nodules
(b) <u>nodular pattern</u> (15–25%):
√ multiple small distinct sharply marginated foci of usually < 2 cm (up to 5 cm) in both hepatic lobes
(c) diffuse <u>infiltrative</u> pattern (7–26%)

Median tumor doubling time: 4–6 (range, 1–19) months
→ 3–12 months follow-up for indeterminate lesions

√ portal vein invasion (25–33–48%)
√ arterioportal shunting (4–63%)
√ invasion of hepatic vein (16%) / IVC (= Budd-Chiari syndrome)
√ occasionally invasion of bile ducts
√ calcifications in ordinary HCC (2–9–25%); however, common in fibrolamellar (30–40%) and sclerosing HCC
√ hepatomegaly and ascites
√ tumor fatty metamorphosis (2–17%)
√ atypical multilocular cystic mass ← necrosis / microscopic hemorrhage

The mural nodules in **multilocular cystic HCC** that correspond to viable tumor components may demonstrate the classic HCC hemodynamics of arterial enhancement and late contrast material washout at both CECT and MR imaging. This feature is critical in differentiating HCC from other cystic neoplasms. Furthermore, if "abnormal internal vessels or a variegated pattern" are observed

in mural nodules, it may strongly indicate HCC.

US (48% sensitive, 98% specific):
- √ variable echogenicity:
  - √ hyperechoic HCC (13%) ← fatty metamorphosis or marked dilatation of sinusoids
  - √ hypoechoic HCC (26%) ← solid tumor
  - √ HCC of mixed echogenicity (61%) ← nonliquefactive tumor necrosis + old hemorrhage
- √ Doppler peak velocity signals > 250 cm/s
- √ calcifications (rare)

Surveillance scan: every 6 months for high-risk patients

NECT (48% sensitive, 70% specific):
- √ hypodense mass / rarely isodense / hyperdense in fatty liver:
  - √ dominant mass with satellite nodules
  - √ mosaic pattern = multiple nodular areas with differing attenuation in larger lesion (up to 63%)
  - √ diffusely infiltrating neoplasm
- √ encapsulated HCC = circular zone of radiolucency surrounding the mass (12–32–67%)

False-positive: confluent fibrosis, regenerative nodule

Biphasic CECT (68% sensitive):
- ◊ 63% sensitivity in cirrhosis, 80% without cirrhosis
- √ enhancement during hepatic arterial phase (80%)
  - ◊ 16% seen on arterial phase only!
- √ decreased attenuation during portal venous phase with inhomogeneous areas of contrast accumulation
- √ isodensity on delayed scans (10%)
- √ thin contrast-enhancing capsule (50%) ← rapid washout
- √ wedge-shaped areas of decreased attenuation (segmental / lobar perfusion defects ← portal vein occlusion by tumor thrombus

Lipiodol® CT (53% sensitive, 88% specific):
- √ hyperdense mass detectable as small as 0.5 cm

MR (81% sensitive):
- ◊ Any solid lesion in a cirrhotic liver that is not a hemangioma is considered HCC until proven otherwise!
- ◊ Dysplastic nodules are rarely seen with imaging!
- √ variable intensity on T1WI:
  - √ most often hypointense relative to liver
  - √ isointense for lesion size < 1.5 cm

Major Imaging Features Favoring HCC
√ masslike configuration:
√ size ≥ 20 mm
√ tumor capsule / pseudocapsule = peripheral rim (ring) enhancement during venous phase
√ discrete margin
√ round shape
√ focal deformity of liver contour
√ displacement of intraparenchymal structures
√ visible on nonenhanced MR, DWI, T2WI, T2*
√ aggressive behavior
√ interval growth: increase ≥ 10 mm in 1 year
√ intralesional necrosis / hemorrhage
√ prominent intralesional arteries
√ local / vascular invasion
√ extrahepatic metastasis
√ arterial phase hyperenhancement:
√ enhancement greater than surrounding liver parenchyma + compared to precontrast phase
√ enhancement may be greater during portal venous phase
√ venous phase hypoenhancement = washout during portal venous / later phase
DDx: fibrotic tissue typically shows delayed enhancement (causing false appearance of hypoenhancement) of a regenerative nodule / hypertrophic pseudomass in liver cirrhosis
√ absent / ↓ uptake of superparamagnetic iron oxide (SPIO) on long T2*
√ tumor thrombus within lumen of vein:
√ arterial phase hyperenhancement + venous phase hypoenhancement of tumor thrombus
√ occluded vein with expanded lumen
√ luminal enhancement not matching time of enhancement in other veins
√ presence of arteries within lumen (in absence of cavernous transformation)
√ markedly restricted / impeded diffusion in lumen

Ancillary Features Favoring Hepatocellular Carcinoma
√ mild to moderate T2 hyperintensity
√ mosaic architecture
√ high signal intensity on DWI
√ intralesional steatosis = ↓ SI on opposed-phase images
√ iron sparing in an iron-overloaded liver

- √ hyperintense areas / hyperintense lesion, particularly if > 1.5 cm in diameter ← lipid / copper / glycogen / blood
  - ◊ Fatty metamorphosis in a cirrhotic nodule is suspicious for HCC!
- √ variable intensity on T2WI relative to liver:
  - √ generally hyperintense / small focus of hyperintensity
    - ◊ Any hypervascular mass in cirrhosis with increased T2 signal similar to that of spleen is suspicious for HCC!
    - ◊ An iron-poor focus within a siderotic nodule on T2WI suggests HCC!
  - √ iso- to hypointense for well-differentiated tumor
- √ "ring" sign (10–78%) = typically thin + discontinuous hypointense capsule on T1WI + T2WI:
  - √ double layer of inner hypointensity (fibrous tissue) + outer hyperintensity (← compressed blood vessels + bile ducts) on T2WI in expansive type of HCC
- √ may contain central scar of fibrosis / calcifications / necrosis hypointense on T1WI + T2WI
- √ variable appearance on DWI:
  - √ often isointense for well-differentiated tumor
  - √ often hyperintense for moderately to poorly differentiated tumor

CEMR:

(a) arterial phase imaging:
- √ marked homogeneous enhancement for lesion < 2 cm:
  - › for 1–2-cm lesion → 3-month follow-up;
  - › for < 1-cm lesion → 6-month follow-up
- √ heterogeneous enhancement for lesion > 2 cm:
  - √ enhancement peripherally (62%) / centrally (7%) / mixed (10%) / no enhancement (21%)
  - √ central scar without much enhancement

(b) portal venous and equilibrium phase:
- √ rapid loss of enhancement becoming isointense / hypointense (= rapid venous washout)
  - ◊ Delayed hypointensity of an arterially enhancing mass in a cirrhotic liver is HCC unless proven otherwise!
- √ progressive delayed enhancement of tumor capsule
- √ "peripheral washout" sign = decrease of contrast material preferentially in periphery of mass while center remains hyperintense (← ? related to vessel distribution with central necrosis / fibrosis and peripherally viable tumor), same as in hypervascular metastasis

- √ improved lesion detectability on T1WI after intravenous administration of superparamagnetic iron oxide (entrapped by Kupffer cells) + gadolinium during late hepatic arterial phase

Characteristic MR features for larger HCC:
- √ mosaic pattern of variable SI on T1WI + T2WI ← confluent small nodules separated by thin septa + areas of tumor necrosis
- √ extracapsular extension with formation of satellite nodules
- √ vascular invasion:
  - √ lack of signal void on SE images
  - √ enhancing intravascular mass during arterial phase
  - √ intravascular filling defect during delayed phase

√ extrahepatic dissemination → distant metastasis + lymph node involvement

NUC:

√ Sulfur colloid scan: single cold spot (70%), multiple defects (15–20%), heterogeneous distribution (10%)

√ Tc-HIDA scan: cold spot / atypical uptake in 4% (delayed images)

√ Gallium-scan: avid accumulation in 70–90% (in 63% greater, in 25% equal, in 12% less uptake than liver)

Angio:

√ "thread and streak" sign = venous and arterial channels located in and around a cast of tumor in a large branch ± trunk of the main portal vein

√ in differentiated HCC: enlarged arterial feeders, coarse neovascularity, vascular lakes, dense tumor stain, arterioportal shunts

√ in anaplastic HCC: vascular encasement, fine neovascularity, displacement of vessels + corkscrew-like vessels of cirrhosis

Prognosis: > 90% overall mortality; 17% resectability rate; 6 months average survival time; 0–10% 5-year survival rate (> 50% for small HCC) → HCC detection of < 2 cm is crucial

Cx: spontaneous rupture (in 7–14% in Asia + Africa)

Rx: (1) Resection

(2) Liver transplant (solitary lesion < 5 cm; up to 3 lesions < 3 cm; no portal / hepatic vein involvement; no metastatic disease)

(3) Radiofrequency ablation for tumors < 3 cm

(4) ^{131}I-antiferritin IgG (remission rate > 40% up to 3 years)

DDx of hypervascular lesion:

(1) Fibrolamellar carcinoma (central scar with calcium, homogeneous tumor without hemorrhage / necrosis)

(2) Hepatocellular adenoma (in young woman using oral contraceptive, in child with glycogen storage disease, anabolic steroid use)

DDx: hepatocarcinoma, cholangiocarcinoma, focal nodular hyperplasia, hemangioma, hepatic adenoma, pseudolesion of cirrhotic liver (mostly < 1-cm enhancing foci not histologically visible)

Infiltrative Hepatocellular Carcinoma

= DIFFUSE HCC, CIRRHOTOMIMETIC HCC, CIRRHOSIS-LIKE HCC (masquerading as cirrhotic nodules)

= characterized by spread of minute tumor nodules throughout a lobe / entire liver

with: hepatitis B virus infection, especially in Asia

• elevated α-fetoprotein: often > 10,000 ng/mL

Imaging sensitivity: 48% for US, 68% for CT, 81% for MR

While a macroscopic growth pattern of infiltrative HCC is uncommon, its histologic features are not unique to this type of HCC.

Infiltrative HCC has a relatively reduced conspicuity during dynamic phases of enhancement ← its permeative infiltrative nature + presence of portal vein thrombosis, resulting in perfusion changes that can effectively conceal the tumor.

√ cryptic spread of distinct minute tumor nodules within hepatic lobe / entire liver:
  √ NO dominant nodule
  √ regular / distinct margin around each tumor nodule
√ tumor contrast characteristics relative to liver parenchyma:
  √ minimal / patchy / miliary enhancement during arterial phase
  √ irregular heterogeneous washout = hypoenhancement during portal ± delayed phase (51%)
  √ reticular appearance during venous + equilibrium phase
  √ lack of hepatospecific contrast agent uptake during hepatobiliary phase
√ extra- / intrahepatic portal vein thrombosis (68–100%)
√ intrahepatic biliary ductal dilatation (13–26%)
√ spread to upper abdominal lymph nodes (10–22%)
√ distant metastases to lung, bone, adrenals (13–23%)
MR:
  √ homo- / heterogeneously hypointense on T1WI
  √ moderately heterogeneously hyperintense on T2WI
  √ hyperintense on DWI with b values of 500–800 sec/mm2
  √ poorly visualized on dynamic contrast-enhanced images

DDx: (1) Confluent fibrosis
(2) Focal hepatic steatosis
(3) Hepatic microabscesses
(4) Intrahepatic cholangiocarcinoma

Prognosis: worst of all growth patterns

Rx: infiltrative HCC is usually a contraindication for resection and transplantation due to decreased survival after surgical resection.

Fibrolamellar Carcinoma of Liver

= uncommon variant of hepatocellular carcinoma arising in young adults without underlying hepatic disease

Prevalence: 1–9% of all HCCs; up to 35% of HCCs in patients < 50 years of age

Mean age: 23 (range, 5–69) years; mostly 2nd–3rd decade (85% < 35 years of age); M÷F = 1÷1

Path: desmoplastic tumor with collagen deposition → fibrous central scar (60–75%) with calcifications (35–55%)

Growth pattern:
(a) large circumscribed nonencapsulated mass (80–90%)
(b) intrahepatic mass with satellite nodules (10–15%)
(c) bilobed mass (5%)
(d) multiple diffuse masses (< 1%)

Histo: large polygonal hepatocyte-like cells with coarse granular eosinophilic cytoplasm growing in sheets / cords / trabeculae separated by broad bands of fibrous stroma arranged in parallel lamellae resulting in a compartmentalized appearance

Risk factors: NONE known; underlying cirrhosis or hepatitis in < 5%

Demographics: USA > Europe; rare in Japan + China; predilection for Caucasians
- abdominal pain, cachexia, palpable RUQ mass, hepatomegaly
- jaundice (5%) ← biliary compression
- gynecomastia (rare) ← conversion of androgens to estrogens by tumor-elaborated enzyme aromatase
- α-fetoprotein usually negative / mildly elevated to < 200 ng/μL (in up to 10%); transaminase levels < 100 IU/L

Mean size: 13 (range, 5–20) cm in diameter

√ well-circumscribed partially / completely encapsulated solitary mass (in 80–90%):
- √ intrahepatic (80%) / pedunculated (20%)
- √ prominent central fibrous scar (45–60%)
- √ punctate / nodular / stellate calcifications (33–68%):
  - √ centrally within scar, < 3 in number, < 5 mm in size
- √ capsular retraction (10%)
- √ intratumoral hemorrhage + necrosis (10%)
- √ vascular invasion (< 5%)

√ mass + small peripheral satellite lesions (10–15%)

√ diffuse multifocal masses (< 1%)

√ regional lymphadenopathy (50–70%) usually in hepatic hilum / hepaticoduodenal ligament

√ distant metastases (20%): lung, peritoneal implants

Abdominal x-ray:
- √ hepatomegaly ± stellate calcifications

US:
- √ well-defined lesion of mixed echogenicity (60%) with predominantly iso- / hyperechoic portions
- √ central hyperechoic scar (33–60%) ± shadowing calcifications

NECT:
- √ mass of heterogeneously low attenuation
- √ lobulated surface contour (in 80%)
- √ prominent stellate / amorphous central scar (20–71%)

CECT:
- √ enhancement of non-scar portion:
  - √ prominent heterogeneous arterial enhancement (in 80%)
  - √ variable attenuation in portal venous phase
  - √ less pronounced enhancement during equilibrium phase
- √ enhancement of scar: none (75%) / delayed (25%)
- √ delayed enhancement of pseudocapsule of compressed liver tissue (15%)

MR:
- √ large well-defined lobulated mass:
  - √ hypointense (86%) / isointense (14%) on T1WI
  - √ hyperintense (85%) / isointense (15%) on T2WI
  - √ homogeneous (80%) / heterogeneous (20%)
- √ hypointense central scar on T1WI + T2WI (in 80%)

CEMR:
- √ early heterogeneous contrast enhancement that fades on subsequent images

√ central scar without enhancement
(DDx: T2-hyperintense myxoid central scar of FNH)

Angio:
√ dense tumor stain
√ enlarged feeding arteries
√ NO arteriovenous / arterioportal shunting
√ avascular central scar

NUC:
√ photopenic area on sulfur colloid scan ← relative lack of Kupffer cells in number + function
√ increased activity during arterial phase + wash-out during delayed imaging on labeled RBC scan
√ nonspecific increased activity on ^{67}Ga scintigraphy

Prognosis: 48% resectability rate; average survival time of 32 months; 67% 5-year survival time

DDx: (1) Focal nodular hyperplasia (young + middle-aged woman, < 5 cm in size, calcifications uncommon, isointense to liver on all CT + MR images with pronounced homogeneous enhancement during arterial phase, myxoid hyperintense central scar on T2WI with delayed enhancement, uptake of sulfur colloid / superparamagnetic iron oxide)
(2) Large cavernous hemangioma (peripheral nodular discontinuous enhancement pattern similar to blood vessels with filling-in on delayed phase)
(3) Hepatocellular adenoma (no central scar, heterogeneous texture ← fat + hemorrhage)
(4) Hepatocellular carcinoma (regions of hemorrhage + necrosis, diseased adjacent liver, ↑ AFP)
(5) Metastasis (multifocal and visible primary)

HEPATOSPLENIC TUBERCULOSIS

Cause: disseminated disease
@ micronodular-miliary involvement
√ innumerable 0.5–2.0-mm nodules
√ hyperechoic liver
@ macronodular involvement (uncommon)
√ hypoattenuating nodules + irregular ill-defined margins
√ minimal central + definite peripheral enhancement
√ T1-hypointense + T2-hyperintense nodules
√ tuberculomas eventually calcify

HYPERPLASTIC CHOLECYSTOSIS

= variety of degenerative + proliferative changes of gallbladder wall characterized by hyperconcentration, hyperexcitability, and hyperexcretion
Frequency: 9–30–50% of all cholecystectomy specimens;
M÷F = 1÷6
Associated with: gallstones in 90%

Adenomyomatosis of Gallbladder

= ADENOMYOMATOUS HYPERPLASIA OF GALLBLADDER
= increase in number + height of mucosal folds
Path: hyperplasia of mucosa + muscularis propria with mucosal outpouching of epithelium-lined cystic spaces into (46%) or all the way through (30%) a thickened muscular layer as tubules / crypts / 2–8 mm saccules (= intramural diverticula = Rokitansky-Aschoff sinus); precipitation of cholesterol crystals in bile trapped in Rokitansky-Aschoff sinuses (= intraluminal cholesterol accumulation)
[Rokitansky, Karl Freiherr von (1804–1878), chair of Pathological Anatomy at Vienna General Hospital, Austria]
[Carl Aschoff (1866–1942), pathologist in Bonn, Germany]
Frequency: 2–5% of all cholecystectomy specimens
Age: > 35 years (develop with increasing age); M÷F = 1÷3
Associated with: (1) Gallstones in 25–75%
(2) Cholesterolosis in 33%
Types:
(a) generalized form = ADENOMYOMATOSIS
√ **"twinkling / comet-tail"** = sound reverberation artifact between cholesterol crystals in Rokitansky-Aschoff sinuses (PATHOGNOMONIC)
N.B.: Rokitansky-Aschoff sinuses of < 5 mm cannot be resolved / identified on abdominal US
√ gallbladder wall thickening + enhancement
√ **"rosary"** sign on CT = enhancing epithelium within intramural diverticula surrounded by relatively unenhanced hypertrophied gallbladder muscularis
√ multiple tiny rounded hyperintense extraluminal cavities:

√ **"string of beads"** sign = high-signal-intensity foci in gallbladder wall on T2WI (92% specific)
√ **"pearl necklace"** sign = multiple round spaces in curvilinear intramural arrangement on MRCP

√ signal voids of intramural calculi (crystals)

(b) segmental form
compartmentalization most often in neck or distal ⅓

(c) localized form in fundus
= solitary ADENOMYOMA with extraluminal diverticula-like formation
√ smooth sessile mass in GB fundus

(d) annular form
√ "hourglass" configuration of GB with transverse congenital septum

DDx: polyposis, papillomatosis, adenoma, cystadenoma, gallbladder carcinoma, metastasis

Cholesterolosis

= abnormal deposition of triglycerides + cholesterol esters in macrophages within lamina propria (foam cells) + in mucosal epithelium

Strawberry Gallbladder

= LIPID CHOLECYSTITIS = CHOLESTEROLOSIS
= planar form of cholesterolosis
= seedlike patchy / diffuse thickening of the villous surface pattern (disseminated micronodules)

Associated with: cholesterol stones in 50–70%
• bright red mucosa with interposed areas of yellow lipid
• not related to serum cholesterol level
√ radiologically not demonstrable

Cholesterol Polyp *(90%)*

= abnormal deposit of cholesterol esters and triglycerides producing a villouslike structure covered with a single layer of epithelium and attached via a delicate stalk

Not associated with: gallstones
Prevalence: 4%; most common (50%) fixed filling defect of gallbladder
Age: 40–50 years; M÷F=1÷3
Location: commonly in middle ⅓ of gallbladder

√ small round smoothly contoured intraluminal lesion:
√ multiple (on average 8) small filling defects *Size:* < 10 mm (rarely up to 20 mm) in diameter
√ "ball on the wall" sign ← lesion attached to wall with stalk (rarely seen)

Prognosis: NO malignant potential
DDx: papilloma, adenoma, inflammatory granuloma

INFLAMMATORY POLYP OF GALLBLADDER

Cause: gallstones, chronic cholecystitis
√ solitary (in ½), 2–5 polyps (in ½)

√ usually < 10 mm in diameter

Prognosis: may incite mucosal epithelial dysplasia (NO definitively increased risk for adenocarcinoma)

◊ Inflammatory polyps have a nonspecific appearance so that the diagnosis may NOT be made with certainty at imaging!

INSPISSATED BILE SYNDROME

= uncommon cause of jaundice in neonate

Associated with: massive hemolysis (Rh incompatibility), hemorrhage (intraabdominal, intracranial, retroperitoneal), increased enterohepatic circulation (Hirschsprüng disease, intestinal atresia, stenosis)

US:

√ sludge in gallbladder

√ sludge within bile ducts + partial / complete obstruction (affected ducts may blend with surrounding hepatic parenchyma)

INTRADUCTAL PAPILLARY MUCINOUS NEOPLASM OF PANCREAS

= IPMN = MUCINOUS DUCTAL ECTASIA = DUCTECTATIC MUCINOUS CYSTIC TUMOR OF PANCREAS = INTRADUCTAL MUCIN-HYPERSECRETING NEOPLASM = MUCINOUS VILLOUS ADENOMATOSIS = MUCIN-PRODUCING PANCREATIC TUMOR

= rare intraductal tumor originating from papillary epithelial lining characterized by voluminous mucin secretions

Path: conglomeration of communicating cysts covered by a rim of normal pancreatic parenchyma + thin fibrous capsule

Histo: mucinous transformation of pancreatic ductal epithelium forming innumerable papillary projections within a typically dilated pancreatic ductal system that contains globules of mucus; papillae are coated with hyperplastic (= adenoma) / atypical (= borderline lesion) / malignant epithelium ← adenoma-carcinoma sequence

Pancreatic ductal imaging is essential to for classification:

(1) establish the diagnosis of IPMN

(2) differentiate among subtypes of IPMN like

(a) main duct IPMN (diffuse / segmental) cystic pattern

(b) mixed or isolated side-branch IPMN

Mean age: 65 years; M > F

- recurrent episodes of dull pain / acute pancreatitis ← impaired outflow of pancreatic secretions:
  - hyperamylasemia (occasionally)
- viscosity of fluid greater than normal serum (89% sensitive, 100% specific)

Location: frequently multifocal; 5–10% involve entire pancreas

◊ Location is an important factor for prognosis!

√ communication between cystic lesion + main pancreatic duct (= most reliable diagnostic finding!):

√ narrow neck at cyst-duct junction

√ mural nodules projecting into main pancreatic duct
√ protrusion of major papilla
ERCP:
- spillage of thick jellylike mucin from ampulla of Vater with protrusion from bulging patulous duodenal papilla
√ plugging of papilla of Vater
√ elongated band- / threadlike / nodular amorphous filling defects in dilated pancreatic duct (= depiction of mucin)
√ usually small mural polypoid / flat tumor
√ dilated pancreatic ductal system in the absence of an obstructive ductal stricture
√ communication between cyst cavity + pancreatic duct
N.B.: escape of contrast material due to excess of mucin / patent papillary orifice hinders filling of ductal tree

Prognosis: low-grade malignancy with better prognosis than pancreatic adenocarcinoma
Signs of malignant transformation:
√ lesion > 3.5 cm in size with thick walls
√ enhancing soft-tissue nodularity
Dx: ERCP (bulging ampulla, mucin pouring from papilla, communication between pancreatic duct + cystic cavity)
Cx: malignancy (57–92% for main-duct IPMN + 20% for branch-duct IPMN)

MRCP (findings suggestive of a malignant IPMN):
√ filling defects / papillary projections within a dilated pancreatic duct
√ main pancreatic duct cysts + dilatation of > 15 mm
√ branch duct dilatation = enlargement by any amount

DDx: (1) Chronic obstructive pancreatitis (calcifications)
(2) Serous / mucinous cystic tumors (NO communication with pancreatic duct, lobulated contour)
(3) Pseudocyst (communication with duct)

Main Duct IPMN

Age: 57 (range, 34–75) years; M÷F = 1÷1
Histo: invasive carcinoma in 60–70%
√ hyperechoic, hyperdense, T2-hypointense filling defect within dilated duct (= enhancing papillary mural nodule / gravity-dependent mucin glob)
√ dilatation of entire main pancreatic duct:
(a) dilatation of entire main pancreatic duct
√ homogeneous hypoechoic, hypodense, T1-hypointense and T2-hyperintense main duct
√ pancreatic parenchymal atrophy
√ dilatation of branch ducts (usually in pancreatic tail + uncinate process)
√ dilatation of major ± minor papilla bulging into duodenal lumen
√ ± obstruction of CBD ← tumor / impacted mucin
Cx: pancreaticobiliary / ~duodenal fistula, pseudomyxoma peritonei
DDx: chronic obstructive pancreatitis (loss of T1 signal + delayed uptake of contrast =

fibrosis)

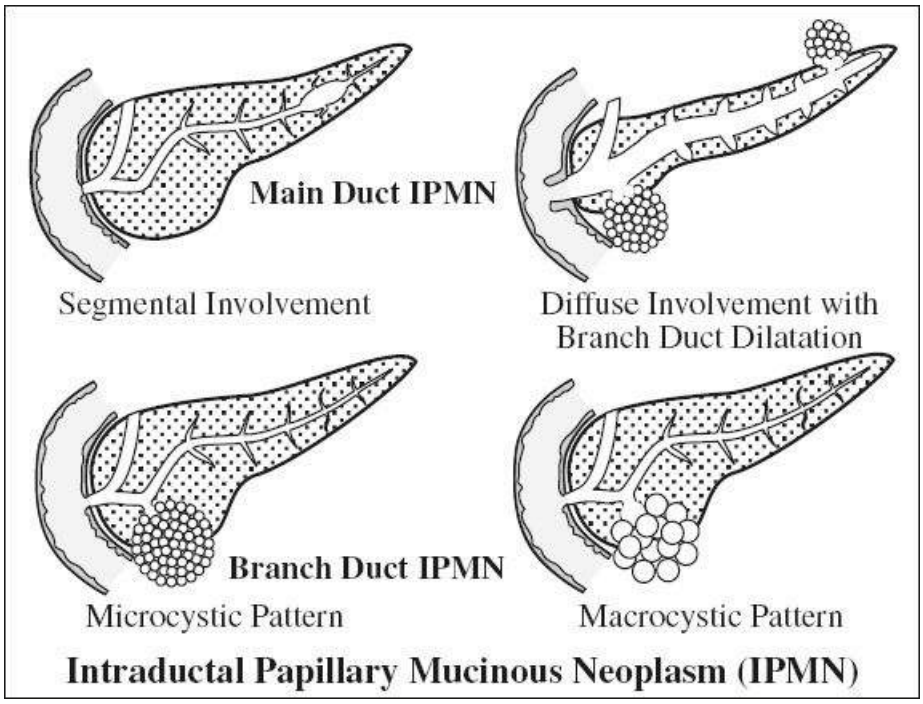
(b) segmental dilatation of main pancreatic duct

√ cyst in pancreatic body / tail + normal remaining pancreatic parenchyma

√ cyst in pancreatic head + upstream dilatation of main pancreatic duct

DDx: peripheral mucinous cystic tumor (main duct almost always normal)

Rx: Whipple operation



Branch Duct IPMN

Age: 63 (range, 37–76) years; M÷F=1÷1

- usually incidental finding when tumor small
- symptoms mimicking acute / chronic pancreatitis

Location: mainly in uncinate process >> pancreatic tail > pancreatic body

Path: macrocystic / microcystic pattern; malignancy suggested by irregular thick wall + septa and solid nodules

Histo: invasive carcinoma in 22%

√ dilatation of multiple side branches (most commonly)

√ round / ovoid small lobulated intraductal mass (frequently not visualized):

√ dilated main pancreatic duct

√ normal main pancreatic duct (almost always normal in small tumor)

◊ Secretin administration distends ducts and enhances detection of communication with main pancreatic duct!

√ uni- / multilocular cyst 10–20 mm large with sparse septa

DDx: mucinous cystadenoma (no communication with main pancreatic duct); pseudocyst (no intraluminal filling defects)

√ grapelike locular appearance = multiple thin septa separating fluid-filled lacunae

DDx: serous cystadenoma (no communication with main pancreatic duct)

√ ± severe pancreatic atrophy
√ protrusion of papilla into duodenum
Cx: seeding to main pancreatic duct resulting in main duct IPMN
Rx: observation (for asymptomatic patient and a lesion of < 3 cm) / partial pancreatectomy

LIPOMA OF LIVER

Extremely rare
• asymptomatic
May be associated with: tuberous sclerosis
Size: few mm – 13 cm
US:
√ well-circumscribed echogenic mass (DDx: hemangioma, angiomyolipoma)
√ striking acoustic refraction (sound velocity in soft tissue 1,540 min/sec, in fat 1,450 min/sec)
CT:
√ homogeneously hypoattenuating mass
√ no contrast enhancement
MR:
√ hyperintense on T1WI
√ hypointense (= signal suppression) on fat-suppressed images
√ NO enhancement after gadolinium chelate administration
Prognosis: no malignant potential

LIVER TRANSPLANT

Cadaveric liver transplantation:
= most common type of liver transplantation in adults
Advantage: › full donor liver transplantation
› usually technically successful
Disadvantage: limited organ availability
Living donor liver transplantation technique:
left lateral hepatectomy including segments II + III

Indications: end-stage acute / chronic liver disease
› chronic viral hepatitis: chronic active hepatitis (4% in childhood)
› metabolic disease: alpha-1 antitrypsin deficiency (9% in childhood), hemochromatosis, Wilson disease
› cholestatic liver disease: primary biliary cirrhosis, primary sclerosing cholangitis, biliary atresia (52% in childhood)
› autoimmune hepatitis
› cryptogenic cirrhosis (6% in childhood)
› alcoholic liver disease
› acute fulminant hepatic failure (11% in childhood): viral hepatitis, drug-induced hepatitis (eg, by acetaminophen, isoniazid), hepatotoxins (eg, mushrooms)

Eligibility for liver transplantation (Milan criteria):
single tumor of < 5 cm / ≤ 3 tumors of 3 cm or smaller

Contraindications: AIDS, extrahepatic malignant tumors, active IVDA / alcohol abuse
Frequency: 112,931 liver transplantations in US between 1988 and 2012; annually 6,000 liver transplantations; 1,500 deaths annually while awaiting transplantation

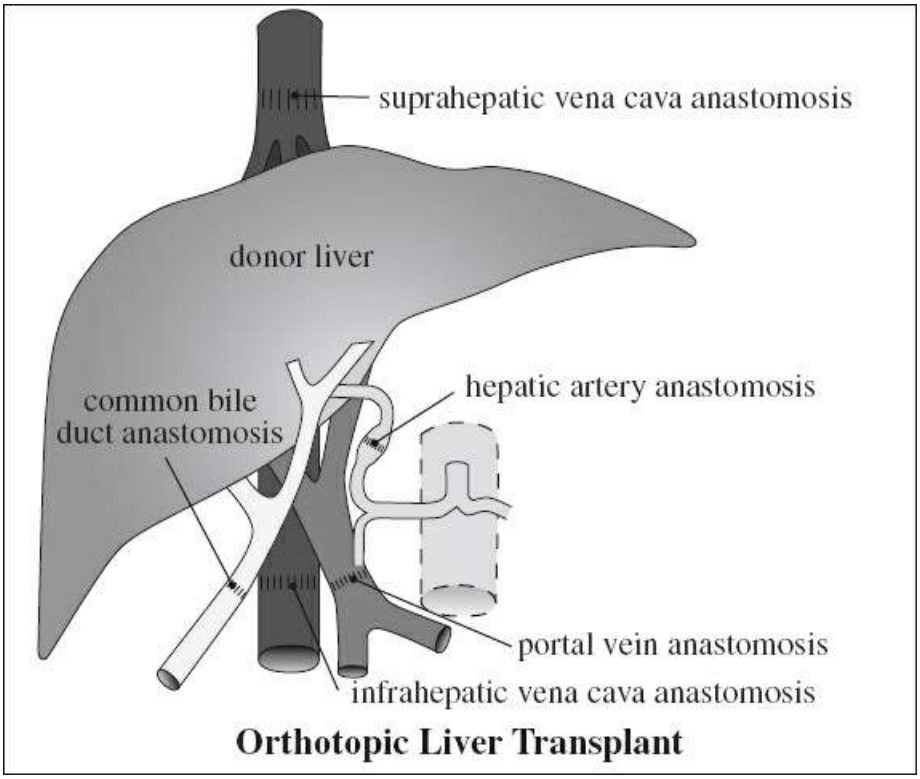
Normal posttransplant findings

(1) Periportal + reperfusion edema (21%)
Cause: lymphedema in early posttransplantation period (= dilatation of lymphatic channels ← lack of normal lymphatic drainage)
√ "starry sky" pattern = diminished liver echogenicity with accentuation of echogenic portal venules
√ "periportal collar" of low attenuation on CT
√ resolution within weeks to months
(2) Pneumobilia
(3) Fluid collection around falciform ligament (11%), at vascular anastomoses (liver hilum, IVC), at biliary anastomosis, in lesser sac
√ present during 1st day; disappears within a few weeks
(4) Small right pleural effusion
(5) Peri- / subhepatic hematoma / free intraabdominal fluid
(6) Anastomotic narrowing of IVC / portal vein
◊ Discrepancies in caliber between donor + recipient vessel have no pathologic significance!
√ wide range of portal vein velocities (15–400 cm/s) with average decrease of 20% over next few days + normalization by 2 years
√ dampened mono- / biphasic hepatic vein waveform ← graft edema / compression by adjacent hematoma

Prognosis: 1- and 5-year graft survival of 82% and 65%

Vascular Complications in Liver Transplant (9%)

◊ Most frequent cause of graft loss
• liver failure, bile leak, abdominal bleeding, septicemia



@ **Thrombosis / stenosis of IVC / hepatic vein** (< 1%)

Cause: size discrepancy between donor + recipient vessels, suprahepatic caval kinking from organ rotation, anastomotic fibrosis, neointimal hyperplasia, chronic thrombosis

- pleural effusions, hepatomegaly, ascites, extremity edema

√ compression of IVC ← swelling of graft
√ reduction in caliber of poststenotic IVC
√ prestenotic dilatation of IVC + hepatic veins
√ persistent monophasic waveform (sensitive but not specific for significance of stenosis; bi- / triphasic waveform excludes significant stenosis)
√ focal narrowing on B-mode imaging
√ 3–4-fold velocity increase compared with prestenotic segment
√ intraluminal echogenic thrombus
√ pressure gradient of > 5 mmHg
√ mosaic pattern of perfusion on CT / MR (Budd-Chiari)

@ **Thrombosis / stenosis of portal vein** (1–3%)

Cause: faulty surgical technique, vessel misalignment, differences in vessel caliber creating turbulent flow, hypercoagulable state, prior portal vein surgery, prior thrombosis in recipient portal vein, increased downstream resistance ← supra-hepatic stricture of IVC, decreased portal inflow

- portal hypertension, liver failure, massive ascites, edema

Duplex US of venous stenosis > 50%
√ 3- to 4-fold increase in peak systolic flow velocity compared with prestenotic segment
√ poststenotic turbulence

√ narrowing of portal vein + poststenotic dilatation
√ increase in number / caliber of collateral vessels
√ filling defect / focal narrowing at anastomosis
Rx: percutaneous transluminal angioplasty ± stent placement, surgical thrombectomy, venous jump graft, creation of portosystemic shunt, retransplantation

@ Hepatic artery
Normal Resistive Index (RI): 0.5 – 0.8

√ < 72 hours after transplantation RI frequently > 0.8 with return to normal in a few days
Cause: older donor age, prolonged period of cold ischemia, hepatic arterial spasm, reperfusion edema, increased portal flow (= inhibition of arterial vasodilator release)

1. **Hepatic artery stenosis** (5–13%)
Location: at / near anastomosis
Cause: clamp injury, arterial spasm, intimal trauma from perfusion catheter, disruption of vasa vasorum
Time of onset: within 3 months after transplantation
√ marked focal increase in peak systolic velocity > 200–300 cm/sec or 2–3 x of prestenotic velocity + poststenotic turbulence in > 50% stenosis (30% sensitive, 96% specific)

√ intrahepatic tardus et parvus waveform:
√ slowed systolic **a**cceleration **t**ime (SAT > 70–80 msec) distal to stenosis (73% sensitive)
√ diminished pulsatility (RI < 0.55) ← ischemia

Pitfall: intrahepatic collateral arteries ← severe aortoiliac atherosclerosis / hepatic artery stenosis)
DDx: normal in early post-transplantation period
√ biliary dilatation (← stricture), infarction, biloma
Cx: hepatic artery thrombosis, hepatic ischemia, biliary stricture, sepsis, graft loss
Rx: revascularization surgery, balloon angioplasty

2. **Hepatic artery thrombosis** (4–12–16% in adults, 9–19–42% in children)
◊Most common vascular complication of liver transplantation (60%)!

Pathophysiology:
Bile duct perfusion: solely by hepatic artery
Arterial bile duct supply: via retrograde collaterals from vessels at 3- and 9-o'clock positions + via gastroduodenal and superior pancreaticoduodenal arcade, which are divided during bile duct transection in donor
Hepatic artery thrombosis → liver infarction, biliary ischemia, necrosis → biliary stricture (anastomotic and nonanastomotic), bile leak, biliary abscess, biliary cast syndrome

Risk factors:
donor death ← intracerebral hemorrhage, donor age > 50 years, previous liver transplant, split segmental graft, interpositional conduit for anastomosis, preexisting celiac artery stenosis
Time of onset: usually within first 2 months
(a) early thrombosis: < 1 month of transplantation ← significant caliber difference between donor + recipient artery, prolonged cold ischemia of donor liver, ABO

blood type incompatibility

(b) late thrombosis: > 1 month of transplantation ← acute rejection / sepsis (CMV infection)

- Three types of clinical presentation:
  (1) Fulminant hepatic necrosis + rapid deterioration
  (2) Bile leak, bile peritonitis, bacteremia, sepsis
  (3) Relapsing bacteremia

CT / MRA / Angio:
√ abrupt cutoff of flow in hepatic artery (usually at anastomotic site)
√ nonenhancement of hepatic artery
√ decreased enhancement of hepatic parenchyma ← ischemia / infarction

US (54–92% sensitive, 64–88% specific):
√ lack of hepatic artery flow
False-positive Doppler (10%):
systemic hypotension, high-grade hepatic artery stenosis, small vessel size, severe hepatic edema (in first 72 hours after transplantation, viral hepatitis, acute rejection)
False-negative Doppler:
arterial collaterals (← chronic thrombosis) with parvus tardus waveform (simulating proximal hepatic artery stenosis)
√ "syndrome of impending thrombosis":
√ loss of arterial diastolic flow
√ dampening of systolic peak
Prognosis: thrombosis in 92%
√ multiple hypoechoic lesions in liver periphery (= infarcts)

Mortality: 27–33–58%; 80% if undiagnosed
Rx: thrombectomy; hepatic artery reconstruction; retransplantation (30% mortality)

3. **Hepatic artery pseudoaneurysm** (uncommon)
   Location: at vascular anastomosis; complication of liver biopsy / angioplasty / focal infection
   Cx: acute shock due to massive intraperitoneal hemorrhage; portal vein fistula; biliary fistula
   Rx: surgical resection, embolization, exclusion by stent placement

Parenchymal Complications in Liver Transplantation

1. Rejection
   ◊ Most common cause of graft failure
   ◊ Can ONLY be diagnosed with liver biopsy!
2. Infarction (10%)
   √ may calcify
   √ may liquefy developing into intrahepatic biloma
3. Graft infection
4. Posttransplant lymphoproliferative disease
5. Neoplasms:
   skin cancer (other than melanoma), Kaposi sarcoma, NHL

Biliary Complications in Liver Transplant (6–25–34%)

◊ 2nd most common cause of liver dysfunction after rejection

Time of onset: within first 3 months

Stricture and leak = the most common biliary complications

1. **Biliary obstruction** (15–18%)
   (a) anastomotic stricture (extrahepatic)
   Cause: iatrogenic trauma → ischemia + scar formation
   (b) nonanastomotic (intrahepatic) stricture
   Cause: hepatic arterial thrombosis / stenosis (in 50%), prolonged preservation time, bacterial / viral cholangitis, rejection, recurrent primary sclerosing cholangitis, cholangiocarcinoma, kinking of redundant CBD, sphincter of Oddi dysfunction
   (c) tension mucocele of allograft cystic duct remnant
   Cause: ligation of cystic duct proximally + distally
   √ extrinsic mass compressing CHD
   √ fluid collection adjacent to CHD
   Cx: ascending cholangitis
2. **Bile leak** (10–15%)

Biliary leaks usually occur within the first few months after transplantation.

   (a) T-tube exit site: 50% within 10 days
   √ free leakage into peritoneal cavity
   √ loculated perihepatic collection
   (b) anastomosis of choledochocholedochostomy:
   70% within 1st postoperative month
   (c) bile duct necrosis (hepatic artery occlusion)
   ◊ The intrahepatic biliary epithelium is perfused solely by the hepatic artery!
   (d) after liver biopsy
   (e) common hepatic duct leak
3. **Biloma formation** (11%)
   within 1st year after transplantation
   Risk factors: hepatic artery thrombosis / stenosis, hepaticojejunostomy
4. **Stone / sludge formation**
   Cause: alteration in bile composition

LYMPHOMA OF LIVER

With de novo focal liver masses the diagnosis of lymphoma is suggested by an absent history of primary malignancy, < 40 years of age, B symptoms, splenic lesions, splenomegaly, and widespread abdominal / mediastinal lymphadenopathy.

US:

√ hypo- to anechoic nodules + absent posterior acoustic enhancement
√ ± "target" appearance (= central hyperechoic + peripheral hypoechoic component)
√ increased peripheral vascularity at Doppler
√ mild inhomogeneous hyperenhancement in arterial phase + contrast agent washout in portal

and late phases

CT:
- √ nodules of soft-tissue attenuation
- √ ± hemorrhage + necrosis
- √ hypovascular during all phases of enhancement
- √ ± rim-enhancement

MRI:
- √ hypo- to isointense nodules on T1WI
- √ moderately hyperintense nodules on T2WI
- √ DWI may allow earlier identification: typically restricted diffusion ← highly cellular mass (Detection rate for CT / MR is < 10%)

CEMR:
- √ hypovascular during all phases of enhancement
- √ ± minimal early enhancement
- √ "target" appearance (15%) = hyperintense poorly enhancing center + peripheral enhancement

PET/CT (modality of choice for staging + treatment response):
- √ avid hypermetabolism

DDx: Hepatocellular carcinoma (arterial phase enhancement, delayed contrast material washout with capsular enhancement, vascular thrombosis, hypometabolic at PET)

Primary Hepatic Lymphoma *(rare)*

Incidence: increased in immunosuppressed patients

Associated with: hepatitis B & C, Epstein-Barr virus

- right upper quadrant pain, jaundice (50%)
- systemic symptoms: fever, weight loss (⅓)
- √ solid solitary liver mass (60%)
- √ multiple heterogeneously enhancing liver masses with dominant mass (35–40%)
- √ diffuse infiltrating disease
- √ ill-defined mass in porta hepatis
- √ ± hepatic hilar lymphadenopathy

In primary hepatic lymphoma distant lymphadenopathy + splenomegaly / splenic lesions + bone marrow disease / leukemic blood profile should NOT occur for at least 6 months after the onset of hepatic disease.

Secondary Hepatic Lymphoma *(common)*

Incidence of liver involvement:
in up to 50% (60% by autopsy) in Hodgkin disease; in up to 20% (50% by autopsy) in NHL

Pattern:

(a) diffuse homogeneous infiltration (80%):
- √ ± hepatomegaly
- √ NO alteration in hepatic architecture

(b) focal nodular lymphoma (in 10%):

√ discrete homogeneous nodules ± miliary pattern

(c) combination of diffuse + nodular lymphoma (3%)

√ paraaortic, celiac, mesenteric, periportal nodes typically involved (lymphadenopathy below level of renal veins)

√ splenic lesions (30–40%)

DDx: Opportunistic infection (fungal microabscesses, septic emboli)

LYMPHOMA OF PANCREAS

Type: NHL (most commonly) with both B- and T-cell lineages

FDG/PET: useful for staging and differentiation of primary from secondary pancreatic lymphoma

A. PRIMARY LYMPHOMA

Frequency: < 2% of extranodal lymphoma; 0.5% of pancreatic tumors

Mean age: 55 (range, 35–75) years

Predisposed: immunocompromised (HIV, transplant recipient)

- abdominal pain (83%), weight loss (50%)
- obstructive jaundice (40%), acute pancreatitis (12%)
- palpable mass (58%)
- CLASSIC fever + chills + night sweats (in only 2%)

Location: pancreatic head > entire gland

Morphology:

(a) focal well-circumscribed mass

Location: pancreatic head (80%)

Size: 8 (range, 2–15) cm

√ large unifocal well-circumscribed homogeneous solid mass:

√ hypoattenuating on CT

√ hypointense on T1WI + intermediate SI on T2WI (higher than pancreas + lower than fluid)

√ infrequently with central cystic area

√ faint contrast enhancement

√ mild dilatation of pancreatic duct

DDx: pancreatic adenocarcinoma (with little pancreatic duct dilatation / tail atrophy)

(b) diffuse form (simulating acute pancreatitis)

√ poorly defined enlarged pancreas

√ slightly lower attenuation compared with normal

√ irregular peripancreatic fat infiltration

√ diffusely reduced homogeneous enhancement

√ hypointense on T1WI + T2WI

DDx: acute pancreatitis

√ invasive growth across anatomic boundaries

√ peripancreatic nodal masses:

√ lymphadenopathy below level of renal veins

√ anterior displacement of entire pancreas

√ intact fat planes between lymph nodes and pancreas

√ NO calcifications

√ envelopment of adjacent vessels WITHOUT vascular invasion / obstruction:
√ peripancreatic vessels displaced + stretched
√ uncommon dilatation of pancreatic + bile duct

B. SECONDARY LYMPHOMA (in 30% of NHL)
√ direct extension from peripancreatic lymphadenopathy

DDx: primary lymphoma (anterior displacement of pancreas, intact fat plane between pancreas + adjacent organs)

DDx: pancreatic adenocarcinoma (gross dilatation of main pancreatic duct, no lymph nodes below level of renal vein, vascular invasion common)

LYMPHOMA OF SPLEEN

Frequency: 3rd most common site of abdominal involvement; may be initial manifestation in large cell lymphoma; most common site of abdominal involvement in Hodgkin disease

N.B.: Splenic involvement is considered extranodal in NHL but nodal in Hodgkin disease!

√ diffuse uniform infiltration
√ ill-defined hypoenhancing foci of < 1 cm in diameter become apparent after contrast enhancement in late venous and equilibrium phase
√ nonspecific splenomegaly ← lymphomatous involvement / reactive process
√ splenic hilar adenopathy

Dx: staging laparotomy necessary as ²/₃ of tumor nodules < 1 cm in size

DDx: disseminated fungal infection of candidiasis / aspergillosis (febrile neutropenic patient, nodules of 2–20 mm in diameter, no lymphadenopathy, peripheral rimlike / central nodular enhancement)

MESENCHYMAL HAMARTOMA OF LIVER

= rare developmental benign cystic liver tumor characterized by proliferative extension along portal tracts; 2nd most common benign liver mass in children after infantile hemangioendothelioma

Pathogenesis: balanced translocation at chromosome 19q13.4 similar to undifferentiated (embryonal) sarcoma

Path: well-marginated solitary liver mass with cysts (in 83%) of a few mm up to 14 cm in size containing clear amber fluid / gelatinous material; no capsule; infrequent hemorrhage and necrosis

Histo: disordered arrangement of primitive fluid-filled mesenchyme, bile ducts, hepatic parenchyma; stromal / cystic predominance

Age peak: 15–24 months (range, newborn to 19 years); in 95% by 5 years of age; M÷F = 3÷2

• slow progressive painless abdominal distension
• anorexia. nausea, vomiting, jaundice
• ± respiratory distress and lower extremity edema

Location: right lobe÷left lobe = 3÷1; 20% pedunculated

Mean size: 16 (range, 5–29) cm

√ grossly discernible cysts in 80%

US:

√ multiple rounded cystic areas on an echogenic background:
√ low-level echoes within cysts (= gelatinous contents)
√ some blood flow in solid portions + septa (color Doppler)
√ may appear solidly echogenic in fetus / younger infant ← microcysts create innumerable tissue-fluid interfaces

CT:
√ multiple lucencies of variable size + attenuation (depending on composition of stromal versus cystic elements)
√ hemorrhage (rare and atypical)
√ enhancement of stromal component

MR:
√ varying SI (varying concentrations of protein in cystic predominance type) / hypointense on T1WI (mesenchymal predominance type)
√ marked hyperintensity of cystic locules on T2WI
√ solid portions of fibrosis hypointense on all sequences

NUC:
√ one / more areas of diminished uptake on sulfur colloid scan

Prognosis: 90% long-term survival

Rx: resection

DDx: (1) Hepatoblastoma (marked elevation of AFP, solid tumor with calcifications)
(2) Focal form of infantile hemangioendothelioma (calcifications in 50%, marked hypervascularity)
(3) Undifferentiated (embryonal) sarcoma (older child at 6–10 years of age, hemorrhage + necrosis)

METASTASIS TO GALLBLADDER

Organ of origin: melanoma (60%), renal cell carcinoma (late in course of disease), lymphoma (in AIDS), malignant fibrous histiocytoma, gastric cancer (in Asia)
› in children: embryonal cell sarcoma, rhabdomyosarcoma

◊ 94% of benign lesions are < 1 cm in diameter; 88% of malignant lesions are > 1 cm in diameter!

DDx: adenocarcinoma (usually associated with gallstones, more common in women + older patients); squamous cell carcinoma; carcinosarcoma, small cell carcinoma

METASTASIS TO LIVER

◊ Most common malignant lesion of the liver
◊ Most common metastatic site after regional lymph nodes

Incidence: 18–20 x greater than primary carcinoma; 22% of all liver tumors in patients with a known malignancy (50% in autopsies)

Organ of origin: colon (42%), stomach (23%), pancreas (21%), breast (14%), lung (13%)
√ involvement of liver + spleen typical in leukemia/lymphoma + melanoma
in children: neuroblastoma, Wilms tumor

• hepatomegaly (70%); abnormal liver enzymes (50–75%)

Location: both lobes (77%), right lobe (20%), left lobe (3%)

Number: multiple (50–98%), solitary (2%)
Size: > 33% smaller than 2 cm
NUC:
sensitivity of 80–95% for lesions > 1.5 cm; lesions < 1.5 cm are frequently missed; sensitivity increases with metastatic deposit size, peripheral location, and use of SPECT
NECT:
important for hypervascular tumors (eg, renal cell carcinoma, carcinoid, islet cell tumors), which may be obscured by CECT
CECT (88–90% sensitive; 99% specific):
◊ Sensitivity decreases relative to NECT if scan obtained only during equilibrium phase of contrast administration
√ lesion enhancement during arterial phase ← metastases are supplied by hepatic artery
√ less enhancement during portal venous phase ← metastases have a negligible portal venous supply
√ extracellular space agents accumulate more in tumor tissue ← metastases have a larger interstitial space
Optimal technique: bolus of contrast followed by dynamic incremental scanning
√ circumferential bead- or bandlike enhancement during arterial phase + peripheral washout on delayed images
√ no (35%), peripheral (37%), mixed (20%), central (8%) enhancement
√ complete isodense fill-in on delayed scans in 5% (DDx: hemangioma)
◊ Lesions of ~ 1 cm can usually be detected!
CT-Angiography (most sensitive imaging modality):
Indication: patients with potentially resectable isolated liver metastases / preoperative before partial hepatectomy → additional lesions are detected in 40–55%
(1) CT arteriography = angiographic catheter in hepatic artery → detects lesions by virtue of increased enhancement
(2) CT arterial portography = angiographic catheter in SMA → detects hypodense lesions on a background of increased enhancement of normal surroundings in portal venous phase
CT-delayed iodine scanning:
= CT performed 4–6 hours following administration of 60 mg iodine results in detection of additional lesions in 27%
US (intraoperative with palpation): > 95% sensitive
MR:
√ usually irregular shape and margin
√ usually hypointense on T1WI
√ heterogeneously hyperintense on DWI + T2WI
√ perilesional fat deposition = metastasis from primary pancreatic insulinoma ← effect of insulin inhibiting oxidation of fatty acids + promoting accumulation of tricglycerides in hepatocytes
CEMR:
√ arterial phase:
√ homogeneously hypervascular for metastasis < 2 cm
√ heterogeneous with ring enhancement if > 2 cm
√ thick hypovascular peripheral rim

√ perilesional ring enhancement ← central tumor necrosis
√ irregular peripheral wash-out during venous phase
√ delayed heterogeneous contrast retention

Rx: (1) Resection

Exclusion criteria for metastasectomy:

(a) advanced stage of primary tumor
(b) > 4 metastases
(c) extrahepatic disease
(d) < 30% normal liver tissue / function available after resection

(2) Radiofrequency ablation

Prognosis: 30–40% 5-year survival after resection

Calcified Liver Metastases

Prevalence: 2–3%

1. Mucinous carcinoma of GI tract (colon, rectum, stomach)
2. Endocrine pancreatic carcinoma
3. Leiomyosarcoma, osteosarcoma
4. Malignant melanoma

Intravenous Contrast Strategies for Liver Lesions

Uniphasic PVP	*Biphasic PP + PVP*	*Triphasic NE + AP + PVP*
Colorectal cancer	Pancreatic cancer	Carcinoid
Gastric cancer		Neuroendocrine
Ovarian cancer		Islet cell tumor
Cervical cancer		Renal cell cancer
Lymphoma		GIST
Multiple myeloma		Thyroid cancer
		? Breast / Melanoma

PVP = portal venous phase; PP = parenchymal phase
AP = arterial phase; NE = nonenhanced

5. Papillary serous ovarian cystadenocarcinoma
6. Lymphoma
7. Pleural mesothelioma
8. Neuroblastoma
9. Breast cancer
10. Medullary carcinoma of the thyroid
11. Renal cell carcinoma
12. Lung carcinoma
13. Testicular carcinoma

mnemonic for mucinous adenocarcinoma: COBS

Colon carcinoma
Ovarian carcinoma
Breast carcinoma

Stomach carcinoma

Hypervascular Liver Metastases

= increased enhancement relative to normal liver during arterial phase + washout on delayed images

1. Primary neuroendocrine tumor:
   (a) Pancreatic endocrine tumor
   (b) Neuroendocrine carcinoma = carcinoid (14%)
   (c) Pheochromocytoma
2. Melanoma (11%)
3. Renal cell carcinoma (8%)
4. Breast carcinoma (some) (2%)
5. Thyroid carcinoma
6. Choriocarcinoma
7. Sarcomas
8. Ovarian cystadenocarcinoma

in ( ) number of lesions seen only during arterial phase

mnemonic: CHIMP

Carcinoid
Hypernephroma
Islet cell carcinoma
Melanoma
Pheochromocytoma

CT:

◊ Triphasic scan recommended!

Detection rate: 87% for NECT, 78% for hepatic arterial phase, 77% for portal venous phase

MR:

√ moderately hypointense on T1WI unless hemorrhagic
√ markedly hyperintense on T2WI (= cystic, necrotic)
√ hyperintense on DWI

CEMR:

√ uniform / peripheral-rim / heterogeneous enhancement
√ "peripheral washout" sign = decrease of contrast material preferentially in periphery of mass while center remains hyperintense on delayed image (? related to vessel distribution with central necrosis / fibrosis and peripherally viable tumor), same as in HCC
√ hypointense / target appearance on 1-hour delayed image after Gd-BenzylOxyPropionicTetraAcetate

Hypovascular Liver Metastases

= decreased enhancement relative to normal liver

1. Stomach
2. Colon / rectum
3. Head & neck

4. Pancreas
5. Lung
6. Breast
7. Transitional cell carcinoma
8. Prostate

√ low SI on T1WI images + iso- to hyperintense on T2WI
√ delayed enhancement during portal venous phase / (occasionally) early ring enhancement
◊ Most conspicuous on portal venous phase images!

Hemorrhagic Liver Metastases

mnemonic: **CT BeComes MR**

Colon carcinoma
Thyroid carcinoma
Breast carcinoma
Choriocarcinoma
Melanoma

Response Evaluation Criteria in Solid Tumors (RECIST) version 1.1				
Lesion Type	*Response Type*			
	Regression: complete	**partial**	**stable**	**Progression**
MEASURABLE TARGET LESIONS				
= longest diameter of ≥ 10 mm (CT slice thickness of ≤ 5 mm) / ≥ 20 mm (nonhelical CT slice thickness of > 10 mm) / ≥ 20 mm (CXR) selected on the basis of size and suitability for accurate repeated measurements (= 2 target lesions per organ)				
Measure SUM of longest diameters of target lesions (≤ 2 per organ + total of ≤ 5)	disappearance of all	relative ⇓ of ≥ 30% ⇓ to < 5 mm reported as 5 mm	no change	≥ 1 new lesions absolute ⇑ of SUM ≥ 5 mm relative ⇑ of SUM ≥ 20% new FDG PET lesion
N.B.: Fragmentation of lesion treated as separate lesions Coalescence of lesions treated as one lesion				
add short-axis measurement of ***lymph node*** if ≥ 15 mm to SUM of target lesions	short-axis ⇓ to < 10 mm			
NONMEASURABLE / NONTARGET LESIONS				
= small lesions with longest diameter of < 10 mm, skeletal metastasis without soft-tissue component, ascites, pleural effusion, lymphangitic spread, leptomeningeal disease, inflammatory breast disease, cystic / necrotic lesion, lesion in irradiated area				
Note presence / absence of each nontarget lesion at baseline and follow-up	disappearance of all nontarget lesions		persistence of ≥ 1 nontarget lesions	appearance of ≥ 1 new lesion progression of existing nontarget lesions
Lymph node with short axis ≥ 10 and < 15 mm	short-axis ⇓ to < 10 mm (= normal node)			

Renal cell carcinoma
and: lung, testicle

√ hyperintense on T1WI

Echogenic Liver Metastases

Prevalence: 25%

1. Colonic carcinoma (mucinous adenocarcinoma) 54%
2. Hepatoma 25%
3. Treated breast carcinoma 21%

Liver Metastases of Mixed Echogenicity

Prevalence: 37.5%

1. Breast cancer 31%
2. Rectal cancer 20%
3. Lung cancer 17%
4. Stomach cancer 14%
5. Anaplastic cancer 11%
6. Cervical cancer 5%
7. Carcinoid 1%

Cystic Liver Metastases

Pathophysiology of cystic metastases:

(a) necrosis of hypervascular metastases ← rapid growth beyond capacity of vascular supply: neuroendocrine tumor, melanoma, GIST
(b) abundant mucin production by mucinous adenocarcinoma: colorectal / ovarian carcinoma
(c) systemic / locoregional treatment

1. Mucinous ovarian carcinoma
2. Colonic carcinoma
3. Sarcoma
4. Melanoma
5. Lung carcinoma
6. Carcinoid tumor

mnemonic: LC GOES

Leiomyosarcoma (and other sarcomas)
Choriocarcinoma
Gastric carcinoma
Ovarian carcinoma
Endometrial carcinoma
Small cell carcinoma

Echopenic Liver Metastases

Prevalence: 37.5%

1. Lymphoma 44%
2. Pancreas 36%
3. Cervical cancer 20%
4. Lung (adenocarcinoma)
5. Nasopharyngeal cancer

T1-Hyperintense Metastasis

1. Melanoma
2. Mucinous carcinoma
3. Carcinoid
4. Hemorrhagic metastasis

Markedly T2-Hyperintense Metastasis

1. Renal cell carcinoma
2. Islet cell tumor
3. Pheochromocytoma
4. Leiomyosarcoma
5. Necrotic metastasis

METASTASIS TO PANCREAS

Frequency: 2–11% (autopsy); 2–5% of all malignancies

Organ of origin: renal cell carcinoma (30%), bronchogenic carcinoma (23%), breast carcinoma (12%), soft-tissue sarcoma + Kaposi sarcoma (8%), colonic carcinoma (6%), melanoma (6%), secondary lymphoma, ovarian cancer, HCC

Time interval since diagnosis of primary:

< 3 years for most primaries; 6–12 years for RCC

• asymptomatic (50–83%) / nonspecific clinical symptoms

Morphology:

(a) well-marginated solitary mass (50–78%)
(b) multiple ovoid masses (5–17%) with discrete smooth margins
(c) diffuse pancreatic enlargement (5–44%)

US:

√ hypo- / hyperechoic mass

NECT:

√ hypo- / isoattenuating mass

CECT (closely resembling enhancement pattern of primary):

√ heterogeneously (60%) / homogeneously (17%) hyperattenuating relative to pancreas
√ hypoattenuating relative to pancreas (20%)
√ isoattenuating relative to pancreas (5%)
√ peripheral enhancement of lesion > 1.5 cm (70%)
√ homogeneous enhancement of small lesion

MR:

√ hypointense on T1WI + hyperintense on T2WI

Concomitant intraabdominal metastases to:

liver (36%), lymph nodes (30%), adrenal glands (30%)

DDx: ductal pancreatic adenocarcinoma (uniformly hypo- / nonenhancing mass, encasement of vessels); neuroendocrine tumor

MILK OF CALCIUM BILE

= LIMY BILE = CALCIUM SOAP

= precipitation of particulate material with high concentration of calcium carbonate, calcium phosphate, calcium bilirubinate

Associated with: chronic cholecystitis + gallstone obstruction of cystic duct

√ diffuse opacification of GB lumen with dependent layering
√ usually functionless GB on oral cholecystogram

US:

√ intermediate features between sludge + gallstones

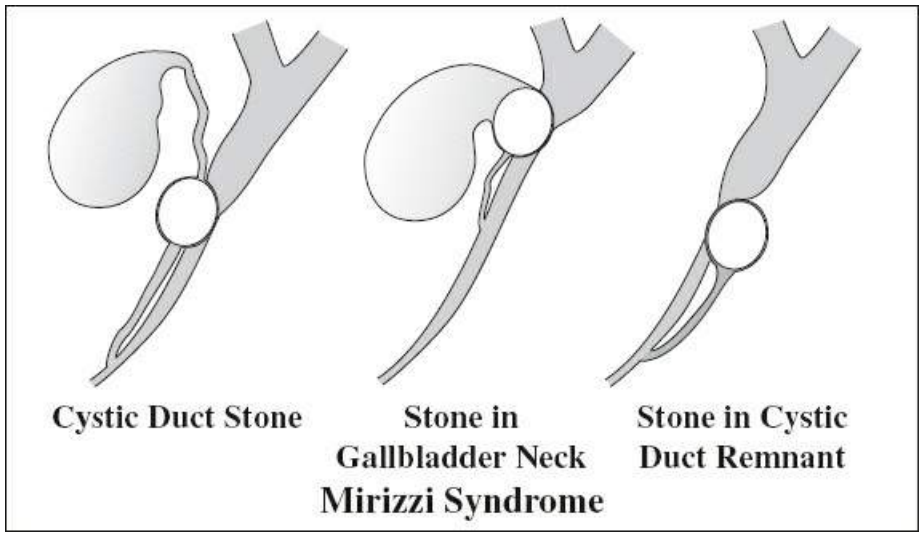
MIRIZZI SYNDROME

= extrinsic right-sided compression of common hepatic duct by large gallstone impacted in Hartmann pouch (at junction of cystic duct and gallbladder neck) / cystic duct remnant; accompanied by chronic inflammatory reaction

Predisposition: long cystic duct coursing parallel to CHD; low insertion of cystic duct into CBD

• jaundice, fever, right upper quadrant pain

Classification (guiding surgical management):



Type 1: simple obstruction of CHD by extrinsic compression WITHOUT fistulization

Type 2: cholecystocholedochal fistula + erosion of CBD wall affecting < ⅓ of bile duct circumference

Type 3 affecting ⅓ to ⅔ of bile duct circumference

Type 4 affecting > ⅔ of bile duct circumference

√ normal CBD

√ TRIAD:

(1) Gallstone impacted in GB neck / cystic duct

(2) Dilatation of intrahepatic and common hepatic ducts

(3) Smooth curved extrinsic narrowing of CHD

Cholangiography:

√ partial obstruction of CHD ← external compression on lateral side of duct / eroding stone

CT:

√ gallstone not always visualized

MR:

√ cholelithiasis with stone in cystic duct

√ focal stricture of CHD

√ dilatation of intrahepatic bile ducts + proximal CHD

√ normal caliber of distal CBD

Cx: cholecystobiliary fistula

Rx: open surgery

DDx: lymphadenopathy, neoplasm of GB / CHD

MUCINOUS CYSTIC NEOPLASM OF PANCREAS

= MACROCYSTIC ADENOMA OF PANCREAS = MUCINOUS CYSTADENOMA

= thick-walled uni- / multilocular low-grade malignant tumor composed of large mucin-containing cystic spaces

Frequency: 10% of pancreatic cystic neoplasm; 1% of all pancreatic neoplasms

Mean age: 47 (range, 20–95) years; in 50% between 40–60 years; M÷F = 1÷9

Path: large smooth round / lobulated multiloculated cystic mass encapsulated by a layer of fibrous connective tissue

Histo: cysts lined by tall columnar, mucin-producing cells subtended by a densely cellular mesenchymal stroma (reminiscent of ovarian stroma = distinguishing feature), often in papillary arrangement; lack of cellular glycogen; similar to biliary and ovarian mucinous tumors

(a) mucinous cystadenoma

(b) mucinous cystadenocarcinoma = stratified papillary epithelium

◊ All mucinous cystic neoplasms should be considered low-grade malignant neoplasms!

• asymptomatic; abdominal pain, anorexia

Location: often in pancreatic tail (90%) / body, head (rare)

Mean size of mass: 10–12 (range, 2–36) cm in diameter

Size of cysts: multi- / unilocular large cysts > 2 cm

Number of cysts: usually < 6 cysts

A pancreatic tumor with cysts of > 2 cm in diameter is a mucinous cystic neoplasm in 93–95%!

√ well-demarcated thick-walled mass with < 2 mm thin septa

√ solid papillary excrescences protrude into the interior of tumor (= sign of malignancy)

√ amorphous discontinuous peripheral mural calcifications (10–15%)

√ hypovascular mass with sparse neovascularity

√ ± vascular encasement and splenic vein occlusion

√ great propensity for invasion of adjacent organs

US:

√ cysts may contain low-level echoes

CT:

√ fine internal septa + small intramural nodules may not be visible ± contrast enhancement → thin-section CT

√ cysts with attenuation values of water; may have different levels of attenuation within different cystic cavities

√ enhancement of cyst walls

MR:

√ unilocular / mildly septated typically mucin-filled cystic lesion of homogeneous T1 hypointensity and T2 hyperintensity (= MR characteristics of simple fluid)

√ mildly thick enhancing septa (frequent)

√ thick delayed-enhancing fibrotic wall

√ pertinent negatives:
√ NO communication with pancreatic duct
√ NO enhancing soft-tissue components

Angio:
√ predominantly avascular mass
√ cyst wall + solid components may demonstrate small areas of vascular blush + neovascularity
√ displacement of surrounding arteries + veins by cysts

Metastases:
√ round thick-walled cystic lesions in liver

Prognosis: invariably transformation into cystadenocarcinoma; 17–63% 5-year survival rate

Dx: biopsy with adequate sampling of cyst lining mandatory to exclude foci of dysplasia / carcinoma in situ

Rx: complete surgical excision (5-year survival rate of 74–90%)

DDx:

(1) Pseudocyst (most common pancreatic cyst): inflammatory changes in peripancreatic fat, pancreatic calcifications, temporal evolution, history of alcoholism, elevated levels of amylase

(2) **Mucinous non-neoplastic cyst**
= mucinous differentiation of epithelial lining without cellular atypia + lack of surrounding ovarian stroma
• no proven sex predilection
√ incidental small (rarely large) unilocular cyst ± thick wall indistinguishable from mucinous cystadenomas
√ NO ductal communication / papillary projections

(3) Lymphangioma / hemangioma

(4) Variants of ductal adenocarcinoma
(a) mucinous colloid adenocarcinoma / ductectatic mucinous tumor of pancreas = mucin-hypersecreting carcinoma
(b) intraductal papillary mucinous neoplasm (IPMN) (communication with pancreatic duct)
(c) adenosquamous carcinoma: squamous component predisposes to necrosis + cystic degeneration
(d) anaplastic adenocarcinoma: lymphadenopathy + metastases at time of presentation

(5) Solid and cystic papillary epithelioid neoplasm: hemorrhagic cystic changes in 20%

(6) Cystic pancreatic endocrine tumor: hypervascular component

(7) Cystic metastases: history of malignant disease

(8) Atypical serous cystadenoma: smaller tumor with greater number of smaller cysts

(9) Sarcoma

(10) Infection: amebiasis, Echinococcus multilocularis

MUCINOUS CYSTADENOCARCINOMA OF PANCREAS

Etiology: adenoma-carcinoma sequence

Histo: invasive elements surrounded by ovarian-type stroma

Age: older than patients with mucinous cystadenoma
MR:
√ > 4-cm large complex cystic pancreatic lesion
√ intracystic enhancing soft tissue
√ soft-tissue nodularity
DDx: Solid pseudopapillary tumor of pancreas
Rx: any enhancing soft tissue within a cystic pancreatic neoplasm is an indication for resection.
Rx: any enhancing soft tissue within a cystic pancreatic neoplasm is an indication for resection.

MULTIPLE BILE DUCT HAMARTOMAS

= BILIARY MICROHAMARTOMAS = VON MEYENBURG COMPLEX
Prevalence: 0.7% at autopsy, 2.8% at microscopy
Etiology: failure of involution of embryonic interlobular bile ducts = part of fibropolycystic liver disease spectrum
Path: communication with biliary system usually obliterated
Histo: cluster of proliferated bile ducts lined by single layer of cuboidal cells embedded in fibrocollagenous tissue with single ramified lumen
May be associated with: fibropolycystic liver disease
Size: 0.1–15 mm
Location: random / scattered; periportal; multiple / solitary
• asymptomatic = incidental discovery
√ nonspecific imaging appearance of small well-defined lesions
√ variable enhancement pattern: none / rim / slow homogeneous
CT:
√ multiple scattered round / oval / irregular hypodense lesions (44% occult on CT)
√ rim of little peripheral / no enhancement
US:
√ multiple small cysts / echogenic areas (if size not resolved)
√ ± comet-tail (ring-down) artifact
MR:
√ small well-defined hypointense lesions on T1WI
√ iso- / slightly hyperintense on T2WI
√ no internal enhancement ± thin rim enhancement of surrounding liver parenchyma on immediate / delayed phase
Angio:
√ multiple areas of abnormal vascularity in form of small grapelike clusters persisting into venous phase
DDx:
1. Metastatic liver disease (more variable in size and attenuation / signal intensity)
2. Simple hepatic cysts (not as numerous or uniformly small)
3. Autosomal dominant polycystic disease (cysts usually larger and more numerous)
4. Microabscesses
5. Granulomata

MULTIPLE ENDOCRINE NEOPLASIA

= MEN = MULTIPLE ENDOCRINE ADENOMAS (MEA)

= familial autosomal dominant adenomatous hyperplasia characterized by neoplasia of 2 or more endocrine organs

Theory: cells of involved principal organs originate from neural crest and produce polypeptide hormones in cytoplasmic granules, which allow amine precursor uptake and decarboxylation = APUD cells

reminder:

MEN 1 = Wermer syndrome PiPaPanc

MEN 2 = Sipple syndrome (type 2A) PhePaM

Types of Multiple Endocrine Neoplasia			
MEN	*Type 1*	*Type 2*	*Type 3*
Pituitary adenoma	+		
Parathyroid adenoma	+	+	
Medullary thyroid carcinoma		+	+
Pancreatic island cell tumor	+		
Pheochromocytoma		+	+
Ganglioneuromatosis			+

MEN 3 = Mucosal neuroma syndrome (type 2B)4 PheMG

MEN 1 Syndrome

= WERMER SYNDROME

[Paul Wermer (1898-1975), internist at Columbia University, NY]

= autosomal dominant syndrome with 95% penetrance

Prevalence: 1÷5,000 to 1÷50,000

Genetics: autosomal dominant MEN1 gene defect encoding protein menin located on chromosome 11q13 = suppressor of cell proliferation

◊ MEN1 mutation present in 21% of sporadic PETs

Organ involvement (PiPaPanc): syn- / metachronous

» in 40% combined involvement of parathyroid gland + pituitary gland + pancreas

1. Parathyroid hyperplasia (97%): multiglandular / (occasionally) adenoma
   - primary HPT (in 95%): usually presenting feature
2. Pancreatic endocrine tumor (30–80%):

   Path: multiple < 5 mm microadenomas producing clinically insignificant active peptides ± few macroadenomas > 5 mm; usually nonmalignant

   ◊ Primary cause of morbidity + mortality!

   (a) gastrinoma (in 50–60%)

   Location: duodenum > pancreas

   √ multiple duodenal microgastrinomas (< 5 mm) account for > 50% of gastrinomas

   (b) insulinoma (in 10–30%)

   Age: more commonly < 40 years

   Location: body + tail of pancreas

◊ coexistence with gastrinomas in 10%

(c) VIPoma

3. Anterior pituitary gland tumor (20–65%)
   (a) nonfunctioning
   (b) prolactin (60%), growth hormone (< 25%), adrenocorticotropic hormone (5%), TSH
   • presenting feature of the syndrome in 10%
4. Thyroid neoplasm
5. Adrenocortical hyperplasia / adenomas (up to 33–40%)
   • rarely functional
6. Pheochromocytoma
7. Carcinoid (2–5%)
   Location: thymus, bronchus, stomach (30-fold increased incidence), duodenum
   ◊ Up to 4% of patients with carcinoid have MEN
7. Lipoma

Mean age: 3rd–4th decade; M÷F = 1÷1

• usually asymptomatic
• multiple facial angiofibromas (in 85–90% of MEN 1 patients)

May be associated with:
thyroid tumor (20%), thymoma, buccal mucosal tumor, colonic polyposis, Ménétrier disease

Screening population: < 35-year old patient with HPT, ≥ 2 endocrine organ tumors, 1st-degree relative of MEN 1 patient

Imaging surveillance:
renal US + abdominal radiograph for abdominal calculi; abdominal MR for islet cell + adrenal tumors + liver mets; pituitary MR for adenoma (every 3 years)

√ typically multiple microadenomas + nonfunctioning pancreatic endocrine tumors throughout pancreas
√ also often functioning tumor, most commonly gastrinoma (in 60%) / insulinoma (in 30%)

Prognosis: premature death from neoplasia (likely due to metachronous multiplicity of pancreatic tumors)

MEN 2 Syndrome

= SIPPLE DISEASE = MEN TYPE 2A
[John H. Sipple (1930-), internist at SUNY in Syracuse]
= autosomal dominant cancer syndrome

Cause: genetic defect on chromosome 10

Organ involvement (PaMPhe):

1. Parathyroid hyperplasia / neoplasia in multiple glands
   • ± hyperparathyroidism (later onset than in MEN 1)
2. Medullary carcinoma of thyroid (almost 100%)
   • serum calcitonin commonly elevated
3. Pheochromocytoma (50%): bilateral in 50%; malignant in 3% diagnosed before (in 10%) / after detection (in 17%) of medullary thyroid carcinoma

May be associated with: carcinoid tumors, Cushing disease
Screening population: all patients with medullary thyroid cancer / pheochromocytoma, 1st-degree relative of MEN 2 patient
Imaging surveillance: abdominal MR for pheochromocytoma (every 3 years); MIBG scintigraphy (optional)

MEN 3 Syndrome

= MUCOSAL NEUROMA SYNDROME = MEN TYPE 2B
Cause: genetic defect on chromosome 10
Organ involvement (MPheG):
1. Medullary carcinoma of thyroid
2. Pheochromocytoma
3. Intestinal ganglioneuromatosis = mucosal neuroma = oral + intestinal neuroganglioneuromatosis
   ◊ Mucosal neuromas are PATHOGNOMONIC
   ◊ Usually precede the appearance of thyroid carcinoma + pheochromocytoma!

- long slender extremities (marfanoid appearance)
- thickened lips ← submucosal nodules
- nodular deformity of tongue (mucosal neuromas of tongue often initially diagnosed by dentists)
- corneal limbus thickening; prognathism
- constipation alternating with diarrhea

@ GI tract
√ thickened / plaquelike colonic wall
√ chronic megacolon = dilated colon with abnormal haustral markings
√ alternating areas of colonic spasm + dilatation (rarely associated with Hirschsprüng disease)
√ multiple submucosal neuromas throughout small bowel, may act as lead point for intussusception

NESIDIOBLASTOSIS

= PERSISTENT HYPERINSULINEMIC HYPOGLYCEMIA OF INFANCY = CONGENITAL HYPERINSULINISM = ADENOMATOUS ISLET CELL HYPERPLASIA = MICROADENOMATOSIS
= tumorlike disorder characterized by proliferation of hyperfunctioning β cells distributed diffusely throughout pancreas or forming a focal mass
Prevalence: 1÷30,000 to 1÷50,000, higher in Ashkenazi Jewish and Saudi Arabian populations
Age: first few hours of life to > 1 year
Path:
(a) diffuse adenomatosis (66–75%)
= nontumoral widespread increase in islet cells
Cause: genetic abnormality
(b) focal adenomatous hyperplasia = nesidioblastoma

- elevated serum insulin ← unregulated release of insulin
- severe persistent hypoglycemia (often resistent to diazoxide / somatostatin analog therapy)

DDx of transient causes of hyperinsulinemic hypoglycemia:
maternal diabetes, Beckwith-Wiedemann syndrome
√ no imaging abnormalities
√ enlarged hyperechoic pancreas

NODULAR REGENERATIVE HYPERPLASIA

= uncommon benign liver disease defined as diffuse nodularity produced by multiple regenerating nodules surrounded by atrophic liver in the absence of fibrosis
◊ Difficult to diagnose at imaging ← variable nonspecific findings + similarity to other hepatocellular lesions!
Associated with: Budd-Chiari syndrome, collagen vascular disease, myelo- and lymphoproliferative syndrome, autoimmune disease, immunosuppressive + antineoplastic drugs
Cause: pulmonary hypertension, right-sided heart failure, passive hepatic congestion, progressive hepatic venous occlusion
Pathogenesis: increased resistance to sinusoidal blood flow → portal hypertension → decrease in portal venous inflow → prolonged exposure to blood-borne hepatopoietins → stimulation of nodular hepatocellular regeneration
Path: lesions resemble FNH containing Kupffer cells surrounded by acinar atrophy without fibrosis
• asymptomatic (50%)
• symptoms of portal hypertension (50%): esophagogastric varices, ascites, splenomegaly
Size of nodules: 1–40 mm
US:
√ well-circumscribed homogeneous hypo- / hyperechoic nodule, if visible at all
CT:
√ hypo- (typically) or isoattenuating nodules
√ typically no enhancement / diffuse mild enhancement
√ heterogeneous hepatic parenchyma
MR:
√ hypo- to iso- to hyperintense on T1WI
√ iso- to minimally hypointense on T2WI (= difficult to visualize!)
√ ± ↓ SI on fat-suppressed T1WI ← intracellular fat
CEMR:
(a) arterial phase:
√ decreased enhancement relative to pancreas
√ multiple small similar-sized enhancing nodules
(b) portal venous + equilibrium phase:
√ fading to isointensity
DDx: HCC rapidly washes out to hypointensity
(b) delayed phase:
√ progressive enhancement
√ hyper- / isointense on 1–hour delayed images after gadobenate dimeglumine = Gd BenzylOxyPropionic-TetraAcetate (Gd-BOPTA = MultiHance®) similar to FNH

PANCREAS DIVISUM

= most common congenital anomaly of pancreatic ductal system

Cause: failure of fusion of ventral + dorsal anlage at 7th week of fetal life

› ventral duct (of Wirsüng) drains ventral anlage only into major papilla corresponding to head and uncinate process

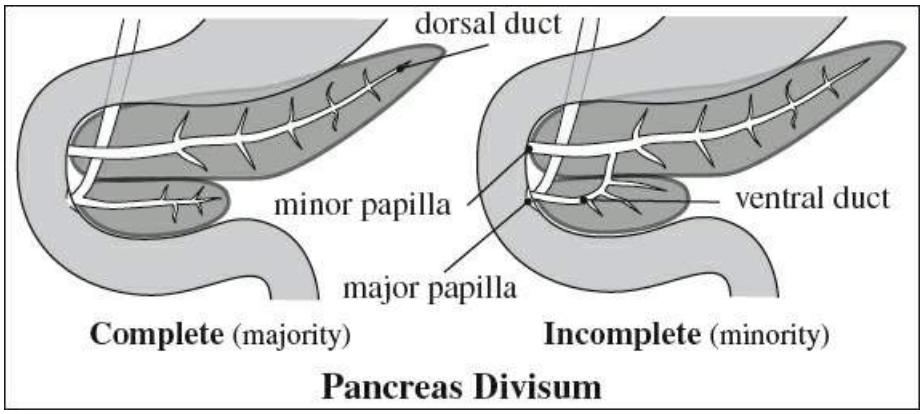
› majority of gland empties into minor papilla via <u>dominant dorsal duct</u> (of Santorini) ± focal dilatation of terminal duct segment (= **santorinicele**) ← relative obstruction

Variations:

(a) no communication between ventral + dorsal duct

(b) incomplete divisum = filamentous communication between ducts (dominant dorsal duct syndrome)

(c) complete absence of ventral duct



Prevalence: 4–14% in autopsy series; 3–8% in ERCP series; 5–10% on MRCPs of normal population; 12–50% in patients with idiopathic recurrent pancreatitis during childhood; in 15–20% of unexplained acute pancreatitis

May be associated with: stenosis of main duct at minor papilla

Hypothesis: relative / actual functional stenosis of minor papilla → obstruction to pancreatic exocrine secretory flow → predisposes to nonalcoholic recurrent pancreatitis in dorsal segment

Age: young / middle-aged adult; M<F

Clinically:

pancreas divisum should be suspected in young / middle-aged adult who presents with recurrent acute pancreatitis / relapsing chronic pancreatitis without any other obvious cause (like gallstones / alcohol consumption)

- usually asymptomatic
- chronic abdominal pain and acute idiopathic / chronic relapsing pancreatitis (in only 5–10% = clinical relevance of pancreas divisum continues to be debated!)

√ "dominant dorsal duct" sign = larger dorsal duct relative to smaller ventral duct

√ continuity of large dorsal pancreatic duct with duct of Santorini draining through minor (accessory) papilla (located 2 cm superior to major papilla)

√ small ventral pancreatic duct (of Wirsüng) drains a portion of pancreatic head including the uncinate process through major papilla after joining with CBD

US:
√ bulky hypoechoic pancreas + peripancreatic inflammation / pseudocyst formation
Endoscopic US (95% sensitive, 97% specific, 99% NPV):
√ absence of "stack sign" (= visualization of bile duct and pancreatic duct running parallel through pancreatic head)
ERCP (Retrograde Endoscopic Pancreatography): DIAGNOSTIC
√ contrast injection into major papilla shows CBD + short narrow ventral pancreatic duct with early arborization and at times highly atretic
√ contrast injection into minor papilla fills dominant dorsal pancreatic duct of larger caliber
√ no communication between ventral + dorsal ducts
Cx: ERCP-induced pancreatitis (5% risk)
CT (90% sensitive, 98% specific, 98% NPV):
√ oblique fat cleft between ventral + dorsal pancreas (25%)
√ failure to see union of dorsal + ventral pancreatic ducts (rare)
MRCP (with secretin stimulation 73–100% sensitive, 97–100% specific):
√ noninvasive multiplanar visualization of pancreatic duct:
√ visualization of main pancreatic (dorsal) duct coursing anterior to CBD before draining into duodenum
√ usually prominent dorsal duct with depiction of relative functional duct obstruction
√ findings of acute pancreatitis: bulky pancreas, pancreatic necrosis, peripancreatic inflammation, pseudocysts
√ findings of chronic pancreatitis: significant atrophy of ventral duct and dilatation of dorsal duct
Dx: by ERCP
Rx: surgical / endoscopic minor papillotomy / sphincterotomy; insertion of stent into minor papilla

PANCREATIC ACINAR CELL CARCINOMA

= rare neoplasm of exocrine origin
Frequency: 1–2% of pancreatic exocrine tumors
Mean age: 62 (range, 40–81) years; M÷F = 86÷14; 87% Caucasian; more common than ductal cell adenocarcinoma in pediatric age group
Path: similar to pancreatoblastoma (= embryonic counterpart)
• biliary obstruction distinctly uncommon
• increased serum lipase ± amylase
• **lipase hypersecretion syndrome** (paraneoplastic syndrome):
= disseminated subcutaneous + intraosseous fat necrosis (usually distal to knees / elbows)
Prevalence: 4–16% of adult patients
Cause: systemic release of tumor-elaborated lipase
• peripheral polyarthropathy; bone infarcts
• painful subcutaneous nodules of fat necrosis resembling erythema nodosum
Location: anywhere in pancreas; frequently exophytic
Size: 10 (range, 2–30) cm
√ soft lobulated well-defined heterogeneous mass

√ partial / complete thin enhancing capsule
√ tumor necrosis usually present
√ punctate / chunky peripheral / central tumor calcifications (33–50%)
√ enhancement less than normal pancreas (greater than ductal adenocarcinomas + less than islet cell tumors)
√ moderately vascular tumor + neovascularity + arterial and venous encasement

Prognosis: median survival of 7–9 months; 57% (26%) [6%] 1-year (3-year) [5-year] survival, slightly better than for ductal adenocarcinoma

DDx: (1) pancreatic adenocarcinoma (small, irregular, locally invasive, without capsule, biliary obstruction if located in head of pancreas)
(2) Nonfunctioning islet-cell tumor
(3) Microcystic cystadenoma
(4) Solid-pseudopapillary tumor
(5) Oncocytic tumor of pancreas
(6) Pancreatoblastoma (in children < 10 years)

PANCREATIC DUCTAL ADENOCARCINOMA

= DUCT CELL ADENOCARCINOMA = PANCREATIC ADENOCARCINOMA

◊ Duct cells comprise only 4% of pancreatic tissue but 85–95% of malignant tumors of pancreas!

Incidence: 12÷100,000 / year (in USA 43,920 new diagnoses in 2012 and 36,800 deaths = 4th leading cause of cancer deaths + 2nd most common cause (after colorectal cancer) of GI cancer–related deaths

Cause: alcohol abuse (4%), diabetes (2 x more frequent than in general population, particularly in females), cigarette smoking (risk factor 2 x)

Genetic risk: hereditary pancreatitis (in 40%), hereditary pancreatic cancer syndrome, hereditary nonpolyposis colon carcinoma, Peutz-Jeghers syndrome, familial atypical multiple mole melanoma, BRCA2

Path: scirrhous infiltrative adenocarcinoma with a dense cellularity + sparse vascularity

Peak age: 7th (range, 4th–8th) decade; M÷F = 2÷1; extremely rare in children

Stage: I = confined to pancreas
II = + regional lymph node metastases
III = + distant spread
◊ At presentation:
› 65% of patients have advanced local disease / distant metastases
› 21% of patients have localized disease with spread to regional lymph nodes
› 14% of patients have tumor confined to pancreas

Growth: aggressive early infiltrative → obstruction of pancreatic duct / common bile duct → invasion of adjacent vessels

Extension:
(a) local extension beyond margins of organ (68%): posteriorly (96%), anteriorly (30%), into porta hepatis (15%), into splenic hilum (13%)
(b) invasion of adjacent organs (42%):
duodenum > stomach > left adrenal gland > spleen > root of small bowel mesentery

(c) local lymph node spread:
pancreaticosplenic nodes accompanying splenic artery, pancreaticoduodenal nodes, superior mesenteric preaortic nodes

Metastases: liver (30–36%), regional lymph nodes > 2 cm (15–28%), ascites from peritoneal carcinomatosis (7–10%), lung (pulmonary nodules / lymphangitic), pleura, bone

- weight loss, anorexia, fatigue, steatorrhea, hyperamylasemia
- pain in hypochondrium radiating to back
- obstructive jaundice (75%):
  - ◊ Most frequent cause of malignant biliary obstruction!
  - painless jaundice (25%)
- acute onset diabetes (25–50%)
- spontaneous vein thrombosis (Trousseau syndrome)

Location: pancreatic head / neck / uncinate process (60–70%); pancreatic body (10–20%); pancreatic tail (5–10%); diffuse pancreatic involvement (5%)

Average size: 2–10 cm (in 60% between 4 and 6 cm)
in pancreatic head: 2.5–3 cm
in pancreatic body + tail: 5–7 cm

√ poorly vascularized predominantly solid soft-tissue lesion
√ delayed enhancement ← contrast material seeps gradually into tumor interstitium
√ cystlike features (8%) ← cystic degeneration, retention cysts, attached pseudocysts

Barium:

UGI:
- √ "antral pad" sign = extrinsic indentation of posteroinferior margin of antrum
- √ "Frostberg inverted-3" sign = inverted 3 contour to medial portion of the duodenal sweep
- √ spiculated duodenal wall + traction + fixation (= neoplastic infiltration of duodenal mucosa / desmoplastic response)
- √ irregular / smooth nodular mass with ampullary cancer
- √ diffuse tethering throughout peritoneal cavity ← intraperitoneal seeding

BE:
- √ localized haustral padding / flattening / narrowing with serrated contour at inferior aspect of transverse colon / splenic flexure

CT (90% accurate for tumor detection, 89–100% PPV for unresectability, 45–79% NPV for resectability):
- √ hypoattenuating lesion best depicted during arterial phase (in 10% nonvisualized isoattenuating tumor)
- √ pancreatic mass (95%) / diffuse enlargement (4%) / normal scan (1%)
- √ mass with central zone of diminished attenuation (75–83%)
- √ cystic-necrotic degeneration (8%)
- √ postobstructive pseudocyst (11%)
- √ calcifications (2%)
- √ <u>indirect signs</u>:
  - √ atrophy of pancreatic body + tail (20%)
  - √ convex deformity of pancreatic contour

√ duct dilatation (58%):
√ 75% biductal with pancreatic + bile duct obstruction = "double-duct" sign of mass in head of pancreas
√ 10% isolated to one duct:
√ dilated pancreatic duct (67%)
√ dilated bile ducts (38%)
√ signs of invasion:
√ obliteration of peripancreatic fat (50%) = pancreas lacks a capsule
√ thickening of Gerota fascia (5%)
√ local tumor extension posteriorly into splenic hilum and porta hepatis (68%)
√ contiguous organ invasion (of duodenum, stomach, mesenteric root) in 42%
√ hepatic metastases (75% sensitive)
CECT (arterial + portal phases):
√ nondepicted isoattenuating pancreatic primary and metastasis (in 10%)
√ portal phase imaging (optimal) for detecting metastatic disease to liver and for assessing peripancreatic veins
√ vascular invasion:
√ thickening of celiac axis / SMA ← invasion of perivascular lymphatics (in 60%)
√ dilated collateral veins (12%)
√ high probability of unresectability if circumferential contiguity of tumor to vessel > 50% (84% sensitive, 98% specific)
√ deformity / thrombosis of vessel = "teardrop" sign of SMV on axial image
US:
√ hypoechoic pancreatic mass
√ focal / diffuse (10%) enlargement of pancreas
√ contour deformity of gland; rounding of uncinate process
√ dilatation of pancreatic ± biliary duct
Endoscopic US:
√ may detect tumors of 2–3 mm in diameter
√ suitable for biopsy of suspect lesions
MR (81% sensitive):
√ hypointense tumor on fat-suppressed T1WI ← scirrhous fibrotic nature
√ iso- to minimally hypointense tumor on T2WI
√ abnormally low SI of pancreatic tail + body on T1WI reducing the contrast relative to focal cancer ← atrophy / secondary chronic pancreatitis
√ complex cystic areas within / adjacent to primary ← adjacent pseudocysts, internal tumor necrosis, or side-branch ductal obstruction
CEMR:
(superior to CT in detecting small tumors + metastases)
√ tumor hypointense compared to gland
√ thin peritumoral rim of greater enhancement
MRCP:
Indication: non–contour-deforming pancreatic mass suspected on CT; small mass of < 2 cm;

hepatic, peritoneal, omental metastases

√ "double duct" sign = abrupt termination of CBD + main pancreatic duct by mass with upstream ductal dilatation

CEMR:

√ hypovascular lesion during arterial + pancreatic parenchymal phase ← desmoplastic fibrotic component

√ progressive enhancement in portal venous + delayed phase ← desmoplasia with large interstitial spaces

√ thin peritumoral rim of enhancement

√ delayed enhancement of obstructed portion of pancreas

PET (85–93% accurate, 46–71% sensitive, 63–100% specific):

√ intense focal FDG uptake ("hot spot") dependent on tumor biology + degree of desmoplastic response

√ superior detection of small metastases

Postop: wait > 6 weeks after surgery to differentiate uptake from postoperative inflammation

PET/CT: improves staging specificity in nonspecific or borderline lymph node enlargement seen on CT; better sensitivity (83%–86%) for tumor depiction in euglycemic patients than in those with elevated glucose levels (42%–69%)

√ may depict < 2 cm small / isoattenuating lesions that are difficult to detect at CT

√ SUV threshold of ≥ 2.0 (100% sensitive, 76–77% specific)

√ SUV threshold of ≥ 4.0 (1.00 PPV, 0.94 NPV)

DDx: mass-forming pancreatitis

Angiography (70% accuracy):

√ hypovascular tumor / neovascularity (50%)

√ arterial encasement: SMA (33%), splenic artery (14%), celiac trunk (11%), hepatic artery (11%), gastroduodenal artery (3%), left renal artery (0.6%)

√ venous obstruction: splenic vein (34%), SMV (10%)

√ venous encasement: SMV (23%), splenic vein (15%), portal vein (4%)

Cholangiography:

√ "rat tail / nipplelike" occlusion of CBD

√ nodular mass / meniscuslike occlusion in ampullary tumors

√ "double duct" sign = abrupt obstruction of common bile duct + pancreatic duct

Pancreatography (abnormal in 97%):

√ abrupt obstruction of main pancreatic duct ← tumor starts in ductal epithelium producing early obstruction:

√ irregular, nodular, rat-tailed, eccentric obstruction

Criteria of Resectability of Pancreatic Adenocarcinoma 89–100% positive predictive value of CT
Unresectable
√ distant metastases
√ SMA encasement > 180° of vessel circumference
√ tumor abutment of celiac axis
√ unreconstructable occlusion of SMV / portal vein
√ invasion of aorta / aortic encasement
Borderline resectable
√ impingement / narrowing of SMV / portal vein
√ short-segment venous occlusion allowing reconstruction
√ encasement of gastroduodenal artery up to hepatic artery
√ tumor abutment of SMA ≤ 180° of vessel circumference

√ localized encasement with prestenotic upstream dilatation

√ acinar defect

Prognosis:

< 20% (2%) [< 5%] 1-year (3-year) [5-year] survival; 14 months (8 months) medial survival after curative (palliative) resection; 5 months without treatment; tumors resectable in only 8–25% at presentation; 5–20% 5-year postoperative survival rate

Survival rate versus tumor size:

100% 5-year survival rate for tumors < 1 cm without parenchymal / vascular / lymphatic invasion; 30% for tumors < 2 cm

Rx: < 10–20% are deemed surgically resectable; palliative chemoradiation

Dx: biopsy with endoscopic US guidance / percutaneous (often preferred) CT-guided biopsy

DDx: focal pancreatitis, islet cell carcinoma, metastasis, lymphoma, normal variant

PANCREATIC ENDOCRINE TUMOR

= PET = PANCREATIC NEUROENDOCRINE TUMOR = PANCREATIC ISLET CELL TUMOR

= predominantly well-differentiated pancreatic / peripancreatic tumor that demonstrates endocrine differentiation

Origin: pluripotential stem cells in ductal epithelium; previously thought to originate from islet of Langerhans; derivatives of APUD (amine precursor uptake and decarboxylation) cell line (APUDoma)

◊ The term islet cell tumor is no longer acceptable because a pancreatic endocrine tumor arises from ductal pluripotent stem cells, rather than from islets of Langerhans

Genetics: sporadic (mostly), familial syndrome (1–2%) with genetic alterations involving MEN1, VHL, NF1, TSC1, TSC2 genes

May be associated with:

MEN 1 (= Wermer syndrome), von Hippel-Lindau syndrome, neurofibromatosis type 1, tuberous sclerosis

◊ Often multiple tumors that manifest at an earlier age!

Prevalence: 1–5÷100,000 population; 1–2% of all pancreatic neoplasms

Mean age: 47 (range, 7–83) years; 25 years for MEN 1; M=F

Path: (a) small tumor: solid well-demarcated, unencapsulated
◊ < 5 mm = microadenoma (only microscopically identifiable) in 10% of autopsied population
(b) large tumor: cystic changes + necrosis + calcifications with often incomplete fibrous pseudocapsule
› well differentiated benign endocrine tumor
› well differentiated endocrine carcinoma
› poorly differentiated endocrine carcinoma (2–3%)

◊ Small tumors tend to be homogeneous, whereas large tumors are more commonly heterogeneous ← areas of cystic change, necrosis, and calcification

Histo: sheets of uniform polygonal cells resembling normal islet cells with round / oval nuclei that have stippled, salt-and-pepper chromatin + eosinophilic granular cytoplasm + numerous stromal vessels
(a) trabecular pattern ± gyriform arrangement
(b) acinar / glandular pattern
(c) medullary / solid pattern
(d) cystic
(e) papillary
(f) angiomatoid
◊ Endocrine differentiation confirmed with Grimelius silver stain / immunohistochemical labeling for chromogranin / synaptophysin

Categories: size, mitotic rate, cell proliferation, invasion (Ki-67 index)

In order of frequency: insulinoma (50%) > gastrinoma (20%) > glucagonoma > VIPoma > somatostatinoma

Average time from onset of symptoms to diagnosis: 2.7 years

Classification:
(a) SYNDROMIC (functioning) pancreatic endocrine tumor (< 50%):
◊ Tumor small at presentation (early symptoms)!
◊ Most syndromic tumors produce multiple hormones!
◊ Named after the predominantly secreted hormone!
(b) NONSYNDROMIC pancreatic endocrine tumor

Location: gastrinoma triangle (most common)

Metastases: in 60–90% to liver ± regional lymph nodes
◊ Liver metastasis are often hypervascular with ringlike enhancement during arterial phase (similar to primary)
◊ A hyperechoic liver metastasis is suggestive of pancreatic endocrine tumor rather than pancreatic adenocarcinoma!

Purpose of imaging:
(1) Localisation of known functioning PET
◊ To avoid the risk of negative laparotomy use CT / MR with their high sensitivity to localize the 4% of tumors missed by intraoperative palpation + intraoperative US
(2) Diagnosis of nonfunctioning pancreatic endocrine tumor
(3) Surgical planning (location, number, spread of tumors)

• unlikely to cause ampullary / ductal obstruction

Size: mostly 1–5 (range, < 1 cm to > 20) cm in diameter
◊ A tumor > 3 cm in diameter with calcifications suggests malignancy!
√ round / ovoid tumor:
√ small homogeneous lesion
√ large heterogeneously enhancing lesion ← cystic degeneration, necrosis, fibrosis, calcification
√ marked enhancement on delayed images ← large interstitial space with loose edematous stroma + abundant blood vessels
√ NO vascular encasement / duct obstruction
US:
(a) transabdominal US (70% sensitive)
(b) endoscopic US (~ 95% sensitive, 93% specific), less sensitive for distal pancreatic body + tail
(c) intraoperative US (combined with palpation by surgeon)
√ round / ovoid mass with smooth margin ± hyperechoic rim:
√ homogeneous / heterogeneous hypoechoic
√ hypervascular pattern
√ ± enlarged peripancreatic lymph nodes
√ ± mostly hyperechoic (occasionally hypoechoic / targetlike) liver metastases
CT (71–82% sensitive):
Method: high resolution + dual phase + distension of stomach and duodenum with water; MPR
◊ Syndromic tumors often small (< 20 mm) + multiple and difficult to detect
√ isoattenuating circumscribed solid mass:
√ tendency to displace surrounding structures
√ hypoattenuating partially / completely cystic PET (in 18%)
CECT:
◊ Early imaging is ESSENTIAL for detection of small tumor:
√ avid enhancement during arterial phase (85% sensitive) ← hypervascularity ← rich capillary network
√ late arterial (pancreatic phase) images (100% sensitive)
√ tumor conspicuity decreases during portal venous phase (11–76% sensitive)
√ hypervascular rim (in 90%) of cystic endocrine tumor
FN: tumor in close proximity to a vessel is easily missed
√ lymph nodes + liver metastases most conspicuous during arterial phase ← hypervascularity:
√ hepatic metastases often with ringlike enhancement
MR (75% sensitive):
T1WI:
√ round / oval circumscribed relatively hypointense mass with / without fat saturation
T2WI:
√ mostly much higher SI compared to normal pancreas
√ may be of intermediate / (less commonly) low signal intensity ← substantial amounts of collagen

CEMR:
√ intense enhancement during arterial + capillary phase
√ homogeneous / ringlike / heterogeneous enhancement
√ T1-hypointense + T2-hyperintense liver metastases (best seen on T2WI with fat suppression):
√ moderate to intense early ringlike enhancement
√ prominent enhancement of lymph node metastases

NUC (70–90% sensitive, only 50% sensitive for gastrinomas and insulinomas):
Useful for: localization of known functioning tumor, DDx of pancreatic mass, evaluation for metastases / recurrence, assessment of receptor status
Somatostatin receptor scintigraphy with ^{111}In-octreotide:
√ sensitivity highest for gastrinoma > 2 cm + lowest for primary insulinoma
√ whole-body scintigraphy detects tumors > 10 mm in size
√ predicts which patients will respond to radionuclide Rx
√ monitors response to therapy
PET:
√ uptake in poorly differentiated pancreatic endocrine tumor

Angio:
√ intense vascular stain in late arterial + capillary phase
Hepatic vein sampling (88% sensitive):
◊ performed together with pancreatic angiography
√ rise in venous hormone concentration after selective injection of secretagogue (eg, calcium) into arteries supplying the pancreas

Prognosis: 82% (56%) 3-year survival rate without (with) hepatic metastases; 50–65% 5-year survival rate ◊ Risk of malignancy increases with tumors > 5 cm

The most reliable indicators of malignancy and poor prognosis are extrapancreatic invasion and metastatic disease defining a well-differentiated tumor as endocrine carcinoma.

Rx: enucleation, partial pancreatectomy, antihormone Rx, chemo- / radionuclide therapy, chemoembolization

DDx: (1) Pancreatic ductal adenocarcinoma (hypovascular, rarely calcified, encasement of SMA + celiac trunk, common ductal involvement, rare central necrosis + cystic degeneration)
(2) Microcystic adenoma (benign tumor, small cysts, older woman)
(3) Metastatic tumor: renal cell carcinoma (clinical Hx)
(4) Solid-pseudopapillary tumor of pancreas (young female, hemorrhagic areas)
(5) Paraganglioma
(6) Sarcoma (rare)

ACTH-producing Tumor

= CORTICOTROPHINOMA
= rare cause of Cushing syndrome
• increased level of serum cortisol
• impaired glucose tolerance > central obesity > hypertension, oligomenorrhea >

osteoporosis > purpura > striae > muscle atrophy

Prognosis: almost all malignant with metastases at time of Dx

Gastrinoma

◊ 2nd most common syndromic pancreatic endocrine tumor (= 50% of insulinoma frequency)

Peak age: 5th decade; 8% in patients < 20 years; M÷F = 1.3÷1

Histo: composed of G cells (in α cells / δ cells)

Gastrinoma symptomatology caused by:

(a) islet cell hyperplasia (10%)

(b) benign adenoma (30%): ½ solitary, ½ multiple (especially in MEN 1)

(c) malignancy (50–60%) with metastases to liver, spleen, lymph nodes, bone

Genetics: sporadic (usually)

◊ 20–25% of all gastrinomas occur in MEN 1

◊ Most common functioning PET in MEN 1

- Zollinger-Ellison syndrome
  → only 0.1% of all cases of peptic ulcer disease!
- markedly ↑ fasting serum levels of gastrin (DIAGNOSTIC): often > 1,000 pg/mL (normal level, < 100 pg/m)
- positive secretin stimulation test

Location: usually solitary, multiple (20–40%)

N.B.: previously pancreas was thought to be the most common location, but many have been peripancreatic nodal metastases from a duodenal tumor

(a) pancreas (20%): mostly in head

(b) ectopic:

› duodenum (80% of sporadic lesions, 90% in MEN1): frequently in gastrinoma triangle; often microadenomas of 1–2 mm in size

› peripancreatic lymph nodes / bile ducts

› stomach, proximal jejunum

› omentum, retroperitoneum

› ovary

Gastrinoma triangle

= triangle bounded by

(1) porta hepatis as apex of triangle (= confluence of cystic duct + common bile duct) superiorly

(2) junction of 2nd and 3rd parts of duodenum inferiorly

(3) neck and body of pancreas medially (OR border of pancreatic body + tail)

Mean size: 3–4 cm (up to 15 cm); in duodenal wall < 1 cm

√ homogeneous ringlike enhancement

√ occasionally calcifications

Angio:

√ hypervascular lesion (70%)

√ hepatic venous sampling after intraarterial stimulation with secretin

Endoscopic US (useful for tumors in duodenal wall and peripancreatic lymph nodes):

√ solid hypoechoic mass

CT:

√ transiently hyperdense on dynamic CT (majority)

MR:

√ low-intensity mass on fat-suppressed T1WI

√ diminished central + peripheral ring enhancement

√ high-intensity mass on fat-suppressed T2WI

NUC:

somatostatin receptor scintigraphy (58–75% sensitive) ← high concentration of somatostatin receptors

Spread:

√ regional lymph node metastasis (may be mistaken for primary because of large size compared to primary)

√ liver metastasis (in 30% at time of diagnosis)

Sensitivity of preoperative localization:

75–93% for ^{111}In-pentetreotide imaging, 77% for arteriography combined with intraarterial injection of secretin, 42–63% for transhepatic portal venous sampling for gastrin, 68–70% for selective angiography, 35% for CT, 25% for US, 20% for MR

Rx: surgery curative in 30%; resection of gastrinoma triangle; medical treatment of Zollinger-Ellison syndrome

Cx: frequently malignant degeneration (60%); multiple gastric carcinoid tumors from ↑ gastrin level

Glucagonoma

◊ 3rd most common syndromic pancreatic endocrine tumor

Incidence: 1÷20,000,000 annually (rare)

Age: 40–60 (range, 19–84) years; M = F

Genetics: almost always sporadic

Rarely associated with: MEN 1

Histo: derived from A cells (α cells) of pancreatic islets

- **4D (glucagonoma) syndrome**

(1) **D**iabetes mellitus

← elevated glucagon counteracting effects of insulin

- plasma glucagon level > 1,000 ng/L (DIAGNOSTIC)

(2) **D**ermatitis

- **necrolytic erythema migrans** ($^{2}/_{3}$)

= painful highly pruritic migrating erythematous macules / papules starting in lower abdomen, groin, genitals spreading to trunk, lower extremity, buttocks, face

Pancreatic Endocrine Tumors					
Type	*Frequency*	*Associated Syndrome*	*Symptoms*	*Average Size*	*Location*
Insulinoma	*50%*	Whipple triad	hypoglycemia, dizziness, vision changes, palpitations	< 2 cm	all of pancreas
Gastrinoma	*20%*	Zollinger-Ellison syndrome	peptic ulcer disease, diarrhea, esophagitis	duodenum: < 1 cm pancreas: 3–4 cm	duodenum > pancreatic head
Glucagonoma		4D syndrome	necrolytic migratory erythema, diabetes, thromboembolism	7–8 cm	pancreatic tail
Vipoma		WDHA syndrome	profuse watery diarrhea, weight loss, hypokalemia	5–6 cm	pancreatic tail
Somatostatinoma		Inhibitory syndrome	diabetes, steatorrhea, diarrhea, cholelithiasis	5–6 cm	pancreatic head
Nonfunctioning		none	abdominal pain, mass, weight loss	5–6 cm	all of pancreas
Poorly differentiated		none / paraneoplastic syndrome	abdominal pain, cachexia, jaundice	6 cm	pancreatic head

Cause: unknown; ? direct effect of glucagon, prostaglandin release; ? deficiency of amino acids, zinc, vitamin B

(3) **D**eep vein thrombosis (rare)

(4) **D**epression

- painful glossitis / stomatitis, diarrhea, weight loss, anemia
- various neurologic + psychiatric symptoms
- elevated glucagon levels (usually 10–20 x that of normal)
- ± elevated levels of insulin, serotonin, gastrin

Location: predominantly in pancreatic body / tail

Mean size: 6.4 (range, 2.5–25.0) cm with solid + necrotic components; in 70% > 5 cm in size

√ hypervascular in 90% → angiographic localization successful in 15%

√ hetero- / homogeneous enhancement with areas of decreased attenuation / intensity

√ uptake of ^{111}In-pentetreotide

Cx: pulmonary thromboembolism

Malignant transformation (in 60–80%):

√ 80% chance of malignancy if tumor > 5 cm in diameter

√ in 50–60% liver / lymph node metastases at time of Dx

Prognosis: 55% 5-year survival rate; ¾ ultimately fatal

Insulinoma

◊ Most common (40%) of syndromic (functioning) PETs!

Incidence: 2–4÷1,000,000 annually

Mean age: 47 years (range, 4th–6th decade); M÷F = 1÷1.4

Genetics: sporadic (usually)

◊ 10–30% of functioning pancreatic endocrine tumors are insulinomas in MEN 1

Associated with: MEN 1, NF1

Insulinoma symptomatology caused by:

(a) single benign adenoma (80–90%)

(b) multiple adenomas / microadenomatosis (2–10%)

(c) diffuse islet cell hyperplasia = nesidioblastosis (5–10%)

(d) malignant adenoma (5–10%)

mnemonic: 10% are associated with MEN 1

10% are multiple (especially in MEN 1)
10% have islet cell hyperplasia
10% are malignant

Histo: composed of β cells (amyloid with green birefringence + Congo red stain is highly suggestive)

- Whipple triad:
  [Allen Oldfather Whipple (1881–1963), professor of surgery at Columbia University]
  (1) Starvation attack (during fasting / after exercise)
  (2) Relief by IV glucose
  (3) Hypoglycemia (fasting glucose < 50 mg/dL)
- neuroglycopenic symptoms: dizziness, diplopia, blurred vision, headaches, confusion, personality changes, coma
- behavorial problems, seizures, coma in young children
- hypoglycemia exacerbated by fasting (98% sensitive) → frequent meals to avoid symptoms
- sweating, palpitations, tremor ← catecholamine release in response to hypoglycemia (less common); obesity
- ↓ fasting glucose level, ↑ serum insulin level
- ↑ level of serum C-peptide (excludes exogenous source)
- firm rubbery palpable mass at surgery (in > 90%)

Location: even distribution throughout pancreas (65% in body + tail); 1–5% in ectopic location; 2–10% multiple

Size: < 1 cm in 40%, < 1.5 cm in 70%, < 2 cm in 90%

◊ Early manifestation ← dramatic clinical syndrome!

√ small homogeneous hyperenhancing tumor

√ heterogeneous enhancement usually in lesions > 2 cm ← cystic change / necrosis

US (20–75% sensitive preoperatively, 75–100% sensitive endoscopically + intraoperatively):

√ round / oval smoothly marginated solid homogeneously hypoechoic mass

Angio:

√ hypervascular tumor (66%) → accurate angiographic localization in 50–90%

√ transhepatic portal venous sampling → correct localization in 95%

√ hepatic venous sampling after intraarterial stimulation with calcium gluconate

CECT (30–75% sensitive):

◊ Use of coronal images is advantageous (DDx to nearby vasculature, identification of pedunculated lesion)

√ hypo- / iso- / hyperattenuating lesion

√ homogeneous hyperenhancement (60%), peripheral ring enhancement (30%)

MR:

√ low signal intensity on fat-suppressed T1WI

√ hyperintense on T2WI + dynamic contrast-enhanced + fat-suppressed inversion recovery images

√ tumors > 2 cm show ring enhancement

Somatostatin receptor scintigraphy (60–70% sensitive)

Prognosis: best among all pancreatic endocrine tumors with overall survival rate similar to general population

Malignant transformation (in 5–10%):
√ lesion usually > 3 cm in diameter
√ metastases in peripancreatic lymph nodes (most often)
Rx: curative surgery of visualized mass / resection of distal tail + body without visualized mass

Nonsyndromic Islet Cell Tumor

= NONFUNCTIONING (CLINICALLY SILENT) ICT = POORLY DIFFERENTIATED NEUROENDOCRINE TUMOR
◊ More common than syndromic pancreatic endocrine tumors ← below threshold of detectability / hypofunctioning / biologically inactive hormone / without clinical syndrome
Frequency: 50% of all pancreatic endocrine tumors
Genetics: sporadic; most common pancreatic endocrine tumor in MEN 1 and VHL syndrome
Histo: derived from either α or β cells characterized by small poorly granular cells with high rate of proliferation and vascular invasion; positive reactivity for chromogranin-A + neurospecific enolase; no reactivity for insulin / glucagon / somatostatin
Mean age: 55 (range, 24–74) years; M > F; younger in MEN 1
• abdominal pain, jaundice, gastric variceal bleeding
• palpable mass, gastric outlet obstruction
• no clinical evidence of hormone production
• ↑ serum chromogranin A level (70% sensitive)
Location: evenly distributed throughout pancreas; anywhere in GI tract
Mean size: 5–6 (range, up to 20) cm; > 5 cm in 72%
◊ Tumor large at presentation and in 90% malignant!
√ most incidentally discovered
√ heterogeneous mass with cystic + necrotic components
√ coarse nodular calcifications (20–25%)
√ contrast enhancement in 83%
√ hypoechoic mass
√ late dense capillary stain
√ large irregular pathologic vessels with early venous filling
NUC:
√ no imaging with ^{111}In-pentetreotide ← absence of somatostatin receptor activity
√ FDG PET imaging is highly accurate and preferred ← high proliferative rate
Spread: metastases to liver + regional nodes in 60–80% at time of diagnosis
Malignant transformation:
√ metastases at time of diagnosis in 80–100%
Prognosis: 60% (44%) 3-year (5-year) survival
Rx: may respond to systemic chemotherapy

Somatostatinoma

Origin: derived from δ cells
Prevalence: < 2% of all well-differentiated PETs
May be associated with: NF1
› for duodenal somatostatinomas → NF1 in 43%

› for pancreatic somatostatinomas → NF1 in 1%

Histo: composed of D cells

Mean age: 50 years; M÷F = 1÷1

- inhibitory syndrome = inhibitory action of somatostatin on other pancreatic + bowel peptides (growth hormone, TSH, insulin, glucagon, gastrin, pepsin, secretin)
- diabetes, steatorrhea, diarrhea, cholelithiasis
- hypochlorhydria, weight loss
- elevated plasma level of somatostatin (DIAGNOSTIC)

Location: pancreatic head (½); periampullary duodenum (½); others in small bowel, colon, rectum

Size: 5– 6 (range 0.6–20) cm

√ hypervascular

√ obstruction of duodenum

Malignant transformation (in 50–90%):

√ metastases in liver / lymph nodes in 50–75% at time of initial diagnosis

VIPoma

= solitary tumor liberating **V**asoactive **I**ntestinal **P**eptide (a peptide not normally secreted by pancreatic islet cells)

Genetics: sporadic; rarely associated with MEN 1

Pathophysiology:

VIP stored in neurons near blood vessels → binds to receptors on intestinal epithelial cells → stimulates production of cyclic adenosine monophosphate (AMP) → relaxation of vascular smooth muscle (= vasodilatation) + secretion of fluid and electrolyte into intestinal lumen → characteristic watery diarrhea (even during fasting)

Path: adenoma / hyperplasia

Histo: composed of D1 cells

Age: 5th–6th decade (range, 2–83 years); M÷F = 1÷1

- WDHA syndrome = **W**atery **D**iarrhea + **H**ypokalemia + **A**chlorhydria (VIP inhibits gastrin production) = **Verner-Morrison syndrome**
- more recently + more accurately described as: WDHH syndrome = profuse **W**atery **D**iarrhea, **H**ypokalemia + **H**ypochlorhydria = "pancreatic cholera"
- dehydration ← massive diarrhea (6–8 L/d)
- weight loss, abdominal pain
- facial flushing (in some patients) ← peripheral vasodilatation mimicking carcinoid syndrome
- ↑ fasting serum VIP levels > 100 pg/mL (HIGHLY SPECIFIC)

Location:

(a) pancreas (75%): from δ cells predominantly in pancreatic tail > body

(b) extrapancreatic + neurogenic (20%): sympathetic ganglia of retroperitoneum + mediastinum, neuroblastoma (in children)

(c) extrapancreatic + nonneurogenic (5%): esophagus, small bowel, colon, liver, kidney

Mean size: ~ 5 cm

√ homogeneous enhancement in smaller lesion

√ cystic change ± calcifications in larger mass

√ mostly hypervascular tumor with solid + necrotic tissue
√ dilatation of gallbladder
√ uptake by ^{111}In-pentetreotide imaging in 88%
√ liver metastasis (usually at time of diagnosis)
Malignant transformation (in 50–80%):
√ metastases in 60–80% at presentation
DDx: small cell carcinoma of lung / neuroblastoma may also cause WDHH syndrome

Cystic Pancreatic Neuroendocrine Tumor (PNET)

= uncommon manifestation (in 17%)
Cause: tumor degeneration
Associated with: multiple endocrine neoplasia syndrome
Mean age: 53 years; M = F
√ vascularized soft-tissue components
√ avidly enhancing rim during arterial phase ← neoplastic neuroendocrine cells lining cyst periphery

PANCREATIC LIPOMATOSIS

= FATTY REPLACEMENT = FATTY INFILTRATION
= deposition of fat cells in pancreatic parenchyma
Predisposing factors:

1. Atherosclerosis of elderly
2. Obesity
3. Steroid therapy
4. Diabetes mellitus
5. Cushing syndrome
6. Chronic pancreatitis
7. Main pancreatic duct obstruction
8. Cystic fibrosis (most common cause in childhood)
9. Malnutrition / dietary deficiency
10. Hepatic disease
11. Hemochromatosis
12. Viral infection
13. Shwachman-Diamond syndrome
14. Johanson-Blizzard syndrome

Matsumoto classification:
* sparing of peribiliary region (in all types)
Ia focal fatty infiltration of pancreatic head WITH sparing of uncinate process + pancreatic body (35%)*
Ib infiltration of pancreatic head + neck + body*
IIa infiltration of uncinate process + pancreatic head WITH sparing of pancreatic body (12%)*
IIb complete infiltration of entire pancreas (18%)*
√ fatty replacement often uneven:
√ increase in AP diameter of pancreatic head with focal fatty replacement = lipomatous

pseudohypertrophy
√ prominently lobulated external contour
US:
√ increased pancreatic echogenicity
CT:
√ "marbling" of pancreatic parenchyma / total fatty replacement / lipomatous pseudohypertrophy
DDx of diffuse fatty replacement: pancreatic agenesis (absence of ductal system)
DDx of focal fatty replacement: neoplasm

Pancreatic Fatty Sparing

= sparing of fatty change in pancreatic head + uncinate process (ventral pancreatic anlage) as initial stage in pancreatic lipomatosis
Histo: ventral pancreatic anlage has smaller + more densely packed acini with scanty / absent interacinar fat
√ absence of mass effect or ductal / vascular displacement
US:
√ rounded / triangular hypoechoic area within pancreatic head / uncinate process + diffusely increased echogenicity in remainder of gland
CT:
√ higher-density region in pancreatic head + uncinate process with diffusely decreased attenuation of pancreatic body + tail

PANCREATIC PSEUDOCYST

= collection of pancreatic secretions / hemorrhagic fat necrosis encapsulated by granulation tissue + fibrous capsule
Etiology: (1) Acute pancreatitis (in 2–4%): pseudocyst develops within 4–6 weeks, matures in 6–8 weeks
(2) Chronic pancreatitis (in 10–15%): alcoholism, hyperlipidemia, hyperparathyroidism, chronic obstruction of pancreatic duct, acute exacerbation of pancreatitis
(3) Trauma / surgery
Frequency: 2–4% in acute pancreatitis;
10–15% in chronic pancreatitis
Location: ²/₃ within pancreas
Atypical location (may dissect along tissue planes in ⅓):
(a) intraperitoneal: mesentery of small bowel / transverse colon / sigmoid colon
(b) retroperitoneal: along psoas muscle; may present as groin mass / in scrotum
(c) intraparenchymal: liver, spleen, kidney
(d) mediastinal (through esophageal hiatus > aortic hiatus > foramen of Morgagni > erosion through diaphragm): may present as neck mass
May communicate with: duodenum, stomach, spleen

Vascularized soft-tissue elements are not a pseudocyst feature.

Plain film / contrast radiograph:
- √ smooth extrinsic indentation of posterior wall of stomach / inner duodenal sweep (80%)
- √ indentation / displacement of splenic flexure / transverse colon (40%)
- √ downward displacement of duodenojejunal junction
- √ gastric outlet obstruction
- √ splaying of renal collecting system / ureteral obstruction

US (pseudocyst detectable in 50–92%; 92–96% accurate):
- √ usually single + unilocular cyst
- √ multilocular in 6%
- √ fluid-debris level / internal echoes ← may contain sequester, blood clot, cellular debris from autolysis
- √ rare septations (= sign of infection / hemorrhage)
- √ may increase in size ← hypertonicity of fluid, communication with pancreatic duct, hemorrhage, erosion of vessel
- √ obstruction of pancreatic duct / CBD

CT:
- √ fluid in pseudocyst (0–30 HU)
- √ cyst wall calcification (extremely rare)

MR:
- √ irregularly marginated (early) / well-circumscribed (after several weeks) fluid collection
- √ thickened enhancing wall
- √ hyperintense contents on T1WI ← blood products / necrotic or proteinaceous debris
- √ hyperintense surrounding tissues on fat-suppressed T2WI ← chemical inflammation / infection

Pancreatography:
- √ communication with pancreatic duct in up to 50–70%

Indications for pseudocyst drainage:
pain, suspected infection, persistence of pseudocyst > 5 cm, increasing size, biliary / gastrointestinal obstruction

Cx (in 40%):
1. Rupture into abdominal cavity, stomach, colon, duodenum
2. Hemorrhage / formation of pseudoaneurysm
3. Infection = pancreatic abscess
   - usually occurs > 4 weeks after acute pancreatitis
   - symptomatology of infection
   - √ gas bubbles (DDx: fistulous communication to GI tract)
   - √ increase in attenuation of fluid contents

   Dx: transcutaneous needle aspiration
4. Intestinal obstruction

Prognosis: spontaneous resolution (in 20–50%) ← rupture into GI tract / pancreatic duct or bile duct

DDx: (1) Mucinous pancreatic cystadenoma (no significant interval change on follow-up)
(2) Cystadenocarcinoma
(3) Necrotic pancreatic carcinoma

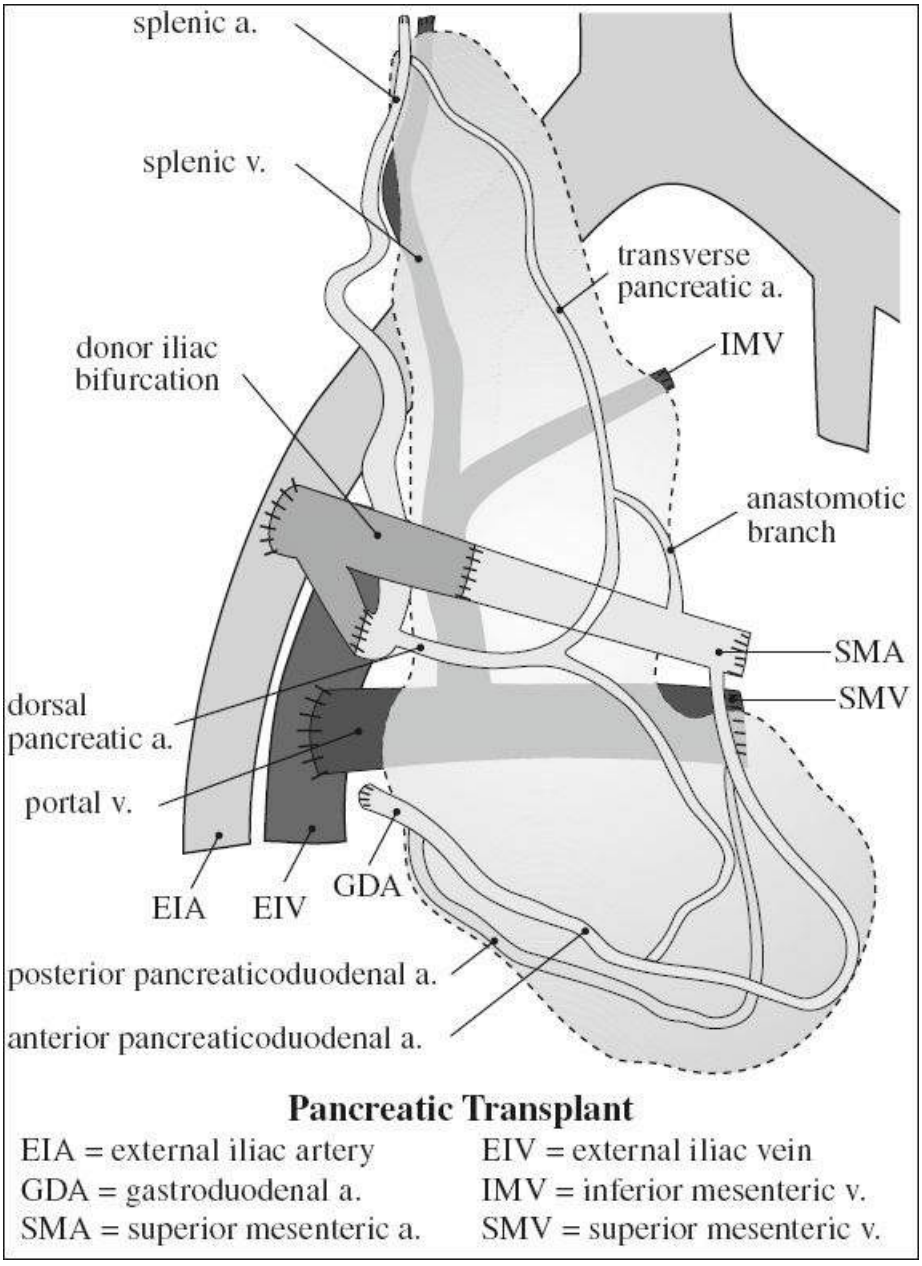
(4) Fluid-filled bowel: small bowel, stomach
(5) Duodenal diverticulum
(6) Aneurysm

PANCREATIC TRANSPLANTATION

Complications: sepsis, rejection, pancreatitis, pseudocyst, pancreatic abscess (22%), anastomotic leak
Prognosis: 40% survival rate > 1 year

Graft-vessel Thrombosis in Pancreatic Transplant (2–19%)

A. Early thrombosis (< 1 month after transplantation)
Cause: technical error in fashioning anastomosis, microvascular damage ← preservation injury



Rx: prompt pancreatectomy

B. Late thrombosis (> 1 month after transplantation)

Cause: alloimmune arteritis with gradual occlusion of small blood vessels

US / CECT:

√ venous > arterial thrombosis

Rejection of Pancreatic Transplant (5–25%)

◊ Graft rejection is primary cause of graft loss

√ all imaging modalities are unreliable

Dx: percutaneous US-guided biopsy

Acute Rejection of Pancreatic Transplant

Time of onset: 1 week– 3 months

Path: autoimmune vasculitis → small vessel occlusion (decreased perfusion) → infarction

- focal tenderness over transplant
- measurement of urinary + serum amylase, blood glucose (nonspecific and poor for diagnosis of rejection)

US (nonspecific):

√ graft enlargement + heterogeneity
√ poor margination of transplant
√ dilated pancreatic duct
√ resistive indices not helpful

DDx: acute pancreatitis, ischemia

Cx: multiple episodes culminate in chronic rejection

Chronic Rejection of Pancreatic Transplant *4–10%*

= major long-term cause of graft failure > first 6 months

Path: small vessel endarteritis → acinar atrophy → interstitial fibrosis

- insidious progressive loss of exocrine, then endocrine function

√ shrunken / disappearing transplant

Graft Pancreatitis

Frequency: up to 35%

Time of onset: < 4 weeks after transplantation

Cause: reperfusion injury

√ nonspecific enlargement + organ heterogeneity
√ peritransplant fluid
√ mural thickening of adjacent bowel

PANCREATITIS

= most common pancreatic disease in children + adults; one of the most common causes of morbidity + mortality worldwide

Cause:

A. CHOLELITHIASIS (50–70%): acute pancreatitis (75%); chronic pancreatitis (20%)
B. ALCOHOLISM (25%): acute pancreatitis (15%); chronic pancreatitis (70%)
C. IDIOPATHIC (20%)
D. METABOLIC DISORDERS
   1. Hypercalcemia in hyperparathyroidism (10%), multiple myeloma, amyloidosis, sarcoidosis
   2. Hereditary pancreatitis: autosomal dominant, only Caucasians affected, most common cause of large spherical pancreatic calcifications in childhood (in 50%), recurrent episodes of pancreatitis, development into pancreatic carcinoma in 20–40%; pronounced dilatation of pancreatic duct; pseudocyst formation (50%); associated with type I hypercholesterolemia
   3. Hyperlipidemia types I and V

4. Cystic fibrosis

E. INFECTION / INFESTATION

1. Viral infection (mumps, hepatitis, Coxsackie virus, mononucleosis)

Drug-Induced Pancreatitis	
Drug Class	*Common Agents*
Antibiotics	metronidazole, tetracyclines, sulfonamides
Diuretics	thiazide, furosemide, ethacrynic acid
Statins	simvastatin
Estrogens	oral contraceptives
ACE inhibitors	captopril, lisinopril, enalapril
Chemotherapeutics	azathioprine, L-asparaginase, Didanosine (2',3'-dideoxyinosine)
Others	sulfasalazine, mesalazine, sodium valproate, phenformin, steroids, acetaminophen, procainamide

2. Parasites (ascariasis, clonorchis)

F. TRAUMA

◊ One of the most common causes of pancreatitis in childhood!

1. Penetrating ulcer
2. Blunt / penetrating trauma; nonaccidental trauma
3. Surgery (in 0.8% of Billroth-II resections, 0.8% of splenectomies, 0.7% of choledochal surgery, 0.4% of aortic graft surgery)

G. STRUCTURAL ABNORMALITIES

1. Pancreas divisum
2. Choledochocele

H. DRUGS (3–5%), > 100 medications have been implicated

Mechanism: pancreatic duct constriction, toxic metabolites, cytotoxic effects → insult to exocrine function and inappropriate accumulation / activation of pancreatic digestive proenzymes

I. MALIGNANCY

Pancreatic carcinoma (in 1%), metastases, lymphoma

J. MULTISYSTEM CONDITIONS

1. Sepsis and shock
2. Hemolytic-uremic syndrome
3. Reye syndrome
4. Systemic lupus erythematosus

Theories of pathogenesis:

reflux of bile / pancreatic enzymes / duodenal succus

(a) terminal duct segment shared by common bile duct and pancreatic duct

(b) obstruction at papilla of Vater from inflammatory stenosis, edema / spasm of sphincter of Oddi, tumor, periduodenal diverticulum

(c) incompetent sphincter of Oddi

Acute Pancreatitis

= inflammatory disease of pancreas producing temporary changes with potential for restoration of normal anatomy and function following resolution

Incidence: > 300,000 hospitalizations annually in USA

- acute epigastric pain radiating to back / chest (peaking after a few hours, resolving in 2–3 days); nausea, vomiting
- ⇑ serum amylase + lipase in blood + urine
- increased amylase-creatinine clearance ratio
- signs of hemorrhagic pancreatitis:
  - Cullen sign = periumbilical ecchymosis
  - Grey-Turner sign = flank ecchymosis
  - Fox sign = infrainguinal ecchymosis
- subcutaneous nodules + fat necrosis + polyarthritis

Clinical definition of acute pancreatitis:

Marshall Scoring System for Acute Pancreatitis

Score	*Respiratory**	*Creatinine [mg/dL]*	*Systolic Pressure [mmHg]*
0	> 400	≤ 1.5	> 90
1	301–400	> 1.5 to ≤ 1.9	< 90, fluid responsive
2	201–300	> 1.9 to ≤ 3.5	< 90, not fluid responsive
3	101–200	> 3.5 to ≤ 5.0	< 90, pH < 7.3
4	< 101	> 5.0	< 90, pH < 7.2

* = ratio of partial pressure of arterial oxygen to fraction of inspired oxygen

organ failure = score ≥ 2 in at least 1 of 3 organ systems

- epigastric pain radiating to back
- serum amylase + lipase > 3 x normal
- characteristic findings on imaging

Clinical phases (revised Atlanta Classification System 2012):

A. First / early clinical phase (during 1st week)

Pathology: early inflammation → peripancreatic edema / ischemia → resolution / permanent necrosis / liquefaction

Severity: based on Marshall scoring system

(a) mild = organ failure resolves within 48 hours

(b) severe = organ failure beyond 48 hours

Other useful severity markers:

- hematocrit, C-reactive protein, LDH, serum / urinary trypsinogen, cytokines
- CT severity index + pleural effusion

◊ Serum amylase + lipase useless to judge severity!

Mortality: 0%

B. Second / late clinical phase beyond 1st week that may persist for weeks – months; characterized by increasing necrosis, ongoing infection, persistent multiorgan failure

- bacteremia + sepsis

Mortality: 5–10% for sterile necrosis; 20–30% for superinfection of necrosis

Role of imaging in acute pancreatitis:

1. Confirm diagnosis in clinical uncertainty
   ◊ NOT needed without signs of severe systemic inflammatory response syndrome!
2. Find cause: cholecystolithiasis, choledocholithiasis, underlying neoplasm
3. Document severity (= extent of necrosis) when patient's condition does not improve / deteriorates
4. Evaluate for complications: extrahepatic biliary dilatation, splenic / portal / mesenteric vein thrombosis, varices, arterial pseudoaneurysm, pleural effusion, ascites, inflammatory changes of stomach, duodenum, small bowel, colon, spleen, kidney, ureter, liver
5. Help to determine when to implement interventional radiologic / endoscopic / surgical treatment
6. Monitor response to treatment

Distribution:

A. Diffuse pancreatitis (52%)
B. Focal pancreatitis (48%): location of head÷tail = 3÷2

Morphologic subtypes:

1. Interstitial edematous pancreatitis 70–80%
2. Necrotizing pancreatitis (more severe form) 20–30%

Abdominal film:

√ "colon cutoff" sign (2–52%) = dilated transverse colon with abrupt change to a gasless descending colon (inflammation via phrenicocolic ligament causes spasm + obstruction at splenic flexure impinging on a paralytic transverse colon)
√ "sentinel loop" (10–55%) = localized segment of gas-containing bowel in duodenum (in 20–45%) / terminal ileum / cecum
√ "renal halo" sign = water-density of inflammation in anterior pararenal space contrasts with perirenal fat; more common on left side
√ mottled appearance of peripancreatic area ← fat necrosis in pancreatic bed, mesentery, omentum
√ intrapancreatic gas bubbles ← acute gangrene / suppurative pancreatitis
√ "gasless abdomen" = fluid-filled bowel associated with vomiting
√ ascites

CXR (findings in 14–71%):

√ pleural effusion (in 10–20%): usually left-sided, elevated amylase levels (in 85%)
√ left-sided diaphragmatic elevation
√ left-sided subsegmental atelectasis (20%)
√ parenchymal infiltrates, pulmonary infarction
√ pulmonary edema, ARDS
√ pleural empyema, pericardial effusion
√ mediastinal abscess, mediastinal pseudocyst
√ pancreaticobronchial / -pleural / -pulmonary fistula

UGI:

√ esophagogastric varices ← splenic vein obstruction

√ diminished duodenal peristalsis
√ widening of retrogastric space ← pancreatic enlargement / inflammation in lesser sac
√ widening of duodenal sweep + downward displacement of ligament of Treitz
√ enlarged tortuous + spiculated edematous rugal folds along antrum + greater curvature of stomach (20%)
√ Poppel sign = edematous swelling of papilla
√ Frostberg "inverted-3" sign = segmental narrowing with fold thickening of duodenum
√ jejunal + ileal fold thickening (proteolytic spread along mesentery)

BE:
√ narrowing, nodularity, fold distortion along inferior haustral row of transverse colon ± descending colon

ERCP (no primary role, replaced by MRCP):
√ long gently tapered narrowing of CBD
√ prestenotic biliary dilatation

Indication: CBD stone removal, pancreatic duct stent placement for stricture / disrupted duct

Cx: exacerbation of pancreatitis, bleeding, perforation of bowel

Bone films (findings in 6%):

Cause: metastatic intramedullary lipolysis + fat necrosis + trabecular bone destruction

Time of onset: usually 3–6 weeks after peak of clinical pancreatitis

√ punched out / permeative mottled destruction of cancellous bone + endosteal erosion
√ aseptic necrosis of femoral / humeral heads
√ metaphyseal infarcts, predominantly in distal femur + proximal tibia

US (visualization of pancreas in 62–78%):
√ hypoechoic diffuse / focal enlargement of pancreas
√ dilatation of pancreatic duct (if head focally involved)
√ perivascular cloaking = spread of inflammatory exudate along perivascular spaces
√ extrapancreatic hypoechoic mass with good acoustic transmission (= phlegmonous pancreatitis)
√ fluid collection: lesser sac (60%), L > R anterior pararenal space (54%), posterior pararenal space (18%), around left lobe of liver (16%), in spleen (9%), mediastinum (3%), iliac fossa, along transverse mesocolon / mesenteric leaves of small intestine

Fate of fluid collection:
(a) complete resolution
(b) pseudocyst formation
(c) bacterial infection = abscess

√ pseudocyst formation (52%): extension into lesser sac, transverse mesocolon, around kidney, mediastinum, lower quadrants of abdomen

CT (modality of choice):
√ no detectable change in size / appearance (29%)
√ enlargement of pancreas with convex margins + indistinctness of gland + parenchymal heterogeneity:
  √ hypodense (5–20 HU) mass in <u>inflammatory pancreatitis</u>; may persist long after complete recovery
  √ hyperdense areas (50–70 HU) in <u>hemorrhagic pancreatitis</u> for 24–48 hr

√ thickening of anterior pararenal fascia
√ "halo" sign = sparing of perirenal space
√ non–contrast-enhancing parenchyma during bolus injection (= pancreatic necrosis)
√ pancreatic + peripancreatic fluid collection

MRI:
√ intra- and extrapancreatic increased T2 signal
√ collection consisting of fluid + nonliquefied material:
  √ T2-hyperintense liquefied component
  √ T2-hypointense nonliquefied component
√ hyperintense SI on fat-saturated T1WI = hemorrhage

MRCP: to evaluate for choledocholithiasis, degree of mass effect on CBD, pancreatic duct stricture / integrity ± communication with collection

N.B.: secretin administration after resolution of acute inflammation to avoid exacerbation

Angiography:
√ may be normal
√ hypovascular areas (15–56%)
√ hypervascularity + increased parenchymal stain (12–45%)
√ venous compression ← edema
√ formation of pseudoaneurysms (in 10% with chronic pancreatitis): splenic artery (50%), pancreatic arcades, gastroduodenal artery

Cx:

Balthazar CT-Severity Index for Acute Pancreatitis

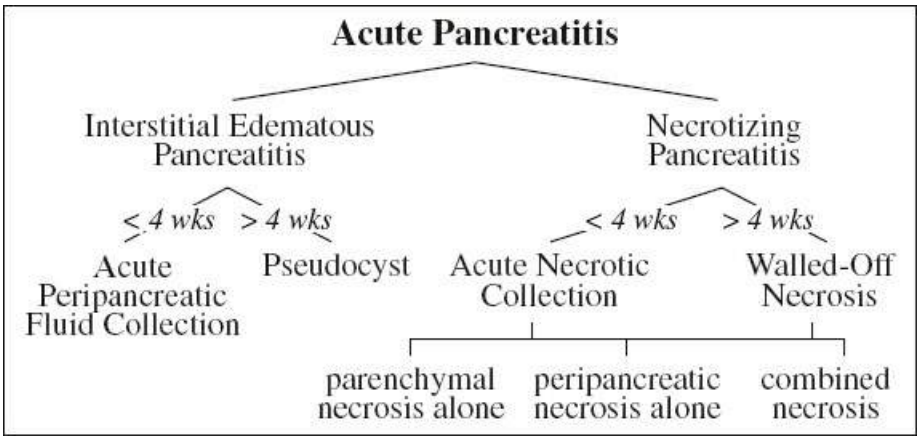
Criteria	*Points*
CT appearance	
Normal pancreas	0
Pancreatic enlargement	1
Pancreatic / peripancreatic inflammation	2
1 fluid collection	3
≥ 2 fluid collection	4
Percentage of necrosis	
None	0
< 30%	2
30–50%	4
> 50%	6

score 0 = 0% mortality;
scores 7–10 = 17% mortality + 92% complication rate

1. Pleural effusion
2. Pseudocyst formation (10%)
3. Hemorrhagic pancreatitis (2–5%)
4. Main pancreatic duct stricture (late Cx)
5. Disconnected pancreatic duct
6. Peripancreatic inflammation

(a) GI tract: stomach, duodenum, small bowel, colon
√ bowel wall thickening, mural hyperenhancement
(b) liver, spleen
(c) kidney, ureter

7. Displacement and compression of adjacent organs
(a) bile duct obstruction
› choledocholithiasis
› mass effect ← inflammation / collection
› stricture ← exposure to proteolytic enzymes
(b) obstruction of stomach
(c) duodenal stricture ← extrinsic compression by enlarged pancreatic head / adjacent fluid collection / duodenal mural edema or hemorrhage
(d) hydronephrosis
◊ At risk for abdominal compartment syndrome
8. Pancreatic ascites
9. Venous thrombosis
Cause: local prothrombotic inflammatory factors, reduced venous flow, mass effect on vein from adjacent necrotic tissue / collection
Location: splenic vein (19–63%) > portal vein (13–25%) > SMV (13–14%)
10. Pseudoaneurysm (typically late Cx)
= digestion of arterial wall by proteolytic enzymes
Frequency: in up to 10% of severe pancreatitis
Location: splenic > gastroduodenal > pancreatico-duodenal > hepatic > left gastric artery
Cx: rupture into preexisting pseudocyst, necrotic collection, gastrointestinal tract, peritoneum, pancreatic parenchyma
Mortality: 37% for rupture, 16–50% for surgery
11. Hemorrhage (1–5%)
Cause: erosion of vasculature, rupture of pseudoaneurysm, rupture of varices
Source: splenic artery, portal vein, splenic vein, small peripancreatic vessels
Location: within pancreatic parenchyma, into fluid collection, into GI tract
Mortality: 34–52%
12. Thoracopancreatic fistula
(a) pancreaticopleural fistula
(b) pancreaticopericardial fistula
(c) pancreaticoesophageal fistula
(d) pancreaticobronchial fistula
(e) mediastinal pseudocyst



BILIARY PANCREATITIS

= gallstone / biliary sludge impaction at ampulla of Vater → ampullary spasm → pancreaticobiliary reflux → obstruction of common bile duct + pancreatic duct

At risk: common pancreaticobiliary channel, pancreas divisum

MR: preferred in suspected choledocholithiasis (more sensitive than CT for detecting gallstones)

HEMORRHAGIC PANCREATITIS

MR:

√ elevated SI on precontrast fat-saturated T1WI

Interstitial Edematous Pancreatitis (IEP) *(70–80%)*

√ localized / diffuse enlargement of pancreas
√ normal homogeneous enhancement
√ normal / "misty" peripancreatic soft tissue
√ ± peripancreatic fat stranding
√ heterogeneous enhancement → repeat scan 5–7 days later for definitive characterization of
(a) interstitial edematous pancreatitis versus
(b) pancreatic necrosis
√ ± peripancreatic fluid collection → eventually pseudocyst

Prognosis: self-limiting with normalization of physical signs + laboratory values within 48–72 hours of conservative therapy

Mortality: 1–5%

Rx: NPO, gastric tube, atropine, analgesics, sedation, prophylactic antibiotics

Necrotizing Pancreatitis *(20–30%)*

= necrosis of pancreatic parenchyma ± peripancreatic tissues as a complication of acute pancreatitis in 25%
{**pancreatic phlegmon** [= misnomer, NO infection!]}

The revised Atlanta Classification System subdivides collections of necrotizing pancreatitis according to time of disease onset:
< 4 weeks after onset WITHOUT discrete wall = **A**cute **N**ecrotic **C**ollection (ANC)
> 4 weeks after onset WITH a discrete wall = **W**alled-**O**ff **N**ecrosis (WON)

ANC and WON can be sterile / infected!
The terms pancreatic abscess, fluid collection, phlegmon are no longer accepted owing to their ambiguity.

Definition: necrosis = nonviable pancreatic tissue that becomes gradually liquefied
Morphologic subtypes (revised Atlanta Classification System of 2012):

(a) pancreatic parenchymal necrosis only (< 5%)
- established by 48–72 hours after disease onset

CT should be performed 3–5 days after presentation because parenchymal pancreatic necrosis cannot be excluded prior to 72 hours after onset!

√ decreased / absent pancreatic parenchymal enhancement = attenuation of < 30 HU during pancreatic parenchymal phase

(b) peripancreatic fat necrosis only (< 20%)
√ mixture of increased attenuation, linear stranding, and fluid collections within peripancreatic fat (DDx: acute interstitial edematous pancreatitis)
√ heterogeneity outside pancreas favors peripancreatic fat necrosis with nonliquefied components ← hemorrhage, necrotic fat
√ liquefied component among fat becomes more apparent after 1 week
Location: commonly retroperitoneum + lesser sac

(c) pancreatic and peripancreatic necrosis (75–80%)
√ combined necrosis with homo- / heterogeneous fluid collections generally becoming walled off (WON) after 4 weeks

Cx: pancreatic duct disruption (~ 50%)
Morbidity: 34–95% due to uncontrolled infection
Mortality: 2–39% due to systemic organ dysfunction, immunosuppression, organ failure

Pancreatic & Peripancreatic Fluid Collection

ACUTE PERIPANCREATIC FLUID COLLECTION (APFC)

= pure extrapancreatic collection WITHOUT solid component during 1st month of interstitial edematous pancreatitis (IEP)
Cause: pancreatic / peripancreatic inflammation; rupture of small peripheral pancreatic branch
Location: adjacent to pancreas conforming to anatomic boundaries of retroperitoneum (extension into lesser sac, anterior pararenal space, transverse mesocolon, small bowel mesentery, retroperitoneum, pelvis)
Content: increased amylase + lipase ← communication with pancreatic ductal system
√ collection of fluid attenuation (near 0 HU):
√ homogeneous and nonenhancing
√ NO discernable wall
Prognosis: spontaneous reabsorption within first few weeks; maturation to pseudocyst

N.B.: Refrain from percutaneous aspiration / drainage to avoid introduction of an infection!

ACUTE NECROTIC COLLECTION (ANC)

= complex collection replacing pancreatic parenchyma during 1st month of necrotizing pancreatitis

Content: nonliquefied + liquefied necrotic debris
◊ Liquefaction of necrotic tissue takes 2–6 weeks!
Location: intrapancreatic / extrapancreatic / both
√ collection of low attenuation:
√ homogeneous / heterogeneous
√ loculated and nonenhancing
√ NO discernable wall (= NO capsule)
√ PATHOGNOMONIC content (if present) of complex heterogeneity, hemorrhage, fat
√ nonliquefied component only discernable on MRI

DDx of Pancreatic & Peripancreatic Fluid Collections

	APFC	*ANC*	*WON*	*Pseudocyst*
Association	IEP	necrotizing pancreatitis	ANC	APFC
Time [month]	< 1st	< 1st	> 1st	> 1st
Location:				
pancreatic	-	+	+	-
peri-	+	+/-		+
Content:	amylase, lipase	liquid + solid	fluid + fat	fluid
homogeneous	+	-/+	-	+
hemorrhage	-	+/-		
fat	-	+/-	+	
Wall:				
discernible	-	-	+	+
enhancing			+	+

√ presence of pancreatic parenchymal necrosis
Prognosis: evolution into
(a) sterile walled-off necrosis (WON) 60%
(b) spontaneous resolution 20%
(c) complicated by infection 20%
Management: CT every 7–10 days to evaluate evolution of pancreatic necrosis + assess for evidence of infection / complications

WALLED-OFF NECROSIS (WON)

= PANCREATIC SEQUESTRATION = NECROMA = ORGANIZED PANCREATIC NECROSIS
= any fluid collection replacing portions of pancreatic parenchyma after 1st month = matured late stage of acute necrotic collection (ANC)
Location: within pancreas / peripancreatic / both
Content: necrotic pancreatic parenchyma + necrotic fat
√ focal / diffuse well-marginated zones of unenhanced pancreatic parenchyma with irregular borders
√ thick enhancing wall between necrosis and adjacent tissue
√ growth of collection favors WON

√ pancreatic ductal dilatation unlikely ← pancreatic fluid decompresses into collection
√ PATHOGNOMONIC if collection is intrapancreatic
√ **saponification** = phospholipases and proteases attack plasma membranes of fat cells → release and hydrolyzation of triglycerides → formation of free fatty acids → combination with serum calcium → precipitation as calcium soaps
Rx: fluid drainage often ineffective
◊ Nonliquefied components require laparoscopic procedure / endoscopic necrosectomy / surgical débridement / percutaneous drain with frequently irrigated large-bore catheter

PSEUDOCYST

= extrapancreatic collection of fluid developing from APFC after 4 weeks
Path: wall of fibrous / granulation tissue; absence of epithelium-lined wall
Frequency: in 10–20% of IEP
Location: adjacent / distant to pancreas
Content: amylase + lipase without necrotic debris
√ well-circumscribed round / oval peripancreatic fluid collection of homogeneously low attenuation < 15 HU
√ well-defined enhancing wall ← fibrous / granulation tissue
◊ Formation of a defined wall takes about 4 weeks!
√ NO nonliquefied component
√ main pancreatic ductal dilatation > 3 mm (frequent) ← compression of pancreatic parenchyma
√ communication with pancreatic ductal system usually seals off
√ persistent pseudocyst after drainage ← continued communication with pancreatic duct
MR:
√ complex cyst dissecting along facial planes:
√ elevated internal T1 signal = blood products
Prognosis: spontaneous resolution in 44%; < 4 cm: resolution anticipated; > 7 cm: treatment recommended; 25% become symptomatic / infected
Cx: hemorrhage, infection, spontaneous rupture into hollow viscera → higher attenuation values
Rx: percutaneous fluid drainage (retroperitoneal approach from flank)

INFECTED COLLECTION

= all 4 types of pancreatic fluid collection can be sterile / infected

The term **"pancreatic abscess"** is no longer used because a collection of pus without pancreatic necrosis does not exist!

Frequency: 2–18%
Timing: most commonly 2–4 weeks after presentation
Cause: bacterial translocation from gut into adjacent necrotic pancreatic parenchyma
◊ Nonliquefied material more likely to become infected!
Organism: (most commonly) E. coli, S. aureus, Enterococcus faecalis
• (nondiagnostic) fever, tachycardia, elevated WBCs
√ gas bubbles in collection (12–22%)

Cause: gas-forming organism (most common: E. coli)
Mortality: 25–70% → diagnosis aggressively pursued!
Dx: image-guided percutaneous aspiration of fluid with positive Gram stain, positive culture for bacteria / fungal organism; 10% FN
Rx: surgical débridement + antibiotics; temporizing percutaneous drainage followed by necrosectomy
DDx of gas: cutaneous / enteric fistula, ruptured duodenum, iatrogenic gas collection (← marsupialization, drainage procedure)

DISCONNECTED PANCREATIC DUCT SYNDROME

Incidence: unknown; in up to 50% after an episode of severe acute necrotizing pancreatitis
Cause: necrosis of ductal epithelium (commonly neck / body); therapeutic intervention (40%)
√ large intrapancreatic collection / longitudinal nonenhancing glandular necrosis (HALLMARK) of > 2 cm
√ viable upstream pancreatic body / tail
√ main pancreatic duct enters collection at 90° angle
√ persistent / growing collection around pancreas
√ persistent drainage of amylase-rich fluid from percutaneously placed catheter despite resolution of fluid collection
ERCP (most sensitive, associated with high morbidity):
√ ductal obstruction at level of fluid collection
√ ± extravasation of contrast material
MRCP (secretin-enhanced):
√ centrally located fluid collection
√ ± dilatation of upstream portion of pancreatic duct and its side branches
Cx: accumulation of fluid around pancreas, pancreatic ascites, pancreaticopleural fistula ← persistent leakage of pancreatic fluid from viable upstream pancreas
Dx: average delay before diagnosis up to 9.3 months
Rx: internal drainage, distal pancreatic resection

Cambridge Classification of Chronic Pancreatitis

Grade	*Main Pancreatic Duct*	*No. of Abnormal Side Branches*
Normal	normal	none
Equivocal	normal	< 3
Mild	normal	≥ 3
Moderate	abnormal	≥ 3
Severe	abnormal	≥ 3

Chronic Pancreatitis

= continued inflammatory disease of pancreas characterized by scarring with irreversible permanent damage to anatomy + function primarily of the exocrine pancreas
Incidence: 3–9÷100,000 per year (in Western countries); annually 120,000 outpatient visits

+ 50,000 hospitalizations

Etiology:

(1) Idiopathic (20%) most common cause of chronic pancreatitis in children
(2) Chronic calcifying pancreatitis
(3) Chronic obstructive pancreatitis

- acute exacerbation of epigastric pain (93%):
  decreasing with time due to progressive destruction of gland, usually painless after 7 years
- jaundice (42%) from common bile duct obstruction
- steatorrhea (80%); negative secretin stimulation test
- diabetes mellitus (58%) ← endocrine insufficiency

√ **"double-duct"** sign = dilatation of CBD and main pancreatic duct, a finding typically associated with chronic pancreatitis
DDx: pancreatic adenocarcinoma

√ **"duct-penetrating"** sign = mass penetrated by an unobstructed pancreatic duct

Plain film:

√ numerous irregular calcifications (in 20–50% of alcoholic pancreatitis)
PATHOGNOMONIC

UGI:

√ displacement of stomach / duodenum by pseudocyst
√ shrinkage / fold induration of stomach (DDx: linitis plastica)
√ stricture of duodenum

Cholangiopancreatography (most sensitive imaging modality):

√ side-branch ectasia = slight ductal ectasia / clubbing of side branches (minimal disease)
√ "nipping" = narrowing of the origins of side branches
√ dilatation > 2 mm, tortuosity, wall rigidity, main ductal stenosis (moderate disease)
√ "beading, chain of lakes, string of pearls" = multifocal dilatation, stenosis, obstruction of main pancreatic duct + side branches (severe disease)
√ intraductal filling defects ← mucinous protein plugs / calculi / debris
√ prolonged emptying of contrast material
√ may have stenosis / obstruction + prestenotic dilatation of CBD
√ filling of pseudocysts (< 50%)

US / CT:

√ irregular (73%) / smooth (15%) / beaded (12%) pancreatic ductal dilatation (in 41–68%)
√ small atrophic pancreas (in 10–54%)
√ pancreatic calcifications (in 4–50–68%)
√ inhomogeneous gland with increased echogenicity (62%)
√ irregular pancreatic contour (45–60%)
√ focal (12–32%) / diffuse (27–45%) pancreatic enlargement during flare up (DDx: pancreatic carcinoma)
√ mostly mild biliary ductal dilatation (29%)
√ intra- / peripancreatic pseudocysts (20–34%)
√ segmental portal hypertension ← splenic vein thrombosis with splenomegaly (in 11%)
√ arterial pseudoaneurysm formation

√ peripancreatic fascial thickening + blurring of organ margins (16%)
√ ascites / pleural effusion (9%)
√ no abnormalities (7%)

MR:
√ loss of SI on fat-suppressed T1WI ← loss of aqueous protein in pancreatic acini ← pancreatic fibrosis
√ delayed diminished heterogeneous contrast enhancement ← loss of capillary network replaced by fibrous tissue

Secretin-enhanced MRCP:
√ **side-branch ductectasia** = one of the EARLIEST findings of chronic pancreatitis
√ main pancreatic duct strictures ± dilatation
√ pseudocyst, fistula
√ loss of MPD distensibility ← reduced compliance
√ loss of duct tapering in pancreatic tail
√ filling defect in MPD ← duct calculus

Angiography:
√ increased tortuosity + angulation of pancreatic arcades + intrahepatic arteries (88%)
√ luminal irregularities / focal fibrotic arterial stenoses (25–75%) / smooth beaded appearance
√ irregular parenchymal stain
√ venous compression / occlusion (20–50%)
√ portoportal shunting + gastric varices without esophageal varices

Cx: pancreatic carcinoma (2–4%), jaundice ← biliary stricture (3–46%), pseudocyst formation, pancreatic ascites, thrombosis of splenic / mesenteric / portal vein

Rx: surgery for infected pseudocyst, GI bleeding from portal hypertension, common bile duct obstruction, gastrointestinal obstruction

DDx: pancreatic carcinoma (extrapancreatic spread)

Chronic Alcoholic Pancreatitis

= characterized by heterogeneous lobular distribution; typically > 8 years of heavy ethanol abuse

Pathophysiology:
thick pancreatic secretions with increased protein concentration → precipitation in pancreatic ductules → obstruction ± calcification of protein plugs

√ protein plugs / calculi within ductal system
√ ductal abnormalities more severe in smaller branches

Chronic Obstructive Pancreatitis

Etiology:
1. Congenital lesion of pancreatic duct
2. Trauma / surgical duct ligation
3. Sphincter of Oddi dysfunction, ampullary stenosis
4. Primary sclerosing cholangitis
5. Idiopathic fibrosing pancreatitis
6. Renal failure

7. Slow growing ampullary tumor
8. Common pancreatic mass: intraductal papillary mucinous tumor, adenocarcinoma, metastasis

DDx of Chronic Pancreatitis from Adenocarcinoma		
Feature	*Chronic Focal Pancreatitis*	*Pancreatic Adenocarcinoma*
Dynamic enhancement	√ early peak	√ peak @ 150–180 sec
	√ delayed wash-out	√ gradual rise
DWI (b value of 600 sec/mm^2)	√ same as pancreas	√ hyperintense to pancreas
ADC	√ higher than normal pancreas	√ lower than normal pancreas / pancreatitis
PET	√ no uptake (88%)	√ increased uptake (98%)

◊ Acute pancreatitis occurs in 3–14% with average delay in cancer diagnosis by 21 months

9. Duodenal lesion: duplication cyst, lipoma, duodenal diverticulum, duodenal adenoma

√ dilatation of main pancreatic duct
√ normal sized / focally or diffusely enlarged / small atrophic gland
√ calcifications uncommon

Autoimmune Pancreatitis AIP *(1.8–11%)*

= PRIMARY / CHRONIC SCLEROSING PANCREATITIS = LYMPHOPLASMACYTIC SCLEROSING PANCREATITIS = NONALCOHOLIC DUCT-DESTRUCTIVE / IDIOPATHIC DUCT-CENTRIC CHRONIC PANCREATITIS = PSEUDOTUMOROUS PANCREATITIS

= unique form of chronic pancreatitis characterized by diffuse inflammatory infiltration by T-lymphocytes and IgG4-positive plasma cells with exuberant fibrosis

Histo: dense periductal lymphoplasmacytic infiltrates

Type 1: lymphoplasmacytic sclerosing pancreatitis with storiform fibrosis and obliterative phlebitis and high rate of relapse
- biliary tract involvement (in up to 80%)

Type 2: idiopathic duct centric pancreatitis with granulocytic epithelial lesions without relapse

Prevalence: 2–5% of chronic pancreatitis
Mean age: 56 (range, 14–77) years; M÷F = 2÷1
Association with other autoimmune conditions:

IgG4-related lesions similar to autoimmune pancreatitis have been identified in many extrapancreatic organs, like bile ducts, gallbladder, lymph nodes, retroperitoneum, mesentery, kidney, lung, breast, prostate gland, skin.

1. Tubulointerstitial nephritis(7–35%)
2. Sialadenitis (12–16%)
3. Sjögren syndrome

4. Primary sclerosing cholangitis (68–88%)
5. Primary biliary cirrhosis
6. Inflammatory bowel disease: ulcerative colitis (17%)
7. Systemic lupus erythematosus
8. Systemic lymphadenopathy
9. Retroperitoneal fibrosis (3–8%)
10. Renal involvement (3–35%)
11. Chronic thyroiditis

Nearly 40% of patients with IgG4-related pancreatitis also have salivary ± lacrimal gland involvement, characterized by bilateral painless glandular swelling, which may precede / accompany pancreatitis / occur in isolation.

- no / mild upper abdominal pain (35%), easy fatigability
- bulging of papilla with obstructive jaundice (63–75%)
- weight loss (35%); diabetes mellitus (42–76%)
- symptoms of pancreatitis at presentation unusual (33%)
- serum level of immunoglobulin G4 (IgG4) > 130 mg/dL (67–94% sensitive, 90–100% specific)
- positivity for ALA (antilactoferrin antibody), ACA II (anti–carbonic anhydrase II antibody), ASMA (anti–smooth muscle antibody), ANA (antinuclear antibody)

Location:

(a) diffuse form: body + tail of pancreas
(b) focal form: head of pancreas
(b) multifocal form: anywhere in pancreas

US:

√ hypoechoic enlarged pancreas

CT:

√ widely varying imaging features depending on degree of fibrosis + inflammatory infiltrate
√ "featureless" pancreas = loss of lobular architecture in diffusely enlarged sausage-shaped pancreas (52%) / focal enlargement of pancreas
√ homogeneously iso- / hypoattenuating parenchyma
√ thin rimlike capsule (of fibrosis)
√ rare calcifications / pseudocysts / vessel encasement
√ minimal hypoattenuating peripancreatic halo = fat stranding of inflammatory tissue around body + tail
√ ± involution of pancreatic tail
√ ± regional lymphadenopathy
√ diffusely narrowed pancreatic duct
√ ± bile duct strictures with upstream ductal dilatation
√ reduced enhancement during parenchymal phase (29–75%)
√ delayed homogeneous enhancement (25–71%)

MR:

√ homogeneously decreased SI on T1WI isointense relative to liver (100%)
√ mildly hyperintense (93%) / variointense on T2WI

√ rim of low SI on T2WI with delayed enhancement
√ delayed retention of contrast material ← widened extracellular extravascular space (70–89%)

CECT /CEMR:
√ SPECIFIC capsulelike rim / halo of low attenuation surrounding pancreas (not seen in any other pancreatic disorder) ← fluid collection / phlegmon / fibrosis (12–48% for CECT, 18–47% for CEMR)

MRCP:
√ diffuse narrowing of main pancreatic duct
√ strictures of pancreaticobiliary tree

ERCP:
√ focal / segmental / diffuse narrowing of main pancreatic duct + nonvisualization of side branches (CHARACTERISTIC):
√ > 3 cm long stenosis of main pancreatic duct
√ < 6 mm diameter of upstream portion of duct
√ "duct-penetrating sign" = continuity of pancreatic duct highly SPECIFIC for a benign pancreatic mass
√ "ice pick sign" = smooth tapered narrowing of upstream pancreatic duct just distal to pancreatic lesion
√ smooth stricture of distal extrapancreatic CBD + dilatation of proximal duct segment (90%) ← extrinsic compression
√ strictures of more proximal bile ducts resembling primary sclerosing cholangitis

PET:

PET/CT is helpful in diagnosis and response assessment to corticosteroid therapy.

√ longitudinal heterogeneous pattern with multiple areas of uptake within pancreas
√ extrapancreatic uptake in lacrimal / salivary glands, biliary system, retroperitoneal space, prostate gland

@ Renal manifestations
√ bilateral small peripheral renal cortical nodules / round lesions / well-defined wedge-shaped lesions / patchy parenchymal lesions
√ involvement of perirenal tissue, renal sinus, renal pelvic wall

@ Pulmonary manifestations
√ retroperitoneal fibrosis
√ pulmonary parenchymal nodules + infiltrates
√ mediastinal adenopathy

Cx: diffuse sclerosis → organ dysfunction

Rx: dramatic response to corticosteroid therapy

DDx: (1) Pancreatic cancer (invasion / encasement of vessels, mass effect, abrupt narrowing of pancreatic duct + significant proximal dilatation, marked atrophy of parenchyma upstream to mass, fluid collection, IgG4-negativity)
(2) Lymphoma
(3) Acute pancreatitis (marked peripancreatic fat stranding, peripancreatic fat necrosis, NO peripancreatic halo)

(4) Chronic pancreatitis (calcifications)

Focal Pancreatitis

= MASS-FORMING / PSEUDOTUMORAL PANCREATITIS

Frequency: 5–10% of pancreatectomies for presumed malignancy

Cause: chronic pancreatitis, autoimmune pancreatitis (25%), groove pancreatitis

◊ NO distinguishing morphologic features from adenocarcinoma clinically + radiographically ← coexistence with inflammation; adenocarcinoma may arise in chronic pancreatitis (2% [65%] after 10 [20] years)

√ "duct penetrating" sign = nondilated / smooth tapering of pancreatic + bile ducts coursing through mass

√ irregularity of pancreatic duct

√ pancreatic calcifications

DDx: adenocarcinoma (abrupt interruption of smoothly dilated pancreatic duct, upstream pancreatic gland atrophy, gradual enhancement)

Groove Pancreatitis

= rare distinct form of chronic segmental pancreatitis characterized by inflammation + fibrous tissue formation in pancreaticoduodenal groove

Prevalence: unknown

Location: groove (= potential space) between pancreatic head + duodenum + common bile duct

Cause: unknown

Types:

(a) segmental form = involvement of pancreatic head + pancreaticoduodenal groove mimicking a mass

(b) pure form = sheetlike fibrotic scar tissue in groove without involvement of pancreatic head

• recurrent vomiting ← duodenal obstruction in 50%

• symptoms of biliary obstruction (in 50%) rarely precede those of duodenal obstruction

√ hypoattenuating sheetlike soft-tissue density

√ hypointense on T1WI + iso- to hyperintense on T2WI

√ delayed enhancement

√ masslike appearance of pancreatic head

Histo: chronic pancreatitis

√ long smooth segmental stricture of intrapancreatic CBD

√ widening of space between distal pancreatic duct + CBD and duodenal lumen

√ thickening ± cystic dystrophy of duodenal wall

DDx: pancreatic adenocarcinoma (vascular invasion, no cystic lesions within mass / thickened duodenal wall)

Hereditary Pancreatitis *(<1%)*

= autosomal dominant disease with recurrent attacks resulting in chronic pancreatitis

Genetics: mutation of cationic trypsinogen genes like PRSS1 (serine peptidase) and CFTR (cystic fibrosis transmembrane regulator) gene; NO mutations in 30%

Age of onset: variable from 5–10 years to 6th decade
√ pancreatic parenchymal calcifications + ductal calculi
√ duct destruction with significant pancreatic atrophy
√ absence of anatomic anomalies
Cx: (1) Exocrine + endocrine pancreatic insufficiency
(2) Pancreatic cancer: 50–70-fold increased risk within 7–30 years of disease onset
◊ Endoscopic US in 6–12-month intervals starting at 30 years of age
Dx: suspect after 2 attacks of acute pancreatitis without explanation like: anatomic anomalies, ampullary / MPD strictures, trauma, viral infection, gallstones, alcohol consumption, drug use, hyperlipidemia
DDx: tropical pancreatitis

Tropical Pancreatitis

= JUVENILE NONALCOHOLIC CHRONIC RELAPSING PANCREATITIS = JUVENILE TROPICAL PANCREATITIS = KWASHIORKOR
= variant of chronic pancreatitis with rapidly progressive course
◊ Most common cause of pancreatitis worldwide!
Geography: southern state of Kerala in India, Indonesia, Asia, Africa, and South America
Etiology:
(1) Protein energy malnutrition → suppression of pancreatic function
(2) Pancreatic ductal anomalies
(3) Food toxicity: chronic cyanide toxicity from cassava
(4) Genetic predisposition: SPINK 1 N34S mutation, CFTR mutation
Mean age: 12.5 years (range, infancy to adulthood); M÷F = 1.6÷1 to 5÷1
• abdominal pain (80–90%), weight loss, steatorrhea
• glucose intolerance / frank diabetes mellitus
√ multiple discrete dense up to 5 cm large pancreatic calculi within dilated pancreatic duct (80%) ± extension into side branches
√ pancreatic atrophy (50%)
Cx: (1) Fibrocalculous pancreatic diabetes (within decade of onset)
(2) Pancreatic adenocarcinoma (by 45 years, responsible for 25% of deaths)

PANCREATOBLASTOMA

= INFANTILE PANCREATIC CARCINOMA
= rare childhood tumor often misdiagnosed as neuroblastoma / hepatoblastoma
Frequency: 0.2% of all pancreatic tumors
◊ Most common pancreatic tumor in young children (< 75 cases in literature)!
Ethnicity: > 50% in Asians
Mean age: 4.5 (range, fetus to 9) years; M÷F = 2÷1
May be associated with: Beckwith-Wiedemann syndrome
Path: displacing tumor of soft consistency with cystic spaces ← hemorrhage / cystic degeneration
Histo: epithelial tissue in organoid arrangement of acinar, trabecular, solid formation separated by dense stromal bands; scattered islands of squamoid corpuscles (CHARACTERISTIC)
Size: 10.6 (range, 1.5–20.0) cm
◊ Organ of origin difficult to establish due to large size!
Location: head of pancreas (50%) uncommonly dilating the biliary tree
• abdominal pain, fatigue, lethargy, weight loss, anorexia
• early satiety, vomiting, constipation
• asymptomatic large palpable mass (slow growing)
• elevated serum α-fetoprotein (25–33%)
√ well-defined smooth lobulated solid / multiloculated solitary mass in region of lesser sac
√ ± small clustered punctate / curvilinear calcifications
√ enhancing septa
US:
√ well-circumscribed hypoechoic / heterogeneous mass with solid + cystic components (with echogenic internal septa)
MR:
√ low (= foci of necrosis) to intermediate SI on T1WI
√ heterogeneous high SI on T2WI
Spread: liver + regional lymph nodes (35%); lung / brain (less common); omentum, cul-de-sac, colon, spleen, kidney, adrenal (rare)
√ hyperattenuating liver metastases
√ regional lymphadenopathy difficult to detect due to large displacing mass
√ rarely vascular invasion
DDx: neuroblastoma, Wilms tumor, hepatoblastoma, NHL, solid-pseudopapillary tumor (adolescent girl)
Rx: complete resection (resectable in 75%) + empirical adjuvant chemotherapy; recurrence after surgery in 14%

PAPILLARY ADENOMA OF BILE DUCTS

= very rare benign tumor of biliary tract
Path: usually solitary tumor / biliary papillomatosis with papillary fronds extending into lumen

Histo: columnar epithelium supported by connective tissue from lamina propria ± mucin production

• biliary obstruction

Location: common bile duct > right / left hepatic duct

√ usually small intraductal mass

√ visualized at cross-sectional imaging only if large enough

√ segmental biliary ductal dilatation

Prognosis: high rate of recurrence after surgical resection

Cx: malignant transformation (rare in solitary adenoma, significant risk in papillomatosis))

PASSIVE HEPATIC CONGESTION

= stasis of blood within liver parenchyma ← impaired hepatic venous drainage ← cardiac disease

Cause: CHF, constrictive pericarditis, pericardial effusion, cardiomyopathy, tricuspid / pulmonary valve disease

Pathophysiology: chronic central venous hypertension transmitted to hepatic sinusoids → centrilobular congestion → hepatic atrophy, necrosis, fibrosis → irreversible **cardiac cirrhosis**

• RUQ pain, hepatomegaly, increased abdominal girth

• elevation of liver enzymes, jaundice

√ hepatomegaly

√ ascites, pleural effusion, pericardial effusion

√ cardiomegaly, congestive heart failure

CECT:

- √ reflux of contrast from RA into IVC → early enhancement of dilated IVC + central hepatic veins during arterial phase
- √ enhancement of portal veins + hepatic arteries + immediately adjacent parenchyma (56%)
- √ delayed antegrade enhancement of hepatic veins during portal venous phase
- √ "reticulated mosaic" pattern = lobular patchy areas of enhancement separated by coarse linear regions of diminished attenuation (100%) during parenchymal phase
- √ globally delayed enhancement (36%)
- √ linear / curvilinear areas of poor enhancement ← delayed enhancement of small + medium-sized hepatic veins
- √ large patchy peripheral areas of poor delayed enhancement
- √ perivascular lymphedema = linear hypoattenuating regions encircling intrahepatic IVC / portal veins:
  - √ diminished periportal attenuation (24%)
  - √ diminished attenuation around intrahepatic IVC (8%)

DDx: Budd-Chiari syndrome (narrowed intrahepatic IVC / hepatic veins; flip-flop pattern between arterial + venous phase in acute disease; caudate lobe hypertrophy; large regenerative nodules in chronic disease)

PELIOSIS

[*pelios*, Greek = purple]

= rare benign disorder characterized by cystic sinusoidal dilatation + multiple blood-filled lacunar spaces between 1 mm and several cm in diameter within organs of the RES

Cause: (a) idiopathic (in 20–50%)

(b) acquired:

› chronic wasting / infection = bacillary peliosis hepatis (Bartonella henselae and quintana, TB, leprosy, AIDS)

› hepatotoxic drugs: androgen-anabolic steroids, corticosteroids, tamoxifen citrate, chemotherapeutic |agents, azathioprine, oral contraceptives, diethylstilbestrol, thorium dioxide injection, arsenic, polyvinyl chloride)

› chronic renal failure

› advanced malignancy: HCC, Hodgkin disease, myeloma, disseminated cancer

› renal / cardiac transplantation

(c) ? congenital: angiomatous malformation

Histo: (1) PHLEBECTATIC peliosis hepatis (early stage)

= endothelial-lined cysts (= ? dilatation of central veins) communicating with dilated hepatic sinusoids + compression of surrounding liver

(2) PARENCHYMAL peliosis hepatis (late stage)

= irregularly shaped cysts without lining communicating with dilated hepatic sinusoids + areas of liver cell necrosis

Associated with: hormonally induced benign / malignant tumors; diabetes mellitus, sprue, necrotizing vasculitis

Location: liver (most common), spleen, bone marrow, lymph nodes, lung

Age: fetal life (rare) to adult life

• incidentally discovered; asymptomatic

√ hepatomegaly, splenomegaly

√ small lesions remain invisible with / without contrast

US:

√ multiple indistinct areas of variable echogenicity:

√ hyperechoic on background of normal liver

√ hypoechoic on background of abnormal echogenic liver

√ ± internal vascularity

CT:

√ focal hypoattenuating area ± internal calcifications

√ increased attenuation in areas of hemorrhage

CECT (variable enhancement pattern):

√ hypoattenuating relative to liver during early phase + centripetally increasing enhancement during later phases (DDx: hemangioma)

√ complete globular vessel-like enhancement during early phase

√ "target" sign (= central enhancement) with centrifugal progression during portal venous phase

√ homogeneously hyperintense on delayed phase

√ ± nonenhancing central areas of thrombosis simulating metastasis / abscess

MR:

√ variable intensity on T1WI (typically hypointense ← subacute blood products

√ commonly and typically hyperintense on T2WI + central areas of increased SI ← necrosis
√ mixed SI ← repeated hemorrhage (deoxyhemoglobin + methemoglobin + siderotic nodules)
√ low SI during arterial phase + contrast accumulation during portal venous + delayed phases

Angio:

√ multiple small (several mm to 1.5 cm) round collections of contrast medium scattered throughout liver in late arterial phase of hepatic arteriogram
√ ± simultaneous opacification of hepatic veins

Prognosis: reversible after drug withdrawal / progression to hepatic failure / intraperitoneal hemorrhage leading to death

CAVE: inadvertent aspiration of a peliotic lesion may be fatal

DDx: hypervascular metastasis (hypo- / isoattenuating to liver in portal venous phase); hemangioma (discontinuous globular enhancement in arterial phase + centripetal progression + mass effect); liver abscess

PORCELAIN GALLBLADDER

= calcium carbonate incrustation of gallbladder wall

Frequency: 0.6–0.8% of cholecystectomy patients; M÷F = 1÷5

Histo: (a) flakes of dystrophic calcium within chronically inflamed + fibrotic muscular wall
(b) microliths scattered diffusely throughout mucosa, submucosa, glandular spaces, Rokitansky-Aschoff sinuses

Associated with: gallstones in 90%

• minimal symptoms
√ curvilinear (muscularis) / granular (mucosal) calcifications in segment of wall / entire wall
√ nonfunctioning GB on oral cholecystogram
√ highly echogenic shadowing curvilinear structure in GB fossa (DDx: stone-filled contracted GB)
√ echogenic GB wall with little acoustic shadowing (DDx: emphysematous cholecystitis)
√ scattered irregular clumps of echoes with posterior acoustic shadowing

Cx: 10–20% develop carcinoma of gallbladder

PORTAL HYPERTENSION

= portal venous pressure > 10 mmHg

• normal hepatic blood flow of 550–900 mL/min (= 25% of cardiac output) passes through portal system (⅔) + through hepatic artery (⅓)

Classification:

A. DYNAMIC / HYPERKINETIC PORTAL HYPERTENSION
CONGENITAL / traumatic / neoplastic arterioportal fistula

B. INCREASED PORTAL RESISTANCE

@ Prehepatic
› portal vein thrombosis: portal phlebitis, oral contraceptives, coagulopathy, neoplastic invasion, pancreatitis, neonatal omphalitis
› portal vein compression: tumor, trauma, lymphadeno-pathy, portal phlebosclerosis, pancreatic pseudocyst

@ Intrahepatic (= obstruction of portal venules)

› presinusoidal

1. Congenital hepatic fibrosis
2. Idiopathic noncirrhotic fibrosis
3. Primary biliary cirrhosis
4. Alpha-1 antitrypsin deficiency
5. Wilson disease
6. Sarcoid liver disease
7. Toxic fibrosis (arsenic, copper, PVC)
8. Reticuloendotheliosis
9. Myelofibrosis
10. Felty syndrome
11. Schistosomiasis
12. Cystic fibrosis
13. Chronic malaria

› sinusoidal

1. Hepatitis
2. Sickle cell disease

› postsinusoidal

1. Cirrhosis (most frequent): Laennec cirrhosis, postnecrotic cirrhosis from hepatitis
2. Venoocclusive disease of liver

@ Posthepatic

1. Budd-Chiari syndrome
2. Constrictive pericarditis
3. CHF (tricuspid incompetence)

Pathophysiology:

continued elevated pressure despite formation of portal venous collateral vessels may be explained by

(a) <u>backward flow theory</u> = hypodynamic flow theory
= increase in sinusoidal pressure ← deposition of collagen in spaces of Disse + hepatocyte swelling
• low / stagnant portal venous flow rates

(b) <u>forward flow theory</u> = hyperdynamic flow theory
= splanchnic flow increases ← mesenteric vasodilators + increase in cardiac output to preserve hepatic perfusion + intrahepatic endogenous vasoconstrictors
• increased portal venous flow rates > 15 mL/min/kg

Flow direction:

(a) hepatopetal (*petere*, Latin = to seek)
(b) hepatofugal (*fugere*, Latin = to flee) = flow reversal
Cause: intrahepatic arterioportal communications (inside portal triads vasa vasorum of portal veins + hepatic arteries connect via bile duct capillaries to portal v.)

• elevated hepatic wedge pressure (HWP) = portal venous pressure; normal values seen in presinusoidal portal hypertension
• caput medusae = drainage from paraumbilical + omental veins through superficial veins of chest (lateral thoracic vein to axillary vein; superficial epigastric vein to internal mammary

vein and subclavian vein) + abdominal wall (circumflex iliac vein and superficial epigastric vein to femoral vein; inferior epigastric vein to external iliac vein)

• hemorrhaging esophageal varices (50%)

@ Splanchnic system:

√ portal vein > 13 mm (57% sensitive, 100% specific)

√ SMV + splenic vein > 10 mm; coronary vein > 4 mm; recanalized umbilical vein > 3 mm (size of vessels NOT related to degree of portal hypertension or presence of collaterals)

√ loss of respiratory increase of splanchnic vein diameters of < 20% (81% sensitive, 100% specific)

√ portal vein aneurysm

√ portal vein thrombosis

√ cavernous transformation of portal vein

√ increased echogenicity + thickening of portal vein walls

Doppler US:

√ continuous monophasic portal venous flow pattern without respiratory fluctuations

√ loss of flow increase in portal venous system during expiration

√ DIAGNOSTIC reduction of peak portal vein velocity to < 16 cm/sec (normally 16–40 cm/sec)

Spontaneous Portosystemic Shunts

Type of Varices	*Frequency (%)*
Coronary venous	80–86
Esophageal	45–65
Paraumbilical	10–43
Abdominal wall	30
Perisplenic	30
Retrogastric / gastric	2–27
Paraesophageal	22
Omental	20
Retroperitoneal-paravertebral	18
Mesenteric	10
Splenorenal	10
Gastrorenal	7

√ DIAGNOSTIC hepatofugal flow in main portal vein

√ **congestive index** > 0.13 cm•sec (= ratio of area of portal vein divided by flow velocity; 67% sensitive)

√ may have bidirectional / hepatofugal (< 10%) flow within spontaneous splenorenal shunts (indicates high incidence of hepatic encephalopathy)

√ dilated hepatic artery may demonstrate elevated resistive index > 0.78

@ Spontaneous portosystemic shunts / collaterals:

◊ Portosystemic shunts are one of the MOST SPECIFIC findings for portal hypertension!

• high frequency of hepatic encephalopathy

√ varices = serpentine tubular rounded structures

√ coronary (left gastric) vein > 5–6 mm (in 26%)
√ gallbladder wall varices in thickened gallbladder wall (in 80% associated with portal vein thrombosis)

(a) connection to SVC
1. Esophageal varices
2. Paraesophageal varices

(b) connection to pulmonary circulation
1. Gastropulmonary shunt (between gastric / esophageal vv. and left pericardiophrenic / inferior pulmonary vv.)
√ lateral bulging of paraspinal interfaces on CXR
√ obliteration of azygoesophageal recess on CXR
√ cardiophrenic angle masses (with membranous obstruction of IVC)

(c) retrograde mesenteric flow
1. Veins of Retzius (= anastomoses between portal vein and IVC)
› ileocolic veins → right gonadal vein → IVC
› pancreaticoduodenal vein → IVC
› proximal small left branches of SMV → left gonadal vein → left renal vein
› ileocolic veins → directly into IVC

(d) retroperitoneal collaterals
1. Splenorenal / splenoadrenorenal shunt
2. Gastrorenal shunt
3. Mesenterorenal shunt (SMV → right renal vein)
4. Mesenterogonadal shunt (ileocolic vein → right testicular vein)
5. Splenocaval shunt (splenic vein → left hypogastric v.)

(e) intrahepatic shunt (portal vein → hepatic veins)

@ **Cruveilhier-von Baumgarten syndrome** (20–35%)
= recanalized paraumbilical veins (NOT recanalized umbilical veins)
√ hypoechoic channel in ligamentum teres
(a) size < 2 mm (in 97% of normal subjects; in 14% of patients with portal hypertension)
(b) size ≥ 2 mm (86% sensitive for portal hypertension)
√ arterial signal on Doppler US in 38%
√ hepatofugal venous flow (82% sensitive, 100% specific for portal hypertension)

@ Spleen
√ splenomegaly (nonspecific; absence does NOT rule out portal hypertension)
√ **Gamna-Gandy nodules** in 13% (= small foci of perifollicular + trabecular hemosiderin deposits after hemorrhage):
√ multiple 3–8-mm low-intensity (blooming) spots on FLASH / GRASS images
√ multiple hyperechoic spots on US
√ multiple faint calcifications on CT

√ ascites (nonspecific)

Cx: Acute gastrointestinal bleeding (mortality of 30–50% during 1st bleeding)

Segmental Portal Hypertension

= splenic vein occlusion / superior mesenteric vein occlusion

PORTAL VEIN ANEURYSM / VARIX

= rare localized saccular / fusiform portal venous dilatation with a portal vein diameter of > 20 mm

Frequency: 3% of all venous aneurysms; most common type of visceral venous aneurysm

Prevalence: 0.6–4.3÷1000 patients

Cause:

(a) congenital: diverticulum formation ← incomplete regression of distal right primitive vitelline vein; vessel wall weakness; anomalous portal vein branching

(b) ACQUIRED: liver cirrhosis; portal hypertension ← portal vein thrombosis; trauma; surgery; pancreatitis

• usually asymptomatic, pain, jaundice, gastrointestinal bleeding

Site: extrahepatic portal vein (63–77%) > splenomesenteric venous confluence > splenic vein > intrahepatic portal vein branch > superior mesenteric vein > inferior mesenteric vein

√ often solitary (80%) and fusiform (97%–100%)

Cx: portal hypertension, spontaneous thrombosis (28%), venous varix rupture, compression of adjacent biliary tree / duodenum / IVC

PORTAL VEIN THROMBOSIS

= PYLETHROMBOSIS

Etiology:

A. IDIOPATHIC (mostly): ? neonatal sepsis

B. SECONDARY:

(1) Cirrhosis + portal hypertension (5%)

(2) Tumor invasion by: HCC (13–44%), pancreatic carcinoma, cholangiocarcinoma, gastric carcinoma, metastasis / extrinsic compression by tumor

(3) Trauma: umbilical venous catheterization; Cx of splenectomy (7%, higher in patients with myelo-proliferative disorders); liver transplantation; percutaneous islet cell transplantation; portosystemic shunt surgery

(4) Hypercoagulable state: blood dyscrasia; clotting disorder; estrogen therapy; severe dehydration, Trousseau

(5) Intraperitoneal inflammatory process (portal vein phlebitis): perinatal omphalitis; pancreatitis; appendicitis; ascending cholangitis

(6) Budd-Chiari syndrome (20%)

Age: predominantly children, young persons

• nonspecific abdominal pain, hematemesis (esophageal varices)

• portal systemic encephalopathy

Types:

A. BLAND portal vein thrombus
in 11.2–15.8% of cirrhosis with portal hypertension

MRCP:

√ NO effect on portal vein caliber

√ low SI on T2WI ← hemosiderin within thrombus

B. MALIGNANT portal vein thrombus in 44% of HCC

MRCP:
- √ expansile dilatation of portal vein
- √ intermediate to high SI on T2WI
- √ arterial neovascularity contiguous with primary
- √ enhancement similar to primary tumor

Course: dependent on degree of thrombosis, extent of collateralization, duration of thrombus

Acute Portal Vein Thrombosis

- may be asymptomatic
- exacerbation of preexisting portal hypertension

Plain film:
- √ hepatosplenomegaly
- √ enlarged azygos vein
- √ paraspinal varices

UGI:
- √ esophageal varices
- √ thickening of bowel wall

US:
- √ echogenic material within vessel lumen (67%) / thrombus may be isoechoic
- √ increase in portal vein diameter (57%):
  - √ enlargement of thrombosed segment > 15 mm (38%)
- √ portosystemic collateral circulation (48%): biliary and gastric tributaries of portal vein (most common)
- √ thickening of lesser omentum

Doppler-US:
- √ NO flow on postprandial color Doppler scans:
  - ◊ Malignant thrombus tends to distend vein + exhibit pulsatile flow, a bland thrombus does not!
- √ decrease in hepatic artery resistive index:
  - √ RI < 0.50 (in acute occlusive portal vein thrombosis)
  - √ minimal decrease / normal RI (in chronic portal vein thrombosis / nonocclusive thrombosis)

NECT:
- √ thrombus usually of high attenuation
- √ decreased attenuation of affected hepatic parenchyma ← edema, depletion of hepatocytes, fibrosis

CECT:
- √ transient high attenuation of hepatic parenchyma during hepatic arterial phase ← increased arterial flow
- √ partial / complete filling defect in portal vein:
  - √ low-density center of portal vein thrombus = portal vein density 20–30 HU less than aortic density
  - √ surrounded by peripheral enhancement

MR:
- √ absent flow void in portal area + abnormal SI in main portal vein

√ hyperintense thrombus on T1WI + T2WI (if < 5 weeks old)
√ filling defect on CEMR
√ iso- / hypointense bland thrombus on T1WI + T2WI
√ heterogeneous hyperintense tumor thrombus on T2WI

Angio:

√ "thread and streaks" sign of tumor thrombus (streaky contrast opacification of tumor vessels)

Cx: (1) Cavernous transformation (19%)
(2) Hepatic infarction
(3) Bowel infarction
(4) Variceal bleeding → shock

Prognosis: partial / complete spontaneous resolution

Chronic Portal Vein Thrombosis

Pathophysiology:

central part (caudate lobe + lateral segment) is well supplied by collateral venous vessels; the peripheral zone (mainly right lobe) receives less portal venous blood resulting in increased arterial inflow

√ **cavernous transformation** (= cavernoma) of portal vein:
√ presence of a racemose conglomerate network of collateral veins (= enlargement of vasa vasorum of portal vein wall) with portal venous flow linking pancreas + duodenum + gallbladder fossa
√ ± dilated pancreaticoduodenal venous arcades ← SMV occlusion
√ ± dilated gastric + gastroepiploic veins ← splenic vein occlusion
√ segmental atrophy of affected liver segments + compensatory hypertrophy of perfused segments:
√ abnormal peripheral high-attenuation patches during hepatic arterial phase
√ decreased enhancement during portal venous phase
√ portoportal channels intrahepatically between segments ← thrombosis of intrahepatic portal vein branches
√ extensive portosystemic collateralization ← extrahepatic portal hypertension
√ splenomegaly
√ ascites

NECT:

√ nonvisualization of extrahepatic portal vein (= fibrotic portal vein)
√ ± calcifications within clot / wall of portal vein

CECT:

√ peripheral scattered areas of high attenuation in liver during hepatic arterial phase
√ multiple serpentine enhancing collateral vessels

US:

√ echogenic / nonvisualized portal vein
√ multiple tubular anechoic channels in hepatic hilum

MR:

√ hypointense portal vein on T1WI + hyperintense on T2WI (2–18 months old)

√ numerous abnormal flow voids in porta hepatis

PORTOSYSTEMIC SHUNT

Congenital Portosystemic Shunt

Congenital Extrahepatic Portosystemic Shunt (CEPS)

= ABERNETHY MALFORMATION

= anastomosis between prehilar portomesenteric PV and a systemic vein (IVC > renal / iliac / azygos vein / RA)

Age:

Type 1: usually early childhood; M÷F = 1÷3

Type 2: intrauterine to 68 years; M÷F = 1÷1

Associated congenital anomalies:

CHD (ASD, VSD, patent foramen ovale, patent ductus arteriosus, tetralogy of Fallot), situs ambiguous, polysplenia, malrotation, duodenal atresia, annular pancreas, skeletal anomalies, GU malformations

Cause:

excessive involution of periduodenal vitelline venous loop / total failure of vitelline veins to establish critical anastomoses with hepatic sinusoids / umbilical veins

› shunt due to persistence of right vitelline vein (shunt drains into retrohepatic IVC) /

› shunt due to persistence of left vitelline vein (shunt drains into IVC or RA above level of hepatic vein confluence)

Types (Morgan & Superina classification):

1. Complete diversion of portal blood into systemic circulation (end-to-side shunt) with absent intrahepatic portal branches
   1a SV / SMV drain separately into systemic vein = complete **atresia of portal vein**
   1b SV + SMV form a common trunk and drain together into a systemic vein
2. Some portal flow is diverted into a systemic vein (side-to-side shunt) with intact intrahepatic PV

Types according to development of venules in portal triads:

I absence of PV + absence of venules = PV **agenesis**

II absence of PV + presence of venules = PV **atresia**

In suspected type 1 CEPS a liver biopsy is necessary to reveal small portal venules within portal triads (not diagnosable by imaging), a finding indicative of a type II shunt.

- symptoms related to abnormal hepatic development:
  - nonspecific liver dysfunction
  - fatty degeneration + atrophy → small liver volume
  - regenerative / hyperplastic nodules → hepatomegaly
- symptoms resulting from the portosystemic shunt:
  - elevated serum levels of ammonia, galactose, other toxic metabolites
  - high galactose levels are useful for screening of newborn
- symptoms from associated congenital abnormalities

√ absence of portal hypertension: NO ascites, NO varices, NO splenomegaly

Portal hypertension with its secondary signs of splenomegaly, ascites, portosystemic collaterals is not seen in CEPS.

√ polysplenia + hypersplenism (frequent)
√ ± congenital biliary atresia, choledochal cyst, intrahepatic gallbladder
US:
√ (often) absent / hypoplastic portal vein
√ enlarged hepatic artery = only vessel seen within hepatoduodenal ligament given atresia of portal vein

Bland vs. Malignant Portal Vein Thrombus

Findings on US, CT, MR	*Bland*	*Malignant*
Echogenicity	hyperechoic (often)	heterogeneous
Attenuation of filling defect	low	higher
Thrombus intensity	iso- to hypo ⇑ ADC	hetero on T2WI, ⇓ ADC
Arterialized flow in thrombus	–	+
Presence of Doppler flow	–	+
Contrast enhancement	–	+
Adjacent tumor	none	contiguous
Portal vein expansion	–	+

√ portal vein draining into IVC
CT / MR angiography:
√ identification of absent portal branches

√ regenerative nodular hyperplasia typically has high signal intensity on T1WI (in 75%).

Transrectal Portal Scintigraphy:
» rectal administration of 123I iodoamphetamine → absorption into IMV → carried to liver
√ simultaneous detection of isotope in liver and lungs
√ abnormal portosystemic shunt index (= lung counts divided by liver counts + lung counts) > 5%

Cx: (1) Intrahepatic tumors: regenerative nodules, FNH, adenoma
(2) Malignancy (rare): hepatoblastoma, HCC
(3) Hepatic (portosystemic) encephalopathy (15%)
(4) Hepatopulmonary syndrome = hypoxemia ← ventilation-perfusion mismatch ← dilatation of intrapulmonary vessels ← diversion of vasoactive mediators into systemic circulation

DDx: (1) Portal vein thrombosis
(2) Intrahepatic shunt

Rx: determination of the type of shunt is important for the planning of definitive treatment

In type 1 CEPS occlusion of the shunt is not an option, because it represents the only drainage route for mesenteric and splenic venous blood. Liver transplantation is the only therapy.

Congenital Intrahepatic Portosystemic Shunt *(rare)*

= abnormal intrahepatic connection between posthilar PV branches and HV / IVC

Cause: trauma, portal hypertension

Types (Park classification):

› more common:

1. Single large vessel connecting RPV to IVC
2. One / more localized shunt(s) in one hepatic segment between peripheral PV branch + HV

› less common:

3. Aneurysmal communication between peripheral PV branch and hepatic veins = focal varix
4. Multiple communications between peripheral PV and HV branches in both hepatic lobes

• hyperammonemia + elevated serum bile acid levels (with persistent shunt patency)

√ enlarged afferent + efferent vessels contiguous with portal + hepatic veins

√ ± abnormal round cystic structure with turbulent flow = focal varix

√ increased flow velocity + phasic waveforms in afferent portal vein branch ← transmitted cardiac pulsations

√ continuous flow with loss of normal triphasic waveform in efferent hepatic vein branch ← increased portal venous inflow

Prognosis: ± spontaneous closure during 1st year of life; at risk for hepatic encephalopathy (in adult life)

Extrahepatic Portosystemic Shunt

(a) congenital (rare)

(b) acquired (most common)

Cause: portal venous hypertension

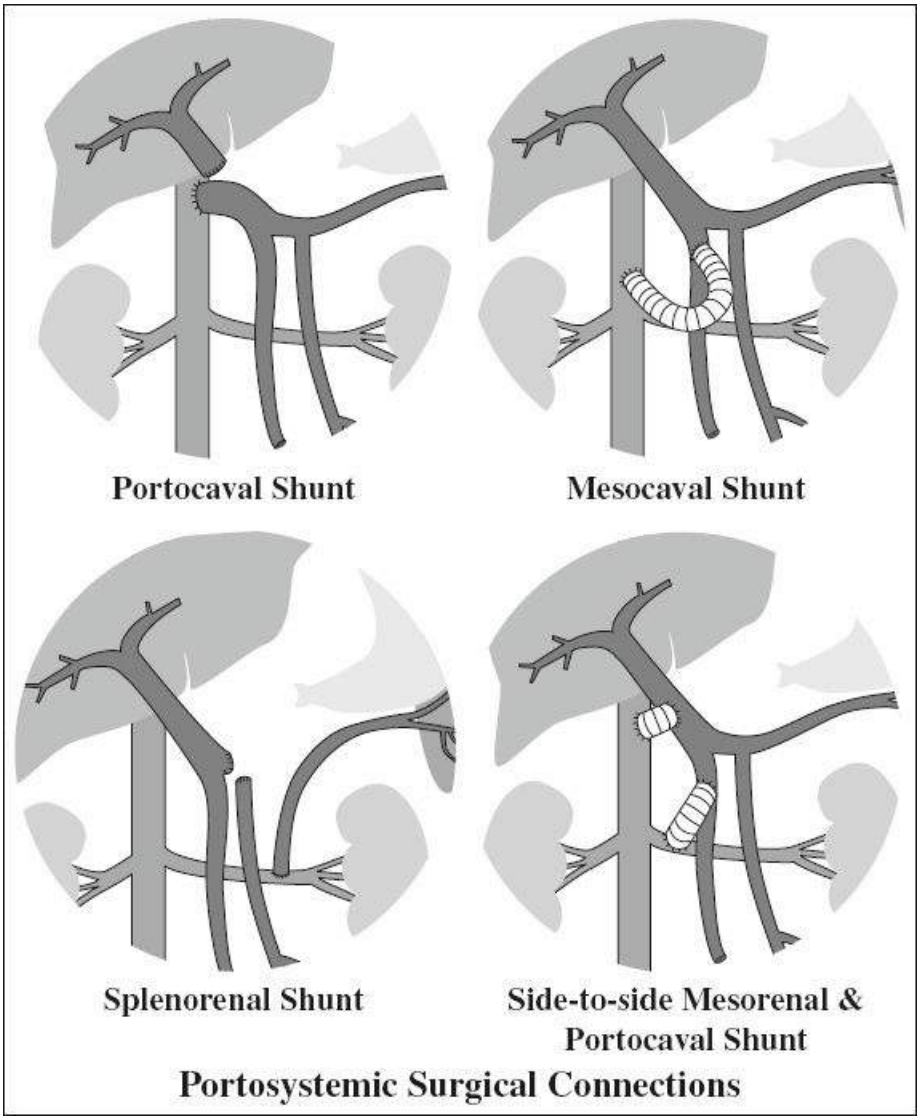
Portosystemic Surgical Connections

A. NONSELECTIVE SHUNT

= decompression of the entire portal system with increased risk of hepatic encephalopathy

1. Portocaval shunt

= portal vein → IVC end-to-side / side-to-side



2. Mesocaval shunt
   = synthetic graft between SMV and IVC
   (a) short "H-graft" to posterior wall of SMV
   (b) long "C-graft" to anterior wall of SMV
   (c) direct mesocaval shunt dividing IVC (rare)
3. Mesorenal shunt
4. Mesoatrial shunt
   = polytetrafluoroethylene graft between anterior wall of SMV superior to pancreas and right atrium coursing through abdomen + diaphragm into right thoracic cavity

B. SELECTIVE SHUNT
   = decompression of parts of the portal system with preservation of blood flow to the liver
   ◊ Contraindicated in patients with ascites
1. Distal splenorenal shunt = Warren shunt (popular)
   = splenic vein → left renal vein

Doppler criteria for shunt patency:

√ increased local velocities
√ turbulence + severe spectral broadening
√ dilatation of recipient vein at shunt site
√ phasic flow pattern in portal tributaries
√ hepatofugal flow in intrahepatic portal vein branches
√ reduction in size + number of portosystemic collaterals
√ reduction / absence of ascites or splenomegaly

Transjugular Intrahepatic Portosystemic Shunt (TIPS)

= portal decompression through percutaneously established shunt with expandable metallic stent between hepatic + portal veins within the liver

Indication: patients with esophageal + gastric variceal hemorrhage / refractory ascites ← advanced liver disease with portal hypertension, hepatorenal syndrome, hepatic hydrothorax, Budd-Chiari syndrome

Success: technical in 96–99%, control of variceal bleeding in 94–100%, control of refractory ascites in 58–84%

Type of stent: 10-mm Wall stent (curved), Palmaz stent (straight), Strecker stent, spiral Z stent
◊ polytetrafluoroethylene (PTFE)-covered stent has a higher patency rate over time

Shunt surveillance:
at regular 3–6-month intervals after initial assessment performed at 1 month after bare stent (Wallstent) placement / 1 month after initial placement of a covered stent

Assessment:
A. MORPHOLOGY
1. Ascites
2. Portosystemic collaterals
3. Size of spleen
4. Diameter of stent (usually 8–10 mm)
5. Configuration of stent: areas of narrowing
6. Extension of stent into portal + hepatic veins

B. HEMODYNAMICS
1. Direction of flow in: extrahepatic portal vein, R + L portal vein, SMV, splenic vein, all 3 hepatic veins, intrahepatic IVC, paraumbilical vein, coronary vein
2. Peak blood flow velocity within main portal vein
3. Peak blood flow velocity within proximal + mid + distal aspects of stent
4. Hepatic artery: PSV, EDV, RI

√ high-velocity turbulent flow (50–270 cm/sec) at least double that of pre-TIPS values
√ superimposed cardiac + respiratory variations
√ increase in hepatic artery velocities from 77 cm/sec (pre-TIPS) to 119 cm/sec (post-TIPS)
√ reversed flow direction within portal vein branches

Cx: A. Obstruction to flow
(1) Shunt obstruction (38%)
(2) Hepatic vein stenosis
B. Trauma

(a) Vascular injury
(1) Hepatic artery pseudoaneurysm
(2) Arterioportal fistula
(2) Intrahepatic / subcapsular hematoma
(3) Hemoperitoneum ← penetration of liver capsule
(b) Biliary injury
(1) Transient bile duct dilatation ← hemobilia
(2) Bile collection

C. Stent dislodgment with embolization to right atrium, pulmonary artery, internal jugular vein

Mortality: < 2% (intraperitoneal hemorrhage)

TIPS Malfunction / Failure

Cause: acute thrombosis, improper stent placement, intimal hyperplasia, change in stent configuration, bulging of liver parenchyma into shunt, iatrogenic dissection of portal vein

Prevalence: 31% at 1 year, 42% at 2 years

• recurrent bleeding = shunt abnormality in 100%

A. > 50% STENOSIS (in 30–80% within 12 months)
= > 50% reduction in diameter of stent lumen / portal pressure gradient > 12–15 mmHg

Site: hepatic vein between stent + IVC > hepatic venous end > in-stent > portal venous end

√ irregular filling defects along wall of shunt on color Doppler
◊ Pseudointimal hyperplasia is isoechoic to blood!

√ generalized decrease in shunt velocity:
√ portal vein inflow velocity < 30 cm/sec

Pre- and Post-TIPS Baseline Study
(under stable fasting conditions)

	Pre-TIPS	*Post-TIPS*
Portal vein velocity (cm/sec)	10–30	40–60
Mean portal vein velocity (cm/sec)	18 ± 6	55 ± 7
Portal pressure (mmHg)	37 ± 8	22 ± 6
Shunt peak velocity (cm/sec)		95 ± 58

√ maximal shunt velocity of < 60 cm/sec (> 95% sensitive + specific)
√ gradual decrease in shunt velocity over 1–6 months ← intimal hyperplasia
√ decrease in peak flow velocity in similar location within stent > 50 cm/sec relative to initial baseline study
√ decrease in maximal portal vein velocity > 33–50% from baseline over time

√ local increase in shunt velocity:
√ velocity transition zone within stent with flow acceleration by a factor of 2
√ abnormally high velocity > 190 cm/sec
√ increase in peak flow velocity in similar location within stent > 50 cm/sec relative to initial baseline study

√ change in flow direction:

√ reversal of portal venous flow direction (100% sensitive, 92% specific, 71% PPV, 100% NPV)
√ change in flow direction in collateral veins from baseline
√ retrograde flow in RHV (developing stenosis of right hepatic venous outflow tract)
√ loss of pulsatility of portal / shunt flow:
√ venous pulsatility index (Vmax – Vmin) ÷ Vmax < 0.16 (94% sensitive, 87% specific)
√ developing / recurring collateral vessels (eg, recanalized umbilical vein)
√ developing / worsening ascites / splenomegaly

B. OCCLUSION
√ absent flow within shunt
√ echogenic material within stent
› acute cause: prolonged procedural catheterization, leakage of bile into / around stent
› delayed cause: pseudointimal hyperplasia, stent shortening with delayed stent expansion

TIPS revision: balloon angioplasty, recanalization, insertion of additional stent, creation of parallel stent

POSTCHOLECYSTECTOMY SYNDROME

= symptoms recurring / persisting after cholecystectomy

Frequency:

mild recurrent symptoms in 9–25%; severe symptoms in 2.6–32.0% (result of 1,930 cholecystectomies):

› completely cured (61%)
› satisfactory improvement with
(a) persistent mild dyspepsia (11%)
(b) mild attacks of pain (24%)
› failure with
(a) occasional attacks of severe pain (3%)
(b) continuous severe distress (1.7%)
(c) recurrent cholangitis (0.7%)

Cause:

A. BILIARY CAUSES
(a) Incomplete surgery
1. Gallbladder / cystic duct remnant
2. Retained stone in cystic duct remnant (1%)
3. Overlooked CBD stone (5%)
(b) Operative trauma
1. Bile duct stricture
2. Bile peritonitis
3. Suture granuloma of cystic duct remnant
(c) Bile duct pathology
1. Fibrosis of sphincter of Oddi

2. Biliary dyskinesia
3. Biliary fistula
4. Cystic duct mucocele

(d) Residual disease in neighboring structures
1. Pancreatitis
2. Hepatitis
3. Cholangitis

(e) Overlooked bile duct neoplasia

B. EXTRABILIARY CAUSES (erroneous preoperative Dx)

(a) Other GI tract disease:
1. Inadequate dentition
2. Hiatus hernia
3. Peptic ulcer
4. Spastic colon

(b) Anxiety state, air swallowing

(c) Abdominal angina

(d) Carcinoma outside gallbladder

(e) Coronary artery disease

PYLEPHLEBITIS

= ACUTE SUPPURATIVE THROMBOPHLEBITIS OF PORTAL VEIN

[*pyle* , Greek = gate]

Cause: diverticulitis, appendicitis, pancreatitis, cholangitis, inflammatory bowel disease, intraabdominal infection with territory drained by portal vein

Organism: gram-negative bacilli

• nonspecific abdominal pain, sepsis

Prognosis: 0–12% (50%) mortality if treated (untreated)

US:

√ acute hyperechoic thrombus

√ hyperechoic shadowing foci within portal venous system = gas in portal vein

CT:

√ portal vein thrombus, portal vein gas

√ hepatic abscesses

√ low-attenuation tubular filling defect (= infected thrombus)expanding portal vein or its tributaries

Cx: hepatic abscess; bowel ischemia from retrograde propagation of thrombus; residual thrombus after successful treatment (frequent)

Rx: culture-specific systemic antibiotic; anticoagulation (controversial)

RICHTER SYNDROME

= development of large cell / diffuse histiocytic lymphoma in patients with CLL

Etiology: transformation / dedifferentiation of CLL lymphocytes

Incidence in CLL patients: 3–10%

Median age: 59 years

Medium time interval after diagnosis of CLL: 24 months
- fever (65%) without evidence of infection
- increasing lymphadenopathy + hepatosplenomegaly (46%)
- weight loss (26%), abdominal pain (26%)

Location: bone marrow, lymph nodes, liver, spleen, bowel, lung, pleura, kidney, dura

Prognosis: median survival time: 4 months from diagnosis of lymphoma; 14% rate of remission rate

SCHISTOSOMIASIS

◊ Major cause of portal hypertension worldwide: 200 million people affected

Parasites:

(a) parasitizing abdominal veins

› tributaries of superior mesenteric vein

1. Schistosoma mansoni: occurs in > 70 million inhabitants of parts of Africa, Middle East, Arabic peninsula, northern part of South America, West Indies, Caribbean

› tributaries of inferior mesenteric + superior hemorrhoidal veins

2. Schistosoma japonicum: Far East, coastal areas of China, Japan, Formosa, Philippines, Celebes

(b) parasitizing venules of urinary bladder

3. Schistosoma haematobium

Infection: cercariae penetrate intact human skin / buccal mucosa from contaminated fresh water (slow-moving streams, irrigation canals, paddy fields, lakes)

Cycle:

cercariae enter lymphatics + blood system via thoracic duct → larvae are transported into mesenteric capillaries → mature in portal system + liver into worms → worms mate and live in pairs within portal vein + tributaries for 10–15 years → female swims against blood flow to reach tributaries of superior mesenteric vein (S. mansoni) / tributaries of inferior mesenteric + superior hemorrhoidal veins (S. japonicum) → deposits eggs in wall of intestines or urinary bladder → eggs seed back to liver via portal vein + become trapped in periportal space or pass with feces → hatch within water to release miracidia → miracidia infect snail hosts → cercariae emerge after maturation from snails

Histo: chronic granulomatous reaction + abundant fibrosis along portal vein branches

- clinically mild infection with chronic course: fever, headache, myalgia, bloody diarrhea, abdominal pain, eosinophilia

@ Liver & spleen (10%)

√ hepatosplenomegaly

√ normal parenchymal echogenicity + small peripheral hyperechoic foci in 50%

√ marked diffuse thickening of echogenic walls of portal venules = periportal fibrosis = clay pipe stem fibrosis

◊ Schistosoma infection is the most frequent cause of liver fibrosis worldwide!

Fibrosis pattern of Schistosomiasis mansoni:

Cause: periportal fibrosis most prominent in central liver (large eggs deposit within central liver)

√ "turtleback / tortoise shell" appearance of liver:

√ thick fibrous bands around portal vein branches radiate from hilum perpendicularly to surface
√ shrunken liver with nodular surface contour
√ calcifications of large eggs (rare)

Fibrosis pattern of Schistosomiasis japonicum:

Cause: widespread peripheral periportal fibrosis (small eggs deposit near liver capsule)
√ thinner fibrous bands give a more uniform polygonal "honeycomb" appearance resembling fish scales
√ calcifications of interlobular septa (common)

√ portal vein dilatation in 73% (= presinusoidal portal hypertension)

@ Biliary tract
√ paucity of 2nd- and 3rd-order biliary branches ← biliary obstruction ← bile duct proliferation ← periportal fibrosis
√ irregular focally narrowed wall contours of bile ducts
√ hyperechoic gallbladder bed + thickened gallbladder wall

@ GI tract
√ gastric + esophageal varices
√ polypoid bowel wall masses (esp. in sigmoid)
√ granulomatous colitis
√ strictures with extensive pericolic inflammation
Cx: ileus

Dx: eggs in multiple fecal examinations
Rx: praziquantel

SHWACHMAN-DIAMOND SYNDROME

= rare autosomal recessive condition characterized by congenital absence of pancreatic exocrine tissue, bone marrow dysfunction, skeletal abnormalities and short stature
◊ 2nd most frequent cause of exocrine pancreatic insufficiency in childhood after cystic fibrosis!
Incidence: 1÷75,000 people
• pancreatic insufficiency, steatorrhea, failure to thrive
• recurrent respiratory and skin infections ← bone marrow hypoplasia; normal electrolytes in sweat
• trend for improvement with time
√ total fatty replacement of pancreas
√ metaphyseal chondrodysplasia resulting in dwarfism
DDx: cystic fibrosis (pancreatic calcifications, cyst formation, abnormal sweat test)

SEROUS CYSTADENOMA OF PANCREAS

= MICROCYSTIC CYSTADENOMA = GLYCOGEN-RICH CYSTADENOMA = MICROCYSTIC PANCREATIC LESION
= benign lobulated neoplasm composed of 1–20 mm small honeycomb cysts containing proteinaceous fluid separated by thin connective tissue septa
Frequency: ~ 50% of all cystic pancreatic neoplasms

Path: cysts separated by fibrous septa that radiate from a central scar, which may be calcified; thin fibrous pseudocapsule

Histo: cyst walls lined by cuboidal / flat glycogen-rich epithelial cells derived from centroacinar cells of pancreas (DDx: lymphangioma)

Types:

(a) classic microcystic form

(b) **oligocystic / macrocystic** form = larger + fewer serous cysts mimicking mucinous cystadenoma

Location: pancreatic head

√ lobulated contour, lack of wall enhancement

(c) solid form = microscopic serous cysts too small to resolve mimicking pancreatic neuroendocrine tumor

Mean age: 65 (range, 34–88) years; in 82% over 60 years of age; M÷F = 1÷2–4

Associated with: von Hippel-Lindau syndrome

• commonly incidental discovery at imaging; palpable mass

• pain, weight loss, malaise, anorexia, fatigue, jaundice

Location: any part of pancreas affected, slight predominance for head + neck

Size of mass: 5.0 (range, 1.4–27.0) cm in diameter

Size of cysts: typically < 10 (range, 1–20) mm; uncommonly a few large cysts (in < 5%) / cyst up to 8 cm in diameter

Number of cysts: > 6; typically innumerable

√ well-demarcated <u>lobulated</u> mass with smooth / nodular contour

√ cysts of honeycomb / bunch of grapes appearance

√ prominent <u>central stellate scar</u> in 30% (CHARACTERISTIC) ← fibrotic walls of collapsed centrally located cyst with tissue retraction

√ amorphous central calcifications (in 18%) in dystrophic area of stellate central scar ("sunburst")

√ ± progressive enlargement over months / years

√ pancreatic duct + CBD may be displaced / encased / obstructed

US:

√ mass as mixture of hypo- and hyperechoic areas

√ may appear as solid predominantly echogenic mass ← multiple acoustic interfaces

CT:

√ attenuation values close to water

√ may appear solid ← small cysts with large amount of fibrous tissue

√ contrast enhancement of septa (may be misleading)

MR:

√ cluster of small hyperintense cysts on T2WI

√ NO visible communication between cysts + pancreatic duct

√ late enhancement of thin fibrous septa

√ signal void in central scar ← coarse calcifications

√ delayed enhancement of scar on contrast-enhanced FLASH

Angio:

√ hypervascular mass with dilated feeding arteries, dense tumor blush, prominent draining

veins, neovascularity, occasional AV shunting, NO vascular encasement

Prognosis: no malignant potential

Rx: surgical excision / follow-up examinations

DDx: malignant mucinous cystic neoplasm (younger age, body + tail of pancreas, > 10 cm large at presentation)

SINUSOIDAL OBSTRUCTION SYNDROME

= SOS = venoocclusive disease

= blockage of small hepatic venules

Predisposition: stem cell / bone marrow recipients

Drugs: myeloablative regimens (eg, busulfan plus cyclophosphamide), dacarbazine, cisplatin, oxaliplatin, carboplatin, total body irradiation

Mechanism: necrosis of sinusoidal endothelial cells → extrusion into hepatic sinusoids → obstruction + congestion

- abdominal pain + swelling, weight gain
- ± elevation of serum enzyme levels

√ hepatomegaly and hepatic congestion

CT:

√ heterogeneous hepatic attenuation

CECT:

√ heterogeneous enhancement ← altered perfusion in areas of increased sinusoidal pressure from venous stasis

√ small obstructed hepatic venules NOT visible at imaging

MR:

√ heterogeneous liver with areas of increased signal intensity on T2WI ← edema

DDx: graft versus host disease, viral hepatitis, sepsis

SOLID PSEUDOPAPILLARY TUMOR OF PANCREAS

= SOLID AND PAPILLARY NEOPLASM = SOLID AND CYSTIC TUMOR = PAPILLARY-CYSTIC NEOPLASM = SOLID AND PAPILLARY EPITHELIAL NEOPLASM = HAMOUDI TUMOR

= rare slow-growing low-grade malignant tumor; often misclassified as nonfunctioning pancreatic endocrine tumor, cystadenoma, or cystadenocarcinoma of pancreas

◊ The classification of solid pseudopapillary tumors as a cystic pancreatic lesion has lead to confusion because many tumors are completely solid. Cystic components are secondary to tumor degeneration varying in size and morphology.

Prevalence: 1–2% of all pancreatic tumors

Mean age: 28 (range, 2–85) years; M÷F = 1÷9; predilection for black and East Asian patients

Path: large well-encapsulated solitary mass with considerable hemorrhagic necrosis + cystic degeneration

◊ Small tumors are predominantly solid

Histo: sheets + cords of cells arranged around a fibrovascular stroma

- vague upper abdominal fullness, discomfort and pain
- nausea, vomiting, gradually enlarging abdominal mass
- jaundice (rare, even with location in pancreatic head)

Location: pancreatic tail (36%), pancreatic head (34%); frequently exophytic obscuring pancreatic origin

Mean size: 6–10 (range, 0.5–34.5) cm

√ well-encapsulated inhomogeneous round / lobulated pancreatic mass with completely solid ± cystic portions ← tumor degeneration

√ may be completely cystic (when complicated by extensive necrosis + internal hemorrhage)

√ compression of adjacent structures without invasion

√ fluid-fluid or fluid-debris level (10–20%) ← hematocrit effect

√ ± stippled / punctate / amorphous dystrophic calcification (33%) rimlike in tumor capsule or chunky inside tumor

√ hypovascular with contrast enhancement less than pancreas / enhancement of solid tissue projecting toward center of mass

US:

√ echogenic rim of tumor capsule

√ echogenic mass with necrotic center / completely cystic with subcapsular rim of tumor

CT:

√ solid tumor component isoattenuating to pancreas

√ cystic component of 20–50 HU

√ hypoattenuating tumor pseudocapsule

MR:

√ hypointense fibrous capsule on T1WI + T2WI (80–100%)

√ solid well-circumscribed tumor:

√ iso- to hypointense on T1WI compared to pancreas

√ mildly increased T2 signal intensity

√ foci of high SI on T1WI (in 80–100%) + variable T2 signal intensity ← variable hemoglobin degradation products from internal hemorrhage (DISTINCTIVE FEATURE)

√ T2 signal intensity close to fluid in mostly cystic variety

CEMR:

√ enhancing soft-tissue components are uniformly present

√ early peripheral heterogeneous / ring enhancement greater than pancreas (70%)

√ gradual accumulation (= progressive fill-in) of contrast material within tumor

DDx: neuroendocrine tumor (early arterial enhancement)

√ hypointense to pancreas on delayed images

Angio:

√ hypo- to avascular with displacement of vessels

√ mild peripheral blush

Prognosis: (1) excellent after excision

(2) metastases (in 7–16%): omentum, lymph nodes, liver (usually solitary)

Rx: complete surgical excision (95% cure rate)

DDx: (1) Cystic neuroendocrine tumor (older age group, hypointense on T1, diffuse / ringlike enhancement)

(2) Microcystic adenoma (innumerable tiny cysts, older age group)

(3) Mucinous cystic neoplasm (large uni- / multilocular cysts, older age group)

(4) Nonfunctioning pancreatic endocrine tumor (hypervascular)

(5) Pleomorphic carcinoma of pancreas (smaller tumor in older patient)
(6) Pancreatoblastoma (childhood tumor)
(7) Calcified hemorrhagic pseudocyst

SPLENIC ANGIOSARCOMA

Prevalence: rare, < 100 cases in literature
Cause: usually NOT due to thorotrast or toxic exposure to vinyl chloride / arsenic as in liver angiosarcoma
Age: 50–60 years
• splenomegaly, abdominal pain
√ multiple nodules of varying size → usually enlarging spleen
√ solitary complex mass with variable contrast enhancement
√ metastasizes to liver (in 70%)
√ spontaneous rupture (in 33%)
MR:
√ focal / diffuse hypointense foci on T1WI + T2WI ← iron deposition from hemorrhage
Prognosis: 20% survival rate after 6 months

SPLENIC HAMARTOMA

= SPLENOMA
= rare typically single nonneoplastic lesion composed of a mixture of normal splenic elements
Etiology: congenital
May be associated with: hamartomas elsewhere as in tuberous sclerosis
Histo: (a) mixture of white + red pulp (most common)
(b) white pulp subtype = aberrant lymphoid tissue
(c) red pulp subtype = aberrant complex of sinusoids
• asymptomatic
CT:
√ attenuation equal to / hypodense to splenic tissue
√ prolonged heterogeneous enhancement
MR:
√ heterogeneously hyperintense on T2WI
√ diffuse heterogeneous enhancement, more homogeneous on delayed images

SPLENIC HEMANGIOMA

Cause: congenital, arising from sinusoidal epithelium
Prevalence: 0.03–14% (autopsy); M > F

◊ Most common primary splenic tumor!

Age: 20–50 years
Histo: proliferation of vascular channels lined by single layer of endothelium; mostly of cavernous type; may contain areas of infarction, hemorrhage, thrombosis, fibrosis
Associated with: generalized angiomatosis, Klippel-Trénaunay-Weber syndrome, Beckwith-Wiedemann syndrome, Turner syndrome

• asymptomatic or pain + fullness in LUQ
√ usually small single lesion < 4 cm, up to 17 cm in size
√ foci of speckled / snowflakelike calcifications
US:
√ well-marginated predominantly hyperechoic lesion
CT:
√ predominantly avascular cystic lesion
√ solid areas hypo- / isodense to normal spleen and enhancing
MR:
√ hypo- / isointense on T1WI + hyperintense on T2WI
√ hypointense areas ← hemosiderin deposits
√ progressive centripetal enhancement with persistent uniform enhancement on delayed images
NUC:
√ no uptake of ^{99m}Tc-sulfur colloid
Prognosis: slow growth, thus becoming symptomatic in adulthood
Cx: (1) Spontaneous splenic rupture (in up to 25%)
(2) Kasabach-Merritt syndrome (= coagulopathy, anemia, thrombocytopenia) with large hemangioma
(3) Portal hypertension
(4) Malignant degeneration

SPLENIC INFARCTION

◊ Most common cause of focal splenic defects!
Cause:
1. Embolic: bacterial endocarditis (responsible in 50%), atherosclerosis with plaque emboli, cardiac thrombus (atrial fibrillation, left ventricular thrombus), metastatic carcinoma
2. Local thrombosis: sickle cell disease (leading to functional asplenia); myelo- / lymphoproliferative disorders (CML most common); polycythemia vera; myelofibrosis with myeloid metaplasia + splenomegaly; Gaucher disease; collagen vascular disease; portal hypertension
3. Vasculitis: periarteritis nodosa
4. Vascular compromise of splenic artery: focal inflammatory process (eg, pancreatitis); thrombus from splenic artery aneurysm; splenic torsion
5. Therapeutic complication: transcatheter hepatic arterial embolization

mnemonic: PSALMS
Pancreatic carcinoma, **P**ancreatitis
Sickle cell disease / trait
Adenocarcinoma of stomach
Leukemia
Mitral stenosis with emboli
Subacute bacterial endocarditis

Anatomy: branches of the splenic artery are noncommunicating end arteries

• LUQ pain, fever; abnormal lactate dehydrogenase levels
• elevated erythrocyte sedimentation rate, leukocytosis
√ single / multiple focal wedge-shaped peripheral defects
√ global infarction
US:
√ initially ill-defined hypoechoic lesion ← inflammation, edema, necrosis
√ later increasingly well-defined echogenic lesion ← organization of infarct with fibrosis
CT phases:
(a) hyperacute phase (day 1)
√ mottled area of increased attenuation on NECT ← hemorrhage
√ large focal hyperattenuating lesion on CECT
√ mottled pattern of contrast enhancement
(b) acute (days 2–4) + subacute phase (days 4–8)
√ focal progressively more well-demarcated areas of decreased attenuation without enhancement
(c) chronic phase (2–4 weeks)
√ size decreases + attenuation returns to normal
√ complete resolution / residual contour defect
√ areas of calcification
Cx: acute febrile illness, abscess formation, pseudocyst formation, splenic rupture, hemorrhage

SPLENOSIS

= posttraumatic autotransplantation of splenic tissue to other sites (heterotopic splenic tissue)
Age: young men with history of trauma / splenectomy
Time of detection: mean age of 10 years (range, 6 months to 32 years) after trauma
Location: diaphragmatic surface, liver, greater omentum, small bowel serosa, parietal peritoneum, pleura after diaphragmatic rupture (attaches to peritoneal / pleural surface)
√ multiple small round / oval lobulated encapsulated sessile masses (implants)
Size: few mm to 3 cm ← limited blood supply from local neovascularization
US:
√ mass of homogeneously hypoechoic echotexture
CT:
√ isodense to normal spleen
√ attenuation identical to normal spleen in all phases of enhancement
MR:
√ hypointense on T1WI
√ heterogeneous enhancement (red + white pulp differences)
√ hyper- / rarely hypointense (← iron deposition) on T2WI
NUC:
√ uptake by ^{99m}Tc-sulfur colloid; ^{111}In-labeled platelets; ^{99m}Tc-heat-damaged RBC (best detection rate without uptake by liver)
Significance:
(1) protects against infection in pediatric patients

(2) may be confused with metastases / lymphoma
(3) responsible for disease recurrence after splenectomy (eg, idiopathic thrombocytopenic purpura)

DDx: accessory spleen

SPONTANEOUS PERFORATION OF COMMON BILE DUCT

Pathogenesis: unknown (? CBD obstruction, localized mural malformation, ischemia, trauma)

Age: 5 weeks to 3 years of age

- vague abdominal distension, varying acholic stools
- mild persistent hyperbilirubinemia

US:

√ biliary ascites / loculated subhepatic fluid
√ localized pseudocholedochal cyst in porta hepatis

Hepatobiliary scintigraphy:

√ radioisotope diffusely throughout peritoneal cavity

THOROTRASTOSIS

Thorotrast = 25% colloidal suspension of thorium dioxide; used as contrast agent between late 1920s and mid 1950s, in particular for cerebral angiography and liver spleen imaging; chemically inert with high atomic number of 90; > 100,000 people injected

Thorium dioxide = consists of 11 radioactive isotopes (Thorium-232 is major isotope); decay by means of alpha, beta, and gamma emission; biologic half-life of 14 billion years; hepatic dose of 1,000–3,000 rad in 20 years

Distribution: phagocytized by RES + deposited in liver (70%), spleen (30%), bone marrow, abdominal lymph nodes (20%)

√ linear network of metallic density contrast material in spleen, lymph nodes, liver
√ spleen may be shrunken / nonfunctional

Cx: hepatic fibrosis, angiosarcoma (50%), cholangiocarcinoma, hepatocellular carcinoma (latency period of 3–40 years; mean 26 years)

TYROSINEMIA

= rare autosomal recessive metabolic disorder

Country: increased prevalence in Canadian province of Quebec and parts of Scandinavia

Biochemistry: deficiency of enzyme fumarylacetoacetase (last step in catabolic pathway of tyrosine, serum methionine, urinary succinylacetone); ↑ levels of serum tyrosine as a precursor of dopamine, norepinephrine, epinephrine, melanin, thyroxin

A. ACUTE FORM
   - fulminant liver failure, often by 1 year of age

B. CHRONIC FORM
   = Fanconi syndrome with renal tubular dysfunction
   - vitamin D-resistant rickets
   - intermittent porphyria-like symptoms

- progressive liver failure in early childhood
- anemia, abnormal liver function tests, ↑ levels of α-fetoprotein

√ hepatosplenomegaly
√ micro- and macronodular cirrhosis (early childhood):
  √ regenerating nodules of 2–20 mm: hyper- (mostly) / iso- / hypoattenuating; hypo- / occasionally hyperechoic
  √ portal hypertension
  √ increased echogenicity (fibrosis + fatty infiltration)
√ nephromegaly with uniformly thickened renal cortices
√ nephrocalcinosis

Prenatal Dx: enzyme deficiency demonstrable in hepatocytes, skin fibroblasts, lymphocytes, amniocytes

Cx: hepatocellular carcinoma (in 37% beyond 2 years of age)

Rx: (1) Diet restricted in phenylalanine + tyrosine (alleviates kidney damage but does not prevent fatal outcome)

(2) 2-2-nitro-4-trifluoro-methylbenzoyl-1,3-cyclohexanedione (NTBC) inhibits 4-hydroxyphenylpyruvate dioxygenase + prevents formation of maleylacetoacetate and fumarylacetoacetate

(3) Liver transplantation (before HCC develops)

UNDIFFERENTIATED SARCOMA OF LIVER

= UNDIFFERENTIATED EMBRYONAL SARCOMA (UES) = MALIGNANT MESENCHYMOMA / SARCOMA

= rare highly malignant tumor of children

Prevalence: 4th–5th most common liver tumor in children

Age: < 2 months (in 5%); 6–10 years (in 52%); by 15 years (in 90%); up to 49 years; M÷F = 1÷1

Path: well-demarcated predominantly solid tumor mixed with cystic gelatinous areas and foci of hemorrhage + necrosis; often with fibrous pseudocapsule

Histo: primitive undifferentiated stellate / spindle-shaped sarcomatous cells closely packed in whorls + sheets / scattered loosely in a myxoid ground substance with foci of hematopoiesis (50%)

• painful RUQ mass and fever (5%)
• mild anemia + leukocytosis (50%)
• elevated liver enzymes (33%); normal α-fetoprotein

Spread: lung, pleura, peritoneum

Location: right lobe (75%); left lobe (10%); both lobes (15%)

Mean size: 14 (range, 10–29) cm

◊ Discordant findings between US (solid) + CT and MR (cystic)!

NUC:
  √ photodefect on sulfur colloid scan

US:
  √ large intrahepatic typically iso- to hyperechoic solid mass
  √ cystic areas up to 4 cm in diameter (foci of necrosis + old hemorrhage + cystic myxoid degeneration)

CT:
  √ cystic multiseptate mass of predominantly water attenuation (88% of tumor volume) due to

myxoid stroma
√ peripheral foci of soft tissue / septa of variable thickness
√ ± central foci of high attenuation (= hemorrhage)
√ occasional fluid-debris level
√ well-defined margins of mass ← dense enhancing peripheral rim of pseudocapsule

CECT:
√ predominantly peripheral enhancement on delayed images

MR:
√ focal mass with multiple cystic spaces, septations (best seen on MRI) and central necrosis
√ predominantly CSF signal intensity on T1WI + T2WI
√ hypointense rim on T1WI + T2WI (= fibrous pseudocapsule)
√ hyperintense areas of hemorrhage on T1WI
√ heterogeneous enhancement of solid components

Angio:
√ hypo- / hypervascular with stretching of vessels
√ scattered foci of neovascularity

Prognosis: frequently death within 12 months

Rx: multiagent chemotherapy followed by resection / liver transplantation

DDx: (1) Mesenchymal hamartoma (generally diagnosed by 2 years of age)
(2) Hydatid cyst (US shows solid nature of mass, delayed enhancement of solid components, peripheral eosinophilia)
(3) Abscess (history of travel / fever)
(4) Hepatoblastoma (uncommonly cystic, younger age group, elevated serum AFP level)
(5) HCC (generally solid, underlying liver disease, elevated serum AFP level)

WANDERING SPLEEN

= ABERRANT / FLOATING / PTOTIC / DRIFTING / DYSTOPIC / DISPLACED / PROLAPSED SPLEEN
= excessively mobile spleen on an elongated pedicle displaced from its usual position in LUQ

Incidence: < 0.2% / year

Cause: embryologically absent / malformed gastrosplenic + splenorenal ligaments; deficient / lax abdominal musculature (prune-belly syndrome, pregnancy)

Age: any (higher frequency in women of childbearing age)

• asymptomatic mobile abdominal / pelvic mass
• chronic vague lower abdominal / back pain
• nausea, vomiting, eructation, flatulence
• acute abdomen ← splenic infarction ← splenic torsion

√ empty splenic fossa + associated soft-tissue mass in center of abdomen / pelvis
√ inverted malpositioned stomach
√ splenic hilum often located anteriorly
√ displaced large spleen ← congestion during torsion

Cx:

1. **Splenic torsion**
   (a) with prolonged venous occlusion: perisplenitis, localized peritonitis, adhesions,

venous thrombosis, hypersplenism
• abdominal pain, nausea, vomiting
• fever, leukocytosis, palpable mass
√ ectopic location + increased size
√ abnormal ovoid / round contour of spleen
√ whorled appearance of twisted splenic pedicle
√ adjacent inflammatory changes + free fluid
CT:
√ low attenuation with heterogeneous enhancement
US:
√ NO flow within spleen on Doppler US
√ elevated resistive index in proximal splenic artery

(b) with arterial occlusion: hemorrhagic infarction, subcapsular / intrasplenic hemorrhage, gangrene, abscess formation, degenerative cysts, functional asplenism, bowel obstruction, necrosis of pancreatic tail

2. GI complications:
@ Stomach: compression, distension, volvulus, traction diverticulum, varices
@ Small bowel: dilatation, obstruction
@ Colon: compression, volvulus, laxity, ptosis

Rx:
1. Splenectomy (4% postsplenectomy sepsis)
2. Splenopexy
3. Conservative treatment (if asymptomatic)

ABDOMEN AND GASTROINTESTINAL TRACT

DIFFERENTIAL DIAGNOSIS OF GASTROINTESTINAL AND ABDOMINAL DISORDERS

ACUTE ABDOMEN IN CHILD

The majority of ER visits for acute abdominopelvic diseases do not require administration of IV contrast for MRI diagnosis

1. Intussusception
2. Appendicitis
3. Obstruction (previous surgery, hernia)
4. Acute gastroenteritis
5. Basilar pneumonia

RIGHT LOWER QUADRANT PAIN

A. Inflammation / Infection
    1. Acute appendicitis

        A normal or even nonvisualized appendix at CT virtually allows exclusion of appendicitis

    2. Crohn disease
    3. Infectious enterocolitis
    4. Neutropenic colitis
    5. Diverticulitis (colon, cecum, Meckel, appendix)
        (a) Colonic diverticulitis
        (b) Right colonic diverticulitis
        (c) Appendiceal diverticulitis
        (d) Meckel diverticulitis
        (e) Ileal diverticulitis

B. Malignancy
    1. Adenocarcinoma: perforation
    2. Lymphoma

C. Omental / mesenteric conditions
    1. Epiploic appendagitis
    2. Omental infarction
    3. Mesenteric adenitis

D. Miscellaneous
    1. Ingestion of nondigestable foreign body
    2. Intussusception
    3. Cecal volvulus
    4. Ischemic colitis

E. Ovarian disorders
    1. Hemorrhagic ovarian cyst
    2. Pelvic endometriosis
    3. Torsion of ovary
    4. Ovarian hyperstimulation syndrome
    5. Ruptured dermoid
F. Tubal disorders
    1. Ectopic pregnancy
    2. Hydrosalpinx
    3. Tubo-ovarian abscess
G. Uterine disorders
    1. Degenerating / torsed leiomyoma
    2. Ovarian vein syndrome
    3. Hematometra
H. Urinary tract disorders
    1. Nephro- and ureterolithiasis
    2. Cystitis

HEMOPERITONEUM

A. Traumatic hemoperitoneum
B. Nontraumatic hemoperitoneum
    (a) **Spontaneous hemoperitoneum**
        1. Highly vascular neoplasm: hepatocellular carcinoma (10–15%), hepatic angiosarcoma, metastases (lung carcinoma, renal cell carcinoma, melanoma), hepatic adenoma (!)
           Risk factors: large size of mass; peripheral / subcapsular location; ⇑ vascularity
           Pathophysiology: invasion of vessels; ⇑ intratumoral pressure; venous congestion ← venous thrombosis; lack of autoregulation of tumor vessels
        2. Splenomegaly → splenic rupture:
           viral infection (CMV, malaria, EBV); congenital disease; metabolic abnormality (Gaucher disease, amyloidosis); neoplasm (leukemia, lymphoma, hemangiomatosis, angiosarcoma)
        3. Gynecologic causes:
           hemorrhagic ovarian cyst (usually corpus luteal / follicular cyst); ectopic pregnancy; HELLP syndrome; endometriosis; uterine rupture
        4. Vascular lesion:
           ruptured arterial aneurysm (abdominal aorta, splenic artery, hepatic artery); ruptured pseudoaneurysm (of hepatic, splenic, gastroduodenal artery) in pancreatitis
    (b) iatrogenic
        1. Anticoagulation (more commonly bleeding into psoas / rectus muscle)
        2. Blood dyscrasias
        3. Invasive procedure / surgery

GASTROINTESTINAL HEMORRHAGE

Incidence: 1–2% of all hospital admissions (300,000 annually); increasing with age
Age: > 65 years (in 70%); M÷F = 2÷1
◊ Upper GI bleed affects younger, lower GI bleed older patients!
Mortality: 10–40% (highest for variceal bleeding); increases with age, shock, comorbidity
Prognosis: in 75–80% spontaneous resolution; in 25% recurrence

Massive acute GI bleeding can be intermittent from minute to minute. Failure to demonstrate active bleeding may therefore not prove cessation of bleeding!

- positive fecal occult blood test: Hemoccult®
- iron deficiency anemia ← slow intermittent bleed
- **hematemesis** = vomiting of fresh blood
- coffee-ground vomit ← partially digested dark blood
- **melena** = black tarry stool
- **hematochezia** = red blood per rectum *chézein* , Greek = defecate

Endoscopy (98% sensitive, 100% specific):
1st line tool for diagnosis + therapy of upper GI bleed.
Cause not identified in 20% of lower + 14% of upper GI bleed
NUC (93% sensitive, 95% specific):
CTA (increasing use, sequential to unenhanced CT):

A 3-phase CT angiogram (CTA = unenhanced + arterial + portal venous phase) provides the best and most reproducible results in acute gastrointestinal bleeding with a high degree of accuracy regarding location and cause!

N.B.: Barium / oral contrast may mask acute bleeding site!
√ hyperattenuating blood clot on unenhanced phase
√ extravascular blush best seen in portal venous phase ← enlarging focus of extravasation with higher attenuation
√ varied bleed morphology: linear jetlike / swirled / circular ellipsoid / pooled cloud-shaped / fluid–contrast level
√ cause of hemorrhage identified in 80%

Imaging of Acute Gastrointestinal Bleeding

Modality	*Bleeding Rate [mL/min]*	*Sensitivity [estimates]*
Endoscopy		95% (upper GI bleed) 53% (lower GI bleed)
^{99m}Tc-labeled RBCs	> 0.1	88%
3-phase CT angio	> 0.35	91% (active bleed) 46% (obscure bleed)
Catheter angiogram	> 0.5	63% (upper GI bleed) 39% (lower GI bleed)

Source:

A. UPPER GASTROINTESTINAL HEMORRHAGE (70%)
= bleeding site proximal to ligament of Treitz
Incidence: 0.1% of all hospital admissions
Mortality: 10%

• hematemesis, coffee-ground emesis, melena
• hematochezia (with rapid bleeding)
◊ Preferred method = endoscopy!
@ Esophagogastric junction
1. Esophageal varices (17–30%): 40% mortality
2. Mallory-Weiss syndrome (7–14%): low mortality
@ Stomach
1. Acute hemorrhagic gastritis (17–27%)
2. Gastric ulcer (10%)
3. Pyloroduodenal ulcer (17–25%)
Mortality: < 10% if under age 60; > 35% if over age 60
@ Other causes:
(a) neoplasm (2–5%)
(b) vascular lesion (2–3%): visceral artery aneurysm, AV malformation, vascular-enteric fistula
Average mortality: 8–10%
Rx:
(1) Transcatheter embolization (method of choice) abundant collaterals except for postoperative stomach
(2) Intraarterial vasopressin infusion (0.2–0.4 U/min)
Prognosis: controls 73% of gastric mucosal bleeding; high recurrence rate

B. LOWER GASTROINTESTINAL HEMORRHAGE (30%)
= bleeding site distal to ligament of Treitz
Incidence: 0.02% of all hospital admissions
Age: 200 x more likely in 80- than in 20-year-old
Mortality: 3.6%
@ Small intestine
tumor (eg, leiomyoma, hemangioma, metastases), ulcer, diverticula (eg, Meckel diverticulum), inflammatory bowel disease (eg, Crohn disease), vascular malformation, visceral artery aneurysm, aortoenteric fistula
@ Colorectal (70%)
› massive bleeding
1. Diverticulum (20–55%)
2. Colonic angiodysplasia (3–40%)
3. Biopsy
› low-rate bleeding
1. Benign / malignant tumor (8–26%)
2. Inflammatory bowel disease (6–22%)
3. Mesenteric varices
Rx:
(1) Intraarterial vasopressin infusion
Prognosis: 90% initial control rate; 30% control rate for recurrent bleeding
(2) Transcatheter embolization requires superselective catheterization using microcatheters + microembolic agents
Cx: 25% risk of bowel infarction + stricture

Obscure GI Bleed

= persisting / recurring bleeding from GI tract without obvious cause after EGD + colonoscopy

Incidence: 5–20% without identifiable bleeding source

Tagged RBC scanning is the most sensitive technique for detecting active arterial + venous bleeding sites over a prolonged period and is useful for intermittent bleeding!

Upper Gastrointestinal Lesion

1. **Cameron lesion**
   = ulcer in hiatal hernia sac with incidence of 5.3%
2. Fundic varices
3. Peptic ulcer
4. Angiectasia
5. Gastric antral vascular ectasia
6. **Dieulafoy lesion**
   [Paul Georges Dieulafoy (1839–1911), French physician and surgeon, chief of Hôtel-Dieu de Paris]
   = exulceratio simplex = uncommon developmental large tortuous 1–5 mm submucosal arteriole that erodes and bleeds
   Location: on lesser curvature of stomach within 6 cm of GE junction (75%), duodenum (14%), colon (5%)

Middle Gastrointestinal Lesion

(a) in patient < 40 years of age
   1. Tumor
   2. Meckel diverticulum
   3. Dieulafoy lesion
   4. Crohn disease
   5. Celiac disease

(b) in patient > 40 years of age
   1. Angiectasia
   2. NSAID enteropathy
   3. Celiac disease

(c) uncommon lesion
   1. Hemobilia
   2. Hemosuccus pancreaticus
   3. Aortoenteric fistula

Lower Gastrointestinal Lesion

1. Angiectasia
2. Neoplasm

Gastrointestinal Bleeding in Infant

(1) Peptic ulcer
(2) Varices

(3) Ulcerated Meckel diverticulum

Gastrointestinal Bleeding in Child

(1) Meckel diverticulum
(2) Juvenile polyp
(3) Inflammatory bowel disease
(4) Clotting disorder
(5) Arteriovenous malformation

Intramural Hemorrhage

A. VASCULITIS
   1. Henoch-Schönlein purpura
B. TRAUMA
   eg, complication of colonoscopic polypectomy
C. COAGULATION DEFECT
   1. Anticoagulant therapy
   2. Thrombocytopenia
   3. Disseminated intravascular coagulation
D. DISEASE WITH COAGULATION DEFECT
   1. Hemophilia
   2. Leukemia, lymphoma
   3. Multiple myeloma
   4. Metastatic carcinoma
   5. Idiopathic thrombocytopenic purpura
E. ISCHEMIC BOWEL DISEASE (often fatal)

• abdominal pain
• melena

Site: submucosal / intramural / mesenteric

√ "stacked coin" / "picket fence" appearance of mucosal folds ← symmetric infiltration of submucosal blood
√ "thumbprinting" = rounded polypoid filling defect ← focal accumulation of hematoma in bowel wall
√ separation + uncoiling of bowel loops
√ narrowing of lumen + localized filling defects (= asymmetric hematoma)
√ no spasm / irritability
√ mechanical obstruction + proximal distension of loops

US:

√ homogeneously hypoechoic symmetric thickening of a long stretch of affected bowel segment
√ ± preservation of mural stratification
√ marked luminal narrowing
√ normal / diminished / absent vascularity at Doppler

Cx: lead point for intussusception

Prognosis: resolution within 2–6 weeks

Scintigraphy for Gastrointestinal Bleeding

Detection depends on:

(1) Rate of hemorrhage

◊ If bleeding not detectable by RBC scintigraphy, it will not be detectable by angiography!

- RBC scan detects bleeding as low as 0.1 mL/min
- Catheter angiography requires bleeding rates of ≥ 0.5 mL/min:
  63% (39%) sensitive for upper (lower) GI bleed
  - ◊ Only 50% of angiograms will be positive after a positive scintigram!
  - ◊ A positive scintigram increases likelihood of a positive angiogram from 22% to 53%!
  - ◊ A hemodynamically unstable patient with systolic pressures < 100 mmHg should go to angiography!

(2) Continuous versus intermittent bleeding: most GI hemorrhages are intermittent

(3) Site of hemorrhage in reference to specific vascular territory: eg, celiac, superior mesenteric, inferior mesenteric artery

(4) Characteristics of radionuclide agent

^{99m}Tc-Labeled Autologous RBCs (In Vivtro Labeling Preferred)

◊ Generally preferred and accepted most sensitive imaging method for lower GI bleeding

◊ Serves to triage patients for angiography as a negative exam predicts a negative arteriogram

Indications: acute / intermittent arterial or venous bleeding; NOT useful in occult bleeding

Pharmacokinetics:

» remains in vascular system for a prolonged period

» liver + spleen activity are low allowing detection of upper GI tract hemorrhage

» low target-to-background ratio (high activity in great vessels, liver, spleen, kidneys, stomach, colon; probably related to free pertechnetate fraction)

Dose: 10–25 mCi

Imaging:

(a) flow imaging at 1 frame every 2 sec for 60 seconds immediately after radiotracer injection

(b) functional imaging at a rate of 1 frame per minute for up to 90 minutes presented as cine clips

(c) additional delayed static images at 2, 4, 6, 12 hours up to 24/36 hr as needed, each time coupled with cine loop

◊ Patient can be reimaged within 24 hours without relabeling RBCs when initial scintigram negative!

Localization of bleeding site:

may be difficult ← (1) rapid transit time (bowel motility can be reduced with 1 mg glucagon IV) or ← (2) too widely spaced time intervals; overall 83% positive correlation with angiography

√ progressive tracer accumulation over time in abnormal location

√ change in appearance over time ← bowel peristalsis

√ bleeding site conforms to bowel anatomy (localizing information may be misleading ← forward / backward peristalsis)

Sensitivity:
in 83–93% correctly identified bleeding site (50–85% within 1st hour, may become positive in 33% only after 12–24 hours); collection as small as 5 mL may be detected; superior to sulfur colloid
» 50% sensitivity for blood loss < 500 mL/24 hours
» > 90% sensitivity for blood loss > 500 mL/24 hours

False positives (5%):
(a) free pertechnetate fraction: physiologic uptake in stomach + intestine, renal pelvis + bladder
◊ Spot view of thyroid shows contamination!
(b) hepatic hemangioma, accessory spleen, varices, inflammation, isolated vascular process (AVM, venous / arterial graft)

False negatives: 9% for bleeding of < 500 mL/24 hours

GASTRIC BLEEDING

Initial test: sampling of gastric content via nasogastric tube / upper endoscopy
Cause: varices, peptic ulcer, angiectasia, gastritis
√ frequently stationary position of radiotracer
False positives:
(a) inefficient labeling with free ^{99m}Tc pertechnetate in normal gastric mucosa
(b) accumulation in accessory spleen / hepatic hemangioma overlapping stomach
√ absence of peristaltic motion

SMALL BOWEL BLEEDING

Other tests: upper + lower endoscopy, double-balloon enteroscopy, capsule endoscopy
Cause: tumor, Meckel diverticulum, Dieulafoy lesion, angiectasia, Crohn disease, celiac disease, hemobilia, aortoenteric fistula
False positives: inflammatory process with hyperemic accumulation of radiotracer (= fixed activity seen on initial flow images)

COLONIC BLEEDING

Initial test: ^{99m}Tc-labeled autologous RBCs
Cause: diverticulosis, angiodysplasia, neoplasm, internal hemorrhoids
False positives: activity in penis / ureter / bladder
◊ Lateral / "tail-on-detector" view!

^{99m}Tc-Sulfur Colloid

Indication: bleeding must be active at time of tracer administration; length of active imaging can be increased by fractionating dose
» Disappearance half-life of 2.5–3.5 minutes (rapidly cleared from blood by RES + low background activity)
» Active bleeding sites detected with rates as low as 0.04–0.1 mL/minute
» Not useful for upper GI bleeding (interference from high activity in liver + spleen) or bleeding near hepatic / splenic flexure

Dose: 10 mCi (370 MBq)

Imaging:

every image should have 500,000–1,000,000 counts with oblique + lateral images as necessary

(a) every 5 sec for 1 minute ("flow study" = radionuclide angiogram)

(b) 60-second images at 2, 5, 10, 15, 20, 30, 40, 60 min; study terminated if no abnormality up to 30 minutes

(c) delayed images at 2, 4, 6, 12 hours

√ extravasation of tracer seen in active bleeding

Specificity: almost 100% (rarely false-positive results due to ectopic RES tissue)

False positives: transplanted kidney, ectopic splenic tissue, modified marrow uptake, male genitalia, arterial graft, aortic aneurysm

^{99m}Tc-Pertechnetate

Indication: bleeding from functioning heterotopic gastric mucosa in Meckel diverticulum / intestinal duplication; consider in adults up to age 25 years; independent of bleeding rate

Pathophysiology: tracer accumulation in mucus-secreting cells

◊ Avoid barium GI studies + endoscopy + irritating bowel preparation prior to study!

Dose: 5–10 mCi (185–370 MBq)

Imaging:

(a) radionuclide angiogram 2–3 sec/frame for 1st minute

(b) sequential 5-minute images up to 20 minutes with 500,000–1,000,000 counts per image

Sensitivity: > 80%

enhanced by

» fasting for 3–6 hours to reduce gastric secretions passing through bowel

» nasogastric tube suction to remove gastric secretions

» premedication with pentagastrin (6 µg/kg SQ 15 min before study) to stimulate gastric secretion of pertechnetate

» premedication with cimetidine (300 mg qid x 48 hours) to reduce release of pertechnetate from mucosa

» voiding just prior to injection

False positives:

bowel inflammation (Barrett esophagus, duodenal ulcer, ulcerative colitis, Crohn disease), enteric duplication, hemangioma, AV malformation, aneurysm, volvulus, intussusception, urinary obstruction, uterine blush

False negatives:

ulcerated epithelium

HETEROTOPIC GASTRIC MUCOSA

= epithelial lesion

1. Esophagus
2. Duodenum
3. Small bowel

4. Meckel diverticulum
5. Duplication cyst

GI ABNORMALITIES IN CHRONIC RENAL FAILURE AND RENAL TRANSPLANTATION

@ Esophagus
1. Esophagitis: candida, CMV, herpes

@ Stomach & duodenum
1. Gastritis
√ thickened gastric folds (38%)
√ edema + erosions
Cause:
(a) imbalance of gastrin levels + gastric acid secretion due to
(1) reduced removal of gastrin from kidney with loss of cortical mass
(2) impaired acid feedback mechanism
(3) hypochlorhydria
(b) opportunistic infection (eg, CMV)
2. Gastric ulcer (3.5%)
3. Duodenal ulcer (2.4%)
4. Duodenitis (47%)

@ Colon

More severely + frequently affected after renal transplantation
1. Progressive distention + pseudoobstruction
Contributing factors: dehydration, alteration of diet, inactivity, nonabsorbable antacids, high-dose steroids
2. Ischemic colitis
(a) primary disease responsible for end-stage renal disease: eg, diabetes, vasculitis
(b) trauma of renal transplantation
3. Diverticulitis
Contributing factors: chronic obstipation, steroids, autonomic nervous dysfunction
4. Pseudomembranous colitis
5. Uremic colitis = nonspecific colitis
6. Spontaneous colonic perforation
Cause: nonocclusive ischemia, diverticula, duodenal + gastric ulcers

@ Pancreas
1. Pancreatitis
Cause: hypercalcemia, steroids, infection, immunosuppressive agents, trauma

@ General
1. GI hemorrhage
Cause: gastritis, ulcer, colonic diverticula, ischemic bowel, infectious colitis, pseudomembranous colitis, nonspecific cecal ulceration
2. Bowel perforation: in 1–4% of transplant recipients
3. Opportunistic infection
Organism: Candida, herpes, CMV, Strongyloides

4. Malignancy
   (a) skin tumors
   (b) lymphoma

IMMUNE-MEDIATED GASTROENTEROCOLITIS

1. Celiac disease
2. Eosinophilic esophagitis
3. Eosinophilic gastroenteritis

ENTEROPATHY

Protein-losing Enteropathy

A. DISEASE WITH MUCOSAL ULCERATION
   1. Carcinoma
   2. Lymphoma
   3. Inflammatory bowel disease
   4. Peptic ulcer disease
B. HYPERTROPHIED GASTRIC RUGAE
   1. Ménétrier disease
C. NONULCERATIVE MUCOSAL DISEASE
   1. Celiac disease
   2. Tropical sprue
   3. Whipple disease
   4. Allergic gastroenteropathy
   5. Gastrocolic fistula
   6. Villous adenoma of colon
D. LYMPHATIC OBSTRUCTION
   1. Intestinal lymphangiectasia
E. HEART DISEASE
   1. Constrictive pericarditis
   2. Tricuspid insufficiency

Malabsorption

= deficient absorption of any essential food materials within small bowel

A. PRIMARY MALABSORPTION
   = the digestive abnormality is the only abnormality present
   1. Celiac disease = nontropical sprue
   2. Tropical sprue
   3. Disaccharidase deficiencies
B. SECONDARY MALABSORPTION
   = occurring during course of gastrointestinal disease
   (a) enteric
      1. Whipple disease
      2. Parasites: hookworm, Giardia, fish tapeworm
      3. Mechanical defects: fistulas, blind loops, adhesions, volvulus, short circuits

4. Neurologic: diabetes, functional diarrhea
5. Inflammatory: enteritis (viral, bacterial, fungal, nonspecific)
6. Endocrine: Zollinger-Ellison syndrome
7. Drugs: neomycin, phenindione, cathartics
8. Collagen disease: scleroderma, lupus, polyarteritis
9. Lymphoma
10. Benign + malignant small bowel tumors
11. Vascular disease
12. CHF, agammaglobulinemia, amyloid, abetalipoproteinemia, intestinal lymphangiectasia

Causes of Radiographic Malabsorption Pattern

General	*Specifics*
Abnormal digestion	
↓ digestive juices	pancreatic / hepatic / biliary insufficiency
↑ digestive juices	Zollinger-Ellison gastrinoma, VIPoma
bowel disease	lactose intolerance, Crohn disease, celiac disease, tropical sprue, chronic ischemia
short small bowel	resection, bypass, Roux-en-Y
long small bowel	dysmotility, narcotics, psychotropics, hypothyroidism, radiation and chemotherapy
Abnormal ingestion	
high fat intaker	binge eating, enteric tube feeding
cathartics, nonabsorbable sugar	MiraLAX®, lactulose, mannitol, sorbitol, maltitol

(b) gastric
vagotomy, gastrectomy, pyloroplasty, gastric fistula (to jejunum, ileum, colon)

(c) pancreatic
pancreatitis, pancreatectomy, pancreatic cancer, cystic fibrosis

(d) hepatobiliary
intra- and extrahepatic biliary obstruction, acute + chronic liver disease

Roentgenographic Signs in Malabsorption

√ SMALL BOWEL WITH NORMAL FOLDS + FLUID
1. Maldigestion (deficiency of bile salt / pancreatic enzymes)
2. Gastric surgery
3. Alactasia

√ SMALL BOWEL WITH NORMAL FOLDS + WET
1. Sprue
2. Dermatitis herpetiformis

√ DILATED DRY SMALL BOWEL
1. Scleroderma

2. Dermatomyositis
3. Pseudoobstruction: no peristaltic activity

√ DILATED WET SMALL BOWEL

1. Sprue
2. Obstruction
3. Blind loop

√ THICKENED STRAIGHT FOLDS + DRY SMALL BOWEL

1. Amyloidosis: malabsorption is unusual
2. Radiation
3. Ischemia
4. Lymphoma (rare)
5. Macroglobulinemia (rare)

√ THICKENED STRAIGHT FOLDS + WET SMALL BOWEL

1. Zollinger-Ellison syndrome
2. Abetalipoproteinemia: rare inherited disease characterized by CNS damage, retinal abnormalities, steatorrhea, acanthocytosis

√ THICKENED NODULAR IRREGULAR FOLDS + DRY SMALL BOWEL

1. Lymphoid hyperplasia
2. Lymphoma
3. Crohn disease
4. Whipple disease
5. Mastocytosis

√ THICKENED NODULAR IRREGULAR FOLDS + WET SMALL BOWEL

1. Lymphangiectasia
2. Giardiasis
3. Whipple disease (rare)

Small Bowel Nodularity with Malabsorption

mnemonic: **W**hat **I**s **H**is **M**ain **A**im? **L**ay **E**ggs, **B**y **G**od

Whipple disease
Intestinal lymphangiectasia
Histiocytosis
Mastocytosis
Amyloidosis
Lymphoma, **L**ymph node hyperplasia
Edema
Blood
Giardiasis

PET IMAGING OF GI TRACT

GI Cancers with Low / Variable FDG Uptake

1. Any well-differentiated cancer
2. Mucinous carcinoma
3. Early MALT lesion

4. Hepatocellular carcinoma

Pathologic Uptake in GI Tract

Preparation: for bowel loop distension a neutral oral contrast agent containing sorbitol and 0.1% barium sulfate (Volumen®) is recommended

@ Esophagus
1. Reflux esophagitis
2. Radiation esophagitis
3. Barrett esophagus
4. Glycogenic acanthosis
5. Esophageal cancer

@ Stomach
1. Gastritis (NSAID, Helicobacter pylori)
2. GIST
3. Lymphoma
4. Adenocarcinoma (variable)

@ Small bowel
1. Inflammatory bowel disease
2. GIST
3. Lymphoma
4. Metastases (melanoma)

@ Colon
1. Inflammatory enterocolitis
2. Appendicitis, diverticulitis, abscess
3. Colon cancer

Abnormal Uptake of Bone Agents in Ascitic, Pleural, Pericardial Effusion

1. Uremic renal disease
2. Infection
3. Malignant effusion

ABDOMINAL MASS

Abdominal Mass in Neonate

A. RENAL (55%)
1. Hydronephrosis (25%)
2. Multicystic dysplastic kidney (15%)
3. Polycystic kidney
4. Mesoblastic nephroma
5. Renal vein thrombosis

B. GENITAL (15%)
1. Ovarian cyst
2. Hydrometrocolpos

C. GASTROINTESTINAL (15%)
1. Duplication

2. Volvulus
3. Cystic meconium peritonitis
4. Mesenteric cyst

D. NONRENAL RETROPERITONEAL (10%)
1. Adrenal hemorrhage
2. Neuroblastoma
3. Teratoma

E. HEPATOBILIARY (5%)
1. Hemangioendothelioma
2. Choledochal cyst
3. Hydrops of gallbladder

Abdominal Mass in Infant & Child

A. RENAL (55%)
1. Wilms tumor (22%)
2. Hydronephrosis (20%)
3. Cystic renal mass
4. Congenital anomaly

B. NONRENAL RETROPERITONEAL (23%)
1. Neuroblastoma (21%)
2. Teratoma

C. GASTROINTESTINAL (18%)
1. Appendiceal abscess (10%)
2. Hepatobiliary (6%)

D. GENITAL (4%)
1. Ovarian cyst / teratoma
2. Hydrometrocolpos

Abdominal Wall Mass

A. TUMOR
(a) benign
1. Desmoid tumor / fibromatosis
2. Lipoma
3. Neuroma
4. Hemangioma

(b) malignant
1. Metastatic implants
2. Primary malignancy
3. Lymphoma

B. COLLECTION
1. Hematoma / seroma
2. Abscess

C. HERNIA / REPAIR
1. Incisional hernia
2. Retained surgical material

3. Suture granuloma
4. Keloid
5. Endometriosis

ABNORMAL INTRAABDOMINAL AIR

Abnormal Air Collection

1. Abnormally located bowel = **Chilaiditi syndrome**
   = symptomatic hepatodiaphragmatic interposition of colon between liver and chest wall
   Prevalence: 0.025%–0.28%
   Cause: increased colonic mobility, reduced liver volume, lax suspensory ligament, phrenic nerve palsy, obesity
2. Pneumoperitoneum
3. Retropneumoperitoneum perforation of duodenum / rectum / ascending + descending colon, diverticulitis, ulcerative disease, endoscopic procedure
4. Gas in bowel wall gastric pneumatosis, phlegmonous gastritis, endoscopy, rupture of lung bulla
5. Gas within abscess located in subphrenic, renal, perirenal, hepatic, pancreatic space, lesser sac
6. Gas in biliary system = pneumobilia
7. Gas in portal venous system

Pneumoperitoneum

Cause:

A. DISRUPTION OF WALL OF HOLLOW VISCUS
   (a) trauma
   (b) iatrogenic perforation
   (c) diseases of GI tract
      1. Perforated gastric / duodenal ulcer
      2. Perforated appendix
      3. Ingested foreign-body perforation
      4. Diverticulitis: ruptured Meckel diverticulum / sigmoid diverticulum, jejunal diverticulosis)
      5. Necrotizing enterocolitis with perforation
      6. Inflammatory bowel disease: eg, toxic megacolon
      7. Obstruction† (gas traversing intact mucosa): neoplasm, imperforate anus, Hirschsprüng disease, meconium ileus
      8. Ruptured pneumatosis cystoides intestinalis† with "**balanced pneumoperitoneum**" (= free intraperitoneal air acts as tamponade of pneumatosis cysts thus maintaining a balance between intracystic air + pneumoperitoneum)
      9. **Idiopathic gastric perforation** = spontaneous perforation in premature infants: congenital gastric muscular wall defect

B. THROUGH PERITONEAL SURFACE
   (a) transperitoneal manipulation

1. Abdominal needle biopsy / catheter placement
2. Mistaken thoracentesis / chest tube placement
3. Endoscopic biopsy

(b) extension from chest†

1. Pneumothorax: ventilation, chest injury
2. Dissection from pneumomediastinum: positive pressure breathing, rupture of bulla / bleb, chest surgery
3. Bronchopleural fistula

(c) intraperitoneal rupture of urinary bladder with indwelling Foley catheter / retrograde cystography

(d) penetrating abdominal injury

C. THROUGH FEMALE GENITAL TRACT†

(a) iatrogenic

1. Perforation of uterus / vagina
2. Culdocentesis
3. Rubin test = tubal patency test
4. Pelvic examination

(b) spontaneous

1. Intercourse, orogenital insufflation
2. Douching
3. Knee-chest exercise, water skiing, horseback riding

D. INTRAPERITONEAL

1. Gas-forming peritonitis
2. Rupture of abscess

Note † = asymptomatic spontaneous pneumoperitoneum without peritonitis

√ air in lesser peritoneal sac

√ gas in scrotum ← open processus vaginalis

<u>Large collection of gas:</u>

√ "abdominal distension, NO gastric air-fluid level

√ "**football**" sign = large pneumoperitoneum outlining entire abdominal cavity

√ "double wall / bas-relief" sign = **Rigler sign**
[Leo Rigler (1896–1979), radiologist in Minneapolis, USA]
= air outlining the luminal + serosal surface of the bowel wall with patient in supine position (usually requires > 1,000 mL of free intraperitoneal gas + intraperitoneal fluid)

√ "**telltale triangle**" sign = triangular air pocket between 3 loops of bowel

√ depiction of diaphragmatic muscle slips = two or three 6–13-cm long and 8–10-mm wide arcuate soft-tissue bands directed vertically inferiorly + arching parallel to diaphragmatic dome superiorly

√ outline of ligaments of anterior inferior abdominal wall:

√ "inverted V" sign = outline of both lateral umbilical ligaments (containing inferior epigastric vessels)

√ outline of medial umbilical ligaments (= obliterated umbilical arteries)

√ "urachus" sign = outline of middle umbilical ligament

RUQ gas (best place to look for small collections):

√ single large area of hyperlucency over the liver
√ oblique linear area of hyperlucency outlining the posteroinferior margin of liver
√ "**doge's cap**" sign = triangular collection of gas in Morison pouch (posterior hepatorenal space)
√ outline of falciform ligament = long vertical line to the right of midline extending from ligamentum teres notch to umbilicus; most common structure outlined
√ "ligamentum teres" sign = air outlining fissure of ligamentum teres hepatis (= posterior free edge of falciform ligament) seen as vertically oriented sharply defined slitlike / oval area of hyperlucency between 10th and 12th rib within 2.5–4.0 cm of right vertebral border 2–7 mm wide and 6–20 mm long
√ ligamentum teres notch = inverted V-shaped area of hyperlucency along undersurface of liver
√ "saddlebag / mustache / cupola" sign = gas trapped below central tendon of diaphragm
√ parahepatic air = gas bubble lateral to right edge of liver

US (85.7% sensitive, 99.6% specific):

√ enhancement of peritoneal stripe
Note: normal peritoneal stripe = single / double hyperechoic line deep to anterior abdominal wall
√ posterior shadowing / reverberation artifacts depending on amount of free air
DDx: intraluminal bowel gas (associated with normal overlying peritoneal stripe)

Iatrogenic Pneumoperitoneum

1. Laparotomy / laparoscopy (58%)
absorbed in 1–24 days dependent on initial amount of air introduced and body habitus (80% in asthenic, 25% in obese patients)
◊ After 3 days free air should be followed with suspicion!
2. Leaking surgical anastomosis
3. Peritoneal dialysis
4. Feeding tube placement
5. Endoscopic perforation
6. Enema tip injury
7. Use of gynecologic instruments
8. Vigorous respiratory resuscitation
9. Diagnostic pneumoperitoneum
10. Diagnostic peritoneal lavage

Miscellaneous Causes of Pneumoperitoneum

1. Drugs: steroids, NSAID
2. Pneumatosis coli / intestinalis
3. Entry through female genital tract: douching, sexual intercourse, insufflation

Spontaneous Pneumoperitoneum

1. Perforated peptic ulcer
2. Ischemia

3. Bowel obstruction
4. Toxic megacolon
5. Inflammation: appendicitis, tuberculosis, necrotizing enterocolitis
6. Benign pneumoperitoneum of systemic sclerosis
7. Malignancy (8–10%): colorectal carcinoma (3–10%), gastrointestinal lymphoma

CT
- √ depiction of primary malignancy + site and extent of perforation
- √ pneumoperitoneum
- √ extravasation of bowel content + oral contrast
- √ contained leak
- √ gas within tumor
- √ formation of enteroenteric fistula

Traumatic Pneumoperitoneum

(a) Blunt trauma
(b) Penetrating trauma:
1. Perforating foreign body: eg, thermometer injury to rectum, vaginal stimulator in rectum
2. Barotrauma:
   (a) compressor air directed toward anus
   (b) pulmonary barotrauma
   (c) mechanical ventilation

Pseudopneumoperitoneum

= process mimicking free air

A. ABDOMINAL GAS
= presence of gas confined to inner layer of abdominal wall but external to parietal peritoneum
(a) gastrointestinal gas
1. "Pseudo-wall" sign = apposition of gas-distended bowel loops
2. Chilaiditi syndrome
3. Diaphragmatic hernia
4. Diverticulum of esophagus / stomach / duodenum
(b) extraintestinal gas
1. Retroperitoneal air: eg, rectal injury
2. Subdiaphragmatic abscess

B. CHEST
1. Pneumothorax
2. Empyema
3. Irregularity of diaphragm
4. Rib fracture

C. FAT
1. Subdiaphragmatic intraperitoneal fat
2. Interposition of omental fat between liver + diaphragm

Pneumoretroperitoneum

Cause:

(1) Traumatic rupture: usually duodenum
(2) Perforation of duodenal ulcer
(3) Gas abscess of pancreas (usually extends into lesser sac)
(4) Urinary tract gas: trauma, infection
(5) Dissected mediastinal air

√ kidney outlined by gas
√ outline of psoas margin ± gas streaks in muscle bundles

Pneumatosis Intestinalis

= PNEUMATOSIS CYSTOIDES INTESTINALIS = BULLOUS EMPHYSEMA OF THE INTESTINE = INTESTINAL GAS CYSTS = PERITONEAL LYMPHOPNEUMATOSIS

= cystic / linear gas collection in bowel wall

Cause:

◊ Attributed to at least 58 causative factors!

A. BOWEL NECROSIS / GANGRENE

◊ Most common + life-threatening cause!

Pathogenesis: damage + disruption of mucosa with entry of gas-forming bacteria into bowel wall (cysts contain 50% hydrogen = evidence of bacterial origin)

Necrotizing enterocolitis, ischemia + infarction (mesenteric thrombosis), neutropenic colitis, sepsis, volvulus, strangulation, emphysematous gastritis, caustic ingestion

Drugs Associated with Pneumatosis Intestinalis

Drug Class	*Common Agents*
Corticosteroids	
Chemotherapeutics	
Cytotoxic agents	methotrexate, etoposide, daunorubicin, cytarabine, fluorouracil, paclitaxel
Tyrosine kinase inhibitor	imatinib
Immunosuppressants	
Antidiabetics	
a-glucosidase inhibitors	voglibose, acarbose, miglitol
Others	lactulose, sorbitol

B. MUCOSAL DISRUPTION

Pathogenesis: increased intestinal gas pressure → overdistension and dissection of gas into bowel wall

(a) intestinal obstruction: pyloric stenosis, annular pancreas, imperforate anus, Hirschsprüng disease, meconium plug syndrome, obstructing neoplasm
(b) intestinal trauma: endoscopy ± biopsy, biliary stent perforation, sclerotherapy, bowel surgery, postoperative bowel anastomosis, penetrating / blunt abdominal trauma, trauma of child abuse, intracatheter jejunal feeding tube, barium enema
(c) infection / inflammation: peptic ulcer disease, intestinal parasites, tuberculosis,

peritonitis, inflammatory bowel disease (Crohn disease, ulcerative colitis, pseudomembranous colitis), neutropenic colitis, toxic megacolon, generalized sepsis; rotavirus gastroenteritis (in children)

(d) ruptured jejunal diverticula, Whipple disease, systemic amyloidosis

C. INCREASED MUCOSAL PERMEABILITY

Pathogenesis: defects in lymphoid tissue of bowel wall allows bacterial gas to enter bowel wall

(a) immunotherapy: graft-versus-host disease, organ transplantation, bone marrow transplantation

(b) others: AIDS enterocolitides, steroid therapy, chemotherapy, radiation therapy, collagen vascular disease (scleroderma, systemic lupus erythematosus, periarteritis dermatomyositis), intestinal bypass enteropathy, diabetes mellitus

D. PULMONARY DISEASE

Pathogenesis: alveolar rupture with air dissecting interstitially along bronchovascular bundles to mediastinum and retroperitoneally along vascular supply of viscera

Cause: chronic obstructive pulmonary disease (chronic bronchitis, emphysema, bullous disease of lung), asthma, cystic fibrosis, chest trauma (barotrauma from mechanical ventilation with positive end-expiratory pressure, chest tube), increased intrathoracic pressure associated with retching + vomiting

E. IDIOPATHIC

Path:

(a) microvesicular type = 10–100-mm cysts / bubbles within lamina propria

√ radiolucent clusters of cysts along contour of bowel wall (best demonstrated on CT)

√ segmental mucosal nodularity

DDx: polyposis at 3D CT colonography

(b) linear / curvilinear type = streaks of gas oriented parallel to bowel wall

Location: small bowel > colon; may be discontinuous with spread to distant sites along mesentery

Pneumatosis in small bowel / colon should be treated as an emergent finding until life-threatening causes such as bowel ischemia and impending perforation are excluded.

Site: subserosa > submucosa >> muscularis propria > mesentery; mesenteric side >> antimesenteric side

√ primary radiologic finding:

√ linear / cystic gas collection within bowel wall paralleling mucosa

√ secondary radiologic findings:

√ ± pneumoperitoneum / pneumoretroperitoneum (asymptomatic large pneumoperitoneum may persist for months / years)

√ ± gas in mesenteric + portal vein

√ free fluid

MR:

√ hypointense signal on 2-D dual-echo GRE MRI with blooming artifact ← effect of air on local magnetic field

US:

√ echogenic reverberation artifacts within bowel wall

DDx: "pseudopneumatosis" intestinalis from foreign bodies / staples within bowel wall, tiny bubbles of air trapped between bowel folds, misregistration of air bubbles outside ultrasound beam

Prognosis:

wide spectrum from innocuous to fatal; clinical outcome impossible to predict based on radiologic features

◊ Linear gas collections probably have a more severe connotation
◊ Pneumatosis of the colon is likely clinically insignificant
◊ Extent of pneumatosis is inversely related to severity of disease
◊ Bowel wall thickening + perienteric soft-tissue stranding = signs of life-threatening ischemia

Soap-bubble Appearance in Abdomen of Neonate

1. Feces in infant fed by mouth
2. Meconium ileus:
   gas mixed with meconium, usually RLQ
3. Meconium plug:
   gas in and around plug, in distribution of colon
4. Necrotizing enterocolitis: submucosal pneumatosis
5. Atresia / severe stenosis: pneumatosis
6. Hirschsprüng disease: impacted stool, sometimes pneumatosis

ABDOMINAL CALCIFICATIONS & OPACITIES

Opaque Material in Bowel

mnemonic: CHIPS

Chloral hydrate
Heavy metals: lead
Iron
Phenothiazines
Salicylates

Diffuse Peritoneal Calcifications

(a) systemic mineral imbalance ("metastatic")
   1. Uremia
   2. Hyperparathyroidism + paraneoplastic HPT

(b) dystrophic ← tissue injury / aging / disease
   › neoplasm
      1. Cystadenoma / serous adenocarcinoma of ovary
         √ granular, sandlike psammomatous calcifications
      2. Pseudomyxoma peritonei
         (a) pseudomucinous adenoma of ovary
         (b) mucocele of appendix
      3. Undifferentiated abdominal malignancy

› infection
1. Tuberculous peritonitis
√ mottled calcifications simulating residual barium
2. Pneumocystis carinii infection

› inflammation
1. Meconium peritonitis
2. Peritoneal dialysis with sclerosing peritonitis
√ sheetlike calcifications surrounding bowel and mesentery
3. Oil granuloma
√ annular / plaquelike calcifications

Focal Alimentary Tract Calcifications

A. ENTEROLITHS= fecalith = coprolith
[faex, *Latin* = dregs; kopros, *Greek* = dung]
1. Appendicolith: in 10–15% of acute appendicitis
2. Stone in Meckel diverticulum
3. Diverticular stone
4. Rectal stone
5. Proximal to partial obstruction: TB, Crohn disease

B. MESENTERIC CALCIFICATIONS
1. Dystrophic calcification of omental fat deposits + appendices epiploicae ← infarction / pancreatitis / TB
2. Cysts: mesenteric cyst, hydatid cyst
3. Calcified mesenteric lipoma

C. INGESTED FOREIGN BODIES

D. TUMOR
1. Mucocele of appendix
√ crescent-shaped / circular calcification
2. Mucinous adenocarcinoma of stomach / colon
= COLLOID CARCINOMA
√ small mottled / punctate calcifications in primary site ± in regional lymph node metastases, adjacent omentum, metastatic liver foci
3. Gastric / esophageal leiomyoma: calcifies in 4%
4. Lipoma

Foreign Objects in Abdominal Cavity

A. INTRALUMINAL OBJECT
(a) pathologic condition
1. Bezoar
2. Gallstone
(b) dislodged stent and tube
1. Biliary stent (in up to 6%)
2. Feeding tube
(c) ingestion of diagnostic device
1. pH meter capsule (Bravo™ pH capsule)

√ 6 x 5.5 x 25 mm metallic device

2. Endoscopic video capsule
   √ 11 x 26 mm metallic device

(d) accidental / nonaccidental ingestion

B. EXTRALUMINAL OBJECT

1. Prosthetic mesh for hernia repair:
   › 0.44 mm thick polypropylene
   √ line of attenuation similar to muscle
   › 1-mm thick polytetrafluoroethylene
   √ line of increased attenuation
2. Dropped gallstone = perforation / spillage: during laparoscopic cholecystectomy (in up to 30%)
3. Dropped surgical clip
4. Migrated / perforated IUD (1÷1,000 insertions)
   Cx in 15%: bowel obstruction, perforation of bowel / urinary bladder / mesentery, rectal stricture, rectouterine fistula
5. Hepatic packing with sponges (for 36–48 hours)
6. Bioabsorbable sponge for hemostasis: Gelfoam®, Surgicel®, microfibrillar collagen
   √ usually absorbed within 7–14 days
   √ mimick abscess due to numerous gas pockets

Packing agents mimic an abscess when imaged prior to absorption by 7–14 days post surgery.

7. Urethral bulking agent:
   › collagen: attenuation similar to soft tissue
   › carbon-coated microbeads: 1500–2000 HU
8. Retained surgical material (1÷1000–1500 surgeries): sponge (69%), instrument (31%)
   At risk: emergency surgery, unplanned change of procedure, obesity

A radiopaque marker on the scout image provides an important clue, but can be distorted by folding, disintegrate over time, or can be misinterpreted (as a calcification / oral contrast agent).

Mimicks of Foreign Bodies:

1. Heterotopic mesenteric ossification
   Cause: trauma, repeated intraabdominal surgeries
   Histo: mature trabeculae
   √ multiple high-density linear branching structures within mesentery extending to peritoneal surface
   √ trabecular architecture unchanged over time
   Cx: small bowel obstruction
   DDx: (1) Dystrophic calcifications
   (2) Extravasation of oral contrast (change in configuration, pooling following gravity, less dense over time)
   (3) Osseous metaplasia (trabecular architecture)
2. Heterotopic ossification in surgical incisions
   = subtype of traumatic myositis ossificans
   Prevalence: 25% of abdominal incisions

Location: vertical midline abdominal incisions (mainly), esp. in linea alba
√ trabecular architecture

3. Bogota bag
= clear sterilized plastic bag used for temporary abdominal closure to monitor secondary peritonitis
√ linear high-attenuation area along the direction of the surgical incision

Abdominal Wall Calcifications

A. IN SOFT TISSUES
1. Hypercalcemic states
2. Idiopathic calcinosis

B. IN MUSCLE
(a) parasites:
1. Cysticercosis = Taenia solium
√ round / slightly elongated calcifications
2. Guinea worm = dracunculiasis
√ stringlike calcifications up to 12 cm long

(b) injection sites from quinine, bismuth, calcium gluconate, calcium penicillin
(c) myositis ossificans

C. IN SKIN
1. Soft-tissue nodules: papilloma, neurofibroma, melanoma, nevi
2. Scar:
√ linear density
3. Colostomy / ileostomy
4. Tattoo markings

Abdominal Vascular Calcifications

A. ARTERIES
1. Atheromatous plaques
2. Arterial calcifications in diabetes mellitus

B. VEINS
phleboliths = calcified thrombus, generally seen below interspinous line
1. Normal / varicose veins
2. Hemangioma

C. LYMPH NODES
1. Histoplasmosis / tuberculosis
2. Chronic granulomatous disease
3. Residual lymphographic contrast
4. Silicosis

ABNORMAL INTRAABDOMINAL FLUID

Ascites

Ascites collects in well-defined areas of stasis / arrested flow:
(1) deep pelvic recesses: retrouterine space / pouch of Douglas in women, retrovesical space in

men
(2) right lower quadrant: near termination of small bowel mesentery at ileocecal junction
(3) superior aspect of the sigmoid mesocolon
(4) right paracolic gutter

Cause:

A. TRANSUDATE (most common cause)
(1) Cirrhosis (75%): poor prognostic sign
(2) Hypoproteinemia
(3) CHF
(4) Constrictive pericarditis
(5) Chronic renal failure
(6) Budd-Chiari syndrome

B. EXUDATE
(1) Carcinomatosis (2nd most common cause)
(2) TB peritonitis (3rd most common cause)
(3) Polyserositis
(4) Pancreatitis
(5) Meigs syndrome

C. HEMORRHAGIC / CHYLOUS FLUID

Early signs (accumulation in pelvis):
√ round central density in pelvis + ill-defined bladder top
√ thickening of peritoneal flank stripe
√ space between properitoneal fat and gut > 3 mm

Late signs:
√ Hellmer sign = medial displacement of lateral liver margins
√ medial displacement of ascending + descending colon
√ obliteration of hepatic + splenic angles
√ bulging flanks
√ gray abdomen
√ floating centralized loops
√ separation of loops

High-density Ascites

1. Tuberculosis: 20–45 HU; may be lower
2. Ovarian tumor
3. Appendiceal tumor

Neonatal Ascites

A. GASTROINTESTINAL
(a) perforation of hollow viscus
1. Meconium peritonitis
(b) inflammatory lesions
1. Meckel diverticulum
2. Appendicitis
(c) cyst rupture

1. Mesenteric cyst
2. Omental cyst
3. Choledochal cyst

B. PORTOHEPATIC
   (a) extrahepatic portal vein obstruction
      1. Atresia of veins
      2. Compression by mass
   (b) intrahepatic portal vein obstruction
      1. Portal cirrhosis: neonatal hepatitis
      2. Biliary cirrhosis: biliary atresia
   (c) bile leakage
      1. Biliary obstruction
      2. Biliary perforation

C. URINARY TRACT
   ◊ Urine ascites (most common cause): lower urinary tract obstruction + upper urinary tract rupture: posterior / anterior urethral valves, ureterovesical / ureteropelvic junction obstruction, renal / bladder rupture, anterior urethral diverticulum, bladder diverticula, neurogenic bladder, extrinsic bladder mass

D. GENITAL
   1. Ruptured ovarian cyst
   2. Hydrometrocolpos

E. HYDROPS FETALIS
   1. Immune hydrops
   2. Nonimmune hydrops: usually cardiac causes

F. MISCELLANEOUS
   1. Chylous ascites
   2. Lymphangiectasia
   3. Congenital syphilis, trauma
   4. Idiopathic

Chylous Ascites

IN ADULTS:	1.	Inflammatory process	35%
	2.	Tumor	30%
	3.	Idiopathic	23%
	4.	Trauma	11%
	5.	Congenital	1%
IN CHILDREN:	1.	Congenital	39%
	2.	Inflammatory process	15%
	3.	Trauma	12%
	4.	Tumor	3%
	5.	Idiopathic	33%

Fluid Collections

mnemonic: BLUSCHINGS

Biloma

Lymphocele, **L**ymphangioma, **L**ymphoma (almost anechoic by US)
Urinoma
Seroma
Cyst: pseudocyst, peritoneal inclusion cyst
Hemorrhage, **H**ematoma: aneurysm, AVM
Infection, Infestation: empyema, abscess, Echinococcus
Neoplasm (necrotic)
G I tract: dilated loops, ileus, duplication
Serosa: ascites, pleural fluid, pericardial effusion

Fluid Collection in Lesser Sac

A. Inflammatory exudate
    1. Acute pancreatitis
    2. Cholecystitis
    3. Perforated gastric ulcer
    4. Left perinephric abscess
    5. Ascending pelvic inflammation (rare): appendicitis, diverticulitis
B. Hemorrhage
    1. Injury of liver / spleen
    2. Hemorrhagic pancreatitis
    3. Bleeding from ruptured neoplasms
C. Postoperative fluid: gastric / hepatobiliary surgery

[D. Ascitic transudate (most common + associated with fluid elsewhere in peritoneal cavity): hepatic / renal failure]

Intraabdominal Cyst in Childhood

1. Omental cyst: greater omentum / lesser sac, multilocular
2. Mesenteric cyst: between leaves of small bowel mesentery
3. Choledochal cyst
4. Intestinal duplication
5. Ovarian cyst
6. Pancreatic pseudocyst
7. Cystic renal tumor
8. Abscess
9. Meckel diverticulum: communication with GI tract
10. Lymphangioma
11. Mesenteric lymphoma
12. Intramural tumor

DYSPHAGIA

= OROPHARYNGEAL IMPAIRMENT = SWALLOWING DYSFUNCTION

Prevalence: 22% in adult primary care population, M÷F = 1÷4; 13% in general population; in up to 50% of nursing home residents

Predisposed: gastroesophageal reflux disease (GERD), stroke, Alzheimer disease, multiple sclerosis, amyotrophic lateral sclerosis, Parkinson disease

Neuromuscular disorders and structural abnormalities increase with age. Look for a cause of dysphagia in elderly patients.

Cause:

(1) Cerebrovascular accident: stroke (most common cause in adults), cerebral palsy, Wallenberg syndrome (lateral medullary syndrome)
  ◊ 29–64% of stroke patients become dysphagic; 20% die from aspiration pneumonia
(2) Brain tumor
(3) Neuromuscular disease: myasthenia gravis, Eaton-Lambert syndrome, amyotrophic lateral sclerosis, muscular dystrophy, myotonic dystrophy, oculopharyngeal muscular dystrophy
(4) Neurodegenerative disorder: Parkinson disease, Alzheimer disease, aging-related changes, Huntington disease, progressive supranuclear palsy
(5) Demyelinating diseases: multiple sclerosis
(6) Connective tissue disease: dermatomyositis, polymyositis, Sjögren syndrome, lupus erythematosus, rheumatoid arthritis, scleroderma
(7) Metabolic disorder: hyperthyroidism, hypothyroidism, diabetes mellitus
(8) infection: poliomyelitis, neurosyphilis, encephalitis, meningitis, sarcoidosis
(9) GI disorder:
  › esophageal diverticulum
  › focal esophageal narrowing
  › extrinsic esophageal compression
  › lower esophageal sphincter hypertension
(10) Trauma: head and neck surgery, radiation therapy, spinal cord injury, traumatic brain injury
(11) Medications

• weight loss, slow eating, change in dietary habits
• recurrent pneumonia

Esophagography: anatomic and functional information about pharynx, esophagus, gastroesophageal junction (GEJ), gastric cardia, esophageal motility, gastroesophageal reflux

Modified barium swallow (standard of reference, performed with a swallowing / speech therapist):
swallowing function + response to therapeutic measures and necessary dietary requirements

Cx: dehydration, malnutrition, aspiration, pneumonia, death

DDx: odynophagia, globus sensation, heartburn

Oropharyngeal Dysphagia

= sensation of blockage / discomfort in throat

Common cause: stroke, head & neck surgery, radiation Rx

Pathophysiology:

› structural: Zenker diverticulum, tumor, web, extrinsic mass, cervical spine disease
› functional:
  (a) laryngeal penetration or aspiration

- coughing / choking before / during / after swallow → aspiration pneumonia

(b) soft-palate insufficiency
- nasal voice / nasal regurgitation

(c) abnormal oral phase of swallowing
- food dribbling, difficulty in chewing

(d) cricopharyngeal dysfunction

- "wet" voice during / after meal
- increased oral secretions, drooling
- chronic low-level secretions: esp. bronchial, chest
- difficulty initiating a swallow, hoarseness, dyspnea

Cx: respiratory problems, malnutrition, dehydration, bronchial spasms, airway obstruction

Substernal / Esophageal Dysphagia

= sensation of discomfort / blockage localized to between thoracic inlet and xiphoid process

Pathophysiology:
- › structural: ring stricture, extrinsic mass, tumor in esophagus / proximal stomach
- › functional: esophageal motility abnormality, gastroesophageal reflux disease (GERD)

- sensation of food sticking in chest / throat
- dysphagia primarily for solids
- oral or pharyngeal regurgitation

MECHANICAL INTESTINAL OBSTRUCTION

= occlusion / constriction of bowel lumen

Prevalence: 20% of acute abdominal admissions
- › 80% small bowel obstruction
- › 20% large bowel obstruction

Disturbances in Motility & Transit

1. Irritable bowel syndrome
2. Functional dyspepsia
3. Gastroparesis
4. Bloating / chronic idiopathic constipation

Air Progression in Neonates

stomach	within minutes after birth
entire small bowel	within 3 hours
sigmoid colon	after 8–9 hours

Cause of Absent Gas in Neonate

1. GI obstruction
2. Mechanical ventilation in severe respiratory distress
3. Continuous gastric suction

Cause of Delayed Passage of Gas in Neonate

1. Traumatic delivery

2. Septicemia
3. Hypoglycemia
4. Brain damage

Passage of Meconium

A. NORMAL
   › in 94% within 24 hours
   › in 99% within 48 hours
   Exceptions: prematurity, severely asphyxiated term infants
B. DELAYED PASSAGE
   1. Hirschsprüng disease
   2. Ileal / jejunal atresia
   3. Meconium ileus
   4. Meconium plug syndrome
   5. Colon atresia
   6. Imperforate anus

Common Causes of Obstruction in Children

Time of presentation:

Nursery	intestinal atresia, midgut volvulus, meconium ileus, Hirschsprü disease, small bowel atresia with meconium ileus, meconium p syndrome, small left colon syndrome, imperforate anus, obstru from duplication cyst
First 3 months	hypertrophic pyloric stenosis, inguinal hernia, Hirschsprüng disease, midgut volvulus
6–24 months	ileocolic intussusception
Childhood	appendicitis

Terminology:

High obstruction = proximal to midileum
   ◊ Rarely needs further radiologic evaluation
   • bilious vomiting (after first feeding)
   • abdominal distention
   √ few dilated bowel loops

Low obstruction = distal ileum / colon
   ◊ More difficult to accurately localize
   ◊ Requires contrast enema examination to diagnose microcolon, position of cecum, level of obstruction
   • abdominal distention + vomiting
   • failure to pass meconium
   √ many dilated intestinal loops

Intestinal Obstruction in Neonate

• abdominal distension, vomiting, failure to pass meconium
1. Duodenal atresia (50%), stenosis (40%), web (10%)
2. Midgut volvulus

3. Jejunal / ileal atresia
4. Meconium ileus
5. Meconium plug syndrome
6. Hirschsprüng disease
7. Necrotizing enterocolitis

NEONATAL OBSTRUCTION WITH MICROCOLON

1. Ileal atresia
2. Distal jejunal atresia
3. Meconium ileus

NEONATAL OBSTRUCTION WITH NORMAL COLON

1. Meconium plug
2. Hirschsprüng disease

Intestinal Obstruction in Infant & Child

1. Hypertrophic pyloric stenosis
2. Appendicitis
3. Intussusception

Gastric Outlet Obstruction

A. CONGENITAL LESION
   1. Antral mucosal diaphragm = antral web
   2. Gastric duplication: usually along greater curvature, abdominal mass in infancy
   3. Hypertrophic pyloric stenosis

B. MALIGNANT NARROWING (most common cause)
   1. Antral carcinoma: cause in adults in 30–35%
   2. Scirrhous carcinoma of pyloric channel
   3. Pancreatic adenocarcinoma
   4. Primary duodenal tumor
   5. Primary biliary tumor
   6. Lymphoma (rarely)

C. INFLAMMATORY NARROWING
   1. Peptic ulcer disease: significantly decreased over last 30 years due to advances in diagnosis + treatment
   2. Corrosive gastritis
   3. Crohn disease, sarcoidosis, syphilis, tuberculosis

D. OTHERS
   1. Prolapsed antral polyp / mucosa
   2. Bezoar
   3. Gastric volvulus
   4. Postoperative stomal edema

Abdominal plain film:

√ large smoothly marginated homogeneous mass displacing transverse colon + small bowel inferiorly

√ one / two air-fluid levels

Duodenal Obstruction

A. CONGENITAL
   1. Annular pancreas
   2. Peritoneal bands = Ladd bands
   3. Aberrant vessel

B. INFLAMMATORY NARROWING
   1. Chronic duodenal ulcer scar
   2. Acute pancreatitis: phlegmon, abscess, pseudocyst
   3. Acute cholecystitis: perforated gallstone

C. INTRAMURAL HEMATOMA
   1. Blunt trauma (accident, child abuse)
   2. Anticoagulant therapy
   3. Blood dyscrasia

D. TUMORAL NARROWING
   1. Primary duodenal tumors
   2. Tumor invasion: pancreas, right kidney, lymph node enlargement

E. EXTRINSIC COMPRESSION
   1. Aortic aneurysm
   2. Pseudoaneurysm

F. OTHERS
   1. Superior mesenteric artery syndrome: extensive burns, body cast, rapid weight loss, prolonged bed rest
   2. Bezoar (in gastrectomized patient)

mnemonic: VA BADD TU BADD

child	adult
Volvulus	**T**umor
Atresia	**U**lcer
Bands	**B**ands
Annular pancreas	**A**nnular pancreas
Duplication	**D**uplication
Diverticulum	**D**iverticulum

Abdominal plain film:
√ "double-bubble" sign = air-fluid levels in stomach + duodenum
√ frequently normal ← absence of gas from vomiting

Jejunal and Ileal Obstruction

= SMALL BOWEL OBSTRUCTION (SBO)

Frequency: accounts for 20% of all surgical admissions

Mortality: 5.5% due to strangulation (paradigm: "Never let the sun rise or set on an obstructed small bowel")

Cause:

A. CONGENITAL
   1. Jejunal atresia
   2. Ileal atresia / stenosis

3. Enteric duplication: located on antimesenteric side, mostly in ileum
4. Midgut volvulus: arrest in rotation + fixation of small bowel during fetal life
5. Mesenteric cyst from meconium peritonitis: located on mesenteric side
6. Meckel diverticulum

B. EXTRINSIC BOWEL LESION
1. Fibrous adhesions (50–80%): previous surgery (80%) peritonitis (15%), congenital / uncertain cause (5%)
◊ Postoperative adhesions are the most common cause!
√ abrupt change in bowel caliber
√ no other apparent cause at transition point
2. Hernia (10%): internal / external
3. Volvulus
4. Mass: extrinsic neoplasm (most commonly due to advanced peritoneal carcinomatosis), abscess, aneurysm, hematoma, endometriosis

C. LUMINAL OCCLUSION
(a) swallowed:
1. Foreign body: in children or in mentally disturbed / disabled patients
2. Bezoar
3. Gallstone
4. Inspissated milk
5. Bolus of Ascaris lumbricoides

(b) after birth:
1. Meconium ileus:
√ microcolon in cystic fibrosis
2. Meconium ileus equivalent

(c) other:
1. Intussusception (< 5% in adults)
2. Tumor (rare): eg, lipoma

D. INTRINSIC BOWEL WALL LESION
(a) neoplasm (< 2%)
1. Adenocarcinoma
2. Carcinoid tumor
3. Lymphoma
4. Gastrointestinal stromal tumor

(b) inflammatory lesion
1. Crohn disease (acute bowel wall thickening, chronic cicatricial stenosis, postsurgical)
2. Tuberculous enteritis
3. Eosinophilic gastroenteritis
4. Parasitic disease

(c) vascular insufficiency
1. Ischemia: arterial / venous occlusion
2. Radiation enteropathy: 1 year post radiation

(d) intramural hemorrhage
1. Blunt trauma

2. Henoch-Schönlein purpura
3. Anticoagulants

(e) strictures

1. Surgical anastomosis
2. Irradiation
3. Potassium chloride tablets
4. Massive deposition of amyloid

Plain abdominal radiograph (50–66% sensitive):

◊ High sensitivity only for high-grade obstruction!

Results: diagnostic in 50–60%; equivocal in 20–30%; normal / nonspecific / misleading in 10–20%

√ "candy cane" appearance in erect position = > 2–3 distended small bowel loops with gas-fluid levels (> 3–5 hours after onset of obstruction):

√ gas-fluid levels > 2.5 cm wide

√ gas-fluid levels differing > 2 cm in height from one another within same bowel loop

√ disparity in size between obstructed loops and contiguous small bowel loops of normal caliber beyond site of obstruction

√ small bowel positioned in center of abdomen

√ little / no gas + stool in colon with complete mechanical obstruction after 12–24 hours

√ "stretch" sign = erectile valvulae conniventes completely encircle bowel lumen

√ "stepladder appearance" in low obstruction (the greater the number of dilated bowel loops, the more distal the site of obstruction)

√ "string-of-beads" indicate peristaltic hyperactivity to overcome mechanical obstruction

√ hyperactive peristalsis / aperistalsis = fatigued small bowel

CAVE: little / no gas in small bowel ← fluid-distended loops may lead one to overlook obstruction

Location of obstruction:

(a) valvulae conniventes high + frequent = jejunum

(b) valvulae conniventes sparse / absent = ileum

Plain abdominal radiographic categories:

1. Normal
   = absence of small intestinal gas / gas within 3–4 variably shaped loops < 2.5 cm in diameter
2. Mild small bowel stasis
   = single / multiple loops of 2.5–3.0 cm in diameter with ≥ 3 air-fluid levels
3. Probable SBO pattern
   = dilated multiple gas- / fluid-filled loops with air-fluid levels + moderate amount of colonic gas
4. Definite SBO pattern
   = clearly disproportionate gaseous / fluid distension of small bowel relative to colon

UGI:

√ "snake head" appearance = active peristalsis forms bulbous head of barium column in an attempt to overcome obstruction

√ barium appears in colon > 12 hr

Enteroclysis for adhesive obstruction:
- √ abrupt change in caliber of bowel with normal caliber / collapsed bowel distal to obstruction
- √ stretched folds of normal pattern
- √ angulated + fixed bowel segment

Enteroclysis categories of SBO (Shrake):

(a) low-grade partial SBO
= sufficient flow of contrast material through point of obstruction so that fold pattern beyond obstruction is readily defined

(b) high-grade partial SBO
= stasis + delay in arrival of contrast so that contrast material is diluted in distended prestenotic loop with minimal contrast in postobstructive loop leading to difficulty in defining fold pattern after transition point

(c) complete SBO
√ no passage of contrast material beyond point of obstruction 3–24 hours after start of examination

CT (66% accurate, 78% specific, 63% sensitive [81–100% sensitive for high-grade obstruction, 48% sensitive for low-grade partial obstruction]):
- √ small bowel dilatation > 2.5 cm proximally with normal-caliber / collapsed loops distally:
  - √ "**small bowel feces**" sign (in 7–8%) = gas bubbles mixed with particulate matter immediately proximal to transition point (DDx: cystic fibrosis)
- √ discrepant caliber at transition zone from dilated to nondilated bowel:
  - √ point of transition = triangular beak immediately beyond dilated segment
  - √ level of obstruction best determined by relative lengths of dilated versus collapsed bowel
  - √ incomplete obstruction = passage of enteric contrast material through transition zone:
    - √ high-grade obstruction = 50% difference in caliber between proximal dilated loops + distal collapsed bowel

DDx: adynamic ileus (distension of entire small bowel)

US (89% accuracy):
- @ bowel motion in acute stage:
  - √ hyperperistalsis of bowel with back-and-forth movement of intraluminal contents + thin gut wall
- @ bowel motion in late stage (= prolonged obstruction):
  - √ aperistalsis ± thick edematous bowel wall
- √ small bowel loops dilated > 3 cm
- √ length of dilated segment > 10 cm
- √ colon collapsed
- √ level of obstruction determined by:

(a) location of dilated bowel loops:
√ bowel distal to obstructing lesion often smaller in diameter than more proximal loops
√ caliber of loops distal to obstructing lesion dependent on completeness of obstruction

(b) pattern of valvulae conniventes

√ **signs of bowel infarction**:

√ free fluid between dilated small bowel loops

√ aperistalsis

√ wall thickness of distended bowel segment > 3 mm

Strangulated Obstruction

= impaired circulation / ischemia of obstructed segment mainly ← delay in establishing diagnosis / surgical Rx

Prevalence: 10% of patients with SBO

At risk: patients with acute complete / high-grade SBO; risk increases over time

TRIAD:

(1) closed-loop obstruction of the involved segment (majority of cases)

(2) mechanical obstruction proximal to the involved segment

(3) venous congestion of the involved loop

CT (63–100% detection rate):

√ slight circumferential thickening of bowel wall:

√ increased wall attenuation

√ "target / halo" sign

√ serrated beaklike narrowing at site of obstruction (32–100% specific) = closed loop with regional mesenteric vascular engorgement + bowel wall thickening at the obstructed segment

√ unusual course of mesenteric vasculature

√ vascular compromise of affected bowel:

√ poor / lack of enhancement of bowel wall (100% SPECIFIC)

√ delayed prolonged enhancement of bowel wall

√ mesenteric haziness ← edema (95% specific)

√ diffuse engorgement of mesenteric vasculature

√ localized mesenteric fluid / hemorrhage

√ large amount of ascites

√ pneumatosis intestinalis

√ gas in portal vein

Prognosis: 20–37% mortality rate (compared with 5–8% for a recently reduced simple obstruction) due to delay in diagnosis: 8% (25%) for surgery performed in < 36 (> 36) hours

CLOSED-LOOP OBSTRUCTION

= obstruction at two adjacent points along the course of the bowel at a single site usually with involvement of mesentery

Pathophysiology: impaired venous ± arterial flow

◊ Most common cause of strangulation!

Cause: adhesion (75%), incarcerated hernia

√ fixation of bowel loop = no change in position:

√ "**coffee bean**" sign = gas-filled loop

√ "pseudotumor" = fluid-filled loop

√ U- or C-shaped dilated bowel loop on CT
√ increasing intraluminal fluid
√ "**beak**" sign = fusiform tapering of bowel ending at point of obstruction on CT / UGI
√ "whirl" sign = twisting of bowel + mesentery ← rotation of bowel around fixed point of obstruction on CT:
√ stretched engorged mesenteric vessels converging toward site of obstruction / torsion ± delayed enhancement
Cx: volvulus

Acquired Small Bowel Obstruction in Childhood

mnemonic: AAIMM
Adhesions
Appendicitis
Intussusception
Incarcerated hernia (most common in infancy)
Malrotation
Meckel diverticulum

Small Bowel Obstruction in Adulthood

mnemonic: SHAVIT
Stone (gallstone ileus)
Hernia (21%)
Adhesion (49%)
Volvulus
Intussusception
Tumor (16%)

SBO IN VIRGIN ABDOMEN OF ADULTHOOD

1. Bowel ischemia including ischemic stricture
2. Primary small bowel neoplasm
3. Metastatic small bowel neoplasm
4. Extrinsic abdominal mass
5. Internal / abdominal wall hernia
6. Crohn disease

Colonic Obstruction

Frequency: 25% of all intestinal obstructions
Cause:

A. NEONATAL COLONIC OBSTRUCTION
1. Meconium plug syndrome
2. Colonic atresia
3. Anorectal malformation: rectal atresia, imperforate anus
4. Hirschsprüng disease
5. **Functional colonic immaturity** (especially in premies + infants of mothers treated with magnesium or high doses of sedatives / opiates, children with septicemia, hypothyroidism, hypoglycemia, diabetic mothers)

› small left colon syndrome
› meconium plug syndrome

B. LUMINAL OBTURATION
1. Fecal impaction
√ bubbly pattern of large mass of stool
2. Fecaloma
3. Gallstone (in sigmoid narrowed by diverticulitis)
4. Intussusception

C. BOWEL WALL LESION
(a) malignant (60–70% of obstructions) predominantly in sigmoid
(b) inflammatory
1. Crohn disease
2. Ulcerative colitis
3. Mesenteric ischemia
4. Sigmoid diverticulitis (15%)
√ stenotic segment > 6 cm
5. Acute pancreatitis
(c) infectious:
› infectious granulomatous process
1. Actinomycosis
2. Tuberculosis
3. Lymphogranuloma venereum
› parasitic disease
1. Amebiasis
2. Schistosomiasis
(d) wall hematoma:
blunt trauma, coagulopathy

D. EXTRINSIC
(a) mass impression
1. Endometriosis
2. Large tumor mass: prostate, bladder, uterus, tubes, ovaries
3. Pelvic abscess
4. Hugely distended bladder
5. Mesenteritis
6. Poorly formed colostomy
(b) severe constriction
1. Volvulus (3rd most common cause): sigmoid colon, cecum, transverse colon, compound volvulus (= ileosigmoid knot)
2. Hernia: transverse colon in diaphragmatic hernia, sigmoid colon in left inguinal hernia
3. Adhesion

Abdominal plain-film patterns:
(a) dilated colon only = competent ileocecal valve
(b) dilated small bowel (25%) = incompetent ileocecal valve
(c) dilated colon + dilated small bowel = ileocecal valve obstruction ← cecal

overdistension

√ gas-fluid levels distal to hepatic flexure (fluid is normal in cecum + ascending colon); sign not valid with diarrhea / saline catharsis / enema

√ cecum most dilated portion (in 75% of cases); critical at 10 cm diameter (high probability for impending perforation)

◊ The lower the obstruction, the more proximal the distension!

BE: Emergency barium enema of unprepared colon in suspected obstruction!
Contraindicated in toxic megacolon, pneumatosis intestinalis, portal vein gas, extraluminal gas

ILEUS

[*ileus* = stasis / inability to push fluid along (term does not distinguish between mechanical and nonmechanical causes)]

= ADYNAMIC / PARALYTIC / NONOBSTRUCTIVE ILEUS

= derangement impairing proper distal propulsion of intestinal contents

Cause:

› in neonate:

1. Hyperbilirubinemia
2. Intracranial hemorrhage
3. Aspiration pneumonia
4. Necrotizing enterocolitis
5. Aganglionosis

› in child / adult:

1. Postoperative ileus
   - usually resolves by 4th postoperative day
2. Visceral pain: obstructing ureteral stone, common bile duct stone, twisted ovarian cyst, blunt abdominal / chest trauma
3. Intraabdominal inflammation / infection: peritonitis, appendicitis, cholecystitis, pancreatitis, salpingitis, abdominal abscess, hemolytic-uremic syndrome, gastroenteritis
4. Ischemic bowel disease
5. Anticholinergic drugs: atropine, propantheline, morphine + derivatives, tricyclic antidepressants, dilantin, phenothiazines, hexamethonium bromide
6. Neuromuscular disorder: diabetes, hypothyroidism, porphyria, lead poisoning, uremia, hypokalemia, amyloidosis, urticaria, sprue, scleroderma, Chagas disease, vagotomy, myotonic dystrophy, CNS trauma, paraplegia, quadriplegia
7. Systemic disease: septic / hypovolemic shock, urticaria
8. Chest disease: lower lobe pneumonia, pleuritis, myocardial infarction, acute pericarditis, CHF
9. Retroperitoneal disease: hemorrhage (spine trauma), abscess

mnemonic: Remember the P's

Pancreatitis
Pendicitis
Peptic ulcer
Perforation

Peritonitis
Pneumonia
Porphyria
Postoperative
Potassium paucity
Pregnancy
Pyelonephritis

• intestinal sounds decreased / absent; abdominal distension
√ large + small bowel ± gastric distension
√ decreased small bowel distension on serial films
√ delayed but free passage of contrast material

US:
√ patent dilated fluid filled bowel lumen
√ minimal peristalsis

Rx: not amenable to surgical correction

Localized Ileus

= isolated distended loop of small / large bowel
= SENTINEL LOOP

Often associated with: adjacent acute inflammatory process

Etiology:

1. Acute pancreatitis: duodenum, jejunum, transverse colon
2. Acute cholecystitis: hepatic flexure of colon
3. Acute appendicitis: terminal ileum, cecum
4. Acute diverticulitis: descending colon
5. Acute ureteral colic: GI tract along course of ureter

Intestinal Pseudoobstruction

A. Transient pseudoobstruction
   1. Electrolyte imbalance
   2. Renal failure
   3. Congestive heart failure
B. Acute colonic pseudoobstruction
C. Chronic pseudoobstruction
   1. Scleroderma
   2. Amyloidosis
D. Idiopathic pseudoobstruction
   1. Chronic intestinal pseudoobstruction syndrome
   2. Megacystis-microcolon-intestinal-hypoperistalsis syndrome

ESOPHAGUS

Esophageal Contractions

◊ Esophageal motor activity needs to be evaluated in recumbent position without influence of gravity!

PERISTALTIC EVENT = coordinated contractions of esophagus
PERISTALTIC SEQUENCE = aboral stripping wave clearing esophagus

Primary Esophageal Peristalsis

= orderly peristaltic sequence with progressive aboral stripping traversing entire esophagus with complete clearance of barium; centrally mediated (medulla) swallow reflex via glossopharyngeal + vagal nerve; initiated by swallowing

√ rapid wave of inhibition followed by slower wave of contraction

◊ Normal peristaltic sequence will be interrupted by repetitive swallowing before peristaltic sequence is complete!

Secondary Esophageal Peristalsis

= local peristaltic wave identical to primary peristalsis but elicited through esophageal distension = sensorimotor stretch reflex

◊ Esophageal motility can be evaluated with barium injection through nasoesophageal tube despite patient's inability to swallow!

Tertiary Esophageal Contractions

= nonpropulsive esophageal motor event characterized by disorderly up-and-down movement of bolus without clearing of esophagus

Cause:

1. Presbyesophagus
2. Diffuse esophageal spasm
3. Hyperactive achalasia
4. Neuromuscular disease:
   diabetes mellitus, parkinsonism, amyotrophic lateral sclerosis, multiple sclerosis, thyrotoxic myopathy, myotonic dystrophy
5. Obstruction of cardia:
   neoplasm, distal esophageal stricture, benign lesion, S/P repair of hiatal hernia

◊ Tertiary activity does not necessarily imply a significant motility disturbance!

Age: in 5–10% of normal adults during 4th–6th decade

(a) nonsegmental = partial luminal indentation

Location: in lower ²/₃ of esophagus

√ spontaneous repetitive nonpropulsive contraction

√ "yo-yo" motion of barium

√ "corkscrew" appearance = scalloped configuration of barium column

√ "rosary bead" / "shish kebab" configuration = compartmentalization of barium column

√ no lumen-obliterating contractions

(b) segmental = luminal obliteration (rare)

√ "curling" = erratic segmental contractions

√ "rosary-bead" appearance

Abnormal Esophageal Peristalsis

A. PRIMARY MOTILITY DISORDERS

1. Achalasia

2. Diffuse esophageal spasm
3. Presbyesophagus
4. Chalasia
5. Congenital tracheoesophageal fistula
6. Intestinal pseudoobstruction

B. SECONDARY MOTILITY DISORDERS

(a) connective tissue disease
1. Scleroderma
2. SLE
3. Rheumatoid arthritis
4. Polymyositis
5. Dermatomyositis
6. Muscular dystrophy

(b) chemical / physical injury
1. Reflux / peptic esophagitis
2. S/P vagotomy
3. Caustic esophagitis
4. Radiotherapy

(c) infection
› fungal: Candidiasis
› parasitic: Chagas disease
› bacterial: TB, diphtheria
› viral: Herpes simplex

(d) metabolic disease
1. Diabetes mellitus
2. Amyloidosis
3. Alcoholism
4. Electrolyte disturbances

(e) endocrine disease
1. Myxedema
2. Thyrotoxicosis

(f) neoplasm

(g) drug-related: atropine, propantheline, curare

(h) muscle disease
1. Myotonic dystrophy
2. Muscular dystrophy
3. Oculopharyngeal dystrophy
4. Myasthenia gravis (= disturbed motility only in striated muscle of upper ⅓ of esophagus)
√ persistent collection of barium in upper third of esophagus
√ findings reversed by cholinesterase inhibitor edrophonium (Tensilon®)

(i) neurologic disease
1. Parkinsonism
2. Multiple sclerosis

3. CNS neoplasm
4. Amyotrophic lateral sclerosis
5. Bulbar poliomyelitis
6. Cerebrovascular disease
7. Huntington chorea
8. Ganglioneuromatosis
9. Wilson disease
10. Friedreich ataxia
11. Familial dysautonomia (Riley-Day)
12. Stiff-man syndrome

Diffuse Esophageal Dilatation

= ACHALASIA PATTERN = MEGAESOPHAGUS

A. ESOPHAGEAL MOTILITY DISORDER
   1. Idiopathic achalasia
   2. Chagas disease: patients commonly from South America; often associated with megacolon + cardiomegaly
   3. Postvagotomy syndrome
   4. Scleroderma
   5. Systemic lupus erythematosus
   6. Presbyesophagus
   7. Ehlers-Danlos syndrome
   8. Diabetic / alcoholic neuropathy
   9. Anticholinergic drugs
   10. Idiopathic intestinal pseudoobstruction = degeneration of innervation
   11. Amyloidosis: associated with macroglossia, thickened small bowel folds
   12. Esophagitis

B. DISTAL OBSTRUCTION
   1. Infiltrating lesion of distal esophagus / gastric cardia (eg, carcinoma) = pseudoachalasia
   2. Benign stricture
   3. Extrinsic compression

mnemonic: MA'S TACO in a SHell
Muscular disorder (eg, myasthenia gravis)
Achalasia
Scleroderma
Trypanosomiasis (Chagas disease)
Amyloidosis
Carcinoma
Obstruction
Stricture (lye, potassium, tetracycline)
Hiatal hernia

Air Esophagram

1. Normal variant

2. Scleroderma
3. Distal obstruction: tumor, stricture, achalasia
4. Thoracic surgery
5. Mediastinal inflammatory disease
6. S/P total laryngectomy: esophageal speech
7. Endotracheal intubation + PEEP

Abnormal Esophageal Folds

A. TRANSVERSE FOLDS
   1. **Feline esophagus**
      frequently seen with gastroesophageal reflux; normally found in cats
      √ transient contraction of longitudinally oriented muscularis mucosae
   2. Fixed transverse folds
      ← scarring from reflux esophagitis
      √ stepladder appearance in distal esophagus

B. LONGITUDINAL FOLDS
   normal: 1–2 mm wide, best seen in collapsed esophagus
   √ > 3 mm with submucosal edema / inflammation
   1. Gastroesophageal reflux
   2. Opportunistic infection
   3. Caustic ingestion
   4. Irradiation

DDx: (1) Varices
   √ tortuous / serpentine folds that can be effaced by esophageal distension
   (2) Varicoid carcinoma
   √ fixed rigid folds with abrupt demarcation due to submucosal spread

Esophageal Inflammation

A. CONTACT INJURY
   (a) reflux related
      1. Peptic ulcer disease
      2. Barrett esophagus
      3. Scleroderma (patulous LES)
      4. Nasogastric intubation
   (b) caustic
      1. Foreign body
      2. Corrosives
   (c) thermic
      habitual ingestion of excessively hot meals / liquids

B. RADIATION INJURY

C. INFECTION
   1. Candidiasis
   2. Herpes simplex virus / CMV
   3. Diphtheria

D. SYSTEMIC DISEASE

(a) dermatologic disorders
- blistering of skin + mucous membranes in response to minor trauma

1. **Epidermolysis bullosa dystrophica**
   Histo: intraepidermal bullae
2. **Benign mucous membrane pemphigoid**
   = rare disease of unknown cause
   Histo: subepidermal bullae without acantholysis
   Age: 4th decade; M < F
   √ esophageal lesions (in 2–13%) most frequent at sites of relative stasis (aortic knob, carina, GE junction):
   √ thin smooth webs arising from anterior aspect
   √ stenoses of variable length
3. Pemphigus vulgaris

(b) others:
1. Crohn disease
2. Graft-versus-host disease
3. Behçet disease
4. Eosinophilic gastroenteritis

Esophageal Ulcer

A. PEPTIC
1. Reflux esophagitis: scleroderma
2. Barrett esophagus
3. Crohn disease
4. Dermatologic disorders: benign mucous membrane pemphigoid, epidermolysis bullosa dystrophica, Behçet disease

B. INFECTIOUS
1. Herpes
2. Cytomegalovirus

C. CONTACT INJURY / EXTERNAL INJURY
1. Corrosives: alkali, strictures in 50%
2. Alcohol-induced esophagitis
3. Drug-induced esophagitis
4. Radiotherapy: smooth stricture at > 4,500 rad
   √ shallow / deep ulcers conforming to radiation portal
5. Nasogastric tube
   √ elongated stricture in middle ⅓ + distal ⅓
6. Endoscopic sclerotherapy

D. MALIGNANT
1. Esophageal carcinoma

Location:
@ Upper esophagus
1. Barrett ulcer in islets of gastric mucosa

@ Midesophagus
1. Herpes esophagitis

2. CMV esophagitis
3. Drug-induced esophagitis

@ Distal esophagus
1. Reflux esophagitis
2. CMV esophagitis

DDx:

(1) Sacculation
= outpouching in distal esophagus due to asymmetric scarring in reflux esophagitis

(2) Esophageal intramural pseudodiverticula

(3) Artifact
(a) tiny precipitates of barium
(b) transient mucosal crinkling in inadequate distension
(c) irregular Z-line

Small Esophageal Ulcer (< 1 cm)

1. Herpes simplex virus type I
2. Drug-induced
3. Reflux esophagitis
4. Behçet disease
5. Benign mucous membrane pemphigoid
6. Acute radiation change

Large Esophageal Ulcer (> 1 cm)

1. Cytomegalovirus
2. Human immunodeficiency virus
3. Carcinoma
4. Drug-induced
5. Barrett esophagus
6. Sclerotherapy for varices

Double-barrel Esophagus

1. Dissecting intramural hematoma from emetogenic injury
2. Mallory-Weiss tear: trauma, esophagoscopy (in 0.25%), bougienage (in 0.5%), ingestion of foreign bodies, spontaneous (bleeding diathesis)
3. Intramural abscess
4. Intraluminal diverticulum
5. Esophageal duplication (if communication with esophageal lumen present)

Esophageal Diverticulum

1. Zenker diverticulum (pharyngoesophageal)
2. Killian-Jamieson diverticulum
3. **Interbronchial diverticulum**
= traction diverticulum
= response to pull from fibrous adhesions following lymph node infection (TB), contains all 3 esophageal layers
Location: usually on right anterolateral wall of interbronchial segment

√ calcified mediastinal nodes

4. **Interaorticobronchial diverticulum**
   = thoracic pulsion diverticulum
   Location: on left anterolateral wall between inferior border of aortic arch + upper margin of left main bronchus
5. **Epiphrenic diverticulum** (rare)
   Location: usually on lateral esophageal wall, right > left, in distal 10 cm
   √ often associated with hiatus hernia
   Cx: overflow aspiration
6. **Intramural esophageal pseudodiverticulosis**
   √ outpouching from mucosal glands

Tracheobronchoesophageal Fistula

= ESOPHAGORESPIRATORY FISTULA

Location:	esophagotracheal	52–57%
	esophagobronchial	37–40%
	esophagopulmonary	3–11%

CXR:
√ recurrent pulmonary consolidation
√ lung abscess
√ pleural effusion

Esophagography:
◊ Use low-osmolar hydrosoluble contrast material
√ may confirm Dx + identify site of fistula

CT:
√ oral contrast in airway lumen + lung parenchyma
√ surrounding soft-tissue thickening

A. CONGENITAL
   1. Congenital tracheoesophageal fistula

B. MALIGNANCY (in 60%)
   1. Lung cancer
      ◊ In < 1% of patients with lung cancer
   2. Metastases to mediastinal lymph nodes
   3. Esophageal cancer
      ◊ In 5–10% of patients with advanced esophageal cancer
      Location: middle ⅓ of esophagus
   4. Treatment of mediastinal malignancy by radiation, chemotherapy, laser, esophageal stent placement

C. TRAUMATIC
   1. Instrumentation: esophagoscopy, bougienage, pneumatic dilatation
   2. Blunt ("crush injury") / penetrating chest trauma
   3. Surgery
   4. Foreign-body perforation
   5. Corrosives

6. Postemetic rupture = Boerhaave syndrome

D. INFECTIOUS / INFLAMMATORY
   1. TB, syphilis, histoplasmosis, actinomycosis, Crohn disease
   2. Perforated diverticulum
   3. Pulmonary sequestration / cyst

Long Smooth Esophageal Narrowing

1. Congenital esophageal stenosis
2. Surgical repair of esophageal atresia
   √ interruption of primary peristaltic wave at anastomosis
   √ secondary contractions may produce retrograde flow with aspiration
   √ impaction of food
3. Caustic burns = alkaline burns
4. Alendronate (= inhibitor of osteoclastic activity)
5. Gastric acid: reflux, hyperemesis gravidarum
6. Intubation: reflux + compromise of circulation
7. Radiotherapy for esophageal carcinoma; tumor of lung, breast, or thymus; lymphoma; metastases to mediastinal lymph nodes
   Onset of stricture: usually 4–8 months post Rx
   Dose: 3,000–5,000 rad
8. Postinfectious: moniliasis (rare)

Focal Esophageal Narrowing

1. **Esophageal web**
   = 1–2-mm thick (vertical length) area of complete / incomplete circumferential narrowing
2. **Esophageal ring**
   = 5–10-mm thick (vertical length) area of complete / incomplete circumferential narrowing
3. **Esophageal stricture**
   = > 10 mm in vertical length
   mnemonic: LETTERS MC
   Lye ingestion
   Esophagitis
   Tumor
   Tube (prolonged nasogastric intubation)
   Epidermolysis bullosa
   Radiation
   Surgery, **S**cleroderma
   Moniliasis
   Congenital

Upper & Midesophageal Stricture

In the setting of hiatal hernia and gastroesophageal reflux, a focal stricture in the midesophagus is highly suggestive of Barrett esophagus.

1. Barrett esophagus

2. Mediastinal radiation therapy
3. Caustic esophagitis
4. Drug-induced stricture
5. Esophageal intramural pseudodiverticulosis
6. Dermatologic disorder: benign mucous membrane pemphigoid, epidermolysis bullosa dystrophica, erythema multiforme major
7. Graft-versus-host disease
8. Congenital esophageal stenosis
   = tracheobronchial remnant / cartilaginous ring in esophageal wall
9. Metastatic cancer (from subcarinal nodes / left mainstem bronchus)

DDx: Primary carcinoma: squamous cell carcinoma

Lower Esophageal Narrowing

mnemonic: SPADE

Scleroderma
Presbyesophagus
Achalasia; **A**nticholinergics
Diffuse esophageal spasm
Esophagitis

LONG DISTAL (LOWER) ESOPHAGEAL STRICTURE

A. SEVERE ACID EXPOSURE
   1. Nasogastric intubation
   2. Zollinger-Ellison syndrome
   3. Alkaline reflux esophagitis

B. INFLAMMATION
   1. Crohn disease

SHORT DISTAL (LOWER) ESOPHAGEAL STRICTURE

1. Reflux-induced ("peptic") esophagitis
2. Scleroderma
3. Carcinoma (adenocarcinoma)
4. Crohn disease
5. Schatzki ring

Esophageal Filling Defect

A. BENIGN TUMORS

< 1% of all clinical esophageal tumors; 20% at autopsy

(a) Subepithelial tumor (75%)
   = nonepithelial, intramural
   1. Leiomyoma (50% of all benign tumors)
      ◊ Most common subepithelial mass in esophagus
   2. Granular cell myoblastoma
   3. Lipoma, fibroma, lipoma, fibrolipoma, myxofibroma, hamartoma, hemangioma, lymphangioma, neurofibroma, schwannoma

√ primary wave stops at level of tumor

√ proximal esophageal dilatation + hypotonicity
√ rigid esophageal wall at site of tumoral implant
√ disorganized / altered / effaced mucosal folds around defect
√ tumor shadow on tangential view extending beyond esophageal margin

(b) Mucosal tumor (25%) = epithelial, intraluminal

1. **Squamous papilloma**
   = most common benign mucosal tumor; rarely multiple (as in esophageal papillomatosis)
   √ small sessile slightly lobulated polyp
   √ average size of 4 mm
2. **Fibrovascular polyp**
3. **Inflammatory esophagogastric polyp**
   = sentinel polyp = bulbous tip of thickened gastric fold
   Cause: sequelae of chronic reflux esophagitis
   Prognosis: no malignant potential
4. **Adenoma**
   = originates in Barrett mucosa
   √ rare sessile / pedunculated polyp
   Cx: malignant degeneration
5. Glycogen acanthosis

B. MALIGNANT TUMORS

◊ 80% of esophageal neoplasms are malignant!

1. Esophageal cancer
2. Carcinoma of cardia (= gastric cancer)
3. Metastases: malignant melanoma, lymphoma (< 1% of gastrointestinal lymphomas), stomach, lung, breast

C. VASCULAR

1. Varices

D. INFECTION / INFLAMMATION

1. Candida / herpes esophagitis
2. Drug-induced inflammatory reaction

E. CONGENITAL / NORMAL VARIANT

1. Prolapsed gastric folds
2. Esophageal duplication cyst (0.5–2.5% of all esophageal tumors)

F. FOREIGN BODIES

1. Retained food particles: chicken bone, fish bone, pins, coins, small toys, meat
2. Undissolved effervescent crystals
3. Air bubbles

Esophageal Mucosal Nodules / Plaques

plaque = discrete irregular / ovoid elevation barely protruding above mucosal surface
nodule = small more rounded elevation

1. Candida esophagitis
2. Reflux esophagitis (early stage)
3. Barrett esophagus

4. Glycogen acanthosis
5. Superficial spreading carcinoma
6. Esophageal varices
7. Artifacts: undissolved effervescent agent, air bubbles, debris

Extrinsic Esophageal Impression

Cervical Causes of Esophageal Impression

A. OSSEOUS LESIONS
   1. Anterior marginal osteophyte / DISH
   2. Anterior disk herniation
   3. Cervical trauma + hematoma
   4. Osteomyelitis
   5. Bone neoplasm

B. ESOPHAGEAL WALL LESIONS
   (a) muscle
      1. Cricopharyngeus
      2. Esophageal web
   (b) vessel
      1. Pharyngeal venous plexus
      2. Lymph node enlargement

C. ENDOCRINE ORGANS
   1. Thyroid / parathyroid enlargement (benign / malignant)
   2. Fibrotic traction after thyroidectomy

D. Retropharyngeal / mediastinal abscess

Thoracic Causes of Esophageal Impression

A. NORMAL INDENTATIONS aortic arch, left mainstem bronchus, left inferior pulmonary vein, diaphragmatic hiatus

B. ABNORMAL VASCULATURE right-sided aortic arch, cervical aortic arch, aortic unfolding, aortic tortuosity, aortic aneurysm, double aortic arch ("reverse S"), coarctation of aorta ("reverse figure 3"), aberrant right subclavian artery = **arteria lusoria** (semilunar / bayonet-shaped imprint upon posterior wall of esophagus), aberrant left pulmonary artery (between trachea + esophagus), anomalous pulmonary venous return (anterior), persistent truncus arteriosus (posterior)

C. CARDIAC CAUSES
   (a) enlargement of chambers
      left atrial / left ventricular enlargement: mitral disease
      (esophageal displacement backward + to the right)
   (b) pericardial mass
      pericardial tumor / cyst / effusion

D. MEDIASTINAL CAUSES mediastinal tumor, lymphadenopathy (metastatic, tuberculous), inflammation, cyst

E. PULMONARY CAUSES pulmonary tumor, bronchogenic cyst, atypical pulmonary fibrosis (retraction)

F. ESOPHAGEAL ABNORMALITIES
   1. Esophageal diverticulum
   2. Paraesophageal hernia
   3. Esophageal duplication

STOMACH

Gastroesophageal Reflux

89% correlation with acid reflux test

Cause:

(1) Decreased pressure of lower esophageal sphincter
  (a) transient-complete relaxation of LES
  (b) low resting pressure of LES
(2) Transient increase in intraabdominal pressure
(3) Short intraabdominal esophageal segment

Age of children: usually 6–9 months, up to 2 years

- poor weight gain, vomiting, aspiration, choking
- asthmatic episodes, stridor, apnea

Detection: upper GI examination with barium, distal esophageal sphincter pressure measurements, 24-hr pH probe measurement in distal esophagus (gold standard), radionuclide examination

Preparation: 4-hour / overnight fasting; abdominal sphygmomanometer (for adults)

Dose: 0.5–1.0 mCi ^{99m}Tc-sulfur colloid in 300 mL of acidified orange juice (150 mL juice + 150 mL 0.1 N hydrochloric acid) followed by "cold" acidified orange juice

Imaging: at 30–60-second intervals for 30–60 min images taken in supine position from anterior; sphygmo-manometer inflated at 20, 40, 60, 80, 100 mmHg

Interpretation:

Reflux (in %) = $[\text{counts}_{\text{esophageal}} - \text{counts}_{\text{background}}] / \text{counts}_{\text{gastric}}) \bullet 100$

√ up to 3% magnitude reflux is normal

√ evidence of pulmonary aspiration (valuable in pediatric age group)

Cx: reflux esophagitis secondary to

(a) <u>delayed clearance time of esophageal acid load</u>: tertiary / repetitive esophageal contractions, supine position of refluxor, aspiration of saliva, stimulation of salivary flow, stretched phrenoesophageal membrane in hiatal hernia
(b) <u>delayed gastric emptying</u>: increased intragastric pressure (gastric outlet obstruction), viral gastropathy, diabetes

Prognosis in childhood:

(1) Self-limiting process with spontaneous resolution by end of infancy (in majority of patients)
(2) Persistent symptoms until age 4 (⅓ of patients)
(3) Death from inanition / recurrent pneumonia (5%)
(4) Cause of recurrent respiratory infections, asthma, failure to thrive, esophagitis, esophageal stricture, chronic blood loss, sudden infant death syndrome (SIDS)

Rx: (1) Conservative therapy:
avoidance of food + drugs that decrease pressure in LES, elevation of head during sleep, acid neutral-ization, cimetidine / ranitidine (reduction of acid production), metoclopramide / domperidone (increase sphincter pressure + promote gastric emptying)

(2) Antireflux surgery

Gastric Emptying

◊ Rates of gastric emptying vary widely between subjects and even in the same subject at different times

Dose: 0.5–1 mCi

(a) ^{99m}Tc-sulfur colloid cooked with egg white / liver pâté as solid food

(b) ^{111}In-DTPA in milk, water, formula, juice for simultaneous measurement of liquid phase

Imaging: 1-minute anterior abdominal images obtained at 0, 10, 30, 60, 90 min in erect position if dual-head camera available; anterior and posterior imaging performed with geometric mean activity calculated

Pharmacokinetics:

79% tracer activity in stomach for solid phase at 10 minutes; 65% at 30 minutes; 33% at 60 minutes; 10% at 90 minutes

Normal result: 50% of activity in stomach at time zero; should empty by 60 ± 30 minutes

√ acutely delayed emptying in stress (pain, cold), drugs (morphine, anticholinergics, L-DOPA, nicotine, β-adrenergic antagonists), postoperative ileus, acute viral gastroenteritis, hyperglycemia, hypokalemia

√ chronically delayed gastric emptying in gastric outlet obstruction, postvagotomy, gastric ulcer, chronic idiopathic intestinal pseudoobstruction, GE reflux, progressive systemic sclerosis, dermatomyositis, spinal cord injury, myotonia dystrophica, familial dysautonomia, anorexia nervosa, hypothyroidism, diabetes mellitus, amyloidosis, uremia

√ abnormally rapid gastric emptying after gastric surgery, Z-E syndrome, duodenal ulcer disease, malabsorption (pancreatic exocrine insufficiency / celiac sprue)

Emergent Gastric Conditions

Mural stratification favors inflammation. Focal / nodular gastritis requires endoscopy and biopsy to exclude malignancy.

A. INFLAMMATION
   1. Emphysematous gastritis
   2. Peptic ulcer disease
   3. Marginal ulcer

B. OBSTRUCTION
   1. Gastric Volvulus
   2. Peptic ulcer disease
   3. Malignancy
   4. Bezoar
   5. Bouveret syndrome
   6. Slipped gastric band
   7. Vertical band gastroplasty

C. PERFORATION
   1. Peptic ulcer disease
   2. Malignancy
   3. Gastric banding

4. Penetrating trauma

D. HEMORRHAGE

E. ISCHEMIA

Gastric Tumor

Gastric Tumor Classification based on Cell Origin (WHO)

A. Epithelial (vast majority of gastric tumors)
Wall layer: mucosa

B. Nonepithelial = intramural = ~~submucosal~~
◊ Don't use "submucosal" in the sense of "deep to mucosa" because submucosa is its own specific layer
Wall layer: submucosa, muscularis propria, serosa

CECT:
√ prominent enhancement of gastric mucosa during arterial phase
√ enhancement of entire gastric wall during later phases without identification of distinct wall layers

Gastric Tumor Classification based on Biologic Behavior

A. MALIGNANT (10–15%)
(a) epithelial / mucosal tumor
1. Adenocarcinoma (> 95%)
2. Lymphoma, MALT
3. Carcinoid tumor
(b) mesenchymal tumor (50%)
1. Sarcoma: leiomyosarcoma, Kaposi sarcoma
2. Metastasis to stomach

B. BENIGN (85–90%)
(a) epithelial / mucosal tumor (50%)
1. Hyperplastic polyp
2. Adenomatous polyp
3. Brunner gland hyperplasia
(b) mesenchymal tumor (50%)

Mesenchymal Tumor of Stomach

= nonepithelial / intramural

A. GIST

B. SOMATIC SOFT TISSUE TUMOR
(a) smooth muscle tumor
1. True leiomyoma
2. True leiomyosarcoma
3. Plexiform fibromyxoma
(b) neural tumor (4% of all benign gastric tumors)
1. Schwannoma
2. Neurofibroma
3. Plexosarcoma

(c) lipocytic tumor
1. Lipoma
2. Liposarcoma

(d) vascular / perivascular tissue
◊ 2% of all benign gastric tumors
1. Glomus tumor (most common)
2. Hemangioma
3. Lymphangioma

(e) inflammatory tumor
1. Inflammatory fibroid polyp
2. Inflammatory myofibroblastic tumor

◊ Carcinoid tumor originates from Kulchitsky cell within gastric mucosa = epithelial origin. Tumor bulk is often submucosal, so they should be included in DDx of submucosal gastric tumors.

MESENCHYMAL GASTRIC TUMOR BY LOCATION

Some tumors are seen more frequently in certain parts of the stomach → tumor location is important for DDx

@ gastric cardia: leiomyoma
@ gastric body: GIST, schwannoma
@ gastric antrum: glomus tumor, inflammatory fibroid polyp, lipoma, ectopic panc

Calcified Gastric Tumor

1. Mucinous adenocarcinoma: miliary / punctate
2. Stromal tumors: amorphous calcifications
3. Hemangioma: clusters of phleboliths

Multiple Gastric Tumors

1. Carcinoid tumors
2. Hyperplastic polyps
3. Adenomatous polyps: familial adenomatous polyposis syndrome
4. Hamartomatous polyps: Peutz-Jeghers syndrome
5. Multiple hamartomas: Cowden disease
6. Metastases (usually intramural)

Congenital Gastric Obstruction

A. COMPLETE OBSTRUCTION

1. **Gastric atresia**
Frequency: < 1% of all GI obstructions
May be associated with: epidermolysis bullosa
Site: antrum + pylorus
• regurgitation of bile-free vomitus within first few hours after birth
√ "single bubble" appearance of air in stomach
√ membranous mucosal diaphragm
2. Congenital peritoneal bands
3. Annular pancreatic tissue

4. Gastric volvulus

B. PARTIAL GASTRIC OUTLET OBSTRUCTION

• cyclic transient postprandial vomiting

1. Incomplete prepyloric diaphragm
2. Antral stenosis
3. Aberrant pancreatic tissue in gastric antrum
4. Antral duplication cyst

Widened Retrogastric Space

A. PANCREATIC MASS (most common cause)

1. Acute + chronic pancreatitis
2. Pancreatic pseudocyst
3. Pancreatic cystadenoma + carcinoma

B. OTHER RETROPERITONEAL MASS

1. Sarcoma
2. Renal tumor, adrenal tumor
3. Lymph node enlargement
4. Abscess, hematoma

C. GASTRIC MASS

1. Leiomyoma, leiomyosarcoma

D. OTHERS

1. Aortic aneurysm
2. Choledochal cyst
3. Obesity
4. Postsurgical disruptions + adhesions
5. Ascites
6. Gross hepatomegaly + enlarged caudate lobe
7. Hernia involving omentum

Gas within Stomach Wall

A. NONINFECTIOUS

1. **Interstitial gastric emphysema**

   = gas accumulation in submucosa / subserosa / or both

   Cause: air from an extrinsic source

   (a) obstructive (← raised intragastric pressure): gastric outlet obstruction, volvulus, overinflation during gastroscopy, profuse severe vomiting

   (b) pulmonary (← rupture + dissection of subpleural blebs in bullous emphysema along esophageal wall / mediastinum): pulmonary emphysema

   (c) traumatic (← mucosal trauma): instrumentation of stomach, recent gastroduodenal surgery, endoscopy (1.6%)

   • benign clinical course with spontaneous resolution

   √ linear lucency conforming to contour of a thin-walled distended stomach

2. **Cystic pneumatosis**

   = PNEUMATOSIS CYSTOIDES INTESTINALIS

   Cause: similar to interstitial gastric emphysema

• little / no gastrointestinal symptoms
√ multiple 1–2-mm gas-filled cysts in wall of stomach and intestines

B. INFECTIOUS
1. Emphysematous gastritis
predisposed: corrosive gastritis, acid ingestion, severe necrotizing gastroenteritis, gastric ulcer disease with intramural perforation, gastric carcinoma, volvulus, gastric infarction

Gastric Atony

= gastric retention in the absence of mechanical obstruction
Pathophysiology: reflex paralysis
• abdominal distension, vomiting
• vascular collapse (decreased venous return)
√ large stomach filled with air + fluid (up to 7,500 mL)
√ retention of barium
√ absent / diminished peristaltic activity
√ patulous pylorus
√ frequently dilated duodenum
DDx: gastric volvulus, pyloric stenosis

Acute Gastric Atony

(may develop within 24–48 hours)
1. Acute gastric dilatation ← decreased arterial perfusion ← ischemia / CHF in old patients, usually fatal
2. Postsurgical atony, ureteral catheterization
3. Immobilization: body cast, paraplegia, postoperative state
4. Abdominal trauma: especially back injury
5. Severe pain: renal / biliary colic, migraine headaches, severe burns
6. Infection: peritonitis, pancreatitis, appendicitis, subphrenic abscess, septicemia

Chronic Gastric Atony

1. Neurologic abnormalities: brain tumor, bulbar poliomyelitis, vagotomy, tabes
2. Muscular abnormalities: scleroderma, muscular dystrophy
3. Drug-induced atony: atropine, morphine, heroin, ganglionic blocking agents
4. Electrolyte imbalance: diabetic ketoacidosis, hypercalcemia, hypocalcemia, hypokalemia, hepatic coma, uremia, myxedema
5. Diabetes mellitus = gastroparesis diabeticorum (0.08% incidence)
6. Emotional distress
7. Lead poisoning
8. Porphyria

Narrowing of Stomach

= **linitis plastica** type of stenosis

A. MALIGNANCY
1. Scirrhous gastric carcinoma (involving portion / all of stomach)
2. Hodgkin lymphoma, NHL

3. Metastatic involvement ← carcinoma of breast, pancreatic carcinoma, colonic carcinoma

B. INFLAMMATION
1. Chronic gastric ulcer disease with intense spasm
2. Pseudo-Billroth-I pattern of Crohn disease
3. Sarcoidosis
   √ polypoid appearance, pyloric hypertrophy
   √ gastric ulcers, duodenal deformity
4. Eosinophilic gastritis
5. Polyarteritis nodosa
6. Stenosing antral gastritis / hypertrophic pyloric stenosis

C. INFECTION
1. Tertiary stage of syphilis
   √ absent mucosal folds + peristalsis
   √ no change over years
2. Tuberculosis (rare)
   √ hyperplastic nodules / ulcerative lesion / annular lesion
   √ pyloric obstruction, may cross into duodenum
3. Histoplasmosis
4. Actinomycosis
5. Strongyloidiasis
6. Phlegmonous gastritis
7. Toxoplasmosis

D. TRAUMA
1. Corrosive gastritis
2. Radiation injury
3. Gastric freezing
4. Hepatic arterial chemotherapy infusion

E. OTHERS
1. Perigastric adhesions: normal mucosa, no interval change, normal peristalsis
2. Amyloidosis
3. Pseudolymphoma
4. Exogastric mass: hepatomegaly, pancreatic pseudocyst

mnemonic: SLIMRAGE
Scirrhous carcinoma of stomach
Lymphoma
Infiltration from adjacent neoplasm
Metastasis (breast carcinoma)
Radiation therapy
Acids (corrosive ingestion)
Granulomatous disease (TB, sarcoidosis, Crohn)
Eosinophilic gastroenteritis

Antral Narrowing

mnemonic: SPICER

Sarcoidosis, **S**yphilis
Peptic ulcer disease
Infection: TB, chronic granulomatous disease of childhood
Cancer (linitis plastica), **C**rohn disease, **C**austic ingestion
Eosinophilic gastritis
Radiation

Antral Pad Sign

= extrinsic impression of the posteroinferior wall of antrum

1. Pancreatic cancer in head / body
2. Pancreatitis
3. Pancreatic pseudocyst
4. Normal / distended gallbladder (patient in RAO position)

Intramural-extramucosal Lesion of Stomach

√ sharply delineated marginal / contour defect
√ stretched folds over intact mucosa
√ acute angle at margins
√ may ulcerate centrally
√ may become pedunculated and acquire polypoid appearance over years

A. NEOPLASTIC
   1. Leiomyoma 48%
   2. Neurogenic tumor 14%
   3. Heterotopic pancreas 12%
   4. Fibrous tumor 11%
   5. Lipoma 7%
   6. Hemangioma 7%
   7. Glomus tumor rare
   8. Carcinoid
   9. Metastatic tumor

B. INFLAMMATION / INFECTION
   1. Granuloma
      (1) Foreign-body granuloma
      (2) Sarcoidosis
      (3) Crohn disease
      (4) Tuberculosis
      (5) Histoplasmosis
   2. Eosinophilic gastritis
   3. Tertiary syphilis: infiltrative / ulcerative / tumorous type
   4. Echinococcal cyst

C. PANCREATIC ABNORMALITIES
   1. Ectopic pancreas
   2. Annular pancreas
   3. Pancreatic pseudocyst

D. DEPOSITS

1. Amyloid
2. Endometriosis
3. Localized hematoma

E. OTHERS
1. Varices: ie, fundal
2. Duplications (4% of all GI tract duplications)

Gastric Filling Defect

A. INTRINSIC WALL LESIONS
(a) benign (most common)
1. Polyp: hyperplastic, adenomatous, villous, hamar- tomatous (Peutz-Jeghers syndrome, Cowden disease)
2. Leiomyoma
3. Granulomatous lesion
(1) Eosinophilic granuloma
(2) Crohn disease
(3) Tuberculosis
(4) Sarcoidosis
4. Pseudolymphoma = benign reactive proliferation of lymphoid tissue
5. Extramedullary hematopoiesis
6. Ectopic pancreas
7. Gastric duplication cyst
8. Intramural hematoma
9. Esophagogastric herniation

(b) malignant
1. Gastric carcinoma, lymphoma
2. Gastric sarcoma: leiomyosarcoma, liposarcoma, leiomyoblastoma
3. Gastric metastases: melanoma, breast, pancreas, colon

B. EXTRINSIC IMPRESSION ON STOMACH
in 70% nonneoplastic (extrinsic pseudotumors in 20%)
(a) normal organ: organomegaly, tortuous aorta, heart, cardiac aneurysm
(b) benign mass: cysts of pancreas, liver, spleen, adrenal, kidney, gastric duplication, postoperative deformity (eg, Nissen fundoplication)
(c) malignant mass: enlarged celiac nodes
(d) inflammatory lesion: left subphrenic abscess / hematoma
› lateral displacement: enlarged liver, aortic aneurysm, enlarged celiac nodes
› medial displacement: splenomegaly, mass in colonic splenic flexure, cardiomegaly, subphrenic abscess

C. INTRALUMINAL GASTRIC MASS
1. Bezoar
2. Foreign bodies: food, pills, blood clot, gallstone

D. TUMOR OF ADJACENT ORGAN
1. Pancreatic carcinoma + cystadenoma
2. Liver carcinoma
3. Carcinoma of gallbladder

4. Colonic carcinoma
5. Renal carcinoma
6. Adrenal carcinoma
7. Lymph node involvement

E. THICKENED GASTRIC FOLDS

Filling Defect of Gastric Remnant

A. IATROGENIC surgical deformity / plication defect, suture granuloma
B. INFLAMMATORY bile reflux gastritis, hyperplastic polyps
C. INTUSSUSCEPTION
   1. **Jejunogastric intussusception**
      (efferent loop in 75%, afferent loop in 25%)
      (a) acute form: high intestinal obstruction, left hypochondriac mass, hematemesis
      (b) chronic / intermittent form: may be self-reducing
      √ "coiled spring" appearance of gastric filling defect
   2. Gastrojejunal / gastroduodenal mucosal prolapse
      • often asymptomatic, bleeding partial obstruction
D. NEOPLASTIC
   1. Gastric stump carcinoma: > 5 years after resection for benign disease; 15% (20%) within 10 (20) years
   2. Recurrent carcinoma (10%) ← incomplete removal of gastric cancer
   3. Malignancy at anastomosis: incomplete resection
E. INTRALUMINAL MATTER: bezoar

mnemonic: PUBLICS

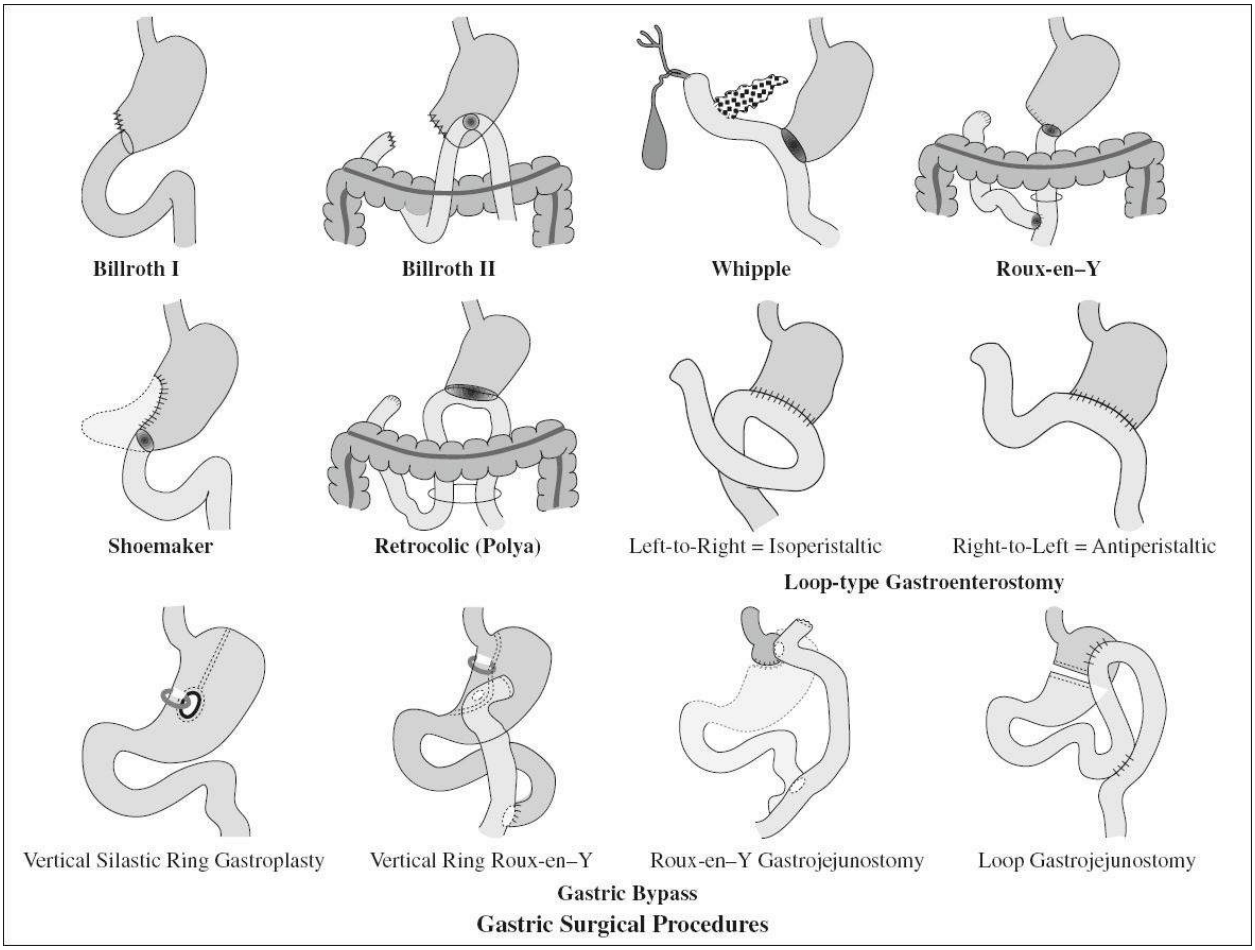
Polyp (hyperplastic polyp due to bile reflux)
Ulcer (anastomotic)
Bezoar, **B**lind loop syndrome
Loop (afferent loop syndrome)
Intussusception at gastrojejunostomy
Cancer (recurrent, residual, de novo)
Surgical deformity, **S**uture granuloma

Thickened Gastric Folds

A. INFLAMMATION / INFECTION
   1. Inflammatory gastritis:
      alcoholic, hypertrophic, antral, corrosive, postirradiation, gastric cooling
   2. Crohn disease
   3. Sarcoidosis
   4. Infectious gastritis:
      bacterial invasion, bacterial toxins from botulism, diphtheria, dysentery, typhoid fever, anisakiasis, TB, syphilis
   5. Pseudolymphoma
B. MALIGNANCY
   1. Lymphoma
   2. Gastric carcinoma

C. INFILTRATIVE PROCESS
   1. Eosinophilic gastritis
   2. Amyloidosis
D. PANCREATIC DISEASE
   1. Pancreatitis
   2. Direct extension from pancreatic carcinoma
E. OTHERS
   1. Zollinger-Ellison syndrome
   2. Ménétrier disease
   3. Gastric varices

mnemonic: ZEAL VOLUMES C3P3



Zollinger-**E**llison syndrome
Amyloidosis
Lymphoid hyperplasia
Varices
Operative defect
Lymphoma
Ulcer disease (peptic)

Ménétrier disease
Eosinophilic gastroenteritis
Syphilis
Crohn disease, **C**arcinoma, **C**orrosive gastritis
Pancreatitis, **P**ancreatic carcinoma,
Postradiation gastritis

Bull's-eye Lesion

A. PRIMARY NEOPLASMS
   1. Leiomyoma, leiomyosarcoma
   2. Lymphoma
   3. Carcinoid
   4. Primary carcinoma
B. HEMATOGENOUS METASTASES
   1. Malignant melanoma
      √ usually spares large bowel
   2. Breast cancer (15%)
      √ scirrhous appearance in stomach
   3. Cancer of lung
   4. Renal cell carcinoma
   5. Kaposi sarcoma
   6. Bladder carcinoma
C. ECTOPIC PANCREAS
   in duodenum / stomach
D. EOSINOPHILIC GRANULOMA
   most frequently in stomach

Complications of Postoperative Stomach

1. Filling defect of gastric remnant
2. Retained gastric antrum
3. Dumping syndrome
4. Afferent loop syndrome
5. Stomal obstruction
   (a) temporary reversible: edema of suture line, abscess / hematoma, potassium deficiency, inadequate electrolyte replacement, hypoproteinemia, hypoacidity
   (b) late mechanical: stomal ulcer (75%)

mnemonic: LOBULATING
Leaks (early)
Obstruction (early)
Bezoar
Ulcer: especially marginal
Loop: afferent loop syndrome
Anemia: macrocytic ← decreased intrinsic factor
Tumor (? increased incidence)
Intussusception

Not feeling well after meals: dumping syndrome
Gastritis: bile reflux

Transpyloric Disease

= LESIONS INVOLVING STOMACH AND DUODENUM

1. Lymphoma: in up to 40% of patients with lymphoma
2. Gastric carcinoma: in 5–25%, but 50 x more common than lymphoma
3. Peptic ulcer disease
4. Tuberculosis: in 10% of gastric TB
5. Crohn disease: pseudo-Billroth-I pattern
6. Strongyloidiasis
7. Eosinophilic gastroenteritis

Transpyloric spread by itself does not make a diagnosis of lymphoma because of the higher incidence of gastric cancer!

DUODENUM

Congenital Duodenal Obstruction

- bile-stained vomiting delayed until after first feeding and increasing progressively

1. Duodenal atresia / severe stenosis
2. Annular pancreas
3. Midgut volvulus
4. Duodenal web
5. Ladd bands
6. Preduodenal portal vein
7. Duodenal duplication cyst

Severe duodenal obstruction is characterized by 2 air-fluid levels on the upright view ("double bubble sign"), the largest below the left hemidiaphragm (= gastric distention), the smaller on the right side of the spine (= dilated proximal duodenum).

Extrinsic Pressure Effect on Duodenum

A. BILE DUCTS
normal impression, dilated CBD, choledochal cyst
B. GALLBLADDER
normal impression, gallbladder hydrops, Courvoisier phenomenon, gallbladder carcinoma, pericholecystic abscess
C. LIVER
hepatomegaly, hypertrophied caudate lobe, anomalous hepatic lobe, hepatic cyst, hepatic tumor
D. RIGHT KIDNEY
bifid collecting system, hydronephrosis, multiple renal cysts, polycystic kidney disease, hypernephroma
E. RIGHT ADRENAL
adrenal carcinoma, enlargement in Addison disease

F. COLON
duodenocolic apposition ← anomalous peritoneal fixation, carcinoma of hepatic flexure
G. VESSELS
lymphadenopathy, duodenal varices, dilated arterial collaterals, aortic aneurysm, intramural / mesenteric hematoma

Widened Duodenal Sweep

A. NORMAL Variant
B. PANCREATIC LESION
1. Acute pancreatitis
2. Groove pancreatitis
3. Pancreatic pseudocyst
4. Pancreatic carcinoma
5. Metastasis to pancreas
6. Pancreatic cystadenoma
C. VASCULAR LESION
1. Lymph node enlargement: lymphoma, metastasis, inflammation
2. Cystic lymphangioma of the mesentery
D. RETROPERITONEAL MASS
1. Aortic aneurysm
2. Choledochal cyst

Thickened Duodenal Folds

A. INFLAMMATION
(a) within bowel wall:
1. Peptic ulcer disease
2. Zollinger-Ellison syndrome
3. Crohn disease (regional enteritis)
4. Lymphoid hyperplasia
5. Uremia
6. Celiac disease
(b) surrounding bowel wall: pancreatitis, cholecystitis
B. INFECTION
giardiasis, TB, strongyloidiasis, disseminated histoplasmosis
C. NEOPLASIA
lymphoma, metastases to peripancreatic nodes
D. DIFFUSE INFILTRATIVE DISORDER
Whipple disease, amyloidosis, mastocytosis, eosinophilic enteritis, intestinal lymphangiectasia
E. VASCULAR DISORDER
duodenal varices, mesenteric arterial collaterals, intramural hemorrhage (trauma, Schönlein-Henoch purpura), chronic duodenal congestion (CHF, portal venous hypertension); lymphangiectasia
F. HYPOPROTEINEMIA
nephrotic syndrome, Ménétrier disease, protein-losing enteropathy

G. GLANDULAR ENLARGEMENT
Brunner gland hyperplasia, cystic fibrosis
mnemonic: BAD HELP
Brunner gland hyperplasia
Amyloidosis
Duodenitis: Z-E syndrome, peptic ulcer
Hemorrhage
Edema, **E**ctopic pancreas
Lymphoma
Pancreatitis, **P**arasites

Duodenal Filling Defect

A. EXTRINSIC gallbladder impression, CBD impression, gas-filled diverticulum
B. INTRINSIC TO WALL
(a) benign neoplastic mass
1. Adenoma
2. Leiomyoma
3. Lipoma
4. Hamartoma (Peutz-Jeghers syndrome)
5. Prolapsed antral polyp
6. Brunner gland adenoma
7. Villous adenoma
8. Islet cell tumor
9. Gangliocytic paraganglioma

(b) malignant neoplastic mass
1. Carcinoid tumor
2. Adenocarcinoma
3. Ampullary cancer
4. Lymphoma
5. Sarcoma
6. Metastasis: stomach, pancreas, gallbladder, colon, kidney, melanoma
7. Retroperitoneal lymph node involvement

(c) nonneoplastic mass
1. Papilla of Vater
2. Choledochocele
3. Duplication cyst
4. Pancreatic pseudocyst
5. Duodenal varix
6. Mesenteric artery collaterals
7. Intramural hematoma
8. Inflammatory mass: adjacent abscess, stitch abscess
9. Ectopic pancreas, heterotopic gastric mucosa
10. Prolapsed antral mucosa
11. Brunner gland hyperplasia
12. Benign lymphoid hyperplasia

13. Flexural pseudopolyp

C. INTRALUMINAL
1. Blood clot
2. Foreign body: fruit pit, gallstone, feeding tube

Duodenal Tumor

Benign Duodenal Tumors

= typically small polyps < 2 cm in diameter

1. GIST 27%
2. Leiomyoma ?
3. Adenomatous polyp 21%
   › villous adenoma
   › tubular adenoma
   › Brunner gland adenoma 17%
4. Lipoma 21%
5. Angiomatous tumor 6%
6. Ectopic pancreas 2%
7. Duodenal cyst 2%
8. Neurofibroma 2%
9. Hamartoma 2%

Malignant Duodenal Tumors

1. Duodenal adenocarcinoma (73%)
2. **Periampullary carcinoma**
   = tumor arising within 1 cm from papilla of Vater
   Origin: ampulla, pancreas, bile duct, duodenum
   At risk: familial adenomatous polyposis
   √ may not be seen at CT / MR due to small size
   √ hypovascular polypoid mass at ampulla
   Associated with: "double duct" sign ← biliary and pancreatic ductal dilatation
   Prognosis: ampullary ca. (best), pancreatic ca. (worst)
3. Malignant GIST (14%)
   most often beyond 1st portion of duodenum
   √ up to 20 cm in size
   √ frequently ulcerated exophytic mass
4. Carcinoid (11%)
5. Lymphoma (2%)
   √ marked wall thickening
   √ bulky periduodenal lymphadenopathy
6. APUDoma
7. Metastasis
8. Leiomyosarcoma

Enlargement of Papilla of Vater

[Abraham Vater (1684–1751), anatomist in Wittenberg, Germany]

A. Normal variant
   identified in 60% of UGI series; atypical location in 3rd portion of duodenum in 8%; 1.5 cm in diameter in 1% of normals
B. Papillary edema
   1. Impacted stone
   2. Pancreatitis (Poppel sign)
   3. Acute duodenal ulcer disease
   4. Papillitis
C. Perivaterian neoplasms
   = tumor mass + lymphatic obstruction
   1. Adenocarcinoma
   2. Adenomatous polyp (premalignant lesion)
      √ irregular surface + erosions
D. Lesions simulating enlarged papilla
   1. Benign spindle cell tumor
   2. Ectopic pancreatic tissue

Duodenal Narrowing

A. DEVELOPMENTAL ANOMALY
   1. Duodenal atresia
   2. Congenital web / duodenal diaphragm
   3. Intraluminal diverticulum
   4. Duodenal duplication cyst
   5. Annular pancreas
   6. Midgut volvulus, peritoneal bands (Ladd bands)
B. INTRINSIC DISORDER
   (a) inflammation / infection
      1. Postbulbar ulcer
      2. Crohn disease
      3. Sprue
      4. Tuberculosis
      5. Strongyloidiasis
   (b) intramural tumor
      1. GIST (90%)
      2. Lipoma, leiomyoblastoma
      3. Hemangioma, lymphangioma
      4. Ectopic pancreatic rest, Brunner gland hamartoma
      5. Duodenal carcinoma, periampullary carcinoma
C. DISEASE IN ADJACENT STRUCTURES
   1. Pancreatitis, pseudocyst, pancreatic carcinoma
   2. Cholecystitis
   3. Contiguous abscess
   4. Metastases to pancreaticoduodenal nodes: lymphoma, lung cancer, breast cancer
D. TRAUMA

1. Duodenal rupture
2. Intramural duodenal hematoma

E. VASCULAR
1. Superior mesenteric artery syndrome
2. Aorticoduodenal fistula
3. Preduodenal portal vein (anterior to descending duodenum)

Dilated Duodenum

Megaduodenum = marked dilatation of entire C-loop
Megabulb = dilatation of duodenal bulb only

A. VASCULAR COMPRESSION
superior mesenteric artery syndrome, abdominal aortic aneurysm, aorticoduodenal fistula

B. PRIMARY DUODENAL ATONY
(a) scleroderma, dermatomyositis, SLE
(b) Chagas disease, aganglionosis, neuropathy, surgical / chemical vagotomy
(c) focal ileus: pancreatitis, cholecystitis, peptic ulcer disease, trauma
(d) altered emotional status, chronic idiopathic intestinal pseudoobstruction

C. INFLAMMATORY / NEOPLASTIC INDURATION OF MESENTERIC ROOT
Crohn disease, tuberculous enteritis, pancreatitis, peptic ulcer disease, strongyloidiasis, metastatic disease

D. FLUID DISTENSION
celiac disease, Zollinger-Ellison syndrome

Benign Wall Thickening of Duodenum

1. **Cystic dystrophy** of duodenal wall
   = dilatation of pancreatic ducts in ectopic pancreatic tissue within wall of 2nd portion of duodenum ← duct obstruction
2. Pancreatic hamartoma
3. Paraduodenal wall cyst
4. Myoadenomatosis
5. Groove pancreatitis

Postbulbar Ulceration

1. Benign postbulbar peptic ulcer (10%)
2. Zollinger-Ellison syndrome
3. Gastrointestinal stromal tumor (GIST)
4. Malignant tumors:
   (a) primary
   adenocarcinoma, lymphoma, sarcoma
   (b) contiguous spread
   pancreas, colon, kidney, gallbladder
   (c) hematogenous spread
   melanoma, Kaposi sarcoma
   (d) lymphogenic spread
   metastases to periduodenal lymph nodes

5. Granulomatous disease: Crohn disease, TB, CMV
6. Aorticoduodenal fistula
7. Mimickers: ectopic pancreas, diverticulum

SMALL BOWEL

Anatomic Predilection for Intestinal Involvement

@ proximal jejunum	diverticulosis, giardiasis, adenocarcinoma, Whipple disease, Z-E syndrome, celiac disease
@ distal ileum	Crohn disease, TB, infectious enteritis, lymphoma, carcinoid, metastases
@ mesenteric border	diverticulosis, Crohn disease, mesenteric hematoma, intraperitoneal spread of tumor
@ antimesenteric border	Meckel diverticulum, sacculations in scleroderma, hematogenous metastases

Increased Fluid within Small Bowel

1. Ingestion
2. Resection / removal of stomach
3. Small-bowel obstruction
4. Enteritis
5. Malabsorption: celiac disease, Whipple disease
6. Peritoneal carcinomatosis

Small Bowel Diverticula

A. TRUE DIVERTICULA
   (a) Duodenal diverticula
      1. Racemose diverticula: bizarre, lobulated
      2. Giant diverticula
      3. Intraluminal diverticula: result of congenital web / diaphragm
   (b) Jejunal diverticulosis
   (c) Meckel diverticulum

B. PSEUDODIVERTICULA
   1. Scleroderma
   2. Crohn disease
   3. Lymphoma
   4. Mesenteric ischemia
   5. Communicating ileal duplication
   6. Giant duodenal ulcer

Small Bowel Ulcer

Aphthous Ulcers of Small Bowel

A. INFECTION
   1. Yersinia enterocolitis (25%)
   2. Salmonellosis

3. Tuberculosis
4. Rickettsiosis

B. INFLAMMATION
1. Crohn disease (22%)
2. Behçet disease
3. Reiter syndrome
4. Ankylosing spondylitis

Large Nonstenotic Ulcers of Small Bowel

1. Primary nonspecific ulcer 47% incidence
2. Yersiniosis 33%
3. Crohn disease 30%
4. Tuberculosis 18%
5. Salmonellosis / shigellosis 7%
6. Meckel diverticulum 5%

Multiple Small Bowel Ulcers

A. DRUGS
1. Potassium tablets
2. Steroids
3. Nonsteroidal antiinflammatory drugs

B. INFECTION / INFLAMMATION
1. Bacillary dysentery
2. Ischemic enteritis
3. Ulcerative jejunoileitis as complication of celiac disease

C. TUMOR
1. Neoplasms
2. Intestinal lymphoma

Cavitary Small Bowel Lesion

A. PRIMARY TUMOR
1. Lymphoma (exoenteric form)
2. Leiomyosarcoma (exoenteric form)
3. Primary adenocarcinoma

B. METASTASIS
1. Malignant melanoma
2. Lung cancer

C. INFLAMMATION
1. Diverticulitis with abscess: Meckel, jejunal
2. Communicating duplication cyst

Separation of Bowel Loops

A. INFILTRATION OF BOWEL WALL / MESENTERY

(a) inflammation / infection
1. Crohn disease
2. TB

3. Radiation injury
4. Retractile mesenteritis
5. Intraperitoneal abscess

(b) deposits
1. Intestinal hemorrhage / mesenteric vascular occlusion
2. Whipple disease
3. Amyloidosis

(c) tumor
1. Carcinoid tumor: local release of serotonin responsible for muscular thickening + fibroplastic proliferation = desmoplastic reaction
2. Primary carcinoma of small bowel (unusual presentation)
3. Lymphoma
4. Neurofibromatosis

B. ASCITES / INTRAPERITONEAL BLEEDING hepatic cirrhosis (75%), peritonitis, peritoneal carcinomatosis, congestive heart failure, constrictive pericarditis, primary / metastatic lymphatic disease

C. EXTRINSIC MASS
1. Intraperitoneal spread of tumor: peritoneal mesothelioma, mesenteric tumors (fibroma, lipoma, fibrosarcoma, leiomyosarcoma, malignant mesenteric lymphoid tumor, metastases)
2. Interloop abscesses / loculated fluid collection
3. Endometriosis
4. Retractile mesenteritis (fibrosis, fatty infiltration, panniculitis)
5. Mesenteric fat deposits
6. Fibrofatty proliferation: Crohn disease, mesenteric panniculitis

Normal Small Bowel Folds & Diarrhea

1. Pancreatic insufficiency
2. Lactase deficiency
3. Lymphoma / pseudolymphoma

Dilated Small Bowel & Normal Folds

mnemonic: SOS

Sprue
Obstruction
Scleroderma

A. EXCESSIVE FLUID

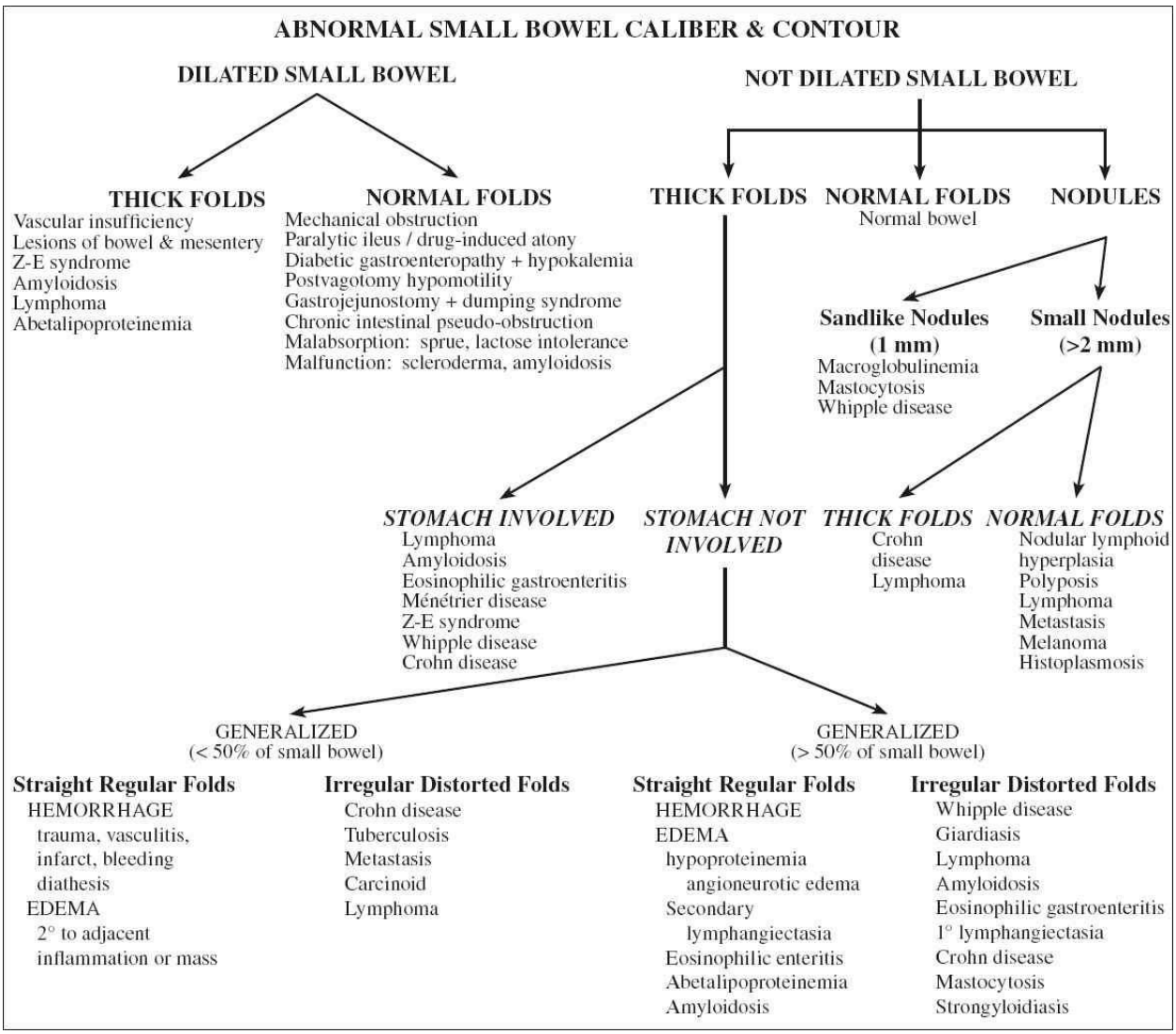
(a) mechanical obstruction ← adhesion, hernia, neoplasm
√ "string-of-beads" sign = air bubbles between mucosal folds in a fluid-filled small bowel
√ "pseudotumor" sign = closed-loop obstruction

(b) malabsorption syndromes
1. Celiac disease, tropical + nontropical sprue
2. Lactase deficiency

B. BOWEL WALL PARALYSIS

= functional ileus = adynamic ileus

1. Surgical vagotomy
2. Chemical vagotomy from drug effects: atropine-like substances, morphine, L-dopa, glucagon
3. Chagas disease
4. Metabolic: hypokalemia, diabetes
5. Intrinsic + extrinsic intraabdominal inflammation
6. Chronic idiopathic pseudoobstruction



C. VASCULAR COMPROMISE

1. Mesenteric ischemia: atherosclerosis
2. Acute radiation enteritis
3. Amyloidosis
4. SLE

D. BOWEL WALL DESTRUCTION

1. Lymphoma
2. Scleroderma: smooth muscle atrophy
3. Dermatomyositis

Abnormal Small Bowel Folds

Abnormal Folds + Increased Intraluminal Fluid

1. Malabsorption syndrome
2. Crohn disease, infectious enteritis
3. Parasitic infestation / giardiasis
4. Ischemia proximal to an obstruction
5. Zollinger-Ellison syndrome
6. Lymphangiectasia, mesenteric lymphadenopathy

Thickened Folds of Stomach & Small Bowel

1. Lymphoma
2. Crohn disease
3. Eosinophilic gastroenteritis
4. Zollinger-Ellison syndrome
5. Ménétrier disease
6. Cirrhosis = gastric varices + hypoproteinemia
7. Amyloidosis
8. Whipple disease
9. Systemic sclerosis

Thickened Smooth Folds ± Dilatation

A. EDEMA
   (a) hypoproteinemia
      1. Cirrhosis
      2. Nephrotic syndrome
      3. Protein-losing enteropathy: celiac disease, Whipple disease
   (b) increased capillary permeability
      1. Angioneurotic edema = angioedema
      2. Gastroenteritis
   (c) increased hydrostatic pressure
      1. Portal venous hypertension
   (d) Zollinger-Ellison syndrome

B. HEMORRHAGE
   (a) vessel injury
      1. Ischemia
      2. Infarction
      3. Trauma
   (b) vasculitis
      1. Connective tissue disease
      2. Henoch-Schönlein purpura
      3. Thrombangiitis obliterans, irradiation

(c) hypocoagulability
1. Hemophilia
2. Anticoagulant therapy
3. Hypofibrinogemia
4. Circulating anticoagulants
5. Fibrinolytic system activation
6. Idiopathic thrombocytopenic purpura
7. Coagulation defects: leukemia, lymphoma, multiple myeloma, metastatic carcinoma
8. Hypoprothrombinemia

C. LYMPHATIC BLOCKAGE
1. Tumor infiltration: lymphoma, pseudolymphoma
2. Irradiation
3. Mesenteric fibrosis
4. Intestinal lymphangiectasia
5. Whipple disease

D. DEPOSITS
1. Eosinophilic enteritis
2. Pneumatosis intestinalis
3. Amyloidosis
4. Abetalipoproteinemia
5. Crohn disease
6. Graft-versus-host disease
7. Immunologic deficiency: hypo- / dysgammaglobulinemia

Thickened Irregular Folds ± Dilatation

A. INFLAMMATION
1. Crohn disease

B. NEOPLASTIC
1. Lymphoma, pseudolymphoma

C. INFECTION
(a) protozoan: giardiasis, strongyloidiasis, hookworm
(b) bacterial: Yersinia enterocolitica, typhoid fever, TB
(c) fungal: histoplasmosis
(d) AIDS-related infection

D. IDIOPATHIC
(a) lymphatic dilatation
1. Lymphangiectasia
2. Inflammatory process, tumor growth, irradiation fibrosis
3. Whipple disease

(b) cellular infiltration
1. Eosinophilic enteritis
2. Mastocytosis

(c) deposits
1. Zollinger-Ellison syndrome

2. Amyloidosis
3. Alpha chain disease: defective secretory IgA system
4. A-β-lipoproteinemia: recessive, retinitis pigmentosa, neurologic disease
5. A-α-lipoproteinemia
6. Fibrocystic disease of the pancreas
7. Polyposis syndrome

mnemonic: G. WILLIAMS

Giardiasis
Whipple disease, **W**aldenström macroglobulinemia
Ischemia
Lymphangiectasia
Lymphoma
Inflammation
Amyloidosis, **A**gammaglobulinemia
Mastocytosis, **M**alabsorption
Soft-tissue neoplasm: carcinoid, lipoma

Tethered Folds

= indicative of desmoplastic reaction
√ kinking, angulation, tethering, separation of bowel loops

1. Carcinoid
2. Postoperative in Gardner syndrome
3. Retractile mesenteritis
4. Hodgkin disease
5. Peritoneal implants
6. Endometriosis
7. Tuberculous peritonitis
8. Mesothelioma
9. Postoperative adhesions

Atrophy of Small Bowel Folds

1. Chronic malabsorption: celiac disease
2. Chronic ischemic changes: radiation injury, amyloidosis
3. Crohn disease in burned-out stage
4. Parasitic infestation: strongyloidiasis
5. Graft-versus-host disease

Ribbonlike Small Bowel

= featureless / tubular nature of small bowel with effacement of folds

1. Graft-versus-host disease
2. Celiac disease
3. Small bowel infection: eg, viral enteritis
4. Injury from radiation / corrosive medication
5. Allergy: eg, soybeans
6. Ischemia

7. Amyloid, mastocytosis
8. Lymphoma, pseudolymphoma
9. Crohn disease

Delayed Small Bowel Transit

= transit time > 6 hr

mnemonic: SPATS DID

Scleroderma
Potassium (hypokalemia)
Anxiety
Thyroid (hypothyroidism)
Sprue
Diabetes (poorly controlled)
Idiopathic
Drugs (opiates, atropine, phenothiazine)

Constricting Lesion of Small Bowel

1. Primary adenocarcinoma (proximal jejunum)
2. Carcinoid (distal ileum)
3. Lymphoma, metastasis
4. Endometriosis
5. Adhesion, mucosal diaphragm
6. Strictures: Crohn disease, radiation enteritis, ischemia, potassium chloride tablets

Multiple Stenotic Lesions of Small Bowel

1. Crohn disease
2. End-stage radiation enteritis
3. Metastatic carcinoma
4. Endometriosis
5. Eosinophilic gastroenteritis
6. Tuberculosis
7. Drug-induced (eg, potassium chloride tablets, NSAIDs)

FEATURELESS BOWEL

1. Crohn disease
2. Chronic graft-versus-host disease
3. Radiation therapy

Small Bowel Filling Defects

Solitary Filling Defect of Small Bowel

A. INTRINSIC TO BOWEL WALL
   (a) benign neoplasm: leiomyoma (97%), adenoma, lipoma, hemangioma, neurofibroma
   (b) malignant primary: adenocarcinoma, lymphoma (desmoplastic response), sarcoma, carcinoid
   (c) metastases: ← melanoma, lung, kidney, breast

(d) inflammation: inflammatory pseudotumor
(e) infection: parasites

B. EXTRINSIC TO BOWEL WALL
1. Duplication cyst
2. Endometrioma

C. INTRALUMINAL
1. Gallstone ileus
2. Parasites: ascariasis, strongyloidiasis
3. Inverted Meckel diverticulum
4. Blood clot
5. Foreign body, bezoar, pills, seeds

Multiple Filling Defects of Small Bowel

A. POLYPOSIS SYNDROMES
1. Peutz-Jeghers syndrome
2. Gardner syndrome
3. Disseminated gastrointestinal polyposis
4. Generalized gastrointestinal juvenile polyposis
5. Cronkhite-Canada syndrome

B. BENIGN TUMORS
1. Multiple simple adenomatous polyps
2. Hemangioma, blue rubber bleb nevus syndrome
3. Leiomyoma, neurofibroma, lipoma
4. Nodular lymphoid hyperplasia
= normal terminal ileum in children + adolescents; may be associated with dysgammaglobulinemia
√ symmetric fairly sharply demarcated filling defects
5. Varices (= multiple phlebectasia in jejunum, oral mucosa, tongue, scrotum)

C. MALIGNANT TUMORS
1. Carcinoid tumor
2. Lymphoma
(a) primary lymphoma (rarely multiple)
(b) secondary lymphoma: GI involvement in 63% of disseminated disease; 19% in small intestine
3. Kaposi sarcoma
4. Subepithelial metastases: melanoma > lung > breast > choriocarcinoma > kidney > stomach, uterus, ovary, pancreas

D. INTRALUMINAL
1. Gallstones
2. Foreign bodies, food particles, seeds, pills
3. Parasites: ascariasis, strongyloidiasis, hookworm, tapeworm

Sandlike Lucencies of Small Bowel

1. Waldenström macroglobulinemia
2. Mastocytosis

3. Histoplasmosis
4. Nodular lymphoid hyperplasia
5. Intestinal lymphangiectasia
6. Eosinophilic gastroenteritis
7. Lymphoma
8. Crohn disease
9. Whipple disease
10. Yersinia enterocolitis
11. Cronkhite-Canada syndrome
12. Cystic fibrosis
13. Food particles / gas bubbles
14. Strongyloides stercoralis

Small Bowel Tumors

Prevalence: 1÷100,000; 1%–2% of all GI neoplasms

Malignant÷benign = 3÷2

Symptomatic malignant÷symptomatic benign = 3÷1

Location of small bowel primaries:

ileum (41%), jejunum (36%), duodenum (18%)

- pain, obstruction, anorexia, weight loss
- bleeding, perforation, jaundice

In order of frequency:

adenocarcinoma > carcinoid tumor > lymphoma > GIST

ROENTGENOGRAPHIC APPEARANCE:

(1) pedunculated intraluminal tumor, usually originating from mucosa
- √ smooth / irregular surface without visible mucosal pattern
- √ moves within intestinal lumen twice the length of the stalk

(2) sessile intraluminal tumor without stalk, usually from tissues outside mucosa
- √ smooth / irregular surface without visible mucosal pattern

(3) intra- / extramural tumor
- √ base of tumor greater than any part projecting into the lumen
- √ mucosal pattern visible, may be stretched

(4) serosal tumor
- √ displacement of adjacent loops
- √ small bowel obstruction (rare)
- √ coil-spring pattern of intussusceptum

CT:
- √ abnormalities associated with small bowel tumors (90%)
- √ small bowel wall > 1.5 cm thick

Cx: small-bowel obstruction (in up to 10%)

Benign Small Bowel Tumors

- asymptomatic (80%)
- melena, intermittent abdominal pain, weakness
- palpable abdominal mass (20%)

Types:

1. GIST 36–49%
2. Adenoma 15–20%
3. Lipoma 14–16%
4. Hemangioma 13–16%
5. Lymphangioma 5%
   Location: duodenum > jejunum > ileum
6. Neurogenic tumor 1%
7. Hamartomatous polyps (Peutz-Jeghers syndrome)
8. Hyperplastic polyp

Malignant Small Bowel Tumors

At risk: Crohn disease, celiac disease, polyposis syndromes, history of small-bowel diverting surgery

- asymptomatic (10–30%)
- pain due to intermittent obstruction (80%)
- weight loss (66%)
- gastrointestinal blood loss (50%)
- palpable abdominal mass (50%)

PRIMARY MALIGNANT SMALL BOWEL TUMOR

1. Adenocarcinoma 40%
2. Carcinoid 33%
3. Lymphoma 16–17%
4. GIST 9–10%
5 Vascular malignancy 1%
6. Fibrosarcoma 0.3%

SECONDARY MALIGNANT SMALL BOWEL TUMOR

◊ Most common neoplasm of small intestines!

CECUM

Ileocecal Valve Abnormalities

A. BENIGN NEOPLASM

1. **Lipomatosis of ileocecal valve**: predominantly in female > 40 years of age
   √ symmetric stellate / rosette pattern
2. Lipoma
3. Adenomatous polyp, villous adenoma
4. Lymphoid hyperplasia

B. PRIMARY MALIGNANT NEOPLASM

1. Adenocarcinoma of cecum
   Incidence: 25% of colonic adenocarcinomas
2. Ileal carcinoid tumor
3. Lymphoma
4. GIST (rare)

C. SECONDARY MALIGNANT NEOPLASM
   1. Adenocarcinoma of terminal ileum / appendix
   2. Direct invasion from ovarian neoplasm / intraperitoneal seeding
   3. Metastasis

D. IDIOPATHIC INFLAMMATION
   1. Crohn disease
   2. Ulcerative colitis
      √ patulous valve, fixed in open position

E. INFECTIOUS CONDITION
   1. Tuberculosis
   2. Infectious ileocecitis
   3. Typhlitis

F. PROLAPSE
   (a) antegrade: indistinguishable from lipomatosis / prolapsing mucosa / neoplasm
   (b) retrograde

G. INTUSSUSCEPTION

H. OTHERS
   1. Cathartic abuse
   2. Ischemic necrosis of cecum
   3. Volvulus
   4. Ileocecal duplication cyst

Coned Cecum

A. INFLAMMATION
   1. Crohn disease
      √ involvement of ascending colon + terminal ileum
   2. Ulcerative colitis
      √ backwash ileitis (in 10%)
      √ gaping ileocecal valve
   3. Appendicitis
   4. Typhlitis
   5. Perforated cecal diverticulum

B. INFECTION
   1. Tuberculosis
      √ colonic involvement more prominent than that of terminal ileum
   2. Amebiasis
      √ involvement of cecum in 90% of amebiasis
      √ thickened ileocecal valve fixed in open position
      √ reflux into normal terminal ileum
      √ skip lesions in colon
   3. Actinomycosis
      • palpable abdominal mass
      • indolent sinus tracts in abdominal wall
   4. Blastomycosis

5. Anisakiasis
6. Typhoid, Yersinia

C. TUMOR
1. Adenocarcinoma of the cecum
   Frequency: 25% of colon cancers; 95% of malignant cecal masses are adenocarcinomas
   √ large polypoid bulky mass causing asymmetric wall thickening
   √ mild pericolic fat infiltration
   √ rarely obstructing
   √ may act as lead point for intussusception
2. Metastasis to cecum

CT Features of Ileocecal Disease

Feature	*Adenocarcinoma*	*Lymphoma*	*Crohn Disease*	*Infectious Ileitis*	*Ischemia / Typhlitis*	*Cecal diverticulitis*
Stratified bowel wall	-	-	+ (if acute)	+	+	+
Bowel wall thickening	severe irregular eccentric	severe smooth ± symmetric	mild, rarely > 2 cm, symmetric	mild / marked, symmetric	mild / marked, symmetric	mild smooth concentric
Length	focal	segmental	segmental	segmental	segmental	focal
Fat stranding	minimal	0 / -	+	+	+	++
Transition to normal	abrupt	gradual	smooth	smooth	smooth	smooth
Fluid	-	-	occasional	occasional	occasional	mesenteric root
Lymphadenopathy	regional	bulky retroperitoneal	regional	regional	-	±
Others	mets	cavitary mass, solid organ + other GI sites involved	skip lesions, creeping fat, fistula, abscess	diarrhea	pneumatosis	inflamed diverticulum

Cecal Filling Defect

A. ABNORMALITIES OF THE APPENDIX
1. Acute appendicitis / appendiceal abscess
2. Crohn disease
3. Inverted appendiceal stump / appendiceal intussusception
4. Mucocele
5. Myxoglobulosis
6. Appendiceal neoplasm: carcinoid tumor (90%), leiomyoma, neuroma, lipoma, adenocarcinoma, metastasis

B. COLONIC LESION
1. Ameboma
2. Primary cecal neoplasm
3. Ileocolic intussusception
4. Lipomatosis of ileocecal valve

C. UNUSUAL ABNORMALITIES
1. Ileocecal diverticulitis (in 50% < age 30 years)
2. Solitary benign ulcer of the cecum
3. Adherent fecolith: eg, in cystic fibrosis
4. Endometriosis
5. Burkitt lymphoma

mnemonic: CECUM TIP SALE

Carcinoma
Enteritis
Carcinoid
Ulcerative colitis
Mucocele of appendix
Tuberculosis
Intussusception
Periappendiceal abscess
Stump of the appendix
Ameboma
Lymphoma
Endometriosis

Pericecal Fat-stranding on CT

1. Appendicitis
2. Crohn disease
3. Tuboovarian abscess
4. Cecal diverticulitis
5. Perforated cecal carcinoma

APPENDIX

Primary Neoplasm of the Appendix

1. Mucocele:
   mucinous adenoma 44%
   adenocarcinoma 23%
2. Colonic-type adenocarcinoma 13%
3. NHL
4. Carcinoid tumor

Appendiceal Intussusception

1. Mucocele
2. Endometrioma
3. Fecolith
4. Foreign body
5. Polyp: juvenile, inflammatory
6. Papilloma
7. Adenoma / adenocarcinoma
8. Carcinoid tumor
9. Postappendectomy stump

COLON

Colon Cutoff Sign

= abrupt termination of colonic gas column at splenic flexure with decompression of the

distal colon due to spasm + obstruction at the splenic flexure impinging on a paralytic transverse colon

A. IMPINGEMENT VIA PHRENICOCOLIC LIGAMENT
   1. Acute pancreatitis / postpancreatitic stricture
   2. Pancreatic / gastric carcinoma
   3. Hemorrhage from rupture of splenic artery / abdominal aortic aneurysm
B. COLONIC DISEASE
   1. Colon cancer
   2. Mesenteric thrombosis
   3. Ischemic colitis
   4. Perforated appendicitis (in 20%)
      N.B.: amputation of gas at the hepatic flexure ← spastic ascending colon

Colonic Thumbprinting

= sharply defined fingerlike marginal indentations at contours of wall

1. ISCHEMIA = Ischemic colitis occlusive vascular disease, hypercoagulability state, hemorrhage into bowel wall (bleeding diathesis, anticoagulants), traumatic intramural hematoma
2. INFLAMMATION ulcerative colitis, Crohn colitis
3. INFECTION
   acute amebiasis, schistosomiasis, strongyloidiasis, cytomegalovirus (in renal transplant recipients), pseudomembranous colitis
4. MALIGNANT LESIONS
   localized primary lymphoma, hematogenous metastases
5. MISCELLANEOUS
   endometriosis, amyloidosis, pneumatosis intestinalis, diverticulosis, diverticulitis, hereditary angioneurotic edema

mnemonic: PSALM II

Pseudomembranous colitis
Schistosomiasis
Amebic colitis
Lymphoma
Metastases (to colon)
Ischemic colitis
Inflammatory bowel disease

Colonic Urticaria Pattern

A. OBSTRUCTION
   1. Obstructing carcinoma
   2. Cecal volvulus
   3. Colonic ileus
B. ISCHEMIA
C. INFECTION / INFLAMMATION
   1. Yersinia enterocolitis
   2. Herpes

3. Crohn disease

D. URTICARIA

Colonic Ulcers

A. IDIOPATHIC
   1. Ulcerative colitis
   2. Crohn colitis

B. ISCHEMIC
   1. Ischemic colitis

C. TRAUMATIC
   1. Radiation injury
   2. Caustic colitis

D. NEOPLASTIC
   1. Primary colonic carcinoma
   2. Metastases: prostate, stomach, lymphoma, leukemia

E. INFLAMMATORY
   1. Pseudomembranous colitis
   2. Pancreatitis
   3. Diverticulitis
   4. Behçet disease
   5. Solitary rectal ulcer syndrome
   6. Nonspecific benign ulceration

F. INFECTION
   (a) protozoan
      1. Amebiasis
      2. Schistosomiasis
      3. Strongyloidiasis
   (b) bacterial
      1. Shigellosis, salmonellosis
      2. Staphylococcal colitis
      3. Tuberculosis
      4. Gonorrheal proctitis
      5. Yersinia colitis
      6. Campylobacter fetus colitis
   (c) fungal
      histoplasmosis, mucormycosis, actinomycosis, candidiasis
   (d) viral
      1. Lymphogranuloma venereum
      2. Herpes proctocolitis
      3. Cytomegalovirus (transplants)

Aphthous Ulcers of Colon

1. Crohn disease
2. Amebic colitis
3. **Yersinia enterocolitis**

Organism: gram-negative
• fever, diarrhea, RLQ pain
Location: terminal ileum
√ thickened folds + ulceration
√ lymphoid nodular hyperplasia

4. Salmonella, shigella infection
5. Herpes virus infection
6. Behçet disease
7. Lymphoma
8. Ischemia

Multiple Bull's-eye Lesions of Colonic Wall

mnemonic: MaCK CLaN
Melanoma and
Carcinoma
Kaposi sarcoma
Carcinoid
Lymphoma and
Neurofibromatosis

Double-tracking of Colon

= longitudinal extraluminal tracks paralleling the colon

1. Diverticulitis: generally 3–6 cm in length
2. Crohn disease: generally > 10 cm
3. Ulcerative colitis
4. Primary carcinoma: wider + more irregular

Pseudomembranous Colitis

= endoscopically diagnosed colonic infection / inflammation characterized by pseudomembranes consisting of an exudate of necrotic cells on a denuded mucosa

1. Clostridium difficile
2. Ischemic colitis: acute / subacute
3. Staphylococcus
4. Shigella
5. Pseudomonas aeruginosa
6. Drugs: chlorpropamide, mercuric compounds, gold, NSAIDs

Accordion Sign

= gross irregular polypoid thickening of colonic wall with wide separation of inner + outer walls

1. Radiation-induced colitis
2. Ischemic colitis
3. Infectious colitis: Clostridium difficile, tuberculosis
4. Typhlitis, neutropenic colitis
5. Inflammation: Crohn disease, ulcerative colitis

◊ The only 2 conditions with wall thickening > 10 mm

6. Lymphangiectasia
7. Intramural hemorrhage

Colonic Narrowing

A. CHRONIC STAGE OF ANY ULCERATING COLITIS
   (a) inflammatory:
      1. Ulcerative colitis
      2. Crohn colitis
      3. Solitary rectal ulcer syndrome
      4. Nonspecific benign ulcer
   (b) infectious:
      1. Amebiasis
      2. Schistosomiasis
      3. Bacillary dysentery
      4. Tuberculosis
      5. Fungal disease
      6. Lymphogranuloma venereum
      7. Herpes zoster
      8. Cytomegalovirus
      9. Strongyloides
   (c) ischemic
      1. Ischemic colitis
   (d) traumatic
      1. Radiation injury
      2. Cathartic colon
      3. Caustic colitis

B. MALIGNANT LESION
   (a) primary
      1. Colonic carcinoma: annular / scirrhous
      2. Complication of ulcerative colitis + Crohn colitis
   (b) metastatic:
      ← prostate, cervix, uterus, kidney, stomach, pancreas, primary intraperitoneal sarcoma
      › hematogenous (eg, breast)
      › lymphangitic spread
      › peritoneal seeding

C. EXTRINSIC PROCESS
   (a) inflammation
      1. Retractile mesenteritis
      2. Diverticulitis
      3. Pancreatitis
   (b) deposits
      1. Amyloidosis
      2. Endometriosis
      3. Pelvic lipomatosis

D. POSTSURGICAL
   1. Adhesive bands
   2. Surgical anastomosis
E. NORMAL
   1. Cannon point

Localized Colonic Narrowing

mnemonic: SCARED CELL-MATE

Schistosomiasis
Carcinoid
Actinomycosis
Radiation
Endometriosis
Diverticulitis
Colitis
Extrinsic lesion
Lymphoma
Lymphogranuloma venereum
Metastasis
Adenocarcinoma
Tuberculosis
Entamoeba histolytica

Microcolon

mnemonic: **MI**a **M**icro**C**olic**A**

Meconium ileus, Meconium peritonitis (cystic fibrosis)
Ileal / jejunal atresia
Megacystis-microcolon-hypoperistalsis syndrome
Colonic atresia (distal to atretic segment)
Aganglionosis (Hirschsprüng disease)

Colonic Filling Defects

Subepithelial Lesion of Colon

SUBEPITHELIAL NEOPLASM OF COLON

= masslike protrusion into lumen covered by normal overlying mucosa at optical colonoscopy

A. Neoplasm with intramural origin
   1. Lipoma
   2. Carcinoid
   3. Lymphoma
   4. Hemangioma
   5. GIST
   6. Hematogenous metastasis:
      melanoma > lung > breast

7. Other primary tumor (rare):
   leiomyoma, schwannoma, leiomyosarcoma, ganglioneuroma, granular cell tumor

B. Neoplasm with extramural origin
   1. Direct invasion by extracolonic tumor: gastric adenocarcinoma
   2. Peritoneal carcinomatosis
   3. Appendiceal tumor

SUBEPITHELIAL NONNEOPLASTIC LESION OF COLON

A. Intramural origin
   (a) vascular lesion:
      1. Internal hemorrhoid
      2. Rectal varix
      3. Venous malformation
   (b) cystic lesion:
      1. Colonic duplication cyst
      2. Lymphangioma
      3. Colitis cystica profunda
   (c) others:
      1. Lymphoid polyp / hyperplasia
      2. Intramural hematoma
      3. Pneumatosis cystoides coli

B. Extramural origin
   1. Endometriosis
   2. Extrinsic impression: uterus, adnexa, aorta, common iliac artery, adjacent GI tract
   3. Presacral lesion

Single Colonic Filling Defect

A. BENIGN TUMOR
   1. Polyp
      (hyperplastic, adenomatous, villous adenoma, villoglandular); most common benign tumor
   2. Lipoma
      Most common intramural tumor; 2nd most common benign tumor; M < F
      Location: ascending colon + cecum > left side of colon
   3. Carcinoid: 10% metastasize
   4. Spindle cell tumor
      (leiomyoma, fibroma, neurofibroma); 4th most common benign tumor; rectum > cecum
   5. Lymphangioma, hemangioma

B. MALIGNANT TUMOR
   (a) primary tumor: carcinoma, sarcoma
   (b) secondary tumor: metastases (breast, stomach, lung, pancreas, kidney, female genital tract), lymphoma, invasion by adjacent tumors

C. INFECTION
   1. Ameboma

2. Polypoid granuloma: schistosomiasis, TB

D. INFLAMMATION
1. Inflammatory pseudopolyp: ulcerative colitis, Crohn disease
2. Periappendiceal abscess
3. Diverticulitis
4. Foreign-body perforation

E. NONSESSILE INTRALUMINAL BODY
1. Fecal impaction
2. Foreign body
3. Gallstone
4. Bolus of Ascaris worms

F. MISCELLANEOUS
1. Endometriosis
   3rd most common benign tumor
   Location: sigmoid colon, rectosigmoid junction (at level of cul-de-sac)
   • may cause bleeding (after invasion of mucosa)
2. Localized amyloid deposition
3. Suture granuloma
4. Intussusception
5. Pseudotumor: ← adhesions, fibrous bands
6. Colitis cystica profunda

Multiple Colonic Filling Defects

A. NEOPLASMS
(a) polyposis syndrome
(b) hematogenous metastases: from breast, lung, stomach, ovary, pancreas, uterus
(c) multiple tumors
› benign: neurofibromatosis, colonic lipomatosis, multiple hamartoma syndrome (Cowden disease)
› malignant: lymphoma, leukemia, adenocarcinoma

B. INFLAMMATORY PSEUDOPOLYPS
ulcerative colitis, Crohn colitis, ischemic colitis, amebiasis, schistosomiasis, strongyloidiasis, trichuriasis

C. ARTIFACTS
feces, air bubbles, oil bubbles, mucous strands, ingested foreign body (eg, corn kernels)

D. MISCELLANEOUS
nodular lymphoid hyperplasia, lymphoid follicular pattern, hemorrhoids, diverticula, pneumatosis intestinalis, colitis cystica profunda, colonic urticaria, submucosal colonic edema ← obstruction, cystic fibrosis, amyloidosis, ulcerative pseudopolyps, proximal to obstruction

mnemonic: MILL P3
Metastases (to colon)
Ischemia (thumbprinting)
Lymphoma
Lymphoid hyperplasia

Polyposis
Pseudopolyposis (with inflammatory bowel disease)
Pneumatosis cystoides

Carpet Lesions of Colon

= flat lobulated lesions with alteration of surface texture + little / no protrusion into lumen
Location: rectum > cecum > ascending colon
Cause:
A. NEOPLASM
1. Tubular / tubulovillous / villous adenoma
2. Familial polyposis
3. Adenocarcinoma
4. Submucosal tumor spread ← adjacent carcinoma

B. MISCELLANEOUS
1. Nonspecific follicular proctitis
2. Biopsy site
3. Endometriosis
4. Rectal varices
5. Colonic urticaria

Colonic Polyp

Terminology:

1. **Polyp**
= mass projecting into the lumen of a hollow viscus above level of mucosa; usually arises from mucosa, may derive from submucosa / muscularis propria
(a) neoplastic polyp: adenoma / carcinoma
(b) nonneoplastic: hamartoma / inflammatory polyp
2. **Pseudopolyp**
= scattered island of inflamed edematous mucosa on a background of denuded mucosa
(a) pseudopolyposis of ulcerative colitis
(b) "cobblestoning" of Crohn disease
3. **Postinflammatory (filiform) polyp**
= fingerlike projection of submucosa covered by mucosa on all sides following healing + regeneration of inflammatory (most common in ulcerative colitis) / ischemic / infectious bowel disease
4. **Adenomatous polyp**
◊ Most commonly seen neoplastic polyp
Histo: tubular > villous > tubulovillous adenoma
5. **Hyperplastic polyp**
◊ Most commonly seen nonneoplastic polyp
6. **Pedunculated polyp**
= attachment to wall via stalk
7. **Sessile polyp**
= attachment to wall via broad base
8. **Flat polyp**

= mass with height > ½ its width

RECTUM & ANUS

Rectal Disease

A. NEOPLASIA
   1. Rectal polyp
   2. Rectal cancer
   3. Multiple lymphomatous polyposis

B. INFLAMMATION
   1. Ulcerative colitis
   2. Perianal fistula of Crohn disease
   3. Solitary rectal ulcer syndrome
   4. Pseudomembranous colitis

C. EXTRAMUCOSAL LESION
   1. Serosal metastasis
   2. Lymph node metastasis
   3. Leiomyoma
   4. Perirectal abscess
   5. Uterine leiomyosarcoma invading rectal wall

Rectal Narrowing

1. Pelvic lipomatosis + fibrolipomatosis
2. Lymphogranuloma venereum
3. Radiation injury of rectum
4. Chronic ulcerative colitis

Enlarged Presacral Space

Normal width: < 5 mm in 95%; abnormal width > 10 mm

A. RECTAL INFLAMMATION / INFECTION
   ulcerative colitis, Crohn colitis, idiopathic proctosigmoiditis, radiation therapy

B. RECTAL INFECTION
   1. Proctitis: TB, amebiasis, lymphogranuloma venereum, radiation, ischemia
   2. Diverticulitis

Differential Diagnosis of Colonic Polyps		
	Single Polyp	*Multiple Polyps*
Neoplastic (10 %)		
epithelial (adenomatous)	Tubular adenoma	Familial multiple polyposis
	Tubulovillous adenoma	Adenomatosis of GI tract
	Villous adenoma	Gardner syndrome
		Turcot syndrome
nonepithelial	Carcinoid	
	Leiomyoma	
	Lipoma	
	Hemangioma, lymphangioma	
	Fibroma, neurofibroma	
Nonneoplastic (90%)		
unclassified	Hyperplastic polyp	Hyperplastic polyposis
hamartomatous	Juvenile polyps	Juvenile polyposis
		Peutz-Jeghers syndrome
		Cronkhite-Canada syndrome
inflammatory	Benign lymphoid polyp	Ulcerative colitis
	Fibroid granulation polyp	

C. BODY FLUIDS / DEPOSITS
   1. Hematoma: surgery, sacral fracture
   2. Pus: perforated appendix, presacral abscess
   3. Serum: edema, venous thrombosis
   4. Deposit of fat: pelvic lipomatosis, Cushing disease
   5. Deposit of amyloid: amyloidosis

D. SACRAL TUMOR
   1. Sacrococcygeal teratoma, anterior sacral meningocele
   2. Chordoma, metastasis to sacrum

E. PRESACRAL TUMOR *(see below)*

F. MISCELLANEOUS
   1. Inguinal hernia containing segment of colon
   2. Colitis cystica profunda
   3. Pelvic lipomatosis

Presacral Tumor

= mass effect on posterior wall of rectum

A. OSTEOCHONDRAL
   1. Giant cell tumor

2. Ewing sarcoma
3. Osteosarcoma of spine
4. Chondrosarcoma
5. Aneurysmal bone cyst

B. NEUROGENIC
1. Neurofibroma
2. Schwannoma
3. Paraganglioma
4. Sacrococcygeal chordoma
5. Dural ectasia
6. Anterior myelomeningocele

C. MESENCHYMAL
1. Hemangioma
2. Myelolipoma
3. Solitary fibrous tumor
4. Castleman disease
5. Retroperitoneal fibrosis
7. GIST
8. Lipoma

D. MALIGNANT RECTAL TUMOR
1. Colorectal carcinoma
2. Cloacogenic carcinoma
3. Lymphoma
4. Sarcoma
5. Hemangioendothelioma
6. Lymph node metastases
7. Prostatic carcinoma, bladder tumors, cervical cancer, ovarian cancer

E. CONGENITAL / DEVELOPMENTAL
(a) developmental cyst:
1. Epidermoid, dermoid
2. Rectal duplication cyst
3. Tailgut cyst

(b) germ cell tumor:
1. Sacrococcygeal teratoma
2. Yolk sac tumor
3. Embryonal cell carcinoma

(d) lymphoproliferative disorder

F. INFECTIOUS / INFLAMMATORY

G. POSTTRAUMATIC

Lesions of Ischiorectal Fossa

A. CONGENITAL AND DEVELOPMENTAL ANOMALIES
1. Gartner duct cyst
2. Klippel-Trénaunay syndrome
3. Tailgut cyst

B. INFLAMMATORY AND HEMORRHAGIC LESIONS
1. Fistula in ano
2. Ischiorectal / perirectal abscess
3. Extraperitoneal pelvic hematoma
4. Rectal perforation

C. SECONDARY NEOPLASM
per direct extension / hematogenous spread:
anorectal / prostatic / pelvic / sacral tumor; lung cancer; melanoma; lymphoma

D. PRIMARY NEOPLASM
1. Aggressive angiomyxoma
2. Lipoma
3. Plexiform neurofibroma
4. Anal adenocarcinoma
5. Squamous cell carcinoma

MURAL STRATIFICATION OF INTESTINAL TRACT

= bowel wall thickening with abnormal separation of bowel layers on cross-sectional imaging = visualization of layers of bowel wall at contrast-material–enhanced CT

CECT:

√ "double halo / target" sign = trilaminar appearance during late arterial phase:
√ contrast enhancement of inner layer:
(1) mucosa + (2) muscularis mucosae
√ nonenhanced interposed layer of (3) submucosa with various degrees of attenuation:
› blood attenuation ← hemorrhage
› soft-tissue attenuation ← inflammatory cells
› low attenuation ← pus
› water attenuation ← intramural edema
› fat attenuation ← past / chronic inflammation
√ contrast enhancement of outer layer:
(4) muscularis propria + (5) serosa

Cause:

◊ Tumor has NOT been reported to cause stratification!

A. BOWEL WALL EDEMA
√ low-density / water-density separation
1. Ulcerative colitis (50%): rectum
2. Proximal to obstructing tumor / intussusception
3. Angioedema

B. INFLAMMATORY CELL INFILTRATE
1. Crohn disease (in up to 50%)
2. Mycobacterium tuberculosis
3. Eosinophilic enteritis
4. Cytomegalovirus
5. Clostridium difficile
6. Entamoeba histolytica

7. Vibrio cholerae
8. Shigella
9. Escherichia coli

C. BOWEL ISCHEMIA / INFARCTION
1. Arterial obstruction: thromboembolism, plaque thrombus
2. Peripheral vasculopathy
3. Venous obstruction: thrombosis, bowel torsion, closed-loop obstruction
4. Hypoperfusion: proximal arterial stenosis potentiated by myocardial infarction, bradycardia, dehydration

N.B.: closed-loop obstruction with signs of bowel infarction is a surgical condition!
- √ signs of bowel infarction:
  - √ free peritoneal fluid
  - √ asymmetric bowel wall enhancement
  - √ persistent enhancement of bowel wall / segmental arteries
  - √ arterial / venous filling defects
  - √ increased density of mesentery
  - √ bowel obstruction

D. INTESTINAL WALL HEMORRHAGE
1. Anticoagulation
2. Blood dyscrasia: thrombocytopenic purpura
3. Blunt trauma
   - √ "snow-cone" appearance of duodenum

Segmental Mural Stratification of Small Bowel
1. Small-vessel vasculitis
2. Small-vessel ischemia
3. Chemotherapy-induced enteritis
4. Radiation therapy
5. ACE inhibitor–induced angioedema

Bowel Wall Thickening in Children

A. INFECTION
1. Gastroenteritis
2. Enterocolitis
3. Pseudomembranous colitis
4. Hemolytic-uremic syndrome
5. Chronic granulomatous disease

B. TRAUMA
1. Duodenal hematoma
2. Hypoperfusion complex

C. NEOPLASM
1. Lymphoma
2. GIST
3. Neurogenic tumors: mesenteric plexiform neurofibroma associated with neurofibromatosis

4. Vascular tumors: hemangioma
5. Colon cancer (2nd decade of life)
6. Langerhans cell histiocytosis

D. INFLAMMATION
1. Crohn disease
2. Ulcerative colitis
3. Typhlitis
4. Inflammatory pseudotumor

The degree of wall thickening is significantly greater in Crohn disease than in ulcerative colitis!

E. AUTOIMMUNE
(a) Collagen vascular disease
1. SLE
2. Scleroderma
(b) Vasculitis:
1. Periarteritis nodosa
2. Henoch-Schönlein purpura

F. Mechanical
1. Mesenteric ischemia
2. Intussusception
3. Acute appendicitis
4. Meckel diverticulum
5. Radiation enteritis

G. OTHERS
1. Celiac disease
2. Lactose intolerance
3. Eosinophilic gastroenteritis
3. Hypoproteinemia
4. Graft-versus-host disease

Fat halo sign

= layer of fat attenuation (-18 to -64 HU) in submucosa sandwiched between inner + outer layer of soft-tissue attenuation of a thickened bowel wall

1. Chronic inflammatory bowel disease: ulcerative colitis (61%), Crohn disease (8%)
2. Graft-versus-host disease
3. Cytoreductive therapy
4. Asymptomatic obese patient

Hyperattenuating Bowel Wall

= hemorrhage secondary to

1. Trauma
2. Henoch-Schönlein purpura
3. Vasculitis

Prolonged Contrast Coating of Bowel Wall

for hours to days

Cause: incorporation of barium into submucosal layer through mucosal ulcers

1. Graft-versus-host disease
2. Ischemic bowel

Aphthous Ulcer

= ulcer crater surrounded by a rim of edema overlying submucosal lymphoid follicle

1. Crohn disease
2. Yersinia enterocolitis
3. Tuberculosis
4. Amebiasis
5. Ischemic enteritis

Hypervascular Subepithelial (Submucosal) Mass

1. Neuroendocrine tumor
2. Gastrointestinal stromal tumor
3. Glomus tumor
4. Hemangioma
5. Angiosarcoma: extremely rare in GI tract
6. Kaposi sarcoma
7. Peripheral nerve sheath tumor
8. Hypervascular metastasis
9. Heterotopic pancreatic tissue

The term *subepithelial* is favored over *submucosal* because lesions in this category do not necessarily arise from the submucosa, but can arise from any layer of the GI wall (intramural) or intraabdominal structures (extramural).

POLYPOSIS SYNDROMES

= more than 100 polyps in number

Mode of transmission:

A. HEREDITARY
   (a) autosomal dominant
      1. Familial (multiple) polyposis
      2. Gardner syndrome
      3. Peutz-Jeghers syndrome
      4. Juvenile polyposis coli
   (b) autosomal recessive
      1. Turcot syndrome

B. NONHEREDITARY
   1. Cronkhite-Canada syndrome
   2. Juvenile polyposis

DDx: polyposis look-alikes on barium studies

1. Postinflammatory polyposis
2. Lymphoid hyperplasia
3. Multiple lymphomatous polyposis

4. Metastases
5. Pneumatosis coli
6. Disseminated gastrointestinal polyps
7. Multiple adenomatous polyps

Adenomatous Polyposis Syndromes

1. Familial (multiple) polyposis
2. Gardner syndrome
3. Turcot syndrome

Hamartomatous Polyposis Syndromes

1. Peutz-Jeghers syndrome* (polyp with central core of smooth muscle)
2. Cowden disease*
3. Juvenile polyposis*
4. Cronkhite-Canada syndrome
5. Bannayan-Riley-Ruvalcaba syndrome

* = increased prevalence of coexisting adenomas and adenoma-carcinoma sequence

PERITONEUM

Lesion of Serosal Membranes

A. PRIMARY NEOPLASM
   (a) malignant
      1. Malignant pleural mesothelioma
      2. Malignant peritoneal mesothelioma
      3. Primary serous papillary carcinoma of peritoneum = serous cystadenocarcinoma of ovary
   (b) benign
      1. Adenomatoid tumor
      2. Benign multicystic mesothelioma
      3. Desmoplastic small round cell tumor
      4. Localized fibrous tumor of pleura
      5. Leiomyomatosis peritonealis disseminata

B. SECONDARY NEOPLASM (more common)
   Spread by: direct extension from an adjacent visceral organ / transcoelomic dissemination / permeation of underlying lymphatics
   (a) pleura: lung, breast, thymus, ovary, pancreas, thyroid, gastrointestinal tract, kidney
   (b) peritoneum: pseudomyxoma peritonei

C. NONNEOPLASTIC LESION
   1. Pleural plaque
   2. Pleural fibrosis
   3. Pericardial cyst
   4. Sclerosing encapsulating peritonitis
   5. Sclerosing mesenteritis
   6. Peritoneal inclusion cyst

Peritoneal Mass

A. SOLID MASS
   1. Peritoneal mesothelioma
   2. Peritoneal carcinomatosis
B. INFILTRATIVE PATTERN
   1. Peritoneal mesothelioma
C. CYSTIC MASS
   1. Multicystic mesothelioma
   2. Pseudomyxoma peritonei
   3. Bacterial / mycobacterial infection

Intraperitoneal Solid Abdominal Mass in a Child

LOCALIZED MASS

1. Inflammatory myofibroblastic tumor
2. Castleman disease
3. Mesenteric fibromatosis
4. Benign mesenchymal mass: lymphatic malformation, infantile hemangioma

DIFFUSE PERITONEAL DISEASE

1. Desmoplastic small round cell tumor
2. Burkitt lymphoma (NHL)
3. Rhabdomyosarcoma

Multiple Peritoneal Masses

A. METASTATIC NEOPLASM
   1. Peritoneal metastases = carcinomatosis
   2. Pseudomyxoma peritonei
   3. Lymphomatosis = body cavity-based lymphoma
   4. Sarcomatosis
      Cause: unusual hematogenous metastases, GIST
B. TUMORLIKE CONDITIONS
   1 Endometriosis
   2. Gliomatosis peritonei
   3. Osseous metaplasia = heterotopic mesenteric ossification
   4. Cartilaginous metaplasia
   5. Splenosis
C. INFECTION / INFLAMMATION
   1. **Granulomatous peritonitis**
      Cause: TB, Histoplasma, Pneumocystis, talc, barium, meconium, bowel contents, ruptured ovarian cyst, bile, gallstones
   3. Sclerosing encapsulating peritonitis
   2. Inflammatory pseudotumor

Diffuse Peritoneal Masses in Children

1. Desmoplastic small round cell tumor

2. Rhabdomyosarcoma
3. Metastatic germ cell tumor
4. Gliomatosis peritonei
5. Metastatic retroperitoneal tumor:
   (a) Neuroblastoma
   (b) Wilms tumor
6. Malignant mesothelioma
7. Peritoneal carcinomatosis
8. Peritoneal seeding of intracranial tumors through ventriculoperitoneal shunt

Peritoneal Calcifications

1. Tuberculosis
2. Amyloidosis
3. Hyperparathyroidism
4. Pseudomyxoma peritonei
5. Peritoneal carcinomatosis
6. Meconium peritonitis

MESENTERY & OMENTUM

Short Mesentery

= shortened line of fixation

1. Malrotation + midgut volvulus
2. Omphalocele
3. Gastroschisis
4. Congenital diaphragmatic hernia
5. Asplenia + polysplenia

"Apple peel" Small Bowel

= distal small intestines spirals around its vascular supply resembling an apple peel resulting in a very short intestine

1. Proximal jejunal atresia
2. Absence of distal superior mesenteric artery
3. Shortening of small bowel distal to atresia
4. Absence of dorsal mesentery

Cx: propensity toward necrotizing enterocolitis

Prognosis: high mortality

Whirlpool Sign of Small Bowel Mesentery

1. Midgut volvulus
2. Internal hernia
3. Adhesions
4. Surgical disruption of normal anatomy

Omental Mass

◊ 33% of primary omental tumors are malignant!
◊ Secondary neoplasms are more frequent than primary!

A. SOLID MASS
   (a) benign
      1. Leiomyoma
      2. Lipoma
      3. Neurofibroma
   (b) malignant
      1. Leiomyosarcoma
      2. Liposarcoma
      3. Fibrosarcoma
      4. Lymphoma
      5. Peritoneal mesothelioma
      6. Hemangiopericytoma
      7. Metastases
   (c) Infection: tuberculosis

B. CYSTIC MASS
   1. Hematoma
   2. Cystic mesothelioma

Omental Cake

= replacement of normal fat of the greater omentum by a soft-tissue density

A. INTRAPERITONEAL TUMOR SPREAD
   1. Peritoneal metastases from abdominal organs
      mnemonic: COPUBS
         Colon
         Ovary
         Pancreas
         Uterus
         Bladder
         Stomach
   2. Metastases from extraabdominal organs: malignant melanoma, breast, lung

B. INFLAMMATION
   1. Tuberculosis
   2. Crohn disease
   3. Phlegmonous pancreatitis
   4. Granulomatous enterocolitis

C. BENIGN TUMOR
   1. Desmoid fibroma
   2. Extramedullary hematopoiesis

D. MALIGNANT TUMOR
   1. Mesothelioma
   2. Lymphomatosis

E. OTHER
   1. Hemoperitoneum

2. Liver cirrhosis with portal hypertension

Mesenteric Mass

A. ROUND SOLID MASS
- ◊ Benign primary tumors >> malignant primary tumors
- ◊ Secondary neoplasms are more frequent than primary
- ◊ Cystic tumors are more common than solid tumors!
- ◊ Malignant solid tumors have a tendency to be located near root of mesentery, benign solid tumors in periphery near bowel!

1. Metastases: especially ← colon, ovary (most frequent neoplasm of mesentery)
2. Lymphoma
3. Leiomyosarcoma: more frequent than leiomyoma
4. Neural tumor : neurofibroma, ganglioneuroma
5. Lipoma (uncommon), lipomatosis, liposarcoma
6. Fibrous histiocytoma
7. Hemangioma
8. Desmoid tumor (most common primary)
9. Desmoplastic small round cell tumor of peritoneum

B. ILL-DEFINED MASS
1. Metastases (ovary)
2. Lymphoma
3. Fibromatosis, fibrosing mesenteritis (associated with Gardner syndrome)
4. Lipodystrophy
5. Mesenteric panniculitis

C. STELLATE MASS
1. Peritoneal mesothelioma
2. Retractile mesenteritis
3. Fibrotic reaction of carcinoid
4. Radiation therapy
5. Desmoid tumor
6. Hodgkin disease
7. Tuberculous peritonitis
8. Ovarian metastases
9. Diverticulitis
10. Pancreatitis

- ◊ A calcified mesenteric mass suggests carcinoid tumor!

D. LOCULATED CYSTIC MASS (2/3)
1. Cystic lymphangioma (most common)
2. Pseudomyxoma peritonei
3. Cystic mesothelioma
4. Mesenteric cyst
5. Mesenteric hematoma
6. Benign cystic teratoma
7. Cystic spindle cell tumor (= centrally necrotic leiomyoma / leiomyosarcoma)

Benign Fibrous Tumor of Mesentery

1. Mesenteric fibromatosis
2. Sclerosing mesenteritis
3. Inflammatory pseudotumor
4. Extrapleural solitary fibrous tumor

Mesenteric / Omental Cysts

= "Bubbles of the belly"

◊ The first step is to determine the organ of origin!

1. Lymphangioma
2. Nonpancreatic pseudocyst
   = sequelae of mesenteric / omental hematoma / abscess
   Path: thick-walled, usually septated cystic mass with hemorrhagic / purulent contents
3. Duplication cyst
4. Mesothelial cyst
5. Enteric cyst
6. Cystic metastasis
7. Cystic mesothelioma

Mesenteric Edema / Congestion

√ increase of mesenteric fat attenuation to –40 to –60 HU

√ loss of sharp interfaces between mesenteric vessels + fat

A. SYSTEMIC FLUID OVERLOAD
   1. Hypoalbuminemia
   2. Liver cirrhosis
   3. Nephrosis
   4. Heart failure

B. LOCAL VESSEL DISEASE
   1. Portal vein thrombosis
   2. Mesenteric vein / artery thrombosis
   3. Vasculitis
   4. SMA dissection

C. CELL INFILTRATE
   1. Malignant neoplasm
   2. Inflammation
   3. Trauma: small hemorrhage

Comb Sign

= vascular dilatation of vasa recta + interconnected arterial arcades aligned as the teeth of a comb

√ multiple tubular tortuous opacities on mesenteric side of ileum

1. Crohn disease
2. Ulcerative colitis
3. Vasculitis: Lupus, polyarteritis nodosa, Behçet disease, Henoch-Schönlein syndrome, microscopic polyangiitis

4. Mesenteric thromboembolism
5. Strangulated bowel obstruction

Fat Ring Sign

= fat-stranding of the fat plane surrounding the root of mesenteric vessels

A. BENIGN
   1. Mesenteric panniculitis
   2. Mesenteric lipodystrophy
   3. Retractile mesenteritis

B. MALIGNANT
   1. Carcinoid
   2. Desmoid tumor
   3. Lymphoma

Misty Mesentery Sign

= subtle increased attenuation in the mesentery at CT often associated with small borderline-sized lymph nodes

1. Normalcy (common finding!)
2. Mesenteric panniculitis
3. Hemorrhage
4. Edema
5. Malignancy

Abdominal Fat Necrosis

1. Epiploic appendagitis
2. Omental infarction
3. Encapsulated fat necrosis
4. Fat saponification from pancreatitis = retroperitoneal fat necrosis

Mimicks:

1. Focal lipohypertrophy
   Cause: insulin injections into subcutaneous tissue in insulin-dependent diabetics
2. Lipodystrophy
   = heterogeneous group of disorders interfering with normal distribution of adipose tissue
3. Liposarcoma

Umbilical Tumor

A. PRIMARY (38%)
   benign / malignant neoplasm, skin tumor

B. METASTASES (30%)
   = "Sister Joseph nodule"
   • firm painful nodule
   • ± ulceration with serosanguinous / purulent discharge
   Cause: gastrointestinal cancer (50%), undetermined (25%), ovarian cancer, pancreatic cancer, small cell carcinoma of lung (very rare)
   Spread:

(a) direct extension from anterior peritoneal surface
(b) extension along embryonic remnants: falciform, median umbilical, omphalomesenteric ligaments
(c) hematogenous
(d) retrograde lymphatic flow from inguinal, axillary, paraaortic nodes
(e) iatrogenic: laparoscopic tract, tract of percutaneous needle biopsy

C. NONNEOPLASTIC
1. Endometriosis (32%)
2. Granuloma
3. Incarcerated hernia

Omphalomesenteric Duct Anomalies
1. Meckel Diverticulum (98%)
2. Omphalomesenteric fistula
3. Omphalomesenteric sinus
4. Omphalomesenteric duct cyst
5. Omphalomesenteric ligament

ABDOMINAL LYMPHADENOPATHY

Regional Patterns of Lymphadenopathy

@ Retrocrural nodes
Abnormal size: > 6 mm
Common cause: lung carcinoma, mesothelioma, lymphoma

@ Gastrohepatic ligament nodes
= superior portion of lesser omentum suspending stomach from liver
Abnormal size: > 8 mm
Common cause: carcinoma of lesser curvature of stomach, distal esophagus, lymphoma, pancreatic cancer, melanoma, colon + breast cancer
DDx: coronary varices

@ Porta hepatis nodes
= in porta hepatis extending down hepatoduodenal ligament, anterior + posterior to portal vein
Abnormal size: > 6 mm
Common cause: carcinoma of gallbladder + biliary tree, liver, stomach, pancreas, colon, lung, breast, chronic hepatitis C
Cx: high extrahepatic biliary obstruction

@ Pancreaticoduodenal nodes
= between duodenal sweep + pancreatic head anterior to IVC
Abnormal size: > 10 mm
Common cause: lymphoma, pancreatic head, colon, stomach, lung, breast cancer

@ Perisplenic nodes
= in splenic hilum
Abnormal size: > 10 mm
Common cause: NHL, leukemia, small bowel neoplasm, ovarian cancer, carcinoma of

right / transverse colon

@ Retroperitoneal nodes
= periaortic, pericaval, interaortocaval
Abnormal size: > 10 mm
Common cause: lymphoma, renal cell, testicular, cervical, prostatic carcinomas

As with malignant retroperitoneal fibrosis, metastatic retro-peritoneal adenopathy typically elevates the aorta off the underlying vertebral body (exceptions have been reported)

@ Celiac and superior mesenteric artery nodes
= preaortic nodes
Normal size: 4.6 mm mean maximum short-axis diameter
Abnormal size: > 10 mm
Common cause: lymphoma, any intraabdominal neoplasm, TB, atypical mycobacterial infection, Whipple disease

@ Ileocecal nodes
= along ileocolic artery
Common cause: mesenteric lymphadenitis, appendicitis, diverticulitis, Crohn disease, SLE, HIV infection

@ Pelvic nodes
= along common, external + internal iliac vessels
Abnormal size: > 15 mm
Common cause: carcinoma of bladder, prostate, cervix, uterus, rectum

Low-attenuation Abdominal Adenopathy

= ENLARGED LYMPH NODE WITH LOW-DENSITY CENTER
√ rim-enhancing nodules + central necrosis
1. Mycobacterial infection (TB, M. avium-intracellulare)
2. Pyogenic infection
3. Whipple disease
4. Lymphoma
5. Metastatic disease after radiation + chemotherapy
6. Lymphangioleiomyomatosis
7. Neurofibromatosis type I
8. Cavitating mesenteric lymph node syndrome

PARASITIC INFESTATION

A. PROTOZOA = one cell parasites
[*protos*, Greek = foremost, earliest; *zoion*, Greek = animal]
(a) genitourinary
1. Trichomoniasis
2. Chlamydomonas
(b) intestinal
1. Giardiasis
2. Amebiasis
3. Cryptosporidiosis

(c) blood
1. Malaria
2. Giardiasis
4. Trypanosomiasis
5. Tuberculosis
6. Toxoplasmosis
8. Filariasis
7. Leishmaniasis

B. PLATYHELMINTHES = flatworms
(a) cestodes (= tapeworms) [*cestus*, Latin = belt, girdle]
1. Echinococcus granulosus
2. Echinococcus multilocularis
3. Cysticercosis

(b) trematodes (flukes) [*trema* , Greek = hole; *odes* , Greek = like]
1. Clonorchiasis
2. Fascioliasis
3. Paragonimiasis
4. Schistosomiasis
› S. haematobium (GU tract) > 95%
› S. mansoni, S. japonicum (GI tract) < 5%

C. NEMATODES = roundworms [*nema*, Greek = thread; *odes*, Greek = like]
1. Strongyloidiasis (= pinworm)
2. Ascariasis
3. Trichuriasis
4. Toxocariasis
5. Angiostrongylosis

› other hookworms: Ancylostoma duodenale, Necator americanus
› other pinworm: Enterobius vermicularis (formerly Oxyuris vermicularis)

Helminthiasis

= infestation caused by Platyhelminthes and Nematoda

Incidence: 2 billion people affected worldwide

Geography: › endemic: in developing countries and places with poor sanitation
› nonendemic: through immigration and travel

- iron-deficiency anemia, seizures
- chronic diarrhea, portal hypertension

Transmission: active penetration of skin by larvae from soil / fecal-oral route / vector arthropods

(a) larval penetration:
1. Schistosomiasis
2. Strongyloidiasis

(b) fecal-oral route:
1. Fascioliasis
2. Ascariasis
3. Trichuriasis

4. Cysticercosis
5. Echinococcosis
6. Toxocariasis
7. Angiostrongylosis

ANATOMY AND FUNCTION OF ABDOMEN AND GASTROINTESTINAL TRACT

GASTROINTESTINAL HORMONES

Cholecystokinin

= CCK = 33 amino acid residues (former name: Pancreozymin); the 5 C-terminal amino acids are identical to those of gastrin, causing similar effects as gastrin; 2.5-min serum half-life

Produced in: duodenal + upper intestinal mucosa

Released by: fatty acids, some amino acids (phenylalanine, methionine), hydrogen ions

Effects:

@ Stomach
- (1) weakly stimulates HCl secretion
- (2) given alone: inhibits gastrin → ↓ in HCl production
- (3) stimulates pepsin secretion
- (4) stimulates gastric motility

@ Pancreas
- (1) stimulates secretion of pancreatic enzymes (= Pancreozymin)
- (2) stimulates bicarbonate secretion: weakly by direct effect; strongly through potentiating effect on secretin
- (3) stimulates insulin release

@ Liver
- (1) stimulates water + bicarbonate secretion

@ Intestine
- (1) stimulates secretion of Brunner glands
- (2) increases motility

@ Biliary tract
- (1) strong stimulator of gallbladder contraction with maximum effect within 5–15 min + return to basal size in 1 hour
- (2) relaxation of sphincter of Oddi

Medication:

sincalide (KINEVAC®) = synthetic C-terminal octapeptide of the hormone cholecystokinin

Gastrointestinal Endocrine Cells		
Cell Type	*Location*	*Secretory Product*
G-cell (gastrin cell)	gastric antrum, duodenum	gastrin
ECL-cell (enterochromaffin -like cell)	gastric fundus and body	histamine
D-cell (somatostatin -producing cell)	stomach, duodenum, jejunum, colon, rectum	somatostatin
EC-cell (enterochromaffin cell)	stomach, duodenum, jejunum, colon, rectum	serotonin, motilin, substance P
CCK-cell (cholecystokinin cell)	duodenum, ileum	cholecystokinin
GIP-cell (gastric inhibitory polypeptide cell)	duodenum, ileum	gastric inhibitory polypeptide
M-cell (motilin cell)	duodenum, jejunum	motilin
S-cell (secretin cell)	duodenum, jejunum	secretin
PP-cell (pancreatic polypeptide cell)	duodenum	pancreatic polypeptide
L-cell (enteroendocrine cell)	jejunum, ileum, colon, rectum	polypeptide YY
N-cell (neurotensin cell)	jejunum, ileum	neurotensin

Use: may be used to empty gallbladder about 30 minutes (to 4 hours) before tracer injection in patients on prolonged fasting (gallbladder atony + retained bile and sludge) ← absence of endogenously produced CCK

Dose for hepatobiliary scintigraphy:

package insert: with slow IV injection of 0.01 µg/kg KINEVAC® over 3 minutes (concentration of 1 µg/mL) the response is too variable

preferred: IV infusion of 0.01 µg/kg KINEVAC® over 30–60 minutes

Useful in: (a) patient fasting > 24 hours / on total parenteral nutrition
(b) acalculous cholecystitis
(c) chronic GB dysfunction
(d) GB ejection fraction

Side effect: increase in biliary-to-bowel transit time, dizziness, flushing, nausea, abdominal cramps, urge to defecate

Contraindications:

acute pancreatitis, acute cholecystitis, obstruction of cystic duct / CBD, appendicitis, peritonitis, pyloric stenosis, peptic ulcer

Gastrin

= 17 amino acid peptide amide

PENTAGASTRIN = acyl derivative of the biologic active C-terminal tetrapeptide amide

Produced in: antral cells + G cells of pancreas

Released by:

(a) vagal stimulation, gastric distension
(b) short-chain alcohol: ethanol, propanol
(c) amino acids: glycine, β-alanine
(d) caffeine
(e) hypercalcemia

mediated by neuroendocrine cholinergic reflexes

Inhibited by: drop in pH of antral mucosa to < 3.5

Effects:

@ Stomach:
(1) stimulation of gastric HCl secretion from parietal cells, which in turn
(2) increases pepsinogen production by chief cells through local reflex
(3) increase in antral motility
(4) trophic effect on gastric mucosa → parietal cell hyperplasia

@ Pancreas
(1) strong increase in enzyme output
(2) weakly stimulates fluid + bicarbonate output
(3) stimulates insulin release

@ Liver
(1) water + bicarbonate secretion

@ Intestine
(1) stimulates secretion of Brunner glands
(2) increases motility

@ Gallbladder
(1) stimulates contraction

@ Esophagus
(1) increases resting pressure of LES

Glucagon

Produced in: α cells (and β cells) of pancreas

Released by: low blood glucose levels

Effects:

@ Intestines
(1) lowers pressure of GE sphincter
(2) hypotonic effect on duodenum > jejunum > stomach > colon

@ Hormones
(1) releases catecholamines from adrenal gland → paralysation of intestinal smooth muscle
(2) increases serum insulin + glucose levels → mobilization of hepatic glycogen

@ Biliary tract
(1) increases bile flow
(2) relaxes gallbladder + sphincter of Oddi

Dose for radiologic imaging: 1 mg maximum

◊ IV administration causes a quick response + rapid dissipation of action!
◊ IM administration prolongs onset + increases length of action!

Half-life: 3–6 min

Side effects: nausea + vomiting, weakness, dizziness (delayed onset of 1.5–4.0 hours after IM administration)

Contraindication:

(1) hypersensitivity / allergy to glucagon: urticaria, periorbital edema, respiratory distress, hypotension, coronary artery spasm (?), circulatory arrest
(2) known hypertensive response to glucagon
(3) pheochromocytoma: glucagon stimulates release of catecholamines
(4) insulinoma: insulin-releasing effect may result in hypoglycemia
(5) glucagonoma
(6) poorly controlled diabetes mellitus

Secretin

= 27–amino acid polypeptide hormone

Produced in: duodenal mucosa

Released by: hydrogen ions providing a pH < 4.5 (usually increase in postprandial intraluminal acidity)

The physiologic effects of secretin include secretion of bicarbonate-rich fluid from pancreatic ductal cells and transient increase in the sphincter of Oddi tone, which improves depiction of the pancreatic duct.

Effects:

@ Stomach
(1) inhibits release of gastrin → ↓ in HCl secretion
(2) stimulates pepsinogen secretion by chief cells (potent pepsigogue)
(3) decreases gastric and duodenal motility + contraction of pyloric sphincter

@ Pancreas
(1) increases alkaline bicarbonate-rich pancreatic secretions (NaHCO3 = sodium bicarbonate)
» bicarbonate = 2 x as much carbonate (CO3) per sodium ion in sodium bicarbonate (NaHCO3) as in sodium carbonate (Na2CO3); crucial role in physiological pH buffering
(2) weakly stimulates enzyme secretion
(3) stimulates insulin release

@ Liver
(1) stimulates water + HCO3- secretion (most potent choleretic)

@ Intestine
(1) stimulates secretion of Brunner glands
(2) inhibits motility

@ Esophagus
(1) opens LES

@ Sphincter of Oddi
(1) transient increase in muscle tone used in SOM (sphincter of Oddi manometry)

Common Indications for Secretin Use during MRCP	
Clinical	*Indication*
Acute recurrent pancreatitis, severe necrotizing pancreatitis	Integrity of MPD
Chronic pancreatitis	Duct stricture / stone
	Pancreatic excretory volume estimate
Pancreatic cystic neoplasm	Side-branch IPMN vs. other cystic neoplasm / pseudocyst
Postoperative pancreas	Pancreaticoenteric anastomosis patency
	Estimate pancreatic exocrine reserve
	Duct dilatation / filling defect / leak
Suspected duct anomaly	Pancreas divisum + variants
	Pancreaticobiliary junction anomaly

Secretin Stimulation Test SST

Indication: (1) Exocrine pancreas dysfunction
(2) Gastrinoma versus peptic ulcer disease
(3) Identification of ampulla of Vater + accessory papilla during ERCP

Drug: purified synthetic human secretin ChiRhoStim®, ChiRhoClin®

Dose: 0.2–0.4 µg/kg IV (~ 16 µg for adult) over 1 minute to avoid side effect of abdominal pain

Initial test dose: for possible allergic reaction

Peak effect: usually at 3–5 minutes after injection

√ ↑ main pancreatic duct (MPD) diameter by > 1 mm
√ ↑ visibility of side branches of MPD
√ ↑ T2 SI in duodenum ← excretion of pancreatic fluid

Adverse effects: (in 0.5%) nausea, flushing, abdominal pain, vomiting, mild acute pancreatitis

Dx of gastrinoma:

release of gastrin from gastrinoma cells is increased → increased serum gastrin level of 200 ng/L above baseline (90% sensitive + specific)

N.B.: normally secretin inhibits release of gastrin

Dx of chronic pancreatitis:

aspiration of intestinal secretions via tube passed into duodenum for 1 hour analyzing volume, pH, bicarbonate concentration in 15-minute aliquots (75% sensitive + 90% specific for chronic pancreatitis)

Contraindication: acute pancreatitis

Somatostatin SS

= growth hormone–inhibiting hormone (GHIH); somatotropin release-inhibiting factor (SRIF); somatotropin release-inhibiting hormone (SRIH)

Produced in: many tissues; principally in nervous + digestive systems

Action: inhibits secretion of several other hormones like growth hormone (GH), thyroid stimulating hormone (TSH), cholecystokinin, insulin

Released by: raised levels of other hormones (feed back); ↑ blood glucose + amino acids (food intake)

Inhibited by: reduced levels of other hormones (feed back)

Effects:

@ Hypothalamus
inhibits pituitary gland → ↓ secretion of GH + TSH
Rx: treatment of acromegaly

@ Pancreas
food intake → ↓ secretion of insulin + glucagon

@ GI tract
(a) local reduction of gastric secretion
(b) gastrointestinal motility
(c) inhibits secretion of gastrin + secretin

EMBRYOLOGY OF ALIMENTARY TRACT

Origin: pouchlike extension of the yolk sac

Division: (1) foregut supplied by celiac artery for bronchopulmo-nary system, stomach, pancreas, proximal duodenum
(2) midgut supplied by superior mesenteric artery (SMA) representing axis of gut rotation: mid-duodenum, jejunum, ileum, appendix, ascending colon, mid-transverse colon
(3) hindgut supplied by inferior mesenteric artery: mid-transverse colon, rectum

at 4 weeks: short straight featureless tube

1st rotation:
(a) duodenum rotates cephalocaudal 90° counterclockwise to a position at right of SMA
(b) colon rotates 90° to left of SMA

at 6 weeks: rapid growth of intraabdominal organs (expansion of liver + GI tract) → bowel herniates into umbilical cord = physiologic umbilical herniation

2nd rotation:
(a) duodenum rotates another 90° (completes 180°) counter-clockwise beneath SMA to a position at left of SMA
(b) colon does not rotate

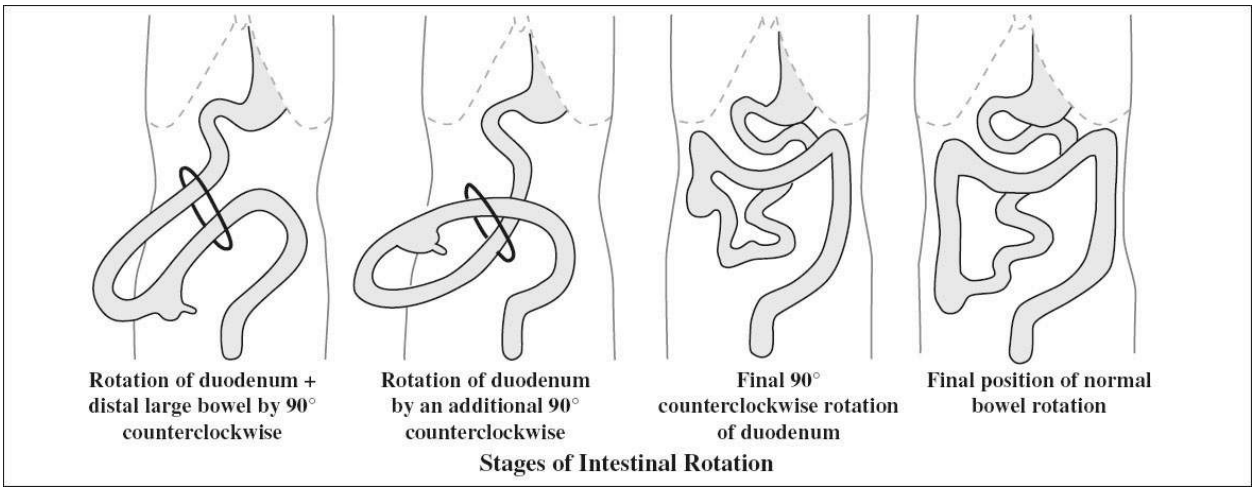
at 10 weeks: bowel returns to abdominal cavity

3rd rotation:
(a) duodenum rotates another 90° (completes 270°) counter-clockwise with duodenojejunal junction resting to left of spine
(b) colon rotates 180° counterclockwise until cecum is located in RLQ by 12th week

Peritoneal fixation of bowel:
› broad-based mesentery extending from ligament of Treitz to ileocecal valve
› colon fuses with retroperitoneum in RLQ with the exception of the most caudal part
› duodenum fixes to retroperitoneum in LUQ

Change in fetal nutrition from yolk sac to placenta:

› during 5th to 7th weeks → regressing omphalomesenteric duct



Stages of Intestinal Rotation

ARTERIAL SUPPLY OF BOWEL

◊ Bowel receives 20% of resting cardiac output (⅔ for intestinal mucosa) which increases up to 35% in postprandial phase

Influence of food:

carbohydrates → earliest + fast rise

fat + proteins → slower + large rise

Celiac Trunk

Location: at ~ T12 = superior border of pancreatic body

Supplies: from distal esophagus to descending duodenum

Branches: common hepatic a. (CHA), left gastric a. (LGA), splenic artery (SpA) with considerable variations in branching pattern

- › CHA branching from SMA (hepatomesenteric type)
- › direct branching of CHA / LGA / SpA from aorta
- › replaced left hepatic artery
- › replaced right hepatic artery

Anastomosis: to SMA via gastroduodenal artery as the 1st branch off the celiac trunk

Superior Mesenteric Artery (SMA)

Supplies: transverse + descending duodenum, jejunum, ileum, large bowel to splenic flexure

Anastomosis: with IMA via marginal artery of Drummond, arcade of Riolan

Inferior Mesenteric Artery (IMA)

Supply for: colon from splenic flexure to rectum

Anastomoses: with lumbar branches of abdominal aorta, sacral artery, internal iliac arteries

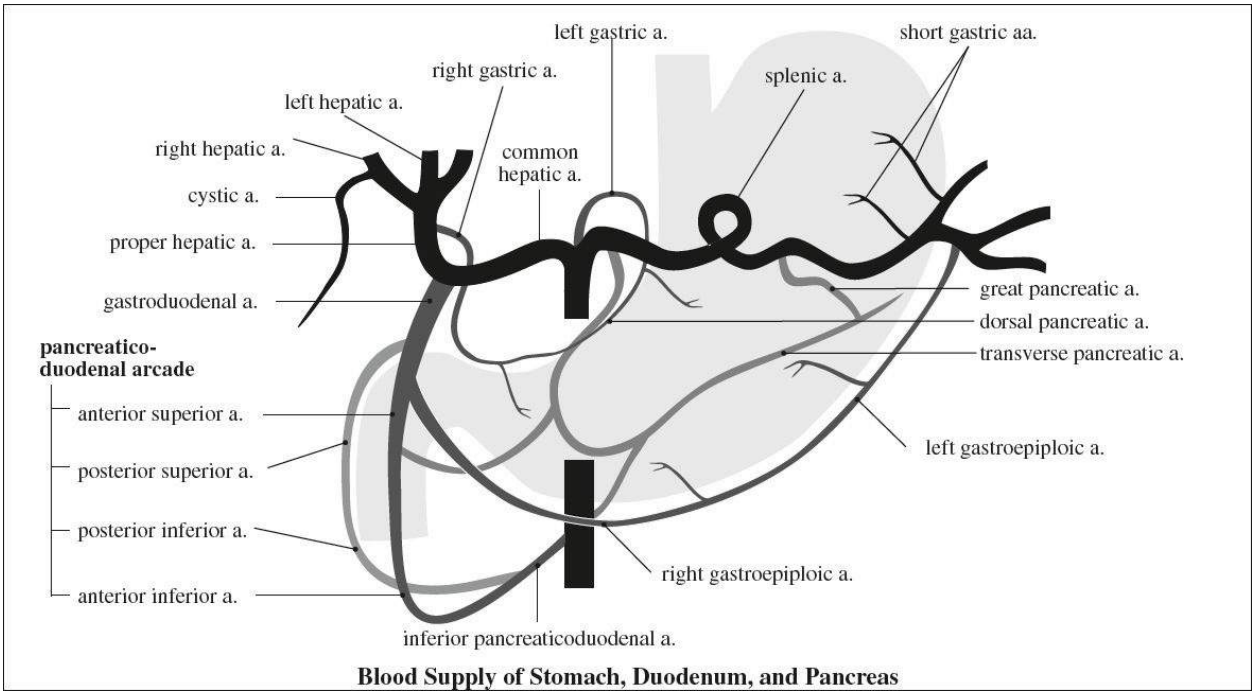
Arterial Arcades

up to 4 arcades are formed by these arteries which continue toward the periphery as

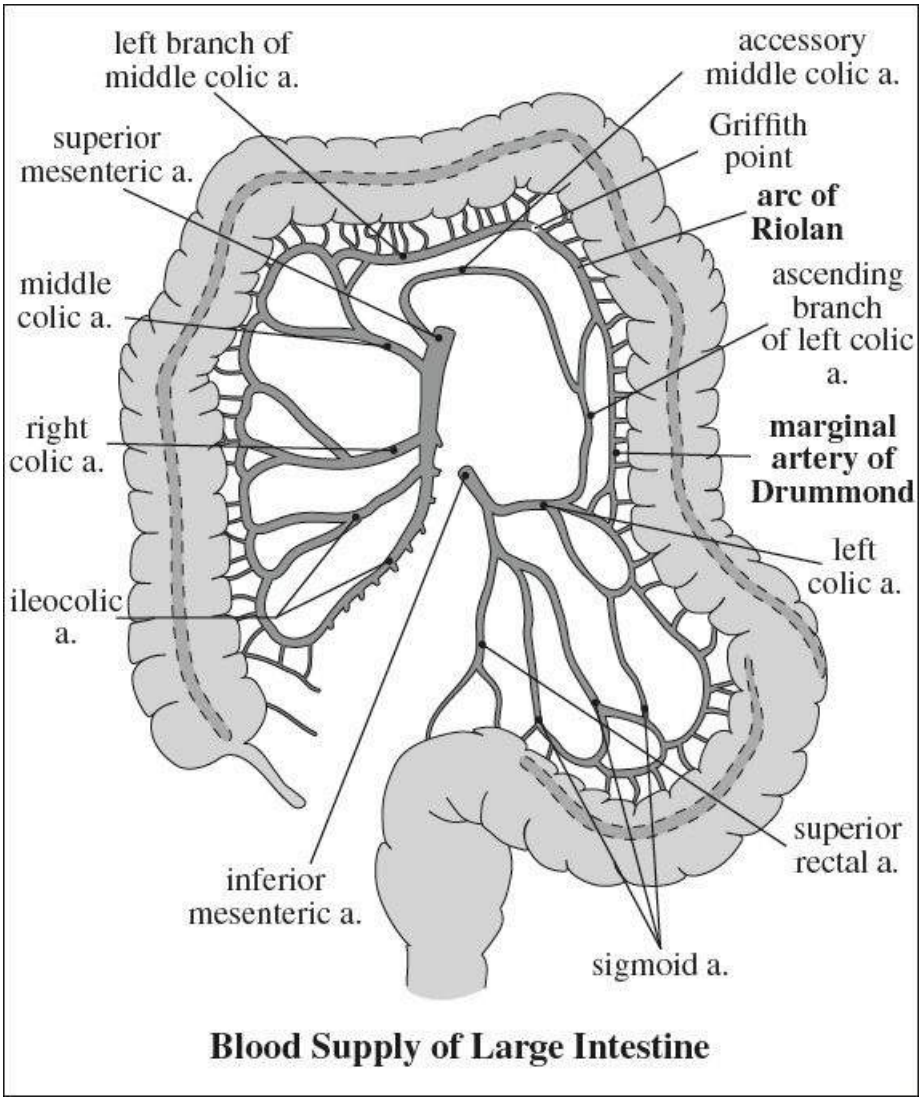
1. Primary parallel circuits for
   a. muscularis propria

b. submucosa
c. mucosa

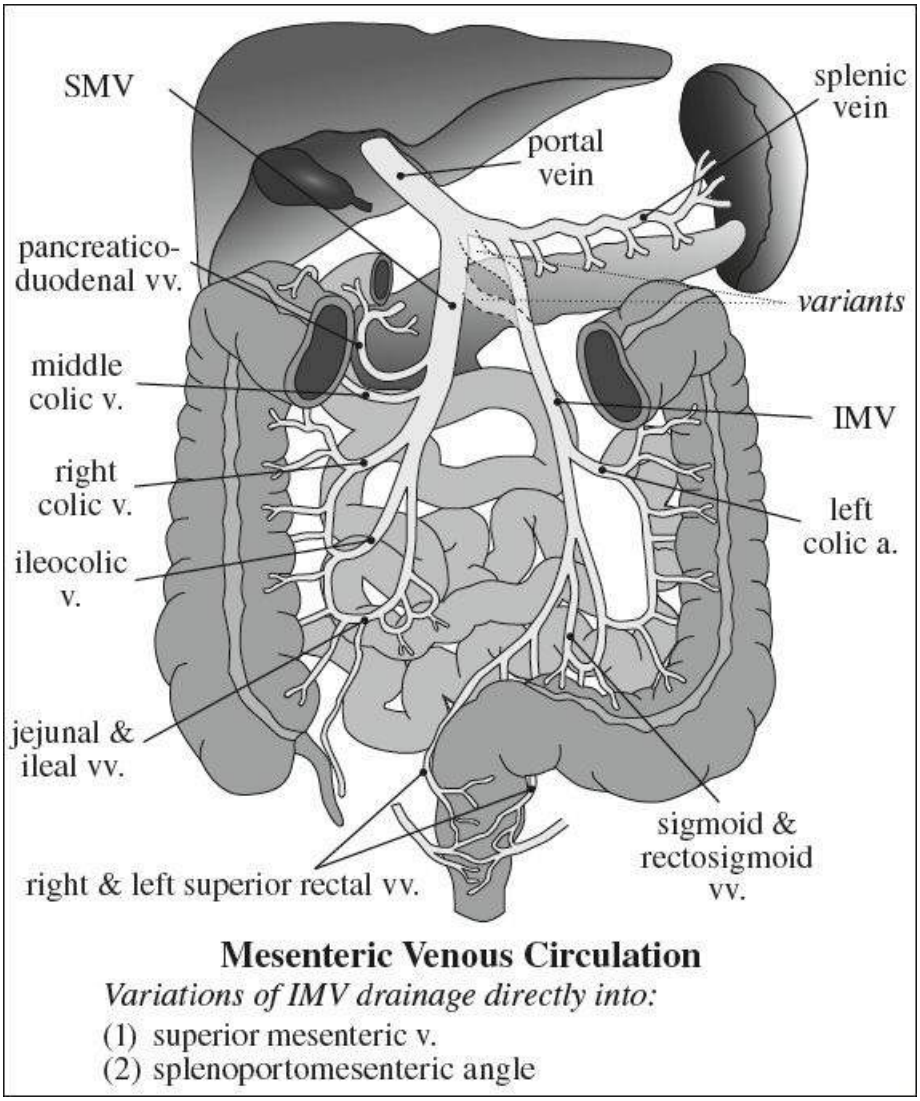
2. Serial circuits of
   a. resistance arterioles
   b. precapillary sphincters
   c. capillaries
   d. postcapillary sphincters
   e. venous capacitance vessels



Blood Supply of Stomach, Duodenum, and Pancreas



Blood Supply of Large Intestine



Mesenteric Venous Circulation

Variations of IMV drainage directly into:

(1) superior mesenteric v.

(2) splenoportomesenteric angle

MESENTERIC VENOUS SYSTEM

Venae Rectae

= multiple small veins along bowel wall that join to form venous arcades

Superior Mesenteric Vein

Drainage for: small bowel, proximal colon to splenic angle

Formed by: jejunoileal, ileocolic, right colic, middle colic, pancreaticoduodenal veins

Inferior Mesenteric Vein

Drainage for: splenic flexure, descending colon, sigmoid colon, part of rectum

Formed by: left colic, sigmoid, rectosigmoid, right and left superior rectal veins

Connects to: SMV directly / splenic vein / angle of splenoportomesenteric confluence

ESOPHAGUS

Esophageal Division

1. Upper third
   cricopharyngeus to superior margin of aortic arch
2. Middle third
   superior margin of aortic arch to inferior pulmonary vein
3. Lower third
   inferior pulmonary vein to gastroesophageal junction

Cricopharyngeus Muscle

= main component of upper esophageal sphincter
√ normally closed between swallows
√ relaxes and opens completely for bolus passage to occur in conjunction with elevation of larynx and pharyngeal constrictors
√ prominent posterior indentation on barium column ← incidental / sign of dysphagia
May be associated with:
pharyngeal constrictor muscle weakness, failure of laryngeal elevation, Zenker diverticulum, response esophageal spasm or GERD

Lower Esophageal Anatomy

A. **Esophageal Vestibule**
= saccular termination of lower esophagus with upper boundary at tubulovestibular junction + lower boundary at esophagogastric junction
√ collapsed during resting state
√ assumes bulbous configuration with swallowing
(a) tubulovestibular junction = A level = junction between tubular and saccular esophagus
(b) phrenic ampulla = bell-shaped part above diaphragm (term should be discarded because of dynamic changes of configuration)
(c) submerged segment = infrahiatal part of esophagus
√ widening / disappearance is indicative of gastroesophageal reflux disease (GERD)

B. **Gastroesophageal Junction**
Function: regulates flow of food + fluid between esophagus and stomach; key defense against gastroesophageal reflux
Barrier: (1) Intrinsic smooth muscle of LES
(2) Extrinsic striated muscle of crural diaphragm
(3) clasp + sling fibers of gastric cardia
Site: at upper level of gastric sling fibers, straddles cardiac incisura demarcating the left lateral margin of GE junction

C. **Z-line** = B level = zigzag-shaped squamocolumnar junction line
◊ Not acceptable criterion for locating GE junction
Site: 1–2 cm above gastric sling fibers

D. **Lower Esophageal Sphincter**
= physiologic 2–4-cm high pressure zone corresponding to esophageal vestibule
√ tightly closed during resting state
√ assumes bulbous configuration with swallowing

Muscular Rings of Esophagus

A Ring

= contracted / hypertrophied muscles in response to incompetent GE sphincter

• rarely symptomatic / dysphagia

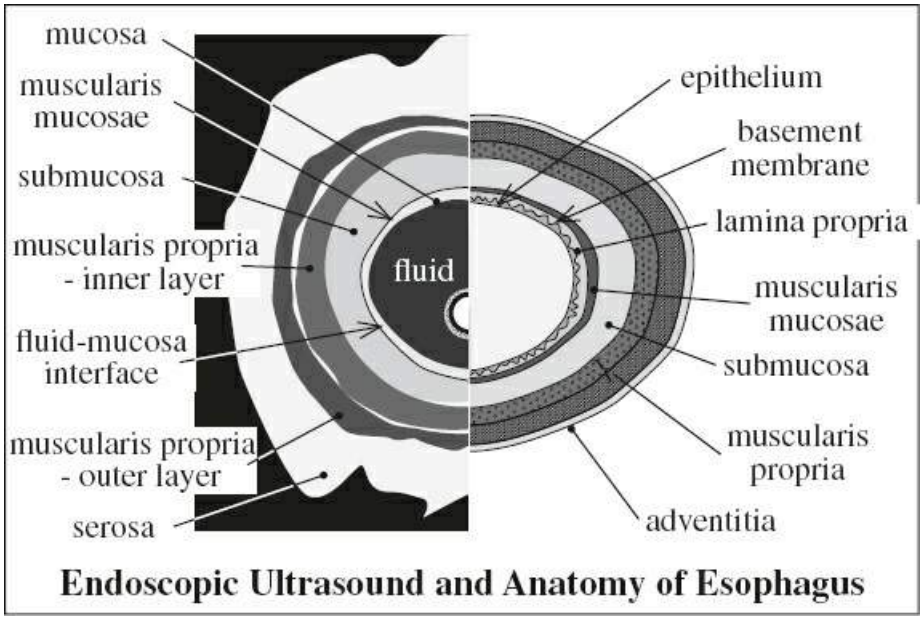
Location: at tubulovestibular junction = superior aspect of vestibule

√ usually 2 cm proximal to GE junction at upper end of vestibule

√ varies in caliber during the same examination, may disappear on maximum distension

√ broad smooth narrowing with thick rounded margins

√ visible only if tubular esophagus above + vestibule below are distended



Endoscopic Ultrasound and Anatomy of Esophagus

B Ring

= sling fibers representing a U-shaped thickening of inner muscle layers with open arm of U toward lesser curvature = inferior aspect of vestibule

Location: < 2 cm from hiatal margins

√ only visible when esophagogastric junction is above hiatus

√ thin ledge-like ring just below the mucosal junction (Z-line)

Layers of Intestinal Wall by Ultrasound

= gut signature

1. Mucosa echogenic
   √ hyperechoic interface of balloon + mucosa
2. Muscularis mucosae hypoechoic
   √ hypoechoic mucosa + muscularis mucosa
3. Submucosa echogenic / hyperechoic
4. Muscularis propria hypoechoic
5. Serosa echogenic / hyperechoic

Most benign conditions preserve the gut signature involving long segments of bowel, while malignant

conditions destroy the gut signature involving short segments of bowel.
Aggressive inflammatory processes cause focal disruption of the gut signature.

SWALLOWING FUNCTION

Preparation: refrain from smoking for 12 hours + from eating for > 4 hours before examination
Provide info on baseline anatomy + swallow physiology: for oral cavity, pharynx, larynx, upper esophagus during deglutition

Technique:

Videofluoroscopic Swallow Study (VFSS) = modified barium swallow study to assess handling of bolus; usually performed together with swallowing / speech pathologist

» patient seated upright in lateral + AP positions
» incremental increase in radiopaque bolus volume + texture of various consistencies like nectar liquid, honey liquid, pureed food, soft solid food, hard solid food (commercially available: E-Z Paque liquid, Varibar® thin liquid, nectar, honey, pudding, graham cracker cookie with pudding)

Document patient behavior + reaction:
episode of refusal, cough, silent aspiration, apnea, bradycardia

CNS involved: cranial nerves V, VII, IX, X, XII; 5 cervical nerves; cortical + subcortical pathways; midbrain; brainstem

Muscles involved: 32 groups of muscles

Developmental: swallowing as early as 11 weeks GA;
suckling at 18–24 weeks GA; nonnutritive
sucking at 27–28 weeks GA; single breath
sucking at 35–36 weeks GA

Phases:

1. Oral preparatory phase
   √ food chewed + mixed with saliva
2. Oral phase
   √ bolus propelled posteriorly to tongue
   Path:
   (a) spillage from mouth
   (b) small bolus formation
   (c) tongue tremor
   (d) incomplete tongue elevation
   (e) early spillage into valleculae prior to initiation of swallow
3. Pharyngeal phase
   √ elevation of soft palate + valleculae (to seal nasopharynx)
   √ elevation of larynx (to close vestibule)
   √ relaxation of cricopharyngeal muscle
   √ contraction of lateral pharyngeal wall

At videofluoroscopy carefully evaluate mechanisms to prevent aspiration: superior + anterior elevation of larynx, closure of larynx, and epiglottic tilt.

Path:
(a) **nasopharyngeal reflux**

(b) **laryngeal penetration** = contrast material enters laryngeal vestibule
Cause: delayed elevation of larynx
(c) **tracheal aspiration** = contrast material enters airway below vocal cord level into proximal trachea
Cause: delayed elevation of larynx, delayed pharyngeal transit time, decreased clearance of bolus with residual in vallecula and pyriform sinus spilling into larynx + trachea

4. Esophageal phase
√ contraction of cricopharyngeal muscle
√ bolus transfer into esophagus
Path: cricopharyngeal achalasia (with reflux of bolus into oropharynx / pooling in pyriform sinus)

STOMACH

Segmental Anatomy of Stomach

1. Cardia
2. Fundus
Dependency: most superior portion when upright most dependent portion when supine
√ stomach bubble on CXR
√ accumulation of intraluminal contents on CT
3. Body
(a) lesser curvature: left and posteriorly on CT
(b) greater curvature: right and anteriorly on CT
√ ≤ 5 mm in thickness (in distended state)
» **Incisura angularis**
= transition to antral-type mucosa
◊ Most common site for gastric ulcers!
4. Antrum
= thickest gastric segment ← most muscular
√ ≤ 12 mm in thickness (in distended state)
√ exhibits the most peristalsis
√ may display mural stratification on CECT
5. Pylorus

Inadequate gastric distention limits diagnostic evaluation and may create a false appearance of thickening or may obscure true disease.
When evaluating abnormal gastric wall thickening in a nondistended stomach, supplementary findings can be helpful in identifying disease.

Trilaminar Gastric Wall on CECT

1. Mucosa: avid enhancement
2. Submucosa: low in attenuation
3. Muscularis propria: high in attenuation
4. Serosa

Suspicious findings:
√ focal / eccentric gastric wall thickening
√ low attenuation / nodularity of gastric wall
√ mucosal hyperenhancement
√ adjacent fat stranding

Gastric Cells

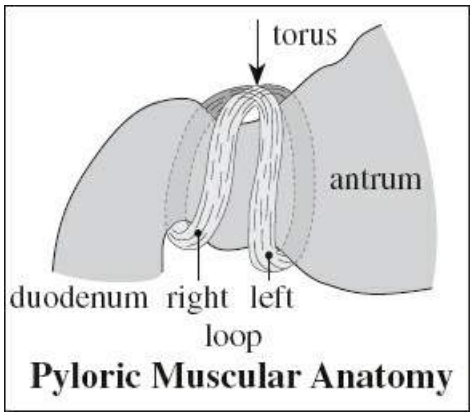
1. Chief cells = peptic / zymogenic cells
   Location: body + fundus
   produce: pepsinogen
2. Parietal cells = oxyntic cells
   Location: body + fundus
   produce: H+, Cl-, intrinsic factor, prostaglandins
3. Mucous neck cells
   produce: mucoprotein, mucopolysaccharide, aminopolysaccharide sulfate
4. Argentaffine cells = enteroendocrine cells
   Location: body + fundus
   produce: glucagon-like substance (A-cells), somatostatin (D-cells), vasoactive intestinal polypeptide (D1-cells), 5-hydroxytryptamine (EC-cells)
5. G-cells
   Location: pylorus
   produce: gastrin

Effect of Bilateral Vagotomy

= cholinergic denervation
(1) decreased MOTILITY of stomach + intestines
(2) decreased GASTRIC SECRETION
(3) decreased TONE OF GALLBLADDER + bile ducts
(4) increased TONE OF SPHINCTERS (Oddi + lower esophageal sphincter)

Pylorus

[*pyloros*, Greek = gatekeeper]
= fan-shaped specialized circular muscle fibers with:
(a) distal sphincteric loop = right canalis loop
√ corresponds to radiologic pyloric sphincter
(b) proximal sphincteric loop = left canalis loop
√ 2 cm proximal to distal sphincteric loop on greater curvature (seen during complete relaxation)
(c) torus
= fibers of both sphincters converge on the lesser curvature side to form a muscular prominence; prolapse of mucosa between sphincteric loops produces a niche simulating ulcer
√ pyloric channel 5–10 mm long, wall thickness of 4–8 mm
√ concentric indentation of the base of the duodenal bulb



SMALL BOWEL

◊ Longest tubular organ in body measuring 550–600 cm (18–22 feet) in length

Segments and Length:

› duodenum of 25–30 cm in length

› mesenteric small bowel:

» jejunum: 10–12 feet in length (= proximal 60%)

» ileum: 6–8 feet in length (= distal 40%)

Mesentery: 15 cm long between ligament of Treitz (musculus suspensorius duodeni) + ileocecal junction

Duodenum

= 1st part of small intestine from pylorus to lig. of Treitz

[Václav (Wenzel) Treitz (1819–1872), Director of the Institute of Pathological Anatomy in Prague]

Borders:

(a) posterior: external edge of IVC, medial surface of right kidney + hilum, psoas muscle

(b) anterior: right transverse colon, mesocolon, floating small bowel loops

(c) medial: pancreatic head

(d) lateral: right hepatic lobe, gallbladder neck, ascending colon

Duodenal Segments

1st segment = duodenal bulb + short postbulbar segment:

Course: passes backward + upward toward neck of GB

Location: intraperitoneal

√ freely movable ← intraperitoneal

2nd segment = descending duodenum

= gentle curve from superior to inferior duodenal flexures with attachment to head of pancreas

Length: 7–10-cm-long tube

Diameter: 35–40-mm

Location: retroperitoneal in anterior pararenal space between posterior parietal peritoneum and anterior perirenal fascia of Gerota

Openings:

(a) major papilla (Vater) ← hepatopancreatic ampulla ← junction of CBD + main pancreatic duct

(b) minor duodenal papilla = opening 2 cm above ampulla ← accessory pancreatic duct of Santorini

3rd segment = horizontal / transverse segment

Course: runs 10–12 cm horizontally to the left

Location: retroperitoneal crossing in front of IVC + aorta + lumbar spine; posterior to mesenteric vessels

4th segment = ascending portion

Course: runs 2–3 cm upward to the left

Location: retroperitoneal ascending to level of duodenojejunal junction

VARIATIONS:

(1) "mobile duodenum" / "water-trap duodenum"
= long postbulbar segment with undulation / redundancy

(2) duodenum inversum / duodenum reflexum
= distal duodenum ascends to the right of spine to the level of duodenal bulb + then crosses spine horizontally + fixated in normal location

Small Bowel Folds

◊ Circumferential small bowel folds (= folds of Kerckring
[Theodor (or Dirk) Kerckring (Kerckeringh, Kerckerinck) (1638–1693), Dutch anatomist and chemical physician]
= valvulae conniventes = plicae circulares) = 2 mucosal layers around a core of submucosa

A. WALL THICKNESS
◊ Small bowel wall thickness > 3 mm at CT is abnormal!

B. NORMAL FOLD THICKNESS
@ jejunum 1.7–2.0 mm > 2.5 mm pathologic
@ ileum 1.4–1.7 mm > 2.0 mm pathologic

C. NORMAL NUMBER OF FOLDS
@ jejunum 4–7 / inch
@ ileum 2–4 / inch

D. NORMAL FOLD HEIGHT
@ jejunum 3.5–7.0 mm
@ ileum 2.0–3.5 mm

E. NORMAL LUMEN DIAMETER
@ upper jejunum 3.0–4.0 cm > 4.5 cm pathologic
@ lower jejunum 2.5–3.5 cm > 4.0 cm pathologic
@ ileum 2.0–2.8 cm > 3.0 cm pathologic

RULE OF 3's:
◊ Wall thickness < 3 mm
◊ Valvulae conniventes < 3 mm
◊ Diameter < 3 cm
◊ Air-fluid levels < 3

Normal Bowel Caliber

◊ Small bowel gradually tapers in diameter from duodenojejunal junction to terminal ileum!

mnemonic: 3-6-9-12

3 cm maximal size of small bowel
- › < 3 cm in jejunum (up to 4 cm during enteroclysis)
- › < 2 cm in ileum (up to 3 cm during enteroclysis)
  - ◊ < 25 mm on CT

6 cm maximal size of transverse colon

9 cm maximal size of cecum

12 cm maximal caliber of cecum before it may burst

Small Bowel Peristalsis

A. INCREASED
1. Vagal stimulation
2. Acetylcholine
3. Anticholinesterase (eg, neostigmine)
4. Cholecystokinin

B. DECREASED
1. Atropine (eg, Pro-Banthine®)
2. Bilateral vagotomy

Ileocecal Valve

= ICV = COLIC VALVE = VALVULA COLI

Composition: symmetric upper + lower lip formed by intrusion of circular muscle layer of ileum into lumen of large intestine

Frenula of ICV: narrow membranous ridges at medial and lateral end of aperture where lips meet

Function: modulation of flow of luminal contents from ileum into colon → minimizing rapid anterograde passage / retrograde flow; minimal sphincteric action (common barium reflux into terminal ileum)

Location: within a cecal fold along medial aspect of cecum

Endoscopic classification:

(a) labial	= slitlike opening
(b) papillary	= dome shaped opening
(c) lipomatous	= substantial deposit of fat within lips

COLON

Colon Transit Time

Sitzmarks diagnostic test:

Indication: adults with severe constipation but otherwise normal GI examination

1. Withhold laxatives / enemas / suppositories for 5 days
2. On day 0 patient takes 1 gelatin capsule (contains 24 radiopaque polyvinyl chloride markers of 1 x 4.5 mm) with water
   - ◊ All markers are usually in colon by 12 hours

3. Take KUB on day 5 to determine location + extent of marker elimination
   - › ≥ 19 markers (80%) expelled = grossly normal colonic transit time
   - › markers scattered about the colon = colonic hypomotility / inertia
   - › markers in rectum / rectosigmoid = functional outlet obstruction (eg, internal rectal prolapse / anismus)
   - › ≥ 5 (20%) retained need follow-up KUB on day 7

Colonic Wall Thickness

< 3 mm = normal
3–4 mm = indeterminate
> 4 mm = pathologic

Cecum

= 1st part of large intestine
Location: most commonly in right iliac fossa below ileocecal valve, resting on iliac + greater psoas muscles
Size: 6.25 cm long; 7.5 cm wide
Attachment: to iliac fossa laterally + medially by peritoneal cecal folds
Layers: thickened bands of longitudinal muscle (= teniae coli) contiguous with distal colon + converging at base of vermiform appendix to form a complete outer longitudinal layer of muscle
√ considerable mobility ← usually almost entirely enveloped by peritoneum

Appendix

Average length: 8–10 cm
Wall thickness of normal appendix: < 2 mm
Diameter of normal appendix: < 6 mm
Location: 2.5 cm inferior to ileocecal valve with its own short triangular mesentery (= mesoappendix)
Function: well-developed lymphoid organ (in childhood) of immunologic importance
√ collapsed or partially filled with fluid / contrast material / air
MR (visualized in up to 65–90%, even in pregnant women):
- ◊ Oral preparation with 300 mL of GastroMARK® + 300 mL of ReadiCat® 2 1–1.5 hours before MRI study
- √ hyperintense center + hypointense wall on T2WI
- √ predominantly low signal intensity on T1WI

RECTUM

= last segment of GI tract
Origin: derived from fetal hindgut
Boundaries: sigmoid colon and anus
Peritoneal investment: proximal portion only
Blood supply: superior + middle hemorrhoidal arteries
Venous drainage:
- › proximal rectum: drained by inferior mesenteric vein

› distal rectum + anorectal junction: drained by internal iliac / inferior mesenteric vein (IMV)
◊ 2 hematogenous metastatic patterns of rectal cancer:
(1) liver metastasis ← via IMV + portal venous system / via endolymphatic spread along course of IMV
(2) lung metastasis ← via internal iliac veins + IVC

Rectosigmoid junction:
superior aspect of rectum = line formed by confluence of taeniae coli muscles on serosal surface of sigmoid (surgical definition); <u>less precise:</u> sacral promontory / peritoneal reflection
<u>endoscopically:</u> extension to 12 cm above anal verge

Anorectal junction: inferior aspect of rectum corresponding to dentate line (anatomic definition)

ANAL CANAL

= 2.5–4.0 cm long terminal part of GI tract extending from anorectal junction to anus

Dentate / pectinate line:
= 5–10 mm wide line dividing upper ⅔ and lower ⅓ of anal canal marking transitional zone between columnar epithelium of GI tract and squamous epithelium of anoderm

Division:
› upper ⅔ of canal
1. Zona columnaris = upper half of canal lined by simple columnar epithelium
   • longitudinal folds joined together into anal valves

› lower ⅓ of canal
2. Zona hemorrhagica = lined by stratified non-keratinized squamous epithelium
3. Zona cutanea = lined by stratified keratinized squamous epithelium

Border between zona hemorrhagica and cutanea:
Hilton's white line / pecten of Jon Stroud

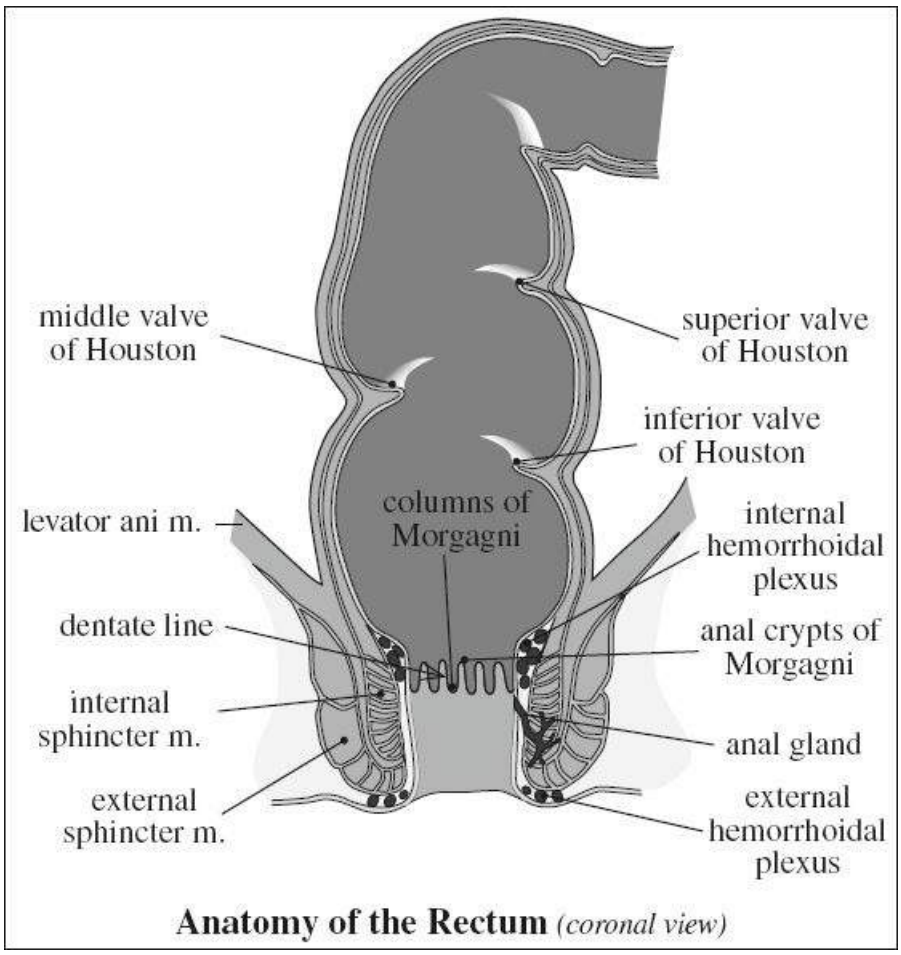
Anal Verge
= distal end of anal canal forming transitional zone between epithelium of moist hairless modified skin of anal canal + dry perianal skin

INTESTINAL FUNCTION

Intestinal Gas

A. INFLUX
1. Aerophagia 2 L
2. Liberation from intestinal tract
   (a) neutralization of bicarbonate in secretions (CO_2) 8 L
   (b) bacterial fermentation (CO_2, H_2, CH_4, H_2S) 15 L
3. Diffusion from blood (N_2, O_2, CO_2)

B. EFFLUX



1. Diffusion from intestines into blood and expulsion from lung 50 L
2. Expulsion from anus 2 L

Intestinal Fluid

A. INFLUX
   1. Oral ingestion 2.5 L
   2. Intestinal secretions 8.2 L
      saliva 1.5 L
      bile 0.5 L
      gastric secretions 2.5 L
      pancreatic secretions 0.7 L
      intestinal secretions 3.0 L

B. EFFLUX
   1. Peranal 0.1 L
   2. Intestinal resorption (primarily in ileum + ascending colon) 10.6 L

Intestinal Transit Time

greatly affected by type of diet

Measurement techniques:

(1) Breath tests: hydrogen; urea-labeled ^{13}C
(2) Scintigraphy
(3) Radiopaque markers
(4) Ingestible wireless motility capsule (measuring pH, pressure, temperature)

◊ It takes ~ 2 hours for a contrast bolus to reach ileocecal valve following esophagram and radiographs of the stomach!

Normal Transit Times:

Stomach:	2–5 hours
Small bowel:	2.5–6.0 hours
Colon:	5–60 hours
Whole gut:	10–73 hours

While it may not be possible to diagnose a specific disease that produces a change in bowel motility, alterations in motility may be used in support of a diagnosis and disease severity.

PELVIC FLOOR

= musculofascial diaphragm inserted on pelvic bones

Function:

› static support to visceral organs: opposing gravity + increased abdominal pressure
› active closure of urogenital hiatus: permitting emptying and continence mechanisms

Pelvic sling: extends obliquely from coccyx toward posterior levator plate just behind anorectal junction

Pelvic floor: (3 layers from cranial to caudal)

(a) endopelvic fascia:
= network of connective tissue that lies deep to peritoneum and supports pelvic organs
› peritoneal reflection fused to underlying connective tissue
› pubocervical fascia (between bladder + vagina)
› **sacrouterine–cardinal ligament complex**
» fascia anteriorly around vagina + uterus
Function: supports vaginal cuff by pulling cervix and upper vagina superiorly + posteriorly toward sacrum
» fusion posteriorly with prerectal fascia
Function: prevents pelvic floor descent
› **arcus tendineus** fasciae pelvis (ATFP) and arcus tendineus levatoris ani (ATLA)
= connective tissue condensations of obturator + levator ani fascia that runs obliquely on pelvic sidewall from pubic symphysis (cranially) to ischial spine (caudally)
Function: provide lateral support by anchoring organs to pelvic side wall

MR:
√ too thin to be recognized except for its condensations: cardinal lig., uterosacral ligament, urethral ligament
√ integrity inferred by efficiency of provided support

(b) **muscular pelvic diaphragm**
consisting mainly of <u>levator ani complex</u> made of
(1) puboperineal
(2) pubovaginal

(3) puboanal component
√ nonvisualized U-shaped sling inserting on inner pubis + passing around anorectal junction (AXIAL plane)
√ encloses urogenital hiatus (= space for urethra + vagina + anal canal)
(4) puborectalis muscle
√ encircles urogenital hiatus
√ responsible for angle between rectum + anal canal
(5) iliococcygeus muscle
√ thin sagittally oriented fan-shaped structure
√ curved shape with inferior concavity (COR plane)
√ inserts laterally to pelvic sidewalls on ATLA
√ inserts medially to pelvic organs
√ forms posteriorly raphe with attachment to external anal sphincter → anococcygeal ligament

Function: at rest tonically contracted
⇒ acting as an anterior sling drawing urethra anteriorly and superiorly relative to bladder base → acute angle between bladder neck and urethra
⇒ anus is drawn anterosuperiorly → acute angle between anus and rectum crucial for gross fecal continence

(c) **urogenital diaphragm**
= diamond-shaped structure consisting of two triangles with transverse perineus muscle as common base
» *anterior triangle:* apex at symphysis pubis; sides at pubic bones
penetrated by: urethra + vagina
» *posterior triangle:* apex at tip of coccyx
penetrated by: anus

› connective tissue = perineal membrane (mainly)
√ visible on MRI as hypointense connective tissue condensation (= perineal body) at insertion of perineus muscle and external anal sphincter interposed between vaginal vestibule and anal canal

› deep transverse perineus muscle
oriented transversely just deep to pelvic diaphragm and anterior to anorectal junction
anchors: external anal sphincter, muscles of urogenital diaphragm, puborectalis muscle, sacrouterine– cardinal ligament complex, prerectal fascia

PERITONEUM

Definitions:
Ligament = formed by two folds of peritoneum supporting a structure within the peritoneal cavity
Omentum = specialized structure connecting stomach to an additional structure: liver, duodenum, colon
Mesentery = two peritoneal folds connecting a portion of bowel to the retroperitoneum

Peritoneal Fluid

Changes in intraperitoneal hydrostatic pressure and anatomic arrangement of the peritoneal recesses result in transcoelomic migration of fluid toward the undersurface of the diaphragm.

Clearance: by subphrenic submesothelial lymphatics augmented by continual circulation of fluid upward to subdiaphragmatic spaces

Cause of motion: fluctuations in intraabdominal pressure during respiration + intestinal peristalsis

Reproducible circulatory pathway:

› Initially toward gravity-dependent spaces:
  (1) deep pelvic recesses (= pouch of Douglas in women / retrovesical space in men)
  (2) lateral paravesical spaces

› Later cephalad ascension to right subdiaphragmatic space:
  (3) right paracolic gutter → right subdiaphragmatic space
  (4) shallow left paracolic gutter
    (a) NO connection to left subdiaphragmatic space ← interruption by phrenicocolic ligament
    (b) NO connection between left and right subdiaphragmatic spaces ← falciform ligament

› Caudal redirection into pelvis:
  (5) by inframesocolic compartment

› Serving as watersheds: all mesenteries = transverse mesocolon, small bowel mesentery, sigmoid mesocolon, peritoneal attachments of ascending + descending colon

Small Bowel Mesentery

Composition: fatty extraperitoneal connective tissue, SMA & SMV and their branches, nerves, lymphatics

Investment: reflection of posterior parietal peritoneum

Function: suspension for 20–25 feet of jejunal + ileal loops

Root: 15 cm long fan-shaped bare area extending obliquely from point of terminal duodenum to cecum in right iliac fossa

Attachment: from duodenojejunal flexure over head of pancreas + 3rd part of duodenum obliquely across aorta, IVC, right ureter, right psoas major muscle

Vascular landmarks: superior mesenteric vessels + branches

Relationship: continuous with anterior pararenal space and root of transverse mesocolon at uncinate process

Peritoneal Spaces

A. RIGHT SUPRAMESOCOLIC SPACE
forms perihepatic space + lesser sac

1. **Right subphrenic / subdiaphragmatic space**
   Location: between right hepatic lobe + diaphragm
   › limited posteriorly by right superior reflection of coronary ligament + right triangular ligament
2. **Right subhepatic / hepatorenal space**: divided into
   (a) anterior right subhepatic space:

Location: posterior to porta hepatis

√ communicates with lesser sac via epiploic foramen (= foramen of Winsløw) [Jacob Benignus Winsløw (1669–1760)], danish-born professor of anatomy at the Jardin du Roi, Paris, France]

(b) posterior right subhepatic space

= Morison pouch = hepatorenal fossa

[James Rutherford Morison (1853–1939), British surgeon and professor at the University of Durham]

◊ Most dependent portion of the abdomen in supine patient!

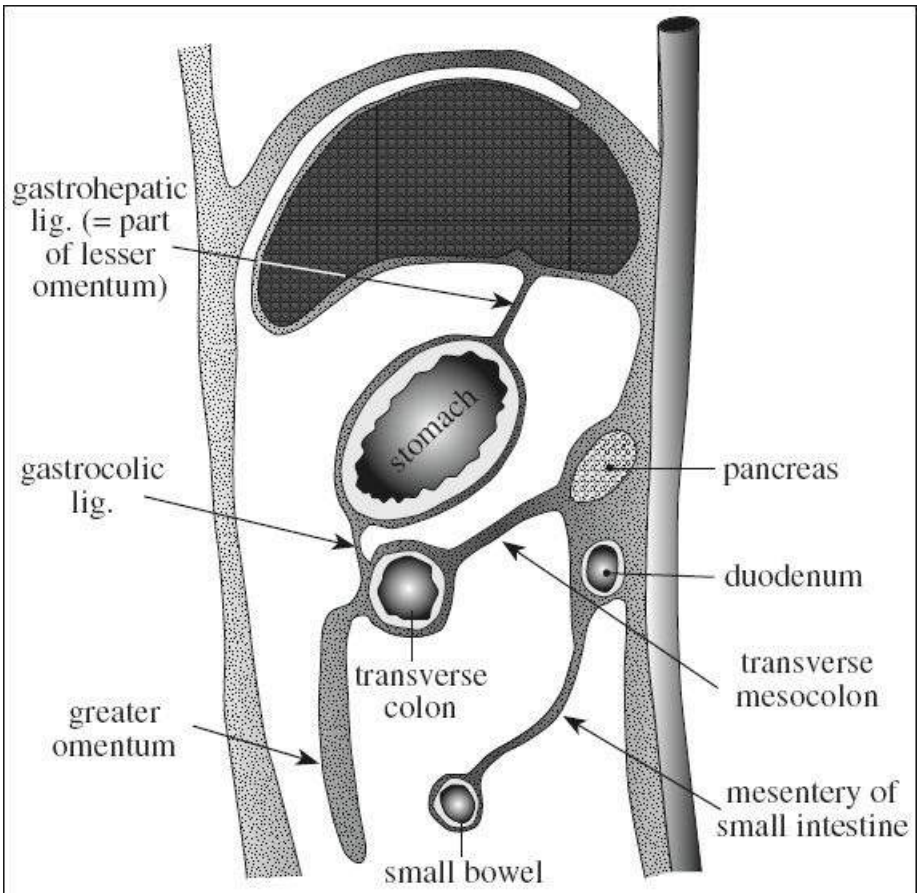
The right subhepatic space is an important site of fluid collections resulting from liver injuries because it is the most gravity-dependent space at this site.

3. **Bare area** of liver

Location: between reflections of right + left coronary ligaments

√ continuous with right anterior pararenal space

4. **Lesser sac / omental bursa**



Relationship of Transverse Mesocolon, Greater Omentum, Small Bowel Mesentery and Ligaments

(a) superior recess:

√ surrounds medial aspect of caudate lobe
√ separated from splenic recess by gastropancreatic fold

(b) splenic recess:
√ extends across midline to splenic hilum

(c) inferior recess:
√ separates stomach from pancreas + transverse mesocolon
√ anteriorly covered by lesser omentum

Compartments: separated by **gastropancreatic fold** ← elevation of posterior parietal peritoneum by left gastric artery into
› smaller medial compartment
› larger lateral compartment

B. LEFT SUPRAMESOCOLIC SPACE forms
1. **Left subphrenic space** artificially divided into
(a) immediate subphrenic space: between diaphragm + gastric fundus
(b) perisplenic space: bounded inferiorly by phrenicocolic ligament
(c) subhepatic space = gastrohepatic recess: located between lateral segment of left hepatic lobe + stomach; separated from right subphrenic space by falciform ligament

C. PARACOLIC SPACES
1. Right + left **paracolic gutter**
Location: lateral to ascending + descending colon

D. INFRAMESOCOLIC SPACES
1. Right **inframesocolic space**
Location: medial to ascending colon
√ limited inferiorly by attachment of small bowel mesentery to cecum
2. Left inframesocolic space
Location: medial to descending colon
√ communicates freely with pelvis
3. Superior + inferior **ileocecal recesses**
Location: above + below terminal ileum
4. **Intersigmoid recess**
Location: along undersurface of sigmoid mesocolon
5. **Retrocecal space**
• present only if peritoneum reflects posterior to cecum

Suspensory Ligaments of Liver

1. **Triangular Ligaments** outline bare area of liver
(a) Right triangular ligament
Origin: fusion of inferior + superior reflections of right coronary ligament
√ long ligament dividing posterior aspect of right perihepatic space into right subphrenic space + posterior right subhepatic space

(b) Left triangular ligament
Origin: fusion of inferior + superior reflections of left coronary ligament
Location: along superior aspect of left hepatic lobe
√ short noncompartmentalizing ligament

2. **Falciform ligament**
   = sickle-shaped fold composed of two layers of peritoneum
   √ incomplete barrier to fluid transfer from right subphrenic to left perihepatic space
   √ continuous with fissure for ligamentum venosum
   Origin: remnant of the most anterior part of the ventral mesentery
   Relationship: ventral surface of liver to anterior abdominal wall; its right layer continues into the superior layer of the coronary ligament, its left layer continues into the anterior layer of the left triangular ligament
   Content: ligamentum teres (= obliterated umbilical vein) in its free inferoposterior margin, recanalized paraumbilical veins

Peritoneal Ligaments of Stomach

1. **Lesser omentum**
   Origin: remnants of dorsal portion of ventral mesentery
   Formed by: gastrohepatic + hepatoduodenal ligaments
   (a) **Gastrohepatic ligament**
   = wedge-shaped ligament arising in fissure of ligamentum venosum
   Relationship: lesser curvature of stomach to fissure of ligamentum venosum (anterior to caudate lobe at medial aspect of liver); subperitoneal areolar tissue of gastrohepatic ligament continues into liver as Glisson capsule
   Content: adipose tissue, left gastric artery, coronary vein, lymph nodes
   Vascular landmark: anastomotic arcade formed by right + left gastric artery & vein along lesser curvature of stomach
   (b) **Hepatoduodenal ligament**
   = double-layered tubular peritoneum = free edge of lesser omentum
   Insertion: between 1st and 2nd portions of duodenum
   Contents: portal triad (main portal vein, proper hepatic artery, common hepatic duct): gallbladder neck; part of cystic duct; ventral anlage of pancreas (until 8th embryonic week)
   Vascular landmarks: proper hepatic artery, portal vein, right gastric vein draining into portal vein
   → forms inferior edge of gastrohepatic ligament
   → forms anterior margin of epiploic foramen
   › extends from proximal duodenum to porta hepatis
2. **Gastrophrenic ligament**
   Origin: anterosuperior portion of dorsal mesentery
   Content: short gastric vessels, varices after splenic vein thrombosis, route of subperitoneal spread of pancreatic exudate
   → courses through immediate subphrenic space
   → suspends stomach from dome of diaphragm
3. **Greater omentum**
   Origin: anteroinferior portion of dorsal mesentery becomes redundant ← growth + rotation of stomach in utero; formed by double reflection of dorsal mesogastrium thus composed of 4 layers of peritoneum
   Attachment: greater curvature of stomach

Content: epiploic artery & vein ← gastroepiploic arcade
Function: containment of intraperitoneal infections
√ inferior continuation of gastrocolic ligament with apronlike extension in anterior abdominal cavity

4. **Gastropancreatic ligament**
   Origin: formed by proximal left gastric artery
   Relationship: posterior aspect of gastric fundus to retroperitoneum
   → partially separates superior recess of lesser sac from splenic recess
5. **Gastrocolic ligament / supracolic omentum**
   = portion of peritoneum between greater gastric curvature and transverse colon
   → forms portion of anterior border of lesser sac
   → forms superior aspect of greater omentum
   Relationship: greater curvature of stomach to superior aspect of transverse colon
   Contiguity: gastrosplenic ligament (on left); transverse mesocolon (posteriorly and on right)
   Content: R and L gastroepiploic arteries form anastomotic arcade along greater curvature of stomach = anatomic landmark for gastrocolic ligament

Peritoneal Ligaments of Spleen

1. **Phrenicocolic ligament**
   = major suspensory ligament of spleen
   Relationship: proximal descending colon to left hemidiaphragm
   → separates left subphrenic space from left paracolic gutter
2. **Splenorenal ligament**
   = major suspensory ligament of spleen
   Origin: most posterior + lateral aspect of dorsal mesentery where it didn't fuse with posterior parietal layer of peritoneum
   Relationship: retroperitoneum (anterior to left kidney) to splenic hilum = anterior pararenal space to posterior aspect of spleen
   Contiguity: with gastrocolic ligament
   Vascular landmarks: distal splenic artery, proximal splenic vein, splenorenal collateral vessels in portal hypertension
   Content: pancreatic tail, splenic vessels
   → forms left posterolateral boundary of lesser sac
3. **Gastrosplenic ligament**
   Origin: remnant of dorsal mesentery
   Relationship: posterolateral wall of gastric fundus and greater curvature to splenic hilum
   Contiguity: with splenorenal ligament medially and posteriorly
   Vascular landmarks: left gastroepiploic vessels; proximal segment of L gastroepiploic vessels
   Content: short gastric vessels
   → forms lateral boundary of lesser sac

Ligaments of Abdomen

The transverse mesocolon divides the peritoneum into the supramesocolic and inframesocolic spaces.

› ***above transverse mesocolon:***

A. VENTRAL MESENTERY gives rise to:
   1. Falciform ligament
   2. Right triangular ligament
   3. Left triangular ligament
   4. Gastrohepatic ligament
   5. Hepatoduodenal ligament

B. DORSAL MESENTERY gives rise to:
   1. Gastrophrenic ligament
   2. Gastropancreatic ligament
   3. Phrenicocolic ligament
   4. Gastrosplenic ligament
   5. Splenorenal ligament
   6. Gastrocolic ligament

› ***below transverse mesocolon:***

A. VENTRAL MESENTERY regresses

B. DORSAL MESENTERY

Origin: during progression of foregut rotation, dorsal mesoduodenum + dorsal mesogastrium fuse with parietal layer of peritoneum pushing head and body of pancreas into retroperitoneum

Contiguity: laterally with splenorenal + phrenicocolic ligaments; anteriorly with root of small bowel mesentery (over uncinate process), greater omentum + gastrocolic ligament

Significance: bare areas establish contiguity between pancreas and transverse colon up to splenic flexure, spleen, and small bowel allowing for subperitoneal spread

√ pericolitis with relative sparing of mucosa and submucosa (15%) ← acute pancreatitis with direct spread of pancreatic enzymes

Cx: colonic perforation

Mortality: increased to 40%

1. **Transverse mesocolon**

= peritoneal fold that suspends transverse colon from retroperitoneum along infraampullary duodenum + anteroinferior edge of pancreas

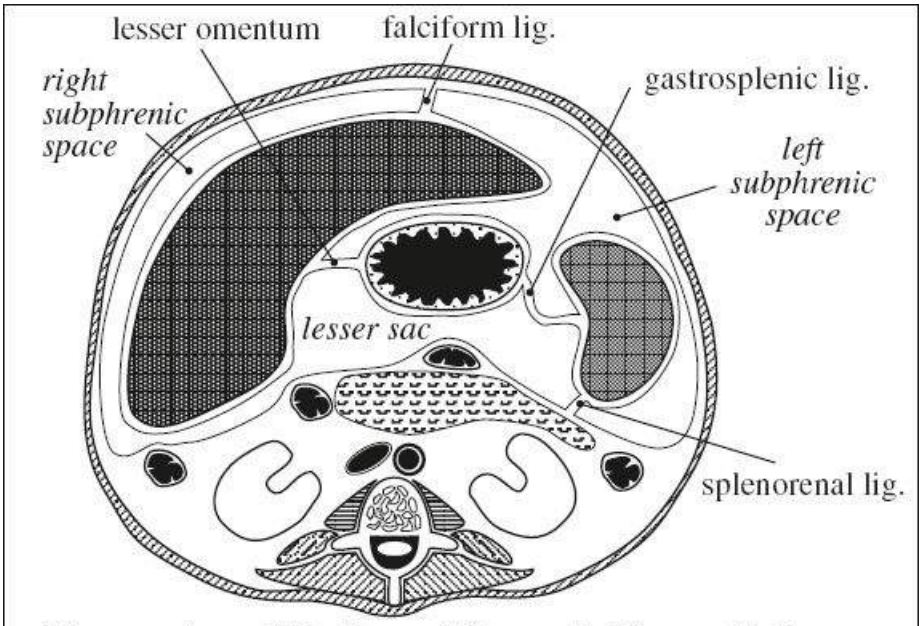
Relationship: transverse colon to pancreas

Vascular landmarks:

middle colic artery & vein, gastrocolic trunk, left middle colic v. to splenic v. / inferior mesenteric v.

√ forms posteroinferior border of lesser sac

Content: internal hernia after Roux-en-Y gastric bypass, spread of pancreatic cancer rendering it inoperable



Ligaments and Peritoneal Spaces in Upper Abdomen

2. **Small bowel mesentery**
   √ suspends small bowel from retroperitoneum
   Location: ligament of Treitz to ileocecal valve
   Content: superior mesenteric vessels + lymph nodes
3. **Sigmoid mesocolon**
   = peritoneal ligament that attaches sigmoid colon to posterior pelvic wall
   Content: sigmoid + hemorrhoidal vessels
4. Greater omentum *(see above)*

Tumors and fluid collections may spread across the peritoneal ligaments (= subperitoneal spread) to involve several contiguous organs.

INGUINAL CANAL

= narrow diagonal tunnel lined by aponeuroses of the 3 abdominal wall muscles

Course: from deep inguinal ring (superiorly posterolateral) to superficial inguinal ring (inferiorly anteromedial)

Content:
(a) male: spermatic cord covered by fascia from all 3 abdominal wall muscle aponeuroses comprising:
- › ductus / vas deferens
- › testicular artery
- › pampiniform plexus
- › genital branch of the genitofemoral nerve

(b) female:
- › round ligament of uterus
- › ilioinguinal nerve to labia majora

Anterior wall: aponeuroses of the external + internal oblique mm.

Superior wall: aponeuroses of internal oblique and transversus abdominis muscles
Posterior wall: transversalis fascia and conjoint tendon of internal oblique + transversalis fascia medially at the pectineal line
Inferior wall: inguinal ligament of Poupart (= folded-up lower border of the external oblique aponeurosis
[François Poupart (1616-1708), French physician, anatomist, entomologist in Paris, France]

Deep / Internal Inguinal Ring

= gap in the transversalis fascia just superior to the inguinal ligament + lateral and posterior to inferior epigastric vessels

Superficial / External Inguinal Ring

= opening in the external oblique aponeurosis just superior + lateral to the pubic tubercle

Inguinal Ligament

= extends from anterior superior iliac spine to the pubic tubercle

ANATOMY OF LYMPH NODES

Paraaortic Nodes

Lateroaortic Nodes

1. Lateroaortic (on left of aorta)
2. Aortocaval (between aorta + IVC)
3. Laterocaval (on right of IVC)
4. Precaval (in front of IVC)
5. Retrocaval (behind IVC)

Preaortic Nodes

Retroaortic Nodes

Iliac Nodes

Common Iliac Nodes

1. Lateral common iliac nodes
   = extension of lateral chain of external iliac nodes
   Location: lateral to common iliac artery
2. Median common iliac nodes
   Location: triangular area between both common iliac arteries from bifurcation of aorta to bifurcation of common iliac arteries
3. Medial common iliac nodes
   Location: lumbosacral fossa (bordered posteromedially by vertebrae, anterolaterally by psoas muscle, anteromedially by common iliac vessels)

Internal Iliac = Hypogastric Nodes

accompany each visceral branch of internal iliac artery

1. Junctional nodes
   Location: at junction between internal + external iliac nodes
2. Sacral + promontory nodes
   Location: central location of presacral space

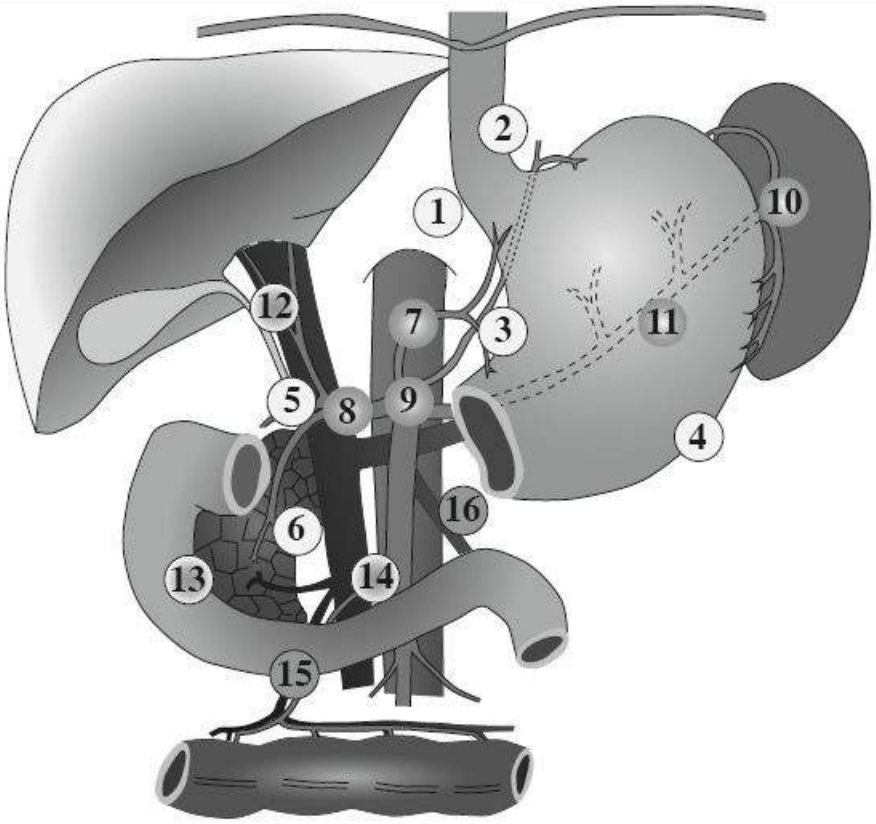
External Iliac Nodes

1. Lateral chain
   Location: lateral relative to external iliac artery)
2. Middle chain
   Location: between external iliac artery + vein)
3. Medial chain = obturator nodes
   Location: medial + posterior to external iliac vein)

Inguinal nodes

demarcated from external iliac nodes by inguinal ligament

1. Superficial inguinal nodes
   Location: subcutis anterior to inguinal ligament along femoral vein + saphenous vein
   Saphenofemoral junction node = sentinel node
2. Deep inguinal nodes
   Location: along common femoral artery + vein



Perigastric Lymph Nodes

Compartment I			
1	right paracardium	2	left paracardium
3	lesser curvature	4	greater curvature
5	suprapylorus	6	infrapylorus
Compartment II			
7	left gastric a.	8	common hepatic a.
9	celiac a.	10	splenic hilum
11	proximal splenic a.		
Compartment III			
		12	hepatoduodenal lig.
13	posterior pancreas	14	superior mesenteric vessels
Compartment IV			
15	middle colic vessels	16	abdominal aorta

ABDOMINAL COMPARTMENT SYNDROME

Cause: pathologic elevation of intraabdominal pressure
- diminished respiratory function, diminished cardiac output

CT:
- √ dense infiltration of the retroperitoneum out of proportion to peritoneal disease
- √ accumulation of retroperitoneal fluid
- √ extrinsic compression of IVC by retroperitoneal hemorrhage / exudate
- √ massive abdominal distension
- √ renal compression
- √ inguinal herniation
- √ enhancing bowel thickening

Rx: emergent surgical decompression

ACHALASIA

= absence of primary esophageal peristalsis (= unorganized peristalsis) + failure of lower esophageal sphincter to relax

Etiology: (a) idiopathic: abnormality of Auerbach plexus / medullary dorsal nucleus; ? neurotropic virus, ? gastrin hypersensitivity
(b) Chagas disease

- often increase in lower esophageal sphincter pressure

√ megaesophagus = dilatation of esophagus beginning in upper ⅓, ultimately entire length
√ absence of primary peristalsis below level of cricopharyngeus
√ nonperistaltic contractions
√ "bird-beak" / "rat tail" deformity = V-shaped conical and symmetric tapering of stenotic segment with most marked narrowing at GE junction
√ Hurst phenomenon = temporary transit through cardia when hydrostatic pressure of barium column is above tonic LES pressure
√ sudden esophageal emptying after ingestion of carbonated beverage (eg, Coke)
√ "vigorous achalasia" = numerous tertiary contractions in nondilated distal esophagus of early achalasia
√ prompt relaxation of LES upon amyl nitrite inhalation (smooth-muscle relaxant)

CXR:
- √ right convex opacity behind right heart border; occasionally left convex opacity if thoracic aorta tortuous
- √ right convex opacity may be tethered by azygos arch allowing for greater dilatation above + below
- √ air-fluid level ← stasis in thoracic esophagus filled with retained secretions + alimentary residue
- √ small / absent gastric air bubble

√ anterior displacement + bowing of trachea (LAT view)
√ patchy bilateral alveolar opacities ← acute / chronic aspiration pneumonia (M. fortuitum-chelonei infection)

Cx: esophageal carcinoma in 2–7% (usually midesophagus)

Rx: pneumatic dilatation / surgical myotomy

DDx: (1) Neoplasm (separation of gastric fundus from diaphragm, normal peristalsis, asymmetric tapering)
(2) Peptic stricture of esophagus

Secondary Achalasia

= carcinoma of cardia / gastric fundus invading esophagus

Age: > 50 years

• duration of symptoms for < 6 months
√ irregular / asymmetric narrowing
√ abrupt transition
√ associated fundal lesion

Pseudoachalasia

• more abrupt onset of symptoms, weight loss

Cause: primary or metastatic tumor
Location: distal esophagus + GE junction
√ dilated esophagus
√ irregular luminal narrowing with lobulated margins
DDx: achalasia (tapered beaklike narrowing of distal esophagus + GE junction)

ADENOMA OF SMALL BOWEL

Location: duodenum (21%), jejunum (36%), ileum (43%) esp. ileocecal valve

Histo:

(1) Hamartomatous polyp (77%): multiple in 47%, ⅓ of multiple lesions associated with Peutz-Jeghers syndrome
(2) Adenomatous polyp (13%): may have malignant potential
(3) Polypoid gastric heterotopic tumor (10%)

ADENOMATOUS COLONIC POLYP

= EPITHELIAL POLYP

Most common benign colonic tumor (68–79%)

Predisposed: previously detected polyp / cancer; family history of polyps / cancer; idiopathic inflammatory bowel disease; Peutz-Jeghers syndrome; Gardner syndrome; familial polyposis

Prevalence: 3% (10%) [26%] in 3rd (7th)) [9th]] decade

Location: sigmoid (26–38%); rectum (21–34%); descending colon (6–18%); transverse colon (12–13%); ascending colon (9–12%); multiple in 35–50% (usually < 5–10 in number)

Histo:

1. **Tubular adenoma** (75%)
   = cylindrical glandular formation lined by stratified columnar epithelium + containing nests of epithelium within lamina propria
   √ usually < 10 mm in diameter
   √ often pedunculated if > 10 mm
   Malignant potential: < 10 mm in 1%; 10–20 mm in 10%; > 20 mm in 35%
2. **Tubulovillous adenoma** (15%)
   = mixture between tubular + villous adenoma
   Malignant potential: < 10 mm in 4%; 10–20 mm in 7%; > 20 mm in 46%
3. **Villous adenoma** (10%)
   = thin frondlike surface projections ("villous fronds")
   • potassium depletion
   √ often > 20 mm in diameter with papillary surface
   √ often broad-based sessile lesion
   Malignant potential: < 10 mm in 10%; 10–20 mm in 10%; > 20 mm in 53%

Adenoma size versus incidence of malignancy:
< 5 mm in 0.5%; 5–9 mm in 1%; 10–20 mm in 5–10%;
> 20 mm in 10–50% malignant
◊ Invasive carcinoma (= penetration of muscularis mucosa):
(a) rare in a pedunculated adenoma of < 15 mm
(b) in 30% of villous adenomas of > 50 mm
◊ All polyps > 10 mm should be removed!
◊ Time for adenoma-carcinoma sequence probably averages 10–15 years!

Probability of coexistent colonic growth:
› synchronous adenoma in 50%
› metachronous adenoma in 30–40%
› synchronous adenocarcinoma in 1.5–5%
› metachronous adenocarcinoma in 5–10%

• asymptomatic (75%), diarrhea, abdominal pain
• peranal hemorrhage (67%)

Colonoscopy: incomplete in 16–43%

BE:
Sensitivity of DCBE in detecting polyps:
< 10 mm 80–83%; > 10 mm 96–97%; all 84–88%; rate of detection of polyps < 10 mm higher with DCBE than SCBE
√ sessile flat / round polyp
√ pedunculated polyp: stalk > 2 cm in length almost always indicative of a benign polyp
√ suggestive of malignancy: irregular lobulated surface, broad base (= width of the base greater than height), retraction of colonic wall (= dimpling / indentation / puckering at base of tumor), interval growth
√ lacelike / reticular surface pattern CHARACTERISTIC for villous adenoma (occasionally in tubular adenoma)

DDx: (1) Nonneoplastic: hyperplastic polyp, inflammatory pseudopolyp, lymphoid tissue, ameboma, tuberculoma, foreign-body granuloma, malakoplakia, heterotopia,

hamartoma

(2) Neoplastic subepithelial: lipoma, leiomyoma, neurofibroma, hemangioma, lymphangioma, endothelioma, myeloblastoma, sarcoma, lymphoma, enteric cyst, duplication, varix, pneumatosis, hematoma, endometriosis

ADENOCARCINOMA OF SMALL BOWEL

Frequency: 35–40% of primary malignant neoplasms of small bowel; ~ 50 x less common than colonic carcinoma

◊ Most common primary tumor of small bowel

Risk factors: familial adenomatous polyposis (FAP), Crohn disease, sprue, Peutz-Jeghers syndrome, hereditary nonpolyposis colon cancer syndrome (Lynch syndrome), congenital bowel duplication, ileostomy, duodenal / jejunal bypass surgery

Histo: mostly moderately to well differentiated; may arise in villous tumors / de novo; no correlation between size and invasiveness

- vague mild abdominal pain, anemia, weight loss
- nausea, vomiting, anorexia

Location: duodenum (54%, especially near ampulla) > jejunum (28%) > ileum (18%)

› in familial adenomatous polyposis: duodenum
› in celiac disease: jejunum
› in Crohn disease: ileum

√ variety of shapes:
- √ annular stricture with "overhanging edges" (60%)
- √ lobulated / ovoid polypoid sessile mass (41%)
  - ◊ Duodenal tumors tend to be papillary / polypoid!
- √ ulcerated plaque / mass (27%)

CT:
- √ soft-tissue mass with heterogeneous attenuation
- √ moderate contrast enhancement

Cx: progressive small bowel obstruction; intussusception; perforation (rare)

Prognosis: poor (often disseminated at time of presentation); 30% 5-year survival rate

DDx: lymphoma (lymphadenopathy more bulky)

Duodenal Adenocarcinoma

= rare tumor that typically abuts but spares / only partially involves the major duodenal papilla

Prevalence: 1.7÷1,000,000; M < F

Location: most often in 2nd + 3rd portion = periampullary neoplasm

(a) suprapapillary: apt to cause obstruction + GI bleeding
(b) peripapillary: extrahepatic jaundice
(c) intrapapillary: GI bleeding

Predisposed: familial adenomatous polyposis syndrome, Crohn disease, celiac disease, neurofibromatosis

May be associated with: Peutz-Jeghers syndrome

√ eccentric duodenal wall thickening ± ulceration:

√ annular lesion with relatively short segment involvement
√ fungating polypoid / intraluminal mass
√ gradual luminal narrowing (most common)
√ luminal obstruction + gastric distention ← larger tumor
√ ± biliary dilatation
CT / MR:
√ hypovascular during all phases
Metastases: to regional lymph nodes (²/₃)
DDx: other periampullary lesions

AFFERENT LOOP SYNDROME

= PROXIMAL LOOP / BLIND LOOP SYNDROME
= partial intermittent obstruction of afferent loop leading to overdistension of loop by gastric juices after Billroth-II gastrojejunostomy
Cause: gastrojejunostomy with left-to-right anastomosis (= proximal jejunal loop attached to greater curvature instead of lesser curvature), mechanical factors (intussusception, adhesion, kinking), inflammatory disease, neoplastic infiltration of local mesentery or anastomosis, idiopathic motor dysfunction
• postprandial epigastric fullness relieved by bilious vomiting
• vitamin B12 deficiency with megaloblastic anemia
• afferent loop with abnormal bacterial flora (Gram negative, resembling colon in quality + quantity)
Abdominal plain film:
√ normal in 85% (no air in lumen of afferent loop)
UGI:
√ preferential emptying of stomach into proximal loop
√ proximal loop stasis
√ regurgitation
CT:
√ rounded water-density masses adjacent to head + tail of pancreas forming a U-shaped loop
√ oral contrast material may not enter loop
√ may result in biliary obstruction (increased pressure at ampulla)
Rx: antibiotic therapy

AIDS

◊ Gastrointestinal involvement ← opportunistic infections + AIDS-associated neoplasms!
◊ Pathologic abnormalities at multiple sites with single / several opportunistic organisms are frequent!

A. VIRAL PATHOGENS

1. **Cytomegalovirus infection**

◊ Most common cause of life-threatening opportunistic viral infection in AIDS patients!
Organism: double-stranded DNA virus of herpes family
Infection: ubiquitous among humans occurring at an early age in populations with poor sanitation + crowded living conditions

◊ Result of reactivation of latent virus in previously infected host!

Prevalence: 13% of all GI diseases in AIDS patients

Path: infection of endothelial cells → small vessel vasculitis → hemorrhage, ischemic necrosis, ulcer

Histo: large mononuclear epithelial / endothelial cells that contain intranuclear / cytoplasmatic inclusions with surrounding inflammation

Location: colon > small bowel (terminal ileum) > esophagus > stomach

@ Esophagus

√ single / multiple large superficial ulcers

@ Small bowel

√ luminal narrowing ← marked bowel wall thickening

√ diffuse irregular fold thickening ← thrombosis and ischemia ← vasculitis

√ penetrating ulcer ± perforation

√ CMV pseudotumor (uncommon)

@ Colon (CMV colitis)

• hematochezia, crampy abdominal pain, fever

√ toxic megacolon

√ discrete small well-defined nodules (similar to lymphoid nodular hyperplasia) throughout colon

√ aphthous ulcers on background of normal mucosa

√ marked bowel wall thickening

√ "double-ring / target" sign on CT ← increased submucosal edema

√ ascites

√ inflammation of pericolonic fat + fascia

Rx: ganciclovir (effective in 75%)

2. **Herpes simplex virus infection**

◊ Result of reactivation of latent virus in previously infected host

Organism: neurotropic DNA virus of herpes family

Prevalence: 70% for type 1, 16% for type 2 (endemic in USA); type 2 much more common in AIDS

Infection: direct inoculation through mucous membrane contact; from dormant state in root ganglia reactivated + transported via efferent nerves to mucocutaneous surface

Location: oral cavity, esophagus, rectum, anus

√ multiple small discrete ulcers

3. **Human immunodeficiency virus infection**

◊ Not an AIDS-defining illness!

Infection: acute HIV-infection with transient immunosuppression / during AIDS

√ > 2-cm large solitary ulcer in the mid- or distal esophagus (HIV-infected cells → alterations in cytokines → infiltration of inflammatory cells into submucosa and destruction of mucosa

Rx: corticosteroids

B. FUNGAL PATHOGENS

1. **Candidiasis**

◊ The absence of thrush does NOT exclude the diagnosis of candida esophagitis!

Organism: commensal fungus Candida albicans

Prevalence: 10–20% (in USA); up to 80% in developing countries

Location: oral cavity, esophagus

√ discrete linear / irregular longitudinally oriented filling defects in esophagus

Cx: disseminated systemic candidiasis (rare; indicative of granulocytopenia from chemotherapy / direct inoculation via catheter)

2. **Histoplasmosis**

Organism: dimorphic opportunistic fungus

Prevalence: 10% GI involvement with disseminated histoplasmosis in AIDS patients

Location: colon > terminal ileum

√ segmental inflammation / apple core lesion / bowel stricture

√ hepatosplenomegaly

√ mesenteric lymphadenopathy

√ diffuse hypoattenuation of spleen

C. PROTOZOAN PATHOGENS

1. **Cryptosporidiosis**

◊ One of the most common causes of enteric + biliary disease in AIDS patients!

Organism: intracellular parasite Cryptosporidium

Prevalence: isolated in 6% of all patients with AIDS; in 16% (in USA) + in up to 48% (in developing countries) of patients with diarrhea

• severe choleralike debilitating diarrhea with fluid loss of 10–17 L/d

Location: jejunum > other small bowel > stomach > colon

√ Cryptosporidium antritis = area of focal gastric thickening + ulceration

√ small bowel dilatation ← increased secretions

√ regular fold thickening + effacement ← atrophy, blunting, fusion, loss of villi

√ "toothpaste" appearance of small bowel (mimicking sprue)

√ dilution of barium ← hypersecretion

√ marked antral narrowing ← extensive inflammation

√ AIDS-related cholangitis

Dx: microscopic identification in stool / biopsy

2. **Pneumocystosis**

◊ Likely to occur in patients treated with aerosolized pentamidine!

Organism: eukaryotic microbe Pneumocystis carinii

Prevalence: pulmonary infection in 75% of AIDS patients; in < 1% dissemination

Location: liver, spleen, lymph nodes

√ hepatic + splenic + nodal punctate calcifications

√ multiple tiny echogenic foci in spleen

√ multiple low-attenuation lesions of varying size in spleen (foamy eosinophilic material) → subsequently progressive rimlike / punctate calcifications

D. BACTERIAL PATHOGENS

1. **Tuberculosis**

◊ Most common cause of serious HIV-related infection worldwide with tendency to occur earlier than other AIDS-defining opportunistic infections!

Prevalence: 4% (in USA) + 43% (in developing countries) of HIV-infected persons
Infection: swallowing of infected sputum; hematogenous spread from pulmonary focus; direct extension from lymph node
Location: lymph nodes, liver, spleen, peritoneum, GI tract (especially ileum, colon, ileocecal valve)
√ low-attenuation mesenteric lymphadenopathy ← suggestive of necrosis
√ segmental ulceration
√ inflammatory stricture
√ hypertrophic lesion resembling polyp or mass

2. **Mycobacterium avium complex infection**

= PSEUDO-WHIPPLE DISEASE IN AIDS
◊ Most common opportunistic infection of bacterial origin in AIDS patients!
◊ Most common nontuberculous mycobacterial infection in AIDS patients!
Organism: facultative intracellular acid-fast bacillus M. avium / M. intracellulare
Infection: invasion of Peyer patches + adjacent mesenteric lymph nodes
Histo: true granulomas with Langhans giant cells and caseous necrosis are rare because infection occurs in patients with advanced disease and a CD4 cell count of < 100/μL
• diarrhea, malabsorption (similar clinical picture as in Whipple disease caused by Mycobacterium avium-intracellulare)
Location: jejunum (most common)
√ mild dilatation of middle + distal small bowel
√ wall thickening of small bowel loops
√ diffuse irregular thickening of mucosal fold and nodularity without ulceration
√ mesenteric + retroperitoneal lymphadenopathy:
√ homogeneous 1.0–1.5 cm nodes of soft-tissue attenuation causing segmental separation of small bowel loops
√ necrotic mesenteric nodes of low attenuation (= pseudo-Whipple disease)
√ hepatosplenomegaly
√ multiple tiny echogenic foci in liver + spleen (occasionally large hypoechoic / low-attenuation lesions)
Dx: (1) Visualization of large numbers of intracellular acid-fast bacilli in foamy histiocytes of tissue specimen
(2) Tissue culture
DDx: Whipple disease (positive with periodic acid-Schiff stain just like M. avium, but not with acid-fast stain, responsive to tetracyclines)

E. OTHER INFECTIONS

1. **Bacillary angiomatosis**

Organism: rickettsia Bartonella henselae
Histo: characteristic pattern of vascular proliferation with bacilli
Location: cutis (mimicking Kaposi sarcoma), liver, spleen, lymph nodes
√ peliosis (= blood-filled cystic spaces) of liver / spleen
√ abdominal lymphadenopathy with contrast enhancement

2. **Isospora belli**

◊ Infection resembles cryptosporidiosis

Organism: protozoan pathogen

Histo: oval oocysts within bowel lumen / epithelial cells; localized inflammation; fold atrophy

Location: small intestine

• severe watery diarrhea

√ fold thickening

F. AIDS-ASSOCIATED NEOPLASMS

1. **Kaposi sarcoma**
2. **Non-Hodgkin lymphoma**

◊ 2nd most common AIDS-associated neoplasm

Prevalence: in 4–10% of AIDS patients (60 x higher risk compared with general population); occurs in all AIDS risk groups

Histo: multiclonal B-cell lymphoma of high / intermediate grade

• at initial presentation widely disseminated disease often with extranodal involvement

Location: CNS, bone marrow, GI tract (stomach, small bowel)

@ Stomach

√ circumferential / focal wall thickening

√ mural mass ± ulceration

@ Small bowel

√ diffuse / focal wall thickening

√ excavated mass

√ solitary / multiple liver lesions

Differential diagnostic considerations:

1. Splenomegaly (31–45%)
   Cause: nonspecific (most), lymphoma, infection (M. avium-intracellulare, P. carinii)
2. Lymphadenopathy (21–60%)
   Cause: reactive hyperplasia (most), Kaposi sarcoma, lymphoma, infections
   Size: < 3 cm in diameter (in 95%)
3. Hepatomegaly (20%)
   Cause: nonspecific, hepatitis, fatty infiltration, lymphoma, Kaposi sarcoma
4. AIDS-related cholangiopathy:
   Organism: CMV, Cryptosporidium
   √ papillary stenosis of CBD
   √ dilatation of extra- and intrahepatic bile ducts
   √ periductal fibrosis
   √ strictures + irregularities of bile ducts resembling primary sclerosing cholangitis
   √ intraluminal polypoid filling defects
5. AIDS-related esophagitis:
   Organism: Candida, herpes simplex, CMV
   √ giant esophageal ulcer: HIV (76%), CMV (14%)
   √ esophageal fistula / perforation: TB, actinomycosis
6. Gastritis
   Organism: CMV (GE junction + prepyloric antrum), Cryptosporidium (antrum)
7. AIDS enteritis

Organism: Cryptosporidium, M. avium complex

8. AIDS colitis
   - › ischemic bowel
   - › acute appendicitis
   - › neutropenic colitis
   - › pseudomembranous colitis
   - › infectious colitis / ileitis
9. Bowel obstruction
   (a) infection
   (b) intussusception: Kaposi sarcoma, lymphoma

AMEBIASIS

= primary infection of colon by protozoan Entamoeba histolytica

Organism: free-living protozoa widespread in water, soil, air

Countries: worldwide distribution, most common in warm climates; South Africa, Egypt, India, Asia, Central + South America (20%); USA (5%)

Route: ingestion of cysts in contaminated food / water → cyst dissolves in small bowel → trophozoites settle in colon; invasion of bowel wall ← proteolytic enzymes and hyaluronidase that lyse intestinal epithelium; may embolize into portal venous + systemic blood system

Histo: amebic invasion of mucosa + submucosa causing tiny ulcers, which spread beneath mucosa + merge into larger areas of necrosis; mucosal sloughing; secondary bacterial infection

- asymptomatic for months / years; fever, headache, nausea
- acute attacks of diarrhea (= loose mucoid bloodstained stools)

Location: (areas of relative stasis) right colon + cecum (90%) > hepatic + splenic flexures > rectosigmoid

BE:

- √ loss of normal haustral pattern with granular appearance ← edema, punctate ulcers
- √ "collarbutton" ulcers
- √ cone-shaped cecum
- √ several cm long stenosis of bowel lumen in transverse colon, sigmoid colon, flexures (result of healing + fibrosis); in multiple segments
- √ ileocecal valve thickened + fixed in open position with reflux
- √ involvement of distal ileum (10%):
  - ◊ Amebiasis spares terminal ileum (in USA)
- √ ameboma = hyperplastic granuloma with bacterial invasion of amebic abscess; usually annular + constricting / intramural mass / cavity continuous with bowel lumen; shrinkage under therapy in 3–4 weeks

CT/US:

- √ amebic liver abscess of "anchovy sauce" content
- √ pericarditis, pericardial effusion

CXR (consequences of subdiaphragmatic abscess):

- √ elevation of right hemidiaphragm

√ pleural effusion ← transdiaphragmatic spread of infection / sterile sympathetic effusion
√ airspace consolidation ± cavitation

Dx: stool examination / rectal biopsy

Cx: (1) Toxic megacolon with perforation
(2) Amebic abscess in liver (2%), brain, lung, pericolic, ischiorectal, subphrenic space
(3) Intussusception in children ← ameboma
(4) Fistula formation: colovesical, rectovesical, rectovaginal, enterocolic, hepatobronchial, bronchobiliary

AMYLOIDOSIS

= group of heterogeneous disorders caused by interstitial deposits of an insoluble fibrillar protein-polysaccharide in various organs impairing tissue function → hypoxia, mucosal edema, hemorrhage, ulceration, mucosal atrophy, muscle atrophy

Cause: (a) prolonged antigenic stimulation of RES by chronic infection
(b) disorder of immunoincompetence
(c) aging
(d) idiopathic

Histo: amorphous eosinophilic hyaline material deposited around terminal blood vessels, stains with Congo red + crystal violet; green birefringence under polarizing light; amyloid fibrils have β-pleated sheet structure (= β fibrilloses)

Biochemical classification:

1. AL amyloidosis
   (A = amyloidosis, L = light chain immunoglobulin)
   • monoclonal protein in serum + urine
   • occurs in primary amyloidosis + myeloma-associated amyloidosis
   Histo: massive deposits in muscularis mucosae + submucosa
   √ thickening of folds with polyps / large nodules
2. SAA amyloidosis (S = secondary, AA = amyloid A)
   • occurs in secondary = reactive amyloidosis
   • cardiomyopathy with restrictive ventricular filling
   Histo: expansion of lamina propria
   √ coarse mucosal pattern + innumerable fine granular elevations
3. AF amyloidosis (A = amyloid, F = familial)
   • AF prealbumin as precursor of fibrils
   • occurs in familial amyloidosis
4. AS amyloidosis (A = amyloid, S = senile)
   • AS prealbumin as precursor of fibrils
   • occurs in senile amyloidosis
   √ massive amyloid deposition
5. AH amyloidosis (A = amyloid, H = hemodialysis)
   • β_2 microglobulin as precursor of fibrils
6. AE amyloidosis (A = amyloid, E = endocrine)
   • calcitonin produced by medullary thyroid carcinoma is precursor of fibrils

7. Transthyretin (ATTR)-related hereditary amyloidosis
   • cardiomyopathy with restrictive ventricular filling
8. β2-microglobulin (Abeta2M)-derived dialysis-related amyloidosis

Reimann classification (1935):

1. **Primary = idiopathic amyloidosis**
   = amyloid immunoglobulin light chain (AL) disease
   = probably autosomal dominant inheritance with immunologically determined dysfunction of plasma cells (clonal B-cell dyscrasia)
   • absence of discernible preceding / concurrent disease
   Location: (predominant involvement of connective tissues + mesenchymal organs): heart (90%), lung (30–70%), liver (35%), spleen (40%), kidneys (35%), adrenals, tongue (40%), GI tract (70%), skin + subcutis (25%), skeletal muscle, joints
   √ tendency for nodular deposition
   Prognosis: ⅓ eventually develop multiple myeloma / B-cell lymphoma / Waldenström macroglobulinemia / other plasma cell neoplasia
2. **Secondary amyloidosis** (most common form)
   = amyloid-associated disease
   • following / coexistent with prolonged infectious / inflammatory processes
   Cause: rheumatoid arthritis (in 20%), Still disease, TB, chronic osteomyelitis, leprosy, chronic pyelonephritis, bronchiectasis, ulcerative colitis, Crohn disease, familial Mediterranean fever, lymphoreticular malignancy, Waldenström macroglobulinemia
   Location: spleen, liver, kidneys (> 80%), breast, tongue, GI tract, connective tissue
   √ small amyloid deposits
3. **Amyloidosis associated with multiple myeloma**
   • may precede development of multiple myeloma
   Frequency: 10–15%
   √ primary amyloidosis with osteolytic lesions in myelomatous disease
4. **Tumor-forming / organ-limited amyloidosis**
   • related to primary type
   (a) hereditary = familial amyloidosis
   (b) senile amyloidosis (limited to heart / brain / pancreas / spleen)
   √ large localized masses

Classification by distribution:

1. **Localized (organ-limited) amyloidosis** (10–20%)
   = deposition of abnormal proteins <u>in one organ</u>
   Cause: usually primary (rarely secondary) form of amyloidosis; attributed to tissue-based immunocyte dyscrasia
   Rx: supportive / localized management
   Dx: (1) NO monoclonal protein in serum / urine
   (2) negative bone marrow biopsy
   (3) NO evidence of systemic involvement
2. **Systemic amyloidosis** (80–90%)
   = deposition of abnormal proteins <u>in wide variety of organs</u>

Prognosis: progressive & fatal (kidney / heart failure)

Dx: (1) bioptic proof of amyloid deposits in subcutaneous fat / rectal mucosa / bone marrow

(2) monoclonal protein in urine, serum

◊ GI involvement more common in primary than in secondary amyloidosis!

• malabsorption (diarrhea, protein loss); occult GI bleeding

• intestinal pseudo-obstruction; macroglossia

@ Esophagus (11%)

√ loss of peristalsis

√ megaesophagus

@ Stomach (37%)

• postprandial epigastric pain + heartburn

• acute erosive hemorrhagic gastritis

(a) diffuse infiltrative form

√ small-sized stomach with rigidity + loss of distensibility simulating linitis plastica ← thickening of gastric wall

√ effaced rugal pattern

√ diminished / absent peristalsis

√ marked retention of food

(b) localized infiltration (often located in antrum)

√ irregularly narrowed + rigid antrum

√ thickened rugae

√ superficial erosions / ulcerations

(c) amyloidoma = well-defined submucosal mass

@ Small bowel (74%)

(a) diffuse form (more common)

√ irregular diffuse thickening of valvulae conniventes of entire small bowel associated with:

√ 2–3-mm micronodules ← ischemia

√ 6–10-mm nodules ← deposition of fibrillar protein in submucosa + lamina propria

√ broadened flat undulated mucosal folds (mucosal atrophy)

√ "jejunalization" of ileum

√ impaired intestinal motility

√ small bowel dilatation

(b) localized form (less common)

√ multiple pea- / marble-sized deposits

√ pseudoobstruction = physical + plain-film findings suggesting mechanical obstruction with patent large + small bowel on barium examination ← involvement of myenteric plexus

Cx: small bowel infarction

@ Colon (27%)

√ pseudopolyps in colon

@ Liver

Path: extracellular deposition of amyloid in the spaces of Disse (= narrow gaps between

endothelial linings of sinusoids and hepatocytes of hepatic lamina) with progressive encroachment on hepatic parenchymal cells + sinusoids

• hepatic function usually preserved

CT:

√ hepatomegaly

√ regions of low attenuation with decreased contrast enhancement

@ Spleen

Histo: (a) nodular form involving lymph follicles

(b) diffuse form infiltrating red pulp

√ discrete masses

√ splenomegaly (4–13%)

MR:

√ T2 values significantly lower than normal

@ Bone

√ bone cysts

Cx: spontaneous splenic rupture (from vascular fragility + acquired coagulopathy)

Dx: by rectal / gingival biopsy

DDx: Whipple disease, intestinal lymphangiectasia, lymphosarcoma

ANGIODYSPLASIA OF COLON

= VASCULAR ECTASIA = ARTERIOVENOUS MALFORMATION (not a true AVM)

Cause: age-related degenerative dilatation of normal vessels in submucosa of bowel wall

Theory: colonic contractions result in dilatation of colonic veins, venules and capillaries forging multiple small arteriovenous communications

Associated with: aortic stenosis (20%); NOT related to extraintestinal angiomatous lesions

Prevalence: most common vascular lesion of GI tract!

at autopsy: 2%

at colonoscopy: 0.8% (at age > 50 years)

◊ Up to 40% of lower GI bleeding in over age 60

Age: majority > 55 years; M = F

Location: (a) cecum + ascending colon (74%)

(b) jejunum, ileum (15%)

(c) descending + sigmoid colon (? 25%)

Site: usually at antimesenteric border

• chronic intermittent low-grade / occasionally massive bleeding

NUC (^{99m}Tc-labeled RBCs):

√ focus of tracer accumulation at site of bowel hemorrhage migrating with peristalsis

BE:

√ no abnormality ← soft submucosal lesion

CT:

√ avidly enhancing plaque / nodule during enteric phase fading during delayed phase of CT arteriography

√ early draining vein during arterial phase

NUC:
√ increased tracer accumulation of ^{99m}Tc-labeled RBC
Angio:
√ "arterial tuft" = cluster / tangle of vessels during arterial phase along antimesenteric border
√ early opacification of draining ileocolic vein
√ densely opacified dilated tortuous ileocolic vein into late venous phase
√ contrast extravasation into bowel lumen (unusual)
Prognosis: spontaneous cessation of bleeding in 80%, recurrent bleeding in 85%
Rx: surgical excision

ANISAKIASIS

= parasitic disease of GI tract
Cause: ingestion of Anisakis larvae present in raw / undercooked fish (mackerel, cod, pollack, herring, whiting, bonito, squid) consumed as sashimi, sushi, ceviche, lomi-lomi
Organism: worm with straight / serpentine / circular threadlike appearance
◊ Site of penetration by larvae determines clinical form!
@ Gastric anisakiasis
• acute gastric pain, nausea, eosinophilia
• vomiting a few hours after ingestion (DDx: acute gastritis, peptic ulcer, neoplasia, food poisoning)
√ mucosal edema
√ about 3 cm long threadlike filling defects (= larvae)
@ Intestinal anisakiasis
• diffuse abdominal tenderness / colicky abdominal pain, nausea, vomiting (DDx: acute appendicitis, regional enteritis, intussusception, ileus, diverticulitis, neoplasia)
• leukocytosis without eosinophilia (frequent)
Histo: marked edema, eosinophilic infiltrates, granuloma formation
√ thickened folds
√ disappearance of Kerckring folds
√ thumbprinting / saw-tooth appearance
√ irregular luminal narrowing
√ eosinophilic ascites (DDx: eosinophilic gastroenteritis, hypereosinophilic syndrome)
Cx: ileus
@ Colonic anisakiasis (rare)
DDx: colonic tumor

ANORECTAL MALFORMATION

= complex group of congenital anomalies involving distal anus, rectum, urinary and genital tracts
Prevalence: 1÷5,000 live births; M > F
Cause: abnormal development of urorectal septum in early fetal life
Embryology:
› 3rd and 4th week GA: dorsal part of yolk sac folds are incorporated into embryo forming the **primitive hindgut** that consists of distal part of transverse, descending and sigmoid colon,

rectum, superior portion of anal canal, epithelium of urinary bladder, and most of the urethra

› 4th week GA: coronal sheet of mesenchyme (= **urorectal septum** = transverse rectovesical septum) → descends caudally between allantois and hindgut → divides primitive cloaca into urogenital sinus ventrally and anorectal canal dorsally; **cloacal membrane** separates cloaca from amniotic cavity

Disturbance leads to: ectopic anal orifice / fistula

› 5th week GA: urorectal septum develops forklike infoldings (Tourneux and Rathke folds) of lateral cloacal walls

› 7th week GA:

(a) urorectal septum fuses with cloacal membrane creating a urogenital membrane ventrally + anal membrane dorsally

(b) **perineum** is formed by fusion of urorectal septum + cloacal membrane

(c) secondary occlusion of anorectal canal by adhesion of wall + formation of an epithelial plug at anus

› 9th week GA: cloacal membrane ruptures by apoptosis forming a ventral urogenital and a dorsal anal orifice

Disturbance leads to: abnormal anus in normal position

In 48–70% associated with other congenital anomalies:

(1) GU anomalies (20–60%): vesicoureteral reflux; hydronephrosis; bi- / unilateral renal agenesis; renal dysplasia; renal ectopia; horseshoe kidney; polycystic kidney; renal duplication; megaureter; bladder exstrophy; micropenis; hypospadia (3.1%); double uterus / vagina; vulvogenital atresia; ambiguous genitalia

(2) Spine (30%): lumbosacral segmentation anomalies with sacral agenesis, vertebral dysplasia, spina bifida; tethered cord; myelomeningocele (0.5%) + occult myelodysplasia

(3) GI anomalies (11%): esophageal atresia ± tracheoesopha-geal fistula (4%); duodenal, jejunal, ileal atresia / stenosis; absent colon; intestinal malrotation; volvulus; Meckel diverticulum

(4) Cardiovascular anomalies (8%): tetralogy of Fallot; ASD; VSD, dextrocardia; coarctation of aorta

(5) Musculoskeletal: hip dislocation / dysplasia; fusion of iliac bones; Madelung deformity; arthrogryposis; clubfoot; polydactyly; syndactyly; limb deficiency

(6) Abdominal wall (2%)

(7) Cleft lip–cleft palate (1.6%)

(8) Down syndrome (1.5%)

(9) Others (8%)

Most common associated syndromes:

(1) VACTERL

(2) **O**mphalocele, **E**xstrophy of bladder, **I**mperforate anus, **S**pinal defect (OEIS)

(3) **Mü**llerian + **R**enal agenesis + **C**ervicothoracic **S**omite dysplasia (MURCS)

(4) Chromosomopathies: Trisomy 13, 18 and 21; uniparental disomy 16; deletion of 22q11.2 and 13q

(5) Numerous other syndromes: caudal regression, Down, fetal alcohol, Ivemark, Klippel-Feil, Opitz, etc.

Wingspread Classification (1984):

1. Low: anal stenosis, anocutaneous (rectoperineal / rectovestibular) fistula
   Rx: corrective surgery on day 2–3 of life ± colostomy
2. Intermediate: anal agenesis without fistula / with rectourethral bulbar fistula
   • passage of meconium through vagina / with urine
   Rx: descending colostomy on day 3 of life
3. High: rectal atresia; anorectal agenesis without fistula / rectourethral prostatic fistula
   • passage of meconium through vagina / with urine

Krickenbeck Classification (2005):

1. Anal stenosis; imperforate anus without fistula / (1) rectoperineal fistula or (2) rectovestibular
2. Anal / anorectal agenesis without fistula / (3) rectourethral bulbar, (4) rectourethral prostatic or (5) rectovesical fistula

OB-US:

◊ Prenatal diagnosis made rarely (in only 16%)!
√ oligohydramnios (26%) + distended bladder
√ abdominal / pelvic cystic mass (52%) ← distended bladder + septate fluid-filled vagina
√ fetal hydronephrosis (49%)
√ fetal ascites (22%)
√ intestinal distension (18%)

Transperineal US:

√ bowel-skin distance on midline SAG (rectal pouch to anus)
  < 15 mm: low type of anorectal malformation
  > 15 mm: high type of anorectal malformation
√ linear tract / fistula may be identified

High-pressure distal colostography:

› Foley catheter through colostomy into distal colon
› gentle traction on inflated balloon for sealing
› manual injection of hydrosoluble contrast material until patient voids

MR:

› transverse images through pubococcygeal plane (= upper border of symphysis pubis + upper border of os coccyx)
› coronal images perpendicular to pubococcygeal plane
√ position of rectal pouch
√ size + morphology + development of levator ani muscle group (levator prostate m. / sphincter vaginae m., puborectalis m., pubococcygeus m., iliococcygeus muscle) + external anal sphincter (subcutaneous, superficial and deep layer)

(1) **Rectal atresia**
= open anus + atretic rectal segment superior to anus + no fistula

(2) **Ectopic anus**
= fistulous opening of bowel ← failure of terminal bowel to descend normally
Site of arrest: high / low colon arrest = above / below puborectal sling
• most common anomaly of anorectal segment
• anal dimple + external sphincter in normal position
Location of fistula: perineum, vestibule, vagina, urethra, bladder, cloaca
√ low small bowel / colonic obstruction

√ "M" line accurately represents level of puborectal muscle = line drawn horizontally through junction of lower ⅓ and upper ⅔ of ischium on lateral radiograph

(3) **Imperforate anus**
= blind ending of terminal bowel + no fistula

(4) **Cloacal malformation**

(5) **Cloacal exstrophy**

ANTRAL-MUCOSAL DIAPHRAGM

= ANTRAL WEB

Age range: 3 months to 80 years

Associated with: gastric ulcer (30–50%)

• symptomatic if opening < 1 cm

Location: usually 1.5 cm from pylorus (range 0–7 cm)

√ constant symmetric band of 2–3 mm thickness traversing the antrum perpendicular to long axis of stomach

√ "double bulb" appearance (in profile)

√ concentric / eccentric orifice

√ normal peristaltic activity

APPENDICITIS

Prevalence: > 250,000 cases annually; 1–4% in children with acute abdominal pain

Lifetime risk: 7–9% in Western world population

Etiology: obstruction of appendiceal lumen by lymphoid hyperplasia (60%), fecolith (33%), foreign body (4%), stricture, tumor, parasite; Crohn disease (in 25%)

Cause: luminal obstruction from

(a) fecolith (11–52%) = hard crushable concretions from inspissation of fecal material + inorganic salts

(b) appendiceal calculus = hard noncrushable calcified stone (7–15%)

(c) lymphoid hyperplasia

(d) foreign body

(e) parasite

(f) primary tumor: carcinoid, adenocarcinoma, Kaposi sarcoma, lymphoma

(g) metastatic tumor: colon cancer, breast cancer

Pathogenesis:

continued secretion of mucus in appendiceal obstruction → elevates intraluminal pressure + distends lumen → venous engorgement → arterial compromise → tissue ischemia (after intraluminal pressure exceeds capillary perfusion pressure)

Peak age: 2nd decade; thereafter declining incidence; M÷F = 3÷2 (in teens / young adults, thereafter 1÷1)

◊ Rare under the age of 2 years!

• 80% clinical accuracy (78–92% in males, 58–85% in females):

Diagnostic dilemma (in 20–35%):

in elderly, ovulating women, infants / young children

◊ 32–45% rate of misdiagnosis in women 20–40 years!

◊ 5–25% false-negative appendectomy rate for children!

- pain:
  - mild poorly localized visceral pain of 4–6 hours duration referred to epigastrium + periumbilical region
  - crampy pain migrates into RLQ pain over appendix = McBurney sign (72%) and becomes continuous + more severe (somatic pain)
- anorexia, nausea, vomiting (40%)
- afebrile / low-grade fever (56%)
  ◊ Suspect perforation with temperature > 38.3°C
- leukocytosis with left shift (88%)

Clinical scoring system: "MANTRELS" score of up to 10

Migration of pain to RLQ 1
Anorexia 1
Nausea and vomiting 1
Tenderness in RLQ 2
Rebound pain 1
Elevated temperature 1
Leukocytosis 2
Shift of WBC count to left 1

Location:

(a) base of appendix (usually): posteromedial wall of cecum + 3 cm below ileocecal valve

◊ Appendix + ileocecal valve are on the same side of cecum

(b) tip of appendix: retrocecal, subcecal, retroileal, preileal, within pelvis (30%), extraperitoneal (5%)

(c) appendicitis in hernia sac (0.13%): inguinal hernia (Amyand hernia), femoral hernia (de Garengeot hernia)

(d) during pregnancy: cecum and appendix increasingly elevated out of pelvis by gravid uterus
◊ Cecal tilt angle of > 90° (on sagittal MR image) → appendix in right upper quadrant

Abdominal plain film (abnormalities seen in < 50%):

◊ Plain-film findings become more distinctive after perforation, while clinical findings subside / simulate other diseases!

√ usually laminated calcified appendicolith in RLQ (in 7–15%):

◊ Appendicolith + abdominal pain → 90% probability of acute appendicitis → high probability for gangrene / perforation!

√ cecal changes:
- √ thickening of cecal wall
- √ water-density mass + paucity / absence of intestinal gas in RLQ (in 24% of perforations)
- √ "cecal ileus" = gas-fluid level in cecum with gangrene ← local paralysis
- √ "colon cutoff" sign = amputation of gas at the hepatic flexure (in 20% of perforations) ← spastic ascending colon

√ small bowel obstruction pattern = small bowel dilatation with air-fluid levels (in 43% of perforations)

√ extraluminal gas (in 33% of perforations):
- √ gas loculation

- √ mottled bacteriogenic gas
- √ pneumoperitoneum (rare)

√ loss of fat planes:
- √ focal increase in thickness of lateral abdominal wall in 32% ← edema between properitoneal fat line + cecum
- √ loss of properitoneal fat line
- √ loss of pelvic fat planes around the bladder / right obturator ← fluid / pus in cul-de-sac
- √ loss of definition of right inferior hepatic outline ← free peritoneal fluid
- √ distortion of psoas margin + flank stripes

√ scoliosis ← muscle irritation

BE / UGI (accuracy 50–84%):

√ failure to fill appendix with barium: normal in up to 35%

√ indentation along medial wall of cecum ← edema at base of appendix / matted omentum / periappendiceal abscess

Oral contrast material within the appendix excludes acute appendicitis.

CT (87–100% sensitive, 89–98% specific, 93–98% accurate, 92–98% PPV, 95–100% NPV):

√ normal appendix visualized in 67–100%:
- √ 1–2 cm below ileocecal junction from posteromedial aspect of cecum with a diameter of up to 10 mm
- ◊ Nonvisualization of the appendix in a patient with RLQ pain virtually excludes acute appendicitis!

√ abnormal appendix:

An ↑ appendiceal caliber alone is not a reliable indicator for appendicitis. However, an ↑ between serial CTs suggests early acute appendicitis, even without adjacent fat stranding.

- √ distended appendiceal lumen > 7 mm in diameter
- √ circumferential wall thickening
- √ homogeneously enhancing wall ± mural stratification (= "target" sign)
- √ appendicolith = homogeneous / ringlike calcification (25%)

√ periappendicular inflammation (98%):
- √ linear streaky densities in periappendicular / pericecal / mesenteric / pelvic fat
- √ subtle clouding of mesentery
- √ local fascial thickening
- √ free peritoneal fluid
- √ localized + mesenteric lymphadenopathy
- √ marked terminal ileal wall thickening
- √ peritonitis
- √ small-bowel obstruction

√ circumferential / focal cecal apical thickening (80%):
- √ "arrowhead" sign = funnel of contrast medium in cecum symmetrically centering about occluded orifice of appendix (30% sensitive, 100% specific)

√ perforated appendix:
- √ defect in the enhancing appendiceal wall
- √ nonvisualization of appendix ← fragmentation

√ phlegmon = diffuse substantial inflammation of periappendiceal fat with ill-defined fluid collections (DDx: ileocolitis with secondary inflammation of appendix)
√ pericecal / mesenteric / interloop / pelvic abscess = poorly encapsulated single / multiple fluid collections containing air / extravasated contrast material
√ extraluminal appendicolith
√ extraluminal air

False-negative CT:

(a) overlapping range in maximal appendiceal diameter between inflamed + uninflamed appendix
(b) appendix mistaken for unopacified bowel
(c) distal appendicitis = inflammation limited to tip
√ abnormal tip of appendix with NORMAL proximal appendix and cecal apex

False-positive CT:

(a) cystic fibrosis (= appendiceal thickening of up to 15 mm)
(b) Crohn disease
(c) Cancer of the appendix

Secondary / reactive appendicitis can be caused by cecal / terminal ileal diverticulitis, terminal ileitis, active Crohn disease, colitis, or an acute gynecologic process.

Graded-compression US (85% sensitive, 92% specific, 78–96% accurate, 91–94% PPV, 89–97% NPV):

◊ Nondiagnostic study in 4% ← inadequate RLQ compression
◊ Useful in ovulating women + infants / children (false-negative appendectomy rate in males 15%, in females 35%)
◊ Normal appendix visualized in 2% of normal adults, but in 50% of normal children
√ noncompressibility of tubular appendix:
√ absence of peristalsis must be confirmed → NOT to mistake small bowel for appendix
√ blind-ending bulbous tip must be demonstrated → NOT to miss distal appendicitis
√ laminated wall with target appearance of ≥ 6 mm in outer wall diameter on cross section (81% specific, 98% PPV, 98% NPV) / mural wall thickness ≥ 2 mm
√ lumen may be distended with anechoic / hyperechoic material
√ pericecal / periappendiceal fluid
√ increased periappendiceal echogenicity (= inflammatory infiltration of mesoappendix / pericecal fat)
√ enlarged mesenteric lymph nodes
√ loss of wall layers = gangrenous appendix
√ perforated appendix (23–73%):
√ loss of echogenic submucosal layer
√ appendix no longer visualized (40–60%)
√ loculated periappendiceal / pelvic fluid collection ± gas bubbles ← abscess
√ prominent hyperechoic mesoappendix / pericecal fat
√ visualization of appendicolith (6%) = bright echogenic focus with clean distal acoustic shadowing
√ gas bubbles localized to perforation site
√ hypoechoic zones with poor margination within inflamed fat ← phlegmonous appendicitis

√ sympathetic thickening of adjacent terminal ileum + ascending colon

False-negative US:

(a) failure to visualize appendix
  › inability of adequate compression
  › aberrant location of appendix: eg, retrocecal
  › appendiceal perforation

(b) early inflammation limited to appendiceal tip

False-positive US:

(a) normal appendix mistaken for appendicitis

(b) alternate diagnosis: Crohn disease, pelvic inflammatory disease, inflamed Meckel diverticulum

(c) spontaneous resolution of acute appendicitis

Color Doppler US:

√ increased conspicuity (= increase in size + number) of circumferential vessels in and around the wall of the appendix ← hyperemia

√ decreased resistance of arterial waveforms

√ continuous / pulsatile venous flow

√ decreased / no perfusion = gangrenous appendicitis

MR (97–100% sensitive, 92–94% specific, 93% accurate):

√ appendiceal diameter > 6–7 mm on single-shot fast SE without luminal air / oral contrast material

√ appendiceal wall thickness > 2 mm, hypointense on T1WI and hyperintense on T2WI

√ ± high luminal SI on T2WI ← fluid-filled lumen

√ periappendiceal bands of high SI on fat-saturated images ← edema / fluid / abscess

√ thickened wall of cecum

√ (occasionally) focal area of low signal intensity in appendiceal lumen on all sequences = appendicolith

Negative predictive value: 100%

√ normal appendix visualized in 80% of pregnant women:
  √ tubular structure ≤ 6 mm
  √ intermediate signal intensity isointense to muscle
  √ central low SI (air / oral contrast) with blooming effect on T2*
  √ progressive cranial displacement of appendix + cecum during pregnancy

Prognosis:

(1) **Abortive appendicitis** = mild acute appendicitis that resolves spontaneously in an early stage of disease (after relief of inciting obstruction) in 8–15%
  • low C-reactive protein
  √ inflamed appendix that returns to normal within 1 week
  Prognosis: 50% recurrence rate

(2) Recurrent appendicitis (10–38%) = repeated similar episodic attacks of RLQ pain → appendectomy showing acute inflammation; in 70% within a year after first event

(3) Chronic appendicitis (1%) = RLQ pain of > 3 weeks + no alternative diagnosis + chronic active inflammation on histology → relief of symptoms after appendectomy

(4) Mortality rate of 1% (associated with perforation)

Cx: perforation (13–30–73%), abscess formation, peritonitis, wound infection, sepsis,

infertility, adhesions, bowel obstruction, death

Rx: an appendicolith is sufficient evidence to perform prophylactic appendectomy in asymptomatic patients (50% have perforation / abscess formation at surgery)

DDx: ◊ Only 22–38% of children referred for suspected appendicitis actually have appendicitis

Nonsurgical mimickers: mesenteric adenitis, terminal infectious ileitis-ileocecitis (Yersinia, Salmonella, Campylobacter) / inflammation (Crohn disease)

Clinical mimickers: appendiceal mucocele, neoplasm

BANNAYAN-RILEY-RUVALCABA SYNDROME

= RUVALCABA-MYHRE-SMITH SYNDROME

Cause: autosomal dominant transmission

• pigmented genital lesions

√ hamartomatous intestinal polyps (in 45%): usually in distal ileum + colon

√ macrocephaly

√ subcutaneous and visceral lipomas + hemangiomas

BARRETT ESOPHAGUS

= BARRETT SYNDROME

[Norman Rupert Barrett (1903–1979), surgeon at St. Thomas Hospital in London, president of Thoracic Surgeons of Great Britain and Ireland in 1962]

= progressive replacement of stratified squamous epithelium by metaplastic columnar epithelium (Barrett epithelium) containing goblet cells but no parietal cells

Cause: chronic gastroesophageal reflux (GERD) → reflux esophagitis → epithelial injury → epithelial metaplasia

Contributing factors:

delayed acid clearance, reduced acid sensitivity, hiatal hernia, duodenogastroesophageal reflux, reduced LES pressure, transient LES relaxation, alcohol, tobacco, obesity, chemotherapy, scleroderma (37%), genetic influence, S/P repair of esophageal atresia / esophagogastric resection / Heller esophagomyotomy

Histo: (1) specialized columnar epithelium (proximal)

(2) junctional-type epithelium (distal to (1))

(3) fundic-type epithelium (most distally)

Prevalence: in general 0.3–4%; in 7–10% of patients with advanced chronic reflux esophagitis

Associated with: moderate + severe esophagitis (94%); NO / mild esophagitis (6%)

Age: 0–15 years and 40–88 years (mean of 55 years); M > F; mainly among Whites

• asymptomatic; dysphagia ← esophageal stricture

• signs of reflux esophagitis: heartburn, substernal chest pain, regurgitation

• low-grade upper intestinal bleeding

Location: middle to lower esophagus

◊ A stricture in the mid- to upper esophagus is less common but more specific for Barrett esophagus

N.B.: the squamocolumnar junction is irregular and lies > 2–3 cm orad from the GE junction

Distribution: circumferential / focal

› mucosal changes:
  √ fine reticular / granular mucosal pattern (3–30%) resembling areae gastricae of the stomach located at distal aspect of midesophageal stricture:
    √ netlike web of thin linear / intersecting barium-filled grooves or crevices surrounding small tufts of mucosa (DDx: reflux esophagitis, acanthosis, leukoplakia, superficial spreading carcinoma, moniliasis / herpes simplex / CMV esophagitis)
  √ thickened irregular mucosal folds (28–86%)
  √ large deep wide-mouthed peptic ulcer (= Barrett ulcer) at upwardly displaced squamocolumnar junction / within columnar epithelium
  √ uptake of ^{99m}Tc-pertechnetate by columnar epithelium

› scarring:
  √ several-cm-long stricture (71%) in lower esophagus (60%) or upper to midesophagus below level of aortic arch (40%) [DDx: peptic stricture without Barrett esophagus]:
    √ ringlike constrictions / smooth tapered segments of concentric narrowing in midesophagus
  √ hiatal hernia (75–94%)

› functional:
  √ gastroesophageal reflux (45–63%)
  √ distal esophageal widening (34–66%) ← abnormal motility

Dx: velvety pinkish red appearance of gastric-type mucosa extending from gastric mucosa into distal esophagus (endoscopy with biopsy)

Cx: (1) Ulceration ± penetration into mediastinum

(2) Stricture

(3) Adenocarcinoma: annual risk of 0.12% (40-fold higher risk than in general population)

  √ plaquelike / focal irregularity / nodularity / sessile polyps

Rx: (1) Stop smoking, avoid bedtime snacks + foods that lower LES pressure, lose excess weight

(2) Suppress gastric acidity: antacids, H_2-receptor antagonists (cimetidine, ranitidine, famotidine), H+K+-adenosintriphosphatase inhibitor (omeprazole)

(3) Improve LES pressure: metoclopramide, bethanechol

(4) Esophageal resection in high-grade dysplasia

BEZOAR

[*padzahr* , Persian = antidote, counterpoison]

= persistent concretions of foreign matter composed of accumulated ingested material in intestines

Pathophysiology: usually formed in stomach → passing into small bowel as part / whole → impaction

Frequency: 0.4% (large endoscopic series)

Etiology: material unable to exit stomach because of large size, indigestibility, gastric outlet obstruction, poor gastric motility (diabetes, mixed connective tissue disease,

myotonic dystrophy, hypothyroidism)

Predisposition:
previous gastric surgery (vagotomy, pyloroplasty, antrectomy, partial gastrectomy), inadequate chewing, missing teeth, dentures, massive overindulgence of food with high fiber contents

• anorexia, bloating, early satiety / may be asymptomatic
√ well-defined focal ovoid mass of soft-tissue attenuation
√ mottled gas pattern
Cx: partial / complete small bowel obstruction
DDx: "small bowel feces" sign (amorphous, affects longer segment, related to adhesion)

Phytobezoar

= poorly digested fibers, skin + seeds of fruits and vegetables usually forming in stomach, ± impaction in small bowel
Frequency: 55% of all bezoars
• history of recent ingestion of pulpy foods
Food: oranges, persimmons (most common, unripe persimmons contain the tannin shibuol that forms a gluelike coagulum after contact with dilute acid)
Site of impaction: stomach, jejunum, ileum
√ intraluminal filling defect without constant site of attachment to bowel wall
√ interstices filled with barium
√ coiled-spring appearance (rare)
Cx: decubitus ulceration + pressure necrosis of bowel wall, perforation, peritonitis
DDx: lobulated / villous adenoma, leiomyosarcoma, metastatic melanoma, intussusception

Trichobezoar

[*trikho* , *thrix*, Greek = hair]
in 80% < age 30 years, almost exclusively in females
Associated with: gastric ulcer in 24–70%

BLUE RUBBER BLEB NEVUS SYNDROME

= BEAN SYNDROME
[William Bennett Bean (1909–1989), head of internal medicine at University of Iowa College of Medicine]
= rare familial disorder characterized by multiple cutaneous + musculoskeletal + gastrointestinal venous malformations predominantly afflicting GI tract (but also liver, spleen, heart, skeletal muscle, lung, kidney, thyroid, eyes, CNS)
Incidence: > 200 cases
Etiology: sporadic / autosomal dominant
Path: thin layer of connective tissue + single layer of endothelial cells surrounding blood-filled ectatic vessels
• blue to black soft rubbery painless 0.1–5.0 cm cutaneous lesions evacuating under pressure + slow refilling (commonly present at birth ± increase in size and number with age) = cutaneous venous malformations
• iron deficiency anemia ← chronic spontaneous hemorrhage

√ multiple polypoid filling defects of various sizes throughout small bowel ← venous malformations
√ intermittent small bowel obstruction ← chronic bleeding
√ multiple phleboliths
MR:
√ hyperintense lesions on T2WI ← slow flow / thrombosis
Cx: intussusception, volvulus; GI hemorrhage; chronic coagulation disorders; hemothorax; hypercalcemia; pressure erosion of bone, osseous + soft-tissue hypertrophy ← hypervascularity
DDx:
(1) Maffucci syndrome (dyschondroplasia + osteochondromas + vascular malformations)
(2) Klippel-Trénaunay-Weber syndrome (port wine stain, vascular malformations, limb hypertrophy)
(3) Kasabach-Merritt syndrome (large vascular malformations + consumptive coagulopathy)
(4) Kaposi sarcoma
(5) Peutz-Jeghers syndrome (congenital polyposis + melanotic cutaneous lesions)
(6) Gardner syndrome (soft-tissue tumors + sebaceous cysts)

BLUNT ABDOMINAL TRAUMA

CT is imaging method of choice for evaluation of stable patients
US imaging in the detection of intraabdominal injury:
86% sensitive, 99% specific, 98% accurate

Traumatic Hemoperitoneum

Prevalence: 29–34% of patients with abdominal visceral injury have NO hemoperitoneum ← intraparenchymal laceration / contusion without penetration of organ capsule
Location: paracolic gutters, pelvis
◊ Most dependent portions in supine position: pouch of Morison (hepatorenal fossa) and pouch of Douglas (pelvic cul-de-sac)
√ hematocrit effect of fresh blood = sedimented RBCs in the dependent portion of a hemoperitoneum

NECT (negative predictive value of 99.6%):
√ high-attenuation ascites (~ 30–45 HU) ← high protein content of unclotted extravascular blood
√ "sentinel clot"(clotted blood attenuation typically 45–70 HU) marks anatomic site + suggests source of bleeding
CECT:
√ high-density site of contrast extravasation ← active ongoing bleeding
√ extravasation always surrounded by lower-density hematoma (DDx: extravasated oral contrast is not surrounded by lower-density material)
CT findings requiring intervention:
(1) Solid-organ injury with active arterial extravasation
(2) Diaphragmatic injury

(3) Bowel and mesenteric injury
(4) Injury to major vessel
(5) Intraperitoneal bladder rupture

US:

√ usually anechoic fluid accumulation in subhepatic space (= Morison pouch) > pouch of Douglas / paravesical space > between bowel loops
DDx: bowel contents, urine, bile, ascites

√ **hemoperitoneum score** = depth of largest fluid collection in cm + 1 point for each additional site with fluid (score of ≤ 2 managed conservatively)

√ hyperechoic / occasionally isoechoic masses ← intraperitoneal clot

Prognosis: 17% of patients without hemoperitoneum require surgical / angiographic intervention

◊ Small pockets of fluid of 10–15 HU found in pelvis in 3–5% of male trauma patients WITHOUT organ injury!

◊ Peritoneal lavage cannot quantify amount of hemoperitoneum → 19–39% rate of nontherapeutic surgeries

◊ The rate of bleeding + presence of active extravasation have the most direct effect on patient care decisions!

DDx of free intraperitoneal fluid < 20 HU:
hemoperitoneum in anemic patient; simple ascites; bile; succus entericus in small bowel perforation; intraperitoneal urine from ruptured bladder

Hypovolemia = Hypoperfusion Complex

= manifestation of tenuous hemodynamic instability even after aggressive resuscitation efforts with IV fluids

√ "collapsed cava" sign = persistent flattening of infrahepatic IVC + flattening of renal veins ← decreased venous return
N.B.: abort CT examination as shock is imminent!

√ small hypodense spleen ← decreased enhancement

√ small aorta + mesenteric arteries ← intense vasoconstriction

√ **shock bowel**:
√ dilatation of fluid-filled intestines
√ diffuse concentric thickening of small bowel
√ intense enhancement ← vasoconstricted mesenteric vessels
√ sparing of colon

√ **shock nephrogram** = increased enhancement of kidneys + lack of renal contrast excretion

√ marked enhancement of adrenal glands

√ intense pancreatic enhancement

√ pancreatic + retroperitoneal edema

Fluid Overload

√ diffuse thickening + edema of bowel wall
√ distended IVC + hepatic veins
√ heterogeneous "nutmeg" appearance of liver
√ "periportal collar" = concentric halo of low attenuation around portal veins

CECT Attenuation Values of Fluid*	
HU	*Description*
0–15–20	bile, urine, intestinal contents
30–45	fresh nonclotted blood (high proteinaceous content (less with low hematocrit / hemorrhage after 48 hour)
45–70–100	clotted blood (close to bleeding site = sentinel clot sign); hematocrit effect (= sedimentation of RBCs with high attenuation)
85–(132)–370	active arterial contrast extravasation surrounded by large hematoma
* during IV contrast administration and assuming an initially normal hematocrit without significant dilution from intraperitoneal fluid (ascites, urine, succus, lavage fluid)	
DDx: (1) Water-soluble enteric contrast in ascites = bowel perforation (2) IV contrast during urographic phase = urinary ascites	

Blunt Trauma to Duodenum

√ retroperitoneal hematoma
√ stranding of retroperitoneal fatty tissue
√ thickening of duodenal wall

1. **Duodenal contusion**
   √ edema / hematoma of the duodenal wall
   √ intramural gas accumulations
   √ focal duodenal wall thickening > 4 mm
   Rx: conservative
2. Hematoma of the duodenal wall
3. **Duodenal perforation** and disruption
   √ retroperitoneal collection of contrast (infrequent)
   √ extraluminal gas
   √ lack of continuity of duodenal wall

Blunt Trauma to Spleen (40%)

◊ Most frequently injured intraperitoneal organ in blunt abdominal trauma (40% of abdominal organ injuries)

Associated with: other solid visceral / bowel injuries (29%); lower rib fractures in 44%, injury to left kidney in 10%, injury to left diaphragm in 2%

◊ 20% of left rib fractures have splenic injury!
◊ 25% of left renal injury have splenic injury!

Scoring of Duodenal Injury (1990) *American Association for the Surgery of Trauma*		
Grade	*Injury*	*Description*
I	hematoma laceration	involvement of single portion of duodenum
II	hematoma laceration	involvement of > 1 portion; disruption of < 50% of circumference
III	laceration	disruption of 50–75% of circumference of 2nd segment, disruption of 50–100% of circumference of 1st, 3rd, 4th segment
IV	laceration	disruption of > 75% of circumference of 2nd segment or involvement of ampulla / distal CBD
V	disruption	massive disruption of duodenopancreatic complex / duodenal devascularization
The extent of transections cannot be reliably evaluated with CT!		

Technique: scanning delay of 60–70 sec to avoid heterogeneous splenic enhancement

CECT (95% accurate):

◊ CT not reliable to determine need for surgical intervention!

√ hemoperitoneum ← disruption of splenic capsule

√ "sentinel clot" (= area of > 60 HU adjacent to spleen) as sensitive predictor of injury = **perisplenic hematoma**

√ **active extravasation**:

√ high-attenuation blush (80–370 HU)

√ focal high-attenuation area in / emanating from injured splenic parenchyma

√ growing larger with time (delayed phase imaging!)

N.B.: active extravasation of contrast material requires emergent surgery in 83–93%

√ mottled parenchymal enhancement = **contusion**

√ hypoattenuating line connecting opposing visceral surfaces = linear parenchymal defect = **splenic laceration**:

√ almost always associated with hemoperitoneum

√ crescentic region of low attenuation along splenic margin flattening / indenting / compressing the normal parenchyma = **subcapsular hematoma**

√ round hypodense inhomogeneous region ± hyperdense clot = **intrasplenic hematoma**

√ hypoattenuating hematoma with complete separation of splenic fragments = laceration traversing two capsular surfaces = **splenic fracture**

√ multiple lacerations = "**shattered spleen**"

US:

√ hyperechoic intraparenchymal region (= acute hematoma / laceration)

√ anechoic intralesional collection (= brisk hemorrhage)

√ diffusely heterogeneous parenchymal pattern containing hyper- and hypoechoic areas (= extensive splenic injury)

√ loss of normal organ contour ← perisplenic clot

Sequelae:

(1) scar / fibrosis

(2) splenic pseudocyst (20–30 HU)
(3) Vascular injury: pseudoaneurysm, AV fistula
(4) delayed splenic rupture
= hemorrhage > 48 hours after trauma

Categories of Splenic Injury (1994 Revision)
American Association for the Surgery of Trauma

Grade	*Injury*	*Description*
I	hematoma	subcapsular < 10% of surface area
	laceration	capsular tear < 1 cm of parenchymal depth
II	hematoma	subcapsular 10–50% of surface area; intraparenchymal < 5 cm in diameter
	laceration	1–3 cm deep without involvement of trabecular vessel
III	hematoma	subcapsular > 50% of surface area; ruptured subcapsular / parenchymal hematoma; intraparenchymal > 10 cm / expanding
	laceration	> 3 cm parenchymal depth / involvement of trabecular vessels
IV	laceration	involvement of segmental / hilar vessels with devascularization of > 25%
V	laceration	completely shattered spleen
	vascular	total splenic devascularization

◊ Does not consider amount of hemoperitoneum, active bleeding, pseudoaneurysm, AV fistula
N.B.: grade III or higher require more often surgical therapy!

Cause: subcapsular hematoma
Prevalence: 0.3–20% of blunt splenic injuries
Time of onset: in 70% within 2 weeks of injury; in 90% within 4 weeks of injury
Prognosis: splenectomy / splenorrhaphy; 80–90% success in nonoperative management
Rx: up to 91% of stable patients can be treated conservatively with observation; transcatheter embolization
◊ Preservation of spleen and its immune function = standard of care
DDx: (1) Normal lobulation / splenic cleft (smoothly contoured, medially located)
(2) Adjacent unopacified jejunum simulating splenic tissue
(3) Early differential enhancement of red and white pulp (scan obtained within 20–50 seconds)
(4) Perisplenic fluid from ascites / urine / succus / bile / lavage

Blunt Trauma to Liver (20%)

Prevalence: 2nd most frequently injured abdominal viscus
Associated with: splenic injury in 45%
• clinical manifestation often delayed by days / weeks
Location: right (posterior segment) > left lobe
Site: perivascular, paralleling right + middle hepatic arteries + posterior branches of right

portal vein, avulsion of right hepatic vein from IVC (13%)

◊ Left lobe injuries are more often associated with damage to duodenum, pancreas, transverse colon

CECT:

√ **liver laceration** = predominantly irregular linear branching / round regions of low attenuation:

(a) superficial ≤ 3 cm deep; (b) > 3 cm in depth

◊ Most frequently identified injury pattern

Associated with:

› retroperitoneal hematoma surrounding IVC ← posterosuperior segment VII laceration of bare area

› hematoma involving adrenal gland

› biloma ← laceration extending into porta hepatis

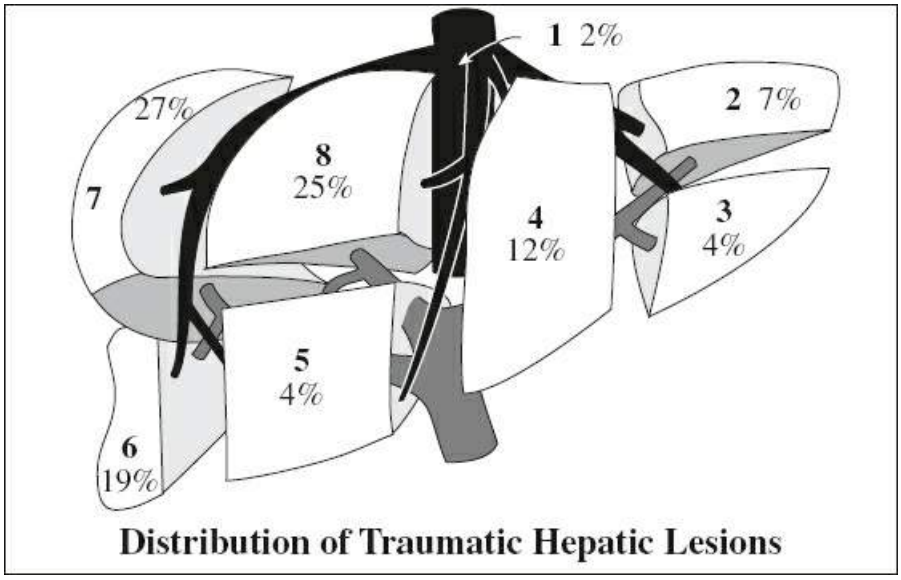
DDx: (1) beam-hardening artifact from adjacent ribs / from air-contrast level in stomach

(2) Focal fatty infiltration

Categories of Liver Injury (1994 Revision)*
American Association for the Surgery of Trauma

Grade	*Injury*	*Description*
I	hematoma	subcapsular < 10% of surface area
	laceration	capsular tear < 1 cm of parenchymal depth
II	hematoma	subcapsular 10–50% of surface area; intraparenchymal < 10 cm in diameter
	laceration	1–3 cm deep and < 10 cm long
III	hematoma	subcapsular > 50% of surface area; ruptured subcapsular / parenchymal; intraparenchymal >10 cm / expanding
	laceration	>3 cm parenchymal depth
IV	laceration	parenchymal disruption 25–75% of lobe; 1–3 Couinaud segments in single lobe
V	laceration	disruption > 75% of single lobe; > 3 Couinaud segments in single lobe
	vascular	juxtahepatic venous injury (HV, IVC)
VI	vascular	hepatic avulsion

* Active bleeding, pseudoaneurysm, AV fistula are not considered!



Distribution of Traumatic Hepatic Lesions

√ **liver hematoma:**
- √ hyperattenuating mass in acute phase of 54 (range, 28–82) HU decreasing over time ← clotted blood:
  - › intraparenchymal hematoma: single / multiple
  - › subcapsular hematoma: lenticular / elliptical configuration flattening underlying liver margin

Resolution: usually within 6–8 weeks

√ <u>active (potentially life-threatening) liver hemorrhage:</u>
- √ focal hyperattenuating area during early phase of 155 (range, 91–274) HU ← extravasated contrast material

Prognosis: 75% become hemodynamically unstable
Rx: angiographic embolization
DDx: focal hyperdense area of 80–350 HU during early phase ← pseudoaneurysm / AV fistula

√ <u>major (life-threatening) hepatic venous injury</u>
= liver laceration or hematoma extending into major hepatic vein / IVC
◊ 3.5 x more frequently associated with arterial bleeding

√ focal / diffuse <u>periportal tracking</u> (in up to 22%)
= areas of low attenuation paralleling portal vein + its branches 2° to
- › dissecting hemorrhage / bile
- › dilated engorged periportal lymphatics ← ↑ central venous pressure ← vigorous IV fluid administration / tension pneumothorax / pericardial tamponade

√ <u>flat IVC</u>
= AP diameter < ¼ of IVC width not caused by external compression
Cause: hypovolemia, poor fluid resuscitation, shock

√ hypodense wedge extending to liver surface = focal hepatic devascularization
√ hemoperitoneum ← violation of liver capsule with inability of liver veins to contract
√ intrahepatic / subcapsular gas, usually ← necrosis

US:

√ localized area of increased intraparenchymal echogenicity (= acute hematoma / laceration)
√ widespread heterogeneous liver echogenicity + absence of normal vascular pattern (= global parenchymal injury)

Cx: in 5–23%
(1) delayed hemorrhage(2–6%)
(2) abscess (0.6–4%) ← superinfection of hematoma / biloma / devascularized hepatic parenchyma
(3) pseudoaneurysm (1%) → hemobilia, melena, hematemesis (decompression into biliary system)
(4) bile peritonitis
(5) biliary fistula: external (to skin / hollow viscus), internal (to intestine / bronchus), biliovascular (to hepatic artery, portal / hepatic vein)

Rx: conservative treatment in up to 80% in adults + 97% in children; transcatheter embolization

Prognosis: healing in 1–6–15 months; 4–12% mortality

Blunt Trauma to Gallbladder (2%)

Associated with: injury to liver (91%), duodenum (54%), spleen (54%)
√ pericholecystic fluid (extraperitoneal location of GB)
√ free intraperitoneal fluid
CECT:
√ blurred contour of GB
√ focal thickening / discontinuity of GB wall
√ intraluminal enhancing mucosal flap
√ blood within GB lumen = attenuation > 50 HU
√ mass effect on adjacent duodenum
√ collapsed GB ← GB rupture
√ focal periportal tracking ← GB rupture
US:
√ focal hypoechoic thickening
√ echogenic mass within GB lumen

Blunt Trauma to GI Tract (5%)

◊ 3rd most common type of injury from blunt trauma to abdominal organs
Cause in children: MVA (lap belts), bicycle handle bar, child abuse
May be associated with: Chance fracture; traumatic hernia (disruption of the rectus abdominis m.)
Mechanism:
(1) crush / compression injury: direct force; near spine
(2) burst injury: sudden increase in intraluminal pressure
(3) shear injury: rapid deceleration at points of transition between mobile and fixed bowel portions

Location: jejunum distal to ligament of Treitz > duodenum > ascending colon at ileocecal valve > descending colon > distal ileum near ileocecal valve

- Classic triad (in only 33%):
  - abdominal pain + tenderness (100% sensitive)
  - abdominal rigidity; absent / decreased bowel sounds
- ↑ temperature + heart rate; ↓ urine output over 24 hours
- lap belt ecchymosis (not highly correlated)
- *Lavage:* 90% sensitive for hemoperitoneum → compromises interpretation of CT exam

N.B.: clinical signs + symptoms may be delayed for 24 hours (increasing mortality to 65%)

US:

√ nonspecific free intraabdominal fluid (86% sensitive, 98% specific)

NECT:

√ abdominal wall injury: SQ fat stranding ("seat belt" sign) ← hematoma ← tear

√ extraintestinal free air (30–60% sensitive, 95% specific):

√ intraperitoneal air: small gas bubbles anteriorly near liver / trapped within leaves of mesentery (with small bowel perforation) / porta hepatis

√ retroperitoneal air (with disruption of duodenum / rectum / colon)

DDx of free air:

◊ Most bowel perforations have no free gas due to:

(a) spontaneous seal of perforation

(b) developing ileus → no passage of gas

(c) rapid reabsorption of small gas collections

√ intramural air

√ hypodense free fluid (90–100% sensitive, 15–25% specific), particularly in interloop location ← perforation

DDx: parenchymal organ injury / osseous injury / large vessel injury / bladder perforation

√ "sentinel clot" sign adjacent to bowel

CECT (84–94% sensitive, 84–99% accurate):

@ bowel injury (CT 94% sensitive, 88% accurate)

Location: small bowel (proximal jejunum, distal ileum) > colon > stomach

√ extravasation of oral contrast material (8–15% sensitive, 100% specific), densest near perforation

DDx: hyperattenuating blood, extravasating vascular contrast material, leak of contrast material ← ruptured urinary tract

√ focal discontinuity of bowel wall = direct evidence (5–10% sensitive, 100% specific)

√ focal bowel wall thickening > 3 mm (= intramural hematoma [55–75% sensitive, 90% specific] / vascular compromise and inflammation ← spilling of bowel contents):

√ ± intestinal obstruction / ileus

DDx: lack of bowel distension

√ abnormal bowel wall enhancement (10–15% sensitive, 90% specific):

√ hyperdense contrast enhancement of injured bowel wall ← delayed venous transit time (20%)

√ lack of bowel wall enhancement (13%) ← bowel infarct, highly SPECIFIC

√ duodenal submucosal / subserosal hematoma → gastric outlet obstruction

@ mesenteric injury (CT 96% sensitive, 96% accurate)

√ mesenteric contrast extravasation (17%)

√ mesenteric vascular beading (39%) = change in caliber

√ abrupt termination of mesenteric artery / vein (35%)

√ mesenteric infiltration (70–77% sensitive, 40–90% specific) = haziness + fat stranding = streaky hyperattenuating infiltration / fluid at mesenteric root ← hemorrhage + inflammatory response

DDx: retractile mesenteritis

√ mesenteric rent → internal hernia

√ mesenteric hematoma (39%)

√ mesenteric pseudoaneurysm

Cx: peritonitis, sepsis, hemorrhage

Prognosis: delay in diagnosis by 8–12 hours increases morbidity + mortality from peritonitis + sepsis

Rx: surgery based on clinical assessment alone has a 40% negative laparotomy rate

CT in Blunt Trauma to Bowel and Mesentery

	Specific CT Findings	*Less Specific Findings*
Bowel	Free intraperitoneal air	Bowel wall thickening
	Bowel discontinuity	Abnormal wall enhancement
	Extraluminal contrast	Mesenteric fat stranding / fluid / air
Mesentery	Extravasation	Mesenteric fat stranding
	Vascular beading	Mesenteric hematoma
	Abrupt vessel termination	Abnormal bowel wall thickening / enhancement

Blunt Trauma to Pancreas (3%)

Mechanism: compression against vertebral column with shear across pancreatic neck

Frequency: < 10% of childhood trauma

Cause: motor vehicle accident (→ compression by seat belt /steering wheel), fall onto handle bars of a bicycle, child abuse

Scoring of Pancreatic Injury (1990)
American Association for the Surgery of Trauma

Grade	*Injury*	*Description*
I	hematoma	minor contusion without duct injury
	laceration	superficial laceration without duct injury
II	hematoma	major contusion without duct injury
	laceration	major laceration without duct injury
III	laceration	distal transection / parenchymal injury with duct injury
IV	laceration	proximal transection / parenchymal injury involving ampulla / bile duct
V	disruption	massive disruption of pancreatic head

Associated with: injury to liver (47%, typically left lobe), spleen (28%), stomach (42%), duodenum (19%, typically in younger patients), major vessel (41%), kidney (23%)

Classification:

I minor contusion / hematoma, capsule + major duct intact
II parenchymal injury without major duct injury
III major ductal injury
IV severe crush injury

- epigastric/ diffuse abdominal pain, vomiting
- leukocytosis, ↑ serum amylase activity

Location: pancreatic body (65%) > tail / head

CT (70–95% sensitive):

√ within first 12 hours normal CT findings in 20–40% → repeat CT at 24–48 hours
√ posttraumatic pancreatitis:
  √ edema / fluid in peripancreatic fat
  √ focal / diffuse pancreatic enlargement
  √ irregularity of pancreatic contour
√ focal area of low-attenuation / enlargement
  (1) **contusion** = diffuse / localized hypoattenuating area within normally enhancing parenchyma
  (2) **laceration** (actual site of laceration difficult to visualize)

N.B.: pancreatic laceration of > 50% of pancreatic diameter suggests ductal injury. Evaluation of the integrity of the main pancreatic duct remains the critical role of MRCP!

  (3) **transection** (fracture) = hypoattenuating linear findings with separated parenchyma
√ pancreatic **hematoma** = mixed / slightly hyperattenuating lesion within margins / in contact with parenchyma
√ fluid / blood accumulation:
  (a) alongside superior mesenteric artery
  (b) in transverse mesocolon / lesser sac
  (c) fluid between pancreas and splenic vein (in up to 90%)
√ thickening of anterior pararenal fascia

Morbidity: 11–62%

Mortality: 5%

Rx: I + II conservative management
III + IV need for surgery within 24 hours
endoscopic stent placement for duct injury

Cx: pancreatic fistula (23%), posttraumatic pancreatitis (10%), pseudocyst (5%), pseudoaneurysm, pneumonia, abscess (increases mortality to 20%)

BOERHAAVE SYNDROME

[Herman Boerhaave (1668–1738), professor of clinical medicine, botany and chemistry at the University of Leiden, Netherlands]

= spontaneous emetogenic injury resulting in rupture of esophagus → extrusion of gastric content into mediastinum / pleural space

Frequency: 1÷6,000 persons
Age: middle-aged men (in 50% with history of alcoholism / heavy drinking)
Cause: violent retching ← food bolus impaction
Pathophysiology:
incomplete cricopharyngeal relaxation during sudden increase in intraabdominal pressure while vomiting → abrupt increase in intraluminal esophageal pressure (barotrauma) in the presence of a moderate to large amount of gastric contents → complete transmural disruption of esophageal wall

- **Mackler triad:**
  - episode of severe retching + forceful vomiting
  - sudden excruciating chest pain (substernal, left chest, neck, pleuritic, epigastric); subcutaneous emphysema
- odynophagia, tachypnea, cyanosis, fever, shock
- NO hematemesis (blood escapes outside esophageal lumen)

√ rent of 2–5 cm in length
Location: 3–6 cm above diaphragm (= 2–3 cm above GE junction), predominantly in left posterolateral wall

CXR:
√ mediastinal widening
√ air-fluid level within mediastinum
√ extravasation of contrast into mediastinum / pleura
√ pneumomediastinum (single most important plain-film finding), pneumopericardium, subcutaneous air:
√ **"V" sign of Naclerio** = localized mediastinal emphysema with air between lower thoracic aorta + diaphragm
[Emil A. Naclerio (1915–1985), thoracic surgeon at Harlem and Columbus Hospitals in New York City]
√ pleural effusion on left >> right side / hydropneumothorax
√ subcutaneous emphysema
√ patchy pulmonary infiltrate

Esophagography(modality of choice):
Technique: initially hydrosoluble contrast medium (in 10% falsely negative) followed by barium if negative
√ submucosal collection
√ extravasation of contrast material
√ esophagopleural fistula (most commonly on left)

The use of hydrosoluble contrast material is preferred over barium in suspected esophageal rupture → risk for mediastinitis as a result of irritation caused by barium.

CT:
√ esophageal wall thickening
√ supradiaphragmatic periesophageal air collection
√ mediastinal fluid collection + pneumomediastinum

BRUNNER GLAND HAMARTOMA

[Johann Conrad Brunner (1653–1727), Swiss professor of anatomy and physiology at the University of Heidelberg, Germany]

Terminology:
Brunner gland hamartoma ≤ 5 mm in diameter
Brunner gland hyperplasia > 5 mm in diameter

Prevalence: 1.2% of all gastric polyps; 5% of all duodenal masses

Etiology: response to gastric acid in duodenum → glands protect duodenal epithelium + optimize pH for pancreatic enzyme activity

Histo: diffusely enlarged hyperplastic glands of Swiss cheese appearance and variable amounts of adipose + smooth muscle + lymphoid tissue + sclerosis

Physiology: mucosal + submucosal Brunner glands contain mucous + serous cells → secrete a clear viscous alkaline mucus into crypts of Lieberkühn

Age: manifest in middle age; M÷F = 1÷1

• incidental / symptomatic (abdominal pain)

MORPHOLOGIC TYPES:
1. Diffuse nodular hyperplasia: throughout duodenum
2. Circumscribed nodular hyperplasia: in suprapapillary portion
3. Single glandular adenoma with polypoid tumorlike dimensions

Location: duodenum (70% bulb, 26% 2nd portion, 4% 3rd portion); prepyloric region (distribution of duodenal glands from vicinity of pylorus to proximal ²/₃ of duodenum)

Mean size: 2.0 (range, 0.5–6.0) cm; rarely up to 11 cm

UGI:
√ multiple nodular filling defects (usually limited to 1st portion of duodenum) with "**cobblestone appearance**" (most common finding)
DDx: polyposis syndromes, lymphoid hyperplasia, heterotopic gastric mucosa, nodular duodenitis
√ smooth single mass ± central ulceration
DDx: adenomatous polyp, lipoma, leiomyoma, leiomyosarcoma, lymphoma, ectopic pancreatic tissue, GIST, carcinoid tumor, adenocarcinoma, pancreatic neoplasm, ampullary neoplasm

Endoscopic US:
◊ Guides appropriate depth of endoscopic biopsy!
√ heterogeneous echogenicity with various amounts of solid + cystic components

NECT:
√ isoattenuating relative to pancreas

CECT:
√ hypoattenuating relative to pancreas (portal venous phase)
√ peripheral rim enhancement (of duodenal mucosa)

Cx: GI bleeding (chronic melena, hematemesis), intestinal obstruction, intussusception

BURKITT LYMPHOMA

= highly aggressive B-cell lymphoma usually found in children or immunocompromised adults
[initially described in a 7-year old Ugandan child in 1958 by Denis Parsons Burkitt (1911–1993), Irish surgeon on Medical Research Council in London]

Prevalence: 1–2% of all NHLs; 1–5% of primary gastrointestinal NHLs in adults

◊ Most common (30–50%) type of pediatric NHL in children < 15 years in USA and western Europe.

Origin: undifferentiated small noncleaved B-cell–derived lymphocyte

Histo: uniform deeply basophilic medium-sized cells containing round nuclei with distinct chromatin and multiple nucleoli; characteristic "starry sky" pattern (= scattered macrophages containing apoptotic cellular debris on a basophilic background) at light microscopy; 99% proliferation index

Genetics: translocation of c-Myc oncogene with one of immuno- globulin genes, most frequently t(8;14)(q24;q32)

Growth rate: fastest growing of all human tumors with a doubling time of about 24 hours

Rx: dramatic response to chemotherapy

Prognosis: 90–98% 5-year survival rate in children with localized disease: 75–89% 2-year disease-free survival rate in children with advanced disease; 50–70% survival in adults

Endemic / African Form of Burkitt Lymphoma

Endemic in areas with malaria:

sub-Saharan Africa, New Guinea (exposure to Plasmodium falciparum has a synergistic effect causing a marked decrease in T-cell surveillance)

Incidence in central Africa:

50–80% of all childhood neoplasms

Associated with: Epstein-Barr virus infection in 95% (implicated as B-cell mitogen in oncogenesis); malaria

Age: 3–10 years

@ Mandible > maxilla / facial bones

• jaw mass; exophthalmos (orbital extension)

√ grossly destructive lesion, spicules of bone growing at right angles

√ large soft-tissue mass

@ Other skeleton (multifocal in 10%)

√ reminiscent of Ewing tumor / reticulum cell sarcoma

√ lamellated periosteal reaction around major long bones

Sporadic / American Form of Burkitt Lymphoma

= NONENDEMIC FORM OF BURKITT LYMPHOMA

= typically manifests with bulky disease because of its rapid doubling time

Incidence in Europe + North America:

35–45% of all pediatric NHL; 3% of all childhood tumors

Median age: 8 (range, 6–15) years; ⅓ between 5 and 9 years; unusual in children < 5 years; most frequently in white boys

• paraplegia; NO peripheral leukemia

• Epstein-Barr virus genome found in only a minority

◊ Widespread extraintestinal disease at presentation (mesenteric ± retroperitoneal

lymphadenopathy) in 70%!

@ Gastrointestinal tract (22–69%)
- abdominal mass, intestinal obstruction
- acute abdominal complaints (30–40%)

Location: terminal ileum, ileocecal region (Peyer patches), mesentery >> stomach, colon

√ well-defined sharply marginated homogeneous large abdominal and pelvic masses (31–64%):
  √ encasement of bowel and mesenteric vessels
  √ invading bowel wall → obstruction
  √ central necrosis in large tumor
√ ± enlarged abdominal lymph nodes
√ malignant ascites (25%–63%)
√ peritoneal thickening / nodularity (42%) along liver capsule and peritoneal reflections ← intraperitoneal seeding
√ usually intraabdominal extranodal involvement with sparing of spleen

Barium:
  √ displacement of bowel loops by a large mass
  √ abnormally separated bowel loops ← extensive bowel wall thickening
  √ narrowing of distal ileum

US:
  √ large hypoechoic masses ± engulfing of bowel / mesenteric vessels
  √ cystic central areas ← necrosis
  √ omental caking (unusual)

CT:
  √ bowel wall thickening / mural masses
  √ "sandwich" sign = enhancing vessels surrounded by mildly enhancing confluent mesenteric mass

MR:
  √ isointense to muscle on T1WI + T2WI:
    √ homogeneous T1 hypointensity
    √ heterogeneous intermediate-to-high SI on T2WI
  √ intense homogeneous enhancement
  √ bright round-to-ovoid lesions > 10 mm in size with restricted diffusion ← lymph node involvement

PET/CT:
  √ highly FDG avid

Cx: intussusception, aneurysmal dilatation, perforation
  ◊ Most common cause of intussusception in children ≥ 4 years

◊ Intussusception and aneurysmal dilatation of bowel suggest lymphoma.

@ Abdominal organs
√ multiple hypoechoic / hypoattenuating lesions of liver + spleen
√ periportal hypoattenuation

@ Genitourinary tract (20%)

Involvement of: kidneys, retroperitoneum, ovary, uterus

√ multiple hypoechoic / hypoattenuating renal masses / diffuse renal enlargement (5%)
√ hydronephrosis (28%)
√ retroperitoneal Burkitt may extend into spinal canal

@ Chest
√ pleural effusion (most common chest abnormality)

@ CNS
√ meningeal infiltration (most commonly)
√ cavernous sinus invasion
√ supra- and parasellar tumor
√ epidural spinal mass ± spinal cord compression

@ Others
salivary glands, thyroid, bone marrow

Immunodeficiency-associated Burkitt Lymphoma

Prevalence: in up to 40% of NHLs in HIV-positive patients
Prognosis: 50–70% survival in adults

CARCINOID SYNDROME

= constellation of clinical findings related to secretion of serotonin + other vasoactive peptides by tumor

Frequency:
› in 7–9% of small bowel carcinoids (most commonly in ileal carcinoids) ← metastases to liver + retroperitoneal Lnn.
› in only 0.7% of pulmonary carcinoids ← rarely metastasize to liver
› in 2–5% of pulmonary carcinoids → developing hepatic metastases during follow-up period

Cause: excess serotonin + tachykinin levels in systemic circulation produced by some carcinoids

Associated with: hepatic / retroperitoneal metastases

Serotonin metabolism:
normally, platelets take up + store circulating serotonin; excess serotonin is inactivated by liver, lung, brain and transformed to 5-hydroxyindoleacetic acid (5-HIAA)

Pathophysiology:
vasoactive substances enter systemic circulation by escaping hepatic degradation → thus bypassing hepatic metabolic pathway to 5-HIAA with
(a) metastases to liver / retroperitoneal nodes
(b) primary pulmonary / ovarian carcinoids

- attacks precipitated / exacerbated by ingestion of food / alcohol emotional stress, exercise
- colicky abdominal pain, recurrent intractable diarrhea (70%)
- asthmatic wheezing ← bronchospasm (15%) caused by tachykinin + bradykinin; excess 5-HIAA in urine
- nausea & vomiting, fever, hypotension (vasomotor instability)
- right-sided **endocardial fibroelastosis** (40–50%)
- skin changes:
  - cutaneous facial flushing + sweating (rare)

- desquamative skin lesions (5%)
- pellagra (7%) from niacin deficiency ← preferential conversion of dietary tryptophan to serotonin rather than niacin
- multiple telangiectasias (25%)

Prognosis: carcinoid syndrome has a higher morbidity & mortality than does the tumor itself!

CARCINOID TUMOR OF GI TRACT

= NEUROENDOCRINE TUMOR OF GI TRACT

[*Karzinoide*, German = carcinoma-like]

= group of well-differentiated tumors of the diffuse endocrine system outside pancreas + thyroid

Commonality: neuroendocrine cells share several antigens with nerve elements (neuroendocrine markers)

Neuroendocrine system:

◊ The majority of neuroendocrine tumors occur within the gastroenteropancreatic (GEP) axis

(a) adrenal medulla, pancreatic islets, paraganglia
(b) parathyroid, pituitary, thyroid C cells
(c) others:
  › GI tract: from hypopharynx to rectum (67–85%)
  › tracheobronchial system (10–29%)
  › biliary tract, gallbladder, liver
  › kidney, urethra, ovary, testis, skin (8%)

Inheritance: sporadic (mostly) / part of complex familial endocrine cancer syndrome (MEN 1, NF 1)

Frequency: 1.9÷100,000 annually worldwide
2nd most common primary tumor of small bowel

Origin: enteroendocrine cells that populate mucosa + submucosa; belong to APUDomas (like pheochromocytoma, medullary carcinoma of thyroid, islet cell tumors of pancreas)

Average age: 61 years; M÷F = 2÷1

Path: firm white / yellow / grey firm submucosal nodule arising from argentophil Kulchitsky cells of epithelial origin in the crypts of Lieberkühn (= argentaffinoma ← affinity for silver stain marking serotonin-containing granules of enterochromaffin EC-cells); invasion of mesentery incites an intense fibrotic reaction

Often the tumor bulk is subepithelial, and they should be included in the DDx of submucosal tumors.

Histo: solid acinar / insular nests of closely packed monomorphic cells, uniform in size, arranged in trabecular / glandular rosette pattern; cytoplasma contains argyrophil secretory granules arranged in distinctive "salt and pepper" pattern of nuclear chromatin; low-grade malignancy resembling adenocarcinoma without its aggressive behavior; malignant through invasion of muscularis

Immunohisto: chromogranin, synaptophysin, neuron-specific enolase, protein gene product 9.5, peptide markers for serotonin and gastrin

Classification based on malignant potential:

1. Well-differentiated neuroendocrine tumor (typical carcinoid tumors) → low-grade malignancy
2. Well-differentiated neuroendocrine carcinoma (atypical carcinoid tumor) with metastases

→ more aggressive

3. Poorly differentiated neuroendocrine carcinoma of high-grade malignancy → poor prognosis
   (a) Large cell neuroendocrine carcinoma (LCNEC)
   (b) Small cell lung carcinoma (SCLC) = majority

Biochemistry:
tumor elaborates excessive amounts of vasoactive substances + neuropeptides (1) ACTH (2) histamine (3) bradykinin (4) kallikrein (5) prostaglandin (6) substance P (7) neurokinin-A (8) serotonin (= 5-hydroxytryptamine ← 5-hydroxytryptophan ← tryptophan), which is metabolized (inactivated) in liver by monamine oxidase into 5-hydroxyindole acetic acid (5-HIAA) and excreted in urine; 5-hydroxytryptophan is destroyed in pulmonary circulation

Associated with: other synchronous / metachronous malignancies (36% at necropsy), especially gastrointestinal adenocarcinoma; neurofibromatosis type 1

- asymptomatic (66%), abdominal pain / bowel obstruction (19%)
- nausea, weight loss (16%), palpable mass (14%), GI bleeding
- elevated serum chromogranin-A (most common marker)
- elevated urinary 5-HIAA (hydroxyindole acetic acid)
- carcinoid syndrome

RULE OF ⅓:
◊ ⅓ occur in small bowel
◊ ⅓ have metastases
◊ ⅓ are multiple
◊ ⅓ have a second malignancy
◊ ⅓ have carcinoid syndrome

Metastases (~ 40% at time of presentation):
mesenteric lymph nodes, liver (in 90% of patients with carcinoid syndrome), peritoneum, lung, bone (osteoblastic)

◊ Symptomatic metastases ← midgut carcinoids in 75%

(a) incidence versus tumor size
tumor of < 1 cm (in 75%) metastasizes in 2%
tumor of 1–2 cm (in 20%) metastasizes in 50%
tumor of > 2 cm (in 5%) metastasizes in 85%

(b) incidence versus location
tumor in ileum (in 28%) metastasizes in 35%
tumor in appendix (in 46%) metastasizes in 3%
tumor in rectum (in 17%) metastasizes in 1%

Visualization of Liver Metastases

	best seen at	*present at*
NECT	35%	3%
CECT in HAP	35%	14%
CECT in PVP	30%	3%

HAP = hepatic arterial-dominant phase of triple phase CT
PVP = portal venous-dominant phase of triple phase CT

Location within GI tract:

◊ 30% are multicentric (Examine entire bowel!)
@ Small bowel (42%)
Frequency: 25% of all small bowel tumors
Location: ileum (91%); jejunum (7%), duodenum (2%); multiple in 15–29–41%
@ Rectum (27%)
@ Appendix (24%)
@ Stomach (9%)
@ Colon (5%)
@ Esophagus (0.05%)
Location outside GI tract:
@ Respiratory tract (20–30%)
@ Others: thyroid, pancreas, biliary tract, teratomas (ovarian, sacrococcygeal, testicular)
Site: intramural mass / intraluminal polypoid nodule
UGI:
√ small smooth submucosal mass (usually < 2 cm) impinging eccentrically on lumen
√ ± ulceration of overlying gastric / intestinal mucosa
√ desmoplastic fibrotic response of mesentery ← high levels of serotonin ← local production by nodal metastases:
√ angulation + kinking of loops → obstruction (DIAGNOSTIC)
√ spiculated / tethered appearance of mucosal folds
√ matting of multiple loops
√ separation of loops ← large mesenteric metastases
CT:
√ primary tumor:
√ small subepithelial avidly enhancing polyp during early phase, often in ileum (dual-phase imaging with water as oral contrast / CT enteroclysis)
√ may become isodense after slow contrast infusion / in portal-venous phase
√ enhancing carpet lesions mimicking Crohn disease
√ regional lymph node metastases:
√ focal conglomerate mesenteric mass often larger than primary tumor
√ low-density lymphadenopathy ← necrosis
√ mesenteric carcinoid tumor (metastasis):
√ "sunburst" appearance = stellate radiating pattern and beading of mesenteric neurovascular bundles ← fibrosis + desmoplastic reaction
√ containing calcifications (in up to 70%)
√ thickening + retraction + shortening of mesentery
√ displacement + kinking + separation of adjacent bowel loops
√ asymmetric / concentric segmental thickening of adjacent bowel loops ← bowel ischemia ← encasement of mesenteric vessels
√ characteristically hyperattenuating + necrotic liver metastases (best visualized during early arterial phase!)
MR:
√ mesenteric tumor isointense to muscle on T1WI + T2WI
Angio:

√ "sunburst" appearance:
√ kinking of small- and medium-sized vessels of a stellate configuration
√ simulated hypervascularity with thickening + foreshortening of mesenteric vessels ← fibrotic retraction
√ mesenteric ischemia:
√ arterial branch stenoses from encasement of medium-sized vessels ← elastic vascular sclerosis with locally elevated serotonin levels
√ venous occlusion / mesenteric varices
√ tumor may be identified as hypervascular mass

NUC (initial procedure of choice for):
(a) localization of occult primary tumor
(b) staging
(c) identification of receptor status for octreotide Rx

(1) ^{111}In-pentetreotide somatostatin-receptor scintigraphy (80–100% of carcinoids contain 5 somatostatin receptor subtypes)
Sensitivity: 80–90% (improved with SPECT-CT fusion)
√ higher frequency of radiotracer uptake in midgut carcinoids + with elevated serotonin levels

(2) ^{123}I- / ^{131}I-MIBG scintigraphy
Sensitivity: 55–70% (lower than for ^{111}In-pentetreotide)
√ type I uptake mechanism for guanethidine

Prognosis: slow progression with average survival time of 3.2 years after diagnosis of liver metastases; 5-year survival of 65% for localized disease + 36% for distant metastatic disease

Rx: resection; somatostatin / SMS 201-995; chemoembolization of hepatic arteries

DDx: oat-cell carcinoma, pancreatic carcinoma, medullary thyroid carcinoma, retractile (sclerosing) mesenteritis, desmoplastic carcinoma / lymphoma

Gastric Carcinoid (9%)

Frequency: 2% of all gastric malignancies

Origin: (enterochromaffin-like) ECL-cell arising from oxyntic (gastric–acid-secreting) mucosa
[*oxyno* , Greek = make sour / acid, to sharpen]

Location: gastric body and fundus

√ one / more small 1–4-cm subepithelial masses:
√ bull's eye appearance when ulcerated
√ one / more sessile / pedunculated polyps
√ avid enhancement in early arterial phase

Type 1 gastric ECL-cell carcinoid (74–80%)

Mean age: 63 years; M÷F = 1÷2.5

Associated with: autoimmune chronic atrophic gastritis

Path: multiple < 1 cm mucosal nodules in gastric fundus / body

Histo: positive stain for chromogranin A + synaptophysin

- often incidental finding during imaging for dyspepsia / chronic atrophic gastritis:
  - hypergastrinemia ← antral G-cell hyperplasia

• ± achlorhydria and pernicious anemia

√ multiple / solitary polyps of < 1 cm in diameter in fundus

Prognosis: tendency for benign biologic behavior; nodal + hepatic metastatic spread in 5%

Type 2 gastric ECL-cell carcinoids (5–10%)

Mean age: 50 years; M÷F = 1÷1

Associated with: Zollinger-Ellison syndrome in MEN 1

◊ 30% of patients with MEN 1 have gastric carcinoid tumors ← altered tumor suppression contributes to development of carcinoids from ECL-cell hyperplasia

Path: multiple mucosal nodules of variable size

• hypergastrinemia → abdominal pain, recurrent peptic ulcers, diarrhea; hypertrophic hypersecretory gastritis

√ multiple masses of variable size on diffuse gastric wall thickening

Prognosis: local nodal metastatic spread in 10–30%

Types 1 and 2 of gastric carcinoids are associated with hypergastrinemia causing proliferation of enterochromaffin- like cells → developing often multiple carcinoid tumors.

Type 3 gastric ECL-cell carcinoids (13%)

= sporadic carcinoid NOT associated with hypergastrinemia

Mean age: 55 years; M÷F = 3÷1

Path: solitary > 2 cm mass in gastric body + fundus

• bleeding, abdominal pain, anorexia, weight loss

√ usually solitary submucosal tumors ± ulceration

Prognosis: metastases at clinical presentation in 50–70%; 20% 5-year survival

DDx of solitary tumor: adenocarcinoma, lymphoma, GIST

Duodenal Carcinoid (2%)

Mean age: 53 (range, 19–90) years; M÷F = 1÷1

Associated with:

(1) Multiple endocrine neoplasia

(2) Neurofibromatosis type 1 for periampullary carcinoids often containing somatostatin-producing D-cells

A. **G-cell (gastrin-producing) carcinoid** (62%)

◊ in ⅓ functioning tumor (= gastrinoma) that produces Zollinger-Ellison syndrome

◊ 85% of sporadic gastrinomas in "gastrinoma triangle"

◊ 90% of MEN 1 patients develop multiple G-cell carcinoids

• abdominal pain + diarrhea (50%) ← hypergastrinemia

• nausea, vomiting, positive secretin stimulation test

• bleeding from multiple + recurrent peptic ulcers

• gastroesophageal reflux ← excess acid production

B. **D-cell (somatostatin-producing) carcinoid** (21%)

Associated with: neurofibromatosis 1 (in up to 50%)

Path: 1–2 cm polypoid nodules in submucosa / infiltrative intramural masses ± ulceration

Histo: densely calcified concentrically laminated psammoma bodies (= psammomatous

somatostatinoma); positive stains for neuron-specific enolase, chromogranin A, synaptophysin, somatostatin; immunoreactivity for gastrin

Location: around ampulla of Vater

- jaundice, pancreatitis ← obstruction of bile duct
- hemorrhage
- somatostatin effects (rare): steatorrhea, diarrhea, diabetes mellitus, hypochlorhydria, anemia, cholelithiasis

UGI:

√ well-defined round intraluminal polypoid mass (52%) / intramural mass (39%) ± focal ulceration

CT:

√ arterial phase enhancement + loss of enhancement during delayed phase

√ metastasis to peripancreatic lymph nodes / liver (in 60–80% at time of diagnosis)

N.B.: positive gastrointestinal contrast material may mask small duodenal mural lesions

Jejunal and Ileal Carcinoid (42%)

Mean age: 65 years; M÷F = 1÷1

Associated with: synchronous / metachronous malignancies (29%): GI adenocarcinoma (most common)

- often asymptomatic
- local symptoms: small bowel obstruction, ischemia, bleeding
- long history of intermittent crampy abdominal pain, weight loss, fatigue, abdominal distension, diarrhea, nausea, vomiting

Path: small firm < 3.5 cm intramural nodule ± protrusion into lumen; multiple in 30%; infiltrative growth into subserosa + mesentery stimulating desmoplastic reaction → multifocal stenoses and occlusions of arteries + veins → intestinal ischemia

SBFT:

√ solitary / multifocal small polypoid nodules / mucosal elevations ± ulceration

√ fixed rigid curved segment of small bowel

US:

√ smooth intraluminal hypoechoic oval masses interrupting submucosal layer

√ thickening + puckering of muscularis propria

√ retraction of wall, invasion of serosa

√ mesenteric metastases of similar echogenicity to primary ± calcification

CT:

› primary tumor

√ large polypoid intramural lesion

√ concentric / asymmetric hypoattenuating mural thickening ("target / halo" sign) ← intestinal ischemia / infiltrating tumor with desmoplastic fibrosis

√ hypervascular nodular wall thickening smooth submucosal mass

√ "hairpin turn" = kinking / curvature of a thickened distorted intestinal wall

› metastatic disease (in 60% at time of diagnosis):

√ large enhancing local mesenteric lymph nodes / masses often exceeding the primary mass in size:

√ stellate mesenteric desmoplastic reaction of "spoke-wheel / sunburst" appearance

NOT associated with a mass = mesenteric soft-tissue stranding and distortion of mesenteric vessels ← fibrosis rather than tumor infiltration
√ well-defined margins ± necrosis
√ faint stippled / coarse dense / diffuse calcifications (70%)
√ miliary peritoneal implants / large masses / mesenteric caking
√ hypervascular liver metastases during arterial phase ± central necrosis

Cx: intussusception

DDx for carcinoids of small intestines:
metastatic disease, primary intestinal adenocarcinoma, lymphoma, GIST, Crohn disease, localized ischemic enteritis

Appendiceal Carcinoid (< 10%–24%)

Commonly benign: slow growth, rarely metastasizing

Incidence at surgery: 0.03–0.70%

- mostly asymptomatic
- symptoms of appendicitis (30–50%)

Age: any; M < F

Site: tip (70%), middle (20%), base (10%) of appendix

Size: usually < 1 cm, rarely > 2 cm

√ focal soft-tissue mass / diffuse circumferential thickening

√ invasion of mesoappendix (11%)

US:
√ persistent fluid-distended appendix without typical signs of appendicitis

Colorectal Carcinoid

Frequency: < 1% of all rectal cancers

Mean age: 66 years (56 years for rectal location)

Location: rectum (27%) >> cecum / ascending colon (5%)

- mostly asymptomatic / abdominal pain, weight loss
- carcinoid syndrome (NOT with common rectal carcinoids)

√ polypoid intramural mass ± intussusception

√ ± ulceration of large tumor

Prognosis: metastatic in 10%

CATHARTIC COLON

= prolonged use of stimulant-irritant cathartics (> 15 years) → chronically increased muscular activity + tonus → neuromuscular incoordination

Agents: castor oil, senna, phenolphthalein, cascara, podophyllum, aloin

Location: involvement of colon proximal to splenic flexure

√ effaced mucosa with flattened smooth surface

√ diminished / absent haustrations

√ "pseudostrictures" = typically smoothly tapered areas of narrowing ← sustained tonus of circular muscles

√ poor evacuation of barium

√ flattened + gaping ileocecal valve

√ shortened but distensible ascending colon
DDx: "burned-out" ulcerative colitis with right-sided predominance (very similar)

CHAGAS DISEASE

[Carlos Chagas (1879–1934), physician in Rio de Janeiro, Brazil]
= damage of ganglion cells by neurotoxin liberated from protozoa Trypanosoma cruzi resulting in aperistalsis of GI tract + dilatation
Histo: decreased number of cells in medullary dorsal motor nucleus + Wallerian degeneration of vagus + decrease / loss of argyrophilic cells in myenteric plexus of Auerbach
Peak age: 30–50 years; M÷F = 1÷1
• foul breath, regurgitation, intermittent / persistent dysphagia
• odynophagia (= fear of swallowing), aspiration
• Mecholyl test: abnormal response indicative of deficient innervation; 2.5–10 mg methacholine subcutaneously followed by severe tetanic nonperistaltic contraction 2–5 minutes after injection, commonly in distal half of esophagus, accompanied by severe pain
@ Dilatative cardiomyopathy (myocarditis)
@ Megacolon (bowels move at intervals of 8 days to 5 months)
Cx: impacted feces, sigmoid volvulus
@ Esophagus: changes as in achalasia

Trypanosomiasis

[*trypano* , Greek = borer; *soma* , Greek = body]
Organism: unicellular parasitic flagellate Trypanosoma cruzi transmitted via vector
Transmission: acquired by insect bite from the Reduviidae family (genera Triatoma, Rhodnius, and Panstrongylus); trypomastigotes inoculation occurs through rubbing of reduviid bug feces into a bite or other skin defect
◊ Endemic to Central + South America (esp. eastern Brazil) with 24 million people infected
• acute febrile illness, acute myocarditis (uncommon)
• facial / unilateral palpebral edema ("Romaña" sign)
@ Heart: chronic myocarditis
Histo: focal / diffuse loss of myocytes, fibrosis, focal atrophy, conduction system involvement
• bundle branch block → complete atrioventricular block
√ severe cardiomegaly ← dilated cardiomyopathy
√ pulmonary edema, septal lines, pleural effusion ← chronic heart failure
@ GI tract: esophagus, colon
• achalasia, megacolon
Dx: direct visualization of trypomastigotes in blood smear; serologic test for chronic manifestation

CHALASIA

= continuously relaxed sphincter with free reflux in the absence of a sliding hernia
Etiology: elevated submerged segment
Cause:

(1) Delayed development of esophagogastric region in newborns
(2) Scleroderma, Raynaud disease
(3) S/P forceful dilatation / myotomy for achalasia

√ free / easily induced reflux

CLOSTRIDIUM DIFFICILE COLITIS

= ANTIBIOTIC-ASSOCIATED COLITIS = PSEUDOMEMBRANOUS COLITIS

= nosocomial epidemic / endemic acute infectious colitis ← Clostridium difficile toxins

Etiologic agent: toxin A (enterotoxin) + toxin B (cytotoxin) produced by C. difficile

Cause: unopposed overgrowth of gram-positive Clostridium difficile ← decrease in normal intestinal flora

Predisposed:

(a) complication of broad-spectrum antibiotics: tetracycline, extended-spectrum penicillins (azlocillin, mezlocillin, piperacillin, ticarcillin, carbenicillin, mecillinam), aminopenicillins (ampicillin, amoxicillin), clindamycin, lincomycin, chloramphenicol, cephalosporins, metronidazole, vancomycin
(b) complication of some chemotherapeutic agents: methotrexate, fluorouracil
(c) following abdominal surgery / renal transplantation / irradiation
(d) prolonged hypotension / hypoperfusion of bowel
(e) shock, uremia
(f) proximal to colonic obstruction
(g) debilitating diseases: lymphosarcoma, leukemia, advanced HIV infection
(h) immunosuppressive therapy with actinomycin D

Histo: pseudomembranes (= exudate composed of leukocytes, fibrin, mucin, sloughed necrotic epithelium held in columns by strands of mucus) on a partially denuded colonic edematous mucosa (mucosa generally intact); reactive edema in lamina propria, submucosa, and eventually subserosa

Clinical manifestations of C. difficile infection:

(1) Absence of symptoms (majority)
(2) Antibiotic-associated colitis without pseudomembrane formation
(3) Pseudomembranous colitis
(4) Fulminant colitis

- profuse watery diarrhea, abdominal cramps, tenderness
- fever, fecal blood, leukocytosis
- less common: chronic diarrhea, dehydration, toxic megacolon, hyperpyrexia, leukemoid reaction, hypoalbuminemia with anasarca

Location: pancolitis (most commonly); rectum (95%); confined to right + transverse colon (5–27–40%)

◊ Radiographic abnormalities in 32% + positive stool toxin assay!

Plain film:

√ adynamic ileus pattern = moderate gaseous distension of small bowel + colon:
  √ small bowel ileus (20%)
  √ colonic ileus (32%)
√ nodular haustral thickening (18%):

√ "thumbprinting" = "transverse banding" = wide perpendicular bands ← marked thickening + distortion of haustral folds (most prominent in transverse colon) ← submucosal hemorrhage + edema
√ diffusely shaggy + irregular surface ← confluent pseudomembranes
√ ascites (7%)

BE (CONTRAINDICATED in severe cases):

Fluoroscopic enemas should be avoided in a patient with pseudomembranous colitis ← risk for perforation

√ pseudoulcerations = barium filling clefts between pseudomembranes
√ irregular ragged polypoid contour of colonic wall
√ discrete multiple plaquelike lesions of 2–4 mm in size (DDx: polyposis, nodular form of lymphoma)

N.B.: risk of colonic perforation in toxic megacolon!

CT (85% sensitive, 48% specific):

√ NO colonic abnormality (12–39%)
√ substantial irregular eccentric colonic wall thickening:
√ wall thickness usually > 4 mm with a mean of 14.7 (range, 3–32) mm in 61–88%

The degree of wall thickening in C. difficile colitis is greater than in any other infectious or inflammatory process involving the bowel except for Crohn disease.

√ segmental / diffuse involvement of entire colon
√ mural hypoattenuation ← edema
√ mural hyperattenuation ← acute inflammation
√ thumbprinting thickened ← edematous haustra
√ "**accordion**" sign (51–70%) = enteric contrast material trapped between distorted thickened closely spaced transverse edematous haustra of low attenuation (simulating intramural tracts), TYPICAL in severe cases
√ smooth (44%) / irregular / polypoid (17%)
√ "target" sign = submucosal edema + homogeneous mucosal enhancement ← hyperemia (best seen during arterial enhancement)
√ colonic dilatation frequent ← transmural inflammation
√ usually DISPROPORTIONATELY mild pericolonic stranding (42%) relative to marked wall thickening
√ ascites in severe cases (15–35%)
√ pneumatosis coli ± portal vein gas in severe cases

Dx: (1) Stool assay for Clostridium difficile cytotoxin (detects toxin B): cumbersome to perform
(2) Enzyme immunoassay test (up to 33% false-negative results): detection of toxin A + B
(3) Stool culture (95% sensitive): not available for 2 days
(4) Pseudomembranes of adherent yellow plaques 2–10 mm in diameter on proctosigmoidoscopy

Cx: peritonitis, toxic megacolon (if dilatation > 6 cm), perforation

Prognosis: 1.1–3.5% overall mortality; most patients recover within 2 weeks

Rx: (1) Discontinuation of suspected antibiotic
(2) Administration of vancomycin / metronidazole (response within 3–4 days)
(3) Attention to fluid and electrolyte balance
(4) Life-saving partial colectomy required in < 1%

DDx: acute stage of ulcerative / Crohn colitis, infectious colitis (eg, enterohemorrhagic E. coli), ischemic colitis, radiation colitis, colonic wall hemorrhage, colonic lymphangiectasia, leukemic infiltration, diverticulitis

COLITIS CYSTICA PROFUNDA

= rare benign chronic condition characterized by dilated sub- mucosal mucin-filled cysts lined by normal colonic epithelium

Etiology: probably related to chronic inflammation

Associated with: solitary rectal ulcer syndrome (as localized polypoid variant)

Age: primarily disease of young adults

- brief periods of bright red rectal bleeding
- mucous / bloody discharge, intermittent diarrhea

Location:
(a) localized to rectum (most commonly) / sigmoid
(b) generalized colonic process (less common)

√ nodular polypoid / cauliflower-like lesions < 2 cm in size, containing no gas
√ spiculations mimicking ulcers (barium-filled clefts between nodules)

DDx: pneumatosis (rarely affects rectum)

COLONIC ATRESIA

Frequency: less common than ileal atresia

Plain radiograph:
√ massive dilatation of colon proximal to obstruction
√ mottled pattern of gas + feces proximal to point of atresia
DDx: often indistinguishable from obstruction of distal ileum

BE:
√ functional microcolon
√ obstruction to retrograde flow of barium

US:
√ dilated hyperechoic distal small bowel + proximal colon ← retained meconium

COLORECTAL CARCINOMA

Most common cancer of GI tract; 3rd most commonly diagnosed malignancy in developed countries in men (after lung and prostate cancer) and women (after lung + breast cancer); 2nd leading cause of cancer deaths

Incidence: 136,830 new cases annually with 50,310 deaths in USA (2014); 11% of all newly diagnosed cancers; 13% of all cancer deaths; 3÷100,000 in 30–34-year-olds; 532÷100,000 for > 85-year-olds

Lifetime probability: 4– 6% of any White person

Risk factors:

1. Personal history of colonic adenoma / carcinoma
   › malignancy in 5% of tubular adenomas
   › malignancy in 30–40% of villous adenomas
   Proof of adenoma-carcinoma sequence:
   (a) frequent coexistence of adenoma + carcinoma
   (b) similar distribution within colon
   (c) consistent proportional prevalence in population having varied magnitudes of colon cancer risk
   (d) increased frequency of carcinoma in patients with adenomas
   (e) reduction of cancer incidence following endoscopic removal of polyps
   (f) all patients with familial adenomatous polyposis syndrome develop colon carcinoma if colon not removed
   (g) similarity of DNA + chromosomal constitution
   ◊ 93% of colorectal carcinomas arise in adenomatous polyps
   ◊ A patient with one adenoma has a 9% chance of having a colorectal carcinoma in the next 15 years!
   ◊ It takes about 7 years for a 1-cm adenoma to become an invasive cancer!
   ◊ 5% of 5-mm adenomas develop into invasive cancers (5 mm = critical mass of intraepithelial neoplasia)!
2. Family history of benign / malignant colorectal tumors in 1st-degree relative (3–5 x risk)
3. Personal history of ovarian / endometrial / breast cancer
4. Dysplasia of colon within flat mucosa
5. Inflammatory bowel disease:
   (a) Ulcerative colitis (3–5% incidence; cumulative incidence of 26% after 25 years of colitic symptoms)
   (b) Crohn disease affecting the colon + rectum (particularly in bypassed loops / in vicinity of chronic fistula)
   Time delay: > 8–10 years of colitis
   Underlying lesion: dysplasia within flat mucosa
6. Prominent lymphoid follicular pattern
7. Pelvic irradiation
8. Ureterosigmoidostomy

Environmental risk factors:
(a) low fiber diet: prevents rapid transit time → increasing contact time between potential toxins and colonic mucosa
(b) increased ingestion of fat + animal protein
(c) obesity
(d) asbestos worker

Genetic risk factors (6% of colorectal carcinomas):
(a) familial adenomatous polyposis syndrome:
familial polyposis, Gardner syndrome, Turcot syndrome
Age: ~ 40 years
(b) certain hamartomatous polyposis syndromes:
Peutz-Jeghers syndrome, juvenile polyposis, Cowden disease
(c) hereditary nonpolyposis colon cancer syndrome

= Lynch syndrome

Screening recommendations (American Cancer Society):

as / more effective than mammographic screening

(a) for persons > 50 years of age: annual fecal occult-blood test + sigmoidoscopy / BE every 3–5 years

(b) for 1st-degree relatives of patients with colon cancer screening should start at age 40

Median age: 71 years for colon cancer; 69 years for rectal cancer; M÷F = 3÷2

Histo:

(1) Adenocarcinoma with varied degrees of differentiation (> 90%)

(2) Mucinous carcinoma (uncommon)

(3) Squamous cell carcinoma + adenoacanthoma (rare)

Metastases (lymphatic / hematogenous venous):

1. Liver (75%; 15–20% at time of surgery) ← portal venous drainage route
2. Mesentery + mesenteric nodes (10–15%)
3. Adrenal (10–14%)
4. Lung (5–50%)
5. Ovary (3–8%) = Krukenberg tumor
6. Psoas muscle tumor deposit
7. Peritoneal metastases:
   (a) malignant ascites: usually associated with poorly differentiated colonic carcinoma
   (b) pseudomyxoma peritonei (< 5%): low-grade colonic adenocarcinoma
8. Bone (5%)
9. Brain (5%)

◊ Because of the absence of lymphatics in the lamina propria colon cancer will not metastasize until it penetrates the muscularis mucosa!

- rectal bleeding, iron deficiency anemia
- change in bowel habits / caliber of stools
- obstruction (poor prognostic indicator), hydronephrosis (13%)
- positive fecal occult blood testing (2–6% positive-result rate; 5–10% positive predictive value; fails to detect 30–50% of colorectal carcinomas + up to 75% of adenomas): Hemoccult® (hematein), HemoQuant® (porphyrins), HemeSelect™ (hemoglobin)
- progressive elevation of carcinoembryonic antigen (CEA) > 10 µg/L indicative of recurrent / metastatic disease
- watery diarrhea + potassium depletion / excessive secretion of mucus + hypoalbuminemia (in large mucin-secreting villous tumor)

Location: "aging gut" = number of right-sided lesions increasing with age ("changing distribution")

(a) left colon (52–61%):
rectum (15–33–41%), sigmoid (20–37%), descending colon (10–11%)
√ commonly annular strictures with obstruction

(b) right colon:
transverse colon (12%), ascending colon (8–16%), cecum (8–10%)
√ commonly polypoid lesions with chronic bleeding + intussusception

(c) rectum: ⅓ of all colorectal cancers

Colonoscopy: cecum not visualized in 10–36%; fails to detect 12% of colonic polyps (10% in

areas never reached by colonoscope)

Cx: perforation in 0.2% (0.02% for BE); death in 1÷5,000 (1÷50,000 for BE)

BE:

Detection of Colonic Polyps on Barium Enemas		
Sensitivity	*Polyp > 1 cm*	*Polyp < 1 cm*
Single contrast barium enema	77–94%	82–97%
Double contrast barium enema	18–72%%	61–83%

√ fungating polypoid carcinoma:
- chronic bleeding, intussusception

√ annular ulcerating carcinoma = "apple core lesion"
= annular constriction ← tumor grows along lymphatic channels that parallel circular muscle fibers of inner layer of the muscularis propria; longitudinal growth is limited with abrupt transition to normal mucosa
- colonic obstruction

√ "saddle lesion" = growth characteristics between polypoid mass + annular constricting lesion

√ scirrhous carcinoma (signet-ring type)
= long-segment stricture without significant mucosal abnormality similar to linitis plastica ← diffuse circumferential + longitudinal tumor infiltration within loose submucosal tissue between muscularis mucosa and muscularis propria
- often seen in ulcerative colitis

√ curvilinear / mottled calcifications are CHARACTERISTIC of mucinous adenocarcinoma (rare)

CT (48–90% staging accuracy, 25–73% for lymph node mets):

√ marked asymmetric colonic wall thickening involving a short segment

√ low-density mass + low-density lymph nodes in mucinous adenocarcinoma (if > 50% of tumor composed of extracellular mucin)

√ abrupt change from normal to abnormal segment of colon

√ psammomatous calcifications in mucinous adenocarcinoma

√ signs of Lnn involvement: single lymph node > 1 cm in diameter / cluster of ≥ 3 nodes < 1 cm / node of any size within mesentery

◊ *Screening CT colonography:* 55–94% sensitive for polyps > 10 mm

CT Staging of Colorectal Cancer *(poor accuracy compared with Astler-Coller classification)*	
Stage 1	intramural polypoid mass
Stage 2	thickening of bowel wall
Stage 3	slight invasion of surrounding tissues
Stage 4	massive invasion of surrounding tissue + adjacent organs / distant metastases

MR: (staging accuracy of 73%, 40% sensitivity for lymph node metastases)

Prognosis:

5-year survival rate of 40–50% (unchanged over past 40 years); 83–90% (70%) [33%]

{5%} with Duke A (B) [C] {D}

Recurrence in ⅓ of patients:

(a) local recurrence at line of anastomosis (60%): within 1 {2} year after resection in 50% {70–80%}

(b) distant metastases (26%)

(c) local recurrence + metastases (14%)

Staging of Colorectal Cancer
(UICC-AJCC Colorectal Cancer Staging System)

Stage	*Grouping*			*5-year Survival*
0	Tis	N0	M0	>95%
I	T1	N0	M0	75–100%
	T2	N0	M0	
II	T3	N0	M0	50–75%
	T4	N0	M0	
III	any T	N1	M0	30–50%
	any T	N2,3	M0	
IV	any T	any N	M1	<10%

Legend:

Tis	carcinoma in situ
T1	invasion of submucosa
T2	invasion of muscularis propria
T3	invasion of subserosa / pericolic tissue
T4	invasion of visceral peritoneum / other organs
N1	1–3 pericolic Lnn
N2	>4 pericolic Lnn
N3	any Lnn along course of a vascular trunk

<u>Risk after detection of colon cancer:</u>

5% for synchronous colon cancer

14% for synchronous cancer with "sentinel polyp"

35% for additional adenomatous polyp

3% for metachronous colon cancer

4% for extracolonic malignancy

Cx: (1) Obstruction (frequently in descending + sigmoid colon) ← relatively larger caliber of right colon allows growth to a larger size before becoming symptomatic by obstruction

(2) Perforation (in up to 10%)

(a) at site of mass: subacute process ← slow gradual infiltration of bowel wall

(b) proximal to mass: necrosis of stercoral ulcer / increased pressure proximal to obstruction

(3) Intussusception (50% of all adult intussusceptions): intestinal lymphoma, GI tumor, metastatic disease

(4) Abscess formation: intraperitoneal (in majority); localized paracolic; extension to flank, thigh, trunk

(5) Fistula formation

(6) Pneumatosis cystoides intestinalis

(7) Pseudomyxoma peritonei ← low-grade adenocarcinoma of colon
(8) Ischemic colitis (in 7%)
Cause: (1) severe colonic distention ← mechanical obstruction (2) stagnated bowel contents → bacterial overgrowth (3) mechanical vascular occlusion (4) invasion of mesenteric root vessels
√ concentric ~ 1 cm thickening of bowel wall
DDx: tumoral segment (irregular thickening of bowel wall by an average of 2 cm)

Rx: (1) Local surgical excision / polypectomy for stage I disease
(2) Right / left hemicolectomy with eventual anastomosis of proximal + distal excision sites
(3) Low anterior resection: > 2 cm of rectum must remain to anastomose the colon
(4) Abdominoperineal resection with colostomy for low rectal carcinoma
(5) Adjuvant chemotherapy for stage II disease (fluorouracil / levamisole)

DDx: (1) Prolapsing ileocecal valve (change on palpation)
(2) Spasm (intact mucosa, released by propantheline bromide)
(3) Diverticulitis

Cecal Adenocarcinoma

• often grow asymptomatic for a long time
√ often large polypoid bulky tumor
√ marked wall thickening + mild pericolic infiltration
√ involvement of distal ileum (10%)

Cx: (1) Obstruction (rare): often large tumor within capacious cecum
(2) Intussusception ← tumor as lead point

Signet Ring Carcinoma *(2.6%)*

= variant of mucin-secreting adenocarcinoma
Age: younger patients
Histo: > 50% of cells have a cell nucleus that is displaced to periphery by large amount of intracytoplasmic mucin
Spread: peritoneal surfaces + lymph nodes (more readily); hepatic parenchymal metastases (less frequent)
√ often elongated infiltrating mass > 5 cm in length mimicking underlying colonic inflammatory process
√ concentric rigid wall thickening of scirrhous / linitis plastica appearance
Dx: mucosal surface may appear intact endoscopically → requires deep-tissue biopsies
Prognosis: poor ← aggressive tumor + frequent local recurrence
DDx: colonic Crohn disease / ischemic colitis

Lynch Syndrome

= HEREDITARY NONPOLYPOSIS COLORECTAL CANCER SYNDROME (HNPCC)
= autosomal dominant disorder with high incidence of colorectal cancers + increased incidence of synchronous and metachronous colorectal cancers
Amsterdam criteria:

(a) ≥ 3 family members of whom 2 are 1st degree relatives of the 3rd family member
(b) family members in ≥ 2 generations
(c) one family member diagnosed < 50 years of age

Lynch I = no associated extracolonic cancer

Lynch II = associated with extracolonic malignancy:
transitional cell carcinoma of ureter + renal pelvis; adenocarcinoma of endometrium, stomach, small bowel, pancreas, biliary tract, brain; hematologic malignancy; carcinoma of skin + larynx

Etiology: autosomal dominant abnormality of chromosome 2 with defect in DNA replication-repair process
(a) accelerated adenoma-carcinoma sequence
(b) dysplasia in flat mucosa of colon

Prevalence: 5–10% of patients with colon cancer; 5 x more common than familial adenomatous polyposis syndrome

Mean age: 45 years

Location: 70% proximal to splenic flexure

Prognosis: better stage for stage of other cancers (5-year survival rate of 65% versus 44% in sporadic cases)

Surveillance: colonoscopy every 1–2 years from ages 22–35

Rectal Cancer

Incidence: 40,340 rectal cancers annually in USA (2005); 0.01% national screening average

- gastrointestinal bleeding, change in bowel habit

Pathologic Staging of Rectal Cancer
(modified Dukes = Astler-Coller classification) and TNM

Astler-Coller/TNM		*Description*	*5-year Survival*
A	T1 N0 M0	limited to submucosa	80%
B		involvement of muscularis propria	
B_1	T2 N0 M0	limited to muscularis propria	70%
B_2	T3 N0 M0	transmural extension	60–65%
	T3a	< 5 mm beyond m. propria	
	T3b	5–10 mm beyond m. propria	
	T3c	> 10 mm beyond m. propria	
C		Lymph node metastases	
C_1	T2 N1 M0	nodes (+), into muscularis	35–45%
C_2	T3 N1 M0	nodes (+), transmural	25%
	T4	invasion of adjacent organs	
	T4a	penetration of visceral peritoneum	
D	M1	distant metastasis	<25%

Two hematogenous metastatic patterns of rectal cancer:
(1) liver metastasis ← via IMV + portal venous system / via endolymphatic spread along course of IMV
(2) lung metastasis ← via internal iliac veins + IVC

Hematogenous metastasis:

dual venous drainage into portal + systemic veins

√ may have lung metastases without liver metastases

Risk of recurrence:

5% for T1

10% for T2 33% for T1, N1 + T2N1

25% for T3 66% for T3N1

50% for T4

Staging accuracy:

› Digital rectal examination: 68–75–83%; limited to lesions within 10 cm of anal verge

› CT: 48–72–92%, better for more extensive regional spread; 25–73% for lymph node involvement

› MR: 74–84–93% with tendency for overstaging

› Transrectal ultrasound: 64–77–94% with tendency for overstaging; limited to nonstenotic lesions < 14 cm from anal verge; 50–83% sensitivity for involved lymph nodes

› PET: 97% sensitive for recurrence

Transrectal US (81% accuracy):

Normal layers = gut signature: → see GI anatomy

√ hypoechoic mass disrupting rectal wall:

√ NO interruption of hyperechoic submucosa = tumor confined to mucosa + submucosa

√ NO interruption of hyperechoic serosa = tumor confined to rectal wall

√ break in outermost hyperechoic layer = tumor penetrates into perirectal fat

√ irregular serrated outer border of muscularis propria (pseudopodia through serosa)

√ hypoechoic perirectal lymph nodes ← tumor involvement

COLONIC VOLVULUS

= most common form of volvulus

Frequency: 2% of bowel obstruction; 11% of intestinal volvulus

Colonic volvulus often has a characteristic appearance at conventional radiography, which may be sufficient for a diagnosis in a large percentage of patients!

Cecal Volvulus (25–40%)

= VOLVULUS OF CECUM

◊ Surgical EMERGENCY ← threat of bowel ischemia + bowel perforation!

= twisting of cecum along its long axis ← closed-loop obstruction ← excess mobility

Frequency: 25–40% of all cases of colonic volvulus

Cause: acquired / congenitally poor fixation of right colon to posterior parietal peritoneum (malrotation + long mesentery) → mobile cecum (10–25% of population)

Trigger: sudden distension by trauma, pregnancy, distal colonic obstruction, pressure, colonic atony, constipation, mesenteric / pelvic mass, recent colonoscopy, previous laparotomy with adhesions, congenital cecal duplication cyst

Pathophysiology of vascular compromise:

(1) Acute mesenteric torsion + strangulation → arterial and venous obstruction

(2) Gradual distension + increase in intraluminal pressure → interferes with perfusion → perforation in 65%

Types: I = axial torsion (40%) = cecum twists in axial plane rotating along its long axis
√ cecum occupies right lower quadrant

II = loop twist (40%) = cecum twists and inverts
√ cecum occupies left upper quadrant

III = **cecal bascule** (20%) [*bascule*, French = seesaw]
= anteromedial + upward folding of cecum over ascending colon WITHOUT twist
Cause: loose mesentery, ? related to adhesion
√ dilated cecum anterior to ascending colon

Age peak: 20–40 years; M > F

- gradual onset of acute cramping abdominal pain
- distention, constipation, vomiting

Plain film (DIAGNOSTIC in < 50%):

√ air- or fluid-filled dilated small bowel

√ collapsed left colon

√ cecal gaseous distension:

√ "kidney-shaped" distended cecum inverts + rotates into left upper quadrant (type II)

√ dilated cecum rotates upward + anterior to ascending colon without twisting (type III)

DDx: gastric distension, SBO, sigmoid volvulus

BE (for confirmation of plain film findings):

√ "bird beak" sign = tapering of afferent + efferent bowel loops pointing to point of torsion

√ "coffee bean" sign = dilated air- and fluid-filled cecum with haustral creases

√ decompressed distal colon

√ inability to reflux much contrast material into dilated proximal colon and terminal ileum

CT:

√ cecum ectopically positioned in upper mid + left abdomen

√ "whirlpool / whirl" sign = twisted loop of bowel with its mesentery + ileocecal vessels (NOT in type III)

√ "coffee bean / bird beak" sign

Cx: (1) Cecal distension > 10–12 cm → means risk of bowel perforation / infarction

(2) **Abdominal compartment syndrome** = increase in abdominal pressure diminishes respiratory function + cardiac output

Sigmoid Volvulus (60–75%)

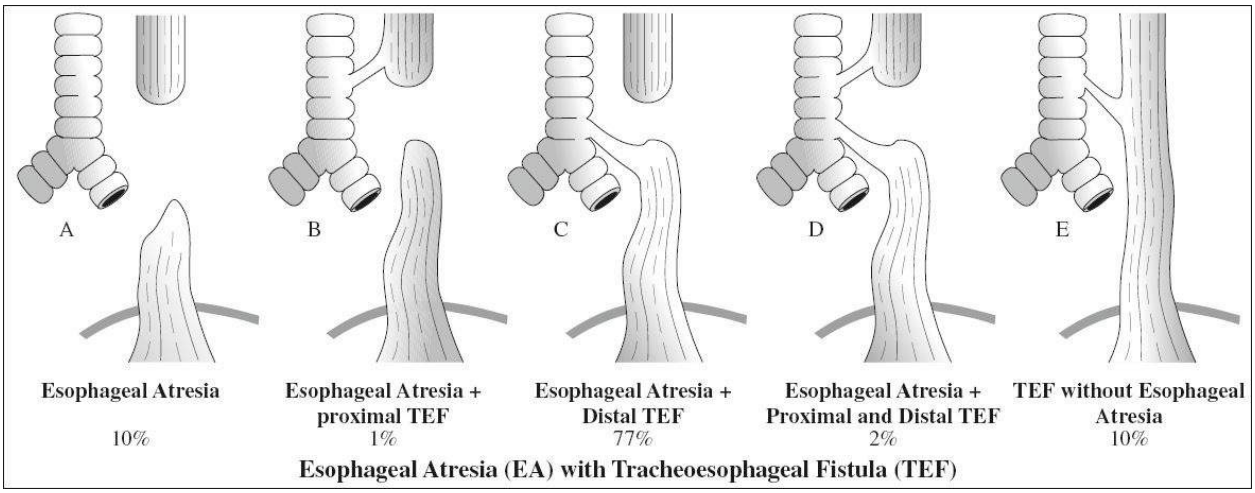
= VOLVULUS OF SIGMOID COLON

Cause: sigmoid twist on mesenteric axis

At risk: chronic constipation, redundancy of sigmoid colon ← high-fiber diet, pregnancy, Chagas disease, hospitalization / institutionalization

Age: usually in elderly > 70 years / psychiatrically disturbed

Degree of torsion: 360° (50%), 180° (35%), 540° (10%)



Esophageal Atresia (EA) with Tracheoesophageal Fistula (TEF)

Plain film:

√ "northern exposure" sign = greatly distended paralyzed loop with fluid-fluid levels arising out of pelvis and extending toward diaphragm beyond level of transverse colon mainly on left side (on film in UPRIGHT position)

√ "coffee-bean sign" = distinct midline crease corresponding to mesenteric root of large gas-distended sigmoid colon (on film in SUPINE position)

√ "white stripe" sign = obliquely oriented center line of the U-shaped closed-loop appearance

√ "three-line" sign = obliquely oriented outer wall + center lines of the U-shaped closed-loop appearance

BE (thin water-soluble contrast material):

√ "bird-of-prey" sign = tapered beaklike distal aspect of twist on barium enema

√ enema may help achieve reduction of volvulus

CT:

√ "whirl" sign = tightly torsed mesentery formed by twisted afferent + efferent loop

Volvulus of Transverse Colon

Frequency: < 5–10% of all cases of colonic volvulus
Cause: abnormal fixation of a long transverse colon
Prognosis: highest mortality of all cases of colonic volvulus ← rare + unsuspected occurrence
√ characteristic beaklike tapering at level of twist
√ "whirl" sign adjacent to transverse colon

CONGENITAL ESOPHAGEAL ATRESIA & TRACHEOESOPHAGEAL FISTULA

= complex of congenital anomalies characterized by failed / incomplete formation of the tubular esophagus or an abnormal communication between esophagus + trachea
Cause: developmental disorder in formation and separation of primitive foregut into trachea + esophagus / vascular compromise
Embryology:
primitive foregut tube develops lateral wall folds that may incompletely connect at any point leaving a fistulous communication; occurs at 3rd–5th week of intrauterine life
Prevalence: 1÷2,000–4,000 livebirths; most common sporadic congenital anomaly diagnosed in childhood
Risk of recurrence in sibling: 1%
Associated anomalies (17–56–70%):

1. Gastrointestinal (20–25%): imperforate anus, pyloric stenosis, duodenal atresia, annular pancreas
2. Cardiac (15–39%): patent ductus arteriosus, ASD, VSD, right-sided aortic arch (5%)
3. Musculoskeletal (24%): radial ray hypoplasia, vertebral anomalies
4. Genitourinary (12%): unilateral renal agenesis
5. Chromosomal (3–19%): trisomy 18, 21, 13
   ◊ Trisomy 18 is present in 75–100% of fetuses + in 3–4% of neonates with esophageal atresia!

mnemonic: ARTICLES
Anal atresia
Renal anomalies
Tracheoesophageal fistula (TEF)
Intestinal atresia / malrotation
Cardiac anomaly: PDA, VSD
Limb anomalies: radial ray hypoplasia, polydactyly
Esophageal atresia
Spinal anomalies

mnemonic: VACTERL
Vertebral anomalies
Anal atresia
Cardiac malformations

Tracheo-
Esophageal fistula
Renal anomalies
Limb anomalies
◊ At least 3 anomalies must be present to suggest VACTERL!

Prevalence: 1÷10,000 to 1÷40,000 live births

- drooling from excessive accumulation of pharyngeal secretions (esophageal atresia = EA)
- obligatory regurgitation of ingested fluids (EA)
- aspiration with coughing + choking during feeding (TEF)
- recurrent pneumonia + progressive respiratory distress of variable severity in neonate (TEF)

Location: between upper ⅓ + lower ⅓ of esophagus just above carina

@ Mediastinum
√ "coiled tube" = inability to pass feeding tube into stomach (esophageal atresia)
√ retrotracheal air-distended pouch of proximal esophagus causing compression / displacement of trachea
√ non- / hypoperistaltic esophageal segment (6–15 cm) in midesophagus
√ food impaction

@ Abdomen
√ gasless abdomen ← esophageal atresia ± proximal TEF = types A + B
√ abdomen distended by bowel gas in 90% ← distal TEF / H-type fistula = types C + D

@ Chest
√ bronchopneumonia with patchy airspace opacity, esp. in dependent upper lobes (in 50%)

OB-US (anomalies not identified before 24 weeks GA):
√ polyhydramnios in 33–60%:
◊ TEF with esophageal atresia = cause of polyhydramnios in only 3%!
√ absence of fluid-distended stomach (in 10–41%; in remaining cases TEF / gastric secretions allow some gastric distension)
√ reduced intraluminal fluid in fetal gut
√ small abdomen (birth weight < 10th percentile in 40%)
√ distended proximal pouch of atretic esophagus
√ ± single umbilical artery

Cx after repair:
(1) Anastomotic leak
(2) Recurrent TEF
(3) Aspiration pneumonia 2° to
(a) esophageal stricture
(b) disordered esophageal motility distal to TEF
(c) gastroesophageal reflux

DDx: pharyngeal pseudodiverticulum (traumatic perforation of posterior pharynx from finger insertion into oropharynx during delivery / tube insertion)

Esophageal Atresia without Fistula = EA Type A

Frequency: 8–10%

Associated anomalies: in 17% (mostly Down syndrome + other atresias of GI tract)

Esophageal Atresia (EA) with Fistula

Associated anomalies: in 30% (mostly cardiovascular)

Type B = esophageal atresia + proximal TEF

Frequency: 0.9–1%

Type C = esophageal atresia + distal TEF

Frequency: 53–86%

Type D = esophageal atresia + proximal and distal TEF

Frequency: 1–2.1%

Tracheoesophageal Fistula without Atresia

= H-SHAPED FISTULA = **Type E**

Frequency: 6–10%

Associated anomalies: in 23% (mostly cardiovascular)

- feeding difficulties with choking
- diagnosis may not be made for several years

√ fistula courses forward and upward from esophagus

mnemonic: No TEF, P, D, P+D, H – 10,1,80,1,10

type **A** = esophageal atresia – **no** TEF = 10%
type B = esophageal atresia – **prox** TEF = 1%
type C = esophageal atresia – **dist** TEF = 80%
type D = esophageal atresia – **prox + dist** = 1%
type E = **H**-type fistula – no atresia = 10%

CONGENITAL ESOPHAGEAL STENOSIS

= rare developmental anomaly

Prevalence: 1÷25,000 to 1÷50,000 live births

Forms:

(1) Tracheobronchial remnant
= incomplete embryologic separation of primitive foregut from respiratory tract
May be associated with: esophageal atresia and tracheoesophageal fistula
Location: lower ⅓ of esophagus
√ ringlike constriction

(2) Fibromuscular stenosis
Location: middle ⅓
√ segmental stricture with a smooth tapered area of concentric narrowing of 1 cm in length
√ circumferential wall thickening on CT

(3) Membranous diaphragm
Location: middle ⅓ of esophagus
√ weblike stenosis

- dysphagia, vomiting, respiratory symptoms

DDx: stricture ← trauma / reflux esophagitis / ingestion of toxic substance

CONGENITAL INTESTINAL ATRESIA

Prevalence: 1÷300 livebirths

Cause: usually sporadic vascular accidents (primary / secondary to volvulus or gastroschisis)
Location: jejunum + ileum (70%), duodenum (25%), colon (5%); may involve multiple sites
√ "triple bubble" sign = intraluminal gas in stomach + duodenal bulb + proximal jejunum as PATHOGNOMONIC sign for jejunal atresia
√ "bulbous bowel segment" sign with curvilinear termination = dilated loop of bowel just proximal to site of atresia ← prolonged impaction of intestinal contents
√ gasless lower abdomen: gut usually air-filled by 4 h after birth
√ meconium peritonitis (6%)
√ polyhydramnios (in 50% ← duodenal / proximal jejunal atresia; rarely in ileal / colonic atresia)
Prognosis: 88% survival for isolated atresia

CRICOPHARYNGEAL ACHALASIA

= hypertrophy of cricopharyngeus muscle (= upper esophageal sphincter) with failure of complete relaxation
Etiology:
1. Normal variant without symptoms: seen in 5–10% of adults
2. Compensatory mechanism to gastroesophageal reflux
3. Neuromuscular dysfunction of deglutition
   (a) primary neural disorders:
   brainstem disorder (bulbar poliomyelitis, syringomyelia, multiple sclerosis, amyotrophic lateral sclerosis); central / peripheral nerve palsy; cerebrovascular occlusive disease; Huntington chorea
   (b) primary muscle disorder:
   myotonic dystrophy; polymyositis; dermatomyositis; sarcoidosis; myopathies ← steroids / thyroid dysfunction; oculopharyngeal myopathy
   (c) myoneural junction disorder:
   myasthenia gravis; diphtheria; tetanus

• mostly asymptomatic, dysphagia
◊ Cineradiography / videotape recording required for demonstration!
√ distension of proximal esophagus + pharynx
√ smoothly outlined shelf- / liplike projection posteriorly at level of cricoid (= pharyngoesophageal junction = level of C5-6)
√ barium may overflow into larynx + trachea
Cx: Zenker diverticulum
Rx: cricopharyngeal myotomy

COWDEN DISEASE

= MULTIPLE HAMARTOMA-NEOPLASIA SYNDROME
= autosomal dominant disease with high penetrance characterized by multiple hamartomas + neoplasms of endodermal, ectodermal, mesodermal origin
Prevalence: 160 cases reported
Cause: susceptibility gene on long arm of chromosome 10 (10q23.2)
Age: 2nd decade

@ Mucocutaneous lesions
  • facial papules, oral papillomas (lips, gingiva, tongue)
  • palmoplantar keratosis, acral keratosis
@ CNS neoplasia
  • macrocephaly
  √ meningioma, glioma
  Associated with: dysplastic cerebellar gangliocytoma
@ Breast lesions (in 50%):
  √ fibrocystic disease + fibroadenomas
  √ breast cancer (20–30%): often bilateral + ductal
@ GI tract
  √ multiple hamartomatous polyps (in 30–60%, commonly in rectosigmoid)
@ Thyroid abnormalities (in 60–70%):
  √ adenomas + goiter
  √ follicular thyroid adenocarcinoma (3–4%)
@ Genitourinary lesions
  √ multiple randomly distributed 1–6-mm hyperechoic avascular masses (= lipomatosis)
@ Skeletal abnormalities

CROHN DISEASE

[Burrill Crohn (1884–1983), gastroenterologist in New York, USA]
= REGIONAL ENTERITIS
= chronic relapsing inflammatory disorder with prolonged unpredictable course characterized by discontinuous + asymmetric involvement of entire GI tract

Cause: unknown; ? diet, smoking, stress, infection, genetics, autoimmune abnormality

Genetic susceptibility:
(1) homozygosity for Nod-2 gene (= intracellular protein in lymphocytes) responsible for binding bacterial endotoxins + initiating a cascade that produces TNF-α (= tumor necrosis factor-alpha)
(2) increased mucosal permeability for enteric bacteria

Incidence: 3.1–14.6÷100,000 annually; high in Caucasians + Jews; 25% during pediatric period
  ◊ 10,000–40,000 new cases annually in USA

Path: transmural (= full-thickness) bowel inflammation with obstructive lymphedema + submucosal lymphoid hyperplasia; aphthous ulcer progresses to longitudinal ulceration typically along mesenteric border; extension into mesentery + adjacent lymph nodes → formation of perienteric sinuses + fistulas + abscesses

In Crohn disease the 1st macroscopic feature to appear is a mucosal aphthous ulceration = a pinpoint ulcer / erosion of mucosa overlying a submucosal lymphoid follicle.

Histo: (a) acute: neutrophilic infiltration, crypt abscesses
(b) chronic: villous atrophy
Noncaseating granulomas with Langhans giant cells and epithelioid cells, edema, fibrosis (in 30%)

Age peaks: 2nd decade + 5th–7th decade (bimodal distribution); M÷F = 1÷1
- recurrent episodes of diarrhea, colicky / steady abdominal pain
- low-grade fever, weight loss, anorexia, occult blood + anemia
- perianal abscess / fistula (40%), malabsorption (30%)

Associated with: erythema nodosum, pyoderma gangrenosum

Rx: (a) lifestyle changes: cessation of smoking

(b) medical: aminosalicylates, corticosteroids; probiotics + antibiotics (modulation of enteric flora); purine synthesis inhibitors like azathioprine + 6-mercapto-purine (downregulation of inflammatory response); infliximab (chimeric antibody binding to TNF-α)

(c) surgical: resection at some point (60–70%)

Outcome: chronic active disease (13%), chronic intermittent disease (73%), in remission for many years (10%)

Intestinal Manifestations of Crohn Disease

Phases: may coexist

(a) Earliest changes
- √ nodular enlargement of lymphoid follicles
- √ blunting / flattening / distortion / straightening / thickening of valvulae conniventes ← obstructive lymphedema, usually first seen in terminal ileum
- √ aphthous ulcers = nodules with shallow central barium collection up to 5 mm in diameter

Location: duodenal bulb, 2nd portion of duodenum, terminal ileum

(b) Advanced nonstenotic phase
- √ <u>skip lesions</u> (90%) = PATHOGNOMONIC discontinuous involvement with intervening normal areas
- √ straightening + rigidity of small bowel loops with luminal narrowing ← spasm + submucosal edema:
  - √ separation + displacement of small bowel loops ← lymphedematous wall thickening + increase in mesenteric fat + enlarged mesenteric lymph nodes + abscess formation after perforation
- √ inflammatory adhesions
- √ thick + blunted small bowel folds ← inflammatory infiltration of lamina propria + submucosa:
  - √ "string" sign = reversible incomplete filling ← edema and spasm ← irritability from severe ulceration
- √ linear mesenteric border ulcers parallel to shortened concave / straight mesenteric border (nearly PATHOGNOMONIC):
  - √ antimesenteric border sacculations = bulging area of normal wall opposite affected scarred wall on mesenteric side = pseudosacculations
  - √ transmural ulcer formation → sinus, fistula, perienteric abscess
- √ **cobblestone appearance** = ulceronodular pattern of serpiginous longitudinal + transverse ulcers separated by areas of edematous residual mucosal islands:
  - √ diffuse mucosal granularity ← 0.5–1-mm round lucencies (= blunted + fused villi

seen EN FACE)
√ pseudopolyps = islands of hyperplastic mucosa between denuded mucosa

(c) Stenotic / obstructive phase
√ "string" sign = irreversible severe narrowing of bowel loop ← marked fibrous thickening of intestinal wall = stricture (in 21%, most frequently in terminal ileum) in combination with severe edema + spasm
√ normal proximal loops may be dilated with stasis ulcers + fecoliths

(d) Reparative phase
√ mucosal denudation (← mucosal atrophy) with focal areas of sparing
√ extensive sessile / pedunculated / filiform postinflammatory regenerative polyposis

US:

Technologic advances in US allow improved visualization of small bowel and mesentery, especially in the pediatric population.

@ bowel wall
√ "pseudokidney / target" sign = circumferential continuous / intermittent diffusely thickened hypoechoic bowel wall (22–65–89%) of 5–20 mm (DDx: ulcerative colitis)
√ loss of normal layering ← transmural edema, inflammation, fibrosis
√ echolucent interruptions of the normally echogenic submucosa
√ decreased peristalsis / aperistalsis ← ganglioneuritis / alteration in interstitial cells of Cajal
√ luminal narrowing:
√ noncompressible rigid and fixed bowel segment
√ upstream distention with fluid-filled loops (12%)
› inflammatory stricture with little fibrosis:
√ loss of normal bowel wall stratification
√ hypoechoic bowel wall ← mural hyperemia
√ increased vascularity of gut wall and adjacent fat on color Doppler
› fibrotic stricture:
√ maintained gut signature
√ prominently echogenic submucosa ← collagen deposition
√ NO increase in wall vascularity

@ perienteric findings on US
√ small amount of intraperitoneal free fluid
√ hypertrophy of mesenteric adipose tissue → separation of bowel loops
√ echogenic ectopic "creeping fat / fat wrapping" (= inflammatory and fibrous tissue) around active region of inflammation extending to antimesenteric surface
√ "comb" sign = increased mesenteric blood flow ← engorgement of vasa recta
√ increased number ± increased size of visualized lymph nodes
√ inflammatory mass = phlegmon (14%) without a discernible wall / walled-off abscess (4%)
√ hypoechoic fistulous tract from serosal surface of bowel that may contain echogenic gas / debris

CT:

@ bowel wall:
√ mucosal hyperenhancement = segmental hyperattenuation of well-distended small bowel loops during late arterial / enteric phase (best seen with bowel lumen distended by negative contrast):
√ "**target" sign** of active inflammation
√ mural stratification:
√ "double halo" configuration (50%) = trilaminar mural stratification = enhancing mucosa + serosa sandwiching submucosa of decreased attenuation:
√ water-density edema = active inflammation
DDx: radiation enteritis, ischemia, mesenteric venous thrombosis, acute pancreatitis
√ fat deposition = abnormally low attenuation of submucosa in long-standing disease
√ bowel wall thickening:
√ mean thickness of 11 (range, 10–20) mm in 82%
DDx: mean of 8 mm for ulcerative colitis
√ asymmetric thickening affecting predominantly mesenteric border
√ bowel wall thickening of homogeneous density
DDx: ulcerative colitis of heterogeneous density
√ skip areas of bowel wall thickening
√ luminal narrowing + proximal dilatation (CT enterography / enteroclysis are highly sensitive):
√ reversible enhancing inflammatory stricture
√ irreversible stricture with lack of enhancement + loss of mural stratification
@ par- / peri- / extraenteric findings on CT
√ "**comb" sign** = hyperemic engorged tortuous vasa recta leading to actively inflamed bowel segment
√ mesenteric fat stranding (= transmural extension of inflammation across serosa with engorgement of hyperemic vasa recta)

CT Findings of Acute and Chronic Crohn Disease

Active Crohn Disease	*Inactive Crohn Disease*
↑ C-reactive protein level	√ submucosal fat deposition
√ mural hyperenhancement	√ pseudosacculation
√ mural stratification ← intramural edema	√ perienteric fibrofatty proliferation
√ mesenteric fat stranding	√ fibrotic strictures
√ comb sign	

√ **"creeping fat / fat wrapping" sign** = almost PATHOGNOMONIC massive fibrofatty proliferation of mesentery along mesenteric border (40%) ← production of tumor necrosis factor a sustaining the inflammatory process:
√ fat attenuation elevated by 20–60 HU
√ separation of small bowel loops (mass effect)
√ remains present in clinically quiescent disease

√ **pseudosacculation** of antimesenteric border ← asymmetric fibrosis of the mesenteric border ← inflammation of mesenteric border of involved segment
√ mild mesenteric lymphadenopathy (18%) with nodes 3–8 mm small
◊ Consider lymphoma / carcinoma with lymph nodes > 10 mm!
√ fistulization / sinus tract (15–40%)
√ mesenteric phlegmon / abscess formation in 15–20% (*DDx:* postoperative blind loop)

MR:
√ aphthous ulcers + intestinal fold thickening
√ bowel wall thickening > 3 mm correlating with Crohn disease activity index
√ fissuring undermining transmural ulcers
√ PATHOGNOMONIC linear ulcers paralleling mesenteric border
√ cobblestoning
√ layered pattern of intense enhancement ← inner + outer enhancing rings (= hyperemic mucosa + serosa) with low-signal-intensity ring (= submucosal edema) in between correlating well with Crohn disease activity index
DDx: "halo" sign of chronic inflammatory bowel disease (low-signal-intensity ring of fat hypertrophy + fibrosis in submucosa)
√ "creeping fat / fat wrapping" sign of fat proliferation
√ "comb" sign
√ mural abscess with rimlike enhancement
√ serosal hypervascularity = nestlike lesions of tiny serpentine hyperintense enhancing vessels adjacent to serosal surface
√ hypointense chronic fibrotic stricture on T1WI + T2WI
√ pseudosacculation on antimesenteric side

Prognosis: recurrence rate of up to 39% after resection (commonly at the site of the new terminal ileum, most frequently during first 2 years after resection); mortality rate of 7% at 5 years, 12% at 10 years after 1st resection

Cx:
(1) Fistula (ileoileal > ileocecal > ileosigmoid)
(2) Intramural sinus tracts
(3) Abscess in up to 20% (DDx: acute appendicitis)
(4) Small bowel obstruction (15%)
(5) Free perforation (1–2%)
(6) Toxic megacolon
(7) Hydronephrosis, generally on right side ← ureteric compression
(8) Adenocarcinoma in ileum / colon (particularly in bypassed loops / in vicinity of chronic fistula)

Patients with Crohn disease are at increased risk for developing adenocarcinoma in affected intestinal segments (4–20 x that of general population, with a prevalence of up to 1.8%)

(9) Lymphoma in large + small bowel

DDx:
(1) Yersinia (in terminal ileum, resolution within 3–4 months)
(2) Tuberculosis (more severe involvement of cecum, pulmonary TB)

(3) Actinomycosis, histoplasmosis, blastomycosis, anisakiasis
(4) Segmental infarction (acute onset, elderly patient)
(5) Radiation ileitis (appropriate history)
(6) Lymphoma (no spasm, luminal narrowing is uncommon, tumor nodules)
(7) Carcinoid tumor (tumor nodules)
(8) Eosinophilic gastroenteritis
(9) Potassium stricture

Location: terminal ileum + ileocecal region (most common)

@ Esophagus (3%)
√ "aphthous" ulcers (early) = discrete superficial ulcers with punctate collections of barium surrounded by halo of edema
√ esophagitis, stricture, fistula (late)
DDx: superficial spreading esophageal carcinoma

@ Stomach (1–2%) = granulomatous gastritis
√ aphthous ulcers (= pinpoint erosions)
√ pseudo–post Billroth-I appearance
√ "ram's horn" sign = poorly distensible smooth tubular narrowed antrum + widened pylorus + narrow duodenal bulb
√ cobblestone appearance of mucosa
√ antral-duodenal fistula

@ Duodenum (4–20%) almost always associated with gastric involvement
Location: duodenal bulb + proximal half of duodenum
UGI:
√ superficial aphthoid erosions (early lesion)
√ thickened nodular folds, cobblestone pattern
√ deep linear ulcer + sacculations of opposing wall
√ multiple eccentric duodenal stenoses with outward ballooning / sacculation between areas of stricture in stenotic phase of Crohn disease ← healing of deep ulcerations with scarring + fibrosis
CT:
√ mural thickening, mucosal hyperemia, periduodenal soft-tissue stranding

@ Small bowel (80%) = REGIONAL ENTERITIS
Location: terminal ileum (alone / in combination in 95% ← high concentration of lymphoid tissue; jejunum / ileum (15–55%); sparing of terminal ileum in 1%
√ picket fence pattern = diffuse irregular segmental thickening + slight nodularity of circular folds
√ aphthous ulcers
√ reduction in / distortion of folds ← ulceration
√ cobblestone mucosa
√ commonly associated with medial cecal defect

@ Colon (22–70%)
= GRANULOMATOUS COLITIS = CROHN COLITIS
Location: particularly on right side with rectum + sigmoid frequently spared; isolated

to colon (in 20%)

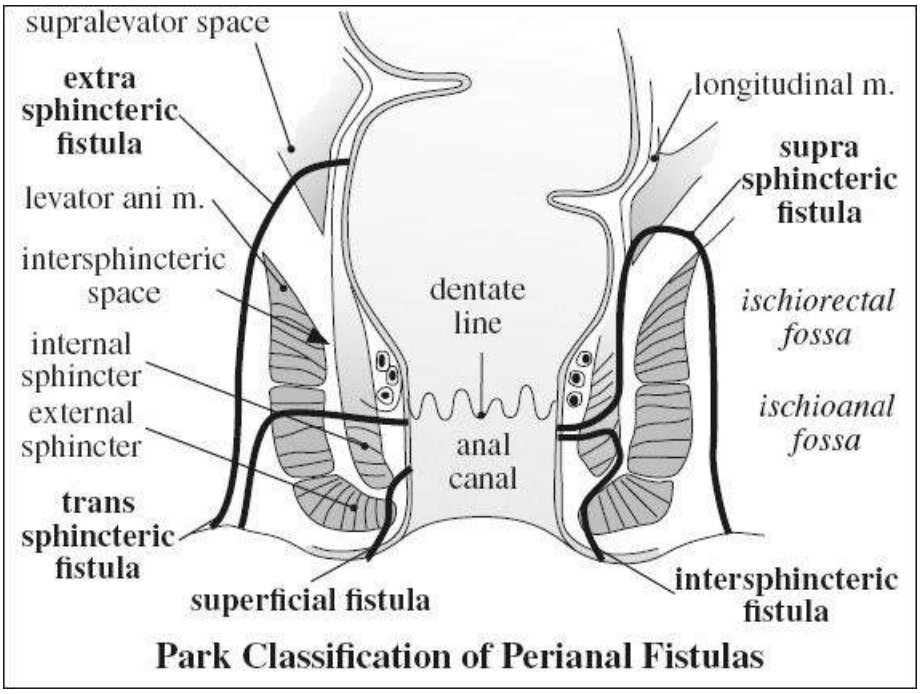
√ feces completely absent / present only in one colonic segment

√ tiny 1–2-mm nodular filling defects (lymphoid follicular pattern)

√ aphthous ulcers of "target / bull's-eye" appearance

√ "transverse stripe" sign = 1-cm-long straight stripes representing contrast medium within deep grooves of coarse mucosal folds

√ long fistulous tracts parallel to bowel lumen



Park Classification of Perianal Fistulas

@ Appendicitis (20%)

@ Rectum (14–50%)

√ deep / collarbutton ulcers

√ rectal sinus tracts

Fistulizing Crohn Disease

= PENETRATING CROHN DISEASE

Frequency: 35% at some time during course of disease with a 20–40% lifetime risk

◊ Crohn disease is 3rd most common cause of fistula / sinus tracts (DDx: iatrogenic [most common cause], diverticula [2nd most common cause])!

Types:

A. Internal fistula

√ hyperenhancing tracts

(a) enteroenteric:

• asymptomatic

Site: most frequently between ileum + cecum

(b) interloop abscess

(d) enterovesical

(e) enterogenital: rectovaginal fistula

B. External / enterocutaneous fistula (8–21%)
= perineal fistula (rectum-to-skin in 54%)
√ isoattenuating tract relative to anorectum

√ positive oral contrast material may better depict fistulous tract BUT obscure mucosal hyperenhancement

Crohn Disease versus Ulcerative Colitis

	Crohn Disease	*Ulcerative Colitis*
Wall	~ 11–13 mm thick	~ 8 mm thick
	eccentric (mesenteric)	symmetric
	segmental	continuous
Distribution	terminal ileum	rectum
	right colon	left colon
Inflammation	transmural	NOT transmural
CT signs	mesenteric comb	
	halo	halo
	creeping mesenteric fat	
	perirectal fat proliferation	perirectal fat proliferation
Cx	fistulae	NO fistulae
	abscesses	

Extraintestinal Manifestations of Crohn Disease

@ Hepatobiliary
1. Fatty infiltration of liver ← steroid therapy, hyperalimentation
2. Hepatic abscess (rare): M÷F = 3÷1
3. Gallstones (15–34%): predominantly cholesterol;
Risk: 3–5 x higher risk than expected; risk correlates with length of diseased ileum / resected ileum / duration of disease
Cause: interrupted enterohepatic circulation with malabsorption of bile salts in terminal ileum
4. Acute cholecystitis
5. Primary sclerosing cholangitis (1%) + hepatoma
6. Bile duct + gallbladder carcinoma
7. Pancreatitis

@ Genitourinary
1. Urolithiasis (5–10%): oxalate (steatorrhea → excess colonic absorption of oxalate) / urate stones
2. Hydronephrosis
3. Renal amyloidosis
4. Focal cystitis
5. Ileoureteral / ileovesical fistula (5–20%)

@ Musculoskeletal

- digital clubbing (11–40%)
- mild self-limiting seronegative peripheral migratory arthritis (15–22%): may precede bowel disease in 10%; severity + course correlates well with severity of intestinal disease; resection of diseased bowel leads to regression of symptoms

1. Hypertrophic osteoarthropathy
2. Ankylosing spondylitis (in 3–16%)
   ◊ Axial skeletal involvement usually precedes onset of GI symptoms!
   - in severity / course unrelated to activity level of bowel disease

   √ symmetric bilateral sacroiliitis
   √ spondylitis with syndesmophytes
3. Peripheral erosive arthritis
   √ small marginal erosions
   √ periostitis
   √ propensity for osseous ankylosis
4. Avascular necrosis of femoral head ← steroid Rx
5. Pelvic osteomyelitis (contiguous involvement)
6. Septic arthritis
7. Muscle abscess
8. Retarded skeletal growth + maturation

@ Erythema nodosum, uveitis

CRONKHITE-CANADA SYNDROME

= nonneoplastic nonhereditary polyps (as in juvenile polyposis) associated with ectodermal abnormalities; no familial predisposition

Prevalence: > 100 cases described

Histo: hamartomatous polyps resemble juvenile / retention polyps = multiple cystic spaces filled with mucin ← degenerative changes; expansion + inflammation of lamina propria

Age: 62 (range, 42–75) years; M < F

- exudative protein-losing enteropathy
- diarrhea ← disaccharidase deficiency, bacterial overgrowth in small intestine
- severe weight loss, anorexia, abdominal pain
- brownish macules of hand + feet, nail atrophy, alopecia

√ multiple polyps
√ thickened gastric rugae

Location: stomach (100%); small bowel (> 50%); colon (100%)

Prognosis: rapidly fatal in women within 6–18 months ← cachexia; tendency toward remission in men

DESMOPLASTIC SMALL ROUND CELL TUMOR

= INTRAABDOMINAL DESMOPLASTIC SMALL ROUND CELL TUMOR OF PERITONEUM

= rare highly malignant tumor belonging to a generic group of small round blue cell tumors (like Ewing sarcoma, neuroblastoma, Wilms tumor, rhabdomyosarcoma, primitive neuroendocrine tumor)

Prevalence: < 50 cases in literature

Median age: 21 (range, 5–30) years; M÷F = 4–9÷1
Origin: mesothelial / submesothelial / subserosal mesenchyme of the abdominal cavity
Path: multinodular unencapsulated mass with focal cystic areas / necrosis / hemorrhage; common serosal implants
Histo: island clusters of small blue cells embedded in a dense desmoplastic fibrous stroma; immunohistochemically positive for epithelial, neural, muscular markers (cytoplasmic keratin + desmin)
Genetics: chromosomal translocation t(11;22)(p13;q12) creating a unique fusion protein of WT1 (Wilms tumor gene) and EWS (Ewing sarcoma family gene)
• palpable intraabdominal mass (64%)
• abdominal pain (52%), increased abdominal girth (8%)
Location: mesentery (particularly retrovesical / rectouterine spaces), retroperitoneum, paratesticular region, posterior mediastinum, pleura, meninges, bone, salivary glands
Spread to: omentum, retroperitoneal and mesenteric lymph nodes, liver, lung, bone (in 50% at initial presentation)

Average size: 11.2 (range, 3–22) cm
√ multiple scattered necrotic peritoneal, omental, and serosal round / ovoid masses without a clear organ of origin
√ usually single dominant (> 10 cm) mass in the retrovesical / retrouterine space / peritoneum / omentum

√ diffuse nodular peritoneal thickening + omental caking
√ tumor spread to serosal surface of liver + spleen (common)
  √ small punctate peritoneal calcifications
  √ cystic areas in mass ← intratumoral necrosis / hemorrhage
√ heterogeneous enhancement
√ scant malignant ascites (37%)
US:
  √ hyper- / hypoechoic mass ← depending on degree of necrosis + hemorrhage
  √ ± echogenic shadowing calcifications
  √ heterogeneous internal vascularity
CT:
  √ small masses of low attenuation (24–36 HU) + uniform enhancement
  √ larger (> 10 cm) mass with central area of low attenuation + heterogeneous enhancement ← necrosis, old hemorrhage
  √ small punctate / amorphous calcifications (30%)
  √ hypoattenuating metastases to liver, abdominal and retroperitoneal lymph nodes
MR:
  √ mass typically hypo- to isointense on T1WI + heterogeneously iso- to hyperintense on T2WI compared with skeletal muscle
  √ foci of T1-hyperintensity ← intratumoral hemorrhage
  √ occasional areas of T2-hypointensity ← densely cellular components / dense desmoplastic stroma
CEMR:
  √ modest heterogeneous enhancement
  √ nonenhancing central foci ← hemorrhage / necrosis / fibromyxoid component

PET (PET/CT 96% sensitive, 98% specific):
√ mean standardized uptake value of 11.1 (range, 3.7–15.0)
Cx: hydronephrosis, bowel obstruction
Prognosis: mean survival time of 17 months
DDx:
(1) in infants / adolescents: rhabdomyosarcoma; neuroblastoma; mesenteric carcinoid; Burkitt lymphoma
(2) in adults: diffuse omental / peritoneal carcinomatosis (← carcinoma of stomach, colon, ovary, pancreas); melanoma; leiomyosarcoma; lymphoma; desmoid tumor; mesothelioma; tumefactive tuberculosis; actinomycosis; Castleman disease; splenosis

DIAPHRAGM DISEASE

= small bowel webs ← NSAIDs
Effect of NSAID: gastric irritation, ulceration of small intestines
Frequency: in 10% of patients receiving long-term NSAIDs
Path: foci of submucosal fibrosis with interruption of adjacent muscularis mucosae
• blood + protein loss, intermittent intestinal obstruction
Location: ileum > jejunum
Enteroclysis:
√ multiple concentric diaphragm-like strictures
DDx: Crohn disease

DIFFUSE ESOPHAGEAL SPASM

Age: more common in patients > 50 years
• severe intermittent chest pain ± dysphagia while swallowing
Location: primarily in distal ²/₃ of esophagus
√ compartmentalization of esophagus by numerous tertiary contractions
√ multiple spontaneous uncoordinated esophageal contractions, often intermittent
√ CLASSIC corkscrew appearance → may obliterate esophageal lumen
Dx: extremely high pressures on manometry

DISACCHARIDASE DEFICIENCY

= enzyme deficiencies for any of the disaccharides (maltose, lactose, etc.)
A. PRIMARY
B. SECONDARY to other diseases (eg, Crohn disease)
Pathophysiology:
(a) unabsorbed disaccharides → produce osmotic diarrhea
(b) bacterial fermentation → produces short-chain volatile fatty acids causing further osmotic + irritant diarrhea
√ normal small bowel series without added lactose
√ abnormal small bowel series done with lactose (50 g added to 600 cm^3 of barium suspension)
√ small + large bowel distension
√ dilution of barium
√ shortening of transit time

DISTAL INTESTINAL OBSTRUCTION SYNDROME

= DIOS = MECONIUM ILEUS EQUIVALENT

= accumulation and impaction of viscid fecal material adherent to intestinal wall in distal part of ileum + proximal part of colon [*viscum* , Latin = birdlime, sticky, slimy, glutinous]

Prevalence: 10–24%% of older child / young adult with cystic fibrosis; 2% in patients < 5 years of age

Cause: tenacious intestinal mucus, steatorrhea ← pancreatic insufficiency, undigested food remnants, disordered intestinal motility with increase in intestinal transit time, fecal stasis

Risk factors: pancreatic insufficiency, history of meconium ileus / DIOS, dehydration, lung transplantation

Age: 2nd–3rd decade of life

- recurrent acute bouts of colicky periumbilical / RLQ pain and vomiting ← fecal impaction / constipation
- palpable cecal mass

√ bubbly granular ileocecal soft-tissue mass in RLQ

√ partial / complete small bowel obstruction ← puttylike fecal material in terminal ileum / right colon

√ thickening of mucosal folds

√ cystic fibrosis of lung

CT:

Location: cecum > ascending colon > transverse colon > descending colon (contiguous involvement)

√ diffuse colonic thickening

√ mural striation (50%)

√ mesenteric soft-tissue infiltration (100%)

√ increased pericolonic fat (60%)

Cx: intussusception, volvulus, perforation, ischemia

Rx: rehydration, stool softeners, oral polyethylene glycol-electrolyte solution (GoLYTELY®), increasing dose of pancreatic enzyme supplements, mucolytic agents (N-acetylcysteine) orally / with Gastrografin® enema

DDx: severe constipation (subacute presentation), appendicitis, partial intestinal obstruction (adhesion / stricture from previous bowel surgery)

DIVERTICULAR DISEASE OF COLON

= saccular outpouching ← overactivity of smooth muscle causes herniation of mucosa + submucosa through a defect in the muscle layer of the colon

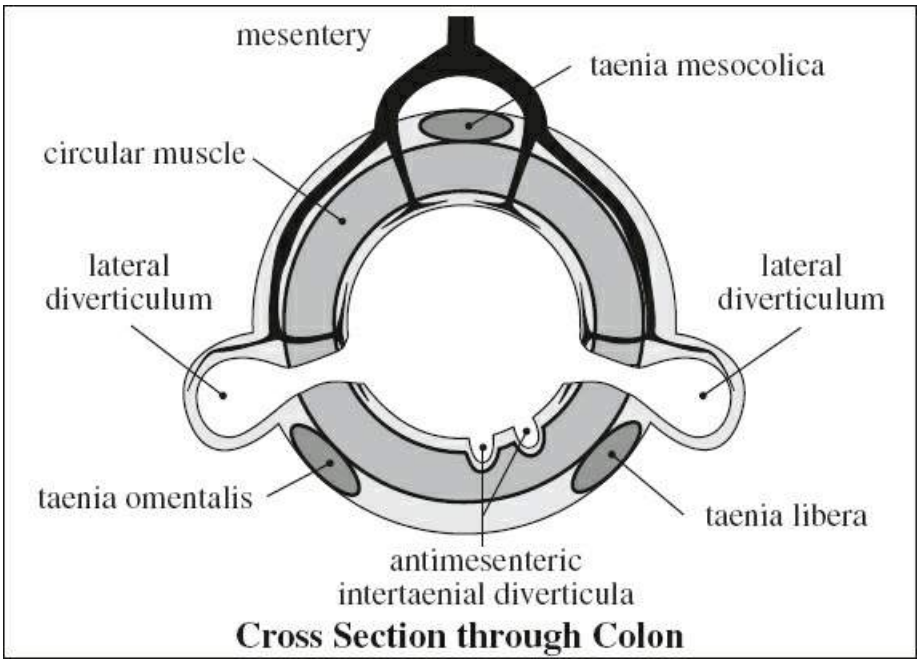
Frequency: 5–10% in 5th decade; 33–48% over age 50; 50–65% past 7th decade; M÷F = 1÷1; most common affliction of colon in developed countries

Cause: decreased fecal bulk (= diet high in refined fiber + low in roughage)

Location: in 80% in sigmoid (= narrowest colonic segment with highest pressure); in 17% distributed over entire colon; in 4–12% isolated to cecum / ascending colon

Prediverticular Disease of Colon

= longitudinal + circular smooth muscle thickening with redundancy of folds ← myostatic contracture
√ "saw-tooth" sign = crowding + thickening of haustral folds ← shortening of colonic segment
√ plump marginal indentations
√ superimposed muscle spasm (relieved by antispasmodics)



Cross Section through Colon

DDx: hemorrhage; ischemia; radiation changes; pseudomembranous colitis

Colonic Diverticulosis

= acquired herniations of mucosa + muscularis mucosae through the muscularis propria with wall components of mucosa, submucosa, serosa = false diverticula of pulsion type
Location: predominantly left-sided colon
Site:
(a) lateral diverticula arise between mesenteric + antimesenteric teniae on opposite sides
(b) antimesenteric intertaenial diverticula opposite of mesenteric side
N.B.: intramural type vasa recta (= nutrient arteries) pass through circular muscle (= weakness in muscular wall) → carried over fundus of diverticulum as it enlarges
√ size: initially tiny (3–10-mm) V-shaped protrusions increasing up to several cm in diameter
√ bubbly appearance of air-containing diverticula
√ residual barium within diverticula from previous study
√ spiky irregular outline (antimesenteric intertaenial ridge is typical site for intramural diverticula)
√ smooth dome-shaped appendages with a short neck
√ may be pointed, attenuated, irregular with variable filling
√ circular line with sharp outer edge + fuzzy blurred inner edge (EN FACE view in double contrast BE)

US:
√ thin-walled round / oval outpouching containing echogenic material that often produces distal acoustic shadowing ← air / feces
√ peridiverticular perienteric fat of normal echogenicity
√ thickened muscularis propria ← hypertrophy
CT:
√ rounded outpouchings containing air ± contrast material (= diverticula)
√ circumferential sawtooth-like thickening of colonic haustra + distorted luminal contour (= muscular hypertrophy)
Cx: bleeding (usually right colon), diverticulitis (usually sigmoid colon)

Giant Colonic Diverticulum *(rare)*
Age: after 6th decade
Path:
(1) Inflammatory diverticulum (66%): wall of dense fibrous tissue + chronic inflammatory cells + foreign body giant cells
(2) Pseudodiverticulum (22%): colonic muscularis propria ends abruptly at neck of pseudodiverticulum ← degeneration of mucosal lining of a pseudodiverticulum
(3) True diverticulum (12%): wall contains all colonic layers ← communicating bowel duplication cyst
• abdominal pain, nausea, vomiting, fever, constipation, diarrhea, melena
Location: sigmoid (93%)
BE:
√ opacification by barium (in 60%)
CT:
√ large gas-, fluid-, stool-filled cavity + thin regular wall
√ NO contrast enhancement / wall thickening unless inflamed
√ ± wall calcifications ← chronic inflammation
Cx: perforation, abscess formation
DDx: volvulus, bowel duplication, Meckel / duodenal diverticulum, infected pancreatic pseudocyst, emphysematous cholecystitis, emphysematous cystitis, vesicoenteric fistula, abscess

Colonic Diverticulitis

= perforation of diverticulum with intramural / localized pericolic inflammatory mass
Frequency: 5% of population; in 10–35% of diverticular disease
Age: in 5–10% > 45 years of age, in 80% > 85 years of age (frequency increasing with age)
Pathogenesis: mucosal abrasion from inspissated fecal material → perforation of thin wall
• evenly distributed lower abdominal pain
• local and rebound tenderness + mass in LLQ (typically)
• nausea, fever (25%), leukocytosis (36%)
• clinical misdiagnosis rate of 34–67%
Location: sigmoid colon (95%), cecum (4%)
√ localized ileus

√ ± pattern of small bowel obstruction → kinking / edema if small bowel adheres to abscess
√ extraluminal gas in abscess / fistula
√ pneumoperitoneum (rare)
BE (77–86% sensitive):
  √ focal area of eccentric luminal narrowing caused by pericolic / intramural inflammatory mass:
    √ annular lesion mimicking carcinoma
  √ marked thickening + distortion of mucosal folds
  √ tethered spiculated mucosal folds
  √ centrally amputated diverticulum
  √ extraluminal contrast = **peridiverticulitis**:
    √ "double-tracking" = pericolonic longitudinal sinus tract
    √ pericolonic collection = peridiverticular abscess
    √ fistula to bladder / small bowel / vagina
CT (79–93% sensitive, 77% specific):
  √ inflamed diverticulum:
    √ pericolic fat stranding = poorly marginated hazy area of ↑ attenuation ± fine linear strands within mesocolic fat (98%)
    √ diverticula (84%) = flask-shaped structures projecting through colonic wall, filled with air / barium / fecal material
    √ "centipede" sign = hyperemic engorged vasa recta
  √ bowel wall thickening:
    √ circumferential bowel wall thickening of > 4 mm (70%) and up to 2 cm
    √ colonic wall thickening extending > 5 cm in length
    √ "double halo" sign = mural stratification = enhancement pattern with inner hyperdense layer + thickened hypodense middle layer + outer hyperdense layer
    √ focally thickened + inflamed colonic wall
    √ "arrowhead" sign = funnel of intraluminal contrast medium / air in focally thickened colonic wall centering about occluded orifice of inflamed diverticulum (27%)
    √ pneumatosis
  √ fluid collection:
    √ fluid at root of sigmoid mesentery
    √ fluid ± air of peritonitis (16%)
    √ frank abscess (47%) = central liquid / gas
  √ tract formation:
    √ fistula formation (14%): most commonly colovesical, also colovaginal, coloenteric, colocutaneous
    √ intramural sinus tracts (9%)
  √ fecolith
  √ colonic obstruction (12%)
  √ ureteral obstruction (7%)

CT Findings of Diverticulitis versus Malignancy	
Diverticulitis	*Malignancy*
√ long segment of involvement >10 cm	√ focal concentric mass
√ double halo / target sign	√ overhanging shoulders
√ fat stranding adjacent to a thickened wall	√ enlarged pericolic nodes

US (85–98% sensitive, 80–97% specific):
- √ thickening of bowel wall > 4 mm (= distance measured between echogenic lumen interface and serosa)
- √ round / oval hypo- / hyperechoic focus protruding from colonic wall + focal disruption of normal layer continuity ± internal acoustic shadowing
- √ regionally ↑ echogenicity adjacent to colonic wall ± ill-defined hypoechoic zones ← inflamed pericolic fat
- √ increased mural vascularity at color Doppler US
- √ pericolic abscess

MR:
- √ chronic colonic wall thickening in affected area
- √ increased SI in pericolonic fat associated with diverticulum on fat-suppressed T2WI

Prognosis: (a) self-limiting (usually) = fecolith + pus evacuate into colonic lumen in 1–2 days
(b) transmural perforation
(c) superficial ulceration
(d) chronic abscess

Cx: (1) Colonic obstruction
(2) Fistula to bladder / vagina / small bowel
(3) Free perforation (rare)
(4) Abscess

DDx: (1) Colonic neoplasm (shorter segment, heaped-up margins, ulcerated mucosa, loss of mural enhancement pattern, pericolic lymph nodes)
(2) Crohn colitis (double-tracking longer than 10 cm)

Rx: antibiotics, surgery (in 25%), percutaneous abscess drainage

Right Colonic Diverticulitis

= reliably benign self-limiting condition

Cause: often congenital solitary true diverticulum

Frequency: 1÷34 to 1÷300 appendectomies

Age: any; peak prevalence at 35–45 years of age

- protracted mild pain mimicking appendicitis
- palpable mass in 33%

- √ solitary diverticulum containing a 12-mm fecolith surrounded by inflamed fat
- √ marked circumferential colonic wall thickening

Cx: pericolonic abscess

Prognosis: spontaneous evacuation into colonic lumen
Rx: conservative; NO indication for surgery
DDx: appendicitis

CECAL DIVERTICULITIS *(5%)*

= usually true diverticulum containing all layers of colonic wall
• generally asymptomatic
• clinically indistinguishable from acute appendicitis
Location: near ileocecal valve (80%)
√ inflammatory changes adjacent to diverticulum
√ normal-appearing appendix

Appendiceal Diverticulitis

= insidious onset of inflammation of uncommon usually acquired diverticulum of appendix
Appendiceal diverticulum: mostly pseudodiverticulum (= herniation of mucosa through muscularis)
Pathogenesis: ?; increased intraluminal pressure ← proximal obstruction
Highly associated with: appendiceal neoplasms
Age: usually > 30 years of age
• lacks migratory pain of classic appendicitis
Site: along mesenteric border of distal ⅓ of appendix; single / multiple
Size: < 5 mm
√ round outpouching beyond margin of appendix
√ may contain fluid / air / enhancing soft tissue
√ prominent enhancement of diverticular wall with surrounding fat stranding
√ increased diameter of wall-thickened hyperenhancing appendix (mimicks acute appendicitis)
Cx: perforation

Colonic Diverticular Hemorrhage

◊ Not related to diverticulitis
Frequency: in 3–25–47% of diverticulosis
Location: 75% located in ascending colon (larger neck + dome of diverticula)
• massive rectal hemorrhage without pain
√ extravasation of radionuclide tracers
√ angiographic contrast pooling in bowel lumen
Prognosis: spontaneous cessation of bleeding in 75%, recurrent bleeding in 25%
Rx: (1) transcatheter infusion of vasoconstrictive agents (Pitressin®)
(2) embolization with Gelfoam®

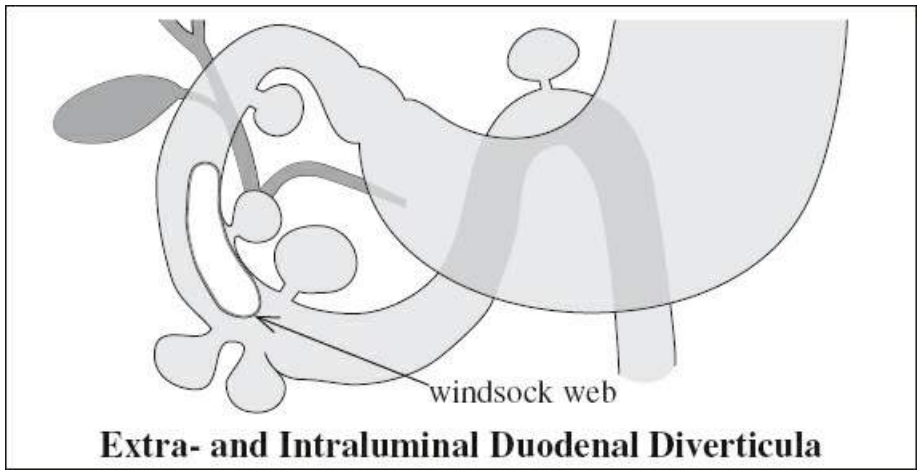
DUMPING SYNDROME

= early postprandial vascular symptomatology of sweating, flushing, palpitation, feeling of weakness and dizziness
Pathophysiology: rapid entering of hypertonic solution into jejunum → resulting in fluid shift from blood compartment into small bowel

Frequency: 1–5%; M÷F = 2÷1
◊ Roentgenologic findings not diagnostic!
√ rapid emptying of barium into small bowel (= loss of gastric reservoir function)
Rx: lying down, diet
DDx: late postprandial hypoglycemia (90–120 min after eating)

DUODENAL ATRESIA

= most common cause of congenital duodenal obstruction; 2nd most common site of gastrointestinal atresias after ileum
Prevalence: 1÷10,000; M÷F = 1÷1
Etiology: defective vacuolization of duodenum between 6th and 11th weeks of fetal life; rarely from vascular insult (extent of obstruction usually involves larger regions with vascular insult)
Age at presentation: first few days of life
• persistent bilious vomiting a few hours after birth / following 1st feeding (75%)
• rapid deterioration ← loss of fluids + electrolytes
Associated anomalies (in 50–60%):
In 30–52% isolated sporadic anomaly
(1) Down syndrome (20–33%)
◊ 25% of fetuses with duodenal atresia have Down syndrome
◊ < 5% of fetuses with Down syndrome have duodenal atresia
(2) CHD (8–30–50%): endocardial cushion defect, VSD



Extra- and Intraluminal Duodenal Diverticula

(3) Gastrointestinal anomalies (26%):
esophageal atresia, biliary atresia, duodenal duplication, imperforate anus, small bowel atresia, malrotation, Ladd bands, Meckel diverticulum, transposed liver, annular pancreas (20%), preduodenal portal vein
(4) Urinary tract anomalies (8%)
(5) Vertebral + rib anomalies (37%)
Location: (a) usually distal to ampulla of Vater (80%)
(b) proximal duodenum (20%)

√ "double bubble" sign = gas-fluid levels in duodenal bulb + gastric fundus
√ total absence of intestinal gas in small / large bowel
√ colon of normal caliber
OB-US (usually not identified prior to 24 weeks GA):
• ± elevated AFP
√ "double bubble" sign = simultaneous distension of stomach + 1st portion of duodenum; continuity of fluid between stomach + duodenum must be demonstrated
√ increased gastric peristalsis
√ polyhydramnios in 3rd trimester (100%)
Prognosis: 36% mortality in neonates
DDx: (1) Prominent incisura angularis → bidissection of stomach
(2) Choledochal cyst
(3) Annular pancreas
(4) Peritoneal bands
(5) Intestinal duplication
Cx: prematurity (40%) ← preterm labor ← polyhydramnios

DUODENAL DIVERTICULUM

Frequency: 1–5% of GI studies; 22% of autopsies
A. PRIMARY / FALSE DIVERTICULUM
= mucosal prolapse through muscularis propria
Site: posteriorly (8%), lateral wall (4%)
B. SECONDARY / TRUE DIVERTICULUM
= all layers of duodenal wall as complication of duodenal / periduodenal inflammation
Location: almost invariably in 1st portion of duodenum
• mostly asymptomatic
√ may be fluid-filled (mimicking pancreatic pseudocyst)
√ may contain foci of air (mimicking pancreatic abscess)
√ contains normal bowel gas / oral contrast material directly communicating with adjacent duodenum
Cx: (1) Perforation + peritonitis
(2) Bowel obstruction
(3) Obstruction of bile duct / pancreatic duct
(4) Bleeding
(5) Diverticulitis

Intraluminal Duodenal Diverticulum

= congenital lesion ← elongation of an incomplete duodenal diaphragm
Age at presentation: young adult
• easy satiety, vomiting, upper abdominal cramping pain
Location: 2nd–3rd portion of duodenum near ampulla of Vater
√ barium-filled sac within duodenal lumen of "windsock, comma, teardrop" appearance (PATHOGNOMONIC picture):

√ anchored to lateral wall of duodenum
√ "halo" sign = duodenal mucosa covers outer + inner wall of diverticulum
√ fluid- / contrast material filled duodenum with thin diverticular wall on CT / MR

DUODENAL HEMATOMA

Cause: blunt abdominal trauma: deceleration injury, endoscopy; bleeding diathesis; anticoagulation therapy
Mechanism: duodenal compression between spine + anterior abdominal wall by seatbelt / handlebar / nonaccidental injury
Age: 80% in children / young adults
Associated with: pancreatic injury in 50–98%, mesenteric and abdominal wall hematoma, spinal fracture
Path: mural hematoma with blood dissecting along submucosal compartment ← separation of mucosa from loose submucosa
Location: 2nd / 3rd portion of duodenum
UGI:
√ circumferential / eccentric duodenal narrowing ← extrinsic compression
√ large filling defect completely occupying + dilating lumen
CT:
√ hyperattenuating (= acute trauma) thickened duodenal wall
√ eccentric mass protruding into the bowel lumen
Mortality: 30%
Cx: bowel obstruction, perforation
Rx: conservative

DUODENAL ULCER

Incidence: 60,000 hospitalizations in USA (2006); 2–3 x more frequent than gastric ulcers; M÷F = 3÷1
Pathophysiology: too much acid in duodenum from
(a) abnormally high gastric secretion
(b) inadequate neutralization
Predisposed: cortisone therapy, severe cerebral injury, after surgery, chronic obstructive pulmonary disease
Location:
(a) bulbar ulcer (95%):
anterior wall (50%), posterior wall (23%), inferior wall (22%), superior wall (5%)
√ bulbar deformity in 85%
(b) postbulbar ulcer (3–5%): medial wall
UGI:
√ round collection of barium in a niche + radiolucent halo of edema + circumferential / eccentric luminal narrowing ← spasm (in acute phase)
√ frequently < 1 cm round / ovoid (5% linear) ulcer niche
√ "kissing ulcers" = ulcers opposite from each other on anterior + posterior wall (in acute

stage)

√ giant duodenal ulcer > 2 cm (rare) with higher morbidity + mortality; may be overlooked by simulating a normal / deformed scarred duodenal bulb

√ "cloverleaf deformity, hourglass stenosis" (in healed stage) with prestenotic dilatation of recesses

CT:

√ outpouching of duodenal wall + adjacent mural thickening + periduodenal fat stranding (acute)

√ radiating folds with central punctate / small linear deposit of contrast material (chronic)

√ eccentric luminal narrowing + smooth round wall indentation (chronic)

Cx: (1) Obstruction (5%) ← edema + spasm (in acute phase) / scarring + fibrosis (subsequent to ulcer healing)

• postprandial nausea & vomiting

(2) Perforation (10–13%): anterior > posterior wall; fistula to gallbladder

(3) Penetration (< 5%) = sealed perforation

(4) Hemorrhage (15%): melena > hematemesis

Prognosis: healing → development of scar

Rx: antral resection (Billroth I) + vagotomy

DUODENAL VARICES

= dilated collateral veins ← portal hypertension (posterior superior pancreaticoduodenal vein)

√ lobulated filling defects (best demonstrated in prone position, maximal luminal distension will obliterate them)

√ commonly associated with fundal + esophageal varices

DUODENAL WEB

= failure of recanalization process in primitive foregut between 9th–11th week GA

May be associated with: Down syndrome, annular pancreas, midgut malrotation, imperforate anus

Types:

(1) Duodenal atresia / complete imperforate web

(2) Windsock web = imperforate intraluminal duodenal diverticulum (IDD)

The shape of the wall of the imperforate intraluminal duodenal diverticulum is affected by peristalsis in the same way a windsock moves with the wind.

(3) Perforated duodenal web = IDD with central / eccentric opening

• symptoms of pancreatitis ± duodenal obstruction

CT / MR:

√ fluid- / contrast–filled blind-ending saccular structure

√ thin enhancing diverticular wall

Cx: pancreatitis ← reflux of duodenal contents through papilla of Vater

DUPLICATION CYST

= GASTROINTESTINAL DUPLICATION CYST

= uncommon congenital anomaly found anywhere along mesenteric side of alimentary tract from tongue to anus

Frequency: 15% of pediatric abdominal masses are gastrointestinal duplication cysts

Theories of formation:

(1) Abortive twinning
(2) Persistent embryologic diverticula
(3) Split notochord
(4) Aberrant luminal recanalization (Bremer): foregut epithelium grows and obliterates lumen (solid stage for esophagus, small bowel, colon) during 6th week GA; → later produces secretions that form vacuoles in the intercellular space; → vacuoles line up longitudinally and coalesce to form new lumen; → failure of an aberrant vacuole to coalesce creates a wall cyst
(5) Intrauterine vascular accident (Favara) associated with alimentary tract atresia in 9%

Age: presentation often in 1st year of life / early childhood

Path: (a) cystic sphere (80%) WITHOUT bowel communication
(b) cystic tubule (20%) communicating with bowel lumen
located in / immediately adjacent to gastrointestinal tract; shares a common muscle wall + blood supply; has a separate mucosal lining; cyst contents usually serous

Histo: wall of smooth muscle lined with alimentary tract mucosa; ectopic mucosa; squamous, transitional, ciliated mucosa; lymphoid aggregates; ganglion cells
◊ Gastric mucosa + pancreatic tissue are the only ectopic tissues of clinical importance!

- mostly asymptomatic, palpable abdominal mass
- respiratory distress (with esophageal duplication)
- nausea, emesis ← partial / complete obstruction

Location: distal ileum (30–33%), esophagus (17–20%), colon (13–30%), jejunum (10–13%), stomach (7%), pylorus (4%), duodenum (4–5%), ileocecal junction (4%), rectum (4%)
◊ In 7–15% concomitant duplications elsewhere within the alimentary tract!

Site: on mesenteric aspect of alimentary canal

Morphology:

(a) large spherical / saccular cyst (82%)
(b) small intramural cyst
(c) tubular sausage-shaped cyst (18%): commonly along small + large bowel; frequently communicates with lumen of adjacent gut

BE:
√ mass extrinsic to bowel lumen

US:
√ elongated tubular / spherical cystic mass with "double-wall / muscular rim" sign:
√ "muscular rim" sign (= echogenic inner mucosal lining + hypoechoic outer rim) in 47%
√ sonolucent content with good through transmission ← clear fluid
√ echogenic content ← hemorrhage + inspissated material
√ cyst paralleling normal bowel lumen

CT:
√ smoothly rounded fluid-filled cyst / tubular structure

√ thin slightly enhancing wall

MR:

√ heterogeneous SI of intracystic fluid on T1WI + homogeneous high SI on T2WI

Cx: (1) Bowel obstruction by intussusception ← cyst at ileocecal junction

(2) Small bowel volvulus ← weight of duplication

(3) Bleeding ← gastric mucosa / pressure necrosis of adjacent mucosa by cyst expansion / from intussusception

√ area of high attenuation ← hemorrhage / proteinaceous material

(4) Infection

√ thick enhancing wall / septum + surrounding inflammation

(5) Malignant transformation

√ enhancing solid focus within cyst

(6) Perforation

Rx: surgical excision

DDx:

(1) Omental cyst (greater omentum / lesser sac, multilocular)
(2) Mesenteric cyst (between leaves of small bowel mesentery)
(3) Choledochal cyst
(4) Ovarian cyst
(5) Pancreatic pseudocyst
(6) Cystic renal tumor
(7) Abscess
(8) Meckel diverticulum (communicates with GI tract)
(9) Lymphangioma
(10) Mesenteric lymphoma
(11) Intramural tumor

Esophageal Duplication Cyst (10–20%)

arises from foregut

Frequency: 10–20% of all alimentary tract duplications; 0.5–2.5% of all esophageal masses; M÷F = 2÷1

Path: contains ectopic gastric mucosa in 43%

Histo: contains no cartilage, lined by alimentary tract mucosa

Associated with: vertebral anomalies (spina bifida, hemivertebra, fusion defects), esophageal atresia, small bowel duplication (18%)

Location: adjacent to esophagus / within esophageal musculature at any level, paraspinal position; R÷L = 2÷1; in right pleural space detached from esophagus (rare)

A. CERVICAL ESOPHAGUS (23%)

- asymptomatic enlarging lateral neck mass
- upper airway obstruction in newborn

DDx: thyroglossal duct cyst, branchial cleft cyst, cystic hygroma, cervical tumor, cervical lymphadenopathy

B. MIDESOPHAGUS (17%)

- severe upper airway obstruction in early infancy

DDx: bronchogenic cyst, neurenteric cyst, intramural esophageal tumor

C. DISTAL ESOPHAGUS (60%)

• frequently asymptomatic

Location: paraspinal

DDx: bronchogenic cyst, neurenteric cyst, intramural esophageal tumor

√ thick-walled closed spherical cyst, almost never communicating

CXR:

√ posterior mediastinal mass ± air-fluid level

√ lobar consolidation + central cavitation ← autodigestion of lung tissue by gastric secretions

√ thoracic vertebral anomalies

UGI:

√ displacement of esophagus by paraesophageal mass

√ intramural extramucosal mass

US:

√ hypoechoic fluid-filled cyst + layered wall:

√ inner echogenic layer (mucosa) and outer hypoechoic layer (muscle)

CT:

√ sharply marginated homogeneous near-water density mass without enhancement

√ contrast-enhancing cyst wall

Cx: (1) Peptic ulceration ← gastric mucosa

(2) Perforation ← penetrating ulcer

(3) Hematemesis ← erosion into esophagus

(4) Hemoptysis + autodigestion of pulmonary tissue ← erosion into tracheobronchial tree

Thoracoabdominal Duplication

= FOREGUT DUPLICATION

= long tubular cyst closed at its cranial end, passing through diaphragm in its own hiatus, in 60% communicating with normal duodenum / jejunum / ileum

Frequency: 2% of all alimentary tract duplications

Associated with: thoracic vertebral anomalies

Histo: gastric mucosa in 29%

Symptomatic age: 50% during neonatal period; 80% within 1st year of life

• severe respiratory distress, chest pain, GI bleeding, anemia

√ tubular right posterior mediastinal mass ± air

√ thoracic vertebral anomaly

√ contrast material may enter through distal connection

Gastric Duplication Cyst (7%)

= intramural gastric cyst lined with secretory epithelium

Frequency: 7% of all alimentary tract duplications

Path: noncommunicating spherical cyst (majority); may communicate with aberrant pancreatic duct; ectopic pancreatic tissue found in 37%

Symptomatic age: infancy; in 75% detected before age 12; M÷F = 1÷2

- pain ← overdistension of cyst, rupture with peritonitis, peptic ulcer formation, internal pancreatitis
- vomiting, anemia, fever
- symptoms mimicking congenital hypertrophic pyloric stenosis (if duplication in antrum / pylorus)

Most common site: greater curvature (65%)

√ paragastric cystic mass up to 12 cm in size, indenting greater curvature
√ seldom communicates with main gastric lumen at one / both ends
√ may enlarge + ulcerate
√ ^{99m}Tc uptake

US:

√ cyst with two wall layers: inner echogenic layer of mucosa + outer hypoechoic layer of muscle
√ clear / debris-containing fluid

Cx: (1) Partial / complete small bowel obstruction
(2) Relapsing pancreatitis (with ductal communication)
(3) Ulceration, perforation, fistula formation

DDx: pancreatic cyst, pancreatic pseudocyst, mesenteric cyst, leiomyoma, adenomatous polyp, hamartoma, lipoma, neurofibroma, teratoma

Small Bowel Duplication Cyst

Frequency: most common of all alimentary tract duplications
Symptomatic age: neonatal period (⅓); < 2 years of age (in 72%)
Path: contains ectopic gastric mucosa in 24%; ectopic pancreatic tissue in jejunum (8%)
May be associated with: small bowel atresia

- neonatal bowel obstruction, intussusception, palpable mass
- acute abdominal pain, GI hemorrhage (may be painless)

Location: ileum (33%), jejunum (10%), ileocecal (4%)
Site: on mesenteric side

√ low small bowel obstruction ± soft-tissue mass
√ cyst may serve as lead point for intussusception

DDx: mesenteric cyst, pancreatic pseudocyst, omental cyst, exophytic hepatic cyst, ovarian cyst

Duodenal Duplication Cyst (5%)

Path: noncommunicating spherical cyst; may contain ectopic gastric mucosa in 21%, small bowel mucosa, pancreatic tissue

- obstructive symptoms, palpable abdominal mass
- hemorrhage ← peptic ulceration
- jaundice ← biliary obstruction
- pancreatitis ← ectopic pancreatic tissue

Location: 1st + 2nd portion of duodenum
Site: on mesenteric side of anterior wall

√ mass in concavity of duodenal C-loop

√ compression + displacement of 1st / 2nd portion of duodenum superiorly + anteriorly
Cholangiography:
√ may communicate with pancreatic ductal system through the aberrant duct of an accessory lobe
Cx: pancreatitis ← perforation of duplication cyst
DDx: pancreatic cyst, pancreatic pseudocyst, choledochal cyst, choledochocele, duodenal intramural tumor, pancreatic tumor

Colorectal Tubular Duplication (6%)

= DUPLICATION OF THE HINDGUT
= double-barreled duplication involving part / all of large bowel with "twin" segment on mesenteric / antimesenteric side
Symptomatic age: neonatal period / infancy; M÷F = 1÷2
May be associated with:
rectogenital / rectourinary fistula; duplication of internal / external genitalia; vertebral anomalies; multisystem congenital anomaly complex
• bowel obstruction / constipation
• passage of feces through vagina
√ simultaneous opacification of true + twin colon
√ duplication may terminate at
(a) 2nd functional anus
(b) imperforate perineal orifice
(c) fistulous communication with GU tract

Colonic Duplication Cyst (7–13%)

= CYSTIC COLONIC DUPLICATION
Frequency: 13% of all alimentary tract duplications
Path: closed spherical cyst; contains gastric mucosa in 2% + ectopic pancreatic tissue in 5%
• abdominal mass, bowel obstruction / constipation
• GI hemorrhage
Location: cecum (40%) ± intussusception
√ air / intestinal matter can enter cyst (20%)

Double Appendix

Rectal Duplication Cyst (4%)

Path: spherical fluid-filled cyst; may contain duodenal / gastric mucosa + pancreatic tissue
Histo: (a) 2 layers of smooth muscle,
(b) continuity with rectum,
(c) mucosal lining similar to rectal mucosa
◊ May contain ectopic gastric mucosa, urothelial mucosa, and pancreatic tissue
Site: presacral space posterior to rectum / anus
Symptomatic age: childhood
• constipation + fecal soiling

• intractable excoriation of perianal skin (with chronic perianal fistula); palpable retrorectal / retroanal mass

√ cystic mass: may be echogenic ← solid material ± gas from communication with rectum

√ spherical cystic lesion that may communicate internally with anorectal lumen / externally with skin surface (20%)

DDx: (1) Anterior meningocele, sacrococcygeal teratoma, retrorectal abscess, pilonidal cyst, sacral bone tumor

(2) Tailgut cyst (no smooth muscle layer)

ENCAPSULATED FAT NECROSIS

Cause: traumatic or ischemic insult → fat degeneration → organization within a thin / thick fibrous capsule

• may be focally tender at palpation

Location: anywhere in body (1st described in breast)

CT:

√ mild mass effect on adjacent structures

√ weak enhancement of capsule

√ ± inflammatory fat stranding + calcification

Prognosis: decrease in size over time

DDx: Liposarcoma (invasion of adjacent organs, no history of surgery, increase in size over time); Failed kidney transplant replaced by fat

ENTERIC CYST

= cyst lined by gastrointestinal mucosa without bowel wall

Etiology: migration of small bowel / colonic diverticulum into mesentery / mesocolon

Path: unilocular thin smooth-walled cyst with serous contents lined by enteric epithelium + thin fibrous wall

US:

√ hypoechoic cystic mass, occasionally with septations

DDx: Duplication cyst (reduplication of bowel wall)

ENTEROCOLITIS

= inflammation / infection of small intestine + colon

Infectious Enterocolitis (Infectious Colitis)

= INFECTIOUS ILEOCECITIS

= self-limited relatively common clinical condition

Cause:

(a) bacterium: Campylobacter jejuni > Salmonella enteritidis > Yersinia enterocolitica + Shigella, E. coli, Staphylococcus, Chlamydia trachomatis, amebiasis, tuberculosis

(b) fungus: histoplasmosis, mucormycosis, actinomycosis

(c) virus: herpesvirus, CMV, rotavirus

Path: bacterial infection limited to mucosa + submucosa of ileum and right colon; layers intact

Age childhood: rotavirus, E. coli, Salmonella, Shigella, Campylobacter
- acute crampy right lower quadrant pain, positive stool culture
- diarrhea: absent / mild / profuse / bloody (dysentery)

Location:
- › proximal small bowel: Giardia and Strongyloides, MAI
- › distal small bowel: Salmonella, Shigella, Yersinia, Campylobacter, Anisakis
- › distal ileum and cecum: tuberculosis, typhlitis, amebiasis
- › pancolitis: Clostridium difficile, cytomegalovirus, E. coli
- › ascending colon: Yersinia, Salmonella, Entamoeba
- › descending + sigmoid colon: schistosomiasis, Shigella
- › rectosigmoid: herpes simplex virus, gonorrhea, Chlamydia trachomatis (lymphogranuloma venereum), Treponema pallidum (gay bowel syndrome)

Associations:
- › lymphadenopathy + splenomegaly: Salmonella

CT:
- √ enhancing circumferential hypodense mural thickening
- √ homogeneous wall enhancement
- √ "empty colon" sign = absence of luminal contents
- √ pericolic fat stranding OFTEN absent with infections
- √ ± multiple air-fluid levels
- √ ± small amount of ascites
- √ ± adjacent lymphadenopathy
- √ NO involvement of appendix / NO abscess / NO fistula
- √ NO obstruction

specific signs:
- √ thumbprinting / accordion sign ← C. difficile
- √ target sign ← Salmonella, Shigella

Dx: clinical (may lead to unnecessary surgery!)

E. coli Infection in Childhood

unlike in adults E. coli infection may result in hemolytic-uremic syndrome

Inflammatory Enterocolitis

A. PRIMARY: inflammatory bowel disease (ulcerative colitis, Crohn disease), vasculitis
B. SECONDARY: chemotherapy, radiation therapy, graft versus host disease, angiotensin-converting enzyme inhibitor–induced enteritis

Age: teen, young adult; 2nd peak in adulthood
- tenesmus, diarrhea, weight loss
- extraintestinal features: large joint arthritis, erythema nodosum, pyoderma gangrenosum

Necrotizing Enterocolitis

= NEC = ischemic bowel disease ← hypoxia, perinatal stress, infection (endotoxin), congenital heart disease

Frequency: most common GI emergency in premature infants
in 1–5% of neonates in ICU;

in 10% of neonates weighing < 1500 g;
in 10% of full-term neonates with CHD

Age: in 90% within first 10 days of life

Pathophysiology:

prematurity → mucosal injury consisting of mucosal ulceration + widespread transmural necrosis → infection, immature immunity, release of vasoconstrictors, inflammatory mediators → passage of bacteria + toxins into bowel wall → increased blood flow + intramural gas → intestinal ischemia → overwhelming sepsis

Organism: not yet isolated; often occurs in miniepidemics within nursery

Risk factors: prematurity (50–80%), perinatal asphyxia, PDA, indomethacin, Hirschsprüng disease, bowel obstruction (small bowel atresia, pyloric stenosis, meconium ileus, meconium plug syndrome)

- feeding intolerance, abdominal distension, bilious emesis
- blood-streaked stools (in 50%); explosive diarrhea
- mild respiratory distress, generalized sepsis with shock

Location: usually in terminal ileum (most commonly involved), cecum, right colon; rarely in stomach, upper bowel

Plain Abdominal Radiography:

◊ Must include horizontal beam cross-table radiograph!

◊ Large bowel may be impossible to differentiate from small bowel!

√ loss of mosaic multifaceted bowel gas pattern (no longer normal array of polygons caused by impression of gas-filled loops on adjacent loops)

√ distension of small bowel and colon (loops wider than vertebral body of L1) ± air-fluid levels, commonly in RLQ (1st and most common sign in 90%):

- √ change from generalized dilatation to asymmetric distribution
- √ "fixed" bowel = persistent abnormal loop of bowel without change on supine vs. prone films / for > 24 hours

√ bowel wall thickening + "thumbprinting"

√ pneumatosis intestinalis (19–80–98%):

- √ black lines of intramural gas often accompanied by white lines representing lifted off mucosa + submucosa
  - › in curvilinear shape (= subserosal) or
  - › bubbly / cystic (= submucosal gas collection from gas-forming organisms / dissection of intraluminal gas)
- √ may disappear within 12 hours
- √ "bubbly" appearance of bowel ← gas in wall / intraluminal gas / fecal matter (intraluminal contents are composed of blood, sloughed colonic mucosa, intraluminal gas, some fecal material)

√ gas in portal venous system in up to 30% (frequently transient, does not imply hopeless outcome):

- √ linear branching radiolucent vessels extending into periphery of liver

√ pneumoperitoneum (immediate surgery required):

- √ triangular lucencies between loops of bowel anterior to liver beneath abdominal wall on cross-table view

US:

√ small individual foci / granular speckled accumulation of hyperechoic gas in dependent portion of bowel wall (DDx: intraluminal gas that changes in position ← peristalsis, respiration, patient position, abdominal compression)
√ portal venous gas:
  √ echogenic foci within portal vein moving with blood flow
  √ sharp bidirectional spikes on Doppler spectrum, audible as crackles
  √ focal / diffuse linear branching pattern of hyperechoic gas in portal veins
√ pneumoperitoneum:
  √ hyperechoic foci of dirty shadowing between anterior surface of liver + abdominal wall / between bowel loops
√ fluid:
  √ ascites ± low-level echoes / septations ← suggestive of perforation
  √ localized intraabdominal fluid collection (= abscess)
  √ increased intraluminal fluid
√ absent peristalsis
√ bowel wall thickness (normal, 1.1–2.6 mm):
  √ "zebra" pattern = bowel wall thickening + increased echogenicity of valvulae conniventes ← edema
  √ bowel wall thinning
√ bowel wall perfusion by color Doppler:
  √ hyperemia: "zebra" pattern (hyperemic valvulae), "Y" pattern (distal mesenteric + subserosal vessels), "ring" pattern (circumferential flow around entire bowel wall)
  √ absent flow ← transmural bowel necrosis

N.B.: Barium enema contraindicated! May be used judiciously in selected cases with radiologic + clinical doubt!

Cx: (1) Inflammatory stricture after healing in 10–30%, in 30% multiple, in 80% in left colon (BE follow-up in survivors)
(2) Bowel perforation in 12–32%

Prognosis: 20–40% mortality (in 64% with perforation)

Rx: bowel rest with nasogastric tube, antibiotics, total parenteral nutrition with adequate hydration, surgery

Neutropenic Colitis (Typhlitis)

= ILEOCECAL SYNDROME [*typhlos*, Greek = blind sac = cecum]
= acute inflammation of cecum, appendix, and occasionally terminal ileum typically in immunosuppressed condition (= neutropenic patients undergoing chemotherapy for malignancy / during posttransplantation period)

Cause: ? probably multifactorial: leukemic / lymphomatous infiltrate, ischemia, mucosal hemorrhage, focal pseudomembranous colitis, infection (esp. CMV)

Histo: edema + ulceration of entire bowel wall → transmural necrosis → perforation possible

Organism: CMV, Pseudomonas, Candida, Klebsiella, E. coli, B. fragilis, Enterobacter, C. difficile

Predisposed: common in childhood leukemia, aplastic anemia, lymphoma,

immunosuppressive therapy (eg, renal transplant), cyclic neutropenia, myelodysplastic syndrome, clinical AIDS

- abdominal pain, may be localized to RLQ
- watery / bloody diarrhea; fullness / palpable mass in RLQ
- fever, neutropenia; hematochezia / occult blood

Location: right colon (cecum + appendix + ascending colon); distal ileum + transverse colon may become secondarily involved

The length of cecum and right colon involved by typhlitis is generally much greater than that associated with appendicitis.

N.B.: Risk of bowel perforation with colonoscopy / contrast enema examination!

√ fluid-filled masslike density in RLQ
√ distension of nearby small bowel loops
√ thumbprinting of ascending colon
√ circumferential thickening of cecal wall > 4 mm
√ occasionally pneumatosis

CT (preferable examination due to risk of perforation):

√ cecal distension
√ circumferential segmental wall thickening (> 1–3 mm) of cecum ± terminal ileum
√ decreased bowel wall attenuation ← edema + necrosis
√ severe stranding of adjacent fat + thickening of fascial planes ← pericolonic inflammation
√ ± pericolonic fluid + intramural pneumatosis

Cx: (1) Perforation
√ pneumatosis coli
√ pneumoperitoneum
(2) Abscess formation
√ pericolic fluid collection

Prognosis: up to 50% mortality ← necrosis, rupture, peritonitis

Rx: (1) Early aggressive medical support (high doses of antibiotics + IV fluids), bowel rest, total parenteral nutrition, electrolyte replacement prior to development of transmural necrosis
(2) Surgery for uncontrollable GI bleeding, obstruction, abscess, transmural necrosis, free perforation, uncontrollable sepsis

DDx: (1) Leukemic / lymphomatous deposits (more eccentric thickening)
(2) Appendicitis with periappendicular abscess (normal cecal wall thickness)
(3) Diverticulitis
(4) Inflammatory bowel disease

EOSINOPHILIC GASTROENTEROPATHY

Eosinophilic Esophagitis

= manifestation of immune-mediated inflammation (allergy) in genetically susceptible individuals

◊ Leading cause of emergency department visits for esophageal food impaction (in up to 50%)

Incidence: 1÷10,000 [2–6÷10,000] annually in children [adults]

Prevalence: 4÷10,000 [27÷10,000] in child [adult]

Peak age: 3rd + 4th decade; M÷F = 3÷1

Histo: PATHOGNOMONIC infiltration of squamous epithelium with > 15–20 eosinophils per high-power field

- chronic nonprogressive dysphagia with solid foods (70%)
- gastroesophageal reflux / heartburn (38%)
- vomiting, regurgitation, hematemesis, weight loss
- history of atopy; asthma, atopic dermatitis, eczema

Seasonal occurrence: symptoms in late summer and fall

Pathophysiology:

hypersensitivity reaction to inhaled / ingested allergens → Th2 type immune response (= cytokines like interleukin 4, 5, 10, 13) → excessive eosinophils → release of cytotoxic chemicals (eg, transforming growth factor beta) → muscular contractions → fibrotic strictures

UGI:

√ smooth long-segment stricture without ulceration + mild mucosal irregularity (most common finding)

√ "ringed esophagus" = multiple fixed rings appearing as closely stacked indentations on esophageal lumen

√ stricture with an irregular ulcerated lumen / granular mucosa

√ small-caliber esophagus → diameter of < 20 mm

Location: mid / distal esophagus

Associated with: hiatal hernia, reflux esophagitis

CT:

√ diffuse mural thickening (nonspecific)

√ occasionally impacted food

Dx: (1) Endoscopy

- esophageal rings (a) fixed (= "esophageal trachealization" (b) transient (= "felinization")
- linear / longitudinal mucosal grooves
- white plaques mimicking candidiasis
- pale fragile mucosa ("crepe paper mucosa") → may fracture with passage of endoscope → risk of esophageal perforation

Rx: dietary modification (98% positive response in children); oral corticosteroids + leukotriene and eotaxin inhibitors; esophageal dilatation (for symptomatic stricture with ↑ risk of perforation)

(2) Biopsy (30% complication rate)

Cx: spontaneous esophageal rupture

DDx: peptic / radiation-induced stricture (indistinguishable)

Eosinophilic Gastroenteritis

= uncommon occasionally self-limited form of gastroenteritis with remissions +

exacerbations characterized by infiltration of eosinophilic leukocytes into wall of GI tract

Prevalence: 1÷100,000

Cause:

(a) primary = idiopathic

(b) secondary = result of systemic condition

1. Hypereosinophilic syndrome
2. Celiac disease
3. Crohn disease
4. Churg-Strauss syndrome
5. Helminthic infection
6. Drugs: enalapril, gemfibrozil, cyclosporine

Histo: fibrous tissue + eosinophilic infiltrate of gastrointestinal mucosa

Peak age: 3rd–5th decade; M÷F = 1.4÷1

A. EOSINOPHILIC GRANULOMA

B. EOSINOPHILIC GASTROENTERITIS

= diffuse type

= eosinophilic infiltration of mucosa (58%), submucosa, muscular layer, serosa of small intestine ± stomach by mature eosinophils (? gastric pendant to Löffler syndrome)

- history of atopy + systemic / food allergy (75%)
- usually marked peripheral eosinophilia (75–100%)
- local symptoms:
  - recurrent episodes of abdominal pain / cramps
  - diarrhea, vomiting, bowel obstruction, acute pancreatitis
  - GI bleed, hematemesis ← ulceration
- systemic symptoms:
  - malabsorption, protein-losing enteropathy → hypoproteinemia, iron-deficiency anemia
  - weight loss, anorexia, failure to thrive
  - delayed puberty, amenorrhea

Location: entire small bowel (particularly jejunum), distal stomach, omentum, mesentery

Layer of involvement: (a) mucosa + submucosa (58%)
(b) muscularis (30%)
(c) serosa (12%)

@ Small bowel (100%)

√ separation of small bowel loops

(a) mucosal type
√ mucosal fold thickening, polyps, nodular thickening, ulcers
√ "araneid limblike" sign = "spider leg" appearance ← diffuse mucosal thickening with contrast material in mucosal sinuses

(b) submucosal type
√ "halo" sign = layered appearance of bowel wall ← submucosal edema

(c) muscular type
√ strictures, bowel wall thickening, intestinal obstruction

√ concentric hypoattenuating bowel wall thickening

√ reduced distensibility + narrowing of lumen

√ motility disturbance → small-bowel obstruction

√ effacement of mucosal pattern

(c) serosal type

√ ascites with peripheral eosinophilia

√ pleural effusion

√ peritoneal stranding, omental thickening

√ mesenteric lymphadenopathy with central necrosis

√ clustering of small bowel loops

√ serosal enhancement

DDx: lymphoma

@ Stomach (80%; almost always limited to antrum)

√ "wet stomach"

(a) mucosal type

√ enlarged gastric rugae / cobblestone nodules / polyps

√ ulcers (rare)

(b) muscular type

√ thickened + rigid wall with narrowed gastric antrum / pylorus

√ bulky intraluminal mass up to 9 cm in size

Cx: pyloric / gastric outlet obstruction

DDx: hypertrophic gastritis, lymphoma, carcinoma

Prognosis: tendency toward spontaneous remission (in ⅓) with frequent relapse

Rx: corticosteroids / removal of sensitizing agent; dietary modification

Eosinophilic Colitis

= non–IgE-mediated allergic disease

Cause: allergy to cow's milk / soy proteins

Age: infants, young adults

In 50% associated with: atopic disease

• abdominal pain

(a) mucosal disease

• bloody diarrhea

(b) muscular disease

√ volvulus, intussusception, perforation

(c) serosal disease

√ ascites

√ segmental / diffuse colonic wall thickening, wall edema

√ pericolonic fat stranding

Dx: increased eosinophils in colonic wall + negative workup for other causes of tissue eosinophilia

Rx: dietary modification (child); corticosteroid / immunosuppressive therapy (adult)

Prognosis: waxing and waning course

EPIPLOIC APPENDAGITIS

= rare self-limiting inflammation of one of 50–100 epiploic / omental appendages

◊ 40 times more common than Meckel diverticulitis!

◊ Relatively unknown amongst clinicians and almost never suspected preoperatively!

Epiploic appendage: small benign 5–50 mm long outpouching of visceral peritoneum containing fat and small blood vessels + arising from serosal surface of colon adjacent to tenia coli

Cause: (a) primary: torsion (exercise) → venous thrombosis
Blood supply: 2 arteries + 1 draining vein
(b) secondary: inflammation of adjacent organ (eg, diverticulitis, appendicitis, cholecystitis)

Associated with: obesity, rapid recent weight loss, hernia, unaccustomed exercise

Age: 4th–5th decade; M > F

Histo: acute infarction with fat necrosis, inflammation, thrombosed vessels with hemorrhagic suffusion

- abrupt onset of very localized nonmigratory LLQ abdominal pain (RLQ in 50%) + rebound tenderness, gradually resolving over 3–7 days
- less frequent: nausea, vomiting, altered bowel function, fever
- palpable mass (10–30%); ± peritoneal signs
- normal / mildly increased (7%) WBCs; NO fever

Location: sigmoid > descending > right hemicolon > appendix
◊ Most commonly mimicks acute diverticulitis!

Site: anterolaterally / (occasionally) anteromedially between colon + abdominal wall

Size: 1.0–3.5–5.0 cm in diameter

√ oval fatty lesion commonly adjacent to sigmoid colon:
  √ stranding of periappendigeal fat
  √ thickening of parietal peritoneum

CT:
  √ pericolic oval-shaped pedunculated mass of fat attenuation (~ -60 HU):
    √ hyperattenuating 2–3 mm peripheral rim (= thickening of adjacent visceral peritoneal lining) in 93%
    √ "central dot" sign / linear focus of high attenuation (= engorged / thrombosed vein / central hemorrhage / necrosis)
  √ ± (often peripheral) calcification ← fat necrosis
  √ eccentric minimal colonic wall thickening

US:
  √ solid hyperechoic noncompressible oval mass at site of maximal tenderness
  √ hypoechoic margin (93%)
  √ absence of central blood flow on color Doppler

MR:
  √ focal lesion with signal intensity of fat
  √ enhancing rim around oval fatty lesion

Cx: adhesion, bowel obstruction, intussusception, peritonitis, abscess, intraperitoneal calcified loose body (after twisting off its pedicle)

Prognosis: spontaneous resolution within 2 weeks clinically + within 6 months on CT

Rx: conservative management with NSAID

DDx: (1) Torsion / infarction of greater omentum = epiploic appendagitis "on steroids"
(2) Sclerosing mesenteritis

(3) Diverticulitis
(4) Appendicitis
(5) Primary tumor / metastasis of mesocolon

ESOPHAGEAL CANCER

Incidence: 4–10% of all gastrointestinal malignancies (3rd most common) worldwide; 1% of all cancers; 16,910 cases with 15,690 deaths annually (USA, 2016); 5.8 cases per 100,000 people; M÷F = 4÷1

High-risk regions: Iran, parts of Africa, Italy, China

At risk: tobacco + alcohol use (synergistic effect); diet low in fresh fruit + vegetables and high in nitrosamines; achalasia (risk factor of 1,000 x), asbestosis, Barrett esophagus, celiac disease, radiation exposure, acid / lye burn (risk factor of 1,000 x), Plummer-Vinson syndrome, tannins, alcohol, tobacco, history of oral / pharyngeal cancer, **tylosis palmaris et plantaris** (defect in tylosis esophageal cancer gene on chromosome 17q25)

mnemonic: BELCH SPAT
Barrett esophagus
EtOH abuse
Lye stricture
Celiac disease
Head and neck tumor
Smoking
Plummer-Vinson syndrome
Achalasia, **A**sbestosis
Tylosis

Cancer Staging (American Joint Commission on Cancer):

TNM system:

Tis high-grade dysplasia
T1a tumor invades lamina propria / muscularis mucosae
T1b tumor invades submucosa
T2 tumor invades muscularis propria
T3 tumor invades adventitia
T4 tumor invades adjacent structures
T4a resectable (pleura, pericardium, diaphragm)
T4b unresectable (aorta, vertebra, trachea)
N0 no regional Lnn metastasis
N1 1–2 regional Lnn metastasis
N2 3–6 regional Lnn metastasis
N3 ≥ 7 regional Lnn metastasis

Stage I	= T1 N0 M0	Stage III	= T3 N1 M0
Stage IIA	= T2/3 N0 M0		or T4,N0/1,M0
Stage IIB	= T1/2 N1 M0	Stage IV	= T1-4 N0/1 M1

T4a cancers are resectable in spite of ← invasion of pleura, peritoneum, pericardium, diaphragm.
T4b cancers are unresectable ← invasion of aorta, carotid a. + v., azygos v., trachea, left main

bronchus, vertebral body.

Lymph node map:

1	supraclavicular	9	inferior pulmonary lig.
2L	paratracheal – L/R	10	hilar L / R
3P	posterior mediastinal	15	diaphragmatic
4	tracheobronchial angle	16	paracardial
5	aortopulmonary	17	left gastric (resectable)
6	anterior mediastinal	18	common hepatic
7	subcarinal	19	splenic
8L	lower paraesophageal	20	celiac (unresectable)
8M	middle paraesophageal		

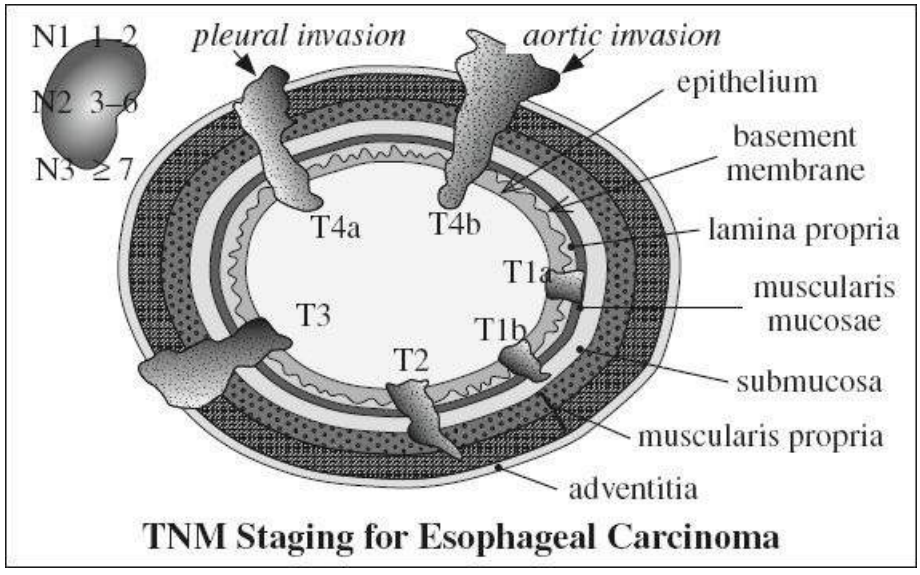
Regional lymph nodes include any paraesophageal lymph nodes from cervical nodes to celiac nodes.

Lnn status is based on location of primary:

N1 = locoregional periesophageal Lnn disease
M1a = metastasis to cervical / celiac nodes
M1b = distant nonregional Lnn disease

(a) in proximal esophageal cancer:
M1a = cervical Lnn involvement
M1b = all other distant metastases

(b) in middle esophageal cancer:
M1a = none available
M1b = metastasis to cervical / celiac axis Lnn



(c) in distal esophageal cancer:
N1 = gastric Lnn involvement
M1a = celiac axis Lnn involvement
M1b = all other distant metastases

CT (30–60% sensitive, 46–58% accurate):
√ intrathoracic/ abdominal lymph node > 10 mm
√ supraclavicular lymph node with short axis > 5 mm
US (72–80% accurate):
√ homogeneously hypoechoic central pattern
√ round lymph node with a short axis of > 10 mm
PET:
√ 51–84% sensitivity for locoregional lymph nodes
√ up to 90% sensitive for metastatic lymph node

CT staging (Moss):
Stage 1 intraluminal tumor / localized wall thickening of 3–5 mm
Stage 2 localized / circumferential wall thickening > 5 mm
Stage 3 contiguous spread into adjacent mediastinum (trachea, thyroid, larynx, bronchi, aorta, lung, pericardium, diaphragm)
√ loss of fat planes (nonspecific ← cachexia, often still resectable)
√ mass in contact with aorta > 90° arc (in 20–70% still resectable)
√ displacement / compression of airway (90–100% accuracy for invasion)
√ esophagotracheal / -bronchial fistula (unresectable)
√ pericardial thickening, pericardial effusion, loss of pericardial fat plane, indentation of heart
Stage 4 distant metastases
√ enlarged abdominal lymph nodes > 10 mm (12–85% accuracy)
√ hepatic, pulmonary, adrenal metastases
√ direct erosion of vertebral body
√ tumor > 3 cm wide = high frequency of extraesophageal spread

Endoscopic US (most accurate modality for T staging):
◊ Can differentiate T1<u>mucosal</u> (suitable for local ablative therapy) from T1 <u>submucosal</u> invasion

Accuracy: 75–82% for T1, 64–82% for T2, 89–94% for T3, 88–100% for T4

Histo:
(1) Squamous cell carcinoma (50–70%)
(2) Adenocarcinoma (30–50%)
(3) Spindle-cell carcinoma (0.5–2.8%)
(4) Sarcoma: GIST, leiomyo-, rhabdomyo-, fibrosarcoma
(5) Mucoepidermoid carcinoma, adenoid cystic carcinoma
(6) Neuroendocrine neoplasm / small cell carcinoma (1%)
(7) Malignant lymphoma
(8) Secondary tumor involvement from: thyroid, larynx
(9) Metastasis from: breast, melanoma, GI tract

• dysphagia (87–95%) of < 6 months' duration
• weight loss (71%), retrosternal pain (46%), regurgitation (29%)

Location: upper ⅓ (15–20%); middle ⅓ (37–44%); lower ⅓ (38–43%)

An esophagogastric junction tumor is considered an esophageal cancer if
(a) the epicenter is within lower thoracic esophagus / at esophagogastric junction, or

(b) the epicenter is within proximal 5 cm of the stomach extending into the esophagus.

Radiologic types:

(1) **Polypoid / fungating form** (most common)
- √ sessile / pedunculated tumor with lobulated surface
- √ protruding, irregular, polycyclic, overhanging, steplike "apple core" lesion

(2) **Ulcerating form**
- √ large ulcer niche within bulging mass

(3) **Infiltrating form**
- √ gradual narrowing with smooth transition (DDx: benign stricture)

(4) **Varicoid form = superficial spreading carcinoma**

= uncommon pattern of dissemination via vasculature + lymphatic system to submucosa

Histo: longitudinal extension of squamous cell carcinoma confined to mucosa / submucosa → secondary intramural tumor deposits

Location: middle + distal segments of esophagus

- √ focal area of confluent tortuous / serpentine longitudinal mucosal nodules / plaques simulating downhill esophageal varices:
  - √ NO change during respiration / patient repositioning

DDx: Candida esophagitis

Metastases:

(a) lymphogenic: anterior jugular chain + supraclavicular nodes (primary in upper ⅓); paraesophageal + subdia-phragmatic nodes (primary in middle ⅓); mediastinal + paracardial + celiac trunk nodes (primary in lower ⅓)

N.B.: (1) mucosal + muscular lymphatic plexuses intercommunicate
(2) lymph may flow upward / downward

(b) hematogenous: liver > lung > bone > adrenal gland > kidney > brain

CXR:
- √ widened azygoesophageal recess with convexity toward right lung (in 30% of distal + midesophageal cancers)
- √ thickening of posterior tracheal stripe + right paratracheal stripe > 3–4 mm (in 11% if tumor is located in upper third of esophagus)
- √ tracheal deviation (10%)
- √ widened mediastinum
- √ posterior tracheal indentation / mass
- √ retrocardiac mass
- √ esophageal air-fluid level
- √ lobulated mass extending into gastric air bubble
- √ repeated aspiration pneumonia ← tracheoesophageal fistula

Barium:
- √ plaquelike / polypoid / ulcerated lesion for <u>superficial lesion</u>
- √ irregular luminal narrowing, ulceration, abrupt shouldered margins for <u>advanced lesion</u>
- √ elevated lesion + rigidity of esophageal wall indicate subepithelial tumor extension

Endoscopic US:
- √ homo- / heterogeneous mass
- √ disruption of esophageal wall layers (staging accuracy of 84%)

√ round well-defined lymph node > 10 mm in diameter (92% accuracy if combined with fine-needle aspiration)

CT:

√ asymmetric / circumferential localized thickening of esophageal wall / soft-tissue mass

√ peak enhancement in late arterial phase (at 35 seconds)

√ mediastinal / aortic invasion:

√ loss of intervening fat planes

√ displacement / indentation of trachea

√ tumor in contact with > 90° of aortic circumference

√ distant metastases (to liver, lung, bone)

PET:

√ avid uptake of primary (unless confined to mucosa) and of metastases (unless microscopic involvement)

◊ Primary tumor NOT identified in up to 20% (33% sensitive compared with 81% for endoscopic ultrasound)

Role of PET:

◊ Cost effective in prevention of noncurative surgery!

(1) Initial staging + detection of unresectable distant disease ← locoregional metastases (32–41% sensitive)

(2) Monitoring effectiveness of therapy (after 2 weeks)

= allows prediction of response to neoadjuvant therapy after only 2 cycles (not sufficiently reliable!)

N.B.: many FPs ← posttreatment esophagitis and ulceration, motion artifacts at level of diaphragm, prior mucosal biopsy during EGD

(3) Monitoring conversion from nonsurgical to surgical lesion

(4) Follow-up after definitive treatment (= restaging)

› local recurrence (100% sensitive, 57% specific)

› recurrent regional disease (92% sensitive, 83% specific)

› distant metastases (95% sensitive, 80% specific)

Cx: fistula formation to trachea (5–10%) / bronchi / mediastinum

Prognosis: 18.4% 5-year survival rate (2012); 0% 5-year survival rate for cancer of cervical esophagus; ²/₃ incurable at presentation; survival rate higher for adenocarcinoma versus squamous cell cancer

Mean survival time:

90 days with subdiaphragmatic lymphadenopathy

180 days with local invasion + abdominal metastases

480 days without evidence of invasion / metastases

Rx: (1) Chemotherapy (fluorouracil, cisplatin, bleomycin sulfate, mitomycin) + surgery

(2) Chemotherapy + irradiation (~ 4,000 cGy)

(3) Chemotherapy + irradiation + surgery

Operative mortality: 3–8%

Squamous Cell Carcinoma (SCC) of Esophagus

= malignant tumor of epithelial cells with stratified squamous differentiation progressing

from precursor lesion of intraepithelial neoplasia

Prevalence: 1.8÷100,000 in USA (↓ probably due to declining tobacco consumption); 20÷100,000 in southern Africa + eastern Asia
◊ Most common esophageal neoplasm worldwide!

Histo: nests of squamous epithelial cells penetrate beyond basement membrane with little desmoplastic response; tumor grade does NOT affect prognosis; intramural metastases in up to 16%

Peak age: 60–74 years; M÷F = 65÷35; Blacks÷Whites = 4÷1

- asymptomatic with superficial cancer (85%)
- progressive dysphagia, odynophagia, weight loss
- chest pain (unrelated to swallowing)

Location: middle > lower > upper third of esophagus

Barium:
√ plaquelike / polypoid / ulcerated lesion for superficial lesion
√ irregular luminal narrowing, ulceration, abrupt shouldered margins for advanced lesion
√ elevated lesion + rigidity of esophageal wall indicate subepithelial tumor extension

Endoscopic US:
√ homo- / heterogeneous mass
√ disruption of esophageal wall layers → staging accuracy of 84%
√ round well-defined lymph node > 10 mm in diameter (92% accuracy if combined with fine-needle aspiration)

CT:
√ asymmetric / circumferential localized thickening of esophageal wall / soft-tissue mass
√ peak enhancement in late arterial phase (35 seconds)
√ mediastinal / aortic invasion:
  √ loss of intervening fat planes
  √ displacement / indentation of trachea
  √ tumor in contact with > 90° of aortic circumference
√ distant metastases (to liver, lung, bone)

PET:
√ avid uptake of primary (unless confined to mucosa) + of metastases (unless microscopic involvement)

Cx: esophageal obstruction, tracheoesophageal fistula

Prognosis: overall 5-year survival rate of 10%

Spindle Cell Carcinoma of Esophagus

= (METAPLASTIC) CARCINOSARCOMA = PSEUDOSARCOMA = PSEUDOSARCOMATOUS CA. = POLYPOID SQUAMOUS CARCINOMA = SARCOMATOID CARCINOMA = SCC WITH SPINDLE-CELL COMPONENT

Prevalence: 0.5–2.8% of all malignant esophageal tumors

Histo: squamous + sarcomatous elements

Path: bulky polypoid intraluminal mass with scalloped smooth / ulcerated surface

Age: > 45 years; M÷F = 4÷1 to 9÷1

- pain, dysphagia, weight loss

Location: usually middle + distal esophagus

√ rapid growth = doubling time of 2.2–5.0 months

Esophagram:

√ large bulky smoothly lobulated intraluminal mass

√ cupola / domed appearance of superior tumor edge

√ expands esophageal lumen to an average diameter of 8 cm WITHOUT obstruction

√ ulceration rare; may be polypoid + pedunculated

CT:

√ expansile hypoattenuating intraluminal mass

√ ± focal esophageal wall thickening at attachment site

Prognosis: similar to SCC with 20% 5-year survival

Spread (in 38–50%): lung, liver

DDx: fibrovascular polyp, myofibroma, pedunculated lipoma, leiomyoma, lymphoma, adenocarcinoma, leiomyosarcoma, fibrosarcoma, rhabdomyosarcoma, melanoma, oat cell carcinoma

Adenocarcinoma of Esophagus

= malignant epithelial neoplasm that almost always arises from

(a) malignant degeneration of underlying columnar-lined epithelium (Barrett epithelium)

› occasionally from

(b) ectopic gastric mucosa in esophagus

(c) submucosal / deep esophageal glands

(d) gastric adenocarcinoma involving GE junction

Prevalence: marked ↑ from 18% (in 1984) to 63% (in 2008) of all malignant esophageal tumors surpassing squamous cell carcinoma in USA

◊ 2nd most common malignant tumor of esophagus in most countries!

◊ 2,500 new cases annually

Path: grossly infiltrating / polypoid / ulcerative lesion

Histo: sequence of progressively severe epithelial dysplasia → mostly well / moderately well differentiated invasive carcinoma with columnar or cuboidal cells in tubular / glandular / cribriform patterns; ± mucinous / signet-ring cell subtypes

Peak age: 7th decade; M÷F = 85÷15; Whites÷Blacks = 5÷1

• asymptomatic (most)

• symptoms of gastroesophageal reflux disease (GERD)

Location: 75% in lower ⅓ of esophagus with marked tendency to extend to gastric cardia + fundus

Adenocarcinoma and SCC have similar morphologic findings. However, adenocarcinomas usually involve the lower ⅓ of the esophagus with a tendency to invade the stomach.

√ imaging features identical to SCC

Prognosis: overall 5-year survival rate of 42% after resection compared to 30% for SCC

ESOPHAGEAL INTRAMURAL PSEUDODIVERTICULOSIS

= dilated excretory ducts of deep mucous glands

Etiology: uncertain

Prevalence: about 100 cases in world literature

In 90% associated with:
diabetes, alcoholism, any severe esophagitis (most often reflux / Candida), esophageal stricture
Site: diffuse / segmental involvement
√ multiple tiny rounded / flask-shaped barium collections in longitudinal rows parallel to long axis of esophagus:
√ appear to "float" outside esophagus without apparent communication with lumen
√ esophageal stricture:
√ short stricture in distal esophagus (common)
√ long stricture in cervical / upper thoracic esophagus (classic)

ESOPHAGEAL TRAUMA

Cause:
A. EXTRALUMINAL:
(1) Blunt trauma = closed chest trauma (10%)
Frequency: 1% of all blunt chest trauma
Location:
(a) cervical / upper thoracic esophagus (82%)
(b) just above gastroesophageal junction along left posterolateral wall
(2) Penetrating trauma
B. INTRALUMINAL:
(1) Iatrogenic injury = complication of instrumentation (most common cause, 55%): endoscopy, dilatation of stricture + stent placement, bougie, disruption of suture line following surgical anastomosis (gastric fundoplication, esophageal myotomy), attempted intubation, thyroidectomy, anterior cervical diskectomy, left atrial radiofrequency ablation
(2) Barotrauma = spontaneous rupture = Boerhaave syndrome (15%)
(4) Foreign body impaction (14%): coin, aluminum pop-tops, metallic button, safety pin, invisible plastic toy leading to perforation (in pediatric age group)
(5) Intrinsic esophageal disease: Barrett ulcer, caustic / infectious esophagitis, esophageal carcinoma
• abrupt onset of retrosternal chest pain (similar to acute myocardial infarction / aortic dissection)
• dysphagia, odynophagia, hematemesis

Intramural Dissection of the Esophagus

= SUBMUCOSAL DISSECTION = INTRAMURAL RUPTURE OF ESOPHAGUS = DISSECTING INTRAMURAL HEMATOMA
= mucosal tear with dissecting hemorrhage into submucosa + involvement of venous plexus
Cause: recent instrumentation, forceful vomiting, spontaneous hemorrhage (anticoagulant therapy, coagulopathy), aortoesophageal fistula, spontaneous
Age: middle-aged; M < F
• hematemesis
Location: usually posterior

Site: distal ← lack of striated muscle
√ well-defined focal filling defect = intramural hematoma simulating retained solid material within lumen
√ luminal narrowing of the esophagus
√ "double-barrel esophagus" = mucosal flap with submucosal distribution of gas / contrast
√ "mucosal stripe" sign = dissected mucosa floating within lumen
√ eccentric / concentric nonenhancing hyperattenuating mass within esophageal wall

CT:
√ symmetric / asymmetric esophageal wall thickening
√ well-defined nonenhancing intramural esophageal mass of high attenuation

Prognosis: progression to frank esophageal rupture / resolution within a few weeks

Transmural Perforation of the Esophagus

= ESOPHAGEAL PERFORATION = ESOPHAGEAL RUPTURE

• rapid onset of overwhelming sepsis: fever, tachycardia, hypotension, shock

Plain film (normal in 9–12%):
√ extensive pneumomediastinum
√ "V" sign of Naclerio = extrapleural air within lower mediastinum between parietal pleura + diaphragm (usually on left)
√ subcutaneous emphysema of the neck
√ delayed widening of the mediastinum ← mediastinitis
√ hydrothorax (after rupture into pleural cavity), usually unilateral on left side
√ hydropneumothorax (often initially missed)
√ left lower lobe atelectasis
√ confirmation with contrast study (90% of contrast esophagrams are positive)

Esophagography (modality of choice for evaluating esophageal rupture):
(1) Water-soluble contrast (in 10% false-negative result)
(2) Barium (if result with water-soluble material negative)
√ extravasation of oral contrast material into mediastinum ± pleural space

CT (modality of choice for penetrating trauma):
√ focal extraluminal air collection at site of tear (92%; most useful sign)
√ periesophageal / mediastinal hematoma / fluid (92%)
√ pleural effusion (75%)
√ esophageal wall thickening

Cx: (1) Acute mediastinitis
(2) Obstruction of SVC
(3) Mediastinal abscess

Prognosis: 20–60% mortality; 90% after 48 hours

Med. emergency: up to 80% survive if primary closure is performed within 24 hours after perforation

Upper / Midesophageal Perforation

Location: at level of cricopharyngeus muscle (most frequent)
√ widening of upper mediastinum

√ right-sided hydrothorax

Distal Esophageal Perforation

Frequency: more common (but not in blunt chest trauma)
Cause: biopsy, dilatation of stricture, Boerhaave syndrome
√ left-sided hydrothorax
√ little mediastinal changes

ESOPHAGEAL VARICES

= plexuses formed by (1) dilated subepithelial and submucosal veins + (2) dilated venae commitantes of vagus nerve outside tunica muscularis
◊ Most common and clinically important collateral vessels of the intrathoracic portosystemic collateral system

Anatomy:
(a) anterior branch connected to left gastric vein
(b) posterior branch connected to azygos + hemiazygos system

Examination Technique:
(a) small amount of barium (not to obscure varices)
(b) relaxation of esophagus (not to compress varices): refrain from swallowing because succeeding swallow initiates a primary peristaltic wave that lasts for 10–30 seconds; sustained Valsalva maneuver precludes from swallowing
(c) in LAO projection with patient recumbent / in Trendelenburg position ± Valsalva maneuver / deep inspiration

Location: lower esophagus

Plain film:
√ lobulated masses in posterior mediastinum (visible in 5–8% of patients with varices)
√ silhouetting of descending aorta
√ abnormal convex contour of azygoesophageal recess at level of gastroesophageal junction

UGI:
√ thickened sinuous interrupted mucosal folds (earliest sign)
√ tortuous radiolucencies of variable size + location
√ "worm-eaten" smooth lobulated filling defects
√ findings may be accentuated after sclerotherapy

CT (> 90% detection rate):
√ nodular thickening of esophageal wall + lobulated outer contour
√ scalloped enhancing nodular masses protruding into esophageal lumen
√ right- / left-sided soft-tissue masses (= paraesophageal varices)
√ marked enhancement following dynamic CT

Cx: variceal hemorrhage at a rate of 10–30% per year; 20–35% mortality with exsanguination in 10–15%

DDx: varicoid carcinoma of esophagus

Uphill Esophageal Varices

= collateral blood flow from portal vein → azygos vein → into SVC (usually lower esophagus drains via left gastric vein into portal vein)

Cause:
(a) intrahepatic obstruction from cirrhosis
◊ In < 5% of patients with portal hypertension
(b) splenic vein thrombosis (usually gastric varices)
(c) obstruction of hepatic veins
(d) IVC obstruction below hepatic veins
(e) IVC obstruction above hepatic vein entrance / CHF
(f) marked splenomegaly / splenic hemangiomatosis (rare)
√ varices in lower ½ of esophagus

Downhill Esophageal Varices

= collateral blood flow from SVC → azygos vein → into IVC / portal venous system (upper esophagus usually drains via azygos vein into SVC)
Cause: obstruction of superior vena cava distal to entry of azygos vein (= superior vena cava syndrome) most commonly due to lung cancer, lymphoma, retrosternal goiter, thymoma, mediastinal fibrosis
√ varices in upper ⅓ of esophagus

Paraesophageal Varices

= part of intrathoracic portosystemic collateral network
• endoscopically not visible
◊ NOT connected to esophageal varices!
Anatomy: supplied by posterior branch of coronary (= left gastric) vein draining into azygos + hemiazygos vv. + vertebral plexus
May be associated with: subcutaneous collateral vessels in chest wall
CXR:
√ lateral bulging of paraspinal interfaces with obliteration of azygoesophageal recess + descending thoracic aortic interface (in 5–8%)
CT:
√ dilated collateral vessels surrounding esophagus + descending thoracic aorta

Cardiophrenic Angle Varices

= dilated pericardiophrenic veins mimicking a tumor
Cause: membranous obstruction of IVC (frequent in cirrhosis)
CXR:
√ undulating masses along cardiac borders
√ widening of both paraspinal interfaces
CECT:
√ enhancing pseudotumor (vascular nature)

ESOPHAGEAL WEB

= complete / incomplete circumferential narrowing caused by 1–2-mm thick (vertical length) shelf-like filling defect projecting into esophageal lumen
Age: middle-aged females
? Association with:

Plummer-Vinson syndrome = Paterson-Kelly syndrome (iron deficiency anemia, stomatitis, glossitis, dysphagia, thyroid disorder, spoon-shaped nails), benign mucous membrane pemphigoid, epidermolysis bullosa dystrophica, GERD

Cause:

mnemonic: BIEP

B-ring (Schatzki ring)
Idiopathic (= symptomatic transverse mucosal fold)
Epidermolysis bullosa
Plummer-Vinson disease

Path: hyperkeratosis + chronic inflammation of submucosa

Histo: mucosal membrane covered by squamous epithelium on superior + inferior surfaces

• mostly asymptomatic (unless severely stenosing)

Location: in cervical esophagus near cricopharyngeus (most common) > thoracic esophagus at squamocolumnar junction of distal esophagus (Schatzki) > lower hypopharynx; occasionally multiple

Site: often anteriorly located

√ visualized during maximal distension (in $^{1}/_{10}$ of a second)

√ arises at right angles from anterior esophageal wall

√ thin delicate membrane of uniform thickness of < 3 mm

Cx: high risk of upper esophageal + hypopharyngeal (postcricoid) carcinoma

Rx: (1) Balloon dilatation
(2) Bougienage during esophagoscopy

DDx: Stricture (circumferential + thicker > 1–2-mm thick [vertical length] area of complete / incomplete circumferential narrowing)

ESOPHAGITIS

Acute Esophagitis

Cause:

mnemonic: CRIER

Corrosives, **C**rohn disease
Reflux
Infection, **I**ntubation
Epidermolysis bullosa
Radiation therapy

√ thickened > 3-mm wide folds with irregular lobulated contour

√ mucosal nodularity ← multiple ulcers + intervening edema

√ erosions

√ vertically oriented ulcers usually 3–10 mm in length

√ inflammatory esophagogastric polyp = proximal gastric fold extending across esophagogastric junction (rare)

√ abnormal motility

CT:

√ diffuse esophageal thickening

√ submucosal edema
√ mucosal enhancement

Candida Esophagitis

= MONILIASIS = CANDIDIASIS

◊ Most common cause of infectious esophagitis!

Organism: C. albicans, C. tropicalis; endogenous (majority) / transmitted by another human / animal; often discovered in diseased skin, GI tract, sputum, female genital tract, urine with an indwelling Foley catheter

Predisposed:

(a) individuals with depressed immunity: hematologic disease, renal transplant, leukemia, chronic debilitating disease, diabetes mellitus, steroids, chemotherapy, AIDS, radiotherapy
◊ Most common type of fungi found with opportunistic infections!

(b) delayed esophageal emptying: scleroderma, strictures, achalasia, S/P fundoplication

(c) antibiotics

Path: patchy, creamy-white plaques covering a friable erythematous mucosa

Histo: mucosal plaques = necrotic epithelial debris + fungal colonies

- severe odynophagia (= painful swallowing from segmental spasm); dysphagia (= difficulty swallowing)
- intense retro- / substernal pain
- associated with thrush (= oropharyngeal moniliasis) in 20–50–80%

Location: predilection for upper ½ of esophagus

√ involvement of long esophageal segments:
√ "cobblestone" appearance = mucosal nodularity in early stage ← growth of colonies on surface
√ longitudinal plaques = grouping of tiny 1–2-mm nodular filling defects with linear orientation (= heaped-up areas of mucosal plaques)
√ shaggy / fuzzy / serrated contour ← coalescent plaques, pseudomembranes, erosions, ulcerations, intramural hemorrhage) in fulminant candidiasis of AIDS

√ narrowed lumen ← spasm, pseudomembranes, marked edema
√ "intramural diverticulosis" = multiple tiny indentations + protrusions
√ sluggish / absent primary peristalsis
√ strictures (rare)
√ mycetoma resembling large intraluminal tumor (rare)

Diagnostic sensitivity: endoscopy (97%), double contrast (88%), single contrast (55%)

Cx: (1) Systemic candidiasis ("microabscesses" in liver, spleen, kidney)
(2) Gastric bezoar ← large fungus ball (after long-standing esophageal candidiasis)

Rx: ketoconazole / fluconazole

DDx: glycogen acanthosis, reflux esophagitis, superficial spreading carcinoma, artifacts (undissolved effervescent crystals, air bubbles, retained food particles), herpes esophagitis, acute caustic ingestion, intramural pseudo-diverticulosis, squamous papillomatosis, Barrett esophagus, epidermolysis bullosa, varices

Caustic Esophagitis

= CORROSIVE ESOPHAGITIS

Corrosive agents: [= strong acids or strong bases]
hydrochloric acid, lye (sodium hydroxide), washing soda (sodium carbonate), household cleaners, iodine, silver nitrate, household bleaches, Clinitest® tablets (tend to be neutralized by gastric acid)

◊ Severity of injury dependent on contact time + concentration of corrosive material!

Associated with: injury to pharynx + stomach (7–8%): antral burns more common with acid (buffering effect of gastric acid on alkali)

Location: middle + lower thirds of esophagus

Stage I : acute necrosis from protein coagulation
- √ mucosal blurring (edema)
- √ diffusely atonic + dilated esophagus
- √ tertiary contractions / spasm

Stage II : frank ulceration in 3–5 days
- √ ulceration + pseudomembranes

Stage III : scarring + stricture from fibroblastic activity
- √ long segmental stricture after 10 days when acute edema subsides (7–30%)
- √ one / more strictures usually 1–3 months after initial injury in unpredictable location
- √ entire esophagus reduced to filiform structure

Cx: (1) Esophageal / gastric perforation during ulcerative stage
(2) Squamous cell carcinoma in injured segment

Rx: dilatation procedure / esophageal replacement surgery

Chronic Esophagitis

√ luminal narrowing with tapered transition to normal + proximal dilatation
√ circumferential / eccentric stricture
√ sacculations = pseudodiverticula

Drug-induced Esophagitis

= contact esophagitis ← oral medications = "pill esophagitis"

Agents: potassium chloride, antibiotics (tetracycline, doxycycline), quinidine, nonsteroidal antiinflammatory agents (aspirin), ascorbic acid, ferrous sulfate ($FeSO_4$), alprenolol chloride, emepronium bromide, alendronate (= inhibitor of osteoclastic activity)

Esophageal injury is usually caustic ← drug's chemical reaction upon direct contact with the esophageal mucosa:
(a) Antibiotics (doxycycline, tetracycline) are acidic resulting in a chemical mucosal burn
(b) Ferrous sulfate and potassium chloride cause injury ← hyperosmolarity + changes in local blood flow

Histo: inflammatory changes + granulation tissue; sometimes with foreign material ± dyskeratotic cells indicative of apoptosis of squamous epithelial cells

- history of taking medication with little / no water immediately before going to bed; severe odynophagia

• rapid clinical improvement after withdrawal of offending agent

Location: midesophagus at site of normal extrinsic impressions by aortic arch / left mainstem bronchus / left atrium

Esophagram:

√ single ulcer / localized cluster of multiple tiny ulcers (more common) distributed circumferentially:

√ EN FACE: central punctate collections of barium surrounded by a radiolucent halo (= mound of edema)

√ IN PROFILE: elongated flat plaquelike filling defects

√ superficial solitary / several discrete ulcers with sharply delineated margins with commonly normal surrounding mucosa

CT:

√ ulcers may be invisible

Esophageal ulcers induced by medications are frequently small and discrete often corresponding to the direct site of contact.

Prognosis: ulcers heal within 7–10 days after cessation of offending medication

DDx: herpes esophagitis (immunosuppressed patient, less localized); reflux esophagitis (heartburn, distal esophagus near GE junction); Crohn esophagitis

Reflux Esophagitis

= esophageal inflammation ← reflux of acid-peptic contents of the stomach

Prevalence: in 20% of gastroesophageal reflux

Pathophysiology: reflux occurs if resting pressure of LES < 5 mmHg (may be normal event if followed by rapid clearing)

Histo: basal cell hyperplasia with wall thickening + thinning of epithelium, mucosal edema + erosions, inflammatory infiltrate

Determinants: (1) Frequency of reflux
(2) Adequacy of clearing mechanism
(3) Volume of refluxed material
(4) Potency of refluxed material
(5) Tissue resistance

Reflux preventing features:

(1) Lower esophageal sphincter
(2) Phrenoesophageal membrane
(3) Length of subdiaphragmatic esophagus
(4) Gastroesophageal angle of His (70–110°)

May be associated with: sliding hiatal hernia (in > 90%), scleroderma, nasogastric intubation

• heartburn, epigastric discomfort, choking, globus hystericus

• retrosternal pain, thoracic / cervical dysphagia

Site: usually lower ⅓ to lower ½ with continuous disease extending proximally from GE junction

Length: usually 1–4 cm

Consider a malignant tumor when a distal esophageal stricture is present in the absence of a hernia!

√ initial esophageal insult:
√ smooth tapered segment of concentric esophageal narrowing ← edema / spasm / stricture
√ poorly defined tiny mucosal elevations ("mucosal granularity") on thickened / nodular longitudinal folds in early stages ← mucosal edema + inflammation
√ single marginal ulcer / erosion at / adjacent to GE junction
√ multiple areas of superficial ulceration in distal esophagus
√ prominent mucosal fold ending in polypoid protuberance within hiatal hernia / cardia

› effect of secondary esophageal scarring:
√ asymmetric narrowing ← asymmetric scarring
√ 1 to 2 sacculations ← outward ballooning of esophageal wall between areas of fibrosis (DDx: ulcer)
√ "felinization" = "stepladder" appearance of longitudinal scarring = fixed transverse ridges with barium trapped in between (DDx: "feline" esophagus)
√ focal cluster of intramural pseudodiverticula
√ very short segment of ringlike narrowing at the GE junction above a hiatal hernia (DDx: Schatzki ring)

› effect on esophageal function:
√ interruption of primary peristalsis at inflamed segment
√ nonperistaltic waves in distal esophagus following deglutition (85%)
√ incomplete relaxation of LES (75%), incompetent sphincter (33%)
√ acid test = abnormal motility elicited by acid barium (pH 1.7)

NUC (pertechnetate):
√ esophageal activity ← Barrett esophagus activity similar to ectopic gastric mucosa

Reflux tests:

1. **Reflux of barium** in RPO position, may be elicited by coughing / deep respiratory movements / swallowing of saliva + water / anteflexion in erect position: only in 50% accurate
2. **Water-siphon test**: in 5% false negative; large number of false positives
3. **Tuttle test** = measurement of esophageal pH: 96% accurate
4. **Radionuclide gastroesophageal reflux test** (typically combined with gastric emptying test):
   Technique: ROI drawn over distal esophagus + compared with time-activity curve over stomach, scaled to 4%
   √ esophageal activity > 4% stomach activity

Cx of reflux:

(a) from acid + pepsin acting on esophageal mucosa:
   1. Motility disturbance
   2. Stricture
   3. Schatzki ring
   4. Barrett esophagus
   5. Iron-deficiency anemia
   6. Reflux / peptic esophagitis

(b) from aspiration of gastric contents

1. Acute aspiration pneumonia
2. Mendelson syndrome
3. Pulmonary fibrosis

Viral Esophagitis

Predisposed: immunocompromised, eg, underlying malignancy, debilitating illness, radiation treatment, steroids, chemotherapy, AIDS

Cytomegalovirus Esophagitis

Organism: member of herpesvirus group
Associated with: AIDS
• severe odynophagia
√ diffusely normal mucosal background
√ one / more giant ovoid flat ulcers (up to several cm in size) near gastroesophageal junction
√ discrete small superficial ulcers indistinguishable from herpes esophagitis (uncommon)
Rx: ganciclovir (relatively toxic)
Dx: endoscopic brushings, biopsy specimen, cultures

Herpes Esophagitis

◊ 2nd most common cause of opportunistic infection!
Organism: Herpes simplex virus type I (DNA core virus) secreted in saliva of 2% of healthy population
Age: 15–30 years; usually males
Predisposed: immunocompromised patient with HIV, organ transplant, and on chemotherapy; may occur in immunocompetent patient
• history of recent exposure to sexual partners with herpetic lesions on lips / buccal mucosa
• flulike prodrome of 3–10 days (headaches, fever, sore throat, upper respiratory symptoms, myalgia)
• severe acute dysphagia / odynophagia
May be associated with: oropharyngeal herpetic lesions / oropharyngeal candidiasis
Location: midesophagus (level of left main bronchus)
√ initially vesicles / blisters that subsequently rupture
√ multiple small discrete superficial punctate / round / linear / serpentine / stellate (often "diamond-shaped") punched-out ulcers surrounded by radiolucent halo of edematous mucosa (in > 50%)
√ intervening mucosa normal (without plaques)
√ multiple plaquelike lesions (only with severe infection)
Dx: rising serum titer for HSV type I, viral culture, biopsy (immunofluorescent staining for HSV antigen, demonstration of intranuclear inclusions)
Rx: oral / intravenous acyclovir
Prognosis: resolution of symptoms in 3–14 days
DDx: drug-induced esophagitis, Crohn disease, esophageal intramural pseudodiverticulosis

Human Immunodeficiency Virus Esophagitis

- maculopapular rash + ulcers of soft palate (occasionally)
- recent seroconversion / known AIDS

√ one / more giant (> 1 cm) flat ovoid / diamond-shaped ulcers (at time of seroconversion) indistinguishable from CMV esophagitis

Dx: per exclusion (brushings, biopsies, cultures negative for CMV)

Rx: oral steroids

DDx: CMV esophagitis, mycobacterial esophagitis, actinomycosis, potassium chloride, quinidine, caustic ingestion, nasogastric intubation, radiation therapy, endoscopic sclerotherapy

FAMILIAL ADENOMATOUS POLYPOSIS

= FAMILIAL MULTIPLE POLYPOSIS

Frequency: 1÷7,000 to 1÷24,000 live births

Genetics: autosomal dominant disease with 80% penetrance; gene localized on chromosome 5; sporadic occurrence in ⅓

Path: tubular / villotubular adenomatous polyps; usually about 1,000 adenomas

Age: polyps appear around puberty

- family history of colonic polyps (66%)
  - ◊ Screening of family members after puberty!
- clinical symptoms begin during 3rd–4th decade (range, 5–55 years)
- vague abdominal pain, weight loss, diarrhea, bloody stools
- protein-losing enteropathy (occasionally)

Associated with:

(1) Hamartomas of stomach in 49%

(2) Adenomas of duodenum in 25%

(3) Periampullary carcinoma

(4) Desmoid tumors in 9–18%: 1000 x fold increased risk; multiple desmoids in 40%

√ "carpet of polyps" = myriad of 2–3 mm (up to 2 cm) polypoid lesions

@ Colon (100%): more numerous in distal colon; always affecting rectum

√ normal haustral pattern

@ Stomach (5%)

@ Small bowel (< 5%)

Cx: malignant transformation of adenomas: colon > stomach > small bowel in 12% [30%] {100%} by 5 [10] {20} years after diagnosis; carcinomatous development usually at age 20–40 years; multiple carcinomas in 48%

- ◊ 331-fold increased risk of small bowel adenocarcinoma compared to general population after colectomy
- ◊ Periampullary carcinoma is the most common cause of death after prophylactic colectomy!

Rx: prophylactic total colectomy in late teens / early twenties before symptoms develop

(1) Permanent ileostomy

(2) Continent endorectal pull-through pouch

(3) Kock pouch (= distal ileum formed into a one-way valve by invaginating the bowel

at skin site)

DDx: other polyposes, lymphoid hyperplasia, lymphosarcoma, ulcerative colitis with inflammatory pseudopolyps

FIBROVASCULAR POLYP OF ESOPHAGUS

= HAMARTOMA = LIPOMA = FIBROMA = FIBROLIPOMA = FIBROMYXOMA = FIBROEPITHELIAL POLYP

= intraluminal esophageal polyp

Prevalence: 1–2% of benign esophageal tumors

Cause: over time enlarging loose submucosal tissue in Laimer triangle just inferior to cricopharyngeus

[Eduard Laimer (1857–1934), anatomist in Graz, Austria]

Path: elongated intraluminal mass of fibrous + adipose tissue of varying proportions covered by normal squamous epithelium

Age: 53 (range, 1–88) years; M > F

- dysphagia (69%), cough, respiratory distress
- regurgitation of polyp into mouth, foreign-body sensation

Site: near level of cricopharyngeus / lower hypopharynx

Size: 7 cm long at time of presentation extending inferiorly as far as into the stomach

Barium:

√ giant sausage-shaped intraluminal mass originating from cervical esophagus (pedicle usually not identified)

CT / MR:

√ heterogeneous mass with areas of soft-tissue and fat attenuation

√ ± punctate calcifications (occasionally)

The cross-sectional appearance of fibrovascular polyps depends on the proportions of fat and fibrous tissue.

Cx: asphyxia + sudden death ← after regurgitation of polyp into pharynx / mouth

Rx: surgical removal (10% recurrence)

FOREIGN BODY INGESTION

Cause:

(a) accidental: patients with altered mental status / dentures

(b) nonaccidental: "body packing" to smuggle illicit drugs (swallowed, inserted into vagina / rectum)

- pain, excessive salivation, cough, difficulty breathing
- nausea, vomiting

Type:

(a) NONDIGESTABLE FOOD COMPONENT: fish / chicken bone, toothpick

(b) HIGH-DENSITY DEVICE: coin, toy, key, battery, jewelry, pin, needle, nail, razor blade, clip, denture, dislodged tooth, crown

Location of intraluminal lodgement:

esophagus (68%), stomach (11.6%), small bowel (3.3%), colon (11.6%)

› trapped in appendix, diverticula, proximal to stricture: calcified seeds + pits, birdshot

CT:

√ wood difficult to recognize:
√ air attenuation in acute phase mimicking bubbles of gas
√ becoming progressively isoattenuating in subacute phase
√ hyperattenuating ← granulomatous reaction
√ calcified in chronic phase
√ ± pneumoperitoneum (rare ← progressive impaction of foreign body in intestinal wall surrounded by fibrin. omentum, bowel loops that prevent leakage of gas)

Cx: (1) Perforation(< 1%): fish / chicken bone, toothpick
Location: predominantly in ileocecal region, rectosigmoid, areas of bowel narrowing, angulation, pouching, diverticula, adhesions, surgical anastomosis
(2) Toxic effect / liquefaction necrosis: button battery
◊ Any battery lodged in esophagus should be removed promptly!

Rx: most foreign bodies are amenable to endoscopic removal

GALLSTONE ILEUS

[misnomer: mechanical obstruction, not ileus]

Frequency: 0.4–5.0% of all intestinal obstructions ← risk increases with age = 20% [24%] of obstruction in patients > 65 [> 70] years; in 1 of 6 perforations; develops in 0.3–0.5% of patients with cholelithiasis

Etiology: biliary disease (90%), peptic ulcer disease, cancer, trauma
◊ Most eroded gallstones are excreted uneventfully!

Mechanism: cholecystoenteric fistula / following endoscopic sphincterotomy

Age: average 65–75 years; M÷F = 1÷4 – 1÷7

- previous history of gallbladder disease
- intermittent episodes of acute colicky abdominal pain (20–30%)
- nausea, vomiting, fever, distension, obstipation

Location: terminal ileum (60%), proximal ileum / distal jejunum (26%), distal ileum (10%), sigmoid colon

The most obstructive gallstones are > 2.5 cm in diameter and located in ileum (60%) / jejunum (26%). The terminal ileum is the narrowest segment and thus the most likely site of obstruction.

√ **Rigler triad** on plain film (in 15%), on CT (in 78%):
1. Partial / complete intestinal obstruction (usually in small bowel), "string of rosary beads" = multiple small amounts of air trapped between dilated + stretched valvulae conniventes (in 86%)
2. Pneumobilia (in 69%)
3. Ectopic calcified gallstone in lower abdomen (in 25%): stones are commonly > 2.5 cm in diameter

√ change in position of previously identified gallstone

UGI / BE:
√ smooth polypoid filling defect (= gallstone) at site of obstruction
√ well-contained localized barium collection lateral to first portion of duodenum (barium-filled collapsed GB + possibly biliary ducts)

Fistulous communication:
cholecystoduodenal (60%), choledochoduodenal, cholecystocolic, choledochocolic, cholecystogastric

CT (91% sensitive):
√ air / enteric contrast in GB (fistula from GB to duodenum)
√ thickened duodenal wall
√ gallstone at transition point of bowel obstruction

Cx: recurrent gallstone ileus in 5–10% (additional silent calculi more proximally)

Rx: removal of stone(s) + cholecystectomy + fistula repair

Prognosis: high mortality of up to 18%

Bouveret Syndrome

[Léon Bouveret (1850–1929), French internist in Lyon]

= gastric outlet obstruction ← impacted gallstone in duodenum / pylorus ← cholecystoenteric fistula

Age: most commonly in elderly woman

• nausea, vomiting, epigastric pain

CT:
√ obstructing ectopic gallstone in distal stomach / duodenum
√ air in gallbladder / biliary tree

Mortality rate: 12–33%

GANGLIOCYTIC PARAGANGLIOMA

= rare benign tumor of the GI tract

Frequency: < 100 cases reported

Origin: pancreatic endocrine rest that remained when the ventral primordium rotated around the duodenum

Age: 50–60 years of age; M÷F = 2÷1

Location: almost exclusively in 2nd portion of duodenum near ampulla of Vater on medial / lateral wall of duodenum

• GI hemorrhage, abdominal pain

√ polypoid smooth-surfaced intraluminal mass
√ homogeneously enhancing mural / extrinsic solid mass of soft-tissue attenuation
√ well-circumscribed hypoechoic mass contiguous with bowel
√ no biliary duct dilatation

DDx: adenocarcinoma (biliary duct dilatation, hypovascular), leiomyosarcoma (cystic internal hemorrhage / necrosis), hemangioma, duplication cyst, choledochal cyst, lipoma, hamartoma, inflammatory fibroid polyp (distal small bowel), lymphoma (isolated in stomach and ileum)

GARDNER SYNDROME

[Eldon John Gardner (1909–1989), geneticist at Utah State University in Logan, Utah]

= autosomal dominant disease with variable penetrance as a variant of familial adenomatous polyposis characterized by a triad of

(1) Colorectal polyposis
(2) Osteomas
(3) Soft-tissue tumors

Incidence: 1÷14,000

Cause: mutation in tumor suppressor gene APC (adenomatous polyposis coli gene) on chromosome 5q21 to 5q22; in 20% new mutation
◊ Familial polyposis + Gardner syndrome may occur in the same family!

Histo: adenomatous polyps → malignant transformation

Age: 15–30 years (range, 2 months – 70 years)

Average life expectancy: 35–40 years

Associated with: ? MEA complex
(1) Periampullary / duodenal carcinoma (12%)
(2) Papillary thyroid carcinoma: often multicentric
(3) Adrenal adenoma / carcinoma
(4) Parathyroid adenoma
(5) Pituitary chromophobe adenoma
(6) Pancreatic neoplasm (4 x of general population)
(7) Hepatoblastoma (800 x of general population)
(8) Hepatocellular carcinoma
(9) Carcinoid, adenoma of small bowel
(10) Nasal angiofibroma
(11) Retroperitoneal leiomyoma
◊ Lifelong screening for malignancies!

◊ Extraintestinal manifestations occur usually earlier than in intestinal polyposis!

• skin pigmentation
• cramping abdominal pain, weight loss, diarrhea

@ Polyposis
Location: colon (100%), stomach (5–68%), duodenum (90%), ampulla of Vater, small bowel (< 5%)
√ multiple colonic polyps appearing during puberty, increasing in number during 3rd–4th decade
√ lymphoid hyperplasia of terminal ileum
√ hamartomas of stomach
√ intussusception
Cx: small bowel / colonic obstruction; malignant transformation

@ Soft-tissue tumors
(a) sebaceous / epidermoid inclusion cysts: scalp, back, face, extremities
(b) fibroma, lipoma, leiomyoma, neurofibroma
(c) **desmoid tumors** (3–10–34%)
Location: abdominal wall; extra- / intraabdominal
◊ Tend to occur after colectomy
√ peritoneal adhesions ← desmoplastic tendency
√ mesenteric fibrosis, retroperitoneal fibrosis
• urinary tract obstruction, bowel obstruction
Prognosis: frequent recurrence (⅓) after resection / radiation therapy

(d) mammary fibromatosis
(e) marked keloid formation, hypertrophied scars (anterior abdominal wall) arise 1–3 years after surgery

@ Osteomatosis of membranous bone (50%)
Location: calvarium, mandible (81%), maxilla, ribs, long bones

@ Long bones
Location of osteomas: paranasal sinuses; outer table of skull (frequent); mandible (at angle)
√ slight shortening + bowing
√ endosteal cortical thickening
√ may have solid periosteal cortical thickening
√ wavy cortical thickening of superior aspect of ribs
√ osteomas / exostoses may protrude from periosteal surface

@ Teeth
√ odontoma, unerupted / supernumerary teeth, hypercementosis
√ tendency toward numerous caries → dental prosthesis at early age

Cx: malignant transformation of colonic polyps in 100% (average age at death is 41 years if untreated); high incidence of carcinoma of duodenum / ampulla of Vater

Prophylaxis: gastrointestinal surveillance, thyroid screening, ophthalmologic evaluation for retinal pigmentation anomalies; screening of family members starting at age 15

Rx: prophylactic total colectomy at about 20 years of age

GASTRIC CARCINOMA

◊ 4th most common cancer worldwide (most prevalent malignancy in Korea, China, Japan), 6th leading cause of cancer deaths

Prevalence: declining with 24,000 cases annually in USA

Risk factors: smoking, nitrites, nitrates, pickled vegetables

Predisposing factors:
H. pylori gastritis, chronic atrophic gastritis, adenomatous + villous polyp (7–27% are malignant), gastrojejunostomy, partial gastrectomy (Billroth II > Billroth I), pernicious anemia (risk factor of 2), Ménétrier disease (?)

Histo: adenocarcinoma (95%); rarely squamous cell carcinoma / adenoacanthoma

Staging (American Joint Committee on Cancer):

T1	tumor invades lamina propria / submucosa
T2	tumor invades muscularis propria / subserosa
T3	tumor penetrates serosa (= visceral peritoneum)
T4a	invasion of adjacent contiguous tissues
T4b	invasion of adjacent organs, diaphragm, abdominal wall
N1	involvement of 1–6 perigastric nodes within 3 cm of primary along greater / lesser curvature
N2	involvement of 7–15 regional nodes > 3 cm from primary along branches of celiac axis
N3	> 15 paraaortic, hepatoduodenal, retropancreatic, mesenteric nodes

M1 distant metastases

◊ Endoscopic US is the most reliable method for T staging with a diagnostic rate of 78%–93%!

Location: mostly distal third of stomach + cardia; 60% on lesser curvature, 10% on greater curvature; esophagogastric junction in 30%; transpyloric spread in 5–25% (for lymphoma 40%)

Probability of malignancy of an ulcer:
at lesser curvature 10–15%, at greater curvature 70%, in fundus 90%

Morphology:

1. Polypoid / fungating carcinoma
2. Ulcerating / penetrating carcinoma (70%)
3. Infiltrating / scirrhous carcinoma (5–15%) = linitis plastica
   Histo: frequently signet ring cell type + increase in fibrous tissue
   Location: antrum, fundus + body (38%)
   √ firmness, rigidity, reduced capacity of stomach, aperistalsis in involved area
   √ granular / polypoid folds with encircling growth
4. Superficial spreading carcinoma
   = confined to mucosa / submucosa; 5-year survival of 90%
   √ patch of nodularity
   √ little loss of elasticity
5. Advanced bulky carcinoma

The depth of mural invasion and presence of extragastric lesions can be determined with endoscopic US and CT.

• GI bleeding, abdominal pain, weight loss

UGI:
√ rigidity
√ filling defect
√ amputation of folds ± ulceration ± stenosis
√ miliary / punctate calcifications ← mucinous adenocarcinoma

CT:
√ irregular nodular luminal surface
√ asymmetric thickening of folds
√ mass of uniform density / varying attenuation
√ wall thickness > 6 mm (with gas distension) and 13 mm (with positive contrast material distension):
  √ diffuse low attenuation in mucinous carcinoma
√ increased density in perigastric fat
√ enhancement exclusively in linitis plastica type
√ nodules of serosal surface ← dilated surface lymphatics
√ diameter of esophagus at gastroesophageal junction larger than adjacent aorta (DDx: hiatal hernia)
√ lymphadenopathy below level of renal pedicle (3%)

Metastases:

1. Direct invasion: along peritoneal ligaments

(a) gastrocolic lig.: transverse colon, pancreas
(b) gastrohepatic + hepatoduodenal ligament: liver

2. Lymphatic: to local lymph nodes
   √ short-axis diameter of 8–10 mm
   √ nearly round shape
   √ central necrosis
   √ marked / heterogeneous enhancement
3. Hematogenous: to liver (most common), adrenals, ovary, bone (1.8%), lymphangitic carcinomatosis of lung (rare)
4. Peritoneal seeding
   › on rectal wall = **Blumer shelf**
   [George Blumer (1872–1962), surgeon at Albany Medical College, Cooper Medical College, University of California Medical School, Yale University]
   › on ovaries = **Krukenberg tumor**
   [Friedrich Ernst Krukenberg (1871–1946), thesis of doctorate on peculiar ovarian tumors, ophthalmologist in Halle, Germany]
5. left supraclavicular lymph node = **Virchow node**
   [Rudolph Carl Virchow (1821–1902), chair of pathology at university of Würzburg and Charité Hospital in Berlin, Germany, editor of Archiv für pathologische Anatomie und Physiologie und für klinische Medizin]

Prognosis: mean survival time of 7–8 months
- › 85% 5-year survival in stage T1
- › 52% 5-year survival in stage T2
- › 47% 5-year survival in stage T3
- › 17% 5-year survival in stage N1-2
- › 5% 5-year survival in stage N3

Early Gastric Cancer (20%)

= invasion limited to mucosa + submucosa (T1 lesion) regardless of lymph node involvement

Classification of Japan Research Society for Gastric Cancer:

Type	I	protruded type = > 5 mm in height with protrusion into gastric lumen (10–20%)
Type	II	superficial type = < 5 mm in height
	IIa	slightly elevated surface (10–20%)
	IIb	flat / almost unrecognizable (2%)
	IIc	slightly depressed surface (50–60%)
Type	III	excavated / ulcerated type (5–10%)

Prognosis: 5-year survival rate of 85–100%

Advanced Gastric Cancer (T2 lesion and higher)

Bormann classification:

Type 1 broad-based elevated polypoid lesion
Type 2 elevated lesion + ulceration + well-demarcated margin
Type 3 elevated lesion + ulceration + ill-defined margin

Type 4 ill-defined flat lesion
Type 5 unclassified, no apparent elevation

Prognosis: 5-year survival rate of 7–27%

Cx: perforation

GASTRIC DIVERTICULUM

◊ stomach is the least common site of diverticula
Frequency: 1÷600 to 1÷2,400 of UGI studies
Etiology: (a) traction ← scarring / periantral inflammation = true diverticulum
(b) pulsion (less common) = false diverticulum
Age: beyond 40 years
Often associated with: aberrant pancreas in antral location
Location: juxtacardiac on posterior wall (75%), prepyloric (15–22%), greater curve (3%)
√ pliability + varying degrees of distension
√ NO mass, edema or rigidity of adjacent folds
DDx: small ulcer in intramural-extramucosal mass

GASTRIC POLYP

Frequency: 1.5–5%, most common benign gastric tumor
Associated with: hyperacidity + ulcers, chronic atrophic gastritis, gastric carcinoma
A. NONNEOPLASTIC
1. **Inflammatory polyp of stomach** (75–90%)
= HYPERPLASTIC POLYP = REGENERATIVE POLYP
Histo: cystically dilated glands lined by gastric epithelium + acute and chronic inflammatory infiltrates in lamina propria
Associated with: chronic atrophic gastritis, pernicious anemia
Location: predominantly in fundus + body; usually multiple
√ sharply delineated polyp with smooth circular border
√ "Mexican hat" sign = stalk seen en face overlying the head of polyp
√ sessile / pedunculated
√ usually < 2 cm in diameter without progression
√ no contour defect of stomach
Prognosis: no malignant potential
2. **Hamartomatous polyp of stomach** (rare)
Histo: densely packed gastric glands + bundles of smooth muscle
Associated with: Peutz-Jeghers syndrome
√ sessile / pedunculated
√ usually < 2 cm in diameter
3. **Retention polyp of stomach** (rare)
Histo: dilated cystic glands + stroma
Associated with: Cronkhite-Canada syndrome
B. NEOPLASTIC
1. **Adenomatous polyp of stomach** (10–20%)
= true neoplasm with malignant potential (10–80%, increasing with size)
Age: increasing incidence with age; M÷F = 2÷1
Histo: intestinal metaplasia (common) + marked cellular atypism
Associated with: Gardner syndrome; coexistent with gastric carcinoma in 35%
Location: more commonly in antrum (antrum spared in Gardner syndrome)

√ broad-based elliptical / mushroom-shaped polyp ± pedicle; usually solitary
√ usually > 2 cm in diameter (in 80%)
√ smooth / irregular lobulated contour

2. **Villous polyp of stomach** (rare)
√ trabeculated / lobulated slightly irregular contour
Cx: malignant transformation

DDx: (1) Ménétrier disease (antrum spared)
(2) Eosinophilic polyp (peripheral eosinophilia, linitis plastica appearance, small bowel changes)
(3) Lymphoma
(4) Carcinoma

GASTRIC ULCER

Benign Gastric Ulcer (95%)

Cause:

A. HORMONAL
1. Zollinger-Ellison syndrome
2. Hyperparathyroidism (in 1.3–24.0%)
duodenum÷stomach = 4÷1; M÷F = 3÷1
◊ Duodenal ulcers predominate in females!
◊ Gastric ulcers predominate in males!
• absence of gastric hypersecretion
3. Steroid-induced ulcer
gastric > duodenal location; frequently multiple + deep ulcers; commonly associated with erosions
• bleeding (in ⅓)
4. Stress, severe prolonged illness
5. Cerebral disease = Cushing ulcer
6. Curling ulcer (burns) (in 0.09–2.60%)
7. Retained gastric antrum
8. Uremia

B. INFLAMMATION
1. Peptic ulcer disease
2. Gastritis
3. Radiation-induced ulcer
4. Intubation
5. Stasis ulcer proximal to pyloric / duodenal obstruction

C. BENIGN MASS
1. Leiomyoma
2. Granulomatous disease
3. Pseudolymphoma (lymphoid hyperplasia)

D. DRUGS
ASA: greater curvature

Pathophysiology: disrupted mucosal barrier (H. pylori) with vulnerability to acid + secretion of large volume of gastric juice containing little acid

Incidence: 5÷10,000; 100,000 annually (USA)

Age peak: 55–65 years; M÷F = 1÷1

Multiplicity:

(a) multiple in 2–8% (17–24% at autopsy), especially in patients on aspirin

(b) coexistent duodenal ulcer in 5–64%; gastric÷duodenal = 1÷3 [1÷7] in adults [children]

• abdominal pain: in 30% at night, 25% precipitated by food

Location: lesser curvature at junction of corpus + antrum within 7 cm from pylorus; proximal half of stomach in older patients (geriatric ulcer); adjacent to GE junction within hiatal hernia

√ ulcer size usually < 2 cm (range 1–250 mm); in 4% > 4 cm

√ round / ovoid / linear shape

√ **Haudek niche** = conical / collar button-shaped barium collection projecting outside gastric contour (profile view)

√ **Hampton line** = 1-mm thin straight lucent line traversing the orifice of the ulcer niche (seen on profile view + with little gastric distension) = ledge of touching overhanging gastric mucosa of undermined benign ulcer

√ ulcer collar = smooth thick lucent band interposed between the niche and gastric lumen ← thickened rim of edematous gastric wall in well-distended stomach

√ ulcer mound = smooth, sharply delineated, gently sloping extensive tissue mass surrounding a benign ulcer ← edema + lack of wall distensibility in well-distended stomach

√ ulcer crater = round / oval barium collection with smooth border on dependent side (viewed en face)

√ halo defect = wide lucent band symmetrically surrounding ulcer ← extensive ulcer mound (viewed en face)

√ ring shadow: ulcer on nondependent side (en face view)

√ radiating thick folds extending directly to crater edge fusing with effaced marginal fold of ulcer collar / halo of ulcer mound

√ incisura defect = smooth, deep, narrow, sharp indentation on greater curvature opposite a niche on lesser curvature at / slightly below the level of the ulcer ← spastic contraction of circular muscle fibers

Prognosis: healing in 50% by 3 weeks, in 100% by 6–8 weeks; slower healing in older patients; only complete healing proves benignancy

Cx: (1) Bleeding

(2) Perforated ulcer

(a) anterior wall / curvatures → into peritoneal space

(b) posterior wall → into lesser sac

√ free intraperitoneal fluid / gas

√ extraluminal oral contrast material

√ wall discontinuity

(3) Fistula

◊ Most common cause of gastrocolic fistula!

Benign Postbulbar Peptic Ulcer *(10%)*

Cause: Helicobacter pylori infection

Age: adulthood; M÷F = 7÷1

Site: majority on medial wall of proximal descending duodenum (upper 2nd portion above major papilla of Vater)

- localized epigastric pain 2–4 hours after meal
- hemorrhage in 66%

√ edema + spasm may obscure ulcer

√ smooth rounded indentation of lateral wall

√ incisura pointing to ulcer

√ occasionally barium reflux into common bile duct

√ ring stricture

√ stress- and drug-induced ulcers heal without deformity

Malignant Gastric Ulcer (5%)

Cause:

1. Gastric carcinoma
2. Lymphoma (2% of all gastric neoplasms)
   √ multiple ulcers with aneurysmal appearance
3. Leiomyosarcoma, neurogenic sarcoma, fibrosarcoma, liposarcoma
4. Metastases
   (a) hematogenic: malignant melanoma, breast cancer, lung cancer
   (b) per continuum: pancreas, colon, kidney

Location: anywhere within stomach; fundal ulcers above level of cardia are usually malignant

√ ulcer location within gastric lumen, ie, not projecting beyond expected margin of stomach (profile view)

√ eccentrically located ulcer within the tumor

√ irregularly shaped ulcer

√ shallow ulcer with width greater than depth

√ nodular ulcer floor

√ abrupt transition between normal mucosa + abnormal tissue at some distance (usually 2–4 cm) from ulcer edge

√ rolled / rounded / shouldered edges surrounding ulcer

√ nodular irregular folds approaching ulcer with fused / clubbed / amputated tips

√ rigidity / lack of distensibility

√ associated large irregular mass

√ **Carman "meniscus" sign** = lenticular barium collection in ulcer crater trapped by heaped up edges; convex relative to lumen on profile view under compression; found in specific type of ulcerating carcinoma, but seen only rarely

[Russell Daniel Carman (1875–1926), professor of radiology at St. Louis and Washington university and head of Mayo section on roentgenology in 1913, president of RSNA and ARRS]

√ **Kirklin meniscus complex** = Carman sign (appearance of crater) + radiolucent slightly elevated rolled border

Prognosis: partial healing may occur

Gastric Ulcer		
Sign	*Benign*	*Malignant*
Crater	round, ovoid	irregular
Radiating folds	symmetric	nodular, clubbed, fused
Areae gastricae	preserved	destroyed
Projection	outside lumen	inside lumen
Ulcer mound	smooth	rolled edge

GASTRIC VARICES

Cause: portal hypertension (varices seen in 2–78%); splenic vein obstruction ← pancreatitis, pancreatic carcinoma, pseudocyst

Location: (a) esophagogastric junction (most common)
(b) along lesser curvature (in 11–75% of patients with portal hypertension / cirrhosis)

Feeding vessels:

1. Left gastric vein (between splenic vein + stomach)
2. Short gastric veins (between spleen + fundus)
3. Retrogastric vein (between splenic vein + GE junction)

• increased prevalence of portosystemic encephalopathy
√ barium study (65–89% rate of detection):
√ lobulated folds / polypoid masses in fundus
√ endoscopy: most practical method
√ splenic portography
√ hepatofugal blood flow along SMV into left gastric + splenic vein

Cx: variceal bleeding in 3–10–36%
◊ Gastric varices bleed less frequently but more severely than esophageal varices!

DDx of small intramural subepithelial mass:
carcinoid tumor, glomus tumor, ectopic pancreas (all usually with stronger enhancement)

GASTRIC VOLVULUS

◊ SURGICAL EMERGENCY!
= abnormal torsion (twisting) of stomach, usually > 180° → complete obstruction → ischemia → perforation
◊ Use the term organoaxial / mesenteroaxial ***rotation*** if obstruction not present!

The term gastric volvulus implies at least 180° gastric rotation WITH gastric outlet obstruction. Organoaxial / mesenteroaxial rotation alone do not define volvulus. Coronal images are often more diagnostic than axial images alone.

Degrees of torsion:

(1) Partial / incomplete volvulus = chronic form (common)
= rotation of stomach < 180° without vascular compromise
• may be asymptomatic

√ ingested contrast may pass through stomach

(2) COMPLETE volvulus = acute form

= rotation of stomach > 180°

◊ Surgical emergency ← increased risk of ischemia, necrosis, perforation, shock

√ stomach becomes dilated + fills with fluid

√ oral contrast is retained in stomach

Etiology:

(a) abnormality of suspensory ligaments

(b) unusually long gastrohepatic + gastrocolic mesenteries

Anatomy of ligaments:

gastrohepatic lig. at lesser curvature; gastrosplenic + gastrocolic ligg. at greater curvature; gastrophrenic lig. at posterior fundus; attachment to esophagus at gastroesophageal junction; attachment to duodenum at pylorus

Predisposing factors:

paraesophageal hernia (33%), ligamentous laxity (sliding hernia), eventration of diaphragm, phrenic nerve paralysis, splenic abnormalities (asplenia, polysplenia, splenomegaly, prior splenectomy), Bochdalek hernia (in children)

Peak age: 40–50 years (in 20% in infants < 1 year of age); most often in elderly with hiatal hernia; M÷F = 1÷1

- may be acute / chronic-recurrent
- **Borchardt triad:**

[Moritz Borchardt (1868–1948), Chief Surgeon at the Rudolf-Virchow and Moabit Public Hospitals in Berlin]

- sudden onset of severe epigastric pain + distension
- intractable retching (= vigorous attempts to vomit) without production of vomitus
- inability to pass nasogastric tube into stomach

CXR:

√ massively distended stomach in LUQ extending into chest /retrocardiac location (= intrathoracic stomach)

√ unexpected location of stomach gas bubble

√ paucity of distal gas

√ air-fluid levels in mediastinum / upper abdomen

Esophagram:

√ incomplete / absent entrance of barium into stomach

√ displaced gastroesophageal junction

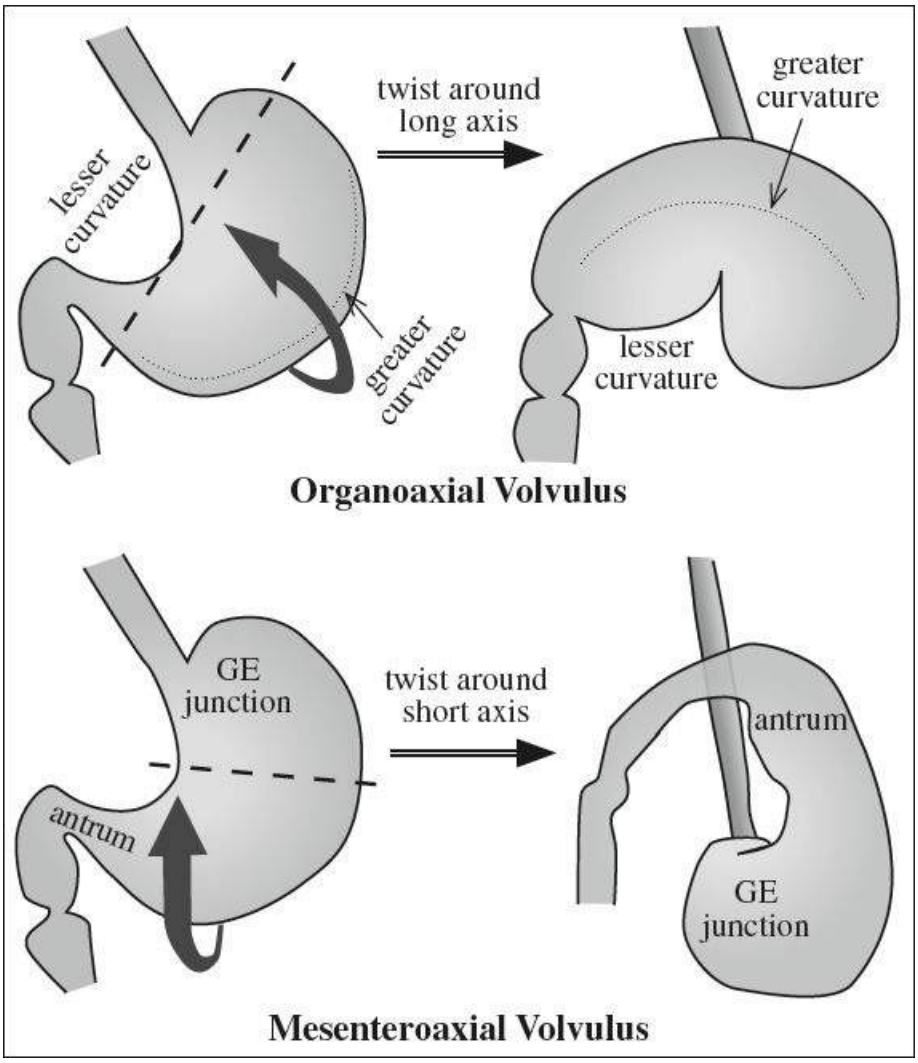
√ barium demonstrates area of twist

Classification:

A. PRIMARY without diaphragmatic defect

B. SECONDARY with diaphragmatic defect

Types:



A. ORGANOAXIAL VOLVULUS (²/₃)

Axis of rotation: around the long axis of stomach connecting GE junction and pylorus

Cause: ligamentous laxity allowing stomach to move abnormally along its long axis + long-standing posttraumatic / paraesophageal hiatal hernia

Age: usually in adulthood

Associated with: diaphragmatic defect (hiatal hernia, diaphragmatic eventration / rupture / large Bochdalek hernia) → migration of stomach into thorax = organoaxial position with twist of < 180°

√ horizontally oriented stomach with a single air-fluid level:

√ "mirror-image" stomach = greater curvature to right of lesser curvature (in vertically oriented stomach)

CT:

√ antrum moves anterosuperiorly + fundus rotates posteroinferiorly:

√ gastroesophageal junction lower than normal

√ "upside-down" stomach = lesser curvature below greater curvature

√ distortion of duodenum

B. MESENTEROAXIAL VOLVULUS (⅓)

Axis of rotation: around short axis that bisects greater and lesser curvatures = the site of mesenteric attachment (gastrohepatic omentum) → twisting vascular supply

Cause: abnormal laxity / absence of peritoneal attachments ← abnormal fusion of fetal mesenteries

Age: usually in childhood

May be associated with: wandering spleen

• idiopathic chronic / intermittent course: asymptomatic / postprandial pain, belching, bloating, vomiting, early satiety

• associated with severe obstruction (of pyloric antrum) ± strangulation (rare)

√ fundus rotates posteroinferiorly

√ usually partial volvulus

√ no underlying diaphragmatic defect

CT:

√ antrum moves above gastroesophageal junction:

√ "right-side up" stomach = antrum / pylorus rotates anterosuperiorly and from right to left

C. COMBINATION (2%)

Cx: intramural emphysema, gastric ischemia / gangrene, necrosis, perforation, mediastinitis, peritonitis, shock, gastric ulceration, hemorrhage, pancreatic necrosis, omental avulsion, splenic rupture

Mortality: 30–42–80% in acute volvulus; 10–13% in chronic volvulus

Rx: open / laparoscopic gastropexy + repair of diaphragmatic hernia

DDx: incarcerated hiatal hernia, gastric atony, acute gastric dilatation, pyloric obstruction

GASTRITIS

= common condition often resulting in submucosal edema and hyperplasia of gastric mucosa

Cause: Helicobacter pylori infection (most common), nonsteroidal anti-inflammatory drugs (NSAIDs), alcohol, systemic illness

• epigastric pain, nausea, vomiting, loss of appetite

Distribution: focal / segmental / diffuse

CT:

√ gastric wall / fold thickening (best appreciated when stomach distended)

√ mural stratification (best during arterial phase):

√ diffuse submucosal low attenuation ← edema

√ mucosal hyperemia

Corrosive Gastritis

Agents:

(a) acid, formaldehyde

• clinically usually silent

Location: esophagus usually unharmed, severe gastric damage, duodenum may be involved (newer potent materials cause atypical distribution)

(b) alkaline

Location: pylorus + antrum most frequently involved

A. ACUTE CHANGES (edema + mucosal sloughing)
   √ marked enlargement of gastric rugae + erosions / ulceration
   √ complete cessation of motor activity
   √ gas in portal venous system
   Cx: perforation
B. CHRONIC CHANGES
   √ firm thick nonpliable wall
   √ stenotic / incontinent pylorus (if involved)
   √ gastric outlet obstruction (cicatrization) after 3–10 weeks

Drug-induced Gastropathy

Cause: NSAIDs (most common worldwide); chemotherapy with cytotoxic agents; alcohol

Mechanism for NSAID:
weakening of mucosal defense mechanisms with increase in acid and pepsin ← reduced prostaglandin synthesis ← inhibition of cyclooxygenase COX enzyme (COX-1 = constitutive enzyme important for basal mucosal blood flow + pH balance; COX-2 = inducible enzyme important in maintaining perfusion for mucosal integrity)

Location: gastric body and antrum along greater curvature (= dependent position as function of gravity)

√ single / multiple discrete punched-out ulcers with sharply defined smooth border:
  √ central punctate collection of barium surrounded by radiolucent halo corresponding to mound of edema
√ linear serpiginous barium collection (= incomplete erosion) surrounded by halo of edema
√ (occasionally) deep ulcer penetrating through muscularis mucosae with involvement of submucosa

DDx: infection, inflammation, malignancy (focal wall thickening > 5 mm, perigastric tissue abnormalities, lymphadenopathy)

Emphysematous Gastritis

= rare but severe form of widespread phlegmonous gastritis subsequent to mucosal disruption characterized by gas in wall of stomach

Cause of mucosal disruption:
ingestion of toxic / corrosive substances (37%), alcohol abuse (22%), gastroenteritis (15%), recent abdominal surgery (15%), gastric infarction, necrotizing enterocolitis, ulcer, acute pancreatitis, adenocarcinoma of stomach, phytobezoar, leukemia, diabetes mellitus, disseminated strongyloidiasis, gastric mucormycosis, after ingestion of large amounts of carbonated beverages

Histo: bacterial invasion of submucosa + subserosa

Organism: hemolytic streptococcus, Clostridium welchii, Clostridium perfringens, E. coli, S. aureus, enterobacter, P. aeruginosa, Klebsiella pneumoniae, Candida

- explosive onset of severe abdominal pain
- nausea, diarrhea, chills, fever, leukocytosis
- bloody foul-smelling emesis ± PATHOGNOMONIC vomiting of a necrotic cast of stomach ← dissection along plane of muscularis mucosae

Plain radiographs:
√ innumerable small gas bubbles silhouetting the stomach in a mottled fashion without positional change
√ thickening of rugal folds
√ ± portal venous gas
GI:
√ cobblestone appearance of mucosa on upper GI
√ intramural penetration of contrast material
CT:
√ gastric wall thickening (DDx: emphysematous gastritis)
√ intramural gas → dissecting into gastric veins + portal venous system
Cx: cicatricial stenosis (21%), sinus tract formation
Prognosis: 60–80% mortality
Rx: broad-spectrum antibiotics + intravenous fluids; emergent surgery for acute perforation
DDx: benign gastric emphysema (recent gastric procedure), gastric ischemia, caustic ingestion

Erosive Gastritis

= HEMORRHAGIC GASTRITIS
Frequency: 0.5–10.0% of GI studies
Etiology (in 50% without causative factors):
(1) Peptic disease: emotional stress, alcohol, acid, corrosives, severe burns, anti-inflammatory agents (aspirin, steroids, phenylbutazone, indomethacin)
(2) Infection: herpes simplex virus, CMV, Candida
(3) Crohn disease: aphthoid ulcers identical in appearance to varioliform erosions
Histo: epithelial defect not penetrating beyond muscularis mucosae
• 10–20% of all GI hemorrhages (usually without significant blood loss); vague dyspepsia, ulcerlike symptoms
Location: antrum, rarely extending into fundus; aligned on surface of gastric rugal folds
√ varioliform <u>complete</u> erosion (95%) = tiny fleck of barium surrounded by radiolucent halo ("target lesion") < 5 mm, usually multiple
√ <u>incomplete erosion</u> (5%) = linear streaks / dots of barium without surrounding mound of edema / inflammation
√ nodularity / scalloping of prominent antral folds
√ contiguous duodenal disease may be present
√ limited distensibility, poor peristalsis / atony, delayed gastric emptying

Phlegmonous Gastritis

Etiology: septicemia, local abscess, postoperative stomach, complication of gastric ulcer / cancer
Organism: Streptococcus
Path: multiple gastric wall abscesses ± communication with lumen
• severe fulminating illness, patient may vomit pus
Location: usually limited to stomach not extending beyond pylorus; submucosa is the most severely affected gastric layer

√ barium dissection into submucosa + serosa

GASTROENTERITIS

= "stomach bug / stomach virus / stomach flu"
= infection involving stomach + small intestine
◊ Most common cause of bowel wall thickening
Organism:
(a) bacteria: Escherichia coli, Shigella, Salmonella, Yersinia, Campylobacter, Staphylococcus
(b) viruses: Rotavirus (very common in winter, between 6 months to 2 years of age), norovirus, Herpes, Cytomegalovirus
(c) parasites: amebiasis in underdeveloped countries
Ingestion: consumption of contaminated water, sharing personal objects
• diarrhea, vomiting, abdominal cramping

GASTROINTESTINAL STROMAL TUMOR

= GIST = SPINDLE CELL / EPITHELIOID TUMOR
Origin: c-KIT-positive interstitial cell of Cajal of myenteric plexus (= pacemaker cell for gut movement)
◊ Most common solid mesenchymal neoplasm of GI tract!
◊ Most common intramural subepithelial neoplasm of GI tract!
Incidence: < 1% of all gastrointestinal tumors; 7–20÷1,000,000 annually; 4500–6000 new cases annually (USA); increased prevalence in NF1
Median age: 55–65 years; M÷F=1÷1
Histo: spindle cell (70–80%) / epithelioid (20–30%) morphology / mixture of both
› expresses transmembrane receptor tyrosine kinase encoded by c-KIT gene (CD117) in 95%; 70% of GISTs coexpress CD34
Location: usually solitary
A. GI TRACT anywhere between esophagus and anus:
› stomach (60–70%)
› small intestine (20–30%): jejunum > duodenum (9%) > ileum
› periampullary (3–5%)
› anorectum (5–7%)
› colon (4%): rare in appendix
› esophagus (2%)
◊ 75% of mesenchymal tumors in the esophagus are leiomyomas and 25% GIST
B. EXTRAINTESTINAL (rare): peritoneum (4%), omentum; mesentery; retroperitoneum
Site: muscularis propria has greatest density of cells of Cajal; endophytic / exophytic to bowel
N.B.: leiomyomas arise from muscularis mucosae!
• early satiety, indigestion, bloating, vague abdominal pain
◊ often not detected until late in their progression
• gastrointestinal bleeding ← mucosal ulceration: hematemesis, melena, hematochezia, anemia
• subtle nonspecific broad-based lesion at optical colonoscopy
Associated with: neurofibromatosis type 1, familial GIST, Carney triad
Spread: (in 50% at presentation)

(a) intraperitoneal: adjacent organ invasion, ascites, omentum, peritoneum
(b) hematogenous: liver metastasis

◊ All GISTs are potentially malignant (30%)!
◊ Lymphadenopathy (rare)!

Staging criteria: based on tumor size, dissemination status, mitotic rate
Mean size: 8.6 cm

@ Stomach (60%)

Frequency: 2–3% of all gastric tumors; most common location of GIST

- nausea, vomiting, weight loss
- abdominal pain + distension, intestinal obstruction

UGI:

√ well-circumscribed mass up to 30 cm in size
√ features of subepithelial mass:
√ lesion margin obtuse / at right angle with gastric wall (in profile)
√ smoothly circumscribed (en face)
√ smooth mucosal surface (common)
√ mucosal ulceration (in up to 60%)
√ polypoid intraluminal mass (in 14%)

US:

√ large well-defined predominantly solid mass with variable echogenicity, often exophytic
√ thick echogenic rim (occasionally)
√ central hypoechoic areas = regions of necrosis

CT:

(a) small < 3 cm tumor:
√ well-defined smooth-walled homogeneous soft-tissue mass with moderate degree of enhancement
√ attenuation similar to muscle

CT features of GISTs < 3 cm overlap with those of other intramural subepithelial masses.

(b) large tumor:
√ large heterogeneous mass with prominent extraluminal location = exoenteric growth with displacement of adjacent organs + vessels
√ extragastric extension into gastrohepatic / gastrosplenic ligament / lesser sac (in 86%)
√ prominent intraluminal component (rare)
√ irregular lobulated margin
√ mucosal ulceration (50%)
√ central areas of low attenuation ← hemorrhage, necrosis, cyst formation
√ large cavity containing air / air-fluid level / oral contrast medium that communicates with gastric lumen (common)
√ rarely calcified (in 3%)

◊ Features of metastatic lesions from GIST are similar to those of the primary tumor!

CECT:

√ tumor vessels visible within tumor

√ hypervascular mass with heterogeneous enhancement
√ peripheral enhancement in 92% (corresponding to viable tumor)

CT Findings suggestive of Malignant GIST:
√ lesion > 5 cm
√ heterogeneous enhancement
√ gastric location
√ metastases
√ cystic-necrotic component

MR:
√ solid tumor portion hypointense on T1WI + intermediate intense to hyperintense on T2WI
√ heterogeneous enhancement of large tumors ← central necrosis + cavitation
√ tumoral hemorrhage varies from high to low SI on T1WI + T2WI depending on age

PET:
√ high sensitivity for detection unless extensively necrotic

DDx: leiomyoma, leiomyosarcoma, schwannoma, neurofibroma, carcinoid

With any hypervascular intramural subepithelial mass > 3 cm GIST should be considered first in the DDx.

@ Small intestine (30%)
◊ 2nd most common site of involvement after stomach
Location: ileum (50%)
@ Periampullary region (3–5%)
@ Anorectum
√ expansion of rectal wall → focal mural mass
Cx: extension into ischiorectal fossa, prostate, vagina
@ Extraintestinal
Age: 31–82 years; M÷F = 1÷2
Location: mesentery, omentum, retroperitoneum

Cx: bowel obstruction (rare)

Rx: (1) Surgery for localized primary
(2) Imatinib mesylate (= tyrosine kinase inhibitor) inhibits growth of GIST (± paradoxical enlargement ← tumor hemorrhage / necrosis)

Response to treatment:
√ decrease in tumor attenuation by > 15% ← myxoid degeneration + hemorrhage + necrosis
√ decrease in tumor size by > 10%
√ apparent "new liver lesions" = lesions initially isodense to hepatic parenchyma become hypodense + visible → no metabolic activity on PET

DDx: new lesions of progressive disease show metabolic activity

GLIOMATOSIS PERITONEI

= benign mature glial implants throughout peritoneum

Cause: ? rupture of ovarian teratoma / metaplasia of peritoneal tissue

Associated with: solid / immature ovarian teratomas, ventriculoperitoneal shunts
Histo: benign mature glial tissue with delicate fibrillar processes and scattered supporting cells
Clue: teratoma with fat and calcifications in one ovary
CT:
√ peritoneal nodules + masses of soft-tissue density
√ omental caking
√ ascites
√ adnexal / pelvic mass suggestive of teratoma
MR:
√ multilobular masses of homogeneously high SI on T2WI
DDx: peritoneal carcinomatosis (indistinguishable)

GIARDIASIS

= overgrowth of commensal parasite Giardia lamblia
Organism:
Giardia lamblia (flagellated protozoan); often harmless contaminant of duodenum + jejunum in motile form (= trophozoite) attached to mucosa by suction disk, nonmotile form (= cyst) shed in feces; capable of pathogenic behavior with invasion of gut wall
Frequency: 1.5–2.0% of USA population, in 3–20% of children in parts of southern USA; infests 4–16% of inhabitants of tropical countries
Predisposed: altered immune mechanism (dysgammaglobulinemia, nodular lymphoid hyperplasia of ileum)
Histo: blunted villi (may be misdiagnosed as celiac disease especially in children), cellular infiltrate of acute + chronic inflammation in lamina propria
• abdominal pain, weight loss, failure to thrive (especially in children)
• spectrum from asymptomatic to severe debilitating diarrhea
• steatorrhea = reduced fat absorption (related to number of organisms) simulating celiac disease
Location: most pronounced in duodenum + jejunum
√ irregular distorted segmental thickening of mucosal folds in duodenum + jejunum (+ normal ileum) ← mucosal edema
√ marked spasm + irritability with rapid change in direction + configuration of folds
√ hypersecretion with blurring + indistinctness of folds
√ hyperperistalsis → rapid transit time
√ segmentation of barium ← motility disturbance + excess intraluminal fluid
√ ± lymphoid hyperplasia (associated with immunoglobulin deficiency state)
Dx: (1) Detection of Giardia lamblia cysts in formed feces or trophozoites in diarrheal stools
(2) Trophozoites in duodenal aspirate / jejunal biopsy
DDx: hookworm Strongyloides infection
Rx: quinacrine (Atabrine®)

GLOMUS TUMOR OF STOMACH

= rare benign vascular tumor that originates from glomus body

Glomus body: modified smooth muscle cells functioning as neuromyoarterial receptors that regulate temperature (= unique arteriovenous shunt) → therefore most abundant in dermis / subcutis of extremities, particularly beneath fingernails

Frequency: 2% of all benign gastric tumors

◊ Most common benign vascular gastric tumor

Path: dilated irregularly shaped thin-walled vessels (= modified capillaries) covered by nests / strands / sheets of glomus cells arising in muscularis propria

Histo: sheets of monotonous round cells interspersed with numerous delicate vessels

Median age: 55 years; M÷F = 3÷7

• asymptomatic / upper GI bleeding

Location: gastric antrum

Size: 1–4 cm in diameter

√ solitary smooth intramural / intraluminal subepithelial mass ± mucosal ulceration

√ change in shape + size during fluoroscopy (similar to lipoma)

√ tiny flecks of calcifications (occasionally)

√ CHARACTERISTIC strong peripheral homogeneous enhancement in arterial + portal venous phases with prolonged enhancement in delayed phase similar to portal vein / IVC / descending aorta

√ SPECIFIC peripheral nodular enhancement pattern + delayed filling-in (reminiscent of hemangioma)

On CT easily differentiated from lipomas because of dense arterial enhancement persisting into delayed phase.

DDx: lipoma, hemangioma, GIST, carcinoid tumor, ectopic pancreas, metastasis

GLYCOGEN ACANTHOSIS

= benign degenerative condition with accumulation of cellular glycogen within squamous epithelial lining of esophagus

Frequency: in up to 15% of endoscoped patients

Etiology: unknown

Age: middle-aged / elderly individuals

Histo: hyperplasia + hypertrophy of squamous mucosal cells ← increased glycogen; no malignant potential

• asymptomatic white oval mucosal plaques of 2–15 mm in diameter on otherwise normal appearing mucosa

Location: middle (common) / upper esophagus, in random distribution

√ multiple 1–3-mm rounded nodules / plaques

Dx: biopsy

DDx: candida esophagitis (lesions disappear under treatment in contrast to glycogen acanthosis), reflux esophagitis

GRAFT-VERSUS-HOST DISEASE

= T lymphocytes from donor bone marrow cause selected epithelial damage of recipient target

organs

Bone marrow transplantation for treatment of:

leukemia, lymphoma, aplastic anemia, immunologic deficit, metabolic disorders of hematopoietic system, some metastatic disease

Frequency: 30–70% of patients with allogeneic (= donor genetically different from host) transplant

Time interval from hematopoietic stem cell transplantation:

(a) acute GVH: less than 100 days

(b) chronic GVH: within 100 days

Target organs: skin, liver, GI tract (small bowel)

@ Skin

- maculopapular rash on face, trunk, extremities
- cholestatic jaundice

@ Liver

- elevation of hepatic enzymes ± liver failure

√ thickening of gallbladder wall ± pericholecystic fluid

√ biliary sludge

√ dilatation of common bile duct

√ enhancement of wall of gallbladder and CBD

Veno-occlusive disease = sinusoidal obstructive syndrome:

Histo: centrilobular hemorrhagic necrosis, venular obliteration, sinusoidal congestion, fibrosis

√ portal hypertension + fluid retention

√ painful hepatomegaly

@ GI tract

- profuse secretory diarrhea ± hemorrhage, weight loss
- abdominal cramping, fever, nausea, vomiting

Path: severe mucosal atrophy / destruction

Location: distal ileum > other small bowel > colon

Plain film:

√ separation of bowel loops ← wall thickening

√ air-fluid levels + small bowel dilatation

√ decreased luminal gas

Barium:

√ shaggy fold thickening

√ "ribbon bowel" = small bowel fold effacement with tubular appearance (DDx: viral enteritis, ischemia, celiac disease, radiation, soybean allergy)

√ "toothpaste / leadpipe / moulage" sign = featureless segment of bowel (chronic stage)

√ loss of haustration, spasm, edema, ulceration, granular mucosal pattern of colon (simulating ulcerative colitis)

√ small bowel "cast" HIGHLY SUGGESTIVE = prolonged coating of abnormal bowel for hours to days ← incorporation of barium into submucosal layer through mucosal ulcers

√ circular collections of contrast material on cross section + parallel tracks on longitudinal section
√ severely decreased transit time

CT:
√ moderate bowel wall thickening < 5.5–8.0 mm: small bowel involved in 75–100%
√ discontinuous involvement (in 41–54%)
√ strictly right colonic involvement (uncommon)
√ fluid-filled distended bowel: colon > 8 cm, small bowel > 3 cm
√ barium (from prior contrast enema weeks ago) may become incorporated into bowel wall

N.B.: oral contrast material should not be given!

√ misty mesentery = mesenteric fat stranding without lymphadenopathy
√ ascites

CECT:
√ abnormally enhancing thin layer of mucosa diffusely involving thickened bowel segments ← mucosal replacement by highly vascular granulation tissue

N.B.: negative oral contrast agent makes hyperattenuating mucosa more conspicuous

√ engorgement of vasa recta = "comb" sign

Cx: infection with opportunistic organisms, eg, Candida albicans, herpes virus, invasive fungal organisms, CMV, Varicella-zoster virus, Epstein-Barr virus, hepatitis viruses, Rotavirus, Adenovirus, Coxsackie virus A and B, P. carinii, pneumococcus

Prognosis: fatal in up to 15% ← opportunistic infection

Rx: steroids + cyclosporine

DDx:
(a) 0–30 days: typhlitis, C. difficile colitis
(b) 31–100 days: viral gastroenteritis / hepatitis, pneumatosis cystoides intestinalis, thrombotic microangiopathy
(c) >100 days: posttransplantation lymphoproliferative disease

GRANULAR CELL TUMOR

= GRANULAR CELL MYOBLASTOMA (misnomer coined in 1926, thought to derive from muscle cells)
= rare mostly benign neoplasm, occasionally locally invasive + metastasizing

Origin: Schwann cell (positive for S-100 marker protein)

Path: infiltrative margins

Histo: nests of ovoid / polygonal cells with small dark regular nuclei and abundant cytoplasm filled with eosinophilic PAS-positive and diastase-resitant granules (= autophagic vacuoles containing cellular debris); separated by collagen bundles; interspersed with branching thin-walled blood vessels

Age: 5th decade; M < F

Location: tongue (most common), subcutaneous tissue (6–8%), oropharynx, GI tract (5–8%), skin, bronchial wall, biliary tract (1%), breast (5%)

Granular Cell Tumor of Gastrointestinal Tract

Site: distal esophagus (2%); in 10% multiple lesions in esophagus; in 9–16% involving additional organs
Size: mostly small tumors < 2 cm incidentally discovered at autopsy / endoscopy
√ small subepithelial mass; hypoechoic on US
CT:
√ moderately enhancing soft-tissue mass with thickening of esophageal wall + partially narrowing esophageal lumen
Cx: malignant degeneration (1–3%)
Rx: endoscopic / surgical removal if > 1 cm in size
DDx: leiomyoma

Granular Cell Tumor of Chest

Age: middle-aged, esp. Black women
√ endobronchial lesion in major bronchi

Granular Cell Tumor of Breast

Prevalence: 1÷1,000 of primary breast tumors; 5–8% of all granular cell tumors; 78% in African-Americans
Mean age: 34 (range, 20–59) years; M÷F = 1÷9
Location: more commonly in upper inner rather than upper outer quadrant
Site: breast parenchyma, hypodermis, dermis
Size: 1–3 cm
• asymmetric painless hard lump with slow growth
• skin fixation / skin retraction / nipple inversion / ulceration mimick malignancy; often fixed to pectoralis fascia
Mammo:
√ round well-demarcated mass / indistinct density / spiculated mass
√ ± calcifications (rare)
US:
√ well-circumscribed / angular / ill-defined spiculated mass
√ posterior acoustic enhancement / shadowing
√ stellate extensions ← tumor insinuating itself into surrounding breast tissue:
√ ± associated skin thickening / retraction (with dermal location)
√ surrounding hyperechoic halo ← infiltrative growth pattern
MR:
√ low to high SI on T2WI + low to intermediate SI on T1WI
√ hyperintense rim on T2WI
√ homogeneous enhancement of varying kinetics / rapid peripheral enhancement
Dx: Fine-needle aspirate may be difficult to interpret!
Rx: wide local excision
DDx: carcinoma, lymphoma, metastasis

HELICOBACTER PYLORI INFECTION

Organism: worldwide gram-negative spiral-shaped bacillus [formerly Campylobacter pylori]
Prevalence: increasing with age; in > 50% of Americans > 60 years of age

Path: surface epithelial damage + inflammation with mucosal infiltration by neutrophils, plasma cells, lymphoid nodules
Location: gastric antrum > proximal half of stomach
Site: beneath mucus layer on surface epithelial cells
• asymptomatic (vast majority); dyspepsia, epigastric pain
√ gastritis (75% prevalence of H. pylori):
  √ thickened gastric folds
  √ polypoid gastritis mimicking malignant tumor
  √ enlarged areae gastricae
√ gastric ulcer (60–80% prevalence of H. pylori)
√ duodenal ulcer (90–100% prevalence of H. pylori)
Dx: (1) Endoscopic brushings + biopsy
(2) Breath test measuring urease activity after ingestion of carbon 14N-labeled urea
(3) Serologic test for IgG antibodies
Rx: triple therapy (= bismuth + metronidazole + tetracycline / amoxicillin) results in 95% cure rate after 2 weeks of therapy

HEMANGIOMA OF GASTROINTESTINAL TRACT

= unusual single / multiple vascular tumors anywhere in GI tract
Frequency: 7–10% of all benign small bowel tumors
Increased incidence in (if multiple):
Maffucci syndrome, Klippel-Trénaunay syndrome, blue rubber-bleb nevus syndrome, Osler-Weber-Rendu disease, Turner syndrome, tuberous sclerosis
Commonly associated with: cutaneous hemangiomas / telangiectasias
Age: any; commonly during infancy / early childhood
• symptomatic (80%):
  • acute intermittent severe bleeding (melena)
  • acute / chronic life-threatening anemia
  • intestinal obstruction, intussusception, perforation
Path: submucosal soft infiltrative polypoid mass
Histo: cavernous / capillary / mixed
Location: jejunum (55%), ileum (42%), duodenum (2%); rare in stomach + colon (mostly rectosigmoid)
Site: submucosal vascular plexus
√ polypoid intramural intraluminal subepithelial mass
√ sessile nodular compressible intraluminal filling defect
√ segmental transmural circumferential bowel wall thickening = diffuse infiltrating abnormality extending into surrounding tissue (= hemangiomatosis)
√ ± virtually PATHOGNOMONIC phleboliths in intestinal wall ← calcified thrombi
CECT:
  √ well-circumscribed avidly enhancing often intraluminal lobulated mass of mixed attenuation supplied by large artery
  √ slow diffuse enhancement + vascular engorgement within adjacent mesentery around mass lesion

Rx: resection ← risk of massive gastrointestinal bleeding
Prognosis: involution during childhood
DDx: GIST, glomus tumor, metastasis

HERNIA

= ABDOMINAL HERNIA
= protrusion of an organ / fascia of an organ through the wall of the cavity that normally contains it
Prevalence: 2nd most common cause (= 10%) of SBO
Nomenclature: according to anatomic site of its orifice
Cx: (1) bowel obstruction
(2) **incarceration** (= irreducible hernia)
[*incarcerare*, Latin = to imprison]
(3) **strangulation** (= constriction of blood flow)
[*strangulare* , Latin = to choke]

External Hernia

= bowel extending outside the abdominal cavity
Frequency: 95% of all hernias
◊ 5% lifetime risk for spontaneous abdominal hernias
Location:
@ Ventral = Anterior abdominal wall hernia
= protrusion of part of peritoneal sac through defect in muscle layers of anterior abdominal wall
Content: fat, omentum, bowel
• abdominal bulge ± Valsalva maneuver
◊ Look for multiple hernias (present in 18–22%)!
√ small-bowel loops extending beyond fascial plane of anterior abdominal wall on lateral view
√ provocative (Valsalva) maneuver facilitates detection
√ luminal narrowing at entry + exit site of hernia orifice
√ fluoroscopic manipulation to document reducibility

1. **Umbilical hernia** (most common)
= usually small protrusion of abdominal contents / fat into anterior abdominal wall via umbilical ring
Prevalence: 4% of all hernias; M < F
Cause: failed closure of umbilical ring, obesity, multiple pregnancies, intraabdominal mass, liver failure, increased intraabdominal pressure, weak abdominal wall
√ may contain fat / small bowel / colon
Cx: strangulation, incarceration
DDx: paraumbilical, spigelian, epigastric, incisional hernia
2. Periumbilical hernia
√ large defect through linea alba ← diastasis of rectus abdominis muscle at

umbilicus

3. Epigastric / hypogastric hernia
   √ in linea alba above / below umbilicus
4. Postoperative / incisional (0.5–14.0%, most common type)
5. Parastomal hernia
   √ one / more intestinal loops alongside loop of ileum / colon leading to stoma
6. Trocar site hernia
   Frequency: 1–3.6%
   √ often Richter type hernia
7. **Spigelian hernia**
   [Adriaan van den Spiegel = Adrianus Spigelius (1578–1625) Flemish anatomist and botanist working in Padua, Italy]
   Frequency: 2% of anterior abdominal hernias
   = acquired ventrolateral hernia through defect in aponeurosis between transverse and rectus muscle of abdomen at junction of semilunar + arcuate lines below umbilicus
   √ hernia sac dissects laterally to rectus abdominis muscle through a fibrous groove (= semicircular / spigelian line)
   √ hernia sac lies beneath an intact external oblique aponeurosis
8. Interparietal / interstitial
   = hernia sac located in fascial plane between abdominal muscles NOT connected to SQ tissue

@ Diaphragmatic hernia

1. Bochdalek hernia
2. Morgagni hernia

@ Lumbar

Location: defect in lumbar muscles below 12th rib + above iliac crest

1. Superior lumbar triangle (Grynfeltt-Lesshaft)
   [Joseph C. Grynfeltt (1840-1913), French surgeon
   Peter Frantsevich Lesshaft (1837–1909), Russian physician]
   Borders: quadratus lumborum muscle (medially), internal oblique muscle (laterally), 12th rib (superiorly)
2. Inferior lumbar triangle (Petit hernia)
   [Jean Louis Petit (1674–1750), inventor of the tourniquet, director of the French Royal Academy of Surgery]
   Borders: external oblique muscle (anteriorly), iliac crest (inferiorly), latissimus dorsi muscle (posteriorly)

@ Pelvic floor

1. Perineal hernia (rare)
   (a) anterior perineal hernia = defect of urogenital diaphragm anterior to superficial transverse perineal m. + lateral to bulbocavernosus m. + medial to ischiocavernosus m. (only in females)
   (b) posterior perineal hernia = defect in levator ani m. / between levator ani m. and coccygeus m. posterior to superficial transverse perineal m.

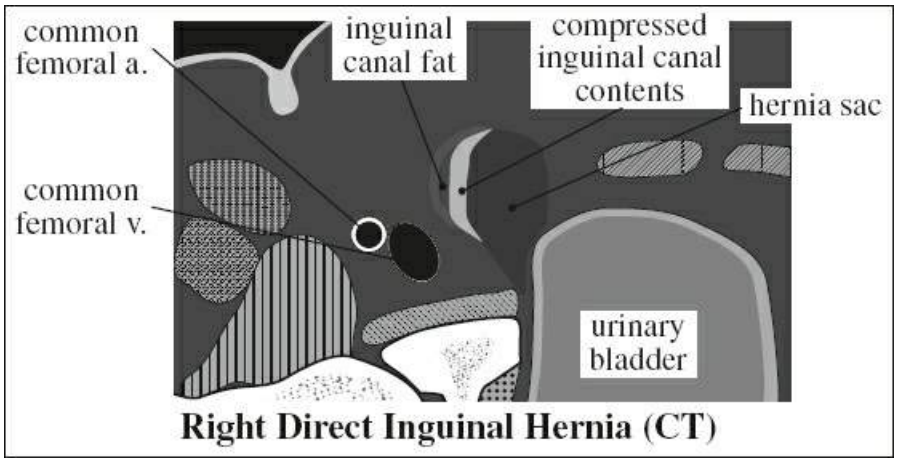
√ defecating proctography

2. Obturator foramen
   √ hernia between pectineus + external obturator mm.
3. Sciatic foramen

@ Groin

1. **Inguinal hernia**
   ◊ Most common type (80%) of spontaneous abdominal wall hernia; M > F
   √ superior + medial to pubic tubercle
   Pubic tubercle:
   = superior border of medial portion of superior pubic ramus
   = attachment point of inguinal ligament

   (a) **Direct inguinal hernia**
   = defect in Hesselbach triangle (bounded by inguinal ligament inferiorly, inferior epigastric artery superolaterally, fused aponeuroses of internal oblique + transverse abdominal muscles medially)
   [Franz Kaspar Hesselbach (1759–1816), surgeon and anatomist in Würzburg, Germany]
   Cause: acquired weakening of transversalis fascia
   Frequency: increases with age
   √ <u>medial</u> to inferior epigastric vessels
   √ hernia contains bowel, mesenteric fat, vessels
   Cx: low risk of strangulation allows for conservative management + monitoring



Right Direct Inguinal Hernia (CT)

   (b) **Indirect inguinal-scrotal hernia**
   ◊ Most common hernia in children ← failure of obliteration of processus vaginalis
   Age: preterm neonates (most common)
   Prevalence: higher in preterm neonates
   Location: R > L
   • clinically inapparent contralateral hernia (88%)
   √ <u>lateral</u> to inferior epigastric vessels originating at deep inguinal ring

√ US visualization of air-bubble movement / intestinal peristalsis / vascularity
√ hernia containing omentum mimicks lipoma
Cx: moderate risk of strangulation (2%)

(c) **Littré hernia** = inguinal hernia containing Meckel diverticulum
[Alexis Littré (1654–1726), French physician and anatomist in Montpellier and Paris]

(d) **Amyand hernia**
[Claudius Amyand (1680-1740), English surgeon who performed first successful appendectomy in 1735]
= appendix within inguinal hernia
Frequency: 1% of all inguinal hernias

DDx: iliopsoas bursa distended by hip joint effusion

2. **Femoral hernia** (5%)
◊ 2nd most common type (5%) of spontaneous abdominal wall hernias, R > L; M÷F = 1÷4 to 1÷6
√ enters femoral canal through femoral ring
Femoral ring:
= most proximal part of femoral canal
Borders: inguinal lig. (anteriorly), pectineal lig. (posteriorly), femoral vein (laterally)
√ lies in femoral triangle:
Borders: deep to deep fascia of thigh, inguinal lig., sartorius m., adductor longus m.
√ inferior and lateral to pubic tubercle
√ medial to femoral vein within femoral canal
√ posterior to inguinal ligament
Cx: highest (40%) rate of (ischemic) strangulation / (irreducible) incarceration of all hernias

3. **Richter hernia** = **Partial enterocele**
[August Gottlieb Richter (1742–1812), surgeon and professor ordinarius in Göttingen, Germany]
= entrapment of antimesenteric border of bowel in hernia orifice, usually seen in older women with femoral hernias
• no palpable mass = difficult to diagnose
√ localized outpouching, possibly incarcerated
√ partial obstruction with patent bowel lumen

Categorization of Internal Hernias	
Type of Orifice	*Category of Hernia*
Normal foramen	foramen of Winsløw
Unusual peritoneal fossa / recess into retroperitoneum	paraduodenal pericecal intersigmoid pelvic internal
Abnormal opening in mesentery / peritoneal ligament	small bowel mesentery greater omentum lesser sac (except Winsløw) transverse mesocolon transmeso- and intramesosigmoid falciform ligament broad ligament Roux-en-Y anastomosis

4. **De Garengeot hernia**
   [René-Jacques Croissent de Garengeot (1683–1759), surgeon-major of the king's regiment of infantry, France]
   = appendix within femoral hernia sac
   Frequency: 0.5–3.3% of all femoral hernias

Internal Hernia

= herniation of bowel through a defect of peritoneum (= peritoneal foramen / recess / fossa), omentum, mesentery or adhesive band into a compartment of the abdominal cavity

Internal hernias are divided into 3 categories on the basis of the type of hernia orifice: (1) normal foramen, (2) unusual peritoneal fossa / recess into the retroperitoneum, and (3) abnormal opening in a mesentery / peritoneal ligament.

Frequency: 5% of all hernias, responsible for < 1% of mechanical small bowel obstruction
Cause of defect: congenital, surgery, trauma, inflammation, circulation
Classification of internal hernias:

(a) retroperitoneal: usually congenital containing a hernia sac
   1. Paraduodenal (ligament of Treitz) 53%
   2. Pericecal / ileocolic 13%
   3. Foramen of Winsløw 8%
   4. Intersigmoid 6%
   5. Supravesical 6%

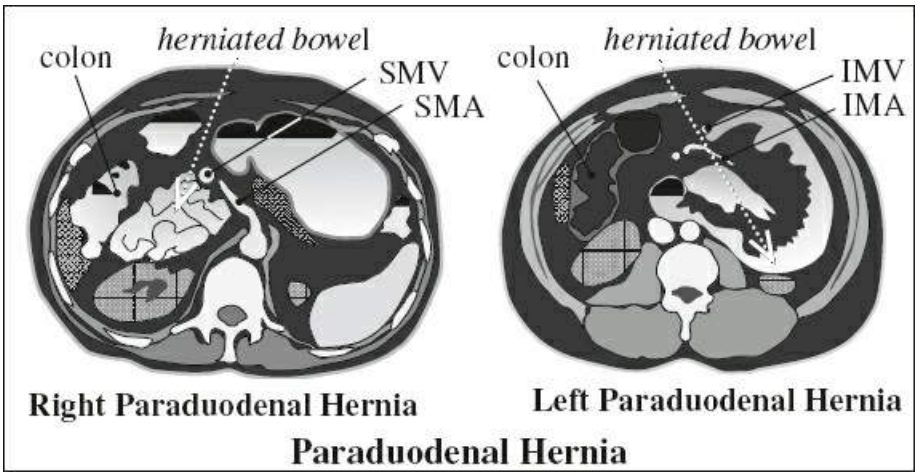
An internal hernia is diagnosed by its saclike closed-loop appearance and displacement of vessels and surrounding structures around the hernia orifice and sac.

(b) anteperitoneal:
   small group of hernias without a peritoneal sac
   1. Transmesenteric (transverse / sigmoid mesocolon) 8%
   2. Transomental 1–4%
   3. Pelvic (including broad ligament)

• epigastric discomfort, periumbilical pain

• recurrent episodes of distension and nausea ← intestinal obstruction (made worse by eating + standing and relieved by fasting + assuming a recumbent position)
N.B.: clinically apparent only when incarcerated → delay in diagnosis may lead to strangulation

√ bowel configuration:
√ saclike mass / cluster of dilated obstructed bowel loops
√ displacement of other abdominal organs



√ mesenteric changes:
√ engorged, stretched, displaced mesenteric vascular pedicle
√ dilated bowel loops with converging vessels at entrance of hernial orifice → impaired venous drainage

Cx: volvulus

Paraduodenal Hernia *(53%)*

= entrapment of small intestine into a congenital fossa

◊ Most common type of internal hernia

(a) LEFT through fossa of Landzert (¾)
[Theodor Bernhard Landzert (1833–1889), Russian anatomist]

Autoptic frequency: 2%

Cause: failure of part of descending mesocolon to fuse with posterior parietal peritoneum

Location: to the left of 4th portion of duodenum at duodenojejunal junction = confluent zone of descending mesocolon + transverse mesocolon + small bowel mesentery

• frequently asymptomatic

√ cluster of dilated small-bowel loops between pancreas + stomach to the left of ligament of Treitz:
√ displacement of gastric wall anteriorly
√ displacement of duodenojejunal flexure and transverse colon inferiorly

√ engorged crowded vessels at entrance of hernia sac

CT:

√ encapsulated bowel loop causes anteromedial displacement of IMV + left colic artery (= landmarks of the right margin of the descending mesocolon)

(b) RIGHT through mesentericoparietal fossa of Waldeyer (¼)

Cause: failure of part of ascending mesocolon to fuse with posterior parietal peritoneum

Predisposed: nonrotation of small bowel

Location: behind the root of small bowel mesentery caudal to SMA and inferior to 3rd portion of duodenum on right side

CT:

√ encapsulated bowel loop displacing the right colic vein (= landmark of left margin of the ascending mesocolon) anteriorly

√ looping of small intestine behind SMA + SMV below transverse portion of duodenum

with nonrotation:

√ SMV located ventral + to left of SMA

√ absence of normal 3rd portion duodenum

Cx: partial / complete obstruction of small intestine (50%)

Lesser Sac Hernia *(1–8%)*

= - FORAMEN OF WINSLØW HERNIA

= 3-cm vertical slit beneath upper part of right border of lesser sac and cephalad to duodenal bulb

Location: anterior to IVC + posterior to hepatoduodenal ligament (portal vein + CBD + hepatic artery)

Predisposing factors:

(1) Enlarged foramen of Winsløw

(2) Excessively mobile intestinal loops ← long mesentery / persistence of ascending mesocolon

Invaginated gut:

(a) small bowel (60–70%): ileum > jejunum, Meckel diverticulum

(b) colon (25–30%): terminal ileum, cecum, appendix, ascending colon

(c) rare: transverse colon, gallbladder, greater omentum

Plain film:

√ gas-containing bowel loops in central upper abdomen

√ distended small bowel loops occupying space between stomach + liver

√ ± cecum + ascending colon absent from usual location

UGI:

√ dilatation of small bowel loops with obstruction in RUQ

BE:

√ ± narrowing / obstruction at hepatic flexure of colon

CT:

√ retrogastric air-fluid collection in lesser sac:

√ ≥ 2 bowel loops in high subhepatic spaces

√ "beak"-shape herniated viscera pointing toward foramen of Winsløw

√ mesenteric vessel between IVC + main portal vein

√ crowded mesenteric vessels between ascending portion of duodenum + pancreatic head
√ anteriorly compressed portal vein
√ absence of ascending colon in right gutter

Pericecal Hernia *(13%)*

4 recesses: superior + inferior ileocecal recess, retrocecal recess, paracolic sulci
√ saclike appearance of ileal loops in right paracolic gutter lateral to cecum + posterior to ascending colon
√ displacement of cecum + ascending colon anteriorly / medially

Falciform Ligament Hernia

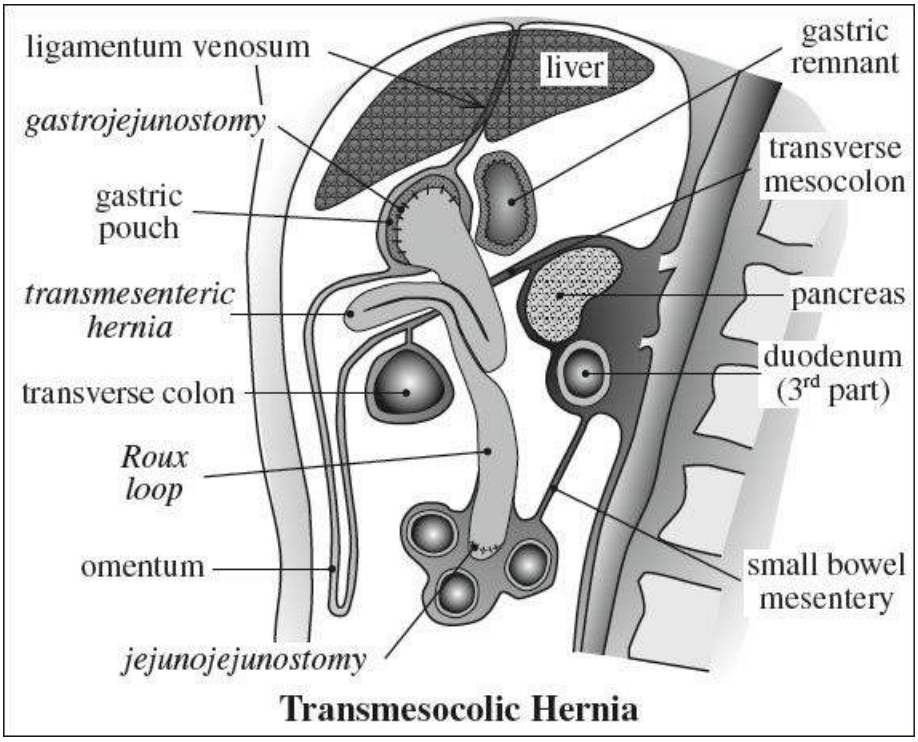
Cause: abnormal opening in falciform ligament
√ closed-loop intestine in front of / slightly caudal to liver

Transmesenteric Hernia *(8%)*

Cause:
(a) in childhood (35%): congenital mesenteric defect 2–5 cm in diameter
Location: close to ligament of Treitz / ileocecal valve
(b) in adulthood: surgery / trauma / inflammation
√ proximal small bowel dilatation = mechanical SBO
CT:
√ clustering of small bowel loops
√ engorged, stretched, crowded mesenteric vascular pedicle
√ displacement of main mesenteric trunk to the right
Cx: small bowel volvulus

Transomental Hernia *(1–4%)*

Type 1: herniation without sac through a free greater omentum (more common)
= slitlike opening 2–10 cm in diameter
Type 2: herniation into lesser sac through gastrocolic lig.
√ closed-loop intestine without saclike appearance, located in most anterior portion of peritoneal cavity
√ omental vessels run vertically around hernia orifice
√ clinical + radiologic findings almost identical to transmesenteric hernia



Transmesocolic Hernia

Sigmoid Mesocolon Hernia *(6%)*

Types: intra-, transmeso-, intermesosigmoid subtypes

√ hernia orifice between sigmoid colon and left psoas major muscle in LLQ

√ small bowel loops posterolateral to sigmoid colon

√ ± herniation sac ± splaying of sigmoid arteries and veins

Internal Supravesical Hernia

√ saclike herniated intestine located anterolaterally to compressed urinary bladder (= retropubic space of Retzius)

Iatrogenic Hernia

TRANSMESOCOLIC HERNIA

Cause: fenestration of transverse mesocolon in construction of Roux-en-Y loop

√ cluster of small-bowel loops (70%)

√ clustered small bowel outside colon compressed against abdominal wall without overlying omental fat (85%)

√ central displacement of colon (92%)

√ displacement of mesenteric trunk (85%)

√ engorged mesenteric vessels (85%)

HERNIA THROUGH BROAD LIGAMENT (4–5%)

= congenital / acquired hernia after laceration / fenestration during surgery or during pregnancy (85%)

CT:

√ cluster of dilated small bowel loops with air-fluid levels in pelvic cavity

compressing rectosigmoid dorsolaterally and uterus ventrally
√ mesenteric vessels of herniated intestine penetrate broad ligament (coronal MPR)
√ enlarged distance between uterus and ovary deviating in opposite directions

Hiatal Hernia

Cause: delay in descent of stomach keeping hiatus large (in children)
Associated with: diverticulosis (25%), reflux esophagitis (25%), duodenal ulcer (20%), gallstones (18%)

Sliding Hiatal Hernia *(99%)*

= AXIAL HERNIA = CONCENTRIC HERNIA
= esophagogastric junction (= termination point of converging gastric folds) > 1.5 cm above diaphragmatic hiatus (= pinched appearance of gastric folds) with portion of peritoneal sac forming part of wall of hernia
Etiology: rupture of phrenicoesophageal membrane ← repetitive stretching with swallowing
Frequency: increasing with age
√ reducible in erect position
√ epiphrenic bulge = entire vestibule + sleeve of stomach are intrathoracic
√ distance between B ring (if visible) + hiatal margin > 2 cm
√ peristalsis ceases above hiatus → end of peristaltic wave delineates esophagogastric junction
√ tortuous esophagus having an eccentric junction with hernia
√ numerous coarse thick gastric folds within suprahiatal pouch (> 6 longitudinal folds)
√ ± gastroesophageal reflux
CT:
√ dehiscence of diaphragmatic crura > 15 mm
√ pseudomass within / above esophageal hiatus
√ increase in fat surrounding distal esophagus ← herniation of omentum through phrenicoesophageal lig.
DDx: normal temporary cephalad motion of esophago-gastric junction by 1–2 cm into chest ← contraction of longitudinal muscle during esophageal peristalsis

Paraesophageal Hernia *(1%)*

= ROLLING HIATAL HERNIA = PARAHIATAL HERNIA
= portion of stomach superiorly displaced into chest with GE junction remaining in subdiaphragmatic position
Cause: absence of gastrosplenic + gastrocolic ligaments; complication of Nissen fundoplication
√ cardia in normal position
√ herniation of portion of stomach anterior to esophagus
√ frequently nonreducible
√ may be associated with gastric ulcer of lesser curvature at level of diaphragmatic hiatus
Cx: organoaxial volvulus, colonic herniation

Totally Intrathoracic Stomach

= defect in central tendon of diaphragm in combination with slight volvulus in transverse axis of stomach behind heart (organoaxial rotation)
√ cardia may be intrathoracic (usually) / subdiaphragmatic
√ great gastric curvature either on right / left side

Congenitally Short Esophagus

(not true hernia, very rare)
= gastric ectopy by lack of lengthening of esophagus
√ nonreducible intrathoracic gastric segment (in erect / supine position)
√ cylindrical / round intrathoracic segment with large sinuous folds
√ short straight esophagus
√ circular narrowing at gastroesophageal junction, frequently with ulcer
√ gastroesophageal reflux

HETEROTOPIC PANCREAS

= pancreatic tissue at aberrant sites that lack a vascular / ductal connection to main pancreatic body
Origin: detachment of branching bud during embryonic gastrointestinal rotation
Prevalence: 1–15% (autoptic)
• usually asymptomatic
• occasionally abdominal pain, GI bleeding, obstruction
Location: upper part of GI tract near pancreas in prepyloric antrum of stomach along greater curvature (90%)
Site: submucosa / muscularis propria
√ flat ovoid intramural subepithelial nodule of < 3 cm
√ intraluminal growth ± central umbilication (= orifice of rudimentary pancreatic duct)
CT:
√ mass with irregular border
√ usually homogeneously enhancing mass with attenuation similar to pancreas
√ occasionally poor enhancement (if pancreatic acini remain a minor component of the mass)

Differentiation of heterotopic pancreas from other subepithelial masses is crucial to avoid unnecessary resection. Its typical location, flat-ovoid shape, intraluminal growth, and irregular border are helpful characteristics.

Rare Cx: pancreatitis, pseudocyst, cystic dystrophy, insulinoma, malignant transformation

HETEROTOPIC MESENTERIC OSSIFICATION

= OSSEOUS METAPLASIA of mesentery and peritoneum
Cause: trauma, repeated intraabdominal operative procedures
Pathogenesis: ? metaplasia of submesothelial mesenchyme; implantation of osteoblasts or periosteum during trauma / procedures
Histo: core of reactive myofibroblasts with hemorrhage + fat necrosis, osteoblastic activity, focal "lace-like" osteoid (DDx: extraskeletal osteosarcoma)
Location: mesentery with extension to peritoneal surface
√ multiple linear-branching structures of high-attenuation

√ trabecular architecture

DDx: (1) Extravasation of oral contrast (changing configuration on serial images, pooling in gravity-dependent locations, becoming less dense with time)

(2) Dystrophic calcifications (typically irregular /punctate / coarse calcifications without trabecular architecture)

HIRSCHSPRÜNG DISEASE

[Harald Hirschsprüng (1830-1916), pediatrician and chief physician of Queen Louisa Hospital for Children in Cøpenhagen, Denmark]

= AGANGLIONOSIS OF THE COLON = AGANGLIONIC MEGACOLON

= complete / partial functional colonic obstruction ← absence of parasympathetic ganglia in muscle (myenteric = Auerbach plexus) + submucosal layers (submucosal = Meissner plexus)

[Leopold Auerbach (1828–1897), German anatomist and professor of neuropathology at the University of Breslau]

[Georg Meissner (1829–1905), professor of anatomy and physiology in Basel, Freiburg and Göttingen, Germany]

Etiology: arrest of craniocaudal migration of neural crest cells along vagal trunks during 5th–12th week → relaxation failure of the aganglionic segment

Prevalence: 1÷5,000–8,000 live births; 15–20% of all neonatal bowel obstructions; usually sporadic; familial in 4%

Age: during first 6 weeks of life of a full-term infant (70–80%); extremely rare in premature infants; usually manifest by 5 years of age; M÷F = 4–9÷1

Associated with: trisomy 21 (in 2%)

Location: at varying distances proximal to anus, usually rectosigmoid (in 80%) and rectum

(a) ultrashort segment (= internal sphincter) (very rare)
(b) short segment disease (80%)
(c) long segment disease (15%)
(d) total colonic aganglionosis (5%)
(e) skip aganglionosis = sparing of rectum (very rare)

- failure to pass meconium within first 48 hours of life
- intermittent constipation + paradoxical diarrhea (25%)
- bilious vomiting, abdominal distension
- rectal manometry with absence of spike activity

√ generalized gaseous distension of bowel loops

BE (study of choice):

√ "transition zone":

√ inverted cone-shaped colon at transition between abnormal + normal bowel (MOST CHARACTERISTIC):

√ dilated stool-filled large + small bowel aborally from transition zone

√ distal aganglionic segment of normal size + free of stool (apparent in 50% during 1st week of life)

√ normal-appearing rectum in 33%

√ short patent colon usually of normal caliber

√ marked retention of barium on delayed postevacuation films after 12–24 hours

√ 10–15-cm segment of persistent corrugated / convoluted rectum (= abnormal uncoordinated contractions of the aganglionic portion of colon) in 31% (DDx: colitis, milk allergy, normal intermittent spasm of rectum)

N.B.: avoid digital exam / cleansing enema prior to radiographic studies!

OB-US:

√ dilated small bowel / dilated colon

CT:

√ narrow transition zone + aboral colonic distension on SAG reformatted view of lower abdomen + pelvis

Cx: (1) Necrotizing enterocolitis
(2) Cecal perforation ← stasis, distension, ischemia
(3) Obstructive uropathy

Dx: full-thickness biopsy of rectum (↑ acetylcholinesterase activity)

Rx: (1) Swenson pull-through procedure
(2) Duhamel operation
(3) Soave procedure

HYPERPLASTIC POLYP OF COLON

= intestinal metaplasia consisting of mucous glands lined by a single layer of columnar epithelium; NO malignant potential

Path: infolding of epithelium into the glandular lumen

Location: rectosigmoid

√ smooth rounded sessile elevation

√ usually < 5 mm in diameter

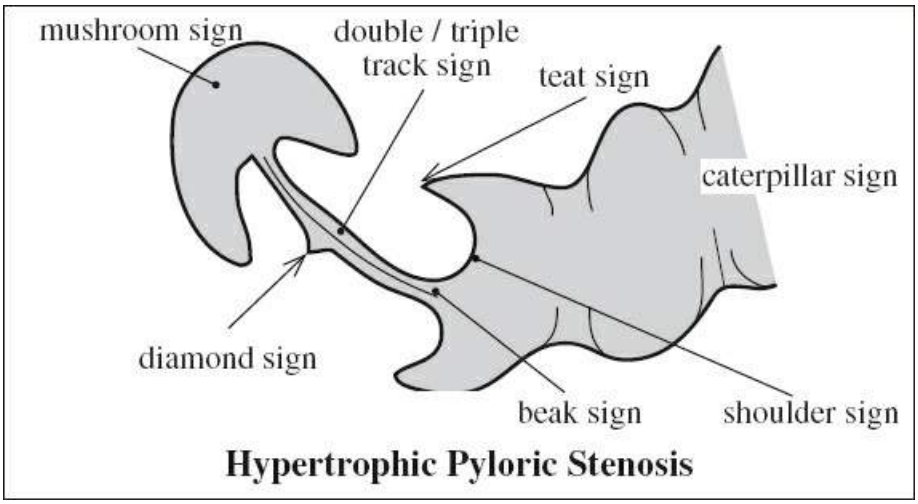
HYPERTROPHIC PYLORIC STENOSIS (HPS)

= idiopathic hypertrophy and hyperplasia of circular muscle fibers of pylorus with proximal extension into gastric antrum

Etiology: inherited as a dominant polygenic trait; increased incidence in firstborn boys; acquired rather than congenital condition

Infantile Form of Hypertrophic Pyloric Stenosis

Age: manifestation between 3rd–12th week of life; peak presentation during 4th week



Frequency: 3÷1,000 births; M÷F = 4–5÷1; 5 x fold increase in 1st-degree relatives

- nonbilious projectile vomiting (sour formula / clear gastric contents) → progression over a period of several weeks after birth (15–20%)
- palpable olive-shaped mass (80% sensitive in experienced hands, up to 14% false positive)
- nasogastric aspirate > 10 mL (92% sensitive, 86% specific)

Abdominal radiograph:

◊ A normal radiograph does not exclude HPS!

√ fluid-filled distended stomach after 2 hours of fasting

√ little bowel gas

UGI (95% sensitivity):

◊ Imaging confirmation is sought by most clinicians to differentiate from gastroesophageal reflux!

Benefit: complete anatomic evaluation of stomach and duodenum; functional assessment of gastroesophageal reflux

Precautions: (1) Empty stomach via nasogastric tube before study

(2) Remove contrast at end of study

√ elongation + narrowing of pyloric canal (2–4 cm in length):

√ "string" sign = passing of small barium streak through elongated pyloric channel (MOST SPECIFIC SIGN)

√ "double / triple track" sign = crowding of mucosal folds in pyloric channel

√ Twining recess = "diamond" sign = transient triangular tentlike cleft / niche in midportion of pyloric canal with apex pointing inferiorly ← mucosal bulging between two separated hypertrophied muscle bundles on the greater curvature side within pyloric channel

√ abnormal configuration of antrum:

√ "pyloric teat" = outpouching along lesser curvature due to disruption of antral peristalsis

√ "shoulder" sign = impression of hypertrophied muscle on distended gastric antrum

√ "antral beaking" = mass impression upon antrum with streak of barium pointing toward pyloric channel

- √ "olive pit" sign = impression of pyloric muscle upon antrum with a tiny amount of barium at orifice seen en face
- √ Kirklin sign = "mushroom" sign = indentation of base of duodenal bulb (in 50%)

√ gastric distension with fluid
√ active gastric hyperperistalsis:
- √ "caterpillar" sign = gastric hyperperistaltic waves

US (method of choice ← direct visualization of HPS):
√ "target" sign = hypoechoic ring of hypertrophied pyloric muscle around echogenic mucosa centrally on cross-section
√ elongated pylorus with thickened muscle:
- √ pyloric muscle wall thickness ≥ 3.0 –3.2 mm
- √ pyloric volume > 1.4 cm^3 (= ¼ π x [maximum pyloric diameter]2 x pyloric length); most criteria independent of contracted or relaxed state (33% false negative)
- √ pyloric length (mm) + 3.64 x muscle thickness (mm) ≥ 25 mm
- √ pyloric transverse diameter ≥ 13 mm with pyloric channel closed
- √ elongated pyloric canal ≥ 16–17 mm in length

√ "cervix" sign = indentation of muscle mass on fluid-filled antrum on longitudinal section
√ "antral nipple" sign = redundant pyloric channel mucosa protruding into gastric antrum
√ exaggerated peristaltic waves
√ delayed gastric emptying of fluid into duodenum

Pitfalls: gastric antrum mistaken for HPS (ingestion of Pedialyte® improves definition of anatomic landmarks)

Cx: hypochloremic metabolic alkalosis

Rx: pyloromyotomy

Prognosis: 2% mortality

DDx:

1. **Infantile pylorospasm**
   = temporary thickening of pyloric muscle
   - √ variable muscle thickness between 1.5 and 3.0 mm
   - √ variable caliber of antral narrowing
   - √ antral peristalsis
   - √ delayed gastric emptying (assure adequate length of real-time observation)
   - √ elongation of pylorus
   - √ gastric content / fluid passes through pyloric channel

   Prognosis: resolves in several days / ? early stage of evolving pyloric stenosis

   Rx: effective with metoclopramide / Bentyl®
2. Gastritis / milk allergy
   - √ circumferential / eccentric thickening of antral mucosa > 2–3 mm
3. Duodenal obstruction from midgut volvulus
   - √ distended descending duodenum
   - √ reversal of SMA and SMV relationship
   - √ "whirlpool" sign = twisting of small bowel mesentery
4. Gastric diaphragm

Adult Form of Hypertrophic Pyloric Stenosis

Cause: secondary to mild infantile form
• acute obstructive symptoms uncommon
• nausea, intermittent vomiting, postprandial distress, heartburn
Associated with:
(1) Peptic ulcer disease (in 50–74%) ← prolonged gastrin production ← stasis of food
(2) Chronic gastritis (54%)
√ persistent elongation (2–4 cm) + concentric narrowing of pyloric channel
√ parallel + preserved mucosal folds
√ antispasmodics show no effect on narrowing
√ proximal benign ulcer (74%), usually near incisura

Focal Pyloric Hypertrophy

= TORUS HYPERPLASIA
= localized muscle hypertrophy on lesser curvature
= milder atypical form of HPS
√ flattening of distal lesser curvature

ILEAL DIVERTICULOSIS

= acquired mucosal herniation of bowel at sites of vascular entry
• usually asymptomatic
Age: > 40 years; M > F
Site: mesenteric border of terminal ileum < 7.5 cm from ileocecal valve
Cx: perforation, bleeding, small bowel obstruction
DDx: acute appendicitis

IMPERFORATE ANUS

Prevalence: 1÷5,000 live births
A. LOW ANOMALY (55%)
= bowel has passed through levator sling
• fistula to perineum / vulva
Rx: readily reparable
B. INTERMEDIATE DEFECT (least common)
= bowel ends within levator muscle as a result of abnormality in posterior migration of rectum
• fistula opening low in vagina / vestibule
Rx: 2- / 3-stage operation
C. HIGH ANOMALY
= bowel ends above levator sling; M > F
• fistulous connection to perineum / vagina / posterior urethra → air in bladder in males / air in vagina in females
Cx: associated malformations more common + more severe
Rx: multiple surgical procedures
√ distance between rectal air and skin will not accurately outline the extent of atretic rectum and anus ← varying length during crying with increase in abdominal pressure + contraction of

levator ani muscle

US:

√ ≤ 15 mm distance between anal dimple + distal rectal pouch on transperineal images → indicates low lesion

OB-US (earliest detection by 20–29 weeks GA):

- absent / low disaccharidase level in amniotic fluid

√ dilated colon in lower pelvis with U- / S-shaped configuration ± intraluminal calcifications

√ normal amniotic fluid (unless also TEF)

√ absence of anal characteristics (= hypoechoic circular rim with central echogenic stripe)

INFLAMMATORY FIBROID POLYP

= VANEK TUMOR = EOSINOPHILIC GRANULOMA = SUBMUCOSAL FIBROMA = FIBROUS POLYPOID LESION

= unusual benign chronic inflammatory lesion

◊ Unrelated to eosinophilic granuloma of lung / bone

Path: arises in submucosa

Histo: spindle cells arranged in whorls around blood vessels with prominent inflammatory cells, particularly eosinophils

Immunohisto: stains for CD34; diffusely positive for vimentin

- usually asymptomatic, NO peripheral eosinophilia
- abdominal pain, GI bleeding ← mucosal ulceration

Location: almost exclusively in stomach: gastric antrum (75%) > gastric body > fundus

Size: 2–5 cm in diameter

√ intraluminal subepithelial polypoid mass / pedunculated polyp with smooth / slightly lobulated contour

Cx: intermittent gastric outlet obstruction

Rx: endoscopic resection

DDx: adenomatous polyp, intraluminal GIST, carcinoid tumor, schwannoma

INFLAMMATORY MYOFIBROBLASTIC TUMOR

= PLASMA CELL GRANULOMA = INFLAMMATORY PSEUDOTUMOR = INFLAMMATORY FIBROSARCOMA = XANTHOMATOUS PSEUDOTUMOR = HISTIOCYTOMA = XANTHOGRANULOMA = FIBROXANTHOMA = PSEUDOLYMPHOMA

= rare neoplasm of intermediate biologic behavior with a low rate (< 5%) of metastases based on cytogenetic studies.

Genetics: rearrangement in anaplastic lymphoma kinase (ALK) gene = tyrosine receptor kinase oncogene (in 50–70%)

Age: any; young adult and child; M < F

Path: solitary multilobular circumscribed solid mass

Histo: myofibroblastic spindle cell proliferation in a loosely myxoid to dense collagenous stroma surrounded by a prominent inflammatory cell infiltrate composed of polyclonal plasma cells, lymphocytes, eosinophils and nonnecrotizing epithelial cell granulomas

Immunohisto: spindle cells reactive with anaplastic lymphoma kinase (ALK) + smooth muscle actin

• fever, weight loss, anemia, thrombocytosis, polyclonal hypergammaglobulinemia (in 25%)
• abdominal pain ← mass effect (most common)

Location: abdominal cavity (mesentery, GI tract), lung, salivary glands, larynx, mediastinum, retroperitoneum, solid organs

Mean size: 7–8 (range, 1–20) cm in diameter

√ nonspecific varied imaging finding depending on site of origin and composition of inflammatory infiltrate and fibrosis

@ mesentery / omentum

√ bulky well-demarcated homo- / heterogeneous spherical / multilobulated mass

US:

√ ill- / well-defined heterogeneous hypo- / hyperechoic solid mass of mixed echotexture

√ ± shadowing echogenic calcifications / central hypoechoic regions

√ prominent vascularity with low-resistance arterial waveform on color Doppler

CT:

√ hypo- / isoattenuating compared with skeletal muscle depending on amount of myxoid / collagenous stroma

√ variably heterogeneous / peripheral enhancement / nonenhancing

√ peritoneal dissemination + lymphadenopathy (rare)

√ (rarely) aggressive intramural masses ± invasion through gastric wall into peritoneal cavity / nearby organs

MR:

√ typically T1-hypointense relative to skeletal muscle and hyperintense on T2WI

√ densely fibrotic tumor may be dark on both sequences

PET/CT:

√ useful in detecting primary tumor, local recurrence, distant metastases

Rx: complete surgical resection → propensity for local recurrence

DDx: (1) Desmoplastic small round cell tumor (diffuse involvement of peritoneal cavity)
(2) Castleman disease (diffuse intense enhancement)
(3) Mesenteric fibromatosis (may encase bowel wall and SMA, family history of colonic polyps)
(4) Burkitt lymphoma (typically diffuse at presentation, rapid doubling rate)
(5) Lipoblastoma (young child, fat attenuation)
(6) Lymphatic malformation (large cystic component, chylous ascites)
(7) Infantile hemangioma (< 1 year of age, intense uniform enhancement, enlarged feeding and draining vessels)
(8) Others: GIST, solitary fibrous tumor, schwannoma, multiple myeloma, solitary plasmacytoma

INTESTINAL LYMPHANGIECTASIA

A. CONGENITAL LYMPHANGIECTASIA

= PRIMARY PROTEIN-LOSING ENTEROPATHY

= generalized congenital malformation of lymphatic system with atresia of the thoracic duct + gross dilatation of small bowel lymphatics; usually sporadic; may be inherited

Age: presentation before 30 years
- asymmetric generalized lymphedema ← protein-losing enteropathy with hypoproteinemia
- chylous pleural effusions (45%)
- diarrhea (60%), steatorrhea (20%), vomiting (15%)
- abdominal pain (15%) + distension
- decreased albumin + globulin, lymphocytopenia (90%)
- decreased serum fibrinogen, transferrin, ceruloplasmin

B. ACQUIRED LYMPHANGIECTASIA

Causes leading to dilatation of intestinal lymphatics:
1. Mesenteric adenitis
2. Retroperitoneal fibrosis
3. Diffuse small bowel lymphoma
4. Pancreatitis
5. Pericardial effusion with obstruction of thoracic duct

- peripheral edema / anasarca (KEY SYMPTOM)
- chylous + serous effusion; malabsorption
- diarrhea, vomiting, abdominal pain, steatorrhea
- hypoproteinemia ← protein loss into intestinal lumen

Path: dilatation of lymph vessels in mucosa + submucosa + abundance of foamy fat-staining macrophages (DDx to Whipple disease: negative for PAS)

√ marked irregular diffuse symmetric thickening of folds in jejunum + ileum ← dilated intestinal lymphatics + hypoproteinemic edema

√ micronodularity ← dilated lacteal vessels in submucosa + lamina propria

√ slight separation + rigidity of folds

√ dilution of barium column ← considerable increase in intestinal secretions from malabsorption

√ no / mild dilatation of bowel

Lymphangiogram (not always diagnostic):

√ hypoplasia of lower extremity lymphatics

√ occlusion of thoracic duct / large tortuous thoracic duct

√ obstruction of cisterna chyli with backflow into mesenteric + intestinal lymphatics

√ hypoplastic lymph nodes

Dx: small bowel biopsy (dilated lymphatics in lamina propria + vascular core)

Rx: low-fat diet with medium-chain triglycerides (direct absorption into portal venous system)

DDx: (1) Whipple disease (more segmentation + fragmentation, wild folds)

(2) Amyloidosis (edema + secretions usually absent)

(3) Hypoalbuminemia (less pronounced symmetric thickening of folds, less prominent secretions)

INTESTINAL PSEUDOOBSTRUCTION

= decreased ability of intestines to push food through

◊ Clinical and radiological findings similar to true intestinal obstruction

√ dilation of various parts of the bowel

A. Primary (idiopathic or inherited)

B. Secondary (due to another disease)

Colonic Pseudoobstruction

= PSEUDOMEGACOLON = ADULT MEGACOLON = ADYNAMIC ILEUS = FUNCTIONAL OBSTRUCTION = IDIOPATHIC LARGE-BOWEL OBSTRUCTION = OGILVIE SYNDROME

[Sir William Heneage Ogilvie (1887–1971), English surgeon at Guy's Hospital, London]

X-ray:

√ nonspecific findings of gaseous distention of colon

√ cecal diameter > 12 cm → colonic decompression

BE:

◊ Avoid if cecal perforation is suspected!

Rx: nasogastric suction, enemas, neostigmine, colonoscopic decompression

DDx: mechanical obstruction, paralytic ileus

Acute Colonic Pseudoobstruction

= rare clinical disorder with signs & symptoms & radiographic appearance of an acute large bowel obstruction but without mechanical obstruction

Pathogenesis:
imbalance in autonomic nervous system (sympathetic overactivity + parasympathetic suppression) after recent significant medical illness / surgical procedure

Cause: retroperitoneal trauma, especially fracture (11–52%), pelvic / abdominal / cardiothoracic surgery (20%), infection (10%), cardiac disease [MI, CHF] (10%)

In 50% associated with:
metabolic imbalance (hypokalemia, hypocalcemia, hypo-magnesemia), drugs (narcotic analgesics, antidepressants, antipsychotic, calcium channel blockers, narcoleptics)

Age: > 60 years / younger patient with spinal disorder; M > F

- abdominal pain (80%), abdominal distension
- nausea & vomiting (80%), obstipation (40%), diarrhea
- fever (37%), bowel sounds present

√ massively dilated colon, especially cecum + right hemicolon (occasionally extending to rectum)

√ normal haustral markings

√ "colon cut-off" sign ← lack of gas in distal colon

√ small bowel air-fluid levels

√ absence of obstructive lesion on enema

Cx: cecal perforation

Prognosis: 15–45% mortality

Rx: nasogastric + rectal suctioning; neostigmine; colonic decompression (if cecum exceeds 10 cm)

DDx: toxic megacolon, mechanical obstruction

Chronic Colonic Pseudoobstruction

= recurrent or persistent pseudobstruction of colon

Path: atrophic changes + decreased numbers of intramural ganglia (= sign of irreversible intramural plexus damage)

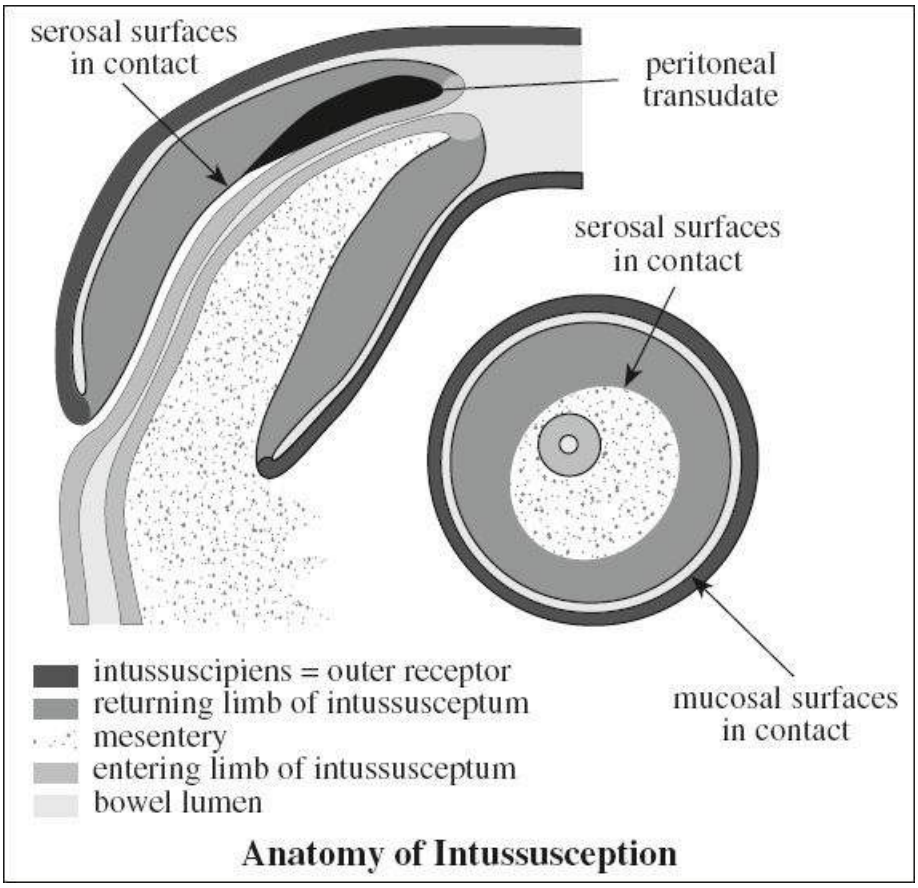
• chronic constipation, repeated obstructive symptoms

CT:

√ marked colonic dilatation: cecum (4–10 cm), transverse colon (8.2–13.7 cm)

√ intermediate transitional zone at / adjacent to splenic flexure (= transition zone of innervation from vagal to sacral nerves for proximal versus distal colon)

◊ Rarely accompanied by perforation!



Anatomy of Intussusception

Chronic Intestinal Pseudoobstruction Syndrome

= nonpropulsive intestine characterized by impaired response to intestinal dilatation without definable cause; ? autosomal dominant

Cause:

(1) Reduced density of interstitial cells of Cajal in colon (= intestinal pacemaker cells)

(2) Neuropathic disorder: amyloidosis, diabetes, multiple sclerosis, brainstem tumor, stroke, spinal cord injury, Parkinsonism, paraneoplastic syndromes (antineuronal nuclear antibodies)

(3) Myopathy: scleroderma

(4) Medication: anticholinergic antidepressant, calcium channel blocker, alpha-2 adrenergic agonists

Age: neonatal period / delayed for months + years,
M÷F = 1÷1

• recurrent attacks of nausea & vomiting (83%)

- abdominal pain (74%), abdominal distension (57%)
- constipation (36%), diarrhea (29%)
- persistently decreased peristalsis

√ esophageal dilation + hypoperistalsis (lower third)
√ excessive duodenal dilation (DDx: megaduodenum, superior mesenteric artery syndrome)
√ mild to marked gaseous distension of proximal small bowel
√ ligament of Treitz may be placed lower than usual
√ delayed transit of barium through affected segments
√ disordered motor activity (on fluoroscopy)
√ small bowel air-fluid levels + distension
√ disturbed intestinal transit

INTUSSUSCEPTION

= telescope-like invagination or prolapse of a segment of intestinal tract (= intussusceptum = donor loop) into the lumen of the adjacent intestinal segment (= intussuscipiens = receiving loop)

◊ The intussuscipiens contains the folded intussusceptum with entering limb + returning limb + their mesentery

Classification by Location: enteroenteric, ileocolic, ileocecal, colocolic

Classification by Cause: benign, malignant, idiopathic, ± lead point

Intussusception in Children (94%)

Prevalence: 2–4÷1,000 live births; most common abdominal emergency of early childhood

◊ Leading cause of acquired bowel obstruction in childhood!

Etiology:

(1) Idiopathic (over 95%): mucosal edema + lymphoid hyperplasia (= enlarged Peyer patches) following viral gastroenteritis; predominantly at ileocecal valve

(2) Lead point (5%):

(a) infants < 30 days of age: Meckel diverticulum (most common), duplication cyst

(b) children > 3 years of age: Burkitt lymphoma, polyp in Peutz-Jeghers syndrome, polypoid hemangioma, enterogenous cyst, ectopic pancreas, suture granuloma, periappendicitis, Henoch-Schönlein purpura, coagulopathy, cystic fibrosis, inspissated meconium

mnemonic: H DIMPL

Henoch-Schönlein purpura
Duplication cyst
Idiopathic (= hypertrophied lymphoid tissue)
Meckel diverticulum
Polyp
Lymphosarcoma

Age: peak incidence between 6 months and 2 years; 3–9 months (40%); < 1 [< 2] {> 3} years (50%) [75%] {< 10%}; M÷F = 2÷1

- classic triad:

(1) Abrupt onset of acute colicky abdominal pain (94%)

(2) Red "currant jelly" stools / hematochezia (66%) usually only after > 48 hours duration
(3) Palpable abdominal mass (59%) / vomiting (91%)
• diarrhea, restlessness, pallor, fever

Location: ileocolic (75–95%) > ileoileocolic (9%) > ileoileal (4%) > colocolic
Tip of intussusceptum: transverse colon + hepatic flexure + ascending colon (90%)

Plain film (40–90% accurate):
◊ Air within cecum excludes diagnosis of ileocecal intussusception!
CAVE: Sigmoid colon may be mistaken for cecum as it is often positioned in RLQ in infants and children!
√ no abnormality in 25%
√ abdominal soft-tissue mass (50–60%), usually in RUQ:
√ "**target**" sign = concentric lucent rim surrounding a soft-tissue mass ← mesenteric fat of intussusceptum
√ "**meniscus**" sign = crescent of intraluminal colonic gas outlining the apex of the intussusceptum
√ loss of inferior hepatic margin

The target and meniscus signs are the most specific radiographic findings of an intussusception.

√ little air in small intestine:
√ paucity of gas in RLQ / pelvis
√ gasless lower abdomen
√ air in displaced appendix
√ small bowel obstruction for several hours (25%):
√ dilated loops of small bowel
√ stacked air-fluid levels
√ pneumoperitoneum (usually > 2–3 days of symptoms)

Antegrade barium study:
√ "coiled spring" appearance
√ beaklike abrupt narrowing of barium column demonstrating a central channel

Diagnostic Enema:
Indication: unusual age of child (< 2 months, > 4 years), high fever, peritoneal signs
Contraindication: free air
√ "meniscus" sign = convex intracolic mass = rounded apex of intussusceptum protrudes into contrast column
√ "coiled spring" sign = edematous mucosal folds of returning limb of intussusceptum outlined by contrast material within lumen of colon

US (98% sensitive, 98% specific, 99% NPV):
√ readily detectable mass over 5.0 x 2.5 cm
√ "crescent-in-doughnut / target / bull's eye" sign (on TRANSVERSE scan) = concentric rings of alternating hypoechoic + hyperechoic layers (= intussuscipiens) with central hyperechoic portion (= mesentery of intussusceptum)
√ "**pseudokidney / sandwich / hay fork**" sign (on LONGITUDINAL scan) = hypoechoic layers on each side of echogenic center of mesenteric fat
√ peritoneal fluid trapped inside intussusception in < 15% (associated with irreducibility + ischemia)

√ echogenic mesentery contains lymph nodes + ceco-appendiceal complex close to base of intussusception
√ color Doppler demonstrates mesenteric vessels dragged between entering + returning wall of intussusceptum:
◊ Absence of blood flow within the intussusceptum → suggests bowel necrosis (47%)!
◊ Presence of blood flow within the intussusceptum is a good predictor of reducibility!

CT:
√ sausage-shaped / targetoid mass of "multiple concentric rings" = 3 concentric cylinders:
(a) central = canal + wall of intussusceptum
(b) middle = crescent of mesenteric fat
(c) outer = returning intussusceptum + intussuscipiens
√ enhancing vessels within mesenteric fat
√ proximal obstruction

Cx: vascular compromise ← incorporation of mesentery (hemorrhage, infarction, acute inflammation)

Hydrostatic / Pneumatic Reduction

< 1% mortality if reduction occurs < 24 hours after onset!

Overall success rate: 70–85%

Contraindications: pneumoperitoneum, peritonitis, hypovolemic shock, severe dehydration
◊ Obtain abdominal radiograph to document absence of perforation before reduction!

Technique:
» Sedation (debated) with morphine sulfate (0.2 mg/kg IM) / fentanyl citrate IV (straining increases intraluminal pressure of distended colon)
» Anal seal with 24-F Foley catheter + balloon inflation to size equal to interpediculate distance of L5; balloon pulled down to levator sling; taped to buttocks; both buttocks firmly taped together
» 60% wt/vol barium sulfate with container between 24–36 inches above level of anus
» Extensive reflux into small bowel desirable to exclude residual ileoileal intussusception
◊ Maximally 3 attempts for 3 minutes each
◊ Manual manipulation increases colonic pressure
◊ Reduction should be accomplished within 10 minutes

"**Rule of 3s**":
(1) 3.5 feet (105 cm) above table (= 120 mmHg)
(2) 3 attempts
(3) 3 minutes between attempts → delay allows venous congestion + edema to subside

Alternative medium:
(1) 1÷4 Gastrografin®-water solution raised to a height of 5 feet (150 cm)
(2) Air (METHOD OF CHOICE): delivers higher intra-colonic pressures, faster, easier, less fluoroscopic time, barium-free colon in case of surgery, smaller tears, less contamination of peritoneal cavity

(3) Ultrasound-guided saline enema: NO limit to procedure time, low perforation rate

Decreased Success Rate:

(1) Duration of symptoms > 48 hours
(2) Significant dehydration
(3) Radiographic signs of small bowel obstruction
(4) Patient age < 3 months or > 5 years
(5) Fluid trapped between layers of intussusception by US
(6) Absence of color flow within intussusception

Cx: perforation (0.4–3.0%, colonic bursting pressure ~ 200 mmHg); reduction of nonviable bowel; incomplete reduction; missed lead point

Prognosis: 10–15% rate of recurrence within first few days

Intussusception in Adults (5–6%)

Frequency: accounts for 1% of all bowel obstructions; 0.05% of CT exams

In adults a lead point intussusception involving the small bowel is generally due to a benign condition and less often due to a neoplasm (usually a metastatic lesion).

Etiology:

A. SPECIFIC CAUSE (80%):
1. Tumor: benign (⅓; lipoma, leiomyoma, adenomatous polyp), malignant ($^1/_5$; lymphoma, metastasis)
2. Postsurgical changes (⅓): adhesions adjacent to sutures / submucosal bowel edema / discoordinated motility
3. Invaginated (= inverted) Meckel diverticulum
4. Prolapsed gastric mucosa
5. Aberrant pancreas
6. Foreign body, feeding tube
7. Chronic ulcer: TB, typhoid
8. Prior gastroenteritis
9. Gastroenterostomy, trauma

spontaneous without anatomic lead point:
celiac disease, scleroderma, Whipple disease, fasting, anxiety, agonal state

B. IDIOPATHIC (20%)

Causes of Adult Intestinal Lead Point Intussusception

Cause	*Small Bowel*	*Large Bowel*
Benign	lipoma, adenomatous polyp, Meckel diverticulum	lipoma, adenomatous polyp
Malignant	metastasis, lymphoma, adenocarcinoma	adenocarcinoma, lymphoma, metastasis
Idiopathic	postoperative adhesion, motility disorder	postoperative adhesion, motility disorder

- recurrent episodes of colicky pain, nausea, vomiting
- abdominal tenderness, distension, change in bowel habits

• palpable mass (in up to 50%), bloody stool (in majority)
Location: ileoileal (40%) > ileocolic (15%), colocolic
small bowel (55%): nonneoplastic (43%), benign neoplasm (40%), malignant neoplasm (17%)
colon (45%): malignant neoplasm (48%), benign neoplasm (21%), nonneoplastic (31%)
Prognosis: self-limiting if intussusception < 3.5 cm in length

Transient (Idiopathic) Intussusception

= temporary short-lived intussusception without clinical significance incidentally detected on abdominal CT
Cause: idiopathic; celiac disease, Crohn disease
• asymptomatic
Location: small bowel, especially jejunum
√ < 3.5 cm in length
√ NO intestinal obstruction, NO lead point

ISCHEMIC COLITIS

= most common manifestation of ischemic injury to GI tract (50%) characterized by acute onset + rapid clinical and radiographic evolutionary changes
Types:
1. Occlusive / thromboembolic ischemic colitis (80%)
2. Nonocclusive ischemic colitis (20%)
   = major mesenteric vessels usually patent
   (a) low systemic flow state: hypovolemic shock, severe heart failure, arrhythmia, renal insufficiency, sepsis
   (b vasoconstricting drugs: cardiotonics, NSAID, amphetamines, cocaine
3. Venous insufficiency

Pathophysiology:
decrease in blood flow to 20% of normal flow associated with small vessel disease (hypoxia) + reperfusion injury when blood flow is reestablished; injury more severe if terminal vascular branches obstructed rather than proximal mesenteric arcades
Path:
(a) injury of mucosa + submucosa (the 2 most sensitive layers to ischemia) → mucosal congestion, patchy necrosis, ulcerations, submucosal edema, hemorrhage
◊ Early mucosal injury is reversible!
(b) injury of muscularis propria (after severe + prolonged ischemia) → can lead to transmural necrosis → fibrotic stricture, perforation, severe sepsis
Precipitating factors:
(a) bowel obstruction: volvulus, carcinoma (proximal dilatation with increased intraluminal pressure and reduced blood flow)
(b) thrombosis: myocardial infarction, oral contraceptives, collagen vascular disease, sickle cell disease, hemolytic-uremic syndrome
(c) trauma: aortoiliac reconstruction (2%) with ligation of IMA, cardiac surgery
(d) idiopathic / spontaneous: mainly in elderly

mnemonic: VINTS

Vasculitis
Incarceration (hernia, volvulus)
Nonocclusive ischemia (shock, CHF)
Thrombosis (atherosclerosis, emboli, polycythemia vera, hyperviscosity)
Spontaneous

Age: usually > 50 years; M = F

- abrupt onset of lower abdominal pain + rectal bleeding
- abdominal tenderness, diarrhea, lack of sepsis
- negative stool cultures

Location: segmental involvement of any part of colon; left colon (46–90%); right colon (30%); entire colon (11%); transverse colon (9%); sigmoid colon (4%); rectum spared <u>most commonly affected "watershed" segments:</u>

(a) **Griffith point** (80%) = junction between distribution of superior + inferior mesenteric arteries at splenic flexure
(b) **point of Sudeck** = anastomotic plexus between inferior mesenteric artery + hypogastric vascular supply at rectosigmoid junction

Mean length of segmental involvement: 19 cm

Plain film (usually normal):

√ segmental thumbprinting = marginal indentations on mesenteric side (rare finding on plain film)

BE (in 90% abnormal):

◊ Double contrast BE is more sensitive than single contrast BE which may efface thumbprinting!
√ thumbprinting (75%) ← submucosal hemorrhage + edema
√ transverse ridging = markedly enlarged mucosal folds with some preserved wall pliability ← spasm
√ serrated mucosa ← inflammatory edema + superficial longitudinal / circumferential ulcerations
√ deep penetrating ulcers (late)

CT (detection rate of 26–39%):

√ symmetric / lobulated segmental thickening of colonic wall between 2 and 20 (mean 8) mm:
  √ shaggy configuration + alternating layers of high and low attenuation (= "double halo" sign) + marked pericolic streakiness of edema (wet appearance in 61%)
  √ sharply defined homogeneously enhancing wall + mild mural thickening (dry appearance in 33%)
√ hyperattenuating mucosa in early stage ← hemorrhage
√ blood clot in SMA / SMV
√ loss of haustral markings
√ irregular narrowed atonic lumen (= thumbprinting)
√ curvilinear collection of intramural gas (pneumatosis coli in 6%) → suggests bowel infarction
√ portal + mesenteric venous gas
√ pneumo- and retropneumoperitoneum (= the only PATHOGNOMONIC sign of transmural

necrosis)

CECT:

- √ hyperenhancing mucosa in early stage ← hyperemia
- √ reduced / absent enhancement in later stage ← intense vasospasm accompanied by bowel dilatation
- √ absent opacification in SMA / SMV distribution

US:

- √ circumferential hypoechoic > 3 mm thick bowel wall
- √ variable loss of mural stratification (= indistinct layers)
- √ abrupt transition from ischemic to normal bowel
- √ absent / diminished color flow in bowel wall = indicator of severity of ischemia (82% sensitive, 92% specific)
- √ absence of arterial signals; however, blood flow on Doppler may represent reperfusion of gut wall
- √ usually unaltered perienteric fat
- √ commonly associated with:
  - √ ascites, luminal bowel distention
  - √ pneumatosis intestinalis, gas within portal veins

Angio (findings similar to inflammatory disease):

- √ normal / slightly attenuated arterial supply
- √ mild acceleration of arteriovenous transit time
- √ small tortuous ectatic draining veins

Prognosis:

(1) Transient ischemia = complete resolution within 1–3 months (76%)

(2) Stricturing ischemia = incomplete delayed healing
   - √ narrowed foldless segment of several cm in length with smooth tapering margins

(3) Gangrene with necrosis + perforation (extremely uncommon)

(4) Mortality rate of 11–36%

DDx of dry appearance: ulcerative / granulomatous colitis

DDx of wet appearance: pseudomembranous colitis, CMV colitis

Ischemic Necrosis of Cecum

= rare spontaneous potentially life-threatening entity

Associated with: chronic heart disease, cardiopulmonary bypass surgery, systemic chemotherapy, cholesterol embolization, aortitis syndrome

Age: elderly

CT:

- √ circumferential cecal wall thickening
- √ mural stratification pattern ← submucosal edema
- √ mild pericolic stranding with normal appendix and absence of diverticula
- √ isolated pneumatosis coli
- √ mesenteric / portal venous gas
- √ pneumoperitoneum

JEJUNAL ATRESIA

◊ Air may be injected through nasogastric tube
◊ BE to exclude 2nd and 3rd areas of atresia
Cause: intrauterine ischemic injury to developing gut
Age: majority presenting during 1st day of life
In 25% associated with: malrotation, volvulus, gastroschisis, omphalocele
• bilious vomiting, abdominal distension, failure to pass meconium
Plain film:
N.B.: difficult to tell colon from small bowel in neonate
√ 2–3 dilated bowel loops
√ absence of gas in lower portion of abdomen
BE:
Purpose: to exclude large-bowel causes of obstruction, show anatomical size of colon, demonstrate meconium ileus
√ microcolon / small colon / colon of normal caliber (due to sufficient intestinal secretions in remaining small bowel)
Cx: meconium peritonitis (5%)

JEJUNAL DIVERTICULAR DISEASE

= JEJUNAL DIVERTICULOSIS
= rarest form of gastrointestinal diverticular disease
Cause: disordered contractions of smooth muscle results in increased intraluminal pressure and mucosal herniation (= pulsion diverticula = false diverticula)
Frequency: 0.5–1.1–2.3% on UGI; 0.3–4.5% of autopsy series; M > F
Age: 6th–7th decades
Location: 80% in jejunum, 15% in ileum (usually solitary), 5% in jejunum + ileum
Site: on mesenteric border near entrance of vasa recti
• intermittent upper abdominal pain, flatulence, episodes of diarrhea (30%)
Size: a few millimeters to > 10 cm
Plain film:
√ air-fluid levels in multiple diverticula
√ slight dilatation of intestinal loops in area of diverticula
BE:
√ may not fill (narrow neck / stagnant secretions)
√ trapped barium on delayed film after 24 hours
Cx:
(1) Blind loop syndrome with bacterial overgrowth
• steatorrhea, diarrhea, malabsorption, weight loss
• megaloblastic anemia ← overgrowth of coliform bacteria leads to deconjugation of bile acids + intraluminal metabolism of vitamin B_{12}
(2) Free perforation = leading cause of pneumoperitoneum without peritonitis (21–40% mortality)
(3) Hemorrhage (few cases)
(4) Diverticulitis
(5) Intestinal obstruction: enterolith ileus

JUVENILE POLYPOSIS

= rare autosomal dominant disease with variable penetrance characterized by development of multiple (> 5) juvenile polyps in GI tract

◊ Most common familial / nonfamilial colonic polyp in children (75%)!

Categories:

A. JUVENILE POLYPOSIS OF INFANCY

Age: 4–6 years (range 1–10 years); M÷F = 3÷2

• protein-losing enteropathy, hemorrhage

√ intussusception

B. COLONIC & GENERALIZED JUVENILE POLYPOSIS

Age: in 85% manifested by 20 years of age

Path: hamartomatous polyps; adenomas may coexist

Histo: little / no smooth muscle; hyperplasia of mucous glands; retention cysts develop with obstruction of gland orifices (multiple mucin-filled spaces); edematous inflamed expanded lamina propria

DDx: familial adenomatous polyposis, Peutz-Jeghers syndrome

• rectal bleeding (95%) most commonly as intermittent bright red hematochezia; abdominal pain ← intussusception

• anemia, diarrhea, constipation; prolapse of polyp / rectum (rare)

Location: rectosigmoid (80%); rare in small bowel + stomach; not in esophagus

√ solitary polyp (75%); multiple polyps (⅓) of smooth round contour

√ lesion of pinpoint size / up to several cm in diameter

√ invariably on stalk of variable length

Dx: (1) Any number of polyps with family history

(2) Polyps throughout the GI tract

(3) > 5–10 polyps in colon

Cx: colorectal cancer by 35 years of age (in 15%)

DDx: solitary juvenile polyps (< 5 polyps, 1% prevalence in children)

KAPOSI SARCOMA

[Moritz Kaposi (1837–1902), dermatologist in Vienna, Austria]

= multicentric low-grade malignant vascular neoplasm originating from endothelial cells of lymphatic / blood vessels

Cause: Human herpes virus type 8 (HHV_8) and other cofactors (eg, cytokine-induced growth)

Frequency: most common AIDS-related neoplasm (40–50%); in 51% of homosexual / bisexual men with AIDS; rare in hemophiliacs; M÷F = 50÷1

Histo: proliferation of spindle cells with numerous extravasated RBCs located in clefts between stromal cells

Almost always associated with: cutaneous disease

Variants:

A. IMMUNE DYSREGULATION

1. Classic (sporadic / Mediterranean) Kaposi sarcoma

Age: 50–80 years; M÷F = 10÷1 to 15÷1

Geography: eastern European, Mediterranean, Askenazi Jews

2. Endemic (African) Kaposi sarcoma
Geography: East Africa, Central Africa
Age: 30–40 years; M÷F = 13÷1 to 17÷1

B. IMMUNOSUPPRESSIVE STATE

3. Iatrogenic (organ transplant-related) Kaposi sarcoma
Prevalence: 6% of all organ transplant recipients and others on immunosuppressive therapy
Mean development time: 21 months
4. AIDS-related (epidemic) Kaposi sarcoma
Prevalence: up to 50% in lifetime of homosexual male > IV drug user > hemophiliac > woman

@ Skin (66%, most frequent site)
• multiple bluish red slightly elevated skin lesions

@ Mucosal disease (56%)
Site: intraoral, pharyngeal, laryngeal, nasal cavity
√ multiple nodular cutaneous / mucosal lesions
√ nonspecific MR: low T1 + high T2 signal intensity
√ CHARACTERISTIC avid enhancement

@ Lymph node involvement (13–80%, 2nd most frequent site):
√ hyperattenuating lymphadenopathy ← vascularity: peripancreatic, porta hepatis, retroperitoneal, mesenteric, inguinal, pelvic
Associated with: high frequency of GI tract involvement

@ GI tract (40–50% of AIDS-related Kaposi sarcomas; 3rd most frequent site):
• usually clinically silent
• concurrent with / after cutaneous disease
◊ GI tract is the only site of involvement in < 5%!
Location: anywhere within GI tract; often multifocal
√ thickened nodular folds
√ single / multiple polypoidal 0.5–3.0-cm subepithelial nodules / masses:
√ ± central umbilication / ulceration (common) = "bull's-eye" / "target" lesions on BE
√ infiltrating linitis plastica lesion (rare)
√ mass enhancement greater than adjacent mucosa ← high tumor vascularity

@ Liver & spleen (34% at autopsy)
√ multiple 5–12-mm nodules hyperechoic on US, hypoattenuating on NECT/CECT indistinguishable from multiple hemangiomas
DDx: metastatic disease, fungal microabscesses, multiple areas of bacillary angiomatosis (= swollen venous lakes in liver)
√ splenomegaly
Prognosis: infrequently contribute to morbidity + mortality

@ Lung (18–47% of patients with cutaneous sarcoma):
= late complication of AIDS
Site: bilateral symmetric peribronchovascular axial interstitium (91%); middle / lower lung zones (92%)
√ coarsening of bronchovascular bundles:

√ tram track opacities
√ peribronchial cuffing
√ septal lines (38–71%)
√ interlobular septal thickening + fissural nodularity
√ numerous perihilar ill-defined asymmetric coalescent clusters of consolidation ± air bronchograms in 45% (= confluent tumor)
√ small (50%) / large (28%) pulmonary nodules ← tumor proliferation extending into parenchyma:
√ "halo" sign = ground-glass opacities surrounding nodule
√ pleural effusion (33–67%), chylothorax (rare)
√ moderate lymphadenopathy (10–35%, late in disease): axillary, mediastinal, hilar
√ thoracic wall masses
@ Musculoskeletal system
√ lytic cortical lesion
√ subcutaneous nodules
Dx: endoscopic visualization + biopsy of mass of red-purple color

KILLIAN-JAMIESON DIVERTICULUM

= rare pulsion diverticulum through muscular gap in anterolateral wall of proximal cervical esophagus inferior to cricopharyngeus muscle
Cause: tightness of cricopharyngeal (= upper esophageal) sphincter → retrograde reflux with increased pressure on relative sidewall weakness
Age: usually > 60 years (same as for Zenker diverticulum)
• almost all asymptomatic
Location: muscular gap at Killian-Jamieson triangle just below cricopharyngeal muscle more inferiorly than Zenker diverticulum; bilateral in 25%
√ predominantly left lateral + anterior outpouching from cervical esophagus
Cx: overflow aspiration

LADD BANDS

= PERITONEAL BANDS
= congenital fibrous stalk of peritoneal tissue
Attachment:
(a) normal: fixates right side of colon to peritoneal wall
(b) malrotation: from RUQ (← malpositioned cecum / hepatic flexure) to right paracolic gutter extending across anterior surface of 2nd / 3rd portion of duodenum
Associated with: malrotation
Cx: duodenal obstruction at its 2nd portion (even without volvulus)
√ oblique termination of duodenal contrast column

LEIOMYOMA

N.B.: In older literature synonymous with GIST (far more frequent, variable risk of progression and metastasis)
Path: arising from muscularis propria

Histo: low to moderate cellularity, intersecting fascicles of spindle cells with eosinophilic cytoplasm, desmin globules (occasionally)
- negative for c-KIT, strongly diffusely positive for desmin + smooth muscle actin (DDx to GIST)

@ Stomach (rare)
Location: gastric cardia
√ low-attenuation mass with endoluminal growth pattern
√ central ulceration for tumor > 2 cm in diameter
Size: 1.3–4.7 cm
DDx: GIST, schwannoma

Leiomyoma of Esophagus

◊ Most common benign subepithelial tumor of esophagus; 50 x less common than esophageal carcinoma
Frequency: 1÷1,119 (autopsy study); 50% of all benign esophageal tumors
Histo: interlacing / palisading pattern of spindle cells with eosinophilic cytoplasm; areas of dense collagen may become calcified
RARE: cystic degeneration, necrosis, ulceration
Age: 4–81 years; 3% in children; M÷F = 2÷1
- usually asymptomatic (due to slow growth)
- dysphagia, odynophagia, dyspepsia usually for > 2 years
- hematemesis if large (rare)

Site: frequently lower + mid ⅓ of esophagus (smooth muscle portion); intramural (97%); multiple leiomyomas in 3–4%
Size: usually < 3 cm (range, 2–15) cm

Leiomyomas have typical findings of an intramural mass = smooth-surfaced crescent-shaped filling defect forming right or slightly obtuse angles with the esophageal wall.

√ smooth slightly lobulated well-defined intramural mass
√ homogeneous contrast enhancement
√ may have coarse calcifications (DDx: GIST)

Barium:
√ smooth-surfaced crescent-shaped filling defect forming right / slightly obtuse angles with esophageal wall
√ deformity of lumen
√ occasionally encircling wall → short stricture
CAVE: high percentage misdiagnosed as extrinsic lesion!

Endoscopic US (89% accuracy):
√ homogeneous hypoechoic mass in muscularis mucosae / submucosa / muscularis propria
√ intact overlying mucosa

CT:
√ homogeneous mediastinal mass in mid to lower esophagus
√ iso- / hypoattenuating to muscle

MR:
√ slightly hyperintense mass on T2WI

PET:
√ usually negative ← low mitotic rate

Rx: endoscopic resection, surgical enucleation, observation

DDx: (1) GIST (positive for CD117 + CD34, central low attenuation, 10 x less frequent than leiomyoma)
(2) Duplication cyst (2nd most common benign lesion of esophagus, manifestation during childhood, may communicate with lumen)
(3) Granular cell tumor (often multiple, less common)
(4) Lymphoma; metastasis

Esophageal Leiomyomatosis

Mean age: 11 (range, 6–18) years; M > F

Cause: (1) Sporadic (50%)
(2) Familial disease (20%): leiomyomas of uterus, vulva, tracheobronchial tree, small bowel, rectum
(3) Alport syndrome (30%) = nephritis, high-frequency sensorineural hearing loss, congenital cataract ← germline deletion of collagen IV subunit genes on X-chromosome

Site: distal ⅓ or ½ of esophagus ± extension into proximal stomach

• slowly progressive dysphagia over years
√ smooth tapered narrowing of distal esophagus over an average length of 6 cm
√ decreased / absent esophageal peristalsis
√ smooth relatively symmetric defect at cardia ← thickened muscle bulging into gastric fundus

CT:
√ marked circumferential wall thickening of up to 4 cm by mass with relatively low soft-tissue attenuation

DDx: (1) Primary achalasia (shorter narrowed segment)
(2) Secondary achalasia (older individual, recent onset of dysphagia)
(3) Stricture from reflux esophagitis
(4) Idiopathic muscular hypertrophy of the esophagus (in late adulthood, corkscrew appearance of esophagus with nonperistaltic contractions, cardia rarely involved)

Leiomyoma of Small Bowel

◊ Most common benign tumor of small bowel

Location: duodenum (21%), jejunum (48%), ileum (31%); single in 97%

Site: mainly serosal (50%), mainly intraluminal (20%), intramural (10%)

Size: < 5 cm (50%), 5–10 cm (25%), > 10 cm (25%)

√ small ulcer + large barium-filled cavity ← central necrosis + communication with lumen
√ hypervascular

LEIOMYOSARCOMA

Frequency: 6% of all soft tissue sarcomas

Origin: smooth muscle cells within walls of blood vessels (most frequent); undifferentiated

mesenchymal cells
Mean age: 50 years
Location: head & neck (nasal cavity, paranasal sinuses), skin, cervical esophagus, larynx
CT:
√ bulky mass remodelling bone
√ little enhancement, uncommon calcifications
MR:
√ iso- to hypointense relative to muscle on T1WI
√ variably hyperintense relative to muscle on T2WI
√ prominent contrast enhancement

Leiomyosarcoma of Small Bowel

Location: duodenum (26%), jejunum (34%), ileum (40%)
√ usually > 6 cm in size
√ nodular mass: intraluminal (10%), intraluminal pedunculated (5%), intramural (15%), chiefly extrinsic (66%)
√ mucosa may be stretched + ulcerated (50%)
√ may show central ulcer pit / fistula communicating with a large necrotic center
√ intussusception

Leiomyosarcoma of Stomach

Frequency: 0.1–3.0% of all gastric malignancies
Age: 10–73 years; M > F
Histo: pleomorphism, hypercellularity, mitotic figures, cystic degeneration, necrosis
• GI bleeding (from ulceration), obstruction
Metastases:
(a) hematogenous to liver, lung, peritoneum; rarely to bone + soft tissue
(b) direct extension into omentum, retroperitoneum
(c) lymph nodes (rare)
Location: 90% in fundus / body of stomach
Site: anterior / posterior wall; endo- / exogastric
Average size: 12 cm
√ intramural mass; large mass tends to be exogastric
√ very frequently ulcerated
√ may be pedunculated
CT:
√ lobulated irregular outline
√ heterogeneous exogastric mass with central zones of low density ← necrosis with liquefaction
√ air / positive contrast within tumor ← ulceration
√ dystrophic calcifications

Carney Triad

Triad of (1) Gastric GIST
(2) Functioning extraadrenal paraganglioma

(3) Pulmonary chondroma

Prevalence: 24 patients reported; M÷F = 1÷11

LIPOMA

= benign submucosal tumor composed of mature adipose tissue surrounded by a fibrous capsule

◊ Most common subepithelial tumor in colon!

Frequency: in colon in 0.25–4.40% (autopsy); 2–3% of all benign gastric tumors

• asymptomatic; may become symptomatic if > 2 cm

• crampy pain, hemorrhage (rare) ← ulcerated overlying mucosa

• "pillow" sign on optical colonoscopy = pale yellow protrusion, soft on probing

Location: colon (particularly cecum + ascending colon) > duodenum > ileum > stomach (gastric antrum) > jejunum > esophagus

Site: endoluminal-submucosal (90%); subserosal (10%)

Size: average 4 cm, up to 30 cm

√ smooth broad-based, sharply outlined, round / ovoid globular mass of 1–3 cm in diameter

√ short thick pedicle in ⅓ ← repeated peristaltic activity (= lead point for intussusception)

Cx: pedunculated lesion (rare) may prolapse through pylorus → intermittent gastric outlet obstruction

Radiography:

√ ± marked radiolucency

Fluoroscopy:

√ change in shape + size on compression ← softness:

√ "squeeze" sign = sausage-shaped mass on postevacuation radiographs

CT:

√ well-circumscribed spheric / ovoid subepithelial mass of uniform fat density (-20 to -120 HU)

√ density increases with inflammation ← ulceration

MR:

√ high fat SI on all sequences

√ loss of SI on fat-suppressed images

Cx: (1) Intussusception (rare)

(2) Central ulceration ← pressure necrosis of overlying mucosa by large lipoma (rare)

Prognosis: NO liposarcomatous degeneration

Rx: none; endoscopic / surgical resection if > 2 cm

DDx: lipomatosis of ileocecal valve (more common, symmetric enlargement of valve)

LYMPHANGIOMA

= congenital malformation of lymphatic vessels → sequestered embryonic lymphatic vessels that have failed to communicate with the rest of the lymphatic / venous system

Path: usually multiloculated large thin-walled cystic mass with chylous / serous / hemorrhagic fluid contents

Location: head & neck (95%); abdomen (mesentery, rarely affecting GI tract); retroperitoneum (< 1%)

• well-defined often compressible cystic submucosal lesion at colonoscopy

√ CHARACTERISTIC involvement of multiple compartments
√ proximal bowel dilatation (in partial bowel obstruction)
US:
√ elongated multiseptated cystic mass with lobules
√ fluid anechoic / with internal echoes / sedimentation
CT:
√ cystic mass with contents of water- to fat-density (chyle)
MR:
√ T1-hypointense + T2-hyperintense ← serous content
√ hyperintense on T1WI + T2WI ← hemorrhage / fat
Rx: surgery (difficult due to intimate attachment to bowel wall)

LYMPHOGRANULOMA VENEREUM

= LGV = sexually transmitted disease caused by virus Chlamydia trachomatis producing a nonspecific granulomatous inflammatory response in infected mucosa (mononuclear cells + macrophages), perirectal lymphatic invasion
Location: rectum ± extension to sigmoid + descending colon
M÷F = 3.4÷1.0
√ narrowing + shortening + straightening of rectosigmoid
√ widening of retrorectal space
√ irregularity of mucosa + ulcerations
√ paracolic abscess
√ fistula to pericolic area, rectum, vagina (common)
Rx: tetracyclines effective in acute phase before scarring has occurred

LYMPHOID HYPERPLASIA

Frequency: normal variant in 13% of BE examinations
Histo: hyperplastic lymph follicles in lamina propria (Peyer patches) ← probably compensatory attempt for immunoglobulin deficiency
Etiology:
(1) Normal in child / young adult
(2) Self-limiting local / systemic inflammation / infection / allergy
(3) May be related to immunodeficiency / dysgammaglobulinemia with small bowel involvement
Age: (a) generally in children < 2 years
(b) in adults invariably associated with late onset immunoglobulin deficiency (IgA, IgM)
Associated with: splenomegaly, large tonsils, eczematous dermatitis, achlorhydria, pernicious anemia, acute pancreatitis, colonic carcinoma
At risk for:
(1) **Good syndrome** (10%)
= gastric carcinoma + benign thymoma + lymphoid hyperplasia
(2) Respiratory infections
(3) Giardia lamblia infection (90%)

(4) Functional thyroid abnormalities

Location: primarily jejunum, may involve entire small bowel, ascending colon + hepatic flexure, seldom in sigmoid / rectum

- malabsorption (diarrhea + steatorrhea)
- low serum concentrations of IgA, IgG, IgM

√ mucosa studded with innumerable 1–3-mm small uniform polypoid lesions

√ lesions may be umbilicated (uncommon)

LYMPHOMA OF GASTROINTESTINAL TRACT

= PRIMARY LYMPHOMA OF BOWEL

Incidence: worldwide 1÷100,000 per year: 4–20% of all NHL; 0.9% of all GI tumors; 10% of patients with abdominal lymphoma have bowel involvement

◊ Most common extranodal manifestation of NHL (up to 20% of all NHL cases)!

◊ Most common gastrointestinal tumor in children!

◊ Extremely rare in Hodgkin disease!

Dx: (1) No palpable superficial nodes (2) Normal CXR (3) Normal WBC count (4) Lymphoma limited to alimentary tract with involvement of only regional nodes (5) No involvement of liver or spleen

Manifestation:

A. LOCALIZED (in early disease):
lymphoid elements in lamina propria and submucosa

B. DIFFUSE (advanced stage after dissemination)

Risk factors: infection with HIV / Helicobacter pylori, long-standing celiac disease, systemic lupus erythematosus, inflammatory bowel disease (2–3-fold increase), immunosuppression (solid organ transplantation, 5-fold increase with immunosuppressive treatment of patients with inflammatory bowel disease)

Predisposed: Arabs + Middle Eastern Jews

Associated with: celiac disease

Age: 1st peak < 10 years + 2nd peak 53 years; M÷F = 3÷2

Histo:

(1) B-cell lymphoma (most common): in stomach

Diffuse large B-cell lymphoma is most commonly found in stomach > ileum + characterized by diffusely infiltrative nodular lesions with extensive ulcerations.

(2) T-cell lymphoma (in celiac disease / peripheral T-cell lymphoma): in small intestine

(3) Extranodal marginal zone B-cell lymphoma *formerly*:

(a) low-grade **M**ucosa-**A**ssociated **L**ymphoid **T**issue 50–72% of all primary gastric lymphomas (see below)

(b) Immunoproliferative small intestinal disease
= Mediterranean / Middle Eastern lymphoma
= special form of MALT lymphoma in young patients of poor socioeconomic status with suspected infectious etiology

May be associated with: enlargement of extraabdominal lymph nodes, malabsorption

- abdominal pain, weight loss

Classification of GI Tract Lymphoma *(WHO 2007)*	
Type of Lymphoma	*Frequency*
B cell	
Diffuse large B-cell lymphoma	38–57%
Extranodal marginal zone B-cell lymphoma	23–48%
Mantle cell lymphoma (polyposis)	< 1–13%
Follicular lymphoma (in duodenum, jejunum)	2–12%
Burkitt lymphoma (in children)	1–5%
Hodgkin lymphoma	< 1%
T cell	
Enteropathy-associated T-cell lymphoma	3%

Lymphomas are a heterogeneous group of neoplasms with varying sites of GI involvement + varying gross and histologic features → wide spectrum of imaging findings

Radiographic morphology:

1. Polypoid / nodular (47%)
   - √ enlarged nodular folds with a range of nodule sizes
   - √ solitary / multiple smooth subepithelial polypoid masses that may ulcerate
   - √ cobblestone pattern ← lymphomatous polyps
   - √ normal / thickened surrounding tissue
   - √ sprue pattern → may cause intussusception
   - √ **multiple lymphomatous polyposis**
     = rare disorder characterized by numerous small polypoid lesions covering long segments of GI tract, typically a manifestation of mantle cell lymphoma
2. Single ulcerative mass (42%)
   - √ circumferential bulky mass in intestinal wall, often extending into mesentery + regional nodes
   - √ asymmetric bowel wall involvement ± exophytic component
   - √ ± intussusception
   - √ obstruction unusual ← tumor soft and pliable without desmoplastic response

   Cx: fistula, perforation

   DDx: simple peptic ulcer, superficial carcinoma
3. Circumferential / constrictive diffusely infiltrative (11%)
   - √ focal / diffuse thickening of bowel wall
   - √ decreased / absent peristalsis
   - √ ± hose- / tubelike segments of luminal narrowing with obstruction (rare) ← desmoplastic response (rare)
   - √ ± ulceration with considerable excavation

   DDx: adenocarcinoma (shorter segment of involvement, more abrupt transition from tumor to normal bowel)
4. Aneurysmal / cavitary
   - √ nonperistaltic segment with circumferential dilatation ← destruction of muscularis propria + autonomic plexus forming large cavity:

√ large mass with only small intramural component
√ irregular lobulated margin ± small nodules at margin of involved segment

√ tumor involvement of mesentery → cavitated endoexoenteric mass filled with enteric contrast:
√ ± ulcer + fistula + aneurysmatic dilatation

DDx: gastrointestinal stromal tumor (GIST), perforated colonic adenocarcinoma, metastatic disease (especially melanoma)

5. Mixed
√ alternating constriction + dilatation with involvement of a lengthy segment

Staging of Primary Gastrointestinal Tract Lymphoma
(Consensus Conference in Luguano, 1993)

Stage	*Involvement*
I	tumor confined to gastrointestinal tract as single primary site / multiple noncontiguous lesions
II	tumor extends into abdominal cavity from primary gastrointestinal site
II_1	local nodal involvement
II_2	distant nodal involvement
III	penetration through serosa to involve adjacent organs / tissues
IV	disseminated extranodal involvement / GI tract lesion with supradiaphragmatic nodal involvement

6. Mesenteric / retroperitoneal adenopathy
√ single / multiple extraluminal masses displacing bowel
√ ill-defined confluent mass engulfing + encasing multiple loops of adjacent bowel
√ "sandwich configuration" = mass surrounding mesenteric vessels that are separated by perivascular fat
√ conglomerate mantle of retroperitoneal + mesenteric mass

CT staging:
Stage I tumor confined to bowel wall
Stage II limited to local nodes
Stage III widespread nodal disease
Stage IV disseminated to bone marrow, liver, other organs

• abdominal pain, weight loss

Location: 10–25% of NHL are extranodal; stomach (50%) > small bowel > ileocecal region (← Peyer patches) > colon + rectum (0.4%) > esophagus; multicentric in 10–50%

Site: originates in submucosa / deep mucosal layer → may be missed at endoscopy

CT:
√ mild to moderate homogeneous circumferential thickening of stomach / bowel wall:
√ hypo- / isoattenuating compared with normal bowel
√ enhances less than normal bowel
√ ± luminal constriction, dilatation, cavitation
√ typically bulky diffuse regional / mesenteric adenopathy
√ enlargement of spleen

MR:
√ wall thickening ± polypoid / ulcerated lesions:
√ heterogeneous increased T2 signal intensity
√ homogeneous intermediate T1 signal intensity
√ mild to moderate enhancement
√ ⇑ SI at DWI (ADC values higher than in gastric cancer)

Lymphadenopathy extending below renal hila or of bulky character makes lymphoma a likely diagnosis!

Prognosis: 71–82% [0%] 2-year survival rate in isolated bowel lymphoma [stage IV disease with bowel involvement]
Cx during chemotherapy: perforation (9–40%), hemorrhage
DDx: Secondary Intestinal Lymphoma (as part of generalized systemic process)
@ Esophagus (< 1%, least common site of GI involvement)
Histo: predominantly B-cell type / MALT
Esophagram:
√ predominantly subepithelial infiltration
√ mucosal ulceration
Esophagram / CT:
√ polypoid mass / nodularity
Cx: perforation, fistulization
@ Stomach (50–70%, most frequently involved site of GI tract)
Frequency:
accounting for only 1–5% of all gastric malignancies; most common site of extranodal lymphoma (25%); isolated primary gastric malignancy in 10%; NHL÷Hodgkin disease = 10÷1
Histo:
(a) low-grade **M**ucosa-**A**ssociated **L**ymphoid **T**issue = **MALT lymphoma** (in 50–70%)
→ development to high-grade B-cell lymphoma over time

Gastric extranodal marginal zone B-cell lymphoma is usually a superficial spreading lesion confined to mucosa + submucosa occurring anywhere in the stomach and often multifocal.

(b) diffuse large B-cell lymphoma
Location: no predilection for any particular gastric region
Site: arises in lymphoid tissue of lamina propria ← chronic Helicobacter pylori gastritis (normally gastric mucosa has no lymphoid tissue!)
Direct extension into: pancreas, spleen, transverse colon, liver
• epigastric pain, dyspepsia

√ gastric lymphoma is suggested by multiple polypoid tumors with central ulceration ("bull's eyes"), giant cavitating lesion, or extensive infiltration with gastric fold thickening!

√ pliant gastric wall
√ duodenum often affected when antrum involved
√ circumscribed mass with endogastric / exogastric (25%) growth
√ abnormal bulge in gastric contour that fills with oral contrast material
√ infiltrative pattern with broad tortuous thickened folds (diffuse form)

√ polypoid / nodular pattern
√ cavitary pattern with large irregular bull's-eye ulcer
√ luminal narrowing / loss of gastric distensibility (rare)
CT:
√ diffuse involvement of entire stomach (50%), typically more than half of gastric circumference
√ segmental involvement (15%)
√ ulcerated mass (8%)
√ average wall thickness of 4–5 cm
√ luminal irregularity (66%)
√ hyperrugosity (58%)
√ perigastric adenopathy (in 50–60%)
Prognosis: 55% 5-year survival rate after resection; MALT may regress completely after antibiotic therapy
DDx: gastric adenocarcinoma (milder more focal wall thickening, tumor infiltration beyond gastric wall = perigastric fat plane not likely preserved, greater tumor enhancement, luminal narrowing, mural rigidity, linitis plastica, smaller lymph nodes above the level of renal veins)

@ Small bowel (20–30% of all abdominal lymphomas)
Frequency: 2nd most common site of GI tract involvement; with 20% most common small bowel malignancy; most common cause of intussusception in children > 6 years
Location: ileum (51%) > jejunum (47%) > duodenum (2%); solitary (75–90%) vs. multiple sites (10–25%)
Site: arising from lymphoid patches of Peyer
√ nodular / multiple polypoid pattern
√ single mass
√ plaquelike thickening of wall > 5 [> 10] cm in length in 80% [20%] (DDx: Crohn disease)
√ irregular segmental thickening of valvulae with corrugated appearance
√ exophytic = endoexoenteric mass
√ mesenteric / retroperitoneal adenopathy
US:
√ hypo- to anechoic circumferential wall thickening
√ destruction of mural stratification
√ nodular / bulky tumor
√ aneurysmal dilatation of the lumen ← destruction of autonomic nerve plexus
√ bowel obstruction (rare) ← no desmoplastic response
√ loss of peristalsis = late sign
√ intussusception
Cx: perforation into adjacent mesentery → formation of confined usually sterile abscess

@ Terminal ileum & cecum
◊ Most common site of primary lymphoma of small and large bowel ← Peyer patches
√ single 1.5 –7.0 cm long / multiple segments of usually marked circumferential symmetric wall thickening:
√ gradual transition to normal bowel

√ homogeneous attenuation + poor enhancement
√ polypoid lesion of variable size → possible lead point for intussusception
√ may extend into appendix
Cx: ulceration → fistulous tract to adjacent bowel loops
DDx: GIST

@ Colon (1.5% of all abdominal lymphomas)
Frequency: less commonly involved than stomach / small bowel
Histo: nearly all non-Hodgkin B-cell lymphoma
Risk factors: immunosuppression (AIDS, organ transplant recipient), inflammatory bowel disease
Location: ileocecal region most commonly involved (85%) > rectosigmoid region
• nonspecific ± gastrointestinal bleeding
√ solitary bulky mass > diffuse infiltration > multifocal polypoid lesions
√ gross mural circumferential / nodular wall thickening in a long segment (with an average length of 5 cm)
√ annular mass ± ulceration
√ paradoxical dilatation ← submucosal lymphoid infiltration weakens muscularis propria
√ slight enhancement
√ massive often absent regional + distant mesenteric + retroperitoneal adenopathy
Rx: surgical resection followed by adjuvant chemotherapy
DDx: neutropenic colitis (contiguous involvement of cecum + ascending colon, mural stratification of affected segment)

Distinguishing CT Findings of Colonic Lymphoma versus Adenocarcinoma
√ extension into terminal ileum
√ well-defined margins + preservation of fat planes
√ no invasion of adjacent structures
√ perforation without desmoplastic reaction
√ severe luminal narrowing without obstruction and with preserved pliability

Diffuse Large B-Cell Lymphoma (38–57%)

Primary GI diffuse large B-cell lymphoma affects commonly stomach > ileum and is characterized by diffusely infiltrative and nodular lesions with extensive ulcerations.

◊ Most common type of GI lymphoma in adults!
Transformation from: extranodal marginal zone lymphoma (concomitant in > ⅓)
Pah: lymphomatous cells involve the bowel wall from submucosa to serosa + may directly invade adjacent structures
Growth pattern: exophytic + annular (± intraluminal) with full-thickness involvement of bowel wall
Location: stomach (most common) > distal ileum

@ Stomach
Barium:
√ diffusely thickened folds / bulky masses

√ deep areas of ulceration / cavitation (frequent)

CT:

√ gastric wall thickness of > 1– 8 cm

√ thin band of mucosal enhancement during early arterial phase

√ delayed homogeneous enhancement of bulky submucosal mass

√ ± low-attenuation areas of necrosis

√ abdominal lymphadenopathy (most)

PET:

√ FDG avidity in 97%

@ Small bowel

√ segmental aneurysmal dilatation (= luminal diameter > 4 cm in area of thickened bowel wall) in 31% ← weakened muscularis propria + destruction of autonomic nerve plexus

Cx: (1) Perforation ← absence of desmoplastic response

(2) Obstruction (uncommon)

DDx: (1) Adenocarcinoma

(2) Inflammation / infection (preserved wall stratification)

Extranodal Marginal Zone B-Cell Lymphoma (23–48%)

= low-grade **M**ucosa-**A**ssociated **L**ymphoid **T**issue = **MALT lymphoma**

= low-grade lymphoma involving cells that arise from the marginal zone surrounding lymphoid follicles

Age: > 50 years; M÷F = 1.2÷1

Location: stomach (85%), small bowel (Mediterranean lymphoma) and colon (12%), esophagus (rare)

Pathophysiology: gram-negative Helicobacter pylori infection → chronic gastritis → reactive lymphoid follicles → MALT lymphoma

Upper GI:

√ < 1 cm round often confluent mucosal nodules (30–52%) ← focal enlargement of the lamina propria

√ shallow ulcer + thickened folds / focal mass (39–50%)

CT:

√ segmental (< 50% of stomach) mild thickening of gastric wall (between 5 and 10 mm)

√ abdominal lymphadenopathy (14–24%)

CECT:

√ iso- / hypoattenuating compared with normal gastric wall

PET (limited):

√ difficult to discern ← indolent growth pattern + background GI accumulation (FDG uptake in only 71%)

Follicular Lymphoma (2–12%)

= low-grade indolent tumor that does not require treatment

◊ Most common nodal lymphoma in Western countries

Median age: 56 (range, 26–81) years; M÷F = 1÷1

Genetics: CD10 positive; overexpression of anti-apoptotic proteins (in 90%) ←

translocation t(14;18)(q32;21)
Location: duodenum, jejunum
√ multiple scattered / confluent small-bowel nodules of varying size
CT (polyps may not be recognizable due to small size):
√ bowel wall thickening (in 15%)
PET (only 46% sensitive)
Progression: may develop into diffuse large B-cell lymphoma
Prognosis: 98 months median relapse-free survival

Mantle Cell Lymphoma (9–13%)
= aggressive form of lymphoma
Histo: pregerminal center-type lymphomatous cells that arise from inner mantle zone of lymphoid follicle
Genetics: overexpression of immunohistochemical marker cyclin D1 ← translocation t(11;14)(q13;q32)
Mean age: 62 years
Location: ileum > ascending colon > rectum
√ lymphomatous polyposis (most common form):
= numerous small polyps / nodules throughout GI tract of up to 4 cm in size
CT (polypoid nature of nodules may not be apparent):
√ nonobstructive bowel wall thickening + mass formation
√ abdominal lymphadenopathy (most)
√ extra-abdominal involvement
Prognosis: poor; median survival of 3–4 years
DDx: (1) Inherited polyposis (family history, in childhood / early adulthood, mucocutaneous pigmentation, fibromatosis, osteomas, dental anomalies)
(2) Blood-borne metastases: breast, lung, malignant melanoma, lymphoma (usually larger lesions, more sporadic, submucosal masses, bull's-eye / target appearance with central ulcer)
(3) Extranodal marginal zone B-cell lymphoma
(4) Follicular lymphoma
Rx: autologous stem cell transplantation

Peripheral T-Cell Lymphoma
Frequency: 5–30% of all NHL
Age: middle age + elderly
Histo: mature T-cell phenotype
Location: bone marrow, skin, lung, liver, GI tract (3%)
Site: small intestine (64%, esp. duodenum + jejunum)
• ± malabsorption
√ multifocal bowel involvement
√ mild (< 1 cm) / 1–2 cm gastric / bowel thickening
√ polypoid mass (rare; common in B-cell lymphoma)
√ thickened plaques, ulcers, strictures

√ nonbulky lymphadenopathy (bulky in B-cell lymphoma)
√ hepatosplenomegaly

T-cell lymphoma compared with large B-cell lymphoma
(a) more frequently involves proximal small bowel
(b) more likely shows multifocal involvement
(c) has a higher frequency of perforation.

Cx: bowel perforation with pneumoperitoneum (41–50% compared with < 30% in B-cell lymphoma)

Enteropathy-associated T-cell Lymphoma

Frequency: 3% of all primary gastrointestinal NHL
Classification:
Type I (80–90%):
Strongly associated with: celiac disease
Type II:
= **Monomorphic CD56+ intestinal lymphoma**

Lymphoma may develop any time during the course of celiac disease, including the time of initial diagnosis.

Median age: 50s; M > F
Location: particularly in proximal small bowel: jejunum / proximal ileum

DDx of Peripheral T-Cell versus Large B-Cell Lymphoma

Feature	*T-cell Lymphoma*	*B-cell Lymphoma*
Small bowel involvement	proximal	distal
Multifocality	50–72%	10–25%
Perforation	41–50%	< 30%
√ polypoid mass	rare	common
Bowel wall character	thickened plaque, ulcer, stricture	exophytic annular mass
Lymphadenopathy	nonbulky	bulky

Barium:
√ thickened nodular folds, ulcers, strictures
CT:
√ circumferential wall thickening
√ ± accompanying lymphadenopathy
√ ± infiltration of mesenteric fat
PET:
√ FDG uptake in 86–100%
Prognosis: poor
Cx: intestinal perforation (16% in Type I, 33% in Type II)
DDx: (1) Diffuse large B-cell lymphoma
(2) Refractory celiac disease (no FDG uptake)

LYMPHOMA OF THE MESENTERY

◊ Most common malignancy involving the mesentery and omentum and most common cause of mesenteric masses
◊ NHL is 3rd most common malignancy in children < 15 years

◊ Mesentery involved in 30–50% of NHL + 4–5% of Hodgkin dz.
Incidence of NHL: 1100 children annually in USA
Associated with: retroperitoneal lymphadenopathy
√ "sandwich" sign = mesenteric lymphadenopathy surrounding mesenteric vessels:
  √ round / oval soft-tissue opacities
  √ irregular masses / lobulated cake-like heterogeneous mass with areas of low attenuation ← necrosis
  √ mildly enhancing
√ "misty mesentery" = mesenteric fat stranding (especially after chemotherapy)
√ direct extension into small bowel
√ displacement of small
DDx: sclerosing mesenteritis, inflammatory infectious / noninfectious disease

MALIGNANT MELANOMA

= develops from melanocytes derived from neural crest cells, arising in preexisting benign nevi (in 20%)
Frequency: 1% of all cancers; increasing at 3.9% annually
Peak prevalence: 40–60 years of age
Risk factors: dysplastic mole, atypical melanocytic hyperplasia, xeroderma pigmentosum, melanoma in first-degree relative, sun-sensitive phenotype, excessive sun exposure
Primary sites: skin, mucous membranes, leptomeninges, eye
• areas of red / white / blue in addition to brown and black colors of benign nevi
• irregular borders with notching + striking protrusions
@ Skin primary
Clark staging:
Level I all tumor cells above basement membrane (in situ lesion)
Level II tumor extends to papillary dermis
Level III tumor extends to interface between papillary + reticular dermis
Level IV tumor extends between bundles of collagen of reticular dermis
Level V tumor invasion of subcutaneous tissue (in 87% metastatic)
Breslow staging:
thin < 0.75 mm depth of invasion
intermediate 0.76–3.99 mm depth of invasion
thick > 4.00 mm depth of invasion
Metastases:
Latent period of 2–20 years after initial diagnosis (most commonly 2–5 years)
Primary site: head + neck (79%), eye (77%), GU system (67%), GI tract (in up to 60%)
@ Lymphadenopathy

› in 23% [75%] with level II + IV [V]
• sentinel node biopsy:
√ intraoperative intradermal injection of dye
√ preoperative lymphoscintigraphy

@ Bone (7–17%)

Prevalence: 30–40% at autopsy
• often initial manifestation of recurrence, poor prognosis
Location: axial skeleton (80%), ribs (38%)
√ predominantly osteolytic
MR of melanotic melanoma:
√ hypo- / isointense on T1WI + T2WI + STIR images (most commonly)
√ hyperintense on T1WI + hypointense on T2WI ← T1-shortening effect of the paramagnetic metals iron + copper bound to melanin
DDx: melanotic / amelanotic <u>hemorrhagic</u> tumor (hyper-intense on T1WI + iso- / hyperintense on T2WI)

@ Lung (70% at autopsy): most common site of relapse
• respiratory failure → most common cause of death

@ Liver (17–23%; 58–66% at autopsy)
√ single / multiple lesions 0.5–15 cm in size
√ larger lesion often necrotic
√ may be partially calcified

@ Spleen (1–5%; 33% at autopsy)
√ single / multiple lesions of variable size
√ solid / cystic

@ GI tract + mesentery (4–8%)
• abdominal pain, GI bleeding
Location: small intestine (35–70%) > colon (14–20%) > stomach (7–20%)
√ multiple hypervascular subepithelial nodules:
√ "bull's-eye / target" appearance on BE = central ulceration ← tendency to outgrow blood supply
√ localized to antimesenteric border of bowel wall ← embolic metastases to intramural rami of vasa recta
√ irregular amorphous cavity (exoenteric growth) in larger lesion ← necrosis, hemorrhage, degenerative change
√ intussusception (10–20%)

@ Kidney (up to 35% at autopsy)

@ Adrenal (11%, up to 50% at autopsy)

@ Subcutis

Prognosis: 30–40% eventually die from this tumor

MALLORY-WEISS SYNDROME

[George Kenneth Mallory (1900–1986), professor of pathology at Boston University]
[Soma Weiss (1898–1942), hungarian born physician-in-chief at Peter Bent Brigham Hospital in Boston]

= mucosal ± submucosal partial thickness tear of distal esophagus ± gastric cardia with involvement of venous plexus

Pathophysiology: violent retching → projection of gastric contents against lower esophagus (similar to Boerhaave syndrome)

Age: 30–60 years; M > F

Predisposed: excessive alcohol consumption

- history of repeated retching / vomiting prior to hematemesis
- massive painless hematemesis

Location: at / above / below (76%) esophagogastric junction

√ 1–4 cm longitudinal collection of barium (single tear in 77%, multiple tears in 23%)

√ extravasation of barium

Angio:

√ bleeding site at gastric cardia

DDx: peptic ulcer / ulcerative gastritis

Rx: supportive

MALROTATION

= abnormal position of small + large bowel ← narrow mesenteric attachment ← arrest in the embryologic development of gut rotation + fixation

Frequency: 1÷500 births

Age: in symptomatic cases: 75% in newborns + 90% in 1st year of life; 5 years average delay in diagnosis; incidental diagnosis in adults

Embryology:

Normal fixation: in LUQ at ligament of Treitz (an extension of the right crus of diaphragm + fibrous tissue around celiac artery, located to left of L2) + RLQ fixation of cecum

Abnormal fixation of mesentery: its upper point below the normal position of ligament of Treitz, its lower point superior + medial to normal cecal position

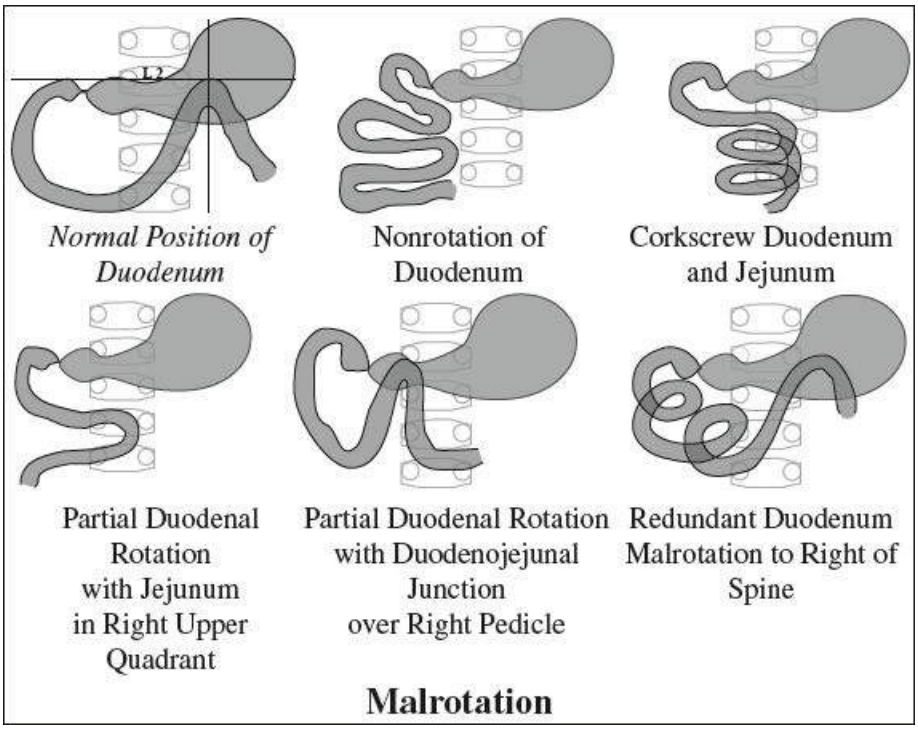
◊ Usually isolated anomaly!

Associated syndromes:

apple-peel intestinal atresia, Cornelia de Lange, Cantrell, cat-eye, chromosomal abnormalities (trisomy 13, 18,21), Coffin-Siris, familial intestinal malrotation, heterotaxy (asplenia, polysplenia), Marfan, Meckel, mobile cecum, prune belly

Associated anomalies:

absence of kidney & ureter, biliary atresia, congenital diaphragmatic hernia (Bochdalek), duodenal web / stenosis / atresia, gastroschisis, Hirschsprüng disease, imperforate anus, intestinal pseudo-obstruction, intussusception, malabsorption, Meckel diverticulum, omphalocele, pyloric stenosis, IVC anomalies, short pancreas, preduodenal portal vein



- symptoms of partial / complete proximal bowel obstruction ← volvulus / peritoneal (Ladd) bands / internal hernia:
  - bilious vomiting (77% of neonates; in 39% within 1st week of life ± abdominal distension
  - recurrent attacks of vomiting + distension (in older children)
  - insidious onset in adulthood with chronic nonspecific symptoms ← intermittent volvulus

Barium meal & barium enema (93–100% sensitive):

Purpose: guess the location of abnormal peritoneal fixation from position of bowel!

√ normal position of duodenum:
- √ 1st portion courses posteriorly
- √ 2nd portion courses inferiorly
- √ 3rd portion courses anteriorly and over spine
- √ 4th portion courses upward to lie at horizontal plane of duodenal bulb or up to 1 vertebral body height inferior

√ clearly abnormal position of duodenum (81%):
- √ duodenum + jejunum to the right of spine (30%)
- √ corkscrew duodenum + jejunum (29%)
- √ duodenojejunal junction low + in midline (22%)

√ unusual abnormal position of duodenum (16%):
- √ duodenojejunal junction over right pedicle
- √ duodenojejunal junction to left of spine but low
- √ duodenal redundancy to right of spine
- √ Z-shape configuration of duodenum + jejunum

√ small bowel on right + colon on left side of abdomen (in 0.2% incidental finding in adults)

√ abnormal position of duodenum + cecum (84%)

√ normal position of duodenum (3%)

√ normal position of cecum (in 5–20%)
DDx: mobile cecum (15%)
15% FP rate:
√ inferior displacement of duodenojejunal junction by distended stomach
√ wandering duodenum = longer meandering course
√ mobile duodenum
√ duodenum inversum
√ displacement of duodenojejunal junction ← renal agenesis, enlargement of spleen, liver transplantation (with cutting of lig. of Treitz), scoliosis, with manual palpation due to lax ligaments in children < 4 years
3–6% FN rate: due to misinterpretation of duodenal course

CT:
√ SMV positioned to left of SMA (80%)
√ aplastic / hypoplastic uncinate process of pancreas

Cx: (1) Midintestinal / midgut volvulus
(2) Duodenal obstruction
(3) Ladd bands
(4) Internal herniation

Mortality: 3–5%

Rx: Ladd procedure

Nonrotation

= midgut loop returns to peritoneal cavity without rotation resulting in weak peritoneal fixation

Frequency: common

• generally asymptomatic: often incidental finding in older children + adults
√ SMA to right of SMV
√ large intestine on left + small intestine on right

Cx: volvulus with "whirl" sign around SMA ← local clockwise rotation

Incomplete Rotation

= failure of midgut loop to complete final 90° of rotation
• prearterial segment of midgut reenters abdomen first toward left side
√ cecum just inferior to pylorus

Cx: duodenal obstruction ← peritoneal bands pass over duodenum)

Reversed Rotation

Frequency: rare

• postarterial segment of midgut reenters abdomen first
= cecum migrates first passing behind SMA toward right thus unwinding the normal counterclockwise rotation of the first stage with additional final 90° clockwise rotation
√ duodenum anterior to SMA
√ transverse colon behind duodenum + SMA

Cx: obstruction of transverse colon ← pressure from SMA

MASTOCYTOSIS

= URTICARIA PIGMENTOSA

= rare systemic disease with mast cell proliferation in skin and RES (lamina propria of small bowel, bone marrow, lymph nodes, liver, spleen) associated with eosinophils + lymphocytes

Age: < 6 months old (in 50%)

Associated with: myeloproliferative disorders, acute nonlymphatic leukemia, malignant lymphoma, mast cell leukemia

Categories:

I indolent mastocytosis (most frequent)
II mastocytosis associated with myeloproliferative / myelodysplastic hematologic disorder
III aggressive / lymphadenopathic mastocytosis with eosinophilia
IV mast cell leukemia (rare)

- diarrhea, malabsorption, steatorrhea, anorexia
- urticaria pigmentosa = cutaneous form (in 80–90%):
  - hyperpigmented skin lesions exhibiting "wheal and flare" phenomenon when disturbed
- abdominal pain, nausea, vomiting
- hypotension with tachycardia, asthma, flushing, headache, gastrointestinal upset with diarrhea, pruritus ← liberation of histamine / prostaglandin D2

  caused by: physical exertion, heat, certain foods, alcohol, nonsteroidal antiinflammatory drugs
- pancytopenia ← chronic neutropenia

@ Skeletal involvement (70%)
- bone and joint pain

Predilected sites: skull, spine, ribs, pelvis, humerus, femur

√ multiple scattered well-defined sclerotic foci with focal / diffuse involvement ← release of histamine by mast cells promotes osteoblastic activity

√ often alternating with areas of bone rarefaction = osteoporosis ← release of heparin + prostaglandin by mast cells activates osteoclasts

@ Reticuloendothelial system

√ hepatomegaly
√ splenomegaly (43–61%)
√ lymphadenopathy: retroperitoneal, periportal, mesenteric
√ Budd-Chiari hepatic venoocclusive disease
√ reversed portal venous flow
√ cavernous transformation of portal vein

@ Abdomen
- nausea, vomiting, diarrhea

√ thickening of omentum + mesentery
√ ascites:
(a) transudative ← liver disease
(b) exudative ← mast cell proliferation of peritoneum

@ Small bowel

√ diffuse irregular thickening of distorted folds
√ generalized 2–3-mm sandlike mucosal nodules ← infiltration by mast cells, lymphocytes,

plasma cells
√ urticaria-like lesions of gastric + intestinal mucosa

Dx: skin / bone marrow biopsy; jejunal biopsy demonstrates an excess of mast cells

Cx: (1) Peptic ulcer disease (release of histamine increases gastric acid secretion)
(2) Leukemia

Rx: antihistamines, histamine decarboxylase inhibitors, sodium chromoglycase; steroids; splenectomy (for symptomatic splenomegaly / hypersplenism)

DDx: carcinoid, pheochromocytoma

MECKEL DIVERTICULUM

= remnant of omphalomesenteric (= vitelline) duct, which usually obliterates by 5th embryonic week

[Johann Friedrich Meckel, the Younger (1781–1833), chairman of surgery and pathological anatomy at University of Halle, Germany]

◊ Most common congenital abnormality of the GI tract!

Frequency: 2–3% of autopsies

Age: majority in children < 10 years of age; M÷F = 1÷1

Path: true diverticulum with all layers of intestinal wall ± connection to umbilicus by fibrous band / omphalomesenteric ligament

Histo: contains ectopic mucosa: gastric / pancreatic / colonic
Frequency of heterotopic gastric mucosa: ⅔ overall; ½ in symptomatic patients; in > 95% with GI hemorrhage

Location: within terminal 6 feet of ileum (= 30–60–100 cm from ileocecal valve); in 94% on antimesenteric side (DDx to ileal diverticulosis on mesenteric side); near midline (± tip attached to umbilicus)

Average length: 2–3 cm

RULE OF 2s: (1) In 2% of population
(2) Symptomatic usually before age 2
(3) Located within 2 feet of ileocecal valve
(4) Two inches (up to 8 cm) in length
(5) Contains 2 types of heterotopic mucosa

• usually asymptomatic
• symptomatic (in 2–4%) because of complications

CT:
√ fluid- or air-filled blind-ending pouch (without Cx) ± particulate matter
√ isolated small bowel obstruction
√ intussusception with small bowel obstruction
√ inverted diverticulum:
  √ central intraluminal area of entrapped fat
  √ surrounded by thick collar of soft-tissue attenuation
√ volvulus
√ inflammatory mass attached to adjacent small bowel
√ intradiverticular enteroliths (3–10%)

√ luminal extravasation of contrast material from bleeding
√ nodular / polypoid intraluminal mass

NUC = "Meckel scan" (> 85% sensitive, > 95% specific, > 83–88% accurate):

◊ ^{99m}Tc-pertechnetate is excreted by mucoid cells of gastric mucosa and not dependent on the presence of parietal cells

N.B.: sensitivity drops after adolescence, because patients who are asymptomatic throughout childhood are less likely to have ectopic gastric mucosa

Preparation:

» No irritative measures for 48 hour (contrast studies, endoscopy, cathartics, enemas, drugs irritating GI tract)
» Fasting for 3–6 hours → results in decreased gastric secretion + diminished bowel peristalsis
» Evacuation of bowel + bladder prior to study

Dose: 5–10–20 mCi (100 µCi/kg) ^{99m}Tc-pertechnetate (adult dose!)

Radiation dose: 0.54 rad/2 mCi for thyroid;
0.3 rad/2 mCi for large intestine;
0.2 rad/2 mCi for stomach

Imaging: immediate continuous anterior imaging for 30–45 minutes / serial images in 5–10-minute intervals for up to 1 hour

√ small focal collection of tracer in RLQ appearing at the same time / shortly after gastric activity
√ tracer activity increases in intensity with time parallel to that of stomach
√ improved visualization through
(a) pentagastrin → stimulates uptake (6 µg/kg SC 20 minutes prior to pertechnetate)
(b) cimetidine → inhibits secretion (maximum 300 mg/dose IV 1 hour prior to pertechnetate)
(c) glucagon → decreases peristalsis (50 µg/kg IM 5–10 minutes prior to pertechnetate)
√ poor visualization with use of perchlorate + atropine → depressed uptake

False-positive results:

(1) Ectopic gastric mucosa in gastrogenic cyst, enteric duplication, normal small bowel, Barrett esophagus
(2) Increased blood pool in AVM, hemangioma, hypervascular tumor, aneurysm
(3) Duodenal ulcer, ulcerative colitis, Crohn disease, appendicitis, laxative abuse
(4) Intussusception, intestinal obstruction, volvulus
(5) Urinary tract obstruction, calyceal diverticulum
(6) Anterior meningomyelocele
(7) Poor technique

mnemonic: HA GUIDI
Hemangioma
Appendicitis
Gastric ectopia
Urinary obstruction
Intussusception
Duplication of bowel
Inflammatory bowel disease

False-negative results:
(1) Insufficient mass of ectopic gastric mucosa
(2) Dilution of intraluminal activity ← hemorrhage / hypersecretion
mnemonic: MIS
Malrotation of ileum
Irritable bowel in RLQ → rapid transit
Small amount of ectopic gastric mucosa

Enteroclysis:
√ elongated, smoothly marginated, clublike, intraluminal mass parallel to long axis of distal ileum = inverted Meckel diverticulum (20%)
√ 0.5–20-cm-long blind pouch on the antimesenteric border of ileum with junctional fold pattern

Angio (59% accuracy):
√ presence of vitelline artery (= anomalous end branch of superior mesenteric artery) is PATHOGNOMONIC

Cx (in 4–20–40%):
(1) Painless GI bleeding: in children < 5 years of age ← ulceration (in 95% ← heterotopic gastric mucosa)
(2) Acute diverticulitis (30%) in adults secondary to
(a) acid secretion from ectopic gastric mucosa
(b) obstruction of diverticulum by enterolith / foreign body
(3) Intestinal obstruction in older child / adult secondary to
(a) volvulus ← omphalomesenteric diverticulum attached to umbilicus by fibrous band
(b) inflammatory adhesion
(c) Intussusception
(d) Littré hernia
(4) Perforation
(5) Neoplasm (rare):
(a) malignant tumor: carcinoid, carcinoma, sarcoma
(b) benign tumor: GIST, leiomyoma
(6) Chronic abdominal pain

MECONIUM ILEUS

= small bowel obstruction ← desiccated meconium pellets impacted in distal ileum
Age: may develop in utero (in 15%)
Associated with:
cystic fibrosis with tenacious + sticky meconium ← deficiency of pancreatic secretions (in almost 100%)

◊ Virtually all infants with meconium ileus prove to have cystic fibrosis
◊ 10–15% of infants with cystic fibrosis present with meconium ileus!

◊ Earliest clinical manifestation of cystic fibrosis!
• abdominal distension, bilious emesis
• failure to pass meconium within 48 hours
√ numerous dilated small bowel loops without air-fluid levels (fluid not present)

√ "bubbly" / "frothy" appearance of intestinal contents
√ "soap-bubble" / "applesauce" appearance in RLQ (in 50–66%) ← admixture of gas with meconium
√ multiple round / oval filling defects in distal ileum + colon
√ functional microcolon ← unused colon in antenatal obstruction
OB-US:
√ unusual echogenic intraluminal areas in small bowel (DDx: normal transient inspissated meconium)
√ usually polyhydramnios
√ fluid-filled dilated small bowel
Cx (in 40–50%): volvulus, ischemia, necrosis, stenosis, atresia, perforation, meconium peritonitis, pseudocyst
Rx: (1) Nonionic contrast media enema (because of risk of bowel perforation)
(2) 17% Hypaque® / Conray™ enema mixed with acetylcysteine (Mucomyst®)
(3) Gastrografin® enema with Tween 80 (attention to fluid + electrolyte balance)
DDx: Hirschsprüng disease, small bowel atresia with meconium ileus, meconium plug syndrome, small left colon syndrome, imperforate anus, obstruction from duplication cyst

MECONIUM PERITONITIS

= sterile chemical peritonitis ← perforation of bowel proximal to high-grade / complete obstruction that seals in utero due to inflammatory response
Frequency: 1÷35,000 livebirths
Age: antenatal perforation after 3rd month of gestation
Cause:
(1) Atresia ← to ischemic event (50%)
(a) of small bowel: usually ileum or jejunum
(b) of colon (uncommon)
(2) Bowel obstruction (46%)
(a) meconium ileus
(b) volvulus, internal hernia
(c) intussusception, congenital bands, Meckel diverticulum
(d) microcolon
(3) Hydrometrocolpos
◊ Meconium peritonitis ← cystic fibrosis diagnosed in utero in 8% + at birth in 15–40%!
◊ Intraperitoneal meconium may calcify within 24 hours!
Types:
A. FIBROADHESIVE TYPE (most common):
= intense chemical reaction of peritoneum, which seals off the perforation
• no evidence for active leak at birth
√ dense mass with calcium deposits
√ calcific plaques scattered throughout peritoneal cavity
B. CYSTIC TYPE
= cystic cavity formed by fixation of bowel loops surrounding the perforation site, which

continues to leak meconium
√ cyst outlined by calcific rim

C. GENERALIZED TYPE
- perforation occurs immediately antenatally
- active leakage of bowel contents

√ complicated ascites

√ intraabdominal calcifications (CONSPICUOUSLY ABSENT in cystic fibrosis):
- √ peripherally calcified pseudocysts
- √ small flecks of calcifications scattered throughout abdomen
- √ larger aggregates of calcifications along inferior surface of liver / flank / processus vaginalis / scrotum

√ obstructive roentgen signs following birth
√ separation of bowel loops by fluid
√ microcolon = "unused colon"
√ meconium hydrocele producing labial mass

US:
- √ highly echogenic linear / clumped foci with posterior acoustic shadowing in scrotum
- √ "snowstorm appearance" = highly echogenic material throughout abdomen in between bowel loops
- √ ill- / well-defined homo- / heterogeneous encysted collections of meconium

OB-US (> 18 weeks EGA):
- √ polyhydramnios (64–71%)
- √ fetal ascites (54–57%)
- √ bowel dilatation (27–29%)
- √ intraabdominal bright echogenic mass
- √ multiple linear / clumped foci of scattered calcifications (85%); may develop within 12 hrs to 8 days after perforation
- √ meconium pseudocyst = well-defined hypoechoic mass surrounded by an echogenic calcified wall (= contained perforation)

DDx: (1) Intraabdominal teratoma
(2) Fetal gallstones
(3) Isolated liver calcifications

Mortality: up to 62%

Prognosis: generally good; surgery may not be required when perforation site is completely healed

MECONIUM PLUG SYNDROME

= local inspissation of meconium leading to low colonic obstruction; probably related to small left colon syndrome as part of the same spectrum of functional immaturity

Age: newborn infant (symptomatic within first 24 hours of life)

Cause: cystic fibrosis (25%), Hirschsprüng disease, prematurity, maternal magnesium sulfate treatment

• abdominal distension, vomiting, failure to pass meconium

√ distended transverse + ascending colon + dilated small bowel (proximal to obstruction)

√ small left colon with change in caliber at splenic flexure
√ occasionally bubbly appearance in colon (DDx: submucosal air in necrotizing enterocolitis)
√ presacral pseudotumor → no gas in rectum
BE:
√ double-contrast effect = barium between meconium plug + colonic wall
Rx: water-soluble enema
DDx: Hirschsprüng disease

MELANOSIS COLI

= benign brown-black discoloration of colonic mucosa
Frequency: 10% of autopsies
Cause: ? chronic anthracene cathartic usage
• asymptomatic
√ nonspecific colonic wall thickening (in severe cases)
Dx: endoscopic
Prognosis: no malignant potential

MéNéTRIER DISEASE

[Pierre Eugène Ménétrier (1859–1935), pathologist in Paris, France]
= GIANT HYPERTROPHIC GASTRITIS = HYPERPLASTIC GASTROPATHY
= rare disease characterized by excessive mucus production and
TRIAD of (1) Giant mucosal hypertrophy + hypersecretion
(2) Hypoproteinemia
(3) Hypochlorhydria
Prevalence: < 1÷200,000
Cause: ? overproduction of polypeptide growth factor α → increasing gastric mucus production + inhibiting gastric acid secretion
Path: mucosal thickness up to 6.0 mm (normal: 0.6–1.0 mm)
Histo: hyperplasia of glandular tissue + microcyst formation
Age: bimodal distribution in children < 10 years (← CMV infection) and adults 20–70 years; M÷F = 1÷3
Associated with: benign gastric ulcer (13–72%)
• epigastric pain, vomiting, anorexia, asthenia, weight loss
• gastrointestinal bleeding, diarrhea
• protein-losing enteropathy with hypoalbuminemia ← loss of albumin into gastric lumen and increased loss of enteric protein + peripheral edema
• absent / decreased acid secretion (> 50%) ← reduction in number of parietal + chief cells
Location: throughout fundus + body, particularly prominent along greater curvature; relative sparing of antrum (involved in 46%) (DDx to lymphoma: usually in antrum)
√ markedly enlarged (> 1 cm in fundus + body with frequent sparing of antrum) and tortuous gastric rugae (no longer parallel to long axis of stomach) resembling cerebral convolutions in spite of adequate gastric distension
√ marked hypersecretion (mucus) → may dilute barium + impair coating of mucosa
√ preserved pliability of stomach

CT:
√ thickened mucosa projecting into gastric lumen + smooth serosal contour
√ nodular symmetric folds
Cx: increased risk of thromboembolic disease
Rx: anticholinergics, prostaglandins, proton pump inhibitors, prednisone, histamine-2 blockers; gastrectomy
DDx: lymphoma (usually in distal stomach + lesser curvature, enlarged nodes, splenomegaly); polypoid variety of gastric carcinoma (rigid gastric folds, mass, ulcer); acute gastritis (H. pylori, CMV, histoplasmosis); infiltrative disease (sarcoidosis, amyloidosis); chronic gastritis; Zollinger-Ellison syndrome (postbulbar ulcer); gastric varices (serpentine form, change in shape and size, confined to cardia + fundus)

MESENTERIC FIBROMATOSIS

= INTRAABDOMINAL FIBROMATOSIS = ABDOMINAL DESMOID
= part of the spectrum of deep fibromatosis
Incidence: 2–4 ÷1,000,000 annually
Mean age: 41 (range, 14–75) years; M÷F=1÷1
Path: nonencapsulated well-circumscribed mass ± infiltrative margins within muscularis propria
Histo: uniform wavy spindle-shaped fibroblasts in a typically uninflamed abundant dense collagenous stroma ± myxoid foci; tentacular melting insinuation into / through muscularis propria of bowel wall; keloidal fiber formation, thick-walled small arteries, thin-walled veins, perivascular microhemorrhages; absent / scant mitoses; NO necrosis
Associated with: Gardner subtype of familial adenomatous polyposis (in 5–13%)
Risk factor: history of abdominal surgery (during past 4 years) in patients with familial adenomatous polyposis (83%)
• family history of Gardner syndrome / hereditary colon cancer
• abdominal pain, palpable abdominal mass
Location: small bowel mesentery (⅔) near origin of SMA > omentum, ileocolic mesentery, transverse / sigmoid mesocolon, omentum, peritoneal ligaments
Size: most 5–10 (up to 30) cm in diameter
Barium / Enteroclysis:
√ displacement of small bowel segments
√ mucosal ulceration ← compromised mesenteric vasculature
√ luminal narrowing / dilatation
√ distorted thickened / effaced small bowel folds
US:
√ solid well-circumscribed heterogeneous mass with variable internal echogenicity (predominantly hypoechoic)
CT:
√ homogeneous soft-tissue attenuation ← highly collagenous stroma similar to skeletal muscle
√ hypoattenuating mass ← myxoid stroma
√ striated / whorled appearance ← alternating collagenous + myxoid areas

√ bowel tethering = bowel encasement
√ encasement of superior mesenteric vessels

CECT:
√ mild homogeneous to heterogeneous enhancement
√ absent enhancement in myxoid lesion
√ similar / greater enhancement compared to muscle in fibrous lesion
√ occasionally marked enhancement

MR:
√ hypo- or isointense signal compared to muscle on T1WI
√ heterogeneously intermediate / high SI on T2WI ← depending on cellularity + amount of collagen versus myxoid stroma

PET:
√ low to moderate heterogeneous uptake
√ mean SUV of 4.54 (maximally up to 8.30)

Cx: gastrointestinal bleeding, small bowel obstruction, fistula formation, bowel perforation

Prognosis: proclivity for local recurrence

Rx: wide surgical excision, less radical surgery / medical therapy with antiestrogens / cytotoxic chemotherapy, postoperative irradiation

DDx:
(1) Malignancy: lymphoma, metastatic disease, soft-tissue sarcoma (lipo-, fibro-, leiomyo-sarcoma, malignant fibrous histiocytoma)
(2) Small-bowel GIST (areas of hemorrhage + necrosis, more cellular without abundant collagenous stroma, positive for CD117 + CD34)
(3) Abdominal fibromatosis (commonly in young women)
(4) Castleman disease
(5) Desmoplastic small round cell tumor

MESENTERIC LYMPHADENITIS

Primary Mesenteric Adenitis

= clinical entity with symptoms related to benign inflammation of lymph nodes without identifiable acute inflammatory condition

Cause: probable infection of the terminal ileum by Yersinia enterocolitica, Y. pseudotuberculosis, viral

Age: children, young adults

• nausea, vomiting, diarrhea, fever, leukocytosis
• diffuse / RLQ pain + tenderness

Location: usually RLQ (immediately anterior to right psoas muscle in 78%, small bowel mesentery in 56%)

√ cluster of (> 3) enlarged (> 5 mm) mesenteric lymph nodes without an identifiable acute inflammatory condition
√ isolated ileal wall thickening (33%)
√ colonic wall thickening (18%)

N.B.: visualization of entire normal appendix is necessary to differentiate from acute appendicitis!

Dx: diagnosis of exclusion

DDx: Secondary mesenteric adenitis as in appendicitis (enlarged nodes immediately anterior to right psoas muscle in 40–82%, nodes less numerous + smaller)

Secondary Mesenteric Adenitis

Cause:

(a) local condition: appendicitis, Crohn disease, diverticulitis

(b) systemic condition: lupus erythematosus, HIV

Age: adults (far more frequent than for primary adenitis)

MESENTERIC ISCHEMIA

= BOWEL ISCHEMIA

Classification of bowel ischemia by the American Gastroenterological Association in 2000:

» MESENTERIC ISCHEMIA

A. ACUTE MESENTERIC ISCHEMIA

(a) arterial (90%)

› occlusive mesenteric infarction (⅔)

1. **SMA embolus**

major: above origin of ileocecal artery

minor: distal to origin of ileocecal artery

2. **SMA thrombosis**

› nonocclusive mesenteric ischemia (⅓)

3. Splanchnic vasoconstriction ← low flow state

(b) venous (10%):

4. Mesenteric vein thrombosis

B. CHRONIC MESENTERIC ISCHEMIA

» COLONIC ISCHEMIA

Etiology:

(a) arterial occlusion / compromise: atheromatous disease, thromboembolic disease, dissecting aortic aneurysm, fibromuscular hyperplasia, arteritis, hypoperfusion (shock, hypovolemia), endotoxin shock, disseminated intravascular coagulation, direct trauma, aortic surgery, stent placement, therapeutic embolization, radiation, antiphospholipid antibody syndrome

› **occlusive mesenteric infarction** (90% mortality)

1. Embolus (40–50%)
2. SMA thrombosis (20–40%) at origin + site of atherosclerotic narrowing (ostium stenosis)

› **nonocclusive mesenteric ischemia** (10% mortality)

1. Preexisting atherosclerosis → low-flow state
2. Bowel vasoconstriction = vasospasm (reflex hypotension, digitalis, ergot preparation, vasopressin, amphetamine, cocaine), pheochromocytoma, familial dysautonomia
3. **Shock bowel** = diffuse small bowel ischemia in hypovolemia and hemorrhagic / cardiogenic / septic shock ← increased bowel permeability to macromolecules + albumin

√ diffuse bowel wall thickening
√ persistent increased enhancement on CT ← slowed perfusion and washout + interstitial leakage of contrast material
√ accumulation of intraluminal fluid ← failed resorption capacity

Arterial involvement:
SMA (5%); celiac artery (4%); IMA (11%)

(b) venous occlusion (< 10%): young patient, often following abdominal surgery
Location: SMV > inferior mesenteric vein > portal vein

(c) systemic low flow state (30%): myocardial infarction, CHF, intraoperative hypotension, arrhythmia, hypovolemia, shock, renal / hepatic disease

(d) bowel obstruction: strangulation by adhesions or bands ± mesenteric vein thrombosis, incarceration of hernia, volvulus, intussusception, pronounced overdistension (prestenotic, distension colitis), ischemic colitis ← endoscopy / enemas / colonic carcinoma (1–7%)

(e) vasculitis: polyarteritis nodosa (50–70%)
√ relatively long segment of bowel involved
√ multiple skip areas in nonsegmental distribution
√ involvement of duodenum is indicative

(f) abdominal inflammation: pancreatitis, appendicitis, diverticulitis, diffuse peritonitis, parasitic infestation

(g) cytotoxic drugs: long-term immunosuppressive drugs for rejection, chemotherapy for leukemia / lymphoma

(h) radiation: > 4,500 cGy

<u>in children:</u>
midgut volvulus, CHD, incarcerated hernia, sickle cell disease (occasionally), necrotizing enterocolitis

Pathophysiology: ischemia leads to
→ inflammatory response (cytokines, platelet-activating factor, tumor necrosis factor released from activated neutrophils, platelets, mast cells, endothelial cells)
→ breakdown of mucosal barrier from
› mild superficial necrosis limited to mucosa (mucosal ulcer) = partial mural bowel ischemia, to
› life-threatening continuous necrosis of all bowel wall layers = transmural bowel infarction
→ invasion of bacteria with bacteremia + sepsis
→ strictures

Distribution:
› small bowel, ascending colon, proximal $^{2}/_{3}$ of transverse colon ← SMA / SMV
› descending colon, sigmoid colon ← IMA / IMV
› splenic flexure, rectosigmoid junction ← watershed zones

Acute Mesenteric Ischemia

Cause:
(a) acute occlusive SMA embolus (in > 50%): usually lodges at bifurcation of middle colic artery + SMA
(b) SMA thrombosis (4–18%; nonocclusive in 25%): frequently involves the proximal

SMA
(c) SMA dissection ← cystic medial necrosis, fibromuscular dysplasia
(d) venous occlusion in 5–10–15% ← hypercoagulability, trauma, portal hypertension, infection, carcinoma, oral contraceptives

- first crampy, then continuous abdominal pain with acute event
- cardiac disease predisposing to embolization
- gut emptying (vomiting / bloody diarrhea)
- gross rectal bleeding, WBC > 12,000/µl with left shift (80%)

Location: (a) any segment of small bowel
(b) cecum (most common), distal transverse colon, splenic flexure

Consequences:
dependent on magnitude of insult, duration of process, adequacy of collaterals

A. REVERSIBLE ISCHEMIA
1. Complete restitution of bowel wall ← abundant collaterals
2. Healing with fibrosis + stricture formation

B. IRREVERSIBLE ISCHEMIA
1. Transmural infarction with bowel perforation

Bowel infarction develops with thrombosis of the small distal mesenteric venous branches.

Plain film:
√ gasless abdomen ← fluid-filled loops from exudation (21%)
√ bowel distension to splenic flexure (= perfusion territory of SMA) in 43%
√ "thumbprinting" (36%) = thickening of bowel wall + valvulae ← edema
√ small bowel pseudoobstruction (most frequently in thrombosis)
√ pneumatosis = dissection of luminal gas into bowel wall (28%)
√ mesenteric + portal vein gas (14%)
√ ascites (14%)

Barium:
√ "scalloping / thumbprinting" = thickening of bowel wall + valvulae
√ "picket fencing" = marked thickening of bowel wall
√ separation + uncoiling of loops
√ narrowed lumen
√ circumferential ulcer

CT (26–73–82% sensitive):
@ Bowel wall thickness
√ circumferential bowel wall thickening (28–52–96%) > 3–5 mm depending on degree of distension:
√ "halo / target" sign = stratification into 3 layers = inner mucosa and outer muscularis propria (rings of high attenuation) separated by layer of low attenuation (submucosal edema ± hemorrhage ± superinfection) in
› ischemic colitis (94%)
› reversible mesenteric ischemia (80%)
› mesenteric infarction (26–38%)
◊ The least specific sign!
◊ NO correlation with the severity of ischemic damage

√ thinning of bowel wall (in acute arterioocclusive transmural infarction) if it becomes gangrenous
√ bowel wall attenuation on NECT:
√ decreased, usually homogeneously ← edema
√ increased ← hemorrhage

@ Bowel wall enhancement
√ diminished enhancement of bowel wall ← compromised blood flow
√ absent enhancement of bowel wall (in 18%, 62% sensitive, 96% specific)
√ engorgement of mesenteric vessels = venous congestion ← stasis
√ increased wall enhancement ← hyperemia in outflow obstruction from mesenteric venous occlusion / during reperfusion after arteriogenic bowel ischemia / in shock bowel) as a good prognostic indicator (33% sensitive, 71% specific)
√ delayed + persistent enhancement ← delayed venous return and arteriospasm

@ Bowel diameter
(a) early reflex spastic ileus
√ contracted gasless bowel in mild mucosal ischemia
(b) intermediate reflex hypotonic ileus
√ dilated gas-filled bowel with paper-thin wall
(c) late paralytic ileus
√ focal / diffuse bowel dilatation (10–56–91%) with gas (43%) / fluid (29%) ← interruption of peristaltic activity ← destruction of intramural nerves + intestinal musculature / irreversible transmural ischemic damage
√ no enhancement
√ pneumatosis

@ Vascular signs
(a) arterial occlusion:
√ hyperattenuating SMA on NECT
√ filling defect with ring enhancement on CECT
√ thumbprinting (26%) = thickening of bowel wall
√ lack of bowel wall enhancement with arterial occlusion
√ concurrent embolic infarction of kidney / spleen
(b) venous thrombosis (15%):
√ enlarged diameter + increased attenuation of SMV on NECT
√ filling defect in SMV / portal vein thrombosis on CECT
√ thumbprinting (64%) = thickening of bowel wall
√ "waterlogging" with marked contrast enhancement of mesentery + bowel wall

√ pneumatosis intestinalis (in 6–28%, 3–14% specific)
= dissection of luminal gas into bowel wall across compromised mucosa signaling irreversible disease:
√ small isolated gas bubbles within wall
√ broad rims of air dissecting the entire bowel wall into two layers
◊ Sign of transmural bowel infarction in 78%

√ gas in portal vein (5–13–36%) / in mesenteric vein (28%) = propagation of intramural gas into mesenteric venous system
◊ Sign of transmural bowel infarction in 81%

@ Extramural signs
√ increased attenuation of mesenteric fat from mesenteric edema (in 68%, 58% sensitive, 79% specific)
√ mesenteric fluid (88% sensitive, 90% specific)
√ ascites (in 43–88%, 75% sensitive, 76% specific)
√ pneumoperitoneum (7%) = perforation of infarcted bowel segment

Cx: bowel necrosis ← occlusion of small vasa recta disallowing collateral flow

Common pitfalls:
(1) Spastic colon misinterpreted as simple contraction, (issue resolved by repeat CT with enema)
(2) Widely distended colonic segment with a wall thickness of 3–5 mm misinterpreted as normal
(3) Small bowel dilatation + air-fluid levels misinterpreted as ileus / pseudoobstruction

Angio (AP and LAT views):
√ occlusion / vasoconstriction / vascular beading
√ embolus lodged at major branching points distal to first 3 cm of SMA

Rx for nonocclusive mesenteric ischemia:
via SMA catheter slow injection of 60 mg papaverine followed by papaverine infusion of 1 mg/minute

NUC:
(a) IV / IA ^{99m}Tc-sulfur colloid / labeled leukocytes, Ga-citrate, ^{99m}Tc-pyrophosphate:
√ tracer accumulation 5 hours after onset of ischemia (more intense uptake with transmural infarcts)
(b) intraperitoneal injection of 133Xe in saline → absorbed by intestine:
√ decreased washout with abnormal perfusion of strangulated bowel

Prognosis:
(1) Massive infarction of small + large bowel if mesenteric embolization occurs proximal to middle colic artery (= limited collateral flow)
(2) Focal segments of intestinal ischemia if mesenteric embolization occurs distal to middle colic artery (= good collateral flow)

Local Cx: bleeding, intestinal perforation, abscess formation, peritonitis

Systemic Cx: hemoconcentration, acidosis, DIC, bone marrow suppression, multiple organ failure (including heart + kidneys)

Mortality: 70–80–92% for intestinal infarction

DDx: typhlitis, Crohn disease, infectious / ulcerative colitis, proctosigmoiditis, sigmoid diverticulitis, other causes of pneumatosis intestinalis / portal venous gas

Chronic Mesenteric Ischemia

= ABDOMINAL / INTESTINAL ANGINA
= intermittent mesenteric ischemia in severe arterial stenosis with inadequate collateralization provoked by food ingestion
• postprandial abdominal pain 15–20 minutes after food intake ← "gastric steal" diverting blood flow away from intestine
◊ Pain out of proportion to physical findings
• fear of eating large meals, weight loss, malabsorption

• reflex emptying of bowel after eating

Barium:

(a) Subacute:

√ flattening of one border

√ pseudosacculation / pseudodiverticula on antimesenteric border

(b) Chronic:

√ 7–10-cm-long smooth pliable strictures

√ dilatation of gut between strictures

√ thinned + atrophic valvulae

Cx: obstruction

Duplex US:

√ celiac trunk occlusion + retrograde perfusion of hepatic artery through SMA

√ PSV > 300 cm/sec and EDV > 45 cm/sec in SMA

√ peak systolic velocity > 160 cm/sec in celiac trunk for > 50% stenosis (57% sensitivity, 100% specificity) during fasting state

Mesenteric Vein Thrombosis

Cause:

A. PRIMARY / IDIOPATHIC (20%)

B. SECONDARY (with predisposing condition):

(1) Infection: acute pancreatitis (24%), sepsis, colonic diverticulitis, appendicitis, peritonitis, abdominal abscess

(2) Inflammatory bowel disease (2%)

(3) Trauma, postoperative state: Roux-en-Y gastric bypass > Nissen fundoplication > partial colectomy > cholecystectomy > appendectomy, pancreaticoduodenectomy (27%)

(4) Mechanical: volvulus, bowel obstruction

(5) Myeloproliferative neoplasm: chronic myelogenous leukemia, polycythemia vera, essential thrombocythemia, primary myelofibrosis

(6) Inheritable hypercoagulable state

(7) Paraneoplastic thromboembolism

(8) Tumor invasion: pancreatic cancer, HCC

(9) Miscellaneous causes: oral contraceptives (5%), pregnancy, chemotherapy

The location of thrombus is often determined by the underlying cause. Hematologic disorders affect small venous branches with progression into larger trunks.

Location: SMV > IMV (6%)

• usually subacute symptomatology over 1–4 weeks

• abdominal pain with rebound / guarding (acute MVT)

• nausea, vomiting, diarrhea

• hematemesis, hematochezia (after bowel necrosis)

√ ileus

√ ascites

√ bowel wall thickening (64%) with "thumbprinting

CT:

› mural signs:
√ pneumatosis intestinalis ← bowel infarction
√ hypoattenuated circumferential bowel wall thickening ← intramural edema / hemorrhage

Bowel wall thickening is more pronounced in venous congestion than in arterial occlusion.

√ "halo / target" sign = abnormally enhancing bowel wall with mural stratification into 2 or 3 thickened layers:
√ hyperattenuating inner ring (= mucosa) + outer ring (= muscularis propria) separated by hypoattenuating middle ring (= submucosal edema)
√ abnormal wall enhancement:
√ increased / normal wall enhancement ← preserved arterial inflow
√ decreased enhancement ← impeded arterial inflow
◊ Highly SPECIFIC for venous bowel infarction!

› vascular signs:
√ portomesenteric venous gas ← bowel infarction
√ hypoattenuating lumen surrounded by well-defined rim-enhancing venous wall ← partial / complete venous filling defect
√ enlargement of major vein ← displacement of venous wall by acute thrombus
√ engorgement of small mesenteric veins ← venous congestion ← thrombosis
√ venous collateral circulation

Upstream venous collateralization occurs more readily with thrombosis of large mesenteric veins than with thrombosis of venae rectae / arcades.

› extramural-nonvascular signs:
√ mesenteric haziness ← venous congestion + superimposed inflammatory edema + ascites
√ bowel dilatation ← interrupted intestinal peristalsis / loss of contractile function ← transmural infarction
√ free intraperitoneal air ← perforated infarcted bowel

US:
√ dilated vein with echogenic thrombus

Cx: bowel ischemia → infarction

Bowel infarction develops in thrombosis of the small distal mesenteric venous branches lacking collaterals.

Mortality: 12–50%

MESOTHELIAL CYST

= MESENTERIC / OMENTAL CYST

Etiology: failure of mesothelial peritoneal surfaces to coalesce

Path: unilocular thin-walled cyst usually with serous, occasionally chylous / hemorrhagic fluid contents

Histo: lined by mesothelial cells + surrounded by thin layer of fibrous tissue

Location: small bowel, mesentery (78%), mesocolon

• asymptomatic

√ single cyst up to several cm in size
√ omental cysts may be pedunculated
CT:
√ near-water density / soft-tissue density
√ ± fluid levels related to fat + water components
Cx: torsion, hemorrhage, intestinal obstruction
DDx: lymphangioma (septations)

METASTASIS TO GASTROINTESTINAL TRACT

GI metastases closely resemble the primary tumor. The radiologic appearance depends mainly on histologic characteristics of the primary / secondary lesion like degree of vascularity relative to growth rate.

Hypervascular Metastasis

1. Malignant melanoma
2. Breast cancer

uncommon:

3. Renal cell carcinoma
4. Choriocarcinoma
5. Neuroendocrine carcinoma
6. Mesenchymal sarcoma

Metastasis to Colon

Spread:

(1) Hematogenous (embolic)
√ subepithelial masses / bull's-eye lesions
√ diffusely infiltrating lesions mimicking inflammatory bowel disease

(2) Direct invasion by contiguous tumor
› ovary inferior border of sigmoid
› left kidney splenic flexure
› pancreatic tail splenic flexure
› pelvis (uterus, bladder) anterior border of rectum
› prostate rectosigmoid

(3) Direct invasion along mesenteric reflections
› stomach transverse colon superior margin
› pancreas transverse colon inferior margin
› omental cake transverse colon superior margin

(4) Intraperitoneal seeding
Origin: ovarian, gastric, colonic, pancreatic cancers (most commonly)
Classic sites of seeding:
› pouch of Douglas (50%): anterior border of rectosigmoid
› lower small bowel mesentery (40%): medial border of cecum
› sigmoid mesocolon (20%): superior border of sigmoid colon
› right paracolic gutter (10%): lateral border of ascending colon

Metastasis to Small Bowel

Origin: colon > stomach > breast > ovary > uterine cervix > melanoma > lung > pancreas

Spread:

(1) Intraperitoneal seeding: primary mucinous tumor of ovary, appendix, colon; breast cancer

(2) Hematogenous dissemination with submucosal deposits: malignant melanoma, breast carcinoma, lung carcinoma, Kaposi sarcoma

(3) Direct extension from adjacent neoplasm: ovary, uterus, prostate, pancreas, colon, kidney

√ fixation + tenting + transverse stretching (= across long axis) of folds ← mesenteric + peritoneal infiltration (most common form)

UGI:

√ single mass protruding into lumen resembling annular carcinoma

√ "bull's-eye" lesions = multiple polypoid masses with sizable ulcer craters

√ obstruction from kinking / annular constriction / large intraluminal mass

√ compression by direct extension of primary tumor / involved nodes

CT:

√ soft-tissue density nodules / masses

√ sheets of tissue causing thickening of bowel wall + mesenteric leaves

√ fixation + angulation of bowel loops (in tumors with desmoplastic response)

√ ascites

Metastasis to Stomach

Organ of origin:

(a) by hematogenous spread: malignant melanoma, breast cancer, lung ca., colon ca., prostate carcinoma, leukemia, secondary lymphoma

√ one / more subepithelial masses

√ target / bull's-eye lesion if centrally ulcerated

√ giant cavitated lesion

√ linitis plastica (usually in breast cancer)

(b) by direct invasion

› Barrett cancer: gastric fundus

› Pancreatic cancer: stomach / duodenal sweep

› Colonic cancer: greater gastric curvature

› Omental cake: greater gastric curvature

• GI bleeding + anemia (40%)

• epigastric pain

√ solitary mass (50%)

√ multiple nodules (30%)

√ linitis plastica (20%): especially in breast cancer

√ multiple umbilicated nodules: malignant melanoma

MIDGUT VOLVULUS

= torsion of entire gut around SMA

◊ MEDICAL EMERGENCY requiring immediate surgery!

Cause: malrotation

Age: most common in neonate / young infant (= acute intestinal obstruction); occasionally in older child / adult (= chronic intestinal obstruction)

In 20% associated with: (1) Duodenal atresia
(2) Duodenal diaphragm
(3) Duodenal stenosis
(4) Annular pancreas

Pathophysiology:

malrotation → abnormally short root of small bowel mesentery → abnormal mobility of midgut → torsion of mesentery; degree of twisting can change ← natural movement of bowel and determines symptomatology; severe volvulus → obstruction of SMV + SMA (= twist of 3 ½ turns) → bowel necrosis

- acute symptoms within first 3 weeks of life in 75%: HALLMARK postprandial intermittent projectile bilious vomiting (60–80%); abdominal distension; shock
- intermittent obstructive symptoms in older child: recurring attacks of nausea, vomiting, and abdominal pain with spontaneous reduction
- failure to thrive ← hypoproteinemic gastroenteropathy ← result of lymphatic + venous obstruction
- "currant jelly" stools / melena (implying vascular compromise)

Plain film:

◊ A normal abdominal radiograph does not exclude the Dx!
√ dilated air-filled duodenal bulb + paucity of gas distally
√ "double bubble" sign = air-fluid levels in stomach + duodenum
√ isolated collection of gas-containing bowel loops distal to obstructed duodenum = gas-filled volvulus = closed-loop obstruction ← nonresorption of intestinal gas ← obstruction of mesenteric veins

UGI (preferred method, 54% sensitive):

N.B.: First exclude perforation on plain films!
◊ UGI not needed if complete obstruction shown on plain film
◊ Nasogastric tube desirable → to decompress fluid-filled stomach with NG tube tip positioned in antropyloric region
√ vertically oriented duodenum that does NOT cross midline with most of small bowel on right side of abdomen
√ dilated proximal duodenum terminates in a distinctive conical / beaked shape
√ duodenal-fold thickening + thumbprinting ← mucosal edema + hemorrhage
√ duodenojejunal junction (ligament of Treitz) located lower than duodenal bulb + usually below and to the right of expected position at / to left of L1 pedicle
√ malrotation = spiral course of midgut (= jejunoileal) loops beyond point of obstruction = "apple-peel / twisted ribbon / corkscrew", "spiral" appearance (in 81%)

BE:

√ abnormally high position of cecum (with isoosmolar water-soluble contrast enema, which is distinguishable from barium suspension used for subsequent UGI)

CT:

√ whorled mesentery = clockwise wrapping of small bowel loops + adjacent mesenteric fat + SMV and tributaries + SMA branches converging to the point of torsion = swirling of vessels in mesenteric root (during volvulus)
√ SMV to left of / posterior to SMA = transposition / reversal of SMA-to-SMV relationship
normal position: SMV to the right of SMA
CAVE: reversal may be seen without malrotation; vessel location may be normal with malrotation
√ inability to visualize 3rd part of duodenum across midline from right to left
√ right- sided small bowel + left-sided colon
√ chylous mesenteric cyst ← interference with lymphatic drainage
√ small bowel dilatation + mucosal hyperattenuation ← global small-bowel ischemia

US:
√ clockwise "whirlpool sign" = color Doppler depiction of SMV wrapping clockwise around superior mesenteric artery
√ distended proximal duodenum with arrowhead-type compression over spine
√ superior mesenteric vein to the left of SMA
√ thick-walled bowel loops below duodenum + to the right of spine associated with free intraperitoneal fluid
√ narrowed mesenteric pedicle

Angio:
√ "barber pole" sign = spiraling of SMA
√ tapering / abrupt termination of mesenteric vessels
√ marked vasoconstriction + prolonged contrast transit time
√ absent venous opacification / dilated tortuous SMV

Cx: (1) Intestinal ischemia in distribution of SMA with occlusion of lymphatics + SMV + SMA → bloody diarrhea, ileus, abdominal distension
(2) Bowel necrosis → surgery → short-gut syndrome → dependence on total parenteral nutrition

Mortality: 3–5%

DDx: (1) Hypertrophic pyloric stenosis (same age group, no bilious vomiting)
(2) Ladd bands

MUCOCELE OF APPENDIX

Mucocele of Appendix

mucocele = macroscopic descriptive term for cystic dilatation of appendix / gallbladder / sinus cavity / salivary gland caused by an accumulation of mucin

Etiology:
(1) Simple mucocele (20%) = retention cyst = cystic dilatation of lumen ← obstruction by fecolith, foreign body, endometriosis, adhesions, postoperative scarring following appendectomy, volvulus, carcinoid, appendiceal carcinoma, carcinoma of cecum
√ mild luminal dilatation rarely > 2 cm in diameter
(2) Focal / diffuse mucosal hyperplasia (5–25%)
(3) Mucinous cystadenoma ← hyperplasia with epithelial atypia (50–63%) = mucin-

secreting tumor
√ marked luminal distention
Cx: perforation with mucous seeding (in 20%)
(4) Mucinous cystadenocarcinoma with stromal invasion (11–20%)
√ severe appendiceal distention by mucin
Cx: 6% risk of perforation + peritoneal implantations
(5) Cystic fibrosis with accumulation of thick mucus

Prevalence: 0.07–0.25% of appendectomy specimens; 8% of appendiceal tumors
Mean age: 55 years; M÷F = 1÷4 to 1÷1
Associated with: colonic adenocarcinoma (6-fold risk), mucin-secreting tumor of ovary

- asymptomatic (25%), ± acute / chronic RLQ pain
- palpable mass in right lower quadrant (in up to 50%)
- altered bowel habits, weight loss, vomiting
- ± elevated CEA, CA 19-9, CA 125

Size: up to 25 cm
BE / plain film:
√ globular, smooth-walled, broad-based mass invaginating into cecum
√ nonfilling of the appendix on BE
√ frequent peripheral punctate / rimlike calcifications ("**porcelain appendix**")
CT:
√ round sharply defined paracecal mass with homogeneous content of near-water / soft-tissue attenuation (depending on amount of mucin)
√ NO adjacent inflammation
√ calcifications of appendiceal wall (< 50%)
US:
√ purely cystic / cystic with gravity-dependent fine internal echoes / complex cystic mass with high-level echoes
√ SPECIFIC sign of multiple echogenic layers of protein macroaggregates / inspissated mucoid material along dilated appendix
√ ± acoustic shadowing if calcifications present
MR:
√ hyperintense tumor on T2WI
√ variably hypo- to isointense on T1WI depending on mucin concentration
√ soft-tissue thickening, infiltration of perifocal fat, irregular mucocele wall = signs of malignancy / secondary inflammation / both
NUC:
√ intense early gallium uptake ← affinity to acid mucopolysaccharides of mucus

Cx: (1) Rupture → pseudomyxoma peritonei
(2) Torsion → gangrene + hemorrhage
(3) Herniation into cecum → bowel obstruction
(4) Intussusception
(5) Right ureteral obstruction

Rx: appendectomy; hemicolectomy (suspected malignancy)
DDx: appendicitis, periappendiceal abscess, mesenteric cyst, enteric duplication cyst, right

ovarian cyst, cystic ovarian neoplasm, hydrosalpinx, tubo-ovarian abscess

Myxoglobulosis

= rare variant of mucocele characterized by clusters of pearly white mucous balls (= intraluminal globules) intermixed with mucus

• usually asymptomatic, may appear as acute appendicitis

√ multiple mobile 1–10-mm small rounded annular nonlaminated calcified spherules (PATHOGNOMONIC)

DDx: inverted appendiceal stump (of inversion-ligation technique), acute appendicitis, cecal carcinoma, phleboliths, calcified lymph nodes

OMENTAL INFARCTION

= rare cause of self-limiting abdominal pain

Pathophysiology:

(a) torsion (rare cause)→ interruption of blood supply to omentum → venous thrombosis

(b) trauma → thrombosis → insufficiency of omental veins

Predisposing factors: obesity, strenuous activity, CHF, digitalis administration, trauma, recent abdominal surgery

A. PRIMARY (idiopathic) OMENTAL INFARCTION (15%)

Cause: bifid omentum, accessory omental tissue, variant vascular supply, marathon running → physiologic shunting with splanchnic vasoconstriction

May be associated with: hypercoagulable state, CHF, vasculitis

Path: hemorrhagic infarction ← vascular compromise ← (a) tenuous blood supply to right edge of omentum, (b) kinking of veins

• precipitated by coughing, straining, overeating, marathon running

Age: pediatric patients

Location: commonly RLQ on inferior right side of omentum

B. SECONDARY OMENTAL INFARCTION (more common)

Cause: postoperative omental adhesion, omental mass, vascular damage related to trauma / inflammation / hernia

Age: adult, M > F

• subacute RLQ / RUQ abdominal pain of a few days duration

• clinical mimicker of acute appendicitis, cholecystitis but in the ABSENCE of GI symptoms of nausea, vomiting, fever

• slightly elevated WBC

Location: mostly between anterior abdominal wall and transverse / ascending colon / cecum

Site: right inferior portion of omentum > left

Size: diameter > 5 cm

CT:

√ solitary encapsulated triangular / oval fatty mass:

√ soft-tissue stranding adjacent to ascending colon = haziness of fat anterior to colon (early / mild infarction)

√ internal heterogeneity ← soft-tissue stranding adjacent to ascending colon

√ whorled pattern of concentric linear fat stranding (in torsion)

√ NO enhancement
√ omental torsion (rare) with swirling of vessels in omentum
√ absent / (rarely) mild thickening of adjacent bowel wall corresponding to site of focal tenderness

US:
√ nonmobile noncompressible hyperechoic tender mass

PET:
√ mild uptake of 18F-fluorodeoxyglucose (FDG)

Dx: clinically difficult; often 1st suggested by radiologist
Cx: omental abscess (rare)
Rx: supportive
DDx: epiploic appendagitis (< 5 cm in diameter, peripheral hyperdense rim, "central dot" sign); diverticulitis (bowel wall thickening)

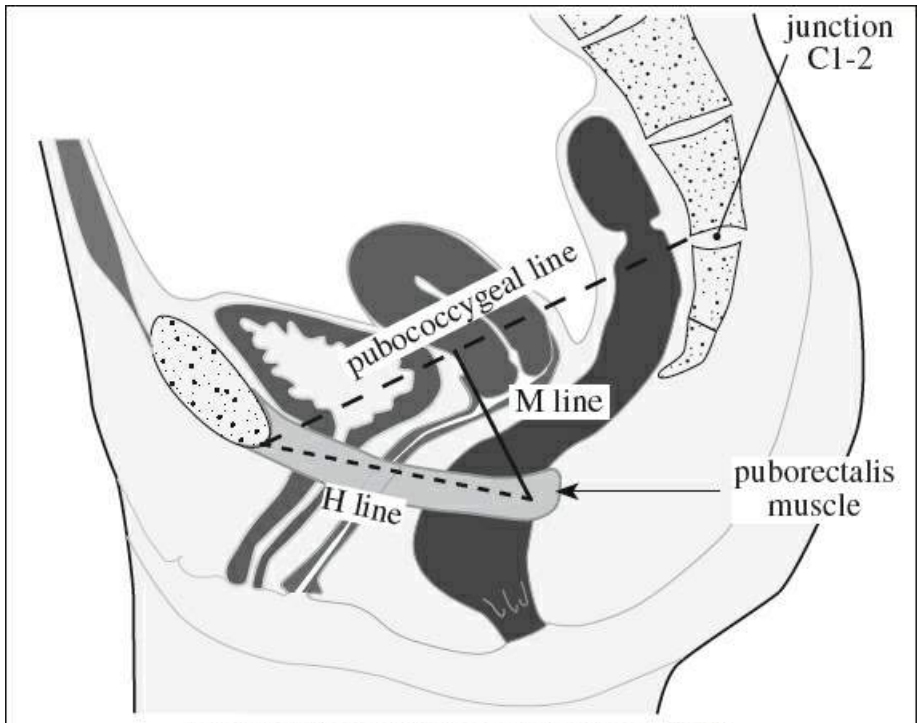
PELVIC FLOOR DYSFUNCTION

= heterogeneous group of disorders presenting with pelvic pain, pressure, dyspareunia, incontinence, incomplete emptying, gross organ protrusion

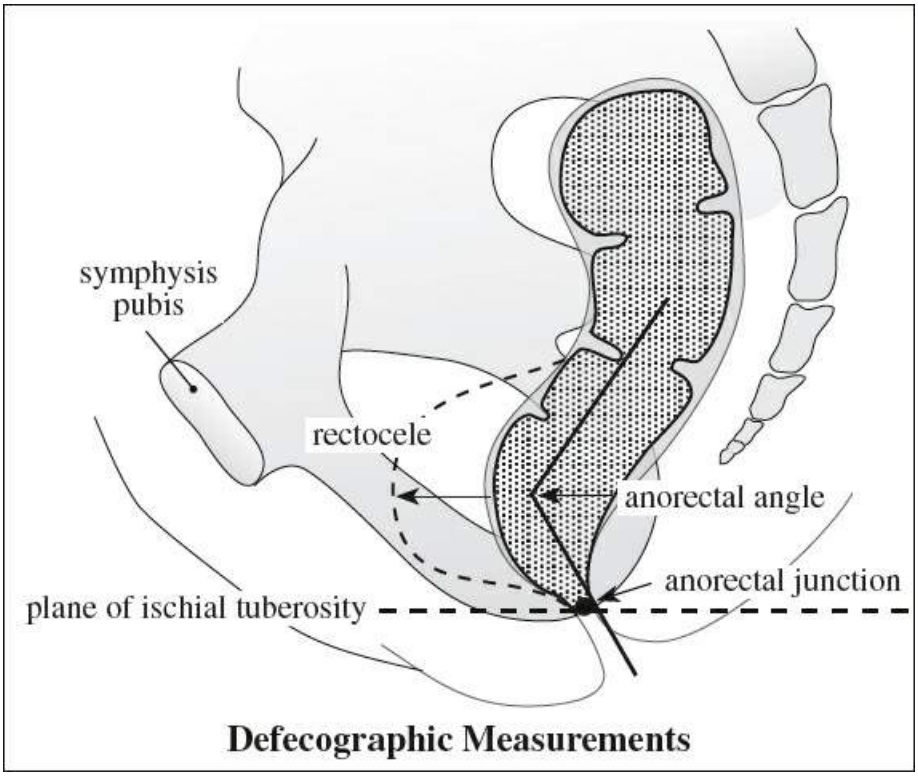
Prevalence: 10–50% of middle-aged / older women increasing with age; 10% requiring surgery

Cause: injury to pelvic floor from surgery / childbirth, denervation of musculature, fascial defect, abnormal synthesis / degradation of collagen

Risk factors: age, menopause, multiparity, complicated vaginal delivery, obesity, collagen-related disorder, hysterectomy



Pelvic Floor Measurements on MR



Midsagittal pelvic MR:

» Draw 3 lines:

(1) Pubococcygeal line from inferior margin of symphysis to junction C1-C2

(2) H-line (**H**iatus of levator ani) along puborectalis muscle sling for structures passing through pelvic floor

√ linear distance measured during straining

(3) M-line (**M**uscular pelvic floor) line from point of posterior puborectalis muscle perpendicular to pubococcygeal line

» HMO evaluation:

(1) **Hiatal size** (**H**-line measurement)

√ hiatal enlargement > 6 cm

Grading: normal < 6 cm, mild 6–8 cm, moderate 8–10 cm, severe > 10 cm

(2) **Pelvic floor descent** (**M**-line measurement)

√ pelvic floor descent > 2 cm

Grading: normal < 2 cm, mild 2–4 cm, moderate 4–6 cm, severe > 6 cm

(3) **Organ prolapse** (any distance below H-line):

= shortest distance between the most caudal aspect of an organ and H line during Valsalva maneuver

Grading: mild / small < 2 cm; moderate 2–4 cm; severe / large ≥ 4 cm

Defecography / Evacuation Proctography:

evacuation time = 15 (range 5–40) seconds

anorectal angle = angle formed between central axis of anal canal + line parallel to posterior wall of rectum

√ 90° at rest and during voluntary contraction (squeeze maneuver)

√ more obtuse during defecation straining (void)

anorectal junction = point of taper of distal rectal ampulla as it merges with the anal canal; position of anorectal junction referenced to plane of ischial tuberosities = 0–3.5 cm; elevation during squeeze of 0–4.5 cm; elevation during void of –3.0–0 cm

rectovaginal space = space between vagina and rectum

perineum = area between external genital organs and anal verge

Pelvic Floor Relaxation

= weakening of pelvic floor support structures consisting of muscles and connective tissue (= pelvic sling) → pelvic floor dysfunction at rest + during activities with ↑ intraabdominal pressure (like coughing, sneezing, urination, defecation)

Components: hiatal enlargement + pelvic floor descent

Rx: surgical mesh reconstruction

Grade	*Hiatal Enlargement*	*Pelvic Floor Descent*
0 (normal)	< 6 cm	0–2 cm
1 (mild)	6–8 cm	2–4 cm
2 (moderate)	8–10 cm	4–6 cm
3 (severe)	≥ 10 cm	≥ 6 cm

Pelvic Floor Prolapse

= abnormal protrusion of a pelvic organ(s) through its respective hiatus

Cause: failure of support structures, perineal hiatal weakening

Cystocele

= prolapse / herniation of bladder through its respective hiatus on anterior vaginal wall

Cause: defect in pubocervical fascia attaching to arcus tendineus fasciae pelvis (ATFP) anterolaterally + to cervix posteriorly

- vaginal bulging → difficult intercourse / dyspareunia
- simple stress urinary incontinence (may be masked in severe case by a kink at the bladder neck ← transverse orientation of urethra)

Voiding video urodynamic study:

√ uncovers urge incontinence from detrusor instability

√ uncovers stress urinary incontinence masked by urethral hypermobility

MR:

√ downward + clockwise bladder rotation ← posterior bladder wall descends disproportionately more than anterior wall (in severe case)

√ descent of bladder base below pubococcygeal line

√ urethral prolapse (= urethral hypermobility)

Rx: pessary: sutures and mesh to approximate original fascial support ± incontinence surgery (sling procedure)

CYSTOURETHROCELE

Cx: ureteral obstruction / hydronephrosis ← entrapment of ureters ← high degree of muscular pelvic floor relaxation

Bladder Outlet Obstruction

Cause: surgical repair for stress urinary incontinence, urethral hypermobility, bladder outlet compression by prolapsing uterus or rectocele, kinking of urethra / bladder outlet in patients with cystocele

- voiding hesitancy, required positional voiding, required manual reduction of prolapse for voiding, frank urinary retention occasionally requiring catheterization

Genital Prolapse

= UTERINE AND VAGINAL VAULT PROLAPSE

Cause: muscle damage + stretching (laxity) / tearing of uterosacral ligaments

- bulging vaginal mass outside external genitalia
- dyspareunia, urinary retention, back pain

MR:

√ descent of vaginal fornix and uterus below PCL
√ progressive uterine retroversion → subsequent prolapse
√ loss of banana-shaped vaginal axis (= loss of elevation of distal vagina by ligaments and muscles)

Rx: pessary, pelvic floor exercises, hysterectomy, vaginal repair

Cx: insidious progressive ureteral obstruction

UTERINE PROCIDENTIA

= uterus prolapse completely outside of hiatus

Enterocele

= CUL-DE-SAC HERNIA

= herniation of peritoneal membrane protruding between uterosacral ligaments at apex of vagina through rectovaginal space (cul-de-sac) and posterior perineum + extending distally into rectovaginal septum, separating rectum from vagina

(a) simple = no associated vaginal vault prolapse
(b) complex = associated with other forms of anterior / posterior vaginal vault prolapse

Content: fat (= peritoneocele), small bowel (= true enterocele), sigmoid colon (= sigmoidocele)

At risk: hysterectomy ← interrupted continuity of pubo-cervical + rectovaginal parts of endopelvic fascia

- symptoms of bowel obstruction, vaginal pressure, dyspareunia, low back pain
- difficult to diagnose on physical examination

Cystocolpoproctography:

◊ fails to demonstrate up to 20% of enteroceles

MR: superior to cystocolpoproctography

Rx: requires peritoneal approach to surgical repair

Sigmoidocele

EVacuation Proctography:

√ prolapse of sigmoid colon between rectum and vagina

Grading: (1) above pubococcygeal line; (2) between pubococcygeal + ischiococcygeal line; (3) below ischiococcygeal line

Cx: obstruction of rectum

Peritoneocele

= MESENTEROCELE

containing liquid / bowel / omentum / mesenteric fat

Evacuation Proctography:

√ extension of rectouterine excavation to below upper third of vagina

Rectocele

= bulging / outpouching of anterior rectal wall anterior to transverse perineus muscle into posterior vaginal wall

Cause: defect in pre- and pararectal fascia and rectovaginal septum

- often missed at physical examination
- impaired emptying → need for digital assistance

Evacuation proctography:

√ measurement of anteroposterior depth of convex wall protrusion extending beyond expected margin of normal rectal wall

√ rectal mucosal prolapse, solitary rectal ulcer

√ incomplete emptying of anterior rectoceles

MR:

√ distance of anterior / posterior rectal wall from anal canal axis

Grading: small < 2 cm; moderate 2–4 cm; large > 4 cm

Cx: obstructed defecation ← dissipation of vector force during straining

Rx: rectovaginal fascia repair / posterior fixation of rectum ± sigmoid / rectal resection

RECTAL PROLAPSE

= descent / infolding of mucosa or entire thickness of rectal wall through anal verge

Cause: chronic straining + fascial disruption

Cx: obstructed defecation → pudendal neuropathy → fecal incontinence; external anal sphincter atrophy

RECTAL INTUSSUSCEPTION

= descent of the entire (full wall) thickness of the rectal wall into anal canal; starting 6–11 cm above anus

Types: internal (intrarectal / intra-anal) or external

√ infolding of < 3 mm in width / > 3 mm in width / intraluminal narrowing / descent into anal canal / external prolapse

√ accompanied by formation of a circular indentation forming a ring pocket

PERITONEAL MESOTHELIOMA

= MALIGNANT MESOTHELIOMA

= uncommon only primary tumor of peritoneum arising from mesothelial cells lining peritoneal cavity

Frequency: 12–33% of all mesotheliomas; 6%–10% of all malignant mesotheliomas

Median age: 50 (range, 55–66) years; M >> F

Associated with: high levels of asbestos exposure (50–70%), esp. exposure to erionite (=

mineral fiber found in Turkey); therapeutic irradiation; exposure to simian virus 40; (rarely) chronic pleural / peritoneal irritation

Origin: (a) expectoration of inhaled asbestos fibers → swallowed → penetration of bowel wall into lymphatics + splanchnic circulation

(b) arise solely from peritoneum (35%)

Spread: intraperitoneal along serosal surfaces; direct invasion of liver, pancreas, bladder, bowel

Location: pleura (67%), peritoneum (30–40%), pericardium (2.5%), processus vaginalis (0.5%)

Path:

(1) Focal (localized) form

√ large mass, usually in upper abdomen + scattered peritoneal nodules in anterior parietal peritoneum becoming confluent and cakelike

Prognosis: good following complete surgical excision

(2) Diffuse (desmoplastic) form

√ diffuse thickening of mesentery, omentum, peritoneum, bowel wall WITHOUT definable mass + spread along serosal surfaces encasing solid / hollow visceral organs

Prognosis: highly aggressive + incurable

Histo: epithelial, sarcomatous, mixed (biphasic / bimorphic) with submesothelial tumor infiltration

• abdominal pain / discomfort, nausea, anorexia, weight loss

• abdominal distention / increasing abdominal girth

√ lymphadenopathy (rare)

UGI:

√ separation of small bowel loops from one another

√ absence of normal peristaltic movements

CT:

√ nodular irregular thickening of peritoneal surfaces / localized masses

√ stellate mesentery (common)= thick neurovascular bundles

√ increased attenuation in mesenteric fat

√ perivascular soft-tissue thickening

√ rigidity of vascular bundle

√ pleated thickening of mesenteric leaves ← infiltrating sheets of tissue

√ bowel wall thickening ← tumor extension to visceral peritoneal surface

√ foci of calcifications (rare)

√ disproportionately small amount of ascites of near-water density

√ omental involvement:

√ finely infiltrated fat with smudged appearance

√ discrete omental nodules

√ omental cake

√ pleural plaque (in 50%)

CECT:

√ homo- / heterogeneous enhancement ← intratumoral mucinous component / cystic degeneration / necrosis

MR:
√ tumor of intermediate to low SI on T1WI
√ tumor of intermediate to high SI on T2WI
NUC:
√ diffuse uptake of 67Gallium
Cx: bowel obstruction
Prognosis: extremely poor ← advanced disease at presentation (most patients die within 1 year)
DDx: peritoneal carcinomatosis (indistinguishable); nonneoplastic condition (eg, tuberculosis)

Multicystic / Cystic Mesothelioma

= BENIGN MULTICYSTIC MESOTHELIOMA = PERITONEAL INCLUSION CYST = PERITONEAL PSEUDOCYST = MULTILOCULAR INCLUSION CYST = ENTRAPPED OVARIAN CYST = INFLAMMATORY CYST OF THE PELVIC PERITONEUM
= accumulation of ovarian fluid contained by peritoneal adhesion / (?) rare benign neoplasm without metastatic potential but tendency for local recurrence
Cause: endometriosis; pelvic inflammatory disease; trauma; prior pelvic surgery in 30–100% (time delay of 6 months to 20 years)
Origin: serosal lining of peritoneum, pleura, pericardium
Pathogenesis: extensive pelvic adhesions → impaired peritoneal clearing → accumulation of ovulated fluid
Path: multiple translucent thin-walled cysts that grow along pelvic peritoneum in grapelike clusters adherent to surface of ovary; intermediate form between benign adenomatoid tumor + malignant peritoneal mesothelioma
Histo: cyst lined by hyperplastic mesothelial cells and fibroglandular tissue with chronic inflammation; filled with watery fluid; positive for calretinin and cytokeratins
◊ Not associated with asbestos exposure!
Mean age: 37 years (premenopausal with active ovaries); M÷F = 1÷5
• chronic or intermittent lower abdominal / pelvic pain
• abdominal distention, tenderness. palpable mass
• dyspareunia, constipation, urinary hesitancy & frequency
Location:
(a) woman: typically in cul-de-sac, along peritoneal surface of uterus and rectum / omentum
(b) men: peritoneal surface of bladder + rectum
(c) upper abdomen: multifocal cysts / freely floating cyst / unilocular cyst
Size: 13 cm of mean diameter
US:
√ single / multiloculated cyst conforming to the shape of the peritoneal cavity + contiguous with normal ovary:
√ "ovary-in-cyst" sign = normal-appearing ipsilateral ovary entrapped by loculated fluid
√ unusual geometric shape with anatomic boundaries
√ NO cyst wall
√ cyst content usually anechoic ± echoes from debris / hemorrhage

√ septa:
√ thin fibrous septa + mesothelial strands (common) resembling a spider web
√ NO septal calcification
√ ± nodular excrescences / thick polypoid incomplete septations

CT:
√ watery fluid attenuation
√ soft-tissue attenuation ← innumerable small cysts / thick-walled cyst
√ septal enhancement

MR:
√ signal pattern typical of serous fluid = low on T1WI, high on T2WI
√ enhancement of septa only
√ may contain hemorrhage

Cx: infertility
Rx: surgery (27–50% risk of recurrence)
Prognosis: good
DDx: Paraovarian cyst (ovoid cyst outside ovary), Hydrosalpinx (visible folds, located outside ovary), Lymphangioma, Intraperitoneal inclusion cyst, Mesenteric cyst, Ovarian cystadenoma / cystadenocarcinoma

PERITONEAL METASTASES

= PERITONEAL CARCINOMATOSIS
= relatively common intraabdominal spread of malignant tumors
Origin: (a) common: ovary, GI primary (stomach, colon)
(b) less common: pancreas, uterus, bladder, appendix
Time of onset:
in 55% at time of diagnosis of nongynecologic primary;
in 70% at time of staging laparotomy for ovarian cancer
• usually asymptomatic at onset
• abdominal enlargement ← ascites
• abdominal pain ← bowel obstruction
Path: tumor nodules studding peritoneal surface; transperitoneal spread with fibrotic host response → replacement of omental fat = omental caking + ovarian metastasis (= Krukenberg tumor)
Histo: adenocarcinoma with abundant mucin + signet ring morphology (most frequent)
√ new onset ascites / massive ascites
√ loculated fluid collections in peritoneal cavity
√ enhancement of peritoneum
√ nodules in areas of relative stasis / arrested flow of peritoneal fluid
Location of arrested flow / stasis of peritoneal fluid:
rectouterine recess (pouch of Douglas), retrovesical space, subhepatic space, right subdiaphragmatic space, root of small bowel mesentery, ileocecal junction, superior aspect of sigmoid mesocolon, right paracolic gutter
◊ Stasis areas = sites of occult tumor
√ desmoplastic reaction at (a) anterior border of rectum (Blumer shelf), (b) mesenteric side of

terminal ileum
√ occasionally sheetlike growth pattern encasing intraperitoneal viscera (DDx: malignant mesothelioma)

US:
√ ascites: anechoic / with low-level echoes of particulate matter (= proteinaceous exudate)
√ hypoechoic tumor nodule / sheetlike mass on visceral / parietal surface
√ echogenic plaquelike omentum floating in ascites / adherent to anterior abdominal wall

CT (25–50% sensitive for tumors < 1 cm):
√ small nodular densities studding peritoneal surface
√ pleated / stellate small bowel mesentery:
√ increased density of linear network in mesenteric fat (= fluid within leaves of mesentery)
√ apparent thickening of mesenteric vessels (= tumor infiltration of perivascular spaces)
√ "omental cake" = thickening of greater omentum
√ adnexal mass of cystic / soft-tissue density (= Krukenberg tumor) ← transperitoneal spread
√ lobulated mass in pouch of Douglas
√ calcified peritoneal implants in serous cystadenocarcinoma of ovary (in up to 40% with stage III / IV disease)

MR (85–90% sensitive for tumors < 1 cm):
√ maximal enhancement of peritoneal implants at 5–10 min

PET (controversial utility):
√ diffuse uptake spreading uniformly throughout abdomen and pelvis obscuring visceral outlines
√ discrete foci of uptake anteriorly within abdomen / dependently within pelvis

Cx: small bowel obstruction

PEUTZ-JEGHERS SYNDROME

[Johannes Peutz (1886–1957), internist in Den Haag, Holland]
[Harold Jeghers (1904–1990), internist in Boston, USA]
= rare syndrome characterized by intestinal polyposis and mucocutaneous pigmentation (= hamartomatosis)

Cause: mutation to serine / threonine kinase 11 (STK11) tumor suppressor gene on chromosome 19p13.3

Genetics: autosomal dominant with incomplete penetrance; often spontaneous mutations

Frequency: 1÷7,000 live births; in 50% familial, in 50% sporadic; most frequent of polyposis syndromes to involve small intestines

Age: at presentation 25 (range 10–30) years; M÷F = 1÷1

Path: multiple small sessile / large pedunculated polyps

Histo: benign hamartomatous (?) polyp with a <u>smooth muscle core</u> arising from muscularis mucosae and arborizing (treelike) extension into lamina propria of polyp (CHARACTERISTIC); misplaced epithelium (= pseudoinvasion) in submucosa, muscularis propria, sub-serosa frequently surrounding mucin-filled spaces

• mucocutaneous pigmentation (similar to freckles):
= 1–5-mm small elongated melanin spots on mucous membranes (lower lips, gums, palate) + facial skin (nose, cheeks, perioral, periorbital) + volar aspects of toes and fingers (100%),

noticeable in first few years of life
◊ NO potential to become malignant
• intermittent cramping abdominal pain ← small bowel intussusception (in 47%)
• rectal bleeding, melena (30%), acute blood loss, chronic hypochromic microcytic anemia ← ulcerated polyps
• prolapse of polyp through anus

Location: small bowel (jejunum + ileum > duodenum) > colon > stomach; mouth + esophagus spared

@ Small bowel (> 95%)
√ multiple usually broad-based polyps separated by wide areas of intervening flat mucosa
√ multilobulated surface of larger polyps
√ myriad of 1–2-mm nodules of up to several cm = carpet of polyps
√ intussusception usually confined to small bowel

@ Colon + rectum (30%)
√ multiple scattered 1–30-mm polyps; NO carpeting

@ Stomach + duodenum (25%)
√ diffuse involvement with multiple polypoid lesions:
√ small / large, sessile / pedunculated polyps

@ Extraintestinal sites: kidney, ureter, gallbladder, bronchial tree, nasal passages
√ adenoma of bronchus + urinary bladder

Cx:

◊ Approximately 60% lifetime incidence of malignancy!

(1) Gastrointestinal adenocarcinoma:
Frequency: 2–3%
Mean age: 40 years of age
Location: stomach, duodenum, colon; small bowel (least common)
(2) Carcinoma of pancreas (13%)
(3) Carcinoma of breast (50% risk by 60 years of age similar to BRCA1 / BRCA2): commonly bilateral + ductal
(4) Ovarian tumor (5%), commonly bilateral: sex cord-stromal tumor of ovary (almost in 100% of patients), mucinous cystic tumor, cystadenoma, granulosa cell tumor
(5) Testicular tumor: Sertoli cell tumor
(6) Endometrial cancer: adenoma malignum of cervix
(= minimal deviation adenocarcinoma = low-grade mucinous tumor of cervix)
(7) Transient intussusception (pedunculated polyp as lead point) → spontaneous reduction or SBO

Rx: (1) Endoscopic removal of all polyps > 5 mm
(2) Surgery is reserved for obstruction, severe bleeding, malignancy
(3) Surveillance screening: hemoglobin level; regular breast, gynecologic, testicular examinations; pelvic, testicular, pancreatic US; endoscopy of upper and lower GI tract; small bowel capsule endoscopy

Prognosis: decreased life expectancy (risk of cancer approaching 40% by 40 years of age)

DDx: familial adenomatous polyposis, juvenile polyposis (similar age), Cowden disease, Cronkhite-Canada syndrome

PNEUMATOSIS CYSTOIDES COLI

= cystic / linear gas collection in colonic wall
Location: submucosal / subserosal

Primary Pneumatosis Cystoides Coli

= benign condition
Location: favors left-sided colon
• simulates polyposis at colonoscopy → release of gas with cyst puncture
√ marked cluster of air-filled cysts in wall of colon

Secondary Pneumatosis

√ more linear gas collection

POSTCRICOID DEFECT

= variable defect seen commonly in the fully distended cervical esophagus; no pathologic value
Etiology: redundancy of mucosa over rich postcricoid submucosal venous plexus
Frequency: in 80% of normal adults
Location: anterior aspect of esophagus at level of cricoid cartilage
√ tumor- / weblike lesion with variable configuration during swallowing
DDx: subepithelial tumor, esophageal web (persistent configuration)

POSTINFLAMMATORY POLYPOSIS

= PSEUDOPOLYPOSIS
= reepithelialized inflammatory polyps as sequelae of mucosal ulceration
Etiology: ulcerative colitis (10–20%); granulomatous colitis (less frequent); schistosomiasis (endemic); amebic colitis (occasionally); toxic megacolon
Pathogenesis: ulcerative undermining of strips of mucosa with reepithelialization of denuded surfaces of tags + bowel wall
Location: most common in left hemicolon, may occur in stomach / small intestine
√ sessile + frondlike appearance (often)
√ filiform polyposis = multiple wormlike projections only attached at their bases (CHARACTERISTIC)
Prognosis: NO malignant potential
DDx: familial polyposis (polyps terminate in bulbous heads)

PRESBYESOPHAGUS

= defect in primary peristalsis + LES relaxation associated with aging
Frequency: 15% [50%] {85%} in 7th [8th] {9th} decade
Associated with: hiatus hernia, reflux
• usually asymptomatic
√ impaired / no primary peristalsis
√ often repetitive nonperistaltic tertiary contractions in distal esophagus
√ mild / moderate esophageal dilatation
√ poor LES relaxation

DDx: diabetes, diffuse esophageal spasm, scleroderma, esophagitis, achalasia, benign stricture, carcinoma

PROGRESSIVE SYSTEMIC SCLEROSIS

= PSS = chronic multisystem autoimmune disorder of connective tissues (collagen-vascular disease) characterized by a widespread pathophysiologic triad of

(1) Autoimmune disease-induced inflammation
(2) Microvascular damage
(3) Fibrosis (= overproduction of collagen → exuberant interstitial fibrosis with atrophy + sclerosis of many organ systems

= **SCLERODERMA** = variety of skin disorders associated with hardening of skin by extent of cutaneous involvement divided into 2 subgroups with different autoantibody profile + survival rate:

(a) DIFFUSE SCLERODERMA
- › skin changes proximal to elbow / knee
- › tendency to involve older women
- › interstitial pulmonary fibrosis more severe
- › organ failure more likely

(b) LIMITED SCLERODERMA (formerly **CREST syndrome**)
- › pulmonary arterial hypertension more common + more severe
- › CREST features more common
  - *CREST*: **C**alcinosis cutis
    Raynaud phenomenon
    Esophageal dysmotility
    Sclerodactyly
    Telangiectasia

May be associated with:
other connective tissue diseases (especially SLE and polymyositis / dermatomyositis)

Etiology: unknown; autoimmune condition with genetic predisposition, may be initiated by environmental antigen (eg, toxic oil syndrome in Spain ← ingestion of adulterated rapeseed oil / ingestion of L-tryptophan)

Incidence: 0.6–122.0÷1,000,000 people annually (higher rates in USA + Australia and among blacks)

Prevalence: 19–75÷100,000 people

Peak age: 45–64 years; M÷F = 1÷3 to 1÷8

Histo: vasculitis + submucosal fibrosis with deposition of collagen in longitudinal layer of muscularis propria + smooth muscle atrophy (initially hypertrophy and finally atrophy of collagen fibers)

- antinuclear antibodies (30–80%):
  - centromere antibody (ACA) specific for limited disease
  - anti–topoisomerase-1 (= antiScl-70) identifies patients with diffuse cutaneous disease
- antibodies to extracellular matrix proteins and type I + IV collagen; rheumatoid factor (35%), LE cells (5%)
- weakness, generalized debility

Increased risk: lung cancer, breast cancer

Stages:

(a) inflammatory phase (several weeks)
- erythema, pruritus, nonpitting edema
- fatigue, arthralgia, myalgia

(b) fibrotic phase (several months to years)
- inflexible skin, loss of function of affected limbs
- contractures, atrophy

Prognosis: 50–67% 5-year survival rate;
◊ Highest mortality among collagen vascular disease ← pulmonary arterial hypertension!

Cardiac Scleroderma

Histo: sclerosis of cardiac muscle (= myocardial fibrosis)
- arrhythmia

√ pericardial effusion (pericarditis)
√ congestive heart failure

Cx: cor pulmonale

Gastrointestinal Scleroderma (in 40–45%)

◊ 3rd most common manifestation of scleroderma (after skin changes + Raynaud phenomenon)
◊ May precede other manifestations!

Path: collagen deposition primarily in tunica muscularis → smooth muscle atrophy + fibrosis
- abdominal pain, diarrhea
- multiple episodes of pseudoobstruction

√ hepatomegaly

@ Esophagus (in 42–97%)
◊ First GI tract location to be involved!

Site: distal ²/₃ (striated muscle in upper ⅓)
- dysphagia (50%), heartburn (30%)

› functional:
√ hypotonia / atony + hypokinesia / aperistalsis in lower ²/₃ of esophagus (dysmotility in > 50%):
√ absent primary peristalsis of esophagus below level of aortic arch
√ chalasia (= patulous lower esophageal sphincter)
√ mild to moderate dilatation of esophagus
√ thin / vanished longitudinal folds
√ deficient esophageal emptying in recumbent position
√ gastroesophageal reflux (70%)
√ normal peristalsis above aortic arch ← striated muscle in proximal ⅓ of esophagus

› severe inflammation & scarring from reflux esophagitis ← poor clearance of peptic acid reflux:
√ erosions + superficial ulcers (= asymptomatic reflux esophagitis: NO protective esophageal contraction)

√ fusiform stricture usually 4–5 cm above GE junction
√ esophageal shortening + sliding hiatal hernia

Cx: peptic stricture, Barrett metaplasia, adenocarcinoma, aspiration pneumonia

@ Stomach (less frequent involvement)
√ gastric dilatation
√ decreased motor activity + delayed emptying

@ Small bowel (in up to 45%)
◊ PSS progresses rapidly once small intestine is involved!
• decreased small bowel motility with delayed intestinal transit time → stasis → bacterial overgrowth → diarrhea → malabsorption
√ pseudo-obstruction = marked dilatation of small bowel (in particular duodenum = megaduodenum, jejunum) simulating small bowel obstruction
CAVE: misdiagnosis of obstruction may lead to exploratory surgery!
√ abrupt cutoff at SMA level ← atrophy of neural cells with hypoperistalsis
√ prolonged transit time with barium retention in duodenum up to 24 hours
√ "hidebound / accordion" pattern (60%) = sharply defined folds of normal thickness with decreased intervalvular distance (valvular packing = tightly packed folds) within dilated segment ← predominant involvement of circular muscle:
√ normal mucosal fold pattern
√ pseudodiverticula (10–40%) = asymmetric sacculations with squared tops + broad bases on mesenteric side ← eccentric smooth muscle atrophy
√ pneumatosis cystoides intestinalis + pneumoperitoneum (occasionally)
√ excess fluid with bacterial overgrowth (= "pseudo–blind loop syndrome")

Cx: transient intussusception without anatomic lead point

@ Colon (up to 40–50%)
• constipation (common), may alternate with diarrhea
√ pseudosacculations + wide-mouthed "diverticula" on antimesenteric side → formed by repetitive bulging through atrophic areas in transverse + descending colon
√ eventually complete loss of haustrations (simulating cathartic colon)
√ marked dilatation (may simulate Hirschsprüng disease)
√ stercoral ulceration ← retained fecal material

Cx: life-threatening barium impaction

DDx: (1) Dermatomyositis (similar radiographic findings)
(2) Sprue (increased secretions, segmentation, fragmentation, dilatation most significant in midjejunum, normal motility)
(3) Obstruction (no esophageal changes, no pseudodiverticula)
(4) Idiopathic intestinal pseudoobstruction (usually in young people)

Localized Scleroderma

= MORPHEA [*morpheus*, Greek = form, structure]
= inflammatory disease that leads to diffuse / localized fibrotic atrophic skin hardening + may affect MSK system
• characterized by ABSENCE OF
• Raynaud phenomenon; digital sclerosis / necrosis

- nailfold capillary changes; involvement of internal organs
- arthralgia (9–17%)

May be associated with: musculoskeletal scleroderma

Musculoskeletal Scleroderma

- edema of distal portion of extremities
- thickened inelastic waxy skin most prominent about face + extremities, symmetrical polyarthralgias (50–80%)
- Raynaud phenomenon (may precede other symptoms by months / years)
- atrophy + thickening of skin and musculature (78%)

@ Fingers
- "sausage digit" = edema of digits associated with loss of transverse skin folds + lack of definition of subcutaneous fat

√ "tapered fingers" = sclerodactyly = atrophy + resorption of soft tissues of fingertips + soft-tissue calcifications

√ acroosteolysis (63–80%)
= "penciling" / "autoamputation" = resorption of distal phalanges of hand beginning at volar aspect of terminal tufts with proximal progression

@ Subcutaneous calcinosis (25–58%)

Location: extensor surface, areas with pressure / friction

√ calcinosis = punctate soft-tissue calcifications of fingertips, axilla, ischial tuberosity, forearm, elbow (over pressure area), lower leg, face

√ calcifications around tendons, bursae, within joints

@ Arthritis
- stiffness in small joints, occasionally in knee, shoulder, wrist; lack of motility → eventually contractures

√ arthritis of interphalangeal joints of hands (25%)

Location: 1st CMC, MCP, DIP, PIP

√ central / marginal erosions (50%):

√ resorption of palmar aspect of terminal phalanges (most frequent sign)

√ bony erosions of carpal bones (trapezium), distal radius + ulna, mandible, ribs, lateral aspect of clavicle, humerus, acromion, mandible, cervical spine

√ joint-space narrowing (late)

DDx: rheumatoid, psoriatic, erosive arthritis

√ soft-tissue swelling ± periarticular osteoporosis

√ NO significant osteoporosis

√ ± flexion contractures of fingers (from tendon sheath inflammation + fibrosis)

@ Ribs

√ erosion of superior aspect of ribs

@ Teeth

√ widening of periodontal membrane

Pulmonary Scleroderma (10–66%)

◊ Organ involvement with the most significant morbidity!

◊ Usually develops within first 3 years of disease

Path: almost 100% involvement in autopsy series
Histo: thickening of basement membrane of alveoli (= fibrosing alveolitis) + small arteries and veins; pattern of usual interstitial pneumonia (UIP) / nonspecific interstitial pneumonitis (NSIP)

- slightly productive, mostly dry cough, atypical chest pain
- exertional progressive dyspnea, fatigue, hematemesis
- pulmonary function abnormalities in the absence of frank roentgenographic changes (TYPICAL DISSOCIATION of clinical, functional, and radiologic evidence)

Location: peripherally, most prominent at both lung bases (where blood flow greatest)
CXR:
√ bibasilar pulmonary fibrosis:
Frequency: 20–65% on CXR, up to 90% on HRCT
√ fine / coarse reticulations / diffuse interstitial infiltrates
√ subpleural fibrocystic spaces (= honeycombing)
√ low lung volumes ← progressive volume loss
√ alveolar changes ← aspiration of refluxed gastric contents with disturbed esophageal motility / mineral oil taken to combat constipation:
√ aspiration pneumonia
√ bronchiolitis
√ dilated esophagus with air esophagram (DDx: achalasia, mediastinitis) with increased frequency of aspiration pneumonia
√ pleural reaction / effusion distinctly uncommon
HRCT:
Pattern: Nonspecific interstitial pneumonia > UIP
√ areas of patchy ground-glass attenuation
√ poorly defined subpleural centrilobular nodules
√ reticular pattern of attenuation
√ traction bronchiectasis + bronchiolectasis; mucous plugs
√ honeycombing
Rx: cyclophosphamide + low-dose prednisolone
Prognosis: ground-glass opacities irreversible even after therapy ← fibrosis NOT inflammation

Cx: (1) Progressive pulmonary fibrosis
(2) Pulmonary arterial hypertension (10–16–33%)
(3) Aspiration pneumonia
(4) Increased incidence of lung cancer

Renal Scleroderma (25%)
Onset: common within 3 years
Histo: fibrinoid necrosis of afferent arterioles (also seen in malignant hypertension)

- hypertensive renal crisis

√ renal cortical necrosis
√ spotty inhomogeneous nephrogram ← constriction + occlusion of arteries

√ concomitant arterial ectasia
Cx: renal failure (from nephrosclerosis)

PROLAPSED ANTRAL MUCOSA

= prolapse of hypertrophic + inflammatory mucosa of gastric antrum into duodenum resulting in pyloric obstruction
√ mushroom- / umbrella- / cauliflower-shaped filling defect at duodenal base
√ filling defect varies in size + shape
√ redundant gastric rugae can be traced from pyloric antrum through pyloric channel
√ gastric hyperperistalsis

PSEUDOMYXOMA PERITONEI

= "jelly belly" = "gelatinous ascites"
= slow insidious accumulation of large amounts of thick mucinous or gelatinous material on peritoneal surfaces
Incidence: 1÷1,000,000 annually
Mean age: 49 (range, 23–83) years; M< F
Etiology:

A. DISSEMINATED PERITONEAL ADENOMUCINOSIS (majority)
Origin: appendix
= benign / borderline / low-grade malignant epithelial cells from ruptured mucocele of the appendix without invasion of stroma
Rx: amenable to surgical debulking
Prognosis: 50% 5-year survival

B. OVARIAN PSEUDOMYXOMA PERITONEI
Origin: ovary
= mucinous tumor, cystadenoma, tumor with low malignant potential, invasive carcinoma that arises in ovarian mature cystic teratoma

C. PERITONEAL MUCINOUS CARCINOMATOSIS (rare)
= invasive high-grade moderately / poorly differentiated mucinous carcinoma
Origin: carcinoma of GI tract (colon < 5%, stomach, appendix), gallbladder, pancreas, uterus, common bile duct, urachal duct, omphalomesenteric duct
Prognosis: 10% 5-year survival

In most cases of pseudomyxoma peritonei the source is an appendiceal mucinous tumor!

• slowly progressive massive abdominal distension
• recurrent abdominal pain, weight loss
√ thickening of peritoneal + omental surfaces
√ omental cake
√ posterior fixation of bowel loops + mesentery
√ voluminous septated / loculated pseudoascites
√ several thin-walled cystic masses of different size throughout abdominal cavity:
√ **Hellmer sign** = focal collection of mucin in right subhepatic space displacing tip of liver medially
√ central displacement of ascending + descending colon and lateral displacement of

properitoneal fat stripe with mucin in paracolic gutter
√ central displacement of intestine
√ scalloped contour of liver + spleen
√ annular / semicircular calcifications (rare but highly suggestive)
CT:
√ intraperitoneal collection of very low attenuation (common) / soft-tissue density (rare)
√ may contain enhancing septa ± calcifications
√ discrete hypoattenuating masses (infrequent)
US:
√ hypoechoic collection (common) / more solid appearance (rare)
√ nonmobile echoes from proteinaceous / bloody / fibrinous exudate
√ echogenic septations
Prognosis: 25–65% median 5-year survival rate
Cx: bowel obstruction
Rx: often requires repeated laparotomies for drainage; need for multiple surgical debulkings
DDx: ascites, peritoneal metastases, pancreatitis with pseudocysts, pyogenic peritonitis, widespread echinococcal disease

RADIATION INJURY

= obliterative endarteritis with irradiation in excess of 4,000–4,500 rad
Frequency: 5%; increased risk after pelvic surgery
Radiosensitivity: small bowel mucosa (most sensitive) > rectum
√ radiographic changes within field of radiation only

Radiation Esophagitis

= from high doses of mediastinal radiation (usually > 5,000 cGy); Adriamycin® can potentiate effects of radiation as low as 500 cGy
• progressive dysphagia 4–8 months after completion of radiation therapy
√ smooth relatively long segment of concentric tapered narrowing within a preexisting radiation portal
DDx: involvement by recurrent tumor

Radiation Gastritis

◊ Permanent radiographic findings of radiation injury appear 1 month to 2 years after therapy
√ gastric ulceration + deformity (pylorus)
√ enlargement + effacement of gastric folds
√ antral narrowing + rigidity (similar to linitis plastica)

Radiation Enteritis

◊ Permanent radiographic findings of radiation injury appear > 1–2 years following irradiation
Predisposed: women (cancer of cervix, endometrium, ovary), patients with bladder cancer
• crampy abdominal pain (from intermittent obstruction)
• persistent diarrhea, occult intestinal hemorrhage
Location: ileum; concomitant radiation damage to colon / rectum

@ ACUTE radiation enteropathy
√ mucosal hyperenhancement
√ irregular nodular thickening of folds with straight transverse course ± ulcerations
√ separation of adjacent bowel loops by > 2 mm
@ CHRONIC radiation enteropathy (after months to years)
√ thickened bowel wall with luminal narrowing
√ multiple strictures + partial mechanical obstruction
√ serrated bowel margin
√ shortening of small bowel
√ fixation + immobilization of bowel loops with similar radiographic appearance between examinations ← dense desmoplastic response to irradiation

CT:
√ increased attenuation of mesentery

DDx: Crohn disease, lymphoma, ischemia, hemorrhage

Radiation Injury of Rectum

◊ Manifestation of radiation colitis can occur up to 15 years following irradiation

Predisposed: 90% in women (with carcinoma of cervix)

• tenesmus, diarrhea, bleeding, constipation

√ ridgelike appearance of mucosa ← submucosal fibrosis

√ irregularly outlined ulcerations (rare)

CT:
√ narrowed partially distensible rectum
√ thick homogeneous rectal wall
√ "target" sign = submucosal circumferential lucency
√ proliferation of perirectal fat > 10 mm
√ thickening of perirectal fascia
√ "halo" sign = increase in pararectal fibrosis

Cx: (1) Obstruction
(2) Colovaginal / coloenteric fistula formation

RECTAL POLYP

Prevalence: 7–50% (more common in older patients)

Path: hyperplastic÷adenomatous polyps = 1÷4

√ tends to flatten out with air distention

Hyperplastic Rectal Polyp

Size: usually < 5 mm

√ not visible adjacent to rectal balloon

Adenomatous Rectal Polyp

√ sessile > pedunculated > flat

√ carpetlike nodular appearance (for villous adenoma)

√ underdistended / redundant rectal mucosa may simulate villous adenoma

RETAINED GASTRIC ANTRUM

Cause: retention of endocrinologically active gastric antrum in continuity with pylorus + duodenum

Pathophysiology: bathing of antrum in alkaline duodenal juice → stimulates secretion of gastrin

Associated with: gastric ulcers in 30–50%

√ duodenogastric reflux of barium through pylorus (DIAGNOSTIC)

√ giant marginal ulcer / several marginal ulcers usually on jejunal side of anastomosis (large false-negative + false-positive rates; correct-positive rate of 28–60%)

√ large amount of secretions

√ edematous mucosa of jejunal anastomotic segment

√ lacy / cobweblike small bowel pattern (hypersecretion)

Cx: gastrojejunocolic fistula

SCHATZKI RING

= LOWER ESOPHAGEAL MUCOSAL RING

[Richard Schatzki (1901–1992), chief of radiology at University Hospital in Leipzig and associate clinical professor of radiology at Harvard Medical School and at Mount Auburn Hospital, Cambridge, MA]

= constant lower esophageal ring (mucosal thickening) presumed to result from reflux esophagitis = thin annular peptic stricture

Frequency: 6–14% of population; old age > young age; M > F

Histo: usually squamous epithelium on upper surface + columnar epithelium on undersurface; may be covered totally by squamous epithelium or columnar epithelium

Associated with: hiatal hernia (typical)

• asymptomatic (if ring > 20 mm), dysphagia (if ring < 12 mm)

Location: near the squamocolumnar junction; in region of B ring at inferior margin of lower esophageal sphincter

Height: 1–3 mm

√ nondistensible concentric transverse ring of shelflike projection with smooth symmetric margins

√ constant shape + size

√ visible only with adequate distension of esophagogastric region and when located above the esophageal hiatus of diaphragm

√ best demonstrated in prone position during arrested deep inspiration with Valsalva maneuver while solid barium column passes through esophagogastric region

√ short esophagus + intrahiatal / intrathoracic gastric segment = sliding hiatal hernia if Schatzki ring located 1–2 cm above diaphragmatic hiatus

Prognosis: decrease in caliber over 5 years (in 25–33%)

Cx: impaction of food bolus (associated with severe chest pain)

Rx: (1) Proper mastication of food

(2) Endoscopic rupture

(3) Esophageal dilatation (radiographically often lack of caliber change after successful dilatation)

DDx: Annular peptic stricture (usually thicker, asymmetric, irregular surface, associated with thickened esophageal folds, serration of esophageal margins)

SCHWANNOMA OF GI TRACT

= rare benign nerve sheath tumor arising from Schwann cell

Frequency: 0.2% (4%) of all (benign) gastric tumor; 2–7% of gastrointestinal mesenchymal tumors

Origin: myenteric plexus within muscularis propria of GI tract

Histo: well-circumscribed unencapsulated tumor characterized by interlacing bundles of spindle cells with wavy cigar-shaped nuclei + collagen; peripheral cuff of peritumoral lymphoid aggregates; areas of hypo- and hypercellularity (Antoni A & B) and Verocay bodies (= lining up of nuclei) are less frequent

Immunohisto: strong + diffuse stain for S-100 protein

Age: 3rd–5th decade; M<F

Location: stomach (60–70%) > colon > rectum

Site: submucosa + muscularis propria

• usually incidental endoscopic finding

• GI bleeding, abdominal pain, obstructive symptoms

√ discrete submucosal mass with exophytic / intramural growth

NECT:

√ low attenuation ← dense spindle cell composition

√ homogeneous attenuation in spite of relatively large size (!)

√ uncommonly calcified

CECT:

√ no / minimal enhancement during arterial phase

√ delayed enhancement during equilibrium phase

Cx: (1) Ulceration ← pressure necrosis of overlying mucosa

(2) Central necrosis ← outgrowing its blood supply

DDx: GIST, leiomyoma, lymphoma

Absence of hemorrhage / necrosis / cavity formation helps distinguish schwannomas from more heterogeneous GIST

SCLEROSING MESENTERITIS

= CHRONIC FIBROSING MESENTERITIS = MULTIFOCAL SUBPERITONEAL SCLEROSIS = SCLEROSING LIPOGRANULO-MATOSIS = PRIMARY LIPOSCLEROSIS OF THE MESENTERY = LIPOSCLEROTIC MESENTERITIS = LIPOGRANULOMA OF THE MESENTERY = ISOLATED LIPODYSTROPHY = SYSTEMIC NODULAR PANNICULITIS= RETROPERITONEAL XANTHOGRANULOMA = MESENTERIC WEBER-CHRISTIAN DISEASE

= rare idiopathic disorder characterized by tumorlike masses in mesentery composed of chronic nonspecific inflammation, fat necrosis, and fibrosis

Etiology: ? trauma, previous surgery, ischemia

Path: solitary / multifocal well-demarcated / diffusely infiltrating (mesenteric thickening) process

Histo: chronic mesenteric inflammation with lipid-laden macrophages (= lipophages) + plasma cells + eosinophils, fat necrosis and fibrosis
◊ NO penetration of muscularis propria!

Stages: based on predominant histopathologic finding in affected mesentery
(1) Mesenteric lipodystrophy
(2) Mesenteric panniculitis
(3) Retractile mesenteritis

Average age: 60 (range, 7–87 years); M÷F = 2÷1
Associated with:
(1) Gardner syndrome, familial polyposis
(2) Fibrosing mediastinitis, retroperitoneal fibrosis
(3) Lymphoma, lymphosarcoma (in 15–69%)
(4) Carcinoid tumor
(5) Metastatic gastric / colonic carcinoma
(6) Whipple lipodystrophy
(7) Weber-Christian disease

- asymptomatic / abdominal pain, palpable abdominal mass
- symptoms of intestinal obstruction / ischemia
- nausea, vomiting, weight loss, pyrexia, diarrhea
- ↑ WBC, ↑ erythrocyte sedimentation rate

Location: root of small bowel mesentery, colonic mesocolon
Site: extending toward mesenteric border; affecting submucosal fat; sparing mucosa
Pathophysiology: inflammatory infiltrate → obstruction of mesenteric lymphatics + mesenteric vessels → submucosal edema + luminal narrowing
Site: small bowel mesentery; occasionally mesocolon, sigmoid mesentery, omentum, retroperitoneum

Plain film:
√ soft-tissue mass with calcifications
√ ± thumbprinting ← vascular congestion
√ SBO: intestinal dilatation, fluid levels, fluid-filled bowel

UGI / Enteroclysis:
√ compression / distortion of duodenum near ligament of Treitz
√ separation of small bowel loops with fixation + kinking + angulation ← shortening + retraction of mesentery
√ irregular fold thickening of small bowel ← reactive mural thickening
√ narrowing + thumbprinting of colon (occasionally)

CT:
√ well-demarcated / ill-defined mesenteric mass:
√ heterogeneous texture of fat density:
√ misty attenuation interspersed with
√ soft-tissue density (= fibrous tissue)
√ single mesenteric root mass (= fibroma)
√ multiple nodules throughout mesentery (= fibromatosis)
√ multiple cystic masses in mesentery (= loose myxomatous composition / lymphatic

cysts):
√ tumoral pseudocapsule = peripheral band of soft-tissue attenuation at the edge of affected mesentery
√ ± small < 5 mm lymph nodes within lesion
√ "fat ring" sign = preservation of fat as a halo of low attenuation surrounding nondisplaced mesenteric vessels
√ punctate / coarse calcifications (uncommon)
√ mesenteric thickening with fine stellate pattern (= radiating strands of fibrosis) extending to bowel border
√ retraction of small bowel loops (= desmoplastic response)
√ rarely associated with retroperitoneal lymphadenopathy

US:
√ heterogeneous mass with hypo- and hyperechoic features

MR:
√ low to intermediate SI on T1WI + very low signal on T2WI
√ high SI on T2WI (= predominant myxomatous change)

Dx: surgical / percutaneous biopsy; diagnosis supported by absence of pancreatitis / inflammatory bowel disease

Prognosis: usually benign self-limited course with complete spontaneous resolution

Cx: compression of mesenteric vessels + formation of collateral vessels ± small bowel ischemia; partial / complete obstruction of small intestines

Rx: steroids + chemotherapy (cyclophosphamide, azathioprine); surgical resection for obstruction

DDx:
(1) Mesenteric fibromatosis = abdominal desmoid (infiltrating melting insinuation into muscularis propria)
(2) Mesenteric lymphoma (no calcifications unless treated, no compressive narrowing of vessels, no "fat-ring" sign, no pseudocapsule); lymphosarcoma
(3) Lipogenic liposarcoma of mesentery
(4) Inflammatory pseudotumor
(5) Mesenteric carcinoid (uptake with octreotide and somatostatin scintigraphy, elevated levels of serum serotonin + urine 5-hydroxyindoleacetic acid, carcinoid syndrome with liver metastases, mural thickening / small bowel masses)
(6) Carcinomatosis; pseudomyxoma peritonei ← metastatic gastric / colonic adenocarcinoma
(7) Crohn disease with fibrofatty proliferation
(8) Pyogenic peritonitis
(9) Whipple disease (polymerase chain reaction to verify causative bacillus, easily curable with antibiotics)

Mesenteric Lipodystrophy (1st stage)

= degeneration and <u>necrosis of mesenteric fat</u>

Path: diffuse mesenteric thickening (42%); solitary (32%) / multiple (26%) discrete mesenteric masses

Histo: sheets of foamy macrophages with scattered lymphocytic infiltration replacing

mesenteric fat
• asymptomatic
√ ± chylous ascites
Prognosis: spontaneous recovery

Mesenteric Panniculitis (2nd stage)
= predominantly chronic inflammatory stage of mesenteritis
Path: diffuse mesenteric thickening with puckering of mesenteric surface ← desmoplastic reaction; adherent mass(es) in root of mesentery; fat necrosis
Histo: infiltrate of plasma cells, foreign body giant cells, foamy macrophages
• crampy abdominal pain; bowel disturbances; low-grade fever
• nausea + vomiting; malaise; mild weight loss
• poorly defined mass (50%) / abdominal fullness
√ "misty mesentery" = mesenteric fat stranding

Retractile Mesenteritis (3rd stage)
= predominantly fibrotic stage of mesenteritis
Histo: collagen deposition, fibrosis, inflammation; calcifications ← fat necrosis
√ narrowing of bowel loop with spiculations → intestinal obstruction
DDx: may be indistinguishable from neoplasia

SCLEROSING PERITONITIS

= ENCAPSULATING PERITONEAL SCLEROSIS = PERITONITIS CHRONICA FIBROSA INCAPSULATA = PERITONEAL FIBROSING SYNDROME
= bowel partially / totally encased / wrapped in thick fibrous membrane forming several compartments that contain loops of small bowel
Cause: ?; idiopathic, chronic irritation of peritoneum
Associated with:
continuous ambulatory peritoneal dialysis (0.7% increasing to 19.4% after 8 years); ventriculoperitoneal shunt; peritoneo-venous shunt; tuberculosis; sarcoidosis; SLE; familial Mediterranean fever; protein S deficiency; liver transplantation; fibrogenic foreign material; GI malignancy; luteinized ovarian thecoma; β-blocker practolol
• recurrent episodes of small bowel obstruction
• weight loss, nausea, anorexia
√ smooth thickening + enhancement of peritoneum
√ "abdominal cocoon" = encasement of small bowel loops by a fibrocollagenous capsule:
√ central clustering of fixated small bowel loops
√ mantle of soft-tissue attenuation
√ peritoneal calcifications of parietal and visceral peritoneum
√ mural fibrosis + thickening of small bowel along its antimesenteric wall → adhesions → narrowing of bowel lumen → small bowel obstruction
√ formation of loculated fluid collections
Cx: small bowel necrosis + perforation
DDx: tuberculosis, amyloidosis, hyperparathyroidism, pseudomyxoma peritonei, peritoneal carcinomatosis, meconium peritonitis

SMALL BOWEL VOLVULUS

= rare life-threatening SURGICAL EMERGENCY

Cause: adhesive bands, internal hernia, external hernia

Pathophysiology:

closed-loop obstruction → bacterial overgrowth → accelerated fluid sequestration + gas production → increased intraluminal pressure + dilatation → compromise of vascular supply to intestinal wall → hemorrhagic infarction → necrosis → perforation

√ poor / absent enhancement of bowel wall

√ "spoke wheel" sign = radial peripheral distribution of distended fluid-filled small-bowel loops around central engorged thickened mesenteric vessels (75%)

√ two collapsed adjacent bowel loops = site of constriction (35%)

√ U-shaped configuration of distended fluid-filled small-bowel loops = radial arrangement of incarcerated fluid-filled dilated loop at periphery of tightly twisted mesentery (30%)

√ "triangular" sign = fusiform tapering of collapsed loop at site of constriction on longitudinal section through loop (15%)

√ "whirl" sign = swirling appearance of twisted mesentery (10%)

Cx: (1) Bowel ischemia in 46% due to closed-loop obstruction + torsion of mesenteric vessels

(2) Bowel necrosis

Mortality: 9%

SMALL LEFT COLON SYNDROME

Cause: transient functional colonic obstruction ← immaturity of mesenteric plexus

Age: newborn infant

Associated with: maternal diabetes mellitus (most common), maternal substance abuse; NOT related to cystic fibrosis

√ colonic caliber becomes abruptly diminutive distal to splenic flexure

√ bowel dilatation proximal to splenic flexure

√ ± meconium plug (as a result and NOT the cause of obstruction)

Prognosis: gradual resolution of functional immaturity over days to weeks

SOLITARY RECTAL ULCER SYNDROME

= MUCOSAL PROLAPSE SYNDROME

= rare condition frequently associated with chronic constipation and pelvic floor dyssynergia

Related disorders with common pathogenesis:

hamartomatous inverted polyp, colitis cystica profunda

Cause: prolapse of anterior rectal wall resulting in mucosal ischemia ← traumatization of rectal mucosa by anal sphincter during defecation (rectal straining / prolapse)

Age: young patients (especially women)

Path: small / large, single / multiple shallow ulcers; 25% broad- based, 18% patchy granular / velvety hyperemic mucosa; rectal stenosis through confluent circumferential lesion

Histo: obliteration of lamina propria mucosae by fibromuscular proliferation of muscularis mucosae, streaming of fibroblasts + muscle fibers between crypts, misplaced mucosal glands deep to muscularis mucosae; diffuse increase in mucosal collagen

- chronic rectal bleeding, passage of mucus
- disordered painful defecation, tenesmus

BE:
- √ central ulceration on anterior rectal wall → regional inflammation → mass effect in surrounding tissue mimicking rectal neoplasm at endoscopy:
  - √ polypoid lesion / nodules (polypoid type)
  - √ flat granular mucosa (flat type)
- √ thickened valves of Houston without ulcer
- √ stricture

Evacuation proctography:
- √ failure of anorectal angle to open while straining
- √ excessive perineal descent

Prognosis:
(1) Little change over time
(2) Considerable change in appearance of lesion
(3) Transfusions necessitated by massive blood loss

Dx: rectal biopsy

DDx: invasive rectal carcinoma, Crohn disease

SPRUE

= classic disease of malabsorption

Path: villous atrophy (truncation) + crypt hyperplasia (elongation of **crypts of Lieberkühn** responsible for water + electrolyte absorption + mucin production) + marked mononuclear round cell infiltration of lamina propria and epithelium (plasma cells, mast cells, lymphocytes, eosinophils)

[Johann Nathanael Lieberkühn (1711–1756), physician inventor of microscopic examination of intestine at Leiden University]

Pathophysiology: loss of villi → decreased absorption of fluid + crypt hyperplasia → production of fluid → chronic excess fluid in small bowel lumen

Location: patchy involvement of duodenum + jejunum > ileum > cecum (decreasing severity toward the distal small intestine)

UGI:
- √ nodularity in fold-free duodenum (= duodenitis)
- √ "bubbly bulb" = peptic duodenitis = mucosal inflammation, gastric metaplasia, Brunner gland hyperplasia

Small bowel follow-through:
- √ small bowel **dilatation** is HALLMARK in untreated celiac disease (70–95%), best seen in mid + distal jejunum ← intestinal hypomotility; degree of dilatation related to severity of disease
- √ hypersecretion-related artifacts:
  - √ air-fluid levels in small bowel (rare)
  - √ **segmentation** = breakup of normal continual barium column creating large masses of barium in dilated segments separated by stringlike strands from adjacent clumps ← excessive fluid; best seen on delayed films

- √ **flocculation** = coarse granular appearance of small clumps of disintegrated barium ← excess fluid best seen at periphery of intestinal segment; occurs especially with steatorrhea
- √ **fragmentation** = scattering = faint irregular stippling of residual barium resembling snowflakes associated with segmentation ← excessive fluid

√ **"moulage" sign** (50%) = smooth contour with effaced featureless folds resembling tubular wax mold ← atrophy of the folds of Kerckring; CHARACTERISTIC of sprue if seen in duodenum + jejunum

√ slow / normal / short transit time:

- √ nonpropulsive asynchronous peristalsis (flaccid + poorly contracting loops)

√ normal / thickened / effaced mucosal folds (depending on degree of hypoproteinemia)

√ colonlike haustrations in well-filled jejunum ← spasm + cicatrization from transverse ulcers

√ transient nonobstructive small bowel intussusception (20%) without anatomic lead point

Enteroclysis:

√ **flip-flop pattern** = "reversal" sign = reversed jejunoileal fold pattern with featureless jejunum ← villous atrophy + compensatory hypertrophy of folds in ileum:

- √ decreased number of folds in proximal jejunum (< 3 folds per inch) ← loss of mucosal surface area
- √ "jejunization" of ileal loops = increased number of folds in distal ileum (> 5 folds per inch) as adaptive response to increased absorptive capability = SPECIFIC

√ tubular featureless lumen

√ mosaic pattern = 1–2-mm polygonal islands of mucosa surrounded by barium-filled distinct grooves (10%)

CT:

CT patterns of celiac disease are small bowel and colonic malabsorption patterns and prominent mesenteric lymph nodes of the small bowel.

@ Small bowel malabsorption pattern:

- √ small bowel dilatation + increased fluid content:
  - √ progressive dilution of enteric contrast material
  - √ flocculation (= precipitating small flecks of barium)
  - √ laminar flow = trilaminar appearance of intraluminal barium separated by a middle layer of low attenuation formed by intrinsic intestinal fluid mimicking intussusception
- √ flaccid dilated small bowel:
  - √ nonobstructing telescoping of small bowel loops
  - √ transient small bowel intussusception (in up to 20%)

@ Colonic malabsorption pattern:

- √ colonic distension (= stagnant hypotonic colon):
  - √ excessive colonic gas accumulation ← undigested sugar + fat are processed by gas-producing bacteria
  - √ fluid-filled colon ← reduction of absorptive capacity
- √ cecal plume (= feathering) of fluid
- √ steatorrhea = stool of fat attenuation (lung windows!)

√ colonic geodes = round spheres of hard rocklike aggregations of fat + fluid + air, which may calcify peripherally with stasis ← fat saponification

@ Mesenteric lymph node prominence

√ mild to moderate mesenteric lymphadenopathy ← follicular hyperplasia ← proliferation of reactive B and T lymphocytes (mimicking lymphoma):

Location: predominantly upper small bowel mesentery

DDx: Crohn disease + mesenteric adenitis (node prominence usually near terminal ileum)

√ lymph nodes of low attenuation (in up to 12%)

√ cavitating lymph nodes (see below)

@ Structural intestinal changes

√ small bowel wall thickening ← inflammation:

√ straightening of valvulae conniventes

√ fold separation

√ reversal of jejunoileal fold pattern (COR reformats!):

√ jejunal villous atrophy

√ ileal jejunization (63% sensitive, 100% specific)

N.B.: > 5 folds per inch in jejunum + < 3 folds per inch in ileum excludes celiac disease

√ colonic fold thickness > 4 mm ← inflammation

√ mesenteric hyperemia = engorgement of mesenteric vessels (during severe active inflammation)

√ mesenteric panniculitis / misty mesentery

√ intramural fat ← sign of chronic inflammation

Location: duodenum + jejunum > right colon

@ Structural extraintestinal changes

√ ascites

√ small atrophic spleen = hyposplenism (30–50%)

√ adenopathy (see above)

√ celiac-associated T-cell lymphoma

US:

√ moderately dilated fluid-filled small intestine

√ thickening of small bowel wall

√ hyperperistalsis (82%)

√ dilated superior mesenteric artery + portal vein

√ liver steatosis ← metabolic derangement from malabsorption

√ mesenteric + retroperitoneal lymphadenopathy (12%)

√ slight ascites (76%)

Dx: (1) Clinical presentation

(2) Jejunal / duodenal biopsy with typical histopathologic features

(3) Improvement of clinical symptoms + intestinal function within 2 weeks of a gluten-free diet (70%)

(4) Improvement of small bowel histology after > 3–6 months of a gluten-free diet

Cause for relapse: hidden dietary gluten, diabetes, bacterial overgrowth, intestinal ulceration,

development of lymphoma

Imaging is important in detecting various complications of celiac disease like lymphoma, ulcerative jejunoileitis, cavitary mesenteric lymph node syndrome, adenocarcinoma of small bowel, SCC of esophagus and pharynx.

Cx:

(1) **Malignant tumors** (in up to 14%)

• recurrent diarrhea / abdominal pain in previously asymptomatic patients under gluten-free diet

◊ Malignant tumors are the most common cause of death

(a) NHL (18% of cancers in celiac disease):

◊ 8% of patients with sprue develop lymphoma

◊ history of celiac disease for > 20 years

Type: enteropathy-associated T-cell lymphoma (85–90%) + extraintestinal lymphoma (mostly Hodgkin disease)

Peak prevalence: 7th decade

Location: terminal ileum (most common)

√ luminal narrowing with mucosal destruction (= ulcer with shouldering of margins)

√ irregularly thickened nodular folds

√ exophytic mass

√ focal aneurysmal bowel dilatation

√ florid lymphadenopathy

(b) adenocarcinoma of small bowel (7%), rectum, stomach

(c) squamous cell carcinoma of esophagus (in 4%) during 6th–7th decade

(d) esophageal cancer

(e) melanoma

(f) other malignancies of oropharynx, ovaries, testicles, thyroid, breast, lungs

(2) **Ulcerative jejunoileitis** (rare)

= multiple chronic benign ulcers

Age: 5th–6th decade

Location: jejunum > ileum > colon

• response to gluten-free diet

√ sausage appearance of small bowel ← circumferential bowel wall thickening

√ fold thickening + ulceration → stricture formation → intestinal obstruction

Cx: hemorrhage, perforation, lymphoma

Prognosis: frequently fatal

Rx: small bowel resection

DDx: enteropathy-associated T-cell lymphoma (may coexist, impossible to differentiate)

(3) **Cavitating mesenteric lymph node syndrome** (rare)

Path: multiple pseudocystic lymph nodes containing chylous fluid (thin milky fluid / thick creamy material) + thin peripheral rim of fibrous material and scant elements of atrophic lymph node structures

• refractory weight loss, fatigue, diarrhea

• target cells + Howell-Jolly bodies in peripheral blood smear (= signs of hyposplenism)

Location: confined to jejunoileal mesentery

√ multiple 2–7-cm large lymph nodes with a central cavity of low attenuation ± fat-fluid levels
√ splenic atrophy
√ villous atrophy of small intestinal mucosa
Prognosis: usually fatal

(4) Sigmoid volvulus (rare)
(5) **CEC syndrome** (in late stage of disease)
= **C**eliac disease + **E**pilepsy + **C**erebral calcification
Countries: Italy, Spain, Argentina
• intractable epilepsy
√ cerebral occipital calcifications identical to Sturge-Weber syndrome (without portwine nevus)

DDx:
(1) Esophageal hypoperistalsis: scleroderma, idiopathic pseudoobstruction
(2) Gastric abnormalities: Zollinger-Ellison syndrome, chronic granulomatous disease, eosinophilic enteritis, amyloidosis, malignancy
(3) Tiny nodular defects on thickened folds: Whipple disease, intestinal lymphangiectasia, Waldenström macroglobulinemia
(4) Small 1–3-mm nodules: lymphoid hyperplasia associated with giardiasis and immunoglobulin deficiency disease, diffuse lymphoma
(5) Small nodules of varying sizes: systemic mastocytosis, amyloidosis, eosinophilic enteritis, Cronkhite-Canada syndrome
(6) Bowel wall narrowing, kinking, scarring, ulceration: regional enteritis, bacterial / parasitic infection, carcinoid, vasculitis, ischemia, irradiation

Celiac Disease

= CELIAC SPRUE = NONTROPICAL SPRUE = GLUTEN-SENSITIVE ENTEROPATHY
[*coeliac* , Greek = abdominal]
= common chronic inflammatory intestinal autoimmune disorder of multifactorial etiology induced in genetically susceptible individuals
Countries: North America, Europe, Australia, India, Pakistan, Middle East, Cuba
Incidence: 1÷100 to 1÷500; 1–3% of general population in Europe and USA; 1÷200 Americans with 60,000 new cases annually; < 10% actually diagnosed with bioptic proof in 2–13÷100,000 adults annually
Age: childhood by age 2 years; 30–40 [40–60] years with M < F [M > F]
Cause: multifactorial; excessive T-cell–mediated immunity to ingested dietary gluten
Irritating agent: gliadin polypeptides in wheat, rye, barley, oats, other grains
Genetics: HLA-DR3-DQ2 heterodimer haplotype (encoded by DQA1 + DQB1 alleles), HLA-DR4-DQ8 haplotype confers an ↑ risk; detected in 15% of 1st-degree relatives (concordance rate of 76% for monozygotic twins + 11% for dizygotic twins)
Associated with: type 1 diabetes (juvenile diabetes), autoimmune thyroid disease, Addison disease, Sjögren syndrome, SLE
Pathophysiology:
anti-tissue transglutaminase antibodies destroy villous extracellular matrix + epithelial

cells → progressive villus inflammation → nodular + thickened duodenal and jejunal folds; villous truncation + crypt hyperplasia → chronic fluid excess in small bowel lumen → stretching of small bowel → delayed transit

- asymptomatic (silent, latent, atypical, subclinical): < 10% of cases are properly diagnosed with an average delay of 20–60 years from onset of symptoms
- intestinal symptoms:
  - severe chronic diarrhea (< 20%) / constipation (15%)
  - failure to thrive, lassitude, fatigue, vomiting
  - weight loss (5%), overweight (39%), obese (13%)
  - crampy abdominal pain (← intussusception), distension
  - flatulence, steatorrhea (CLASSIC but found only in minority of patients)
- extraintestinal symptoms:
  - dermatitis herpetiformis (= pruritic bullous skin rash), aphthous stomatitis, alopecia
  - anemia from iron / folate / vitamin B12 deficiency
  - hepatitis, hypertransaminasemia (elevated alkaline phosphatase + liver enzymes), cholangitis
  - coagulopathy, guaiac-positive stools from bleeding diathesis, prolonged prothrombin time
  - peripheral neuropathy, depression, cerebellar ataxia, dementia, seizures
  - short stature, pubertal delay, infertility
  - idiopathic osteopenia with bone pain; arthralgia
  - dental enamel defects (10–40%)
  - low serum levels of cholesterol, calcium, albumin
- Serologic testing for antibodies to gliadin + endomysium in screening + monitoring compliance
  - anti-tissue transglutaminase IgA antibodies (*DDx:* juvenile diabetes, inflammatory bowel disease, arthritides)
  - antiendomysial antibodies

Small bowel follow-through: mostly replaced by endoscopy, antibody testing, CT enteroclysis!

> √ features of malabsorption pattern in celiac disease include duodenitis, dilution, dilatation, slow transit, flocculation, moulage, reversal of jejunal-ileal fold pattern, and transient small bowel intussusception.

With delay in diagnosis for > 10 years at risk for:
iron deficiency anemia, lactose intolerance, osteoporosis with increase in fracture risk, miscarriage, low birth weight, lymphoma, seizures, depression

Dx: IgA autoantibodies for tissue transglutaminase, antiendomysial antibodies, HLA-DQB1 typing

Rx: gluten-free diet: corn, rice, tapioca, soya, millet, vitamin supplements

Tropical Sprue

Etiology: infectious agent cured with antibiotics; geographic distribution (India, Far East, Puerto Rico)

Age: any age group

- glossitis, hepatosplenomegaly

- macrocytic anemia + leukopenia

Prognosis: spontaneous resolution after months / years

Rx: responds well to folic acid + broad-spectrum antibiotics

STRONGYLOIDIASIS

[*strongylos* , Greek = round; *eidos* , Greek = form]

Organism: helminthic parasite Strongyloides stercoralis (2.2 mm long, 50 μm in diameter); capable of reproducing within (primary) human host [*stercus* , Latin = excrement]

Prevalence: 30–35 million cases globally; 0.4–4% in USA

Country: tropical + subtropical regions, parts of Europe, southeastern USA (endemic in eastern Kentucky, rural Tennessee), Puerto Rico

Primary host: humans

Infection: filiform larva enters body through skin / mucous membranes (from contaminated soil)

Cycle:

filariform larva penetrates skin → passes from subcutaneous / submucosal sites via lymphatic + venous circulation to lung → larva breaks into alveolar spaces and ascends bronchi + trachea;

larva swallowed → settles in duodenum + upper jejunum (lives in tunnels between enterocytes) → larva matures into parasitic female adult worm → produces eggs through parthenogenesis (= asexual reproduction) → worm deposits eggs into the intestinal lumen → ova hatch immediately into nonmigratory rhabditiform larvae (1st larval stage) → excreted in feces

[*parthenos* , Greek = virgin; *genesis* , Greek = creation]

Autoinfection (endogenous reinfection):

rhabditiform larva may remain in intestines long enough to metamorphose into infective filariform larva → penetrates intestinal mucosa / perianal skin → reenters venous system repeating life cycle in same host

Path: edema + inflammation of intestinal wall ← invasion by larvae; flattening of villi; ova in mucosal crypts

Histo: intact larvae seen with Gömöri methenamine silver stain

- asymptomatic for many years (in majority)
- midepigastric pain mimicking peptic ulcer disease
- severe malnutrition (malabsorption, steatorrhea), weight loss
- larva currens = recurrent allergic pruritic cutaneous skin reaction at site of larval penetration within 24 hours in area of buttocks + upper thighs in patients with autoinfection
- worms, larvae, eggs in stool
- peripheral blood eosinophilia (extremely common)
- elevated levels of immunoglobulin E

@ Intestine

√ paralytic ileus (due to massive intestinal infestation):

√ mild to moderate dilatation of proximal ²/₃ of duodenum + jejunum

√ edematous irregular mucosal folds

√ ulcerations

√ stricture of 3rd + 4th part of duodenum

√ rigid pipestem appearance + irregular narrowing of duodenum (in advanced cases)

@ Lung

√ transient pulmonary opacities

Dx: filariform larvae in stool (single stool sample in 70% negative), sputum samples / bronchial washings / bronchial / lung biopsy specimens, CNS samples
Rx: thiabendazole (90% efficacy rate)
Prognosis: high mortality in undernourished patients
DDx: Crohn disease, lymphoma, tuberculosis, other causes of enterocolitis

Strongyloides Hyperinfection Syndrome

= life-threatening parasitic infestation = chronic pathway of continuous autoinfection → widespread dissemination + extensive tissue invasion in immunocompromised host with malignancy, autoimmune disease, malnutrition
• gram-negative bacteremia, septicemia ← spillage of gut organisms into bloodstream at time of larval penetration of intestinal wall)
• crampy abdominal pain, nausea, diarrhea
• persistent vomiting, hematemesis
√ thickened colonic wall ← florid transmural granulomatous inflammatory colitis caused by invasive larvae
@ Heart, skeletal muscle, lymph nodes, liver
• endocarditis, peritonitis
@ CNS
(a) meningitis ← larvae in pia arachnoid
(b) global ischemia, atrophy, microinfarcts ← capillary obstruction
@ Lung
Histo: foreign body reaction resulting in inflammatory pneumonitis + pulmonary hemorrhage
• ± dyspnea, cough, sputum production, wheezing
• hemoptysis
√ fine miliary nodules (rare)
√ diffuse reticulonodular interstitial opacities
√ ill-defined patchy fleeting (migratory) airspace consolidation typically resolving in 1–2 weeks
√ bilateral segmental / lobar opacities (with heavy infestation) ← extensive pneumonia:
√ cavitation + abscess formation ← superimposed bacterial infection
√ adult ARDS may develop
√ pleural effusion
Prognosis: 70% mortality in AIDS patients

TAILGUT CYST

= RETRORECTAL CYSTIC HAMARTOMA
Cause: incomplete regression of embryonic tailgut (= the portion distal to future as yet undeveloped anus)
Average age: 35 years; M < F
Histo: several types of epithelia + elements of intestinal epithelium, smooth muscle within cyst wall
• asymptomatic / urinary frequency

• rectal / perineal pain, painless rectal bleeding
• fever, acute pelvic pain ← secondary infection

Location: retrorectal / midline presacral space ± extension into ischiorectal fossa

√ well-defined thin-walled multicystic / unilocular cyst within perirectal space adhering to sacrum / rectum
√ clear fluid / mucoid fluid with internal echoes
√ mild enhancement of uncomplicated cyst
√ thick enhancing wall ± surrounding inflammation / air-fluid level ← secondary infection

Cx: (1) Repeated perirectal abscesses, recurring anorectal fistula (secondary infection)
(2) Degeneration into mucinous adenocarcinoma (rare)

◊ Asymmetric irregular wall thickening and heterogeneous enhancement raises suspicion for malignant change within a duplication cyst.

Rx: complete surgical excision

DDx: (1) Epidermoid / dermoid cyst
(2) Rectal duplication cyst
(3) Anterior meningocele
(4) Cystic lymphangioma

TOXIC MEGACOLON

= acute transmural fulminant colitis characterized by neurogenic loss of motor tone + rapid development of nonobstructive colonic dilatation + loss of haustra

Etiology:

1. Ulcerative colitis (most common, in < 5%)
2. Crohn disease
3. Amebiasis, salmonellosis
4. Pseudomembranous colitis
5. Ischemic colitis

Pathogenesis: inflammation that extends deep beneath colonic mucosa → damage to muscularis propria → colonic dilatation and loss of haustra

Histo: widespread sloughing of mucosa + thinning of frequently necrotic muscle layers

• systemic toxicity, profuse bloody diarrhea

√ colonic ileus with marked dilatation of transverse colon > 5.5–6.0 cm ← gas influx into nondependent colonic segment in supine patient
√ few air-fluid levels
√ increasing caliber of colon on serial radiographs without redundancy
√ loss of normal colonic haustra + interhaustral folds
√ coarsely irregular mucosal surface
√ pseudopolyposis = mucosal islands in denuded ulcerated colonic wall
√ pneumatosis coli

US:

√ colonic dilatation >6 cm
√ marked decrease in colonic wall thickness to < 2 mm
√ increased free fluid

CT:
√ distended colon filled with large amounts of fluid + air
√ distorted haustral pattern
√ irregular nodular contour of thinned wall
√ intramural air / small collections (= pneumatosis coli)
Cx: perforation ± pneumoperitoneum; rectal carcinoma
BE: CONTRAINDICATED due to risk of perforation
Morbidity: from electrolyte disturbance, fluid loss, hemorrhage, perforation
Prognosis: 20% mortality

TUBERCULOSIS OF ABDOMEN

◊ Most common manifestation of extrapulmonary tuberculosis (solid viscera > GI tract)
Endemic in: sub-Saharan Africa and Southeast Asia
Organism: M. tuberculosis, M. bovis, M. avium-intracellulare

Tuberculous Abdominal Lymphadenopathy (55–66%)

Frequency: 55–66% of patients with abdominal TB
Location: mesenteric, peripancreatic, omental, retroperitoneal
√ enlarged node with hypoattenuating center (40–60%) + hyperattenuating enhancing rim ← caseous necrosis
√ conglomerate lymph node masses of mixed attenuation
√ enlarged lymph nodes of homogeneous attenuation
√ > 3 normal / mildly enlarged homogeneous lymph nodes
√ NO obstruction of bile ducts / GI tract, / urinary tract (if present consider alternative diagnosis)

Tuberculous Peritonitis (33%)

◊ Most common presentation of abdominal tuberculosis (in 33%) associated with widespread abdominal disease!
Cause: hematogenous spread / rupture of mesenteric node / rupture of GI deposit / fallopian tube involvement
Types:
A. WET TYPE (90%) = exudative ascites
• large amount of freely distributed / loculated viscous fluid
√ high-density ascites of 20–45 HU ← high protein contents + leukocytes
√ mildly thickened smooth peritoneum
√ pronounced peritoneal enhancement
√ 5-mm macronodules in mesentery
√ thin omental line ← fibrous wall covering the infiltrated omentum
√ calcifications
B. FIBROTIC-FIXED TYPE (60%) = large cakelike masses with separation + fixation of bowel loops
√ irregular mottled masses of soft-tissue density in omentum + mesentery (common)
√ separation / fixation of matted loops of bowel
√ loculated ascites (occasionally)

C. DRY / PLASTIC TYPE (10%) = large mesenteric caseous adenopathy + adhesions
√ enhancing peritoneal thickening + caseous nodules
√ dense adhesions ← fibrous peritoneal reaction
√ smudged / caked / thickened / masslike omentum
Cx: small bowel obstruction ← adhesions from serosal tubercles
DDx: disseminated peritoneal malignancy, nontuberculous peritonitis, mesothelioma

Tuberculosis of GI tract (rare)

Rarely encountered in Western Hemisphere; increased incidence in AIDS; usually associated with pulmonary tuberculosis (in 6–38%)
Etiology:
(1) Ingestion of tuberculous sputum
(2) Hematogenous spread from tuberculous focus in lung to submucosal lymph nodes
◊ Radiographic evidence of pulmonary TB in < 50%
(3) Primary infection by cow milk (Mycobacterium bovis)
Path:
(a) ulcerative form (most frequent): ulcers with their long axis perpendicular to axis of intestine, undermining + pseudopolyps
(b) hypertrophic form: thickening of bowel wall (transmural granulomatous process)
Age: 20–40 years
• weight loss, abdominal pain (80–90%), nausea, vomiting
• tuberculin skin test negative in most patients with primary intestinal TB
Location: ileocecal region (cecum > terminal ileum) > ascending colon > jejunum > appendix > duodenum > stomach > sigmoid > rectum
◊ Skip areas of luminal narrowing + ileocecal valve involvement strongly suggest TB!
@ Ileocecal area (80–90%)
◊ Most commonly affected bowel segment!
Cause: relative stagnation of intestinal contents + abundance of lymphoid tissue (Peyer patches)
√ irregular thickened nodular folds in terminal ileum
√ **Stierlin** sign = rapid emptying (= hypermotility) of narrowed (spastic) terminal ileum into shortened rigid obliterated cecum on BE (earliest manifestation)
√ thickened ileocecal valve ← mass effect of edema
√ **Fleischner** sign = "inverted umbrella" defect = wide gaping patulous ileocecal valve associated with narrowing of the immediately adjacent terminal ileum
√ deep fissures + large shallow linear / stellate ulcers with CHARACTERISTIC elevated margins following the orientation of lymphoid follicles (ie, longitudinal in terminal ileum and transverse in colon)
√ sinus tracts (rare) / enterocutaneous fistulas / perforation
√ symmetric annular "napkin ring" stenoses
CT:
√ asymmetric circumferential wall thickening of ileocecal valve + medial wall of cecum + terminal ileum
√ exophytic extension engulfing terminal ileum

√ localized massive mesenteric lymphadenopathy with central areas of low attenuation

DDx: Crohn disease, amebiasis, cecal carcinoma

@ Colon

Site: segmental colonic involvement, esp. on right side

√ rigid contracted cone-shaped shrunken cecum ← spasm / transmural fibrosis

√ shortened "amputated" cecum ← retraction of cecum out of iliac fossa ← fibrosis of mesocolon

√ spiculations + wall thickening

√ diffuse ulcerating colitis + pseudopolyps

√ short hourglass strictures

DDx: ulcerative colitis, Crohn disease, amebiasis (spares terminal ileum), colitis of bacillary dysentery, ischemic colitis, pseudomembranous colitis

@ Gastroduodenal

Site: simultaneous involvement of antrum + pylorus + duodenum

√ stenotic pylorus with gastric outlet obstruction

√ narrowed antrum (= linitis plastica appearance)

√ antral sinus tract / fistula

√ multiple large and deep ulcerations on lesser curvature simulating peptic ulcer disease

√ thickened duodenal folds with irregular contour / dilatation

DDx: carcinoma, lymphoma, syphilis

@ Esophagus

◊ Least common GI tract manifestation

Cause: secondary involvement from adjacent tuberculous lymphadenitis / primary TB

Location: level of carina

√ deep ulceration

√ stricture

√ mass

√ intramural dissection / fistula formation → sinus tract formation

TRICHURIASIS

◊ 3rd most common roundworm infection in humans

Organism: Trichuris trichiura

Infection: fecal-oral route

Cycle: after elimination in feces eggs become embryonate and infective within 15 to 30 days → ingestion of eggs → release of larvae in small intestine → larvae mature during migration to cecum + ascending colon → adult worms attaches to mucosa

Barium enema:

√ small elongated filling defects

Dx: stool sample

DDx: lymphoid hyperplasia, aphthous ulcers

TURCOT SYNDROME

= autosomal recessive disease with

(a) colonic polyposis

(b) CNS tumors (especially supratentorial glioblastoma, occasionally medulloblastoma)

Age: symptomatic during 2nd decade

Histo: adenomatous polyps

• diarrhea, seizures

√ multiple 1–30-mm polyps in colon + rectum

Cx: malignant transformation of colonic polyps in 100%

Prognosis: death from brain tumor in 2nd + 3rd decade

ULCERATIVE COLITIS

= common idiopathic superficial inflammatory bowel disease with continuous concentric + symmetric colonic involvement

Etiology: ? hypersensitivity / autoimmune disease

Incidence: 2–14÷100,000 annually

◊ 7,000–46,000 new cases annually in USA

Prevalence: 37–246÷100,000 in North America

Path: predominantly mucosal + submucosal inflammation with neutrophilic infiltrates + exudate + edema + crypt abscesses (HALLMARK) resulting in shallow ulceration

Age peaks: 15–25 years + 50–60 years (bimodal distribution); M÷F = 1.3÷1

• alternating periods of remission + exacerbation

• chronic diarrhea, rectal bleeding, abdominal pain / cramps

• electrolyte depletion, fever, systemic toxicity (malaise)

Extracolonic manifestations:

• iritis, erythema nodosum, pyoderma gangrenosum

• pericholangitis, chronic active hepatitis, primary sclerosing cholangitis, fatty liver, thrombotic complications

• spondylitis, peripheral arthritis, coincidental rheumatoid arthritis (10–20%)

Location: begins in rectum (proctitis in 55%, rectum spared in 4%) with proximal progression, left-sided colitis (30%), pancolitis (15%); relatively uniform symmetric involvement of bowel

@ Rectosigmoid in 95% (diagnosed by rectal biopsy); continuous circumferential involvement often limited to left side of colon

@ Colitis extending proximally to splenic flexure = universal colitis

@ Terminal ileum in 10–25% (= "backwash ileitis")

Plain film:

√ hyperplastic mucosa, polypoid mucosa, deep ulcers

√ diffuse dilatation with loss of haustral markings

√ toxic megacolon

√ free intraperitoneal gas

√ complete absence of fecal residue ← inflammation

BE:

(a) acute stage

√ narrowing + incomplete filling ← spasm + irritability

√ fine mucosal granularity = stippling of barium coat ← diffuse mucosal edema + hyperemia + superficial erosions

√ spicules + serrated bowel margins = tiny superficial ulcers
√ "collar button" ulcers = undermining of ulcers
√ "double-tracking" = longitudinal submucosal ulceration over several cm
√ hazy / fuzzy quality of bowel contour ← excessive secretions / mucin production
√ "thumbprinting" = symmetric thickening of colonic folds
√ pseudopolyps = scattered islands of edematous mucosa + reepithelialized granulation tissue within areas of denuded mucosa
√ widening of presacral space
√ obliterated rectal folds = valves of Houston (43%)

(b) subacute stage
√ distorted irregular haustra
√ inflammatory polyps = sessile frondlike / rarely pedunculated lesions (= localized mucosal inflammation resulting in polypoid protuberance)
√ coarse granular mucosa (= mucosal replacement by granulation tissue)

(c) chronic stage
√ shortening of colon with depression of flexures ← reversible spasm of longitudinal muscle
√ "leadpipe" colon = rigidity + symmetric narrowing of lumen on BE:
← hypertrophic regeneration of muscularis mucosae
← contraction of enlarged muscle layer
← strictures compromising luminal distensibility
← fat deposition within submucosal layer
√ widening of haustral clefts / complete loss of haustrations ← hypertrophy of muscularis mucosae + fibrosis (DDx: cathartic colon)
√ "burnt-out colon" = fairly distensible colon WITHOUT haustral markings + without mucosal pattern
√ hazy / fuzzy quality of bowel contour ← excessive secretions
√ postinflammatory polyps (12–19%) = small sessile nodules / long wormlike branching + bridging outgrowths (= filiform polyposis)
√ "**backwash ileitis**" (5–30%) involving 4–25 cm of terminal ileum with patulous ileocecal valve + absent peristalsis + granularity

US:
√ thickening, hyperemia, loss of haustra
√ preserved mural stratification

CT/MR:

CT enterography is not used for the diagnosis or staging of ulcerative colitis as it is less sensitive than endoscopy and principally assesses the small bowel.

◊ Often normal early in course of disease!
√ colonic wall thickening 3.5–11.6 mm (normal < 3 mm; indeterminate = 3–4 mm; pathologic > 4 mm)
√ mural stratification:
√ submucosal stripe = enhancement of mucosa but not submucosa
√ dilatation of vasa recta
√ inflammatory pseudopolyp

√ widening of presacral space ← perirectal extramural fat proliferation

Mural stratification, dilatation of vasa recta, colonic wall thickening, and inflammatory pseudopolyps are seen in both ulcerative colitis and Crohn colitis!

NUC:

√ positive on ^{99m}Tc–hexamethylpropylene amine (HMPAO)-labeled leukocytes

Dx: colonoscopy

Cx:

(1) Toxic megacolon (in 5%) (DDx: granulomatous / ischemic / amebic colitis)
- ◊ Most common cause of death in ulcerative colitis!
- ◊ Develops within 3 months of diagnosis (in 30%)

(2) Colonic adenocarcinoma (3–5%):

Risk: starts after 8–10 years of disease onset; risk progresses at 0.5–1.0% annually for 10–20 years + at 0.9% per year thereafter; higher risk with pancolitis + onset of disease in < 15 years of age

DDx of Crohn Disease versus Ulcerative Colitis

	Crohn Disease	*Ulcerative Colitis*
mnemonic: LUCIFER M		
Location	right	left
Ulcers	deep	shallow
Contraction	–	+
Ileocecal valve	thickened	gaping
Fistulae	+	–
Eccentricity	+	–
Rate of carcinoma	(↑)	↑↑
Megacolon	unusual	+
Skip lesions	+	–
Pseudopolyps	+	–
Abscess / fistula	+	–
Fibrofatty proliferation	+	–
Full thickness enhancement	+ (transmural)	– (mucosal + submucosal
Increased SI of mucosa	+	–
Submucosal stripe	-	+
Wall thickening	+ (11 mm)	+ (8 mm)
Wall enhancement	+	+
Increased SI of pericolic fat	+	+
Comb sign	+	+
Loss of haustrations	±	+
Enlarged lymph nodes	+	+

Usually associated with: total colitis

Location: rectosigmoid > descending colon, distal transverse colon

√ narrowed segment of 2–6 cm in length with eccentric lumen + irregular contour + flattened rigid tapered margins = scirrhous carcinoma
√ annular / polypoid carcinoma
Prognosis: synchronous lesions in 35%
◊ Surveillance is recommended!

(3) Colonic strictures (10%)
Smooth contour with fusiform pliable tapering margins, usually short + single stricture; commonly in sigmoid / rectum / transverse colon; usually after minimum of 5 years of disease; rarely cause for obstruction (DDx: colonic carcinoma)

(4) Perforation

DDx: (1) Familial polyposis (no inflammatory changes)
(2) Cathartic colon (more extensive in right colon)

VILLOUS ADENOMA

√ solitary sessile polypoid mass with numerous frondlike projections of reticular "soap bubble" appearance ← retention of contrast material in clefts between tumor projections

Villous Adenoma of Colon

Frequency: 7% of all colonic tumors
Age: presentation late in life; M = F
Location: rectum + sigmoid (75%), cecum, ileocecal valve; 2% of all tumors in rectum + colon
Associated with: other GI tumors (25%)

- sensation of incomplete evacuation, rectal bleeding, weakness
- excretion of copious amounts of thick mucus, fatigability
- diarrhea + electrolyte depletion syndrome in 4% (dehydration, hypokalemia, hyponatremia)

√ may completely encircle the colon
√ broad-based sessile bulky tumor often > 20 mm in diameter:
√ innumerable papillary mucosal projections ("villous fronds") with reticular / granular surface pattern (if villous elements constitute > 75% of tumor, diagnosis can be made on BE):
√ spongelike corrugated appearance (= barium within interstices)
√ striated "brushlike" surface
√ soft pliable tumor with change in shape:
√ apparent decrease in size on postevacuation films

CT:
√ heterogeneous low attenuation on CT ← capacious mucin becoming trapped within papillary projections + crevices

Prognosis: higher malignant potential than tubular adenoma
Cx: malignant transformation / invasion (in 36%) related to size of tumor < 5 cm (9%); > 5 cm (55%); > 10 cm (100%)

Villous Adenoma of Duodenum

Prevalence: 1% [50%] of all [benign] duodenal neoplasms; more common in colon + rectum

Average age: 56 years; M=F
Associated with: Gardner syndrome, familial adenomatous polypoid syndrome
• asymptomatic, vague dyspepsia, bowel obstruction (rare)
• occult upper GI bleeding, anemia, ± obstructive jaundice
Location: 2nd duodenal segment near major papilla of Vater
Size: 3–9 cm
√ sessile soft mostly nonobstructive mass
√ "lace" / "soap bubble" pattern ← frondlike projections
√ preservation of peristaltic activity + bowel distensibility
CT:
√ variegated attenuation + variable enhancement patterns
√ CHARACTERISTIC surface gyral pattern for large tumor
Cx: bowel obstruction
Prognosis: 30%–60% risk for malignant transformation

WALDENSTRÖM MACROGLOBULINEMIA

= low-grade lymphoid malignancy (= plasma cell dyscrasia) composed of mature plasmacytoid lymphocytes with production of abnormal monoclonal IgM protein
Incidence: 0.53÷100,000 annually; frequency 10–15% of multiple myeloma
Histo: macroglobulin proteinaceous hyaline material fills lacteals in lamina propria of small bowel villi with secondary lymphatic distension + edema
Mean age: 63 years; M > F
• fatigue, weight loss, diarrhea, steatorrhea, malabsorption
• anemia, bleeding diathesis, IgM elevation
• hyperviscosity syndrome (20%) = bleeding, visual changes, neurologic abnormalities
@ Small bowel (rarely involved)
√ small bowel dilatation
√ diffuse irregular thickening of valvulae conniventes with spikelike configuration (jejunum + proximal ileum)
√ granular surface of punctate 1–2-mm nodules (deposition of immunoglobulin M in submucosa + lamina propria)
@ Bone marrow involvement (91–98%)
(a) diffuse replacement of bone marrow (56%)
(b) variegated replacement of bone marrow (35%)
√ compression fractures of spine (48%)
√ diffuse demineralization of spine
√ lytic lesions on bone surveys (in up to 20%)
MR (pre- and postcontrast T1WI preferred):
√ marrow iso- / hypointense to muscle on T1WI
√ enhancement of abnormal marrow on T1WI
@ Lymph nodes
√ lymphadenopathy (43%)
@ Liver & spleen
√ hepatosplenomegaly

Dx: (1) Characteristic M-spike in serum / urine electrophoresis
(2) Abnormal lymphoplasmacytoid cells in bone marrow / lymph nodes
Prognosis: may occasionally progress to full-blown lymphoma
DDx: multiple myeloma (lymphadenopathy rare, lytic lesions in 31%)

WHIPPLE DISEASE

[George Whipple (1878–1976), pathologist in Rochester, USA]
= INTESTINAL LIPODYSTROPHY
= sporadically occurring chronic bacterial multisystem disease
Etiology: infection with gram-positive bacterium (Tropheryma whipplei) closely related to actinobacteria; in 1–11% (12–26%) of fecal samples in healthy population (sewage workers) in Europe
Incidence: 30 cases annually
Genetics: whites of European heritage predisposed → colonization of bacterium throughout GI tract + lymphoreticular system + CNS
Histo: PAS-positive material (periodic acid Schiff) = glycoprotein (from bacterial cell wall) within foamy macrophages in the submucosa of the jejunum + fat deposits within intestinal submucosa and lymph nodes causing lymphatic obstruction + dilatation
Mean age: 50 years (range, 4th–6th decade); M÷F = 8÷1; Caucasians
- 4 cardinal symptoms:
  - recurrent migratory arthralgias / nondeforming arthritis
  - chronic steatorrhea ← malabsorption
  - weight loss → severe wasting
  - abdominal pain → abdominal distention ← ascites and lymphadenopathy (late finding)
- polyserositis, low-grade fever
- generalized peripheral lymphadenopathy (50%)
- hyperpigmentation of skin similar to Addison disease
- pale shaggy yellow plaques / erosions in postbulbar duodenum on endoscopy

Organ involvement: small bowel (particularly jejunum), lymph nodes, heart valves, joints, CNS, liver, lung, eyes, skin (virtually every organ system)
@ MSK (67%) arthritis may precede Whipple disease up to 10 years (10%)
@ Abdomen (15%)
√ moderate irregular diffuse fold thickening of jejunum + duodenum + (to a lesser degree) ileum ← mucosal and submucosal infiltration by Whipple bacilli + PAS- positive macrophages + lymphatic obstruction
√ micronodularity (= swollen villi) + wild mucosal pattern
√ hypersecretion, segmentation, fragmentation (occasionally if accompanied by hyperproteinemia)
√ NO / minimal distension of small bowel
√ NO rigidity of folds, NO ulcerations
√ NORMAL transit time
√ hepatosplenomegaly
√ mesenteric and retroperitoneal nodes of low attenuation are CHARACTERISTIC of Whipple disease

CT:
√ bulky 3–4-cm low-density lymph nodes in mesenteric root + retroperitoneum ← lymphatic obstruction and intranodal deposition of extracellular lipids
√ thickening of small bowel wall
√ hepatosplenomegaly
√ ascites
√ pneumatosis intestinalis
√ pleuropericarditis
√ sacroiliitis
US:
√ echogenic lymph nodes

@ CNS (33%)
Location: mesial temporal lobe, midbrain, thalamus, hypothalamus
√ patchy nodular enhancement
√ hyperintense regions on FLAIR ← atrophy / gliosis

Dx: endoscopically guided biopsy of small bowel mucosa, abdominal / peripheral lymph node biopsy

Rx: long-term broad-spectrum antibiotics (tetracycline) with 17–35% relapse rate; long-term trimethoprim-sulfamethoxazole

DDx: (1) Sprue (marked dilatation, no fold thickening, pronounced segmentation + fragmentation)
(2) Intestinal lymphangiectasia (thickened folds throughout small bowel)
(3) Amyloidosis
(4) Lymphoma

YERSINIOSIS

Organism: Gram-negative bacillus Yersinia enterocolitica
• self-limited diarrhea
Location: usually confined to terminal ileum
√ irregular segmental thickening of folds
√ ± aphthous ulcers / larger area of ulceration

ZENKER DIVERTICULUM

= PHARYNGOESOPHAGEAL DIVERTICULUM
[Friedrich Albert von Zenker (1825–1898), German pathologist, Dresden city hospital and chair at Erlangen University]
= outpouching of posterior hypopharyngeal wall = pulsion diverticulum with herniation of mucosa + submucosa through muscle bundles (**pseudodiverticulum**)
Prevalence: 0.01–0.11% (overall); higher in elderly women
◊ Most common diverticulum of UGI tract!
Etiology: cricopharyngeal dysfunction (cricopharyngeal achalasia / premature closure) → increased intraluminal pressure (pulsion diverticulum)
Associated with: hiatal hernia, gastroduodenal ulcer, midesophageal diverticulum, esophageal spasm, achalasia, GERD

Age: > 60 years (50% occur in 7th–8th decade); M÷F = 1÷3
- compressible neck mass, noisy deglutition, chronic cough
- upper esophageal dysphagia (98%), weight loss
- regurgitation + aspiration of undigested food
- halitosis (= foul breath)

Location: pharyngoesophageal junction in midline of Killian dehiscence / triangle of Laimer (= focal hypopharyn-geal weakness at cleavage plane between inferior pharyngeal constrictor m. + cricopharyngeus m. or between oblique + transverse fibers of cricopharyngeus m.), at level of C5-6

[Gustav Killian (1860–1921), laryngologist and founder of bronchoscopy, ordinarius for throat and nose disease in Freiburg, Germany]

Barium pharyngography:
- √ posterior + inferior barium extension in upper half of semilunar depression on posterior wall of esophagus in midline / slightly toward left (above cricopharyngeal m.)
- √ barium-filled sac extending caudally behind + usually to left of esophagus
- √ partial / complete obstruction of esophagus from external pressure of sac contents → dysphagia
- √ partial barium reflux from diverticulum into hypopharynx
- √ continual growth with successive enlargement

CXR:
- √ air-fluid level in superior mediastinum

Cx: overflow aspiration pneumonia (30%); esophageal perforation; carcinoma (0.48%)

Rx: surgical excision + cricopharyngeal myotomy

ZOLLINGER-ELLISON SYNDROME

[Robert Milton Zollinger (1903–1992), chairman of surgery at Ohio State University, editor in chief of Am J Surg 1958–1986]

(Edwin Homer Ellison (1918–1970), chairman of surgery at Marquette University, Milwaukee]

= peptic ulcer diathesis ← marked hypersecretion of gastric acid ← gastrin-secreting islet cell neoplasm (gastrinoma)

Incidence: 0.1% of all peptic ulcer disease

Cause:

A. GASTRINOMA (90%)
   = gastrin-producing non-β islet cell tumor of pancreas

B. PSEUDO Z-E SYNDROME = COWLEY SYNDROME
   = antral G-cell hyperplasia (10%) = increase in number of G-cells in gastric antrum
   - lack of gastrin elevation after secretin injection
   - exaggerated gastrin elevation after protein meal

Age: middle age; M > F
- clinical tetrad:

(1) Gastric hypersecretion: refractory response to histamine stimulation test concerning HCl concentration; increased basal secretion (> 60% of augmented secretion is diagnostic)
(2) Hypergastrinemia > 1000 ng/L (during fasting)
(3) Hyperacidity with basal acid output > 15 mEq/hr / occasionally hypoacidity

(4) Diarrhea (30%), steatorrhea (40%) ← malabsorption ← inactivation of pancreatic lipase + damage to small bowel mucosa ← large volumes of gastric acid with low pH; may be sole complaint in 10%, frequently nocturnal

- epigastric pain (90%): mild nonspecific to severe recurrent intractable pain, gastroesophageal reflux, heartburn
- ulcer perforation with GI bleeding (30%)
- positive secretin stimulation test
- ↑ fasting serum levels of gastrin (DIAGNOSTIC): often > 1,000 pg/mL (< 100 pg/mL is normal)

√ peptic ulcers

◊ An unusual location in postbulbar duodenum / proximal jejunum + atypical course should suggest the diagnosis!

Location: duodenal bulb (65%) + stomach (20%), jejunum near ligament of Treitz (25%), duodenal C-loop (5%), distal esophagus (5%)

Multiplicity: solitary ulcer (90%), multiple ulcers (10%)

√ recurrent / intractable ulcers

√ marginal ulcers in postgastrectomy patient

(a) on gastric side of anastomosis

(b) on mesenteric border of efferent loop

√ prominence of areae gastricae ← hyperplasia of parietal cells

√ enlarged thickened rugal folds in gastric fundus + upper body

√ sluggish gastric peristalsis ← ? hypokalemia

√ "wet stomach" = dilution of barium with poor coating by excess secretions in nondilated nonobstructed stomach

√ gastroesophageal reflux (common) + esophagitis

Location: unusually long strictures in distal esophagus (may be initial manifestation of disease)

Cause: increased acidity of peptic acid reflux

√ dilatation of duodenum + upper small bowel ← fluid overload

√ thickened folds in duodenum + jejunum ← edema

√ rapid small-bowel transit time

mnemonic: FUSED

Folds: thickened gastric folds

Ulcers: often multiple, postbulbar

Secretions increased (refractory to histamine)

Edema: of proximal small bowel

Diarrhea

Cx: (1) Malignant islet cell tumor (in 60%)

(2) Liver metastases will continue to stimulate gastric secretion

Rx: (1) Control of gastric hypersecretion:

(a) H_2-receptor antagonist: cimetidine, ranitidine, famotidine

(b) Hydrogen-potassium adenosine triphosphatase inhibitor (omeprazole)

(2) Resection of gastrinoma if found (because of malignant potential)

(3) Total gastrectomy

UROGENITAL TRACT

DIFFERENTIAL DIAGNOSIS OF UROGENITAL DISORDERS

RENAL FAILURE

= reduction in renal function

• rise in serum creatinine > 2.5 mg/dL

Acute Renal Failure (ARF)

= clinical condition associated with rapid steadily increasing azotemia ± oliguria (< 500 mL urine per day) over days / weeks

Etiology:

A. PRERENAL

= renal hypoperfusion ← systemic illness

1. Fluid + electrolyte depletion
2. Hemorrhage
3. Hepatic failure + hepatorenal syndrome
   √ abnormally elevated resistive index
4. Congestive heart failure
5. Sepsis
   √ resistive index < 0.75 in 80% of kidneys

Frequency: 70% of community-acquired ARF (glomerulonephritis); 40% of hospital-acquired ARF (acute tubular necrosis)

B. RENAL (most common)

1. Acute tubular necrosis: ischemia, nephrotoxins, radiographic contrast, hemoglobulinuria, myoglobulinuria, myocardial infarction, burns
   √ resistive index ≥ 0.75 in 91% of kidneys
2. Acute glomerulonephritis + small vessel disease: acute poststrep glomerulonephritis, rapidly progressive glomerulonephritis, lupus, polyarteritis nodosa, Schönlein-Henoch purpura, subacute bacterial endocarditis, serum sickness, Goodpasture syndrome, malignant hypertension, hemolytic uremic syndrome, drug-related vasculitis, abruptio placentae
   √ normal resistive index < 0.70
3. Acute tubulointerstitial nephritis: drug reaction, pyelonephritis, papillary necrosis
   √ abnormal resistive index
4. Intrarenal precipitation: hypercalcemia, urate, myeloma protein
5. Arterial / venous obstruction
6. Acute cortical necrosis

C. POSTRENAL (5%)

= result of outflow obstruction (rare)

1. Prostatism

2. Tumors of bladder, retroperitoneum, pelvis
3. Calculus

√ hydronephrosis

◊ 30–35% of acutely obstructed kidneys (< 36 hours) have no hydronephrosis!

D. CONGENITAL

bilateral renal agenesis / dysplasia / infantile polycystic kidney disease, congenital nephrotic syndrome, congenital nephritis, perinatal hypoxia

Frequency: ATN + prerenal disease account for 75% of acute renal failure; 5–7% of all hospitalized patients

- asymptomatic
- elevated creatinine normal range: 0.5–1.0 mg/dL (about 45–90 µmol/L) for women + 0.7–1.2 mg/dL (60–110 µmol/L) for men

Prognosis: 20–70% mortality

Chronic Renal Failure (CRF)

= decrease in renal function over months / years

Incidence: end-stage renal disease in 0.01% of USA population; annually 85,000 patients undergo hemodialysis + 8,000 renal transplantations

Etiology:

A. INFLAMMATION / INFECTION
1. Glomerulonephritis
2. Chronic pyelonephritis
3. Tuberculosis
4. Sarcoidosis

B. VASCULAR
1. Renal vascular disease
2. Bilateral renal vein thrombosis

C. DYSPROTEINEMIA
1. Myeloma
2. Amyloid
3. Cryoglobulinemia
4. Waldenström macroglobulinemia

D. METABOLIC
1. Diabetes
2. Gout
3. Hypercalcemia
4. Hyperoxaluria
5. Cystinosis
6. Fabry disease
7. Calcinosis

E. CONGENITAL
1. Polycystic kidney disease
2. Multicystic dysplastic kidney
3. Medullary cystic disease
4. Alport syndrome

5. Infantile nephrotic syndrome

F. MISCELLANEOUS
1. Hepatorenal syndrome
2. Radiation

Musculoskeletal Manifestations of CRF

1. Renal osteodystrophy = combination of 2° HPT, osteoporosis, osteosclerosis, osteomalacia, soft-tissue and vascular calcifications
2. Aluminum toxicity (1–30%)
3. Amyloid deposition
   Path: amyloid consists of β2-microglobulin
   Organs: bone, tenosynovium (carpal tunnel syndrome), vertebral disk, articular cartilage + capsule, ligament, muscle
4. Destructive spondyloarthropathy (15%)
   √ diskovertebral junction erosion + sclerosis
   √ vertebral body compression
   √ disk space narrowing
   √ Schmorl node formation
   √ lack of osteophytosis
   √ facet involvement with subluxation
5. Tendon rupture
6. Crystal deposition disease
   Type: calcium hydroxyapatite, CPPD, calcium oxalate, monosodium urate
7. Osteomyelitis + septic arthritis
8. Avascular necrosis (in up to 40%)

DIABETES INSIPIDUS

= characterized by daily production of very large volume of dilute urine (specific gravity < 1.005, < 200 mOsm/L)

Pituitary Diabetes Insipidus

= HYPOTHALAMIC DIABETES INSIPIDUS
= VASOPRESSIN-SENSITIVE DIABETES INSIPIDUS
= vasopressin (ADH) production is reduced to < 10%

Cause:

A. IDIOPATHIC (27%)
   septooptic dysplasia / rare familial (autosomal dominant X-linked) / sporadic disorder
   Histo: atrophic supraoptic nucleus
   • never associated with anterior pituitary dysfunction

B. PITUITARY DESTRUCTION BY TUMOR / INFILTRATIVE DISORDER (32%):
   in childhood: hypothalamic glioma, tuber cinereum hamartoma, craniopharyngioma, Langerhans histiocytosis, germinoma, leukemia, complication of meningitis
   in adulthood: sarcoidosis, TB, metastasis
   • in 60% associated with anterior pituitary dysfunction

C. PITUITARY DESTRUCTION BY SURGERY (20%)
- always associated with anterior pituitary dysfunction

D. HEAD INJURY (17%)
- in 20% associated with anterior pituitary dysfunction

◊ A lesion in the posterior pituitary will NOT produce diabetes insipidus, because it is simply the storage space for vasopressin

Psychogenic Water Intoxication

= compulsive intake of large amounts of fluid → inhibits normal vasopressin production

• water deprivation test

Nephrogenic Diabetes Insipidus

= poor reabsorption of water in collecting ducts ← end-organ resistance to vasopressin

Cause:

A. CONGENITAL
1. Rare X-linked recessive genetic disorder with unresponsiveness of tubules + collecting system to vasopressin (in infants + young males) with variable expression
2. Autosomal dominant form (rare)

B. ACQUIRED = nephrogenic DI syndrome
= disorders affecting the medulla / distal nephrons:
medullary + polycystic disease, sickle cell nephropathy, postobstructive uropathy, reflux nephropathy, chronic uremic nephropathy, unilateral renal artery stenosis, acute tubular necrosis, drug toxicity, analgesic nephropathy, hypokalemic + hypercalcemic nephropathy, amyloidosis, sarcoidosis

- symptoms in infancy:
  - vomiting ← hypernatremic dehydration
  - mental retardation
  - caloric growth failure ← water favored over formula
- symptoms after infancy:
  - increased fluid intake; avoiding urination

√ bilateral hydroureteronephrosis

Rx: thiazide diuretics, low-salt diet, encouragement of frequent micturition, indomethacin

PRIMARY ALDOSTERONISM

= inappropriate autonomous hypersecretion of aldosterone WITHOUT activation of renin-angiotensin-aldosterone axis

Frequency: 5–15% of unselected hypertensive patients
◊ Most common cause of secondary hypertension!

Biochemistry: mineralocorticoid production in zona glomerulosa

Cause: (main role of radiology)

(1) **Aldosterone-producing adenoma** (APA) 33–66%

Age: often found in patients < 40 years

Size: < 2 cm (usually)

Rx: adrenalectomy

(2) **Bilateral adrenal hyperplasia** (BAH) 33–66%
Age: often found in older patients > 40 years
√ enlargement of both adrenal glands
Rx: aldosterone antagonists (eplerenone)
(3) **Unilateral adrenal hyperplasia** < 1%
Rx: adrenalectomy
(4) Adrenal carcinoma rare
(5) Type 1 familial hyperaldosteronism rare
(5) Type 2 familial hyperaldosteronism rare

- hypertension
- hyperaldosteronism, suppressed renin, hypernatremia
- abnormal aldosterone (↑)-renin (↓)ratio, metabolic alkalosis
- failure to suppress plasma aldosterone levels by oral salt-loading / IV administration of saline solution / fluorocortisone

CT (40–100% sensitive) & MR (70–100% sensitive):
√ small adrenal nodule:
√ macronodule > 10 mm
√ micronodule < 10 mm
√ mean adrenal limb width ≥ 5 mm = BAH

Adrenal vein sampling:
= blood samples taken from IVC + both adrenal veins during infusion of adrenocorticotropic hormone
√ cortisol ratio of adrenal vein÷IVC > 2÷1
√ lateralization ratio = adrenal vein÷adrenal vein:
√ > 4 = aldosterone hypersecretion
√ < 3 = BAH

NUC (^{131}Iodine–6-β-iodomethylnorcholesterol = NP-59 or Selenium-75–6-β-selenomethylcholesterol):
› dexamethasone depression increases sensitivity
√ unilateral early uptake < 5 days = APA
√ symmetric early uptake < 5 days = BAH
√ symmetric late uptake > 5 days = normal

HYPERCALCEMIA

mnemonic: SHAMPOO DIRT
Sarcoidosis
Hyperparathyroidism, **H**yperthyroidism
Alkali-milk syndrome
Metastases, Myeloma
Paget disease
Osteogenesis imperfecta
Osteopetrosis
D vitamin intoxication
Immobility

Renal tubular acidosis
Thiazides

POLYCYTHEMIA

Cause: increased level of erythropoietin (acting on erythroid stem cells) ← decrease in pO2; erythropoietin precursor is produced in juxtaglomerular epithelioid cells of kidney + converted in blood

A. RENAL
   (a) intrarenal
      1. Vascular impairment
      2. Renal cell carcinoma (5%)
      3. Wilms tumor
      4. Benign fibroma
      5. Simple cyst (14%)
      6. Polycystic kidney disease
   (b) postrenal
      1. Obstructive uropathy (14%)
B. EXTRARENAL
   (a) liver disease
      1. Hepatoma
      2. Regenerating hepatic cells
   (b) adrenal disease
      1. Pheochromocytoma
      2. Aldosteronoma
      3. Cushing disease
C. CNS DISEASE
      1. Cerebellar hemangioblastoma
D. LARGE UTERINE MYOMAS

Pertinent negatives: NOT in renal vein thrombosis, multicystic dysplastic kidney, medullary sponge kidney

ARTERIAL HYPERTENSION

A. PRIMARY / ESSENTIAL HYPERTENSION (85–90%)
B. SECONDARY HYPERTENSION
   (a) Renal parenchymal disease (5–10%)
   (b) Potentially curable secondary hypertension (1–2%)
      › vascular
      1. Renovascular disease 0.18–4.4%
      2. Coarctation 0.6%
      › hormonal
      1. Pheochromocytoma 0.04–0.2%
      2. Cushing syndrome 0.3%
      3. Primary aldosteronism 0.01–0.4%
      4. Hyperthyroidism

5. Myxedema

› renal

1. Unilateral renal disease

Renovascular Hypertension

= normalization of blood pressure following nephrectomy / reestablishment of normal renal blood flow (Diagnosis made in retrospect)

Prevalence: 1–5% of general population; 2nd most common cause of potentially curable hypertension

Pathophysiology:

usually > 50% stenosis at any level in renovascular bed → mildly reduced pressure in glomerular afferent arteriole (pressure falls precipitously in > 80% stenosis); reduced pressure → stimulates release of renin → followed by angiotensin-II and aldosterone causing

(a) constriction of efferent glomerular arterioles
(b) increase in systemic hypertension
(c) sodium retention

Cause:

1. Atherosclerosis (60–90%) in individuals > 50 years
2. Fibromuscular dysplasia (10–35%) in women < 40 years
3. Neurofibromatosis
4. Pheochromocytoma
5. Fibrous bands: congenital stenosis, retroperitoneal fibrosis, postradiation artery stenosis
6. Arteritis: Buerger disease, polyarteritis nodosa, Takayasu disease, thrombangiitis obliterans, syphilitic arteritis
7. Arteriovenous malformation / fistula
   - renin-mediated hypertension ← renal ischemia distal to fistula
8. Thromboembolic disease: eg, atrial fibrillation, prosthetic valve thrombi, cardiac myxoma, paradoxical emboli, atheromatous emboli
9. Renal artery aneurysm
10. Extrinsic compression: eg, renal cyst, neoplasm, chronic subcapsular hematoma (= Page kidney)
11. Middle aortic syndrome, aortic dissection, dissecting aortic aneurysm
12. Posttraumatic renovascular hypertension
    (a) occlusion of main renal artery
    (b) significant stenosis by intimal flap
    (c) severe renal contusion
    (d) segmental renal artery branch injury

◊ Renal artery stenosis in 77% of hypertensive patients!
◊ Renal artery stenosis in 32–49% of normotensive patients!
◊ After restoration of normal renal blood flow 15–20% of patients remain hypertensive!

Clinical findings that suggest renovascular disease:

1. Onset of HTN < 30 years and > 50 years of age

2. Hypertension refractory to therapy
3. Accelerated / malignant hypertension
4. Unexplained large increases in blood pressure above previously controlled / baseline values
5. Symptomatic hypertension

Rx: (1) Relieving renal artery stenosis
(2) Angiotensin-converting enzyme inhibitor

Hypertension in Children

Prevalence: 1–3%

1. Coarse renal cortex scarring 36%
2. Glomerulonephritis 23%
3. Coarctation of aorta 10%
4. Renovascular disease 10%
5. Polycystic renal disease 6%
6. Hemolytic-uremic syndrome 4%
7. Catecholamine excess: pheochromocytoma, neuroblastoma 3%
8. Renal tumor 2%
9. Essential hypertension 3%

Renin Elevation

1. Juxtaglomerular cell tumor
2. Wilms tumor
3. Hypernephroma
4. Lung cancer
5. Paraovarian tumor
6. Fallopian tube adenocarcinoma
7. Epithelial liver hamartoma
8. Orbital hemangiopericytoma
9. Pancreatic cancer
10. Angiolymphoid hyperplasia

ARTERIAL HYPOTENSION

Cause: intrarenal hypovolemia, primary vasoconstriction, reduced glomerular filtration, depletion of intratubular urine volume

◊ May occur as a contrast reaction!
◊ Urogram reverts to normal after reversion of hypotension!
√ bilateral small smooth kidneys (compared with size on preliminary films)
√ increasingly dense nephrogram
√ usually NO opacification of collecting system
√ initially opacification of collecting system if hypotension occurs during contrast injection

URINARY TRACT INFECTION

= pure growths of > 100,000 organisms/mL urine

Prevalence: 3% of girls + 1% of boys during first 10 years of life

Underlying radiologic abnormality:

1. Vesicoureteral reflux = VUR (30–40%)
2. Obstructive uropathy (8%)
3. Reflux nephropathy / scar formation (6%)
   - ◊ The prevalence of an underlying radiologic abnormality depends on age, sex, and frequency of previous infections!

Imaging objective:

1. Identify patients at risk for reflux nephropathy
2. Detect reflux nephropathy / scars
3. Detect obstructive uropathy
4. Minimize radiation, morbidity, and cost

VCUG:

for children < 5 years of age with infection; normal results in 60–70%

Renal cortical scintigraphy (DMSA / glucoheptonate): to detect acute pyelonephritis (risk for scarring) / scar; VUR poses twice the risk of cortical defects than without VUR

CILIOPATHY

= DISORDER OF PRIMARY CILIA (cilia line ducts of kidney + liver and are integral to proper renal + hepatic development

1. Autosomal recessive polycystic kidney disease
2. Autosomal dominant polycystic kidney disease
3. Medullary cystic disease
4. Multicystic kidney disease
5. Meckel-Gruber syndrome
6. Joubert syndrome
7. Orodigitofacial syndrome
8. Asphyxiating thoracic dysplasia
9. Chondroectodermal dysplasia
10. Short-rib polydactyly syndrome
11. Sensenbrenner syndrome (cranioectodermal dysplasia)
12. Weyers acrofacial dysostosis (nail anomalies, polydactyly, oral-facial defects)

GAS IN URINARY TRACT

A. RENAL EMPHYSEMA = renal / perirenal gas
   1. Emphysematous pyelonephritis
   2. Emphysematous pyelitis
   3. Gas-forming perinephric abscess
   4. Perinephric emphysema

B. BLADDER
   1. Emphysematous cystitis

C. TRAUMA
   1. Penetrating trauma
   2. Ureterosigmoidostomy, ileal conduit, catheterization with vesicoureteral reflux,

percutaneous procedure
CAVE: anomalous posterior position of colon

3. Infarction of renal carcinoma: therapeutic / spontaneous

D. FISTULA TO URINARY TRACT
Connection: bronchus / cutis / GI tract (colon > duodenum > stomach > small bowel > appendix)

1. Inflammation: chronic purulent renal infection, diverticulitis, Crohn disease
2. Neoplastic: colonic carcinoma

RETROPERITONEUM

70–80% of primary retroperitoneal neoplasms are malignant accounting for 0.1–0.2% of all malignancies in the body.

Primary Malignant Tumor of Retroperitoneum

1. Lymphoma most common retroperitoneal malignancy (33%)
2. Retroperitoneal liposarcoma most common primary retroperitoneal sarcoma (33%)
   √ contrast enhancement of thick irregular nodular septa
3. Leiomyosarcoma
   2nd most common primary retroperitoneal sarcoma (28%)

A retroperitoneal mass with extensive necrosis and contiguous involvement of a vessel is highly suggestive of a leiomyosarcoma.

4. Malignant fibrous histiocytoma 3rd most common primary retroperitoneal sarcoma (19%)
   √ dystrophic calcifications in 25%

Mantle-like Soft-tissue Mass Surrounding Aorta

1. Lymphoma
   √ homogeneous mass with irregular lobular margins
   √ "floating aorta" sign (= anterior displacement of aorta)
2. Retroperitoneal fibrosis
   √ tethering of ureters + IVC
3. Erdheim-Chester disease
   √ perinephric fibrosis + bone lesions

Cystic Retroperitoneal Masses

A. NEOPLASTIC

1. Cystic degeneration of solid neoplasm:
   › paraganglioma
   › schwannoma (neurilemmoma)
   » ancient schwannoma
   › leiomyosarcoma
2. Cystic teratoma
3. Retroperitoneal lymphangioma (1% of all retroperitoneal neoplasms)
4. Lymphangiomatosis

5. Lymphangiomyomatosis
6. Cystadenoma / cystadenocarcinoma: mucinous / serous
7. Cystic mesothelioma

B. CYSTS:
1. Müllerian cyst
   • obese woman under hormonal replacement therapy
2. Epidermoid cyst
   Location: midline presacral
   √ unilocular
3. Tailgut cyst
4. Pseudocyst
   • Hx of acute pancreatitis, elevated amylase level

C. NONNEOPLASTIC: hematoma, urinoma, lymphocele

Cystic Mass with Areas of Solid Enhancement

1. Myxoid liposarcoma
2. Schwannoma
3. Neurofibroma

Neurogenic tumors are common along sympathetic ganglia in the paraspinal region and in adrenal medulla / organ of Zuckerkandl (paraaortic bodies). Less commonly neurogenic tumors occur in urinary bladder, abdominal wall, bowel wall, or gallbladder.

Cystic Mass with Slowly Progressive Enhancement

1. Lymphangioleiomyoma
2. Urinoma

Low-density Retroperitoneal Mass

1. Lipoma
   √ sharply marginated, homogeneously fatty mass
2. Lymphangioma
   √ similar to lipoma if enough fat content
3. Renal angiomyolipoma
4. Adrenal myelolipoma
5. Xanthogranulomatous pyelonephritis
6. Metastatic retroperitoneal tumors
7. Renal cell carcinoma
8. Fibrosarcoma, fibrous histiocytoma, mesenchymal sarcoma, malignant teratoma
   √ density close to muscle
9. Retroperitoneal liposarcoma
10. Lipoblastoma
11. Hibernoma

Fat-containing Presacral Mass

1. Lipoma
2. Lipomatosis
3. Liposarcoma: infiltrative growth

4. Teratoma: younger individual
5. Myelolipoma: elderly patient

The differentiation of presacral myelolipoma from other fat-containing lesions may not always be possible with imaging alone.

Heterogeneous Fat-containing Retroperitoneal Mass

1. Dedifferentiated Liposarcoma
2. Myelolipoma
   √ positive for erythroid elements on ^{99m}Tc-sulfur colloid
3. Angiomyolipoma

Classification of Solid Retroperitoneal Masses by Tissue Component

Description	*Benign*	*Malignant*
Hematologic / lymphoid		*most common retroperitoneal malignancy*
		lymphoma, posttransplant lymphoproliferative disease, extramedullary plasmacytoma
Mesodermal		*0.1–0.2% of all malignancies*
adipose tissue	lipoma, pelvic lipomatosis, hibernoma, myelolipoma, angiomyolipoma ◊ The deeper + more centrally located a fatty mass resides the more likely it is malignant!	liposarcoma, myxoid liposarcoma, lipoblastoma
connective tissue	fibroma	malignant fibrous histiocytoma, fibrosarcoma, chondrosarcoma, synovial cell sarcoma
smooth muscle	leiomyoma	leiomyosarcoma
striated muscle	rhabdomyoma	rhabdomyosarcoma
blood vessels	hemangioma, hemangiopericytoma	angiosarcoma
perivascular epithelioid cells	perivascular epithelioid cell tumor (PEcoma): angiomyolipoma, lymphangioleiomyomatosis, clear cell "sugar" tumor, clear cell myomelanocytic tumor, pigmented melanotic tumor	malignant pericytoma, sarcoma of perivascular cells
interstitial cells of Cajal	GIST	
primitive mesenchyme	myxoma	myxosarcoma, malignant mesenchymoma
notochordal remnant	chordoma	
miscellaneous	fibromatosis, desmoid tumor, angiomyofibroblastoma, xanthogranuloma	
Neurogenic		
nerve sheath	schwannoma, neurofibroma, neurofibromatosis	malignant peripheral nerve sheath tumor, neurogenic sarcoma, neurofibrosarcoma
sympathetic ganglionic cells	ganglioneuroma, ganglioneuroblastoma	neuroblastoma
chromaffin tissue = paraganglionic cells	paraganglioma, pheochromocytoma	malignant paraganglioma / pheochromocytoma
Germ cell, sex cord		
germ cell	mature teratoma, immature teratoma	seminoma, malignant teratoma, embryonal carcinoma, yolk sac tumor, choriocarcinoma, mixed germ cell tumor
sex cord stromal	granulosa cell tumor, thecoma, Sertoli-Leydig cell tumor	

Vascular Retroperitoneal Mass

A. INFLAMMATORY
B. LYMPHOPROLIFERATIVE
   1. Lymphoma
   2. Unicentric Castleman disease

C. MESENCHYMAL TUMOR
   1. Sarcoma
   2. Solitary fibrous tumor
   3. Leiomyoma
   4. GIST
   5. Hemangiopericytoma
   6. Congenital pelvic AVM

D. OTHERS
   1. Carcinoid
   2. Retroperitoneal paraganglioma

Calcified Retroperitoneal Mass

A. NONTUMORAL
   1. Exuberant callus formation
   2. Posttraumatic calcified hematoma
   3. Myositis ossificans
   4. Foreign body granuloma
   5. Encapsulated textiloma / gossypiboma
      (*gossypium*, Latin = cotton)
      Cause: retained surgical sponge, gauze, towel

B. BENIGN NEOPLASM
   1. Ganglioneuroma
   2. Schwannoma
   3. Paraganglioma
   4. Hemangioma
   5. Mature teratoma

C. MALIGNANT NEOPLASM
   1. Malignant fibrous histiocytoma
   2. Dedifferentiated liposarcoma
   3. Leiomyosarcoma
   4. Malignant mesenchymoma
   5. Malignant teratoma
   6. Extraskeletal osteosarcoma
   7. Chondrosarcoma
   8. Ewing sarcoma

Retroperitoneal Fluid

1. Traumatic injury to: pancreas, duodenum, renal collecting system
2. Retroperitoneal hemorrhage
3. Hypoperfusion shock complex
4. Abdominal compartment syndrome
5. Resuscitation effect

Disorders of Perirenal Space

A. PRIMARY LESION

(a) benign
1. Extramedullary hematopoiesis
2. Extraadrenal myelolipoma
3. Castleman disease
4. Erdheim-Chester disease

(b) malignant
1. Lymphoma / leukemia
2. Metastasis (lung)

B. RENAL LESION WITH EXTENSION

(a) benign
1. Angiomyolipoma
2. Xanthogranulomatous pyelonephritis
3. Leiomyoma
4. Hemangioma
5. Lymphangioma

(b) malignant
1. Renal cell carcinoma

C. RETROPERITONEAL LESION WITH EXTENSION

(a) BENIGN
1. Retroperitoneal fibrosis

(b) MALIGNANT
1. Lymphoma / leukemia
2. Metastatic lymphadenopathy
3. Malignant fibrous histiocytoma
4. Liposarcoma
5. Plasma cell neoplasm

Solitary Perirenal Mass

A. benign
1. XGP
2. Castleman disease
3. Hemangioma
4. Leiomyoma

B. malignant
1. RCC
2. Malignant fibrous histiocytoma
3. Lymphoma / leukemia

C. BORDERLINE
1. Hemangiopericytoma
2. GIST

Rindlike Perirenal Mass

1. Lymphoma
2. Retroperitoneal fibrosis
3. Erdheim-Chester disease

Multiple Perirenal Masses

1. Metastases: malignant melanoma; cancer of lung, breast, prostate
2. Plasma cell neoplasm: multiple myeloma, plasmacytoma, plasma cell leukemia

Fat-containing Perirenal Mass

1. Angiomyolipoma
2. Retroperitoneal liposarcoma
3. Extramedullary hematopoiesis
4. Extraadrenal myelolipoma

ADRENAL GLAND

Functioning Adrenal Mass

1. Cushing syndrome and Cushing disease
2. Primary aldosteronism
3. Pheochromocytoma

Adrenal Medullary Disease

1. Neuroblastoma
2. Ganglioneuroblastoma
3. Ganglioneuroma
4. Pheochromocytoma

Adrenal Cortical Disease

1. Adrenocortical hyperplasia
2. Adrenocortical adenoma
3. Adrenocortical carcinoma
4. Cushing syndrome
5. Conn syndrome
6. Adrenogenital syndromes

Adrenocortical Hyperfunction

1. Adrenogenital syndrome
2. Conn syndrome = hyperaldosteronism
3. Cushing syndrome = hypercortisolism

Bilateral Adrenal Masses

1. Metastases (50%)
2. Lymphoma (50% of secondary lymphomas, 50% bilateral)
3. Adenoma (20%)
4. Pheochromocytoma (10%)
5. Myelolipoma (5–13%)
6. Adrenocortical carcinoma (2–6%)
7. Hemorrhage
8. Granulomatous infection (usually bilaterally asymmetric)
9. Hyperplasia (usually bilaterally symmetric)

mnemonic: 4 H PM
Hodgkin disease
Hyperplasia
Hemorrhage
Histoplasmosis / TB
Pheochromocytoma
Metastasis

Granulomatous Disease
Organism: tuberculosis, histoplasmosis, blastomycosis
√ usually bilateral homogeneous adrenal enlargement in acute phase
√ sometimes cystic / calcified adrenals in chronic phase
Cx: tuberculous adrenal atrophy → adrenal hypofunction → Addison disease

Incidental Unilateral Adrenal Mass = Incidentaloma
= incidental discovery of a clinically silent adrenal mass of > 10 mm in a patient without known cancer
Prevalence: 4–9% of all CT exams (in 0.2% of patients 20–29 years, in 7% of elderly); 1.0–4.2% of population
Concern for: primary adrenal cortical carcinoma, metastasis, Cushing disease, pheochromocytoma, aldosteronoma versus nonfunctioning adenoma
◊ With a Hx of malignancy an adrenal nodule is a metastasis in merely 26–36%!
◊ 97–98% of incidentalomas are benign and insignificant!
◊ Most adenomas can be accurately characterized by NECT + MR ± CECT
◊ Follow-up imaging has a limited role
◊ Biopsy only if CT + MR do NOT indicate adenoma / PET-CT suggests metastasis
mnemonic: PLAN My HAM
Pheochromocytoma (6%)
Lymphoma
Adenoma (71%): functioning (1%)
Neuroblastoma
Myelolipoma
Hemorrhage
Adenocarcinoma (4%)
Metastasis (2–3%)

Bilaterality of Adrenal Incidentaloma
Frequency: in < 30% of adenomas
DDx: metastasis, lymphoma, infection, hyperplasia, hemorrhage

Morphologic Criteria of Adrenal Incidentaloma
(a) Size of lesion (too unreliable as only criterion)
Principle: Larger lesions are more likely malignant and more likely symptomatic!
› with known malignancy

< 3 cm: 87% are benign
> 3 cm: 95% are malignant
› without known malignancy
> 4 cm: 70% are malignant
> 6 cm: 85% are malignant
Rx: excision for incidentaloma > 5 cm

(b) Change in size
◊ Any increase in size after 6 months can be considered malignant!
CAVE: rare adenomas + myelolipomas can slightly increase in size

(c) Margin of lesion
◊ Irregular borders usually indicate malignancy!
◊ Multinodularity is usually benign!

(d) Internal texture
◊ Large necrotic areas signify malignancy
◊ Small metastases are often homogeneous

Problematic features of any adrenal mass: diffusely heterogeneous attenuation / focal areas of low attenuation / thickened wall

LIPID-SENSITIVE IMAGING OF ADRENAL INCIDENTALOMA

Principle: a benign adrenal mass contains intracytoplasmic fat, a malignancy does not
Substrate: cholesterol, fatty acids, neutral fat
Distribution: 70% of adenomas are lipid-rich; 30% of adenomas are lipid-poor + indeterminate

NECT attenuation (HU_{NECT}):
◊ dependent on scanner type + scanning technique!
ROI: in center of mass covering at least 50% of cross-sectional area
≤ 10 HU_{NECT} = benign lipid-rich adenoma / cyst
> 10 HU_{NECT} = indeterminate / lipid-poor adenoma
Sensitivity for adenomas: 56–71%
Specificity for adenomas: 98%
False-positive rate: 4%

For all practical purposes a < 3 cm homogeneous lesion that measures ≤ 10 HU at NECT is an adrenocortical adenoma!

CT histogram for NECT / CECT:
√ > 10% of pixel count below 0 HU indicates adenoma (sensitivity of 71% for NECT, 12% for CECT)

Chemical shift imaging MR (CSI):
Physics: fat protons precess at lower frequency than water protons
Useful: if lesion < 30 HU on NECT

(a) qualitatively (and effective):
√ fat + water summate to intermediate SI on in-phase images
√ fat + water signals cancel each other out to a low signal intensity on out-of-phase images

Most adenomas show a significant decrease in signal intensity on the out-of-phase images!

(b) quantitative method (rarely used in practice)

√ adrenal-to-spleen SI ratio (SIR) < 0.71

$SIR = SIR_{in\text{-}phase} \div SIR_{opposed\text{-}phase}$

√ signal intensity index (SII) > 16.5%

$SII = (SI_{in\text{-}phase} - SI_{opposed\text{-}phase}) \div SIin\text{-}phase \times 100$

Results: on average 67% of all indeterminate adrenal adenomas > 10 HU are lipid rich on CSI:

100% of adenomas measuring 10–20 HU

75% of adenomas measuring 20–30 HU

13% of adenomas measuring ≥ 30 HU

Indeterminate: lipid-poor adenomas with low lipid-to-water proton ratio per voxel

PERFUSION IMAGING OF ADRENAL INCIDENTALOMA BY CT

= CT washout scan (most effective test)

Principle: malignant vessels have an increased capillary permeability with prolonged retention of contrast material

Input values:

» 60-second scan ($HU_{CECT\ 1\ min}$)

» 15-minute delayed scan ($HU_{CECT\ 15\ min}$)

» ± precontrast CT (HU_{NECT})

(a) **Relative Percentage Washout (RPW)** (if unenhanced CT not available)

$= [HU_{CECT\ 1\ min} - HU_{CECT\ 15\ min}] / [HU_{CECT\ 1\ min}] \bullet 100\%$

washout > 60% = lipid-poor adenoma

washout ≤ 60% = indeterminate mass

Results: 96% sensitive + 100% specific

Absolute and Relative Washout of Adrenal Masses
Szolar DH et al.: Radiology 2005; 234:479–485

Adrenal Mass	*Absolute Washout [%]*	*Relative Washout [%]*
Adenoma	62 ± 17	108 ± 87
Adrenocortical carcinoma	34 ± 9	13 ± 12
Pheochromocytoma	22 ± 12	14 ± 7
Metastasis	31 ± 16	19 ± 11

(b) **Absolute Percentage Washout** (APW) (if unenhanced CT available)

= [HUCECT 1 min – HUCECT 15 min] / [HUCECT 1 min – HUNECT] • 100%

washout > 40% = lipid-poor adenoma

washout ≤ 40% = indeterminate mass

Results: 88% sensitive + 96% specific

Lesions with RPW of < 40% / APW of < 60% are almost always malignant!

◊ A mass with absolute enhancement > 110–120 HU + APW of > 60% + RPW of > 40% suggests a pheochromocytoma

FUNCTIONAL IMAGING WITH 18F-FDG PET

Principle: FDG trapped intracellularly by metabolically active malignant lesion

Use: modality of choice in known malignancy
◊ 50% of incidentalomas in cancer patients represent metastatic disease!
Internal reference organ: liver
SUV: > 4 for metastatic disease ← lung, colon, melanoma, lymphoma
FN: pulmonary carcinoid, lung cancer with strong bronchioloalveolar component, hemorrhagic / necrotic tumor, lesion < 10 mm in size
FP: 5% of adrenal adenomas, pheochromocytoma, adrenal endothelial cyst, inflammation, infection
Results: 93–100% sensitive, 80–100% specific, 99% accurate

ENDOCRINOLOGIC FUNCTION TEST IN INCIDENTALOMA

Use: recommended for lesions > 4 cm
Frequency: 6%
Yield:
› 94% nonfunctioning adrenal adenoma
› 6% functioning adrenal adenoma
» cortisol production (5%) → Cushing syndrome
» aldosterone (< 2%) → Conn syndrome
» catecholamines → pheochromocytoma
» sex hormone (1%)

ADRENAL BIOPSY

Indication: inconclusive / contradictory adrenal imaging with high clinical suspicion for metastasis from an underlying extraadrenal malignancy
Diagnostic accuracy: 83–96%
Insufficient material: 4–19%
Cx: bleeding, pneumothorax, infection, tumor tracking in 8–12%
N.B.: several deaths reported after Bx of pheochromocytoma

Adrenal Mass with specific CT Attenuation

1. Acute hemorrhage: 50–90 HU
2. Adrenal myelolipoma: fat attenuation
3. Adrenal cyst: fluid attenuation

Fat-containing Adrenal Mass

(a) intracellular fat → SI loss on out-of-phase images
1. Adrenal adenoma
(b) macroscopic fat → SI loss on fat-saturated images
1. Myelolipoma

Adrenal Mass with Small Foci of Fat

◊ Not every adrenal mass with a small amount of fat is a myelolipoma!
1. Myelolipoma
2. Adrenocortical adenoma with myelolipomatous changes
3. Adrenocortical carcinoma
4. Pheochromocytoma

Small Unilateral Adrenal Tumor

1. Cortical adenoma (in 1–9% of autopsies)
   √ < 10 HU imply an adenoma (in 96%)
2. Metastasis
3. Pheochromocytoma
4. Asymmetric hyperplasia
5. Granulomatous disease (TB, histoplasmosis)
   √ diffuse enlargement / discrete mass
   √ ± central cystic changes ± calcification
6. Myelolipoma

Large Solid Adrenal Mass

Large tumors ≥ 6 cm are highly suspicious for malignancy!

1. Adrenocortical carcinoma
2. Pheochromocytoma
3. Neuroblastoma / ganglioneuroma
4. Myelolipoma
5. Metastasis
6. Hemorrhage
7. Inflammation
8. Abscess (eg, histoplasmosis, tuberculosis)
9. Hemangioma

Malignant Adrenal Mass

1. Adrenocortical carcinoma
2. Angiosarcoma
3. Lymphoma
4. Malignant pheochromocytoma
5. Neuroblastoma
6. Metastasis
7. **Collision tumor**
   = concomitant benign adenoma + metastasis
   Frequency: in 2% of patients with known primary
   N.B.: Percutaneous biopsy may be falsely negative ← sampling of the benign component!

Benign Adrenal Lesion

1. Adenoma
2. Myelolipoma
3. Adrenal cyst
4. Adrenal hemorrhage
5. Ganglioneuroma
6. Schwannoma
7. Hemangioma
8. Lymphangioma of adrenal gland

9. Granuloma
10. Pheochromocytoma
11. Adenomatoid tumor
12. Oncocytoma of adrenal gland

Adrenal Tumor in Childhood

1. Neuroblastoma (most common extracranial solid tumor)
2. Pheochromocytoma
3. Adrenocortical carcinoma
4. Lymphoma

Cystic Adrenal Mass

1. Pseudocyst: old hemorrhage / infarction
2. Vascular cystic space (endothelial lining): lymphangioma, hemangioma
3. True cyst (epithelial lining): glandular cyst, embryonal cyst, mesothelial inclusion cyst
4. Parasitic cyst: hydatid cyst
5. Hemorrhagic complication / degeneration of a tumor:
   cystic adenoma, cystic pheochromocytoma, cystic adenomatoid tumor, cystic adrenocortical carcinoma, schwannoma with cystic degeneration
6. Neuroblastoma (rare)
7. Cortical adenoma with low density

Adrenal Calcification

A. TUMOR
   1. Neuroblastoma
   2. Pheochromocytoma
   3. Adrenal adenoma
   4. Adrenal carcinoma
   5. Dermoid
B. VASCULAR
   1. Hemorrhage (neonatal, sepsis)
C. INFECTION
   1. Tuberculosis
   2. Histoplasmosis
   3. Waterhouse-Friderichsen syndrome
D. ENDOCRINE
   1. Addison disease (TB)
E. OTHERS
   1. Wolman disease

Adrenal Hemorrhage

Unilateral Adrenal Hemorrhage

A. TRAUMA (80%)
B. BLEEDING INTO UNDERLYING ADRENAL TUMOR
   1. Pseudocyst

2. Myelolipoma
3. Hemangioma
4. Pheochromocytoma
5. Adrenocortical adenoma / carcinoma
6. Metastasis: bronchogenic carcinoma, angiosarcoma, melanoma

Bilateral Adrenal Hemorrhage

A. NEONATAL STRESS

◊ Most common neonatal lesion of adrenal gland

1. Difficult labor / delivery: forceps / breech delivery
2. Asphyxia / hypoxia ← prematurity
3. Septicemia
4. Hemorrhagic disorders: DIC, hypoprothrombinemia
5. Extracorporeal membrane oxygenation (in 4%)
6. Thrombus extending from renal vein thrombosis

Predisposed: infants large for gestational age, infants of diabetic mothers

Age: 1st week of life

Site: R÷L = 7÷3; bilateral in 10%

B. ADULT STRESS

Pathophysiology:

stress → severalfold ⇑ in endogenous secretion of adrenocorticotropic hormone → ⇑ in adrenal vascularity; ⇑ in catecholamines, thrombin, fibrin, endotoxin during shock → venoconstriction + venous thrombosis → intraglandular hemorrhage

1. Surgery: orthotopic liver transplantation
2. Sepsis: Waterhouse-Friderichsen syndrome (= fulminant meningococcemia); Pseudomonas infection; other gram-negative organisms
3. Burns
4. Hypotension
5. Pregnancy
6. Cardiovascular disease
7. Exogenous adrenocorticotropic hormone
8. Exogenous steroids

C. HEMORRHAGIC DIATHESIS & COAGULOPATHY

1. Anticoagulant therapy (heparin, coumadin): during initial 3 weeks
2. Disseminated intravascular coagulopathy
3. Antiphospholipid syndrome ± systemic lupus erythematosus (hypercoagulable state causes adrenal vein thrombosis + venous infarction)

KIDNEY

Developmental Renal Anomalies

Numerary Renal Anomaly

1. Supernumerary kidney
2. Complete / partial renal duplication

3. Abortive calyx
4. Unicaliceal (unipapillary) kidney

Renal Underdevelopment

1. Congenital renal hypoplasia
2. Renal agenesis
3. Renal dysgenesis

Renal Ectopia

Normal location of kidneys: 1st–3rd lumbar vertebra
Prevalence: 0.2% (autopsy series)
Cause: failure of kidney to ascend by 8 weeks GA
At risk of: infection, calculi, hydronephrosis ← UPJ obstruction
√ unusual developmental "funny-looking calyces" often misinterpreted as obstructive
√ loop-to-loop colon = abnormal looped configuration of colon occupying the renal fossa

LONGITUDINAL RENAL ECTOPIA

Location: pelvic, sacral, lower lumbar level, intrathoracic; L > R
√ must demonstrate aberrant arteries
DDx: displacement through diaphragmatic hernia (nonaberrant); hypermobile kidney

Pelvic Kidney

= ectopic kidney ← failure of renal ascent
Prevalence: 1÷725 births
May be associated with:
(1) Vesicoureteral reflux
(2) Hydronephrosis ← abnormally high insertion of ureter into renal pelvis
(3) Hypospadia (common)
(4) Contralateral renal agenesis
√ blood supply via iliac vessels / aorta
√ nonrotation = anteriorly positioned renal pelvis (common)

CROSSED RENAL ECTOPIA

= kidney located on opposite side of midline from its ureteral orifice; usually L > R and crossed kidney inferior to normal kidney
(a) fused (common)
(b) separate (rare)
Cause: ? faulty development of ureteral bud, vascular obstruction of renal ascent
Associated with: obstruction urolithiasis, infection, reflux, megaureter, hypospadia, cryptorchidism, urethral valves, multicystic dysplasia
√ invariably aberrant renal arteries
√ distal ureter inserts into trigone on the side of origin

RENAL FUSION ANOMALIES

= "lump / cake, disk, horseshoe"
Cx: aberrant arteries may cross and obstruct ureter

Horseshoe Kidney

= fusion of lower renal poles with isthmus across midline anterior to aorta

Prevalence: 1÷400 live births

Associated with: vertebral, anorectal, tracheal, esophageal malformations

√ anomalous vascular supply

√ anomalous renal rotation

Cx: varying degrees of obstruction, stone formation, infection

Disc / Pancake Kidney

= bilateral fused pelvic kidneys

Associated with: abnormal testicular descent, tetralogy of Fallot, vaginal agenesis, sacral agenesis, caudal regression, anal anomalies

RENAL MALROTATION

√ collecting structures may be positioned ventrally (most common), lateral (rare), dorsal (rarer), transverse (along AP axis)

√ "funny-looking calices" = developmental usually nonobstructive ectasia

Absent Renal Outline on Plain Film

A. ABSENT KIDNEY
   1. Congenital absence
   2. S/P nephrectomy
B. SMALL KIDNEY
   1. Renal hypoplasia
   2. Renal atrophy
C. RENAL ECTOPIA
   1. Pelvic kidney
   2. Crossed fused ectopia
   3. Intrathoracic kidney
D. OBLITERATION OF PERIRENAL FAT
   1. Perirenal abscess
   2. Perirenal hematoma
   3. Renal tumors

Perinephric Fat Stranding

√ nonspecific perirenal cobwebs

Pathophysiology: engorged lymphatics, edema, fluid extravasation from pyelosinus

1. Acute obstructing renal calculus: ureteral colic
2. Infection
3. Infarction
4. Neoplasm
5. Trauma
6. Renal vein thrombosis

Nonvisualized Kidney on Excretory Urography

A. ABSENCE OF KIDNEY

1. Agenesis
2. Surgical absence
3. Renal ectopia

B. LOSS OF PERFUSION
1. Chronic infarction
2. Unilateral renal vein thrombosis

C. TRAUMA
1. Thrombosis of main renal artery
2. Severe contusion → renal vasospasm
3. Avulsion of renal pedicle

D. HIGH-GRADE URINARY OBSTRUCTION
1. Hydronephrosis
2. Ureteropelvic junction obstruction

E. REPLACED NORMAL RENAL PARENCHYMA
1. Multicystic dysplastic kidney
2. Unilateral polycystic kidney disease
3. Renal tumor (RCC, TCC, Wilms tumor)
4. Xanthogranulomatous pyelonephritis

Faceless Kidney

= absence of normal components of renal sinus (renal parenchyma, fat and collecting system) on cross-sectional imaging

1. Duplicated collecting system
2. Urothelial renal tumor (TCC, SCC)
3. Lymphoma of kidney
4. Inflammatory / infectious mass

Unilateral Large Smooth Kidney

A. PRERENAL
(a) arterial: acute arterial infarction
(b) venous: acute renal vein thrombosis

B. INTRARENAL
(a) congenital: duplicated pelvicaliceal system, crossed fused ectopia, multicystic dysplastic kidney, adult polycystic kidney (in 8% unilateral)
(b) infectious: acute bacterial nephritis
(c) adaptation: compensatory hypertrophy

C. POSTRENAL
(a) collecting system: obstructive uropathy

mnemonic: AROMA

Acute pyelonephritis
Renal vein thrombosis
Obstructive uropathy
Miscellaneous (compensatory hypertrophy, duplication)
Arterial obstruction (infarction)

Bilateral Large Kidneys

Average renal length by x-ray: M = 13 cm; F = 12.5 cm

1. PROTEIN DEPOSITION amyloidosis, multiple myeloma
2. INTERSTITIAL FLUID ACCUMULATION acute tubular necrosis, acute cortical necrosis, acute arterial infarction, renal vein thrombosis
3. CELLULAR INFILTRATION
   (a) Inflammatory cells: acute interstitial / bacterial nephritis
   (b) Malignant cells: leukemia / lymphoma, bilateral Wilms tumor, nephroblastomatosis
4. PROLIFERATIVE / NECROTIZING DISORDERS
   (a) Glomerulonephritis (GN) acute (poststreptococcal) GN, rapidly progressive GN, idiopathic membranous GN, glomerulosclerosis, lobular GN, IgA nephropathy, membranoproliferative GN, glomerulosclerosis related to heroin abuse
   (b) Multisystem disease polyarteritis nodosa, systemic lupus erythematosus, Wegener granulomatosis, allergic angiitis, diabetic glomerulosclerosis, Goodpasture syndrome (lung hemorrhage + glomerulonephritis), Schönlein-Henoch syndrome (anaphylactoid purpura), thrombotic thrombocytopenic purpura, focal glomerulonephritis associated with subacute bacterial endocarditis
5. URINE OUTFLOW OBSTRUCTION bilateral hydronephrosis: congenital / acquired
6. HORMONAL STIMULUS acromegaly, compensatory hypertrophy, nephromegaly associated with cirrhosis / hyperalimentation / diabetes mellitus
7. DEVELOPMENTAL bilateral renal duplication, horseshoe kidney, polycystic kidney disease
8. MISCELLANEOUS acute urate nephropathy, glycogen storage disease, hemophilia, sickle cell disease, Fabry disease, physiologic response to contrast material and diuretics

mnemonic: FOG P

Fluid: edema of kidney (ATN, acute cortical necrosis)
Other: leukemia, acromegaly, sickle cell anemia, bilateral duplication, acute urate nephropathy
Glomerular disease: acute GN, lupus, polyarteritis nodosa, diabetes mellitus
Protein deposition: multiple myeloma, amyloidosis

Bilateral Small Kidneys

A. PRERENAL = VASCULAR
   1. Arterial hypotension (acute)
   2. Generalized arteriosclerosis
   3. Atheroembolic disease
   4. Benign & malignant nephrosclerosis
B. INTRARENAL
   1. Hereditary nephropathies: medullary cystic disease, hereditary chronic nephritis (Alport syndrome)
   2. Chronic glomerulonephritis
   3. Amyloidosis (late)
C. POSTRENAL
   1. Papillary necrosis
D. CAUSES OF UNILATERAL SMALL KIDNEY above causes occurring bilaterally

mnemonic: CAPE HANA
Chronic glomerulonephritis
Arteriosclerosis
Papillary necrosis
Embolic disease ← atherosclerosis
Hypotension
Alport syndrome
Nephrosclerosis
Amyloidosis (late)

Unilateral Small Kidney

A. PRERENAL = VASCULAR
   1. Lobar infarction
   2. Chronic infarction
   3. Renal artery stenosis
   4. Radiation nephritis
B. INTRARENAL = PARENCHYMAL
   1. Congenital hypoplasia
   2. Multicystic dysplastic kidney (in adult)
   3. Postinflammatory atrophy
C. POSTRENAL = COLLECTING SYSTEM
   1. Reflux nephropathy = chronic atrophic pyelonephritis
   2. Postobstructive atrophy

mnemonic: RIP R HIP
Reflux atrophy
Ischemia: renal artery stenosis
Postobstructive atrophy
Radiation therapy
Hypoplasia: congenital
Infarction
Postinflammatory atrophy

Increased Echogenicity of Renal Cortex

= RENAL MEDICAL DISEASE
= diffuse increase in cortical echogenicity with preservation of corticomedullary junction
Path: deposition of collagen / calcium in interstitial, glomerular, tubular, vascular disease
√ echointensity of cortex greater than liver / spleen ± equal to renal sinus
√ renal size may be normal; enlarged kidneys suggest active stage of renal disease; small kidneys suggest chronic + often end-stage renal disease
Cause:
1. Acute / chronic glomerulonephritis
2. Renal transplant rejection
3. Lupus nephritis
4. Hypertensive nephrosclerosis
5. Renal cortical necrosis

6. Methemoglobulinuric renal failure
7. Alport syndrome
8. Amyloidosis
9. Diabetic nephrosclerosis
10. Nephrotoxin-induced acute tubular necrosis
11. End-stage renal disease

Hyperechoic Renal Pyramids in Children

A. MEDULLARY NEPHROCALCINOSIS
B. METABOLIC DISEASE
   1. Gout
   2. Lesch-Nyhan syndrome (urate)
   3. Fanconi syndrome
   4. Glycogen storage disease (distal RTA)
   5. Wilson disease (distal RTA)
   6. Alpha-1 antitrypsin deficiency
   7. Tyrosinemia
   8. Cystinosis
   9. Oxalosis
   10. Crohn disease
C. HYPOKALEMIA
   1. Primary aldosteronism
   2. Pseudo-Bartter syndrome
D. PROTEIN DEPOSITS
   1. Infant dehydration with presumed Tamm-Horsfall proteinuria
   2. Toxic shock syndrome
E. VASCULAR CONGESTION
   1. Sickle cell disease
F. INFECTION
   1. Candida / CMV nephritis
   2. AIDS-associated Mycobacterium avium-intracellulare
G. FIBROSIS OF RENAL PYRAMIDS
H. CYSTIC MEDULLARY DISEASE
   1. Medullary sponge kidney
   2. Congenital hepatic fibrosis with tubular ectasia
I. INTRARENAL REFLUX
   1. Chronic pyelonephritis

Hyperechoic Pyramids in Neonate

1. Transient hyperechogenicity (4–58%): resolves within 10 days or longer in prematurity
   Cause: uncertain
2. Obstructed hydronephrosis
3. Ischemia: ATN, medullary / cortical necrosis, renal vein thrombosis
4. Infection: candida
5. Polycystic kidney disease: ADPKD, Beckwith-Wiedemann syndrome

6. Metabolic

Iron Accumulation in Kidney

A. RENAL CORTEX
   1. Paroxysmal nocturnal hemoglobulinuria (= intravascular extrasplenic hemolysis)
   2. Sickle cell anemia

B. RENAL MEDULLA
   1. Hemorrhagic fever with renal syndrome (uncommon viral illness caused by Hantavirus)

Triad: (1) Renal medullary hemorrhage
(2) Right atrial hemorrhage
(3) Necrosis of anterior pituitary

Cold Defect on Renal Scintigraphy

mnemonic: CHAT SIN

Cyst
Hematoma
Abscess
Tumor
Scar
Infarct
Neoplasm

Abnormal Uptake of Bone Agents within Kidneys

1. Effect of chemotherapeutic drugs: bleomycin, cyclophosphamide, doxorubicin, mitomycin C, 6-mercaptopurine
2. S/P radiation therapy
3. Metastatic calcification
4. Pyelonephritis
5. Acute tubular necrosis
6. Iron overload
7. Multiple myeloma
8. Renal vein thrombosis
9. Ureteral obstruction

Incidental Urinary Tract Abnormalities during Bone Scintigraphy

> 50% of injected dose of ^{99m}Tc-MDP is excreted by 3 hours

A. Bilateral diffuse increased uptake
   = uptake greater than that of lumbar spine
   (a) excess tissue calcium
      1. Hyperparathyroidism
      2. Hypercalcemia
      3. Osteosarcoma metastatic to kidney
   (b) tissue damage
      1. Drug-induced nephrotoxicity
         › chemotherapy: eg, cyclophosphamide, vincristine, doxorubicin, bleomycin,

mitomycin-C, S-6-mercaptopurine, mitoxantrone
› aminoglycosides
› amphotericin B
2. Radiation therapy
3. Necrotic renal cell carcinoma (rare)
4. Renal metastasis (rare)
5. Acute pyelonephritis
6. Acute tubular necrosis
7. Multiple myeloma

(c) iron overload
1. Sickle cell anemia
2. Thalassemia major

mnemonic: RICH CON
Radiation therapy to kidney
Iron overload
Chemotherapy (cytoxan, vincristine, doxorubicin)
Hyperparathyroidism
Calcification (metastatic), **C**arcinoma
Obstruction (urinary)
Nephritis, **N**ormal variant

B. Bilateral decreased renal uptake
(a) loss of renal function
1. End-stage renal disease
(b) increased osteoblastic activity (= superscan)

C. Focally decreased renal uptake
(a) space-occupying lesion replacing renal parenchyma
1. Abscess
2. Cyst
3. Primary / metastatic renal neoplasm

(b) scar
1. Infarct
2. Chronic pyelonephritis
3. Partial nephrectomy

D. Uni- / bilateral focally increased GU uptake ← urine accumulation
1. Normal upper pole calyces: in supine position
2. Urinary tract diversion / ileal conduit
3. Urinoma

E. Change in location of kidney
1. Congenital anomaly: eg, pelvic kidney

Depression of Renal Margins

1. Fetal lobation
√ notching between normal calyces
2. Splenic impression
√ flattened upper outer margin of left kidney

3. Chronic atrophic pyelonephritis
   √ indentation over clubbed calyces
4. Renal infarct
   √ normal calyces
5. Chronic renal ischemia
   √ normal calyces

Enlargement of Iliopsoas Compartment

A. INFECTION
   (a) from retroperitoneal organs
      1. Renal infection
      2. Complicated pancreatitis
      3. Postoperative aortic graft infection
   (b) from spine
      1. Osteomyelitis / postoperative complication of bone surgery
      2. Diskitis / postoperative complication ← disk surgery
   (c) from GI tract
      1. Crohn disease
      2. Appendicitis
   (d) others
      1. Pelvic inflammatory disease / postpartum infection
      2. Sepsis
B. HEMORRHAGE
   1. Coagulopathy and anticoagulant therapy
   2. Ruptured aortic aneurysm
   3. Postoperative aneurysm repair / other surgery / trauma
C. NEOPLASTIC DISEASE
   (a) extrinsic
      1. Lymphoma
      2. Metastatic lymphadenopathy
      3. Bone metastases with soft-tissue involvement
      4. Retroperitoneal sarcoma
   (b) intrinsic
      1. Muscle tumors
      2. Nervous system tumors
      3. Lipoma / liposarcoma
D. MISCELLANEOUS
   1. Pseudoenlargement of psoas muscle compared with de facto atrophy of contralateral side in neuromuscular dz
   2. Fluid collection: urinoma, lymphocele, pancreatic pseudocyst, enlargement of iliopsoas bursa
   3. Pelvic venous thrombosis
      √ diffuse swelling of all muscles (edema)

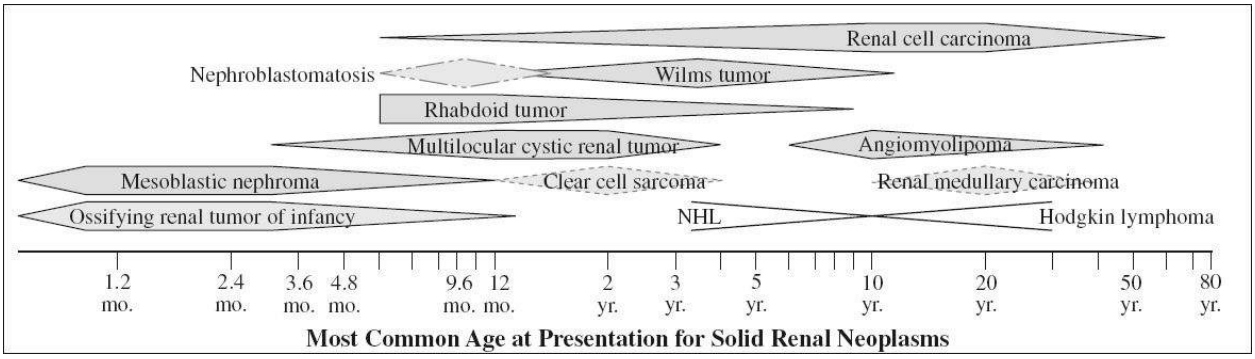
RENAL MASS

Renal Tumors in Adults by Histology (WHO 2004)

A. Renal cell tumor
B. Metanephric tumor
C. Mesenchymal tumor
   (a) benign:
      1. Angiomyolipoma
      2. Leiomyoma of kidney
      3. Hemangioma of kidney
      4. Lymphangioma of kidney
      5. Juxtaglomerular cell tumor
      6. Renomedullary interstitial cell tumor
      7. Solitary fibrous tumor
      8. others: lipoma, schwannoma
   (b) malignant:
      ◊ Primary renal sarcomas account for 1–3% of all malignant renal tumors!
      1. Leiomyosarcoma of kidney (50–60%)
      2. Others: synovial sarcoma, osteosarcoma, fibrosarcoma, rhabdomyosarcoma, angiosarcoma, malignant fibrous histiocytoma, solitary fibrous tumor
D. Mixed mesenchymal and epithelial tumor
E. Neuroendocrine tumor
F. Germ cell tumor

Renal Mass in Neonate

A. UNILATERAL
   1. Multicystic kidney (15%)
   2. Hydronephrosis (25%)
      (a) UPJ obstruction
      (b) upper moiety of duplication
   3. Renal vein thrombosis
   4. Mesoblastic nephroma
      ◊ Most common primary renal neoplasm in 1st month of life
   5. Rare: Wilms tumor, teratoma



Most Common Age at Presentation for Solid Renal Neoplasms

B. BILATERAL

1. Hydronephrosis
2. Polycystic kidney disease
3. Multicystic kidney + contralateral hydronephrosis
4. Nephroblastomatosis
5. Bilateral multicystic kidney

Renal Tumors in 1st Decade of Life

1. Wilms tumor
2. Cystic nephroma and cystic partially differentiated nephroblastoma
3. Mesoblastic nephroma
4. Clear cell sarcoma
5. Rhabdoid tumor
6. Ossifying renal tumor of infancy
7. Renal cell carcinoma
8. Angiomyolipoma
9. Metanephric stromal tumor

Renal Mass in Older Child

A. SINGLE MASS
   (a) single solid mass
      1. Wilms tumor 87%
      2. Clear cell sarcoma of kidney 6%
      3. Mesoblastic nephroma 2%
      4. Rhabdoid tumor 2%
      5. Renal cell carcinoma < 0.5%
      6. Teratoma
      7. Intrarenal neuroblastoma
   (b) single cystic mass
      1. Focal hydronephrosis
      2. Multilocular cystic nephroma
      3. Traumatic cyst, abscess

B. MULTIPLE MASSES
   1. Nephroblastomatosis
   2. Multiple Wilms tumors
   3. Angiomyolipoma
   4. Lymphoma (< 0.5%)
   5. Leukemia
   6. Adult polycystic kidney disease
   7. Abscesses

Bilateral Renal Masses

A. MALIGNANT TUMOR
   1. Malignant lymphoma / Hodgkin disease
   2. Metastases
   3. Renal cell carcinoma

4. Wilms tumor

B. BENIGN TUMOR
   1. Angiomyolipoma
   2. Nephroblastomatosis

C. CYSTS
   1. Adult polycystic kidney disease
   2. Acquired cystic kidney disease

Unilateral Renal Mass

Solid Renal Mass

A. TUMORS
   (a) primary malignant:
   › epithelial tumor of renal parenchyma: adenocarcinoma (83%), papillary neoplasm (14%), chromophobe carcinoma (4%), renal neuroendocrine tumors (carcinoid, small cell carcinoma), Wilms tumor (6%)
   › epithelial tumor of renal pelvis: TCC (8%), squamous cell carcinoma
   › medullary tumor: renal medullary carcinoma, renal collecting duct carcinoma = Bellini duct carcinoma (1%)
   › renal sarcoma (2%)
   <u>in horseshoe kidney:</u>
   adenocarcinoma (45%), Wilms tumor (28%), transitional cell carcinoma (20%)
   (b) secondary malignant: malignant lymphoma / Hodgkin disease, metastases, invasive transitional cell carcinoma
   (c) benign: adenoma, oncocytoma, hamartoma (mesoblastic nephroma, angiomyolipoma, myolipoma, lipoma, leiomyoma, fibroma), hemangioma

B. INFLAMMATORY MASSES
   acute focal pyelonephritis, renal abscess, malakoplakia, xanthogranulomatous pyelonephritis, tuberculoma

Fluid-filled Renal Lesion

A. CYSTS
   1. Simple renal cyst
      √ simple fluid attenuation of 0–20 HU
   2. Complicated renal cyst
   3. Inherited cystic disease:
      multicystic dysplastic kidney disease (Potter type II), multilocular cystic nephroma
   4. Focal hydronephrosis

B. VASCULAR
   1. Arteriovenous malformation
   2. Arteriovenous fistula

C. CYSTIC MASS
   1. Renal cell carcinoma

◊ Lesions < 1 cm often cannot be clearly characterized!
◊ Lesions 1–1.5 cm can often be ignored, particularly in elderly / patients with significant

other disease

Calcified Renal Mass

◊ A calcified renal mass is malignant in 75% of cases!
◊ Lesions with
(a) nonperipheral calcifications are malignant in 87%!
(b) peripheral calcifications are malignant in 20%!

A. MALIGNANT TUMOR
1. Renal cell carcinoma (calcifies in 8–20%)
√ calcifications generally nonperipheral, sometimes along fibrous capsule
2. Wilms tumor
3. Transitional cell carcinoma (rare)
4. Osteosarcoma of renal capsule
5. Metastasis

B. INFECTION
1. Abscess
◊ Tuberculous abscess frequently calcifies!
◊ Pyogenic abscess rarely calcifies!
2. Echinococcal cyst
◊ Renal involvement in 3% of hydatid disease;
◊ 50% of echinococcal cysts calcify
3. Xanthogranulomatous pyelonephritis
√ large obstructive calculus in > 70%

C. CYSTS
◊ Calcification is related to prior hemorrhage / infection!
1. Simple renal cyst (calcifies in 1–3%)
√ thin peripheral "eggshell"-like calcification
2. Multicystic dysplastic kidney (in adult)
3. Autosomal dominant polycystic kidney disease
4. Milk of calcium: cyst, caliceal diverticulum, obstructed hydrocalyx
DDx: residual pantopaque used in cyst puncture

D. VASCULAR
1. Subcapsular / perirenal hematoma
2. Renal artery aneurysm
√ circular cracked eggshell appearance
3. Congenital / posttraumatic arteriovenous malformation
4. Arteriosclerosis: in severe atherosclerotic disease, diabetes mellitus, hyperparathyroidism
5. Sloughed papilla: in papillary necrosis
6. Hemangioma

Avascular Mass in Kidney

mnemonic: CHEAT
Cyst
Hematoma

Edema
Abscess
Tumor

Growth Pattern of Renal Lesions

Renal Lesion with Expansile Growth Pattern

1. Renal cell carcinoma
2. Oncocytoma
3. Angiomyolipoma
4. Juxtaglomerular tumor
5. Metastatic tumor: eg, lymphoma
6. Mesenchymal tumor

Renal Lesions with Infiltrative Growth Pattern

Imaging hallmarks:

√ growth initially respects renal contour
√ invasion of normal structures
√ poorly defined interface between normal renal parenchyma and lesion
√ enlarged kidney with preservation of reniform shape

IVP:

√ decreased / absent nephrogram

Angio:

√ vascular encasement, pruning, amputation
√ no vascular displacement

CT:

√ poorly marginated area of diminished enhancement
√ encasement of collecting system without displacement
√ replacement of renal sinus fat

US:

√ poorly circumscribed hypo- / hyperechoic regions

A. NEOPLASM
   (a) lymphoproliferative
      1. Lymphoma / leukemia
      2. Extramedullary plasmacytoma
   (b) epithelial tumor of renal parenchyma
      1. Renal cell carcinoma (unusual)
      2. High-grade and sarcomatoid type of RCC
   (c) epithelial tumors of the renal pelvis
      1. Invasive transitional cell carcinoma

√ mass arises from collecting system

      2. Squamous cell carcinoma
   (d) medullary tumor of uncertain cell origin
      1. Collecting duct carcinoma
      2. Renal medullary carcinoma

(e) metastases: esp. lung cancer
(f) renal sarcomas
(g) pediatric tumor
1. Mesoblastic nephroma
2. Rhabdoid tumor of the kidney
3. Nephroblastomatosis
4. Primitive neuroectodermal tumor
5. Wilms tumor (unusual)

B. INFLAMMATION
1. Bacterial pyelonephritis
2. Xanthogranulomatous pyelonephritis
3. Renal parenchymal malakoplakia

Local Bulge in Renal Contour

A. CYST
1. Simple renal cyst

B. TUMOR
1. Adenocarcinoma
2. Angiomyolipoma
3. Pseudotumor

C. INFECTION
1. Subcapsular abscess
2. XGP

D. TRAUMA
1. Subcapsular hematoma

E. DILATED COLLECTING SYSTEM

Hyperechoic Renal Nodule

A. MALIGNANT TUMOR
1. Renal cell carcinoma
2. Angiosarcoma
3. Liposarcoma
4. Undifferentiated sarcoma
5. Lymphoma

B. BENIGN TUMOR
1. Angiomyolipoma
2. Lipoma
3. Oncocytoma
4. Cavernous hemangioma

C. INFARCT

D. HEMATOMA

Focal Area of Increased Renal Echogenicity

A. NONNEOPLASTIC
1. Chronic renal infarction

2. Acute focal bacterial nephritis

B. BENIGN TUMOR
   1. Angiomyolipoma
   2. Cavernous renal hemangioma
   3. Oncocytoma

C. MALIGNANCY
   1. Renal cell carcinoma
   2. Angiosarcoma
   3. Undifferentiated sarcoma
   4. Metastasis

Hyperattenuating Renal Mass on NECT

= attenuation higher than
   (a) renal parenchyma (> 40 HU)
   (b) > 20 HU (more restrictive definition)

Pathogenesis:
   (a) elevated iron content
   (b) blood breakdown products, high protein content, colloid formation
   (c) infection
   (d) transient iodine accumulation in cyst
   (e) completely solid mass
   (f) diffuse microcalcifications

A. BENIGN
   1. Complicated benign cyst: hemorrhagic, protein-rich, gelatinous (most common), eg, in autosomal dominant polycystic kidney disease
   2. Hematoma, renal contusion
   3. Vascular abnormality: AVM, pseudoaneurysm, aneurysm, thrombosed renal vein
   4. Focal inflammation: focal bacterial nephritis
   5. Angiomyolipoma (4–5% without fat)
   6. Metanephric adenoma
   7. Leiomyoma

B. MALIGNANT
   1. Malignant multiseptate cyst: multilocular cystic nephroma, cystic renal cell carcinoma
   2. Renal cell carcinoma (2% hyperattenuating)
   3. Papillary renal cell carcinoma
   4. Lymphoma (rare)
   5. Oncocytoma (rare)
   6. Metastasis from thyroid carcinoma

Fat-containing Renal Mass

1. Angiomyolipoma
2. Lipoma, liposarcoma
3. Teratoma
4. Wilms tumor
5. Xanthogranulomatous pyelonephritis

6. Oncocytoma engulfing renal sinus fat
7. Renal cell carcinoma
   (a) invasion of perirenal fat
   (b) intratumoral metaplasia into fatty marrow (in 32% of RCCs < 3 cm in diameter)

◊ If a lesion contains fat + calcium RCC is likely, NOT angiomyolipoma!

Renal Pseudotumor

= normal renal tissue mimicking a renal mass

A. PRIMARY / CONGENITAL

1. **Large column of Bertin**
   = LARGE SEPTUM / CLOISON OF BERTIN = LARGE CLOISON = FOCAL CORTICAL HYPERPLASIA = BENIGN CORTICAL REST = FOCAL RENAL HYPERTROPHY
   = persistence of normal septal cortex / excessive infolding of cortex usually in the presence of partial or complete duplication
   Location: between upper and interpolar portion
   √ mass < 3 cm in largest diameter
   √ lateral indentation of renal sinus
   √ "deformation" of adjacent calyces + infundibula
   √ mass continuous with renal cortex
   √ enhancement pattern like renal cortex
   √ echogenicity similar to cortex
2. **Dromedary hump**
   = SUBCAPSULAR NODULE = SPLENIC BUMP
   Cause: prolonged pressure by spleen during fetal development
   Location: in mid portion of lateral border of left kidney
   √ triangular contour + elongation of middle calyx
   √ enhancement pattern like renal cortex
3. **Hilar lip**
   = SUPRA- / INFRAHILAR BULGE
   = medial part of kidney above / below sinus
   Location: most frequently medial to left kidney just above renal pelvis (on transaxial scan)
   √ enhancement pattern like cortex with medulla
4. **Fetal lobation**
   = PERSISTENT CORTICAL LOBATION = REN LOBATUS
   = 14 individual lobes with centrilobar cortex located around calyces
5. **Lobar dysmorphism** complete diminutive lobe situated deep within renal substance with its own diminutive calyx in its central portion = calyx of nonresorbed normal junctional parenchyma between upper + lower subkidneys

B. ACQUIRED

1. **Nodular compensatory hypertrophy** areas of unaffected tissue in the presence of focal renal scarring from chronic atrophic pyelonephritis (= reflux nephropathy), surgery, trauma, infarction
   √ hypertrophy usually evident within 2 months; less likely to occur > age 50

√ "mass" enhances identically to renal parenchyma

DDx: accessory spleen, medial lobule of spleen, splenosis, normal / abnormal bowel, pancreatic disease, gallbladder, adrenal abnormalities

Dx: static radionuclide imaging / renal arteriography / CT

Pseudokidney Sign

= sonographic mass of reniform appearance with a central hyperechoic region surrounded by a hyperechoic region

1. Intussusception
2. Necrotizing enterocolitis
3. Midgut volvulus
4. Sigmoid volvulus
5. Crohn disease

False-positive:

feces in colon, perforated Meckel diverticulum with malrotation + Ladd bands, psoas muscle, hematoma

RENAL CYSTIC DISEASE

Potter Classification

= POTTER SYNDROME

= any renal condition associated with severe oligohydramnios

• peculiar facies with wide-set eyes, parrot-beak nose, pliable low-set ears, receding chin

Type I : infantile PCKD

Type II : multicystic dysplastic kidney disease, multilocular cystic nephroma

IIa : kidneys of normal / increased size

IIb : kidneys reduced in size

Type III : adult PCKD, tuberous sclerosis, medullary sponge kidney

Type IV : small cortical cysts / cystic dysplasia ← ureteropelvic junction obstruction

Renal Cystic Disease

A. GENETIC CYSTIC DISEASE
   1. Autosomal dominant polycystic kidney disease
   2. Autosomal recessive polycystic kidney disease
   3. Medullary sponge kidney
   4. Medullary cystic disease
   5. Glomerulocystic kidney disease

B. OBSTRUCTIVE CYSTIC DISEASE
   1. Multicystic dysplastic kidney
   2. Segmental / focal renal dysplasia
   3. Familial renal dysplasia

C. ACQUIRED CYSTIC DISEASE
   1. Simple cyst
   2. Parapelvic cyst
   3. Acquired cystic disease of uremia

4. Infectious cysts: TB, Echinococcus, abscess
5. Medullary necrosis
6. Pyelogenic cyst
7. Lithium-induced nephropathy

D. CYSTS ASSOCIATED WITH SYSTEMIC DISEASE
1. Tuberous sclerosis
2. Von Hippel-Lindau disease

E. CYSTIC TUMORS
1. Multilocular cystic nephroma
2. Cystic Wilms tumor
3. Cystic renal cell carcinoma
4. Mixed epithelial and stromal tumor

Focal Renal Cystic Disease

1. Mixed epithelial and stromal tumor
2. Multilocular cystic nephroma
3. Pyelocalyceal diverticulum

Acquired Multifocal Cystic Renal Disease

1. Glomerulocystic kidney disease
2. Lithium-induced nephropathy
3. Acquired cystic kidney disease
4. Multicystic dysplastic kidney
5. Localized cystic renal disease
6. Renal sinus cyst

Cystic Kidney Infection

1. Renal abscess
2. Renal aspergillosis
3. Renal echinococcosis

Renal Cystic Disease in Adults

A. HEREDITARY
1. Autosomal dominant polycystic kidney disease
2. Von Hippel-Lindau disease
3. Tuberous sclerosis complex
4. Medullary cystic kidney disease

B. NONHEREDITARY
1. Acquired cystic kidney disease
2. Medullary sponge kidney
3. Multicystic dysplastic kidney
4. Localized renal cystic disease

Syndromes with Multiple Cortical Renal Cysts

1. Von Hippel-Lindau syndrome
2. Tuberous sclerosis

3. Meckel-Gruber syndrome
4. Jeune syndrome
5. Zellweger syndrome = cerebrohepatorenal syndrome
6. Conradi syndrome = chondrodysplasia punctata
7. Orofacialdigital syndrome
8. Trisomy 13
9. Turner syndrome
10. Dandy-Walker malformation

Multiloculated Renal Mass

= > 3–4 septations

Rx: most multiloculated renal masses are treated with excision / nephrectomy

A. NEOPLASTIC DISEASE
   1. Cystic renal cell carcinoma
   2. Multilocular cystic renal tumor
      (a) adult cystic nephroma
      (b) cystic partially differentiated nephroblastoma
   3. Cystic Wilms tumor
   4. Necrotic tumor
      (a) mesoblastic nephroma
      (b) clear cell sarcoma

B. RENAL CYSTIC DISEASE
   1. Localized renal cystic disease
   2. Septated cyst
   3. Multicystic dysplastic kidney
   3. Segmental multicystic dysplasia
   4. Complicated cyst

C. INFLAMMATORY DISEASE
   1. Echinococcus
   2. Segmental XGP
   3. Abscess
   4. Malakoplakia

D. VASCULAR LESIONS
   1. AV fistula
   2. Organizing hematoma

ABNORMAL NEPHROGRAM

Absence of Nephrogram

Global Absence of Nephrogram

Pathophysiology: complete renal ischemia ← occlusion of main renal artery

1. Injury to vascular pedicle during blunt abdominal trauma
2. Thromboembolic disease
3. Renal artery dissection: spontaneous, traumatic, iatrogenic

Segmental Absence of Nephrogram

A. SPACE-OCCUPYING PROCESS
   1. Neoplasm
   2. Cyst
   3. Abscess

B. FOCAL RENAL INFARCTION
   1. Arterial embolus / thrombosis
   2. Vasculitis, collagen-vascular disease
   3. Sickle cell anemia
   4. Septic shock
   5. Renal vein thrombosis

Rim Nephrogram

= rim of cortex receiving collateral blood flow from capsular, peripelvic, and periureteric vessels

◊ Most specific indicator of renovascular compromise!

√ 2–4-mm peripheral band of cortical opacification

Cause:
1. Acute total main renal artery occlusion: in 50% of cases with renal infarction
2. Renal vein thrombosis
3. Acute tubular necrosis
4. Severe chronic urinary obstruction

DDx: severe hydronephrosis (rim / shell nephrogram surrounding dilated calyces)

Unilateral Delayed Nephrogram

A. OBSTRUCTIVE UROPATHY

B. REDUCTION IN RENAL blood flow
   1. Renal artery stenosis
   2. Renal vein thrombosis

Striated Nephrogram

= streaky linear bands of alternating hyper- and hypoattenuation parallel to axis of tubules + collecting ducts during excretory phase

Cause:

stasis of contrast material in dilated collecting ducts on background of edematous renal parenchyma ← diminished concentration of contrast material in tubules ← ischemia + tubular obstruction by inflammatory cells + debris

A. UNILATERAL
   1. Acute ureteric obstruction
   2. Acute bacterial nephritis / pyelonephritis
   3. Renal contusion
   4. Renal vein thrombosis

B. BILATERAL
   1. Acute pyelonephritis
   2. Intratubular obstruction: Tamm-Horsfall proteinuria, rhabdomyolysis with myoglobinuria

3. Systemic hypotension
4. Autosomal recessive PCKD
5. Medullary sponge kidney
6. Medullary cystic disease

mnemonic: CHOIR BOY

Contusion
Hypotension (systemic)
Obstruction (ureteral)
Intratubular obstruction
Renal vein thrombosis
Bacterial nephritis (acute)
Obstruction (ureteral) — it is so common!
Yes, also cystic diseases: infantile PCKD, medullary cystic disease, medullary sponge kidney

Persistent Nephrogram

A. BILATERAL GLOBAL
   1. Systemic hypotension
   2. Intratubular obstruction from protein:
      Tamm-Horsfall, Bence-Jones, myoglobin
   3. Tubular damage by contrast material
B. UNILATERAL GLOBAL
   1. Renal artery stenosis
   2. Renal vein thrombosis
   3. Urinary tract obstruction
C. SEGMENTAL
   1. Obstructed moiety of duplicated collecting system
   2. Obstructing renal calculus
   3. Obstructing neoplasm
   4. Focal stricture
   5. Focal parenchymal disease: tubulointerstitial infection

Abnormal Nephrogram due to Impaired Perfusion

A. SYSTEMIC HYPOTENSIVE REACTION as a reaction to contrast material / cardiac failure / dehydration / shock

Pathophysiology:

drop in perfusion pressure after contrast reaches kidney → increased salt + water reabsorption and slowed tubular transit

√ prolonged bilateral dense nephrograms = persistent increasing nephrogram
√ decrease in renal size
√ loss of pyelogram after initial opacification

NUC (use of glomerular filtration agent [eg, ^{99m}Tc-DTPA] preferred)
√ prolonged cortical transit + reduced excretion

B. RENAL ARTERY STENOSIS
√ decreased nephrographic opacity + rim nephrogram

√ hyperconcentration in collecting system
√ ureteral notching
NUC (glomerular filtration agent [eg, ^{99m}Tc-DTPA] preferred):
√ decreased perfusion with prolonged excretory phase

C. IMPAIRED PERFUSION OF SMALL ARTERIES
Trueta shunting = transient rerouting of blood flow from cortex to medulla
Cause:
(a) reflex vasospasm during arterial angiography ← catheter trauma / pressure injection of highly concentrated contrast medium
(b) chronic renal disorders: collagen vascular disease, malignant nephrosclerosis, chronic glomerulonephritis
(c) necrotizing vasculitis (polyarteritis nodosa), scleroderma, hypertensive nephrosclerosis
CT, Angio:
√ inhomogeneous opacification of cortex
√ **spotted nephrogram**
IVP:
√ irregular cortical nephrogram = spotted nephrogram (DDx: scleroderma, hypertensive nephrosclerosis)

D. ACUTE VENOUS OUTFLOW OBSTRUCTION in renal vein thrombosis
√ obstructive nephrogram
√ progressive increase in opacity of entire kidney

Abnormal Nephrogram due to Impaired Tubular Transit

NUC: before decrease in renal function → use of glomerular filtration agent (eg, ^{99m}Tc-DTPA); with decrease in renal function → use of plasma flow agents (eg, ^{99m}Tc-MAG_3 / ^{123}I-Hippuran®) is preferred

Cause:

A. EXTRARENAL: ureteric obstruction (eg, stone)
√ obstructive nephrogram
NUC:
√ continuous increase in renal activity
√ dilatation of collecting system

B. INTRARENAL
(a) segmental: limb of duplication system, caliceal obstruction, interstitial edema
√ segmental nephrogram
(b) protein precipitation: Tamm-Horsfall protein (a normal mucoprotein product of proximal nephrons), Bence-Jones protein (multiple myeloma), uric acid precipitation (acute urate nephropathy), myoglobulinuria, hyperproteinuric state
√ striated nephrogram
NUC:
√ prolonged cortical transit time + prolonged excretory phase

Abnormal Nephrogram due to Abnormal Tubular Function

Pathophysiology:

A. PROXIMAL TUBULE

Function: reabsorbs almost all of glucose, amino acids, phosphate, bicarbonate

- glycosuria: Toni-Fanconi syndrome
- aminoaciduria: cystinuria
- phosphaturia: phosphate diabetes, thiazides
- HCO3– wasting: proximal renal tubular acidosis

B. DISTAL TUBULE

Function: absorbs most of water

- diabetes insipidus, secretes H+
- distal renal tubular acidosis

1. Acute tubular necrosis
   √ immediate persistent nephrogram (common)
   √ progressive increasing opacity (rare)
2. Contrast-induced renal failure

Striated Angiographic Nephrogram

= random patchy densities reflecting redistribution of blood flow from the cortical vasculature to vasa recta of medulla

1. Obliterative diseases of renal microvasculature:
   polyarteritis nodosa, scleroderma, necrotizing angiitis, catheter-induced vasospasm
2. Acute bacterial nephritis
3. Renal vein thrombosis

Increasingly Dense Nephrogram

= initially faint nephrogram becoming increasingly dense over hours to days

Mechanism:

(a) diminished plasma clearance of contrast material
(b) leakage of contrast material into renal interstitial space
(c) increase in tubular transit time

Cause:

A. VASCULAR = diminished perfusion
   1. Systemic arterial hypotension (bilateral)
   2. Severe main renal artery stenosis (unilateral)
   3. Acute tubular necrosis (in 33%):
      ← contrast material nephrotoxicity
   4. Acute renal vein thrombosis

B. INTRARENAL
   1. Acute glomerular disease

C. COLLECTING SYSTEM
   1. Intratubular obstruction
      (a) uric acid crystals = acute urate nephropathy
      (b) precipitation of Bence-Jones protein = myeloma nephropathy
      (c) Tamm-Horsfall protein: in severely dehydrated infants / children
   2. Acute extrarenal obstruction: ureteral calculus

Vicarious Contrast Material Excretion during IVP

= biliary contrast material detected radiographically following intravenous administration of contrast material

Normal contrast excretion:

< 2% of urographic dose of diatrizoates + iothalamates are handled by hepatobiliary excretion

Pathophysiology: increase in protein binding ← prolonged intravascular contact + acidosis

Cause:

1. Uremia (reduction in glomerular filtration + uremia-associated acidosis)
2. Acute unilateral obstruction (increase in circulation time + transient intracellular acidosis)
3. Spontaneous urinary extravasation (prolonged vascular contact of contrast material)

RENAL DOPPLER

A. NORMAL RENAL DOPPLER

√ resistive index (RI) of 0.70 = upper limit of normal

Elevation of RI:

› significant systemic hypotension
› markedly decreased heart rate
› perinephric / subcapsular fluid collection
› in neonates + infants

B. RENAL MEDICAL DISEASE

Elevation of RI:

more likely with vascular / tubulointerstitial process: less likely with glomerular disease

May be useful in predicting clinical outcome in:

› hemolytic-uremic syndrome
› acute renal failure
› nonazotemic patients with severe liver disease

C. RENAL ARTERY STENOSIS

D. RENAL VEIN THROMBOSIS

COLLECTING SYSTEM

Spontaneous Urinary Contrast Extravasation

= SPONTANEOUS PYELORENAL BACKFLOW

Etiology: physiologic "safety valve" for obstructed urinary tract with pressures of 80–100 mmHg in collecting system ← ipsilateral ureteral obstruction ← distal stone impaction; pressure is proportional to degree + duration of acute obstruction + dose of contrast material

Prevalence: 0.1–18%; M > F (male ureter less compliant)

Criteria: absence of

(a) recent ureteral instrumentation
(b) previous renal / ureteral surgery
(c) destructive urinary tract lesion

(d) external trauma
(e) external compression
(f) pressure necrosis due to stone

Types:

1. **Pyelotubular backflow**
   = opacification of terminal portions of collecting ducts (= papillary ducts = ducts of Bellini) as a physiologic phenomenon (in 13% with low osmolality + in 0.4% with high osmolality contrast media), wrongly termed "backflow"
   √ wedge-shaped brushlike lines from calyx toward periphery
2. **Pyelosinus backflow**
   = contrast extravasation from ruptured fornices along infundibula, renal pelvis, proximal ureter; most common form
   Cx: urinoma, retroperitoneal fibrosis
3. **Pyelointerstitial backflow**
   = contrast flow from pyramids into subcapsular tubules
4. **Pyelolymphatic backflow**
   = contrast extravasation into periforniceal + peripelvic lymphatics
   √ visualization of small lymphatics draining medially
5. **Pyelovenous backflow**
   = forniceal rupture into interlobar / arcuate veins; rare

Widened Collecting System & Ureter

Fetal pyelectasis:

AP diameter of renal pelvis < 5 mm < 20 weeks MA
< 8 mm 20–30 weeks MA
< 10 mm > 30 weeks MA

A. OBSTRUCTIVE UROPATHY
B. NONOBSTRUCTIVE WIDENING
   (a) congenital
      1. Megacalycosis
         = underdevelopment of papillae; usually unilateral
      2. Congenital primary megaureter
         = widened ureter with normally tapered distal end
      3. Megacystis-megaureter syndrome
      4. Prune-belly syndrome
      5. Bardet-Biedl syndrome
      6. Beckwith-Wiedemann syndrome
      7. Megalourethra
   (b) increased urine volume
      1. High-flow states: diabetes insipidus, osmotic diuresis, dehydrated patient undergoing rehydration, unilateral kidney
      2. Vesicoureteral reflux
   (c) atony of renal collecting system
      1. Infection: ie, acute pyelonephritis

2. Pregnancy
3. Retroperitoneal fibrosis

(d) overdistended urinary bladder

(e) previous long-standing significant obstruction: dilatation remains in spite of relief of obstruction

Caliceal Abnormalities

A. OPACIFICATION OF COLLECTING TUBULES
1. Pyelorenal backflow
2. Medullary sponge kidney

B. PAPILLARY CAVITY
1. Papillary necrosis
2. Caliceal diverticulum
3. Tuberculosis / brucellosis

C. LOCALIZED CALIECTASIS
1. Reflux nephropathy = chronic atrophic pyelonephritis
2. Compound calyx
3. Hydrocalyx
4. Congenital megacalyx
5. Localized postobstructive caliectasis
6. Localized tuberculosis / papillary necrosis

D. GENERALIZED CALIECTASIS
1. Postobstructive atrophy
2. Congenital megacalices
3. Obstructive uropathy (hydronephrosis)
4. Nonobstructive hydronephrosis
5. Diabetes insipidus

Filling Defect in Collecting System

mnemonic: 6 C"s & 2 P's

Clot
Cancer
Cyst
Calculus
Candida + other fungi
Cystitis cystica
Polyp
Papilla (sloughed)

Nonopaque Intraluminal Mass in Collecting System

A. NONOPAQUE CALCULUS uric acid, xanthine, matrix
√ smooth, rounded, not attached

B. TISSUE SLOUGH
1. Papillary necrosis
2. Cholesteatoma

3. Fungus ball = conglomeration of fibrillar hyphae
4. Inspissated debris ("mucopus")

C. VASCULAR
1. Blood clot: history of hematuria
√ change in appearance over time

D. FOREIGN MATERIAL
1. Air from bladder via reverse peristalsis, direct trauma, renoalimentary fistula
2. Foreign matter

Mucosal Mass in Collecting System

A. NEOPLASTIC
(a) benign tumor
1. Aberrant papilla = papilla without calyx protruding into major infundibulum
2. Endometriosis
3. Fibroepithelial polyp

(b) malignant tumor
› uroepithelial tumors
1. Transitional cell carcinoma (85–91%)
2. Squamous cell carcinoma (7–10–15%)
Predisposing factors: calculi (50–60%), chronic infection, leukoplakia, phenacetin abuse
√ infiltrating / superficially spreading
3. Mucinous adenocarcinoma
= metaplastic transformation
4. Sarcoma (extremely rare)

› metastases: breast (most common), melanoma, stomach, lung, cervix, colon, prostate

B. INFLAMMATION / INFECTION
1. Tuberculosis
2. Candidiasis
3. Schistosomiasis
4. Pyeloureteritis cystica
5. Leukoplakia
6. Malakoplakia
7. Xanthogranulomatous pyelonephritis

C. VASCULAR
(a) submucosal hemorrhage
1. Trauma
2. Anticoagulant therapy
3. Acquired circulating anticoagulants
4. Complication of crystalluria / microlithiasis
√ thumbprinting with progressive improvement

(b) vascular notching
1. Ureteropelvic varices
2. Renal vein occlusion

3. IVC occlusion
4. Vascular malformation
5. Retroaortic left renal vein
6. "Nutcracker" effect on left renal vein between aorta and SMA
7. Polyarteritis nodosa

D. PROMINENT MUCOSAL FOLDS
1. Redundant longitudinal mucosal folds of intermittent hydronephrosis: UPJ obstruction, vesicoureteral reflux / after relief of obstruction
2. Chemical / mechanical irritation
3. Urticaria: Stevens-Johnson syndrome = erythema multiforme bullosa
4. Leukoplakia = squamous metaplasia
5. Ureteral diverticulosis = rupture of the roofs of cysts in ureteritis cystica

Effaced Collecting System

A. EXTRINSIC COMPRESSION
(a) Uni- / bilateral global enlargement of renal parenchyma
(b) Renal sinus masses
1. Hemorrhage
2. Parapelvic cyst
3. Sinus lipomatosis

B. SPASM / INFLAMMATION
(a) infection
1. Acute pyelonephritis
2. Acute bacterial nephritis
3. Acute tuberculosis
(b) hematuria

C. INFILTRATION
1. Malignant uroepithelial tumors

D. OLIGURIA
1. Antidiuretic state
2. Renal ischemia
3. Oliguric renal failure

RENAL SINUS

Renal Sinus Mass

A. TUMOR
   (a) renal pelvis
      1. Transitional cell carcinoma (90%)
      2. Squamous cell carcinoma (9%)
      3. Mucinous adenocarcinoma (1%)
   (b) renal parenchyma
      1. Renal cell carcinoma
      2. Multilocular cystic nephroma
      3. Plasmacytoma
   (c) mesenchymal tumor (rare): hemangioma, lipoma, angiomyolipoma, fibroma, leiomyoma, neurogenic tumor, teratoma; sarcomas (eg, leiomyosarcoma)
   (d) retroperitoneal
      1. Lymphoma
      2. Metastasis to sinus lymph nodes
      3. Myeloid metaplasia
B. NONTUMOROUS CONDITION
   (a) fat
      1. Sinus lipomatosis
   (b) fluid
      1. Renal sinus cyst
      2. Urinoma
   (c) vessels
      1. Renal artery aneurysm
         √ annular calcifications in > 50%
         DDx: renal calculus
      2. Arteriovenous communication
      3. Renal varix

Hypoechoic Renal Sinus

A. SOLID
   1. Fibrolipomatosis
   2. Column of Bertin
   3. Duplex kidney
   4. TCC / RCC
B. CYSTIC
   1. Renal sinus cysts
   2. Caliectasis
   3. Dilated veins, varix
   4. Aneurysm, arteriovenous malformation

RENAL CALCIFICATION

Retroperitoneal Calcification

A. NEOPLASM
   1. Wilms tumor (in 10%)
   2. Neuroblastoma (in 50%): fine granular / stippled / amorphous
   3. Teratoma: cartilage / bone / teeth, pseudodigits, pseudolimbs
   4. Cavernous hemangioma: phleboliths

B. INFECTION
   1. Tuberculous psoas abscess
   2. Hydatid cyst
   3. Alkaline-encrusted cystitis and pyelitis

C. TRAUMA
   1. Old hematoma

Nephrocalcinosis

= diffuse fine radiologically demonstrable calcifications deposited as calcium salts in renal parenchyma

DDx: **Nephrolithiasis** (= "kidney stones" = renal calculi = radiopaque / nonradiopaque hard crystalline minerals formed within lumen of the urinary tract (renal collecting system, ureter, bladder = urolithiasis)

nephros, Greek = kidney; *lithos*, Greek = stone; *calx*, Latin = lime; *calculus*, Latin = pebble; *osis*, Greek = abnormal condition = "full of"

Prevalence: 0.1–6%; M > F

Cause:

mnemonic: MARC
Medullary sponge kidney
Alkali excess
Renal medullary / cortical necrosis, **R**TA
Chronic glomerulonephritis
Hyperoxaluria, **H**ypercalcemia, **H**ypercalciuria

Medullary Nephrocalcinosis *(95%)*

= calcifications involving the distal convoluted tubules in the loops of Henle

Frequency: 95% of all nephrocalcinoses

Cause:

A. HYPERCALCIURIA
   (a) endocrine
      1. Hyperparathyroidism in 5% (1° >> 2°)
      2. Paraneoplastic syndrome of lung + kidney ← ectopic parathormone production
      3. Cushing syndrome
      4. Diabetes insipidus
      5. Hyperthyroidism / hypothyroidism
      6. Glycogen storage disease Type I
   (b) alimentary
      1. Absorptive hypercalcemia

2. Milk-alkali syndrome = excess calcium + alkali ← milk + antacids
3. Hypervitaminosis D
4. Beryllium poisoning

(c) osseous
1. Osseous metastases, multiple myeloma
2. Prolonged immobilization
3. Progressive senile osteoporosis

(d) renal
1. Medullary sponge kidney
2. Distal renal tubular acidosis (in 73% of primary RTA)
3. Chronic glomerulonephritis
4. **Bartter syndrome** tubular disorder with potassium + sodium wasting, hyperplasia of juxtaglomerular apparatus, hyperaldosteronism, hypokalemic alkalosis, and normal blood pressure

(e) drug therapy
1. Furosemide (in infants)
2. Prolonged ACTH therapy
3. Vitamin E (orally)
4. Vitamin D excess
5. Calcium (orally)
6. Nephrotoxic drugs: outdated tetracycline, amphotericin B

(f) miscellaneous
1. Sarcoidosis
2. Idiopathic hypercalciuria
3. Idiopathic hypercalcemia
4. Sjögren syndrome (distal RTA)

(g) genetic
1. Williams syndrome
2. Kenny-Caffey syndrome

B. HYPEROXALURIA = OXALOSIS

C. HYPERURICOSURIA = urate crystal deposition
1. Gouty kidney (adult)
2. Lesch-Nyhan syndrome (child)

D. URINARY STASIS
1. Milk-of-calcium in pyelocaliceal diverticulum
2. Medullary sponge kidney

E. DYSTROPHIC CALCIFICATION
1. Renal papillary necrosis ← especially analgesic nephropathy
2. Chronic pyelonephritis
3. Sickle cell disease
4. Renal tuberculosis

mnemonic: HAM HOP
Hyperparathyroidism
Acidosis (renal tubular)
Medullary sponge kidney

Hypercalcemia / hypercalciuria (sarcoidosis, milk-alkali syndrome, hypervitaminosis D)
Oxalosis
Papillary necrosis

√ normal-sized / occasionally enlarged kidneys (medullary sponge kidney)
√ small poorly defined / large coarse granular calcifications in renal pyramids:
  √ uniform deposition: hyperparathyroidism / distal renal tubular acidosis (type 1)
  √ asymmetric deposition in dilated collecting ducts within papillary tips: medullary sponge kidney

US:
  √ absence of hypoechoic papillary structures (earliest sign)
  √ hyperechoic rim at corticomedullary junction + around tip and sides of pyramids
  √ solitary focus of hyperechogenicity at tip of pyramid near fornix
  √ increased echogenicity of renal pyramids ± shadowing (no acoustic shadowing with small + light calcifications)

DDx of hyperechoic medulla in newborns:
oliguria with transient tubular blockage by Tamm-Horsfall proteinuria
Cx: often followed by urolithiasis

MEDULLARY NEPHROCALCINOSIS in CHILDREN

- NORMOCALCEMIA + HYPERCALCIURIA
  (a) iatrogenic
    1. Furosemide
    2. Corticotropin therapy
  (b) noniatrogenic
    1. Distal renal tubular acidosis
    2. Idiopathic hypercalciuria
    3. Bartter syndrome
    4. Hyperprostaglandin E syndrome
    5. Hypomagnesemia
    6. Cushing syndrome
    7. Cystinosis
    8. Glycogen storage disease Type 1
    9. Tyrosinemia
    10. Beckwith-Wiedemann syndrome
    11. Hypothyroidism
- Hypercalcemia + Hypercalciuria
  1. X-linked hypophospatemic rickets
  2. Hyperparathyroidism
  3. Hypophosphatasia
  4. Sarcoidosis
  5. Vitamin D intoxication
  6. Williams syndrome
  7. Subcutaneous fat necrosis
  8. Idiopathic infantile hypercalcemia

- Normocalcemia + Normocalciuria
  1. Acetazolamide
  2. Hyperoxaluria

Cortical Nephrocalcinosis *(5%)*

= calcium deposition in renal cortex

Frequency: 5% of all nephrocalcinoses

Cause:

1. Acute cortical necrosis
2. Chronic glomerulonephritis
3. Alport syndrome
4. Congenital oxalosis, primary hyperoxaluria
5. Chronic paraneoplastic hypercalcemia
6. Toxic: ethylene glycol, methoxyflurane
7. Sickle cell disease
8. Rejected renal transplant

mnemonic: COAG

Cortical necrosis (acute)
Oxalosis
Alport syndrome
Glomerulonephritis (chronic)

√ thin rim of calcification with a "tramline" appearance
√ spotty appearance (= preferential deposition in necrotic glomeruli)

US:

√ homogeneously increased echogenicity of renal parenchyma > liver echogenicity

Calcification of Pyelocaliceal System

1. Staghorn calculus
2. Nephrolithiasis
3. Papillary necrosis
4. Renal tuberculosis
5. Leukoplakia
6. Alkaline-encrusted pyelitis
7. Primary carcinoma of renal pelvis
8. Renal pelvic argyrosis ← contact with silver nitrate
9. Amyloidosis

Spontaneous Retroperitoneal Hemorrhage

A. RENAL TUMOR (57–63%)
   (a) malignant tumor (30–33%)
      1. RCC (33%)
      2. TCC of renal pelvis
      3. Wilms tumor
      4. Lipo-, fibro-, angiosarcoma
   (b) benign tumor (24–33%)

1. Angiomyolipoma (16–24%)
2. Lipoma
3. Adenoma
4. Fibromyoma
5. Ruptured hemorrhagic cyst

B. VASCULAR DISEASE (18–26%)
1. Ruptured renal artery aneurysm
2. Vasculitis: eg, polyarteritis nodosa in 13%
3. Arteriovenous malformation
4. Segmental renal infarction

C. INFLAMMATION / INFECTION (7–10%)
1. Abscess (in 50% of infections)
2. Acute / chronic nephritis

D. COAGULOPATHY
1. Anticoagulant therapy (in 4.3–6.6% of IV heparin, in 01.–0.6% of oral anticoagulants)
Source: idiopathic (42%), tumor (21%), stone disease (17%), hemorrhagic cystitis
2. Bleeding diathesis
3. Long-term hemodialysis

E. PRIMARY ADRENAL CYST / TUMOR
1. Pheochromocytoma
◊ Massive bleed ← an undiagnosed pheochromocytoma has been lethal in 50%!
2. Pseudocyst
3. Myelolipoma
4. Hemangioma
5. Adrenocortical adenoma / carcinoma
6. Metastasis

• flank pain of sudden onset

◊ Follow-up CT may be indicated at 3 and 6 months if the source of blood remains indeterminate!

◊ Surgical exploration must be considered to uncover a small renal tumor if the cause of hemorrhage is not determined radiologically!

Subcapsular Hematoma

√ subcapsular mass with flattening of renal parenchyma

√ total resorption / formation of pseudocapsule with calcification

Angio:

√ avascular mass

Cx: Page kidney (ischemia, release of renin, HTN)

URETER

Congenital Ureteral Abnormalities

A. URETERAL DUPLICATION (most common)
1. Complete ureteral duplication
2. Partial ureteral duplication

B. SMOOTH MUSCLE DYSFUNCTION
   1. UPJ obstruction
   2. Primary megaureter
C. ABNORMAL TERMINATION OF SINGLE URETER
   1. Ectopic ureter
   2. Ureterocele
   3. Vesicoureteral reflux

Ureteral Deviation in Course

A. LUMBAR URETER
   (a) lateral deviation (common)
      1. Hypertrophy of psoas muscle
      2. Enlargement of paracaval / para-aortic lymph nodes
      3. Aneurysmal dilatation of aorta
      4. Neurogenic tumors
      5. Fluid collections: abscess, urinoma, lymphocele, hematoma
   (b) medial deviation
      1. Retrocaval ureter (on right side only)
      2. Circumcaval ureter
      3. Retroperitoneal fibrosis
      4. Inflammatory aortic aneurysm
B. PELVIC URETER
   (a) medial deviation
      1. Hypertrophy of iliopsoas muscle
      2. Enlargement of iliac lymph nodes
      3. Aneurysmal dilatation of iliac vessels
      4. Bladder diverticulum at UVJ (= Hutch diverticulum)
      5. Following abdominoperineal surgery + retroperitoneal lymph node dissection
      6. Pelvic lipomatosis
   (b) lateral deviation with extrinsic compression
      1. Pelvic mass: eg, fibroids, ovarian tumor
      2. Herniated ureter through inguinal canal
C. INTENTIONAL SURGICAL DIVERSION
   ileal conduit, continent cutaneous diversion, orthotopic neobladder

Ureteral Dilatation / Hydroureter

A dilated ureter is not necessarily obstructed; an obstructed ureter is not always dilated.

Size of ureter: > 3 mm

A. OBSTRUCTION
   1. Ureterolithiasis
B. CONGENITAL
   1. Chronic vesicoureteral reflux
   2. Posterior urethral valves
   3. Megaloureter

4. Prune-belly syndrome
5. Ectopic ureter
6. Ureterocele

C. INFECTION / INFLAMMATION impairing ureteral peristalsis
1. UTI: eg, E. coli, Pseudomonas, Citrobacter
2. Appendicitis
3. Diverticulitis

D. COMPRESSION
1. Pelvic / abdominal mass
2. Vessel:
   › retroiliac / retrocaval course of ureter
   › ovarian vein syndrome

Unilateral Hydroureter

(a) obstruction: calculus, tumor, clot, sloughed papilla, stricture, extrinsic compression, mass effect
(b) resolved obstruction (if distension was severe)

Bilateral Hydroureter

1. Polyuria / diuresis
2. Bladder outlet obstruction
3. Neurogenic bladder
4. Pregnancy: R > L

Megaureter

A. VESICOURETERAL REFLUX
(a) primary vesicoureteral reflux
1. Primary reflux megaureter
   Cause: abnormal ureteral tunnel at UVJ
2. Prune belly syndrome

(b) secondary vesicoureteral reflux
1. Hypertonic neurogenic bladder
2. Bladder outlet obstruction
3. Posterior urethral valves

B. OBSTRUCTION
(a) primary obstruction
1. Intrinsic ureteral obstruction: stone, stricture, tumor
2. Ectopic ureter
3. Ureterocele
4. Ureteral duplication
   √ tortuous dilated ureter of upper moiety

(b) secondary obstruction
1. Retroperitoneal obstruction: tumor, fibrosis, aortic aneurysm
2. Bladder wall mass
3. Bladder outlet obstruction: eg, prostatic enlargement

C. nonreflux-nonobstructed MEGAURETER
   1. Congenital primary megaureter = megaloureter
   2. Polyuria: eg, diabetes insipidus, acute diuresis
   3. Infection
   4. Ureter remaining wide after relief of obstruction

mnemonic: DiaPOUR
Diabetes insipidus
Primary megaureter
Obstruction (recent / old)
UVJ obstruction
Reflux

Ureteral Stricture

A stricture is a fixed narrowing with proximal dilatation.

A. INTRINSIC CAUSE
   (a) mucosal
      1. Primary ureteral tumors
      2. Inflammation ← stone passage
   (b) mural
      1. Endometriosis
         common disorder in menstruating women (15%); ureteral involvement is rare and indicates widespread pelvic disease
         √ abrupt smooth stricture of 0.5–2.5 cm length
         √ rectosigmoid involvement on BE
      2. Infection: tuberculosis, schistosomiasis
      3. Traumatic / iatrogenic
         ureterolithotomy, endoscopic stone extraction, gynecologic procedures (esp. hysterectomy), ureteral anastomosis (urinary diversion)
      4. Amyloidosis
         √ distal stricture with submucosal calcification
      5. Nonspecific (rare)

B. EXTRINSIC CAUSE
   1. Endometriosis: extrinsic form÷intrinsic form = 4÷1
   2. Abscess: tuboovarian, appendiceal, perisigmoidal
   3. Inflammatory bowel disease: eg, Crohn disease, diverticulitis
   4. Radiation fibrosis
   5. Tumor encasement / metastasis: cervix, endometrium, ovary, rectum, prostate, breast, lymphoma
   6. Iliac artery aneurysm → perianeurysmal fibrosis

mnemonic: MISTER
Metastasis (extrinsic / intrinsic)
Inflammation from calculus
Schistosomiasis
Tuberculosis, **T**ransitional cell carcinoma, **T**rauma

Endometriosis + other periureteral inflammatory process
Radiation therapy, **R**etroperitoneal fibrosis

Physiologic narrowing is common and characterized by absence of proximal dilatation and rapid changeability.

DDx: Physiologic narrowing
1. Ongoing peristalsis → incomplete opacification resolved on delayed images
2. Anatomic: UPJ, pelvic brim, UVJ, abrupt turn / kink

Ureteral Filling Defect

A. FIXED
   (a) neoplasm
      1. Urothelial neoplasm
      2. Metastasis
      3. Fibroepithelial polyp
   (b) inflammation / infection
      1. Polyureteritis cystica
      2. Tuberculosis
      3. Fungus: Candida, Aspergillus
      4. Schistosomiasis
      4. Endometriosis
B. MOBILE
   1. Stone = urolithiasis
   2. Sloughed papilla
   3. Blood clot
      Cause: trauma, stone, malignancy, anticoagulation
      √ NO enhancement
      √ density of > 50 HU relative to urine and surrounding soft tissues on NECT
      √ clot resolution at follow-up imaging studies
C. MULTIPLE
   1. Polyureteritis cystica
   2. Malakoplakia
   3. Multifocal urothelial cell cancer

Any ureteral filling defect of soft-tissue attenuation must be considered malignant and requires ureteroscopic assessment, biopsy, and cytologic analysis.

Ureteral Calcification

A. URETERAL LUMEN
   1. Stone: migrated from kidney
   2. Stone: in ureteral diverticulum / ureterocele
   3. Stone street = “Steinstrasse” = collection of stone fragments in distal ureter following lithotripsy
B. URETERAL WALL
   1. Schistosomiasis
   2. Tuberculosis

3. Amyloid infiltration
4. Ureteral tumor

DDx: (1) Phlebolith in gonadal vein (multiple, not along course of ureter, centrally radiolucent)
(2) Orally administered contrast material trapped in appendix / diverticulum
(3) Dermoid cyst with calcification
(4) Silastic fallopian tube band
(5) Radiation seeds used for prostate cancer

URINARY BLADDER

Bilateral Narrowing of Urinary Bladder

A. WITH ELEVATION OF BLADDER FLOOR
1. Pelvic lipomatosis
2. Pelvic hematoma
Cause: trauma, anticoagulant therapy, spontaneous rupture of blood vessels, blood dyscrasia (rare), bleeding neoplasm (rare)
3. Chronic cystitis

B. WITH SUPERIOR COMPRESSION OF BLADDER
1. Thrombosis of IVC
Cause: trauma, hypercoagulability state (oral contra-ceptives), extension of thrombi from lower extremity, abdominal sepsis, Budd-Chiari syndrome, compression of IVC by neoplasm
√ collaterals: ← gonadal veins, ascending lumbar veins, vertebral plexus, retroperitoneal veins, portal vein (via hemorrhoidal veins)
√ notching of distal ureter by ureteral veins
2. Pelvic lymphadenopathy
Cause: lymphoma (most often), prostatic carcinoma
√ polycyclic asymmetric compression of bladder
√ medial displacement of pelvic segment of ureters
√ lateral displacement of upper ureters
3. Hypertrophy of iliopsoas muscles
4. Bilateral pelvic masses
(a) bilateral lymphocysts (after radical pelvic surgery)
(b) bilateral urinomas
(c) bilateral pelvic abscesses
5. Retroperitoneal fibrosis
6. Large iliac artery aneurysms

Inverted Pear / Teardrop-shaped Urinary Bladder

mnemonic: PHALL
Psoas hypertrophy
Hematoma (pelvic)
Aneurysm (bilateral common / external iliac artery)

Lipomatosis, pelvic
Lymphadenopathy (pelvic)

Small Bladder Capacity

Cause:

A. THICKENED / FIBROTIC BLADDER WALL
   1. Interstitial cystitis
   2. Tuberculous cystitis
   3. Cystitis cystica
   4. Schistosomiasis
   5. Trauma: surgical resection, radiation therapy

B. DISUSE OF BLADDER

- urinary frequency
- progressive rise in bladder pressure during filling

√ reduced bladder compliance
√ thickened bladder wall + decreased bladder volume
√ vesicoureteral reflux

Bladder Wall Thickening

Normal bladder wall thickness (regardless of age + gender):
< 5 mm in nondistended bladders
< 3 mm in well-distended bladders

A. TUMOR
   1. Neurofibromatosis

B. INFECTION / INFLAMMATION
   1. Cystitis

C. MUSCULAR HYPERTROPHY
   1. Neurogenic bladder
   2. Bladder outlet obstruction (eg, posterior urethral valves)

D. UNDERDISTENDED BLADDER

Urinary Bladder Wall Masses

A. CONGENITAL
   1. Congenital septum
   2. Simple ureterocele
   3. Ectopic ureterocele

B. BLADDER TUMOR

C. INFLAMMATION / INFECTION
   1. Cystitis: hemorrhagic cystitis, abacterial cystitis, bullous cystitis, edematous cystitis, interstitial cystitis, cystitis cystica, eosinophilic cystitis, granulomatous cystitis, emphysematous cystitis, cyclophosphamide cystitis, cystitis glandularis (premalignant lesion with villous lesions in bladder dome from proliferation of “intestinelike” glands in submucosa)
   2. Tuberculosis
   3. Schistosomiasis

4. Malakoplakia
5. Extravesical inflammation:
   (a) Diverticulitis
   (b) Crohn disease
   (c) endometriosis

D. HEMATOMA
after instrumentation, surgery, trauma

Bladder Tumor

Frequency: 2–6% of all tumors

A. EPITHELIAL TUMORS (95%)
1. Urothelial carcinoma = transitional cell carcinoma (90%)
2. Squamous cell carcinoma (4% in USA) worst prognosis; ← chronic disorders (chronic irritation from indwelling catheters, infection, stricture, calculi), cyclophosphamide, smoking, intravesical bacillus Calmette-Guérin, bladder diverticula, schistosomiasis (> 50% of bladder tumors in countries with endemic bilharziasis)
3. Adenocarcinoma (1%) most common in bladder exstrophy, less common in cystitis glandularis + urachal carcinoma
   ◊ Metastatic adenocarcinoma (← colon, prostate, rectum) more common than primary
4. Small cell / neuroendocrine carcinoma (< 0.5%)
   = highly aggressive tumor with invasive disease in 94% at presentation
   Age: 20–91 years; M÷F = 3÷1 to 5÷1
   • hematuria (88%)
   Size: 3–8 cm
   √ large polypoid / nodular tumor
   Prognosis: 16% 5-year survival rate
5. Carcinoid
   Mean size: 6 mm
6. Melanoma (extremely rare)

B. NONEPITHELIAL / MESENCHYMAL TUMORS
(a) primary benign bladder tumor originating from
› muscle
1. **Leiomyoma** (0.43%)
   ◊ Most common nonepithelial tumor
   Age: 22–78 years; M÷F = 1÷1
   • hematuria ← ulceration
   Location: arise in submucosa
   Site: submucosal (7%) / intravesical (63%) / extravesical (30%)
   √ solid homogeneous mass
   √ smooth indentation of bladder wall
   √ intraluminal mass ± degeneration
2. Rhabdomyoma (rare)

› nerve
1. **Neurofibroma** / NF1 in 60%
   √ typically of low attenuation on CT

√ hypointense mass on T1WI
√ "target" sign on T2WI in plexiform neurofibroma= central hypointense fibrosis surrounded by hyperintense myxoid stroma

2. **Paraganglioma** = pheochromocytoma (0.1%)
◊ 1% of all pheochromocytomas
Age: 10–78 years; M < F
Origin: paraganglia of bladder wall
- adrenergic attack in 50% during micturition ("micturition attack") or bladder filling (headaches, weakness)
- intermittent hypertension
- elevated catecholamine levels

√ submucosal mass
√ ring calcification around circumference
√ marked enhancement (KEY FEATURE)
N.B.: biopsy may incite hypertensive crisis!
Prognosis: 7% are malignant

› fat
1. Lipoma

› fibrous tissue
1. Fibroma
2. Solitary fibrous tumor

› blood vessels
1. Hemangioma
Age: 58 (range, 19–76) years during adulthood; 50% during childhood
Median size: 7 (range, 2–30) mm
2. Plasmacytoma
3. Nephrogenic adenoma
Associated with: cystitis cystica / cystitis glandularis

(b) primary malignant bladder tumor

1. **Primary lymphoma**
◊ 2nd most common nonepithelial tumor of bladder
Age: 40 years; M÷F = 1÷3
Histo: low-grade B-cell mucosa-associated lymphoid tissue (MALT) / diffuse large B-cell type
Location: submucosa; at base + trigone of bladder

2. **Rhabdomyosarcoma**
Age: 1st and 2nd decades of life
◊ Most common bladder tumor in patients < 10 years

3. **Leiomyosarcoma**
◊ Most common nonepithelial malignant bladder tumor
Age: mainly > 40 (range, 25–88) years; M÷F = 3÷1
Location: rarely at trigone
Mean size: 7 cm
√ poorly circumscribed invasive mass

√ heterogeneous texture ← necrosis (common)

4. Osteosarcoma

(c) secondary bladder tumor

1. Metastases
   1.5% of all bladder malignancies
   Origin: melanoma > stomach > breast > kidney > lung
   √ solitary / multiple nodules
2. Lymphoma
   autoptic bladder involvement in 15% of NHL, in 5% of Hodgkin disease
3. Leukemia
   microscopic involvement in 22% at autopsy
4. Direct extension (common)
   ← prostate, rectum, sigmoid, cervix, ovary
5. Endometriosis
   Location: on posterior wall
   • urinary symptoms in 80%

Bladder Calcification

Bladder Calculus

1. **Stasis calculus** (70%)
   in bladder outflow obstruction, bladder diverticula, cystocele, neuropathic bladder dysfunction
   Associated with: gram-negative lower urinary tract infection (in 30%), esp. Proteus
2. **Migrant calculus**
   = renal calculi spontaneously passing into bladder
3. **Foreign body nidus calculus**
   ← self-introduced objects, urinary stent, chronic catheterization, bladder wall-penetrating bone fragments, prostatic chips, nonabsorbable suture material, fragments of Foley balloon catheter, pubic hair, presence of intestinal mucosa (in bladder augmentation, ileal conduit, repaired bladder exstrophy)
4. **Idiopathic / primary / endemic calculus**
   Countries: North Africa, India, Indonesia
   Age: in young boys of low socioeconomic class (nutritional deficiency?)

Prevalence: India (13÷100,000); less common in western hemisphere
Number of stones: solitary (86%); multiple (in up to 25%)
Composition: magnesium ammonium phosphate (50%), calcium salts (31%), uric acid origin (5%)

• hematuria, recurrent UTIs, pelvic pain, irritative / obstructive voiding symptoms
Rx: surgical extraction, lithotripsy, alkalinization of urine
Rate of recurrence: 41%

Bladder Wall Calcification

A. INFLAMMATION

1. Schistosomiasis (50%)

√ relatively normal distensibility of bladder
√ thin arcuate pattern of calcification

2. Tuberculosis
   √ bladder markedly contracted
3. Cystitis: postirradiation cystitis, alkaline incrusted cystitis and pyelitis, cytotoxin cystitis
4. Bacillary UTI (extremely uncommon)
5. Encrusted foreign material

B. NEOPLASM
1. Primary neoplasm of bladder: TCC, squamous cell carcinoma, leiomyosarcoma, hemangioma, neuroblastoma, osteogenic sarcoma
2. Urachal carcinoma

mnemonic: SCRITT
Schistosomiasis
Cytoxan
Radiation
Interstitial cystitis
Tuberculosis
Transitional cell carcinoma

Mass Extrinsic to Urinary Bladder

A. NORMAL / ENLARGED ORGAN
1. Uterus: leiomyomatous uterus, pregnant uterus
2. Distended rectosigmoid
3. Ectopic pelvic kidney
4. Prostate cancer / BPH

B. SOLID PELVIC TUMOR
1. Lymphadenopathy
2. Bone tumor ← sacrum / coccyx
3. Rectosigmoid mass
4. Hip arthroplasty
5. Neurogenic neoplasm, meningomyelocele
6. Pelvic lipomatosis / liposarcoma

C. CYSTIC PELVIC LESION
(a) congenital / developmental
1. Urachal cyst
2. Müllerian duct cyst
3. Gartner duct cyst
4. Anterior meningocele
5. Hydrometrocolpos

(b) related to trauma
1. Hematoma: eg, rectus sheath hematoma
2. Urinoma
3. Lymphocele
4. Abscess

5. Aneurysm
6. Mesenteric cyst

(c) cyst of genitalia
1. Prostatic cyst
2. Cyst of seminal vesicle
3. Cyst of vas deferens
4. Ovarian cyst
5. Hydrosalpinx
6. Vaginal cyst

(d) cyst of urinary bladder
1. Bladder diverticulum

(e) cyst of GI tract
1. Peritoneal inclusion cyst
2. Fluid-filled bowel

Bladder Perforation

A. Trauma
1. Blunt trauma
2. Penetrating trauma
3. Iatrogenic: pelvic surgery, cystoscopy, suprapubic or transurethral placement of a Foley catheter (especially a long-term indwelling catheter), bladder biopsy, ureteral stent manipulation

B. Spontaneous

Pathophysiology: increase in bladder pressure + weakening of mucosa
1. Urinary tract infection
2. Urinary retention
3. Vaginal delivery
4. Alcoholism
5. Bladder calculi
6. Radiation therapy
7. Foley catheter malposition

VOIDING DYSFUNCTION

A. FAILURE TO STORE URINE
- urinary frequency, urgency, incontinence

(a) bladder causes
1. Involuntary detrusor contractions
   - › detrusor instability: idiopathic / neurogenic
   - › detrusor hyperreflexia ← upper cord lesion
2. Poor bladder compliance
   - › detrusor hyperreflexia
   - › bladder wall fibrosis
3. Sensory urgency
   - › infection, inflammation, irritation
   - › neoplasia

4. Vesicovaginal fistula
5. Psychogenic condition

(b) sphincter causes
1. Stress incontinence
2. Sphincteric incontinence

(c) extravesical ectopic insertion of ureter in females

B. FAILURE TO EMPTY BLADDER
- poor flow, straining, hesitancy
- inability to completely empty bladder

(a) bladder causes
1. Detrusor areflexia ← sacral arc lesion
2. Impaired detrusor contractility ← myogenic
3. Psychogenic condition

(b) bladder outlet obstruction
1. Bladder neck contracture
2. Prostatic enlargement
3. Detrusor-external sphincter dyssynergia
4. Scarring from surgery / radiation therapy
5. Ectopic ureterocele
6. Urethral stenosis
7. Urethral kinking: eg, ← cystocele

Urinary Incontinence

1. Stress incontinence
2. Vesicovaginal / ureterovaginal fistula
3. Urge incontinence
4. Psychogenic incontinence
5. Overflow incontinence
   ← lesions of sacral spinal cord / sacral reflex arc or severe outlet obstruction
6. Reflex voiding
   (a) hyperreflexive lesion ← lesion of upper spinal cord
   (b) uninhibited / unstable bladder
7. Continual dribbling
   = extravesical ectopic termination of ureter

Associated with pelvic floor dysfunction:
1. Stress urinary incontinence
2. Overactive bladder = urge incontinence
3. Bladder outlet obstruction

Stress Incontinence

= SPHINCTER WEAKNESS INCONTINENCE= URETHRAL INCOMPETENCE
= involuntary loss of urine during physical activity such as coughing, sneezing, laughing, exercise

Cause:
(a) male: S/P prostatectomy with damage to distal sphincter

(b) female: congenital bladder neck weakness, pregnancy, childbirth, aging ← changes in anatomic relationship of urethra + bladder base

• frequency, urgency (involuntary filling of bladder neck)
√ opening of bladder neck during coughing
√ impairment of milk-back mechanism (= retrograde emptying of urethra during interruption of voiding phase does not occur)
√ urethrovesical descent (in types I + II)

Chain cystography:
√ posterior urethrovesical angle (= angle between posterior urethra + bladder base) increased > 100°
√ upper urethral axis (= angle between upper urethra + vertical line) increased > 35°

MR:
√ urethral hypermobility (80–90%) ← laxity of urethral supporting structures:
√ rotational descent during straining = rotation of urethral axis from vertical to horizontal to a position > 30° from its resting axis
√ funneling = bladder neck + proximal urethra pushed low + appearing widely patent (SAG view)

Detrusor Instability

= MOTOR URGE INCONTINENCE = UNSTABLE BLADDER
= sudden contraction of detrusor muscle often related to inflammation / infection / nervous system diseases
◊ Condition resembles that of immature bladder before toilet training

Pathophysiology: likely induced by bladder outlet obstruction

Patient groups:
(1) Symptoms of nocturnal enuresis + frequency / incontinence dating back to childhood
(2) Idiopathic instability occurring in middle age
(3) Outflow obstruction commonly in men with BPH / women with pelvic floor dysfunction
(4) Degenerative instability ← cardiovascular + neurologic disease later in life

• frequency, urgency, urge incontinence, occasionally nocturia
• hesitancy + difficulty in voiding may occur in men without significant prostatic hypertrophy
√ involuntary bladder contractions with NO relationship to bladder distension
√ progressively vigorous contractions during bladder filling
√ postural instability limited to upright position
√ impaired milk-back mechanism ← high bladder pressure
√ strong contractions following bladder emptying

Cx: thickening of bladder wall, bladder diverticula
Rx: treatment of obstruction, anticholinergic drug (oxybutynin), operative increase in bladder capacity

Sensitive Bladder (Sensory Urgency)

Cause: cystitis (reduced compliance), some cases of stress incontinence (filling of bladder neck induces urgency)

• frequency, urgency, sometimes nocturia
√ patient uncomfortable with low bladder filling
√ no abnormal rise in bladder pressure
√ normal voiding function

Detrusor-Sphincter Dyssynergia

= overactivity of bladder neck muscle with failure to relax at beginning of voiding
Cause: spinal cord lesion / trauma above level of sacral outflow
• difficulty in voiding ± frequency
• lifelong history of poor stream
√ collarlike indentation of bladder neck during voiding (= persistent / intermittent narrowing of membranous urethra)
√ may have high voiding pressure + reduced flow
√ trapping of contrast in urethra during interruption of flow
√ massive reflux into prostatic ducts during voiding ← high pressure within prostatic urethra
√ severely trabeculated "Christmas-tree" bladder + bilateral hydroureteronephrosis
Rx: bladder neck incision

Hinman Syndrome

= NONNEUROGENIC NEUROGENIC BLADDER [NNNB] = DETRUSOR-SPHINCTER DYSSYNERGIA
Cause: no neurologic / anatomic obstructive disease; distinctly abnormal family dynamics (in 50%)
Age: some time after toilet training with onset during early / late childhood / puberty
• clinical criteria:
(1) Intact perineal sensation + anal tone
(2) Normal anatomy + function of lower extremities
(3) Absence of skin lesions overlying sacrum
(4) Normal lumbosacral spine at plain radiography
(5) Normal spinal cord at MR imaging
√ high-pressure uninhibited detrusor contractions
√ lack of coordination between detrusor contraction + periurethral striated sphincter relaxation
√ inability to suppress bladder contractions
√ normal response of detrusor muscle to reflex stimulation
√ increased bladder capacity + pressure
√ sphincter activity may increase paradoxically during detrusor contraction
US:
√ trabeculated bladder
√ dilatation of upper urinary tracts
√ renal damage
VCUG:
√ urethra normal during early voiding
√ urethral distension after contraction of external sphincter as voiding progresses
√ ureterovesical obstruction / reflux

Rx: suggestion therapy + hypnosis, bladder retraining, biofeedback, anticholinergic drugs

Wetting

1. Enuresis
   = manifestation of neuromuscular vesicourethral immaturity; M÷F = 3÷2
   • intermittent wetting, usually at night during sleep
   • often positive history of enuresis from one parent
   • normal physical examination
   √ no structural abnormality; urography NOT indicated
2. Epispadia
3. Sacral agenesis
   = segmental defect (below S2) with deficiency of nerves that innervate bladder, urethra, rectum, feet
   ◊ Children of diabetic mothers are affected in 17%!
4. Extravesical infrasphincteric ectopic ureter
   only affects girls, as boys do NOT have infrasphincteric ureteral orifices
   (a) ureter draining upper pole of duplex system → exits below urethral sphincter (90%)
   (b) ureter draining single system → ectopic extravesical orifice (10%)
5. Synechia vulvae
   = adhesive fusion of minor labia → directs urine primarily into vagina, from where it dribbles out post micturition
6. Vaginal reflux
   in obese older girls with fat thighs and fat labia
7. Miscellaneous
   posterior urethral valves, urethral stricture, urethral diverticula

Prostatic Obstruction

= urethral compression by hypertrophic prostatic tissue
• difficulty in voiding, reduction in flow rate
√ high-pressure bladder
√ slow + prolonged flow
√ increase in bladder capacity with reduced contractility (late)

SCROTUM

Acutely Symptomatic Scrotum

= acute unilateral scrotal swelling ± pain
Cause:
epididymitis÷torsion = 3÷2 < 20 years of age
epididymitis÷torsion = 9÷1 > 20 years of age

A. ISCHEMIA
   1. Acute testicular torsion (20%)
   2. Torsion of appendix testis
   3. Testicular infarction

B. INFECTION / INFLAMMATION (75–80%)

1. Acute epididymitis
2. Orchitis
3. Intrascrotal abscess
4. Henoch-Schönlein purpura
5. Kawasaki syndrome
6. Insect bite
7. Acute hydrocele
8. Fournier gangrene

C. HEMORRHAGE
1. Testicular trauma
2. Hemorrhage into testicular tumor

D. HERNIA
1. Scrotal fat necrosis
2. Strangulated hernia

Scrotal Wall Thickening

1. **Acute idiopathic scrotal edema**
   Frequency: 20–30% of all acute scrotal disorders
   Age: 5–11 years (range, 18 months to 14 years)
   • subcutaneous scrotal edema, erythema
   • minimal pain, afebrile, peripheral eosinophilia
   Prognosis: spontaneous resolution in 72 hours to 4 days
2. Epididymo-orchitis
3. Testicular torsion
4. Torsion of testicular / epididymal appendage
5. Trauma
6. Henoch-Schönlein purpura
7. Cx of ventriculoperitoneal shunt
8. Cx of peritoneal dialysis ← ? leakage of fluid into the anterior abdominal wall with dissection into scrotum
9. Acute hemorrhagic edema of infancy
   = similar to Henoch-Schönlein purpura
   Age: 5 months – 2 years

Testicular Blood Flow

Increased Testicular Blood Flow

1. Orchitis
2. Torsion-detorsion sequence
3. Torsion of appendix testis / epididymis
4. Abscess
5. Tumor

Decreased Testicular Blood Flow

1. Torsion
2. Infarct

Scrotal Gas

1. Fournier gangrene
2. Scrotal abscess
3. Scrotal hernia with gas-containing bowel
4. Scrotal emphysema from bowel perforation
5. Extension of subcutaneous emphysema
6. Air leakage + dissection ← faulty chest tube positioning

Groin Mass

A. CONGENITAL
   1. Encysted hydrocele
      = peritoneal fluid remnant of processus vaginalis
      (a) of spermatic cord (male)
      (b) of canal of Nuck (female equivalent)
   2. Retractile testis

B. HERNIA
   1. Inguinal-scrotal hernia
   2. Femoral hernia

C. VASCULAR
   1. Hematoma
   2. Pseudoaneurysm
   3. Varicocele
   4. Varices of greater saphenous vein

D. INFECTIOUS / INFLAMMATORY
   1. Inflammation of ileopectineal bursa
   2. Synovial osteochondromatosis of hip joint
   3. Groin abscess

E. NEOPLASM
   1. Lipoma (most common benign tumor)
   2. Inguinal lymph node metastases ← cancer of lower vagina, vulva, penis, lower rectum, anus, lower extremity

Scrotal mass

US is used to distinguish between
(a) intratesticular masses (more commonly malignant) and extratesticular masses (more commonly benign)
(b) intratesticular solid masses (often malignant) and cystic lesions (usually benign).

Most frequent conditions:

1. Inflammation 48%
2. Hydrocele 24%
3. Torsion 9%
4. Varicocele 7%
5. Spermatocele 4%

6. Cysts 4%
7. Malignant tumor 2%
8. Benign tumor 0.7%

◊ Sonographic differentiation of intra- from extratesticular masses is 80–95% accurate!

MRI's ability to characterize soft tissue helps to differentiate benign from malignant neoplasms or predict the presence of malignant disease.

Benign Tumors and Tumorlike Conditions

= benign mesenchymal tumors

1. Lipoma
2. Hemangioma
3. Lymphangioma
4. Leiomyoma
5. Nerve sheath tumor
6. Angiomyofibroblastoma (AMF)-like tumor
7. Fibrous pseudotumor

Intratesticular Mass

◊ 90–95% of testicular tumors are malignant!

(a) benign
   1. Leydig cell hyperplasia
   2. Intratesticular lipoma
   3. Adrenal rest tumor

(b) potentially malignant
   1. Leydig cell tumor
   2. Sertoli cell tumor

(c) malignant
   1. Germ cell tumor
   2. Lymphoma

(d) pseudotumor
   1. Orchitis
   2. Abscess
   3. Testicular infarction
   4. Testicular hematoma
   5. Postbiopsy defect

MULTIPLE INTRATESTICULAR MASSES

1. Lymphoma / leukemia
2. Primary testicular tumor
3. Chronic infection: epididymo-orchitis
4. Metastases: ← prostate, kidney, melanoma
5. Granulomatous disease: sarcoidosis, TB
6. Leydig cell hyperplasia

◊ The prevalence of synchronous / metachronous bilateral testicular neoplasms is 1–3%!

PREPUBERTAL TESTICULAR MASS

◊ Only 0.5–5.0% of all intratesticular tumors occur in patients < 15 years of age

A. Primary tumor
   (a) Germ cell tumors (70–90%):
      1. Yolk sac tumor ≤ 2 years
      2. Teratoma ≤ 5 years
   (b) Sex cord-stromal tumors (10–30%):
      1. Leydig cell tumor 3–9 years
      2. Sertoli cell tumor commonly < 1 year
      3. Gonadoblastoma after puberty
      4. Fibroma, lipoma, hemangioma, sarcoma, adrenal rest

B. Secondary tumor
   1. Lymphoproliferative tumor: leukemia, lymphoma
   2. Solid tumor: Wilms, neuroblastoma, rhabdomyosarcoma, retinoblastoma
   3. Others: sinus histiocytosis, Langerhans cell histiocytosis, tuberculous orchitis

Paratesticular Mass

◊ Only 4% of all scrotal tumors!

paratesticular = group of extratesticular lesions not readily identified as originating from a particular tissue

PARATESTICULAR INFLAMMATORY MASS

1. Sarcoidosis of epididymis
2. Inflammatory nodule of epididymitis
3. **Sperm granuloma**
   = foreign body giant cell reaction to extravasated sperm
   Autopsy: in 42% of postvasectomy patients
   Location: cut end of vas deferens
   √ well-defined hypoechoic solid mass / masses
4. **Scrotal calculi** = "scrotal pearls"
   = freely mobile calcified bodies between layers of tunica vaginalis
   Cause: fibrinous debris in long-standing hydrocele / following torsion of appendix testis or epididymis / dislodged fibrous pseudotumor
   √ central nidus of discrete acoustic shadow / "comet-tail" artifact (= calcium hydroxyapatite) surrounded by fibrous tissue
5. **Sclerosing lipogranuloma**
   (a) primary sclerosing lipogranuloma
   (b) secondary sclerosing lipogranuloma
   Cause: injection of liquid paraffin, vegetable oil, silicon into scrotal sac
   √ gradually increasing hypoechoic mass
   √ heterogeneous mass with intravoxel fat SI on MRI
   √ avid heterogeneous enhancement
6. Spermatic cord hematoma

PARATESTICULAR TUMOR

◊ The majority of paratesticular tumors are derived from the spermatic cord!

◊ Sarcomas are the most common spermatic cord tumor!

A. EPIDIDYMAL TUMOR
B. SPERMATIC CORD TUMOR
   (a) benign: lipoma > fibroma > dermoid cyst > lymphangioma
   (b) malignant: sarcoma
C. SCROTAL TUNICA TUMOR

Benign Paratesticular Tumor (75–97%)

1. Spermatic cord lipoma (most common)
2. Adenomatoid tumor (2nd most common)
3. Fibrous pseudotumor of scrotum (3rd)
4. Epidermoid inclusion cyst
5. Polyorchidism
6. Leiomyoma
7. Cord fibroma
   = reactive nodular proliferation of paratesticular tissue
8. **Papillary epididymal cystadenoma**
   Frequency: in up to 60% of patients with Von Hippel-Lindau disease
   √ solid mass with a few cystic spaces
   √ multiloculated cystic lesion with small papillary projections
9. Others: herniated omentum, adrenal rest, carcinoid, cholesteatoma

Lipomas are the most common extratesticular neoplasm of the scrotum, discovered in 22% of hernia repairs.

Malignant Paratesticular Tumor (3–25%)

The majority of malignant tumors in the nonepididymal extratesticular soft tissues are sarcomas that arise from the spermatic cord.

1. Sarcomas:
   (a) primarily in adults: undifferentiated sarcoma (30%), leiomyo-, lipo-, fibro-, myxochondro-sarcoma, malignant fibrous histiocytoma
   (b) children: rhabdomyosarcoma (20%), embryonal sarcoma

   Well-differentiated liposarcoma tends to have large amounts of macroscopic fat relative to enhancing soft tissue, while dedifferentiated liposarcomas may have only small amounts of macroscopic fat within a mostly soft-tissue mass.

2. Mesothelioma of tunica (in 15% malignant)
3. Metastases (8%): ← prostate > kidney > stomach > colon > ileal carcinoid tumor > pancreas

Primary Tumor of Tunica Vaginalis

1. Adenomatoid tumor
2. Scrotal tunica cyst
3. Mesothelioma
4. Lipoma
5. Leiomyoma

6. Sarcoma: rhabdo-, lipo-, leiomyo-

Extratesticular Fluid Collection

1. Hydrocele, pyocele, hematocele ← surgery, trauma, neoplasm
2. Spermatic cord hydrocele: encysted / funicular
   √ fluid collection superior to testis
   √ NO communication with scrotal sac
3. Varicocele
4. Spermatocele (exclusively after puberty)
   = single / multiple retention cysts filled with fluid + spermatozoa + cellular debris
   Cause: obstruction + dilatation of efferent ductal system
   • frequently following vasectomy
   Location: commonly in head of epididymis
   √ up to a few cm in size ± septations
5. Epididymal cyst
   = cyst without spermatozoa of lymphatic origin (less common than spermatoceles)
   • status post vasectomy
   Location: anywhere within epididymis
   √ wide range of sizes
6. Lymphangioma, hemangioma
7. Lymphocele
8. Abscess
9. Scrotal hernia = bowel in inguinal hernia
   √ peristalsing hypoechoic bowel musculature

CONGENITAL ANOMALIES OF PROCESSUS VAGINALIS

1. Patent processus vaginalis
   • may remain asymptomatic
   • patent at birth (20%), usually closes in 1st year
   Conditions for delayed / nonclosure:
   premature birth, cystic fibrosis, Ehlers-Danlos syndrome, hip dysplasia, peritoneal dialysis, ventriculoperitoneal shunt
   Cx: failure of testis to descend into scrotum, gliding testis, communicating hydrocele, indirect inguinoscrotal hernia
2. Hydrocele of spermatic cord
   (a) communicating = fluid collection extending from pelvis through deep inguinal ring to scrotum
   (b) funicular = fluid collection communicating with peritoneum at deep inguinal ring (= peritoneal diverticulum) as potential indirect hernia
   √ become larger with ⇑ intraperitoneal pressure
   Rx: herniotomy
   (c) encysted = isolated fluid collection between deep inguinal ring and superior pole of testis
   Location: anywhere along spermatic cord
   √ ovoid / round cyst in the groin

3. Inguinoscrotal hernia

Cystic Lesion of Testis

Prevalence: 4–10% (increasing with age)
• asymptomatic
A. NONNEOPLASTIC
1. **Intratesticular cyst**
Prevalence: 8–10%
Cause: ? trauma, prior inflammation, surgery
Age: > 40 years
• nonpalpable
Often associated with: spermatocele, dilated rete testis
Location: related to rete testis (in 92%)
√ usually solitary 2–20-mm simple cyst
DDx: cystic neoplasm
2. **Tunica albuginea cyst** / scrotal tunica cyst
Cause: fluid within mesothelial rests; fluid from blind-ending efferent ductules
Histo: cyst lined by nonciliated cuboidal cells; contains serous fluid + cellular debris
Mean age: 40 years
• palpable firm nodule
Location: upper anterior / lateral aspect of testis
Site: subcapsular / tunica vaginalis
√ solitary uni- / multilocular 2–5-mm marginally located cyst
3. **Intratesticular tubular ectasia**
= DILATATION OF RETE TESTIS = CYSTIC TRANSFORMATION OF THE RETE TESTIS
Cause: partial / complete obliteration of efferent ductules
Age: > 55 years
Often associated with: spermatocele
• nonpalpable
Location: mediastinum testis, frequently asymmetrically bilateral
√ elliptical hypoechoic branching tubular structures ± cysts
√ ± epididymal cysts / spermatoceles
MR:
√ hypointense on T1WI
√ iso- to hyperintense on T2WI
DDx: teratoma
4. **Intratesticular spermatocele**
= cyst containing mature spermatozoa
Location: attached to mediastinum testis
5. **Intratesticular varicocele**
• ± pain ← related to passive congestion
√ multiple anechoic serpiginous tubules
√ characteristic venous flow pattern increasing with Valsalva on Doppler
Infrequently associated with: extratesticular varicocele
6. Intratesticular abscess

Cause: epididymoorchitis, trauma, testicular infarction, mumps
√ collection with low-level echoes, shaggy irregular wall, occasionally hypervascular margin

7. Intratesticular infarction
   √ avascular hypoechoic mass
8. Congenital cystic dysplasia of testis (extremely rare)

B. BENIGN TUMOR
1. Epidermoid inclusion cyst / keratin cyst of testis

C. MALIGNANCY
◊ 24% of all testicular tumors have a cystic component!
• palpable
√ in combination with solid elements
DDx: hematoma, inflammation, seminoma, Leydig cell tumor

Infiltrative Process of Testis and Epididymis

1. Epididymoorchitis
2. Sarcoidosis
3. Lymphoma
4. Tuberculosis
5. Leukemia

Epididymal Enlargement with Hypoechoic Foci

1. Epididymitis
2. Sperm granulomas
3. Tuberculosis
4. Lymphogranuloma venereum
5. Granuloma inguinale
6. Filarial granuloma
7. Fungal disease
8. Lymphoproliferative disease
9. Metastases

Enlargement and Hyperemia of Epididymis

1. Epididymoorchitis
2. Trauma

Cystic Lesions of Epididymis

1. Epididymal cyst
   Prevalence: in up to 40%
   May be associated with: intratesticular tubular ectasia
   √ single / multiple / bilateral
   DDx: loculated hydrocele
2. Spermatocele
   √ may contain low-level echoes
3. Cystic degeneration of epididymis

PROSTATE

Large Utricle

1. Prune belly syndrome
2. Imperforate anus of high type
3. Down syndrome
4. Hypospadia
5. Posterior urethral valves

Extraprostatic Cyst

1. **Seminal Vesicle Cyst**
   Cause: congenital / acquired
   Age: 10–40 years
   May be associated with: ipsilateral renal agenesis, autosomal dominant polycystic kidney disease
   • asymptomatic, chronic recurrent prostatitis / epididymitis
   • painful ejaculation, perineal / testicular pain
   • urgency, hesitancy, tenesmus, pain upon defecation
   • hematuria, hematospermia, infertility; urethral discharge
   • acute urinary retention, constipation ← bladder / bowel obstruction
   Size: usually < 5 cm
   √ well-defined intraseminal unilocular round / oval cyst
2. **Vas Deferens Cyst**
   √ cyst superior to prostate along course of vas deferens
3. **Cowper Duct Cyst**
   Cause: congenital / acquired
   Location: posterior / posterolateral to posterior urethra
   • mostly asymptomatic, hematuria, urinary obstruction

DDx: ureterocele, TURP defect, bladder diverticulum, hydroureter, ectopic insertion of ureter

Prostatic Cyst

A. MEDIAN CYST
   1. Utricle cyst
   2. Müllerian duct cyst
B. PARAMEDIAN CYST
   1. Ejaculatory duct cyst
C. LATERAL CYST
   1. Prostatic retention cyst
   2. Cystic degeneration of BPH
   3. Cystic carcinoma of prostate / multilocular prostatic cystadenoma, papillary adenocarcinoma
      • hemorrhagic aspirate!
      √ solid tissue invaginating into cyst
   4. Cyst associated with infection

(a) Cavitary / diverticular prostatitis
(b) Prostatic abscess
(c) Parasitic cyst (Echinococcus, bilharziasis)

Hypoechoic Lesion of Prostate

1. Adenocarcinoma 35%
2. Benign prostatic hyperplasia 18%
   √ rarely originating in peripheral zone
3. "Normal" prostatic tissue 18%
   (a) cluster of prostate retention cysts
   (b) prominent ejaculatory / other dilated duct
   (c) external sphincter veins
   (d) neurovascular bundle
   (e) seminal vesicle
   (f) sonographic artifact
4. Acute / chronic prostatitis 14%
5. Granulomatous prostatitis 1%
   most frequently ← intravesical Calmette-Guérin bacillus (BCG) therapy for bladder cancer
6. Atrophy 10%
   • occurs in 70% of young healthy men
   ◊ May be confused with carcinoma histologically!
7. Prostatic dysplasia 6%

Hypointense T2 Signal of Prostate

1. Adenocarcinoma
2. Post-biopsy hemorrhage
   ◊ Wait 6–8 weeks after biopsy before MR imaging
3. Bacterial prostatitis, fibrosis, scarring
4. Hyperplastic nodules
5. Hormonal / radiation treatment
6. Anterior fibromuscular stroma

DDx: The normal central zone appears homogeneously hypointense on T2WI and dark on ADC map of 42–84-year old men mimicking prostate cancer. Location and symmetry of the central zone help to differentiate it from prostate cancer, although it is asymmetric in 20%.

PENIS

Painful Penile Induration

A. INFLAMMATION / INFECTION
   1. Peyronie disease
   2. Cavernositis
      Cause: self-administration of intracavernosal drug, prosthesis implantation
   3. Spongiositis
      Cause: improper catheterization, endoscopic manipulation

4. Cellulitis
5. Balanitis

B. VASCULAR
1. Dorsal vein thrombosis
2. Corporal thrombosis
3. Low-flow priapism
4. **Calciphylaxis**
   = life-threatening disorder characterized by progressive vascular calcification + ischemic tissue loss in patients with end-stage renal disease
5. **Penile Mondor disease**
   = thrombosis / thrombophlebitis in superficial dorsal vein of penis of poorly understood cause

C. TRAUMA
1. Penile fracture

D. TUMOR

URETHRA

Congenital Urethral Anomalies

A. Anomaly of number
1. Duplication of urethra

B. Anomaly of form
1. Posterior urethral valves
2. Congenital stricture
3. Congenital polyp
4. Congenital diverticulum

C. Malformation of urethral groove
1. **Epispadia**
   = absent roof of urethra with opening anywhere between base of bladder and glans penis
   Associated with: bladder exstrophy
   • urinary incontinence from incompetent bladder neck / urethral sphincter
   √ abnormally wide symphysis pubis (> 1 cm)
2. **Hypospadia**
   = congenital defect of anterior urethra with opening anywhere along ventral aspect of penile shaft

Urethral Stricture

= fibrous scarring of anterior urethra ← collagen + fibroblast proliferation; ± spongiofibrosis = scar in surrounding corpus spongiosum

A. Inflammation
1. Infectious urethritis: ← eg, gonococcal urethritis
2. Balanitis xerotica obliterans

B. Trauma
1. Straddle injury

2. Instrumentation: pressure necrosis ← indwelling catheter
3. Surgery: TURP, open radical prostatectomy → "bladder neck contracture"

C. Congenital

Cowper (Bulbourethral) Gland Lesions

Analogous to Bartholin glands in females

Prevalence: 2.3% (autopsy)

Location: within urogenital diaphragm

1. Retention cyst
   Cx: prenatal death from urinary obstruction
2. Infectious / traumatic cyst
   - asymptomatic (most)
   - hematuria, bloody urethral discharge, postvoid dribbling

Periurethral Cyst

◊ NO communication with urethra

A. Vaginal cyst
   1. Gartner duct cyst
   2. Bartholin gland cyst
   4. Müllerian cyst
      Site: anterolateral vaginal wall
   5. Vaginal (epidermal) inclusion cyst
      Site: lower posterior / lateral vaginal wall

B. Paraurethral cyst
   1. Skene duct cyst
   2. Urethral diverticulum
   3. **Urethral caruncle**
      Cause: distal urethral prolapse in hypoestrogenic postmenopausal woman
      Histo: hyperplastic squamous epithelium with submucosal vascularity, fibrosis, inflammation
      Location: posterior margin of external urethral meatus
      - asymptomatic, pain, hematuria
      - soft exophytic lesion of the meatus

C. Other periurethral lesions
   1. Perineal-vulvovaginal endometrioma
      Site: distal urethra
   2. Injected collagen
      Cause: treatment of stress incontinence
      √ hyperintense nodules in urethral wall on T2WI

Cx: infection, hemorrhage, rupture

DDx: ectopic ureter, ureterocele

Urethral Tumor

A. MALIGNANT
   1. Urethral carcinoma

2. Metastasis: ← bladder, prostate, rectum, spermatic cord, testis, melanoma

B. BENIGN

1. Fibroepithelial polyp
2. Transitional cell papilloma
   Age: older patient
   Location: in prostatic / bulbomembranous urethra
   ◊ Frequently associated with concomitant bladder papillomas
3. Adenomatous polyp
   Age: young men
   Histo: columnar epithelium ← aberrant prostatic epithelium
   Location: adjacent to verumontanum
   • hematuria
4. Penile squamous papilloma
5. Urethral leiomyoma (female)
   √ well-defined homogeneous tumor with increased vascularity
   √ T1-hypointense + T2-hyperintense relative to muscle + uniform enhancement
6. Others: caruncle, urethral mucosal prolapse, inflammatory tags (in female)

CALCIFICATIONS OF MALE GENITAL TRACT

A. VAS DEFERENS

1. Diabetes mellitus: in muscular outer layer
2. Degenerative changes
3. TB, syphilis, nonspecific UTI: intraluminal

B. SEMINAL VESICLES

gonorrhea, TB, schistosomiasis, bilharziasis

C. PROSTATE

calcified corpora amylacea, TB

AMBIGUOUS GENITALIA

= INTERSEX

= external genitalia that are not clearly of either sex

Prevalence: 1÷1,000 live births

◊ Only 4–7% of infants with disorders of sex development (DSD) have ambiguous genitalia

Indication for postnatal evaluation:

- cryptorchidism = neither testis palpable
- epi- / hypospadia combined with unilateral undescended / nonpalpable testis
- clitoromegaly = clitoral hypertrophy
- foreshortened vulva; labial fusion
- single urogenital tract opening = urogenital sinus
- inguinal hernia containing gonad in phenotypic female

Indication for evaluation of older patients:

- unrecognized genital ambiguity
- female inguinal hernia; delayed / incomplete puberty

- female virilization; primary amenorrhea
- phenotypic male breast development
- cyclical gross hematuria in phenotypic male

Cause:

A. Abnormal hormone levels
   1. Congenital adrenal hyperplasia (most commonly)
   2. Transplacental passage of hormones
   3. True hermaphroditism

B. Anomalies of external genitalia not hormonally mediated (eg, micropenis)

Laboratory tests:

1. Karyotype analysis for sex chromosome determination
2. 17-hydroxyprogesterone level: elevation suggests CAH
3. 11-deoxycortisol, 11-deoxycorticosterone levels:
   › elevated in 11-b-hydroxylase deficiency in CAH
   › depressed in 21-hydroxylase deficiency in CAH
4. Testosterone-to-dihydrotestosterone ratio: > 20÷1 indicates 5a-reductase deficiency
5. hCG-stimulation test: nonresponse indicates nonfunctioning Leydig cells / anorchia / luteinizing hormone receptor defect
6. Antimüllerian hormone + inhibin B levels: normal values suggest normal Sertoli cell function with presence of at least one testis

Imaging Evaluation:

1. Ultrasound of kidneys, adrenals, pelvis, inguinal, perineal, anal regions
2. Voiding cystourethrogram, genitography
3. MRI: greater sensitivity for intraabdominal gonads

Terminology:

Sex = what a person is biologically; sex assignment based on
(1) Karyotype
(2) Gonadal biopsy
(3) Genital anatomy

Gender = what a person becomes socially

Female Pseudohermaphroditism

= FEMALE INTERSEX = 46,XX DISORDER OF SEX DEVELOPMENT

Cause: exposure to excessive androgens in 1st trimester ←
(a) congenital adrenogenital syndrome
(b) maternal drug ingestion (progestational agents, androgens)
(c) masculinizing ovarian tumor

Karyotype: 46,XX

- masculinized external genitalia:
  - penislike clitoris ← prominent corpora cavernosa + corpus spongiosum
  - rugose labioscrotum
- uterus + vagina may be filled with urine via urogenital sinus

√ normal ovaries, fallopian tubes, uterus, vagina
√ enlarged adrenal glands ←adrenal hyperplasia
√ no testicular tissue / internal wolffian duct derivatives

Male Pseudohermaphroditism

= 46,XY DISORDER OF SEX DEVELOPMENT

Cause: fetal testis with

(a) ↓ testosterone synthesis

(b) ↓ dihydrotestosterone production (= substance responsible for masculinization of external genitalia) ← 5α- reductase deficiency

(b) no testosterone production ← early destruction / dysgenesis of testes

(c) complete / incomplete androgen insensitivity ← androgen receptor defect (= testicular feminization)

Karyotype: 46,XY

• undermasculinized / ambiguous external genitalia

[• apparent hypergonadotropic primary amenorrhea]

√ commonly undescended normal / mildly defective bilateral testes

√ prostatic tissue

√ no müllerian duct derivatives (production of müllerian regression factor by testes not affected)

√ occasionally blind-ending vaginal pouch emptying into perineum (= pseudovagina) / through urethra (= urogenital sinus)

Gonadal Dysgenesis

characterized by abnormal gonadal organization and function with gonads often partially / completely replaced by fibrous stroma (= streak gonad)

(1) **Mixed gonadal dysgenesis**

= testis on one side + gonadal streak on other side

Karyotype: 45,XO / 46,XY karyotype or other mosaics with a Y chromosome

• ambiguous external genitalia

√ small / rudimentary uterus + vagina

√ fallopian tube present on side of streak gonad

√ urogenital sinus commonly empties at base of phallus

√ dysgenetic gonads ← inability to secrete müllerian regression factor

Cx: gonadal neoplasia

(2) **Pure XY gonadal dysgenesis**

Karyotype: 46, XY

√ bilateral streak gonads / dysgenetic testes

√ müllerian + wolffian duct derivatives both absent / partially developed

(3) **XY gonadal agenesis**

= vanishing testes syndrome = testicular resorption in early fetal life of unknown cause

Karyotype: 46,XY

• ambiguous external genitalia / female phenotype

√ absent testes

√ müllerian + wolffian duct derivatives both absent / partially developed

True Hermaphroditism

= TRUE INTERSEX = OVOTESTICULAR DISORDER OF SEX DEVELOPMENT

= condition characterized by presence of ovarian + testicular tissue either separate or in same

gonad (= ovotestis in 64%)

Gonads:

(a) ovary on one + testis on other side (30%)

(b) ovary / testis on one + ovotestis on other side (50%)

(c) bilateral ovotestes (20%)

Location: in pelvis predominantly ovarian tissue; in scrotum / inguinal region predominantly testicular tissue

Prevalence: rare (500 cases in world literature); < 10% of all intersex conditions

Age: diagnosed within first 2 decades (75%)

Karyotype: 46,XX (80%) / 46,XY (10%) / mosaicism (10%)

Classification:

Class I : normal female genitalia (80%)
Class II : enlarged clitoris
Class III : partially fused labioscrotal folds
Class IV : fused labioscrotal folds
Class V : hypoplastic scrotum + penoscrotal hypospadia
Class VI : normal male genitalia

- ambiguous external + internal genitalia, inguinal hernia
- lower abdominal pain ← endometriosis
- lower abdominal tumor (dysgerminoma, myomatous uterus)

Reared as boy:

- cryptorchidism
- short penis
- slight degree of hypospadia
- urogenital sinus at base of penis
- penile urethra (extremely rare)
- effective spermatogenesis (rare)

Reared as girl:

- development of breasts
- hematuria (= menstruation via urogenital sinus opening) in 50%
- internal female organs + female fertility
- amenorrhea
- separate urethral + vaginal openings (uncommon)

√ hypoplastic uterus (in virtually 100%)

√ ovotestis with heterogeneous appearance ← combination of testicular tissue + ovarian follicles

√ internal gonadal duct fits the gonad:

√ deferent duct on side of testis

√ fallopian tube on side of ovary

√ ipsilateral fallopian tube absent ← suppression of development by fetal testis

√ testis / testicular portion of ovotestis usually dysgenetic

MALE INFERTILITY

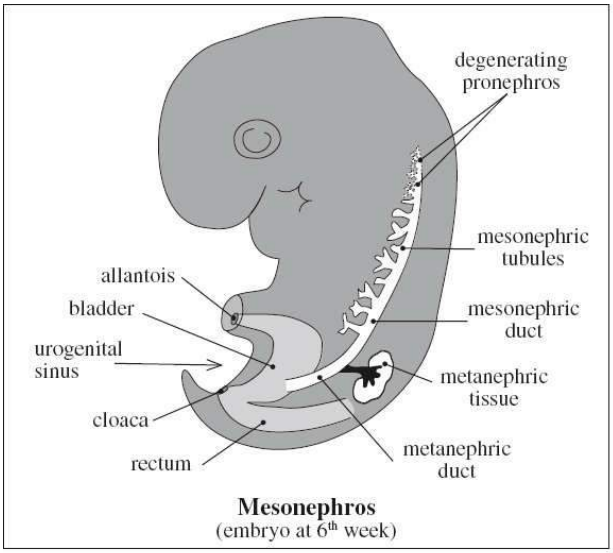
A. CONGENITAL

(a) Wolffian duct anomalies
    1. Renal agenesis / atrophy
    2. Vas deferens agenesis / cyst
    3. Seminal vesicle agenesis / cyst
    4. Ejaculatory duct cyst
(b) Müllerian duct anomalies
    1. Müllerian duct cyst
    2. Utricle cyst

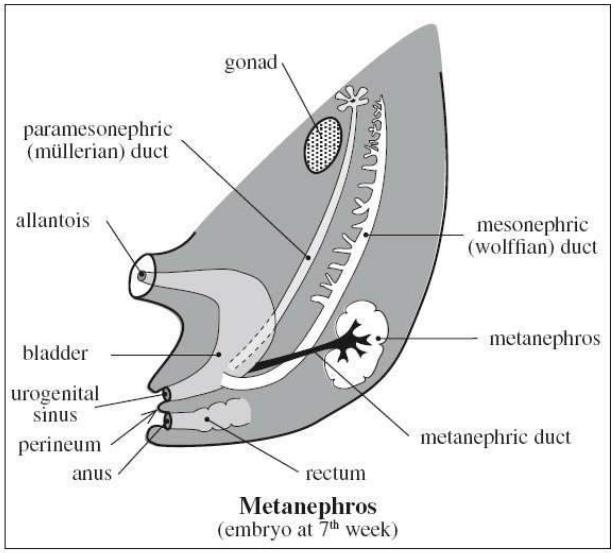
B. ACQUIRED
    1. Cowper duct cyst
    2. Prostatic cyst in peripheral zone

C. INFECTIOUS
    1. Prostatitis

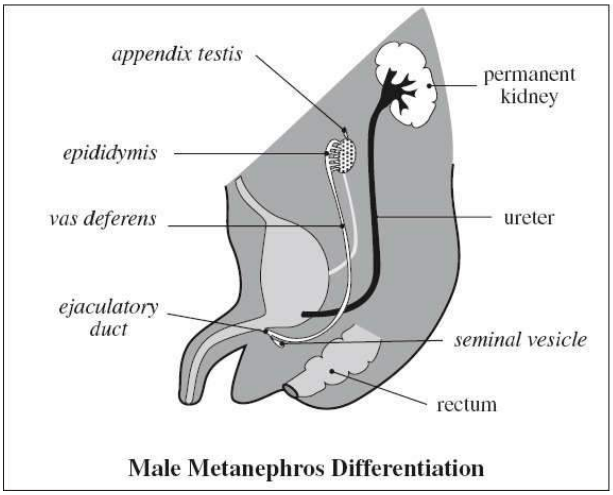
D. HORMONAL
    • semen low in volume, acid pH, without fructose
    1. Seminal vesicle atrophy
       = seminal vesicles < 7 mm in width
    2. Seminal vesicle hypoplasia
       = seminal vesicles < 11 mm + > 7 mm in width



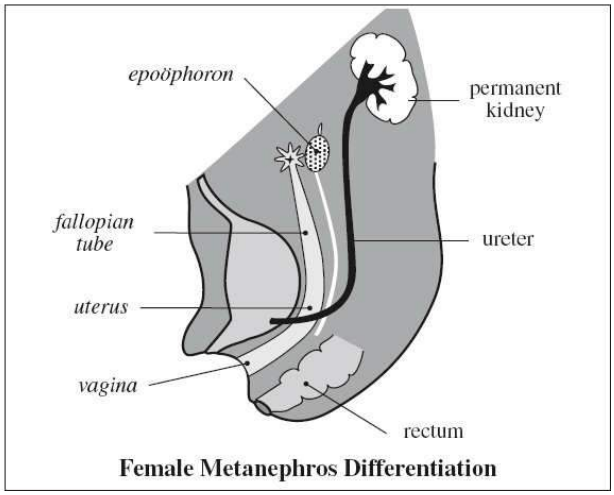
Mesonephros
(embryo at 6th week)



Metanephros
(embryo at 7th week)



Male Metanephros Differentiation



Female Metanephros Differentiation

UROGENITAL EMBRYOLOGY

Pronephros = forekidney

develops from mesoderm during 3rd week of gestation; involutes during 4th week of gestation
→ vestigial remnant / complete absence

Mesonephros = midkidney

develops during 4th week of gestation immediately caudal to pronephros, functions as interim kidney; degenerates around 8 weeks of gestation

(a) mesonephric tubules
→ paradidymis, epididymis, efferent ductules (M); epinephron (F)

(b) mesonephric (wolffian) duct
→ appendix epididymis, vas deferens, ejaculatory duct, seminal vesicles (M); vanishes (F)
[Caspar Friedrich Wolff (1733–1794), German anatomist, biologist, and embryologist in Berlin and St. Petersburg, cofounder of embryology, established doctrine of germ layers]
mnemonic: **G**ardener's **SEED**
» female: **G**artner duct, cyst
» male: **S**eminal vesicle
Epididymis
Ejaculatory duct
Ductus deferens

Paramesonephric (Müllerian) Duct
(grows alongside mesonephric duct)
[Johannes Peter Müller (1801–1858), German physiologist and comparative anatomist in Bonn and Berlin]
Male: degenerates ← production of müllerian inhibiting factor (MIF) by Sertoli cells of testis at about 6 weeks GA
→ prostatic utricle + appendix testis
Female: induced by wolffian duct at 5 weeks GA; grows caudally → joins in midline → fuses with outgrowth of urogenital sinus
→ uterus, fallopian tubes

Metanephros = hindkidney = permanent kidney

(1) **metanephric diverticulum** (ureteric bud) buds from mesonephric duct near its entry into the cloaca at 4th week; it lengthens + grows toward nephrogenic cord which becomes the metanephric blastema that divides and forms
→ ureter (mesonephric duct)
→ renal pelvis (first 4 dividing generations of duct)
→ calices (second 4 dividing generations of duct)
→ collecting tubules (10–12 generations of duct)
(2) **metanephric blastema** (= nephrogenic mesoderm) forms nephrons under the influence of ureteral bud → the end of collecting tubules induce clusters of metanephric blastema cells located at the periphery and along the sides of the medullary ray (= pyramid) except around the papilla
(3) **metanephric vesicles** form within clusters of metanephric blastema cells + elongate into S-shaped tubules which, by 12th week of gestation, result in
→ glomerulus
→ proximal convoluted tubule
→ loop of Henle
[Friedrich Gustav Jakob Henle (1809–1885), German pathologist and anatomist in Berlin, Zürich, Göttingen]
→ distal convoluted tubule
→ connective tissue

◊ Polycystic kidney disease is believed to be a failure of linkage!

Urogenital Sinus

forms from cloaca
→ develops into bladder + urethra (+ prostate)

Bladder

develops in 2nd–4th embryonal month

Urachus

= narrowed apex of fetal bladder continuous with allantoic stalk at the umbilicus
→ forms median umbilical ligament
(a) supravesical portion
(b) intramural portion
(c) intramucosal portion

SEX DEVELOPMENT

Indifferent Stage of Sexual Differentiation

Period: until 7th week of GA
Composition of undifferentiated gonad:

(1) Mesenchyme
condensation of mesenchyme forms genital ridges on both sides of midline between 6th thoracic and 2nd sacral segments; differentiates into interstitial (Leydig) cells within seminiferous tubules (= supporting stromal cells of testicular interstitium, including endothelial cells and vascular smooth muscle cells)

(2) Mesothelium
genital ridges are covered by proliferating mesothelium (coelomic epithelium); differentiates into Sertoli / supporting cells of the seminiferous tubules; forms tunica albuginea (vaginalis) as the serous covering of the testes

(3) Germ cells
form in wall of yolk sac and migrate along hindgut into genital ridge; differentiate into spermatogonia within seminiferous tubules; give rise to most testicular tumors

Chromosomes

› determine genotypic sex
› issue complex signaling pathways + hormones → modify primordial mesodermal cells → phenotypic sex

Formation of Testis

Period: around 8–12 weeks GA

- sex-determining factor localized on short arm of Y chromosome (SRY gene) → initiates male sex differentiation = seminiferous tubules
- Leydig cells secrete testosterone → stimulating growth of mesonephric (wolffian) structures
- Sertoli cells secrete müllerian-inhibiting factor → leading to regression of paramesonephric (müllerian) duct

Testicular Migration

@	inguinal canal:	by 21 weeks
@	scrotum:	by 30 weeks at birth (in 97% of full-term infants) during first 3 months of life (most)

Prenatal Evaluation of Sex

◊ Imaging of genitalia recommended only when
(a) medically indicated
(b) in twin gestation

Successful imaging of genitalia:
› in 60% by 14–18 weeks GA
› in 80–100% > 20 weeks GA

Errors in imaging of genitalia:
√ adducted fetal legs
√ US beam at wrong angle

Female:
√ 3 parallel lines between legs on transverse US
√ 3 bumps with clitoris in midline directed caudally

Male:
√ small semicircular structure (= scrotal sac)
√ penis in midline directed anteriorly and superiorly
√ visualization of testes in scrotum in late 2nd trimester

Ambiguous genitalia:
√ thorough fetal survey to detect associated anomalies
√ repeated US examinations with early GA
√ MRI with present oligohydramnios / multiple anomalies

RENAL ANATOMY

Adult Kidney

› forms by fusion of superior + inferior subkidneys (= metanephric lobes); the line of fusion runs obliquely forward and upward
√ separation of upper + lower groups of calices
√ indentation of cortical contour + echogenic line (= interrenicular septum = **junctional parenchymal defect**) delineates junctional parenchyma (often referred to as hypertrophic column of Bertin)
› consists of 20,000 lobules within 14 lobes (reniculi)
› initially located in pelvic region ventral to sacrum, ascending cranially at 9 weeks of gestation ← body growth caudal to kidneys + straightening of body curvature
› renal hilum at first ventrally located, eventually rotating medially by 90 degrees with renal ascent

Reniculus = renal lobe

= central core of medullary tissue enveloped by
(a) centrilobar cortex (= cortical arch) that covers the base of the pyramid → subsequently

forming the renal cortex with loss of grooves

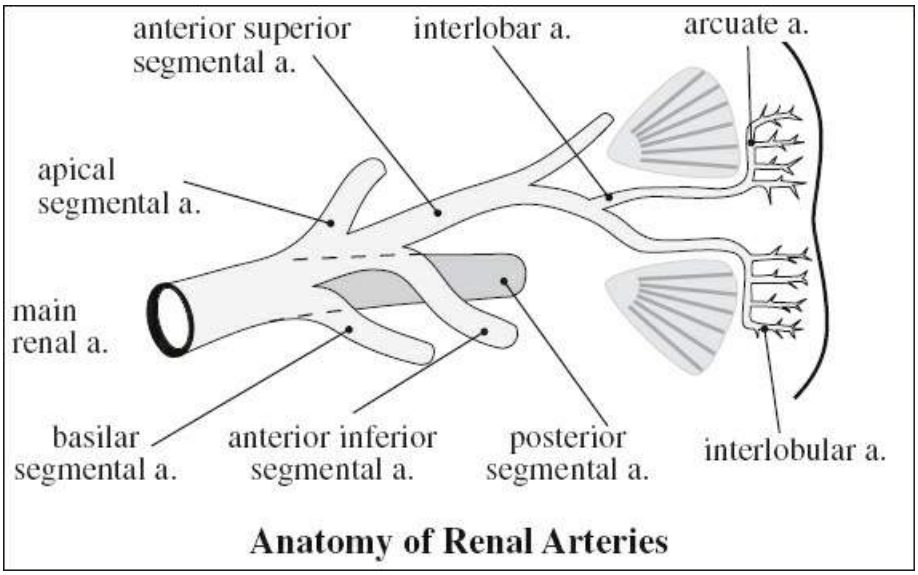
(b) mural cortex that wraps around sides of pyramid → and fuses with the mural cortex of adjacent lobe → to form renal septum (= column of Bertin)

› renal lobes completed by 28 weeks GA

√ ren lobatus (= interlobar surface grooves) present in fetus and infant, rare in adulthood

√ assimilation of independent lobes > 28 weeks GA makes renal surface smoother

› nephrogenesis completed by 36 weeks GA



Anatomy of Renal Arteries

Renal Size (in cm)

› < 1 year of age: 4.98 + 0.155 x age (in months)

› > 1 year of age: 6.79 + 0.22 x age (in years)

› adulthood: R kidney 10.74 ± 1.35 (SD); L kidney 11.10 ± 1.15 (SD)

› ratio of renal length (RL) to distance between first 4 lumbar transverse processes (4 TP) = 1.04 ± 0.22

Renal Echogenicity

A. ADULTHOOD

liver ≥ spleen ≥ renal cortex > renal medulla

B. INFANCY (in neonate up to 6 months of age)

√ cortex may be more echogenic than adjacent normal liver / spleen

Cause: glomeruli occupy 18% of cortex in neonate compared with 9% in adult

√ increase in corticomedullary differentiation

Cause: ratio of cortex to medulla 1.64÷1 in neonate compared with 2.59÷1 in adult

√ hypoechoic pyramids appear relatively large

Cause: thin immature cortex in neonate

N.B.: may be misinterpreted as dilated calices / renal cystic disease

√ renal sinus echogenicity less prominent

Cause: paucity of fat

Renal Vascular Anatomy

Hilar Arteries

Entry: renal hilum

1st order: main renal arteries at level of L1 / upper margin of L2

2nd order: 5 segmental branches = apical, anterior superior, anterior inferior, posterior, basilar

Extrahilar branching:

= branching of main renal artery prior to reaching hilum

Entry: renal hilum / direct as polar arteries

› early branching: within 1.5 cm from aorta

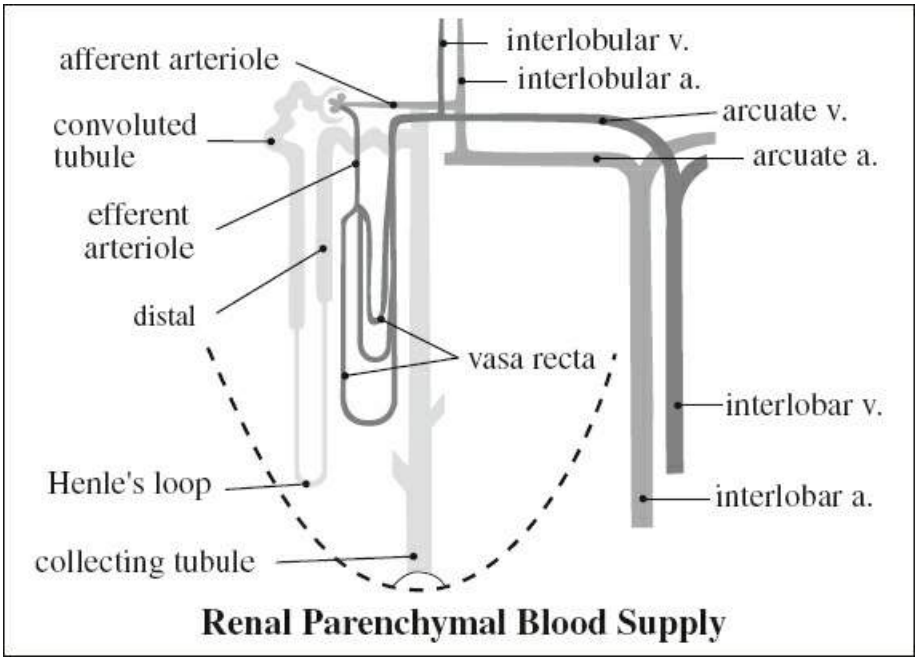
Resistive index: < 0.70 1 SD of several measurements = 0.04

Renal Polar Artery

Entry: without going through renal hilum directly into renal parenchyma at the poles

Types: superior polar artery; inferior polar artery (with supply of upper urinary tract)

Origin: main renal a., contralateral main renal a., aorta, iliac a., superior mesenteric a., inferior mesenteric a., celiac a., middle colic a., lumbar a., gonadal a., middle sacral a.



Renal Parenchymal Blood Supply

Capsular artery

= tiny vessels perfusing the renal capsule coursing tangentially to renal margin

Origin: main renal a., branch renal a., other retroperitoneal aa. (lumbar a.)

Anatomic Renal Artery Variants

Multiple renal arteries (25–30%):

unilaterally (32%); bilaterally (12%)

Number of renal arteries per kidney:

(a) one 71%
(b) two 24%
› 2 hilar arteries 12%
› 1 hilar + 1 superior polar artery 7%
› 1 hilar + 1 inferior polar artery 5%
(b) three 4%
(c) more than three 1%

◊ More than 2 renal arteries per kidney is a contraindication for donation! A small superior polar artery < 2 mm in diameter may be sacrificed.

Separate aortic ostium:

Main renal artery
= vessel with the greatest diameter

Accessory renal artery
= vessel with smaller diameter
= segmental artery originating from aorta / iliac a.

Supplementary artery:

Entry: renal hilum

Origin: aorta, iliac a., internal spermatic a., SMA, IMA, celiac trunk, middle colic a., lumbar a., middle sacral a., contralateral renal a.

Supply: lower pole (72%) > upper pole

Aberrant renal artery:

= segmental artery arising from superior mesenteric artery / internal spermatic artery

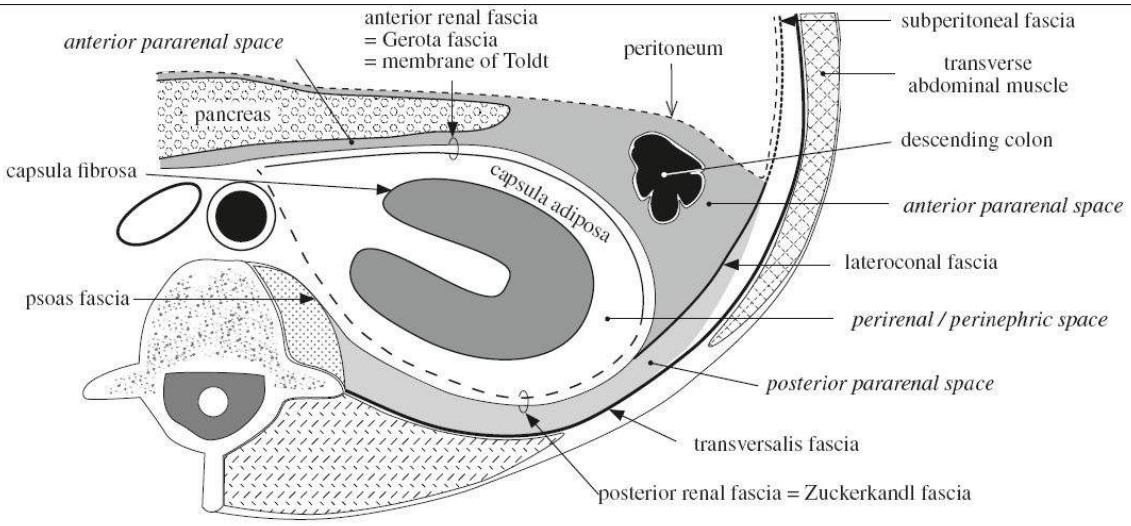
Renal Veins

Single right renal vein

without major extrarenal tributaries (85%)
with major extrarenal tributaries:
(a) right adrenal vein (30%)
(b) right gonadal vein (7%)
(c) lumbar + hemiazygos veins (3%)

Single preaortic left renal vein

without major extrarenal tributaries (86%)
with major extrarenal tributaries:
(a) left adrenal vein
(b) hemiazygos vein
(c) lumbar vein
(d) ascending lumbar vein
(e) left gonadal vein



Renal Fascia (of Gerota) and potential Anterior and Posterior Pararenal Spaces

Anatomic Renal Vein Variants

MULTIPLE RIGHT RENAL VEINS (15–30%)

(a) single right renal vein divides just before union with IVC 4%
(b) right gonadal vein joins the renal vein 6%
(c) accessory branch of adrenal vein enters right renal vein 31%
(d) lumbar / azygos vv. enter right renal vein 3%

CIRCUMAORTIC LEFT RENAL VEIN (5–6–17%)

SINGLE RETROAORTIC LEFT RENAL VEIN (2–3%)

LUMBAR VEINS JOINING LEFT RENAL VEIN (75%)

URETER

= retroperitoneal muscular conduit that carries urine from renal pelvis to urinary bladder

Histo: (a) inner cell layer of watertight urothelium surrounded by
(b) outer layer of smooth muscle → coordinated contraction

Origin: ureteropelvic junction at intra / extrarenal pelvis
Terminus: ureterovesical junction
Length: ~ 25 cm
Diameter: < 3 mm

Congenital Ureteral Abnormalities

A. URETERAL DUPLICATION
   1. Complete ureteral duplication
   2. Partial ureteral duplication
B. SMOOTH MUSCLE DYSFUNCTION
   1. UPJ obstruction
   2. Primary congenital megaureter

C. ABNORMAL TERMINATION OF SINGLE URETER
   1. Ectopic ureter
   2. Ureterocele
   3. Vesicoureteral reflux

Extrarenal Pelvis

= normal anatomic variant in which the renal pelvis lies predominantly outside of the renal sinus
√ may be dilated under normal circumstances
   DDx: UPJ obstruction, distal obstruction
√ NO associated caliectasis
√ normal size of ureter

RETROPERITONEUM

= space posterior to peritoneal cavity extending from diaphragm to pelvic brim; separated from peritoneum anteriorly by posterior peritoneal fascia; bounded posteriorly by transversalis fascia
(a) anterior border: posterior peritoneal fascia (posterior to peritoneum)
(b) posterior border: transversalis fascia (attaches to psoas muscle)

Retroperitoneal Compartments

A. **Anterior pararenal space**
   Boundaries: posterior parietal peritoneum (anteriorly), anterior renal fascia (posteriorly), lateroconal fascia (laterally)
   → superiorly joins with posterior renal fascia and attaches to crux of diaphragm
   → in the middle blends with connective tissues of central prevertebral space around great vessels
   → inferiorly joins with posterior renal fascia and attaches to great vessels
   (a) pancreaticoduodenal space
      Contents: pancreas, duodenum, root of small bowel mesentery
   (b) pericolonic space
      Contents: ascending colon + descending colon
B. **Perirenal / perinephric space** = capsula adiposa
   Boundaries: fascia renalis = Gerota fascia = anterior (membrane of Toldt) + posterior (Zuckerkandl) renal fasciae
   [Carl Toldt (1840–1920), Austrian anatomist, professor of anatomy in Prague and Vienna]
   subdivided into multiple compartments by thin fibrous lamellae + incomplete bridging septa (Kunin septa) that attach to anterior + posterior renal fascia
   → forms superiorly closed inverted cone around adrenal gland + perirenal fat + upper half of kidney; fixed to diaphragmatic fascia above; abuts bare area of liver (R) + subphrenic space (L)
   → inferiorly forms cone around perirenal fat + lower pole of kidney blending with iliac fascia below
   → laterally closed by fusion of anterior + posterior sheath
   → medially open communicating with central prevertebral space

Contents: kidneys, adrenal glands, proximal renal collecting system, proximal ureters, perirenal fat, renal hilar vessels, lymphatic vessels

The perirenal fascia is not made up of distinct unilaminated fascia; rather, it is composed of multiple layers of variably fused embryonic mesentery, creating potential spaces between the retroperitoneal spaces.

C. **Posterior pararenal space**
   Boundaries: posterior renal fascia, transversalis fascia, fascia over psoas muscle continuous with transversalis fascia
   Contents: fat, no organs
D. Great vessel space

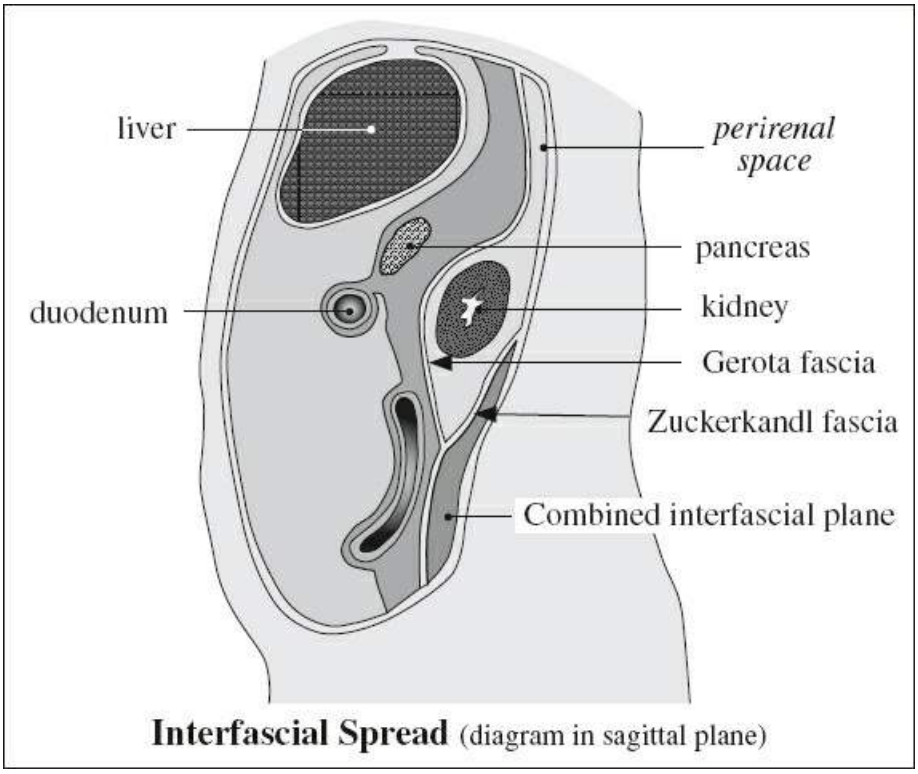
Interfascial spread is the spread of fluid within the layers of the retroperitoneal fascia and is a common route of disease across the midline within the retroperitoneum and from the abdomen to the pelvis along the retromesenteric, retrorenal, and interfascial planes.

Potential Routes of Interfascial Communication

Cause: laminar + variably fused + expandable fasciae
A. Retromesenteric plane
B. Retrorenal space
C. Lateroconal space

Organ of Zuckerkandl

= PARAAORTIC BODIES (DDx to *aortic bodies* which are chemoreceptors near thoracic aorta regulating circulation)
[Emil Zuckerkandl (1849–1910], Hungarian-Austrian anatomist at the universities of Utrecht, Graz, and Vienna, colleague of Carl Freiherr von Rokitansky]
= diffuse group of neuroendocrine sympathetic fibers constituting the chromaffin body → possible source of pheochromocytoma
Origin: neural crest
Location: at aortic bifurcation / at origin of IMA
Function: homeostatic regulator of blood pressure → by secretion of catecholamines into fetal circulation → involuting during 3rd trimester



Interfascial Spread (diagram in sagittal plane)

RENAL HORMONES

Antidiuretic Hormone (ADH)

Production site: supraoptic nuclei of hypothalamus, transported to neurohypophysis
Stimulus: fluid loss → increase in osmolality
Effects: (1) 10 x increase in permeability of collecting ducts (= concentrated urine)
(2) decreased blood flow through vasa recta leads to increased hypertonicity of interstitium (= countercurrent multiplier mechanism)

Renin-Aldosterone Mechanism

› receptors in juxtaglomerular apparatus register intraglomerular capillary hydraulic pressure, one of the main determinants of the glomerular filtration rate (GFR);
› receptors regulate the release of **renin** as an autoregulatory feedback mechanism → to maintain intraglomerular hydraulic pressure;
› renin mediates conversion of angiotensin to angiotensin-I → which is then cleaved by angiotensin converting enzyme (ACE) into angiotensin-II

Angiotensin-II Effect

› constriction of efferent postglomerular arterioles → ⇑ intraglomerular capillary hydraulic pressure + GFR
› systemic arteriolar constriction (= most potent vasoconstrictor of biologic systems) → causes systemic hypertension
› release of **aldosterone** → which increases sodium retention by renal tubules
→ leads to an increase in blood volume + blood pressure if both kidneys are affected

→ leads to compensatory natriuresis if only one kidney is affected

◊ ACE inhibitors (eg, captopril) produce a dramatic decrease in blood pressure!

RENAL PHYSIOLOGY

Perfusion: 1.2–1.3 L of blood per minute (= 20–25% of total cardiac output)

Urine output: 1 L/d

Filtration: substances of up to 4 nm (excluding substances > 8 nm), threshold at molecular weight of ≈ 40,000

Glomerular Filtration Rate (GFR)

$[P] \times GFR = [U] \times U_{vol}$

$GFR = \{[U] \times U_{vol}\} / [P]$ = 125 mL/min = 20% of RPF

Substrate: inulin; ^{99m}Tc-DTPA

Tubular Secretion (Tm)

$[U] \times U_{vol} = [P] \times GFR + Tm$

$Tm = \{[U] \times U_{vol}\} - \{[P] \times GFR\}$

Substrate: p-aminohippurate (PAH); ^{131}I-Hippuran

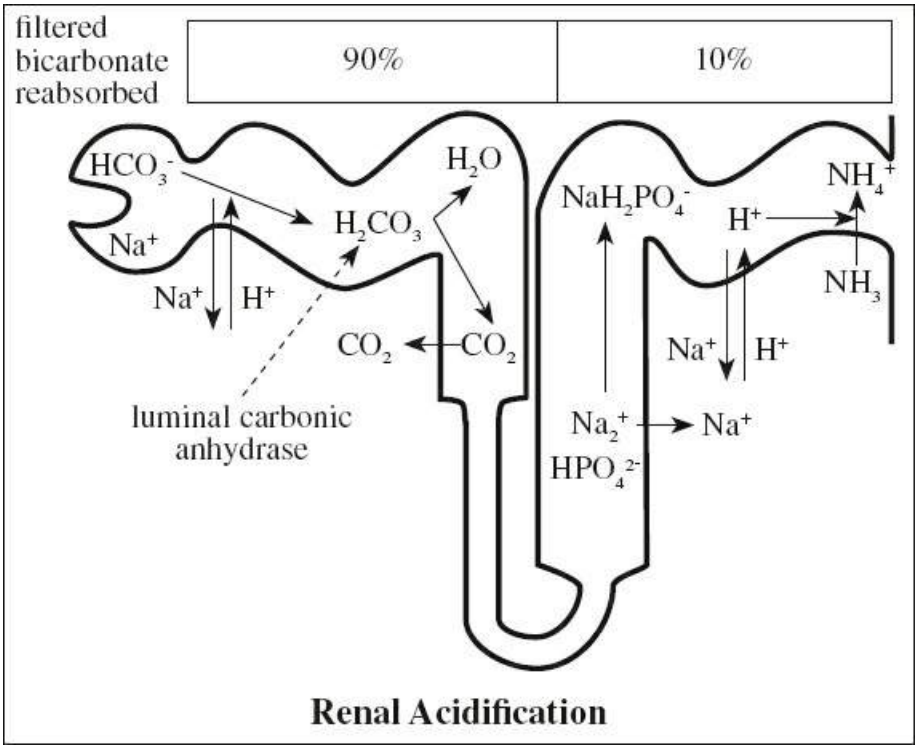
Renal Plasma Flow (RPF)

$[P] \times RPF = [U] \times U_{vol}$

RPF = {[U] x U vol } / [P]

Substrate: p-aminohippurate

[P] = concentration in plasma
GFR = glomerular filtration rate
[U] = concentration in urine
U vol = urine volume
Tm = transport maximum (across tubular cells)
RPF = renal plasma flow



Renal Acidification

Renal Acidification Mechanism

Proximal tubule:

reabsorption of 90% of filtered bicarbonate by luminal Na+/H+ exchange and Na+/HCO3 – cotransport at basolateral membrane

regulated by: luminal carbonic anhydrase

influenced by: luminal HCO3– concentration, extracellular fluid volume, parathormone, K+, aldosterone

Distal nephron:

active secretion of H+ against a steep urine-to-blood gradient across luminal cell membrane by H+-ATPase pump → facilitated by Na+ reabsorption → resulting in reabsorption of 10% of filtered bicarbonate, formation of ammonium (NH4+) and titratable acidity

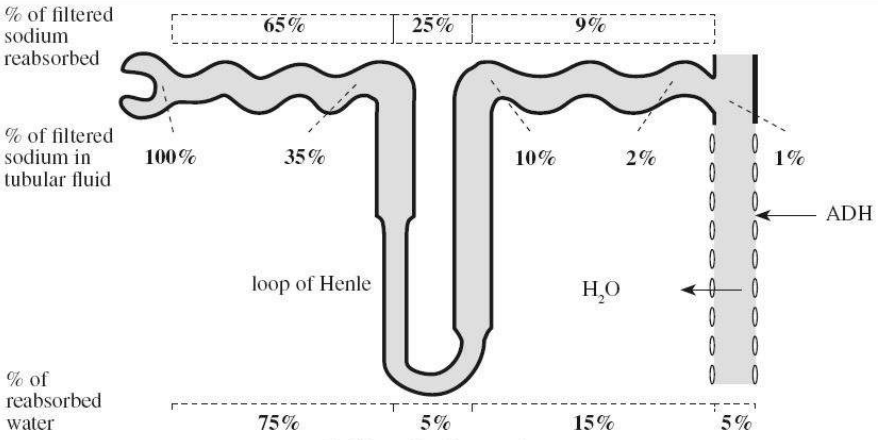
Ammonium excretion:

Ammonia (NH3) is formed in proximal tubule as a product of catabolism of glutamine + other amino acids; combination with secreted H+ to NH4+ takes place in distal nephron

Titratable acidity: divalent basic phosphate is converted into monovalent acid form in distal tubule

Renal Imaging in Newborn Infant

◊ Low glomerular filtration rate (GFR):



Sodium Reabsorption

Hypertonicity is maintained within the medullary interstitium by the countercurrent multiplier system of the loop of Henle and the vasa recta; ADH increases permeability of collecting ducts for water

on first day of life: 21% of adult values
by 2 weeks of age: 44% of adult values
at end of 1st year: close to adult values

◊ Limited capacity to concentrate urine

IVP:

√ occasional failure of renal visualization

NUC:

√ improved visualization on radionuclide studies

Normal Nephrographic Phases / Progression

1. **Vascular phase**
   = CORTICAL ARTERIOGRAM
   = contrast material in interlobular arteries + glomeruli
   Timing after IV injection: 10–15–25 seconds (arm-to-kidney circulation time)
   Duration: transient vascular phase of < 0.5 seconds
2. **Cortical phase**
   = CORTICAL NEPHROGRAM
   = contrast medium in cortical capillaries + peritubular spaces + cortical tubular lumina
   Timing after IV injection: 25–45–70 seconds
   Timing after intraarterial injection: 2–3 seconds
   CT:
   √ exclusive renal cortical enhancement with minimally enhancing renal medulla (= corticomedullary differentiation)
3. **Parenchymal phase**
   = GENERALIZED / DIFFUSE / TUBULAR NEPHROGRAM
   = contrast material in loops of Henle + collecting tubules
   Timing after IV injection: 60–85–120 seconds (max)
   √ enhancement of both cortex and medulla
   N.B.: most valuable phase for detecting renal masses
4. **Excretory phase**

= contrast material in collecting system
Timing after IV injection: beginning at 2–3–5 minutes

Contrast Excretion

UROGRAPHIC DENSITY depends on [U] = {[P] x GFR} / Uvol

1. Concentration of contrast material in plasma [P] is a function of
   (a) total iodine dose
   (b) contrast injection rate
   (c) volume distribution
   Rapid decline of concentration of contrast material in vessels due to:
   (1) rapid mixing within vascular compartment
   (2) diffusion into extravascular extracellular fluid space (capillary permeation)
   (3) renal excretion
2. Glomerular filtration rate (GFR): 99% filtered
3. Urine volume (Uvol):
   (a) in dehydrated state → increased ADH activity → higher concentrations of contrast material

◊ Dehydration is considered a risk-potentiating factor for nephrotoxicity!

   (b) in volume-expanded state → decreased ADH activity → lower concentrations of contrast material

◊ Patients with CHF require higher doses of contrast material!

A. MEGLUMINE
no metabolization, excreted by glomerular filtration alone
Meglumine effect of osmotic diuresis:
(a) lower concentration of urinary iodine per mL urine
(b) greater distension of collecting system
N.B.: Avoid meglumine in "at risk" patients (higher incidence of contrast reactions than sodium!)

B. SODIUM
extensive reabsorption by tubules with delayed excretion
Sodium effect of reabsorption:
(a) increased concentration of urinary iodine (improved visualization)
(b) less distension of collecting system (ureteral compression necessary)

ADRENAL GLAND

Function: regulation of metabolism, salt and water balance, response to stress, sexual function
From periphery to centrum:
(a) renin-angiotensin–dependent <u>outer</u> adrenal cortex
zona glomerulosa = mineralocorticoid (aldosterone)
(b) corticotropin-dependent <u>inner</u> adrenal cortex:
zona fasciculata = glucocorticoids (cortisol)
zona reticularis = sex steroids (androgen, estrogen) + gonadocorticoids
(c) medulla = catecholamines (epinephrine, norepinephrine)
mnemonic: **G**lomerular **F**iltration **R**ate **M**ay **G**ive **A**nswers

Glomerulosa
Fasciculata
Reticularis
Mineralocorticoids
Glucocorticoids
Androgens

@ IN FETUS
responsible for masculinization of external genitalia

@ IN NEONATAL PERIOD
Normal weight: 5–10 g at birth
◊ Rapid regression of fetal cortex during first 6 weeks of life!
√ central echogenic stripe (= medulla) surrounded by thick hypoechoic region (= adrenal cortex)

@ IN ADULTHOOD
Normal size: 3–5 (L) x 3 (W) x 1 cm (thick)
Normal thickness: 2–6 mm
◊ Each limb of the adrenal gland should not be thicker than the crus of the diaphragm
Normal weight: 3–5 g (5–10 g at birth)
Visualization by CT : left side 100%, right side 99%
by US : left side 45%, right side 80%

Adrenal Vascular Anatomy

Adrenal Arteries

(1) superior suprarenal artery ← inferior phrenic artery
(2) middle suprarenal artery ← abdominal aorta
(3) inferior suprarenal artery ← renal artery
50–60 small adrenal branches from 3 main adrenal arteries form a subcapsular plexus → drains into medullary sinusoids
Supply: inferior phrenic a., directly from aorta, renal artery
(a) all 3 sources in 34%
(b) two sources in 61%
(c) single source in 5% (renal a. only in 2%)
forming superior, middle, inferior adrenal arteries
◊ The renal artery contributes in 71%!
◊ Gonadal artery contributes in 60% in fetal circulation!

Adrenal Veins

"Vascular dam" = gland is drained by an intrinsically vulnerable network of relatively few venules
(1) Single right adrenal vein drains into IVC (69%)
(2) Accessory right adrenal vein drains into renal v. (31%)
(3) Left adrenal vein enters left renal vein (almost always) / inferior phrenic vein

BLADDER

Bladder capacity [mL] = (age in years + 2) x 30

Layers of Bladder Wall (from inner to outer)

(1) Uroepithelium = 3–7 layers of stratified flat cells; able to change shape from cuboidal to flattened as the bladder distends (= transitional epithelium)
(2) Lamina propria: very vascular
(3) Muscularis propria = complex network of interlacing bundles of smooth detrusor muscle; fibers merge with prostate capsule / anterior vagina + pelvic floor muscles
(4) Adventitia = connective tissue + serosal covering formed by peritoneum at bladder dome

SCROTUM

= cutaneous fibromuscular sac containing testes + extratesticular tissues

Scrotal Sac

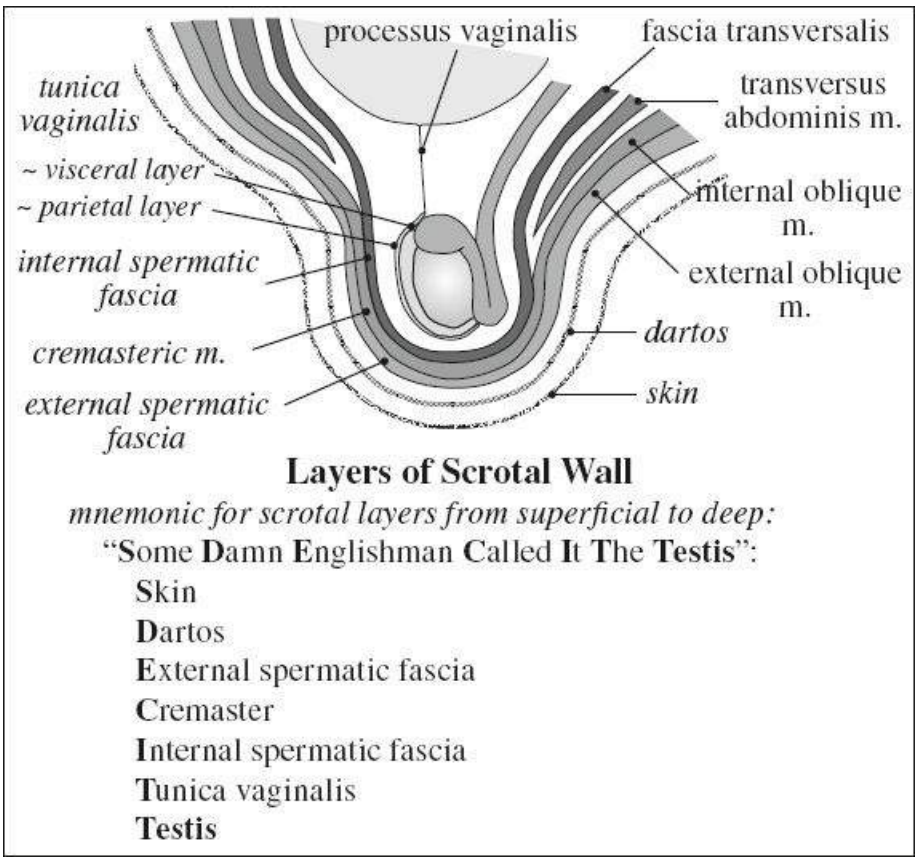
Scrotal wall thickness: 2–8 mm (3–6 mm in 89%)
Layers of scrotal sac:

1. Pigmented Skin
2. Dartos muscle and fascia
3. External spermatic fascia ← external oblique muscle
4. Cremaster muscle and fascia ← internal oblique muscle
5. Internal spermatic fascia ← transversalis fascia
6. Tunica vaginalis

Processus Vaginalis

= socklike evagination (outpouching) of the parietal peritoneum at 13 weeks EGA
› forms anterior to developing testis + ligamentous cord
› elongates caudally through abdominal wall into scrotal folds
› becomes ensheathed by fascial extensions of abdominal wall (from inner to outer layer):
– fascia transversalis → internal spermatic fascia
– internal oblique muscle → cremaster muscle
– external oblique muscle → external spermatic fascia
WITHOUT contribution by transversus abdominis m.

Function: guides testicular descent from abdomen to scrotum at 7th–9th months of fetal life



Layers of Scrotal Wall

mnemonic for scrotal layers from superficial to deep:

"**S**ome **D**amn **E**nglishman **C**alled **I**t **T**he **Testis**":

Skin
Dartos
External spermatic fascia
Cremaster
Internal spermatic fascia
Tunica vaginalis
Testis

(a) superior portion: becomes obliterated in 3 steps
  (1) closure of deep inguinal ring
  (2) closure of area above testis
  (3) atresia between these constrictions

(b) scrotal portion:
peritoneum-lined cavity surrounding anterior surface of the testis = tunica vaginalis
  (1) parietal layer envelops all but the posterior aspect of testis
  (2) visceral layer closely adherent to the tunica albuginea

Content: 1–2 mL of serous fluid

Testis

Embryology: descent from abdomen to scrotum between 7th and 9th months of gestation

Average size of testis: **3**.0 **x** 2.0–3.0 x 3.8–5.0 cm (decreasing with age)

Length of testis: 3–5.5 cm (mature); 1–1.5 cm (newborn)

Testicular cysts: in 8% of normals (average size 2–3 mm), numbers increasing with age

Anatomy: 200–300 lobules each containing 400–600 seminiferous tubules; each tubule is 30–80 cm long with a total length of 300–980 m

Histo: (1) spermatogonia (adjacent to basement membrane) → spermatocytes → spermatids → spermatozoa

(2) nondividing Sertoli cells provide the support structure; their tight cell junctions are responsible for the blood-testis barrier

(3) interstitium (= space between seminiferous tubules) contains connective tissue, lymphatics, blood vessels, mast cells, Leydig cells (= principal source of testosterone production)

Appendix Testis

= HYDATID OF MORGAGNI
= small stalked appendage at upper pole of testis
Frequency: 92% of testes
Origin: remnant of paramesonephric duct
Appendix testis÷appendix epididymis = 9÷1

Tunica Albuginea

= tough fibrous capsule of testis with great tensile strength (sustaining forces of up to 50 kg without rupturing)
› posterior surface invaginates into testicular parenchyma at mediastinum testis → divides testis into lobules
› externally covered by visceral layer of tunica vaginalis (= flattened layer of mesothelium)
√ echogenic rim surrounding the testis

TUNICA VASCULOSA

= composed of capsular arteries, applied internally to tunica albuginea

Tunica Vaginalis

= 2-layered serous membrane as inferior extension of processus vaginalis of peritoneum forming a mesothelium-lined sac that covers entire testis except for the posterior border
(a) inner visceral layer: envelopes most of testis and epididymis
(b) outer parietal layer: lines internal spermatic fascia
Hydrocele: fluid accumulation in potential space between layers of tunica vaginalis (small to moderate in 14% of normals)

Mediastinum Testis

= converging point of ~ 400 cone-shaped lobules separated by fibrous septa + seminiferous tubules forming larger tubuli recti and draining into the rete testis (= 15–20 efferent ductules)
= incomplete septum acting as entry and exit point for ducts, nerves, vessels (= hilum of testis)
√ posteriorly located linear echogenic region extending longitudinally 5–8 mm from the edge

Epididymis

= tortuous tightly folded canal forming the efferent route from testis; consists of head (= globus major), body, tail (= globus minor)

Location	:	superolateral aspect of testis
Length	:	7 cm
Globus major	:	11 x 7 x 6 mm (decreasing with age); located atop superior pole of

testis

Epididymal body	:	2–4 mm thick
Epididymal tail	:	continues as vas deferens
Epididymal cysts	:	occur in 30% of normals (average size of 4 mm)
Epididymal calcification	:	in 3%

Appendix epididymis

= small stalked appendage of globus major near upper pole of testes; occasionally duplicated

Frequency: 20–33% of epididymes

Origin: remnant of mesonephric (wolffian) duct; regarded as detached efferent duct

Spermatic Cord

Course: originates in scrotum → leaves scrotum via superficial inguinal ring → passes through inguinal canal → and through deep inguinal ring

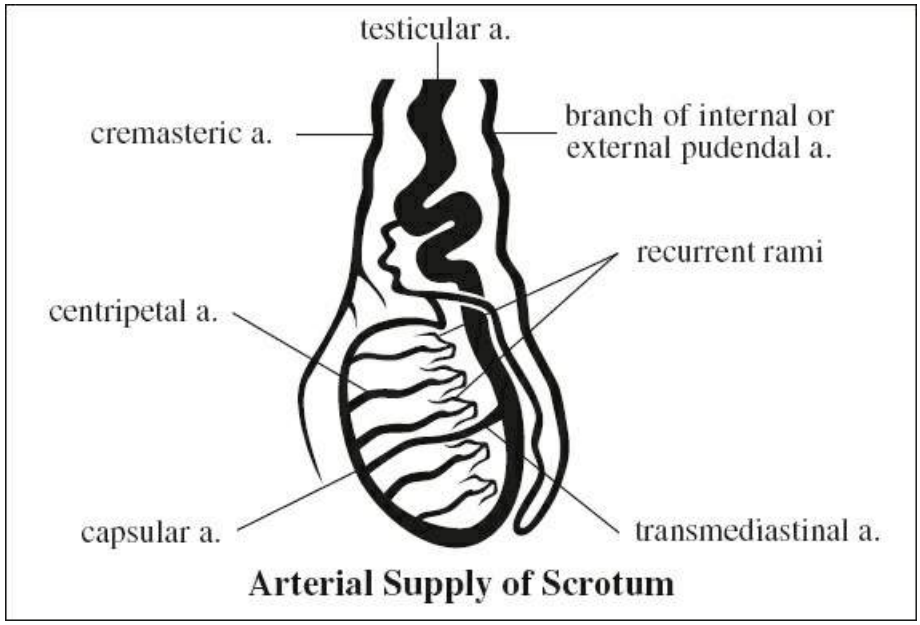
Components: testicular + deferential + cremasteric aa., pampiniform plexus of veins, vas deferens, nerves, lymphatics

Cover: (from superficial to deep) external spermatic fascia, cremasteric m. + fascia, internal spermatic fascia

Gonadal Vascular Anatomy

Gonadal Artery

Origin: ventral surface of aorta (83%) a few cm below the origin of renal arteries / from renal artery or arteries (17%):



Arterial Supply of Scrotum

(a) R from renal a. + L from aorta (6%)

(b) R from aorta + L from renal a. (4%)
(c) R + L from both renal arteries (4%)

Course: L anterior to left renal vein (20%);
R behind IVC + anterior to right renal vein

Gonadal Vein

R: drains into IVC (93%) / right renal vein (7%)
L: drains into left renal vein
Multiple gonadal veins (15%)

Lymphatic drainage follows venous drainage: testes drain into paraaortic and paracaval lymph nodes.

Blood Flow To Testis

Peak systolic velocity: 4–10–19 cm/sec
End-diastolic velocity: 2–5–8 cm/sec
Resistive index: 0.60 (range, 0.44 – 0.75)

ZONAL ANATOMY OF PROSTATE

Normal weight : 20 ± 6 g
Normal size : 2.8 cm (craniocaudad), 2.8 cm (anteroposterior), 4.8 cm (width)

A. OUTER / PERIPHERAL GLAND
   1. Central zone (25% of glandular tissue):
      surrounds ejaculatory ducts from their entrance at prostatic base to verumontanum
   2. Peripheral zone (70% of glandular tissue):
      extends from base of prostate to apex along rectal surface

√ outer gland is hyperintense on T2WI
√ surrounded by thin hypointense rim on T2WI ← anatomic / true capsule

B. INNER / CENTRAL GLAND
   1. Transition zone (5% of glandular tissue):
      on each side of internal sphincter; enlarges with BPH
   2. Periurethral zone (1% of glandular tissue):
      surrounding urethra

√ inner gland is hypointense on T2WI

C. ANTERIOR FIBROMUSCULAR STROMA
   √ hypointense on T2WI

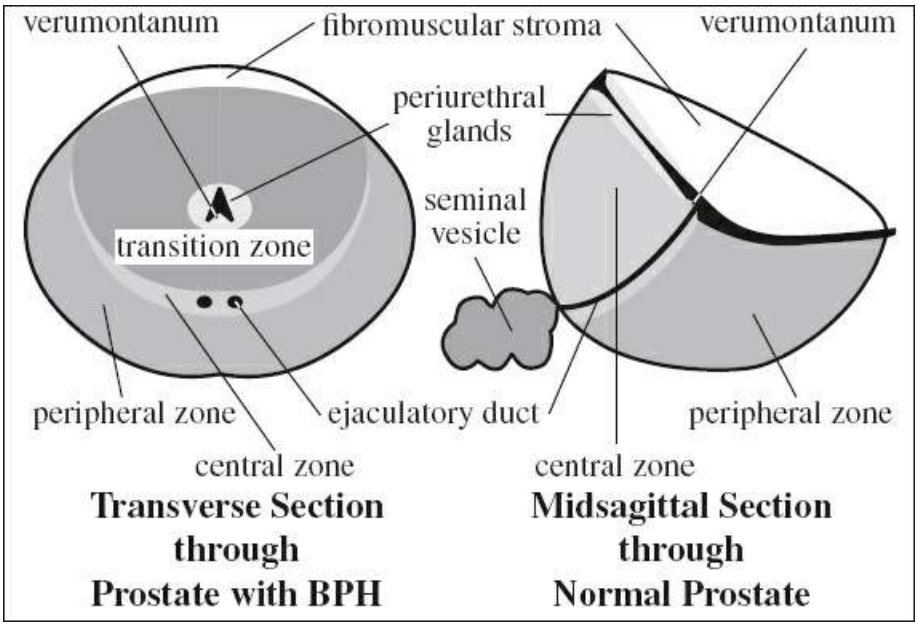
◊ Zonal anatomy is best depicted on high-resolution T2WI

SEMINAL VESICLES (SV)

Origin: separate symmetric buds extend from distal mesonephric duct (vas deferens) just proximal to ejaculatory duct
Connection: SV join distal part of vas deferens forming ejaculatory duct which drains into prostatic urethra through verumontanum

√ symmetric and of smooth saccular appearance
√ 1–2 mm thin wall

Size: 3 cm in length, 1.5 cm in diameter
Volume: 13.7 mL



VAS DEFERENS

Origin: mesonephric duct
Ampulla: 4 ± 1 mm (distal segment of vas deferens just before junction with seminal vesicle)

EJACULATORY DUCT

Origin: mesonephric duct
Diameter: 4–8 mm

URETHRA

Male Urethra

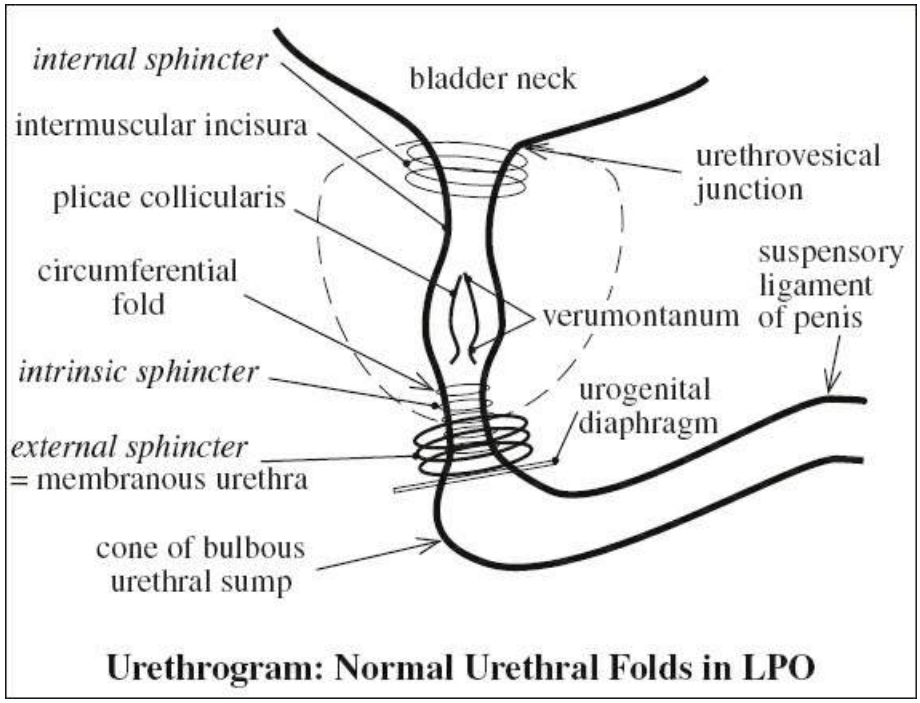
Length: 17.5–20.0 cm

A. POSTERIOR URETHRA

1. **Prostatic urethra**
   = 3.5-cm long segment from vesical neck to triangular ligament at urogenital diaphragm
   › **urethral crest** = posteriorly located longitudinal ridge of smooth muscle with overlying prominent fold from bladder neck to membranous urethra
   › **verumontanum** = colliculus seminalis
   = 1 cm long ovoid mound at posterior wall of prostatic urethra with a small saccular depression centrally (= prostatic utricle representing the fused end of vestigial müllerian ducts)
   › multiple small orifices of ducts from prostate gland acini exit at floor of prostatic urethra around verumontanum

› orifices of the paired ejaculatory ducts just distal + lateral to utricle
› contains involuntary *internal urethral sphincter* (composed of smooth muscle) for primary passive continence

2. **Membranous urethra**
= 1.0–1.5 cm long portion traversing urogenital diaphragm; anchored to anterior pubic arch by paired puboprostatic ligaments
› contains 2 muscles:
(a) voluntary *external urethral sphincter* (composed of striated muscle with contributions from levator ani complex) for active continence
(b) involuntary *intrinsic urethral sphincter* (composed of smooth muscle) for secondary passive continence



Urethrogram: Normal Urethral Folds in LPO

Associated with:
2 cm long pea-sized **bulbourethral glands of Cowper** that lie laterally + posteriorly between fasciae and sphincter urethrae in urogenital diaphragm → empty into bulbous urethral sump
[William Cowper FRS (1666–1709), English surgeon and anatomist in London]

B. ANTERIOR = CAVERNOUS URETHRA
= segment from external meatus to inferior edge of urogenital diaphragm through corpus spongiosum

1. **Bulbous urethra**
• entirely internal
› located in crura of corpus spongiosum
(a) "sump" = proximal dilated portion of urethra
(b) "cone" = conical shape of urethra at bulbomembranous junction
2. **Penile (= pendulous) urethra**

- entirely external
- › beginning at penoscrotal junction + terminating in glans penis

3. Fossa navicularis: 1.0–1.5 cm in length
4. External meatus

Associated with:

many small branched tubular **periurethral glands of Littré** that terminate in recesses (lacunae of Morgagni) and are most numerous at dorsal aspect of penile urethra + in bulbous urethral sump

Cx: recurring urethral discharge following chronic urethritis; latent gonorrheal urethritis; stricture formation

Female Urethra

Size: 3–5 cm in length, 6 mm in diameter

Course: from bladder neck at urethrovesical junction obliquely forward + downward to vestibule forming external meatus between labia minora

Epithelium: transitional cell epithelium (proximal ⅓), stratified squamous epithelium (distal ⅔)

Two sets of glands:

(a) periurethral glands
terminate in 6–30 paraurethral ducts that drain into distal urethra

(b) paraurethral glands = **glands of Skene**
[Alexander Johnston Chalmers Skene (1837–1900), Scottish gynecologist, Professor of Disease of Women at Long Island College Hospital]
(= derivatives of urogenital sinus + homologues of prostatic ducts)

Function: urethral lubrication during sexual intercourse

- › formed by an interdependent conducting system
- › exit on either side of external meatus of the urethra anteriorly draining into vaginal vestibule

Cx: chronic gonorrheal urethritis

1. Intrapelvic urethra
= upper ⅔ of urethra that lies behind symphysis pubis

Muscles: › inner layer: longitudinal smooth muscle
› outer layer: circular smooth muscle; thinner

2. Membranous urethra
surrounded by sphincter membranacea urethrae (weaker less important structure than in male)

Muscle: compressor urethrae muscle (formerly known as deep transverse perineal muscle)

Function: compresses + elongates urethra → improving continence

3. Perineal urethra
lower ⅓ extending from superior fascia of urogenital diaphragm to external meatus between labia minora

Muscle: striated urethrovaginal sphincter reinforcing the 2 concentric layers of smooth muscle

MR:
√ targetlike urethral sphincters on AXIAL plane:
√ average thickness of 4 mm
√ hypointense striated-muscle of outer sphincter
√ surrounding smooth-muscle of inner sphincter
√ innermost mucosa-submucosa
√ hypointense tubular retropubic structure on SAG view

PENIS

Layers of Penile Shaft

1. Dartos fascia separates skin from loose layer of subcutaneous connective tissue
2. Buck fascia
   = fascia penis profunda surrounding corpora cavernosa only
   [Gurdon Buck (1807–1877), pioneer military plastic surgeon during the Civil War, Columbia University + New York Hospital]
3. Tunica albuginea: surrounding corpora cavernosa (thick) and corpus spongiosum (thin)

Corpora cavernosa

= dorsally located paired structures consisting of venous sinusoids surrounded by strong fascial sheath (= tunica albuginea)
Function: erection

Corpus spongiosum

= ventrally located midline structure surrounding urethra terminating in glans penis + surrounded by tunica albuginea
Attached to: ischial tuberosity via crura

Perfusion of Penis

A. ARTERIAL INFLOW:
   1. Dorsal artery: lateral to deep dorsal vein
      Supply for: glans penis, skin
   2. Cavernosal artery: located in center of corpus callosum; terminal branch of internal pudendal artery
      Supply for: corpus cavernosum during erection
   3. Bulbourethral artery
      Supply for: urethral bulb + posterior corpus spongiosum
B. VENOUS DRAINAGE:
   1. Superficial dorsal vein = superficial to Buck fascia
   2. Deep dorsal vein = deep to Buck fascia

RENAL, ADRENAL, URETERAL, VESICAL, AND SCROTAL DISORDERS

ABORTIVE CALYX

= developmental anomaly with short blind-ending outpouching of pyramid without papillary invagination

Location: (a) renal pelvis
(b) infundibulum (mostly upper pole)

ACQUIRED CYSTIC KIDNEY DISEASE

= ACQUIRED CYSTIC DISEASE OF UREMIA

= development of numerous fluid-filled renal cysts in end-stage kidney disease without hereditary causes

◊ Successful transplant probably stops development of additional cysts, but does not affect malignant potential!

Prevalence: in 8–13% before dialysis
in 13% after 2 years of hemodialysis,
in 50% after 6 years of hemodialysis,
in 87% after 9 years of hemodialysis,
in 100% after 10 years of hemodialysis;
in 25% of renal allograft recipients

Proposed etiologies:
compensatory hypertrophy of functional nephrons ← tissue destruction
(a) renal tubular obstruction ← interstitial fibrosis
(b) renal tubular expansion ← epithelial hyperplasia
(c) cyst development ← increased fluid secretion

Not correlated with: race, cause of renal failure, method of dialysis (hemodialysis / peritoneal)

At increased risk: older men; M÷F = 3÷1

Histo: cysts lined by flattened cuboidal epithelium with papillary proliferations within renal cortex + medulla

Associated with:
(a) small papillary / tubular / solid clear-cell adenomas (in 13–20%): ~ 1 cm in diameter
(b) renal cell carcinoma (in 3–7%): 7-year interval between transplantation + detection of renal cell carcinoma

√ small hypoplastic end-stage kidneys (< 280 g)

√ multiple ½–3-cm cysts bilaterally (early = small, late = large): must have at least 3 cysts in each kidney

√ occasionally progressive renal enlargement due to cysts

US:
√ atrophic echogenic kidneys

√ cysts of varying size and complexity

Dx: > 3 cysts + NO history of hereditary cystic disease

Cx: spontaneous hemorrhage into cyst (macrohematuria / retroperitoneal hemorrhage from cyst rupture); cyst infection; ureteral stones; malignancy (risk factors are male sex + increased length of time on dialysis)

Renal malignancy develops in 3–7% of patients with acquired cystic kidney disease

AIDS

- azotemia, proteinuria, hematuria, pyuria (in 38–68% sometime during illness); progressive renal failure (10%)

1. **HIV-associated nephropathy** (up to 40%)

= characterized by nephrotic-range proteinuria + rapidly progressive renal failure, primarily occurring in African-Americans

Histo: focal + segmental glomerulosclerosis with collapsed glomerular tufts (= collapsing glomerulopathy), sparse interstitial infiltrates, severe tubular atrophy and dilatation containing protein casts

- nephrotic range proteinuria
- early + rapidly progressive renal failure

√ normal-sized (majority) / globally enlarged kidneys:

√ bulbous shape with loss of reniform appearance

US (best screening test):

√ increased cortical echogenicity (33–89%) greater than liver and approaching that of renal sinus

√ thickening of pelvicaliceal system

√ "decreased renal sinus fat" sign (in up to 49%) ← renal edema invading renal sinus fat

√ decreased corticomedullary differentiation

CT:

√ medullary hyperattenuation (14%)

√ striated nephrogram on CECT ← dilated protein-filled tubules

MR:

√ loss of corticomedullary differentiation

Prognosis: 100% mortality within 6 months

DDx: infection, acute tubular necrosis

2. **Renal infection with Pneumocystis jirovecii** (8%)

◊ More frequent since introduction of prophylactic aerosolized pentamidine therapy encouraging extrapulmonic spread (< 1%) due to inadequate systemic distribution of drug!

√ punctate renal calcifications confined to cortex ← areas of infiltrate + subsequent destruction of renal tubules (DDx: CMV, Mycobacterium avium-intracellulare)

√ associated areas of increased echogenicity in spleen, liver, lymph nodes, adrenal glands ← calcifications / protein

3. **Other renal infections**

Candida albicans, Aspergillus, disseminated pulmonary tuberculosis, M. avium-intracellulare

√ focal microabscesses + hydronephrosis

4. **Renal lymphoma** (3–12%)
   = AIDS-RELATED LYMPHOMA
   = highly aggressive often extranodal B-cell lymphomas (centroblastic, lymphoblastic, immunoblastic);
   NHL > Burkitt lymphoma, Hodgkin disease
   √ bilateral multiple renal masses:
   √ slightly hyperattenuating relative to renal parenchyma on NECT
   √ hypoattenuating homogeneous masses during nephrographic phase on CECT
   √ direct extension of retroperitoneal lymphadenopathy engulfing kidney, renal sinus, ureter
5. Kaposi sarcoma (27%)
   = AIDS-defining illness usually in patients with CD4 lymphocyte count < 150–200 cells/mm3
   Histo: renal tissue replaced + infiltrated by proliferation of spindle cells with characteristic small vascular spaces + demonstrable nuclear staining for HHV_8
   √ renal enlargement + irregular hypoattenuating areas in renal cortex
6. HAART-related nephropathy
   [**h**ighly **a**ctive **a**ntiretroviral **t**herapy]
   • acute renal failure ← renal tubular damage from nucleotide reverse-transcriptase inhibitors (tenofovir, adefovir, cidofovir)
   • dyslipidemia, insulin resistance, fat redistribution
   • hypertension
   √ renal calculi (in up to 20%) ← indinavir and nelfinavir
   √ renal artery stenosis
7. **Cystitis** (22%)
   Organism: routine gram-negative species, Candida, beta-hemolytic streptococci, Salmonella, CMV
   √ bladder wall thickening

ACUTE CORTICAL NECROSIS

= rare form of acute renal failure

Etiology:

(a) ischemia ← vasospasm of small vessels
(b) toxic damage to glomerular capillary endothelium
(c) primary intravascular thrombosis

At risk:

(a) Obstetric patient (most often): abruptio placentae = premature separation of placenta with concealed hemorrhage (50%), septic abortion, placenta previa
(b) Children: severe dehydration + fever, infection, hemolytic uremic syndrome, transfusion reaction
(c) Adults: sepsis, severe dehydration, acute prolonged shock, myocardial failure, burns, venomous snakebite, abdominal aortic surgery, hyperacute renal transplant rejection

Histo: patchy / universal necrosis of renal cortex + proximal convoluted structures ← distension of glomerular capillaries with dehemoglobulinized RBCs; medulla and 1–2

mm of peripheral cortex are spared

• protracted + severe oliguria / anuria

Distribution: diffuse / multifocal; mostly bilateral

A. EARLY SIGNS

√ diffusely enlarged smooth kidneys

√ absent / faint nephrogram

CT:

√ enhancing interlobar and arcuate arteries adjacent to nonenhancing cortex (arterial phase)

√ "reversed rim" sign = enhancement of medulla + nonenhancement of hypoattenuating cortex (parenchymal phase)

Cause: sustained hypotension for 1 hour

√ rim of subcapsular cortical enhancement ← collateral blood flow from cortical vessels

√ enhancement of juxtamedullary zone of cortex

US:

√ loss of normal corticomedullary region with hypoechoic outer rim of cortex

NUC:

√ severely impaired renal perfusion

B. LATE SIGNS

√ small kidney (after a few months)

√ "tramline" / punctate calcifications along margins of viable and necrotic tissue (as early as 1–2 months)

US:

√ hyperechoic cortex with acoustic shadowing

Prognosis: poor chance of recovery

ACUTE INTERSTITIAL NEPHRITIS

= infiltration of interstitium by lymphocytes, plasma cells, eosinophils, few PMNs + edema

Cause: allergic / idiosyncratic reaction to drug exposure (penicillin, methicillin, sulfonamides, ampicillin, cephalotin, anticoagulants, phenindione, diphenylhydantoin)

• eosinophilia (develops 5 days to 5 weeks after exposure)

√ large smooth kidneys with thick parenchyma

√ normal / diminished contrast density

US:

√ normal / increased echogenicity

ACUTE TUBULAR NECROSIS

= ACUTE VASOMOTOR NEPHROPATHY

= temporary reversible marked reduction in tubular flow rate

Etiology:

(a) DRUGS: bichloride of mercury, ethylene glycol (antifreeze), carbon tetrachloride, bismuth, arsenic, uranium, urographic contrast material (esp. when associated with glomerulosclerosis in diabetes mellitus), aminoglycosides (gentamicin, kanamycin)

(b) ISCHEMIA: major trauma, massive hemorrhage, postpartum hemorrhage, crush injury,

myoglobulinuria, compartmental syndrome, septic shock, cardiogenic shock, burns, transfusion reaction, severe dehydration, pancreatitis, gastroenteritis, renal transplantation, cardiac surgery, biliary surgery, aortic resection

Pathophysiology: profound reduction in renal blood flow ← elevated arteriolar resistance

√ smooth large kidneys, especially increase in AP diameter > 4.63 cm ← interstitial edema
√ diminished / absent opacification of collecting system
√ immediate persistent dense nephrogram (75%)
√ increasingly dense persistent nephrogram (25%)
√ diffuse calcifications (rare)

US:
√ normal to diminished echogenicity of medulla
√ sharp delineation of swollen pyramids
√ normal (89%) / increased (11%) echogenicity of cortex
√ elevated resistive index ≥ 0.75 (in 91% excluding patients with hepatorenal syndrome); unusual in prerenal azotemia

Angio:
√ normal arterial tree with delayed emptying of intrarenal vessels
√ slightly delayed / normal venous opacification

NUC:
√ well-maintained renal perfusion
√ poor concentration of ^{99m}Tc-glucoheptonate / ^{99m}Tc-DTPA
√ better renal visualization on immediate postinjection images than on delayed images
√ progressive parenchymal accumulation of ^{131}I-Hippuran / ^{99m}Tc-MAG_3
√ no excretion

ADDISON DISEASE

= PRIMARY ADRENAL INSUFFICIENCY

◊ 90% of adrenal cortex must be destroyed!

Course: acute (adrenal apoplexy), subacute (disease present for < 2 years), chronic

Acute Primary Adrenal Insufficiency

= ADDISONIAN CRISIS = ADRENAL APOPLEXY

Cause: bilateral adrenal hemorrhage most commonly due to stress from surgery / sepsis / hypotension with shock / hemorrhagic diathesis, anticoagulation therapy

- abdominal / back pain
- fever (70%), hyperpyrexia, lethargy, nausea, vomiting

√ bilateral adrenal enlargement with areas of increased attenuation

Cx: catastrophic hypotension + shock

Chronic Primary Adrenal Insufficiency

Cause:

1. Idiopathic adrenal atrophy (60–70%): likely autoimmune disorder
2. Fungal infection: histoplasmosis, blastomycosis, coccidioidomycosis
3. Granulomatous disease: tuberculosis, sarcoidosis
4. Bilateral metastatic disease (rare)

• hyponatremia, hyperkalemia, azotemia, hypercalcemia
√ diminutive glands ← idiopathic atrophy + chronic inflammation
√ calcifications (in 25% of chronic course)

ADENOMATOID TUMOR OF SCROTUM

= benign slow-growing mesothelial neoplasm
Frequency: 30% of all extratesticular masses;
2nd most common extratesticular mass (after lipoma)
Age: 2nd–4th decade
Histo: epithelial-like cells + stroma of hyalinized / loose collagen with varying amounts of smooth muscle + elastic fibers
Origin: epididymal tail
Location: epididymis > tunica vaginalis, spermatic cord (rare)
Site: L > R; lower pole÷upper pole = 4÷1
Size: 0.4–5.0 cm (usually < 2 cm)
• hard painless scrotal mass
√ smooth round paratesticular mass at periphery of testis:
√ well-marginated solid hypoechoic mass with echogenicity equal to / greater than testis
√ indentation of the testicular contour
MR:
√ isointense relative to testis on T1WI
√ slightly hypointense relative to testis on T2WI
√ enhancement similar to testicular enhancement
DDx: germ cell tumor, granulomatous epididymitis (painful, avascular), metastasis from B-cell ALL / NHL

ADRENAL CYST

Frequency: 0.06–0.18% (at autopsy)
Age: 3rd–5th decades (most commonly); M÷F = 1÷3 to 1÷2
Path: (a) vascular / endothelial cyst (45–48%)
(b) pseudocyst (39–42%)
(c) epithelial lining = true simple cyst (9–10%)
(d) parasitic cyst (7%)
Location: mostly solitary; R÷L = 1÷1; bilateral in 8–15%
Mean size: 5.3 cm; < 5 cm in diameter in 50% (up to 20 cm)
• asymptomatic, unless very large / infected / ruptured / bled into
√ well-circumscribed encapsulated uni- / multilocular lesion with internal septa
√ thin wall of < 3 mm in thickness (unless pseudocyst)
√ lack of central enhancement ± wall and septal enhancement
√ calcifications:
(a) peripheral / mural: rimlike / nodular (51–69%)
(b) central (rarely): in intracystic septation (19%) / punctate within intracystic hemorrhage (5%)
(c) scattered throughout the lesion

Radiography:
√ inferior displacement of ipsilateral kidney
US:
√ well-circumscribed hypo- to anechoic lesion
CT:
√ well-circumscribed nonenhancing hypoattenuating lesion of < 20 HU (near-water density); higher attenuation with hemorrhage / intracystic debris / crystals
MR:
√ uniformly hypointense on T1WI + hyperintense on T2WI
√ NO enhancement
√ T1 hyperintense signal ← hemorrhage
√ ± septations / soft-tissue component ← hemorrhage / hyalinized thrombus
Cx: hypertension; hemorrhage; infection; rupture with retroperitoneal hemorrhage
Prognosis: interval increase in cyst size in 60%
Rx: (1) Resection of cyst > 5 cm ← risk of hemorrhage
(2) Functional symptomatic cyst
(3) Cyst worrisome for malignancy
DDx: (a) benign
1. Cystic pheochromocytoma
2. Cystic adenomatoid tumor
3. Schwannoma
4. Adrenocortical adenoma (contrast enhancement, no wall, no peripheral calcification)
5. Hemangioma

(b) benign
1. Cystic adrenocortical carcinoma (thick-walled lesion > 7 cm in size; extremely rare)
2. Metastatic disease

Vascular / Endothelial Adrenal Cyst (45–48%)

Cause: 1. Simple cyst without soft-tissue component
2. Lymphangioma
3. Hemangioma

Histo: lined by cells resembling normal endothelium
√ multilocular thin-walled cyst containing serous / serosanguinous / clear fluid
√ scattered / central septal calcifications in 15–30%

Adrenal Pseudocyst (39–42%)

Cause:
1. Previous hemorrhage / infarction
2. Hemorrhagic complication of benign vascular neoplasm / malformation
3. Cystic degeneration / hemorrhage of primary adrenal mass

Histo: wall consists of dense hyalinized material + occasional calcification / osseous metaplasia; adrenal cortical cells can be found in wall

• amorphous material + blood products as content
√ typically unilocular thick-walled cyst > 3.5 mm
√ internal scattered echogenicity ← debris / fluid-fluid levels from recent hemorrhage
√ peripheral calcifications

True Simple / Epithelial Adrenal Cyst (9–10%)

Cause: 1. Glandular / retention cyst
2. Embryonal cyst
3. Cystic adenoma
4. Mesothelial inclusion cyst

Histo: simple epithelial lining
√ unilocular thin-walled cyst

Parasitic Adrenal Cyst (7%)

Cause: usually Echinococcus granulosus
Path: purely cystic to more complex contents depending on stage of infection
√ variable internal complexity ← daughter vesicles, freed scolices, brood capsules
√ septal / mural calcifications
√ "water lily" sign
√ extra-adrenal foci of hydatid disease

ADRENAL HEMORRHAGE

Site: medulla with variable degree of cortical involvement
• sudden / gradual onset of lower chest / upper abdominal / flank / back pain; shocklike symptoms = signs of massive blood loss
• acute adrenal insufficiency (rare): manifesting as hypotension + hyponatremia + hyperkalemia
√ round / oval mass displacing kidney inferiorly + IVC anteriorly
√ uniform adrenal enlargement gradually decreasing in size over 6–8 weeks (follow-up for 2–3 months)
√ complete resolution with time:
√ ± rimlike curvilinear / eggshell calcifications > 1 year
√ no enhancement
NECT:
@ acute stage (< 7 days):
√ round / oval mass (in 83%) located in medulla + stretching cortex around hematoma:
√ hyperattenuating (50–90 HU) similar to most neoplasms in acute stage → slowly decreasing over time
N.B.: Follow-up required to confirm regression!
√ obliteration of gland by diffuse irregular hemorrhage (in 9%)
√ periadrenal fat stranding
√ asymmetric thickening of diaphragmatic crus ← periadrenal hemorrhage
@ chronic stage (> 7 weeks):
√ mass with hypoattenuating center ± calcifications = adrenal pseudocyst (DDx: adrenal adenoma)

US (modality of choice for neonate):
√ complex solid heterogeneously hyperechoic mass during early stage
√ mixed echogenicity with centrally hypoechoic region (as liquefaction occurs)
√ peripheral curvilinear hyperechoic calcifications appearing within 1–2 weeks
√ completely anechoic / cystlike in chronic stage
√ avascularity on color Doppler / power Doppler
MR:
@ acute stage (< 7 days):
= high concentration of intracellular deoxyhemoglobin with preferential T2 proton relaxation enhancement
√ isointense / slightly hypointense on T1WI
√ markedly hypointense on T2WI
@ subacute stage (7 days–7 weeks):
= T1 shortening ← paramagnetic effect of free methemoglobin (Fe3+) ← produced by oxidation of hemoglobin (Fe2+)
√ hyperintensity on T1WI and T2WI appearing in periphery with filling in (over several weeks)
√ hematoma may be multilocular, each locule with its own different signal intensity
@ chronic stage (> 7 weeks):
= T2 proton relaxation enhancement ← hemosiderin deposition + presence of a fibrous capsule
√ hypointense rim on T1WI + T2WI
√ "blooming effect" (= magnetic susceptibility) of hemosiderin in gradient-echo imaging
Rx: supportive; prompt glucocorticoid administration with concomitant intravenous saline therapy for acute adrenal insufficiency

Nontraumatic Adrenal Hemorrhage (20%)

Incidence: in 1.8% (autopsy study)
Cause: (1) Stress: severe burn, sepsis, surgery, hypotension
(2) Hemorrhagic diathesis: anticoagulant therapy
(3) Coagulopathy
(4) Underlying adrenal mass: adrenocortical adenoma / carcinoma, myelolipoma, pheochromocytoma, metastasis, neuroblastoma
Location: typically bilateral
DDx: neuroblastoma (stippled calcifications, increase in vanillylmandelic acid, no decrease on follow-up)

Blunt Trauma to Adrenal Gland (80%)

Incidence: in 28% of autopsies; in 2% of trauma CTs
◊ Adrenal injury means exposure to major force!
Mechanism:
(a) direct crush injury between spine and liver / spleen
(b) acutely increased adrenal venous pressure ← transmitted from compressed IVC / adrenal venous sampling

(c) IVC-adrenal vein thrombosis
(d) shear injury to small adrenal vessels (from rotational / deceleration forces)

Often associated with: injury to liver + kidney

Location: R÷L÷bilateral = 75÷15÷10

Prognosis: (1) unilateral hematoma: spontaneous resolution without sequelae
(2) bilateral hemorrhage: acute primary adrenal insufficiency (rare) is life-threatening

DDx: preexisting adrenal mass → repeat imaging after 8–10 weeks!

ADRENOCORTICAL ADENOMA

◊ Most common tumor of adrenal gland!

Prevalence: 1–2% in general population; age-dependent 6.6–8.7% at autopsies (small tumors in 50% of autopsies)

◊ In a patient with lung carcinoma a solitary small adrenal mass is more likely an adenoma than a metastasis!

Path: atypical intralesional cystic degeneration / less often hemorrhage

Histo: clear cells arranged in cords with abundant <u>intracellular</u> (= intracytoplasmic) pale-staining lipid; rich delicate vascular network

◊ Detection of lipid by CT / MRI is NOT 100% specific!

DDx: metastatic clear cell renal cell carcinoma, pheochromocytoma, adrenocortical carcinoma

◊ No lipid may mean a benign lipid-free adenoma!

◊ Fat cell aggregates (<u>macroscopic fat</u>) may be present!

DDx: lipomatous / myelolipomatous metaplasia

• usually nonfunctioning

Average size: 2.0–2.5 cm: usually < 5 cm in size

√ well-defined homogeneous (87%) sharply marginated mass

√ small adenomas < 1 cm often go undetected

√ contralateral gland often normal / atrophic

NECT:

Categories:

(a) lipid-rich adenoma < 10 HU (60–90% of all adenomas)
(b) lipid-poor adenoma > 10 HU (up to 40%)

√ soft-tissue density / cystic density (mimicked by high cholesterol content) with poor correlation between functional status and HU number:

√ < 0 HU on NECT (47% sensitive, 100% specific)

√ <u>≤ 10 HU on NECT</u> (79% sensitive, 96% specific)

√ < 18 HU on NECT (85% sensitive, 100% specific)

√ > 10% negative pixels on histogram (100% specific)

√ homogeneous attenuation (87%)

CECT:

√ homogeneous (58%) enhancement

√ < 37 HU on 5–15-min delayed CECT is DIAGNOSTIC of adenoma

Washout Technique:

Rationale: adenomas show significantly more initial enhancement than nonadenomas

(1) Attenuation before contrast administration = ANECT

(2) Early attenuation at 60 sec = Aearly

(3) Delayed attenuation at 10–15 min = Adelayed

(4) Absolute percentage washout (Wabs / APW)

$W_{abs} = [1 – (A_{delayed} – A_{NECT}) / (A_{early} – A_{NECT})] \bullet 100$

√ washout > 40% = adenoma

√ washout ≤ 40% = indeterminate mass

(5) Relative percentage washout (W_{rel} / RPW) useful when the NECT value is not known

$W_{rel} = [(A_{early} – A_{delayed})/A_{early}] \bullet 100$

√ washout > 60% = adenoma

√ washout ≤ 60% = indeterminate mass

Angio:

√ tumor blush + neovascularity; occasionally hypovascular

√ pooling of contrast material

√ enlarged central vein with high flow

√ arcuate displacement of intraadrenal veins

√ bilateral adrenal venous sampling → in up to 40% unsuccessful in localizing

MR:

√ isointense mass relative to liver + hyperintense relative to spleen on T1WI ← short T1 time of lipid

√ iso- / hypointense mass (rarely hyperintense) to spleen on T2WI

√ marked hypointensity compared with spleen / skeletal muscle on opposed-phase GRE images ← destructive interference of lipid and water signals = phase cancellation of fat + water protons in same voxel in 95% of adenomas (> 90% accurate)

√ signal loss of ≥ 20% on opposed-phase image

√ India ink effect = characteristic black lines outlining interface between organ + adjacent fat (chemical shift artifact)

√ small round foci of altered SI ← cystic changes / hemorrhage / variation in vascularity

CEMR:

√ uniform enhancement on immediate early imaging

√ adenomas tend to enhance less rapidly + less intensely than metastases on time-enhancement curves

√ relatively rapid washout of contrast material compared with metastases with return to baseline at 15 minutes ← lack of large interstitial spaces of edema + necrosis (DDx: metastases tend to have higher signal intensities [however 20–30% overlap])

US:

√ well-circumscribed round or oval lesion of slightly heterogeneous mixed echogenicity

Atypical appearance:

◊ Occasional intralesional cystic degeneration / hemorrhage make an accurate diagnosis more challenging!

√ adenoma may calcify → often in areas of old hemorrhage

DDx: pheochromocytoma, adrenocortical carcinoma, metastasis, functioning adenoma

Nonhyperfunctioning Adrenocortical Adenoma

characterized by
(a) normal lab values of adrenal hormones
(b) NO pituitary shutdown of the contralateral gland
(c) activity on NP-59 radionuclide scans

Prevalence: incidental finding in 0.6–1.5% of CT examinations, in 3–9% at autopsy
√ surveillance CT to confirm lack of growth
Rx: surgical removal for masses 3–5 cm as indeterminate potentially malignant neoplasms
DDx: metastasis

Hyperfunctioning Adrenocortical Adenoma

√ contralateral adrenal atrophy ← suppression of pituitary ACTH by elevated cortisol levels

1. Primary hyperaldosteronism = Conn syndrome (80%)
   Pathophysiology: secretion of aldosterone by an adenoma is pulsatile
   √ ACTH infusion incites a dramatic increase in levels of cortisol + aldosterone for venous sampling
2. Cushing syndrome (10%)
3. Virilization
   (a) hirsutism + clitoromegaly in girls
   (b) pseudopuberty in boys
   ◊ Most common type of hormone elevation in children!
   • elevated testosterone levels > 0.55 ng/mL
4. Feminization (estrogen production)
   √ contralateral atrophic gland ← ACTH suppression with autonomous adenoma
   √ unilateral focus of ^{131}I NP-59 radioactivity + contralateral absence of iodocholesterol accumulation (DDx: hyperplasia [bilateral activity])

ADRENOCORTICAL CARCINOMA

Prevalence: 1–2÷1,000,000 people; 0.3–0.4% of all pediatric neoplasms (3 x more likely than adrenal adenoma)
Age: biphasic distribution (1st + 4th–5th decade); M÷F = 1÷1.5
May be associated with:
hemihypertrophy, Li-Fraumeni syndrome, Beckwith-Wiedemann syndrome, Carney complex, congenital adrenal hyperplasia, MEN 1, astrocytomas
Path: large lobulated tumor, often with cystic / necrotic / hemorrhagic center
Histo: differentiation of benign from malignant solely on the basis of histologic features may be difficult

• abdominal / back pain, palpable abdominal mass
• weight loss, early satiety
• 20% nonfunctioning
• 50% hyperfunctioning (in 10–15% Cushing syndrome, occasionally Conn syndrome, feminization, adrenogenital syndrome with virilization) inversely related to size
• hypertension (common in all syndrome types)

Location: left÷right adrenal = 53÷47; bilateral in 10%

Median size: 10–12 cm (range, 4–25 cm); usually > 5 cm; in 70% > 6 cm in diameter

A heterogeneous enhancing adrenal mass > 4 cm in diameter has a high likelihood of malignancy!

√ frequently heterogeneous mass with irregular margins + displacement of regional structures
√ occasionally calcified (in 19–33%)
√ invasion of IVC, liver, kidney, diaphragm (multiplanar imaging helpful)
√ metastases to liver, regional lymph nodes, lung, bone, brain

◊ Metastases are the only reliable sign of malignancy!
◊ Large size + calcifications suggest malignancy!

CT:
- √ tumor attenuation typically > 10 HU
- √ central areas of low attenuation ← tumor necrosis
- √ heterogeneous enhancement (= foci of hemorrhage + central necrosis) + thin peripheral rim of enhancement

CECT:
- √ peripheral nodular enhancement (in 88%)
- √ venous tumor thrombus
- √ relative percentage washout (RPW) of < 40% at 15 min
- √ slow absolute washout of < 60% at 15 min

US:
- √ well-defined round / oblong mass with lobulated contours
- √ homogeneous echotexture in small tumor
- √ complex echo pattern in large tumor with hyperechoic + hypoechoic regions ← hemorrhage + necrosis

MR:
- √ tumor of low T1 signal + heterogeneously high T2 signal
- √ heterogeneous areas hyperintense to liver on T1WI + T2WI ← internal hemorrhage + necrosis frequent:
  - √ high SI on T1WI ← methemoglobin
  - √ high SI on T2WI ← necrosis
  - √ loss of SI on out-of-phase imaging ← intracytoplasmic lipid

CEMR:
- √ heterogeneous enhancement pattern with slow washout
- √ nodular enhancement + central hypoperfusion

Angio:
- √ enlarged adrenal arteries
- √ neovascularity, occasionally with parasitization
- √ AV shunting; multiple draining veins

NUC:
- √ usually bilateral nonvisualization with ^{131}I NP-59 (= carcinomatous side does not visualize because amount of uptake is small for size of lesion; contralateral side does not visualize because carcinoma is releasing sufficient hormone to cause pituitary feedback shutdown of contralateral gland)

PET:

√ hypermetabolic tumor on 18F-FDG with adrenal-to-liver max SUV ratio of > 1.45 (100% sensitive, 88% specific)

Biopsy: may appear histologically benign in well-differentiated adenocarcinoma
◊ Sampling error with fine-needle aspiration possible; use core biopsy instead

Prognosis: 0% 5-year survival rate

DDx: metastasis (similar signal intensities on MR); adrenocortical adenoma (mass of < 10 HU, >40% relative washout, > 60% absolute washout); myelolipoma (intralesional bulk fat)

Adrenocortical Neoplasm in Children

Incidence: 3÷1,000,000 annually; less common than neuro- blastoma but more common than pheochromocytoma

Mean age: 8 years (range, 6 months to 19 years); ⅔ younger than 5 years of age; M÷F = 2.2÷1.0

Path: adenoma = solitary spherical well-demarcated unencapsulated tumor of < 50 g
carcinoma = multinodular tumor with areas of hemorrhage + necrosis of > 100–500 g

Histo: NO reliable features to distinguish between adenoma and carcinoma!

Associated with:

(1) Beckwith-Wiedemann syndrome (3%)
2nd most common abdominal tumor after Wilms tumor

(2) Li-Fraumeni syndrome = SBLA (sarcoma, breast and brain tumors, laryngeal carcinoma, adrenocortical carcinoma)
[Frederick Pei Li (1940–), American epidemiologist at Harvard School of Public Health and Harvard Medical School in Boston]
[Joseph F. Fraumeni, Jr. (1933–), American epidemiologist at Harvard School of Public Health in Boston]
• alteration of p53 tumor suppressor gene located on short arm of chromosome 17, band 13

(3) Familial Carney complex = cardiac myxoma + Sertoli cell tumor + adrenocortical neoplasm

(4) MEN 1 = pituitary prolactinoma + pancreatic islet cell tumor + parathyroid hyperplasia + adrenocortical neoplasm

- palpable abdominal mass (57%)
- gonadotropin-independent production of endogenous androgens + cortisol (92%):
  - virilization in female
    = herculean habitus (increased muscle mass), clitoromegaly, facial hair, advanced pubic + axillary hair development, advanced bone age
  - isosexual precocious puberty in male
    = early development of acne, pubic hair, penile enlargement
  - mixed endocrine syndrome with cushingoid features (less frequent)
- other endocrine abnormalities (unusual):
  - pure Cushing syndrome
  - feminization in boys ← secretion of estrogen
  - Conn syndrome (primary hyperaldosteronism)
- increase in 24-hour urinary ketosteroid excretion

• increased levels of serum cortisol, testosterone, androstenedione, estradiol

Metastases: lung > liver > tumor invasion of IVC (35%) > peritoneum (29%) > pleura + diaphragm (24%) > abdominal lymph nodes (24%) > kidney (18%)

US:

√ 3–22-cm round / ovoid well-circumscribed mass
√ lobulated border (common)
√ thin echogenic capsule-like rim (27%)
√ homogeneous mass hypo- / isoechoic to kidney
√ heterogeneous mass with centrally hypoechoic regions (= tumor necrosis) if large
√ tumor calcification (19%)

CECT:

√ well-circumscribed mass with thin rim
√ heterogeneous predominantly peripheral enhancement if lesion large
√ fine / coarse calcification (24%)

MR:

√ iso- / slightly hypointense to liver on T1WI
√ hyperintense to liver on T2WI
√ uniform signal loss at chemical shift imaging ← intracytoplasmic lipid

PET/CT:

√ hypermetabolic primary tumor + metastases
√ secondary findings ← excess serum cortisol of Cushing syndrome:
  √ hyperattenuating / hyperechoic renal pyramids ← hypercalcemia
  √ increase in retroperitoneal fatty tissue ← obesity

Rx: surgery

Prognosis of adrenocortical carcinoma:

survival rate of 70% [13%] for children < 5 years [> 5 years] of age; death within 1–2 years after diagnosis

DDx: (1) Neuroblastoma (encasing vascular structures, punctate calcifications, crosses midline, extradural extension through neural foramina, ill child, often already metastatic, increase in catecholamines)
(2) Pheochromocytoma (older child, headaches)
(3) Adrenal hemorrhage (neonate, temporal evolution)
(4) Metastasis (extremely rare)

ADRENOCORTICAL HYPERPLASIA

= ADRENAL CORTICAL HYPERPLASIA

◊ Responsible for 8% of Cushing syndrome and 10–20% of hyperaldosteronism!

Cause:

1. Corticotropin-dependent (85%): pituitary causes, ectopic ACTH production, CRF (corticotropin-releasing factor)production
2. Primary pigmented nodular adrenocortical hyperplasia
3. Primary aldosteronism (rare)

Prevalence: 0.51% increasing with age (autopsy); 4 x increased in patients with malignancy

Age: 70–80% in adults; 19% in children

Location: typically bilateral
Types:
(1) **Smooth diffuse hyperplasia** (common)
√ smooth to slightly lobular thickening of entire adrenal gland while maintaining its overall normal inverted-V or inverted-Y appearance
◊ In 45% of patients with Cushing syndrome
(2) **Cortical nodular hyperplasia** (less common)
Prevalence: increasing with age (autopsy)
Histo: mild nodularity (50%), distinct nodularity (15%)
Age: 65 years
Site: multifocal
√ focal hypo- to isoattenuating micro- / macronodules (= nodules up to 2.5 cm)
√ background of normal adrenal tissue / atrophic intervening cortex
◊ In 3% of patients with Cushing syndrome
Angio:
√ minimally increased hypervascularity
√ focal accumulation of contrast medium
√ normal venogram / may show enlarged gland
√ adrenal venous sampling to direct therapy in symptomatic patients ← results NOT ALWAYS CONCORDANT with imaging findings
NUC:
√ asymmetric bilateral NP-59 uptake (related to urinary cortisol excretion) WITHOUT dexamethasone suppression in Cushing syndrome
√ bilateral foci of NP-59 uptake WITH dexamethasone suppression (nondiagnostic ≥ 5 days)
Rx: no treatment in the absence of clinical / biochemical evidence of adrenocortical hyperfunction

ACTH-independent Macronodular Hyperplasia

= MACRONODULAR HYPERPLASIA WITH MARKED ADRENAL ENLARGEMENT
Etiology: unknown
• clinical features of hyperaldosteronism / Cushing syndrome
• suppressed ACTH ← active production of hormones
√ bilateral enlarged adrenal glands (often > 5 cm) with macronodules

Primary Pigmented Nodular Adrenocortical Disease

√ normal to slightly enlarged adrenals + small nodules + atrophy of intervening cortex
Associated with: Carney complex

ADRENAL REST TUMOR

= ADRENOCORTICAL REST
Prevalence: 7–15% of newborns; 1.6% of adults
◊ Adrenal rests only form masses after exposure to elevated levels of adrenocorticotropic hormone
Associated with conditions of ⇑ circulating ACTH:

(1) Congenital adrenal hyperplasia
(2) Cushing syndrome
(3) Addison disease

• increase in cortisol levels (testicular vein sampling is DIAGNOSTIC)

Location: near testicular hilum; usually bilateral

US:

√ multiple hypoechoic nodules
√ may become hyperechoic with acoustic shadowing

MR:

√ nodules isointense relative to normal testis on T1WI
√ nodules hypointense relative to normal testis on T2WI
√ diffuse enhancement after contrast administration

ADRENOGENITAL SYNDROMES

A. CONGENITAL TYPE = **Congenital Adrenal Hyperplasia**

= autosomal recessive enzyme defect

Incidence: 1÷15,000 in most white populations

Cause: mutation of CYP21A2 (in 90%)

Pathophysiology (in 90–95%):

21-hydroxylase deficiency → impaired cortisol + aldosterone synthesis → hyponatremia + hypokalemia + hypotension → ⇑ ACTH stimulation by pituitary gland (negative feedback mechanism) → ⇑ production of steroid precursors → diverted to production of androgens

Age: manifestation most often in neonatal period; M < F

Path: cerebriform appearance of cortical hyperplasia (weight increase to 2–4 x of normal); multilobular bilateral masses near rete testis (adrenocortical rests)

• excess of androgenic steroids:
› F: virilization of female fetus:
• pseudohermaphroditism (= clitoral hypertrophy, ambiguous external genitalia, urogenital sinus)
› M: precocious puberty in male → rapid growth at 3–7 years of age
• salt wasting ← diminished aldosterone production (in 75%):
• life-threatening hypovolemic salt-wasting adrenal crisis (during first 2 weeks of life)

@ Adrenal glands

√ ± symmetrically enlarged + thickened adrenal glands:
√ adrenal limb > 4 mm thick
√ coiled / cerebriform appearance
√ central echogenic stripe replaced by diffusely stippled echoes
√ massive bilateral myelolipomas ← long-standing / poorly treated congenital adrenal hyperplasia

@ Gonads (55%)

(a) females
√ typically normal gonads in females
√ cystic ovaries mimicking polycystic ovaries (76%)

(b) males
√ bilateral multinodular adrenocortical rests in rete testis (= mediastinum testis) in postpubertal boys (in 25%):
√ growth of adrenocortical rests ← effect of ACTH
√ usually hypoechoic < 5 mm masses
√ occasionally heterogeneously hyperechoic adrenals ± acoustic shadowing
√ iso- / slightly hyperintense on T1WI + hypointense on T2WI compared to adjacent testicular parenchyma

Rx: cortisone ± mineralocorticoids

B. ACQUIRED TYPE

M < F

(a) adrenal hyperplasia / adenoma / carcinoma: occasionally bilateral myelolipomas
(b) ovarian / testicular tumor
(c) gonadotropin-producing tumor: pineal, hypothalamic tumor, choriocarcinoma
• virilization; Cushing syndrome

ALKALINE-ENCRUSTED CYSTITIS AND PYELITIS

= chronic severe urinary tract infection affecting urothelial lining

Cause: nosocomial infection with urease-producing bacterium, most commonly Corynebacterium → producing alkaline urine

Predisposed: immunocompromised patient (esp. renal transplant patient), after invasive urologic procedure

Path: mucosal inflammation + encrustation of urothelial lining with struvite + calcium phosphate

• fever, hematuria, dysuria, suprapubic pain
• ammonia-like smell of urine

NECT:

√ diffuse thin / coarse superficial linear urothelial calcifications

Site: collecting system, ureter, bladder; often bilateral

Dx: culture positive > 48 hr for urea-splitting micro-organism

Cx: septic shock, graft failure

Rx: antibiotics, oral acidification of urine

AMYLOIDOSIS

= accumulation of extracellular eosinophilic amyloid protein

• gross hematuria (60%), urethral bleeding
• dysuria, frequency, cystitis, acute renal failure

GU location: bladder (50%), ureter (25%), urethra (20%), renal pelvis (6%)

@ Urinary bladder (50%)

Cause: ? chronic cystitis

Histo: stromal + muscle deposits of amyloid

• painless gross hematuria ← mucosal ulceration
• irritative symptoms

Site: posterior + posterolateral wall of bladder (68%) > multiple areas (65%)

√ nonspecific filling defects + distortion of bladder outline
√ CHARACTERISTIC linear submucosal / intramural calcifications
DDx: schistosomiasis mansoni, TB, urothelial carcinoma, other neoplasm
√ variable degrees of decreased contrast enhancement
√ decreased SI in bladder wall on T2WI
DDx: desmoplastic metastasis + bladder wall lymphoma (↓ T2-SI); urothelial carcinoma (↑ T2-SI)

@ Renal involvement
Frequency: 1° amyloidosis (35%),
2° amyloidosis (in > 80%)
• nephrotic-range proteinuria, renal insufficiency
√ smooth normal to large kidneys with increase in parenchymal thickness (acute stage)
√ small kidneys = cortical atrophy (in 50% of late stage)
√ occasionally attenuated collecting system
√ nephrographic density normal to diminished
√ amorphous renal calcifications
√ focal renal parenchymal mass lesions
US:
√ diffusely increased cortical echogenicity ← deposition of amyloid in glomeruli and interstitium
√ obscuration of arcuate arteries
√ preservation of corticomedullary differentiation
Cx: renal vein thrombosis → renal failure

@ Renal pelvis (6%)
√ calcification in submucosal deposit
√ irregular filling defect on excretory urography
√ hypointense amyloid deposit on T2WI (DDx: lymphoma, desmoplastic metastasis)
√ variable to NO enhancement

@ Ureter (25%)
Site: distal ureter; rarely bilateral
√ focal / diffuse areas of wall thickening + filling defects
√ irregular ureteral narrowing + stricture → hydronephrosis
√ linear submucosal / intramural calcifications

@ Urethra (rare)
• hematuria, dysuria, urethral obstruction
√ narrowing of urethra with filling defects
√ foci of increased echogenicity + posterior shadowing within corpus spongiosum
√ hypointense urethral + periurethral lesions on T2WI
Dx: urethroscopy + transurethral biopsy
DDx: urethral neoplasm

@ Seminal vesicles
= **senile localized amyloidosis of seminal vesicles**
Frequency: in 21% of men > 75 years of age (autopsy)
Site: symmetric involvement of both SV

DDx: invasion of SV by prostate cancer
Dx: transrectal biopsy

@ Retroperitoneum
√ diffuse infiltration encasing kidneys, aorta, IVC, pancreas
√ replacement of retroperitoneal fat with soft-tissue
√ focal retroperitoneal mass
MR:
√ intermediate T1 signal intensity
√ decreased T2 signal intensity

ANALGESIC NEPHROPATHY

= renal damage from ingestion of salicylates in combination with phenacetin / acetaminophen in a cumulative dose of 1 kg

Prevalence: USA (2–10%), Australia (20%)

Age: middle-aged; M÷F = 1÷4

- gross hematuria, hypertension
- renal colic (passage of renal tissue)
- renal insufficiency (2–10% of all end-stage renal failures)
- **Analgesic syndrome**: history of psychiatric therapy, abuse of alcohol + laxatives, headaches, pain in cervical + lumbar spine, peptic ulcer, anemia, splenomegaly, arteriosclerosis, premature aging

√ papillary necrosis
√ scarring of renal parenchyma ("wavy outline"); bilateral in 66%, unilateral in 5%
√ renal atrophy
√ papillary urothelial tumors in calices / pelvis (mostly TCC / squamous cell carcinoma), in 5% bilateral

ANGIOMYOLIPOMA

= AML = **Renal choristoma** (= benign tumor composed of tissues not normally occurring within the organ of origin)

N.B.: normal cells / tissues in an abnormal location!
[= ***Renal Hamartoma*** (improper name since fat and smooth muscle do normally occur within renal parenchyma]

= most common benign mesenchymal tumor of kidney composed of varying admixtures of thick-walled blood vessels, smooth muscle cells and mature fat (→ hence name!)

Prevalence: 0.3–2.0% of all renal tumors; 1% of all surgically removed renal tumors

Genetics: (a) sporadic (50–70%)
(b) inherited with tuberous sclerosis (30–50%), neurofibromatosis, vHL syndrome

Path: large infiltrating necrotic tumor without true capsule, 88% extending through renal capsule, hemorrhage (characteristic lack of complete elastic layer of vessels predisposes to aneurysm formation); tumor continues to grow during childhood + early adulthood

Histo:

(a) classic triphasic (92%): tumor composed of mature fat, aggregates of dysmorphic / thick-

walled blood vessels, epitheloid immature smooth muscle; coexpresses melanocytic markers (HMB-45, melan-A) and smooth muscle markers (smooth muscle actin, calponin), negative for epithelial markers

(b) monophasic epitheloid (8%): high degree of association with tuberous sclerosis + aggressive behavior

Average age: 41 years; M÷F = 1÷2

- small lesions are asymptomatic (60%)
- acute flank / abdominal pain in 87%

◊ Angiomyolipomas > 4 cm are symptomatic in 82–94% ← spontaneous bleeding in 50–60%!

- gross hematuria, anemia, hypertension
- **Wunderlich syndrome** = hemorrhagic shock ← massive bleeding into angiomyolipoma or into retroperitoneum (10%)

Location: renal parenchyma; renal hilum; may be exophytic perirenal / completely extrarenal (retroperitoneum, solid + hollow organs, skin, gynecologic region)

Mean size: 9 cm (range, few mm to 30 cm) in diameter

√ hypervascular mass with large feeding arteries, multiple aneurysms, laking without shunting, tortuous circumferential vessels, whorled parenchymal + venous phase

US:

√ homogeneously echogenic mass similar to sinus fat (DDx to renal cell carcinoma)

CT:

(a) ordinary AML (in 95%):

√ negative attenuation values

◊ Even a small amount of fat within a solid mass on NECT secures the diagnosis!

(b) minimal-fat AML (in 5%)

= angiomyolipoma with microscopic fat only mimicks RCC

√ hyperattenuating (53%) / isoattenuating (26%) / hypoattenuating (21%) mass (DDx: RCC)

√ homogeneous prolonged tumor enhancement

MR:

√ markedly hyperintense adipose tissue relative to renal parenchyma + isointense relative to fat on T1WI

√ demonstration of fat on selective fat-suppression sequence

√ prominent signal loss relative to other tissues on fat-suppressed / opposed-phase images with respect to in-phase images ← intravoxel coexistence of fat and water:

√ characteristic India ink artifact at interface between mass and normal renal parenchyma on opposed-phase T1WI

√ central portions of lesion do not demonstrate changes in signal intensity compared with in-phase images

√ variable SI on T2WI:

√ homogeneously high SI at single-shot T2WI with large fatty mass

√ homogeneously low SI relative to renal parenchyma in lipid-poor angiomyolipomas on T2WI

√ decreased signal intensity on Gd-enhanced images (DDx: RCC enhances)

Cx: (1) Hemorrhage with spontaneous rupture (25%) ← tumor > 4 cm / intratumoral aneurysm > 5 mm
(2) Growth into renal vein / IVC
◊ Not necessarily implying malignant transformation
(3) Renal failure

Rx: (1) Annual follow-up of lesions < 4 cm
(2) Semiannual follow-up of lesions ≥ 4 cm
(3) Emergency laparotomy (in 25%): nephrectomy, tumor resection
(4) Selective arterial embolization with hemorrhage
(5) Prophylactic surgery in pregnant women
(6) Screening for tuberous sclerosis

DDx: renal / perirenal lipoma or liposarcoma; Wilms tumor / renal cell carcinoma (occasionally contains fat if large, but also calcium); clear cell RCC with small amount of intracellular fat

Isolated Angiomyolipoma (50–70%)

= SPORADIC ANGIOMYOLIPOMA

Mean age: 43 (range, 27–72) years; M÷F = 1÷4

• flank pain, hematuria, palpable mass
√ solitary + unilateral (in 80% on R side) AML, NO stigmata of tuberous sclerosis
√ stable over long periods of time

Angiomyolipoma *Associated with TS* (30–50%)

Mean age: 17 years; usually present by 10 years; M÷F = 1÷1

◊ In 70–80–95% of patients with tuberous sclerosis
◊ May be the only evidence of tuberous sclerosis
√ commonly large + bilateral + multifocal AMLs with macroscopic fat
√ tendency for growth + hemorrhage

ARTERIOVENOUS RENAL CONNECTION

√ early enhancement of draining vein + renal vein + IVC
√ intraparenchymal / subcapsular / perirenal hematoma (as a result of bleeding)

Rx: transcatheter intraarterial occlusion, surgery

Arteriovenous Malformation (20–30%)

Cause: (1) Congenital AVM
• asymptomatic; M < F
(2) Acquired AVM: trauma, spontaneous rupture of aneurysm, very vascular malignant neoplasm

Histo:
(a) cirsoid AVM = multiple coiled vascular channels grouped in cluster
(b) cavernous AVM = single well-defined artery feeding into a single vein (rare)

• gross hematuria

Location: adjacent to collecting system
√ large unifocal mass:
  √ focally attenuated and displaced collecting system
  √ homogeneously enhancing mass
  √ curvilinear calcification
√ supplied by multiple segmental / interlobar arteries of normal caliber
√ draining into one / more veins
US:
  √ tubular anechoic structure (DDx: hydronephrosis, hydrocalyx)
Cx: subcapsular / perinephric hematoma (rare)

Arteriovenous Fistula (70–80%)

M > F
Cause: (1) Acquired: trauma (stab wound, percutaneous needle biopsy, percutaneous nephrostomy, nephrolithotripsy), surgery, tumor, inflammation, erosion of aneurysm into vein
(2) Idiopathic
Path: single dilated feeding artery + single draining vein
• asymptomatic with abdominal bruit / abdominal pain
• persistent / delayed gross hematuria (common)
√ tortuous varices over time
√ enlargement of renal vein

US:
  √ focal area of aliasing / color saturation ← high flow rate + vessel tortuosity
  √ ⇑ flow velocity + ⇓ resistance in feeding artery
  √ arterial pulsations in draining vein

Angio:
  √ detailed vascular anatomy for planning embolic occlusion
  √ diminished nephrogram ± cortical atrophy distal to fistula ← reduced flow to renal segment
Cx: (1) Cardiomegaly + high-output cardiac failure (50%)
(2) Renin-mediated hypertension
(3) Hydronephrosis
Prognosis: spontaneous closure within a few months

BENIGN PROSTATIC HYPERTROPHY

= BENIGN PROSTATIC HYPERPLASIA
Prevalence: 50% between ages 51 + 60 years; 75–80% of all men > 80 years of age
Histo: fibromyoadenomatous nodule (most common), muscular + fibromuscular + fibroadenomatous + stromal nodules
Age: initial growth onset < 30 years of age; onset of clinical symptoms at 60 ± 9 years
• sensation of full bladder, nocturia, trouble initiating micturition
• decreased urine caliber + force

• dribbling at termination of micturition

Location: transition + periurethral zone proximal to verumontanum forming "lateral lobes" (82%), "median lobe" (12%)

√ oval (61%) / round (22%) / pear-shaped (17%) enlargement of central gland

√ posterior + lateral displacement of outer gland (= prostate proper) creating cleavage plane of fibrous tissue between hyperplastic tissue + compressed prostatic tissue (= surgical capsule) often demarcated by displaced intraductal calcifications

Cx: bladder outflow obstruction

Rx: (1) Surgery: open prostatectomy (glands > 80 g), trans-urethral resection of prostate = TURP (glands < 80 g)

◊ Only 4–5% of patients need surgical treatment!

(2) Drugs: α-blockers (for stromal hyperplasia); androgen deprivation (suppression of LHRH / inhibition of Leydig cell synthesis of testosterone / competition for androgen receptor binding sites) + α-blockers (for glandular hyperplasia)

Prostatic Retention Cyst

= dilatation of glandular acini in BPH

Cause: acquired obstruction of glandular ductule

Age: 5th–6th decade

Location: transition / central / peripheral zone

√ 1–2-cm smooth-walled unilocular cyst

Cystic Degeneration of BPH

◊ Most common cystic lesion of prostate!

Location: transition zone

√ usually small cyst within nodules of benign prostatic hyperplasia

BLADDER CANCER

Prevalence: 76,960 new cases annually + 16,390 deaths (2016) 4th (10th) most common cancer in males (females); 5% of all new malignant neoplasms; most common tumor of genitourinary tract

Histo: (a) urothelial: transitional cell carcinoma (90%)

(b) squamous cell carcinoma (6–8%)

(c) adenocarcinoma (rare): resembling serous papillary cancer of ovary

(d) mixed histology: small cell neuroendocrine, micropapillary, sarcomatoid, plasmacytoid

Age: 3.1% [8%] in patients < 44 [45–54] years; usually in patients > 65 years; twice as frequent > 80 years; M÷F = 3–5÷1

T-Staging: primary question "Is there muscle invasion (T2)?"

N-Staging: obturator node (most common), nodes above aortic bifurcation (17%), presacral adenopathy (8%); accuracy of CT (70–90%) > MR (64–92%)

Staging accuracy: 50% clinically; 32–80% for CT; 72–96% for MR

Overstaging due to: edema following endoscopy / endoscopic resection, fibrosis from radiation therapy

• painless gross hematuria / microhematuria (80–90%)
• frequency, dysuria, pelvic pain / pressure

Presentation:

(1) Superficial papillary lesion (70%): papilloma, inverted papilloma, papillary urothelial neoplasm of low malignant potential (PUNLMP), low-grade and high-grade papillary urothelial carcinoma; in 20% progressing to invasive cancer
(2) Aggressive invasive de novo tumor (20%)
(3) Metastatic tumor (10%)

Location: bladder base (80%); lateral wall of bladder, bladder diverticulum (in 0.8–10.8%); single (in 60%)

Staging of Bladder Cancer

Jewett-Strong	*TNM*	*Histopathologic Findings*
O	T0	no primary tumor
	Ta	papillary tumor confined to mucosa = noninvasive
	Tis	carcinoma in situ
A	T1	invasion of lamina propria
B	T2	invasion of muscle
B1	T2a	of inner half of muscle
B2	T2b	of outer half of muscle
C	T3	of perivesical fat
	T3a	microscopic
	T3b	macroscopic
D	T4	invasion of surrounding organs
D1	T4a	seminal vesicles, prostate, vagina, rectum
	T4b	pelvic / abdominal wall
	N1	metastasis to single node ≤ 2 cm
	N2	metastasis to single node of 2–5 cm / in multiple nodes ≤ 5 cm
	N3	metastasis to single node > 5 cm
D2	N4	lymph node metastasis above bifurcation of common iliac arteries
	M1	distant metastasis (lung, liver, bone)

Size: < 2.5 cm (in > 50%)

√ intraluminal papillary / nodular mass
√ focal / diffuse wall thickening
√ ureteral obstruction ← muscle invasion

IVP (70% accuracy rate):

√ irregular filling defect with broad base and fronds (DDx: rectal gas marginated by Simpson's white line)
√ < 1% calcified

US:

√ papillary hypoechoic mass protruding into lumen
√ vascularity on Doppler imaging

CT urography (90% sensitive + specific):
◊ Cystoscopy always required to detect small flat lesions!
◊ Delay CT for > 7 days after instrumentation!
√ nodular / arched tumoral calcifications (< 5%) typically encrusting the surface
√ early tumor enhancement
√ increased attenuation of perivesical fat with invasion

MR (staging modality of choice, 52–93% accuracy):
√ tumor isointense to bladder muscle on T1WI + hyperintense on T2WI
√ T1WI optimal to detect invasion of perivesical fat + metastases to lymph nodes + bone
√ T2WI optimal to differentiate tumor from fibrosis and to evaluate tumor depth (SI differences between inner + outer layers of muscularis propria)
√ enhancement differentiates between early enhancing mucosa, submucosa, tumor, nonenhancing muscle, edema + fibrosis

Prognosis: 40–70% recurrence rate

Transitional Cell Carcinoma of Bladder

Classification:
(a) noninvasive / superficial flat / papillary (80–85%)
(b) muscle-invasive / nonpapillary (20–25%)

◊ Synchronous upper tract TCC in 2%
◊ Metachronous upper tract TCC in 6%

Metachronous bladder TCC:
› in 23–40% of primary renal TCC after 15–48 months
› in 20–50% of primary ureteral TCC after 10–24 months
› in 4% of bladder primaries up to 20 years later (²/₃ within 2 years)

Synchronous bladder TCC:
› in 24% of primary renal pelvic involvement
› in 39% of primary ureteral involvement
› in 2% of primary bladder involvement

Prognosis: overall 82% 5-year survival rate; after cystectomy 55–80% 5-year survival with tumor confined to lamina propria, 40% with invasion of muscularis propria, 20% with invasion of perivesical fat, 6% for metastatic cancer

Rx: cystoscopic resection, intravesical mitomycin C, radical cystectomy with urinary diversion

Noninvasive / Superficial / Papillary TCC (80–85%)

Grade: low-grade lesion, usually multifocal

Origin: hyperplastic epithelium

Prognosis: good; 50% rate of recurrence; evolve into muscle-invasive cancer if untreated

Genetics: activate mutation of HRAS gene and fibroblast growth factor

Muscle-invasive / Nonpapillary TCC *(20–25%)*

Grade: higher histologic grade
Origin: severe dysplasia / carcinoma in situ
Genetics: structural + functional defects in p53 and retinoblastoma tumor suppressor pathways

Squamous Cell Carcinoma of Urinary Bladder

Risk factors: long-term catheterization, nonfunctioning bladder, urinary tract calculi, bladder diverticulum (2–10% risk), chronic infection by Schistosoma hematobium
Prognosis: worse than urothelial cancer

BLADDER DIVERTICULUM

= cavity formed by herniation of bladder mucosa through muscular wall, joined to bladder cavity by constricted neck
Prevalence: 1.7% in children
Average age: 57 years; M÷F = 9÷1
Site: areas of congenital weakness of muscular wall at
(a) urethral meatus
(b) posterolateral wall (Hutch diverticulum = paraureteral)
√ hypoechoic fluid-filled structure continuous with bladder wall
√ may appear complex ← thickened wall / debris / soft-tissue component
√ may contain calculi
Cx: (1) Bladder cancer in 0.8–10% ← urinary stasis ← chronic mucosal irritation ← prolonged exposure to urinary carcinogens (average age of 66 years)
(2) Ureteral obstruction
(3) Ureteral reflux
DDx: pelvic cyst

Primary Diverticulum (40%)

= CONGENITAL / IDIOPATHIC DIVERTICULUM
√ in 3% single diverticulum
(a) WITH vesicoureteral reflux
1. Hutch diverticulum in paraureteral region
(b) WITHOUT vesicoureteral reflux

Secondary Diverticulum (60%)

√ in 50% multiple diverticula
(a) postoperative state
(b) associated with bladder outlet obstruction
1. Posterior urethral valves
2. Urethral stricture
3. Large ureterocele
4. Neurogenic dysfunction
5. Enlarged prostate
6. Bladder neck stenosis

(c) associated with congenital syndromes

1. Prune belly syndrome
2. Menkes kinky-hair syndrome
3. Williams syndrome
4. Ehlers-Danlos type 9 syndrome
5. Diamond-Blackfan syndrome

Multiple Diverticula in Children

1. Neurogenic dysfunction
2. Posterior urethral valves
3. Prune belly syndrome

BLADDER EXSTROPHY

= EPISPADIA-EXSTROPHY COMPLEX

= failure of lower abdominal wall + anterior bladder wall to close normally

Prevalence: 1÷30,000 to 1÷40,000 live births; M > F

Etiology: incomplete retraction of cloacal membrane prevents normal midline migration of mesoderm→ resulting in incomplete midline closure of infraumbilical abdominal wall; size of persistent cloacal membrane at time of rupture accounts for different degrees of severity

- urinary bladder exposed + open anteriorly
- mucosa everted through abdominal wall defect
- bladder margins continuous with margins of abdominal wall
- epispadia + short / split penis (male); bifid clitoris (female)
- maldescended testes

May be associated with:

wide linea alba, omphalocele, limb defects (eg, club feet), renal malformation (horseshoe kidney, renal agenesis), incomplete testicular descent, GI obstruction, bilateral inguinal hernias, imperforate anus, cardiac anomalies, hydrocephalus, meningomyelocele

male: epispadia, short or split penis (common);

female: bifid clitoris, uterine and vaginal anomalies

√ persistently "absent" urinary bladder (HALLMARK) → urine is released immediately into amniotic cavity through opening between bladder and abdominal wall.

√ irregular thickening of everted posterior bladder wall ← inflammation of exposed mucosa

√ ventral defect of infraumbilical abdominal wall

√ low position of umbilicus

√ pubic diastasis = widening of pubic symphysis

DDx: cloacal exstrophy (NO extruded bowel loops, abnormal rectum)

Cx: urinary incontinence, infertility, pyelonephritis, bladder carcinoma (4%)

Rx: primary closure, bladder excision with urinary diversion

Closed Exstrophy = Pseudoexstrophy

= persistent large cloacal membrane without rupture

- anterior wall of bladder covered by thin bilaminar epithelial membrane

√ infraumbilical musculoskeletal defect

√ subcutaneous position of bladder

CHOLESTEATOMA

= KERATIN BALL
= keratinized squamous epithelium shed into lumen
Pathogenesis: long-standing urinary infection may result in squamous metaplasia of transitional epithelium
• history of UTIs; repeated episodes of renal colic with passage of "white tissue flakes"
Location: renal pelvis > upper ureter
√ mottled / stringy "onion-skin" filling defect in calices / renal pelvis
√ dilatation of pelvicaliceal system (with obstruction)
√ calcification of keratinized material possible
◊ Not a premalignant condition!

CHRONIC GLOMERULONEPHRITIS

Cause: acute poststreptococcal glomerulonephritis
• late presentation without prior clinically apparent acute phase
• hypertension, renal failure
√ small smooth kidneys with wasted parenchyma
√ normal papillae + calices
√ patchy nephrogram with diminished density of contrast medium
√ cortical calcification (uncommon)
US:
√ increased echogenicity
√ small kidneys with vicarious sinus lipomatosis
Angio:
√ marked reduction in renal blood flow
√ reflux of contrast material into aorta
√ severely pruned + tortuous interlobar and arcuate arteries
√ nonvisualization of interlobular arteries
√ delayed contrast clearance from interlobar arteries

CLEAR CELL SARCOMA OF KIDNEY

= BONE-METASTASIZING RENAL TUMOR OF CHILDHOOD
= rare highly malignant mesenchymal renal neoplasm of childhood with propensity for bone metastasis (rare for Wilms)
Incidence: 20 cases annually in USA; 4–5% of primary renal neoplasms in childhood; 2nd most common renal malignancy after Wilms
Mean age: 3 (range, 1–6) years; M÷F= 2÷1
Path: always unilateral unicentric soft well-circumscribed mass replacing most of the kidney / centered in renal medulla; hemorrhage + necrosis (in 70%); hilar lymphovascular infiltration (30%); extension into renal vein (5%)
Histo: composed of well-defined polygonal to stellate cells with vacuolization, ovoid to rounded nuclei, prominent capillary pattern + tendency toward cyst formation separated

by slightly thickened septa
• increasing abdominal girth + palpable abdominal mass
• lethargy, weight loss, hematuria, bone pain (infrequent)
√ expansile well-demarcated mass (8–16 cm) with dominant soft-tissue component
√ cystic component of varying size (few mm to 5 cm) + multiplicity (58%)
√ amorphous / linear calcifications (25%)
√ renal mass crossing midline (58%)
√ NO intravascular extension
√ lytic / sclerotic / mixed metastatic bone lesions
Metastases to: lymph nodes (30%), bone (13–20%), lung, brain, liver; in 5–18% metastatic at presentation
US:
√ inhomogeneous renal mass of soft-tissue density
√ well-defined hypoechoic central area (= necrosis)
√ mass with fluid-filled anechoic cystic spaces
√ large fluid-filled spaces + echogenic septa may predominate
CT:
√ heterogeneous enhancement less than that of normal renal parenchyma
√ low-attenuation areas ← hemorrhage / necrosis
√ water-density areas ← cysts
MR:
√ low to intermediate signal intensity on T1WI
√ high signal intensity on T2WI
NUC:
√ bone scan recommended after diagnosis is established
Prognosis: 60–70% long-term survival rate; aggressive behavior (worse than Wilms tumor) with higher rate of relapse + mortality
DDx: cystic form of Wilms tumor (vascular invasion), multilocular cystic nephroma, cystic dysplasia

CONDYLOMA ACUMINATA

= VENEREAL WART = PENILE SQUAMOUS PAPILLOMA
Cause: viral infection
Histo: squamous papilloma
@ Skin
• soft sessile verucca of penile glans / shaft / prepuce
@ Urethra
Prevalence: 0.5–5% of male patients with cutaneous disease
N.B.: retrograde urethrography NOT recommended as it may cause retrograde seeding!
Voiding cystourethrography:
√ multiple papillary filling defects in anterior urethra
√ ± extension into bladder (rare)
Rx: instillation of podophyllin, thiotepa, 5-fluorouracil into urethra

CONGENITAL RENAL HYPOPLASIA

= miniaturization with reduction in number of renal lobes, number of calices and papillae, amount of nephrons
(+ smallness of cells)

VARIANT: **Ask-Upmark kidney** = aglomerular focal hypoplasia

√ unilateral small kidney
√ decreased number of papillae + calices (5 or less)
√ hypertrophied contralateral kidney
√ absent renal artery
√ hypoplastic disorganized renal veins

CONN SYNDROME

= PRIMARY HYPERALDOSTERONISM = PRIMARY ALDOSTERONISM
= autonomous excess secretion of the mineralocorticoid aldosterone with hypertension + spontaneous hypokalemia

Prevalence: 2–15% of hypertensive population
Age: 3rd–5th decade; M÷F = 1÷2
Cause of aldosteronism:

(a) responsive to corticotropin
  › aldosterone-producing adenoma
  › primary adrenal hyperplasia
(b) responsive to renin-angiotensin system
  › aldosterone-producing renin-responsive adenoma
  › bilateral adrenal glomerulosa hyperplasia
  › familial form of aldosteronism

- hypertension ← hypernatremia
- hypokalemia (80–90%, induced by administering large amounts of sodium chloride for 3–5 days):
  - muscle weakness, cardiac arrhythmia
  - carbohydrate intolerance, nephrogenic diabetes insipidus
- depletion of magnesium, metabolic alkalosis
- increased urinary excretion of aldosterone + metabolites
- plasma aldosterone-to-renin ratio (test of choice):
  - nonsuppressible elevation in plasma aldosterone concentration
  - suppressed plasma renin levels

Path:

(a) bilateral idiopathic adrenal hyperplasia (60%):
  = idiopathic hyperaldosteronism = focal / diffuse hyperplasia of glomerulosa zone accompanied by micro- / macroscopic nodules
(b) adrenocortical adenoma (40%): solitary aldosteronoma (65–70%); multiple (13%); microadenomatosis (6%)
(c) adrenocortical carcinoma (< 1%)

Average size: 1.7 (range, 0.5–3.5) cm
Location: L > R; bilateral in 6%

Adrenal venography : 76% accurate
Adrenal venous blood sampling : 95% accurate, 75% sensitive
CT (60–80% sensitive):
√ mass of soft-tissue density / low attenuation
◊ Among hyperfunctioning adrenal adenomas aldosteronomas have the lowest attenuation!
√ usually hypervascular, rarely hypovascular
√ both glands normal in size ← micronodules
√ nodular / multinodular adrenal gland(s) ← hyperplasia
NUC:
√ ^{131}I NP-59 uptake following dexamethasone suppression:
√ bilateral early visualization (< 5 days) implies adrenal hyperplasia
√ unilateral early visualization implies adenoma
√ late bilateral visualization (> 5 days) may be normal
Dx: elevated plasma aldosterone concentration + suppressed plasma renin activity
Diagnostic endocrine tests:
postural stimulation test, short saline infusion test, 18-hydroxycorticosterone concentration
Cave:
◊ Adenoma in one gland + nonhyperfunctioning adenoma in other gland can suggest bilateral adrenal hyperplasia
◊ Dominant macronodule of one gland in bilateral adrenal hyperplasia can simulate adenoma
Solution: Adrenal venous blood sampling to determine appropriate therapy
Rx: adrenalectomy for neoplasms (75% long-term cure rate for hypertension); medical treatment for hyperplasia

CONTRAST NEPHROPATHY

= CONTRAST-INDUCED RENAL FAILURE
= increase in serum creatinine of ≥ 1 mg/dL ± 25–50% of baseline creatinine level after intravascular contrast administration
Patients at risk:
1. Preexisting renal insufficiency
2. Insulin-dependent diabetes mellitus
3. Large volume of contrast media
4. Concomitant administration of other nephrotoxic drugs: aminoglycosides, nonsteroidal anti-inflammatory agents
5. American Heart Association class IV congestive heart failure
6. Hyperuricemia

Contrast Medium-induced Risk of Nephropathy	
Test	*Threshold*
Serum creatinine level	> 1.6 mg/dL
Estimated glomerular filtration rate*	< 45 mL/min

* Online Calculator using age, race, gender, body weight and plasma creatinine: http://www.medcalc.com/gfr.html ; http://www.mcw.edu/calculators/creatinine.htm

◊ A serum creatinine level of > 4.5 mg/dL causes acute renal failure in 60% of nondiabetics + 100% of diabetics!

◊ IV LOCM is an independent risk factor for acute kidney injury post CECT for a serum creatinine ≥ 1.6 mg/dL

Previously considered but no longer accepted risk factors:

dehydration, hypertension, proteinuria, peripheral vascular disease, age > 65 years, multiple myeloma

◊ IV LOCM is NOT a risk factor for acute kidney injury post CECT with a stable serum creatinine < 1.5 mg/dL

Mechanism:

increase in renal perfusion by vasodilatation (via prostaglandin I2 ± E2) → followed by vasoconstriction (via angiotensin II, norepinephrine, vasopressin)

Time course:

(a) rise in serum creatinine within 1–2 days
(b) peak at 4–7 days
(c) return to normal by 10–14 days

√ persistent nephrogram on plain film
√ cortical attenuation > 140 HU on CT after 24-hour delay

Recommendation:

◊ Employ nonionic contrast media (LOCM appears safe in patients without renal dysfunction / underlying risk factors in doses as large as 800 mL [300 mg iodine per mL])

◊ Do NOT exceed maximum allowed dose (**Cigarroa formula** for HOCM): 5 mL x body weight (kg)

Contrast limit (mL) 60% by weight = serum creatinine (mg/100 mL)

CUSHING SYNDROME

= HYPERCORTISOLISM

= excessive glucocorticoid from either exogenous / endogenous sources

Etiology:

A. ACTH-(PITUITARY)-DEPENDENT (70%)

= overproduction of corticotropin

1. **Cushing disease** (68–90% of endogenous causes)

= overproduction of pituitary ACTH → non-autonomous adrenal hyperplasia

Cause:

(a) basophilic / chromophobe adenoma
(b) overactive pituitary
(c) ACTH-producing primary elsewhere

√ normal adrenal glands
√ diffuse adrenal enlargement
√ macronodular adrenal hyperplasia (in up to 85%)

◊ Micronodular hyperplasia is NOT seen on imaging

2. **Paraneoplastic ectopic ACTH production** (12–20%): bronchial / thymic carcinoid > pheochromocytoma, pancreatic islet cell tumor (10%), oat cell carcinoma of lung (8%), liver cancer, prostate cancer, ovarian cancer, breast cancer, bronchial adenoma,

medullary carcinoma of thyroid, thymoma
◊ Bronchial + thymic carcinoids are often < 1 cm at the time they produce Cushing syndrome!
◊ Islet cell tumors are large + often metastatic by the time they produce Cushing syndrome!
Recommendation: thin-section CT of chest

3. Exogenous ACTH
4. Hypothalamic dysfunction
5. Production of corticotropin-releasing factor (rare)

B. ACTH-(PITUITARY)-INDEPENDENT (30%)

(a) primary adrenal abnormality (18%):
= autonomous cortisol production by adrenal gland

1. **Adrenocortical adenoma**
(10–20% of cases; 10% in adults, 15% in children)
√ often > 2 cm in size
→ readily visualized by CT / MRI
√ atrophy of remaining adrenal tissue ← adenoma suppresses ACTH levels
◊ A hyperfunctioning adenoma does NOT always cause atrophy of the adrenal glands, but normal / thickened adrenal limbs should raise concern for ACTH-dependency!
2. **Adrenocortical carcinoma**
(5–10% of cases; 10% in adults, 66% in children)
3. Ectopic ACTH production / ectopic corticotropic-releasing factor (CRF) secretion
4. Primary pigmented nodular adrenocortical (< 1%)hyperplasia (rare; in children + young adults)
√ multiple small bilateral nodules / normal adrenal
4. Massive macronodular hyperplasia with marked adrenal enlargement (< 1%)
√ multiple bilateral macronodules

(b) exogenous cortisol (12%)

Prevalence: 1÷1,000 autopsies; M÷F = 1÷4
Age: 30–40 years (highest incidence); more often following pregnancy

• central / truncal obesity, buffalo hump, moon face, facial plethora
• purple abdominal striae, acne, hirsutism, amenorrhea
• fatigue, mood changes, proximal muscle weakness
• hypertension, atherosclerosis, edema
• impaired glucose tolerance = glycosuria / diabetes
• elevated plasma cortisol levels
• hypokalemia ← excess cortisol binding Na+/K+ pump acting like aldosterone
• excessive excretion of urinary 17-hydroxy-corticosteroids
• elevated peripheral ACTH level
• dexamethasone suppression test / metyrapone test
√ retarded bone maturation
√ most often axial osteoporosis
√ stippled calvarium

√ demineralized dorsum sellae
√ excess callus formation

Cx: (1) Pathologic fractures of vertebrae + ribs with excessive callus formation
(2) Aseptic necrosis of hips
(3) Bone infarcts
(4) Delayed skeletal maturation in children

DDx of Cushing syndrome:

(a) focal unilateral adrenal mass
- √ 2–4-cm focal mass in one adrenal gland + atrophy of contralateral gland = adrenal adenoma
- √ > 4-cm large focal mass with central necrosis in one adrenal gland + atrophy of contralateral gland = adrenal adenocarcinoma

(b) bilateral adrenal enlargement
- √ diffuse uniform thickening = Cushing disease

(c) Multiple bilateral adrenal nodules
- √ macronodules = multinodular hyperplasia of long-standing Cushing disease
- √ large nodules (autonomous ACTH-independent) = massive macronodular hyperplasia
- √ small nodules = primary pigmented nodular adrenocortical disease

CYSTITIS

= bacterial infection; M < F
• frequency, dysuria, hematuria, reduced bladder capacity
√ cystogram insensitive

US:
- √ focal / multifocal / circumferential isoechoic bladder wall thickening
- √ decrease in bladder wall thickening during bladder distension (eg, instillation of sterile saline via a urethral catheter)
- √ bullous lesions
- √ intact mucosa

DDx: bladder neoplasm, ureterocele, pseudoureterocele, neurofibromatosis, pseudosarcomatous myofibroblastic proliferations

Cystitis Cystica

= CYSTITIS FOLLICULARIS = CYSTITIS GLANDULARIS = BULLOUS CYSTITIS
= nonspecific chronic reactive inflammatory process of bladder wall
Age: any; M > F
Histo: metaplasia of urothelium → proliferation into buds (nests of von Brunn) → growth into lamina propria → differentiation into cystic deposits (cystitis **cystica**) or intestinal columnar mucin-secreting glands formed of goblets cells (cystitis **glandularis**)
• frequency, dysuria, urgency, hematuria
• cystoscopy: cobblestone mucosa; papillary / polypoid mass
√ multiple small round cystlike mucosal elevations
√ filling defects
√ intact muscle layer

May be associated with: pelvic lipomatosis → bladder obstruction and chronic infection
Prognosis: potentially malignant in adults

Emphysematous Cystitis

= uncommon complication of urinary tract infection by gas-forming organism almost PATHOGNOMONIC of poorly controlled diabetes (= bacterial fermentation of glucose)
Age: > 50 years; M÷F = 1÷2
Predisposed: diabetes mellitus, neurogenic bladder, bladder outlet obstruction, chronic UTI
Organism: E. coli, E. aerogenes, P. mirabilis, S. aureus, streptococci, Clostridium perfringens, Nocardia, Candida
May be associated with: emphysematous pyelitis / pyelonephritis
• pneumaturia (rare)
Plain film:
√ translucent streaky irregular area / ring of air bubbles in bladder wall
√ intraluminal air-fluid level
US:
√ shadowing echogenic foci within area of bladder wall thickening
CT (most specific modality)
DDx: (a) Gas within bladder:
trauma, urinary tract instrumentation, enterovesical fistula
(b) Gas external to bladder:
rectal gas, emphysematous vaginitis, pneumatosis cystoides intestinalis, gas gangrene of uterus

Eosinophilic Cystitis

= rare chronic inflammatory disease
Prevalence: 83 adult cases in literature
Mean age: 42–48 years; M÷F = 1.3÷1.0
Cause: idiopathic (29%); atopy; after bladder surgery; adverse reaction to drugs + food; parasitic / nonparasitic urinary tract infections; autoimmune disorder; eosinophilic enteritis
Histo: transmural infiltrate of eosinophils with variable degree of fibrosis + muscle necrosis of detrusor
• hematuria, frequency, dysuria, pain
• peripheral eosinophilia (0–43%)
√ single / multiple bladder masses ± cystic component
√ normal / thickened bladder wall
√ small contracted bladder (in fibrotic stage)
√ isointense mass relative to muscle on T2WI
√ hyperintense mass relative to muscle on T1WI with enhancement
Prognosis: usually benign self-limiting course, if cause removed

Granulomatous Cystitis = Tuberculous Cystitis

√ irritable hypertonic bladder with decreased capacity
√ disease process usually starts at trigone spreading upward and laterally

√ calcification of bladder wall (rare)

Hemorrhagic Cystitis

Cause: unclear
(a) nonspecific: negative culture
(b) bacterial: E. coli (in 17%)
(c) viral (adenovirus in 19%): negative culture, viral exanthem
(d) cytotoxic: cyclophosphamide (Cytoxan®), in 15% of patients within 1st year of treatment

√ echogenic mobile clumps of solid material (= intraluminal blood clot)

Interstitial Cystitis

Age: postmenopausal female

• pink pseudoulceration of bladder mucosa characteristically at vertex of bladder (= **Hunner ulcer**)

Bullous Edema of Bladder Wall

Cause: continuous internal contact with Foley catheter, involvement of bladder wall by external contact in pelvic inflammatory conditions (eg, Crohn disease, appendicitis, diverticulitis)

√ smoothly thickened / polypoid redundant hypoechoic mucosa

ECTOPIC URETER

= abnormal distal insertion outside bladder trigone

Associated with: duplication of ureter

Site of insertion of ectopic ureter:

› in female <u>infrasphincteric</u> insertion: bladder neck, upper urethra, uterus, cervix, vaginal vestibule, vagina, fallopian tube, rectum
• incontinence after toilet training ← ureteral insertion below level of external urethral sphincter
• WETTING in upright females = intermittent / constant dribbling
• urinary tract infection

› in male <u>always suprasphincteric</u> insertion: posterior urethra, seminal vesicle (seminal vesical cyst), vas deferens, low in bladder, bladder neck, prostatic urethra, ejaculatory duct
• NO enuresis in males after toilet training ← ureteral insertion above level of external urethral sphincter
• epididymitis / orchitis in preadolescent male
• urge incontinence (insertion into posterior urethra)
√ often associated with ureteral obstruction

EJACULATORY DUCT CYST

Cause: congenital / acquired obstruction of ejaculatory duct

• perineal pain, dysuria, ejaculatory pain, hematospermia
• major cause of male infertility (= low-volume oligospermia / azoospermia)

Location: along expected course of ejaculatory duct

√ intraprostatic cyst within central zone
√ aspirate contains spermatozoa / fructose with normal testicular function
√ cyst commonly contains calculi
√ cystic dilatation of ipsilateral seminal vesicle
√ contrast injection into cyst outlines seminal vesicle

EPIDIDYMITIS

Acute Epididymitis

◊ Most common acute pathologic process in postpubertal age

Cause: retrograde ascending urinary tract infection; instrumentation + prostatitis (in older men); chemical (Amiodarone); posttraumatic; vasculitis (Henoch-Schönlein Purpura); idiopathic

Incidence: 634,000 cases annually

Age: › child < 2 years (23% of children):
imperforate anus, ureteral ectopia to seminal vesicle, bladder exstrophy, neurogenic bladder, posterior urethral valves, dysfunctional voiding
› child > 6 years (77% of children)
› < 18 years (common)
› 19–25 years (very common)
› > 25 years (extremely common)
› > 30 years (almost all cases of scrotal pain)

Organism: E. coli + S. aureus (85%), Gonococcus (12%), TB (2%); nonspecific (? chemical) epididymitis in 20%
(a) child + > 35 years of age: Escherichia coli + Proteus mirabilis, CMV with AIDS
(b) < 35 years of age: Chlamydia trachomatis, Neisseria gonorrhoeae

• fever, increasing scrotal pain over 1–2 days
• hemiscrotal swelling + tenderness + erythema
• pyuria (95%), positive urine culture, leukocytosis (50%)
• dysuria + frequency (25%), prostatic tenderness (infrequent)

Site: may begin with focal epididymitis (25%) often in epididymal tail → body → head (most common)
◊ Subsequent spread to testis (common): global orchitis (frequent), focal orchitis (10%)

US:
√ enlarged heterogeneous epididymis:
√ enlarged head suggests hematogenous spread
√ enlarged tail suggests retrograde reflux from prostate / urine
√ hypoechoic epididymis relative to testis ← edema
√ reactive hydrocele ± thickening of scrotal wall
√ enlarged spermatic cord containing hyperechoic fat
√ thickening of tunica albuginea (in severe infection)

Color Duplex (91% sensitive, 100% specific):
√ increased number + concentration of identifiable vessels in affected region (=

hyperemia)
√ peak systolic velocity (PSV) > 15 cm/sec with PSV ratio > 1.9 compared with normal side
√ detection of venous flow
√ diastolic flow reversal in testicular artery ← epididymal edema with obstruction of venous outflow

NUC (true positive rate of 99%):
√ symmetric perfusion of iliac + femoral vessels
√ markedly increased perfusion through spermatic cord vessels (= testicular + deferential arteries)
√ curvilinear increased activity laterally in hemiscrotum on static images (also centrally if testis involved)
√ increased activity of scrotal contents on static images ← hyperemia + increased capillary permeability

Rx: antimicrobial therapy, scrotal elevation, bed rest, analgesics, ice packs

Cx:
(1) Epididymo-orchitis (20–40%) (see below)
(2) Epididymal abscess (6%)
√ central hypoechoic region of liquefaction with absence of color Doppler signals
(3) Testicular abscess (6%)
(4) Testicular infarction (3%) ← extrinsic compression of testicular blood flow
(5) Late testicular atrophy (21%)
(6) Hydro- / pyocele
(7) Fournier gangrene

DDx:
(1) Testicular abscess (→ increased perfusion with centrally decreased uptake)
(2) Hydrocele (→ normal perfusion, no uptake)
(3) Testicular tumor (→ slightly increased perfusion; in- / decreased uptake; no associated epididymal hyperemia on CFI; positive tumor markers: hCG, AFP)

Acute Epididymo-orchitis

= progression of epididymal infection → focal / diffuse involvement of testis

Frequency: 20–40%

Age: two peaks at > 15 years (sexually active) and > 50 years (with BPH)

• Prhen sign = pain associated with epididymo-orchitis improves with elevation of testes above level of pubic symphysis

Cx: testicular necrosis ← infarction ← compromised testicular venous outflow ← edema

Chronic Epididymitis

= GRANULOMATOUS ORCHITIS

= granulomatous reaction to sperm / microorganisms

• painful mass

Site: mostly tail

US:
√ enlarged heterogeneous hyperechoic epididymis
√ NO increased blood flow
DDx: epididymal adenomatoid tumor (painless)

ERECTILE DYSFUNCTION

= IMPOTENCE (term replaced due to negative connotation)
= inability to have / maintain a penile erection sufficient for vaginal penetration in 50% or more attempts during intercourse
Prevalence: 10 million Americans
Physiology:
(a) psychogenic phase:
- stimuli from thalamic nuclei, rhinencephalon, limbic system converge in medial preoptic anterior hypothalamic area

(b) neurologic phase:
- sacral nerve roots (S2–S4) contribute fibers to pelvic sympathetic plexus
- stimulation of cavernous nerve (parasympathetic nerve) → changes in blood flow → full erection
- stimulation of pudendal nerve (motor nerve) → contraction of bulbocavernosus + ischiocavernosus muscle → occlusion of veins → rigid erection

Risk factors: hypertension, diabetes, smoking, CAD, peripheral vascular disease, pelvic trauma / surgery, blood lipid abnormalities
Cause:
A. ORGANIC (majority)
1. Endocrine disorder reducing serum testosterone / increasing serum prolactin
2. Vascular disease (10–20%): increasing with age
   (a) failure to fill (arteriogenic)
   (b) failure to store (venogenic)
3. Neurogenic disease (10%) = failure to initiate:
   (a) neurologic disorder: multiple sclerosis, spinal cord injury, cervical spondylosis, spinal arachnoiditis, pelvic trauma, temporal lobe / idiopathic epilepsy, Alzheimer disease, Parkinson disease, tabes dorsalis, amyloidosis, primary autonomic insufficiency, cerebrovascular accidents, primary / metastatic tumor
   (b) surgical injury to nerves: damage to pelvic sympathetic nerves / cavernous nerve during radical prostatectomy / cystectomy
4. Chronic disease: diabetes mellitus (2 million); drugs (antihypertensives, anticonvulsants, alcohol, narcotics, psychotropic agents)
5. Endorgan disease: priapism

B. PSYCHOGENIC

Penile-brachial index (normal > 1.0):
= highest penile artery pressure over mean brachial pressure
√ < 0.70 suggests large vessel disease
Rx: (1) Surgery:
(a) vascular reconstructive surgery

(b) penile prosthesis placement
› nonhydraulic: semirigid, malleable, positionable
› hydraulic

(2) Oral / intracavernosal injection of vasoactive agents

(3) Nonsurgical external devices: vacuum erection devices

(4) Sex therapy

EXTRAGONADAL GERM CELL TUMOR

= PRIMARY EXTRAGONADAL GERM CELL TUMOR

Frequency: 1.0–2.5% of germ cell tumors; M > F

Origin: aberrant primordial germ cell rests ←

(a) faulty migration from yolk sac / endoderm to urogenital ridge

(b) physiologic germ cell distribution to liver, bone marrow, brain

Histo: seminoma (rare in retroperitoneum) / nonseminomatous germ cell tumor (embryonal carcinoma, yolk sac tumor, choriocarcinoma, teratoma, mixed germ cell tumor)

◊ 80% of mediastinal germ cell tumors are benign!

• elevated α-fetoprotein: embryonal carcinoma, yolk sac tumor

• elevated β-hCG: choriocarcinoma

Location: along midline from pineal to sacrococcygeal region, mediastinum > retroperitoneum

◊ The anterior mediastinum is the most common site of extragonadal germ cell tumors!

Site: near midline between T6 and S2

◊ A midline mass is more suggestive of a primary tumor than metastasis!

CT/MR:

› seminoma:

√ large lobulated well-defined homogeneous solid mass with ringlike / speckled calcifications

√ hypointense fibrous septa on T2WI

√ contrast enhancement of septa

› nonseminoma:

√ heterogeneous tumor with areas of hemorrhage + necrosis

√ heterogeneous contrast enhancement

√ ± flow voids ← hypervascularity

√ ± invasion of adjacent structures

Dx: after exclusion of primary gonadal source

Prognosis: worse compared to gonadal location

DDx: metastasis from gonadal primary (in 30%)

FIBROEPITHELIAL POLYP

= FIBROUS POLYP = FIBROEPITHELIOMA = VASCULAR FIBROUS POLYP = POLYPOID FIBROMA

Origin: embryonic

Histo: mesodermal tumor with fibrovascular stroma covered by normal transitional cell epithelium

Age: in child / young adult 20–40 years

Multiplicity: usually solitary
√ mobile elongated cylindrical filling defect on a thin stalk
√ multilocular wormlike appearance with smooth margins
√ (occasionally) frondlike appearance
@ Ureter
◊ Most common nonepithelial tumor of ureter!
Site: proximal ureter
• intermittent abdominal / flank pain
• gross hematuria (rare)
@ Urethra
• hematuria at birth, obstructive voiding symptoms
Site: verumontanum
√ polyp may extend through bladder neck into bladder
√ extension into midpoint of bulbar urethra during voiding phase of cystourethrography
Cx: bladder outlet obstruction

FIBROUS PSEUDOTUMOR OF SCROTUM

= NODULAR PERIORCHITIS = NODULAR FIBROSIS
= uncommon benign reactive fibrous proliferation
Frequency: 3rd most common paratesticular mass (after lipoma and epididymal adenomatoid tumor)
Cause: often related to prior inflammation / infection / trauma
Origin: tunica vaginalis (most common)
Histo: dense fibrous tissue with interspersed fibroblasts and mixed inflammatory cells
Associated with: hydrocele (50%)
• history of trauma, surgery, infection, inflammation
• mimicks malignancy at physical examination
Size: up to 8 cm in diameter
√ hypoechoic mass(es) arising from tunica vaginalis (76%):
√ shadowing ← dense fibrosis / internal calcifications
√ uniformly low signal intensity on T1WI + T2WI like fibroma
√ slow persistent variable enhancement
√ may dislodge (as "scrotal pearl")
√ single / multiple hypoechoic / hyperechoic nodules arising from epididymis / spermatic cord / tunica albuginea
√ diffuse fibrous pseudotumor (= **fibromatous periorchitis**):
√ thickening of inner surface of tunica vaginalis ← diffuse proliferative encasement of testis
√ focal linear calcification + ossification
√ **inflammatory pseudotumor of paratesticular lymph node**
= predominantly hypoechoic lymph node ← spindle cell proliferation in connective tissue framework of hilum and capsule

FOURNIER GANGRENE

= FULMINANT NECROTIZING FASCIITIS

[Jean Alfred Fournier (1832–1914), venereologist in Paris, France]
= uncommon potentially lethal polymicrobial necrotizing fasciitis of the perineal, perianal or genital areas
Prevalence: 500 cases in literature
Predisposed: diabetes mellitus (present in 40–60%), alcoholism, HIV, neutropenia
Organism: (a) aerobes: E. coli, S. aureus, Proteus species, enterococci
(b) anaerobes: Bacteroides fragilis, anaerobic streptococci, clostridia
◊ Synergistic action between aerobes + anaerobes!
Source of infection:
◊ In 90% primary focus of infection is recognizable!
(a) colorectal: colorectal cancer, inflammatory bowel disease, perirectal abscess, perianal / perirectal / ischiorectal abscess, anal fissure, colonic perforation
(b) urologic: epididymitis, orchitis, urethral stricture with extravasation, urethral instrumentation, chronic urinary tract infection, circumcision
(c) cutaneous: pressure ulcer of skin, IM injection, hidradenitis, insect bite, burn
(d) female: septic abortion, vulvar / Bartholin gland abscess, hysterectomy, episiotomy
(e) occult (10%)
Path: obliterative endarteritis with ensuing cutaneous + subcutaneous necrosis and gangrene, cellulitis, myositis, fasciitis (rate of fascial destruction as high as 2–3 cm/hr)
Age: newborn to elderly; M÷F = 10÷1
◊ SURGICAL EMERGENCY!
• pain, fever, leukocytosis
• scrotal tenderness, erythema, swelling, crepitation
CT (modality of choice):
√ gas in scrotal wall + perineum
√ scrotal skin thickening + normal testes
◊ Scan entire abdomen + pelvis to find source of infection!
Mortality: 7–75% = UROLOGIC EMERGENCY
Rx: antibiotic therapy + debridement + hyperbaric oxygen
DDx: epididymoorchitis, gas-containing scrotal abscess, scrotal hernia with gas-containing bowel, scrotal emphysema from bowel perforation, extension of subcutaneous emphysema, air leakage + dissection due to faulty chest tube positioning

GANGLIONEUROBLASTOMA

= pediatric tumor of sympathetic nervous system of intermediate grade (cellular maturity between malignant neuroblastoma and benign ganglioneuroma); metastatic potential
Frequency: less common than neuroblastoma / ganglioneuroma
Age: 2–4 years; rare in adults; M÷F = 1÷1
Location: posterior mediastinum, abdomen
√ extension through neural foramen into epidural space
√ nerve root / spinal cord compression

GANGLIONEUROMA

= rare benign neoplastic growth of sympathetic ganglia evolving from a spontaneously regressed

(1%) neuroblastoma or induced by chemotherapy / occurring spontaneously de novo
Path: usually larger than nerve sheath tumor
Histo: mixture of Schwann cells + mature ganglion cells (predominating over glial cells)
Age: older than for neuroblastoma; < 20 years (42–60%), 20–39 years (39%), 40–80 years (19%); M÷F = 1÷1
Location: anywhere along paravertebral sympathetic plexus
(a) extraadrenal
posterior mediastinum (25–43%); retroperitoneum (32–52%); pelvis (9%); neck (8–9%); GI tract (rare)associated with MEN 2b
(b) adrenal medulla (20–30%)
Elaborated hormones: catecholamines, vasoactive intestinal polypeptides, androgenic hormones
• usually asymptomatic / pain
• respiratory symptoms, local pressure (40%)
• rarely hormone-active: diarrhea, sweating, hypertension, virilization, myasthenia gravis
Average size: 8 cm (up to 20 cm)
√ spherical / elliptical large lobulated well-defined encapsulated slow-growing mass
√ tendency to surround blood vessels without compromising the lumen
√ dumbbell-shaped mass extending from paraspinous region through neural foramen into epidural space
√ discrete punctate calcifications (8–27%)
√ unusually homogeneous / mildly heterogeneous mass for its large size
√ variable contrast enhancement
CT:
√ homogeneous / mildly heterogeneous hypoattenuating mass with a density of < 40 HU (less than that of muscle)
CECT:
√ homogeneously hypoattenuating mass compared to muscle
√ surrounds vessels without vascular narrowing / occlusion
MR:
√ homogeneous + isointense with muscle on T1WI
√ hyperintense to muscle on T2WI with varying signal intensities ← depending on composition of myxoid / cellular / collagen components):
√ ± whorled appearance ← interlacing bundles of longitudinal + transverse Schwann cells / collagen fibers
√ gradual delayed enhancement
Prognosis: good after surgical resection
DDx: neurofibroma (no calcification), schwannoma (no calcification), ganglioneuroblastoma, neuroblastoma (coarse calcifications)

Gastrointestinal Ganglioneuroma

Manifestation:
1. Focal polypoid lesions = ganglioneuromas
• asymptomatic
√ well-circumscribed round / oval lobulated hypoattenuating masses

2. Multifocal polyps = ganglioneuromatous polyposis
   Location in NF1: colon, rectum
3. Diffuse infiltrating lesions = ganglioneuromatosis
   - disturbance in gastrointestinal motility (Hirschsprüng-like condition, chronic colonic pseudo-obstruction, megacolon)

   Location in NF1: colon, rectum
   √ diffuse / focal mural thickening
   √ diffuse high-attenuation mural thickening

GENITOURINARY DIABETES MELLITUS

A. CHRONIC GU EFFECTS
   1. Papillary necrosis
   2. Renal artery stenosis
   3. Vas deferens calcification

B. URINARY TRACT INFECTIONS
   1. Renal and perirenal abscess
   2. Emphysematous pyelonephritis
   3. Emphysematous cystitis
   4. Fungal infection: Candida, Aspergillus
   5. Xanthogranulomatous pyelonephritis

C. GENITAL INFECTION
   1. Fournier gangrene
   2. Postmenopausal tuboovarian abscess

Diabetic Nephropathy

= defined as persistent proteinuria (> 500 mg of albumin/24 hours) + retinopathy + elevated blood pressure

◊ Most common cause of end-stage renal disease!

Prevalence: 35–45% of IDDM; < 20% of NIDDM; M > F

Histo: diffuse intercapillary glomerulosclerosis

Early:

√ renal enlargement (= renal hypertrophy with glomerular expansion)

Late:

√ progressive decrease in size
√ diffuse cortical hyperechogenicity with gradual loss of corticomedullary differentiation
√ resistive index > 0.7 (very late)

IVP:

√ contrast material may induce renal failure (= rise in serum creatinine level 1–5 days after exposure)

◊ Keep patient well hydrated with 0.45% saline!

Mortality: 90% after 40 years of age

Diabetic Cystopathy

Cause: autonomous peripheral neuropathy

Histo: vacuolation of ganglion cells in bladder wall, giant sympathetic neurons,

hypochromatic ganglion cells, demyelination
- insidious impairment of bladder sensation
- decreased reflex detrusor activity

√ enlarged postvoid residual urine volume

Cx: vesicoureteral reflux, recurrent pyelonephritis, pyohydronephrosis, overflow incontinence

GLOMERULOCYSTIC KIDNEY DISEASE

= GCKD = rare form of cystic renal disease characterized by cystic dilatation of Bowman capsule

Genetics: often inherited autosomal-dominant disease in families with ADPKD / component of hereditary syndromes (tuberous sclerosis, orofacialdigital syndrome, short rib polydactyly group of skeletal dysplasias); also sporadic cases

Age: neonate, young child

Histo: uniform cystic dilatation of Bowman capsule around glomerulus

- symptoms of renal failure
- accompanying infantile congenital malformations

Site: primarily in cortical subcapsular distribution sparing tubular portions of nephron

√ normal-sized / hypoplastic kidneys

US:

√ small round cysts in renal cortex

√ cortical hyperechogenicity ← if cysts difficult to define

NEMR (preferred imaging modality):

√ numerous T2-hyperintense lesions predominantly in subcapsular portion of renal cortex

DDx: ADPKD (much larger diffusely distributed renal cysts)

HEMANGIOMA OF ADRENAL GLAND

= rare benign vasoformative stromal tumor of adrenal gland

Prevalence: 1÷10,000 autopsies

Histo: cavernous > capillary type

- typically asymptomatic for hemangiomas < 2 cm

√ often large mass (usually > 10 cm in diameter, up to 22 cm) owing to their indolent nature

√ highly vascular mass with multiple peripheral nodular areas of marked enhancement after contrast bolus injection:

√ NO complete fill in of contrast material

√ calcifications (28–87%) from previous hemorrhage / multiple CHARACTERISTIC phleboliths

√ persistent enhancement on delayed imaging

CT:

√ central low attenuation (necrosis / fibrosis)

MR:

√ mass hypointense relative to liver on T1WI + central hyperintensity ← hemorrhage / necrosis

√ usually markedly hyperintense on T2WI, especially in central portion

√ variable appearance after hemorrhage, thrombosis, necrosis, fibrosis

Cx: hemorrhage

HEMANGIOMA OF KIDNEY

= uncommon benign vascular tumor
Origin: embryonic rest of unipotent angioblastic cells
Prevalence: 1÷2,000 to 1÷30,000; M=F
Peak age: young to middle-aged adults
May be associated with: Klippel-Trénaunay syndrome, Sturge-Weber syndrome
Path: unencapsulated tumor
Histo: cavernous variant (widely dilated vessels) > capillary variant (slit-like vascular spaces)
Location: medulla (90%), renal pelvis
Size: mostly < 2 cm
• mostly asymptomatic
• recurrent episodes of hematuria, colicky abdominal pain
√ intense arterial enhancement persisting into venous phase
CT:
√ lobulated hypo- to isoattenuating soft-tissue mass
√ multiple phleboliths (uncommon)
MR:
√ homogeneously hypointense mass on T1WI
√ hyperintense on T2WI

HEMANGIOMA OF URINARY BLADDER

Frequency: 0.6% of primary bladder neoplasms;
0.3% of all bladder tumors
Age: < 20 years (in > 50%); M÷F = 1÷1
May be associated with:
(a) additional hemangiomas in 30%
(b) Klippel-Trénaunay syndrome
(c) Sturge-Weber syndrome
Histo: capillary / venous / cavernous / hemangiolymphomatous form
• recurrent gross painless hematuria
• cutaneous hemangiomas over abdomen, perineum, thighs in 25–30%
Location: dome, posterolateral wall
Site: limited to submucosa (33%), muscular wall, perivesical tissue
√ compressible solitary (⅔) / multiple (⅓) masses:
√ rounded well-marginated intraluminal mass
√ diffuse bladder wall thickening + punctate calcifications (= phleboliths)
IVP:
√ rounded / lobulated filling defect
US:
√ solid predominantly hyperechoic mass
√ hypoechoic spaces within thickened bladder wall

CAVE: high risk of intractable hemorrhage at biopsy!

HEMOLYTIC-UREMIC SYNDROME

= characterized by microangiopathic hemolytic anemia with typical features of DIC

◊ Most common cause of acute renal failure in children requiring dialysis!

Cause: ? triggered by an autoimmune response to infection

(1) Infection: enterotoxic E. coli, > Shigella dysenteriae I, Streptococcus pneumoniae, Salmonella typhi, Coxsackie virus, ECHO virus, adenovirus

(2) Associated medical condition: pregnancy, SLE + other collagen vascular disease, malignancy, malignant hypertension

(3) Drugs: oral contraceptives, cyclosporine, mitomycin, 5-fluorouracil

Pathogenesis: capillary and endothelial injury to kidney → mechanical damage of RBCs + formation of hyaline microthrombi within renal vasculature + focal infarction

Age: usually children < 2 years

Histo: microangiopathy including endothelial swelling + thrombus formation in glomerulus + renal arterioles

CLASSIC TRIAD:

(1) Microangiopathic hemolytic anemia

(2) Thrombocytopenia

(3) Acute oliguric / anuric renal failure → uremia

- recent bout of gastroenteritis (commonly with E. coli)
- sudden pallor, irritability, bloody diarrhea, convulsions
- dyspnea ← fluid retention, heart failure, pleural effusion
- rapid rise in blood urea nitrogen level out of proportion to plasma creatinine level ← cell lysis

@ Kidney (sometimes only organ involved):

√ kidneys of normal / slightly increased size

√ hyperechoic cortex

Doppler-US:

√ diastolic flow absent / reversed / reduced (= increase in resistance to flow)

√ return to normal waveforms predates return of urine output

Scintigraphy:

√ lack of renal perfusion

@ Liver: hepatomegaly, hepatitis

@ Pancreas: diabetes mellitus

@ Heart: myocarditis

@ Muscle: rhabdomyolysis

@ Intestines:

√ mural stratification + narrowing of bowel lumen

√ pericolonic fat stranding

Cx: perforation, intussusception, infectious colitis

@ Brain (20–50%): drowsiness, personality changes, coma, hemiparesis, seizures (up to 40%)

Prognosis: complete spontaneous recovery (in 85%)

HEREDITARY CHRONIC NEPHRITIS

= ALPORT SYNDROME
= probably autosomal dominant trait with presence of fat-filled macrophages ("foam cells") in corticomedullary junction and medulla
(a) males: progressive renal insufficiency, death usually before age 50
(b) females: nonprogressive
• polyuria, salt wasting, hyposthenuria, NO hypertension
• anemia, nerve deafness
• ocular abnormalities: congenital cataracts, nystagmus, myopia, spherophakia
√ small smooth kidneys
√ diminished density of contrast material
√ cortical calcifications

HORSESHOE KIDNEY

= two kidneys joined at poles by parenchymal / fibrous isthmus
Prevalence: 1–4÷1,000 births; 0.2–1.0% (autopsy series); M÷F = 2–3÷1
◊ Most common fusion anomaly!
Associated with:
cardiovascular anomaly, skeletal anomaly, CNS anomaly, anorectal malformation, genitourinary anomaly (hypospadia, undescended testis, bicornuate uterus, ureteral duplication), trisomy 18, Turner syndrome (60%)
In 50% associated with:
(1) Caudal ectopia
(2) Vesicoureteral reflux
(3) Hydronephrosis ← UPJ obstruction
√ fusion of R + L kidney at lower (90%) / upper (10%) pole
√ renal long axis medially oriented
√ isthmus at L4-5 between aorta + inferior mesenteric artery
√ renal pelves and ureters situated anteriorly
√ multiple renal arteries including isthmus artery
Cx: infection, renal calculi

HYDROCELE

= abnormal collection of fluid between parietal and visceral layers of tunica vaginalis
◊ Most common cause of painless scrotal swelling
◊ Most common type of fluid collection in scrotum
US:
√ anechoic, good back wall, through-transmission
√ COMPLICATED HYDROCELE = hydrocele with low-level echoes ± septations = hematocele / pyocele / cholesterol crystals / protein aggregates

Primary = Idiopathic Hydrocele

without predisposing lesion as congenital defect of lymphatic drainage = failure of mesothelial lining to reabsorb fluid

Secondary = Acquired Hydrocele

Age: > older child to adulthood

(a) inflammation: epididymitis, epididymoorchitis
(b) testicular tumor (in 10–40% of malignancies)
(c) trauma / postsurgical
◊ 50% of acquired hydroceles are due to trauma!
(d) torsion, infarction

Congenital Encysted Hydrocele

= ascites trapped in scrotum through communication with peritoneal cavity (= open processus vaginalis)

May be associated with: inguinal hernia

• resolves within 2 years (in 80%)

Infantile Hydrocele

= hydrocele with fingerlike extension into funicular process but WITHOUT communication with peritoneal cavity

HYDRONEPHROSIS

A. OBSTRUCTIVE UROPATHY = HYDRONEPHROSIS
= dilatation of collecting structures without functional deficit

B. OBSTRUCTIVE NEPHROPATHY = dilatation of collecting system with renal <u>functional impairment</u>

Grading system of hydronephrosis by US:

Grade 0 = homogeneous central renal sinus complex without separation of central sinus echoes
Grade 1 = separation of central sinus echoes of ovoid configuration; continuous echogenic sinus periphery; 52% predictive value for obstruction
Grade 2 = separation of central sinus echoes of rounded configuration; dilated calices connecting with renal pelvis; continuity of echogenic sinus periphery
Grade 3 = replacement of major portions of renal sinus; discontinuity of echogenic sinus periphery

Amount of collecting system dilatation depends on:

(a) duration of obstruction
(b) renal output
(c) presence of spontaneous decompression
◊ Amount of residual renal cortex is of prognostic significance!

Acute Hydronephrosis

Cause:

(1) Passage of calculus
(2) Sulfonamide crystallization in nonalkalinized urine
(3) Passage of blood clot ← carcinoma, AV malformation, trauma, anticoagulant therapy
(4) Sloughed necrotic papilla
(5) Ureteral edema following instrumentation

(6) Suture on ureter
(7) Normal pregnancy

• pain (50%), UTI (36%), nausea + vomiting (33%)
√ normal-sized kidney with normal parenchymal thickness
√ increasingly dense nephrogram
√ delayed opacification of collecting system ← decreased glomerular filtration
√ increasingly dense nephrogram over time (= "obstructed nephrogram")
√ dilated collecting system + ureter
√ widening of forniceal angles
√ delayed images demonstrate site of obstruction at the end of a persistent column of contrast material in a dilated urinary collecting system
√ vicarious contrast excretion through gallbladder (uncommon)

US:
√ separation of renal sinus echoes
False-negatives:
staghorn calculus filling entire collecting system, hyperacute renal obstruction (system not yet dilated), spontaneous decompression of obstruction, fluid-depleted patient with partial obstruction, dehydrated neonate
False-positives:
full bladder, increased urine flow (overhydration, medications, following urography, diabetes insipidus, diuresis in nonoliguric azotemia), acute pyelonephritis, postobstructive / postsurgical dilatation, vesicoureteral reflux
Imposters:
parapelvic cysts, sinus vessels, prominent extrarenal pelvis
√ ureteral jet not detectable / trickling flow:
CAVE: in 25% ureteral jets NOT detectable ← insufficient differences in specific gravity between ureteral urine and urine in urinary bladder in normals
√ ureteral jet absent in 13% of pregnant patients without ureteral obstruction
N.B.: turning pregnant patient into contralateral decubitus position will make jet visible

Duplex US:
√ mean RI of 0.77 ± 0.05 versus 0.63 ± 0.06 in nonobstructed kidney
Caution: RI often normal in chronic obstruction; nonobstructive renal disease may elevate RIs
√ ≥ 0.08 difference in RI in right-to-left comparison with unilateral obstruction

Cx: spontaneous urinary extravasation (10–18%) from forniceal / pelvic tear (= pyelosinus reflux)

Chronic Hydronephrosis

= most frequent cause of abdominal mass in first 6 months of life (= 25% of all neonatal abdominal masses)

Cause:
(a) acquired: benign + malignant tumors of the ureter; ureteral strictures; retroperitoneal tumor / fibrosis; neurogenic bladder; benign prostatic hyperplasia; cervical / prostatic carcinoma; pelvic mass (lymphoma, abscess, ovarian); urethral polyps; urethral

neoplasm; acquired urethral strictures

(b) congenital: ureteropelvic junction obstruction (most common); posterior urethral valves; ectopic ureterocele; congenital ureterovesical obstruction; prune-belly syndrome; primary megaureter

• insidious course

√ large kidney with wasted parenchyma

√ diminished nephrographic density ← decreased clearance

√ early "rim" sign (= thin band of radiodensity surrounding calices)

√ "crescent" sign = concentrated contrast material in collecting tubules arranged parallel to margin of dilated calices ← reversible incomplete prolonged obstruction

√ delayed opacification of collecting system

√ moderate to marked widening of collecting system

√ tortuous dilated ureter

CT:

√ hypoenhancement of renal parenchyma during corticomedullary + nephrographic phases

√ delayed persistent nephrogram sign

NUC:

√ photopenic area during vascular phase

√ accumulation of radionuclide tracer within hydronephrotic collecting system on delayed images

Cx: superimposed infection (= pyonephrosis)

Congenital Hydronephrosis

Mostly isolated malformation

Prevalence: 1÷100–300 births

Risk of recurrence: 2–3% for siblings

Age at presentation: 25% by age 1 year,
55% by age 5 years

Cause:

1. UPJ obstruction 22–40–67%
2. Posterior urethral valves 18%
3. Ectopic ureterocele 14%
4. Prune belly syndrome 12%
5. Ureteral + UVJ obstruction 8%
6. Others: severe vesicoureteral reflux, bladder neck obstruction, hypertrophy of verumontanum, urethral diverticulum, congenital urethral strictures, anterior urethral valves, meatal stenosis

May be associated with: Down syndrome (in 17–25%)

• palpable abdominal mass

• intermittent flank + periumbilical pain

• failure to thrive, vomiting, hematuria, infection

Location: 70% unilateral

OB-US:

√ AP diameter of renal pelvis ≥ 5 mm between 15–20 weeks, ≥ 8 mm at 20–30 weeks, ≥ 10 mm after 30 weeks MA

◊ Pyelectasis < 7.0 mm after 32 weeks EGA is highly predictive of a normal postnatal outcome

√ ratio of AP diameter of renal pelvis to kidney > 50%

√ caliceal distension communicating with renal pelvis

◊ Postnatal evaluation after 4–7 days of age (because of ↓ GFR + relative dehydration in first days of life)!

Prognosis: parenchymal atrophy + renal impairment (dependent on severity + duration)

Focal Hydronephrosis

= HYDROCALICOSIS = HYDROCALYX

= obstructed drainage of one portion of kidney

Cause: (1) Congenital: partial / complete duplication
(2) Infectious stricture: eg, TB
(3) Infundibular calculus
(4) Tumor
(5) Trauma

√ unifocal mass, commonly in upper pole

√ absent polar group of calices (early)

√ dilated polar group (late) with displacement of adjacent calices

√ delayed opacification in obstructed group

√ focally replaced nephrogram

US:

√ anechoic cystic lesion with smooth margins

CT:

√ focal area of water density with smooth margin + thick wall

Hydronephrosis in Pregnancy

1. **Physiologic hydronephrosis / dilatation**

Prevalence: 80%; in up to 90% by 3rd trimester

Cause:
(a) hormonal: relaxation of ureteric smooth muscle in response to progesterone
(b) mechanical: gravid uterus compresses ureter at pelvic brim near crossing of iliac vessels with right ureter taking a more acute angle

• asymptomatic / may manifest as abdominal pain

Time of onset: as early as 6–10 weeks of gestation

Location: right (85–90%), left (15–67%)

Not associated with: renal enlargement / perinephric fluid

√ gradual smooth tapering of mid to distal ureter ← extrinsic compression between gravid uterus + iliopsoas

√ ureter widened only to level of sacral promontory

Prognosis: resolution within a few weeks to 6 months after delivery

2. **"Overdistension syndrome"**

Cause: obstruction by gravid uterus

• pain mimicking renal colic

3. **Acute (obstructive) hydronephrosis**
   Cause: change in position of fetus, diuresis, passage of stone into ureter
   • constant pain ± nausea and vomiting
   √ renal enlargement
   √ increased perirenal fluid ← lymphatic congestion / forniceal rupture
   √ ureterovesical stone → ureter dilated distal to sacral promontory

IgG4-RELATED RENAL DISEASE

Renal lesions in patients with pancreatic disease have been used to differentiate autoimmune pancreatitis from pancreatic cancer.

Histo: tubulointerstitial nephritis with fibrosis + abundant IgG4-positive plasma cell infiltration
√ bilateral round / wedge-shaped peripheral cortical lesions (most common)
√ diffuse patchy renal involvement
√ rim of soft tissue around kidney
√ bilateral nodules in renal sinus
√ diffuse wall thickening of renal pelvis

INFLAMMATORY PSEUDOTUMOR OF BLADDER

= PSEUDOSARCOMATOUS FIBROMYXOID TUMOR
Cause: ? response to infection, inflammation or malignancy
Age: 38 (range, 15–74) years; M÷F = 11÷6
Path: ulcerating bleeding mass
Histo: loosely packed spindle cells within myxoid matrix
• hematuria, voiding symptoms, fever, iron deficiency anemia
Location: reported in every organ of body
Site: spares trigone
√ locally aggressive single exophytic / polypoid 2–8 cm bladder mass ± ulceration
√ may invade through bladder wall with extravesical component
√ ringlike peripheral enhancement + poor central enhancement ← necrosis
MR:
√ heterogeneous mass with central hyperintense component surrounded by hypointense periphery on T2WI
Rx: surgery, high-dose steroids, radiation therapy
DDx: rhabdomyosarcoma, myxoid leiomyosarcoma

JUXTAGLOMERULAR CELL TUMOR

= RENINOMA
= very rare benign renin-secreting tumor
Origin: juxtaglomerular cells of adult kidney
Prevalence: < 30 cases reported
Origin: myoendocrine cell arising from afferent arterioles of glomeruli
Path: small foci of hemorrhage + pseudocapsule
Histo: tumor resembles hemangiopericytoma composed of sheets / trabeculae of round to

polygonal cells;
CHARACTERISTIC renin granules on electron microscopy

Mean age: 24 (range, 7–58) years; 50% < 21 years; M÷F = 1÷2

- typical features of primary reninism:
  - marked + sustained hypertension, often accelerated and poorly controlled
  - secondary hyperaldosteronism with hypokalemia
  - hyperreninemia → in the absence of renal artery stenosis
- moderate to severe headaches + muscle aches
- hypertensive retinopathy, polydipsia, polyuria, enuresis

Location: just beneath renal capsule

Size: usually 2–3 (range, 0.8–6.5) cm

√ well-circumscribed renal mass

US:

√ echogenic mass ± areas of necrosis / hemorrhage

NECT (thin overlapping cuts):

√ hypo- to isodense tumor

CECT:

√ hypovascular mass on arterial phase ← renin-induced vascoconstriction

√ moderate enhancement during delayed phase

MR:

√ hypointense mass relative to renal parenchyma on precontrast T1WI + T2WI

√ early low-level peripheral enhancement on T1WI

√ washout of contrast material from periphery + filling in of central tumor portion on delayed T1WI

Angio:

√ (easily overlooked) hypo- / avascular tumor (in 43%)

√ renal vein sampling yields high renin level on affected side

Dx: combination of elevated renin without renal arterial lesion + hypovascular solid renal mass

Rx: surgical excision

LEIOMYOMA OF KIDNEY

= CAPSULOMA

= rare benign mesenchymal neoplasms that mostly occurs in asymptomatic adults

Prevalence: 5% at autopsy (average size of 5 mm)

Origin: smooth muscle cells of renal capsule, muscularis of renal pelvis, wall of cortical vessels

Path: well-encapsulated solid mass containing hemorrhage (17%) / cystic degeneration (27%) / irregular calcifications

Histo: interlacing bundles of smooth muscle cells in a whorled arrangement without nuclear pleomorphism; immunoreactivity to smooth muscle markers (actin, desmin)

Associated with: tuberous sclerosis

Median age: 42 years; M < F; Whites > Blacks

Location: 53% subcapsular, 37% capsular, 10% at renal pelvis

Mean size: 12 cm
• palpable mass if large (50%), hematuria (20%)
√ well-circumscribed exophytic solid lesion ± cleavage plane between tumor and cortex
√ areas of hemorrhage + cystic / myxoid degeneration + dense calcifications in larger tumor
CT:
√ relatively homogeneous peripherally located hyperattenuating solid mass causing cortical buckling
√ relatively homogeneous enhancement
MR:
√ homogeneously low SI on T1WI + T2WI
Angio:
√ hypo- to hypervascular nonspecific mass
DDx: renal leiomyosarcoma, renal cell carcinoma

LEIOMYOSARCOMA OF KIDNEY

◊ Most common sarcoma of adult kidney (50–60% of all renal sarcomas)!
Age: 40–70 years; M÷F = 1÷1
Path: large well-circumscribed encapsulated tumor with focal areas of necrosis
Histo: spindle cells in fascicular / plexiform / haphazard growth pattern interspersed with variable amount of connective tissue; positive for α-smooth muscle actin, desmin, calponin
• flank pain, abdominal mass, hematuria
Location: renal capsule, parenchyma, smooth muscle fibers of renal pelvis / main renal vein
√ expansile well-defined solid mass
√ heterogeneous enhancement + delayed enhancing fibrous stroma
√ central necrosis / multiloculated cystic mass for large tumors
MR:
√ soft-tissue mass of heterogeneous SI on T1WI + T2WI
Prognosis: aggressive + rapidly progressive; 29–36% 5-year survival rate

LEUKEMIA

= clonal proliferation of lymphoblasts (acute leukemia) or small lymphocytes (chronic leukemia)
◊ Most common malignant cause of bilateral global renal enlargement!
Prevalence: renal involvement in 50% of children + in 65% of adults at autopsy
A. DIFFUSE INVOLVEMENT (most common)
› leukemic cells infiltrate the interstitial tissue + renal sinus; tubules are replaced (more common in lymphocytic than in granulocytic forms); no relationship to peripheral white blood cell count
• hypertension; renal impairment ← leukemic infiltrate, hyperuricemia, septicemia, hemorrhage
√ moderate to massive nephromegaly bilaterally with smooth contours
√ normal or diminished density on nephrogram
√ occasionally attenuated collecting system (DDx: renal sinus lipomatosis)

√ nonopaque filling defects on IVP ← clot, uric acid
√ renal / subcapsular / perinephric hemorrhage frequent
√ retroperitoneal lymphadenopathy
US:
√ loss of definition + distortion of central sinus complex
√ normal to increased coarse echoes throughout renal cortex with preservation of renal medulla
√ single / multiple focal anechoic masses

B. FOCAL ACCUMULATION OF LEUKEMIC CELLS (rare)
chloroma (= granulocytic sarcoma) of acute myeloblastic leukemia, myeloblastoma, myeloblastic sarcoma
• may antedate other manifestations of leukemia
√ unifocal mass in renal cortex / renal sinus

DDx: Hodgkin disease, malignant lymphoma, multiple myeloma

LEUKOPLAKIA

= KERATINIZING SQUAMOUS METAPLASIA / DYSPLASIA = DYSKERATOSIS

Cause: chronic infection (80%) / stones (40%)
Histo: large confluent areas / scattered patches of squamous metaplasia of transitional cell epithelium with keratinization + cellular atypia in deeper layers
Peak age: 4th–5th decade;
M÷F = 1÷1 (with involvement of renal pelvis)
M÷F = 4÷1 (with involvement of bladder)
• hematuria (30%), recurrent UTIs
• PATHOGNOMONIC passage of gritty flakes, soft-tissue stones, white chunks of tissue (= desquamated keratinized epithelial layers) → leading to colic, fever, chills
Location: bladder > renal pelvis > ureter; bilateral in 10%
√ corrugated / striated irregularities of pelvicaliceal walls; localized / generalized
√ plaquelike intraluminal mass with "onion skin" pattern of contrast material in interstices
√ caliectasis + pyelectasis common (with obstruction)
√ ridging / filling defects of ureter
√ associated with calculi in 25–50%
Cx: premalignant condition for epidermoid carcinoma in 12% (controversial!)

LEYDIG CELL HYPERPLASIA

= rare benign condition characterized by an increased number of Leydig cells
• asymptomatic (in adults)
• precocious puberty (in childhood) ← hormone secretion
Location: frequently bilateral; multifocal
Size: 1–6 mm
√ hypo- / hyperechoic, T2-hypointense intratesticular nodule(s)
√ variable vascularity ± avid enhancement

LIPOMA OF SPERMATIC CORD

= EXTRATESTICULAR / PARATESTICULAR LIPOMA
Frequency: most common extratesticular tumor
US:
√ well-defined homogeneous scrotal mass
√ NO internal flow on color Doppler
MR:
√ homogeneous high SI on T1WI (DDx: hematoma, proteinaceous cyst)
√ hyperintense paratesticular mass on T2WI
√ india-ink = black boundary artifact and signal suppression on out-of-phase imaging
√ signal suppression on fat-suppressed images

LIPOMA OF SCROTUM

= INTRATESTICULAR LIPOMA
= rare benign fat-containing tumor
Location: epididymis, spermatic cord, tunica vaginalis
US:
√ well-defined homogeneous hyperechoic nonshadowing lesion
√ NO color Doppler flow signals (frequent)
CT:
√ homogeneous attenuation similar to subcutaneous fat
MR:
√ high signal intensity on T1WI and T2WI
√ loss of signal intensity on frequency-selective fat-saturated images
√ NO enhancement

Lipoma can be differentiated from liposarcoma by the lack of any enhancing soft tissue within a lipoma.

Testicular Lipomatosis

Cause: exclusively in Cowden disease
US:
√ multiple nonshadowing hyperechoic small round foci of varying sizes
MR:
√ multiple high SI foci on T1WI

LITHIUM-INDUCED NEPHROTOXICITY

• clinical and laboratory data typically sufficient for diagnosis
Clinical categories:
1. Acute intoxication
2. Nephrogenic diabetes insipidus (most common)
   Rx: reversible with drug cessation
3. Chronic focal interstitial nephritis
   = progressive nonreversible chronic renal insufficiency
   Histo: tubular atrophy, glomerulosclerosis, interstitial fibrosis, distal tubular dilatation with microcyst formation

√ typically normal-sized kidneys

√ abundant uniformly distributed renal microcysts
√ 1–2 mm microcysts (in 33–62%)
Site: cortex and medulla
CT:
√ multiple tiny hypoattenuating lesions
MR (best depiction of number + size of cysts):
√ multiple T2-hyperintense foci

CT and MR findings typically include normal-sized kidneys with abundant and uniformly distributed renal microcysts.

DDx: autosomal dominant polycystic kidney disease, glomerulocystic kidney disease, medullary cystic kidney disease, acquired cystic kidney disease

LOCALIZED CYSTIC DISEASE OF KIDNEY

= SEGMENTAL RENAL CYSTIC DISEASE
= rare nonprogressive condition characterized by replacement of portion / entire renal parenchyma of one kidney with cysts
• mostly asymptomatic, NO impairment of renal function
• abdominal pain, hematuria, hypertension
Genetics: nonhereditary
Pathogenesis: ? acquired maldevelopment
Path: multicystic lesion composed of cysts of varying sizes separated by normal / atrophic renal parenchyma without surrounding capsule
Histo: dilated ducts and tubules varying in size from mm to several cm lined by single layer of flattened epithelium
Location: unilateral in one kidney
√ conglomerate mass of cluster of variably sized + tightly spaced cysts separated by enhancing / atrophic renal tissue:
√ intervening parenchyma may be stretched + attenuated (DDx: thick septations, impossible to distinguish)
√ NO surrounding capsule
√ remaining renal parenchyma of affected / contralateral kidney may contain a few scattered cysts
√ normal excretion of uninvolved segments
Prognosis: not progressive
DDx: (1) Autosomal dominant polycystic kidney disease (bilateral, positive family history, cysts in other visceral organs)
(2) Multicystic dysplastic kidney (absent pelvicaliceal system + absent / hypoplastic renal vessels)
(3) Cystic neoplasm (capsule, coronal plane helpful)

Intervening normally enhancing renal parenchyma + absence of a surrounding capsule distinguishes localized cystic renal disease from cystic nephroma and multiloculated cystic renal cell carcinoma.

LYMPHOCELE

= fluid-filled cyst without epithelial lining

Frequency: in 12–30% after radical lymphadenectomy / renal transplantation (within 4–8 weeks after surgery)

Cause:

1. Complication of radical lymphadenectomy to assess lymph node status in malignancy
2. Lymphatic leakage from allograft / allograft bed

Location: at sites of lymph node dissection; frequently in pelvic / abdominal retroperitoneum, axilla, groin

Time to discovery: 3–8 weeks after surgery

- mostly asymptomatic, edema of abdominal wall / scrotum / labia
- lower limb edema ← pressure effect on veins
- hydronephrosis ← pressure effect on ureter

√ unilocular thin-walled fluid-filled structure

√ photopenic region with displacement / impression on renal transplant / urinary bladder

√ rarely calcification of wall

Dx: aspiration / drainage with biochemical analysis (creatinine + urea nitrogen + protein + electrolyte components similar to serum)

- predominantly lymphocytes, few leukocytes

Cx: hemorrhage; superinfection; compression of adjacent structures if large

Rx: sclerotherapy with povidone-iodine / doxycycline / ethanol / bleomycin; long-term catheter drainage / surgical marsupialization

DDx: hematoma; seroma; abscess; cystic tumor recurrence (enhancing soft-tissue component)

Cystic Degeneration of Lymph Node

Cause: squamous cell carcinoma (from uterine cervix, vagina, vulva, urinary bladder)

√ thin-walled cystic lymph node

DDx: lymphocele; lymphangioleiomyomatosis

LYMPHOMA OF KIDNEY

Prevalence: in 3–8% (by CT), 30–60% (by autopsy); occurs usually late in disease

◊ The kidneys are the 2nd most commonly affected anatomic entity aside from hematopoietic and reticuloendothelial organs!

Path: initially lymphomatous cells grow in interstitium; nephrons, collecting ducts, blood vessels serve as framework for tumor expansion; with continued growth → parenchymal compression + destruction

Types:

A. NON-HODGKIN LYMPHOMA (more common)

(a) SECONDARY ← systemic disease

Type: typically intermediate + high-grade B-cell type

At risk: immunocompromised patients with uncontrolled Epstein-Barr virus proliferation in patients with HIV infection / organ transplantation (esp. after cyclosporine therapy), ataxia-telangiectasia

(b) PRIMARY renal lymphoma (< 1%)

arising in renal hilar nodes / renal parenchyma

B. HODGKIN DISEASE (< 1%)

Prevalence: renal involvement in 13% of autopsies

Patterns of involvement:

(1) Hematogenous dissemination (bilateral in 75%):

› multiple foci (50–65%):

√ multiple hypoenhancing 1–3 cm usually bilateral renal masses

› single mass (10–25%):

√ solitary homogeneous hypovascular renal mass (in 10–20%) with minimal enhancement mimicking a primary renal neoplasm:

√ distortion of renal contour with larger mass

√ ± invasion of perirenal space / renal hilum

› diffuse infiltration (in 20%) along scaffolding of normal interstitial tissue, almost always bilateral:

√ nephromegaly with preservation of renal contour ← primarily interstitial lymphomatous infiltration

√ poorly enhancing areas in kidneys

› rindlike perinephric soft-tissue mass

√ invasion / compression of kidney without significant effect on renal function

(2) Direct extension from retroperitoneal mass / adenopathy (25–30%):

√ cloaking of renal vessels without obstruction

√ occasionally displacement of involved kidney

Cx: hydronephrosis

(3) Isolated perinephric lymphoma (< 10%)

• clinically silent (50%), palpable mass, hematuria
• flank pain, weight loss, fever, night sweats
• compromised renal function: urinary tract obstruction, renal vein compression, diffuse infiltration of kidney, superimposed infarct, amyloidosis, hypercalcemia

Associated with: splenomegaly, lymphadenopathy

◊ Look for other sites of multisystemic involvement in bone marrow, liver, GI tract, lung, heart, CNS!

√ unilateral÷bilateral = 1÷3
√ multiple nodular masses (29–61%): 1.0–4.5 cm in size
√ solitary tumor (10–25%): bulky up to 15 cm in size (7%) / small (7–48%)
√ spread from retroperitoneal disease with involvement via transcapsular / hilar invasion (25–30%)
√ perinephric lymphoma (< 10%):

(a) direct extension from retroperitoneal disease

(b) transcapsular growth of renal parenchymal disease

◊ A tumor surrounding kidney without parenchymal compression or compromise in function is virtually PATHOGNOMONIC of lymphoma

√ renal sinus infiltration
√ small curvilinear areas of high attenuation
√ thickening of fascia of Gerota

√ perirenal nodules / plaques of soft-tissue density
√ mass contiguous with retroperitoneal disease
√ nephromegaly ← diffuse infiltration of interstitium (6–19%) sparing glomeruli and tubules):
√ preservation of renal contour
√ almost always bilateral
√ encasement / deformation of pelvicaliceal system
• clinically silent → presenting with ⇓ renal function
√ patency of renal vessels despite tumor encasement is CHARACTERISTIC
√ wall thickening + enhancement of renal pelvis and ureter
NECT:
√ mass with slightly higher attenuation than normal surrounding parenchyma
CT (nephrographic phase most sensitive for detection):
√ usually homogeneous poorly marginated masses less dense than renal parenchyma + decreased enhancement compared with renal parenchyma
MR:
√ iso- to hypointense SI on T1WI relative to normal cortex
√ hypointense on T2WI relative to normal cortex
√ lymphomatous deposits enhance less than normal parenchyma ± progressive delayed enhancement
US:
√ single / multiple anechoic / hypoechoic masses:
√ may show increased through transmission
√ renal enlargement + decreased parenchymal echoes
√ loss of renal sinus echoes
√ little lesion vascularity + displacement of renal vessels
PET:
√ hypermetabolic activity
Angio:
√ neovascularity, encasement, vascular displacement (occasionally palisade-like configuration)
DDx of nodular mass:
(1) RCC (more heterogeneous, vascular invasion)
(2) Metastases ← lung, breast, stomach, melanoma, synchronous renal cell cancer
(3) Acute pyelonephritis, septic emboli, renal infarct, abscess
DDx of perinephric lymphoma:
sarcoma arising from renal capsule, perinephric metastases, perinephric hematoma, retroperitoneal fibrosis, amyloidosis, extramedullary hematopoiesis
DDx of infiltrative tumor:
TCC, acute / xanthogranulomatous pyelonephritis

MALAKOPLAKIA

[*malaka* , Greek = soft; *plakos* , Greek = flat surface]
= uncommon chronic granulomatous inflammatory response to gram-negative infection that can affect any organ

Frequency: < 200 cases reported
Organism: E. coli (in 94%)
Predisposed: diabetes mellitus, immunocompromised
Pathogenesis: altered host response to infection at the macrophage level = engulfed organisms remain viable + become a source for recurring infection
Histo: submucosal histiocytic granulomas containing large foamy mononuclear cells (Hansemann macrophages) with calcified intracytoplasmic basophilic PAS-positive inclusion bodies (Michaelis-Gutmann bodies = **calculospherules**) consisting of incompletely destroyed E. coli bacterium surrounded by lipoprotein membranes
Peak age: 5th–7th decade; M÷F = 1÷4
- recurrent urinary tract infections: hesitancy, dysuria, frequency
- variable proteinuria, leukocytes + erythrocytes in urine
- gross hematuria
- cystoscopy: raised soft yellow-brown lesion < 3 cm in diameter, nodules, papillary lesions, hemorrhagic masses, necrotic ulcerations

Location:
› bladder > lower ²/₃ of ureter > upper ureter > renal pelvis; multifocal in 75%; bilateral in 50%
› outside urinary tract

@ Bladder (40%) / ureter
√ multiple nodular dome-shaped smooth mural filling defects of collecting system
√ scalloped appearance if lesions confluent
√ generalized pelviureteral dilatation (if obstructive)
√ vesicoureteral reflux
√ circumferential bladder wall thickening
√ invasion of perivesical space
DDx: pyeloureteritis cystica

@ Kidney (16%)
√ diffuse renal enlargement (bilateral involvement unusual)
√ displacement of pelvicaliceal system + distortion of central sinus complex
√ multifocal parenchymal masses → ± diminished / absent nephrogram
√ urinary tract calcification rare
US:
√ lesions of variable echogenicity
CT:
√ ill-defined low-attenuation lesions
√ ± perinephric extension
DDx: infiltrative neoplasm; XGP (unilateral, urinary tract calcification)
Rx: antibiotics, ascorbic acid, cholinergic agonist

MALPOSITIONED TESTIS

= MALDESCENDED TESTIS
Testicles are normally within scrotum by 28–32 weeks MA
Prevalence: early 3rd trimester in 10%; at birth in 3.7–6.0% (in babies > 2,500 g in 3.4%; in

premature babies in 30%); beyond 3 months of age in 1%

Test sensitivity:

MR modality of choice; 84–96% sensitive; 100% specific

US: 20–45–88% (very sensitive in inguinal canal); 78% specific, 88% accurate

CT: 95% (testis < 1 cm cannot be detected)

√ no spermatic cord in inguinal canal

Venography: 50–90%

Laparoscopy: most reliable method

Cx: (1) Sterility

(2) Malignancy: most commonly seminoma, 30–50 x risk increase = 1÷1,000 men annually; 4–11% of all testicular tumors found in cryptorchidism; risk remains increased even after orchiopexy

◊ Annual screening until at least age 35!

(3) Torsion: 10 x risk in cryptorchidism

Rx: surgery / orchiopexy at 9–12 months of age

DDx: (1) Rudimentary testis

(2) Pars intravaginalis gubernaculum = nonatrophied bulbous termination

(3) Congenital absence = monorchia / anorchia (in 3–5%)

◊ Nonpalpable testes are agenetic in 15–63% of term infants!

Cryptorchidism (20–29%)

= arrested migration of testis along its normal course through internal inguinal ring, inguinal canal, external inguinal ring into scrotal sac

Prevalence: 9–30% in premature infants;
3.4–5.8% in full-term infants

Pathophysiologic theory:

generalized defect in embryogenesis results in bilateral dysgenetic gonads

Theory supported by:

› cancer risk extends to contralateral testis

› orchiopexy does not decrease cancer risk

› cancer risk increases with degree of ectopy

Associated with: prune belly syndrome (bilateral cryptorchidism), Prader-Willi syndrome, Beckwith-Wiedemann syndrome, Noonan syndrome, Laurence-Moon-Biedl syndrome, trisomies 13, 18, 21

• nonpalpable testis means:

› in 41% testis atrophic / absent

› in 39% testis distal to external inguinal ring / in inguinal canal

› in 20% testis intraabdominal

Location: bilateral in 10%

(a) canalicular = between internal + external inguinal ring (70%)

(b) prescrotal region = high scrotal position below external inguinal ring (20%)

(c) abdominal (10%)

◊ The most craniad possible point of an undescended testis is the lower pole of the

ipsilateral kidney!
√ failure to visualize testis within scrotum
√ empty ipsilateral scrotal sac + intra-abdominal mass
US:
√ often small atrophic testis with generalized decreased / similar echogenicity compared to contralateral testis
√ identification of mediastinum testis is necessary
√ ± testicular microlithiasis
MR (key tool in localization of undescended testis; 62% sensitive):
√ signal characteristics similar to contralateral / normal testis
√ usually homogeneously hypointense on T1WI
√ homogeneously hyperintense on T2WI
√ markedly hyperintense on DWI
DDx: lymph node

Ectopia Testis (1%)
= deviation from the usual pathway
Location:
(a) interstitial = groin (on external oblique muscle)
(b) pubopenile = root of penis, perineal, femoral triangle, on opposite side

Pseudocryptorchidism (70%)
= RETRACTILE TESTIS
= unusually spastic cremasteric muscle

Undescended Testis
= retractile testis + cryptorchidism

MECKEL-GRUBER SYNDROME

= autosomal-recessive perinatally lethal disease characterized by occipital encephalocele, polycystic kidneys, polydactyly

Prevalence: 1÷12,000 to 1÷50,000;
more common among Yemenite Jews

Risk of recurrence: 25%; carrier frequency of 1÷56

• history of affected siblings, microphthalmia

OB-US:

√ large polycystic kidneys containing 2–10-mm cysts
√ occipital encephalocele
√ postaxial polydactyly
√ other intracranial abnormalities: microcephaly, Dandy-Walker malformation
√ cleft lip and palate
√ cardiac anomalies
√ ductal plate malformation of liver
√ ambiguous genitalia in males
√ moderate-to-severe oligohydramnios (onset midtrimester)
√ inability to visualize urine in fetal bladder

OB management:

1. Chromosomal analysis to exclude trisomy 13 (if no prior family history)
2. Option of pregnancy termination < 24 weeks GA
3. Nonintervention for fetal distress > 24 weeks GA

Prognosis: invariably fatal at birth ← pulmonary hypoplasia with renal failure

DDx: trisomy 13

MEDULLARY CYSTIC DISEASE

= NEPHRONOPHTHISIS

= autosomal dominant salt-wasting nephropathy characterized by multiple medullary cysts + tubulointerstitial nephropathy

Genetics: mutations in > 13 different recessive genes → ciliary dysfunction

(a) MCKD1 gene located on chromosome 1p12 encoding an as of yet unidentified protein product
(b) MCKD2 gene located on chromosome 16p12 encoding protein uromodulin (Tamm-Horsfall glycoprotein)
(c) NPHP1, NPHP2, NPHP3 (nephronophthisis) mutations

Path: tubulointerstitial fibrosis → small kidneys with 1.0–1.5 cm corticomedullary cysts (in 70%)

Histo: variable number of medullary cysts (100 μm to 2 cm) + progressive periglomerular and interstitial fibrosis + tubular atrophy with dilatation of proximal tubules

Types:

(1) **Medullary Cystic Disease** = ADULT ONSETautosomal dominant, in young adults, rapidly progressive course with uremia + death in 2 years
Median age at uremia: 62 (50–70) years

(2) **Juvenile Nephronophthisis** = JUVENILE ONSET = UREMIC MEDULLARY CYSTIC DISEASE
autosomal recessive, in children 3–6 years, average duration of 10 years before uremia and death occurs
Median age at uremia: 32 (20–60) years
(3) **Infantile nephronophthisis**

May be associated with: retinal degeneration
- urinary concentration defect → hyposthenuria + salt-wasting
- polyuria, polydipsia → dehydration
- failure to thrive, growth retardation (in early teens)
- uremia, severe anemia, normal sediment
- hypertension (only in late phase)
- adult-onset hyperuricemia + gout

Size of kidneys: small to normal
Size of cysts: < 3 cm
√ smoothly contoured kidneys with thin cortex
IVP:
√ poor opacification of renal collecting system
√ "medullary nephrogram" = medullary striations persistent for up to 2 hours; occasionally replaced by sharply defined multiple thin-walled lucencies
Retrograde pyelogram:
√ communication between collecting system + cysts
US / CT / MR:
√ increased parenchymal echogenicity + poor corticomedullary differentiation
√ multiple small medullary / corticomedullary cysts (70%) (secondary feature NOT essential for diagnosis)
DDx: medullary sponge kidney, multicystic dysplastic kidney, lithium-induced renal disease

MEDULLARY RENAL TUMOR

Frequency: 1–2% of all renal cancers

Collecting Duct Carcinoma

= BELLINI DUCT CARCINOMA
Frequency: ~ 100 cases reported in literature
Mean age: 55 (range, 13–80) years
Histo: mostly high-grade tumor
- abdominal pain, flank mass, hematuria

◊ In 40% metastasized at presentation
√ infiltrative neoplasm centered in medulla:
√ renal sinus invasion
√ extension into cortex (frequent)
√ ± coexisting expansile component
√ large tumor at presentation
US: √hyperechoic mass
Angio: √hypovascular mass

MR: √hypointense mass on T2WI
Prognosis: aggressive clinical course with 33% surviving > 2 years

Renal Medullary Carcinoma

= highly aggressive malignant tumor of epithelial origin occurring almost exclusively in adolescent / young adult blacks with sickle cell trait / hemoglobin SC disease (termed "7th sickle cell nephropathy") but NOT with hemoglobin SS (sickle cell) disease
Origin: distal collecting duct / epithelium of papilla; ? aggressive form of collecting duct carcinoma
Mean age: 20 (range, 11–39) years; M÷F = 3÷1 (if < 24 years of age) and 1÷1 (if > 24 years of age)
Histo: poorly differentiated tumor cells within a desmoplastic stroma + mixed with reticular, yolk saclike, adenoid cystic components
• abdominal / flank pain, gross hematuria
• palpable mass, weight loss, fever
• metastases at presentation common: regional lymph nodes, liver, lung, bone
√ large ill-defined mass centered in renal medulla:
  √ heterogeneous ← varying amounts of hemorrhage and necrosis
  √ extension into renal sinus and cortex
  √ ± peripheral caliectasis
  √ heterogeneous enhancement
√ reniform enlargement with shape of kidney preserved
√ small peripheral satellite nodules
Prognosis: mean survival rate of 15 weeks from diagnosis
DDx: transitional cell carcinoma, rhabdoid tumor

MEDULLARY SPONGE KIDNEY

= congenital developmental abnormality characterized by ectasia + cystic dilatation of intrapyramidal / intrapapillary portions of medullary collecting ducts (= first few generations of metanephric duct branchings)
Prevalence: 1÷5,000 persons; in 0.5% of IVPs; in 12–20% of patients with calcified kidney stones
Age: 3rd–4th decade
Genetics: mostly sporadic, occasionally autosomal dominant
Pathogenesis: ? disruption in ureteric bud-metanephros interface during embryogenesis → abnormal formation of medullary collecting ducts
Histo: ectasia of medullary + papillary collecting ducts with small < 1 cm cysts in medulla which are lined by columnar / transitional cell epithelium
May be associated with:
congenital hemihypertrophy, Beckwith-Wiedemann syndrome, Caroli syndrome, Wilms tumor, horseshoe kidney, Ehlers-Danlos syndrome, parathyroid adenoma
• mostly asymptomatic; hematuria, renal colic, fever, dysuria
Location: usually both kidneys + all pyramids; may be unilateral (in up to 25%); may be segmental + involve only one pyramid (up to 25%)

√ persistent thick dense paintbrushlike streaks of contrast material ("bunch of flowers") extending from surface of papilla into medulla ← pooling of contrast material in dilated medullary collecting ducts
√ striated / beaded appearance of medullary collecting ducts → distortion of calices (in severe cases)
√ medullary nephrocalcinosis (40–80%) with one / more calculi of up to 5 mm clustered in papillary region ← urinary stasis + hypercalciuria / acidification defects / distal renal tubular acidosis

US:
√ echogenic medulla (in absence of stones)

Cx:
(1) Nephrolithiasis
(2) Renal calculi = urolithiasis
(3) Hematuria
(4) Urinary tract infection
(5) Progressive renal failure (in severe cases)

Dx:
(1) Opacification of stone-free papillary cysts
(2) Accumulation of contrast material around calculi within ectatic tubules / cysts

DDx:
(1) Normal variant ("papillary blush" without distinct streaks / nephrocalcinosis / pyramidal enlargement)
(2) Renal tuberculosis (larger more irregular calcifications + cavitations + strictures + ulcerations)
(3) Papillary necrosis ("sloughed papilla + caliceal ring" sign)
(4) Medullary nephrocalcinosis (no ectatic ducts / cysts, calcifications beyond pyramids)
(5) Juvenile polycystic kidney disease (bilateral renal enlargement + hepatic periportal fibrosis)
(6) Caliceal diverticulum (small, solitary, located between pyramids)

MEGACALICOSIS

= CONGENITAL MEGACALICES
= nonprogressive caliceal dilatation caused by hypoplastic medullary pyramids
Age: any age; M >> F
May be associated with: primary megaureter
• normal glomerular filtration rate
Site: entire kidney / part of kidney; unilateral >> bilateral
√ kidney usually enlarged with prominent fetal lobation
√ reduced parenchymal thickness (medulla affected, NOT cortex):
√ normal DMSA scintigram
√ mosaic-like arrangement of dilated calices (polygonal faceted appearance, NOT globular as in obstruction)
√ increased number of calices (> 15)
√ ABSENT caliceal cupping (semilunar instead of pyramidal configuration of papillae)
√ NO dilatation of pelvis / ureters, NORMAL contrast excretion

Cx: (1) Hematuria
(2) Stone formation

MEGACYSTIS-MICROCOLON SYNDROME

= MEGALOCYSTIS-MICROCOLON-INTESTINAL HYPOPERISTALSIS SYNDROME (MMIH)
= functional obstruction of bladder + colon characterized by
(a) enlarged urinary bladder
(b) small colon
(c) strikingly short small intestine suspended on a primitive dorsal mesentery
(d) markedly enlarged hydronephrotic kidneys with little remaining parenchyma

Prevalence: 26 cases reported; M÷F = 1÷7
May be associated with: diaphragmatic hernia, PDA, teeth at birth

- distended abdomen (large bladder + dilated small bowel loops)
- intestinal pseudoobstruction (poor emptying of stomach, NO peristaltic activity of small bowel); overflow incontinence

OB-US:
√ normal amount of amniotic fluid / polyhydramnios (in spite of dilated bladder = "nonobstructive obstruction")
√ massive + progressive bladder distension with poor emptying
√ bilateral megaloureters
√ ± hydronephrosis
√ female sex

BE:
√ microcolon (= transient feature of "unused colon") with narrow rectum + sigmoid
√ malrotation / malfixation or foreshortening of small bowel

VCUG
√ distended unobstructed bladder with poor / absent muscular function

Prognosis: lethal in most cases (at a few months of age)

MEGALOURETER

= CONGENITAL PRIMARY MEGAURETER = TERMINAL URETERECTASIS = ACHALASIA OF URETER = URETEROVESICAL JUNCTION OBSTRUCTION
= intrinsic congenital dilatation of lower juxtavesical orthotopic ureter ≥ 7 mm ← intrinsic smooth muscle dysfunction and abnormal peristalsis

Cause: aperistaltic juxtavesical (1.5 cm long) segment ← faulty development of muscle layers of ureter with too much collagen / too much muscle (functional, NOT mechanical obstruction) = "Hirschsprüng disease of ureter"

Frequency: 2nd most common cause of hydronephrosis in fetus and newborn
Age: any; M÷F = 2–5÷1
Associated disorders (in 40%):
(a) contralateral: UPJ obstruction, reflux, ureterocele, ureteral duplication, renal ectopia, renal agenesis
(b) ipsilateral: caliceal diverticulum, megacalycosis, papillary necrosis

- asymptomatic (mostly), abdominal mass, pain

• hematuria, infection

Location: L÷R = 3÷1, bilateral in 15–40%

Grading system:

I (mild) = distal ⅓ of ureter involved

II (moderate) = entire ureter involved ± caliectasis

III (severe) = entire ureter + moderate to marked caliectasis

√ prominent localized dilatation of pelvic ureter (up to 5 cm in diameter) usually not progressive, but may involve entire ureter + collecting system

√ vigorous nonpropulsive to-and-fro motion in dilated segment

√ functional "beaking" / gradual tapering (= smoothly tapered narrowing) of abnormal distal ureter without peristalsis

√ NO reflux, NO stenosis

Secondary Megaureter

= ureteral dilatation ← any other cause than primary megaureter

Cause: neurogenic bladder, bladder outlet obstruction, posterior urethral valve, obstructing calculus

MESOBLASTIC NEPHROMA

= FETAL RENAL HAMARTOMA = LEIOMYOMATOUS HAMARTOMA = BENIGN CONGENITAL WILMS TUMOR = BENIGN FETAL HAMARTOMA = FETAL MESENCHYMAL TUMOR = FIBROMYXOMA = BOLANDE TUMOR = CONGENITAL FIBROSARCOMA = CONGENITAL MESOBLASTIC NEPHROMA (CMN)

= nonfamilial benign fibromyomatoid mass arising from renal connective tissue; first described in 1967

Incidence: most common solid renal neoplasm discovered in 2nd / 3rd trimester, in neonate or in infant < 1 year; 3–6% of all renal neoplasms in children

Peak age: 1–3 months; 90% within 1st year of life; rare after the age of 6 months; may occasionally go undetected until adulthood; M÷F=1.5÷1

Path: solid unencapsulated mass infiltrating renal parenchyma (derived from early nephrogenic mesenchyme) → sparing renal pelvis + vascular pedicle

Subtypes:

1. **Classic** benign mesoblastic nephroma (< ⅓)
   = represents infantile fibromatosis
   Age: < 3 months
   Path: little hemorrhage + cystic / necrotic change
   Histo: monomorphic tumor composed of uniform elongated spindle cells arranged in bundles resembling leiomyoma with interspersed areas of entrapped normal embryonic glomeruli, tubules vessels, hematopoietic cells, cartilage
   √ often infiltrative tumor with extension into renal hilum / perinephric fat
2. **Cellular** aggressive mesoblastic nephroma (42–63%)
   = visceral form of infantile fibrosarcoma
   Age: > 3 months
   Path: identical to infantile fibrosarcoma; much larger soft fleshy tumor; tendency to

invade perinephric fat + connective tissue; multicystic areas of intratumoral hemorrhage and fluid accumulation (cysts + necrosis)

Histo: haphazardly arranged sheets of spindle cells with limited tendency to form interlacing bundles

√ fluid-filled spaces ← hemorrhage, necrosis, cyst formation

3. Both patterns (in 10–20%)

In 14% associated with: prematurity, polyhydramnios, GI + GU tract malformations, neuroblastoma

• large palpable abdominal / flank mass within first 6 months of life (most common); hypercalcemia, anemia, vomiting

• hematuria (20%) / hypertension (4%) ← ↑ renin production

√ large usually solid intrarenal mass:

√ usually replaces 60–90% of renal parenchyma

√ typically involves renal sinus

√ may produce multiple cystic spaces ← hemorrhage, necrosis

√ infiltrative growth:

√ NO sharp cleavage plane toward normal parenchyma

√ may extend beyond capsule (common)

√ involvement of renal hilum without invasion of vessels

√ calcifications (rare)

√ NO venous extension (DDx: Wilms tumor)

√ NO invasion of collecting system

IVP:

√ large noncalcified renal mass with distortion of collecting system

√ usually NO herniation into renal pelvis (DDx: MLCN)

CECT:

√ minimal predominantly peripheral enhancement ← functioning entrapped renal elements at tumor periphery

√ areas of low attenuation in large lesions ← hemorrhage / necrosis

MR:

√ iso- to hypointense on T1WI

√ variable from markedly hypo- to hyperintense on T2WI

√ restricted diffusion in solid portion ← increased cellularity

√ focal areas of T1 shortening ← hemorrhage

US:

√ evenly echogenic tumor resembling uterine fibroids

√ "ring" sign = concentric rings of alternating hyper- and hypoechogenicity surrounding tumor ← peripheral dilated blood vessels

√ homogeneously hypoechoic tumor

√ complex heterogeneous mass with hemorrhage + cyst formation + necrosis

OB-US (prenatal detection often possible in 3rd trimester):

• rapid unexplained increase in fundal height

• premature delivery, increased renin levels

√ polyhydramnios, hydrops

Cx: pre-term labor, premature rupture of membranes

Angio:

√ hypervascular mass with neovascularity + displacement of adjacent vessels

Cx: (1) Transformation to metastasizing spindle cell sarcoma (rare)

(2) Metastases to lung, brain, bone (rare)

Dx: Cellular CMN is indistinguishable from Wilms tumor.
While Wilms tumor is the most common pediatric renal tumor, congenital mesoblastic nephroma is more common in young infants. With bilateral tumors, venous invasion, or pulmonary metastases Wilms tumor is more likely.

Rx: radical nephrectomy with wide surgical margin; 10% relapse (← local recurrence / metastases to lung, heart, bone, brain, liver)

Prognosis: excellent (imaging follow-up for 1 year)

DDx: (1) Wilms tumor (peaks at 3–4 years, history of nephroblastomatosis, associated congenital syndromes, bilateral, vascular invasion, pulmonary metastases)

(2) Clear cell sarcoma (age >1 year; bone metastases)

(3) Rhabdoid tumor (local + distant metastases to lung, abdominal lymph nodes, liver, bone; associated with intracranial tumor)

(4) Multilocular cystic nephroma (boys between 3 months and 4 years; well-circumscribed encapsulated multiloculated cystic mass + enhancing septa)

(5) Neuroblastoma (inferior displacement of ipsilateral kidney; encasement of adjacent blood vessels, crosses midline, invasion of spinal canal, tumoral calcifications)

(6) Ossifying renal tumor of infancy (calcified osteoid matrix)

METANEPHRIC ADENOMA

= NEPHROGENIC ADENOFIBROMA = EMBRYONAL ADENOMA

Age: any (range, 15 months – 83 years); M < F

Histo: proliferation of spindle-shaped mesenchymal cells encasing nodules of embryonal epithelium; numerous psammoma bodies

- pain, hematoma, flank mass
- hypercalcemia, polycythemia, hypertension

US:

√ well-defined solid hypovascular mass

√ hypo- / hyperechoic / cystic with mural nodule

CT:

√ iso- / hypoattenuating mass + little enhancement

√ ± small calcifications

Rx: local resection with sparing of kidney

METASTASIS TO ADRENAL GLAND

Frequency: 4th most common site of metastatic disease in the body; in 3% of all autopsy cases (in 27% with known primary)

◊ 50% of adrenal masses in oncologic patients represent benign nonhyperfunctioning

adenomas!
◊ An adrenal mass in a patient with a malignancy is a metastasis in 30–40%!

Origin: lung (40%), breast (20%), colon, stomach, lymphoma, malignant melanoma, renal cell carcinoma, prostate, pancreas, thyroid

Location: bilateral (49%); L÷R = 1.5÷1; **collision tumor** = rare coexistence of metastasis + adenoma

√ large heterogeneously attenuating mass with irregular contour and progressive heterogeneous enhancement

MR:
√ lack of signal loss on out-of-phase images (DDx: adrenal adenoma)
√ low-signal intensity on T1WI ← edema, necrosis
√ heterogeneous high-signal intensity on T2WI

CEMR:
√ strong rapid progressive enhancement
√ prolonged retention of contrast material ← large interstitial spaces of edema + necrosis

PET:
√ 18F-fluorodeoxyglucose uptake in 100% with rare false-positive results

Dx: biopsy

DDx: adenoma (intracytoplasmic lipid → chemical shift artifact + significant decrease in SI on out-of-phase GRE)

METASTASIS TO KIDNEY

◊ Most common malignant tumor of the kidney (2–3 times as frequent as primaries in autopsy studies)!
◊ 5th most common site of metastases (after lung, liver, bone, adrenals)!

Frequency: 7–13% in large autopsy series

◊ Renal metastases typically means advanced disease!

<u>most common primaries:</u>
bronchus, breast, GI tract, opposite kidney, non-Hodgkin lymphoma, colon, neuroblastoma (in children)

<u>less common primaries:</u>
stomach, cervix, ovary, pancreas, prostate, chloroma, myeloblastoma, myeloblastic sarcoma, melanoma (45% incidence), osteogenic sarcoma, choriocarcinoma (10–50% incidence), Hodgkin lymphoma, rhabdomyosarcoma

• usually asymptomatic
√ bilateral multiple small masses ← brief survival of patient
√ solitary exophytic mass (in colon cancer)
√ perinephric tumor (in melanoma)
√ infiltrative growth pattern

DDx on CT: lymphoma, bilateral RCC, multiple renal infarcts, acute focal bacterial nephritis, infiltrating TCC

METASTASIS TO URETER

◊ Hematogenous metastases to the ureter are rare!

most common primaries: breast, GI tract, prostate, cervix

MIXED EPITHELIAL AND STROMAL TUMOR

= MEST = LEIOMYOMATOUS RENAL HAMARTOMA = CYSTIC HAMARTOMA OF RENAL PELVIS = ADULT TYPE MESOBLASTIC NEPHROMA = MULTILOCULAR CYST WITH OVARIAN STROMA

Prevalence: < 100 cases reported in literature

Average age: 56 (range, 17–84) years; M÷F = 1÷11

Associated with: oral estrogen supplements / contraceptives

Path: benign complex solid + cystic renal tumor

Histo: › stromal spindle cells mimicking ovarian stroma with estrogen + progesterone receptors, and
› epithelium-lined cysts / microcysts

- hematuria, flank pain, palpable mass, urinary tract infection
- asymptomatic (¼)

√ well-circumscribed expansile multiseptate complex (= cystic and solid) mass
√ may herniate into renal pelvis
√ variable contrast enhancement of intervening septa
√ delayed contrast enhancement
√ ± adipose tissue
√ ± enhancing mural nodule / mural calcifications
√ ± intralesional hemorrhage

US:
√ heterogeneous hyperechoic / partially cystic mass

MR:
√ cystic region with T1 hypointensity + T2 hyperintensity
√ nodular component T1 hyperintense + T2 hypointense

Rx: surgery (impossible DDx from cystic RRC)

DDx: (1) Multilocular cystic renal tumor – adult cystic nephroma
(2) Cystic renal cell carcinoma
(3) Complex renal cyst
(4) Multicystic dysplastic kidney
(5) Obstructed duplicated renal collecting system
(6) Renal abscess

MÜLLERIAN DUCT CYST

= failed regression of paramesonephric (= müllerian) duct which usually regresses by 3rd fetal month

Prevalence: 4–5% of male newborns; in 1% of men

Peak age: 20–40 years

- obstructive / irritative urinary tract symptoms
- suprapubic / rectal pain, hematuria
- infertility ← most common cause of ejaculatory duct obstruction

Location: arises from region of verumontanum slightly lateral to midline

◊ No communication with genital tract / urethra; connected by thin stalk
Associated with: typically NO other congenital anomalies; renal agenesis (rare)
√ large teardrop-shaped intraprostatic cyst usually with extension superolaterally above prostate
√ aspirate contains serous / mucous clear brown / green fluid (hemorrhage + debris), NOT spermatozoa
√ commonly contains calculi
MR:
√ increased signal on T1WI ← hemorrhage, protein
Cx: infection, hemorrhage, carcinomatous transformation
DDx: posterior bladder diverticulum, urethral diverticulum, utricle cyst, vas deferens cyst, seminal vesicle cyst

MULTICYSTIC DYSPLASTIC KIDNEY

= MULTICYSTIC DYSGENETIC KIDNEY (MCDK) = MULTICYSTIC KIDNEY (MCK) = Potter Type II
= nonheritable developmental disorder in which kidney is replaced by nonfunctioning noncommunicating cysts
◊ 2nd most common cause of an abdominal mass in neonate (after hydronephrosis)!
◊ Most common form of cystic disease in infants!
Prevalence: 1÷4,300 (for unilateral MCDK), 1÷10,000 (for bilateral MCDK) live births; M÷F = 2÷1 (for unilateral MCDK); more common among infants of diabetic mothers
Risk of recurrence: 2–3%
Genetics: sporadic NOT familial
Etiology: obstruction / atresia of ureter during metanephric stage before 8–10 weeks GA
Pathophysiology: interference with ureteral bud division → inhibiting induction and maturation of nephrons and various stromal renal elements; collecting tubules enlarge into cysts
Histo: immature glomeruli + tubules reduced in number + whirling mesenchymal tissue, cartilage (33%), cysts
• abdominal mass
• asymptomatic if unilateral (may go undetected until adulthood)
• recurrent urinary tract infections, intermittent abdominal pain, nausea + vomiting, hematuria, failure to thrive
• fatal ← pulmonary hypoplasia if bilateral
Fatal form: bilateral MCDK (4.5–21%), contralateral renal agenesis (0–11%)
Location:
1. UNILATERAL multicystic dysplastic kidney (80–90%)
most common form (80–90%); L÷R = 2÷1
Cause: pelvoinfundibular atresia
In 33 (range, 20–50)% associated with anomalies of the contralateral kidney:
(1) Vesicoureteral reflux 15–43%
(2) Ureteropelvic junction obstruction 7–27%
(3) Horseshoe kidney 5–9%
(4) Ureteral anomalies 5%

(5) Renal hypoplasia 4%
(6) Megaloureter
(7) Malrotation
(8) Renal agenesis

Associated with anomalies of the ipsilateral kidney:

(1) Vesicoureteral reflux (25%)
(2) Ectopic ureter

2. SEGMENTAL / focal renal dysplasia
= "multilocular cyst" secondary to
(a) high-grade obstruction of upper pole moiety in duplex kidney from ectopic ureterocele
(b) single obstructed infundibulum
3. BILATERAL cystic dysplasia
in the presence of severe obstruction in utero from posterior urethral valves / urethral atresia with oligohydramnios + pulmonary hypoplasia
Prognosis: lethal

Potter types:

(1) Multicystic kidney (Potter IIa)
√ large kidney with multiple large cysts + little visible renal parenchyma
(2) Hypoplastic / diminutive form (Potter IIb)
√ echogenic small kidney

Time of appearance:

(A) RELATED TO SITE OF OBSTRUCTION
@ ureteropelvic junction
√ single / several large / multiple medium-sized cysts in large kidney
@ distal ureter / urethra
√ small / no cysts in small kidney

(B) RELATED TO TIME OF INSULT
(a) early onset between 8th and 11th week
√ small / atretic renal pelvis + calices
√ 10–20 cysts + loss of reniform appearance
(b) late onset = HYDRONEPHROTIC FORM
√ large central cyst (= dilated pelvis) often communicating with cysts
√ some renal function may be demonstrated

√ imaging appearance of MCDK varies by age:
√ large kidney with lobulated contour in infancy
√ often incidental finding of small kidney in adult (as little as 1 g ← arrested growth)
√ calcification: curvilinear / ringlike in wall of cysts in 30% of adults, rarely in children
√ central region of soft tissue
√ peripheral noncommunicating cysts ± calcifications
√ absence / severe atrophy of ipsilateral ureter + renal collecting system + renal vasculature
√ contralateral renal hypertrophy
√ contralateral vesicoureteral reflux (VUR) in 5–43%

NUC (^{99m}Tc-MAG 3):

◊ NUC preferred over IVP in first month of life as concentrating ability of even normal

neonatal kidneys is suboptimal!

√ NO function

DDx: severe hydronephrosis (peripheral activity), UPJ obstruction (minimal uptake)

US:

√ normal renal architecture replaced by:

√ random cysts of varying shape + size ("cluster of grapes") with largest cyst in peripheral nonmedial location (100% accurate)

√ cysts separated by septa (100% accurate)

√ no communication between multiple cysts (93% accurate)

√ cysts begin to disappear in infancy

√ central sinus complex absent (100% accurate)

√ no identification of parenchymal rim or corticomedullary differentiation (74% accurate)

√ oligohydramnios in bilateral MCDK / unilateral MCDK + contralateral urinary obstruction

Angio:

√ absent / hypoplastic renal artery; angiography unnecessary since a DDx to long-standing functionless kidney is not possible

OB management:

(1) Routine antenatal care + evaluation by pediatric urologist following delivery if unilateral

(2) Option of pregnancy termination if ≤ 24 weeks GA

(3) Nonintervention for fetal distress if > 24 weeks GA

Cx: (1) Renin-dependent hypertension (rare)

(2) Malignancy in < 1÷330

Rx: (1) Follow-up in 3–4-month intervals in first year (isolated reports of developing malignancy)

(2) Nephrectomy (in hypertension / massive renal enlargement)

(3) Assessment of contralateral kidney for VUR

DDx: (1) Hydronephrosis

(2) Renal dysplasia with cysts (associated with partial obstruction)

MULTILOCULAR CYSTIC RENAL TUMOR

= MCRT = MULTILOCULAR CYSTIC NEPHROMA (MLCN) = POLYCYSTIC NEPHROBLASTOMA = WELL-DIFFERENTIATED POLYCYSTIC WILMS TUMOR = BENIGN CYSTIC (PARTIALLY) DIFFERENTIATED NEPHROBLASTOMA = MULTILOCULAR CYSTIC NEPHROMA = PERLMAN TUMOR = MULTILOCULAR RENAL CYST = CYSTIC ADENOMA / HAMARTOMA / LYMPHANGIOMA = PARTIALLY POLYCYSTIC KIDNEY

= rare nonhereditary benign renal neoplasm originating from metanephric blastema possibly representing the benign end of a spectrum with solid Wilms tumor at the malignant end

Age: bimodal age + sex distribution: < 4 years in 73% male, > 4 years in 89% female

(a) 3 months to 2 years of age (65%), 5–30 years (5%); M÷F = 2÷1

(b) > 30 (mostly, 40–60) years (30%); M÷F = 1÷8

◊ 90% of tumors in males occur in first 2 years of life (peak 3–24 months)!

◊ Most of the lesions in females occur between ages 4 and 20 or 40 and 60!

Path: solitary large well-circumscribed multiseptated mass of noncommunicating loculi,

surrounded by thick fibrous capsule + compressed renal parenchyma

Solid tumor portion: thin fibrous septa
◊ Solid nodules are absent!
Content of loculi: colorless fluid / thick myxoid material
Size of loculi: between a few mm to 4 cm
√ tumor tendency to herniate into collecting system

Histo: (gross anatomic + radiologic features are identical)

1. **Adult cystic nephroma**
   fibrous tissue septa of undifferentiated mesenchymal and primitive glomerulotubular elements surround cysts lined by flattened eosinophilic cuboidal epithelium partially protruding into lumen in a hobnail / teardrop appearance; NO blastemal / other embryonal elements
   • typically seen in adult women
2. **Cystic partially differentiated nephroblastoma** (CPDN)
   predominantly cystic lesion with septa containing primitive metanephric blastema
   • primarily in young boys
   ◊ No association with Wilms tumor!

• commonly asymptomatic painless abdominal mass
• ± sudden and rapid enlargement, pain, urinary tract infection
• hematuria ← tumor herniation into renal collecting system

Location: unilateral, often replacing an entire renal pole (usually lower pole)
Size of tumor: 5–10 cm (range, few cm to 33 cm)
√ contrast enhancement of capsule + septations ← tortuous fine vessels course through septa
√ curvilinear to flocculent calcification of septa / capsule in 5%
√ absence of intratumoral / perinephric hemorrhage

IVP:
√ distortion of calices / hydronephrosis ← nonfunctional mass
√ tendency for herniation of tumor cysts into renal pelvis and proximal ureter is CHARACTERISTIC (but nonspecific as it also occurs in Wilms tumor + RCC)

US:
√ cystic mass with claw / beak shape of adjacent normal renal parenchyma ← intrarenal origin:
√ cluster of cysts separated by thick septa (SUGGESTIVE):
√ NO solid / nodular elements
√ occasionally solid echogenic character ← closely packed acoustic interfaces with very small cysts / jellylike contents
√ ± associated urinary tract obstruction

CT:
√ well-circumscribed (CHARACTERISTIC) multiseptated cystic renal mass:
√ tumor encapsulated by thick fibrous capsule
√ attenuation of cysts equal to / higher than water ← gelatinous fluid
√ multicystic = cluster of noncommunicating honeycombed cysts between a few mm and 4 cm in size
√ cysts separated by variably enhancing thick septa

√ closely packed septa may appear as solid nodules but are separated by very small cystic spaces

MR:

√ multicystic mass of low signal intensity on T1WI + hyperintense on T2WI

√ hypointense capsule and septa on all sequences

√ variable SI of cyst content on T1WI ← old hemorrhage / concentrated protein

√ enhancing septa

Cx: local recurrence / coexistent Wilms tumor (very rare)

Rx: nephrectomy with excellent prognosis

DDx:
(1) Cystic Wilms tumor (overlapping age, expansile solid masses of nephroblastomatous tissue)
(2) Clear cell sarcoma (poor prognosis)
(3) Cystic mesoblastic nephroma (most common renal tumor of infancy)
(4) Cystic RCC (mean age of 10 years)
(5) Segmental form of multicystic dysplastic kidney (pre- / perinatal discovery in a duplex kidney)
(6) Complex renal cysts
(7) Mixed epithelial and stromal tumor
(8) Severe hydronephrosis (cysts communicating with one another and with a large central cyst)
(9) Complicated benign cyst / polycystic kidney disease

MULTIPLE MYELOMA

◊ It is essential that dehydration be avoided!

Impairment of renal function:

(1) Precipitation of abnormal proteins (Bence-Jones ± Tamm-Horsfall protein casts) within tubule lumen (30–50%)
(2) Toxicity of Bence-Jones proteins on tubules
(3) Impaired renal blood flow ← increased blood viscosity
(4) Amyloidosis
(5) Nephrocalcinosis from hypercalcemia

◊ Contrast-induced renal failure in multiple myeloma is not seen with greatly increased frequency!

• Tamm-Horsfall proteinuria (tubular cell secretion)

√ smooth normal to large kidneys (initially), becoming small over time

√ occasionally attenuated pelvoinfundibulocaliceal system

√ normal to diminished contrast material density; increasingly dense in acute oliguric failure

US:

√ normal to increased echogenicity

NUC in bone scintigraphy:

√ nonspecific increased parenchymal activity

MYCETOMA

= FUNGUS BALL

Organism: typically Candida, Aspergillus, Mucor, Cryptococcus, Phycomycetes, Actinomycetes mostly mycelial (M-form) or occasionally yeast cells (Y-form)

Predisposed: diabetics, debilitating illness, prolonged antibiotic therapy, leukemia, lymphoma, thymoma, immunosuppression

- flank pain, passing of tissue, hematuria (extremely rare)
- renal candidiasis associated with candidemia
- Candida cystitis preceded by vaginal candidiasis

√ unilateral nonvisualization of kidney (most frequent)
√ large irregular filling defect extending into dilated calices (retrograde contrast study)
√ necrotizing papillitis from Candida nephritis (common)
√ lacelike pattern (on antegrade contrast study)

MYELOLIPOMA

= uncommon benign tumor composed of hematopoietic cells + mature fat resembling bone marrow

Prevalence: 0.08–0.20% (autopsy series); 3–6% of all incidental primary adrenal tumors

Mean age: 55 years (for adrenal myelolipoma); M÷F = 2÷3; 64 years (for extraadrenal myelolipoma)

Cause: chronic ACTH elevation → metaplasia of adrenocortical cells precipitated by chronic stress / degeneration

Path: mature fat (0–100%) interspersed with hematopoietic cells resembling bone marrow + pseudocapsule

Histo: variable mixture of megakaryocytes, myeloid and leukocyte precursor cells, erythroid cells, lymphocytes

Associated with: endocrine disorders in 7% (Cushing syndrome, Conn syndrome, 21-hydroxylase deficiency, 17-hydroxylase deficiency); nonhyperfunctioning adenoma (15%)

◊ Long-standing / poorly treated congenital adrenal hyperplasia may develop massive bilateral myelolipomas!

- usually clinically occult
- pain (from spontaneous hemorrhage if large)

Location:
(a) adrenal myelolipoma (85%)
› isolated adrenal myelolipoma
› adrenal myelolipoma with hemorrhage
(b) extraadrenal myelolipoma (15%):
› retroperitoneal (12%): presacral space (6%), abdomen, stomach, liver, muscle fascia
› intrathoracic (3%): mediastinum, lung
Predilection for: perirenal + presacral spaces

Site: unilateral÷bilateral = 10÷1; RT÷LT = 3÷1

Mean size: 10 (range, 2–17) cm;
enlargement with hemorrhage (11%)

X-ray:

√ soft lucent mass with rim of residual normal adrenal cortex

US:

√ heterogeneous predominantly hyperechoic (= fat + myeloid tissue) mass interspersed with hypoechoic regions (= pure fat)

√ ± hypoechoic areas of hemorrhage

CT:

√ heterogeneous mass composed of:

√ fat of –74 (range, –30 to –115) HU:

√ 50–90% fat in adrenal myelolipoma

√ < 50% fat in extraadrenal myelolipoma

√ interspersed "smoky" areas of higher attenuation of +20–30 HU (= admixture of fat + marrowlike elements)

√ occasionally tiny foci of fat (< 10% fat)

√ small punctate calcifications from previous hemorrhage:

√ calcifications in up to 24% of adrenal myelolipomas

√ calcifications in 10% of extraadrenal myelolipomas

√ ± enhancement of soft-tissue component

In general, macroscopic fat-containing adrenal lesions are myelolipomas characteristically identified at CT!

MR:

√ intermediate SI on T2WI similar to spleen / heterogeneous high signal (admixture with hematopoietic tissue + myeloid tissue + hemorrhage)

N.B.: pure fat may demonstrate no SI decrease on opposed-phase images dependent on proportion of fat to water in an image voxel

(a) for lesion with predominantly mature adipose tissue

√ homogeneously hyperintense mass on T1WI

√ intermediate SI on T2WI

√ signal dropout on fat-suppressed images

(b) for lesion with mixture of fatty + myeloid elements

√ heterogeneous masses containing foci of fat SI intermixed with focal high SI on T2WI + contrast enhancement on T1WI

(c) for lesion with predominantly myeloid elements

√ nodules hypointense relative to liver on T1WI

√ hyperintense relative to liver on T2WI

√ contrast enhancement on T1WI

NUC:

√ uptake of ^{99m}Tc-sulfur colloid in erythropoietic elements

Cx: acute retroperitoneal hemorrhage ← myeloid elements with increase in size > 5 cm (12%)

Dx: percutaneous needle biopsy with demonstration of megakaryocytes

Rx: surgical excision of (a) symptomatic lesion (b) enlarging lesion (c) lesion > 7 cm in diameter → increased risk of hemorrhage (d) lesion of diagnostic uncertainty

DDx: adrenocortical carcinoma with lipomatous metaplasia, adrenal lipoma, adrenal teratoma, adrenal adenoma with degenerative and myelolipomatous changes, liposarcoma (unencapsulated + less well defined + infiltrative without hemorrhage),

pheochromocytoma

NEPHROBLASTOMATOSIS

= multiple / diffuse NEPHROGENIC RESTS
= dysontogenetic process with persistence of embryonic renal parenchyma (= metanephric blastema) within the renal cortex > 36 weeks GA

Prevalence: in 1% of infant kidneys (at autopsy); in 41% with unilateral Wilms tumor, in 94% with metachronous contralateral Wilms tumor, in 99% with bilateral Wilms tumor
◊ Usually absent in infants > 4 months of age

Pathogenesis: embryonal renal tissue in mature kidney after birth retains potential to form nephroblastoma / Wilms tumor

A. **Perilobar nephrogenic rest** (0.87%)
Path: multiple rests forming a well-circumscribed smooth band at periphery of lobe (cortex / column of Bertin)
Histo: predominantly blastemal tissue
Associated with:
(1) Beckwith-Wiedemann syndrome (gigantism, macroglossia, omphalocele, genitourinary anomalies)
(2) Hemihypertrophy → 3% develop Wilms tumor
(3) Perlman syndrome (visceromegaly, gigantism, cryptorchidism, polyhydramnios, characteristic facies)
(4) Trisomy 18 syndrome
• abnormal chromosome band 11p15 (Wilms tumor gene 2) in up to 77% of patients with perilobar rests
• mean age presenting with neoplasia: 36 months

B. **Intralobar nephrogenic rest** (0.10%)
Path: single / few rests with irregular indistinct margins located centrally anywhere within a lobe → higher risk of developing neoplasia
Histo: predominantly stromal + epithelial tissue
Associated with:
(1) **Drash syndrome** (ambiguous genitalia in genotypic males, progressive renal failure): 78% with intralobar rests + 11% with perilobar rests
(2) **Sporadic aniridia**: 100% with intralobar rests + 20% with perilobar rests → 33% likelihood of Wilms tumor
(3) **WAGR syndrome** (Wilms tumor, aniridia, genital abnormalities, mental retardation)
• abnormal chromosome band 11p13 (Wilms tumor gene 1)
• mean age presenting with neoplasia: 16 months

Age: < 2 years of age; neonatal period, infancy, childhood

Histologic subtypes:
(a) dormant (nascent): nephrogenic rests the size of a glomerulus primarily composed of blastemal + epithelial elements; no malignant potential
(b) sclerotic (regressing / obsolescent): microscopic rests primarily composed of stromal elements; nonmalignant
(c) hyperplastic: spherical / irregular / oval proliferation of most or all cell elements

(d) neoplastic: expansile mass ← proliferation of a single cell line

• clinically occult in vast majority / renal enlargement

√ peripheral rind of nephrogenic rests that compress normal renal tissue toward the center of the kidney

US (least sensitive technique):

√ hypo-, iso-, or hyperechoic nodules distorting renal shape

√ ± enlargement of kidney causing diffuse hyperechogenicity and poor corticomedullary differentiation

CT (modality of choice):

√ hypo- to isoattenuating nodules

√ striated enhancement pattern / no enhancement

MR (43% sensitivity, 58% sensitivity with enhancement):

√ renal enlargement

√ absent corticomedullary differentiation

√ homogeneously hypo- to isointense foci on T1WI

√ homogeneously T1-hypointense lesions after enhancement

√ iso- to slightly hyperintense on T2WI

Cx: malignant transformation (in 1%) into Wilms tumor / cystic partially differentiated nephroblastoma

√ increase in size of nephrogenic rest

√ increasing tissue heterogeneity

√ developing a spherical masslike configuration

Screening: for children with associated syndromes baseline CT at diagnosis at 6 months of age + follow-up sonograms every 3 months until age 8 years

Rx: radiologic follow-up / chemotherapy (for biopsy-proved hyperplastic nephrogenic rests similar to stage I Wilms tumor)

Multifocal (Juvenile) Nephroblastomatosis

most common form

= isolated macroscopic nephrogenic rests

√ may escape detection with imaging

√ ± nodular mass effect on pelvicaliceal structures

√ kidneys may be enlarged

√ lobulated contour of kidney

US:

√ hypoechoic / isoechoic / hyperechoic nodules

CECT (preferred study):

√ nodules with less enhancement than renal parenchyma

Superficial Diffuse Nephroblastomatosis

= LATE INFANTILE NEPHROBLASTOMATOSIS

= superficial continuous rind of rests around medulla (= perilobar type)

Age: < 2 years

√ nephromegaly

US:

√ loss of corticomedullary differentiation
√ kidneys diffusely echogenic / of normal echogenicity
√ cysts of variable size
CECT:
√ thick rind at periphery of kidney with poor / striated enhancement
DDx: autosomal recessive polycystic kidney disease, leukemia, lymphoma
◊ Strong association with Wilms tumor!

Universal / Panlobar (Infantile) Nephroblastomatosis

rare form
= entire renal parenchyma diffusely involved
• may develop renal failure
√ bilateral renal enlargement (infiltrative growth)

NEPHROGENIC ADENOMA

= uncommon benign metaplastic response to urothelial injury / prolonged irritation
Cause: (a) trauma: pelvic trauma, surgery in lower urinary tract, endoscopic procedure, renal transplantation (after a mean of 50 months)
(b) irritation: calculi, chronic bacterial infection, irradiation, intravesical chemotherapy, immunosuppressive therapy
Age: 3 weeks to 83 years; M÷F = 3÷1 (more common in females if < 20 years of age)
Path: discrete raised papillary / polypoid / cystic areas projecting from epithelial surface
Histo: variable number of small tubules (resembling loops of Henle and collecting ducts) + cysts + papillae lined with a single layer of cuboidal / low columnar cells
• asymptomatic; hematuria, dysuria, bladder instability
Location: bladder (72%), renal pelvis, ureter, urethra; strong correlation between location + site of insult to urothelium
Size: usually 1 mm, up to 7 cm in diameter
√ papillary / polypoid filling defect
Prognosis: high likelihood of recurrence; rarely malignant transformation
Rx: resection / fulguration
DDx: inflammatory / malignant urothelial lesions

NEUROBLASTOMA

Most common solid abdominal mass of infancy (12.3% of all perinatal neoplasms), 4th most common malignant tumor in infancy (after leukemia, lymphoma, CNS tumor); 2nd most common tumor in childhood (Wilms tumor more common in older children), 8% of all childhood cancers; 15% of cancer deaths in children; 30% of all fetal (congenital) tumors
Incidence: 9.5÷1,000,000 live births; 650 new cases annually in USA; 20% hereditary
Origin: neural crest in adrenal medulla / along sympathetic chain
Path: round irregular lobulated mass of 50–150 g with areas of hemorrhage + necrosis
Histo: small round cells slightly larger than lymphocytes with scant cytoplasm; **Horner-Wright rosettes** = one / two layers of primitive neuroblasts surrounding a central zone of tangled neurofibrillary processes (= neuropils)

Median age: 22 months; 25% (50%) [79%] {97%} in 1st year (< 2 years) [< 4 years] {< 10 years}; M÷F = 1÷1 occasionally present at birth or 1st seen in adults;

May be associated with: aganglionosis of bowel, CHD

- constitutional symptoms:
  - fever (30%), weight loss, malaise, failure to thrive
- symptoms of mass effect:
  - pain, urinary retention, frequency of evacuation, constipation
  - bone pain, limp, inability to walk (20%)
- palpable abdominal mass (45–54%)
- cerebellar ataxia:
  - myoclonus of trunk + extremities
  - opsomyoclonus (20%) = spontaneous conjugate + chaotic eye movements (sign of cerebellar disease)
- "raccoon" sign = orbital ecchymosis / proptosis (12%)
- increased catecholamine production (75–90%):
  - in 95% excreted in urine as vanillylmandelic acid (VMA) / homovanillic acid (HVA)
  - paroxysmal episodes of:
    - flushing, tachycardia, headaches, hyperglycemia
    - hypertension (in up to 30%)
    - intractable diarrhea (9%) ← increase in vasoactive intestinal polypeptides (VIP)
    - acute cerebellar encephalopathy
    - rise in body temperature / sweating
- positive bone marrow aspiration (70%)

Stage:

I confined to organ of origin
II local extension not crossing midline
III extension across midline
IV metastatic to distant lymph nodes, liver, bone, brain, lung
IVs stages I + II with disease confined to liver (25%) > skin > bone marrow (< 10%) WITHOUT radiographic evidence of skeletal metastases

Metastases:

bone (60%), regional lymph nodes (42%), orbit (20%), liver (15%), intracranial (14%), lung (10%)

◊ Metastases are the 1st manifestation in up to 60–70%!

› **Hutchinson syndrome**
(1) Primary adrenal neuroblastoma
(2) Extensive skeletal metastases, esp. skull
√ widened cranial sutures = sutural diastasis ← subjacent dural metastases
√ hair-on-end appearance of skull
(3) Proptosis
(4) Bone pain

› **Pepper syndrome**
(1) Primary adrenal neuroblastoma
(2) Massive hepatomegaly from metastases

› **Blueberry muffin syndrome**

(1) Primary adrenal neuroblastoma
(2) Multiple metastatic skin lesions

◊ Bone marrow aspirate is positive in 50–70% at time of initial diagnosis!
◊ ⅔ of patients > 2 years have disseminated disease!

MR (modality of choice):
√ focal T2-hyperintense areas
√ enhancing lesions on fat-suppressed T1WI

@ Skeletal metastases:
• paraplegia / extremity weakness ← spinal canal extension
√ periosteal new-bone formation
√ osteolytic focus / multicentric lytic lesions
√ "black eyes / raccoon" sign ← metastasis to both lateral orbital walls (common)
√ lucent horizontal metaphyseal line
√ vertical linear radiolucent streaks in metadiaphysis of long bones
√ pathologic fracture
√ vertebral collapse
√ sclerotic lesions ← healing
DDx: Ewing sarcoma, rhabdomyosarcoma, leukemia, lymphoma

@ Intracranial + maxillofacial metastases:
Site: dura, brain substance

@ Orbital metastasis (20–55%):
• periorbital ecchymosis ("raccoon eyes"); bilateral in ½
• periorbital swelling, subconjunctival hemorrhage, ocular mobility disturbance, strabismus
• atrophy of the optic head
√ uni- / bilateral proptosis
√ soft-tissue mass originating in diploic space of bony orbit with extension beyond inner + outer tables
√ high attenuation relative to muscle with small calcific foci
√ tumor hypointense to muscle on T1WI
√ slightly hyperintense to muscle on T2WI
√ avid heterogeneous contrast enhancement
√ no tumor extension into preseptal soft tissues
DDx: rhabdomyosarcoma

@ Pulmonary metastases:
√ nodular infiltrates
√ rib erosion
√ mediastinal + retrocrural lymphadenopathy (common)

@ Mesenteric / peritoneal metastases:
√ spread through subperitoneal space (common)
√ peritoneal metastases typically not calcified

Location: anywhere within sympathetic neural chain

@ Abdomen (70%):
(a) adrenal (36–67%): almost always unilateral

(b) both adrenals (7–10%)
(c) extraadrenal in sympathetic chain (18%)

@ Thorax + posterior mediastinum (20%): aortic bodies
@ Neck (5%): carotid ganglia
@ Pelvis (2–3%): organ of Zuckerkandl
@ Skull, olfactory bulb, cerebellum, cerebrum (2%)
@ Other sites (10%): eg, intrarenal (very rare)
@ Unknown (10%)

Clue: large calcified retroperitoneal mass encircling the aorta with extension into neural foramina

√ large suprarenal mass with irregular shape + margins (82%):
√ displacement of kidney
√ inseparable from kidney ± invasion of kidney (10–32%) along the vascular pathways
√ propensity for extension into spinal canal through neural foramen with erosion of pedicles (15%)
√ extension across midline (55%) (DDx: Wilms tumor)
√ stippled / coarse amorphous calcifications (frequent)
√ retroperitoneal adenopathy / contiguous extension (73%)
√ retrocrural adenopathy (27%)
√ encasement of IVC + aorta, celiac axis, SMA (32%):

N.B.: caval involvement = indicator of unresectability

√ liver metastases (18–66%); invasion of liver (5%)

IVP:
√ "drooping lily" sign = displacement of kidney inferolaterally without distortion of collecting system
√ hydronephrosis (24%)
√ calcifications in 36–50% on KUB

CT:
√ heterogeneous texture with low-density areas ← hemorrhage + necrosis (55%)
√ calcifications in up to 85%
√ variable contrast enhancement

MR (most sensitive modality ← high soft-tissue contrast):
√ hyperintense heterogeneous mass on T2WI
√ enhancing heterogeneous low SI on T1WI
√ areas of high SI on T1WI ← intratumoral hemorrhage
√ areas of high SI on T2WI ← cystic changes

Angio:
√ hypo- / hypervascular mass

US:
√ hyperechoic poorly defined mass with acoustic shadowing (calcifications):
√ hypoechoic areas of heterogeneous texture ← hemorrhage / necrosis

OB-US:

Time of Dx: 1st identified in 3rd trimester (earliest at 20 weeks GA); usually at 36 weeks GA

• (occasionally) maternal hypertension + preeclampsia ← fetal catecholamines reaching maternal circulation

Location: right suprarenal; adrenal÷extraadrenal = 9÷1 (compared to 3.5÷6.5 in pediatric age group)

√ cystic (50%) / mixed cystic + solid / solid adrenal mass

√ may exhibit acoustic shadowing (calcifications)

√ displacement of adjacent kidney inferiorly + laterally

√ hydrops fetalis ← severe anemia ← metastases to bone marrow, mechanical compression of IVC, hypersecretion of aldosterone

√ polyhydramnios

Prognosis: 90–96% survival rate (better than for neonates)

NUC (bone scan sensitivity better than radiography):

√ increased radiotracer uptake on bone scan (60%):

√ purely lytic lesions may present as photopenic areas

CAVE: symmetric lytic neuroblastoma metastases occur frequently in metaphyseal areas where normal epiphyseal activity obscures lesions

√ soft-tissue uptake of ^{99m}Tc-phosphate in 60%

√ frequently 67Ga uptake in primary site of neuroblastoma

√ focal uptake of ^{131}I- / ^{123}I-MIBG radioactivity (82% sensitive; 88% specific) → method of choice

PET-CT (sensitive + specific)

Prognosis:

› 2-year survival rate versus age at presentation:

60% if patient's age < 1 year

20% if patient's age 1–2 years

10% if patient's age > 2 years

◊ May revert to benign ganglioneuroma in 0.2%!

› Survival rate versus stage:

80% for stage I

60% for stage II

30% for stage III

7% for stage IV

75–87% for stage IVs

DDx: adrenal hemorrhage, exophytic Wilms tumor, mesoblastic nephroma, multicystic kidney, retroperitoneal teratoma, infradiaphragmatic extralobar sequestration, hepatic hamartoma / hemangioma, splenic cyst

NEUROGENIC BLADDER

Neuroanatomy: bladder innervation of detrusor muscle by parasympathetic nerves S2–S4

Etiology: congenital (myelomeningocele); trauma; neoplasm (spinal, CNS); infection (herpes, polio); inflammation (multiple sclerosis, syrinx); systemic disorder (diabetes, pernicious anemia)

A. SPASTIC BLADDER

"upper motor neuron" lesion above conus

B. ATONIC BLADDER

"lower motor neuron lesion" below conus

ORCHITIS

Etiology:

(a) bacterial infection ascending from bladder associated with epididymitis

(b) viral infection

› complication of **mumps** in 20–35%:

Age: adolescents + young adults

Time of onset: usually within 3–5 days of infection

√ unilateral (bilateral) orchitis in 90% (10%);

√ parotitis precedes orchitis in 84%, simultaneous in 3%, later in 4%; without parotitis in 10%

› Coxsackie virus

Location: diffuse / focal

√ increased testicular blood flow

√ ± diffuse enlargement of testis

√ ± reactive hydrocele + thickening of scrotal wall

√ decreased testicular echogenicity

MR:

√ heterogeneously decreased SI on T1WI

√ increased SI on T2WI

√ avid homogeneous enhancement

Cx: ischemia ← increased intratesticular pressure; pyocele; testicular rupture

Focal Orchitis

Cause: usually epididymitis

√ ill-defined hypoechoic lesion of crescent / amorphous shape

√ peripheral adjacent to abnormal epididymis

√ increased / no color Doppler flow

DDx: neoplasm (mimicked by focal orchitis)

Granulomatous Orchitis

(a) TB, syphilis, fungi, parasites

√ tendency to involve epididymis first

(b) sarcoidosis (genital tract affected in 5%)

√ multiple hypo- / hyperechoic masses within testis / epididymis

Diffuse Orchitis

DDx: leukemia, lymphoma

OSSIFYING RENAL TUMOR OF INFANCY

= extremely rare benign renal mass originating from urothelium

Prevalence: only 11 cases in literature

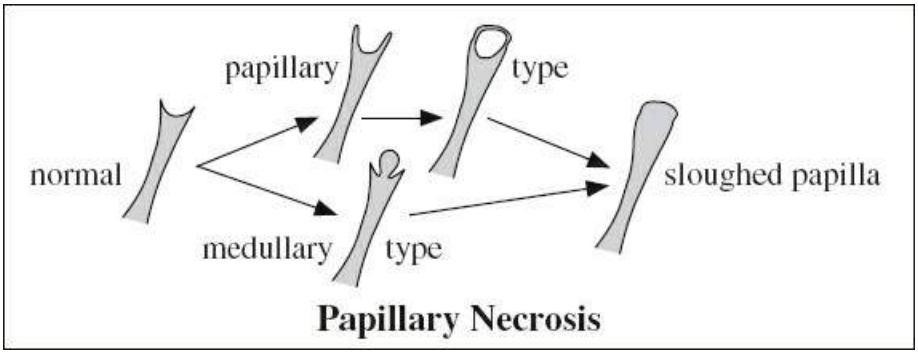
Age: 6 days–14 months; M > F

Histo: osteoid core, osteoblasts, spindle cells

• hematuria
Location: L > R kidney; attached to renal papilla
Site: upper pole
√ 2–3-cm polypoid mass:
  √ calcified (in 80%) resembling a staghorn calculus
  √ filling defect of collecting system
  √ partial obstruction of collecting system
√ echogenic mass + shadowing
√ poor enhancement on CT
Rx: nephron-sparing resection curative
DDx: staghorn calculus

PAGE KIDNEY

= renin-angiotensin–mediated hypertension ← constrictive ischemic nephropathy (= reduction of blood flow to kidney) ← renal compression in a perinephric / subcapsular location
Etiology: (1) Spontaneous hematoma (most common)
(2) Blunt trauma with chronic contained subcapsular hematoma / perirenal scarring
(3) Cyst
(4) Tumor
√ (compressive) subcapsular fluid collection:
  √ indentation / flattening of renal margin
  √ distortion of renal contour + thinning of renal parenchyma
√ kidney surrounded by fibrotic band ± calcification
√ stretching + splaying of intrarenal vessels
√ enlarged + displaced capsular artery
√ delayed nephrogram



√ slow arterial washout
√ elevated resistive index at spectral Doppler
√ globally decreased renal function at perfusion scintigraphy

PAPILLARY NECROSIS

= NECROTIZING PAPILLITIS

= ischemic coagulative necrosis of renal papilla (loops of Henle + vasa recta) ← interstitial nephritis (interstitial edema) or intrinsic vascular obstruction

Cause:

mnemonic: POSTCARD

Pyelonephritis
Obstructive uropathy
Sickle cell disease
Tuberculosis, **T**rauma
Cirrhosis = alcoholism, **C**oagulopathy
Analgesic nephropathy
Renal vein thrombosis
Diabetes mellitus (50%)

also: nonsteroidal anti-inflammatory drugs (NSAID), dehydration, severe infantile diarrhea, hemophilia, Christmas disease, acute tubular necrosis, transplant rejection, postpartum state, high-dose urography, intravesical instillation of formalin, thyroid cancer

Types:

1. Necrosis in situ = necrotic papilla detaches but remains unextruded within its bed
2. Medullary type (partial papillary slough) = single irregular cavity located concentric / eccentric in papilla with long axis paralleling the long axis of the papilla + communicating with calyx
   √ central necrosis at tip of pyramid
3. Papillary type (total papillary slough)
   √ detachment of papilla begins in caliceal fornix

Phases:

(1) Enlargement of papilla (papillary swelling)
(2) Fine projections of contrast material alongside papilla (tract formation)
(3) Medullary cavitation / complete slough of papilla

- flank pain, dysuria, fever, chills, ureteral colic, hypertension
- acute oliguric renal failure
- proteinuria, pyuria, hematuria, leukocytosis

Location: (a) localized / diffuse
(b) bilateral distribution: systemic cause
(c) unilateral: obstruction, renal vein thrombosis, acute bacterial nephritis

√ normal or small kidney ← analgesic nephropathy
√ large kidney ← acute fulminant disease
√ smooth / wavy renal contour ← analgesic nephropathy)
√ calcification of necrotic papilla: papillary / curvilinear / ringlike

IVP:

√ multiple small collections of contrast material in papilla:
√ "lobster claw" sign = subtle streak of contrast material extending from fornix parallel to long axis of papilla
√ centric / eccentric, thin and short / bulbous cavitation of papilla
√ displaced collecting system ← enlarged septal cortex ← edema

√ necrosis of entire papilla:
√ widened fornix ← necrotic shrinkage of papilla
√ "signet ring" sign = ring shadow of papilla → outlining detached papilla within contrast material-filled cavity
√ club-shaped / saccular calyx ← sloughed papilla
√ intraluminal nonopaque filling defect in calyx / pelvis / ureter ← expelled sloughed papilla
√ loss of renal function:
√ diminished density of contrast material in nephrogram; rarely increasingly dense
√ wasted parenchymal thickness

US:
√ multiple round / triangular cystic spaces in medulla with echo reflections of arcuate arteries at periphery of cystic spaces

Cx: acute ureteral obstruction after sloughing of papilla; higher incidence of transitional cell carcinoma in analgesic abusers (8 x); higher incidence of squamous cell carcinoma

DDx: (1) Postobstructive renal atrophy
(2) Congenital megacalices (normal renal function)
(3) Hydronephrosis (dilated infundibula, blunting of all calices)
(4) Parapelvic cyst
(5) Caliceal diverticulum (adjacent to fornix / infundibulum)

PAROXYSMAL NOCTURNAL HEMOGLOBINURIA

= rare acquired disorder of nonmalignant hematopoietic stem cells

Cause: infection, transfusion, radiographic contrast material, exercise, drugs, immunization, surgery

Pathophysiology:
destruction of abnormally sensitive RBCs + granulocytes + platelets by activated complement; complement activation of abnormal platelets + release of thrombogenic material from lysed RBCs

- increased susceptibility to infections
- intravascular hemolysis:
  - hemoglobinuria, pancytopenia / aplasia
  - chronic iron deficiency anemia
- venous thrombosis in uncommon sites:
  - acute (tubulointerstitial nephritis) / chronic renal failure (small vessel thrombosis)
  - cerebral vein thrombosis
  - thrombosis of mesenteric vein + splenic vein + portal vein
  - hepatic vein thrombosis (= Budd-Chiari syndrome) involving tertiary + secondary venous radicles

MR:
√ low SI of renal cortex on T1WI + T2WI ← hemosiderin deposition ← free hemoglobin is filtered across renal glomeruli + reabsorbed by proximal convoluted tubular cells ← intravascular hemolysis
√ usually decreased iron concentration in liver + spleen unless transfusions were given (DDx

to other hemolytic anemias)

Prognosis: venous thrombosis is a major cause of death

PELVIC LIPOMATOSIS & FIBROLIPOMATOSIS

= nonmalignant overgrowth of adipose tissue with minimal fibrotic + inflammatory components compressing soft-tissue structures within pelvis

Prevalence: 0.6÷100,000 to 1.7÷100,000

Cause: unknown; ? UTIs, obesity, endocrine dysfunction

Mean age: 48 (range, 9–80) years; M÷F = 10÷1 to 18÷1; racial predilection for blacks (67%); obesity NOT contributing factor

Path: unencapsulated mature homogeneous white fat separated by thin fibrous septa

- often incidental finding
- urinary tract symptoms (50%): frequency, dysuria, nocturia, urgency, hematuria, sensation of incomplete emptying, suprapubic tenderness, recurrent urinary tract infections
- GI symptoms (20%): constipation, nausea, vomiting, tenesmus, rectal bleeding, ribbonlike stools with mucus
- generalized symptoms: lower abdominal pain, low back pain, flank pain, fever
- edema of lower extremities

@ GU tract
- √ elongation + elevation of urinary bladder with symmetric inverted pear shape / teardrop
- √ elongation of posterior urethra
- √ medial / lateral displacement of lower ureters
- √ pelvic lucency (CT confirmatory)

@ GI tract
- √ straightening + elongation + narrowing of rectum
- √ stretching + elevation of rectosigmoid and sigmoid colon out of pelvis
- √ increase in sacrorectal space > 10 mm

@ Vessels
- √ stretching + thinning of femoral veins

Cx of fibrolipomatosis:

(1) Ureteral obstruction with hydroureteronephrosis (40% within 5 years)
(2) IVC obstruction + deep vein thrombosis
(3) Ureteral calculi
(4) Hypertension

Rx: urinary diversion (39%) to prevent end stage renal disease; screening for proliferative bladder lesions

PENILE CARCINOMA

Prevalence: 0.4% of all male malignancies in US; 1% in Western countries; 10–20% of all malignancies in Asian, African, South American males

Cause: uncircumcised men (smegma ← poor hygiene ← presence of foreskin / phimosis); chronic inflammation (balano-posthitis, lichen sclerosus et atrophicus); human papilloma virus 16 & 18; psoralen / ultraviolet A photochemotherapy for psoriasis treatment

Histo: squamous cell carcinoma (95%), sarcoma (epitheloid ~, Kaposi ~, leiomyo~, rhabdomyo~), melanoma, basal cell carcinoma, lymphoma

Age: 6th and 7th decade; < 25% are less than 40 years of age

• palpable inguinal nodes (30–60% of SCC): ½ reactive, ½ metastatic

Location: glans (48%) > prepuce (21%) > glans + prepuce (9%) > coronal sulcus (6%) > shaft (2%)

Spread: (a) superficial inguinal nodes ← skin + prepuce

(b) deep inguinal + external iliac nodes ← glans

(c) internal iliac nodes ← erectile tissue + penile urethra

› Nodal disease in 20% of T1 + in 47–66% of T2–T4 tumors

› Nodal disease in 42% of superficial spreading SCC

› Nodal disease in 82% of deep vertical growth

MR:

√ solitary ill-defined infiltrating tumor:

√ hypointense relative to corpora on T1WI + T2WI

√ enhancement with Gd (less than corpora)

MRI can assess (1) extent of penile cancer, (2) depth of invasion into corpora cavernosa ± urethra, (3) involvement of inguinal + pelvic lymph nodes.

Rx: circumcision, partial / total penectomy ± inguinal lymphadenectomy; radiation therapy

PENILE FIBROMATOSIS

= PEYRONIE DISEASE = INDURATIO PENIS PLASTICA

[François Gigot de La Peyronie (1678–1747), chief of surgery at the Hôtel-Dieu in Paris and Montpellier, surgeon to King Louis XI]

= benign acquired condition characterized by chronic inflammation → fibrosis + focal thickening of tunica albuginea

Prevalence: 3%

Age: 40–60 years

Cause: ? aberrant healing response to minor penile trauma

Associated with: palmar fibromatosis (Dupuytren contracture) in 16–20%, plantar fibromatosis, Paget disease of bone, diabetes mellitus, gout

• abnormal penile curvature during erection → erectile dysfunction; painful penile induration

• palpable albugineal plaques along corpora cavernosa

Site: dorsal > ventral > lateral aspect of penis, intercorporeal septum

US (68% sensitive):

√ focal hyperechoic thickening of tunica albuginea with shadowing ← calcification

√ focal nonshadowing echogenic thickening of tunica

√ nodular echogenic thickening of intercorporeal septum

√ iso- / hypoechoic plaques (rare)

MR (61% sensitive):

√ hypointense focal thickening of tunica on T1WI + T2WI

√ enhancement during active inflammation

DDx: (1) Congenital penile curvature

(2) Dorsal vein thrombosis

(3) **Penile calciphylaxis** = acute life-threatening condition in end-stage renal disease with occlusion of arterial flow to penis

(4) Penile fibrosis ← prolonged priapism, trauma, removal of penile prosthesis, intracavernosal injections for erectile dysfunction

(5) Penile malignancy

PENILE FRACTURE

= tear in tunica albuginea → rupture of corpus cavernosum

Associated with: urethral injury (in 10–20%)
- blood at urethral meatus

Cause: blunt / penetrating (rare) trauma; powerful lateral motions of the erect penis (frequently during sexual intercourse)

Age: younger man; often related to sports

- excruciating pain, bruising, rapid detumescence

US (difficult in identifying site + extent of tunica albuginea involvement)

Hereditary Syndromes Associated with Pheochromocytoma

Syndrome	*Risk of Tumor [%]*	*Mutated Gene*
Multiple endocrine neoplasia	50	RET
Neurofibromatosis 1	1	NF1
von Hippel-Lindau disease	10–20	VHL
Familial paraganglioma syndrome	~ 20	SDHB, SDHC, SDHD*

* SDH = succinate dehydrogenase (SDH) subunits B, C, or D

MR:

√ focal disruption of T1- and T2-hypointense tunica albuginea

√ adjacent T2-hyperintense hematoma

◊ With a scrotal hematoma / hematocele the radiologist should be vigilant in looking for associated penile / testicular injury.

DDx: penile contusion (focal area of hypointensity in a normally T2-bright corpus cavernosum)

PHEOCHROMOCYTOMA

= ADRENAL MEDULLARY PARAGANGLIOMA

= rare catecholamine-secreting tumor of chromaffin tissue; responsible for 0.1–0.9% of hypertensive individuals

Prevalence: 0.13% in autopsy series; increasing occurrence of incidentalomas by cross-sectional imaging

Incidence: 2–8÷1,000,000 annually

Origin: neuroectodermal tissue

Path: well-circumscribed 3–5 cm mass with central degenerative changes of fibrosis / cystic

change; larger lesions are often hemorrhagic / cystic

Histo: chromaffin tumor cells contain chromogranin within secretory granule forming CHARACTERISTIC clusters of tumor cells = "**Zellballen**"; architectural patterns are
(a) combination of alveolar + trabecular (36%)
(b) predominantly alveolar = nesting (35%)
(c) predominantly trabecular (27%)

Age: 5% in childhood

N.B.: Any physical contact can precipitate cardiac arrhythmia + malignant hypertension

• symptomatology ← excess catecholamine production (norepinephrine > epinephrine):
  • asymptomatic (9–10%)
  • headaches, sweating, flushing, palpitations, tachycardia, anxiety, tremor, nausea, vomiting, abdominal pain, chest pain
  • paroxysmal (47–53%) / sustained (37%) hypertension
    (a) elevated catecholamine
    (b) functional renal vasoconstriction
    (c) renal artery stenosis: fibrosis, intimal proliferation, tumor encasement
  • hypoglycemia during hypertensive crisis

Dx (biochemical confirmation):
  • plasma metanephrine level > 1.1 nmol/L
  • plasma normetanephrine concentration > 2.2 nmol/L
  • elevated urine vanillylmandelic acid (VMA) in 54%; in up to 22% false-negative result because VMA is not excreted

Associated heritable conditions (in 10–25%):

√ usually with bilateral pheochromocytomas + extraadrenal sympathetic and parasympathetic paragangliomas

(1) Multiple endocrine neoplasia (MEN):
  ◊ malignant transformation in 5–10%
  √ pheochromocytoma small + asymptomatic in 50%

(2) Neuroectodermal disorder
  (a) neurofibromatosis type 1 (in 0.1–5.7%)
  (b) Von Hippel-Lindau disease
  (c) tuberous sclerosis
  (d) Sturge-Weber syndrome
  ◊ 10% of patients with neurofibromatosis (NF1) / von Hippel-Lindau disease have pheochromocytoma!

(3) Familial paraganglioma syndrome / pheochromocytosis

(4) Carney syndrome

mnemonic: VEIN
Von Hippel-Lindau
Endocrine neoplasia (MEN 2)
Inherited (congenital) pheochromocytoma
Neurofibromatosis (von Recklinghausen disease)

RULE OF TENS ("ten-percent tumor"):
10% bilateral 10% extraadrenal

10% multiple 10% familial / syndromic
10% malignant 10% nonfunctioning

Location: (a) intraabdominal (98%), medulla of adrenal gland (>90%)
(b) extraadrenal paragangliomas of sympathetic nervous system (from base of brain to urinary bladder) including organ of Zuckerkandl, bladder wall, retroperitoneum, heart, mediastinum, glomus jugulare body

Size: mean diameter 5.3 (range, 2.6–11.2) cm
- clinically silent lesions tend to be large
- large lesions are often nonfunctioning

√ discrete round / oval mass:
- √ marked heterogeneity ← degeneration, necrosis, fibrosis, cystic change, intracellular lipid degeneration, calcification
- √ small / large necrotic areas in 90% ± fluid-fluid level
- √ scattered punctate (= speckled) calcifications in 10–29%

The "imaging chameleon" pheochromocytoma should be considered in any adrenal lesion of low-attenuation / avid washout / dominant cystic component!

CT (93–100% sensitive):

Localization: accurate in 91% with tumor > 2 cm in size; up to 40% in extraadrenal location are missed by CT

- √ solid / cystic / complex mass with low-density areas ← hemorrhage / cystic degeneration / necrosis
- √ tumor attenuation of similar density as surrounding soft tissue with a mean of 36 ± 10 HU
- √ may rarely have abundant intracellular fat of < 10 HU
- √ may have macroscopic fat of < 30 HU ← lipid degeneration (DDx: myelolipoma)
- √ ± calcifications

CECT:

Cave: IV injection of iodinated contrast material MAY precipitate a hypertensive crisis in patients not on α-adrenergic blockers! Nonionic low-osmolar IV contrast media are SAFE!

- √ usually avid contrast enhancement ← capillary-rich framework
  - ◊ Absolute enhancement of > 110–120 HU is INDICATIVE of a pheochromocytoma!
- √ variable contrast wash-out patterns, occasionally similar to adrenocortical adenoma:
  - √ relative washout > 40% (in 25% of pheochromocytomas)
  - √ absolute washout > 60% (in 29% of pheochromocytomas)

NUC:

- √ increased uptake with ^{131}I- / ^{123}I-metaiodobenzylguanidine (MIBG = 80–90% sensitive; 98% specific)

Useful:
(a) with clear clinical / laboratory evidence of tumor but no adrenal abnormality on CT / MR
(b) in detecting extraadrenal pheochromocytomas / bilaterality / metastases by whole-body scintigraphy
(c) in diagnosing postoperative recurrence

PET (72–98% sensitive):

√ increased uptake (DDx: metastasis)

US:

√ well-marginated ovoid purely solid (68%) / complex (16%) / cystic tumor (16%)

√ homo- (46%) / heterogeneously (54%) solid tumor: isoechoic + hypoechoic (77%) / hyperechoic (23%) to renal parenchyma

√ heterogeneity introduced by hemorrhage / necrosis

MR (method of choice):

√ iso- / slightly hypointense to liver on T1WI

√ may contain areas of high SI on T1WI ← hemorrhage (20%) / fat

√ hyperintense compared with spleen on T2WI (in 11%) ← intratumoral cystic regions

N.B.: 30% are hypointense + may be confused with malignancy / benign adenoma

√ contains central heterogeneous areas of decreased SI in 35% on T2WI ← necrosis / hemorrhage / calcifications

√ no change in SI between in-phase + opposed-phase T1WI images ← no substantial amount of cytoplasmic lipid

CEMR:

√ rapid marked homo- / inhomogeneous enhancement (not routinely used as it does not increase sensitivity)

√ extremely hyperintense ("light bulb" sign) ← avid enhancement

Angio:

N.B.: intraarterial injection CONTRAINDICATED → may induce hypertensive crisis

√ localization by aortography in > 91%

√ usually hypervascular lesion with intense tumor blush

√ slow washout of contrast material

√ enlarged feeding arteries + neovascularity (= "spoke-wheel" pattern)

√ parasitization from intrarenal perforating branches

√ venous blood sampling (at different levels in IVC)

Cave: indiscriminate biopsy may trigger a catastrophic crisis and must be avoided requiring consultation with endocrine + anesthesia services and appropriate endocrine blockade

Cx: (1) Malignancy in 2–14% with (± hormonally active) metastases to bone, lymph nodes, liver, lung

(2) Spontaneous retroperitoneal hemorrhage → lethal in 50% if tumor previously undiagnosed

◊ Most common cause of spontaneous retroperitoneal hemorrhage from a primary adrenal tumor!

Rx: (1) Surgical removal curative

(2) Alpha-adrenergic blocker (phenoxybenzamine / phentolamine)

(3) Beta-adrenergic blocker (propranolol)

(4) ^{131}I-MIBG used to treat metastases

DDx: nonfunctioning adrenal adenoma, adrenocortical carcinoma, adrenal cyst, metastatic disease

PLASMACYTOMA OF KIDNEY

= group of malignant disorders involving differentiated B lymphocytes or plasma cells

Classification:

A. SOLITARY = PLASMACYTOMA (5%)
B. MULTIPLE = MULTIPLE MYELOMA (95%):
autoptically involves kidney in 17%

Distribution of primary extramedullary plasmacytoma:

(a) skeleton (95%)
(b) nonskeletal sites (5%): upper respiratory tract

• monoclonal immunoglobulin / Bence-Jones proteinuria
√ well-circumscribed mass / infiltrative lesion
DDx: indistinguishable from other renal primaries

POLYCYSTIC KIDNEY DISEASE

Autosomal Dominant Polycystic Kidney Disease

= ADPKD = ADULT POLYCYSTIC KIDNEY DISEASE= Potter type III
[Edith Louise Potter(1901–1993], American pathologist in Chicago]
= characterized by bilaterally enlarged kidneys with multiple expansile cysts along nephron

Prevalence: 1÷500–1,000 live births; affects 300,000–600,000 Americans; 5–10% of dialysis patients
◊ Most common heritable renal disorder!
◊ 3rd most common cause of end-stage renal disease!

Genetics:

hereditary (90%) or spontaneous mutation (10%) of
(a) PKD1 gene located on short arm of chromosome 16p13.3 encoding protein polycystin-1 (85%)
(b) PKD2 gene located on long arm of chromosome 4q13–23 encoding protein polycystin-2 (15%) = milder form of disease with later age of onset

localized in cell membrane of primary cilia of renal tubular epithelial cells → both polycystin proteins interact to form a calcium2+-channel receptor
◊ Genetic testing identifies only 70% of individuals with ADPKD

Pathophysiology:

deranged function of polycystin proteins → ciliary dysfunction → overproliferation of tubular epithelial cells with ↑ tubular fluid secretion → tubular ectasia + cyst formation

Path: cysts form as outpouchings of nephron → become disconnected from nephron early on → continued growth into round (rather than tubular) shape of up to several cm in diameter → compression of tubules and glomeruli

Histo: abnormal rate of tubule divisions (Potter type III) with hypoplasia of portions of tubules left behind as the ureteral bud advances; cystic dilatation of Bowman capsule / loop of Henle / proximal convoluted tubule coexisting with normal tissue

Mean age at diagnosis:

43 years; early clinical manifestations < 15 years of age in 2% (with rare neonatal / infantile onset); M÷F = 1÷1

Onset of cyst formation:

54% (72%) [86%] in 1st decade (2nd decade) [3rd decade]; morphologic evidence in all

patients by age 80

Minimum diagnostic criteria in screening exam for cysts to confirm diagnosis of ADPKD:

15–39 years ≥ 3 uni- / bilateral cysts

40–59 years ≥ 2 cysts in each kidney

> 60 years ≥ 4 cysts in each kidney

Associated with:

(1) Cysts in: liver (40%), pancreas (9%); rare in spleen, arachnoid membrane, lung, thyroid, ovary, uterus, testis, seminal vesicle, epididymis, bladder

(2) Saccular "berry" aneurysm of cerebral arteries (3–15%)

◊ Screening recommended to start at age 20 years

(3) Aortic aneurysm, aortic dissection

(4) Mitral valve abnormalities (26%)

(4) Abdominal wall hernia

(5) Colonic diverticulosis

- usually asymptomatic → symptomatic at mean age of 35 years ← cysts grow with age; disease is slowly progressive with nearly 100% penetrance and great variation in expressivity
- hypertension (50–70%), hematuria, proteinuria
- azotemia ← replacement of renal parenchyma by cysts
- lumbar / abdominal pain

Size of kidney: up to 40 cm in length; up to 8 kg in weight

Renal volume: mean of > 1,000 mL (normal mean = 150 mL) with mean annual increase of 63 mL

◊ Volume measurements by MR may be used to monitor disease progression!

√ enlargement of both kidneys with innumerable cysts of varied size + diffuse distribution

√ cysts may calcify in curvilinear rim- / ringlike irregular amorphous fashion

√ elongated + distorted + attenuated collecting system

√ nodular puddling of contrast material on delayed images

√ "Swiss cheese" nephrogram = multiple lesions of varying size with smooth margins

√ polycystic kidneys shrink after beginning of renal failure, after renal transplantation, or on chronic hemodialysis

√ liver cysts (may be identified without renal involvement):

√ isolated from bile ducts (DDx ARPKD)

√ liver cyst size + number increase with advancing age → liver function preserved

Cx: mass effect, intracyst hemorrhage / infection

NUC: poor renal function on ^{99m}Tc-DTPA scan

√ multiple areas of diminished activity, cortical activity only in areas of functioning cortex

US:

√ multiple cysts in cortical region (usually seen in 50% by 10 years of age)

√ diffusely echogenic when cysts small (children)

√ renal contour poorly demarcated

N.B.: A normal US examination cannot exclude ADPKD until after age 35 years!

In a child with known PKD1 mutation ≥ 3 renal cysts / cyst in liver establishes the

diagnosis!

OB-US:

√ kidneys normal in size / mildly enlarged

√ echogenic kidneys similar to infantile PCKD (usually in 3rd trimester, may be unilateral (earliest sonographic diagnosis at 14 weeks GA):

√ hyperechoic cortex + relatively hypoechoic medulla → increased corticomedullary differentiation

√ ± few macroscopic small round cysts in cortex and medulla (rare)

√ normal amount of amniotic fluid / oligohydramnios ← renal function usually not impaired

Atypical rare presentation:

(a) unilateral adult PCKD

(b) segmental adult PCKD

(c) adult PCKD in utero / neonatal period

Cx:

(1) Death from uremia in late adulthood (59%) / cerebral hemorrhage ← hypertension / ruptured aneurysm (13%) / cardiac complications (mean age 50 years)

◊ NO increased risk of renal cell carcinoma!

About 50% of ADPKD patients will develop end-stage renal disease.

(2) Renal calculi (20%): mostly urate

(3) Cyst infection

(4) Cyst rupture

(5) Cyst hemorrhage (66%):

• common cause of acute flank pain

√ hyperattenuated cyst content on CT

√ calcifications frequent, which may take years

(6) Liver dysfunction (sporadically): hepatomegaly, liver failure, Budd-Chiari syndrome

◊ NO increased risk for renal cell carcinoma unless on prolonged dialysis

DDx:

(1) Multiple simple cysts (less diffuse, no family history)

(2) Glomerulocystic disease

(3) Von Hippel-Lindau disease (cerebellar hemangioblastoma, retinal hemangiomas, occasionally pheochromocytomas)

(4) Acquired uremic cystic disease (kidneys small, no renal function, transplant)

(5) Infantile PCKD (usually microscopic cysts)

Autosomal Recessive Polycystic Kidney Disease

= ARPKD = INFANTILE POLYCYSTIC KIDNEY DISEASE = POLY-CYSTIC DISEASE OF CHILDHOOD = Potter Type I

= most common ciliopathy affecting kidney + liver to varying degrees

Prevalence: 1÷22,000 live births; F = M; carrier frequency of 1÷70

Mean age: 2.5 years (at presentation)

Genetics: mutations in PKHD1 (polycystic kidney hepatic disease 1) gene located on chromosome 6p12 → encodes protein fibrocystin-polyductin localizing to primary cilia of epithelial cells that line renal tubules (collecting ducts) + intrahepatic bile

ducts

Pathogenesis:

symmetric circumferential epithelial proliferation results in tubular lengthening + fusiform dilatation of collecting ducts; abnormal epithelium becomes secretory instead of resorptive; secreted fluid is rich in epithelial growth factors stimulating further epithelial proliferation

Path:

@ Kidney:

numerous nonobstructive fusiform dilated + elongated collecting tubules with radial orientation extending from enlarged medulla into compressed cortex; associated renal interstitial edema + fibrosis; increased separation of a normal number of glomeruli → progressive cystic degeneration into peripheral cortical microcysts of 1–3 mm in diameter with occasional macrocyst

√ spongelike texture of renal parenchyma

• diminished concentrating ability of kidneys, azotemia

@ Liver:

malformation of ductal plate → congenital hepatic fibrosis = irregularly formed ectatic nonobstructive intrahepatic bile ducts increased in number with atypical branching pattern + septa of fibrosed portal tracts → disproportionate enlargement of left lobe

@ Pancreas: pancreatic fibrosis

◊ The greater the percentage of abnormal collecting tubules, the more severe the renal compromise and the earlier the clinical presentation!

◊ The less severe the renal findings, the more severe the hepatic findings!

Blythe & Ockenden classification:

A. PERINATAL FORM (most common)

90% of tubules show cystic changes

• onset of renal failure in utero, Potter sequence

• large palpable flank masses, small thorax, respiratory distress, oliguria in neonate

√ both kidneys enlarged

√ oligohydramnios + dystocia ← large abdominal mass

Prognosis: death from renal failure / respiratory insufficiency (pulmonary hypoplasia) within 24 hours in 75%, within 1 year in 93%; uniformly fatal

B. NEONATAL FORM

60% of tubules show ectasia + minimal hepatic fibrosis + bile duct proliferation

• onset of renal failure within 1st month of life

Prognosis: death from renal failure / hypertension / left ventricular failure within 1st year of life

C. INFANTILE FORM

25% of renal tubules involved + mild / moderate periportal fibrosis

• disease appears by 3–6 months of age

Prognosis: death from chronic renal failure / systemic arterial hypertension / portal hypertension

D. JUVENILE FORM

10% of tubules involved + gross hepatic fibrosis + bile duct proliferation

• disease appears at 6 months to 5 years of age

√ portal hypertension:
- thrombocytopenia ← hypersplenism
- gastroesophageal variceal bleeding

√ hepatosplenomegaly
√ ascites

Prognosis: death from portal hypertension

Radiography
√ abdominal distension
√ gas-filled bowel loops deviated centrally
√ small bell-shaped thorax → severe pulmonary hypoplasia
√ pneumothorax / pneumomediastinum

IVP:
√ bilateral gross smooth renal enlargement
√ faint nephrogram + blotchy opacification on initial images
√ increasingly dense nephrogram
√ poor visualization of collecting system
√ "sunburst nephrogram" = striated nephrogram with persistent radiating opaque streaks (= collecting ducts) on delayed images
√ prominent fetal lobation
√ poor opacification + contrast excretion ← impaired renal function

CT:
√ kidneys of low attenuation ← stagnant urine in dilated collecting ducts
√ prolonged corticomedullary phase
√ striated nephrogram ← contrast material accumulating in dilated collecting ducts

MR:
√ enlarged kidneys darker than normal on T1WI
√ hyperintense renal parenchyma on T2WI:
√ homogeneously T2-bright kidneys
√ multiple rounded 1–2-mm discrete tubular cystic foci
√ large 1–2-cm macrocysts

GU-US:
√ hyperechoic enlarged kidneys ← increased number of acoustic interfaces ← unresolved 1–2-mm cystic / ectatic dilatation of renal tubules
√ increased renal through-transmission ← fluid content of cysts:
√ high-spatial-resolution US may resolve tiny dilated tubular cysts:
√ isolated medullary disease (in 37%)
√ corticomedullary involvement (in 63%)
√ normal renal cortex → ~ normal renal function
√ loss of corticomedullary differentiation → poor visualization of renal sinus + renal borders
√ thin rim of hypoechoic cortex
√ occasionally discrete macrocysts < 1 cm with tendency to become larger + more numerous over time (in older children) resembling adult medullary sponge kidney
√ small bladder

Liver-US:

• portal venous hypertension (5–13 years of age)
√ disproportionate enlargement of left hepatic lobe
√ patchy / diffuse heterogeneously coarse liver echogenicity:
  √ increased echogenicity of portal tracts = echogenic periportal thickening ← fibrosis
√ tubular cystic dilatation of small intrahepatic bile ducts:
  √ "**central dot**" sign = portal vein + hepatic artery branches completely surrounded by dilated intrahepatic bile duct
  √ cysts in continuity with bile ducts
√ dilated extrahepatic bile ducts + elongated hydropic gallbladder (in up to 55%)
√ splenomegaly
√ ascites
√ enlarged splenic v., portal v. + splanchnic collateral veins (gastroesophageal varices, "recanalized" paraumbilical veins, spontaneous splenorenal shunts)
√ increased stiffness on liver elastography ← fibrosis

OB-US (diagnostic as early as 15–17 weeks GA):
• decreased fetal urine output
• Potter facies: low-set + flattened ears, short + snubbed nose, deep eye creases, micrognathia
√ progressive massive renal enlargement (10–20 x larger than normal):
  √ renal÷abdominal circumference ratio > 0.30
√ hyperechoic renal parenchyma = echogenic medulla with relative sparing of cortex
√ nonvisualization of urine in fetal bladder (in severe cases)
√ severe oligohydramnios (33%) by 20 weeks GA → oligohydramnios / Potter sequence
  mnemonic: POTTER
    Pulmonary hypoplasia
    Oligohydramnios
    Twisted wrinkly skin
    Twisted Potter face
    Extremity defects
    Renal agenesis, bilateral
√ small / absent urinary bladder
√ small fetal thorax with pulmonary hypoplasia
√ club foot
√ congenital dislocation of hips

OB management:
(1) Chromosome studies to determine if other malformations present (eg, trisomy 13 / 18)
(2) Option of pregnancy termination < 24 weeks
(3) Nonintervention for fetal distress > 24 weeks if severe oligohydramnios present

Risk of recurrence: 25%

DDx: Meckel-Gruber syndrome, adult polycystic kidney disease (absence of tiny tubular cysts, cysts in parents), nephronophthisis, cystic renal dysplasia (round cysts), tuberous sclerosis (cortical rather than medullary cysts, angiomyolipomas)

POLYORCHIDISM

= SUPERNUMERARY TESTIS
= rare congenital anomaly, in which > 2 testes are present
Cause: developmental accident in union / division of genital ridge + mesonephric ducts ← peritoneal bands
Associated with: maldescent of one supernumerary testis (15–50%), inguinal hernia (30%), hydrocele, epididymitis, varicocele, infertility, cryptorchidism (40%), malignancy
• painless extratesticular scrotal mass
Location: left > right
√ duplication of testis + single epididymis (most common)
√ bridging vessels between supernumerary + normal testis
Cx: torsion (13–15%) ← ↑ mobility of supernumerary testis
Rx: orchiopexy
DDx: splenogonadal fusion

POSTERIOR URETHRAL VALVES

= congenital thick folds of mucous membrane located in posterior urethra (prostatic + membranous) distal to verumontanum
Type I: (most common) mucosal folds (vestiges of wolffian duct) extend anteroinferiorly from the caudal aspect of the verumontanum, often fusing anteriorly at a lower level
Type II: (rare) mucosal folds extend anterosuperiorly from verumontanum toward bladder neck (nonobstructive normal variant, probably a consequence of bladder outlet obstruction)
Type III: diaphragm-like membrane located below the verumontanum = abnormal canalization of urogenital membrane
Prevalence: 1÷5,000 to 1÷8,000 boys; most common cause of urinary tract obstruction + leading cause of end-stage renal disease among boys
Time of discovery: prenatal (8%), neonatal (34%), 1st year (32%), 2nd–16th year (23%), adult (3%)
• urinary tract infection (fever, vomiting) in 36%
• obstructive symptoms in 32% (hesitancy, straining, dribbling [20%], enuresis [20%]); failure to thrive (13%)
• palpable kidneys / bladder in neonate (21%), hematuria (5%)
VCUG:
√ vesicoureteral reflux, mainly on left side (in 33%)
√ fusiform distension + elongation of proximal posterior urethra persisting throughout voiding
√ transverse / curvilinear filling defect in posterior urethra
√ diminution of urethral caliber distal to severe obstruction
√ hypertrophy of bladder neck
√ trabeculation + sacculation of bladder wall
√ large postvoid bladder residual
US:
√ male gender
√ oligohydramnios (related to severity + duration of obstruction)
√ hypoplastic / multicystic dysplastic kidney (if early occurrence)

√ bilateral hydroureteronephrosis → pulmonary hypoplasia
√ dilated renal pelvis may be absent in renal dysplasia / rupture of bladder / pelviureteral atresia
√ overdistended urinary bladder (= megacystis) in 30%
√ thick-walled urinary bladder + trabeculations (best seen after decompression)
√ urine leak: urinoma, urine ascites, urothorax
√ "pear / keyhole" bladder = thick-walled bladder + dilated posterior urethra (on perineal scan)
√ dilated utricle (perineal scan)

OB management:
(1) Induction of labor as soon as fetal lung maturity established (if diagnosed during last 10 weeks of pregnancy)
(2) Vesicoamniotic shunting may be contemplated if diagnosed remote from term (68% survivors) with good prognostic parameters of fetal urinary sodium < 100 mEq/dL + chloride < 90 mEq/dL + osmolality < 210 mOsm/dL

Cx: (1) Neonatal urine leak: ascites, urothorax, urinoma (13%)
(2) Neonatal pneumothorax / pneumomediastinum (in 9%)
(3) Prune belly syndrome
(4) Renal dysplasia (if obstruction occurs early during gestation)

Prognosis: depends upon duration of obstruction prior to corrective surgery; poor prognosis if associated with vesicoureteral reflux; nephrectomy for irreversible damage (13%)

DDx: (1) UPJ obstruction
(2) UVJ obstruction
(3) Primary megaureter
(4) Massive vesicoureteral reflux
(5) Megacystis-microcolon-intestinal hypoperistalsis syndrome

POSTINFLAMMATORY RENAL ATROPHY

= acute bacterial nephritis with irreversible ischemia as unusual form of severe gram-negative bacterial infection in patients with altered host resistance in spite of proper antibiotic treatment

Histo: occlusion of interlobar arteries / vasospasm
√ small smooth kidney
√ papillary necrosis in acute phase

POSTOBSTRUCTIVE RENAL ATROPHY

= generalized papillary atrophy usually following successful surgical correction of urinary tract obstruction and progressing in spite of relief of obstruction
√ small smooth kidney, usually unilateral
√ dilated calices with effaced papillae
√ thinned cortex

PRIAPISM

= prolonged penile erection not associated with sexual arousal
[*Priapus* , Greek mythology = god of fertility]
Types:
(1) LOW-FLOW / ischemic / venoocclusive form (common): characterized by ischemia, venous stasis, pooling of blood within corpora cavernosa
Cause: intracavernosal injection of vasoactive agent (papaverine, prostaglandin), sickle cell disease, hematopoietic malignancy, hypercoagulable state
◊ SURGICAL EMERGENCY!
• painful erection
• corporeal aspiration of nonoxygenated blood (with low oxygen tension in blood gas analysis)
√ sluggish flow / blood stasis in corpora cavernosa:
√ sedimentation of blood with fluid-fluid level
√ decreased venous outflow
√ decreased arterial inflow
√ intracavernosal thrombosis
Rx: cavernosal aspiration + irrigation, cavernosal injection of α-adrenergic receptor agonists (phenylephrine), anticoagulation, shunt procedure
Cx: cavernosal tissue fibrosis → permanent erectile dysfunction (in 50% in spite of Rx)
(2) HIGH-FLOW / arterial / nonischemic form (rare):
characterized by unregulated arterial inflow of blood into corpora cavernosa ← usually arterial injury
Cause: perineal / penile trauma
• subsequent persistent painless erection
• corporeal aspiration of oxygenated blood (with high oxygen tension in blood gas analysis)
Color Doppler US:
√ high blood flow in cavernosal artery
√ focal blush of abnormal intracavernosal flow adjacent to cavernosal artery from arterial-sinusoidal fistula / pseudoaneurysm
Rx: percutaneous transcatheter embolization; arterial ligation

PROSTATE CANCER

Incidence:
doubles with each decade after age 50; 129÷100,000 new cases annually in USA (2012); 3rd most common new malignancy in USA in 2016 (after female breast cancer + lung cancer); in 35% of men > 45 years of age (autopsies)
◊ 14% of males will develop prostate cancer (= lifetime risk)!
Racial factors: White > Black > Hispanic > Asian
Risk factors: advancing age, presence of testes, cadmium exposure, animal fat intake; ≥ 1 first-degree relative
Histo: adenocarcinoma (common); rare cancers: transitional cell cancer, adenoid cystic cancer, endometrioid neoplasm of verumontanum, carcinosarcoma, sarcoma, lymphoma
Histo for adenocarcinoma:

nuclear anaplasia + large nucleoli in secretory cells, disturbed architecture, invasive growth

Premalignant change:

(1) Prostatic intraepithelial neoplasia (**PIN**)
= premalignant lesion frequently associated with invasive carcinoma next to it / elsewhere in the gland

(2) Atypical adenomatous hyperplasia = proliferation of newly formed small acini

Grading (**Gleason score** 2–10):

1,2,3	glands surrounded by 1 row of epithelial cells
4	absence of complete gland formation
5	sheets of malignant cells

low numbers refer to well-differentiated, high numbers to anaplastic tumors; primary predominant grade (1–5) is added to secondary less representative area with highest degree of dedifferentiation (1–5)

◊ Gleason grading is in only 80% reproducible!

◊ Gleason grade ≥ 7 has worse prognosis

- Clinical categories:
  1. **Latent carcinoma** = usually discovered at autopsy of a patient without signs or symptoms referable to the prostate (26–73%)
  2. **Incidental carcinoma** = discovered in 6–20% of specimens obtained during transurethral resection for clinically benign prostatic hyperplasia
  3. **Occult carcinoma** = found at biopsy of metastatically involved bone lesion / lymph node in a patient without symptoms of prostatic disease
  4. **Clinical carcinoma** = cancer detected by digital rectal examination based on induration / irregularity / nodule
     - digital rectal exam is 30–60% accurate for differentiating stage B from stage C disease
- elevated **P**rostate-**S**pecific **A**ntigen (**PSA**)
  (= glycoprotein produced by prostatic epithelium) is measured by a monoclonal radioimmunoassay (Hybritech®, most commonly used: normal value of 0.1–4 ng/mL)

  ◊ 19–30% of prostate cancers have normal PSA!

  ◊ Cancers of < 1 mL usually do not elevate PSA!

  Confined disease (stage B and less) & PSA level:

  75% of patients with PSA of < 4 ng/mL

  53% of patients with PSA of 4–10 ng/mL

  2% of patients with PSA of > 30 ng/mL

  ◊ 16% of normal men have PSA > 4 ng/mL

  ◊ Benign conditions with PSA elevation: benign prostatic hypertrophy, acute urinary retention, acute prostatitis, prostatic intraepithelial neoplasia (PIN)
  - ↓ free-to-total PSA ratio:
    < 15% is highly suggestive of cancer,
    < 25% detects 95% of detectable cancers
  - ↑ **PSA density**
    = volume corrected PSA level [= prostate volume (height x width x length x 0.523) / PSA value]:
    > 0.12 (90% sensitive, 51% specific for cancer)

◊ Each gram of malignant prostate tissue produces 3.5 ng/mL PSA versus 0.3 ng/mL PSA for BPH!

- ↑ **PSA velocity** = serial PSA evaluation
  > 0.75 ng x mL-1 x yr-1

Staging of Prostate Cancer *American Joint Committee on Cancer*		
T0		No evidence of primary tumor
T1		Clinically inapparent nonpalpable nonvisible tumor
	T1a	< 3 microscopic foci of cancer / ≤ 5% of resected tissue
	T1b	> 3 microscopic foci of cancer / > 5% of resected tissue
	T1c	tumor diagnosed by needle biopsy
T2		Tumor clinically present + confined to prostate
	T2a	tumor ≤ 1.5 cm, < ½ of one lobe
	T2b	tumor > 1.5 cm / > ½ of one lobe (unilateral)
	T2c	tumor involves both lobes (bilateral)
T3		Extension through prostatic capsule
	T3a	unilateral
	T3b	bilateral
	T3c	invasion of seminal vesicles
T4		Tumor fixed / invading adjacent structures other than seminal vesicles
	T4a	invasion of bladder neck, external sphincter, rectum
	T4b	invasion of levator ani muscle and/or fixed to pelvic wall
N		Involvement of regional lymph nodes
	N1	metastasis in a single node ≤ 2 cm
	N2	metastasis in a single node > 2 and < 5 cm / multiple lymph nodes affected
	N3	metastasis in a lymph node ≥ 5 cm
M		Distant metastasis
	M1a	nonregional lymph nodes
	M1b	bone
M1c		other site ± bone

Staging of Prostate Cancer *American Urological Association System* *(modified Jewitt-Whitmore Staging System)*	
A	No palpable lesion
A_1	focal well-differentiated tumor < 1.5 cm
A_2	diffuse poorly differentiated tumor; > 5% of chips from TURP contain cancer
B	Palpable tumor confined to prostate
B_1	lesion < 1.5 cm in diameter confined to one lobe
B_2	tumor ≥ 1.5 cm / involving more than one lobe
C	Localized tumor with capsular involvement
C_1	capsular invasion
C_2	capsular penetration
C_3	seminal vesicle involvement
D	Distant metastasis
D_1	involvement of pelvic lymph nodes
D_2	distant nodes involved
D_3	metastases to bone / soft tissues / organs

Staging:

- ◊ At initial presentation > 75% have stage C + D!
- ◊ 40% of patient believed to have organ-confined disease have extraprostatic disease at radical prostatectomy

Benign Conditions Mimicking Prostate Cancer at MRI	
Condition	*Histologic & Anatomic Features*
Normal anatomy	
Anterior fibromuscular stroma	dense fibromuscular band anterior to transition zone
Surgical capsule	band of fibromuscular + compressed glandular tissue between transition + peripheral zone
Central zone	complex crowded glands + dense stroma surrounding ejaculatory ducts
Periprostatic vein	venous plexus closely associated with pseudocapsule
Periprostatic lymph nodes	Lnn adjacent to lateral / posterolateral prostate
Benign pathology	
Stroma-rich BPH	stromal fibromuscular proliferation in transition zone (rarely in peripheral zone)
Bacterial prostatitis	inflammatory infiltrate (neutrophils + lymphocytes) ± glandular atrophy
Mycobacterial granulomatous prostatitis	granulomatous inflammation ± central caseation
Malakoplakia	granulomatous inflammation + Michaelis-Gutman bodies
Atrophy	crowded glands with scan cytoplasm + nuclear crowding
Necrosis	coagulative necrosis + surrounding inflammatory infiltrate
Calcification	concreted prostatic secretions / calcified corpora amylacea

Escape routes through prostatic capsule are:

(1) Capsular margin at neurovascular bundle posterolaterally (80%) ← intrinsic weakness of capsule at this location

(2) Apex

(3) Seminal vesicles!

Staging accuracy for local [advanced] disease:

46 [66%] for US, 57 [77%] for MR

◊ Extracapsular disease is common at > 3.8 cm^3 tumor volume!

Metastases to lymph nodes:

0% (3–7%) [5%] {10–12%} in stage A1 (A2) [B1] {B2}; 54–57% in stage C; 10% [70–93%] with Gleason grade ≤ 5 [9 / 10]

√ size > 10 mm (25–78% sensitive, 77–98% specific)

√ MR-enhancement with ultrasmall superparamagnetic iron oxide particles (USPIO) for nodal mapping is superior

Predictors for bone metastases:

- PSA > 20; Gleason score of 8–10
- clinical stage of > T3; bone symptoms

Location of cancer: peripheral zone (70%), transition zone (20%), central zone (10%); multifocal in 40%

MR imaging findings suggestive of transition zone cancer:
√ homogeneous low T2 signal intensity ("erased charcoal sign") + ill-defined margins + lack of capsule + lenticular shape + invasion of anterior fibromuscular stroma

US (21% positive predictive value):
√ hypoechoic (61%) / mixed (2%) / hyperechoic (2%) lesion; undetectable isoechoic lesion (35%)
√ asymmetric enlargement of gland
√ deformed contour of prostate = "irregular bulge" sign (75% PPV)
√ heterogeneous texture

Size versus rate of detection:
≤ 5 mm (36%), 6–10 mm (65%), 11–15 mm (53%), 16–20 mm (84%), 21–25 mm (92%), ≥ 26 mm (75%)

MR (useful for targeted biopsy):
√ low-signal abnormality within the normally high-signal glandular tissue of the peripheral zone on T2WI
√ tumor isointense relative to surrounding gland on T1WI
√ extracapsular extension (90% specific, 15% sensitive):
√ direct tumor extension beyond prostate
√ decreased SI in periprostatic fat adjacent to capsule near tumor on T1WI + T2WI (capsule optimally depicted on T1WI ← demarcation by periprostatic fat of high SI)
√ capsular thickening
√ irregular focal bulge in contour of capsule near tumor (24–38% sensitive, 77–88% specific)
√ angulated glandular contour
√ irregular spiculated margin
√ flattening / obliteration of rectoprostatic angle (24–50% sensitive, 81–95% specific)
√ asymmetry of neurovascular bundle (21–38% sensitive, 81–95% specific)
√ tumor enveloping neurovascular bundle
√ low-signal lesion on T2WI within seminal vesicles that are normally of high-SI (43–71% sensitive, 99% specific)

CEMR:
√ enhancement of cancer relative to surrounding tissue:
√ calculation of peak enhancement parameters
√ area enhancing within 30–60 sec

MR spectroscopy (metabolic mapping of entire gland):
√ ⇑ choline-citrate ratio > 2 SD:
√ ↓ citrate levels ← conversion from citrate-producing to citrate-oxidating metabolism
√ ↑ cholin levels ← increased turnover of phospholipid cell membrane in proliferating malignant tissue

N.B.: creatinine peak may be inseparable from cholin peak

DDx: post-biopsy hemorrhage → low signal on T2WI + high signal on T1WI; inflammation; fibrosis; scarring

Prognosis: increase in tumor volume increases probability of capsular penetration, metastasis, histologic dedifferentiation; 100% (28%) 5-year survival for localized disease (metastatic cancer)

Mortality: 20.7÷100,000 (2013); 26,120 deaths annually (2016)

Screening recommendation (American Urological Association, American Cancer Society): PSA level measurements + digital rectal exam annually

Dx: transrectal biopsy

Sextant biopsy: 83% PPV, 37%NPV, 30% of cancers are missed, localization inaccurate

◊ 40% accuracy of biopsy for Gleason grade

Rx: (1) Watchful waiting

(2) Radical prostatectomy for disease confined to capsule → life expectancy > 15 years

(3) Radiation therapy for

(a) disease confined to capsule → life expectancy < 15 years

(b) disease outside capsule, no spread

(4) Hormonal therapy: orchiectomy, diethylstilbestrol, leuprolide acetate (for widely metastatic disease)

(5) Cryosurgery

(6) Chemotherapy

PROSTATIC ABSCESS

Age: 5th–6th decade

Agent: E. coli (main cause)

- urinary frequency, urgency, dysuria, hematuria
- perineal / lower back pain, fever, chills
- focally enlarged tender prostate

√ hypo- / anechoic mass with irregular wall + septations

PROSTATITIS

Bacterial Prostatitis

Prevalence: 9.7%

Consider prostatitis with a clinical history of urinary ± sexual symptoms, fluctuating PSA levels, or PSA response to antibiotics.

Distribution: diffuse / focal

Location: peripheral zone (common); transition zone mimicking "erased charcoal" appearance of prostate carcinoma

MR:

√ low T2 signal intensity ← increased inflammatory cellular infiltrates

√ mildly to moderately restricted diffusion (less than in prostate cancer)

CEMR:

√ increased early enhancement (similar to prostate cancer)

Acute Bacterial Prostatitis (uncommon)

Cause: intraprostatic reflux of infected urine, prostatic Bx
Organisms: Escherichia coli, Enterococcus, Proteus
Age: young men
Histo: influx of neutrophils
• local and systemic symptoms
√ enlarged reactive lymph nodes

Chronic Bacterial Prostatitis

Cause: undertreated acute prostatitis, recurrent infection, lower urinary tract obstruction in older men
Histo: influx of lymphocytes, often with glandular atrophy
• indolent (without systemic symptoms)
• lower GU tract symptoms

CAVITARY / DIVERTICULAR PROSTATITIS

Cause: fibrosis of chronic prostatitis constricts ducts leading to stagnation of exudate + breakdown of intraacinar septa with cavity formation
• history of long-standing inflammatory condition
√ "Swiss cheese" appearance of prostate

Granulomatous Prostatitis

• clinically often mistaken for prostate cancer
Types:
(1) Idiopathic: nonspecific and nonnecrotic
(2) Infective: specific, nonnecrotic / necrotic
(3) Iatrogenic: postsurgical
(4) Malakoplakia
(5) Systemic granulomatous disease

Florid granulomatous prostatitis may demonstrate extraprostatic extension like prostate cancer, both entities of a similar appearance at MRI.

DDx: clinically often mistaken for prostate cancer

Idiopathic Granulomatous Prostatitis *(60–78%)*

= nonspecific nonnecrotic prostatitis
Cause: not clear
• often self-limiting
No association with: systemic diseases

Sarcoid Prostatitis *(rare)*

= idiopathic multisystem noncaseating granulomatous disease
Predilection for: African-Americans
Histo: nonspecific histology
• mostly asymptomatic; elevated PSA level

Dx: based on clinical-radiologic correlation + exclusion of other granulomatous disease entities

Iatrogenic Granulomatous Prostatitis

Incidence: 2nd most common type

Cause: transurethral resection of prostate / bladder ← reaction to altered epithelium + stroma from intervention

Histo: palisaded histiocytoid granulomas with central necrotizing / fibrinoid necrosis surrounded by infiltrative eosinophils

Infective Granulomatous Prostatitis

Cause: mycobacterium tuberculosis (← hematogenous spread / direct extension from adjacent organs); development after intravesical bacillus Calmette-Guérin therapy for bladder cancer; Treponema pallidum; viruses (herpes zoster); fungi (Cryptococcus, Candida, Aspergillus)

Histo: well-formed granulomas with epithelioid cell + multinucleated giant cell infiltration +/- central necrosis (caseation)

Predisposing risk factors: Hx of tuberculosis infection, bacillus Calmette-Guérin therapy, immunosuppressive state

- mostly asymptomatic, elevated PSA level
- indurated prostate at digital rectal examination

√ area of hypointensity on T2WI associated with diffusion restriction

√ moderate / marked enhancement on dynamic images

NONNECROTIC GRANULOMATOUS PROSTATITIS

Histo: highly cellular simulating prostate cancer

MR:

√ area of hypointensity on T2WI associated with restricted diffusion in the peripheral zone

√ moderate / marked enhancement

DDx: prostate cancer

NECROTIC GRANULOMATOUS PROSTATITIS

Histo: central necrosis (caseation)

MR:

√ area of central hyperintensity on T2WI

√ focal hyperintensity on high-b-value images

√ marked diffusion restriction

√ NO enhancement

Malakoplakia

= rare granulomatous inflammatory condition associated with recurrent infection

Path: granulomatous infiltration with Michaelis-Gutmann bodies, which may represent abnormality of intraphagosomal digestion of macrophages

- bulging and irregularity of prostatic capsule

MR:

√ diffuse low T2 signal intensity, diffusion restriction
√ hyperenhancement
DDx: prostate cancer

PRUNE BELLY SYNDROME

= EAGLE-BARRETT SYNDROME
= congenital nonhereditary multisystem disorder; almost exclusively in males
TRIAD: 1. Abdominal wall muscle deficiency (wrinkled "prune belly" appearance of abdominal wall)
2. Nonobstructed markedly distended redundant ureters ± hydronephrosis and variable degree of renal dysplasia
3. Bilateral undescended testes (cryptorchidism)
Etiology:
(1) Primary mesodermal arrest at 6–10 weeks GA:
abundance of fibrous tissue with sparsely placed smooth muscle throughout urinary tract
(2) Massive abdominal distension with pressure effects on abdominal wall musculature: ← bladder outlet obstruction (10–20%) / urine ascites / intestinal perforation with ascites / cystic abdominal masses / megacystis-microcolon-intestinal hypoperistalsis syndrome causing pressure atrophy of abdominal wall muscles; bladder distension interfering with descent of testes
(3) Dysgenesis of yolk sac
Prevalence: 1÷29,000 to 1÷50,000 live births; M÷F = 19÷1; increased prevalence in Nigeria + Saskatchewan, Canada
Groups:
(1) Severe urethral obstruction ← urethral atresia [most commonly] / valves
Associated with:
malrotation (most common anomaly), intestinal atresia, imperforate anus, skeletal abnormalities (meningo-myelocele, scoliosis, pectus carinatum /excavatum, arthrogryposis, clubfoot, dislocation of hip, lower limb hemimelia, sacral agenesis, polydactyly), CHD (VSD, pulmonary artery stenosis), Hirschsprüng disease, congenital cystic adenomatoid malformation of lung
√ bladder wall hypertrophy
√ bilateral cystic renal dysplasia
Prognosis: in 20% [50%] death within 1 month [2 years] ← renal failure ± pulmonary insufficiency
(2) Functional abnormality of bladder emptying (more common) with no associated abnormalities
√ large floppy urinary bladder
√ large urachal remnant
√ dilated posterior urethra (without obstruction)
√ utricle
√ vesicoureteral reflux
√ dilated tortuous ureters + focal areas of narrowing
√ lobulated kidneys with dilated collecting system of bizarre shape

Prognosis: chronic urinary tract problems

- wrinkled flaccid appearance of hypotonic abdominal wall with bulging flanks ← agenesis / hypoplasia of muscles in lower parts of abdominal wall ventrally + laterally:
  transverse muscle > rectus abdominis muscle below umbilicus > internal + external oblique muscle > rectus abdominis muscle above umbilicus
- bilateral cryptorchidism (ESSENTIAL COMPONENT) with increased risk for malignant degeneration
- ± impaired renal function

OB-US:

√ enlarged bladder, dilated ureters
√ abnormal abdominal wall
√ normal / decreased AFI

DDx: posterior urethral valves

@ Bladder

√ thickened bladder wall without trabeculations ← replacement by fibrocytes + collagen
√ large distended urinary bladder with a capacity of 600–800 mL
√ intramural bladder calcifications
√ persistence of patent urachus ± calcification
√ widely patent bladder neck
√ laterally placed ureteric orifices

@ Urethra

√ elongated + dilated prostatic urethra with tapering of membranous urethra
√ small / absent verumontanum
√ absent / markedly hypoplastic prostate → infertility and enlarged prostatic urethra
√ enlarged prostatic utricle (= small epithelium-lined diverticulum representing the remnant of the fused caudal ends of the müllerian ducts)
√ urethral obstruction: stenosis / atresia / dorsal chordae / posterior urethral valves (in 20%)
√ scaphoid megalourethra (70%)
(a) complete / fusiform megalourethra (rare)
= complete absence / marked deficiency of corpora cavernosa + corpus spongiosum
(b) incomplete / scaphoid megalourethra (common)
= congenital absence / deficiency of corpus spongiosum with a normal glans + navicular fossa

@ Ureters

Histo: diffuse increase in connective tissue with replacement of smooth muscle
√ massively dilated tortuous elongated ureters affecting the lower ⅓ more profoundly (HALLMARK)
√ poor ureteral peristalsis ← decrease in number of nerves + degeneration of nonmyelinated Schwann fibers
√ alternating narrowed + dilated ureteral segments
√ vesicoureteral reflux (> 70%)

@ Kidneys

√ asymmetry of renal size + lobulated contours

√ no / mild (> 50%) hydronephrosis
√ caliceal dilatation ± diverticula
√ renal calcifications
√ renal dysplasia with cystic dysplastic changes, oligohydramnios, pulmonary hypoplasia (in severe cases due to a combination defect of ureteric bud + metanephron)

@ Lung (55%)
√ pulmonary hypoplasia
√ cystic adenomatoid malformation
Cx: respiratory infections ← ineffective cough

@ Musculoskeletal (50%):
scoliosis, pectus deformity, arthrogryposis, clubfoot, valgus foot, hemimelia, dislocation of hip, sacral agenesis, polydactyly

@ Gastrointestinal anomalies (30%):
malrotation, atresia, stenosis, volvulus, imperforate anus, Hirschsprüng disease, gastroschisis

@ Cardiovascular (10%): VSD, PDA, tetralogy of Fallot

Cx: chronic renal failure / urosepsis / respiratory failure (30% die within first 2 years of life)

Rx: internal urethrotomy, cutaneous vesicostomy, reduction cystoplasty, ureteral reimplantation, orchiopexy at 1–2 years of age, renal transplantation after bilateral nephroureterectomy, abdominoplasty

PYELOCALICEAL DIVERTICULUM

= PYELOGENIC CYST = PERICALICEAL CYST = CALICEAL DIVERTICULUM

= uroepithelium-lined urine-filled cavity within renal cortex communicating with renal collecting system

TYPE I (connecting with minor calyx):
more common; connected to caliceal cup, usually at fornix; bulbous shape; narrow connecting infundibulum of varying length; few millimeters in diameter; in polar region especially upper pole

TYPE II (connecting with major calyx / renal pelvis):
interpolar region; communicates directly with pelvis; usually larger and rounder; neck short and not easily identified

Prevalence: 2.1–4.5÷1000 intravenous urograms

Cause:
(1) Congenital: developmental origin from ureteral bud remnant ← obstruction of peripheral aberrant "minicalyx" / failure of regression of 3rd–4th-generation ureteric bud
(2) Acquired (less common): reflux, obstructing stone, infection, rupture of simple cyst / abscess, infundibular achalasia / spasm, hydrocalyx ← inflammatory fibrosis of an infundibulum

√ appearance of simple cyst
√ opacification during excretory phase may be delayed and remain so for prolonged period → layering of contrast medium
√ mass effect on adjacent pelvicaliceal system if large enough

US:

√ anechoic cyst
√ ± layering mobile echogenic material ← formation of single / multiple stones (50%) / milk of calcium (fluid-calcium level)

Cx: hemorrhage, recurrent infection, cyst rupture, malignancy (exceedingly rare)

DDx: ruptured simple nephrogenic cyst, evacuated abscess / hematoma, renal papillary necrosis, medullary sponge kidney, hydrocalyx ← infundibular narrowing from TB / crossing vessel / stone / infiltrating carcinoma

PYELONEPHRITIS

= upper urinary tract infection with pelvic + caliceal + parenchymal inflammation

◊ The Society of Uroradiology recommends eliminating the terms (acute focal) bacterial nephritis, lobar nephritis, lobar nephronia, preabscess, renal cellulitis, renal phlegmon, renal carbuncle!

Acute Pyelonephritis

= episodic bacterial infection of kidney with acute inflammation, usually involving pyelocaliceal lining + renal parenchyma centrifugally along medullary rays

Risk factors:

1. Vesicoureteral reflux in children
2. Obstruction, stasis, stone in adults (5%)

Pathway of infection:

(a) **ascending bacterial infection** ← (usually) P-fimbriated E. coli (fimbriae facilitate adherence to mucosal surface): initial colonization of ureter in areas of turbulent flow → paralysis of ureteral smooth muscle → dilatation + functional obstruction of collecting system

(b) **vesicoureteral reflux** + pyelotubular backflow: P-fimbriated E. coli NOT necessary for infection

(c) **hematogenous** spread (12–20%) with gram-positive cocci

Path: thickened urothelium with multifocally / globally edematous kidney; radiating yellow-white stripes / wedges extending from papillary tip to cortical surface in a patchy distribution + sharply demarcated from adjacent spared parenchyma by 48–72 hours

Histo: tubulointerstitial nephritis = leukocytic migration from interstitium into lumen of tubules → destruction of tubule cells by released enzymes → bacterial invasion of interstitium by 48–72 hours

Organism: E. coli > Proteus > Klebsiella, Enterobacter, Pseudomonas

Age: most commonly 15–30 years; M << F

Prevalence: 1–2% of all pregnant women

- fever, chills, flank pain + tenderness
- pyuria, bacteriuria, positive urine culture
- ± microscopic hematuria / bacteremia; leukocytosis

Indication for imaging in adults:

(1) Diabetes
(2) Analgesic abuse
(3) Neuropathic bladder

(4) History of urinary tract stones
(5) Atypical organism: eg, proteus
(6) Poor response to antibiotics
(7) Frequent recurrences
(8) Immunocompromise

IVP (abnormal in 25%):
√ smooth normal / enlarged kidney(s), focal >> diffuse involvement of kidney
√ diminished nephrographic density (global / wedge-shaped / patchy)
√ immediate persistent dense nephrogram, rarely striated
√ nonvisualization of kidney ← severe pyelonephritis (rare)
√ "tree-barking" = mucosal striations (rare)
√ compression of collecting system ← edema
√ delayed opacification of collecting system
√ nonobstructive ureteral dilatation ← effect of endotoxins (rare)

CT:
√ thickening of Gerota fascia + thickened bridging septa / stranding ← perinephric inflammation
√ generalized renal enlargement / focal swelling
√ obliteration of renal sinus
√ thickening of walls of renal pelvis + calices
√ mild dilatation of renal pelvis + ureter
√ area of high attenuation on unenhanced sca(= hemorrhagic bacterial nephritis)

CECT (abnormal in 65–90%):
√ hypoattenuating (80–90 HU) wedge-shaped area of cortex extending from papilla to renal capsule during nephrographic phase (= lobar segments of hypoperfusion + edema)
√ striated nephrogram
√ poor corticomedullary differentiation
√ dense parenchymal staining on scan delayed by 3–6 hours in area of earlier diminished enhancement ← functioning renal parenchyma
√ soft-tissue filling defect in collecting system ← papillary necrosis, inflammatory debris, blood clot
√ caliceal effacement

US (abnormal in < 50%):
◊ Pyelonephritis is difficult to detect sonographically!
√ swollen kidney of decreased echogenicity
√ loss of central sinus complex
√ wedge-shaped hypo- / isoechoic zones, rarely hyperechoic ← hemorrhage
√ thickened sonolucent corticomedullary bands
√ blurred corticomedullary junctions
√ localized increase in size + echogenicity of perinephric fat ± fat within renal sinus
√ localized perinephric exudate
√ thickening of wall of renal pelvis
√ focally decreased blood flow on power Doppler

MR:
√ perinephric edema surrounding enlarged kidney

√ wedge-shaped foci of persistent increased SI on contrast-enhanced fast inversion recovery / T2WI

Renal cortical scintigraphy (^{99m}Tc-DMSA):

√ focal areas of diminished uptake (in 90%)

Prognosis:

(1) Quick response to antibiotic treatment will leave no scars

(2) Delayed treatment of acute pyelonephritis during first 3 years of life can severely affect renal function later in life → decreased renal function, hypertension (33%), end-stage renal disease (10%)

Cx: (1) Renal abscess (near-water density lesion without enhancement)

(2) Scarring of affected renal lobes often in children + in up to 43% in adults

(3) Maternal septic shock (3%)

(4) Premature labor (17%)

Acute Focal Pyelonephritis

= LOBAR NEPHRONIA = ACUTE FOCAL BACTERIAL NEPHRITIS = CARBUNCLE = RENAL CELLULITIS = RENAL PHLEGMON

= focal variant of acute pyelonephritis with single / multiple areas of suppuration + necrosis

Organism: E. coli > Proteus > Klebsiella

Predisposed: patients with altered host resistance (diabetes [60%], immunosuppression), trauma, chronic catheterization, mechanical / functional obstruction

• fever, flank pain, pyuria

Site: usually involves entire renal lobe

√ ^{67}Ga uptake

√ vesicoureteral reflux often present

IVP:

√ focal area of absent nephrogram / distorted pyelogram

US:

√ hypoechoic mass with ill-defined margins and disruption of corticomedullary border

√ NOT a fluid collection

CT:

√ hypoattenuating zone with poorly defined transition to surrounding parenchyma

√ less than normal parenchymal enhancement

MR:

√ area of low signal intensity on T1WI

√ hyperintense center on T2WI ← fluid, necrosis

Angio:

√ renal arteries displaced, renal veins compressed

DDx: abscess (no enhancement on CT)

Cx: scarring, abscess

Acute Suppurative Pyelonephritis

= ACUTE DIFFUSE BACTERIAL NEPHRITIS

= more severe and extensive form of acute pyelonephritis → may lead to diffuse necrosis (=

phlegmon)
Organism: Proteus, Klebsiella > E. coli
Predisposed: diabetics (60%)

Emphysematous Pyelitis

= gas confined to renal pelvis + calices
Organism: E. coli
Predisposed: diabetes mellitus (50%); M÷F = 1÷3
May be associated with: emphysematous cystitis (rare)
• pyuria
√ gas pyelogram outlining pelvicaliceal system
√ dilated renal collecting system (frequent)
√ ± gas in ureters
DDx: reflux of gas / air from bladder or urinary diversion

Emphysematous Pyelonephritis

= life-threatening acute fulminant necrotizing infection of kidney and perirenal tissues associated with gas formation
Organism: E. coli (68%), Klebsiella pneumoniae (9%), Proteus mirabilis, Pseudomonas, Enterobacter, Candida, Clostridia (exceptionally rare)
Path: acute and chronic necrotizing pyelonephritis with multiple cortical abscesses
Mechanism: pyelonephritis → ischemia + low O2 tension with anaerobic metabolism; facultative anaerobe organisms form CO_2 with fermentation of necrotic tissue / tissue glucose
Predisposed: immunocompromised patients, esp. diabetics (in 87–97% of cases); ureteral obstruction (in 20–40%)
Average age: 54 years; M÷F = 1÷2
May be associated with: XGP
• features of acute severe pyelonephritis (chills, fever, flank pain, lethargy, confusion) not responding to Rx
• positive blood + urine cultures (in majority), urosepsis, shock
• fever of unknown origin + NO localizing signs in 18%
• multiple associated medical problems: uncontrolled hyperglycemia, acidosis, dehydration, electrolyte imbalance
Location: in 5–7% bilateral
√ parenchymal destruction
√ absent / decreased contrast excretion ← compromised renal function
Type I (33%):
√ streaky / mottled gas in interstitium of renal parenchyma radiating from medulla to cortex
√ crescent of subcapsular / perinephric gas
√ NO fluid collection ← no effective immune response
Prognosis: 69% mortality
Type II (66%):
√ bubbly / loculated intrarenal gas (infers presence of abscess)
√ renal / perirenal fluid collection

√ gas within collecting system (85%)
Prognosis: 18% mortality
US:
√ high-amplitude echoes within renal sinus / renal parenchyma associated with "dirty" shadowing / "comet tail" reverberations
CAVE: (1) Kidney may be completely obscured by large amount of gas in perinephric space (DDx: surrounding bowel gas)
(2) Gas may be confused with renal calculi
CT (most reliable + sensitive modality):
√ mottled areas of low attenuation extending radially along pyramids
√ extensive involvement of kidney + perinephric space
√ air extending through Gerota fascia into retroperitoneal space
√ occasionally gas in renal veins
MR:
√ signal void on T1WI + T2WI (DDx: renal calculi, rapidly flowing blood)
Mortality: 60–75% under antibiotic Rx; 21–29% after antibiotic Rx + nephrectomy; 80% with extension into perirenal space
Rx: antibiotic therapy + nephrectomy; drainage procedure for coexisting obstruction
DDx: emphysematous pyelitis (gas in collecting system but not in parenchyma, diabetes in 50%, less grave prognosis)

Fungal Pyelonephritis

Organism: Candida, Aspergillus, Mucor, Coccidioides, Cryptococcus, Actinomyces, Nocardia, Torulopsis
At risk: diabetes, drug addiction, leukemia, debilitation, immunosuppression
√ pyelonephritis, papillary necrosis, renal abscess
√ fungus ball

Xanthogranulomatous Pyelonephritis

= rare chronic suppurative granulomatous infection characterized by progressive parenchymal destruction ← chronic renal obstruction ← calculus, stricture, carcinoma
Cause: abnormal host response to bacterial infection
Prevalence: 681,000 surgically proven cases of chronic pyelonephritis
Organism: Proteus mirabilis, E. coli, S. aureus
Risk factors: female gender, diabetes
Associated with: nephrolithiasis (staghorn calculus in 50%)
Path: replacement of corticomedullary junction with soft yellow nodules; calices filled with pus and debris
Histo: diffuse infiltration by plasma cells + histiocytes + lipid-laden macrophages (xanthoma cells)
Pathophysiology:
infection of renal pelvis, which the host is unable to eradicate; macrophages become enlarged with undigested bacteria gradually replacing the renal parenchyma + perinephric space
Peak age: 45–65 years; all ages affected, may occur in infants; M÷F = 1÷3–1:4; typically in

perimenopausal woman

- pyuria 95%
- flank pain 80%
- fever 70%
- palpable mass 50%
- weight loss 50%
- microscopic hematuria 50%
- elevated ESR; reversible elevated liver function tests (50%) ← inflammation of portal triads

◊ Symptomatic for 6 months prior to diagnosis in 40%!

A. DIFFUSE XGP (83–90%)
= massive renal enlargement, lithiasis, peripelvic fibrosis, hydronephrosis, lobulated masses replacing parenchyma

B. SEGMENTAL / FOCAL XGP (10–17%)
= tumefactive form ← obstructed single infundibulum / one moiety of duplex system
DDx: renal cell carcinoma

IVP:
√ global enlargement of kidney (smooth contour uncommon) / focal renal mass (less frequent)
√ contracted pelvis with dilated calices
√ focally absent / totally absent nephrogram (80%)
√ centrally obstructing calculus:
√ staghorn calculus in 75%
√ extension of inflammation into perirenal space, pararenal space, ipsilateral psoas muscle, colon, spleen, diaphragm, posterior abdominal wall, skin

Retrograde:
√ complete obstruction at ureteropelvic junction / infundibulum / proximal ureter
√ contracted renal pelvis, dilated deformed calices + nodular filling defects
√ irregular parenchymal masses with cavitation

CT:
√ enlargement of kidney
√ obstructive staghorn-like calculus
√ hydronephrosis + abscesses:
√ "**bear paw**" sign = low-attenuation fatty masses arranged in a "hydronephrotic" pattern replacing renal parenchyma (= replacement fibrolipomatosis with attenuation values of less than water)
√ extension into perinephric space + retroperitoneum (simulating an infiltrative malignancy)
√ heterogeneous parenchymal / NO enhancement

US:
√ hypoechoic dilated calices with echogenic rim
√ hypoechoic masses frequently with low-level internal echoes replacing renal parenchyma
√ loss of corticomedullary junction
√ parenchymal calcifications (uncommon)

MR:
√ renal parenchyma replaced by dilated calices + abscess cavities of intermediate SI on T1WI and high SI on T2WI
√ ± marked enhancement of cavity walls
√ signal void of calculus within collecting system
Angio:
√ stretching of segmental / interlobar arteries around large avascular masses
√ hypervascularity / blush around periphery of masses in late arterial phase (= granulation tissue)
√ venous encasement + occlusion
DDx: pyonephrosis, long-standing hydronephrosis, avascular tumor
Rx: nephrectomy

PYELOURETERITIS CYSTICA

= POLYURETERITIS CYSTICA
= hyperplastic noncommunicating cystic transitional epithelial cell collections projecting into ureteral lumen
◊ Indicative of past / present urinary tract infection!
Cause: chronic urinary tract irritant ← stone / infection
Histo: numerous small submucosal epithelial-lined cysts representing cystic degeneration of epithelial cell nests within lamina propria (**cell nests of von Brunn**) formed by downward proliferation of buds of surface epithelium that have become detached from the mucosa
Organism: E. coli > M. tuberculosis, Enterococcus, Proteus, schistosomiasis
Predisposed: diabetics
Age: 6th decade; more prevalent in women
• no specific symptoms; ± hematuria
Location: bladder >> proximal ⅓ of ureter > ureteropelvic junction; unilateral >> bilateral
√ multiple small round smooth lucent filling defects of 2–3 mm in size; scattered discrete / clustered
√ persist unchanged for years in spite of antibiotic therapy
Cx: increased incidence of transitional cell carcinoma
Dx: biopsy to exclude malignancy
DDx: (1) Spreading / multifocal TCC
(2) Vascular ureteral notching
(3) Multiple blood clots
(4) Multiple polyps
(5) Allergic urticaria of mucosa
(6) Submucosal hemorrhage (eg, anticoagulation)

PYONEPHROSIS

= presence of pus in dilated collecting system (= infected hydronephrosis)
Path: purulent exudate composed of sloughed urothelium + inflammatory cells from early

formation of microabscesses + necrotizing papillitis

Organism: most commonly E. coli

US:

√ dispersed / dependent internal echoes within dilated pelvicaliceal system

√ shifting urine-debris level

√ dense peripheral echoes in nondependent location + shadowing (gas from infection)

Cx: (1) Renal microabscesses + necrotizing papillitis

(2) XGP

(3) Renal / perinephric abscess

(4) Fistula to duodenum, colon, pleura

RADIATION NEPHRITIS

Histo: interstitial fibrosis, tubule atrophy, glomerular sclerosis, sclerosis of arteries of all sizes, hyalinization of afferent arterioles, thickening of renal capsule

Threshold dose: 2,300 rad over 5 weeks

• clinically resembling chronic glomerulonephritis

√ normal / small smooth kidney consistent with radiation field

√ parenchymal thickness diminished (globally / focally; related to radiation field)

√ diminished nephrographic density

REFLUX ATROPHY

Cause: increased hydrostatic pressure of pelvicaliceal urine with atrophy of nephrons ← long-standing vesicoureteral reflux

√ small smooth kidney with loss of parenchymal thickness

√ widened collecting system with effaced papillae

√ longitudinal striations ← redundant mucosa when collecting system is collapsed

◊ Do NOT confuse with reflux nephropathy!

REFLUX NEPHROPATHY

= CHRONIC ATROPHIC PYELONEPHRITIS

= ascending bacterial urinary tract infection ← reflux of infected urine from lower tract + tubulointerstitial inflammation in childhood (hardly ever endangers adult kidney)

◊ Most common cause of a small scarred kidney!

Etiology: 3 essential elements:

(1) Infected urine

(2) Vesicoureteral reflux

(3) Intrarenal reflux

Age: usually young adults (subclinical diagnosis starting in childhood); M < F

• fever, flank pain, frequency, dysuria, hypertension, renal failure

• may have no history of significant symptoms

Site: predominantly affecting poles of kidneys ← presence of compound calices having distorted **papillary ducts of Bellini** (= papillae with gaping openings instead of slitlike openings of interpolar papillae)

√ normal / small kidney; uni- / bilateral; uni- / multifocal
√ focal parenchymal thinning with contour depression in upper / lower pole (more compound papillae in upper pole), scar formation only up to age 4
√ retracted papilla with clubbed calyx subjacent to scar
√ contralateral / focal compensatory hypertrophy (= renal pseudotumor)
√ dilated ureters ← reflux, sometimes with linear striations (= redundant / edematous mucosa)
US:
√ focally increased echogenicity within cortex ← scar
Angio:
√ small tortuous intrarenal arteries, pruning of intrarenal vessels
√ vascular stenoses, occlusion, aneurysms
√ inhomogeneous nephrographic phase
NUC (^{99m}Tc-glucoheptonate / DMSA with SPECT most sensitive method):
√ focal / multifocal photon-deficient areas
Cx: (1) Hypertension
(2) Obstetric complications
(3) Renal failure

RENAL ABSCESS

= PYOGENIC RENAL ABSCESS = KIDNEY ABSCESS
= usually complication of renal inflammation with liquefactive necrosis; 2% of all renal masses
Cause: typically complication of acute untreated / incompletely treated pyelonephritis / ascending UTI; hematogenous seeding via bacteremia
Pathway of infection:
(a) ascending (80%): associated with obstruction (UPJ, ureter, calculus)
Organism: E. coli, Proteus
(b) hematogenous (20%): infection from skin, teeth, lung, tonsils, endocarditis, intravenous drug abuse
Organism: staphylococcus aureus
Predisposed: diabetic (twice as frequent compared with nondiabetic); immunocompromised; pregnancy
• positive urine (blood) culture in 33% (50%)
• may have negative urine analysis / culture (in up to 20%)
• pyuria, hematuria (absent if abscess isolated within parenchyma)
IVP:
√ focal mass displacing collecting system
CECT:
√ well-defined hypoattenuating irregular focal round renal mass:
√ thick rim / halo of enhancing wall / pseudocapsule
√ no enhancement of center of abscess
√ ± presence of gas
√ thickened septa + Gerota fascia
√ perinephric fat obliteration ← perinephric extension
US:

√ slightly hypoechoic (early), hypo- to anechoic (late) mass
√ irregular margins + increased through-transmission
√ ± septations ± microbubbles of gas

MR:
√ heterogeneous thick-rimmed complex T1-hypointense and T2-hyperintense lesion replacing renal parenchyma
√ restricted diffusion
√ surrounding thick hypointense rim on T2WI
√ elevated perinephric SI on T2WI
√ blooming artifact on GRE ← gas

NUC (^{67}Ga-citrate / ^{111}In leukocytes):
√ hot spot

DDx: renal cyst; cystic renal cell carcinoma

Perinephric / Perirenal Abscess

Cause:
(1) Acute pyelonephritis with extension of renal abscess through capsule
(2) Adjacent retroperitoneal infection: eg, perforation of colon cancer, psoas abscess
(3) Deep penetrating subcutaneous abscess
(4) Hematogenous spread

Predisposed: diabetics (in 30%), urolithiasis, septic emboli
◊ 14–75% of patients with perinephric abscess have diabetes mellitus!

Organism: in up to 30% different from abscess

√ loss of psoas margin / obscuration of renal contour
√ renal displacement
√ focal renal mass
√ scoliosis concave to involved side
√ respiratory immobility of kidney = renal fixation
√ occasionally gas in renal fossa
√ unilateral impaired excretion
√ pleural effusion

RENAL ADENOMA

◊ Small adenoma < 3 cm should be considered a renal cell carcinoma of low metastatic potential = borderline renal cell carcinoma!

Frequency: in 7–15–23% of adults (autopsies); most common cortical lesion; increasing with age (in 10% of patients < 40 years of age, in 40% of patients > 70 years of age); increased frequency in tobacco users + patients on long-term dialysis

Age: usually > 30 years; M÷F = 3÷1

Types:

(1) Papillary adenoma / cystadenoma (38%)
(2) Tubular adenoma (38%)
(3) Mixed type adenoma (21%)
(4) Alveolar adenoma (3%) = precursor of RCC

√ solitary in 75%, multiple in 25%

√ usually < 3 cm in size; subcapsular cortical location

√ impossible to differentiate from renal cell carcinoma

Cx: premalignant (adenoma-carcinoma sequence)

Prognosis: average growth rate of 0.4 (range, 0.2–3.5) cm annually; tumors growing < 0.25 cm annually rarely metastasize; tumors growing > 0.6 cm annually frequently metastasize

RENAL AGENESIS

Mechanism:

(a) formation failure
= failure of ureteral bud to form
• hemitrigone = absence of ipsilateral trigone + ureteral orifice

(b) induction failure
= failure of growing ureteral bud to induce metanephric tissue
• blind-ending ureter

Unilateral Renal Agenesis

Prevalence: 1÷600 to 1÷1,000 pregnancies; M÷F = 1.8÷1

Risk of recurrence: 4.5%

Often coexisting with other anomalies:

1. Genital abnormalities:
   (a) in male (10–15%): **Zinner syndrome**
   = rare congenital abnormality of the mesonephric (Wolffian) duct = TRIAD of (1) hypoplasia or agenesis of testis / vas deferens, (2) seminal vesicle cyst, (3) ipsilateral ejaculatory duct obstruction
   [Alfred Zinner (?1887–1967), urologist in Wien, Austria]
   (b) in female (25–50%): unicornuate / bicornuate / hypoplastic / absent uterus, absent / aplastic vagina
   ◊ 90% of women with renal agenesis have uterine anomalies
   ◊ 30–40% of women with uterine anomalies have renal agenesis
2. Turner syndrome, trisomy, Fanconi anemia, Laurence-Moon-Biedl syndrome

Location: L > R
√ visualization of single kidney (DDx: additional kidney in ectopic location)
√ absent adrenal gland (11%)
√ absent / rudimentary renal vessels
√ colon occupies renal fossa
√ compensatory contralateral renal hypertrophy (50%)

Bilateral Renal Agenesis

= POTTER SYNDROME
Prevalence: 1÷3,000 to 1÷10,000 pregnancies; M÷F = 2.5÷1
Risk of recurrence: < 1%
• **Potter's facies** = low-set ears, redundant skin, parrot-beaked nose, receding chin
◊ US sensitivity is ONLY 69–73% ← decreased visualization from oligohydramnios + discoid-shaped adrenal glands simulating kidneys!
√ severe oligohydramnios (after 14 weeks MA)
√ bilateral absence of kidneys, ureters, renal arteries (after 12 weeks)
√ inability to visualize renal arteries by color duplex
√ inability to visualize urine in fetal bladder (after 13 weeks) ← bladder agenesis / hypoplasia; negative furosemide test (20–60 mg IV) NOT diagnostic (fetuses with severe IUGR may not be capable of diuresis)
√ flattened discoid shape of adrenals ← absence of pressure by kidney
√ bell-shaped thorax in mid to late 3rd trimester ← pulmonary hypoplasia
√ compression deformities of extremities → clubfoot, flexion contractures, joint dislocations (eg, hip)
Prognosis: stillbirths (24–38%); invariably fatal in the first days of life ← pulmonary hypoplasia
DDx: functional cause of in utero renal failure (eg, severe IUGR)

Potter Sequence

= hypoplasia of lungs, bowing of legs, broad hands, loose skin, growth retardation associated with long-standing severe oligohydramnios
Cause: renal agenesis, urethral obstruction, prolonged rupture of membranes, severe IUGR

RENAL ARTERY ANEURYSM

Incidence: 0.01–0.10%; 22% of visceral aneurysms
Cause: medial fibrodysplasia, penetrating trauma
Age: 50–61 years; M÷F = 1÷1
Location: R > L; 1st-order branch of main renal artery (usually)
Type:
(a) saccular (80%): near first bifurcation of main renal artery; variety of causes (congenital; associated with medial fibroplasia + atherosclerosis)
(b) fusiform (20%): ← advanced renal artery medial fibrodysplasia; not calcified
(c) dissecting: traumatic, spontaneous (atherosclerosis, intimal fibroplasia, perimedial fibroplasia), iatrogenic

• usually asymptomatic (in > 50%)

Rx: Endovascular therapy (> 80% success rate)

Cx: (1) Hypertension (unusual)

(2) Perinephric / retroperitoneal hemorrhage (rare) with increased risk in peripartum women

(3) Formation of AV fistula

(4) Peripheral renal embolization ← mural thrombus

(5) Thrombosis

(6) Hematuria

Extrarenal Aneurysm *(⅔)*

A. TRUE ANEURYSM
   1. Atherosclerotic (most common)
   2. Fibromuscular dysplasia
   3. Pregnancy
   4. Mesenchymal disease: neurofibromatosis, Ehlers-Danlos syndrome

B. FALSE ANEURYSM
   1. Trauma; renal artery angioplasty
   2. Behçet disease
   3. **Mycotic aneurysm** 2.5% of all aneurysms

      Cause: bacteremia, SBE, perivascular extension of inflammation

      Organism: Streptococcus, Staphylococcus, Pneumococcus, Salmonella

√ incomplete / complete ring of calcification

√ variable enhancement (depending on amount of thrombus)

Rx: (1) Conservative in asymptomatic patient for well-calcified aneurysm < 2 cm in diameter

(2) Surgery for (a) interval growth, (b) emboli to kidney, (c) in woman of childbearing age, (d) diminished renal function / ischemia / hypertension / dissection

Intrarenal Aneurysm *(⅓)*

in interlobar and more peripheral branches

A. CONGENITAL (most common)
   1. Congenital renal aneurysm

      Age at Dx: 30 years or older; M÷F = 1÷1

      • hypertension in 25% ← segmental renal ischemia

      √ saccular aneurysm close to vascular bifurcations, may calcify

      √ often bilateral

      Rx: surgical / endovascular repair for aneurysm > 1.0 cm in hypertensive patient / for aneurysm > 1.5 cm in asymptomatic normotensive patient

B. ARTERITIS
   1. Polyarteritis nodosa
   2. SLE
   3. Allergic vasculitis
   4. Wegener granulomatosis

5. Transplant rejection
6. Drug-abuse vasculitis
   ◊ Kidney most commonly affected organ!
   Cause:
   (a) immunologic injury from circulating hepatitis antigen-antibody complexes producing a necrotizing angiitis
   (b) bacterial endocarditis
   (c) drug-related
   (d) impurity-related
   Drugs: methamphetamine, heroin, LSD
   √ multiple small aneurysms in interlobar branches near corticomedullary junction
   √ inhomogeneous spotty nephrogram

C. DEGENERATIVE: Atherosclerosis (may calcify)
D. TUMOR
   1. Neoplasm (RCC in 14%; adult Wilms tumor)
   2. Hamartoma (angiomyolipoma in 50%)
   3. Metastatic arterial myxoma
   4. Vascular malformation
E. MESENCHYMAL DISEASE
   1. Neurofibromatosis
   2. Fibroplasia
F. TRAUMA
G. INFECTION: syphilis, tuberculosis

RENAL ARTERY STENOSIS

Prevalence: 1–2–4% of hypertensive individuals; 4.3 % of autopsies; 10% of hypertensive individuals with coronary artery disease; 25% of patients with hypertension that is difficult to control; in 45% of patients with malignant hypertension; in 45% of patients with peripheral vascular disease

Cause:

1. Atherosclerosis (60–90%): mostly in proximal 2 cm of main renal artery
   ◊ Any of multiple renal arteries (occurring in 14–28% of the population) may be affected!
2. Fibromuscular dysplasia (10–30%)
3. Others (< 10%): thromboembolic disease, arterial dissection, infrarenal aortic aneurysm, arteriovenous fistula, vasculitis (Buerger disease, Takayasu disease, polyarteritis nodosa, postradiation), neurofibromatosis, retroperitoneal fibrosis

Pathophysiology:

↓ perfusion pressure of glomeruli → stimulates production of renin in juxtaglomerular apparatus + angiotensin II in kidney; renin converts circulating angiotensinogen (α2-globulin) into angiotensin I → subsequently converted by angiotensin-converting enzyme (ACE present in vascular endothelium) → into angiotensin II releasing aldosterone; aldosterone increases salt + water retention; angiotensin II + aldosterone vasoconstrict vessels (especially intraglomerular efferent arteriole to maintain filtration pressure)

◊ ACE inhibition may impair overall renal function ← disruption of autoregulatory

mechanism of GFR (with renal artery stenosis in both kidneys / solitary kidney)

Renin production stimuli:

(a) baroreceptors in afferent glomerular arteriole sense ⇓ stretching of arteriolar wall with diminished blood flow

(b) chemoreceptors of macula densa located in first part of the distal tubule sense a ⇓ amount of sodium and chloride (which have been largely reabsorbed ← low GFR)

Histo: tubular atrophy and shrinkage of glomeruli

- abdominal / flank pain, hematuria, oliguria, anuria
- renin-mediated hypertension ← ischemia
- low urine sodium concentration

Hemodynamic significance determined by:

(a) elevated renin levels in ipsilateral renal vein ≥ 1.5÷1

(b) presence of collateral vessels

(c) greater than 70% stenosis with poststenotic dilatation

(d) transstenotic pressure gradient ≥ 40 mmHg

(e) decrease in renal size

◊ 15–20% of patients remain hypertensive after restoration of normal renal blood flow (= renal artery stenosis without renovascular hypertension)!

Patient selection criteria for screening test:

= clinical signs associated with moderate-to-high risk of renovascular hypertension (HTN):

1. Abrupt onset or severe HTN
2. HTN resistant to 3-drug therapy in compliant patient
3. Abdominal / flank bruits
4. Unexplained azotemia in elderly patient with HTN
5. Worsening renal function during antihypertensive therapy, especially with ACEIs
6. Grade 3 / 4 hypertensive retinopathy
7. Occlusive disease in other vascular beds
8. Onset of HTN < 30 years or > 55 years of age
9. Recurrent pulmonary edema in elderly patient with HTN
10. HTN in infants with an umbilical artery catheter
11. HTN in children

√ normal / decreased renal size (R 2 cm < L; L 1.5 cm < R) with smooth contour

√ vascular calcifications (aneurysm / atherosclerosis)

IVP (60% true-positive rate, 22% false-negative rate):

√ delayed appearance of contrast material ← decreased glomerular filtration

√ increased density of contrast material ← increased water reabsorption

√ delayed washout of contrast material ← prolonged urine transit time

√ lack of distension of collecting system

√ global attenuation of contrast density; urogram may be normal with adequate collateral circulation

√ notching of proximal ureter ← enlargement of collateral vessels

CT:

√ prolongation of cortical nephrographic phase + persistent corticomedullary differentiation

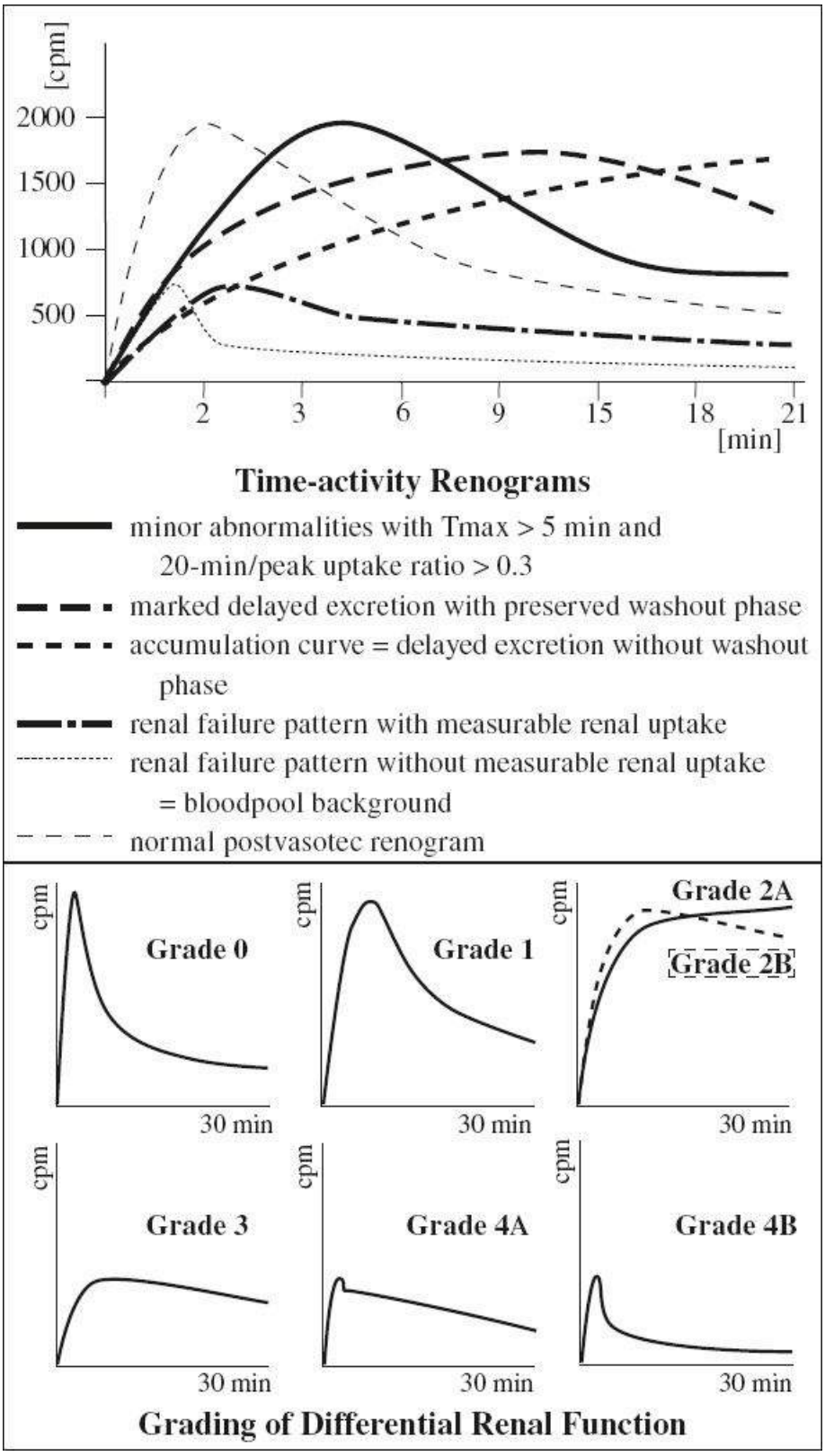
√ CT angiography (2–3-mm collimation, pitch ≤ 1.5–2.0): specificity of real-time interactive volume rendering > maximum-intensity projection > shaded-surface display

MRA (> 95% sensitive, > 90% specific):

√ tendency to overestimate stenosis

Limitations:

› evaluation of branch vessels
› presence of metallic stent
› detection of accessory arteries
› evaluation of small renal arteries



Angiography:

(a) conventional angiography = "gold standard" test

(b) intravenous digital subtraction angiography:
does not address hemodynamic significance

ACE inhibitor scintigraphy (51–96% sensitive, 80–93% specific):

= screening test for renovascular hypertension (not renal artery stenosis) with angiotensin-converting enzyme inhibitor (ACEI) challenge

◊ ACE inhibition may impair overall renal function due to disruption of autoregulatory mechanism of GFR (with renal artery stenosis in both kidneys / solitary kidney)

Pharmacology:

affected kidney responds to decreased arteriolar flow by releasing renin + angiotensin II (= extremely potent vasoconstrictor acting on the efferent renal arteriole to increase filtration pressure) in juxtaglomerular apparatus; ACE inhibitors (eg, captopril, enalapril) → block ACE (angiotensin-converting enzyme) → reduces GFR (51–96% sensitive, 80–93% specific)

√ unilateral parenchymal retention after ACEI: reduced GFR → ⇓ urinary output + ⇑ radiotracer retention
= > 90% probability of renovascular hypertension

√ change in grade of differential renal function from baseline grade 0 / 1 by > 1 grade
= high probability for renal artery stenosis

√ abnormal baseline curve without change
= indeterminate for renovascular hypertension

√ functional improvement following ACEI challenge
= low probability for renovascular hypertension

Semiquantitative interpretation of time-activity renograms:

√ normal ACE inhibitor scintigram (< 10% probability for renovascular hypertension)

√ criteria for high probability (> 90%):

√ worsening of scintigraphic curve

√ reduction in relative uptake with > 10% change after ACE inhibition

√ prolongation of parenchymal transit time with > 2 min delay of excretion into renal pelvis

√ ⇑ in 20-minute peak uptake ratio > 0.15 from baseline

√ prolongation of T_{max} of > 2 min / 40%

√ asymmetry of renal uptake < 40% of total renal uptake

√ bilateral symmetrical changes are usually due to:

(a) hypotension
(b) salt depletion
(c) use of calcium channel blockers
(d) low urine flow rate

Decreased accuracy with:

(1) Bilateral renal artery stenosis
(2) Impaired renal function
(3) Urinary obstruction
(4) Chronic ACE inhibitor therapy

Sources of error:

(1) Failure to administer ACEIs properly:

(a) ingestion of food within 4 hours of taking captopril
(b) paravenous infiltration

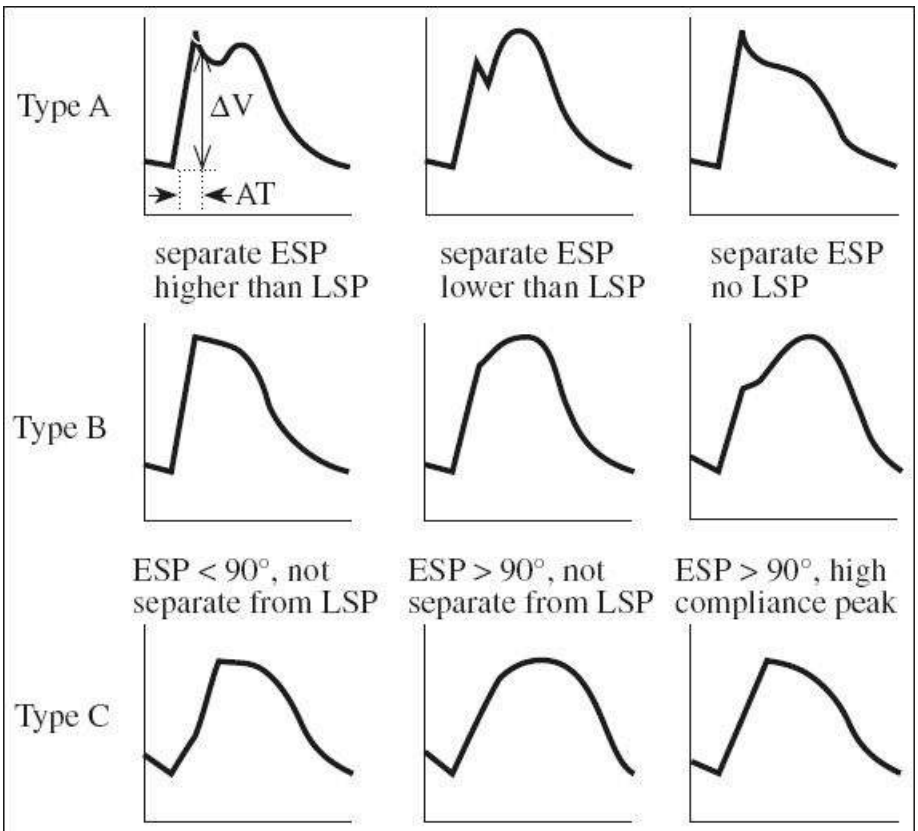
(2) Causes of abnormal whole-kidney renograms:
(a) renal pelvic retention
(b) dehydration
(c) hypotension
(d) full bladder impairing drainage

Duplex US:

(1) direct signs = visualization of renal artery stenosis
√ peak systolic velocity > 150 cm/sec for angles < 60° or 180 cm/sec for angles > 70° (with many false positives due to suboptimal Doppler angles)
√ ratio of peak renal artery velocity to peak aortic center stream velocity > 3.5 (for > 60% stenosis; 0–91% sensitive, 37–97% specific)
√ poststenotic spectral broadening ± flow reversal
√ absence of blood flow during diastole (for > 50% stenosis)
√ NO detectable Doppler signal with good visualization of renal artery (= arterial occlusion)

Problems:
(a) technically inadequate examination (gas, corpulence, respiratory motion) in 6–49%; US usually limited to children + thin adults
(b) multiple renal arteries in 16–28%
(c) "false" tracings from large collateral vessels / reconstituted segments of main renal artery
(d) need to visualize entire length of renal artery
(e) transmitted cardiac / aortic pulsations obscure renal artery waveform recordings

(2) indirect signs = analysis of intrarenal arterial Doppler waveforms
(a) pattern recognition
√ dampened appearance = tardus-parvus pulse
[*tardus*, Latin = late arrival; *parvus*, Latin = attenuated peak]
√ loss of early systolic peak (not necessarily abnormal!)
√ segmental arterial flow detectable with renal artery occlusion ← collateral circulation
(b) quantitative criteria



Variants of Normal Renal Artery Doppler Waveforms

Type A: early systolic peak (ESP) at the end of the early rise

Type B: no peak but rise remains straight

Type C: abnormal spectra with slowed rise time

AT = acceleration time; ΔV = velocity difference between ESP velocity and late diastolic velocity; ESP = early systolic peak
LSP = late systolic peak; acceleration index (AI) = ΔV/AT

Duplex Results for > 60% Renal Artery Stenosis			
	Sensitivity	*Specificity*	*Accuracy*
AT ≥ 0.07 sec	81%	95%	91%
AI < 300 cm/s²	89%	86%	87%
Absent ESP	92%	96%	95%

√ acceleration index of < 370–470 cm/s2 = ΔV/ΔT = tangential inclination of Doppler waveform in early systole (single most sensitive screening parameter)
√ delay in acceleration / pulse rise time of > 0.05–0.08 sec = gradual slope of Doppler waveform during early systole
√ ΔRI > 5% between both kidneys (82% sensitive + 92% specific for stenosis > 50%, 100% sensitive + 94% specific for stenosis ≥ 60%)
√ RI < 0.56
√ attenuated (= parvus) Doppler waveform amplitude = decrease in peak systolic

velocity to < 20–30 cm/s
Problems: technically inadequate examination in 0–2%
False-negative US: stenosis in accessory renal artery
False-positive US: coarctation

Arteriosclerotic Renal Artery Disease

Frequency: in up to 6% of hypertensive patients; most common cause of secondary hypertension
Age: > 50 years; M > F
Path: lesion primarily involving intima
- worsening of preexistent hypertension
- abrupt onset of severe hypertension > 180/110 mmHg
- vascular bruit in 40–50% (present in 20% of hypertensive patients without renal artery stenosis)

Associated with: severe arteriosclerosis of aorta, cerebral, coronary, peripheral arteries
Location: main renal artery (93%) + additional stenosis of renal artery branch (7%); bilateral in 31%
√ eccentric stenosis in proximal 2 cm of renal artery, frequently involving orifice
√ decrease in renal length over time (= high-grade renal artery stenosis with risk for occlusion)
Prognosis: progression of atherosclerotic lesion (40–45%) to renal atrophy, arterial occlusion, ischemic renal failure
Cx: azotemia with
(a) bilateral renal artery stenoses
(b) unilateral renal artery stenosis + poorly functioning contralateral kidney
◊ Reversible azotemia may be induced by treatment with angiotensin-converting enzyme inhibitors / sodium nitroprusside!

Rx: (1) Three-step antihypertensive therapy (control of hypertension difficult)
(2) Angiotensin-converting enzyme inhibitors (eg, captopril PO, enalaprilat IV)
(3) Renal artery angioplasty (80% success for nonostial lesion, 25–30% for ostial lesion)
(4) Surgical revascularization (80–90% success for any lesion location)
› hypertension improved in 66%
› improvement / stabilization of renal function in 27–80%

Fibromuscular Dysplasia of Renal Artery

Prevalence: 4÷1000 symptomatic patients of renal artery + 2÷1000 of extracranial carotid artery involvement (2007); 35% of renal artery stenoses; 25% of all cases of renovascular hypertension
Age: most common cause of renovascular hypertension in children + young adults < 30–40 years; M÷F = 1÷3
Associated with: fibromuscular dysplasia of other aortic branches in 1–2%: celiac artery, hepatic artery, splenic artery, mesenteric artery, iliac artery, internal carotid artery

• hypertension, progressive renal insufficiency

Sites: mid and distal main renal artery (79%), renal artery branches (4%), combination (17%); proximal ⅓ of main renal artery spared in 98%; bilateral in ²/₃; R÷L = 4÷1

Types:

1. Intimal fibroplasia = intimal hyperplasia
   - √ narrow annular radiolucent band in main renal artery + major segmental branches; often bilateral
   - √ poststenotic fusiform dilatation
2. Medial fibroplasia with microaneurysm
   - √ "string-of-beads / **string-of-pearls** sign" = alternating areas of stenoses + aneurysms in mid + distal renal artery + branches; usually bilateral
3. Fibromuscular hyperplasia
   - √ long smooth tubular narrowing of main renal artery and branches
4. Perimedial fibroplasia
   - √ beading without aneurysm formation of distal (mostly right) main renal artery
5. Medial dissection
   - √ false channel in main renal artery + branches
6. Adventitial fibroplasia
   - √ long segmental stenosis of main renal artery + large branches

Prognosis: progression of lesion in 20% → decline in renal function

Cx: (1) Giant aneurysm
(2) AV fistula between renal artery + vein (in medial fibroplasia)

Rx: (1) Resection of diseased segment with end-to-end anastomosis
(2) Replacement by autogenous vein graft, excision + repair by patch angioplasty
(3) Transluminal balloon angioplasty (90% success rate with very low restenosis rate)

Neurofibromatosis of Renal Artery

Hypertension in neurofibromatosis due to:
(1) Pheochromocytoma
(2) Renal artery stenosis

◊ Renal artery involvement mainly seen in children!

Types:
(a) mesodermal dysplasia of arterial wall with fibrous transformation (common)
(b) narrowing of main renal artery by periarterial neurofibroma (rare)

√ saccular funnel-shaped aneurysm involving aorta / main renal artery
√ smooth / nodular stenosis (mural / adventitial neurofibroma) in proximal renal artery
√ intrarenal aneurysm (rare)

DDx: fibromuscular dysplasia; congenital renal artery stenosis

RENAL CELL CARCINOMA

= RCC = RENAL ADENOCARCINOMA = HYPERNEPHROMA

Prevalence: 2–3% of all adult visceral cancers (frequency approximates ovarian cancer, gastric cancer, pancreatic cancer, leukemia); 65,000 new RCCs in USA annually with 13,500 deaths (2012); 85–90% of all renal malignant primaries in adults; 7th / 12th

most common malignancy in men / women; 61% found incidentally with imaging

Age: 6th–7th decade (generally > 40 years); median age of 55 years; 2% occur in children in first 2 decades of life; frequency increasing with age; M÷F = 1.6÷1

Path: arises from proximal tubular cells

Tumor growth pattern:

papillary (5–15%, best prognosis); trabecular / tubular / cystic / solid (poorer prognosis)

Associated with familial and hereditary syndromes:

(1) von Hippel–Lindau syndrome
(2) **Birt-Hogg-Dubé syndrome**: rare autosomal dominant disease characterized by hair follicle hamartomas, renal tumors, pulmonary cysts
(3) Hereditary papillary renal cancer

Predisposed:

(1) Von Hippel-Lindau syndrome (10–25%): multiple often small intracystic tumors (hemangioblastoma, retinal angioma, renal cysts) manifesting at a young age
(2) Hemodialysis (in 1.4–2.6%)
(3) Acquired cystic disease of uremia (3.3–6.1%; 7 x increased risk)
(4) Tobacco; phenacetin abuse
(5) Obesity

Histopathologic subtypes associated with different prognosis:

(a) clear cell RCC (65–80%)
(b) multilocular clear cell RCC (< 1%)
(c) papillary RCC (15–20%) = pRCC
(d) chromophobe RCC (4–11%)
(e) collecting duct carcinoma of Bellini (< 1%)
(f) renal medullary carcinoma
(g) unclassified
- › Xp11 translocation carcinoma
- › carcinoma associated with neuroblastoma
- › mucinous tubular spindle cell carcinoma

Grading (Fuhrman):

Grade 1 tumor cells with 10-µm small round uniform nuclei without nucleoli
Grade 2 tumor cells with 15-µm nuclei, subtle irregular outline and with nucleoli
Grade 3 tumor cells with 20-µm nuclei obvious irregular outline and prominent larger nucleoli
Grade 4 tumor cells with bizarre multilobed nuclei and heavy clumps of chromatin

Staging:

Staging of Renal Cell Carcinoma *American Joint Committee on Cancer (2002)*	
T1	tumor ≤ 7 cm confined to kidney
T2	tumor > 7 cm confined to kidney
T3	invasion of perinephric fat / adrenal gland / major vein
T4	extension beyond Gerota fascia / distant metastasis

Staging accuracy: 84–91% for CT; 82–96% for MR; poor for US

Regional extension: into lymph nodes (9–23%); into main renal vein (21–35%); into IVC (4–10%)

Multiple RCC: commonly in Von Hippel-Lindau syndrome; hereditary RCC; sporadic in 4–15%; bilateral in 1–3%

Metastasis:

- hematuria (56%), flank pain (36%), weight loss (27%), fever (11–15%); normochromic normocytic anemia (28–40%)
- classic triad of flank pain + gross hematuria + palpable renal mass (4–9%); varicocele (2%)
- **Stauffer syndrome** (15%) = nephrogenic hepatopathy = hepatosplenomegaly + abnormal liver function in absence of hepatic metastases (? tumor hepatotoxin)
- Paraneoplastic syndromes: erythrocytosis (2%); hypercalcemia ← parathormone, prostaglandin, vitamin D metabolites)

√ well-marginated often lobulated solitary mass:
  √ focal bulge in renal contour
  √ enlargement of affected part of kidney
√ calcification (15–20%): usually central + amorphous or peripheral + curvilinear in cystic RCC
√ extrinsic compression / displacement / invasion of renal pelvis + calices
√ cysts:
  (a) cystic necrotic tumor (40%)
  (b) cystadenocarcinoma (2–5%)
  (c) renal cell carcinoma in wall of cyst (3%)
√ tumor growth into renal vein (23%) / IVC (in up to 16%) → conveys poor prognosis
√ infiltrative growth pattern (6%) with ill-defined margin

IVP:
  √ diminished function ← parenchymal replacement, hydronephrosis
  √ absence of contrast excretion ← renal vein occlusion
  √ pyelotumoral backflow = necrotic part of tumor fills with contrast material

NECT:
  √ homogeneous solid mass of > 20 HU ← if ≤ 3 cm lesion
  √ heterogeneous hemorrhagic / necrotic mass ← if > 3 cm
  √ calcifications in up to 30%
  √ perinephric fat stranding (50%) ← edema, vascular engorgement, previous inflammation, tumor invasion
  √ ± subcapsular / perinephric hemorrhage
  √ nodal enlargement of > 1 cm (43% PPV, 96% NPV) (DDx: benign inflammation as reactive immune response)

  Falsely negative in corticomedullary phase:
    (1) a small tumor may enhance to the same degree as renal parenchyma
    (2) centrally located tumor mistaken for medulla

CECT:
  √ mostly heterogeneous enhancement ← cystic areas / necrosis:
    √ enhancement of > 12 HU compared with NECT
    √ enhancement to a similar degree as renal cortex
    √ enhancement to a lesser degree than renal cortex = papillary / chromophobe RCC

√ metastases show similar enhancement as primary
√ enhancing nodule in perinephric space (46% sensitive for perinephric spread)
√ renal vein thrombus (92% PPV, 97% NPV):
√ low-attenuation filling defect in corticomedullary phase (MOST SPECIFIC SIGN)
√ abrupt change in caliber of vein
√ presence of collateral veins
√ heterogeneous enhancement of malignant thrombus

US:
√ hyperechoic mass (in 20–50%), mostly in small tumors < 3 cm (78%), occasionally in large tumors (32%):
√ markedly hyperechoic, ie, isoechoic to renal sinus fat in 4–12% of small tumors (DDx: angiomyolipoma)
√ anechoic rim (in 84% of small hyperechoic RCCs) ← pseudocapsule of compressed renal tissue (NOT seen in angiomyolipoma)
√ isoechoic (30–86%) / hypoechoic (10–12%), mostly in larger tumors
√ cystic lesion with increase in acoustic transmission (2–13%) ← extensive liquefaction necrosis (DDx: complicated cyst)
√ inhomogeneity ← hemorrhage, necrosis, cystic degeneration

MR (best modality to assess stage III + IV disease):
√ hyper- / iso- (most) / hypointense relative to renal parenchyma:
√ often low to medium signal intensity on T1WI
√ hyperintense areas on T1WI + hypointense on T2WI ← usually from hemorrhage
√ heterogeneous hyperintensity on T2WI
√ mild decrease in SI on opposed-phase images ← diffuse microscopic intracellular lipid in cRCC
√ imaging at 2 to 5 minutes post contrast injection is critical for the detection of small renal mass (= less enhancement than in normal renal tissue)

PET (sensitivity inferior to CT and MR):
√ inconsistent FDG uptake ← hypo- / isometabolism relative to background + lack of accessibility of FDG ← heterogeneity of glucose transporter expression
◊ Malignancy cannot be ruled out with a negative study!

Angio:
√ typically hypervascular (95%) with puddling of contrast + occasional AV shunting
√ enlarged tortuous poorly tapering feeding vessels
√ coarse neovascularity + formation of small aneurysms
√ parasitization of lumbar, adrenal, subcostal, mesenteric artery branches
√ poorly defined tumor margins

Prognosis:
◊ Tumor stage + histologic grade are the most important prognosticators!
› 5-year survival rates for stages I, II, III, IV are 85–100%, 45–65%, 20–40%, 0–10%;
› 10-year survival rates for stages I, II, III, IV are 56%, 28%, 20%, 3%
› 4.4% 3-year survival rate if untreated
› papillary carcinomas have a better prognosis than nonpapillary carcinomas!
› clear cell + granular cell cancers have a better prognosis than spindle cell + anaplastic

cancers

Recurrence: in 11% after 10 years

Rx:

(1) Radical nephrectomy (2–5% operative mortality)
N.B.: chemo- / radiation- / immunotherapy cannot cure metastatic renal cell carcinoma!

(2) Nephron-sparing surgery (partial nephrectomy) with solitary functioning kidney, compromised renal function, multiple bilateral tumors, small RCC (< 3 cm in diameter, polar, cortical, far from renal hilum / sinus / collecting system)

(3) < 5% of metastatic RCCs respond to chemotherapy; only 20% respond to interleukin-2 / interferon-α

(4) Targeting tumor-angiogenesis: sunitinib and temsirolimus

Chromophobe Renal Cell Carcinoma

Prevalence: 4–11%

Associated with: Birt-Hogg-Dubé syndrome

Origin: intercalated cells of renal cortex

Differentiation of Renal Cyst vs. Neoplasm by CT

CT Feature	*Cyst*	*Neoplasm*
Shape	round, oval	irregular
Margin	smooth	lobulated
Wall	thin, not measurable	thick
Interface	sharp, distinct	indistinct
Density	0–20 HU	> 30 HU
Enhancement	< 10–20 HU	> 10–20 HU
Portal venous phase	< 70 HU	> 70 HU
Vascular invasion	none	yes

Path: solid growth, rarely necrotic even in large tumor

Histo: round to polygonal cells with well-defined cytoplasmic border, abundant pale eosinophilic cytoplasm, fine reticular pattern, perinuclear halo

Median age: 6th decade (range, 31–75 years)

Average size: 8.0 (range, 1.3–20.0) cm

√ less hypervascular than clear cell RCC

√ cystic changes within solid tumor (rare)

√ spokewheel enhancement (? related to oncocytoma)

Prognosis: 5-year survival rate of 90%; better than for cRCC

Collecting Duct Renal Cell Carcinoma

= highly aggressive subtype of RCC

Site: centered in pelvicaliceal system

√ infiltrative growth pattern with medullary epicenter

√ large lesions: heterogeneous ← areas of necrosis, hemorrhage, calcifications

MR:

√ typically low SI on T2WI with hypovascularity

Prognosis: 5-year survival rate of < 5%

Clear Cell Renal Cell Carcinoma (cRCC)

= CONVENTIONAL RCC = cRCC
Prevalence: 60–80% of all RCCs
Associated with: von Hippel–Lindau syndrome
Origin: derived from epithelium of proximal convoluted tubule → cortical location and expansile growth
Path: central necrosis (common); may be predominantly cystic with only minor solid enhancing component
Histo: rich in cytoplasmic glycogen + lipid content that washes away (hence "clear") during tissue processing; extensive thin-walled sinusoid-like vessels
Genetics: translocation of short arm of chromosome 3; mutation of von Hippel–Lindau tumor suppressor gene → synthesizes protein that suppresses hypoxia-induced genes involved in angiogenesis
Location: in cortex as exophytic hypervascular solid mass
√ heterogeneous appearance ← macroscopic areas of necrosis, hemorrhage, cystic changes, calcifications
√ greater degree of enhancement than other subtypes ← CHARACTERISTIC network of small sinusoid blood vessels
MR:
- √ tumor isointense to renal parenchyma on T1WI
- √ tumor hyperintense to renal parenchyma on T2WI
- √ SI loss within solid portions on opposed-phase compared with in-phase images ← cytoplasmic fat (in 60%)
- √ ± hypointense rim on both T1- and T2-weighted images = pseudocapsule of compressed adjacent renal parenchyma:
  - √ interruption of pseudocapsule ← invasion of perirenal fat in advanced tumor stage
- √ imaging of tumor necrosis:
  - √ homogeneously hypointense area in center of mass on T1WI that is hypo- to hyperintense on T2WI
  - √ solid rim of tumor peripherally
  - √ lack of enhancement in necrotic area + marked enhancement of viable tumor component
- √ imaging of intratumoral hemorrhage:
  - √ high signal intensity on both T1- and T2WI = subacute to chronic hemorrhage
  - √ hypointense on both T1- and T2WI = long-standing hemorrhage predominantly containing hemosiderin
- √ hypervascularity during cortical phase ← network of small sinusoid-like blood vessels
- √ renal vein tumor thrombus = higher-stage tumor

Prognosis: 5-year survival rate of 55–60%; poorer than for chromophobe or pRCC

Cystic Renal Cell Carcinoma

Prevalence: 4–15% of all RCCs
Spectrum:

(a) **Unilocular cystic RCC** (50%)
= extensive necrosis of a previously solid RCC / intrinsic cystic growth of a cystadenocarcinoma / papillary RCC
√ fluid-filled mass without criteria of a renal cyst
(b) **Multilocular RCC** (30%)
= intrinsic multilocular growth; impossible to distinguish from multilocular cystic nephroma
√ septated variable-sized cysts + septal calcifications
(c) **Mural nodule in cystic RCC** (20%)
√ asymmetric cystic tumor necrosis
√ tumor arising in wall of preexisting cyst
√ tubular dilatation with secondary cyst formation from tumor obstruction

√ characteristics of a fluid-filled cystic mass:
√ calcifications
√ atypical contents:
√ high attenuation > 20 HU at NECT
√ signal intensity atypical for water at MRI
√ solid component with internal echoes failing to show acoustic enhancement at US
√ septations
√ multiple locules
√ contrast enhancement
√ wall thickening > 2–3 mm
√ nodularity

CT (triple phase):
√ > 15 HU change within solid portion (DDx: cystic angiomyolipoma, oncocytoma, infection)
√ rarely 10–15 HU change (DDx: papillary RCC, volume averaging, motion, streak artifact, imperfect placement of ROI)

DDx: complicated renal cyst

Metastatic Renal Cell Carcinoma

18–28% of patients have clinically apparent multiple synchronous distant metastases at presentation

50% will develop metachronous metastases during follow-up after nephrectomy (in 85% within 3 years)

Incidence of metastatic disease:

(a) tumors < 3 cm : 2.6%
(b) tumors 3–5 cm : 15.4%
(c) tumors > 5 cm : 78.6%

Number of sites: single÷multiple sites = 3÷2

Spread to:

lung (45–55%) > bone (32%) > lymph nodes (22–34%); liver (20–33%); pancreas(1.6–11%); adrenals (4.3–19%); contralateral kidney (11%); brain (6%); heart (5%); spleen (5%); bowel (4%); skin (3%); ureter (rare)

(a) hematogenous: venous extension (20–35%)
› ascending into IVC → right chambers → lung → systemic circulation
› descending (= venous reflux) into adrenal, gonadal, second lumbar veins → (often ipsilateral) ovary / testis / adrenal gland
› with venous thrombosis → retroperitoneal and paravertebral Batson plexus
(b) lymphatic:
» regional lymph nodes (N): renal hilar and retroperitoneal (paraaortic + paracaval) nodes
› mediastinal, pelvic, inguinal nodes (M1)
› invasion of thoracic duct → thoracic (mediastinal and hilar) / supraclavicular nodes

• cough, bone pain, hemoptysis (as initial symptoms of metastatic disease present in 9%)

CT:
√ tumor metastases tend to be hypervascular
√ some metastases (eg, clear cell RCC) are detected only during arterial phase
√ hypovascular metastases are best detected during the nephrographic phase

Bone scintigraphy:
√ negative uptake for bone metastases if lesion purely lytic without associated reactive bone formation

Papillary Renal Cell Carcinoma (pRCC)

Prevalence: 10–15% (2nd most common) of all RCCs
Age: 3rd–8th decade; M÷F = 2÷1 to 4÷1
Origin: derived from epithelium of proximal convoluted tubules
Associated with: end-stage renal disease
Path: cystic necrosis + degeneration frequent; familial form associated with trisomy 7 & 17 & loss of Y chromosome in males (similar to papillary adenoma)
Histo: cells surrounding fronds of delicate fibrovascular core; macrophages infiltrating papillary stalks
(a) basophilic = small cuboidal cells with uniform nuclei covering thin papillae
(b) eosinophilic = large eosinophilic cells with pleomorphic nuclei
Growth pattern: papillary, tubular, tubulopapillary
Location: most common of multifocal / bilateral renal tumors!
√ typically hypovascular → enhances to a lesser degree compared with clear cell RCC
√ homogeneous slow growing well-encapsulated tumor
√ peripheral calcifications frequent

CECT:
√ little contrast enhancement in all phases to a lesser degree than renal cortex (DDx to hypervascular cRCC)
√ usually homogeneous enhancement if < 3 cm
√ heterogeneous enhancement if > 3 cm (DDx to usually homogeneously enhancing chromophobe RCC)

MR:
√ fibrous capsule (frequent)
√ hypointense on T1WI + T2WI (DDx to hyperintense cRCC on T2WI)
√ low-grade basophilic (type I) tumor:

√ homogeneously low SI on T2WI
√ hypovascular homogeneous low-level enhancement
√ high-grade eosinophilic (type II) tumor:
√ complex tumor appearance ← hemorrhage + necrosis
√ enhancing papillary projections at periphery of cystic hemorrhagic mass
US:
√ frequently hypoechoic mass
Prognosis: 5-year survival rate of 80–90%; favorable (smaller mean diameter, lower stage, later metastases than cRCC)
DDx: renal cyst (enhancement of < 10 HU / pseudoenhancement, cyst by US + MR)

Renal Cell Carcinoma in Childhood

Frequency: 7% of all primary renal tumors during first 2 decades of life;
in childhood: Wilms tumor÷RCC = 30÷1
in 2nd decade: Wilms tumor÷RCC = 1÷1
Mean age: 9 years
• palpable abdominal mass (60%), abdominal pain (50%)
• hematuria (30–60%), hypertension due to renin production
• polycythemia ← erythropoietin production
• bone resorption ← parathyroid hormone production
Increased risk of renal cell carcinoma:
Von Hippel-Lindau disease in 10–25% (cerebellar hemangioblastoma, retinal angioma, pancreatic cysts + tumors, pheochromocytoma, renal cysts + tumors)
Metastases (20%): lung, bone, liver, brain
Cx: intravascular extension (25%)
Prognosis: 64% overall survival rate
DDx: Wilms tumor (younger age, larger at presentation, calcifications less frequent [9% versus 25%], less dense / homogeneous)

RENAL CYST

Simple Cortical Renal Cyst

= acquired lesion possibly secondary to tubular obstruction; accounts for 62% of all renal masses
Frequency: in 1–2% (3–5%) of all urograms (autopsies)
Age: peak incidence after age 30; increasing frequency with age (0.22% in pediatric age group, 50% over age 50)
Path: low cuboidal / flattened epithelium surrounded by 1–2-mm thick fibrous wall containing clear / slightly yellow serous fluid
May be associated with:
tuberous sclerosis, Von Hippel-Lindau disease, Caroli disease, neurofibromatosis
√ large and unifocal when peripheral
√ focal attenuation + displacement of collecting system
√ focally replaced nephrogram with smooth margin
√ "beak / **claw**" sign = effaced wedge of renal parenchyma

√ delicate filamentous often undulating septa (10–15%)
√ curvilinear calcification (1–3%) in wall / septa
√ milk of calcium in dependent portion = always benign

CT / MR Features of Cystic Renal Lesions
Bosniak Classification

Class	*Description*	*Findings*	*Malignant*
I	simple cyst	√ well-defined round mass of water attenuation √ hairline-thin smooth imperceptible wall √ no enhancement	~ 0%
II	minimally complicated cyst	√ cluster of cysts / septated cyst √ fine curvilinear calcification √ minimally irregular wall √ high-density content in < 3 cm cyst	~ 0%
IIF	Follow-up lesion (initially 6 months, then yearly)	√ several hairline-thin septa √ wall / septa with perceived enhancement √ thick nodular calcium √ intrarenal >3 cm high-density lesion	~ 5%
III	complicated (surgical) lesion: hemorrhagic / infected cyst, MLCN, cystic neoplasm	√ irregular thickened septa √ measurable enhancement √ coarse irregular calcification √ irregular margin √ multiloculated lesion √ uniform wall thickening √ nonenhancing nodular mass	~ 50%
IV	clearly malignant cystic lesion	√ large cystic / necrotic component √ irregular wall thickening √ solid enhancing elements	> 90%

N.B.: measurement of cyst wall thickness not accurate in a completely intrarenal cyst

US (90–100% accuracy of US & CT):
- √ spherical / ovoid in shape
- √ anechoic content without internal echoes
- √ smooth clearly demarcated back wall
- √ acoustic enhancement of tissue beyond cyst (= positive through transmission) ← unattenuated sound reflections
- √ refraction along sidewalls

CT (100% accuracy):
- √ near-water–density lesion (0–20 HU) with thin wall + smooth interface with renal parenchyma
  - *N.B.:* Accuracy of HU measurements depends on: patient size, mass size, size of region examined, CT scanner type & manufacturer, CT technique, image noise, partial

volume averaging, pseudoenhancement

√ no enhancement (< 12 HU)

MR:

√ most sensitive modality for cysts < 10 mm

√ < 15% enhancement after 0.1 mmol/kg gadolinium on spoiled GE T1WI without fat sat and without retuning = $(SI_{post} - SI_{pre}) \div SI_{pre} \times 100$

Cystography:

√ smooth wall, clear aspirate with low lactic dehydrogenase, no fat content

Cx: (1) Hemorrhage in 1–11.5%

(2) Infection in 2.5%

(3) Tumor within cyst in < 1%

PSEUDOENHANCEMENT

= artificial elevation of Hounsfield unit measurements of renal cyst measured on CECT images

◊ Most frequently occurs in intrarenal cyst of < 2 cm during peak parenchymal enhancement

Cause: secondary to image reconstruction algorithm used to adjust for beam-hardening effects

√ simple fluid attenuation of < 10 HU on NECT images

√ simple renal cyst mischaracterized as solid mass

Recommendation if suspected: US / MR

Atypical / Complicated Renal Cyst

Path: calcification, hemorrhage, septations, wall-thickening, nodularity

Histo: inflammatory cells + granulation tissue + neovascularity ← host reparative response to hemorrhage, infection, inflammation, ischemia

US:

√ cyst content of low-level echoes / layers of echoes

√ cyst septations ± reverberation artifacts

√ ± shadowing calcifications

CT:

› Bosniak II cyst

√ fine calcifications ± short segment of slightly thickened calcification in cyst wall / septa

√ ± few hairline-thin septa

√ nonenhancing homogeneously hyperattenuating (> 20 HU) lesion measuring ≤ 3 cm

› Bosniak IIF cyst (0.01% chance of malignancy)

√ several thin internal septations without measurable enhancement

√ few nodular calcifications

√ smooth thickening of cyst wall

√ nonenhancing hyperattenuating (> 20 HU) cyst > 3 cm ± completely intrarenal

◊ cyst content of > 70 HU on NECT in > 99.9% benign

› Bosniak III cyst (30–100% chance of malignancy)

√ thick irregular walls ± numerous septa with measurable enhancement

√ ± thick nodular calcifications in cyst wall and septa

DDx: RCC, cystic nephroma, mixed epithelial and stromal tumor (MEST), benign multiloculated cyst, hemorrhagic cyst, renal abscess, hematoma, renal artery aneurysm

Rx: serial follow-up, surgery

› Bosniak IV cyst (= malignant until proven otherwise)

√ enhancing nodular soft-tissue component

Rx: surgery

Dx: cyst puncture + aspiration

Hemorrhagic Renal Cyst

Cause: trauma, varices, bleeding diathesis

• rust-colored puttylike material

√ uni- / multilocular cyst separated by thick septa

√ thick fibrous ± calcified wall

√ fibrin ball inside cyst (rare)

CT:

√ increased density ← acute hemorrhage / high protein contents (= hyperattenuating cyst with ~ 60–90 HU)

√ no contrast enhancement

MR:

√ usually iso- to hyperintense on T1WI ← methemoglobin + hyperintense on T2WI ← lysis of RBCs

√ NO suppression on fat-saturated T1WI

√ variable signal intensities (dependent on amount + acuity of hemorrhage, hemoglobin degradation product, degree of RBC lysis, protein content)

√ hematocrit effect ← settling of RBCs at cyst bottom

Infected Renal Cyst

Cause: hematogenous dissemination of bacteria, ascending urinary tract infection

Mean age: 61 years; in 94% females

• history of no response to antibiotic Rx for acute pyelonephritis; leukocyturia

US:

√ thickened irregular cyst wall (22%)

√ internal septations (11%)

√ wall calcification (occasionally)

√ minute debris either diffusely / fluid-fluid level in dependent portion of cyst

√ amorphous solid conglomerates

√ round sharply marginated lesion

High-density Renal Cyst

= completely homogeneous cyst content ≥ 20 HU (often 50–90 HU) without enhancement

1. Proteinaceous content (20–40 HU)
   √ simple cyst on US
2. Hemorrhage (> 40 HU)

√ complex cyst on US

3. Infection
4. Calcification
5. Communication with calyx
6. Streak artifact

√ pseudoenhancement *(see above)*

◊ Cyst wall cannot be evaluated in high-attenuation cysts!

◊ Considered a Bosniak Class II lesion if:
≤ 3 cm in size, partially exophytic, round, sharply marginated, homogeneous, nonenhancing

◊ A homogeneous renal mass with attenuation > 70 HU on NECT is benign with a 99% probability!

Cyst of Renal Pelvis

= generic term for spherical fluid-filled mass intimately attached to renal pelvis without connection to pelvicaliceal system

Prevalence: 1.5% (autopsies); 4–6% of all renal cysts

Age: mostly during 5th–6th decade

• clear straw-colored serous fluid

√ soft-tissue density in renal sinus

√ anechoic mass(es) with acoustic enhancement

DDx: hydronephrosis

Renal Sinus Cyst

= PERIPELVIC CYST = PARAPELVIC LYMPHATIC CYST = PARAPELVIC LYMPHANGIECTASIA

= multiple small confluent cysts arising from renal sinus

Etiology: probably ectatic lymphatic channels from lymphatic obstruction; ? posttraumatic extravasation of urine / blood; ? mesonephric remnant; ? remnant of wolffian body; ? outpouchings of renal pelvis; ? duplication anomaly

• almost always asymptomatic

Location: frequently bilateral

√ multiple small renal sinus cysts

√ focal displacement + smooth effacement of collecting system

√ rarely curvilinear calcification of cyst wall (4%)

IVP:

√ stretching of collecting system when generalized (indistinguishable from sinus lipomatosis)

NECT / US:

√ multiple confluent cysts (mimicking hydronephrosis)

CECT:

√ high-attenuation contrast fills collecting system but not cyst

Prognosis: NO change on long-term follow-up

Parapelvic Cyst

= protrusion of medial parenchymal cyst into sinus fat

Histo: lined with single epithelial layer
- hematuria ← cyst rupture
- pain ← obstructive caliectasis / infection
- renovascular hypertension ← compression of renal arteries

Location: usually single unilateral cyst, may be multiple

√ simple cortical renal cyst that extends into renal sinus fat

Cx: (1) Caliectasis / localized hydronephrosis) ← compression of collecting system
(2) hypertension ← compression of renal artery
(3) infection, hemorrhage

Rx: cyst ablation with 95% ethanol if symptomatic

RENAL DYSGENESIS

= undifferentiated tissue of renal anlage

◊ Pathologic NOT radiologic diagnosis

√ renal vessels usually absent; occasionally small vascular channels

RENAL INFARCTION

Cause:

1. TRAUMA
   blunt abdominal trauma with traumatic avulsion / occlusion of renal artery, penetrating vascular injury, surgery
2. EMBOLISM
   (a) Cardiac: rheumatic heart disease with arrhythmia (atrial fibrillation), myocardial infarction, prosthetic valve, myocardial trauma, left atrial / mural thrombus, myocardial tumor, subacute bacterial endocarditis → septic emboli
   (b) Catheters: angiographic catheter manipulation, transcatheter embolization, umbilical artery catheter above level of renal arteries
3. ARTERIAL THROMBOSIS
   arteriosclerosis, aneurysm or dissection of aorta / renal artery, thrombangiitis obliterans, polyarteritis nodosa, syphilitic cardiovascular disease, sickle cell disease, paraneoplastic syndrome (Trousseau syndrome), hypercoagulable state
4. VASCULITIS
   polyarteritis nodosa, SLE, drug-induced vasculitis
5. Sudden complete renal vein thrombosis

Acute Renal Infarction

- sudden onset of flank / back pain
- ± hematuria, proteinuria, fever, leukocytosis

√ normal / large kidney with smooth contour

√ normal / expanded parenchymal thickness

√ normal / attenuated collecting system, often only opacified by retrograde pyelography

√ absent / diminished nephrogram with cortical rim enhancement, rarely striations

CT:

√ wedge-shaped area of absent enhancement

√ edematous enlargement of kidney (with large infarct)
√ "cortical rim" sign within several days after global infarction

US:
√ diminished echogenicity (within < 24 hours)
√ normal echogenicity (echoes appear within 7 days)

NUC (SPECT imaging with ^{99m}Tc-DMSA):
√ photon-deficient area

Rx: thrombolytic therapy, supportive hemodialysis, transcatheter thrombembolectomy, surgery

Lobar Renal Infarction

Early signs:
√ focal attenuation of collecting system ← tissue swelling
√ focally absent nephrogram (triangular with base at cortex)

Late signs:
√ normal / small kidney(s)
√ focally wasted parenchyma with NORMAL interpapillary line (portion of lobe / whole lobe / several adjacent lobes)

CT:
√ nonperfused area corresponding to vascular division
√ "cortical rim" sign (subacute) = thin rim of preserved subcapsular perfusion ← capsular perforators

US:
√ focally increased echogenicity

Chronic Renal Infarction

Path: all elements of kidney atrophied with replacement by interstitial fibrosis
√ normal / small kidney with smooth contour
√ globally wasted parenchyma
√ diminished / absent contrast material density

US:
√ increased echogenicity (by 17 days)

Angio:
√ normal intrarenal venous architecture
√ late visualization of renal arteries on abdominal aortogram

Atheroembolic Renal Disease

= dislodgment of multiple atheromatous emboli from the aorta into renal circulation → below level of arcuate arteries
√ normal / small kidneys with smooth contour or shallow depressions
√ wasted parenchymal thickness
√ diminished density of contrast material

CT:
√ patchy nephrographic distribution

Angio:

√ embolic occlusion

Arteriosclerotic Renal Disease

= disseminated process involving most of the interlobar + arcuate arteries causing uniform shrinkage of kidney

Age: generally over 60 years

Accelerated development in:

scleroderma, polyarteritis nodosa, chronic tophaceous gout

• often associated with hypertension (= nephrosclerosis)

√ normal / small kidneys

√ smooth contour with random shallow contour depressions ← infarctions

√ uniform loss of cortical thickness

√ normal / effaced collecting system ← fat proliferation

√ increased pelvic radiolucency (vicarious sinus fat proliferation)

√ calcification of medium-sized intrarenal arteries

US:

√ increased echogenicity possible

√ increased size of renal sinus echoes ← fatty replacement

Nephrosclerosis

Histo: thickening + hyalinization of afferent arterioles, proliferative endarteritis, necrotizing arteriolitis, necrotizing glomerulitis

• arterial hypertension

(a) benign nephrosclerosis

(b) malignant nephrosclerosis (rapid deterioration of renal function)

√ radiographic appearance similar to arteriosclerotic kidney

RENAL SARCOMA

Frequency: 1% of malignant renal parenchymal tumors

Subtypes: leiomyosarcoma (> 50%), angiosarcoma, hemangiopericytoma, rhabdomyosarcoma, fibrosarcoma, osteosarcoma

√ considerable variation in growth pattern:

√ expansile mass (most commonly)

√ infiltrative growth (rhabdomyosarcoma, angiosarcoma)

Dx: by exclusion of sarcomatoid renal carcinoma + primary retroperitoneal sarcoma with direct extension into kidney

RENAL TRANSPLANT

Frequency: 316,493 transplants between 1988 and 2012 in US; 17,107 transplants annually in USA (2014)

Complications in 10%:

◊ Problematic period between 4 days and 3 weeks after surgery!

• hypertension in 50% (from rejection / arterial stenosis)

(a) immediate: ATN, acute humeral rejection, renovascular thrombosis, perinephric hematoma, graft infection + abscess

(b) early (> 1–4 weeks): acute rejection, renal vein thrombosis, urinary tract obstruction, urine leak, urinoma

(c) late (> 1 month): acute + chronic rejection, ureteral stricture, VUR, renal artery stenosis, arteriovenous fistula, pseudoaneurysm, lymhocele, seroma

Prognosis: organ survival at 1 (5) years in 89–95% (67–80%); 13–24 years half-life for transplant from living related donor

Renal Allograft Dysfunction *relative to Time since Surgery*	
Immediate to 1st 48 hr	*Day 2 to 7*
1. Hyperacute rejection	1. ATN
2. Renal vein thrombosis	2. RVT
3. Discordant size	
>1 week postop	*Delayed*
1. Acute rejection	1. Chronic rejection
2. ATN	2. Drug toxicity
	3. Obstruction
	4. Infection
	5. Extrinsic compression

Renal Transplant Scintigram				
	Early study (<24 hr post transplantation)		*Late study (>5 days post transplantation)*	
	Flow	*Excretion*	*Flow*	*Excretion*
Acute tubular necrosis	normal / ↓	↓	normal / ↓	↓
Hyperacute rejection	absent	absent		
Acute rejection	↓	↓	worsening	worsening
Chronic rejection	↓	↓	↓	↓

Acute Tubular Necrosis in Renal Transplant

= primary nonfunction within 72 hours of transplantation followed by improvement within a few days to 1 month

◊ Most common cause of "delayed" graft function"

Cause: preservation injury ← prolonged ischemia (cold ischemia time > 24–30 hours), reperfusion injury

› ATN more frequent in cadaveric than living-related donor transplant ← donor hypotension

› ATN greater in transplants with > 1 renal artery

› ATN related to length of ischemic interval ← prolonged organ storage

Histo: sloughed renal tubular epithelium + surrounding edema

Pathophysiology: relative preservation of renal perfusion + minimal / absent urinary excretion

• no constitutional symptoms; elevated urine sodium

• oliguria may begin immediately after transplantation / may be delayed for several days

US:

√ transient enlargement of transplant

√ transient increase in resistive index

NUC (^{99m}Tc mertiatide preferred):

= 1st-line imaging modality!

◊ Limited diagnostic value if serum creatinine > 6 mg/dL

√ normal / slightly decreased transplant perfusion:

√ delayed time from Tmax to one-half maximal activity

√ decreased + delayed radiopharmaceutical uptake:

√ delayed transit time + delayed Tmax

√ delayed / decreased / absent excretion of radiotracer with prolonged cortical retention:

√ high 20-minute to 3-minute ratio

DDx: acute rejection (serial studies help to differentiate)

Rejection of Renal Transplant

◊ Most common cause of parenchymal failure!

◊ Rejection occurs in all transplants to some degree!

Hyperacute Rejection of Renal Transplant (rare)

= humeral rejection with preformed circulating antibodies present in recipient at time of transplantation, usually following retransplantation

Path: thrombosed arterioles + cortical necrosis

Time of onset: within minutes after transplantation

◊ In practice never imaged!

√ complete absence of renal perfusion + renal function on ^{99m}Tc-DTPA scan (DDx: complete arterial / venous occlusion)

Rx: requires immediate reoperation

Accelerated Acute Rejection of Renal Transplant

= combination of antibody + cell-mediated rejection

Time of onset: 2–5 days after transplantation

Acute Rejection of Renal Transplant (in up to 40%)

= cellular rejection predominantly dependent on cellular immunity

◊ Most common type of allograft rejection

Time of onset: any time, typically within 5 days to 6 months; peak incidence at 2nd–5th week

Prevalence: in 50% at least 1 episode in 1st year

Path:

(a) acute interstitial rejection

= edema of interstitium with lymphocytic infiltration of capillaries + lymphatics

(b) acute vascular rejection (rare)

= proliferative endovasculitis + vessel thrombosis

• malaise, fever, weight gain; graft tenderness

• low urine sodium, increase in serum creatinine

• hypertension, oliguria, proteinuria

US (30–50% negative predictive value):

√ increase in renal volume from edema:

√ ↓ renal sinus fat + ↑ cortical thickness (most predictive)

√ loss of corticomedullary differentiation

√ thickening of pelvoinfundibular wall

√ diminished echogenicity of renal sinus fat

Doppler US (higher accuracy than morphologic parameters):

√ initially decrease in resistive index (? autoregulatory mechanism)

√ increase in resistive index > 0.80 (with increasing severity of rejection)

(a) ≤ 0.70 without any form of rejection (57% NPV)

(b) > 0.90 (100% PPV, 26% sensitivity)

√ reversal of diastolic flow

NUC:

√ typically ↓ renal perfusion + ↓ graft function + high background radiotracer activity

√ initially perfusion may be normal with only function decreased (DDx to ATN may not be possible on single study)

√ subsequent exams (1–3-day intervals) demonstrate decreasing renal perfusion

√ prolonged excretory phase

√ poor and inhomogeneous nephrogram

Angio:

√ rapid tapering + pruning of interlobar arteries

√ multiple stenoses + occlusions

√ nonvisualization of interlobular arteries

√ prolonged arterial opacification (normally < 2 seconds)

DDx: acute tubular necrosis (develops within first few days)

Chronic Rejection of Renal Transplant

= slow relentless progressive process resulting in interstitial scarring

◊ Most common cause of late graft loss

Histo: endothelial proliferation in small arteries + arterioles; interstitial cellular infiltration + fibrosis; tubular atrophy; glomerular lesions (? recurrence of patient's original glomerulonephritis)

Time of onset: months to years after transplantation

• progressive decline of renal function

√ progressive volume loss → small kidney with thin cortex

√ diminished number of intrarenal vessels

√ vascular pruning / stenoses / occlusions → commonly focal cortical scarring

√ mild hydronephrosis

NUC:

√ small graft with poor perfusion + globally decreased function

Drug Nephrotoxicity

Nephrotoxic potential of calcineurin inhibitors:

cyclosporine (vasoconstrictive effect on afferent glomerular arterioles) > OKT3 >

tacrolimus (FK-506)
◊ Effects are dose-dependent and accentuated by dehydration + decreased renal perfusion
Action: impedes rejection process with narrow therapeutic window
Histo: (a) acutely: damage to tubules, microthrombosis of kidney ← activation of coagulation cascade
(b) chronically: hyaline deposition within arterial walls
√ no change in renal size
√ no change (?) / elevation of resistive index
NUC:
√ depressed effective renal plasma flow
√ no parenchymal retention

Urologic Problems with Renal Transplant

◊ US is 1st-line imaging modality!

Ureteral Obstruction of Renal Transplant *(2–10%)*
(a) acute: secondary to technical problems
(b) late: secondary to ischemia / previous extravasation
Cause: ischemic stricture (most commonly at ureterovesical junction), ureteral kinking, (transient) edema at ureteroneocystostomy, ureteropelvic fibrosis, crossing vessels, blood clot, fungus ball, calculus, tumor, perinephric fluid collection (hematoma, lymphocele)
• rising serum creatinine level, oliguria
√ pyelocaliectasis
√ normal resistive index strongly argues against obstruction unless ureteral leak is present
NUC (only 18% sensitive ← impaired uptake)
DDx: diminished ureteral tone ← denervation

Urine Extravasation of Renal Transplant *(1–5%)*
Cause:
(1) Distal ureteral necrosis ← interruption of blood supply (early) / vascular insufficiency ← rejection (late)
(2) Leakage from ureteroneocystostomy site (related to surgical technique / distal ureteral necrosis)
(3) Leakage from anterior cystostomy closure site
(4) Segmental renal infarction
• high creatinine level in fluid collection
Prognosis: high morbidity + mortality ← death from transplant infection + septicemia

Paratransplant Fluid Collection *(in up to 50%)*
Dx: percutaneous fluid aspiration
Cx: Page kidney
(1) **Lymphocele** (0.6–18%)
Onset: within 4–8 weeks after transplantation
√ mean diameter of 11 cm

√ thick septa (50%) + internal debris
DDx: urinoma (radiotracer uptake)

(2) **Urinoma** (rare)
Onset: in early postoperative period

(3) **Hematoma, seroma, abscess**
Onset: in early postoperative period
√ small crescentic peritransplant fluid collection (as normal sequelae of surgery)
√ photopenic region with displacement / impression on renal transplant / urinary bladder
Prognosis: small hematomas typically resolve spontaneously within a few weeks

mnemonic: HAUL
Hematoma
Abscess
Urinoma
Lymphocele

Vascular Problems with Renal Transplant (10%)

◊ Doppler US is 1st-line imaging modality!

A. PRERENAL

1. **Renal artery stenosis** (1–4%)
◊ Transient elevation of velocities in immediate postop. period ← vessel wall edema / arterial spasm!
Time of onset: late = within 3 years; cadaver kidney > young donor kidney > living-related donor kidney
Location:
(a) short-segment stenosis at anastomosis: technical (75%)
Cause: use of clamp / cannula, trauma, ischemia of donor vessel
(b) long-segment stenosis of proximal artery (close to anastomosis) > distal artery
Cause: trauma during allograft harvesting, faulty operative technique, chronic rejection, atherosclerosis, kinking, scar formation
• recent onset of hypertension / severe hypertension refractory to multiple drug regimens
◊ 1–5% of all causes of posttransplant hypertension (nonrenovascular hypertension in 65%)
• unexplained graft dysfunction
• nonspecific audible bruit over graft (occasionally)
√ surrounding soft-tissue "speckle" ← vibration
√ increase in peak systolic velocity > 180–210 cm/s
√ 2÷1 ratio between peak stenotic and poststenotic velocities
√ main renal artery / external iliac artery ratio > 3.5 (normally < 2.0)
√ marked poststenotic turbulence (supportive evidence)
√ dampened signals distal to stenosis (= tardus-parvus waveform)
√ increase in acceleration time (= pulse rise time) of intrarenal arteries
NUC (low sensitivity):
√ ↓ perfusion + cortical uptake, photopenic graft

Angio:
√ standard test for detection of arterial stenosis ± intravascular treatment
Cx (0.5–2.3%): hemorrhage, intimal flap, AV fistula

2. **Renal artery thrombosis** (1–6%)
Cause: rejection, faulty surgical technique (torsion / kinking / angulation of anastomosis)
Time of onset: within first 48 hours – 1st week
Predisposed: allografts with disparate vessel size, multiple anastomoses, arterial dissection ← faulty handling, rejection
• early sudden onset of anuria
• graft tenderness + swelling
(a) global
√ absence of perfusion, uptake, excretion
√ failure to demonstrate intrarenal arterial / venous flow
Prognosis: graft loss
(b) segmental (late complication)
√ segmental infarction ← occlusion of polar artery
√ hypo- / hyperechoic area ± cortical thickening
√ no flow in affected area

3. **Pseudoaneurysm** (in up to 17%)
Cause: percutaneous biopsy with laceration of arterial wall, faulty surgical technique, perivascular infection
Location:
(a) extrarenal at anastomotic site (uncommon): ← suture rupture, anastomotic leakage, vessel wall ischemia
(b) intrarenal, mostly of arcuate arteries: following needle biopsy, mycotic infection
√ mimics renal cyst
√ disorganized flow / to-and-fro waveform
Prognosis: spontaneous regression frequent
Cx: spontaneous rupture

4. **Arteriovenous fistula** (in 2–18%)
Cause: percutaneous biopsy with simultaneous laceration of artery and vein, faulty surgical technique, perivascular infection
• hypertension, hematuria, high-output cardiac failure
US:
√ high-velocity low-resistance flow in feeding artery
√ pulsatile "arterialized" waveform in draining vein
√ turbulence + high-frequency velocity shift
√ exaggerated focal color around lesion (= bruit = perivascular soft-tissue vibration)
Angio (gold standard + allows treatment):
√ rapid contrast appearance in IVC
√ decreased density on nephrogram
Prognosis: 70% resolve within 1–2 years

Cx: renal ischemia (with large lesion), persistent hematuria, rupture

5. **Renal allograft necrosis / infarct**

= total lack of perfusion in an area of renal cortex associated with variable degrees of medullary necrosis

Cause: rejection, surgical ligature, preexistent arterial lesion, severe ATN, prolonged time of warm ischemia

Pattern:

1. Small focal necrosis
2. Large isolated area of infarction ← segmental arterial occlusion)
3. Outer cortical necrosis
4. Cortical necrosis with large patches
5. Diffuse cortical necrosis
6. Cortical + medullary necrosis
7. Necrosis of whole kidney ← occlusion of main renal artery

MR:

√ slightly hyperintense ← ischemic necrosis / hypointense ← hemorrhagic necrosis / isointense area on T2WI

√ hypointense areas on Gd-DTPA images

US:

√ hypoechoic ← ischemic necrosis / iso- or hyperechoic areas ← hemorrhagic necrosis

√ swollen area ← probably cortical edema

√ absence of arterial perfusion by color duplex (not sensitive for small infarcts / superficial cortical necrosis)

√ elevated resistive indexes + no / reversed diastolic flow

B. POSTRENAL

1. **Renal / iliac vein thrombosis** (4.2–5%)

Cause:

(a) immediately: injury to epithelium at site of renal vein anastomosis, extrinsic compression by fluid collection (hematoma, lymphocele)

(b) after 1st week: acute rejection, reduced intrarenal arterial flow, hypovolemia, propagation of iliofemoral vein thrombosis

• abrupt onset of oliguria, graft tenderness

• hematuria, proteinuria

√ enlarged hypoechoic transplant

√ prolonged arterial transit time without arterial occlusions + arterial spasms

√ diminished cortical perfusion

√ absent venous flow

√ "U-shaped" / plateau-like reversal of diastolic arterial flow

√ decreased systolic rise time

NUC:

√ lack of perfusion (but no graft photopenia)

2. **Renal vein stenosis**

Cause: perivascular fibrosis, compression from adjacent perinephric fluid collection

√ color aliasing

√ 3–4-fold increase in velocity

High Vascular Impedance of Renal Transplant

= pulsatility index (A – B ÷ mean) > 1.8 or resistive index (A – B ÷ B) of Doppler signals of 0.75–0.80 indicate a reduction in diastolic flow velocity

Cause:

(a) intrinsic vascular obstruction
   1. Acute vascular rejection (later stage)
   2. Renal vein obstruction

(b) increased intraparenchymal pressure
   1. Severe ATN
   2. Severe pyelonephritis:
      CMV, herpes, E. coli, C. albicans
   3. Extrarenal compression:
      large collection, hematoma, discordant size
   4. Urinary obstruction (doubted!)
   5. Excessive pressure by transducer

Gastrointestinal Problems with Renal Transplant

Prevalence: 40%

1. Gastrointestinal hemorrhage
   (a) upper GI tract bleeding:
      gastric erosions, gastric / duodenal ulcers
      Mortality rate: 2–3 x of normal
   (b) lower GI tract bleeding:
      hemorrhoids, pseudomembranous colitis, cecal ulcers, colonic polyps
2. GI tract perforation (3%)
   Cause: spontaneous, antacid impaction, perinephric abscess, diverticular disease
   Location: colon > small bowel > gastroduodenal
   Mortality rate: approaches 75% (because of delayed Dx)

Hypertension with Renal Transplant

◊ Leading cause of death in renal transplant recipient!

Prevalence: up to 60% 1 year after transplantation

Cause:

A. TRANSPLANT RELATED
   1. Acute transplant rejection
   2. Chronic rejection
   3. Cyclosporine toxicity
   4. Ureteral obstruction
   5. Renal artery stenosis (1–5%)
      (a) accelerated atherosclerosis
      (b) postsurgical fibrosis at anastomosis

B. NOT TRANSPLANT RELATED
   1. Renin production of native kidney

2. Original renal disease involving transplant
3. Development of essential hypertension

Aseptic Necrosis with Renal Transplant

Most common long-term disabling complication; femoral head most common site; bilateral in 59–80%

Frequency: 6–15–29% within 3 years after surgery

Mean time of onset: 9–19 (range, 5–126) months after transplantation when symptoms develop

Risk factors:

dose + method of glucocorticoid administration, duration + quality of dialysis before transplantation, secondary hyperparathyroidism, allograft dysfunction, liver disease, previous transplantation, iron overload, increased protein catabolism during dialysis

Pathophysiology of corticosteroid therapy:

(1) Fat embolism → fat globules occlude subchondral end arteries
(2) Increase in fat cell volume in closed marrow space → ↑ intramedullary pressure → diminished perfusion
(3) Osteopenia → increased bone fragility
(4) Reduced sensibility to pain → loss of protection against excessive stress

Histo: fragmentation, compression, resorption of dead bone, proliferation of granulation tissue, revascularization, production of new bone

• 40% asymptomatic, joint pain, restriction of movement

Sites: femoral head, femoral condyles (lateral > medial condyle), humeral head

√ subchondral bone resorption
√ patchy osteosclerosis
√ collapse / fragmentation of bone

MR abbreviated T1WI protocol = test of choice!

RENAL TUBULAR ACIDOSIS

= clinical syndrome characterized by tubular insufficiency to resorb bicarbonate, excrete hydrogen ion, or both (= nonanion gap metabolic acidosis)

• failure to thrive

Proximal Renal Tubular Acidosis

= TYPE 2 RTA

= impaired capacity to absorb HCO3 – in proximal tubule → bicarbonate in urine at lower plasma levels than normal

Pathogenesis:

? defect in Na+/HCO3 – cotransport at basolateral membrane; deficit of carbonic anhydrase; parathyroid hormone activates cyclic AMP → inhibits carbonic anhydrase → hypocalcemia of hyperparathyroidism + various types of Fanconi syndrome

• self-limited acidosis (= bicarbonate loss stops once bicarbonate threshold of about 15 mEq/L is reached)

• unimpaired ability to lower urine pH (pH 4.5–7.8 depending on level of plasma bicarbonate) by normal excretion of H+

• hypokalemia ← hyperaldosteronism ← decreased proximal resorption of NaCl
√ rickets / osteomalacia
N.B.: NEVER nephrocalcinosis / nephrolithiasis ← normal urinary citrate excretion, low urine pH, self-limited less severe acidosis with less calcium release from bone
Dx: bicarbonate titration test, large requirement of alkali to sustain plasma bicarbonate level at 22 mmol/L
Rx: administration of alkali ± potassium ± hydrochloro-thiazide

Infantile Type of Primary Proximal RTA

Age: diagnosed within first 18 months of life; usually male patient
- excessive vomiting in early infancy
- growth retardation (< 3rd percentile)
- metabolic hyperchloremic acidosis
- normal quantities of net acid excretion

Prognosis: transient type with spontaneous remission

Secondary Proximal RTA

= tubular defect of bicarbonate resorption associated with other tubular dysfunction / generalized disease

Cause:
› Fanconi syndrome, cystinosis, Lowe syndrome, hereditary fructose intolerance, glycogen storage disease, galactosemia, tyrosinemia, Wilson disease, Leigh syndrome
› 1° + 2° hyperparathyroidism, vitamin D deficiency, mineralocorticoid deficiency, osteopetrosis
› medullary cystic disease, renal transplantation, vascular accident to kidney in newborn period, multiple myeloma, amyloidosis, nephrotic syndrome, cyanotic CHD, Sjögren syndrome
› intoxication with cadmium, outdated tetracycline, methylchromone, 6-mercaptopurine

Distal Renal Tubular Acidosis

= TYPE 1 RTA (first type discovered)
= impaired ability to secrete H+ in distal tubule despite low levels of plasma bicarbonate (urine cannot be acidified with pH invariably high at > 5.5–6.0)

Pathophysiology:

primary defect of nonacidification of urine followed by
(a) hyperchloremia:
small constant loss of serum sodium bicarbonate (NaHCO3) without concomitant loss of chloride (= NaCl retention) → shrinkage of ECF volume
(b) chronic severe + progressive acidosis (← inability to excrete the usual endogenously produced nonvolatile acid) leads to:
› mobilization of calcium + phosphate from bone (osteomalacia)
› growth retardation
› hypercalciuria → 2° hyperparathyroidism
› loss of phosphate → osteomalacia / rickets
(c) nephrocalcinosis + nephrolithiasis ← combination of hypercalciuria + elevated urine

pH + marked reduction in urinary citrate

(d) potassium wastage with hyperkaliuria + hypokalemia ← constant small loss of sodium bicarbonate in urine, reduction of ECF space, 2° hyperaldosteronism, increase in sodium-potassium exchange in distal tubule

Path: calcium deposits accompanied by chronic interstitial nephritis with cellular infiltration, tubular atrophy, glomerular sclerosis

- muscle weakness, hyporeflexia, paralysis ← hypokalemia
- bone pain ← osteomalacia
- polyuria ← defect in urinary concentrating ability as a result of nephrocalcinosis + potassium deficiency
- low plasma bicarbonate, hypokalemia, loss of sodium
- hyperchloremic acidosis ← impaired ability to excrete the usual endogenous load of nonvolatile acid
- alkaline urine = urine pH > 5.0–5.5
- hypercalciuria ← continued mobilization of calcium + phosphate from bone ← metabolic acidosis
- hypocitraturia ← increased proximal tubular reabsorption of citrate

Dx: acid load test with ammonium chloride (NH_4Cl)

Rx: administration of a mixture of sodium + potassium bicarbonate

Cx: interstitial nephritis, chronic renal failure (damage from nephrocalcinosis + secondary pyelonephritis), bone lesions, nephrocalcinosis, nephrolithiasis

Permanent Distal Renal Tubular Acidosis

= ADULT TYPE OF PRIMARY DISTAL RTA = BUTLER-ALBRIGHT SYNDROME

Genetics: mostly sporadic; may be autosomal dominant

Age: children + adults (usually not diagnosed before age 2); F > M

- vomiting, constipation, polyuria, dehydration
- failure to thrive, growth retardation, anorexia
- polyuria ← renal concentrating defect
- potassium loss → flaccid paralysis
- bone pain + pathologic fractures in adolescents + adults ← osteomalacia
- low serum pH, low bicarbonate concentration
- elevation of chloride, urinary pH of 6.0–6.5

√ rickets / osteomalacia

√ moderately retarded bone age

√ medullary nephrocalcinosis / nephrolithiasis (as early as 1 month of age)

Secondary Distal Renal Tubular Acidosis

(a) systemic conditions:

› starvation, malnutrition, sickle cell disease

› primary hyperthyroidism + nephrocalcinosis, 1° hyperparathyroidism + nephrocalcinosis, vitamin D intoxication, idiopathic hypercalcemia, idiopathic hypercalciuria + nephrocalcinosis

› amphotericin B nephropathy, toxicity to lithium, toluene sniffing

› hepatic cirrhosis, fructose intolerance with nephrocalcinosis, Ehlers-Danlos

syndrome, Marfan syndrome, elliptocytosis

(b) renal conditions: renal tubular necrosis, renal transplantation, medullary sponge kidney, obstructive uropathy

(c) hypergammaglobulinemic states (? autoimmune process): idiopathic hypergammaglobulinemia, chronic active hepatitis, hyperglobulinemic purpura, Sjögren syndrome, cryoglobulinemia, systemic lupus erythematosus, lupoid hepatitis, fibrosing alveolitis

Transient Distal Renal Acidosis

= INFANTILE TYPE OF PRIMARY DISTAL RTA

= LIGHTWOOD SYNDROME = SALT-LOSING NEPHRITIS

= transient self-limited form of infancy (only observed within 1st year of life) with unclear pathophysiology, probably due to vitamin D intoxication

• NO nephrocalcinosis

RENAL VEIN THROMBOSIS

Prevalence: 0.5% (autopsy)

Cause:

A. Intrinsic

= thrombotic process begins intrarenally within small intrarenal veins ← acidosis, hemoconcentration, disseminated intravascular coagulation, intrarenal arteriolar constriction reducing venous flow

(a) antenatally: abruptio placentae

(b) neonates (most common): advanced maternal age, glycosuria in infants of diabetic mothers, dehydration from vomiting, diarrhea, enterocolitis, sepsis, polycythemia, birth trauma, left adrenal hemorrhage, prematurity

(c) adults: pyelonephritis, amyloidosis, polyarteritis nodosa, sickle cell anemia, thrombosis of IVC, low flow states (CHF, constrictive pericarditis), diabetic nephropathy, sarcoidosis

› hypercoagulable state:

» nephrotic syndrome: membranous + membrano-proliferative glomerulonephritis (most common), lupoid nephrosis

» SLE

» inherited hypercoagulable state: deficiency of antithrombin III / protein C / protein S

› mechanical process:

» trauma

» neoplasm: renal neoplasia (50%: RCC, TCC, Wilms tumor), left adrenal carcinoma

» abscess

» aneurysm

› left ovarian vein thrombosis

B. Extrinsic umbilical vein catheterization, thrombosis of IVC with extension into renal vein, malpositioned IVC filter, carcinoma of pancreatic tail invading renal vein (in 75%), pancreatitis, lymphoma, retroperitoneal sarcoma, retroperitoneal fibrosis, metastases to

retroperitoneum (bronchogenic carcinoma)

mnemonic: TEST MAN

Thrombophlebitis
Enterocolitis (dehydration)
Sickle cell disease, **S**ystemic lupus erythematosus
Trauma
Membranous glomerulonephritis
Amyloidosis
Neoplasm

Radiographic appearance varies with:

(1) Rapidity of venous occlusion
(2) Extent of occlusion
(3) Availability of collateral circulation
(4) Site of occlusion in relation to collateral pathways

Pathophysiology: formation of collateral channels develops at 24 hours + peaks at 2 weeks after onset of occlusion

Collaterals: ureteral vein to vesicular veins, pericapsular veins to lumbar veins, azygos vein, portal vein

on left (in addition): gonadal vein, adrenal vein, inferior phrenic veins

Acute Renal Vein Thrombosis

Path: hemorrhagic renal infarction + edema from ruptured venules + capillaries without time for effective development of collaterals

- gross hematuria, proteinuria, anuria, hypertension, azotemia
- asymptomatic / painful flank mass
- consumptive thrombocytopenia

Location: more common on left (longer left renal vein)

√ focal hemorrhagic infarction + capsular rupture
√ smooth enlargement of kidney ← edema + hemorrhage

IVP:
√ initially faint + delayed dense nephrogram
√ range of completely normal to pyelocaliceal nonvisualization

US:
√ focal / generalized areas of increased echogenicity ← hemorrhage / edema
√ loss of corticomedullary differentiation
√ thrombus within distended renal vein / IVC

Doppler-US:
√ venous flow present in segmental veins + collateral veins overlying renal hilum mimicking patency of main renal v.
√ steady / less pulsatile venous flow compared with contralateral main renal vein
√ main renal vein not traceable into IVC on color Doppler
√ elevated resistive index > 0.70 ± reversed end-diastolic renal arterial flow in native kidney

CT:
√ prolonged cortical nephrographic phase with coarse striations + persistent

corticomedullary differentiation
√ edema in renal sinus + perinephric space
√ thickened renal fascia + perirenal stranding
√ development of collateral venous vessels
√ retroperitoneal hemorrhage

MR:
√ high signal intensity on T1WI + T2WI

Angio:
√ poorly filling cortical arteries
√ absent inflow from renal vein into IVC
√ thrombus extending into IVC

NUC:
√ no characteristic pattern on sequential functional study
√ markedly decreased / absent perfusion
√ delayed radiotracer uptake + excretion
√ retention of ^{99m}Tc mertiatide

DDx: acute renal artery occlusion; chronically nonfunctioning kidney

Cx: (1) Pulmonary emboli (50%)
(2) Severe renal atrophy (may show complete recovery)

Subacute Renal Vein Thrombosis

= good collateral drainage; impaired function with steady state or recanalization
√ enlarged edematous boggy kidney
√ slightly diminished / normal nephrographic density (may increase over time)
√ compression of collecting system ("spidery calices")
√ hypoechoic large kidney
√ collateral veins allow venous efflux → normalizing arterial waveform
√ main renal vein appears small ← recanalization

Chronic Renal Vein Thrombosis

= indolent stage
• 80–90% asymptomatic
• nephrotic syndrome (= proteinuria, hypercholesterolemia, anasarca)
√ normal excretory urogram in 25% (with good collateral circulation especially if left side affected)
√ notching of collecting system + proximal ureter
√ retroperitoneal dilated collaterals
√ lacelike intrarenal pattern of calcifications

US:
√ branching linear calcifications (calcified thrombus)
√ small atrophic echogenic kidney

CT:
√ attenuated renal vein ← retraction of blood clot + IVC thrombus (24%)
√ collaterals along proximal + middle ureter + perirenal
√ prolonged corticomedullary differentiation

√ delayed / absent pyelocaliceal opacification + attenuated collecting system
√ thickening of Gerota fascia
Arteriography:
√ enlarged venous collaterals on delayed images

RENOMEDULLARY INTERSTITIAL CELL TUMOR

= MEDULLARY FIBROMA
= rare benign often incidental mesenchymal neoplasm of kidney
Frequency: 50% of autopsies in adults
Origin: interstitial cells of medulla
Histo: stellate spindle cells on basophilic stroma
Size: < 5 mm (most)
• asymptomatic, (rarely) flank pain and hematuria
Location: renal pyramid
√ small nonenhancing noncalcified hypoattenuating solid mass
√ hypointense on T1WI + T2WI (← rich collagen content)

RETROCAVAL URETER

= CIRCUMCAVAL URETER
Etiology: abnormality in embryogenesis of IVC with persistence of right posterior cardinal vein ventral to ureter + failure of right supracardinal system to develop
Prevalence: 0.07%; M÷F = 3÷1
• symptoms of right ureteral obstruction
√ proximal right ureter swings medially over pedicle of L3-4, passes behind IVC, and emerges to right of aorta → returns to its normal position anterior to iliac vessels
√ varying degrees of hydronephrosis + proximal hydrouretero-nephrosis
Cx: recurrent urinary tract infections

RETROPERITONEAL FAT NECROSIS

Cause: fat saponification ← autodigestion of pancreatic parenchyma + peripancreatic fat ← release of lipolytic enzymes ← pancreatitis
Pathophysiology:
phospholipases + proteases attack plasma membranes of fat cells → release and hydrolyzation of triglycerides → production of free fatty acids → combining with serum calcium → precipitate as calcium soap
• hypocalcemia (associated with severe pancreatitis)
√ scattered nodules of fat necrosis throughout retroperitoneum + abdominal cavity:
√ mass effect + delayed contrast enhancement
DDx: peritoneal carcinomatosis

RETROPERITONEAL FIBROSIS

= RPF = ORMOND DISEASE = CHRONIC PERIAORTITIS = PERIURETERITIS FIBROSA = GEROTA FASCIITIS = SCLEROSING RETROPERITONEAL GRANULOMA
[John Kelso Ormond (1886–1978), surgeon-in-chief of urology division at Henry Ford Hospital,

Detroit]

= uncommon collagen vascular disease of unknown cause characterized by aggressive confluent fibroproliferative masses in retroperitoneal space leading to progressive encasement of retroperitoneal structures, especially ureters

Pathogenesis:

(a) probably autoimmune disease with antibodies to insoluble ceroid + oxidized low-density lipoproteins (by-products of aortic plaque, which has penetrated locally into media) leading to systemic vasculitis

(b) systemic autoimmune / inflammatory disease frequently associated with systemic lupus erythematosus, ankylosing spondylitis, Wegener granulomatosis, antineutrophil cytoplasmic antibody (ANCA)-positive rapidly progressive glomerulonephritis, primary biliary cirrhosis

(c) immunoglobulin G4 (IgG4)-related disease (= multifocal fibrosclerosis)

Classification:

A. Primary / idiopathic retroperitoneal fibrosis (⅔)

With idiopathic RPF the fibroinflammatory tissue entraps both ureters in most cases causing obstructive uropathy (in 56–100%) and subsequent renal failure. Some patients present late with nonfunctioning kidneys.

B. Secondary retroperitoneal fibrosis (⅓)

(1) Drugs (12%): derivatives of ergot alkaloids (methysergide, ergotamine, lysergic acid diethylamide [LSD]), beta-blocker, phenacetin, hydralazine, methyldopa, amphetamines

(2) Malignancy (in up to 8%): desmoplastic response to: lymphoma, Hodgkin disease, carcinoid, retroperitoneal metastases (breast, lung, thyroid, GI tract, GU organs)

- positive tumor markers

√ anterior displacement of aorta + IVC

√ nodularity of retroperitoneal mass

√ hyperintense SI on T2WI

(3) Infection = desmoplastic response to: histoplasmosis, tuberculosis, actinomycosis

(4) Retroperitoneal fluid collection / hematoma / urine extravasation: ← major trauma, major surgery

(5) Aneurysm of aorta / iliac arteries: desmoplastic response to chronic periaortitis

(6) Connective tissue disease: eg, polyarteritis nodosa

(7) Radiation therapy: fibrosis limited to radiation field

Prevalence: 1.3÷100,000 to 1÷200,000

Peak age: 40–65 years; M÷F = 2÷1 to 3÷1

Path: hard retroperitoneal plaque with ill-defined margins enveloping abdominal aorta, iliac vessels, IVC, ureters

Histo:

(a) early: immature fibrotic process with capillary proliferation + diffuse perivascular infiltrate of T and B lymphocytes, plasma cells + fibroblasts in loose matrix of collagen fibers

(b) later: mature plaque composed of relatively acellular and avascular hyalinized collagen + scattered calcifications

May be associated with: asbestos exposure
- weight loss, nausea, malaise, anorexia, low-grade fever
- dull pain in costovertebral angle, back, abdomen (90%)
- obstructive uropathy → oliguria → anuria → renal insufficiency (50–60%)
- renal vessel involvement (2–35%) → hypertension → renal insufficiency
- lymphatic + venous obstruction → lower extremity edema, deep vein thrombosis (6%), hydrocele (10%), scrotal swelling, varicocele
- compression of arteries → bowel ischemia, claudication (occasionally)
- high erythrocyte sedimentation rate (ESR), anemia
- high levels of C-reactive protein (80–100%)
- tests for antinuclear antibodies may be positive

Location: plaque typically begins around aortic bifurcation (L4-5) extending cephalad to renal hilum / surrounding kidney, duodenum, pancreas and spleen; rarely extends below pelvic rim, but may extend caudad to bladder + rectosigmoid

Retroperitoneal fibrosis most commonly surrounds the infrarenal abdominal aorta and proximal common iliac arteries.

√ tethering of aorta / IVC to vertebrae without anterior displacement
√ usually mild uni- / bilateral pyelocaliectasis → hydronephrosis → renal failure (56–100%)
◊ Diagnostic clue: incongruity between severe degree of renal failure + mild degree of hydronephrosis!

IVP / retrograde pyelography:
√ Classic TRIAD:
(1) Ureterectasis above L4-5 ← interference with peristalsis
(2) Medial deviation of ureters in middle third, typically bilateral = **maiden waist** deformity
(3) Gradual tapering of ureters at lower lumbar spine / upper sacral region ← extrinsic compression

DDx: primary ureteral tumor, periureteral lymph nodes, inflammatory ureteral stricture

US (poor sensitivity):
√ hypo- / isoechoic well-demarcated irregularly contoured homogeneous mass with smooth margins anterior to lower lumbar spine / sacral promontory
√ varying degrees of uni- / bilateral hydronephrosis
√ NO flow on Doppler imaging

CT:
√ well-delimited irregular periaortic rindlike layer of soft tissue isoattenuating to muscle
√ contrast enhancement (during active inflammation of immature plaque)
√ localized reactive infracentimetric lymphadenopathy (25%)
√ NO aortic displacement (!)

CT / MR allow comprehensive evaluation of morphology, location and extent of RPF + involvement of adjacent organs and vascular structures. They may detect diseases often associated with idiopathic RPF (eg, autoimmune pancreatitis) or an underlying cause of secondary RPF (eg, malignancy).

MR:
◊ In impaired renal function use HASTE + RARE urography

√ low to medium homogeneous signal intensity on T1WI
√ T2WI:
(a) acute phase → inflammatory edema
√ heterogeneous high SI on T2WI (DDx: malignancy)
√ early soft-tissue enhancement mirrors degree of inflammatory activity
(b) chronic phase → dense fibrotic plaque
√ low SI on T2WI
√ little / NO enhancement during venous phase
√ delayed enhancement

NUC:
√ 67Ga-citrate uptake during active inflammation
√ little / NO gallium uptake in chronic fibrotic stage

PET:
√ increased uptake of FDG paralleling degree of activity
√ may detect remote disease (multifocal fibrosclerosis, infectious / neoplastic disease, other autoimmune process)

^{18}F-FDG PET is the most sensitive modality for
(a) assessing metabolic activity of residual masses,
(b) demonstrating relapse.

Dx: open surgical / laparoscopic biopsy preferred for differentiation of benign from malignant disease

Histologic evaluation of biopsy tissue is mandatory to establish a definitive diagnosis if there are (a) findings suggestive of underlying malignancy or infection; (b) atypical location of the retroperitoneal mass (eg, pelvic, peripancreatic, perirenal); (c) progression of the mass or absence of response to immunosuppressive therapy.

Prognosis: chronic relapsing course

The most important challenge is to differentiate benign from malignant RPF because benign forms of RPF have a good outcome, whereas RPF secondary to malignancy has a poor prognosis.

DDx: (1) Perianeurysmal fibrosis (dilated encased aorta)
(2) Malignant retroperitoneal fibrosis / sarcoma (mass with irregular lobular / nodular margins, more cephalad location, anterior displacement of aorta, edema, Doppler flow, contrast enhancement)
(3) Retroperitoneal lymphadenopathy, lymphoma (anterior elevation of aorta / IVC off vertebral body)
(4) Primary amyloidosis
(5) Subacute retroperitoneal hematoma

Rx: (1) Withdrawal of possible causative agent
(2) Interventional relief of urinary obstruction
(3) Corticosteroids / immunotherapeutic drugs
(4) Disease-modifying antirheumatic drugs, tamoxifen
(5) Ureterolysis for refractory cases

RETROPERITONEAL LEIOMYOSARCOMA

Frequency: 2nd most common (28%) primary retroperitoneal malignancy (after liposarcoma)
Path: necrosis + cystic degeneration + hemorrhage in large tumor; calcifications uncommon
Age: 5th–6th decade; M÷F = 1÷6

- abdominal mass, pain, weight loss, nausea, vomiting
- abdominal distension, change in defecation habits, leg edema, back / radicular pain, frequency of urination
- hemoperitoneum, GI bleeding, dystocia, paraplegia

Site:
(a) retroperitoneal space without attachment to organs
(b) wall of inferior vena cava (in 6% of leiomyosarcomas)
Size: average diameter > 10 cm
Metastases:
frequently hematogenous, less commonly lymphatic dissemination
(a) common sites: liver, lung, brain, peritoneum
(b) rare sites: skin, soft tissue, bone, kidney, omentum
◊ Distant metastases present at time of diagnosis in 40%
Dx: extensive necrosis in a retroperitoneal mass with contiguous involvement of a vessel!
DDx: (1) Liposarcoma (fat content)
(2) Malignant fibrous histiocytoma (not as necrotic)
(3) Lymphoma (nonnecrotic, tends to envelop IVC + aorta)
(4) Primary adrenal tumor
(5) Bland IVC thrombus (NO enhancement / luminal enlargement)
Rx: (1) Complete excision (resectable in 10–75%)
(2) Partial resection (reduction in tumor size)
(3) Adjuvant chemotherapy / radiotherapy
Prognosis: local recurrence in 40–70%; death within 5 years in 80–87% with extraluminal tumors

Extravascular Leiomyosarcoma (62%)

Path: extraluminal (= completely extravascular) large tumor with extensive necrosis
IVP:
√ large soft-tissue mass with displacement of
(a) kidney + ureter
(b) gas-containing ascending / descending colon
√ well-defined fat plane between mass and kidney
√ obstruction of kidney (ureteral involvement)
√ usually not calcified
US:
√ solid mass isoechoic to liver / rarely hyperechoic
√ complex mass with cystic spaces + irregular walls
CT:
√ lobulated mass often > 10 cm in size

√ large cystic areas of tumor necrosis in center of mass
√ areas of high attenuation ± fluid-debris level with recent hemorrhage
√ homogeneously solid with small tumor

MR:
√ intermediate intensity on T1WI with low-intensity areas of necrosis
√ inhomogeneous intermediate to high SI on T2WI ← high water content of cystic areas
√ ± fluid-debris level ← hemorrhage

Angio:
√ hypervascular tumor with blood supply from lumbar, celiac, mesenteric, renal arteries
√ avascular center surrounded by thick hypervascular rind

Intravascular Leiomyosarcoma (5%)

Path: intraluminal (= completely intravascular) polypoid mass firmly attached to vessel wall
Location: between diaphragm + renal veins, may extend along entire length of IVC + into heart
√ small solid mass within IVC
√ gradual expansion / obstruction of IVC
√ intratumoral vascularity confirmed by Doppler
√ irregular enhancement (CT bolus injection)
Cx: (1) Budd-Chiari syndrome (intrahepatic segment of IVC)
(2) Nephrotic syndrome ← IVC segment involved between hepatic + renal veins
(3) Edema of lower extremities ← IVC segment below renal veins without adequate collateralization
(4) Tumor embolus to lung
Prognosis: better for middle segment of IVC (between hepatic + renal veins) than other segments

Extra- & Intravascular Leiomyosarcoma (33%)

√ solid / necrotic extraluminal mass not originating from a retroperitoneal organ with contiguous intravascular enhancing component (PATHOGNOMONIC)

Intramural Leiomyosarcoma (extremely rare)

RETROPERITONEAL LIPOSARCOMA

= slow-growing tumor that displaces rather than infiltrates surrounding tissue and rarely metastasizes
Frequency: most common (33%) of primary malignant retroperitoneal sarcomas; 95% of all fatty retroperitoneal tumors
Histo:
› biologically least aggressive
(a) well-differentiated lipogenic type (most common):
√ radiodensity of fat
› biologically intermediate aggressiveness
(b) myxoid type (more common in younger population):

√ radiodensity between water + muscle
√ solid appearance on US
› biologically highly aggressive
√ radiodensity of muscle for (c), (d), (e)
(c) round cell type
(d) pleomorphic type (least common)
(e) dedifferentiated (10–15%) ← long latent period

Age: most commonly 50–70 years; M = F

• abdominal pain, weight loss, anemia, palpable mass

Site: anterior to spine + psoas muscle > paraspinal + posterior pararenal space

Size: average diameter > 20 cm

CT:

√ solid pattern: inhomogeneous poorly marginated infiltrating mass with contrast enhancement
√ mixed pattern: focal fatty areas (–40 to –20 HU) + areas of higher density (+20 HU)
√ pseudocystic pattern: water-density mass ← averaging of fatty + solid connective-tissue elements
√ calcifications in up to 12% (= important sign of dedifferentiation of an initially well-differentiated type)
◊ Recurrent tumors have higher attenuation values than fat!

MR:

√ hyperintense on T1WI
√ intermediate SI on T2WI; more hyperintense for myxoid type ← mucopolysaccharide content
√ loss of fat signal intensity on fat-suppressed sequence
√ enhancing thick irregular nodular septa

Angio:

√ hypovascular without vessel dilatation / capillary staining / laking

Prognosis: local recurrence in 90%; most radiosensitive of soft-tissue sarcomas; 32% overall 5-year survival

DDx: malignant fibrous histiocytoma, leiomyosarcoma, desmoid tumor, encapsulated fat necrosis

RETROPERITONEAL LYMPHANGIOMA

Lymphangioma of Adrenal Gland

= exceedingly rare tumor usually discovered incidentally

Prevalence: 0.06%

Age: any; peaks during 3rd–6th decade of life

CT:

√ thin-walled multilocular cystic lesion near fluid attenuation
√ thin septa WITHOUT internal enhancement

MR:

√ decreased SI on T1WI + increased intensity on T2WI

DDx: adrenal cyst, hemangioma, cystic pheochromocytoma, schwannoma with cystic degeneration

Lymphangioma of Kidney

= RENAL LYMPHANGIECTASIA / LYMPHANGIOMATOSIS

Frequency: rare benign renal tumor (50 cases in literature)

Origin: developmental anomaly of perirenal lymphatic system / true neoplasm (monosomy, trisomy 7q, defect in vHL gene)

Path: (a) well-encapsulated unilateral mass
(b) bilateral multilocular cystic mass with clear fluid

Histo: multiple communicating cysts lined by flattened endothelial cells; multiple septa containing entrapped renal tubules, lymphoid cells, smooth muscle elements

Age: adulthood ($^2/_3$); M÷F = 1÷1

• mostly asymptomatic, flank pain, abdominal mass, hematuria

Location: renal sinus, perinephric region; (commonly) bilateral

√ uni- / multilocular cystic mass

MR:

√ hypointense on T1WI + uniformly hyperintense on T2WI

√ variable SI of intracystic fluid (depending on presence of hemorrhage / debris / protein content)

Prognosis: spontaneous regression (occasionally)

Decompensated Lymphangiectasia

= exacerbation during pregnancy

• hypertension, flank pain

√ increasing perinephric collection, ascites

RETROPERITONEAL LYMPHOMA

Frequency: most common retroperitoneal malignancy

Histo: Hodgkin disease / NHL

A. PRIMARY lymphoma = confined to single organ + immediately adjacent lymph nodes

B. SECONDARY lymphoma (more common)

Location: bilateral in 50%

US:

√ heterogeneous predominantly hypoechoic mass ← varying degrees of hemorrhage and necrosis

CT:

√ well-defined homogeneous hypoattenuating mass spreading between normal structures without compressing them:

√ mass enveloping normal constituents of renal sinus

√ often contiguous spread into perinephric space

√ ± anterior displacement of IVC and aorta ("**floating aorta**")

√ rarely calcified + necrotic prior to therapy

CECT:
√ mild to moderate homogeneous contrast enhancement
√ slow washout on delayed images
MR:
√ isointense to muscle on T1WI
√ iso- to hyperintense on T2WI
√ moderate homogeneous / patchy enhancement
Cx: obstruction of ureters + IVC

Hodgkin Disease

Age: bimodal distribution in 20s and 60s
Extent: limited disease involving mediastinum + spleen
√ enlarged paraaortic lymph nodes in 25%

Non-Hodgkin Lymphoma

Age: 40–70 years
Extent: commonly extranodal disease in liver, spleen, bowel at an advanced stage
√ retroperitoneal mass in 14%
√ enlarged paraaortic lymph nodes in 55%
√ mesenteric lymphadenopathy (frequent)

Posttherapy Lymphoma

Path: soft-tissue masses persist as fibrosis
MR:
√ low signal intensity on T2WI + minimal enhancement
FDG-PET:
√ no uptake in fibrosis
√ hypermetabolic activity in viable tumor

RETROPERITONEAL ONCOCYTOMA

Oncocytoma of Adrenal Gland

= ONCOCYTIC ADRENOCORTICAL ADENOMA / NEOPLASM
Median age: 46 years; M÷F = 1÷1.8
Histo: abundant deeply eosinophilic (mitochondria-rich) cells; positive for vimentin, melan A, inhibin-α, calretinin; ± immunoreactive for synaptophysin + mitochondrial antigen $MTCO_2$; variably positive for CK8, CK18, CD10
Location: L÷R = 1.5÷1
Mean size: 9 cm
• asymptomatic (70%)
• symptomatic (30%) due to steroid production → Cushing syndrome, virilization, feminization
√ well-marginated often large mass with heterogeneous enhancement of nonspecific appearance
Cx: malignant transformation

Oncocytoma of Kidney

= PROXIMAL TUBULAR ADENOMA = BENIGN OXYPHILIC ADENOMA
= rare form of a benign hypervascular adenoma
Prevalence: 3–7% of solid renal masses
Median age: 65 (range, 26–94) years; M÷F = 1.6÷1 to 2.5÷1
Path: well-encapsulated tan-colored tumor of well-differentiated proximal tubular cells + oncocytes
Histo: oncocytes = large uniformly round epithelial cells with granular oxyphilic / eosinophilic cytoplasm ← large number of mitochondria; no clear cytoplasm; similar to oncocytic tumors seen in thyroid, parathyroid, salivary glands, adrenals
Location: rarely multicentric / bilateral / metachronous
• majority asymptomatic, occasionally hypertension
Tumor size: 6.0–7.5 (range, 0.1–26.0) cm
√ renal mass of homogeneously low attenuation / hypoechogenicity (in > 50%)
√ well-demarcated with pseudocapsule
√ central stellate scar in 30% (in lesions > 3 cm in diameter ← organization of central infarction + hemorrhage after tumor growth has outstripped blood supply)
√ invasion of renal capsule / renal vein in large tumors
MR:
√ typically spherical well-defined mass
√ hypointense relative to renal parenchyma on T1WI (70%)
√ hyperintense relative to renal parenchyma on T2WI (67%)
√ prominent enhancement of mass
√ central stellate scar:
√ hypointense on T1WI + hyperintense on T2WI
√ less enhancement than remainder of mass
√ scar may show delayed enhancement
√ nonspecific well-defined hypointense capsule (in < 50%)
Angio:
√ spoke-wheel configuration in 80% (DDx: renal cell ca.)
√ homogeneously dense parenchymal phase (71%)
√ NO contrast puddling / arteriovenous shunting / renal vein invasion
NUC:
√ photopenic area on ^{99m}Tc-DMSA ← tubular cells do not function normally
Dx: percutaneous needle biopsy unreliable
◊ Pathologic diagnosis requires entire tumor because a well-differentiated renal cell carcinoma may have oncocytic features!
Rx: local resection / heminephrectomy
Prognosis: death from malignancy following surgery (3%)

RETROPERITONEAL PARAGANGLIOMA

= EXTRAADRENAL PHEOCHROMOCYTOMA
Location: anywhere in sympathetic nervous system from neck to sacrum; subdiaphragmatic in 98%

(a) adrenal medulla (85–90%) = *pheochromocytoma*
(b) extraadrenal (10–15% in adults, 31% in children)
= *paraganglioma*:
› diaphragm to lower poles of kidney 50%
› lower poles of kidney to bifurcation 30%
» organ of Zuckerkandl at origin of inferior mesenteric artery 2–5%
› pelvis 10%
» gonads, urinary bladder 1%
› thorax 10%
adherent to / involving LA

Multiplicity: 10% in nonfamilial adult cases
32% in nonfamilial childhood cases
65% in familial syndromes

√ well-defined hypervascular mass in pelvic retroperitoneum along course of common iliac vessels

CT (90% sensitive):
√ large well-defined lobular tumor
√ fluid-fluid level ← hemorrhage + necrosis
√ punctate calcifications (in 15%)
√ intense contrast enhancement

MRI (90% sensitive):
√ signal voids on T1WI
√ "lightbulb" high SI (unusual) with superimposed variable heterogeneous SI (← hemorrhage) on T2WI

NUC:
√ high uptake of m-iodobenzylguanidine (MIBG) with ^{123}I / ^{131}I (77–95% sensitive, 95–100% specific)
√ ^{111}In-pentetreotide scintigraphy (up to 94% sensitive) for lesions > 1.5 cm

PET:
√ 18F–fluorodihydroxyphenylalanine (98% sensitive, up to 100% specific), especially for predominantly noradrenaline-secreting and hereditary types

Cave: Percutaneous biopsy of a hypervascular retroperitoneal mass without adequate laboratory evaluation and prebiopsy preparation (like pharmacologic blockade) must be avoided, since it can result in hypertensive crisis or even death.

Cx: (1) Malignancy: 30–40% of paragangliomas
√ local invasion
√ metastases (in 22–50%): versus 2–10% in pheochromocytomas
(2) Rupture with retroperitoneal hemorrhage

DDx: (1) Nerve sheath tumor
(2) Hypervascular lymphadenopathy: metastasis / Castleman disease
(3) Hypervascular soft-tissue sarcoma

Paraganglioma of Organ of Zuckerkandl

Frequency: 135 cases in literature

Age: 20–40 years
May be associated with:
(1) Multiple endocrine neoplasia type 2a (MEN 2a)
(2) Neurofibromatosis
(3) von Hippel−Lindau disease
(4) Triad of Carney
- functional (¾): associated with hypertension
- nonfunctional (¼): abdominal pain / mass

RETROPERITONEAL TERATOMA

= germ cell tumor with somatic differentiation of cells producing mature but disorganized tissues of > 2 embryonic layers (ectoderm, mesoderm, endoderm)

Frequency: 1–11% of all primary retroperitoneal tumors; < 10% of all teratomas located in retroperitoneum; 3rd most common tumor of retroperitoneum in children (after neuroblastoma + Wilms tumor)

Origin: interruption of normal embryologic migration of pluripotent primordial germ cells from yolk sac to genital ridge

Path: benign (mature = dermoid cyst / immature) or malignant

Histo: cysts lined by epithelium of ectodermal and endodermal origin + glial tissue + mesodermal components (fat, bone, cartilage); may harbor various malignancies of germ cell (seminoma, embryonal cell carcinoma, yolk sac tumor) or somatic (rhabdomyosarcoma, chondrosarcoma, liposarcoma) origin

Age: bimodal distribution with peaks in first 6 months + early adulthood; M÷F = 1÷2 to 1÷3.4

Location: retroperitoneum (< 10%), ovary, testis, anterior mediastinum, presacral + coccygeal area

Site: midline (common), left side, suprarenal fossa

- asymptomatic (most); fixed palpable midline mass, abdominal tenderness, progressive abdominal distension
- nausea, vomiting, pain, GU symptoms, lower extremity swelling (after growth)

√ varied appearance from predominantly cystic to completely solid mass:
√ containing fat (in 61–83%)
√ congealed / linear / shardlike / toothlike calcifications (in 83–93%)
√ wall nodules (= Rokitansky nodules) in cystic component

√ necrosis + hemorrhage → suggest malignancy

Rx: surgical resection

Prognosis: excellent for benign teratoma; poor with malignant teratoma (adults÷children = 26%÷7%)

Immature Teratoma (< 1%)

Age: younger age group (< 20 years) than mature teratomas
Histo: > 10% undifferentiated tissue
Location: near upper pole of left kidney
√ predominantly solid with scattered areas of fat and coarse + ill-defined calcifications
√ occasionally cystic component

Mature Retroperitoneal Teratoma (99%)

= DERMOID CYST

Histo: well-differentiated tissue from at least 2 germ cell layers: ectodermal (in 100%), mesodermal (in 90%), endodermal (in majority of lesions)

√ predominantly cystic

√ villiform solid component (= Rokitansky protuberance) in 81%

√ toothlike / well-defined calcification (56%)

√ fat (93%)

Dx: A fat-fluid level of sebum with chemical shift between fat and fluid are PATHOGNOMONIC .

Cx: malignant degeneration (2–3%): in ¼ of children and 1/10 of adults

Malignant Teratoma

Histo: malignant tissue of germ cell / non-germ cell origin

• elevated a-fetoprotein (in 50%)

√ irregular mass with invasion of adjacent structures + vessels

Prognosis: poor with germ cell lesions or lesions with rhabdomyosarcomatous / neural differentiation

RHABDOID TUMOR OF KIDNEY

◊ Most aggressive renal neoplasm of childhood!

Frequency: < 2% of pediatric renal tumors

Mean age: 11–17 months; 6–12 months of age (25%), < 1 year [< 2 years] of age 60% [80%]; M÷F = 1.5÷1

Origin: renal sinus

Histo: monomorphic noncohesive large cells with prominent nucleoli + abundant eosinophilic cytoplasm (superficial resemblance to skeletal muscle, hence name); filamentous intracytoplasmic inclusions (CHARACTERISTIC)

Associated with: syn- / metachronous primary brain tumor of neuroectodermal origin (medulloblastoma, ependymoma, cerebellar / brainstem astrocytoma, PNET)

Metastatic to: lung, liver, brain

• paraneoplastic hypercalcemia (occasionally)

√ centrally located heterogeneous renal mass:

√ indistinct borders with infiltration of medulla + sinus

√ PROMINENT peripheral crescent-shaped subcapsular fluid collection in 70% (subcapsular hematoma in 47% / necrotic cavity in 53%)

Subcapsular hemorrhage suggests rhabdoid tumor; however, since Wilms tumor is so much more common, a tumor with this finding is more likely to be a Wilms tumor than a rhabdoid tumor.

√ SUGGESTIVE multilobulated architecture, esp. if surrounded by low-attenuation material ← old hemorrhage / necrosis

√ curvilinear calcifications outlining tumor lobules (2/3)

√ may invade renal vein and IVC

√ midline mass in posterior fossa of skull

√ metastatic (in 80%) to lung, liver, retroperitoneal lymph nodes, abdomen, brain, bone

Prognosis: 20% 18-month survival rate

DDx: (1) Wilms tumor

(2) Mesoblastic nephroma (young infant, subcapsular fluid collection, no lymphadenopathy)

RHABDOMYOSARCOMA

= rapidly growing aggressive malignancy frequently invading adjacent bones and soft tissues

Origin: pluripotential mesenchymal cell with capacity to differentiate into skeletal muscle (rhabdomyoblasts resemble primitive striated muscle cells; NOT from striated muscle)

Frequency:

4–10% of cancers in children < 15 years of age (ranking 4th after CNS neoplasm, neuroblastoma, Wilms tumor);

5–15% of all adult sarcomas; 35% of pediatric sarcomas

◊ Most common soft-tissue tumor in childhood (60%)

Incidence: 4.5 (1.3)÷1,000,000 annually in USA in white (black)

Age: bimodal age distribution: 1–4 years (1st peak), 14–19 years (2nd smaller peak); < 11 years (70%); M÷F = 2÷1

Associated with: Li-Fraumeni syndrome, neurofibromatosis type 1, Beckwith-Wiedemann syndrome, DICER1 mutation (familial pleuropulmonary blastoma)

Histo: arising from small undifferentiated "blue cells" with scant cytoplasm + primitive-appearing nuclei; perineural invasion common

(1) embryonal type (70–80%)

Variant: polypoidal form = **sarcoma botryoides** [*bótry* , Greek = bunch of grapes] = grapelike

Age: newborn – 15 years

(2) alveolar type (10–15–20%, worst prognosis)

Age: 10 – 25 years

(3) pleomorphic type (10%, poor prognosis)

Peak age: 45 years; rare in children

Location: primarily large muscles of extremities

√ variable amounts of hemorrhage + necrosis

(4) mixture of two types

DDx of other small round blue cell tumors:

neuroblastoma, Ewing sarcoma, primitive neuroecto-dermal tumor, lymphoma, desmoplastic small round cell tumor

Location: head + neck (35–40%), trigone and bladder neck (18– 21%), extremities (18–23%), orbit (10%), trunk (7–8%), retroperitoneum (6–7%), perineum + anus (2%), other sites (7%); intraperitoneal involvement (10%)

Spread: 15–20% have metastatic disease at presentation

Head & Neck Rhabdomyosarcoma *(40%)*

Frequency: 10% of all rhabdomyosarcomas; 3rd most common primary childhood malignancy of head and neck (following CNS neoplasm + retinoblastoma)

◊ Most common primary extracranial tumor invading cranial vault in childhood

Classification of head & neck tumors:

(a) orbital (25–35%) (see below)

(b) parameningeal (50%): middle ear, paranasal sinus, mastoid process, pterygopalatine fossa, nasopharyngeal musculature (⅓) especially in masticator space

√ MR to assess intracranial extension (in up to 55%)

◊ Parameningeal disease carries the worst prognosis!

(c) nonparameningeal = superficial (25%)

Metastases: lung, cortical bone, lymph nodes (10–20%) > bone marrow, liver

◊ Metastases in 10–20% at time of diagnosis!

• cranial nerve palsy

√ bulky nasopharyngeal mass

√ extension into cranial vault through fissures + foramina (up to 35%) usually involving cavernous sinus

√ bone destruction by direct invasion

√ mild to moderate uniform diffuse contrast enhancement

CT:

√ poorly defined relatively homogeneous mass isodense to brain

√ expanded foramen / fissure

MR (imaging modality of choice):

√ SI intermediate between muscle and fat on T1WI + hyperintense on T2WI

Prognosis: 12.5% 5-year survival (better than in extremities)

DDx: fibrosarcoma, hemangioma, lymphangioma, lymphoma, mastoiditis, lymphadenopathy, Langerhans cell histiocytosis

Rhabdomyosarcoma of Orbit

◊ Most common primary extraocular malignancy in a child

Frequency:

25%–35% of head and neck rhabdomyosarcomas; 3–4% of all pediatric orbital masses:

› 10% as primary tumor of orbit

› 10% as metastasis / from invasion of orbit ← nasopharynx, pterygopalatine fossa, infratemporal fossa, paranasal sinuses (= parameningeal site)

Histo: embryonal form (most common) in young children; alveolar form (less common) generally affecting older children / adolescents; pleomorphic type extremely rare in orbit

Mean age: 6–8 (range, infancy – 68) years; 90% by 16 years of age; M÷F = 5÷3

Rarely associated with: neurofibromatosis

• rapidly progressive unilateral proptosis / globe displacement

• conjunctival + palpebral swelling (DDx orbital cellulitis)

Staging: I localized completely resected tumor

II residual microscopic disease after surgery

III gross residual disease after biopsy

IV distant metastases at onset

Location:

(a) extraconal (37–87%): superonasal quadrant / superior orbit / retrobulbar (71%), lid

(22%), conjunctiva (7%)
(b) intra- and extraconal (13–47%)
√ TYPICALLY thickening of eyelid
√ large soft-tissue density mass with ill-defined margins:
√ mass often contiguous with adjacent extraocular muscle ← muscle displaced / encased (without enlargement of muscle belly)
√ globe often distorted / displaced but rarely invaded
√ ± invasion of adjacent preseptal space, paranasal sinus (20%), nasal cavity, intracranial cavity (3%)
√ moderate to marked generalized enhancement
√ cavitary mass with ringlike enhancement (rare)
CT (sensitive for bone erosion):
√ extraconal well-circumscribed ovoid irregular homogeneous mass isoattenuating to muscle:
√ necrosis + hemorrhage (uncommon)
√ bone erosion (in 30–40%) at presentation
MR (sensitive for intracranial extension):
√ homogeneous mass isointense / minimally hyperintense to muscle / brain on T1WI:
√ areas of high signal intensity on T1WI and T2WI ← foci of subacute hemorrhage
√ hyperintense to muscle, fat and brain on T2WI
√ moderate to marked uniform internal enhancement
US:
√ heterogeneous well-defined irregular mass of low to medium echogenicity
√ variable vascular flow pattern on Doppler US

Metastases: (a) hematogenous: lung, bone marrow
(b) lymphatic (rare): cervical lymph nodes

Prognosis:
(1) 40% survival after exenteration
(2) 80–90% 5-year survival after biopsy / surgical debulking followed by radiation therapy (4,000–5,000 rad) + chemotherapy (vincristine, cyclophosphamide, doxorubicin)

DDx: (1) Subperiosteal hemorrhage (bone erosion during resolution)
(2) Orbital cellulitis with abscess (fever, leukocytosis)
(3) Dermoid cyst (cystic appearance, internal fat attenuation, calcification, fluid level, bone depression near zygomaticofrontal suture)
(4) Capillary hemangioma (growth during 1.0–1.5 year of life, ipsilateral cutaneous hemangiomas, peripheral + internal flow voids)
(5) Venous-lymphatic malformation (multiloculated cystic with ill-defined border, fluid-fluid levels, peripheral enhancement, phleboliths)
(6) Langerhans cell histiocytosis (pronounced bone destruction, diabetes insipidus)
(7) Leukemia (peripheral blood smear)
(8) Lymphoma (lacrimal gland involvement, encasement of globe, hypointense on T2WI)

Genitourinary Rhabdomyosarcoma

Frequency: 4–8% of all malignant solid tumors in children < 15 years of age (ranking 4th after CNS neoplasm, neuroblastoma, Wilms tumor); 10–25% of all sarcomas; annual incidence of 4.5 [1.3]÷1,000,000 in white [black] children

Age: bimodal distribution with peaks at 7 years + at adolescence; white÷black = 3÷1; M÷F = 6÷4

Path: firm fleshy lobulated mass with infiltrative margin / well-defined pseudocapsule; composed of smooth grapelike clusters if intraluminal (= sarcoma botryoides)

Histo (Horn & Enterline):

(a) embryonal (56%)
(b) botryoid (5%) = subtype of embryonal rhabdomyosarcoma
(c) alveolar (20%): worst prognosis
(d) pleomorphic (1%): mostly in adults

DDx: primitive neuroectodermal tumor, extraosseous Ewing sarcoma, synovial cell sarcoma, fibrosarcoma, alveolar soft part sarcoma, hemangiopericytoma, undifferentiated sarcoma, neuroblastoma

√ nonspecific imaging features:

√ homogeneous echogenicity similar to muscle ± hypoechoic areas on US ← hemorrhage / necrosis
√ heterogeneous lesion with calcifications + necrosis
√ ± hyperemia with high diastolic flow component
√ bulky pelvic mass of heterogeneous attenuation
√ hypointense on T1WI + hyperintense on T2WI with heterogeneous enhancement
√ diffuse tumor vascularity on angio

Prognosis:

(a) 14–35% 5-year survival with radical surgery
(b) 60–90% 3-year survival with chemotherapy added

◊ Local recurrence is common!

Bladder-Prostate Rhabdomyosarcoma

◊ 5% of all rhabdomyosarcomas occur in genitourinary tract
◊ Most common bladder tumor in patients < 10 years

Age: in first 3 years of life; M÷F = 3÷1

Associated with: congenital anomalies of the brain, neurofibromatosis, nephroblastoma

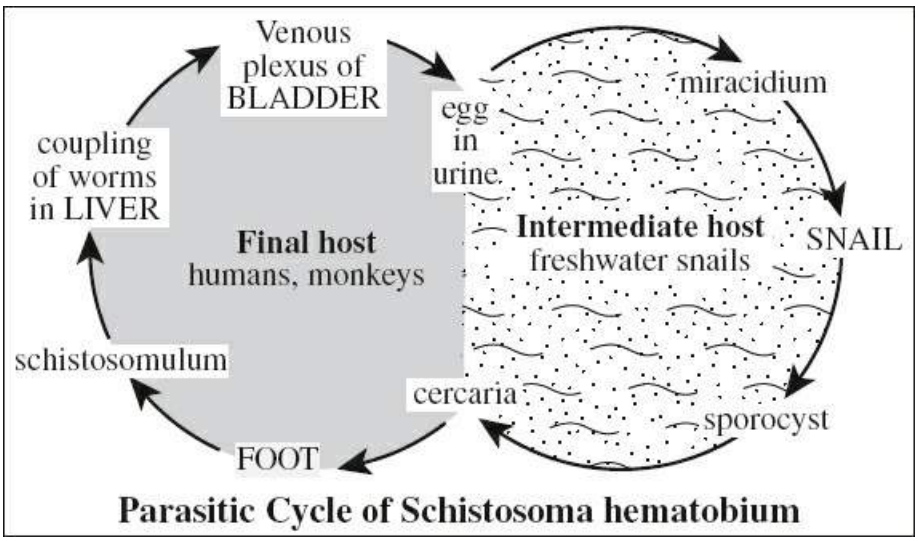
Histo: embryonal (90%), alveolar (10%)

Location: trigone of urinary bladder / prostate (tumor infiltrating both)

- abdominal pain + distension (from bladder outlet obstruction), urinary retention, palpable bladder
- urinary frequency + dysuria (← urinary tract infection)
- hematuria (unusual late manifestation)
- strangury (= painful urge to void without success)

√ polypoid intraluminal tumor mass
√ elevation of bladder floor with obstruction of bladder neck + large postvoid residual
√ ± invasion of periurethral / perivesical tissues
√ retroperitoneal lymph node enlargement

MR:
√ low signal intensity on T1WI + hyperintense on T2WI
√ heterogeneous enhancement
Rx: chemotherapy prior to surgery
DDx: polyp, hemangioma, ectopic ureterocele, hemorrhagic cystitis



Rhabdomyosarcoma of Female Genital Tract

Location: vulva / vagina (infancy), cervix (reproductive years), uterine corpus (postmenopausal)
• vulvar / perineal / vaginal mass
• vaginal bleeding / discharge / protruding grapelike mass
DDx: polyp, urethral prolapse, hydrometrocolpos, neoplasm
Prognosis: 91% 5-year survival rate for nonmetastatic rhabdomyosarcoma of genital tract

VAGINAL RHABDOMYOSARCOMA

Age: very young children (almost exclusively)
Histo: commonly botryoid
√ large solid heterogeneous hypoechoic mass posterior to urinary bladder

Paratesticular Rhabdomyosarcoma

◊ Most common extratesticular neoplasm in children!
Age: childhood, 2nd age peak in adolescence
Histo: embryonal subtype (majority)
Location: spermatic cord, testis, penis, epididymis
• painless scrotal swelling
• palpable nontransilluminating intrascrotal tumor
• bulky abdominal (lymphadenopathy)
√ hypervascular hypo- / hyperechoic solid mass
√ displacement / compression / infiltration of adjacent epididymis + testis
Prognosis: 73–89% 3-year survival rate
DDx: hydrocele, epididymitis, testicular neoplasm

Abdominal Rhabdomyosarcoma *(rare)*

Location: peritoneum, mesentery, omentum
√ omental caking (primary disease)
US:
√ predominantly solid mixed-echogenicity mass
√ markedly increased color flow
CT:
√ mild to moderate ascites
√ hypoattenuating intraperitoneal + mesenteric nodules and masses
√ variable enhancement

SCHISTOSOMIASIS

= BILHARZIASIS = SNAIL FEVER
[*schisto*, Greek = split; *soma*, Greek = body]
[Theodor Maximilian Bilharz (1825–1862), German physician and parasitologist, chair of descriptive anatomy at Kasr el Aïn, Cairo]
◊ One of the most protean diseases in humans (> 200 million people infected in Africa, Asia, and the Americas)!
◊ 2nd most common cause of mortality among parasitic infections after malaria → 500,000 deaths annually!
◊ The most prevalent waterborne disease!
Organism: S. haematobium (GU tract) > 95%;
S. mansoni, S. japonicum (GI tract) < 5%
Contact: exposure of skin to water contaminated with cercariae excreted by snails as a result of unsanitary disposal of human and animal wastes combined with repeated daily contact with contaminated freshwater (eg, fishing, farming, swimming, bathing, recreation)
• dermatitis = **swimmer's itch** (common manifestation) ← juvenile worms enter circulatory system
• "**Katayama fever**" = fever, chills, sweating, cough (occasional) ← adult female worms develop in GU and GI tracts
Rx: praziquantel (destroys adult worms + incites eggs to hatch), albendazole

Schistosoma Hematobium

Prevalence: 8% of world's population; 25% in Africa
Endemic to: South Africa, Egypt, Nigeria, Tanzania, Zimbabwe; South America; Carribean; Middle East; Asia; Puerto Rico
Life cycle:
female parasite resides within venules of urinary bladder → eggs erode bladder mucosa → excreted with urine and feces → hatch in fresh water into larval **miracidia**
larvae invade aquatic / amphibious fresh-water snails (= intermediate host) of genus Bulinus → miracidia develop into adult **sporocytes** → in 4–6 weeks thousands of fork-tailed free swimming 1-mm long **cercariae** are released → pass into surrounding body of water
→ death within 72 hours OR

penetration of human skin (usually foot) where they lose their tail → pass into lymphatics + thoracic duct → travel to RT heart + lungs → LT heart + mesenteric capillaries → reach portal vein where they mature into **adult worms** + copulate (in 21 days after penetration) → return into pelvic venous plexus where they may live for many years

Histo: eggs incite granulomatous response + fibrosis → polypoid lesions (acute phase) and ultimately SCC (chronic phase); large number of eggs calcify in bladder wall without viable eggs in urine

Definite Dx: eggs found at urine microscopy

- frequency, urgency, dysuria
- terminal microscopic hematuria, hemospermia
- albuminuria in the nephrotic range (most common)
- suprapubic pain; dull flank pain (from hydronephrosis)
- hypertrophic, ulcerative, fistulous, wart-like lesions of vulva + perineum (can be mistaken for condylomata lata)
- index of infectious severity = urine egg count

Location: lower ureters + bladder

@ Urinary bladder

Pathogenesis:

chronic irritation of mucosa → proliferation of urothelium into buds (von Brunn nests) → growth into lamina propria →

(a) cystic deposits = **cystitis cystica**

(b) intestinal mucin-secreting glands (goblet cells) = **cystitis glandularis**

√ polypoid filling defects + mucosal irregularities in urinary bladder (pseudotubercles, papillomas) during acute phase ← cystitis cystica

√ bladder wall calcifications (in 4–56%): curvilinear / coarse / floccular, beginning at base parallel to upper aspect of pubic bone, involving all wall layers:

√ calcified bladder resembling a fetal head (PATHOGNOMONIC)

◊ Calcifications present with an abundance of calcified dead ova in submucosa in chronic stage

√ thick-walled fibrotic "flat-topped" bladder with high insertion of ureters

√ reduced bladder capacity (fibrotic stage) → significant postvoid residual

√ vesical calculi (in 39%), distal ureteral calcification (in 34%), honeycombed calcification of seminal vesicles

Cx: **Squamous cell carcinoma of bladder** (SCC)

Age: 30–50 years (exposed early in childhood with 20–30-year latency period)

Location: posterior bladder wall, rarely trigone

√ nodular / fungating filling defect (80%)

√ diffuse / focal region of wall thickening

√ multiple tumors (25%)

√ discontinuous calcifications

@ Ureter (in up to 65%)

√ persistent filling defect of distal ureteral segment with ureterectasis ← peristaltic disorganization ← focal egg deposition

√ beaded appearance of ureter:

√ air bubble-like filling defect = **ureteritis cystica**
√ multiple inflammatory pseudopolyps in ureter ← granulomas (= bilharziomas)
√ ureteral strictures in distal third (in 8%, L > R), most commonly in intravesical portion with cobra-head configuration = **pseudoureterocele**; **Makar stricture** = focal stricture at L3
√ linear wall calcifications = **ureteritis calcinosa** (PATHOGNOMONIC)
√ vesicoureteral reflux (in up to 30%)
√ striation of renal pelvis + proximal ureter in 21% (DDx: normal in 3%, other urinary tract infection, vesicoureteric reflux
Cx: hydroureteronephrosis ← cessation of peristalsis

@ Urethra
√ polyps in fossa navicularis of urethra
√ urethral stricture with perineal and scrotal fistulas

@ Scrotum
√ testicular + epididymal lesions simulating malignancy
√ tunica vaginalis shows septate collections, multiple calcifications, diffuse / nodular enlargement ← granulomatous inflammatory reaction
DDx: malignancy, infarction, epididymo-orchitis

Schistosoma Mansoni & Japonicum

Organism:

A. **Schistosoma mansoni**
Endemic to: Africa, Saudi Arabia, Madagascar, Brazil, Surinam, Venezuela, Puerto Rico, Middle East
Path: eggs deposited along large portal veins of liver hilum

B. **Schistosoma japonicum**
Endemic to: east Asia, China, Philippines
Path: eggs deposited in peripheral small portal veins

Intermediate host: snail

Life cycle:

(a) within snail : **miracidia** mature into **cercariae** → released into water + swim → penetrate skin / intestinal wall of human host
(b) within human: <u>in mesenteric veins</u>
› migration via blood + lymph vessels into lung → afterward liver → eggs released into portal circulation
› adult worm inhabits inferior mesenteric + portal veins
› eggs excreted in human feces → reach water → hatching of miracidia → infection of snails

Path: (a) **intestinal schistosomiasis**:
› exudative granulomatous response (proctocolitis) → formation of inflammatory polyps, fibrosis, wall thickening, colonic stenosis

(b) **hepatosplenic schistosomiasis**:
› liver granulomas → periportal (Symmers) fibrosis → fibrosis-induced presinusoidal portal hypertension
› chronic endothelial inflammation → venous thrombosis

Dx: eggs identified in stool specimen / rectal biopsy

Cx: (1) Splenomegaly with siderotic nodules

(2) Portal vein thrombosis with collateral circulation → gastrointestinal hemorrhage

(3) Portal cholangiopathy → cavernous transformation of portal vein → biliary obstruction with jaundice

(4) Portal hypertension → eggs shunted from portal system into pulmonary vasculature

@ GI tract

√ esophageal varices ← portal hypertension

√ polypoid calcifying bowel lesions ← eggs of S. mansoni trapped in bowel wall + inciting granulomatous reaction)

DDx: isolated intestinal schistosomiasis may be indistinguishable from other forms of proctocolitis.

@ Liver

√ severe splenomegaly with siderotic nodules

√ atrophy of right hepatic lobe + widening of fissures

√ portal hypertension ← fibrosing granulomatous reaction within presinusoidal portal veins ← ova migrating into portal venous system

√ periportal hyperechogenicity

√ gallbladder wall thickening

MR:

√ high-signal-intensity bands along portal tracts on T2WI ← periportal fibrosis

√ low signal intensity bands on T1WI enhance during venous phase

Advanced-stage hepatosplenic schistosomiasis causes marked morphologic changes in the liver with periportal fibrosis, signs of portal hypertension and severe splenomegaly with siderotic nodules.

@ Lung

› early form (3–8 weeks after parasitic penetration)

- shortness of breath, wheezing, dry cough
- eosinophilia ← immunologic type 3 reaction
- **Katayama fever** = pulmonary symptoms coincide with febrile illness ← immunologic reaction to parasite eggs

Associated with: hepatosplenomegaly, hepatitis, urticaria, arthralgia

√ diffuse small nodular granulomatous lung lesions with ill-defined borders

√ reticulonodular pattern (less common)

√ bilateral diffuse ground-glass opacities / hyperattenuation

› late form = granulomatous type 4 reaction to eggs deposited in pulmonary vasculature → intimal fibrosis, pulmonary hypertension, cor pulmonale

- dyspnea, chest pain, fatigue, palpitations, cough
- right-sided heart failure (late)

√ cardiomegaly

√ enlargement of RV + pulmonary artery + azygos vein (from portal hypertension)

SCHWANNOMA OF ADRENAL GLAND

= benign nerve sheath tumor of neural crest origin
Location: retroperitoneum (3%), adrenal gland (rare)
Age: 20–40 years
CT:
√ heterogeneously enhancing hypoattenuating mass
MR:
√ marked variability depending on degree of degeneration
√ isointense signal to muscle on T1WI
√ hyperintensity on T2WI
DDx: pheochromocytoma, malignant tumor

SCROTAL ABSCESS

Etiology:
(1) Complication of epididymoorchitis (often in diabetics), missed testicular torsion, gangrenous tumor, infected hematoma after trauma, primary pyogenic orchitis
(2) Systemic infection: mumps, smallpox, scarlet fever, influenza, typhoid, syphilis, TB
(3) Septic dissemination: sinusitis, osteomyelitis, cholecystitis, appendicitis
Predisposed: diabetics
NUC:
√ marked increase in perfusion = hot hemiscrotum with photon-deficient area representing the abscess on ^{99m}Tc-pertechnetate scan (DDx: chronic torsion)
√ increased scrotal uptake with leukocyte imaging
US:
√ hypoechoic / complex fluid collection (differentiation of intra- from extratesticular abscess location possible):
√ intratesticular abscess with low-level internal echoes + shaggy wall
√ focal area of absent color Doppler flow
√ hypervascular surrounding testicular parenchyma
√ skin thickening
√ hydrocele
MR:
√ hypointense on T1WI + hyperintense on T2WI ← fluid content
√ hypointense rim on T2WI
√ nonenhancing lesion + avid enhancement of surrounding tissue
√ central hyperintensity on DWI with corresponding low signal on ADC map ← restricted diffusion of abscess cavity
Cx: (1) Pyocele
(2) Fistulous tract to skin (T1-hypointense linearity with corresponding hyperintensity on fat-suppressed T2WI)

SEMINAL VESICLE CYST

√ cystic mass posterior to urinary bladder (DDx: müllerian duct cyst)
√ dilated ejaculatory duct

Acquired Seminal Vesicle Cyst

Etiology:

1. Autosomal dominant polycystic kidney disease
   √ bilateral seminal vesicle cysts
2. Invasive bladder tumor
3. Infection
4. Benign prostatic hypertrophy
5. Ejaculatory duct obstruction

Congenital Seminal Vesicle Cyst

Associated with: anomalies of ipsilateral mesonephric duct:

Etiology:

(1) Ectopic insertion of ipsilateral ureter 92% into bladder neck / posterior prostatic urethra / ejaculatory duct / seminal vesicle
(2) Ipsilateral renal dysgenesis 80%
(3) Duplication of collecting system 8%
(4) Vas deferens agenesis

Symptomatic age: 21–41 years

- abdominal / flank / pelvic / perineal pain exacerbated by ejaculation, epididymitis in prepubertal boy
- dysuria, frequent urination, recurrent urinary tract infection

SINUS LIPOMATOSIS

= PERIPELVIC LIPOMATOSIS = PELVIC FIBROLIPOMATOSIS = PERIPELVIC FAT PROLIFERATION

Etiology:

(1) Normal increase with aging and obesity
(2) Proliferation of sinus fat
   (a) vicarious proliferation (usually unilateral) (= replacement lipomatosis) see below
   (b) metabolic proliferation (bilateral) ← increased exogenous / endogenous steroids
(3) Extravasation of urine → proliferation of fatty granulation tissue
(4) Normal variant

Age: 6th–7th decade

- asymptomatic

√ kidney may be enlarged
√ elongated "spiderlike / trumpetlike" pelvicaliceal system
√ infundibula arranged in "spoke-wheel" pattern
√ parenchymal thickness diminished with underlying disease
√ occasionally focal fat deposit with localized deformity of collecting system

Plain film:
√ diminished sinus density = radiolucent sinus

CT:
√ unequivocal fat values

US:
√ echodense / patchy hypoechoic sinus complex

Replacement Lipomatosis / Fibrolipomatosis

= extreme form of renal sinus lipomatosis ← renal destruction / atrophy

Associated with: infection, long-term hydronephrosis, calculi (70%)

Path: marked proliferation of hyperplastic sinus fat with extremely atrophied cortex + varying degrees of hydro- / pyonephrosis, acute / chronic pyelonephritis

√ kidney enlarged by a fatty sinus mass and outlined by an extremely thin cortex:

√ fat characteristically distributed within renal sinus + perinephric space

√ staghorn calculus inside an enlarged renal outline

√ poorly functioning / nonfunctioning kidney

DDx: xanthogranulomatous pyelonephritis, lipoma, angiomyolipoma, liposarcoma (focal mass effect on intrarenal collecting system, no calculus, no parenchymal renal atrophy)

SKENE DUCT CYST

= paraurethral retention cyst
Origin: urogenital sinus
Cause: inflammatory obstruction of paraurethral ducts
Histo: stratified squamous epithelium
Location: lateral to external urethral meatus
√ round / oval T2-hyperintense lesion
DDx: Bartholin gland cyst (similar location)

SPERMATIC CORD TORSION

= TESTICULAR TORSION = TWISTING OF SPERMATIC CORD
◊ Most common scrotal disorder in children, 20% of acute scrotal pathology
Incidence: 1÷4,000 to 1÷25,000 males of < 25 years annually; 10-fold risk in undescended testis
Etiology:
(1) Intravaginal torsion (= torsion distal to attachment of tunica vaginalis) = **"bell and clapper" deformity** = high insertion of tunica vaginalis on spermatic cord in 12% of males
Site: in 5% bilateral ← anomalous suspension of contralateral testis found in 80%
Age: any, predominantly adolescence
(2) Extravaginal torsion (10%) = torsion proximal to attach-ment of tunica vaginalis involving testis + tunica vaginalis ← loose attachment of testicular tunics to scrotum
Age: in utero (mostly) + perinatal period; may be bilateral
• testis necrotic at birth → swollen + discolored hemiscrotum
√ complex hydrocele + calcification of tunica albuginea
(3) Abnormally loose mesorchium between testis + epididymis
Pathophysiology: blood flow compromise → venous obstruction followed by arterial obstruction
Peak age: newborn period + puberty (13–16 years); < 20 [> 21] {> 30} years in 74–85% [26%] {9%}
Cx: testicular atrophy (in 33–45%)

Acute Testicular Torsion

= symptoms present for < 24 hours
• 70% of patients present within first 6 hours from onset of pain:
  • sudden severe pain in 100% (frequently at night)
  • negative urine analysis (98%), nausea + vomiting (50%)
  • history of similar episode in same / contralateral testis (42%); history of trauma / extreme exertion (13%)
  • scrotal swelling + tenderness (42%)
  • leukocytosis (32%), low-grade fever (20%)
• Brunzel sign = elevated horizontal lie of testis
• Ger sign = skin pitting at scrotal base

◊ SURGICAL EMERGENCY!

Testicular viability related to:

(a) degree of torsion (720° necessary for complete ischemia)

Degree of torsion and blood flow:

- testis usually turns medially up to 1,080°

√ diminished blood flow in < 180°-torsion at 1 hour

√ absent blood flow in any degree of torsion > 4 hours

(b) length of ischemia

Salvage rate versus time from onset of pain to surgery

97–100% < 6 hrs	57% 6–12 hrs
35% 12–24 hrs	0–9% > 24 hrs

◊ Irreversible ischemic damage begins at 3–6 hours after onset of torsion!

(c) intermittent torsion

◊ Spontaneous detorsion in 7%

√ hyperemia after spontaneous detorsion

US (80–90% sensitivity):

√ testicular echogenicity:

√ normal grey-scale appearance (within 1–3–6 hours)

√ diffusely hypoechoic echotexture (> 6 hours)

√ heterogeneous echotexture ← ischemic necrosis

√ testicular size:

√ normal size = 80% salvage rate

√ testicular + epididymal enlargement with decreased echogenicity (within 8–24 hours)

◊ Torsion has no / minimal epididymal flow (DDx: acute epididymitis has increased flow)

√ extratesticular findings:

√ scrotal skin thickening

√ hydrocele (occasionally)

√ "torsion knot" sign = twisted enlarged spermatic cord with spiraling vessels at external inguinal orifice

√ intrascrotal portion of cord round / ovoid / curled with epididymal head wrapped around it

√ inverted orientation of testis + epididymis + cord (in 6%)

Pitfall: dilated cord mistaken for abnormal epididymis

Color duplex (86% sensitive, 100% specific, 97% accurate):

N.B.: contralateral testis = internal normal control (!)

√ loss of spermatic cord Doppler signal (44% sensitive, 67% specific)

√ absence of testicular + epididymal flow (DDx: global testicular infarction)

√ diminished flow (veins affected before arteries) ← incomplete (< 360°) / intermittent torsion:

√ some arterial flow persists (in 20% of torsions)

√ high-resistance waveform = decreased / reversed arterial flow in diastole

False-negative: torsion-detorsion sequence, incomplete torsion < 360 degrees

False-positive: in small boys < 4 years of age (= limitation of color Doppler sensitivity)

NUC (98% accuracy):

Dose: 5–15 mCi ^{99m}Tc-pertechnetate

Imaging: at 2- to 5-sec intervals for 1 min (vascular phase); at 5-min intervals for 20 minutes (tissue phase)

√ decreased perfusion / occasionally normal

√ "**nubbin**" sign = bump of activity extending medially from iliac artery ← reactive increased blood flow in spermatic cord with abrupt termination

√ rounded cold area replacing testis (requires knowledge of side + location of painful testis)

Rx: (1) Detorsion (***should be attempted by radiologist***):

◊ Twist testis outward + laterally by 180° like "opening a book"! May have to be repeated; successful in $^{2}/_{3}$

(2) Orchiopexy

DDx: epididymo-orchitis (more gradual onset of pain, however, in 5% sudden onset of pain)

Subacute Testicular Torsion

= MISSED TESTICULAR TORSION

= symptoms present for > 24 hours + less than 10 days

US:

√ enlarged / normal-sized testis with heterogeneous punctate / diffusely increased echotexture

√ ⇑ peritesticular flow without parenchymal blood flow

Pitfall: increased flow in scrotal wall mistaken for intrascrotal inflammatory disease

NUC:

√ normal NUC angiogram / "nubbin" sign

√ "doughnut" sign = decreased testicular activity with rim hyperemia of dartos perfusion

MR:

√ enlarged spermatic cord without increase in vascularity

√ whirlpool pattern (twisting of spermatic cord)

√ torsion knot = low-signal-intensity focus at point of twist (= displacement of free protons from epicenter of twist)

Chronic Testicular Torsion

√ small atrophied homogeneously hypoechoic testis

√ enlarged echogenic epididymis

Appendix Testis Torsion

= TORSION OF TESTICULAR APPENDAGE

◊ Most common cause of scrotal pain in pediatric population; accounts for 5% of scrotal pathology

Prevalence: 31–67%

Age: prepubertal male aged 7–14 years

- gradual / sudden intense pain localized to upper pole of testis
- "blue dot" sign (21%) = PATHOGNOMONIC nodule visible as bluish dot beneath skin in upper scrotum

Location: near superior pole of testis; L > R
√ ovoid complex hypo- to hyperechoic extratesticular 4–16 mm mass in superior aspect of scrotum
√ mass without color Doppler flow signals
√ reactive noninfectious epididymo-orchitis:
  √ mildly enlarged epididymal head (75%)
  √ hyperemia of ipsilateral epididymis (60%) + scrotal wall (53%) + testis (13%) simulating acute epididymo-orchitis
  √ reactive hydrocele + scrotal skin thickening
√ NO Doppler signal within twisted appendage
√ hypervascularisation of epididymis + scrotal tunics
√ "scrotal pearl" = **scrotolith** = calcified detached remnant of twisted appendix testis on follow-up US within days
Rx: bed rest, NSAID

SQUAMOUS CELL CARCINOMA OF KIDNEY

Frequency: 5–10% of all urothelial tumors; 1% of renal neoplasms; 2nd most common malignancy of pelvic urothelium after TCC
Age: 60–70 years; M÷F = 2:1
Path: flat ulcerating mass + extensive induration
Associated with: chronic irritation of urothelium by renal infection + calculi (25–60%)
• painless hematuria
• flank pain (with ureteropelvic junction obstruction)
√ infiltrating renal process
√ nonfunctional kidney:
  √ ureteropelvic junction obstruction (common)
√ presence of faceted calculi (40–80%)
IVP:
  √ stricture that may simulate extrinsic cause
Angio:
  √ arterial encasement + occlusion + neovascularity
  √ enlarged pelvic + ureteric arteries
  √ occlusion of renal vein / branches (41%)
CT:
  √ thickening of pelvicaliceal wall (with superficial spread over large areas)
  √ enlarged kidney maintaining reniform shape:
    √ infiltrating growth into sinus + parenchyma
    √ tumor mass infrequent
  √ no contrast excretion ← obstruction
Prognosis: worse than TCC ← early metastases; 33% 1-year survival rate
DDx: xanthogranulomatous pyelonephritis (radiologically indistinguishable)

SUPERNUMERARY KIDNEY

= aberrant division of nephrogenic cord into two metanephric tails (rare)

Associated with: horseshoe kidney, vaginal atresia, duplicated female urethra, duplicated penis
Location: most commonly on left side of abdomen caudal to normal kidney
√ supernumerary ureter may insert into ipsilateral kidney / directly into bladder / ectopic site
Cx: hydronephrosis, pyonephrosis, pyelonephritis, cysts, calculi, carcinoma, papillary cystadenoma, Wilms tumor

TESTICULAR CANCER

◊ Most common neoplasm in males between ages 15 and 35 years; 0.5% of all cancers in males; 4–6% of all male genitourinary tumors; 1% of all childhood malignancies; 4th most common cause of death from malignancy between ages 15–34 years (12%)
Incidence annually: 5.7÷100,000 in 2016 (4.1÷100,000 in 1975); 1÷263 males; 8,720 new cases in USA (2016)
Peak age: 25–35 years; 71–90 years; infants < 3 years: yolk sac tumor + teratoma; White÷Black = 4.5÷1
Risk factors:
(1) Prior testicular cancer (20 x risk = 2–5%)
(2) Maldescension = cryptorchidism (10 x risk)
5% for abdominal site, 1.25% for inguinal site
Rx: orchiopexy
(3) Family history of testicular cancer (6 x risk for 1st-degree relative = 2%)
more prevalent in Caucasian race, Jewish religion
(4) Infertility (0.4–1.1% prevalence of intratubular germ cell neoplasia)
(5) Intersex syndrome: gonadal dysgenesis, true hermaphroditism, pseudohermaphroditism

- painless enlarging testis / mass (90%), however:
  - acute scrotal pain (10%, from intratumoral hemorrhage)
- "heaviness / fullness" in lower abdomen / scrotum
- gynecomastia, virilization

Location: mostly unilateral; contralateral tumor develops eventually in 8%
Metastases: at presentation in 4–14%
(a) lymphatic dissemination
testicular lymphatic drainage follows gonadal veins to
› interaortocaval chain at L2 (for right testicular tumor)
› left paraaortic nodes between renal vein, aorta, ureter and inferior mesenteric artery
› along thoracic duct
› left supraclavicular nodes
› lungs
(b) hematogenous dissemination (usually late) to lung > liver, brain, bone
◊ Choriocarcinoma has a proclivity for early hematogenous spread (especially to brain)!
(c) direct extension through tunica albuginea to skin (rare and late) / epididymis → spread to inguinal + iliac nodes
Histo: may be different from that of primary tumor indicating totipotential nature of germ cells
Tumor markers (elevated in 80% at time of diagnosis):
α- yolk sac tumors, mixed germ cell tumors with yolk sac elements

fetoprotein:

β-hCG: seminoma, choriocarcinoma (tumors containing syncytiotrophoblasts)

LDH: correlates with bulk of disease (nonspecific as it is produced by multiple organs)

US (92–98% sensitive, 95.0–99.8% specific):

Color duplex:

√ tumor < 1.5 cm is hypovascular in 86%, > 1.6 cm hypervascular in 95% (DDx: orchitis associated with epididymal hyperemia)

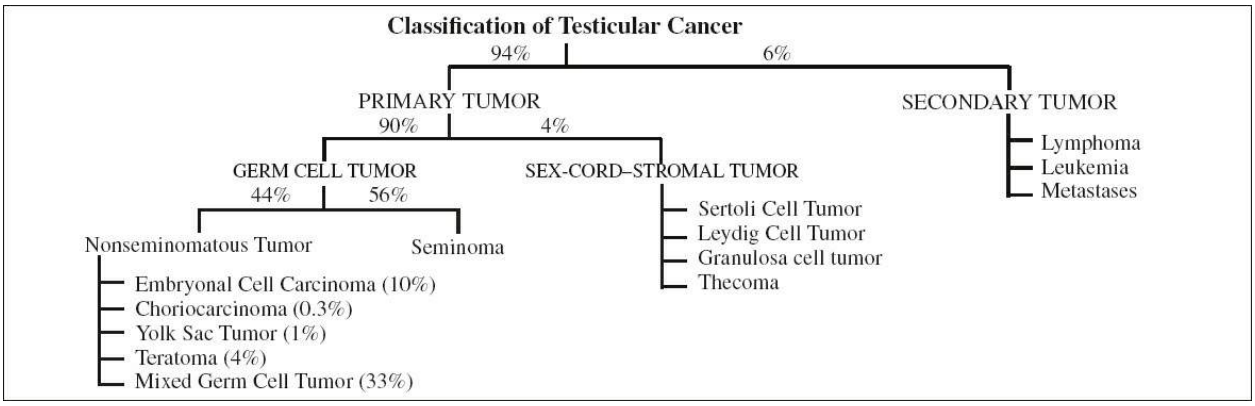
√ distortion of vessels

Age Group of Testicular Tumors	
Yolk sac tumor / teratoma	1st decade
Choriocarcinoma	2nd + 3rd decade
Embryonal cell carcinoma	3rd decade
Seminoma	4th decade
Lymphoma	7th decade

Staging of Testicular Cancer *(American Joint Committee on Cancer)*	
pTX	primary tumor not available (no orchiectomy)
pT0	no primary tumor found
pTis	intratubular germ cell tumor (carcinoma in situ)
pT1	limited to testis + epididymis
pT2	same as pT1 + vascular / lymphatic invasion or involvement of tunica vaginalis
pT3	invasion of spermatic cord
pT4	invasion of scrotum
pN0	negative lymph nodes
pN1	node ≤20 mm; or ≤ 5 nodes involved all <20 mm
pN2	node between 20 and 50 mm; or > 5 nodes none > 50 mm
pN3	node mass > 50 mm
M0	no distant metastasis
M1	distant metastasis
S0	all markers normal
S1	LDH < 1.5 x ULN + hCG <5,000 mIU/mL + AFP < 1,000 ng/mL
S2	LDH < 1.5–10 x ULN ± hCG 5,000–50,000 mIU/mL ± AFP 1,000–10,000 ng/mL
S3	LDH > 10 x ULN ± hCG >50,000 mIU/mL ± AFP > 10,000 ng/mL

ULN = upper limits of normal

Testicular Cancer Stage Grouping	
I	limited to testis + spermatic cord
II	metastases to lymph nodes below diaphragm
II A	nonpalpable < 2 cm in diameter
II B	moderate mass = 2–5 cm in diameter
II C	bulky mass > 5 cm in diameter
III	metastases to lymph nodes above diaphragm
III A	confined to lymphatic system
III B	extranodal metastases



MR:

√ tumors isointense to testicular parenchyma on T1WI + T2WI

Prognosis: > 93% [85–90%] 5-year survival rate for stage I [stage II]; complete remission under chemotherapy in 65–75%; relapse in 10–20% within 18 months

Most cases of testicular cancer are curable as a result of advances in chemotherapy.

DDx:

Imaging overlap exists between testicular tumors and nontumorous conditions. Correlation with clinical history is critical to avoid unnecessary surgery.

(1) Testicular infarction
(2) Testicular hematoma
(3) Orchitis: acute / granulomatous
(4) Epidermoid cyst
(5) Syndromic lesion:
  (a) adrenal rests in congenital adrenal hyperplasia
  (b) lipomatosis in Cowden disease

Rx: inguinal orchiectomy (first-line treatment)

About 95% of testicular cancers are germ cell tumors, and 5% are sex-cord–stromal tumors. Approximately 50% of germ cell tumors are seminomas, and about 50% are nonseminomatous germ cell tumors (NSGCTs).

Germ Cell Tumor (95%)

Origin: primitive spermatogenic cell

(a) one histologic type in 65%
- › from unipotential nondifferentiated gonadal line:
  1. Seminoma
- › along a totipotential line → forming differentiated nonseminomatous tumors (more aggressive than seminoma):
  1. Embryonal carcinoma (slightly differentiated)
  2. Teratoma (embryonic differentiation)
  3. Yolk sac tumor (extraembryonic differentiation)
  4. Choriocarcinoma (extraembryonic differentiation)

(b) mixed lesion
- › from totipotential cells developing along several pathways (embryonal carcinoma being the most common component of mixed lesions)
  1. Teratocarcinoma (= teratoma + embryonal cell ca.)
     - ◊ 2nd most common after seminoma, may occasionally undergo spontaneous regression
  2. Embryonal cell carcinoma + seminoma
  3. Seminoma + teratoma

(c) **Growing Teratoma Syndrome**:
= evolution of mixed germ cell tumor → into mature teratoma after chemotherapy (in 40%) → followed by interval growth despite maintaining a benign histology

mnemonic: YES CT
Yolk sac tumor
Embryonal cell carcinoma
Seminoma
Choriocarcinoma
Teratoma

Seminoma (35–50%)

◊ Most common tumor in undescended testis!
◊ Most common pure germ cell tumor!

Average age: 40.5 years (slightly older patient compared with other germ cell tumors)
Stem cell: unipotential cell line
Histo: uniform cellular morphology resembling primitive germ cells
(1) Typical seminoma 85%
(2) Anaplastic seminoma 10%
(3) Spermatocytic seminoma 5%
Presentation: in 75% limited to testis;
in 20% retroperitoneal lymphadenopathy;
in 5% extranodal metastases
Associated with: testicular microlithiasis

• serum α-fetoprotein normal in pure seminomas
• β-hCG elevation (in 5–25%) ← produced by syncytiotrophoblastic giant cells

√ usually homogeneous hypoechoic mass:
√ round / lobulated / multiple confluent nodules

√ entire testis replaced (> 50%)
√ cystic component (10%) ± fluid-debris level
√ confined within tunica albuginea (= less aggressive)
√ calcifications / cystic spaces (infrequent)
√ may be multifocal
√ bilateral in 1–3%, almost always asynchronous
MR:
√ homogeneously hypointense on T2WI
√ enhancing bandlike areas of low SI on T1WI + T2WI ← fibrovascular septa
Rx: very sensitive to radiation ± chemotherapy
Prognosis: 10-year survival rate of 75–85%; 19% develop pulmonary metastases

Nonseminomatous Tumor

Frequency: 50% of all germ cell tumors
Stem cell: totipotential embryonal cell line with varying degrees of differentiation into embryonal, teratoma, yolk sac, or choriocarcinoma cells
Age: 20–30 years
• ⇑ α-fetoprotein level (in 50–60%)
√ heterogeneous echotexture (71%)
√ cystic spaces (61%)
√ irregular ill-defined margins (45%)
√ echogenic foci ← calcifications (35%)

EMBRYONAL CELL CARCINOMA (20–25%)

◊ Second most common testicular tumor!
◊ Most common component of mixed germ cell tumors (embryonal cells present in 87%); often associated with teratoma
Histo: primitive anaplastic epithelial cells resembling early embryonic cells; in 3% as pure form
Age: 25–35 years and < 2 years
Spread: most aggressive testicular tumor, visceral metastases
• ± α-fetoprotein elevation
√ hypoechoic mass with heterogeneous areas:
√ ill-defined borders
√ areas of increased echogenicity ← hemorrhage
√ cystic areas ← necrosis
√ may show invasion of tunica albuginea (common)
Rx: less sensitive to radiation
Prognosis: 30–35% 5-year survival rate

MIXED GERM CELL TUMOR

= malignant neoplasm with more than 1 germ cell tumor component excluding seminoma with syncytiotropho-blastic cells
Frequency: 69% of all nonseminomatous + 32% of all testicular germ cell tumors
Components: embryonal cell (most common, often combined with teratoma / seminoma / yolk sac tumor)

Average age: 30 years
• ↑ α-fetoprotein (in 60%), ↑ β-hCG levels (in 55%)
√ unilateral mass with a mixture of solid + cystic components ← necrosis, hemorrhage, cystic degeneration
√ calcifications (in 40%)

TERATOMA (4–10%)
Prevalence: 1÷1,000,000;
◊ 2nd most common testicular tumor in young boys ≤ 5 years (75%)
Histo: consists of elements from > 1 germ cell layer (keratin, muscle, bone, cartilage, hair, mucous glands, neural tissue); 2–3% as pure form (in adult)
(a) mature
(b) immature
(c) malignant areas
Age: within first 4 years of life; benign in children; may transform into malignancy in adulthood
• serum α-fetoprotein usually normal
√ well-circumscribed heterogeneous complex mass:
√ anechoic / complex cysts with variable echogenicity ← serous, mucoid, keratinous fluid
√ markedly echogenic components ← cartilage, calcification, fibrosis, scar formation
√ echogenic intratumoral fat
Prognosis:
variable biologic behavior: benign in prepubertal testes BUT may metastasize in postpubertal testes with nonteratomatous germ cell elements; metastases to lymph nodes, bone, liver in 30% within 5 years

EPIDERMOID CYST / KERATIN CYST OF TESTIS (1%)
= "monodermal dermoid"
= benign teratoma with only ectodermal components / squamous metaplasia of surface mesothelium
Origin: ? monodermal development of a teratoma, ? meta- plasia of rete testis / seminiferous epithelium
Age: 20–40 (range, 3–77) years; primarily in white + Asian population
Histo: cyst contains keratin debris / other desquamated material; wall composed of fibrous tissue + lined by keratinizing stratified squamous epithelium
• smooth firm painless testicular nodule
• negative tumor marker status
Location: R (>) L; solitary >> multiple >> bilateral
Size: 1–3 (range 0.5–10.5) cm in diameter
√ sharply circumscribed encapsulated round lesion:
√ "**onion-skin**" / ringed appearance of alternating hypo- and hyperechogenicity (= alternating layers of compacted keratin + loosely arranged desquamated squamous cells):
√ well-defined rim = hyperechoic fibrous cyst wall ± shadowing from

calcifications / ossification
√ hypoechoic cyst contents (= laminated keratin debris)
√ "target / bull's eye" appearance ← echogenic center ← compacted keratin / calcification
√ confined by tunica albuginea
√ diffuse testicular enlargement (10%)
√ NO blood flow on Doppler (avascular lesion)
MR:
√ target appearance:
√ fibrous capsule of low SI on T1WI + T2WI
√ cyst content (water and lipid) of high SI on T1WI + T2WI
√ alternating concentric rings of low + high SI
√ center of mass of low SI ← keratin debris ± central calcification
√ NO enhancement
Prognosis: no malignant potential
Rx: enucleation + frozen section (testis-sparing surgery to avoid orchiectomy)

CHORIOCARCINOMA (1–3%)

Prevalence: in 0.3% in pure form; in 8–16% of mixed germ cell tumors
Peak age: 20–30 years
Histo: admixture of cytotrophoblastic + syncytiotrophoblastic cells
Spread: may rapidly metastasize (lung, liver, GI tract, brain) without evidence of choriocarcinoma in primary lesion, pulmonary metastases develop in 81%
• symptoms of metastatic disease while primary not yet palpable
• serum β-hCG always elevated → gynecomastia in 10%
N.B.: choriocarcinoma has a proclivity for hemorrhage in primary site and metastases!
√ often small tumor of mixed echotexture ← hemorrhage, necrosis, calcifications
√ indistinct margins of pulmonary metastases ← hemorrhage
Prognosis: death usually within 1 year of diagnosis; nearly 0–48% 5-year survival rate

YOLK SAC TUMOR = ENDODERMAL SINUS TUMOR

Equivalent to endodermal sinus tumor of ovary
Prevalence: most common germ cell tumor
◊ 80% of childhood testicular tumors!
◊ Present in 44% of mixed germ cell tumors of adults
Age: ≤ 2 years (80%)
• serum α-fetoprotein elevated in > 90% (exclusive to yolk sac elements)
√ nonspecific imaging findings:
√ testicular enlargement ± identifiable mass
√ hypoechoic areas (frequent) ← necrosis
√ pulmonary metastases (most common site of recurrent disease)

Sex Cord-Stromal Tumor = Interstitial Cell Tumor

Prevalence: 4% of all testicular tumors; 10–30% during childhood
Origin: supporting tissues of testis (sex cord + stromal cells)

- precocious virilism (10% in children)
- painless testicular mass without endocrine abnormalities
- gynecomastia (adults >> children)
- loss of libido, impotence (adults)

Spread: in 20% at initial diagnosis; metastases to lymph nodes (70%), liver (45%), lung (40%), bone (25%)

Rx: orchiectomy; conservative resection under ultrasound guidance

Prognosis: malignant in 10–20%

Leydig Cell Tumor

Prevalence: 1–3% of all testicular tumors

Origin: interstitial cells forming the fibrovascular stroma

Age: 3–6 years; 20% in patients < 10 years; 25% between ages 30 and 50 years; 25% in patients > 50 years

Histo: usually polygonal large cells with abundant cytoplasm; intracytoplasmic / intranuclear cylindric / rectangular / rhomboid structures = Reinke crystals

- endocrinopathy (in 30%) → secretion of androgens or estrogens (direct production of estradiol / aromatization of testosterone moiety) by the tumor:
  - precocious puberty / virilization
  - gynecomastia (in 30%); decreased libido

Laterality: unilateral + solitary; 3% bilateral

Size: 3–5 cm

US:

√ usually small homogeneous hypoechoic / occasionally echogenic nodule
√ ± cystic areas in 25% ← hemorrhage / necrosis
√ lacking internal vascularity + prominent circumferential blood flow on Doppler

MR:

√ isointense on T1WI + hypointense on T2WI compared to surrounding normal testis
√ hyperintense capsule on T2WI
√ internal high SI on T2WI ← central scar
√ marked homogeneous enhancement

Prognosis: benign÷malignant = 9÷1

Rx: enucleation to preserve fertility (if benign); radical orchiectomy + retroperitoneal lymphadenectomy

Sertoli Cell Tumor

Prevalence: 0.4–1.5% of all testicular tumors

Origin: sex cord (derived from Sertoli cells of seminiferous tubules)

Histo: moderate to abundant eosinophilic cytoplasm / pale ← lipid accumulation; ± Charcot-Böttcher crystals (specific cytoplasmic inclusion bodies)

Subtype: **l**arge-**c**ell **c**alcifying **S**ertoli **c**ell **t**umor

Age: most < 40 years; 30% in children

- may secrete estrogens → gynecomastia in 3%

Laterality: unilateral; may be bilateral + multifocal

US:

√ multicystic "spoke-wheel" appearance
√ diffusely ⇑ inhomogeneous echogenicity in enlarged testis (occasionally) ← dense collagenous matrix
√ well-circumscribed round / lobulated hypoechoic nodules + surrounding thin hypoechoic rims (usually)
√ dense echogenic foci ← calcified scars = "burned-out" tumor

LARGE-CELL CALCIFYING SERTOLI CELL TUMOR

= LCCSCT = most common histologic variant in children + adolescents
• precocious puberty ← testosterone production
Associated with: Peutz-Jeghers syndrome, Carney syndrome (almost exclusively)
US:
√ echogenic nodule with acoustic shadowing
√ multiple bilateral (20%) large areas of calcifications
MR:
√ homogeneously isointense on T1WI + hyperintense on T2WI
√ variably homogeneous / rim enhancement
Prognosis: benign÷malignant = 9÷1
Rx: radical orchiectomy (may be delayed to bank sperm)

Gonadoblastoma

= primitive gonadal stroma tumor (exceedingly rare) containing sex cord-stromal elements + germ cells
Histo: dysgenetic lesion not neoplasm
• abnormal karyotype in 80%: intersex status, phenotypically female

Nonprimary Testicular Tumors

Metastases to Testis (in 0.7% of autopsies)

Mean age: 55 years
(a) in adults: prostate (35%) > lung (19%) > melanoma (9%), colon (9%) > kidney (7%), bladder, thyroid
◊ More common than germ cell tumors in males > 50 years of age!
(b) in children: neuroblastoma, retinoblastoma, Wilms tumor, rhabdomyosarcoma
√ often multiple and bilateral (in 8–15%)
√ mostly hypoechoic, occasionally echogenic masses

Lymphoma of Testis

Frequency: 1–9% of all testicular tumors; in 1% of patients with NHL / ALL
Age: most common testicular tumor in men > age 60; median age of 37 years in immunocompromised
Presentation:
(a) primary testicular lymphoma (rare)
(b) secondary involvement:
› initial manifestation of clinically occult disease
› site of recurrent disease in established lymphoma

◊ Metachronous involvement (in 80%) months to years following orchiectomy

Histo: NHL = almost exclusively B-cell lymphoma (most commonly diffuse large cell lymphoma > follicular lymphoma, mucosa-associated lymphoid tissue, plasmacytoma, granulocytic sarcoma)

Associated with: widespread dissemination to skin, lung, CNS (6–17%), Waldeyer ring (6%)

- painless testicular enlargement over weeks to months
- weight loss, anorexia, fever, weakness (initial complaint in 25%)

Location: bilateral in 38%; synchronous in 20%

◊ The most common bilateral testicular tumor!

√ enlarged diffusely hypoechoic testis ← ill-defined diffuse infiltrative process
√ multiple focal hypoechoic masses
√ epididymis + spermatic cord + skin commonly infiltrated
√ increased blood flow on color Doppler

MR:

√ testis replaced by tissue hypointense on T1WI + T2WI
√ low-level enhancement less than normal testis
√ one / more focal masses
√ frequent extension outside testis into epididymis

Prognosis: poor; median survival of 12 months; 12–35% 5-year survival

DDx: epididymo-orchitis (tender, improvement on Rx), sarcoid (African-American), tuberculosis, leukemia (often prior history of treated leukemia)

Leukemia of Testis

Prevalence: 60–92% on autopsy; 8–16% on clinical examination during therapy; up to 41% on clinical examination after therapy

◊ Occult testicular tumor often found in patients in bone marrow remission (gonadal barrier = blood-testis barrier to chemotherapy)

√ uni- / bilateral tumors:
√ diffuse / focal
√ hypo- or hyperechoic

Burned-out Tumor of Testis

= AZZOPARDI TUMOR = REGRESSED GERM CELL TUMOR

= widespread metastatic disease + spontaneous regression of testicular malignancy ← teratocarcinoma

Histo: minute amounts of residual tumor / dense deposit of collagen + scattered inflammatory cells

Pathogenesis: tumor with high metabolic rate outgrows its own blood supply

√ small primary tumor:
√ hypoechoic lesion
√ highly echogenic focal lesion (= scarred tumor residue)
√ ± shadowing (= focal calcification)

√ metastases to retroperitoneum, mediastinum, cervical / axillary / supraclavicular lymph nodes, lung, liver

Second Testicular Tumor

Prevalence: 1–5% of all testicular cancers

US: a testicular abnormality is malignant in only 50%!

SYNCHRONOUS TESTICULAR TUMOR

= development of 2 separate primary tumors ← NO lymphatic / vascular connections between testes

Frequency: 10% of bilateral tumors

Histo: identical

Rx: bilateral orchiectomy; for small tumors testis-preserving surgery + radiation therapy

METACHRONOUS TESTICULAR TUMOR

= subsequent development of second primary tumor

Frequency: 90% of bilateral tumors

Risk for second tumor in cryptorchidism:

15% for inguinal, 30% for abdominal location

Risk for second contralateral tumor:

increased by 500–1,000 x; bilaterality in 1.1–4.4%;

Development interval between 1st + 2nd tumor:

4 months to 25 years

◊ Detected in 47% [60%] {75%} by 2 [5] {10} years

TESTICULAR INFARCTION

= extremely rare

Cause: torsion, trauma, acute epididymo-orchitis, leukemia, embolus (eg, bacterial endocarditis, sickle cell disease, polycythemia), vasculitis (eg, polyarteritis nodosa, Henoch-Schönlein purpura), hernia repair (testicular atrophy in 0.5% after first repair, in 0.8–5% after recurrent repair)

Age: 20–40 years

Location: often in periphery with extension to capsule

• painful testis, soft to palpation

√ focal hypoechoic wedge-shaped region without flow (most common)

√ hyperechoic regions ← hemorrhage / fibrosis

√ decrease in testicular size over time ← fibrosis

√ diffusely hypoechoic small testis

MR:

√ hypo- / (typically) isointense to normal testis on T1WI:

√ may have high SI on T1WI ← hemorrhage

√ hypointense to normal testis on T2WI

√ avascular area + enhancing rim on contrast administration

DDx: malignancy (difficult differentiation)

TESTICULAR MICROLITHIASIS

Definition: > 5 microliths per image; ≤ 5 microliths per image = limited microlithiasis

Etiology: defect in phagocytotic activity of Sertoli cells leaving degenerated intratubular debris behind

Prevalence: 0.6%; 5% in asymptomatic men aged 18–35 years

May be associated with:

testicular germ cell tumor (40%), cryptorchidism, subfertility, infertility, Klinefelter syndrome, testicular infarcts, granulomas, male pseudohermaphroditism, Down syndrome, pulmonary alveolar microlithiasis, congenital urethroperineal fistula

Histo: laminated concretions within lumen of seminiferous tubules

• asymptomatic, uncommon incidental finding

√ 1–2-mm (> 5) hyperechoic nonshadowing foci scattered throughout the parenchyma of both testes (PATHOGNOMONIC):

√ may be asymmetrically distributed, unilateral, clustered in periphery

Cx: concurrent germ cell tumor in up to 40% (21.6 x risk)

Prognosis: the vast majority of patients with testicular microlithiasis will not develop testicular cancer

◊ Testicular microlithiasis is not a premalignant condition and does not cause testicular cancer!

Recommendation: follow up in 6–12-month intervals to screen for testicular tumors (contested)

DDx: postinflammatory changes, scars, granulomatous changes, benign adenomatoid tumor, hemorrhage with infarction, large-cell calcifying Sertoli cell tumor

TESTICULAR TRAUMA

= SCROTAL TRAUMA

Frequency: < 1% of all traumas

Cause:

(a) blunt force (crushing of testis against symphysis / between thighs): sporting activity (> 50%), motor vehicle accident (9–17%)
Pathophysiology: contusion → hematoma → fracture → rupture

(b) penetrating: sharp object (knife), missile (bullet), animal bite, self mutilation

(c) iatrogenic: complication of herniorrhaphy

(d) degloving injury: genital skin entrapped in rotating machinery

(e) thermal injury

Peak age: 10–30 years

Site: R > L (superior location with propensity to become trapped against pubis / inner thigh)

√ hematoma in scrotal wall / between layers of tunica vaginalis (= hematocele) / in epididymis / in testis

√ uriniferous hydrocele ← perforated bulbous urethra

Cx: torsion in 5–8% ← sudden forceful cremasteric contraction on "bell and clapper" deformity

Testicular Dislocation

Cause: impact against fuel tank of motor cycle

At risk: patients with wide inguinal ring / indirect inguinal hernia / atrophic testis

Site: superficial inguinal (50%), pubic (18%), canalicular (8%), penile (8%),

intraabdominal (6%), perineal (4%), crural (2%)

Testicular Fracture

= break / discontinuity in testicular parenchyma
Frequency: 17% of testicular trauma
√ linear hypoechoic + avascular band disrupting the architecture (= fracture line)
√ smooth outer contour with intact tunica albuginea
√ usually preserved vascular flow
Rx: conservative / debridement along fracture line

Testicular Hematoma

• may be quite large ← surrounding scrotal elasticity
US:
√ over time age-dependent rapid change in echo character of hematoma + decrease in size
(a) hyperacute / acute hematoma
√ initially hyperechoic acute hematoma
√ later isoechoic → reexamination after 12–24 hours
(b) chronic hematoma
√ hypoechoic / anechoic mass decreasing in size
√ absence of internal vascularity (DDx: tumor)
√ peripheral hyperemia in infected hematoma (40% incidence)
√ developing testicular cyst ← subacute / chronic liquefaction of hematoma
MR:
√ hyperintense hematoma on T1WI
√ hypointense hemosiderin rim on T2WI
NB.: Follow-up all hematomas to resolution!
◊ 40% of hematomas become infected + lead to necrosis!
◊ Testicular cancer is incidentally identified in 10–15% of patients with scrotal trauma!
Rx: conservative (ice pack, NSAID)

Testicular Rupture

= tear / rupture of tunica albuginea with protrusion of seminiferous tubules
Pathophysiology: 50 kg of force ruptures tunica albuginea
◊ SURGICAL EMERGENCY!
US (100% sensitive, 65% specific):
√ disruption of tunica albuginea = discontinuity of echogenic testicular outline (50% sensitive, 76% specific)
√ abnormal testicular contour = extrusion of testicular parenchyma (difficult DDx: peritesticular hematoma)
◊ Err on the side of overcalling!
√ heterogeneous echotexture of testis with areas of ⇓ / ⇑ echogenicity ← hemorrhage ± necrosis (DDx: intratesticular hematoma without rupture)
√ avascular region on color duplex ← disruption of tunica vasculosa (DDx: hematoma)
√ thickened scrotal wall ← hematoma of scrotal wall

√ hematocele, may show thickening + calcification of tunica vaginalis if chronic

MR (long examination time):

√ area of heterogeneously low SI on T2WI

√ interruption of hypointense fibrous tunica albuginea

Rx: immediate surgical repair → preservation of fertility + hormonal function / orchiectomy

Salvageability: 80–90% if surgical repair occurs < 72 hours after trauma; 30–55% if surgical repair occurs > 72 hours after trauma

DDx: laceration, contusion, hemorrhage

TRANSITIONAL CELL CARCINOMA

= UROTHELIAL CELL CARCINOMA

◊ Most common urinary tract cancer in USA + Europe!

Mean age: 68 years; M÷F = 2.7÷1; Whites > Blacks

Pathogenesis: chemical carcinogens act locally on epithelium (= field of change), action enhanced by length of contact time (eg, stasis / diverticulum / horseshoe kidney)

Risk factors:

(1) Cigarette smoking (2–3 x): dose-response relation to pack-years; 50–60% in M, 33% in F

(2) Chemical carcinogens: aniline dye, benzidine, aromatic amines, azo dyes in textile, rubber, petroleum, printing, plastic manufacturing, arsenic in drinking water (lag time of 10 years)

(3) Antineoplastic alkylating agents: carmustine, busulfan, cyclophosphamide (lag time of 6.5 years)

(4) Analgesic abuse (8 x increase): long-term use of phenacetin → capillosclerosis + renal pelvic TCC

(5) **B**alkan nephropathy (= progressive renal failure + development of bilateral and multiple tumors) ← unintentional ingestion of aristolochic acid in seeds of the Aristolochia clematitis plant (contaminating flour)

(6) Recurrent / chronic urinary tract infection (esp. Schistosoma haematobium)

(7) Heavy caffeine consumption (?)

Growth pattern:

(a) papillary lesion with predominantly exophytic growth
= frondlike structure with central fibrovascular core lined by epithelial layer
› broad based
› pedunculated

(b) infiltrating: usually higher grade + less common

(c) carcinoma in situ

Grade: usually correlates with stage
1 = cells slightly anaplastic
2 = intermediate features
3 = marked cellular pleomorphism

Location: typically multifocal

@ Lower urinary tract (95%)

1. Urinary bladder: 30–50 x more common than upper urinary tract

@ Upper urinary tract (5%)
2. Kidney (3.75%): calyx > renal pelvis
3. Ureter (1.25%): 75% in lower ⅓ — 25% in upper ⅔

Spread: mucosal extension, regional lymph nodes (early involvement), hematogenous (liver, bone, lung)

Prognosis: multicentricity means poor survival; frequent synchronous + metachronous tumors requires vigilant urologic + radiographic follow-up

Follow-up: annual CT x 2 years; cystoscopy 4 x 3 months for 1st year, 2 x 6 month in 2nd year, yearly thereafter for early detection of metachronous bladder TCC

Renal TCC

Prevalence: 7% of all renal neoplasms; bilateral in 2–4%; 90% of all tumors arising from renal pelvic urothelium

Age: 6th & 7th decades; M÷F = 3÷1

Site: extrarenal part of renal pelvis > infundibulocaliceal region

◊ Synchronous bilateral renal TCC in 1–2%
◊ Metachronous renal TCC in 11–13%
◊ Metachronous bladder TCC in 23–40% after 15–48 months

Excretory Urogram:

√ single / multiple sessile / pedunculated mulberry-like filling defects in renal pelvis (35%):
  √ "stipple" sign = contrast material trapped in interstices of papillary lesion (DDx: blood clot, fungus ball)
√ dilated calyx with filling defect (26%) ← stricture / complete obstruction of infundibulum:
  √ ± focal delayed increasingly dense nephrogram
  √ caliceal amputation (19%) = "**phantom calyx**" = failure to opacify ← obstruction (DDx: TB stricture of infundibulum)
  √ "**oncocalyx**" = contrast outlining distended calyx completely filled with tumor
√ absent / decreased excretion with renal atrophy (13%) ← long-standing obstruction of ureteropelvic junction
√ renal enlargement:
  √ large bean-shaped kidney ← infiltrative tumor invasion of renal parenchyma
  √ hydronephrosis (6%) ← tumor obstructing ureteropelvic junction
√ tumor calcifications in 2–7%

Staging of Transitional Cell Cancer of Kidney		
TNM	*AJCC*	*Description*
Tx	...	primary tumor cannot be assessed
T0	...	no evidence of primary tumor
Tis	0	in situ lesion
Ta	...	noninvasive papillary carcinoma
T1	I	invasion of subepithelial connective tissue
T2	II	confined to muscularis layer
T3	III	invasion of renal parenchyma / peripelvic soft tissues
T4	IV	extension beyond renal capsule
N0		negative lymph nodes
N1		single node ≤ 20 mm
N2		single node > 20 – ≤ 50 mm / multiple nodes ≤ 50 mm
N3		node > 50 mm
M0		no distant metastasis
M1		distant metastasis: lung, retroperitoneum, bone

Retrograde pyelography:
- √ smooth / irregular / stippled intraluminal filling defect
- √ irregular papillary / nodular mucosa
- √ "amputated" calyx ± focal hydronephrosis
- √ "oncocalyx" = tumor-filled distended calyx
- √ calculus ← urinary stasis

US:
- √ bulky hypoechoic (similar to renal parenchyma) / slightly hyperechoic mass lesion
- √ infiltrative without disruption of renal contour
- √ splitting / separation of central renal sinus complex
- √ ± caliectasis without pelviectasis

NECT:
- √ tumor density of 5–30 HU:
  - √ hyperattenuating relative to urine + renal parenchyma
  - √ hypoattenuating relative to clot (40–80 HU) / calculus (> 100 HU)
- √ hydronephrosis / hydrocalyx (most frequent finding)
- √ "faceless" kidney on cross-sectional imaging → coronal imaging helpful

CECT (36–52–83% staging accuracy):
- √ focal or diffuse mural thickening of pelvicaliceal wall
- √ pelvicaliceal irregularity
- √ oncocalyx
- √ central sessile solid filling defect centrifugally expanding renal pelvis
- √ obliteration / compression of renal sinus fat
- √ invasion of renal parenchyma (infiltrating growth pattern) with preservation of reniform shape
  (DDx: expansile RCC distorting renal contour)

√ coarse punctate calcific deposits (0.7–6.7%) may mimic urinary calculi
√ variable enhancement of tumor

MR:
√ typically isointense relative to renal medulla on T1WI
√ hypointense filling defect in hyperintense urine on T2WI
√ hypointense soft-tissue mass infiltrating renal parenchyma of intermediate SI
√ hypoenhancing tumor mass on postcontrast imaging, (rarely) avidly enhancing
√ enhancing focal filling defect in collecting system

Dx: cytologic analysis of urine (selective lavage, ureteral urine collection, brush biopsy, ureteroscopy

DDx: papilloma (benign lesion, fronds lined by normal epithelium), blood clot

Prognosis: 77–80% 5-year survival rate without invasion of muscularis mucosa; 5% 5-year survival rate with invasion of muscularis mucosa

Rx: total nephroureterectomy + excision of ipsilateral ureteric orifice with cuff of bladder

Ureteral TCC

Incidence: 1% of all upper urinary tract cancers

Site: lower ⅓ (70%), mid ⅓ (15%), upper ⅓ (15%)
◊ Synchronous TCC in both ureters in 2–9%
◊ Metachronous upper tract TCC in 11–13%
◊ Metachronous bladder TCC in 20–50% (within 2 years of surgical treatment)

Excretory Urogram:
√ nonfunctioning kidney in advanced tumor (46%)
√ hydronephrosis ± hydroureter (34%)
√ single / multiple ureteral filling defects (19%) ± surface stippling
√ irregular nontapering narrowing of ureteral lumen

Retrograde pyelography:
√ stricture suggestive of malignancy:
  √ ureteric fixation + nontapering margins
  √ eccentric / circumferential stricture
√ "champagne glass / chalice / goblet" sign = focal expansion of ureter around + distal to intraluminal slow growing polypoid tumor ← mechanical dilatation ← to-and-fro peristalsis of mass
√ Bergman sign = "catheter-coiling" sign = coiling of catheter on retrograde catheterization below the mass

CT:
√ enhancing intraluminal soft-tissue mass
√ eccentric / circumferential thickening of ureteral wall
√ periureteric fat stranding ← extramural spread

TRAUMA TO BLADDER

Cause:
1. Blunt injury (67–86%): often associated with pelvic fractures
2. Penetrating injury (14–33%)

Associated with: pelvic fracture in 70%

Indications for urethrogram:
- blood at urethral meatus, inability to pass Foley catheter
- "floating" prostate

√ diastasis of symphysis

√ "pie-in-the-sky bladder" = high position of opacified bladder within pelvis ← large pelvic hematoma with disruption of bladder moorings + associated urethral injury

CT cystogram:

Technique:

» prior to IV contrast instill up to 400 mL of diluted contrast solution via Foley catheter under gravity flow → clamp Foley to maintain bladder distension, OR

» clamp Foley → IV contrast injection → delayed imaging after 180–300 seconds after opacification of bladder

√ focal thickening of bladder wall = contusion

√ contrast extravasation

Bladder Contusion *(most common injury)*

= intramural hematoma

√ no extravasation

√ lack of normal distensibility

√ crescent-shaped filling defect in contrast-distended bladder

Interstitial Bladder Injury *(uncommon)*

= bladder tear without serosal involvement

Bladder Rupture

Cystography: diagnostic in > 85%; false-negatives if tear sealed by hematoma / mesentery

CT:

√ unusual fluid / gas collection

√ abnormal location of Foley catheter

√ defect in enhancing bladder wall

Extraperitoneal Rupture of Bladder (80–90%)

Cause: pelvic fracture (sharp bony spicule) or avulsion tear at fixation points of puboprostatic ligaments → separation of fascial planes between bladder + pelvis

Location: tear usually close to base of bladder anterolaterally

Plain film:

√ "pear-shaped" bladder

√ loss of obturator fat planes

√ paralytic ileus

√ upward displacement of ileal loops

Contrast examination:

√ flame-shaped contrast extravasation into perivesical fat, best seen on postvoid films, may extend into thigh / anterior abdominal wall

CT:

√ relatively contained extravasated fluid isoattenuating to fluid in bladder:

√ limited to perivesical (Retzius) space = simple
√ extravasated contrast extends to prevesical space, thigh, scrotum, perineum = complex

US:
√ "bladder within a bladder" = bladder surrounded by fluid collection

Rx: conservative (urinary drainage via Foley); surgery

Intraperitoneal Rupture of Bladder (10–20%)

Cause:
(a) usually as a result of invasive procedure (cystoscopy), stab wound, surgery
(b) blunt trauma with sudden rise in intravesical pressure (= distended bladder at time of impact)

Location: tear usually at dome of bladder

√ contrast extravasation (requires adequate bladder filling) into paracolic gutters, rectovesical / rectouterine pouch
√ contrast outlining / surrounding intraperitoneal structures (small bowel loops + mesentery)
√ extravasated contrast less dense than in bladder ← contrast dilution within large intraperitoneal space
√ uriniferous ascites

Rx: surgery

TRAUMA TO KIDNEY

Frequency: 3–10% of injuries in emergency department

◊ 95–98% of isolated renal injuries are considered minor injuries and managed nonsurgically!

Indications for imaging:
(1) Penetrating injury + gross hematuria
(2) Blunt trauma + microscopic hematuria + hypotension < 90 mmHg
(3) Blunt trauma + known association with renal injuries (eg, rapid deceleration, fall from a height, direct contusion / hematoma of flank soft tissues, fracture of lower ribs / transverse processes / thoracolumbar spine)

(4) Microscopic hematuria + positive peritoneal lavage
◊ Only 0.1–0.5% of hemodynamically stable patients with microscopic hematuria have significant urinary tract injury!

Classification:

I. MINOR RENAL INJURY (75–85%)
√ no / limited perinephric hematoma
DDx: respiratory motion artifact (low-attenuation area surrounding kidney)
√ no extravasation of urine (= no caliceal disruption)

1. **Intrarenal hemorrhage / hematoma = renal contusion**
√ hyperattenuating area of 40–70 HU (= acute clotted blood) on NECT
√ sharply / poorly defined round / ovoid area of decreased enhancement during CECT (DDx: renal infarction with no enhancement)
√ focal area of striation on delayed nephrogram
√ area of persistent contrast material staining on very delayed scan

2. **Subcapsular hematoma**
   √ round / lenticular-shaped fluid collection + flattening of subjacent parenchyma
3. **Perinephric hematoma** without extension to collecting system / medulla
   √ defects in periphery of renal parenchyma
   √ ± limited perinephric hematoma with attenuation values of 45–90 HU
   ◊ Subcapsular / perinephric hematoma usually proportional to extent of injury
4. Small subsegmental **cortical infarct**
   Cause: stretching + thrombotic occlusion of accessory renal artery / capsular artery / segmental artery
   √ sharply demarcated wedge-shaped area of decreased contrast enhancement

Rx: observation

II. MAJOR RENAL LACERATION (10%)

= complete cortical laceration / fracture extending to medulla ± collecting system

√ laceration connecting two cortical surfaces = renal fracture = separation of renal poles

√ ± devascularization of renal parenchyma

(a) without involvement of collecting system:

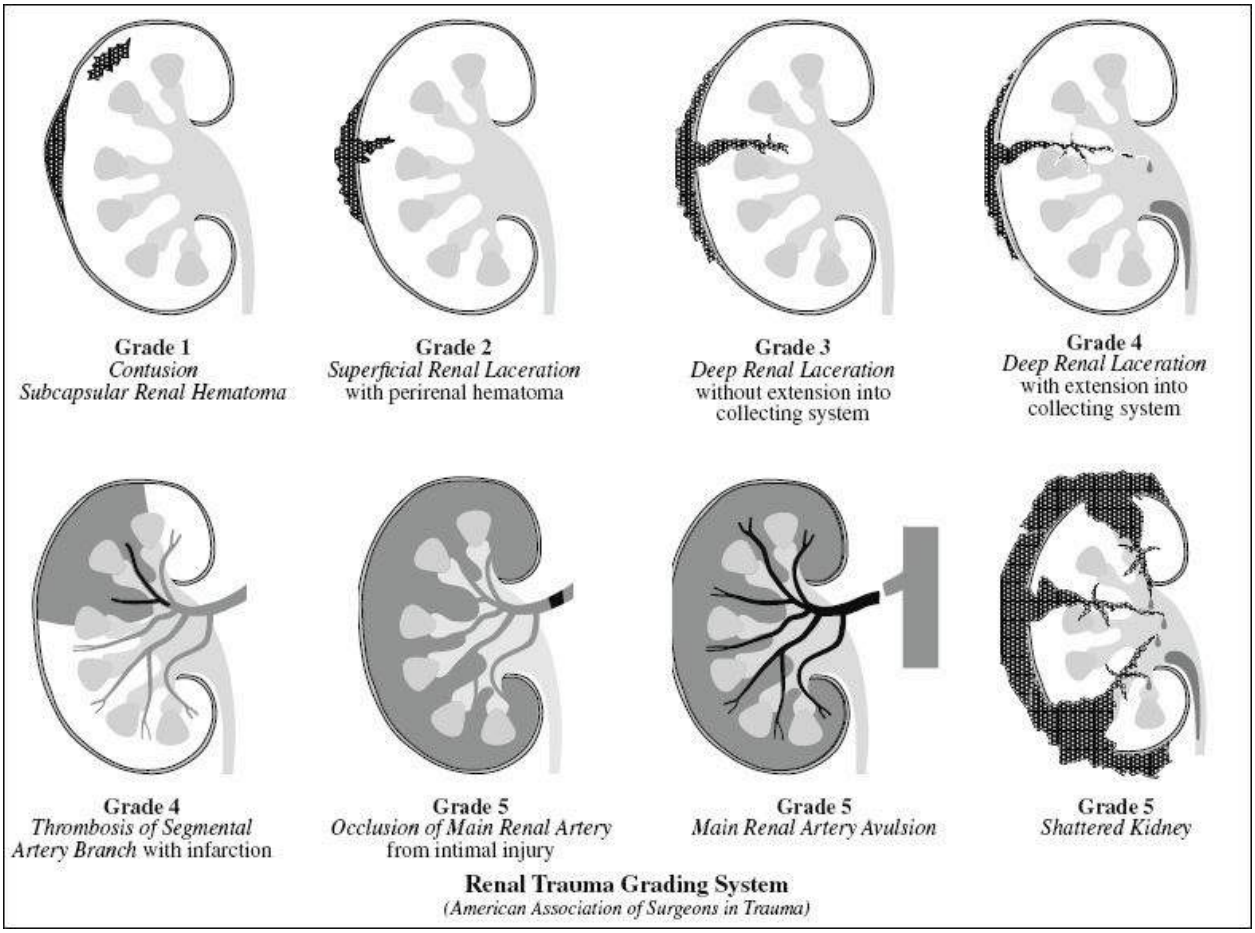
√ nonenhancing deep parenchymal cleft filled with hematoma on CECT

√ perirenal hematoma from capsular disruption

Kidney Injury Scale
American Association for the Surgery of Trauma (**AAST**)

Grade	*Injury*	*Description (based on surgical findings)*
I	contusion	hematuria + normal urologic studies
	hematoma	subcapsular nonexpanding, no laceration
II	hematoma	nonexpanding perirenal, confined to renal retroperitoneum
	laceration	< 1 cm parenchymal depth of renal cortex, no urinary extravasation
III	laceration	> 1 cm parenchymal depth of renal cortex, no collecting system rupture / urinary extravasation
IV	laceration	parenchymal laceration extending through renal cortex, medulla, collecting system
	vascular	main renal artery / vein injury + contained hemorrhage
V	laceration	completely shattered kidney
	vascular	avulsion of renal hilum with devascularization of kidney

◊ Advance one grade for multiple injuries to same organ



(b) with involvement of collecting system:
- √ urine extravasation of contrast material on delayed images 3–5 minutes after injection
- √ perinephric fluid during portal venous phase → suspect urinoma!

(c) active hemorrhage / pseudoaneurysm:
- ◊ Hemodynamic decompensation may be imminent in 38%!
- √ intense contrast enhancement within a laceration / hematoma during early phase:
  - √ linear / flamelike contrast extravasation of 80–370 HU or within 10–15 HU of aortic density

Rx: variable (clinical judgement required)

III. CATASTROPHIC RENAL INJURY (5%)

√ extravasation of contrast material with patchy areas of 85–370 HU (= active bleeding)

1. Multiple renal lacerations = **shattered kidney**
   - √ multiple separate renal fragments
   - √ lack of enhancement of part of kidney ← segmental renal arterial infarctions
   - √ ± cortical rim nephrogram (= enhancement of renal periphery through intact capsular / collateral vessels)

   Rx: surgical exploration / nephrectomy
2. **Vascular injury of renal pedicle**

   = occlusion of main renal artery ← intimal flap

• hematuria may be absent
√ abrupt termination of main renal artery just beyond its origin
√ minimal hematoma around proximal renal artery
√ absence of perinephric hematoma (HALLMARK)
√ absent nephrogram on affected side
√ retrograde opacification of ipsilateral renal vein
√ cortical rim nephrogram (develops > 8 hours after injury)
Prognosis: high risk of ongoing hemorrhage
Rx: revascularization procedure (in 14% return of renal function)

3. **Avulsion of renal artery** (rare)
= tearing of tunica muscularis + adventitia
√ absent contrast enhancement (= global infarct)
√ extensive medial perirenal hematoma
√ active arterial bleeding
Prognosis: life-threatening
4. **Thrombosis / laceration of renal vein** (rare)
√ intraluminal thrombus in dilated renal vein
√ acute venous hypertension:
√ nephromegaly
√ diminished nephrogram
√ delayed nephrographic progression
√ decreased excretion

IV. INJURY OF URETEROPELVIC JUNCTION (rare)
= laceration (= incomplete tear in 60%) / avulsion (= complete transection) of ureter at UPJ
Mechanism: tension on renal pedicle by sudden deceleration
Age: usually young boys
Associated with: fracture of transverse process (30%)
• gross / microscopic hematuria (53–60%)
N.B.: delayed imaging to check for urine leak!
√ massive extravasation of contrast material medially in the region of UPJ
√ nonfilling of affected ureter (with avulsion)
√ ± circumferential perinephric urinoma
Early Cx: urinoma formation (1–7%), infected urinoma, perinephric abscess, sepsis, delayed bleeding ← arteriovenous fistula / pseudoaneurysm
Late Cx: posttraumatic renovascular hypertension, hydro- nephrosis, calculus formation, chronic pyelonephritis

Blunt Trauma to Kidney

Frequency: 80–90% of all renal injuries
Cause: motor vehicle accident, fight, assault, contact sports, fall from a height
Mechanism: (a) crush injury (> 80%) = direct blow with renal laceration by lower ribs
(b) sudden deceleration → renal artery tear
Associated with: other organ injury in 75%; fracture of lower ribs / thoracolumbar spine /

transverse processes of L-spine

- contusion / hematoma of flank
- > 95% hematuria (> 5 RBCs per high-power field):

  N.B.: poor correlation between severity of hematuria + severity of renal injury

  ◊ With gross hematuria 25% have significant injuries!

  ◊ With renal pedicle injury 24% have no hematuria!

  ◊ Normotensive patients with microscopic hematuria (< 35 RBCs per high-power field) have a significant renal injury in < 0.2%!

Location: simultaneous upper + lower GU tract injury in < 5%

Rx: The only absolute indication for surgery is life-threatening active bleeding! Urine leaks will close spontaneously in 87%!

Penetrating Renal Trauma

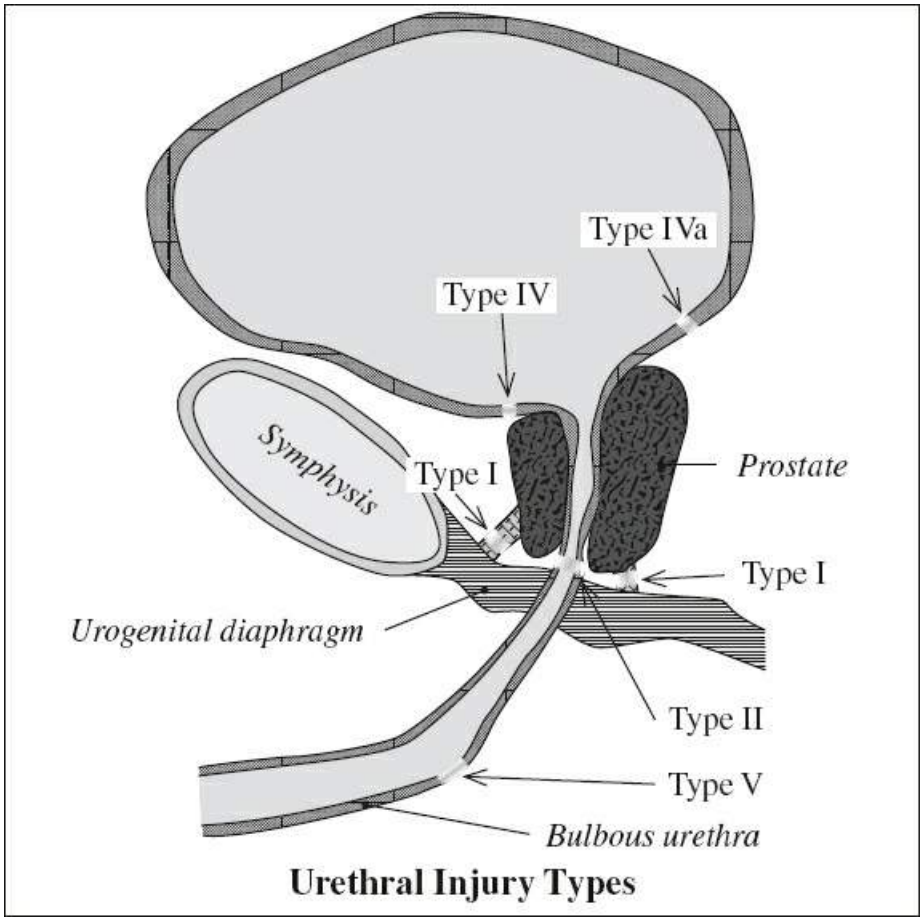
Frequency: 10–20% of all renal trauma

Cause: gunshot, stab wound, shrapnel, biopsy

Associated with: multiorgan injuries in 80%

Cx: (1) infection ← "dirty" contaminated wound

(2) "bullet / buckshot colic", "birdshot calculus" = ureteral obstruction ← migrating missile



Urethral Injury Types

Classification System of Urethral Injury at Urethrography (Goldman)		
Type	*Injury*	*Urethrographic Signs*
I	stretching of posterior urethra	√ intact stretched urethra
II	disruption of urethra above urogenital diaphragm	√ extravasation above urogenital diaphragm
III	disruption of membranous urethra with extension below urogenital diaphragm to involve anterior urethra	√ extravasation below urogenital diaphragm ± extension to pelvis / perineum √ intact bladder neck
IV	bladder neck injury with extension to proximal urethra	√ extraperitoneal extravasation √ bladder neck disruption
IVa	bladder base injury simulating type IV	√ periurethral extravasation √ bladder base disruption
V	isolated anterior urethral injury	√ extravasation below urogenital diaphragm confined to anterior urethra

TRAUMA TO URETHRA

Frequency: in 4–14% of pelvic fractures in males, in < 6% of pelvic fractures in females
Associated with: bladder laceration in up to 20%
Location:
(a) posterior urethra (in 4–14% of pelvic fractures)
(b) anterior urethra (often isolated) ← straddle injury

- gross hematuria, blood at meatus (50%), swelling / hematoma of perineum / penis, "high-riding" prostate at digital exam
- inability to void

N.B.: blind urethral catheterization is contraindicated!

CT (indirect findings):
√ pelvic diastasis / fractures
√ distortion of periprostatic structures
√ hematoma of ischiocavernosus / obturator muscle
√ excretory contrast extravasation around bladder base

Urethrographic technique:
(a) **ascending (retrograde) urethrography**
» external occlusion with Knutsson / Brodney clamp
» internal occlusion with inflatable balloon (6–8-F Foley with 5 mL balloon / HSG catheter with 3 mL balloon)
(b) **descending (antegrade) urethrography**
» bladder filling with 350–400 mL contrast
» imaging during micturation + after voiding
(c) **ascending pericatheter urethrography**

» 4–6-F pediatric catheter with balloon inflated in navicular fossa alongside indwelling catheter
» gradually advance 4–6-F feeding tube ± seal with tightly tied ribbon gauze around penis proximal to glans

(d) **descending pericatheter urethrography**
= voiding around indwelling catheter
» indwelling catheter pushed deeper into bladder ± deflation of balloon (avoid dislodging catheter!)

Rx: suprapubic catheter for urethral / bladder injury

Cx: (1) Urethral stricture (38–100%)
(2) Impotence (in up to 40%)
(3) Incontinence (30%)

TUBERCULOSIS OF GU TRACT

The urogenital tract is the 2nd most common site after lung; almost always affects the kidney first
= hematogenous focus from lung / bone / GI tract

Age: usually before age 50; M > F

Path: organisms lodge in periglomerular capillaries; breakdown in host immunity results in extensive necrosis + fibrosis (coalescing cortical granulomas); organisms spill down the nephrons and become trapped in the narrow segment of the loop of Henle forming ulcerocavernous papillary lesions, which erode into collecting system

Spread:
(a) contiguous: from renal parenchyma → along urothelium → to infundibula, renal pelvis, ureter, bladder
(b) hematogenous (rare): epididymis, testis
◊ It is unusual for genitourinary sites to be affected without involvement of kidney first!

- gross / microscopic hematuria
- "sterile" pyuria, frequency, urgency, dysuria
- history of previous clinical TB (15–20%) → lag time of 2–40 years

IVP (abnormal in 85–90%)

Adrenal Tuberculosis *6%*

◊ 5th most common site of extrapulmonary tuberculosis
• Addisonian type clinical picture
√ bilaterally enlarged glands (91%)
√ low-attenuation center + peripheral enhancement (47%)
√ dotlike calcifications (59%)

Renal Tuberculosis

◊ Renal TB in 5–10% of patients with pulmonary TB!
◊ Radiographic evidence of pulmonary TB in < 50% of patients with renal TB (only 5% have active cavitary TB)!

Location: unilateral (75%)

√ <u>renal size:</u> enlarged (early) / small (late) / normal (most common):

√ "putty kidney" = tuberculous pyonephrosis from ureteral stricture
√ autonephrectomy = small shrunken scarred nonfunctioning kidney ± dystrophic calcifications
√ cortical scars, often associated with parenchymal calcifications:
√ distortion of collecting system ← adjacent cortical scarring
√ displacement of collecting system ← tuberculoma of low attenuation (initial infection)
√ "moth-eaten calyx" = "smudged" papillae = irregular feathery appearance of surface of papilla ← erosion (earliest sign) → progression to papillary necrosis
√ cavities communicating with collecting system:
√ irregular tract formations from calyx into papilla
√ large irregular cavities with extensive destruction
√ blunted dilated calices = papillary necrosis
√ strictures of infundibula / renal pelvis:
√ dilated calices (hydrocalycosis) often with sharply defined circumferential narrowing (infundibular strictures) at one / several sites (most common finding)
√ caliceal truncation
√ "phantom calyx" / amputated calyx = incomplete visualization of calyx ← infundibular stenosis
√ reduced capacity of renal pelvis
√ Kerr kink = kinking of renal pelvis
√ hydronephrosis with irregular margins + filling defects ← caseous debris
√ mural thickening of collecting system
√ dystrophic amorphous parenchymal calcifications (50%)
√ in tuberculomas (in 24–44%): amorphous / granular / curvilinear / punctate / confluent ("toothpaste") / involving entire kidney ("**putty kidney**"):
√ nephrolithiasis (in 10%)
√ globally poor renal function
√ infection may extend into peri- / pararenal space + psoas
CT:
√ triangular / ringlike calcifications within renal collecting system (= papillary necrosis)

Ureteral Tuberculosis

Frequency: in 50% of genitourinary TB; always with evidence of renal involvement as it spreads from kidney
Location: either end of ureter (most commonly distal ⅓), usually asymmetric, may be unilateral
√ ureteral filling defects ← mucosal granulomas
√ "**saw-tooth ureter**" = irregular jagged contour ← dilatation from ureterovesical junction obstruction + multiple small mucosal ulcerations + wall edema (early changes)
√ strictures (late changes):
Site: pelviureteric junction, across pelvic brim, at vesicoureteric junction
"beaded ureter" = alternating areas of strictures + dilatations
"corkscrew ureter" = marked tortuosity with strictures + dilatations
"**pipestem ureter**" = rigid aperistaltic foreshortened thick and straight ureter
√ vesicoureteral reflux through "fixed" patulous orifice

√ ureteral calcifications uncommon (usually in distal portion)
CT:
√ thickening of ureteral wall with periureteric inflammation

Bladder Tuberculosis

= infection from renal source causes interstitial cystitis
√ thickened bladder wall (= muscle hypertrophy + inflammatory tuberculomas)
√ filling defects ← multiple granulomas
√ bladder wall ulcerations
√ "shrunken bladder" = scarred bladder with diminished capacity
√ "thimble bladder" = diminutive irregular bladder
√ bladder wall calcifications (rare)
Cx: fistula / sinus tract / vesicoureteral reflux ← fibrosis of ureteral orifice

Male Genital Tuberculosis

√ calcifications in 10% (diabetes more common cause)
(1) Tuberculous prostatitis / prostatic abscess:
√ hypoechoic irregular area in peripheral zone
√ hypoattenuating prostatic lesion ← foci of caseous necrosis + inflammation
√ hypointense diffuse radiating streaky areas on T2WI (= "watermelon" sign)
√ peripheral enhancement
(2) Tuberculous epididymitis
ascending / descending route of infection
√ diffusely enlarged / nonspecific nodular epididymis of heterogeneous echogenicity
√ hydrocele, sinus tract, calcifications
(3) Tuberculous orchitis (rare)
direct extension from epididymal infection, rarely from hematogenous spread
DDx: brucellosis, fungal infections (identical picture)

Female Genital Tuberculosis

Prevalence: 1.3% involve genital tract (fallopian tube in 34%)
(1) Salpingitis (94%): mostly bilateral
√ thick-walled serpentine juxtauterine structure
√ intense enhancement
√ beaded appearance of salpinges ← multiple constrictions
√ tubal obstruction is unusual
(2) Tuboovarian abscess: → extension into extraperitoneal compartment
√ loculated ascites
√ omental + mesenteric soft-tissue infiltration
√ peritoneal thickening + nodularity
√ enlarged necrotic lymph nodes (= lymphadenitis)
DDx: peritoneal carcinomatosis
Cx: tuberculous peritonitis (in up to 50%): may mimic ovarian cancer ← elevated CA-125

UNICALICEAL (UNIPAPILLARY) KIDNEY

Path: OLIGOMEGANEPHRONIA = reduced number of nephrons and enlargement of glomeruli
Associated with: absence of contralateral kidney, other anomalies
• hypertension, proteinuria, azotemia

URACHAL ANOMALIES

urachus = median umbilical ligament = thick fibrous cord as the remnant of the allantois (= endodermal outgrowth from yolk sac into stalk), which regresses at 5th month of development; bounded by transverse fascia ventrally + parietal peritoneum dorsally (space of Retzius)
Cx: infection (23%), intestinal obstruction, hemorrhage into cyst, peritonitis from rupture, malignant degeneration

Alternating Sinus = Umbilical-Urachal Fistula

= cystic dilatation of urachus periodically emptying into bladder / umbilicus

Patent Urachus

= fistula between bladder and umbilicus
Prevalence: 1÷200,000 live births
• urine draining from umbilicus

Urachal Cyst (30%)

= gradually enlarging cyst ← closure of both ends of urachus
Prevalence: 1÷5,000 (at autopsy); 30% of all urachal anomalies
• asymptomatic in children unless rupture occurs
• symptomatic in adults ← enlargement / infection
√ cystic extraperitoneal mass
√ no communication with bladder or umbilicus

Urachal / Vesicourachal Diverticulum (3%)

= urachus communicates only with bladder dome

Urachal Sinus

= urachus patent only at umbilicus
Associated with: urachal cyst
• umbilical mass / inflammation ± drainage
√ thickened tubular structure with echogenic center

URACHAL CARCINOMA

= rare tumor arising from the urachus (= vestigial remnant of cloaca + allantois) within space of Retzius
Frequency: 0.01% of all adult cancers;
0.17–0.34% of all bladder cancers;
20–40% of all primary bladder adenocarcinomas
Histo:
(a) adenocarcinoma (84–90%), in 75% mucin producing
◊ 34% of all bladder adenocarcinomas are urachal in origin

Cause: columnar epithelial metaplasia of transitional cell epithelium in urachal remnant

(b) urothelial cancer (3%), sarcoma, squamous cell carcinoma

◊ 75% of urachal neoplasms in patients < 20 years of age are sarcomas!

Stages of Urachal Carcinoma	
I	cancer limited to urachus
II	invasion limited to urachus
III A	local invasion of bladder
III B	invasion of abdominal wall
III C	invasion of peritoneum
III D	invasion of other viscera
IV A	metastases to local lymph nodes
IV B	distant metastases (liver)

Age: 40–70 years; M÷F = 2÷1 to 3÷1

- suprapubic mass, abdominal pain; mucous micturition (25%)
- irritative voiding symptoms: dysuria, abdominal pain
- discharge of blood, pus from umbilicus, hematuria (71%)

Location: supravesical, midline, anterior (80%), extraperitoneally in space of Retzius

Site: close to bladder (90%); along course of urachus / at umbilical end (10%)

√ midline mass anterosuperior to vesical dome in the space of Retzius with predominantly muscular / extravesical involvement

√ tumor bulk outside bladder + invasion of bladder dome (88%)

√ mean tumor size of 6 cm

√ often peripheral curvilinear / punctate stippled psammomatous calcifications (50–72%)
PATHOGNOMONIC for mucinous adenocarcinoma

√ heterogeneous enhancement

US:

√ midline fluid-filled cavity with mixed echogenicity + calcifications adjacent to anterior abdominal wall

CT:

√ low-attenuation mass in 60% (mucin)

MR:

√ markedly increased SI on T2WI ← mucin

Cx: pseudomyxoma peritonei (in peritoneal carcinomatosis); metastasis to pelvic lymph nodes, lung, brain, liver, bone

Prognosis: 7–61% 5-year survival rate

Rx: radical cystectomy; often local recurrence within 2 years

DDx: infected benign urachal cyst; primary benign bladder tumor (adenoma, fibroadenoma, fibromyxoma, hamartoma); primary malignant bladder tumor (adenocarcinoma, transitional cell carcinoma); secondary bladder tumor (metastasis from colon, prostate, female genital tract); desmoid tumor

URETERAL DUPLICATION

= RENAL DUPLICATION

Ureteral duplication is the most common congenital anomaly of the urinary tract.

Complete Duplication of Ureter *(0.2%)*

Cause: second ureteral bud arising from mesonephric duct leading to complete ureteral duplication

Prevalence: 0.2% of live births; M÷F = 1÷2; in 15–40% bilateral

Risk of recurrence: 12% in 1st-degree relatives

Increased risk for: UTI, obstruction, vesicoureteral reflux

Embryology: ureters develop from separate ureteric buds originating from a single wolffian duct

√ duplicated ureter may be orthotopic

√ renal enlargement

√ tortuous dilated lower pole ureter

US:

√ two separate echodense renal sinuses + pelves separated by parenchymal bridge

IVP:

√ poor / nonvisualization of upper pole collecting system (delayed films):

√ "**drooping lily**" sign = hydronephrosis + decreased function of obstructed upper pole moiety causing downward displacement of lower pole calices

√ lateral + downward displacement of lower pole collecting system + ureter:

√ "nubbin" sign = scarring, atrophy, and decreased function of lower pole moiety may simulate a renal mass

√ displacement of proximal orifice upward

VCUG:

√ ureterocele

√ reflux into lower moiety (rare)

Cx: (1) Vesicoureteral reflux (most commonly)
(2) Ectopic ureteral insertion
(3) Ectopic ureterocele
(4) Ureteropelvic junction obstruction of lower pole

Weigert-Meyer Rule

= the upper pole ureter terminates inferior and medial to the lower pole ureter

(a) upper moiety ureter
remains with wolffian duct longer → passes through bladder wall → inserts ectopic <u>inferior and medial to lower moiety ureter</u> below the level of the trigone / into any wolffian duct derivative

(b) lower moiety ureter
drains lower pole and interpolar portion; is incorporated into developing bladder first → ascends during bladder growth → enters bladder at trigone

Upper Moiety Ureter

Three possible distal configurations:

1. Ureterocele
2. Ectopic ureter

3. Normal insertion into bladder

◊ Subject to ureteral obstruction ← stenosis at ectopic ureteral insertion / ectopic ureterocele / aberrant artery crossing!

◊ The ectopic ureteral orifice is inferior + medial to orthotopic ureteral orifice!

Associated with: significant renal dysplasia

Site of insertion of ectopic ureter

Cx: upper pole obstructive hydronephrosis

LOWER MOIETY URETER

◊ Subject to vesicoureteral reflux ← abnormal UVJ valve mechanism ← shortened ureteral tunnel at bladder insertion!

Cx: lower pole of duplex kidney may atrophy (in 50%) ← chronic pyelonephritis ← reflux nephropathy (= reflux ± infection)

√ clubbed calices underneath focal scars

Incomplete / Partial Duplication of Ureter *(0.6%)*

= initially separate upper + lower pole ureters fuse proximal to UVJ into a common ureter

Development: branching of ascending single ureteral bud (= one ureteral orifice + common distal ureter) before reaching metanephric blastema

Prevalence: in 0.6% of urograms

Associated with: ureteropelvic junction obstruction of lower renal pole

• frequently clinically insignificant

√ bifid ureter (in early branching)

√ bifid pelvis (in late branching)

√ ureteroureteral reflux = "yo-yo" / "saddle" / "seesaw" peristalsis = urine moves down the cephalad ureter + refluxes up the lower pole ureter and vice versa

√ asymmetric dilatation of one ureteral segment

√ upper pole ureter may end blindly (seen on retrograde injection only)

Cx: urinary tract infections

URETEROCELE

= bulbous dilatation / cystic ectasia of subepithelial segment of intravesical ureter

Prevalence: 1÷5,000 to 1÷12,000 children

IVP:

√ early filling of bulbous terminal ureter ("**cobra head** / spring onion" sign) projecting into urinary bladder

√ surrounded by a thin radiolucent halo (= combined thickness of ureteral wall + prolapsed bladder mucosa)

VCUG:

√ round / oval lucent defect near trigone

√ effacement with increased bladder distension

√ ± eversion during voiding

Simple Ureterocele

= ORTHOTOPIC URETEROCELE

= congenital prolapse of dilated distal ureter + orifice into bladder lumen at the usual location of the trigone, typically seen with single ureter

Presentation: incidental finding in adults; M÷F = 2÷3; bilateral in 33%

Cx:

(1) Pyelocaliceal dilatation

(2) Prolapse into bladder neck / urethra → obstruction (rare)

(3) Wall thickening ← edema from impacted stone / infection

Ectopic Ureterocele

= ureteral bud arising in an abnormal cephalad position from the mesonephric duct and moving caudally resulting in an ureteral orifice distal to trigone within / outside bladder

Frequency: in 10% bilateral

(a) in single nonduplicated system (20%)

M÷F = 1÷1

• hypoplastic / absent ipsilateral trigone

√ poorly visualized / nonvisualized kidney

√ small / poorly functioning kidney

(b) in upper moiety ureter of duplex kidney (80%)

M÷F = 1÷4 to 1÷8

Cx: (1) Bladder outlet obstruction ← ectopic ureterocele prolapsing into bladder neck / urethra

(2) Contralateral ureteral obstruction (if ectopic ureterocele large)

(3) Multicystic dysplastic kidney (the further the orifice from normal site of insertion, the more dysplastic the kidney!)

Pseudoureterocele

= obstruction of an otherwise normal intramural ureter mimicking simple ureterocele

Cause:

(a) Tumor
bladder tumor (most common in adults), invasion by cervical cancer, pheochromocytoma of intravesical ureter

(b) Edema
from impacted ureteral calculus (most common in children), radiation cystitis, following ureteral instrumentation, schistosomiasis

√ NO protrusion of ureter into bladder lumen (oblique views + cystoscopy normal)

√ thick irregular radiolucent halo surrounding bulbous terminal ureter

Dx: cystoscopy

URETEROPELVIC JUNCTION OBSTRUCTION

Primary UPJ Obstruction

= congenital partial functional / anatomic obstruction at junction of renal pelvis + proximal ureter

Prevalence: 1÷20,000 live births

◊ Most common cause of fetal / neonatal hydronephrosis!

Cause:

A. INTRINSIC FUNCTIONAL CAUSE

= embryonic insult to smooth muscle cells → adynamic aperistaltic proximal ureteral segment → impaired formation of urine bolus

(1) Replacement of UPJ muscle by excessive local collagen deposition

(2) Abnormal arrangement of junction muscles causing dysmotility (69%)

(3) Abnormal intercellular conduction

B. EXTRINSIC MECHANICAL / ANATOMIC CAUSE

(1) Crossing aberrant vessels (11–79%):

› branch of main renal artery / vein

› accessory branch from aorta / iliac artery / IVC

√ vessel to lower renal pole (in 25–39% of adult patients): anterior to UPJ (90–95%), posterior to UPJ (5–10%)

(2) Luminal narrowing by mucosal folds (= stenosis or valve) in upper ureter

(3) Periureteral fibrosis (= adventitial bands) ← recurrent urinary tract infections

(4) Insertional abnormality

› primary high ureteral insertion

› developing over time with renal pelvic distension

(5) Fixed kink / angulation

Age at discovery: in utero; < 15 years (25%); > 40 years (50%); M÷F = 5÷1

Associated anomalies (27%):

vesicoureteral reflux, bilateral ureteral duplication, bilateral obstructed megaureter, contralateral multicystic dysplastic kidney, contralateral renal agenesis, meatal stenosis, hypospadia

Location: left > right side; bilateral (10–20–40%)

• abdominal mass, intermittent flank pain

• Dietl crisis = "**beer-drinker's hydronephrosis**"

[Jozef Dietl (1804- 1878), Polish physician, pioneer of balneology and mayor of Kraków]

= intermittent flank pain typically after a large volume of fluid intake and subsequent diuresis (classically in college freshmen after excessive alcohol intake)

• hematuria, renal stones, UTI, pyelonephritis

√ hugely dilated largely extrarenal pelvis:

√ draped over lower pole vessel as inverted teardrop shape

√ proximal ureter hooking over lower pole vessel

√ variable degree of caliceal dilatation

√ NO dilatation of ureter

IVP:

√ sharply defined narrowing at UPJ

√ pelvicaliectasis without ureterectasis

√ anterior rotation of pelvis

√ broad tangential sharply defined extrinsic compression (in arterial crossing)

√ longitudinal striae of redundant mucosa (in dehydrated state)

√ late changes: unilateral renal enlargement, diminished opacification, wasting of kidney

substance
√ "**balloon-on-a-string**" sign:
√ caliceal crescents surrounding dilated collecting system
√ eccentric exit of ureter from dilated renal pelvis
CT / MRI:
√ accurate detection of crossing vessels (100% PPV) during late arterial phase
NUC: confirms obstruction at UPJ + determines function
OB-US:
√ progressive enlargement of renal pelvis + branching infundibula + calices
√ anteroposterior diameter of renal pelvis ≥ 10 mm
√ large unilocular fluid collection (severely dilated collecting system)
DDx: multicystic dysplastic kidney, perinephric urinoma
ADDITIONAL TESTS:
(1) Diuresis excretory urography (Whitfield): accurate in 85%
(2) Diuresis renography (^{131}Iodine-iodohippurate sodium / ^{99m}Tc-DTPA)
(3) Pressure flow urodynamic study (Whitaker test)
Rx: early surgical correction (ante- / retrograde endopyelotomy, open / laparoscopic dismembered pyeloplasty) to preserve renal function

Secondary UPJ Obstruction

Cause:
(1) Infection: eosinophilic ureteritis, XGP
(2) Stones
(3) Ischemia
(4) Iatrogenic injury
(5) Aortic aneurysm
(6) Renal cyst

URETHRAL CARCINOMA

Prevalence: < 1% of all urologic cancers
Age: 6th–7th decade; M÷F = 1÷4

Urethral Carcinoma of Male Urethra

Cause: chronic urethritis from venereal disease (25–44%) + urethral strictures (50–88%)
• palpable mass in perineum / along shaft of urethra
• periurethral abscess, obstructive voiding symptoms
• urethrocutaneous fistula, serosanguinous discharge
√ urethral stricture
Site: @ Prostatic urethra (10%):
TCC (90%) > squamous cell ca. (10%)
@ Bulbomembranous urethra (60%):
squamous cell ca. (80%) > TCC (10%) > adenocarcinoma + undifferentiated carcinoma (10%)
@ Penile urethra (30%):
squamous cell ca. (90%) > TCC (10%)

Histo:

1. Squamous cell carcinoma (70–80%)
2. Transitional cell carcinoma (16%) part of multifocal urothelial neoplasia; in 10% after cystectomy for bladder tumor
3. Adenocarcinoma (6%) in bulbous urethra originating in glands of Cowper / Littré
4. Malignant melanoma, leiomyosarcoma, rhabdomyosarcoma, fibrosarcoma (rare)
5. Metastases from bladder / prostatic carcinoma (rare)

Stage I: confined to subepithelial connective tissue
Stage II: invasion of corpus spongiosum / prostate / periurethral muscle
Stage III: invasion of corpus cavernosum + bladder neck beyond prostatic capsule
Stage IV: invasion of other organs
Spread: direct extension + regional lymph nodes (superficial + deep inguinal + external iliac nodes from anterior urethra; pelvic nodes from posterior urethra)
MR:
√ mass hypointense relative to normal corpora on T1WI + T2WI

Urethral Carcinoma of Female Urethra

Prevalence: < 0.02% of all malignancies in women
Cause: chronic irritation, urinary tract infection, proliferative lesions (caruncle, papilloma, adenoma, polyp, leukoplakia)
Risk factor: human papilloma virus infection, urethral diverticulum
Histo:

1. Squamous cell carcinoma (70%):
   Site: distal ²/₃ of urethra + meatus
   √ lobulated exophytic / deeply infiltrating lesion
   √ irregularly marginated hypo- / isoechoic mass
   √ T2-hypointense with heterogeneous enhancement
2. TCC (8–24%):
   Site: posterior ⅓ of urethra
   √ lobulated iso- to hypointense on T1WI + T2WI
   √ heterogeneous contrast enhancement
3. Adenocarcinoma (10–18–28%):
   Site: urethrovulvar junction from periurethral glands of Skene (40%), urethral diverticulum (60%)
   ◊ similarity to nephrogenic adenoma, immunostaining for PSA + prostate acid phosphatase
   √ exophytic diverticular tumor
   √ T2-hyperintense + peripheral rim of low SI
   √ variably heterogeneous contrast enhancement
4. Secondary tumor: contiguous extension from bladder, cervix, vagina, anus

Age: > 50 years
MR (best on SAG T2WI):
√ mass hypointense on T1WI + hyperintense on T2WI
@ Cancer of the anterior urethra (46%)
Site: distal ⅓ of urethra

- urethral bleeding, urinary frequency, dysuria
- palpable mass at urethral orifice

Spread: superficial + deep inguinal nodes

Rx: local surgical excision

@ Cancer of the entire urethra

Histo: SCC (60%), TCC (20%), adenocarcinoma (10%), undifferentiated ca. / sarcoma (8%), melanoma (2%)

- urinary retention, urethral abscess, urethrovaginal fistula

Spread: (a) local extension: into bladder neck, vagina, vulva
(b) lymphatic: external iliac, hypogastric, obturator nodes (for posterior urethra)

Rx: surgery, radiation, chemotherapy

Prognosis: poor (in 50% metastatic at presentation); survival rate of 50% for distal tumor, survival rate of 6% for proximal tumor

DDx: markedly inflamed diverticulum

URETHRAL DIVERTICULUM

= protrusion of urethra into periurethral fascia

Prevalence: 0.6–6% of women

Age: 26–74 years; 6 x more common in black women (?)

Histo: same as urethral mucosa

- asymptomatic (3–20%); fluid / pus may be expressed from urethra
- tender cystic swelling protruding from anterior wall of vagina
- classic "triad of Ds": **d**ysuria (45%), **d**yspareunia, postvoid **d**ribbling
- vague nonspecific urinary tract symptoms mimicking chronic / interstitial cystitis, periurethral cysts / fibrosis, urethrocele, carcinoma in situ of the bladder / urethra, detrusor instability:
  - urinary frequency / urgency (67%)
  - recurrent urinary tract infections (40%)
  - urinary incontinence (9–32–70%), urine retention, pelvic pain

Congenital Urethral Diverticulum

Cause: ectopic cloacal epithelium

M > F

Acquired Urethral Diverticulum

Prevalence: in 1.4% of women with stress incontinence; M < F

Cause:

(1) Obstruction of paraurethral glands (of Skene) → subsequent infection (E. coli, gonococci, chlamydia) of dilated periurethral gland → rupture into urethra

(2) Trauma: catheterization / childbirth / disruption of periurethral fascia during bladder neck suspension surgery

May be associated with: cloacal epithelium, wolffian / müllerian duct remnant

Site: posterolateral aspect of midurethra at level of pubic symphysis

Voiding cystourethrography (65% accurate):

√ rounded / elongated sac connected to urethra

US:

√ echogenic focus with distinct acoustic shadow ← stone

MR:

√ cystic T2-hyperintense lesion with various degrees of extensions around the circumference of urethra:

√ oval / U-shaped "saddlebag" / circumferential

√ single / multiple

√ unilocular / multiseptated

√ narrow / wide neck

√ heterogeneous hyperintense signal compared with urine on T1WI if content is proteinaceous / hemorrhagic

√ fluid-fluid level on T2WI if inflammation present

Cx: (1) Infection

(2) Stone formation (in up to 5–10%)

(3) Malignant degeneration to adenocarcinoma (60%) > TCC (30%) > squamous cell carcinoma (10%)

Rx: transvaginal / endoscopic diverticulectomy with resection of neck (to prevent recurrence)

DDx: (1) Vaginal cyst (Gartner duct cyst, paramesonephric cyst, müllerian duct cyst, epithelial inclusion cyst)

(2) Ectopic ureterocele

(3) Endometrioma

(4) Urethral tumor

URINOMA

= uriniferous perirenal pseudocyst ← tear in collecting system with continued renal function

Etiology:

A. NONOBSTRUCTIVE: blunt / penetrating trauma, surgery, infection, calculus erosion

B. OBSTRUCTIVE:

(1) Ureteral obstruction (calculus, surgical ligature, neoplasm)

(2) Bladder outlet obstruction (posterior urethral valves)

◊ Augmented by sudden diuretic load of urographic contrast material!

Path: fibroblastic cavity (in 5–12 days), dense connective tissue encapsulation (in 3–6 weeks)

- pain, malaise, nausea, fever
- hematuria (10–50%), fluctuant tender mass
- discharge from wound (in early postoperative period)

Location:

√ cystic mass in perirenal space = localized perirenal urinoma (most common)

√ cystic mass filling entire perirenal space = diffuse perirenal urinoma

√ sickle-shaped collection = subcapsular urinoma

√ encapsulated expanding intrarenal cystic mass separating renal tissue fragments = intrarenal urinoma

Plain radiography:
√ soft-tissue mass obliterating retroperitoneal structures
√ superior + lateral displacement of kidney
CT:
√ extravasation of contrast material
√ smooth thin-walled cavity (–10 to +30 HU)
√ frequently associated with urine ascites
√ rarely septated + smaller than lymphocele
NUC:
√ progressive radiotracer activity within collection
Cx: retroperitoneal fibrosis, stricture of upper ureter, perinephric abscess, rupture into peritoneal cavity
◊ Renal dysplasia of affected kidney in almost 100% when detected in utero!
Dx: aspirated fluid with high urea concentration
DDx: lymphocele, hematoma, abscess, renal cyst, pancreatic pseudocyst, ascites

UROLITHIASIS

= NEPHROLITHIASIS
◊ Most common cause of calcification within the kidney:
› 12% of population develop a renal stone by age 70;
◊ 2–3% of population experience an attack of acute renal colic during their lifetime
◊ Patients with acute flank pain have ureteral calculi in 67–95%
Annual incidence: 1–2÷1,000; 1,200,000 annually in USA
Age: 30–60 years; M÷F = 4÷1
Anderson-Carr-Randall theory of renal stone formation:
abnormally high calcium excretion exceeds lymphatic capacity, microaggregates of calcium (present in the normal kidney) occur in medulla → ⇑ in size → migrate toward caliceal epithelium and → rupture into calices to form calculi
(a) nucleation theory
= crystal / foreign body initiates formation in urine supersaturated with crystallizing salt
(b) stone matrix theory
= organic matrix of urinary proteins + serum serves as framework for deposition of crystals
(c) inhibitor theory
= little / no concentration of urinary stone inhibitors (citrate, pyrophosphate, glycosaminoglycan, nephrocalcin, Tamm-Horsfall protein) → crystal formation
Stone composition in order of frequency:
calcium oxalate mono- and dihydrate 40–60%
calcium phosphate 20–60%
struvite 5–15%
uric acid 5–10%
brushite 2–4%
cystine 1–3%
Cause:

genetics, diet, employment, geography, history of UTI

◊ 70–80% of patients with first-time stones have a specific metabolic disorder (idiopathic hypercalciuria, secondary hypercalciuria (sarcoidosis, hyperparathyroidism), hyperuricosuria (gout, Lesch-Nyhan syndrome, hyperoxaluria, cystinuria)

Radiographic Opacity and Frequency of Urolithiasis

Mineral Composition	*Description*	*Frequency*	*Opacity*	*NECT [HU]*	*Factors*
Calcium stones		70–80%	+++		
1. Calcium oxalate		20–30%	+++		underlying metabolic disorder; hard to fragment
(a) Calcium oxalate monohydrate (= whewellite)	√ small highly opaque			1700–2800	
(b) Calcium oxalate dihydrate (= wedellite)	√ ± spiculated / mamillated ("mulberry stone")				
(c) Calcium oxalate-phosphate (calcium oxalate plus apatite)		30–40%	+++		
2. Calcium hydrogen phosphate (= brushite)		2–4%	+++	1700–2800	hard to fragment
3. Calcium phosphate (= hydroxyapatite)	• rarely pure (= laminated), occasionally forms in infected alkaline urine	20–60%	+++	1200–1600	usually no metabolic abnormality
Cystine stone		1–3%		600–1100	renal tubular defect; hard to fragment
Struvite stones	√ mildly opaque	5–15%	++	600–900	renal infection
1. Magnesium ammonium phosphate (= struvite)	√ laminated ← urea-splitting organisms (usually Proteus)	1%	++		most common constituent of staghorn calculus
2. Struvite plus calcium phosphate	• associated with infection	15–20%	++		
Uric acid stone	√ radiolucent	5–10%	-	200–450	pH < 5.8
Xanthine stone	√ nonopaque	extremely rare	-	> 200	
Matrix stone (mucoprotein / mucopolysaccharide)	√ nonopaque	rare	-	15–200	pure matrix stones may not be visible

Interventional Procedures for Urolithiasis

Treatment	*Location & Size of Stone*	*Advantage*	*Disadvantage*
Shock wave lithotripsy (SWL)	kidney < 1 cm; ureter < 1 cm	least invasive, good success rate, under sedation / anesthetics	poor success for cystine stones / stones > 1000 HU
Ureteroscopy with semirigid lithotripsy	distal ureter < 1 cm; proximal ureter < 1 cm (in woman)	stones refractory to SWL, high stone-free rate (better than SWL)	invasive, general / spinal-epidural anesthesia
Ureteroscopy with flexible lithotripsy	proximal ureter stone < 1 cm kidney stone < 1.5 cm	stones refractory to SWL, high stone-free rate (better than SWL)	invasive, general / spinal-epidural anesthesia
Percutaneous nephrolithotomy (PCNL)	proximal ureter stone < 1.5 cm kidney stone < 1.5 cm staghorn calculus	highest stone-free rate for large kidney + upper ureter stones	most invasive, may require blood transfusion
Ureterolithotomy: open / laparoscopic	large stone in middle / distal ureter	most effective for large stones	rarely used
Pyelolithotomy: open / laparoscopic	large stone: unbranched in renal pelvis / in horseshoe kidney	most effective for very large stones	rarely used
Anatrophic nephrolithotomy	full staghorn calculus	alternative to multiple-track PCNL	rarely used

1. **Hypercalciuria**
   - with hypercalcemia (50%): primary hyperparathyroidism, milk-alkali syndrome, hypervitaminosis D, malignant neoplasm, Paget disease, prolonged immobilization, sarcoidosis, adrenal insufficiency, hyper- and hypothyroidism, renal transplantation
   - with normocalcemia (30–60%): obstruction, urinary tract infection, vesical diverticulum, horseshoe kidney, medullary sponge kidney, renal tubular acidosis, malignant neoplasm, Paget disease, Cushing syndrome, prolonged immobilization,

idiopathic hypercalciuria, acetazolamide therapy, sarcoidosis

(a) ABSORPTIVE HYPERCALCIURIA
= increased intestinal absorption of calcium
Cause: increase in 1,25-dihydroxy-vitamin D levels (50%)

(b) RENAL HYPERCALCIURIA
= abnormal renal calcium leak
Cause: diet high in sodium, urinary tract infection (33%)

(c) RESORPTIVE HYPERCALCIURIA
= increased bone demineralization ← subtle hyper-parathyroidism

(d) IDIOPATHIC
√ attenuation of calcium stones > 1,000 HU similar to bone cortex

2. **Hyperoxaluria**= OXALOSIS

◊ Hyperoxaluria has a stronger correlation to severity of stone disease than hypercalciuria!

Physiology:

◊ 85% of urinary oxalate is produced endogenously in liver!

◊ Oxalic acid is present in many foods but poorly absorbed in healthy individuals resulting in increase in urinary oxalate by only 2–3%!

1. **Primary hyperoxaluria** (more common)
= HEREDITARY HYPEROXALURIA
= rare autosomal recessive inherited enzyme deficiency of carboligase → diffuse oxalate deposition in kidneys, heart, blood vessels, lung, spleen, bone marrow

Type I = deficient ketoglutarate-glyoxylate carboxylase
• glycolic aciduria

Type II = D-glycerate dehydrogenase deficiency
• D-glyceric aciduria

Age: usually < 5 years
Prognosis: early death in childhood

2. **Secondary / enteric hyperoxaluria** (rare)
Cause: disturbance of bile acid metabolism after excess oxalate absorption from bowel after jejunoileal bypass, ileal resection, blind loop syndrome, Crohn disease; increased ingestion (green leafy vegetables), pyridoxine deficiency, ethylene glycol poisoning, methoxyflurane anesthesia

3. **Hyperuricosuria**

• uric acid lithiasis (15–20%); stones form in acid urine
• M > F; usually familial
• multiple small hard smooth yellow / red-brown radiolucent stones

(a) WITH HYPERURICEMIA:
gout (25–50%) ← excessive intake of meat, fish, poultry; myeloproliferative diseases; antimitotic drugs; chemo- / radiation therapy; uricosuric agents; Lesch-Nyhan syndrome

(b) WITH NORMOURICEMIA:
idiopathic; occurrence in concentrated acidic urine → becomes supersaturated with undissociated uric acid (hot climate, ileostomy)

√ bright well-defined stone of medium-high attenuation (> 150 HU [300–500 HU])

Rx: raising urinary pH (potassium citrate / sodium bicarbonate)

4. **Cystinuria** (stones form in acid urine)
   = autosomal recessive disorder with tubular inability to reabsorb cystine, ornithine, lysine, arginine
   Age of onset: after 10 years (usually young girls)
   • multiple soft / hard, pink / yellow radiopaque stones
   Rx: (1) Decreased intake of methionine
   (2) Alkalinization of urine
5. **Xanthinuria**
   = inherited autosomal recessive deficiency of xanthine oxidase ← failure of normal oxidation of purines
6. **Urinary tract infection**
   Cause: urea-splitting organisms (Proteus mirabilis, P. vulgaris, Haemophilus influenzae, S. aureus, Ureaplasma urealyticum) + alkaline environment (pH > 7.19)
   ◊ May lead to magnesium ammonium phosphate = struvite stones
   Predisposed: women (M÷F = 1÷2), neurogenic bladder, urinary diversion, indwelling catheter, lower-urinary-tract voiding dysfunction
   √ often branching into staghorn calculi
   √ most struvite stones are radiopaque, but poorly mineralized matrix stones are not
7. Any condition causing nephrocalcinosis
8. Idiopathic calcium urolithiasis
9. Indinavir (protease inhibitor for treatment of HIV type 1) → precipitation of drug crystals in renal tubule
   • rectangular brown puttylike nonradiopaque stones
   √ detectable sonographically / IVP / CECT

NECT:

All urinary tract calculi are of high attenuation measuring > 200 HU (except for indinavir calculi, which have soft-tissue attenuation) and may be obscured by contrast material!

Radiographic Shape of Kidney Stone

1. **Staghorn** calculus (resembling antlers of a stag):
   = branched calculus filling the entire bifid renal collecting system
   Cause: recurrent urinary tract infections from bacterial pathogens producing alkaline urine (the only stone more common in females)
   Composition: struvite (= mixture of calcium, magnesium, ammonium, phosphate) / cystine / uric acid
2. **Fragmented staghorn**
   = incomplete branched calculus
   Cause: infection complicated by obstruction
   (a) pyonephrosis
   (b) XGP
3. **Jack stone** (resembling a child's toy jack)
   = stone of spiked configuration
   Composition: calcium oxalate dihydrate

Location: urinary bladder > kidney

4. **Mulberry stone** = mamillated contour
   Composition: calcium oxalate dihydrate
5. **Hemp-seed calculi**
   = multiple small stones of similar size with lapidary appearance (like cut gems)
   [*lapis*, Latin = stone; *lapidarius* = stonecutter]
   Composition: calcium oxalate / calcium phosphate
   Location: caliceal diverticulum, cyst, hydronephrosis)
6. **Milk of calcium** (with urine-calcium level)
   Composition: calcium carbonate
   Location: any epithelium-lined structure directly communicating with the collecting system (caliceal diverticulum, hydrocalyx, renal cyst)

Nonradiopaque Stones

mnemonic: SMUX

Struvite (rarely of pure magnesium ammonium phosphate)
Matrix stone (mucoprotein, mucopolysaccharide)
Uric acid
Xanthine

Calculi often Associated with Infection

mnemonic: S and M

Struvite (magnesium ammonium phosphate ± calcium phosphate)
Matrix stone (mucoprotein, mucopolysaccharide)

Acute Obstruction by Ureteric Calculi

= URETEROLITHIASIS

- renal colic = acute severe spasmodic / steady continuous flank pain
- frequently radiating into pelvis / groin / scrotum / labia
- hematuria (85%): absent in completely obstructing stone

Site: at points of ureteral narrowing

(a) ureterovesical junction (UVJ)
(b) ureteropelvic junction (UPJ)
(c) iliac vessel crossing

Frequency of Stones	*Location*
37%	in proximal ureter
7%	in midureter
33%	in distal ureter
18%	at ureterovesical junction

Plain radiography = KUB (45% sensitive, 77% specific):

Useful: planning ESWL, monitoring stone fragments in 1–2-week intervals
Visualization:

◊ 90% of urinary calculi are radiopaque

Confounding factors: small size of calculus, overlying bowel gas / fecal matter, osseous structures (transverse process, sacrum), extrarenal calcifications (gallstone, calcific

pancreatitis, mesenteric lymph node, arterial calcification, phlebolith), obesity
◊ Stones may be present in 30% of the time when KUB is negative!
◊ 60% of calcifications along expected course of ureter on symptomatic side are ureteric stones!

IVP (64–97% sensitive, 92–94% specific, 31–48% FN):
◊ Most common cause of ureteral filling defects at IVP!
√ delayed opacification of collecting system: degree of obstruction displayed by time delay of appearance of contrast material (physiologic information)
√ persistent delayed nephrogram increasing in intensity with time
√ hydroureteronephrosis
√ column of contrast material proximal to obstructing stone
◊ Nonobstructing calculi may be difficult to detect

US (37% sensitive):
√ highly echogenic focus + acoustic shadow within dilated ureter
√ unilateral hydronephrosis (11–35% FN, up to 10% FP rate)
DDx: physiologic dilatation in pregnancy
√ RI (resistive index) > 0.70 in symptomatic kidney within 6 hours after acute obstruction (partial obstruction, antecedent IVP may alter RI)
N.B.: normal pregnancy does NOT alter RI
√ difference in RI between kidneys of ≥ 0.04
√ absent ureteral jet / continuous low-level flow on affected side (jet may be present with partially obstructing calculus)
N.B.: 15% falsely positive during pregnancy
√ direct visualization of prevesical calculus by transabdominal / transrectal / transvaginal US

NECT (95–98% sensitive, 96–100% specific, 97% accurate):
◊ Helical NECT is the most accurate technique and gold standard for detecting urinary tract calculi!
Advantages:
(a) visualization of all calculi (= stone burden)
(b) short exam time (3–5 minutes)
(c) avoidance of IV contrast
(d) detection of extraurinary causes of flank pain (in 16–45%)
(e) information about stone composition and fragility
√ calcified stone within ureter (PATHOGNOMONIC):
DDx: phlebolith → no continuity with the ureter
√ all stone compositions readily detectable (except unmineralized stone matrix + stones related to protease inhibitor indinavir [Crixivan®] for HIV treatment)
√ proximal ureteral dilatation + normal caliber distally
√ stone at ureterovesical junction
DDx: stone passed into bladder (stone falls anteriorly in prone position)
√ "**soft-tissue rim**" sign (50–77% sensitive, 92% specific):
= halo of soft-tissue attenuation around calcific focus ← thickening of ureteral wall surrounding impacted small ureteric calculus ← edema within 4–24 hours after

obstruction
√ visible in 90% of stones < 4 mm
√ not visible in 33% of stones > 5 mm ← thinning of ureteral wall by impaction of larger stones
DDx: gonadal vein phlebolith (in front of upper ureter, lateral to mid ureter); 2–8% of phleboliths have a "soft-tissue rim" sign
√ secondary signs of urinary tract obstruction (in 96%):
√ asymmetric stranding of perinephric fat (in 65%, 76% sensitive, 90% specific) with loss of well-defined fat-kidney interface due to
(a) fluid within bridging septa of perinephric fat ← increased lymphatic pressure
◊ A higher degree of perinephric edema means a higher degree of obstruction!
(b) focal nonlinear fluid collection of extravasated urine ← forniceal rupture
√ periureteral edema (in 31%)
√ hydronephrosis (in 69%, 83% sensitive, 94% specific) = rounded fluid-filled calices and infundibula partially obliterating the renal sinus fat; seen early
DDx: extrarenal pelvis, parapelvic cysts
√ hydroureter above stone (87% sensitive, 90% specific) continuous with renal pelvis
√ unilateral renal enlargement (71% sensitive, 89% specific)
√ thickening of lateroconal fascia
√ perinephric edema
√ unilateral absence of white pyramid (= loss of the occasional incidental finding of high-attenuation medullary pyramids in normal kidneys)
False negatives (2–7%):
(a) volume averaging (= stone small relative to collimation)
(b) patients treated with indinavir
Stone burden:
√ greatest dimension of stone in magnified bone window setting
√ stone volume for large / staghorn calculi → SWL failure likely with a stone of > 700 mm3
Stone fragility:
√ stone heterogeneity → susceptible to fragmentation
√ stone homogeneity → harder to fragment

MR:
◊ May be helpful when use of contrast media / radiation is undesirable (pregnancy, children)!
√ renal enlargement
√ perinephric fluid ← lymphatic congestion / forniceal rupture
√ periureteral edema associated with urinary obstruction
√ abrupt change in ureteral caliber
√ dilatation distal to sacral promontory ← suspect ureterovesical junction stone
√ dark signal void (low SI of filling defect) in ureter (DDx: flow artifact on T2 single-shot fast SE images)
◊ insensitive for most renal / ureteral stones of < 1 cm

Visualization of stones in the urinary tract is challenging with MRI, particularly for intrarenal stones and

those at the ureterovesical junction.

NUC (DTPA, MAG3):
√ initially diminished uptake during renal perfusion phase
√ prolonged nephrographic phase
√ delayed excretion into collecting system
√ delayed transit of radiotracer with accumulation in obstructed collecting system
√ no clearing effect of IV furosemide injection

Advantages: quantitative assessment of renal function

Cx: xanthogranulomatous pyelonephritis

Rx: (1) Medical expulsive therapy: α-blocker, calcium channel blocker, steroids, NSAID

(2) Hydration (during strenuous physical activity, at bedtime, within 3 hours after meal) maintaining urine output of 2–3 L/days

(3) Diet: restrict amounts of protein, sodium, calcium

(4) Drugs: thiazide diuretics (lowers urinary calcium), allopurinol (lowers urate + oxalate excretion)

(5) Extracorporeal shock wave lithotripsy (ESWL)

DDx: (1) Recent passage of stone

(2) **Phlebolith**

√ "**comet-tail**" sign = extension of curvilinear soft-tissue band from stone (in 65%)
√ comet nucleus ← calcified phlebolith
√ comet tail ← noncalcified gonadal vein
√ low-attenuation center (visible in 9%, detectable with profile analysis in 21%)

(3) Arterial calcification

(4) Calcified lymph node

(5) Surgical clip

Prognosis:

(1) Spontaneous passage of ureteral calculi (in 93%)

Stone size	*passes in*
< 4 mm	90%
≤ 5 mm	68%
4–6 mm	50%
5–10 mm	47%

◊ Stones > 6 mm rarely pass!

(2) Without treatment stone recurrence is 10% at 1 year, 33% at 5 years, 50% at 10 years, 75% by 20 years

UTRICLE CYST

= dilatation of prostatic utricle (sometimes believed to be a remnant of the müllerian duct)

Prevalence: 1–5% of general population

Age: 1st–2nd decade

• postvoid dribbling, suprapubic / rectal pain, hematuria

• obstructive / irritative urinary tract symptoms

Often associated with:

hypospadia, intersex disorders, incomplete testicular descent, ipsilateral renal agenesis

Location: arise in midline from verumontanum

◊ Free communication with urethra

√ usually 8–10-mm long pear-shaped cyst posterior to urethra

√ NO extension above base of prostate (DDx: müllerian duct cyst, usually larger with extension above base of prostate)

Dx: endoscopic catheterization with aspiration of white / brown fluid occasionally containing spermatozoa

Cx: recurrent epididymitis, hematospermia, carcinomatous metaplasia

VARICOCELE

= abnormal dilatation + tortuosity of plexus pampiniformis ← retrograde flow into internal spermatic vein

Components of pampiniform plexus:

(a) internal spermatic vein (ventral location) draining testis

(b) vein of vas deferens (mediodorsal) draining epididymis

(c) cremasteric vein (laterodorsal location) draining scrotal wall

US:

√ multiple hypoechoic serpiginous tubular structures, initially superior and lateral, later posterior and inferior to testis

√ containing low-level echoes if flow slow

Grading of Varicocele

Grade	*Relaxed State*	*During Valsalva*
Normal	2.2 mm	2.7 mm
Small varicocele	2.5–4.0 mm	↑ by 1.0 mm
Moderate varicocele	4.0–5.0 mm	↑ by 1.2–1.5 mm
Large varicocele	> 5.0 mm	↑ by > 1.5 mm

Idiopathic / Primary Varicocele

Cause: incompetent / absent valve at level of left renal vein / IVC on right side

Prevalence:

(a) clinical varicocele: in 8–15% of adult males, in 21–39% of infertile men

(b) subclinical varicocele: in 40–75% of infertile men

Theoretical causes for infertility:

(1) Increase in local temperature

(2) Reflux of toxic substances from adrenal gland (countercurrent exchange of norepinephrine from refluxing renal venous blood into testicular arterial blood at the level of the pampiniform plexus)

(3) Alteration in Leydig cell function

(4) Hypoxia of germinative tissue ← venous reflux resulting in venous hypertension + stasis

• scrotal pain, scrotal swelling with "bag of worms" quality
• abnormal spermatogram: impaired motility, immature sperm, oligospermia

Location: left side (78%), bilateral (16%), right side (6%)

Reasons for left-sided prevalence:

(a) left testicular vein longer
(b) left testicular vein enters left renal vein at right angle
(c) compression of left renal vein by left testicular artery in some men
(d) compression of left testicular vein by descending colon distended with feces

Bidirectional Doppler sonography (erect with quiet breathing):

(1) SHUNT TYPE (86%): insufficient distal valves allow spontaneous + continuous reflux from internal spermatic vein (retrograde flow) into cremasteric vein + vein of vas deferens (where flow is orthograde) via collaterals
• sperm quality diminished
• clinically plexus type (grade II + III) = medium-sized + large varicoceles
√ continuous reflux during Valsalva maneuver

(2) STOP TYPE / PRESSURE TYPE (14%): intact intrascrotal valves allow only brief period of reflux from spermatic vein into pampiniform plexus under Valsalva maneuver
• sperm quality normal
• clinically central type (grade 0 + I) = subclinical + small varicocele
√ short phase of initial retrograde flow

US (almost 100% sensitive + specific):
√ diameter of dominant vein in upright position at inguinal canal

Dx: documentation of venous reflux

Cx: testicular atrophy (volume measurement of testes!)

Rx: (1) Ivanissevitch procedure = surgery
(2) Transcatheter spermatic vein occlusion
◊ Treatment improves sperm quality in up to 53%

Secondary Varicocele

= compression of left renal vein by tumor, aberrant renal artery, obstructed renal vein, hydronephrosis, cirrhosis
• nondecompressible varicocele
◊ Check left renal vein!

VESICOURETERIC REFLUX

= abnormal valve mechanism at UVJ resulting in reflux, ureteral dilatation, clubbed calices, eventual renal scarring

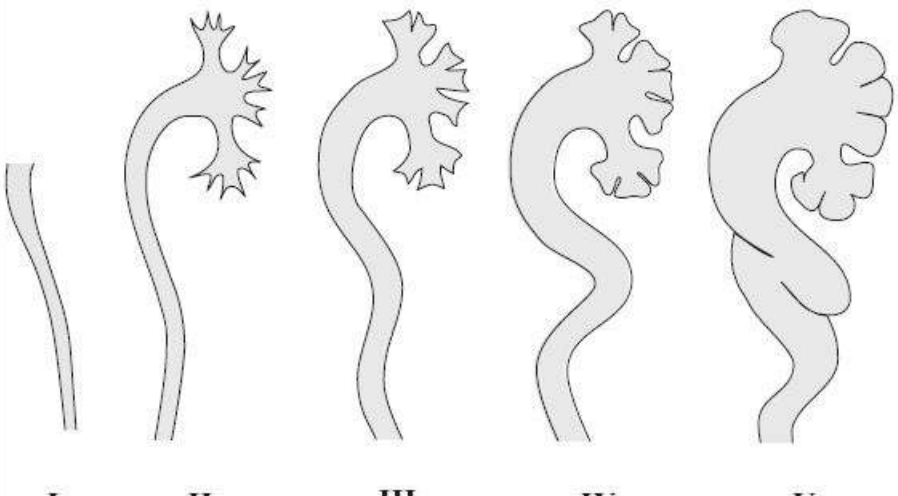
A. CONGENITAL REFLUX = PRIMARY REFLUX

= incompetence of ureterovesical junction ← abnormal tunneling of distal ureter through bladder wall

Prevalence: in 9–10% of normal Caucasian babies; in 1.4% of school girls; in 30% of children with a first episode of UTI

• short submucosal ureteral tunnel (normally has a length/width ratio of 4÷1)
• large laterally located ureteral orifice

Location: uni- / bilateral (frequently involves lower pole ureter in total ureteral duplication)



Grading of Vesicoureteral Reflux
(International Reflux System)

Grades of Vesicoureteral Reflux by VCUG

Grade I	√ reflux into ureter
Grade II	√ reflux into pelvicaliceal system (without caliceal dilatation / blunting)
Grade III	√ all of the above + mild dilatation of ureter and pelvicaliceal system √ distinct forniceal angles + papillary impressions
Grade IV	√ reflux into tortuous ureter + moderately dilated pelvicaliceal system √ blunted forniceal angles √ distinct papillary impressions
Grade V	√ reflux into markedly dilated and tortuous ureter + markedly dilated pelvicaliceal system √ obliteration of forniceal angles + papillary impressions

√ renal scars in 22–50%

Prognosis: disappears spontaneously in 80%

Cx: reflux atrophy / nephropathy in 22–50%; end-stage renal disease in 5–15% of adults

B. ACQUIRED REFLUX = SECONDARY REFLUX

1. Paraureteric diverticulum = Hutch diverticulum
2. Duplication with ureterocele

3. Cystitis (in 29–50%)
4. Urethral obstruction (urethral valves)
5. Neurogenic bladder
6. Absence of abdominal musculature (prune belly syndrome)

Cx: renal scarring with UTI (30–60%)

Estimated radiation dose to ovaries:

(a) usual fluoroscopy: 300 mrad
(c) tailored low-dose fluoroscopy: 3 mrad
(b) radionuclide cystography: 2 mrad

US (74% of kidneys with VUR may be normal by US):

√ intermittent hydroureteronephrosis = variable size of collecting system
√ redundant mucosa causing apparent thickening of renal pelvic wall
√ large thin-walled bladder
√ midline-to-orifice distance > 7–9 mm has high probability of vesicoureteric reflux

Prognosis:

All grades of reflux can be outgrown:

› 80% [46%] of grade I–II [III] outgrow reflux within 5 years
› 50% of grade IV continue to have reflux 9 years after initial diagnosis

Renal scarring: > 20% chance for grade III–V reflux; 2–3% chance for grade I–II reflux

Rx: (1) Grade IV–V require surgery to avoid renal scarring + renal impairment + hypertension (except in infants

(2) Periureteral diverticulum requires surgery (grade of reflux not prognostic)

◊ Grade I–III resolve with maturation of the UV junction

WILMS TUMOR

[Carl Max Wilhelm Wilms (1867–1918), pathologist and chair of surgery at the University of Heidelberg]

= NEPHROBLASTOMA

◊ Most common malignant abdominal neoplasm in children 1–8 years old (10%)!
◊ 3rd most common malignancy in childhood (after leukemia + brain tumors; neuroblastoma more common in infancy)!
◊ 3rd most common (87%) of all renal masses in childhood (after hydronephrosis + multicystic dysplastic kidney)!

Prevalence: 7–8÷1,000,000 children; 500 new cases annually in USA (2015, stable for years); familial in 1–2%

Peak age: 2–3 years (range, 3 months – 11 years); rare in neonates (0.16%) and during 1st year; 50% < 3 years; 80% < 5 years; 90% < 8 years; M÷F = 1÷1; more common in blacks

Histo: arises from undifferentiated metanephric blastema (= nephrogenic rests) with variable amounts of blastema, stroma, epithelium; occasionally mesodermal derivatives of striated / smooth muscle, fat, bone, cartilage = "teratoid Wilms tumor"

(a) unfavorable histologic character = presence of anaplasia in 6.2%: localized / diffuse
(b) favorable histologic character (90%)

◊ Multilocular cystic nephroma, mesoblastic nephroma, nephro-blastomatosis are related to the

more favorable types of Wilms tumor!

Genetics: multifactorial; abnormal WT1 gene on locus 11p13 with WAGR syndrome (**W**ilms tumor, **a**niridia, **g**enitourinary abnormalities, mental **r**etardation) or Drash syndrome; abnormal WT2 gene on locus 11p15 with Beckwith-Wiedemann syndrome or hemihypertrophy; familial Wilms tumor in 1%

Staging of Wilms Tumor (stage each kidney separately) *(National Wilms Tumor Study Group)*	
I	tumor limited to kidney (renal capsule intact)
II	extracapsular extension into perirenal tissue / renal vessels outside kidney / lymph nodes
III	not totally resectable (peritoneal implants, other than paraaortic nodes involved, invasion of vital structures)
IV	hematogenous metastases (lung in 85%, liver in 20%, bone in 0.8%, brain [rare]) / lymph node metastases outside abdomen or pelvis
V	bilateral renal involvement at diagnosis (4–13%)

Syndromic Wilms tumor (in 10–14%) associated with:

(1) Sporadic aniridia (= severe hypoplasia of iris)
- ◊ 33% of sporadic aniridia patients develop Wilms tumor!

(2) Beckwith-Wiedemann syndrome
- ◊ 10–20% of patients with Beckwith-Wiedemann syndrome develop Wilms tumor!

(3) **Hemihypertrophy**: total / segmental / crossed (2.5%)
- ◊ Ipsilateral or contralateral kidney affected
- ◊ Increased incidence of all embryonal tumors (adrenal cortical neoplasms, hepatoblastoma)

(4) Genitourinary disorders (4.4%):
- (a) **Drash syndrome**: male pseudohermaphroditism, progressive glomerulonephritis
- (b) Renal anomalies: horseshoe kidney, duplex / solitary / fused kidney
- (c) Genital anomalies: cryptorchidism (2.8%), hypospadia (1.8%), ambiguous genitalia

Screening recommendations (up to age 7 years):

CT at 6 months of age followed by US every 3 months

Staging:

› evaluate for
- invasion of adjacent organs
- involvement of regional lymph nodes
- involvement of the other kidney
- spread to the peritoneum
- metastatic disease

› screen contralateral kidney
› examine renal vein + IVC

√ signs of tumor rupture:
- √ poorly defined tumor margins
- √ perinephric fat stranding
- √ retroperitoneal fluid
- √ ipsilateral pleural effusion
- √ peritoneal fluid beyond cul-de-sac

- asymptomatic palpable abdominal mass (90%), often discovered by a parent
- hypertension (in up to 25%) ← renin production by tumor / vascular compression by tumor
- abdominal pain (25%), low-grade fever (15%)
- gross hematuria (7–15%) ← invasion of renal pelvis
- microscopic hematuria (15–25%)
- hemorrhage after minor trauma
- ascites ← venous obstruction; varicocele ← left-sided tumor

RULE OF 10's:
- › 10% unfavorable histology
- › 10% multifocal in one kidney
- › 10% bilateral
- › 10% vascular invasion
- › 10% calcifications
- › 10% pulmonary metastases at presentation

Location: usually solitary lesion; multifocal within one kidney (12%); syn- / metachronous bilateral tumors (7%) with nephrogenic rests in 94–99%

√ large tumor → average size of 12 cm in diameter

√ expansile intrarenal growth:
- √ sharply marginated with compression of renal tissue = pseudocapsule
- √ distorted "clobbered" / dilated calices
- √ displacement of major vessels, rather than encasement

√ curvilinear / phlebolithic calcifications in 5% on plain film, in 15% on CT (DDx: regular stippled calcifications in 85% of neuroblastomas)

√ tumor invasion of renal vein and IVC (4–10%); extension into right atrium (in 21% of cases with IVC invasion)

√ tumor may cross midline

√ poor / nonexcretion of IV contrast ← invasion or compression of hilar vessels + collecting system / extensive tumor infiltration of renal parenchyma

US:
- √ predominantly solid spherical mass:
  - √ heterogeneous echogenicity (frequent):
    - √ irregular anechoic areas ← cyst formation + central necrosis + hemorrhage
    - √ echogenic areas ← calcium (9%) / fat
  - √ fairly evenly echogenic (rare)

CT (preferred modality):
- √ large well-circumscribed heterogeneous partially cystic intrarenal mass ← old hemorrhage + necrosis (71%), cyst formation, fat, calcifications (15%)
- √ beak / claw of renal tissue extends partially around mass
- √ tumor less enhancing than renal parenchyma

CECT (ALARA dose → ONLY portal venous phase necessary):
- √ nodal / hepatic metastases
- √ tumor extension into renal vein / IVC
- √ contralateral synchronous tumor/ nephrogenic rests

MR:
- √ typically heterogeneous lobulated hypointense compared with normal renal parenchyma on T1WI
- √ foci of increased T1 signal intensity ← hemorrhage
- √ hyper- or isointense on T2WI

NUC:
- √ nonfunctioning kidney (10%)
- √ hypo- / iso- / hyperperfusion on radionuclide angiogram
- √ absent tracer accumulation on delayed static images
- √ displacement of kidney + distortion of collecting system

PET:
- √ FDG-avid primary + metastatic Wilms tumor
- √ may be useful to detect active / residual disease and identify nonresponders of neoadjuvant chemotherapy

Angio:
- √ hypervascular tumor: enlarged tortuous vessels, coarse neovascularity; small arterial aneurysms; vascular lakes
- √ parasitization of vascular supply

Spread with rupture through renal capsule:
- √ broad-based subdiaphragmatic masses on surface of liver and spleen
- √ omental caking

Cx: tumor rupture

Rx: presurgical chemotherapy + nephrectomy + adjuvant chemotherapy ± radiation therapy

Prognosis: survival rate ← depending on pathologic pattern, age at time of diagnosis, extent of disease; 4-year relapse-free survival: 91% for stage I; 88% for stage II; 79% for stage III; 78–84% for stage IV

DDx: Age is the most important consideration formulating a DDx

(1) Neuroblastoma (encasement / elevation of aorta, many regular stippled calcifications, displacement of kidney, tumor crossing midline behind aorta, extension through neural foramina into spinal canal, skeletal metastases)
(2) Congenital mesoblastic nephroma (in fetus / neonate)
(3) RCC (2nd decade of life, renal vein extension)
(4) Clear cell sarcoma (early skeletal metastases)
(5) Rhabdoid tumor (subcapsular hemorrhage, brain tumor in posterior fossa)
(6) Infection: acute bacterial nephritis, renal abscess

WOLMAN DISEASE

[Moshe Wolman (1914–?), chairman of pathology at University of Tel-Aviv, Israel]

= PRIMARY FAMILIAL XANTHOMATOSIS

= rare autosomal recessive lipidosis with accumulation of cholesterol esters and triglycerides in visceral foam cells + various tissues (liver, spleen, lymph nodes, adrenal cortex, small bowel)

Etiology: deficiency of lysosomal acid esterase / acid lipase

• malabsorption in neonatal period: failure to thrive, diarrhea, steatorrhea, vomiting

• delayed growth, diminished muscle mass, abdominal distension
√ hepatosplenomegaly
√ extensive bilateral punctate calcifications (calcification of fatty-acid soaps) throughout enlarged adrenals (maintaining their normal triangular shape) are DIAGNOSTIC
√ enlarged fat-containing lymph nodes
√ small bowel wall thickening ← infiltration of mucosa of small bowel by lipid-filled histiocytes impairing absorption
√ generalized osteoporosis

CT & MR: attenuation + signal intensities consistent with deposition of lipids

Dx: assay of leukocytes / cultured skin fibroblasts

Prognosis: death occurs within first 6 months of life

OBSTETRICS AND GYNECOLOGY

DIFFERENTIAL DIAGNOSIS OF OBSTETRIC AND GYNECOLOGIC DISORDERS

PELVIC PAIN

Chronic Pelvic Pain

= nonmenstrual pain of > 6 months duration

Prevalence: 15% in women between 18 and 50 years; 10–40% of all gynecologic outpatient visits; 35% of diagnostic laparoscopies; 15% of all hysterectomies

Age: typically < 35 years; Whites > Blacks

Pelvic Pain in Young Woman

A. Most common*
   1. Hemorrhagic ovarian cyst
   2. Pelvic inflammatory disease (PID)
   3. Ectopic pregnancy
B. Less frequent*
   1. Torsion of ovary
   2. Massive ovarian edema
   3. Endometriosis
   4. Degenerating fibroid
   5. Pelvic congestion syndrome
C. Post partum
   1. Endometritis
   2. Ovarian vein thrombosis

* β-hCG results influence options

Pelvic Pain in Nongynecological Condition

1. Appendicitis
2. Diverticulitis
3. Epiploic appendagitis
4. Crohn disease
5. Infectious ileocolitis
6. Colonic malignancy
7. Ureterolithiasis

Pelvic Pain in Pediatric Age Group

1. Ovarian torsion
   (a) of normal ovary

Cause: excessive mobility of ovary in childhood

(b) with ovarian mass:

› functional cyst (60%)

› neoplasm (40%):

» benign mature teratoma (66%)

» malignancy (33%): germ cell tumor (60–75%), epithelial tumor (10–20%), stromal tumor (10%)

2. Hemorrhagic ovarian cyst
3. Pelvic inflammatory disease
4. Ectopic pregnancy

Pelvic Pain in Pregnancy

Confounding factors:

1. Nonspecific leukocytosis
2. Displacement of structures from their normal locations by gravid uterus
3. Difficult abdominal examination
4. Nonspecific nausea and vomiting

A. PROBLEMS WITH THE PREGNANCY

1. Failed pregnancy
2. Ectopic pregnancy
3. Placental abruption
4. Placenta previa

B. PROBLEMS WITH PELVIC ORGANS

(a) Uterus

1. Degenerating fibroid ← altered blood supply with enlargement during pregnancy

(b) Ovary

1. Ruptured hemorrhagic corpus luteum cyst
2. Adnexal mass ← rupture / rapid enlargement
3. Ovarian torsion / edema

(c) General

1. Endometriosis
2. PID: pregnancy decreases risk of PID

C. NONOBSTETRICAL PROBLEMS

(a) GI tract

1. Acute appendicitis
2. Inflammatory bowel disease: peak age 15–25 years
3. Diverticulitis: no increase during pregnancy
4. Small bowel obstruction / ileus

(b) Hepatobiliary

1. Cholelithiasis / choledocholithiasis
2. Acute cholecystitis
3. Pancreatitis: mostly secondary to gallstones
4. HELLP syndrome
5. Acute fatty liver

(c) GU tract

1. Physiologic hydronephrosis
2. Obstructing ureteral stone

(d) Vascular

1. Venous thromboembolic disease
2. Ovarian vein enlargement / thrombosis

GENERAL OBSTETRICS

Parity Nomenclature (for pregnancies < 20 weeks)

example: G_5P_{4004}

Gravida 5 pregnancies

Parity

mnemonic: FPAL

Full term	4 full term
Preterm	0 preterm
Abortion	0 abortion
Living	4 living

Level I Obstetric Ultrasound

Indication: MS-AFP ≥ 2.5 multiples of mean (MoM) between 14 and 18 weeks MA

Limited scope of examination to identify frequent causes of MS-AFP elevation in 20–50% of pregnancies:

1. Gestational age ≥ 2 weeks more advanced than estimated clinically (18%)
2. Multiple gestations (10%)
3. Unsuspected fetal demise (5%)
4. Obvious fetal NTD / abdominal wall defect

Outcome: no cause identified in 50–80%

Recommendation if level I ultrasound is unrevealing:

(1) Amniocentesis for AF-AFP → normal results in > 90%

(2) Level II obstetric ultrasound (skipping amniocentesis)

Level II Obstetric Ultrasound

Indication: AF-AFP ≥ 2 MoM

Accuracy: identification of abnormal fetuses in 99%

Examination targeted for:

1. Open neural tube defect: anencephaly, encephalocele, open spina bifida, amniotic band syndrome resulting in open neural tube defect
2. Closed neural axis anomaly: hydrocephalus, Dandy-Walker malformation
3. Abdominal wall defect: gastroschisis, omphalocele, gastropleuroschisis from amniotic band syndrome
4. Upper GI obstruction: esophageal atresia ± tracheoesophageal fistula, duodenal obstruction
5. Cystic hygroma

6. Teratoma: sacrococcygeal, lingual, retropharyngeal
7. Renal anomalies: obstructive uropathy, renal agenesis, multicystic dysplastic kidney, congenital Finnish nephrosis

◊ Risk of fetal chromosomal anomaly is only 0.6–1.1% with normal level II sonogram!

MATERNAL SERUM SCREENING

Alpha-fetoprotein

= glycoprotein as major circulatory protein of early fetus

Origin: formed initially by yolk sac + fetal gut (4–8 weeks), later by fetal liver

Detectable in

(a) fetal serum
- concentration peaks at 14–15 weeks followed by progressive decline

(b) amniotic fluid (AF-AFP) is a result of
- › fetal urination
- › fetal gastrointestinal secretions
- › transudation across fetal membranes: amnion, placenta
- › transudation across immature fetal epithelium
- concentration peaks early in 2nd trimester followed by progressive decline

(c) maternal circulation (MS-AFP) ← leakage from amniotic fluid across placenta
- levels start to rise at 7th week, peak at 32nd week, and decline toward end of pregnancy

◊ Either high / low MS-AFP is associated with 34% of all major congenital defect

At the end of the 1st trimester AFP is present:

in fetal plasma in milligram quantities
in amniotic fluid in microgram quantities
in maternal serum in nanogram quantities

Reported in MoM = multiples of mean to standardize interpretation among laboratories

Elevated Alpha-fetoprotein

- screening at 16–18 weeks GA

◊ Values must be corrected for dates, maternal weight, race, presence of diabetes (diabetes has depressing effect on MS-AFP so that lower levels may be associated with NTDs)

Associated with:

A. LABORATORY ERROR

B. ERRONEOUS DATES (18%):
GA ≥ 2 weeks more advanced sonographically than by clinical estimate (AFP levels rise 15% per week during 16–18-week window)

C. MULTIPLE GESTATIONS (14%)

D. FETAL DEMISE (7%) / fetal distress / threatened abortion

E. FETAL ANOMALIES (61%)

1. Neural tube defects (51%):
anencephaly (30%), myelomeningocele (18%), encephalocele (3%), forebrain malformation
Prevalence: 1.6÷1,000 births in USA; 6÷1,000 births in Great Britain

◊ In 90% as 1st time event!

Risk of recurrence: 3% after one affected child; 6% after 2 affected children

2. Ventral wall defects (21%):
   gastroschisis, omphalocele (sensitivity of 50%)
3. Proximal fetal gut obstruction:
   esophageal / duodenal atresia
   → diminished AFP degradation in small bowel
4. Cystic hygroma, teratoma: pharyngeal, sacral
5. Amniotic band syndrome:
   asymmetric cephalocele, gastropleuroschisis
6. Renal abnormalities:
   multicystic dysplastic kidney, renal agenesis, pelviectasis, congenital Finnish nephrosis → typically ≥ 10 MoM + negative amniotic fluid acetylcholinesterase
7. Oligohydramnios

F. PLACENTAL LESION
   altering the placentomaternal barrier
   1. Chorioangioma
   2. Peri- and intraplacental hematoma
      → resulting in fetomaternal hemorrhage
   3. Placental lakes, infarct, intervillous thrombosis

G. LOW BIRTH WEIGHT

H. Normal pregnancy + MATERNAL DISORDER
   1. Hepatitis
   2. Hepatoma

I. Fetal-maternal blood mixing:
   collection of MS-AFP samples after amniocentesis

mnemonic: GEM MINER CO

Gastroschisis
Esophageal atresia
Multiple gestations
Mole
Incorrect menstrual dates
Neural tube defects
Error: laboratory
Renal disease in fetus: autosomal recessive polycystic kidney disease, renal dysplasia, obstructive uropathy, congenital Finnish nephrosis
Chorioangioma
Omphalocele

ELEVATED MATERNAL SERUM AFP (MS-AFP)

= defined as ≥ 2.5 MoM / equivalent to the 5th percentile: 4.5 MoM for multiple gestations

Power of detection at ≥ 2.5 MoM cutoff:
98% for gastroschisis
90% for anencephalic fetuses

75–80% for open spinal defects
70% for omphaloceles

Prevalence: 2–5% screen-positive rate (in 16% normal MS-AFP on retesting); 6–15% of fetuses have some type of major congenital defect; in 1.3÷1,000 tests fetal anomaly detected

◊ The higher the AFP elevation the higher the probability of fetal anomalies

◊ 20–38% of women with unexplained high MS-AFP (ie, in the absence of fetal abnormality) suffer adverse pregnancy outcomes (premature birth, preeclampsia, 2–4 x IUGR, 10 x perinatal mortality, 10 x placental abruption)!

ELEVATED AMNIOTIC FLUID AFP (AF-AFP)

= defined as ≥ 2 MoM (< 2 MoM has a 97% NPV)

Prevalence: < 10% of women with elevated MS-AFP and "unrevealing" level I US exam

• amniotic fluid also tested for karyotype + acetylcholinesterase (= neurotransmitter enzyme present when neural tissue is exposed)

◊ 66% of fetuses with ↑ maternal AF-AFP are normal!

◊ A targeted level II ultrasound exam will show fetal anomalies in 33%!

Low Alpha-fetoprotein

= MS-AFP ≤ 0.5 / AF-AFP ≤ 0.72 MoM

Prevalence: 3%

1. Autosomal trisomy syndromes: trisomy 21, 18, 13
   ◊ 20% of trisomy 21 fetuses are found in women with low MS-AFP after adjustment for age!
2. Absence of fetal tissues: eg, hydatidiform mole
3. Fetal demise
4. Misdated pregnancy
5. Normal pregnancy
6. Patient not pregnant

Use of Karyotyping

Frequency: 11–35% of fetuses with sonographically identified abnormalities have chromosomal abnormalities

A. FETAL ANOMALIES

1. CNS anomalies: holoprosencephaly (43–59%), Dandy-Walker malformation (29–50%), cerebellar hypoplasia, agenesis of corpus callosum, myelomeningocele (33–50%)
2. Cystic hygroma (72%): Turner syndrome
3. Omphalocele (30–40%)
4. Cardiac malformations
5. Nonimmune hydrops
6. Duodenal atresia
7. Severe early-onset IUGR: trisomy 18, 13, triploidy
8. Congenital diaphragmatic hernia

9. Bone-echodense bowel (20%): trisomy 21

B. MATERNAL RISK FACTORS
1. Advanced age
2. Low serum alpha-fetoprotein
3. Abnormal triple screen of maternal serum
4. History of previous chromosomally abnormal pregnancy (1% risk of recurrence)

Aneuploid Risk of Major Anomalies

Structural Defect	*Incidence*	*Aneuploidy*	
		Risk	*Most common*
Cystic hygroma	1:6,000	60-75%	45X, 21,18,13, XXY
Hydrops	1:4,000	30–80%	13,21,18,45X
Holoprosencephaly	1:16,000	40–60%	13,18,18p
Cardiac defects	1:125	5–30%	21,18,13,22
AV canal		40–70%	21
Omphalocele	1:5,800	30–40%	13,18
Duodenal atresia	1:10,000	20–30%	21
Diaphragmatic hernia	1:4,000	20–25%	13,18,21,45X
Bladder outlet obstruction	1:1,000	20–25%	13,18
Limb reduction	1:2,000	8%	18
Clubfoot	1:830	6%	18,13,4p-,18q-
Hydrocephalus	1:1,250	3–8%	13,18, triploidy
Facial cleft	1:700	1%	13,18,deletions
Prune belly	1:40,000	low	18,13,45X
Single umbilical artery	1:100	minimal	
Bowel obstruction	1:4,000	minimal	
Gastroschisis	1:12,000	minimal	

C. PLANNED INTENSE INTRAUTERINE MANAGEMENT

Fetal anomalies not associated with chromosomal anomalies:
1. Gastroschisis
2. Unilateral renal anomaly
3. Intestinal obstruction distal to duodenal bulb
4. Off-midline unilateral cleft lip
5. Fetal teratoma: sacrococcygeal / anterior cervical
6. Isolated single umbilical artery

AMNIOTIC FLUID VOLUME

Production:

(a) 1st trimester: dialysate of maternal + fetal serum across the noncornified fetal skin

(b) 2nd + 3rd trimester: fetal urine (600–800 cm^3/d near term), fetal lungs (600–800 cm^3/d near term), amniotic membrane

Absorption:

fetal swallowing + GI absorption, fetal lung absorption, clearance by placenta

Assessment of amniotic fluid volume by:

(1) Subjective assessment ("Gestalt" method):
quick + efficient, accounts for GA-related variations in fluid volume, considered the most accurate if performed by experienced operator, operator + interpreter must be identical, no documentation, variations on serial scans difficult to appreciate

(2) Depth of largest vertical pocket:
simple + quick (used in BPP), pockets > 2 cm may be found in crevices between fetal parts with moderately severe oligohydramnios, does not account for GA-related variations

(3) Four-quadrant Amniotic Fluid Index (AFI):
fairly quick, probably correlates better with fluid volume than any single measurement, may not accurately reflect overall fluid volume, may be affected by fetal movement during measurements

(4) Planimetric measurement of total intrauterine volume

(5) Dye / para-aminohippurate dilution technique:
800 cm^3 at 34 weeks, 500 cm^3 > 34 weeks

Polyhydramnios

= amniotic fluid volume > 1,500–2,000 cm^3 at term

Prevalence: 1.1–2–3.5%

√ fetus does not fill the AP diameter of uterus

√ single largest pocket devoid of fetal parts / cord > 8 cm in vertical direction

√ AFI ≥ 20–24 cm

Prognosis: 64% perinatal mortality with severe polyhydramnios

Etiology:

A. IDIOPATHIC (35%)

Associated with: macrosomia in 19–37%

Suggested cause:

(1) Increased renal vascular flow

(2) Bulk flow of water across surface of fetus + umbilical cord + placenta + membranes

B. MATERNAL CAUSES (36%)

1. Diabetes (25%)
2. Isoimmunization: Rh incompatibility (11%)]
3. Placental tumors: chorioangioma

C. FETAL ANOMALIES (20%)

(a) gastrointestinal anomalies (6–16%):
impairment of fetal swallowing (esophageal atresia in 3%); high intestinal atresias / obstruction of duodenum / proximal small bowel (1.2–1.8%), omphalocele, meconium peritonitis

(b) nonimmune hydrops (16%)

(c) neural tube defects (9–16%):
anencephaly, hydranencephaly, holoprosencephaly, myelomeningocele, ventriculomegaly, agenesis of corpus callosum, encephalocele, microcephaly

(d) chest anomalies (12%):

diaphragmatic hernia, cystic adenomatoid malformation, tracheal atresia, mediastinal teratoma, primary pulmonary hypoplasia, extralobar sequestration, congenital chylothorax

(e) skeletal dysplasias (11%):
dwarfism (thanatophoric dysplasia, achondroplasia), kyphoscoliosis, platyspondyly

(f) chromosomal abnormalities (9%):
trisomy 21, 18, 13

(g) cardiac anomalies (5%):
VSD, truncus arteriosus, ectopia cordis, septal rhabdomyoma, arrhythmia

(h) genitourinary malformations:
unilateral UPJ obstruction, unilateral multicystic dysplastic kidney, mesoblastic nephroma

Cause: ? hormonally mediated polyuria

(i) miscellaneous (8%):
cystic hygroma, facial tumors, cleft lip / palate, teratoma, amniotic band syndrome, congenital pancreatic cyst

◊ In polyhydramnios efforts to detect fetal anomalies should be directed at SGA fetuses!

mnemonic: TARDI
Twins
Anomalies, fetal
Rh incompatibility
Diabetes
Idiopathic

Oligohydramnios

= amniotic fluid volume < 500 cm^3 at term
√ single largest pocket devoid of fetal parts / cord ≤ 1–2 cm in vertical direction
√ AFI ≤ 5–7 cm

Etiology:

mnemonic: DRIPP
Demise of fetus / Drugs (Motrin® therapy for tocolysis of preterm labor)
Renal anomalies, bilateral (= inadequate urine production): renal agenesis / dysgenesis, infantile polycystic kidney disease, prune belly syndrome, posterior urethral valves, urethral atresia, cloacal anomalies

◊ 20-fold increase in incidence of fetal anomalies with oligohydramnios!

N.B.: bilateral renal obstruction, if combined with intestinal obstruction, may be associated with polyhydramnios

IUGR: ← reduced renal perfusion
Premature rupture of membranes (most common)
Postmaturity

Cx: pulmonary hypoplasia, cord compression
Prognosis: 77–100% perinatal mortality with 2nd trimester oligohydramnios

ABNORMAL FIRST TRIMESTER FINDINGS

Time of onset: prior to 8–10 weeks

First Trimester Bleeding

= VAGINAL BLEEDING IN FIRST TRIMESTER

Frequency: 15–25% of all pregnancies, of which 50% terminate in abortion

A. INTRAUTERINE CONCEPTUS IDENTIFIED
   1. Threatened abortion
   2. Embryonic demise
   3. Blighted ovum
   4. Gestational trophoblastic disease
   5. Implantation bleed: 3–4 weeks after last menstrual period
   6. Subchorionic hemorrhage
   7. Low-lying placenta previa
   8. Twin loss

B. NORMAL ENDOMETRIAL CAVITY
   (a) with β-hCG level > 1,800 mIU/mL
      1. Recent spontaneous abortion
      2. Ectopic pregnancy
   (b) with β-hCG level < 1,800 mIU/mL
      1. Very early IUP
      2. Ectopic pregnancy

C. SAC VULNERABILITY
   1. Leiomyoma
   2. Intrauterine contraceptive device

Hemoperitoneum during Pregnancy

= hemorrhage in cul-de-sac (= rectouterine pouch)

1. Hemorrhagic corpus luteum cyst
2. Placenta accreta
3. Spontaneous abortion
4. Ectopic pregnancy
5. HELLP syndrome
6. Uterine rupture

Poor Prognostic Indicators in Early Pregnancy
√ irregular contour / low-lying position of gestational sac
√ calcified yolk sac > 7 mm in diameter
√ empty enlarged / expanded amnion
√ amorphous shape of embryo
√ embryonic bradycardia of ≤ 85 bpm
√ hydropic embryo
√ large subchorionic hemorrhage encircling > ²/₃ of gestational sac circumference

US Findings Diagnostic of Pregnancy Failure
√ no heartbeat with CRL of ≥ 7 mm
√ no embryo with mean sac diameter of ≥ 25 mm
√ no heartbeat ≥ 2 weeks after appearance of gestational sac without yolk sac
√ no heartbeat ≥ 11 days after appearance of gestational sac with yolk sac

US Findings Suspicious of Pregnancy Failure
√ no heartbeat with CRL of < 7 mm
√ no embryo with mean sac diameter of 16–25 mm
√ no heartbeat 7–13 days after appearance of gestational sac without yolk sac
√ no heartbeat 7–10 days after appearance of gestational sac with yolk sac
√ no embryo ≥ 6 weeks after last menstrual period
√ no embryo with empty amnion
√ no embryo with yolk sac > 7 mm
√ small gestational sac relative to size of embryo with a < 5-mm difference between mean sac diameter and CRL

Abnormal Sonographic Findings in 1st Trimester

1. Embryonic demise = abortion (clinical term)
2. Nondevelopment = blighted ovum
3. Maldevelopment = hydatidiform mole

Empty Gestational Sac

1. Normal early IUP between 5 and 7 weeks MA
2. Blighted ovum

DDx: Pseudosac of ectopic pregnancy

Gestational Sac in Low Position

1. Abortion in progress
   √ no placental blood flow
2. Cervical ectopic pregnancy
3. Fundal fibroid compressing sac downward

Pregnancy of Unknown Location

= normal pelvic US = transient state of early pregnancy during which no definite IUP is visualized at US with normal adnexa

= positive β-hCG without IUP

mnemonic: HERE

HCG-producing tumor (rare)
Ectopic pregnancy: occult
Recent completed spontaneous abortion

Early intrauterine pregnancy

In a hemodynamically stable patient with a pregnancy of unknown location, it is less harmful to wait, follow the β-hCG levels, and repeat the US examination than to presumptively treat an ectopic pregnancy.

hCG-producing Tumor

1. Gestational trophoblastic disease: hydatidiform mole, gestational choriocarcinoma
2. Ovarian malignant germ cell tumor
3. Nontesticular teratoma
4. Nontrophoblastic tumor: hepatoma, neuroendocrine tumor, breast cancer, pancreatic cancer, cervical cancer, gastric cancer, malignant phyllodes tumor
5. Spurious laboratory finding

Thickened Central Cavity Complex

1. Intrauterine blood
2. Retained products of conception following an incomplete spontaneous abortion
3. Early intrauterine not yet visible pregnancy
4. Decidual reaction ← ectopic pregnancy

Uterus Large for Dates

1. Multiple gestation pregnancy
2. Inaccurate menstrual history
3. Fibroids
4. Polyhydramnios
5. Hydatidiform mole
6. Fetal macrosomia

Intrauterine Membrane in Pregnancy

A. MEMBRANE OF MATERNAL ORIGIN
   1. Uterine septum
      = incomplete resorption of sagittal septum between the fused two müllerian ducts
   2. Amniotic sheet / shelf
      = folding of amniochorionic membrane around uterine synechia
      √ synechia often thins during uterine stretching + disappears as pregnancy progresses
   3. Wisps of umbilical cord

B. MEMBRANE OF FETAL ORIGIN
   1. Intertwin membrane
      = apposing membrane of multiple pregnancy / residual sac of blighted twin pregnancy
   2. Amniotic band
      = rent within amnion
   3. Chorioamnionic separation
      = incomplete fusion / hemorrhagic separation of amnion (= inner membrane) and chorion (= outer membrane)
   4. Subchorionic hemorrhage = chorioamnionic elevation
      = separation of chorionic membrane from decidua

- implantation bleed of early pregnancy

C. FIBRIN STRAND

Cause: hemorrhage during transplacental amniocentesis

mnemonic: STABS

Separation (chorioamnionic)
Twins (intertwin membrane)
Abruption
Bands (amniotic band syndrome)
Synechia

Dilated Cervix

1. Inevitable abortion
2. Premature labor
   = spontaneous onset of palpable, regularly occurring uterine contractions between 20 and 37 weeks MA
3. Incompetent cervix

PLACENTA

Abnormal Placental Size

◊ Placental mass tends to reflect fetal mass!

A. ENLARGEMENT OF PLACENTA = **Placentomegaly**
   = > 5 cm thick in sections obtained at right angles to long axis of placenta
   (a) maternal disease
      1. Maternal diabetes ← villous edema
      2. Chronic intrauterine infections: eg, syphilis
      3. Maternal anemia: normal histology
      4. Alpha-thalassemia
   (b) fetal disease
      1. Hemolytic disease of the newborn ← villous edema + hyperplasia ← immunologic incompatibility including Rh sensitization
      2. Umbilical vein obstruction
      3. Fetal high-output failure:
         large chorioangioma, arteriovenous fistula
      4. Fetal malformation:
         Beckwith-Wiedemann syndrome, sacrococcygeal teratoma, chromosomal abnormality, fetal hydrops
      5. Twin-twin transfusion syndrome
   (c) fetomaternal hemorrhage
   (d) placental abnormalities
      1. Molar pregnancy
      2. Chorioangioma
      3. Intraplacental hemorrhage

   mnemonic: HAD IT
   Hydrops

Abruption
Diabetes mellitus
Infection
Triploidy

B. DECREASE IN PLACENTAL SIZE
   1. Preeclampsia: associated with placental infarcts in 33–60%
   2. IUGR
   3. Chromosomal abnormality
   4. Intrauterine infection

Vascular Spaces of the Placenta

1. "**Placental cysts**"
   = large fetal veins located between amnion + chorion anastomosing with umbilical vein
   √ sluggish blood flow (detectable by real-time observation)
2. **Basal veins**
   = decidual + uterine veins
   √ lacy appearing network of veins underneath placenta
   DDx: placental abruption
3. **Intraplacental venous lakes**
   √ intraplacental sonolucent spaces
   √ whirlpool motion pattern of flowing blood

Placental Causes of Antepartum Hemorrhage

= vaginal bleeding between 20 wks GA and delivery

1. Placenta previa
2. Placental abruption = placental hematoma
   › on fetal side
      (a) Subchorionic = preplacental hematoma
   › on maternal side
      (b) Retroplacental hematoma
      (c) Intraplacental hematoma

Macroscopic Lesion of the Placenta

1. **Intervillous thrombosis** (36%)
   = intraplacental areas of hemorrhage
   Etiology: breaks in villous capillaries with bleeding from fetal vessels
   √ irregular sonolucent intraplacental lesions (mm to cm range)
   √ blood flow may be observed within lesion
   Significance: fetal-maternal hemorrhage (Rh sensitization, elevated AFP levels)
2. **Perivillous fibrin deposition** (22%)
   = nonlaminated collection of fibrin deposition
   Etiology: thrombosis of intervillous space
   Significance: none
3. **Septal cyst** (19%)
   Etiology: obstruction of septal venous drainage by edematous villi

√ 5–10-mm cyst within septum
Significance: none

4. **Placental infarct** (25%)
   = coagulation necrosis of villi
   Etiology: disorder of maternal vessels, retroplacental hemorrhage
   √ not visualized unless hemorrhagic
   √ well-circumscribed mass with hyperechoic / mixed echo pattern
   Significance: dependent on extent + associated maternal condition
5. **Subchorionic fibrin deposition** (20%)
   = laminated collection of fibrin deposition
   Etiology: thrombosis of maternal blood in subchorionic space
   √ subchorionic sonolucent area
   Significance: none
6. **Massive subchorial thrombus**
   = BREUS MOLE = PREPLACENTAL HEMORRHAGE

Placental Tumor

A. TROPHOBLASTIC
   1. Complete hydatidiform mole
   2. Partial hydatidiform mole
   3. Invasive mole
   4. Choriocarcinoma
B. NONTROPHOBLASTIC
   1. Chorioangioma (in up to 1% of placentas)
   2. Teratoma (rare)
   3. Metastatic lesion (rare): melanoma, breast carcinoma, bronchial carcinoma

Unbalanced Intertwin Transfusion

= unbalanced intertwin transfusion through vascular anastomoses between 2 circulations of monochorionic twins

A. ACUTE = Twin-embolization syndrome
B. CHRONIC = Twin-twin transfusion syndrome
C. REVERSE = Acardiac twinning

UMBILICAL CORD

Abnormal Umbilical Cord Insertion

1. Marginal cord insertion
   = cord insertion < 1–2 cm from placental edge
   Frequency: 5–7% of pregnancies
2. Battledore placenta
   [battledore = flat wooden paddle in ancient form of badminton]
   = cord insertion on edge of placenta = extreme marginal
   • no clinical significance
3. Velamentous cord insertion

4. Vasa previa

Distortion Abnormality of Umbilical Cord

1. **Cord torsion**
   = excessive twisting of cord as rare form of cord constriction
   Timing: any time during pregnancy; more common during 2nd and 3rd trimester
   √ evaluation of pitch value of cord coiling
   √ abnormal S/D flow velocity ratio of umbilical artery
   Cx: critically reduced fetal blood flow and fetal hypoxia, oligohydramnios, IUGR, and fetal death
   Dx: difficult to diagnose prenatally; mostly detected during postnatal examination
2. **Cord entanglement**
   Cause: nearby umbilical cord insertions on single placenta in monoamniotic twin pregnancy
   √ branching pattern at level of entanglement
   √ end systolic notch on umbilical artery waveform ← vascular compression / narrowing
   Cx: vascular compromise in one / both fetuses → fetal demise
3. **Noncoiled "straight" cord**
   counterclockwise÷clockwise umbilical cords = 7÷1
   right-handed÷left-handed persons = 7÷1
   Prevalence: 3.7–5%
   √ absent vascular coiling for entire length of visible cord
   At risk for: intrauterine death (8%), stillbirth, fetal anomalies (24%), prematurity, intrapartum heart rate decelerations, fetal distress, meconium staining
4. Body cord
   = loop around fetal body / any fetal body part
5. Nuchal cord

Umbilical Cord Lesion

A. DEVELOPMENTAL CORD LESION
   1. **Umbilical hernia**
      = protrusion from anterior abdominal wall with normal insertion of umbilical vessels
      Predisposed:
      Blacks, low-birth-weight infants, trisomy 21, congenital hypothyroidism, Beckwith-Wiedemann syndrome, mucopolysaccharidoses
      Prognosis: spontaneous closure in first 3 years of life
   2. Umbilical cord cyst
B. ACQUIRED CORD LESION
   1. **False knot**
      (a) exaggerated looping of cord vessels → focal dilatation of cord
      (b) focal accumulation of Wharton jelly
      (c) varix of umbilical vessel
      • clinically insignificant
      √ knoblike protrusion / bulge of cord
   2. **True knot**

Prevalence: 1% of pregnancies
Cause: excessive fetal movements
Predisposed: long cord, polyhydramnios, small fetus, monoamniotic twins
√ "hanging noose" sign = segment of umbilical cord closely surrounded by another loop of cord
√ local distension / thrombosis of umbilical vein near cord knot resembling an umbilical cyst
√ tortuosity of cord at level of knot
Cx: vascular occlusion → fetal asphyxia → fetal demise
OB management: expectant (mostly loose knot with marginal impact on fetal well-being)

3. **Umbilical cord hematoma**
= rupture of the wall of the umbilical vein ← mechanical trauma (cordocentesis, torsion, loops, knots, traction) / congenital weakness of vessel wall
Prevalence: 0.02% of pregnancies
Location: near fetal insertion of umbilical cord (most common)
√ hyper- / hypoechoic mass 1–2 cm in size, multiple (in 18%)
Cx: rupture into amniotic cavity → exsanguination
Prognosis: 52% overall perinatal fetal mortality
4. Neoplasm
(a) **Angiomyxoma / hemangioma of cord**
Prevalence: 22 cases in literature
Histo: multiple vascular channels lined by benign endothelium surrounded by edema + myxomatous degeneration of Wharton jelly
Associated with: single umbilical artery
• increased maternal serum α-fetoprotein level
Location: more frequently near placental insertion of umbilical cord
√ hyperechoic / multicystic mass within cord
√ may be associated with pseudocyst (= localized collection of edema)
√ blood flow on Doppler
Cx: premature delivery, stillbirth, hydramnios, nonimmune hydrops, massive hemorrhage ← rupture
(b) Other tumors: myxosarcoma, dermoid, teratoma

Umbilical Cord Cyst

◊ Umbilical cord cysts persisting into 2nd + 3rd trimester are frequently accompanied by fetal anomalies: angiomyxoma of cord, hernia, intestinal obstruction, urinary tract obstruction, urachal anomalies, imperforate anus, TE fistula, omphalocele, cardiac defect, trisomy 18

Location: toward fetal insertion of cord

A. UMBILICAL CORD PSEUDOCYST (common)
= **Mucoid degeneration of umbilical cord**
= **Wharton jelly cyst**
Histo: localized edema + liquefaction of Wharton jelly without epithelial lining
Commonly associated with: omphalocele

√ focal thickening of Wharton jelly

Prognosis: usually resolved by 12 weeks MA

B. TRUE UMBILICAL CORD CYST (rare)

Prevalence: 3.4% of 1st trimester pregnancies; 20% persist into 2nd trimester

Histo: lined by single layer of flattened epithelium

Rarely associated with: fetal structural anomaly, aneuploidy

Size: 4–60 mm in diameter

1. **Omphalomesenteric duct cyst**
   Site: eccentric in cord
2. **Allantoic cyst**
   = remnant of umbilical vesicle / allantois; usually degenerates by 6 weeks
   Site: in center of cord
3. **Amniotic inclusion cyst**
   = amniotic epithelium trapped within umbilical cord

Vascular Abnormalities of Umbilical Cord

1. Single umbilical artery
2. **Persistent Right Umbilical Vein (PRUV)**
   = regression of left umbilical vein → abnormal course of blood flow in fetal liver
   Frequency: 0.1–0.3%
   Cause: altered development of umbilical cord during 4th –7th week GA
   May be associated with: situs inversus, heterotaxy, anomalies of GU / GI tract, heart, skeletal development
   Path of blood flow:
   (a) intrahepatic PRUV = isolated right umbilical vein joins fetal portal system at sinus venosus + gives rise to ductus venosus
   (b) extrahepatic PRUV = right umbilical vein bypasses liver and drains into RA / IVC / right iliac vein + absent ductus venosus
   √ fetal portal vein curves toward (rather than parallel to) stomach
   √ fetal gallbladder between umbilical vein and stomach + medial (rather than lateral) to umbilical vein
   √ umbilical vein connects to right (rather than left) portal vein
3. **Umbilical vein / Cord varix**
   Frequency: < 4% of all umbilical cord abnormalities
   May be associated with: aneuploidy (6%), other fetal anomalies (28%)
   Site: intraamniotic / intraabdominal, intrahepatic / extrahepatic
   Normal size of umbilical vein: 3 mm at 15 weeks GA, 8 mm at term
   √ fusiform dilatation of umbilical vein > 9 mm
   √ transverse diameter of extrahepatic umbilical vein > 1.5 x greater than intrahepatic component
   √ vein diameter > 2 SD above mean diameter for GA
   √ fetal hydrops, anemia, IUGR
   Cx: (1) Thrombosis with subsequent fetal death
   (2) Partial thrombosis with IUGR

◊ Serial US examinations are recommended from diagnosis to delivery!

Prognosis: usually no clinical significance

4. **Umbilical artery aneurysm** Often associated with single umbilical artery, aneuploidy, fetal structural abnormalities

SMALL-FOR-GESTATIONAL AGE FETUS (SGA)

= generic clinical term describing a group of perinates at / below 10th percentile for gestational age without reference to etiology

1. Fetus of appropriate growth (misdiagnosed as small)
2. Small normal fetus = constitutionally small fetus (80–85%)
   ◊ No indication for surveillance / intervention!
3. Small abnormal fetus = primary growth failure associated with karyotype anomaly / fetal infection (5–10%)
   ◊ Active intervention is of no benefit!
4. Dysmature fetus = IUGR = growth failure as a result of uteroplacental insufficiency (10–15%)
   ◊ Intensive management is likely of benefit!

FETAL OVERGROWTH DISORDER

1. Beckwith-Wiedemann syndrome
2. Simpson-Golabi-Behmenl syndrome
3. Perlman syndrome

FETAL SKELETAL DYSPLASIA

= DWARFISM

= heterogeneous group of bone growth disorders resulting in abnormal shape + size of the skeleton

◊ More than 200 skeletal dysplasias are known, but only a few are frequent:
- › thanatophoric dysplasia
- › osteogenesis imperfecta type II
- › achondrogenesis
- › heterozygous achondroplasia

Birth prevalence:

2.3÷10,000–7.6÷10,000 births for all skeletal dysplasias; 1.5÷10,000 births for lethal skeletal dysplasias

Prognosis: 51% mortality ← hypoplastic lungs: 23% stillbirths, 32% death in 1st week of life

Terminology:

Amelia	=	absence of limb
Hemimelia	=	absence of distal parts
Micromelia	=	shortening involves entire limb (eg, humerus, radius + ulna, hand)
Rhizomelia	=	shortening involves proximal segment (ie, humerus / femur) [*rhiza*, Greek = root of extremity = shoulder / hip]
Mesomelia	=	shortening involves intermediate segment (ie, radius + ulna / tibia +

fibula)
[*mesos*, Greek= middle]

Acromelia = shortening involves distal segment (eg, hand)

Meromelia = partial absence of a limb

Phocomelia = proximal reduction with distal parts attached to trunk

Preaxial polydactyly = extra digit on radial / tibial side

Postaxial polydactyly = extra digit on ulnar / fibular side

Classification:

(1) OSTEOCHONDRODYSPLASIA
= abnormalities of cartilage / bone growth and development
(a) identifiable at birth:
› usually lethal: achondrogenesis, fibrochondrogenesis, thanatophoric dysplasia, short rib syndrome
› usually nonlethal: chondrodysplasia punctata, camptomelic dysplasia, achondroplasia, diastrophic dysplasia, chondroectodermal dysplasia, Jeune syndrome, spondyloepiphyseal dysplasia congenita, mesomelic dysplasia, cleidocranial dysplasia, otopalatodigital syndrome
(b) identifiable in later life: hypochondroplasia, dyschondrosteosis, spondylometaphyseal dysplasia, acromicric dysplasia
(c) abnormal bone density: osteopetrosis, pyknodysostosis, Melnick-Needles syndrome

(2) DYSOSTOSIS
= malformation of individual bones singly / in combination
(a) with cranial + facial involvement: craniosynostosis, craniofacial dysostosis (Crouzon), acrocephalosyndactyly, acrocephalopolysyndactyly, branchial arch syndromes (Treacher-Collins, Franceschetti, acrofacial dysostosis, oculoauriculo-vertebral dysostosis, hemifacial microsomia, oculomandibulofacial syndrome)
(b) with predominant axial involvement: vertebral segmentation defects (Klippel-Feil), Sprengel anomaly, spondylocostal dysostosis, oculovertebral syndrome
(c) with predominant involvement of extremities: **acheiria** (= absence of hands), **apodia** (= absence of feet), polydactyly, syndactyly, camptodactyly, Rubinstein-Taybi syndrome, pancytopenia-dysmelia syndrome (Fanconi), Blackfan-Diamond anemia with thumb anomaly, thrombocytopenia-radial aplasia syndrome, cardiomelic syndromes (Holt-Oram), focal femoral deficiency, multiple synostoses

(3) IDIOPATHIC OSTEOLYSIS
= disorders with multifocal resorption of bone

(4) CHROMOSOMAL ABERRATION

(5) PRIMARY METABOLIC DISORDER
(a) calcium / phosphorus: hypophosphatasia
(b) complex carbohydrates: mucopolysaccharidosis

Assessment of:

1. **Long bones** for absence, hypoplasia, malformation, curvature, degree of mineralization, fractures, premature ossification centers

- √ shortening of long bones (common characteristic)
  - ◊ Femur length > 5 mm below 2 standard deviations suggests skeletal dysplasia!
  - √ FL÷foot length < 0.9 = suggests skeletal dysplasia
- √ limb shortening of 40–60% of the mean in thanatophoric dysplasia + OI type II
- √ limb shortening of > 30% of the mean in achondrogenesis

2. **Thorax** for shape, abnormal rib size, absence / hypoplasia of clavicles, presence of scapula
   - √ Chest Circumference < 5th percentile (= lung hypoplasia)
   - √ Chest Circumference÷AC < 5th percentile
   - √ heart area÷chest area < 5th percentile
   - √ FL÷AC < 0.16 = suggests lung hypoplasia
2. **Hand & foot** for clinodactyly, syndactyly, pre- or postaxial polydactyly
   - √ "hitchhiker's thumb", radial ray anomaly, absence of thumb
   - √ "rocker-bottom" foot, clubbed foot
4. **Skull** for size, shape (brachycephaly, scaphocephaly, craniosynostosis, frontal bossing, cloverleaf skull), degree of mineralization
   - √ HC and BPD
   - √ binocular and interocular diameter
   - √ micrognathia, short upper lip, abnormally shaped ears
4. **Spine** for relative total length, scoliosis, mineralization of vertebral bodies, integrity of neural arches, vertebral height, absence of segments
5. **Pelvis** for shape

Associated with: polyhydramnios

DDx features: mineralization, bowing, fractures, number of digits, fetal movement, thoracic measurement, associated anomalies, age of onset

DDx: constitutionally short limbs, severe IUGR

Micromelic Dwarfism

= disproportionate shortening of entire leg

A. Mild micromelic dwarfism
   1. Jeune syndrome
   2. Chondroectodermal dysplasia
   3. Diastrophic dwarfism

B. Mild bowed micromelic dwarfism
   1. Camptomelic dysplasia
   2. Osteogenesis imperfecta, type III

C. Severe micromelic dwarfism
   1. Thanatophoric dysplasia
   2. Osteogenesis imperfecta, type II
   3. Homozygous achondroplasia
   4. Hypophosphatasia
   5. Short-rib polydactyly syndrome
   6. Fibrochondrogenesis

Acromelic Dwarfism

Asphyxiating thoracic dysplasia

Rhizomelic Dwarfism

mnemonic: MA CAT

Metatrophic dwarfism
Achondrogenesis (most severe shortening)
Chondrodysplasia punctata: autosomal recessive
Achondroplasia, heterozygous
Thanatophoric dysplasia

Osteochondrodysplasia

A. Failure of
   (a) articular cartilage: spondyloepiphyseal dysplasia
   (b) ossification center: multiple epiphyseal dysplasia
   (c) proliferating cartilage: achondroplasia
   (d) spongiosa formation: hypophosphatasia
   (e) spongiosa absorption: osteopetrosis
   (f) periosteal bone: osteogenesis imperfecta
   (g) endosteal bone: idiopathic osteoporosis
B. Excess of
   (a) articular cartilage: dysplasia epiphysealis hemimelica
   (b) hypertrophic cartilage: enchondromatosis
   (c) spongiosa: multiple exostosis
   (d) periosteal bone: progressive diaphyseal dysplasia
   (e) endosteal bone: hyperphosphatemia

Lethal Bone Dysplasia

in order of frequency:

1. Thanatophoric dysplasia
2. Osteogenesis imperfecta type II
3. Achondrogenesis type I + II
4. Jeune syndrome (may be nonlethal)
5. Hypophosphatasia, congenital lethal form
6. Chondroectodermal dysplasia (usually nonlethal)
7. Chondrodysplasia punctata, rhizomelic type
8. Camptomelic dysplasia
9. Short-rib polydactyly syndrome
10. Homozygous achondroplasia

◊ Lethal short-limbed dysplasias typically are manifest on sonograms < 24 weeks MA!

Nonlethal Dwarfism

1. Achondroplasia (heterozygous)
2. Asphyxiating thoracic dysplasia
3. Chondroectodermal dysplasia
4. Chondrodysplasia punctata

5. Spondyloepiphyseal dysplasia (congenital)
6. Diastrophic dysplasia
7. Metatrophic dwarfism
8. Hypochondroplasia

Late-onset Dwarfism

1. Spondyloepiphyseal dysplasia tarda
2. Multiple epiphyseal dysplasia
3. Pseudoachondroplasia
4. Metaphyseal chondrodysplasia
5. Dyschondrosteosis
6. Cleidocranial dysostosis
7. Progressive diaphyseal dysplasia

Hypomineralization in Fetus

A. DIFFUSE
    1. Osteogenesis imperfecta
    2. Hypophosphatasia
B. SPINE
    1. Achondrogenesis

Large Head in Fetus

1. Achondroplasia
2. Thanatophoric dysplasia

Narrow Hypoplastic Chest in Fetus

1. Short-rib polydactyly syndrome
2. Asphyxiating thoracic dysplasia
3. Chondroectodermal dysplasia
4. Camptomelic dysplasia
5. Thanatophoric dysplasia
6. Homozygous achondroplasia
7. Achondrogenesis
8. Hypophosphatasia
9. Osteogenesis imperfecta

Platyspondyly

1. Thanatophoric dysplasia
2. Osteogenesis imperfecta type II
3. Achondroplasia
4. Morquio syndrome

Bowed Long Bones in Fetus

1. Camptomelic syndrome
2. Osteogenesis imperfecta
3. Thanatophoric dysplasia

4. Hypophosphatasia

Bone Fractures in Fetus

1. Osteogenesis imperfecta
2. Hypophosphatasia
3. Achondrogenesis

Acrocephalosyndactyly

= syndrome characterized by
(1) increased height of skull vault ← generalized craniosynostosis (= acrocephaly, oxycephaly)
(2) syndactyly of fingers / toes

Type 1: Apert syndrome
Type 2: Crouzon syndrome
Type 3: Saethre-Chotzen syndrome
Type 4: Wardenburg type
Type 5: Pfeiffer syndrome

Acrocephalopolysyndactyly

Type 1: Noack syndrome
Type 2: Carpenter syndrome
Type 3: Sakati-Nyhan-Tisdale syndrome
Type 4: Goodman syndrome
Type 5: Pfeiffer syndrome

LIMB REDUCTION ANOMALIES

Prevalence: 0.49 ÷10,000 births

Isolated Extremity Amputation

1. Amniotic band syndrome
2. Exposure to teratogen
3. Vascular accident

Aplasia / Hypoplasia of Radius

mnemonic: **T**he **F**urry **C**at **H**it **M**y **D**og

Thrombocytopenia–absent radius syndrome
Fanconi anemia
Cornelia de Lange syndrome
Holt-Oram syndrome
Myositis ossificans progressiva (thumb only)
Diastrophic dwarfism ("hitchhiker's thumb")

Pubic Bone Maldevelopment

mnemonic: CHIEF

Cleidocranial dysostosis
Hypospadia, epispadia

Idiopathic
Exstrophy of bladder
F for syringomyelia

Fetal Hand Anomalies

Best time for assessment:
late 1st to middle 2nd trimester ← ossification of metacarpals beginning at 12 weeks EGA + frequent fetal movement

◊ Complete fetal work-up needed for associated anomalies!

Normal findings:
› unossified hypoechogenic carpus
› 5 hyperechoic + cylindric metacarpal bones
› 5 independent digits of different lengths with 3 ossified phalanges (2 for thumb)
› normal radius, ulna, humerus
› flexion (fist) + extension (unclenched hand)

Classification:
(a) abnormal alignment: clenched hand, camptodactyly, clinodactyly, akinesia deformation sequence, clubhand, phocomelia
(b) thumb anomalies: macrodactyly, trident hand
(c) abnormal number: polydactyly, syndactyly, ectrodactyly

Camptodactyly

= flexion contracture of PIP joint of any finger
Cause: karyotype anomaly (trisomy 18, 13, 15) or contracture syndrome; may be isolated
Location: often asymmetric
Prognosis: may progress during infancy / childhood

Clenched Hand

= index finger overlaps clenched fist formed by other digits
Cause: trisomy 18, akinesia-hypokinesia syndromes, temporarily closed normal fist
√ proximal interphalangeal articulation of index finger flexed + ulnarly deviated
√ adducted thumb

Clinodactyly

= fixed abnormal deviation of 5th finger in radioulnar plane (= radial angulation of DIP joint) ← abnormally small size of middle phalanx
Cause: trisomy 21 (in up to 60%), triploidy; isolated familial clinodactyly; normal in 18%

Clubhand

= permanently deviated axis of wrist + usually closed hand
Classification:
(a) Radial clubhand associated with preaxial deficits (ranging from mild hypoplasia of thumb to complete absence of radius)
(b) Ulnar clubhand ← ulnar deficiency

Ectrodactyly

= SPLIT / CLEFT HAND = LOBSTER CLAW HAND

= longitudinal deficiency of central digits

Cause: EEC (ectrodactyly, ectodermal dysplasia, cleft lip or palate), Roberts syndrome

Pathogenesis: failure of median apical ectodermal ridge in developing limb bud

May be associated with: syndactyly, aplasia, hypoplasia of residual phalanges + metacarpals

√ deep V- or U-shaped central defect

DDx: oligodactyly (= reduced number of well-formed fingers), constrictive amniotic bands

Macrodactyly

= overgrowth of all structures of affected (commonly radial) fingers

Cause: proteus syndrome, neurofibromatosis type 1

Phocomelia

= missing / foreshortened arm / forearm with presence of hand

Cause:

(1) Thalidomide
(2) Roberts syndrome = autosomal recessive disorder associated with tetraphocomelia with more severe upper-limb deformities, facial cleft, polyhydramnios
(3) TAR syndrome
(4) Grebe syndrome = autosomal recessive disorder associated with marked hypomelia (more severe in lower limbs increasing in severity distally)

Polydactyly

= presence of supernumerary digits

Incidence: 1÷683 pregnancies;

◊ Most common hand anomaly!

Cause: trisomy 13, short-rib-polydactyly syndrome, asphyxiating thoracic dystrophy (Jeune syndrome), Smith-Lemli-Opitz syndrome

ULNAR / POSTAXIAL POLYDACTYLY (more frequent)

affecting 5th finger

Cause:

(1) Trisomy 13
(2) Meckel-Gruber syndrome
(3) Short-rib polydactyly syndrome
(4) Ellis-van Creveld syndrome
(5) **Smith-Lemli-Opitz syndrome** (= intrauterine growth retardation + characteristic high level of 7-dehydrocholesterol)
(6) **Hydrolethalus syndrome** (= heart and brain defects, cleft lip / palate, abnormally shaped nose / jaw, incomplete lung development causing stillbirth / death within a few days after birth)
(7) **Bardet-Biedl syndrome** = medullary cystic kidney disease without encephalocele, progressive renal dystrophy, obesity, hypogonadism, learning

difficulties

RADIAL / PREAXIAL POLYDACTYLY (less frequent)

affecting thumb

Cause:

(1) Holt-Oram syndrome
(2) Short-rib–polydactyly syndrome
(3) Carpenter syndrome
(4) Trisomy 21
(5) VACTERL association
(6) Fanconi anemia
(7) Orodigitofacial syndrome

POLYSYNDACTYLY

= association of polydactyly with syndactyly

Syndactyly

= abnormal connection between adjacent digits

Incidence: 2–3÷10,000 live births

Location: commonly between 2nd + 3rd digit

Classification: simple (between soft tissues), complex (between bones), complete (entire length of finger), incomplete (sparing of distal part)

Cause: Poland sequence, Apert syndrome and other acrocephalosyndactylies, triploidy, Roberts syndrome, familial syndactyly (autosomal dominant, with variable expressivity and incomplete penetrance), constriction band sequence

Trident Hand

= same length of last 4 fingers

Cause: various chondrodysplasias

Overlapping Digit

trisomy 18

Hitchhiker's Thumb

diastrophic dysplasia

Flexion Contractures

trisomy 13 + 18, fetal akinesia deformation sequence

Limb Reduction

congenital varicella, hypoglossia-hyperdactyly syndrome

Amputation

amniotic band syndrome

Drug-induced Musculoskeletal Embryopathy

Thalidomide

= sedative-hypnotic nonbarbiturate (sold 1954–1961)
Critical period: 34–50 days after most recent menstrual period
• increased miscarriage, increased stillbirth rate
• 40% increased infant mortality
√ narrowing, disorganization, destruction of joints
√ hemimelia = absence / gross shortening of distal portion of one / more limbs (esp. radius + thumb)
√ phocomelia = attachment of hands + feet to abbreviated arms and legs
√ amelia = congenital absence of one / more arms / legs
√ fusion / absence of paired bones

Anticonvulsant Drugs
Prevalence: 0.4% of pregnancies
Drugs: valproic acid, carbamazepine, phenytoin, phenobarbital
√ diminished bone mineral density
√ poorly developed diaphyses of long bones
√ anomalies of phalanges:
  √ hypoplastic terminal phalanges associated with dysplastic nails
  √ hyperphalangism
√ congenital heart disease, cleft lip + palate, urinary tract anomalies, syndromes of dysmorphism, mental retardation

Folic Acid Antagonists
Drugs: aminopterin, methotrexate
Critical period: 6–8 weeks after conception
√ growth retardation
√ osteoporosis
√ talipes equinovarus, foreshortened extremities, absent digits, syndactyly, anomalous ribs
√ CNS anomalies, cardiac abnormalities

Vitamin A and Retinoids
• anomalies of external ear, facial dysmorphism
√ CNS, craniofacial, cardiovascular, thymic malformations
√ hydrocephalus, microcephalus

Warfarin
Critical period: 6–9 weeks GA
Frequency: 10%
√ stippled ossification centers in vertebrae, proximal femora, tarsal + carpal bones

FETAL CNS ANOMALIES
Prevalence: 2÷1,000 births in USA; 90% as 1st time occurrence
Recurrence: 2–3% after 1st, 6% after 2nd occurrence
√ ventricular atrium + cisterna magna are two sensitive anatomic markers for normal brain development!
A. HYDROCEPHALUS

1. Aqueductal stenosis
2. Communicating hydrocephalus
3. Dandy-Walker malformation
4. Choroid plexus papilloma

B. NEURAL TUBE DEFECT

Prevalence: 1÷500–600 live births

Risk of recurrence: 3–4%

1. Spina bifida
2. Anencephaly
3. Acrania
4. Encephalocele (8–15%)
5. Porencephaly
6. Hydranencephaly
7. Holoprosencephaly
8. Iniencephaly
9. Microcephaly
10. Agenesis of corpus callosum
11. Lissencephaly
12. Arachnoid cyst
13. Choroid plexus cyst
14. Vein of Galen aneurysm
15. Schizencephaly

Associated with: trisomy 13 and 18

Increased risk: low parity, low socioeconomic status, relative infertility, diabetes, obesity, anticonvulsants, folate deficiency

C. INTRACRANIAL NEOPLASM

1. Teratoma (> 50%): benign / malignant

   Location: originate from base of skull
2. Glioblastoma
3. Astrocytoma

Fetal Ventriculomegaly

Cause:

A. MORPHOLOGIC ANOMALY (70–80%):
   1. Spina bifida (30–65%)
   2. Dandy-Walker malformation
   3. Encephalocele
   4. Holoprosencephaly
   5. Agenesis of corpus callosum

B. ABNORMAL KARYOTYPE (10–20%)

C. VIRAL INFECTION

◊ 20–40% of concurrent anomalies are missed by ultrasound!

√ "dangling" choroid plexus

√ width of ventricular atrium > 10 mm

Prognosis: 21% survival rate; 50% with intellectual impairment

Isolated Mild Ventriculomegaly

= atrial width of 10–15 mm

Prevalence: 1÷700 in low-risk population

◊ Most common brain anomaly on prenatal sonograms

Associated structural anomalies (9%):

periventricular leukomalacia, subependymal / germinal matrix hemorrhage, partial agenesis of corpus callosum, heterotopia, parenchymal dysplasia

Associated chromosomal anomalies: in 4%

Recommendation: MR to diagnose associated structural anomalies

Prognosis: 80% with isolated mild ventriculomegaly have normal motor + intellectual function at ≥ 12 months of age

Lemon Sign

= flat / inwardly scalloped contour of both frontal bones

1. **Spina bifida**
   Prevalence for fetuses ≤ 24 weeks: 98%
   (90–93% sensitive, 98–99% specific, 84% PPV for high-risk population, 6% PPV for low-risk population)
   Prevalence for fetuses > 24 weeks: 13%
   (disappears in 3rd trimester)
2. Encephalocele
3. Agenesis of corpus callosum
4. Thanatophoric dysplasia
5. Cystic hygroma
6. Congenital diaphragmatic hernia
7. Fetal hydronephrosis
8. Umbilical vein varix
9. Normal fetus (in 0.7–1.3%)

Prenatal Intracranial Calcifications

1. Toxoplasmosis
2. CMV infection
3. Tuberous sclerosis
4. Sturge-Weber syndrome
5. Venous sinus thrombosis
6. Teratoma

Cystic Intracranial Lesion

mnemonic: CHAP VAN

Choroid plexus cyst
Hydrocephalus, **H**oloprosencephaly, **H**ydranencephaly
Agenesis of corpus callosum + cystic dilatation of 3rd ventricle
Porencephaly (= schizencephaly)
Vein of Galen aneurysm
Arachnoid cyst

Neoplasm: cystic teratoma

Abnormal Cisterna Magna

Normal size between 15 and 25 weeks MA:
> 2 to < 10 mm (usually 4–9 mm) in 94–97% of fetuses

A. SMALL CISTERNA MAGNA + "banana" sign
   1. Chiari II malformation (with myelomeningocele)
   2. Occipital cephalocele
   3. Severe hydrocephalus

B. LARGE CISTERNA MAGNA
   1. Megacisterna magna
      √ cerebellum + vermis remain intact
   2. Arachnoid cyst
      √ en bloc displacement of cerebellum + vermis
   3. Cerebellar hypoplasia
   4. Dandy-Walker syndrome (with vermian agenesis)

FETAL ORBITAL ANOMALIES

Hypotelorism

1. Holoprosencephaly
2. Chromosomal abnormalities: trisomy 13
3. Microcephaly, trigonocephaly
4. Maternal phenylketonuria
5. Meckel-Gruber syndrome
6. Myotonic dystrophy
7. Williams syndrome
8. Oculodental dysplasia

Hypertelorism

1. Median cleft syndrome: cleft lip / palate
2. Craniosynostosis: Apert / Crouzon syndrome
3. Pena-Shokeir syndrome
4. Frontal / ethmoidal, sphenoidal encephalocele
5. Dilantin / phenytoin effect

Orbital and Periorbital Masses

1. Dacryocystocele
2. Anterior encephalocele
3. Glioma
4. Hemangioma
5. Teratoma

FETAL NECK ANOMALIES

1. Cervical myelomeningocele

2. Occipital cephalocele
3. Cystic hygroma / lymphangioma
4. Teratoma
5. Branchial cleft cyst
6. Enlarged thyroid
7. Sarcoma

Nuchal Skin Thickening

= NUCHAL SONOLUCENCY / FULLNESS / EDEMA

= skin thickening of posterior neck measured between calvarium + dorsal skin margin
  (a) ≥ 3 mm during 9–13 weeks MA
  (b) ≥ 5 mm during 14–21 weeks MA
  (c) ≥ 6 mm during 19–24 weeks MA
  ◊ The smallest measurement should be used!

Image plane: axial / transverse image (slightly craniad to that of the BPD measurement) that includes cavum septi pellucidi, cerebellar hemisphere and cisterna magna (transcerebellar diameter view)

Prevalence: among the most common anomaly in 1st trimester + early 2nd trimester

Cause:

A. NORMAL VARIANT (0.06%)
B. CHROMOSOMAL DISORDERS trisomy 21 (in 45–80%), Turner syndrome (45 XO), Noonan syndrome, trisomy 18, XXX syndrome, XYY syndrome, XXXX syndrome, XXXXY syndrome, 18p-syndrome, 13q-syndrome
   ◊ 30–40% of fetuses with Down syndrome have nuchal skin thickening!
C. NONCHROMOSOMAL DISORDERS
   1. Multiple pterygium syndrome = Escobar syndrome
   2. Klippel-Feil syndrome: fusion of cervical vertebrae, CHD, deafness (30%), cleft palate
   3. Zellweger syndrome = cerebrohepatorenal syndrome: large forehead, flat facies, macrogyria, hepatomegaly, cystic kidney disease, contractures of extremities
   4. Robert syndrome
   5. Cumming syndrome

√ larger lymphangiomas with radiating septations are usually found with trisomy 18
√ nuchal fullness ≥ 3 mm during 1st trimester is seen in trisomy 21 / 18 / 13 (30–50% PPV)
√ often reverting to normal by 16–18 weeks
√ septations within nuchal translucency carries a 20- to 200-fold risk for chromosomal anomalies compared with normal

Sensitivity: 2–44–75% for detection of trisomy 21

Specificity: 99% for detection of trisomy 21

PPV: 69%

Positive screen: 1.2–3.0% in general population (exceeding 0.5% risk of amniocentesis)

False positives: 0.5–2–8.5%

OB management: thorough sonographic evaluation at 18–20 weeks MA

DDx: chorioamnionic separation

Protruding Tongue

1. Macroglossia
2. Lymphangioma of the tongue

Macroglossia

1. Beckwith-Wiedemann syndrome
2. Down syndrome
3. Hypothyroidism
4. Mental retardation

FETAL CHEST ANOMALIES

Pulmonary Underdevelopment

Pulmonary Aplasia

= rudimentary bronchus ending in blind pouch + absence of parenchyma + vessels

Frequency: 1÷10,000; R÷L = 1÷1

CT:

√ diffuse opacification of involved hemithorax
√ ipsilateral mediastinal shift
√ absence of ipsilateral pulmonary tissue + artery
√ bronchus terminates in dilated short blind pouch

Pulmonary Hypoplasia

= completely formed but congenitally small bronchus with rudimentary parenchyma + small vessels

Cause:

A. PRIMARY / idiopathic pulmonary hypoplasia (rare)
B. SECONDARY pulmonary hypoplasia limiting space for lung development
    (a) Intrathoracic lung compression
        1. Intrathoracic mass
        2. Mediastinal mass
        3. Large hydrothorax
        4. Lymphatic malformation
        5. Agenesis of diaphragm
    (b) Extrathoracic lung compression (= Potter syndrome)
        1. Prolonged oligohydramnios (20–25%) ← renal agenesis, bilateral cystic renal disease, obstructive uropathy, premature rupture of membranes
        2. Fetal ascites
    (c) Dysplasia of thoracic cage
        1. Jeune
        2. Thanatophoric dystrophy
        3. Ellis-van Creveld
        4. Severe achondroplasia
    (d) Others ← reduced breathing activity
        1. Muscular disease

2. Neurologic condition
3. Chromosomal abnormality

Path: absolute decrease in lung volume / weight for GA

√ thoracic circumference (TC) < 5th percentile for EGA
√ TC÷AC length ratio < 0.32
√ FL÷AC ratio < 0.16
√ small hyperlucent lung ← oligemia
√ diminutive ipsilateral pulmonary artery
√ hyperlucent contralateral lung ← compensatory hyperexpansion
√ ipsilateral mediastinal shift

Congenital Chest Malformation

1. Congenital pulmonary airway malformation
2. Congenital diaphragmatic hernia (CDH)
3. Bronchopulmonary sequestration (BPS)
4. Congenital hydrothorax
5. Congenital lobar emphysema
6. Congenital high airway obstruction syndrome

Intrathoracic Mass

in order of frequency:

1. Congenital diaphragmatic hernia / eventration
2. Congenital pulmonary airway malformation
3. Bronchopulmonary sequestration
4. Bronchogenic cyst
5. Bronchial atresia

Unilateral Chest Mass

1. Congenital diaphragmatic hernia
2. Congenital pulmonary airway malformation
3. Bronchopulmonary sequestration
4. Bronchogenic cyst
5. Unilateral bronchial atresia / stenosis

Bilateral Chest Masses

1. **Laryngeal / tracheal atresia**
   √ pulmonary hyperplasia
   √ symmetrically enlarged echogenic lungs
   √ dilated fluid-filled trachea + bronchi
   √ inverted hemidiaphragms
   √ diminutive heart amongst enlarged lungs
   √ ± hydrops
2. Congenital high airway obstruction
2. Bilateral congenital pulmonary airway malformation
3. Bilateral congenital diaphragmatic herniae

Mediastinal Mass

1. Goiter
2. Cystic hygroma
3. Pericardial teratoma
4. Neuroblastoma

Cystic Chest Mass

1. Bronchogenic cyst
2. Enteric cyst
3. Neurenteric cyst
4. Cystic adenomatoid malformation type I
5. Congenital diaphragmatic hernia
6. Pericardial cyst
7. Mediastinal meningocele

Complex Chest Mass

1. Congenital diaphragmatic hernia
2. Congenital pulmonary airway malformation
3. Bronchopulmonary sequestration
4. Complex enteric cyst
5. Pericardial teratoma

Solid Chest Mass

1. Congenital diaphragmatic hernia: bowel ± liver
2. Cystic adenomatoid malformation type III
3. Pulmonary sequestration
4. Obstructed lung ← bronchial atresia, laryngeal atresia, bronchogenic cyst
5. Bronchopulmonary foregut malformation
6. Pericardial tumor
7. Heterotopic brain tissue

Regressing Fetal Chest Mass

1. Cystic adenomatoid malformation
2. Bronchopulmonary sequestration

Chest Wall Mass

1. Hemangioma
2. Cystic hygroma
3. Teratoma
4. Hamartoma
5. Thoracic myelomeningocele

Pleural Effusion

1. Primary idiopathic chylothorax (most common)
2. Hydrops fetalis (multiple causes)
3. Chromosome anomaly: trisomy 21, 45 XO (mostly)

4. Pulmonary lymphangiectasia / cystic hygroma
5. Lung mass: cystic adenomatoid malformation, bronchopulmonary sequestration, congenital diaphragmatic hernia, chest wall hamartoma (uncommon)
6. Pulmonary vein atresia
7. Idiopathic

FETAL CARDIAC ANOMALIES

Prevalence: 1÷125 births = 0.8% of population; most common of all congenital malformations (40%)

◊ 90% occur as isolated multifactorial traits with a recurrence risk of 2–4%

◊ 10% are associated with multiple birth defects

◊ responsible for 50% of childhood deaths from congenital malformations

Antenatal sonographic diagnosis to prompt cardiac evaluation:

A. ABNORMALITIES IN CARDIAC POSITION

B. CNS
   1. Hydrocephalus
   2. Microcephaly
   3. Agenesis of corpus callosum
   4. Encephalocele: Meckel-Gruber syndrome

C. GASTROINTESTINAL
   1. Esophageal atresia
   2. Duodenal atresia
   3. Situs abnormalities
   4. Diaphragmatic hernia

D. VENTRAL WALL DEFECT
   1. Omphalocele
   2. Ectopia cordis

E. RENAL
   1. Bilateral renal agenesis
   2. Dysplastic kidneys

F. TWINS
   1. Conjoined twins

Prenatal Risk Factors for Congenital Heart Disease

A. FETAL RISK FACTORS
   1. Symmetric IUGR
   2. Arrhythmias
      (a) fixed fetal bradycardia (50%) ≤ 110 bpm
      (b) tachycardia (low risk)
      (c) irregular: PACs, PVCs (low risk)
   3. Abnormal fetal karyotype: CHD in Down syndrome (40%); in trisomy 18 / 13 (> 90%); in Turner syndrome (35%)
   4. Extracardiac somatic anomalies by US: omphaloceles (20%), duodenal atresia, hydrocephaly, spina bifida, VACTERL
   5. Nonimmune hydrops (30–35%)

6. Oligo- / polyhydramnios

B. MATERNAL RISK FACTORS
   1. Maternal heart disease (10%)
   2. Insulin-dependent diabetes mellitus (4–5%)
   3. Phenylketonuria (in 15% if maternal phenylalanine > 15%)
   4. Collagen vascular disease: SLE
   5. Viral infection: rubella
   6. Drugs
      (a) phenytoin: in 2% PS, AS, coarctation, PDA
      (b) trimethadione: in 20% transposition, tetralogy, hypoplastic left heart
      (c) sex hormones (in 3%)
      (d) lithium (7%): Ebstein anomaly, tricuspid atresia
      (e) alcohol (25% of fetal alcohol syndrome): VSD, ASD
      (f) retinoic acid = isotretinoin (?15%)
   7. Paternal CHD (risk uncertain)

C. MENDELIAN SYNDROMES
   1. Tuberous sclerosis
   2. Ellis-van Creveld syndrome
   3. Noonan syndrome

D. FAMILIAL RISK FACTORS FOR RECURRENCE OF HEART DISEASE
   › overall incidence : 6–8÷1,000 live births
   › affected sibling : 1–4% (risk doubled)
   › affected parent : 2.5–4%

◊ In 50% of neonates with CHD there is no identifiable risk factor!

Poor prognostic features:
(1) Intrauterine cardiac failure → hydrops
(2) Severe trisomy: 18, 13
(3) Hypoplastic left heart + endocardial fibroelastosis
(4) Delivery in center without pediatric cardiology

In Utero Detection of Cardiac Anomalies

A. ABNORMAL HEART POSITION
   1. Diaphragmatic hernia
   2. Lung anomaly
   3. Pleural effusion
   4. Cardiac defect

B. CHAMBER ENLARGEMENT

⇑ RA:	⇑ LA:
1. Tricuspid regurgitation	1. Mitral stenosis
2. Tricuspid valve dysplasia	2. Aortic stenosis
3. Ebstein anomaly	
⇑ RV:	**⇑ LV:**
1. Coarctation	1 Aortic stenosis
2. Normal in 3rd trimester	2 Cardiomyopathy

C. ABNORMAL FOUR-CHAMBER VIEW
   1. Septal rhabdomyoma
   2. Endocardial cushion defect
   3. Ventricular septal defect
   4. Ebstein anomaly
   5. Single ventricle

D. VENTRICULAR DISPROPORTION
   1. Hypoplastic right / left ventricle
   2. Hypoplastic aortic arch
   3. Aortic / subaortic stenosis
   4. Coarctation of aorta
   5. Ostium primum defect

E. INCREASED AORTIC ROOT DIMENSION
   1. Tetralogy of Fallot
   2. Truncus arteriosus
   3. Hypoplastic left ventricle with transposition

F. DECREASED AORTIC ROOT DIMENSION
   1. Coarctation of aorta
   2. Hypoplastic left ventricle

◊ 26–80% of serious cardiac anomalies can be detected on four-chamber view!
◊ Increased sensitivity > 20 weeks + by including outflow views!

Structural Cardiac Abnormalities & Fetal Hydrops

1. Atrioventricular septal defect + complete heart block
2. Hypoplastic left heart
3. Critical aortic stenosis
4. Cardiac tumor
5. Ectopia cordis
6. Dilated cardiomyopathy
7. Ebstein anomaly
8. Pulmonary atresia

Fetal Echocardiographic Views

Identification of fetal RV:

√ RV lies closest to anterior chest wall
√ foramen ovale flap seen within LA
√ prominent moderator band + papillary muscles in RV

A. FOUR-CHAMBER VIEW
   1. Position of heart within thorax
   2. Number of cardiac chambers
   3. Ventricular proportion
   4. Integrity of atrial + ventricular septa
   5. Position + size + excursion of AV valves
B. LONG-AXIS VIEW OF LV OUTFLOW TRACT
   = PARASTERNAL LONG-AXIS VIEW
   1. Continuity between ventricular septum + anterior aortic wall
   2. Caliber of aortic outflow tract
   3. Excursion of aortic valve leaflets
C. SHORT-AXIS VIEW OF OUTFLOW TRACTS
   1. Spatial relationship between aorta + pulmonary artery
   2. Caliber of aortic + pulmonary outflow tracts
D. AORTIC ARCH VIEW

Echogenic Intracardiac Focus

Cause: mineralization of a papillary muscle

◊ Isolated anomaly in 90%!

1. Trisomy 21 (in 30% of affected fetuses)
2. Trisomy 13 (in 50% of affected fetuses)
3. Normal pregnancy (4% in a population at high risk for fetal anomalies)

FETAL GASTROINTESTINAL ANOMALIES

1. Esophageal atresia ± tracheoesophageal fistula
2. Duodenal atresia
3. Meconium peritonitis
4. Hirschsprüng disease
5. Choledochal cyst
6. Mesenteric cyst

Fetal Abdominal Wall Defect

Prevalence: 6÷2,000 pregnancies; 6÷10,000 births

The American Institute of Ultrasound in Medicine mandates demonstration of the umbilical cord insertion on the fetal abdomen during 2nd + 3rd trimester US exams.

(a) normal cord insertion (CI)
   › defect to right of CI: gastroschisis
   › defect below CI: bladder exstrophy

(b) abnormal cord insertion
   › low defect + absent bladder: cloacal exstrophy
   › CI on membrane: omphalocele
   › high defect: pentalogy of Cantrell
   › no defined distribution: abdominoschisis, limb-body wall complex

Fetal Hepatomegaly

A. CONGENITAL INFECTIONS
   1. CMV
B. SEVERE HEMOLYTIC DISEASE
C. SYNDROMES
   1. Beckwith-Wiedemann syndrome
   2. Zellweger syndrome

Intraabdominal Echogenic Mass in Fetus

A. ABDOMEN
   1. Echogenic bowel
   2. Enteric duplication cyst (rarely echogenic)
   3. Subdiaphragmatic extralobar pulmonary sequestration (4÷1 left-sided predominance)
B. LIVER
   1. Hepatic hemangioma
   2. Hepatic mesenchymal hamartoma composed of multiple microcysts
C. ADRENAL / RENAL
   1. Neuroblastoma
   2. Adrenal hemorrhage
   3. Mesoblastic nephroma

Nonvisualization of Fetal Stomach

◊ Fetal swallowing begins at 11 weeks MA

Normal: stomach is visualized in almost all normal fetuses by 13–14 weeks (definitely by 19 weeks)

Prevalence: 2%

Cause:

1. Physiologic gastric emptying / intermittent swallowing
   ◊ Repeat scan after 30 min!
2. Oligohydramnios
3. CNS depression / abnormalities impairing swallowing
4. Abnormal position of stomach:
   √ stomach on contralateral side (situs inversus)
   √ congenital diaphragmatic hernia
5. Esophageal atresia ± tracheoesophageal fistula
   ◊ Nonvisualization of fetal stomach and polyhydramnios in 33% fetuses with esophageal atresia after 24 weeks MA!
6. Cleft lip / palate → impairing normal swallowing

Rx: repeat ultrasound scan

Double Bubble Sign

= fluid-filled stomach + proximal duodenum

◊ A persistently fluid-filled duodenum is always abnormal!

A. DUODENAL OBSTRUCTION
   1. Duodenal atresia (usually not seen < 24 weeks MA)

Cause: in 30% due to Down syndrome

2. Severe duodenal stenosis
3. Duodenal web
4. Duodenal duplication cyst

B. PERIDUODENAL ANOMALY
1. Ladd bands
2. Annular pancreas
3. Preduodenal portal vein

C. DISTAL OBSTRUCTION
1. Midgut volvulus
2. Malrotation

mnemonic: LADS
Ladd bands / malrotation
Annular pancreas
Duodenal atresia
Stenosis (duodenal)

Dilated Bowel in Fetus

1. Meconium ileus
   ◊ All newborns with meconium ileus have cystic fibrosis!
   ◊ 10–15% of newborns with cystic fibrosis present with meconium ileus!
2. "Apple peel" atresia of small bowel
3. Jejunal atresia
4. Megacystis-microcolon-intestinal hypoperistalsis syndrome
5. Colonic aganglionosis = Hirschsprüng disease
   (may be associated with Down syndrome)
6. Anorectal atresia: associated with CNS abnormalities, part of VACTERL complex

Bowel Obstruction in Fetus

Etiology: intestinal atresia / stenosis secondary to vascular accident, volvulus, meconium ileus, intussusception after organogenesis

Prevalence: imperforate anus 1÷3,000; small bowel 1÷5,000; colon 1÷20,000

Pathologic types:

I one / more transverse diaphragms
II blind-ending loops connected by fibrous string
III complete separation of blind-ending loops
IV apple-peel atresia of small bowel ← occlusion of SMA branch

Associated with: GI anomalies in 45% (malrotation, duplication, microcolon, esophageal atresia)

√ multiple distended bowel loops > 7 mm in diameter
√ increased peristalsis
√ polyhydramnios (if obstruction above level of mid jejunum; exceptions are esophageal atresia + tracheoesophageal fistula) ← fetal inability to cycle amniotic fluid through gut

Cx: Meconium peritonitis (50%)

DDx: (1) Other cystic masses: duodenal atresia, hydronephrosis, ovarian cyst, mesenteric cyst
(2) Chronic chloride diarrhea

Hyperechoic Fetal Bowel

◊ Most common echogenic mass in fetal abdomen

Definition: bowel echogenicity ≥ bone

Prevalence: 0.2–1.0% of 2nd trimester fetuses

Cause: (?) "constipation" in utero ← decreased swallowing, hypoperistalsis, bowel obstruction + increased fluid absorption, ingestion of blood

1. Normal small bowel variant (especially < 20 weeks MA) with resolution on follow-up sonogram toward end of 2nd trimester (in 50–70%)
2. Normal colon variant in 3rd trimester ← echogenic meconium
3. Meconium ileus
   ◊ Increased abdominal echogenicity is seen in 60–70% of fetuses with cystic fibrosis!
4. Chromosomal abnormality (3–25%)
   (a) Down syndrome (5–14%)
   (b) Trisomy 13, 18
   (c) Turner syndrome
5. Severe IUGR (16%)
6. Intraamniotic bleeding with subsequent swallowing of blood by fetus

Prognosis:

5-fold increase in risk for adverse fetal outcome (due to chromosomal abnormality, other anomalies, placental abruption, perinatal death [8–16%], IUGR [67–23%])

◊ 30–50% of fetuses with echogenic bowel in 2nd trimester will have poor outcome!

Management: parental testing for cystic fibrosis, careful fetal anatomic survey, follow-up for growth assessment

Hyperechoic Adrenal Gland in Fetus

seen routinely on US > 30–32 weeks GA

1. Acute adrenal hemorrhage
2. Exophytic renal tumor: mesoblastic nephroma
3. Neuroblastoma
4. Subdiaphragmatic extralobar sequestration

Intraabdominal Calcifications in Fetus

◊ Isolated liver calcifications are relatively frequent (1÷1,750 pregnancies) and of no clinical significance!

Scattered Calcifications

A. PERITONEAL
   1. Meconium peritonitis
   2. Plastic peritonitis associated with hydrometrocolpos
B. CONGENITAL INFECTION

1. Toxoplasmosis
2. Cytomegalovirus

Focal Calcification

A. TUMOR
   1. Hepatoblastoma
   2. Metastatic neuroblastoma
   3. Hemangioma / hemangioendothelioma
   4. Teratoma
   5. Ovarian dermoid

B. OTHERS
   1. Fetal gallstones (> 28 weeks EGA)
      Cause: hemolytic disease, cholestasis, maternal drug use
      Prognosis: resolution before / after delivery

Cystic Mass in Fetal Abdomen

Incidence: abdominal cyst in 1÷500 – 1÷1,000 live births; 1÷2,625 pregnancies

A. POSTERIOR MID ABDOMEN
   1. Simple renal cyst
   2. Hydroureteronephrosis
   3. Multicystic dysplastic kidney
   4. Paranephric collection = urinoma
   5. Lymphangioma
   6. Cystic neuroblastoma

B. RIGHT UPPER QUADRANT
   1. Liver cyst
   2. Choledochal cyst

C. LEFT UPPER QUADRANT
   1. Splenic cyst

D. ANTERIOR MID ABDOMEN
   1. Gastrointestinal duplication cyst
   2. Mesenteric cyst
   3. Meconium pseudocyst
   4. Dilated bowel
   5. Urachal cyst

E. LOWER ABDOMEN
   1. Fetal ovarian cyst (*see below*)
   2. Hydrometrocolpos
   3. Meningocele
   4. Sacrococcygeal teratoma
   5. Ureterocele

Fetal Ovarian Cyst

◊ Most common intraabdominal mass in female fetus

Incidence: clinically significant ovarian cyst in 1÷2500 live births

Time of development: 3rd trimester
Cause: elevated hormone levels ← fetal pituitary gonadotropins, placental human chorionic gonadotropins, maternal estrogens

1. Simple ovarian cyst
2. Complex ovarian cyst

Prognosis: < 5 cm cyst: spontaneous resolution (69%), > 5 cm cyst: spontaneous resolution (15%)

Rx: The most conservative postpartum approach is a period of observation because many cysts will regress spontaneously.

Fetal Ascites

A. ASCITES + FETAL HYDROPS
   1. Immune hydrops
   2. Nonimmune hydrops
B. ISOLATED ASCITES
   1. Urinary ascites
   2. Meconium peritonitis
   3. Bowel rupture
   4. Ruptured ovarian cyst
   5. Hydrometrocolpos
   6. Glycogen storage disease

Solid-appearing Fetal Abdominal Mass

1. Neoplasm: neuroblastoma, mesoblastic nephroma, liver tumor (eg, hemangioendothelioma)
2. Abdominal bronchopulmonary sequestration
3. Fetus in fetu

FETAL URINARY TRACT ANOMALIES

Prevalence: 0.25%–1.00% liveborn infants (OB-US); 1÷100 to 1÷200 neonates (pediatrics)
Types:

1. Bilateral renal agenesis
2. Infantile polycystic kidney disease
3. Adult polycystic kidney disease
4. Multicystic dysplastic kidney
5. Ureteropelvic junction obstruction
6. Megaureter
7. Posterior urethral valves
8. Prune belly syndrome
9. Megacystis-microcolon-intestinal hypoperistalsis syndrome
10. Mesoblastic nephroma
11. Wilms tumor
12. Neuroblastoma

Associated with: chromosome abnormalities in 12% (74% trisomy, 10% deletion, 9% sex chromosome aneuploidy, 6% triploidy)

• fetal urine production: 5 mL/hour at 20 weeks MA; 56 mL/hour at 40 weeks MA
√ bladder volume: 1 mL at 20 weeks MA; 36 mL at 40 weeks MA
√ filling + emptying of fetal urinary bladder occurs every 10–30 (range 7–43) minutes
√ increased renal parenchymal echogenicity indicates renal abnormality in 80%
√ fetal hydronephrosis
= AP diameter of renal pelvis > 5 mm at 15–20 weeks, ≥ 8 mm at 20–30 weeks, ≥ 10 mm at > 30 weeks

FETAL TUMOR

= CONGENITAL TUMOR
= mass in fetus + newborn manifesting in first 3 months of life
Prevalence: 1.7–13.5÷100,000 live births
Common features: polyhydramnios (⅓), associated congenital anomalies (20%), hydrops (17%)

A. EXTRACRANIAL TERATOMA (most common)
Location: typically along midline of body
Origin: during amoeba-like migration from yolk sac wall to genital ridges a few pluripotential primordial germ cells become isolated in aberrant locations and grow
Path: all 3 germ cell layers:
(a) ectoderm (dominant): neural tissue
(b) mesoderm (common): fat, bone, smooth muscle, cartilage
(c) endoderm (least common): respiratory epithelium, gastrointestinal tissue
Histo: (a) mature
(b) immature: primitive neuroglial tissue + neuroepithelial rosettes; (occasionally) malignant: yolk sac tumor / embryonal carcinoma
1. Sacrococcygeal teratoma (70–80%)
2. Teratoma of head & neck (10–20%)
3. Chest & abdomen teratoma (< 10%)
4. **Fetus in fetu**
= highly differentiated "fetiform" teratoma / parasitic monochorionic diamniotic twin embedded in retroperitoneal location of host

B. NEUROBLASTOMA (30%)
C. SOFT-TISSUE TUMOR (12–22%)
(a) benign: fibromatosis, digital fibromatosis, myofibromatosis, fibrous hamartoma
(b) malignant: infantile fibrosarcoma, rhabdosarcoma, primitive neuroectodermal tumor, rhabdoid tumor, hemangiopericytoma
(b) developmental vascular: hemangioma, lymphangioma, AV malformation
D. INTRACRANIAL TUMOR (10%)
Location: pineal region, suprasellar area, cerebral hemispheres
Site: supratentorial > infratentorial (unlike pediatric age)
√ macrocephaly, hydrocephalus, polyhydramnios ← depressed swallowing ← hypothalamic dysfunction
Mortality: 97% (except for lipoma)

DDx: intracranial hemorrhage

1. Intracranial teratoma (50% of all fetal CNS tumors)
2. Astrocytoma
3. Lipoma (10%)
4. Choroid plexus papilloma (5–9%)
5. Craniopharyngioma
6. Primitive neuroectodermal tumor (3.4–13.2%)

E. RENAL TUMOR (5%)

1. Mesoblastic nephroma
2. Wilms tumor
3. Rhabdoid tumor

F. LIVER TUMOR (5%)

1. Hemangioendothelioma
2. Mesenchymal hamartoma
3. Hepatoblastoma
4. Metastases: ← neuroblastoma + leukemia

G. **Congenital leukemia**

Prevalence: 4.7÷1,000,000 live births
Prognosis: poor ← rapidly progressive course
Age: first 4–6 weeks of infancy
Associated with: congenital leukemia of Down syndrome (15-fold increase of leukemia)
OB-US:

√ hepatosplenomegaly → ↑ abdominal circumference
√ hydrops ← fetal anemia / leukemic infiltrate of myocardium / visceral fibrosis with ↑ vascular resistance

DDx: infection, metastatic neuroblastoma

GENERAL GYNECOLOGY

Pelvic Features of Estrogen Stimulation

√ increased thickness + volume of uterus
√ fundocervical ratio > 2
√ echogenic endometrium
√ appearance of ovaries NOT USEFUL (because of widely varying ovarian volumes + normal visualization of follicles at all ages)

Precocious Puberty

= development of secondary sex characteristics < 8 years of age in girls / < 9 years of age in boys
• premature thelarche / adrenarche / menarche
√ significantly advanced bone age (may limit adult height potential)
Terminology:

(a) isosexual precocity = secondary sex characteristics appropriate for patient's gender
(b) heterosexual precocity = secondary sex characteristics inappropriate for patient's gender

› virilization in girls
› feminization in boys

(c) gonadotropin-dependent = true precocious puberty

(d) gonadotropin-independent = pseudoprecocious puberty

Source: pituitary – adrenal – gonad

Central Precocious Puberty

= TRUE PRECOCIOUS PUBERTY = TRUE ISOSEXUAL PRECOCITY = COMPLETE PRECOCIOUS PUBERTY

= isosexual gonadotropin-dependent early development of gonads + secondary sex characteristics with ovulation before 8 years of age

Cause:

A. IDIOPATHIC (66–80%) F > M activation of hypothalamic-pituitary-gonadal axis
= hypothalamic release of GnRH → pituitary gonadotropin secretion → ovulation / spermatogenesis

B. ORGANIC (13–42%) M >> F
(1) Lesion of pituitary gland / hypothalamus: eg, tuber cinereum hamartoma, cyst
(2) Increased intracranial pressure: eg, postmeningitic hydrocephalus
(3) Traumatic brain injury
(4) Empty sella
(5) Congenital toxoplasmosis
(6) Septo-optic dysplasia, pituitary duplication

• increased levels of estrogen, advanced bone age
• increased gonadotropin levels after LHRH stimulation
√ bilateral adult-sized ovaries (1.2–12 cm^3) with bilateral cysts of < 9 mm
√ dominance of corpus over cervix length
◊ Uterine size + shape are more reliable indicators of estrogen stimulation!

Rx: long-acting gonadotropin-releasing hormone analogue

Radiologic workup:

(1) Bone age assessment
(2) Pelvic ultrasound for evidence of maturation of uterus + ovaries
(3) Search for estrogen-producing lesion: functioning ovarian cysts, juvenile granulosa cell tumor of ovary, feminizing adrenal cortical tumor

Peripheral Precocious Puberty

= PSEUDOPRECOCIOUS PUBERTY = PSEUDOSEXUAL PRECOCITY = INCOMPLETE PRECOCIOUS PUBERTY

= iso- / heterosexual pubertal changes independent of secretion of pituitary gonadotropins =early development of secondary sex characteristics without ovulation

Cause:

A. ISOSEXUAL PPP IN FEMALES

1. Autonomously functioning ovarian follicular cyst (most common cause)
√ asymmetric ovarian enlargement (one ovary 2.4–7 cm^3) with macrocysts (> 9 mm)
√ pubertal morphology + size of uterus ← estrogen stimulation

2. Estrogen-secreting ovarian tumor: eg, granulosa cell tumor, gonadoblastoma, thecoma, choriocarcinoma
3. Feminizing adrenocortical neoplasm

rare others: McCune-Albright syndrome, untreated hypothyroidism, neurofibromatosis (NF1), hepatoblastoma, estrogen ingestion (food, topical cream)

B. HETEROSEXUAL PPP IN FEMALES
1. Virilizing adrenocortical neoplasm (ACN)
2. Congenital adrenal hyperplasia (CAH)

C. ISOSEXUAL PPP IN BOYS
1. Sex cord-stromal tumor of testis
2. hCG-secreting tumors stimulating Leydig cells: hepatoblastoma, mediastinal teratoma, some testicular germ cell tumors, suprasellar germinoma

- low gonadotropin levels after LHRH stimulation
- high serum estradiol level, low serum levels of FSH + LH
- normal bone age; uterine bleeding ← withdrawal of estrogen stimulation upon cyst rupture

√ prepubertal small uterus + ovaries
√ asymmetric ovarian enlargement (one ovary 2.4–7 cm^3) with macrocysts (> 9 mm)
√ ± unilateral follicular ovarian cyst characterized by internal daughter cyst

Isolated Premature Adrenarche

= axillary and pubic hair development ← action of adrenal androgens in girls 1–3 years of age

- increased levels of adrenal androgens independent of stimulation by adrenocorticotropic hormone (ACTH)

√ prepubertal uterus + ovaries (0.1–1.0 cm^3)
√ normal / slightly advanced bone age

Isolated Premature Thelarche

= breast enlargement in girls 1–3 years of age
◊ May occur without endocrine abnormalities
√ prepubertal uterus + ovaries
√ normal / slightly advanced bone age

Infertility

= failure to conceive after 1 year of unprotected intercourse

Incidence: affects 10–15% of couples = 7.4 million women in 2010

Etiology:

A. FEMALE FACTORS (55%):
› Tubal disease (10–20–40%): congenital anomalies, DES exposure, pelvic inflammatory disease, salpingitis isthmica nodosa, endometriosis, postoperative factors, polyp, neoplasm, ectopic pregnancy
› Uterine factors (2–5%): bicornuate uterus, septate uterus, DES exposure, intrauterine adhesions, endometrial inflammation / infection, uterine neoplasm, complications

after pregnancy, leiomyoma
› Ovulatory disorder (10–20%): premature ovarian failure, gonadal dysgenesis, polycystic ovary syndrome
› Pelvic factors (20–25%)
› Cervical factors (5–10%)

B. MALE FACTORS (40%)
C. COMBINATION OF FACTORS (15–25%)
D. UNKNOWN CAUSE (5–10%)

Tests:

- history + physical examination
- laboratory tests (mainly hormonal), postcoital test
- basal body temperature measurement, cervical culture
- endometrial biopsy, sonographic monitoring of ovaries
- in vitro mucus penetration test, sperm agglutination studies
- laparoscopy + hysteroscopy, hysterosalpingography

Fallopian Tube Occlusion, Irregularity and Adhesions

Frequency: 30–40%

1. Pelvic inflammatory disease
   (a) granulomatous salpingitis: TB
   (b) parasitic infection
2. Congenital anomaly
3. Postsurgical anomaly
4. Tubal spasm
5. Intraluminal endometriosis
6. Salpingitis isthmica nodosa

Intrauterine Filling Defect on HSG

1. Intrauterine synechiae
2. Submucosal leiomyoma
3. Endometrial polyps
4. Blood clot
5. Air bubbles

Uterine Contour Irregularities

1. Adenomyosis
2. Leiomyoma
3. Müllerian duct anomalies (up to 25%)

Cervical Anomalies

1. Cervical factor infertility (10%)
   = inadequate quality / volume of cervical mucus
2. Cervical stenosis

Ovarian Abnormalities

A. PRIMARY

1. Nonfunctioning ovaries
2. Premature ovarian failure
3. Gonadal dysgenesis

B. SECONDARY
1. Polycystic ovary syndrome
2. Endometriosis
3. Ovarian cancer

Amenorrhea

Primary Amenorrhea

Definition:

(a) no menarche by 16 years of age
(b) no thelarche / adrenarche by 14 years of age
(c) no menarche > 3 years after adrenarche + thelarche

Cause:

A. FEMALE ANATOMIC ANOMALIES
= Müllerian (uterovaginal) anomalies (20%)

B. CONGENITAL DISORDERS OF SEXUAL DIFFERENTIATION
(a) pure gonadal dysgenesis = Turner syndrome (33%)
√ bilateral dysfunctional / streak gonads
(b) mixed gonadal dysgenesis
√ testis + streak gonad
Risk: in 25% development of dysgerminoma / gonadoblastoma in dysgenetic gonads with Y chromosome

C. OVARIAN FAILURE / DYSFUNCTION

D. HYPOTHALAMIC / PITUITARY CAUSES (15%)

E. CONSTITUTIONAL DELAY (10%)

F. OTHERS: eg, systemic, psychiatric illness (22%)

√ absent / streak gonads + infantile uterus:

1. **Hypogonadotropic hypogonadism**
• low / normal LH + FSH levels
(a) hypothalamic dysfunction: hypothalamic tumor, **Kallmann disease** (= lack of pulsatile GnRH release), systemic illness, constitutional growth delay, extreme physical / psychological / nutritional stress (cystic fibrosis, sickle cell disease, Crohn disease), irradiation
(b) pituitary dysfunction: disruption of pituitary stalk from child abuse, head trauma
2. **Hypergonadotropic hypogonadism**
= ovarian tissue fails to respond to endogenous gonadotropins
• high LH + FSH levels
(a) abnormal karyotype: Turner syndrome, XY gonadal dysgenesis
(b) irradiation, chemotherapy, autoimmune disease (eg, autoimmune oophoritis)

√ absent uterus:

1. **Testicular feminization** = male intersex = male pseudohermaphroditism ← end-organ insensitivity to testosterone

2. **Müllerian dysgenesis** (= Mayer-Rokitansky-Küster-Hauser syndrome)
   √ normal fallopian tubes + ovaries
   Associated with: unilateral renal abnormality (50%), skeletal abnormality (12%)

√ small infantile uterus:
1. Androgen-producing virilizing tumor of adolescent ovary ← usually Sertoli-Leydig cell tumor
   √ unilateral adnexal mass
2. Turner syndrome
3. In utero exposure to diethylstilbestrol

√ normal uterus + unilateral ovarian tumor:
1. Estrogen-producing ovarian tumor with disruption of menstrual cycle: granulosa cell tumor, thecoma

√ hematometrocolpos:
(a) neonate = congenital uterovaginal obstruction
   1. Urogenital sinus / cloacal malformation
      √ pelviabdominal cystic mass with fluid-debris level in fetal US during 3rd trimester
      √ renal dysplasia / obstruction
(b) teenager
   1. Imperforate hymen
   2. Transverse vaginal septum
      › in upper vagina (45%)
      › in mid vagina (40%)
      › in lower vagina (15%)

√ hematometra
1. Cervical dysgenesis

√ bilateral ovarian enlargement:
1. Polycystic ovary syndrome
   (= Stein-Leventhal syndrome): most common cause of secondary amenorrhea

Secondary Amenorrhea

1. Pregnancy: most common cause in girls > 9 years of age
2. Polycystic ovary syndrome (main pathologic cause)
3. Asherman syndrome
4. All causes of primary amenorrhea

Oligomenorrhea

Definition: < 9 menstrual cycles per year

Calcifications of Female Genital Tract

A. UTERUS
   1. Uterine fibroid
   2. Arcuate arteries
B. OVARIES
   1. Dermoid cyst (50%)

2. Papillary cystadenoma (psammomatous bodies)
3. Cystadenocarcinoma
4. Hemangiopericytoma
5. Gonadoblastoma
6. Chronic ovarian torsion
7. Pseudomyxoma peritonei

C. FALLOPIAN TUBES
1. Tuberculous salpingitis

D. PLACENTA

E. LITHOPEDION

Psammoma Bodies in Tumor

1. Papillary serous cystadenoma / cystadenocarcinoma
2. Mucinous carcinoma of colon
3. Papillary thyroid cancer
4. Meningioma

Free Fluid in Cul-de-sac

1. Follicular rupture
2. Ovulation
3. Ectopic pregnancy
4. S/P culdocentesis
5. Ovarian neoplasm
6. Pelvic inflammatory disease

PELVIC MASS

Frequency of Pelvic Masses

1. Benign adnexal cyst 34%
2. Leiomyoma 14%
3. Cancer 14%
4. Dermoid 13%
5. Endometriosis 10%
6. Pelvic inflammatory disease 8%

Cystic Pelvic Mass

A. CYSTIC ADNEXAL MASS

B. EXTRAADNEXAL CYSTIC MASS

(a) intraperitoneal

@ Peritoneum

1. Peritoneal inclusion cyst
2. Paraovarian cyst

@ Bowel

1. Mucocele of the appendix
2. Mesenteric cyst

3. Fluid-distended bowel

@ Fallopian tube
1. Hydro-, pyo-, hematosalpinx
2. Ectopic gestation

@ Uterus
1. Pedunculated / parasitized leiomyoma with cystic degeneration
2. Cystic adenomyosis
3. Unicornuate uterus with obstructed rudimentary horn

(b) extraperitoneal

@ Presacral space
1. Spinal meningeal cyst
2. Retrorectal developmental cyst: dermoid, epidermoid, enteric tailgut / duplication cyst

@ Lymphatics
1. Lymphocele
2. Cystic degeneration of lymph node
3. Lymphangioleiomyomatosis
4. Lymphangioma

(c) intra- and extraperitoneal
1. Loculated pelvic abscess: appendiceal, diverticular, postoperative, Crohn disease, tuberculous, pelvic actinomycosis
2. Hematoma
3. Bladder diverticulum

Complex Pelvic Mass

mnemonic: CHEETAH

Cystadenoma / **C**ystadenocarcinoma
Hemorrhagic cyst
Endometrioma
Ectopic pregnancy
Teratoma: dermoid
Abscess ← adjacent appendicitis, etc.
Hematoma in pelvis

Solid Pelvic Mass

1. Pedunculated myoma (most common)
2. Fibroma
3. Adenofibroma
4. Thecoma
5. Brenner tumor

Fatty Pelvic Mass

A. UTERUS
1. Lipoleiomyoma
2. Fibromyolipoma

B. OVARY
   1. Benign cystic ovarian teratoma
   2. Malignant degeneration of cystic teratoma
   3. Nonteratomatous lipomatous ovarian tumor

C. PELVIS
   1. Benign pelvic lipoma
   2. Liposarcoma
   3. Lipoblastic lymphadenopathy

Extrauterine Pelvic Mass

1. Solid adnexal mass
2. Metastatic disease
3. Lymphoma
4. Pelvic kidney
5. Rectosigmoid carcinoma
6. Bladder carcinoma
7. Retroperitoneal tumor / fibrosis
8. Intraperitoneal fat
9. Vascular mass / malformation
10. Hematoma
11. Bowel

ADNEXA

Adnexal Mass

A. CYSTIC OVARIAN MASS
   1. Physiologic ovarian cyst:
      › Graafian follicle: at midcycle < 25 mm
      › Corpus luteum: after midcycle < 15 mm
   2. Functional / retention cyst
   3. Endometrioma
   4. Tuboovarian abscess
   5. Dermoid cyst
   6. Ectopic pregnancy
   7. Serous / mucinous ovarian tumor
   8. Ovarian hyperstimulation cysts
   9. Massive ovarian edema

B. EXTRAOVARIAN CYSTIC LESION
   1. Hydrosalpinx
   2. Paraovarian cyst / cystadenoma
   3. Peritoneal inclusion cyst

C. SOLID OVARIAN
   1. Ovarian tumor
   2. Torsion of ovary
   3. Oophoritis

4. Stein-Leventhal syndrome
5. Ovarian fibromatosis

D. SOLID EXTRA-OVARIAN
1. Fallopian tube carcinoma
2. Pedunculated fibroid

Ovarian Mass with Low Resistive Flow

Low resistance flow = RI < 0.5 or PI ≤ 1.0

1. Physiologic corpus luteum
2. Inflammatory mass
3. Endometrioma
4. Mesothelial cyst
5. Benign tumor: serous / mucinous cystadenoma, mature cystic teratoma, cystadenofibroma
6. Malignant ovarian tumor
   ◊ Some malignancies have high resistive blood flow!

Hemorrhagic Adnexal Lesion

1. Endometriosis
2. Hemorrhagic ovarian cyst
3. Hemorrhagic foci of adenomyosis
4. Hematosalpinx

Low-intensity Adnexal Lesion on T1WI

1. Fibroma
2. Fibrothecoma
3. Cystadenofibroma
4. Brenner tumor
5. Ovarian fibromatosis
6. Krukenberg tumor
7. Wall of chronic pelvic abscess
8. Pedunculated leiomyoma

High-intensity Adnexal Lesion on T1WI

= T1-shortening ← fat, hemorrhage, high protein

1. Endometrioma
   √ frequently multilocular + bilateral
   √ shading (= signal loss) on T2WI
2. Hemorrhagic ovarian cyst
   √ unilocular
   √ no shading
   √ resolution with time
3. Dermoid
   √ chemical shift artifact
   √ signal drop-out after fat suppression
4. Mucinous cystic neoplasm

√ signal intensity less than fat / blood

5. Ovarian carcinoma
   √ solid components, septations
   √ large size

LOW SI OF T1-HYPERINTENSE ADNEXAL MASS ON STIR

1. Fat of mature cystic teratoma
2. Hemorrhagic ovarian cyst
3. Endometrioma

◊ Use selective fat-suppressed T1WI to identify fat!

Low-intensity Adnexal Lesion on T2WI

A. Blood products
   1. Endometrioma
   2. Hemorrhagic cyst
   3. Hematosalpinx
   4. Cystic adenomyosis
B. Smooth muscle
   1. Uterine leiomyoma
C. Fibrous tissue
   1. Ovarian fibroma
   2. Theca cell tumor of ovary
   3. Cystadenofibroma
   4. Ovarian fibromatosis
   5. Pelvic aggressive fibromatosis
D. Mixed cellularity
   1. Brenner tumor
   2. Struma ovarii
   3. Krukenberg tumor

T2-isointense Pelvic Mass Relative to Muscle

A. Uterine origin
   1. Cystic adenomyosis: ↑ T1WI
   2. Leiomyoma: enhancing
B. Adnexal origin
   (a) ↑ T1WI without enhancement
      1. Endometrioma
      2. Hematosalpinx

Classification of Surface Epithelial Neoplasms by Cell Type			
Frequency	*Benign*	*Borderline (4–14%)*	*Malignant*
50%	Serous cystadenoma	Serous borderline tumor *resembling ciliated columnar cells of fallopian tube*	Serous cystadenocarcinoma
15–30%	Endometrioid cystadenoma	Endometrioid borderline tumor *resembling endometrial adenocarcinoma*	Endometrioid adenocarcinoma
15%	Mucinous cystadenoma	Mucinous borderline tumor *resembling endocervical canal epithelium*	Mucinous adenocarcinoma
5%	Benign clear cell tumor	Borderline clear cell tumor *mesonephroid tumor*	Clear cell adenocarcinoma
2.5%	Transitional cell (Brenner) tumor	Brenner tumor of borderline malignancy	Transitional cell carcinoma (non-Brenner type)
Clinical Features			
Age		young woman	6th–7th decade
Solid component	minimal amount	moderate amount	marked amount
Papillary projections	none / minimal (13%)	none / minimal (13%)	abundant (67%), in 38% with domineering solid component
Extraovarian tumor implants		noninvasive	invasive
+ retro-peritoneal Lnn.		21%	
+ Doppler blood flow		90%	92%
↑ CA-125		90%	high

(b) ↓ T1WI with enhancement
1. Fibroma
2. Fibrothecoma
3. Cystadenofibroma
4. Struma ovarii

T2-Hyperintense Adnexal Mass Brighter than Muscle

(a) ↑ T1WI
› without enhancement
1. Hemorrhagic cyst
› with enhancement
2. Malignant transformation of endometrioma

(b) ↓ T1WI
› without enhancement
1. Mucinous cystic neoplasm
› with enhancement
2. Krukenberg tumor

Adnexal Mass with Restricted Diffusion

1. Malignancy
2. Benign hemorrhagic ovarian cyst
3. Endometrioma
4. Benign mature cystic teratoma

Adnexal Mass in Pregnancy

Prevalence: 0.5–1.2%

A. RESOLVING BY 14–16 WEEKS EGA

1. Corpus luteum cyst
2. Theca lutein cyst

B. PERSISTENT ADNEXAL MASS

1. Benign
   correctly diagnosed by US: 95% of dermoids, 80% of endometriomas, 71% of simple cysts
2. Malignant (0.1–0.8%)

Ovarian Tumor

- abdominal discomfort, vomiting, flatulence, dyspnea
- acute pain from torsion / hemorrhage; menstrual irregularity
- chronic pain ← slowly enlarging mass, impaction, adhesions

Radiologic guidelines:

◊ Imaging features of ovarian neoplasms virtually never allow a specific diagnosis. Regardless of further differentiation patients always undergo surgery!

Signs suggestive of benignancy:

√ unilocularity of cyst
√ thin wall < 3 mm
√ minimal septations
√ absence of papillary projection

Signs suggestive of malignancy:

√ solid nonfatty nonfibrous tissue (most POWERFUL PREDICTOR of malignancy!)
√ many solid-tissue elements in a complex lesion
√ wall thickness > 3 mm
√ inner wall irregularities / papillary projections
√ thick septations > 3 mm
√ increased echogenicity within a cyst

Age: 13% of neoplasms malignant in premenopause; 45% of neoplasms malignant in postmenopause

Cx: (1) Torsion (in 10–20%)
(2) Rupture (rare)
(3) Infection

Terminology:

prefix "cyst-": cystic component present
suffix "fibroma": > 50% fibrous component
"tumor of low malignant potential": borderline malignant

Classification:

◊ 75% of ovarian neoplasms are benign
◊ 21% of ovarian neoplasms are malignant
◊ 4% of ovarian neoplasms are borderline malignant

The proportion of malignant tumors increases with age:
< 20 years of age 4%
> 50 years of age 40%

Tumor of Surface Epithelium (60–70%)

= EPITHELIAL OVARIAN TUMOR

Origin: arising from precursors from outside the ovary = surface epithelium / mesothelium

Frequency: 60% of all ovarian tumors; 85% of all ovarian malignancies; 50% occur > 65 years of age

Age peak: 6th–7th decade; rare before puberty

√ primarily uni- / multilocular cystic mass

√ ↑ amounts of solid tissue (mural nodules, vascular solid component) correlate with likelihood of malignancy

√ papillary projections in benign tumor (13%) / borderline tumor (67%) / malignant neoplasm (38%)

√ propensity for early peritoneal + lymphatic spread:

- √ ascites
- √ peritoneal studding
- √ omental cake
- √ perihepatic diaphragmatic implants
- √ retroperitoneal lymphadenopathy

Germ Cell Tumor (20–25%)

◊ 40% of germ cell tumors are malignant

Age: commonly in young women

(a) BENIGN (95%)

1. Dermoid cyst = mature cystic teratoma
   = the only benign variety

(b) MALIGNANT (5%)

= ovarian malignant germ cell tumor (OMGCT

Types: dysgerminoma (1.9%), immature teratoma (1.3%), endodermal sinus / yolk sac tumor (1.0%), malignant mixed germ cell tumor (0.7%), embryonal carcinoma (0.1%), choriocarcinoma (0.1%), malignant struma ovarii tumor

Fat within a solid ovarian tumor is characteristic of a teratoma = mature teratoma ± malignant degeneration / immature teratoma / mixed GCT with immature elements

Sex Cord-Stromal Tumor (5–8%)

usually has more than one cell type + arises from two groups of cells:

› primitive sex cord cells, which form from the coelomic epithelium (= primordial peritoneum) and differentiate into granulosa cells + Sertoli cells

› stromal cells (fibroblasts, theca cells, Leydig cells) derive from the mesonephros mesenchyma of the genital ridge

Age: broad range of ages

• most present at stage I with good prognosis

• absent tumor markers

◊ Often manifest with tumor-mediated hormonal effects

√ NO papillary projections

√ lack of fat + calcifications

Malignant Ovarian Epithelial versus Germ Cell Tumor		
Characteristic	*Epithelial Tumor*	*Germ Cell Tumor*
Prevalence	much more common	less common
Highest incidence	> 65 years of age	15–19 years of age
Age affected	older woman	girl / young woman
Race affected	more in whites	more in blacks + Asians
Bilaterality	serous (58%), mucinous (21%), clear cell (13%), endometrioid (27%)	4% (usually unilateral)
Tumor marker	CA-125	α-fetoprotein + β-hCG
Endocrine signs	None	isosexual precocity, carcinoid syndrome
5-year survival rate	44% (depending on stage)	dysgerminoma (100%), other malignant GCT (85%)

› hyperestrogenic tumors: granulosa cell tumor, thecoma, stromal luteoma
› virilizing tumors: Sertoli-Leydig cell tumor, steroid cell tumor (Sertoli cell tumor, Leydig cell tumor)

Size versus risk of malignancy: < 5 cm in 3%
5–10 cm in 10%
> 10 cm in 65%

A. GRANULOSA-STROMAL CELL TUMOR
   1. Juvenile granulosa cell tumor multicystic
   2. Adult granulosa cell tumor solid
   3. Thecoma solid
   4. Fibroma solid
   5. Fibrosarcoma
   6. Sclerosing stromal tumor

B. SERTOLI-STROMAL CELL TUMOR
   1. Sertoli-Leydig tumor solid
   2. Sertoli cell = arrhenoblastoma solid
   3. Leydig cell

C. STEROID CELL TUMOR = LIPID CELL TUMOR
   1. Stromal luteoma
   2. Leydig cell tumor = hilus cell tumor
   3. Steroid cell tumor, not otherwise specified

D. OTHER
   1. Gynandroblastoma
   2. Sex cord tumor with annular tubules
      associated with Peutz-Jeghers syndrome (30% of all tumors with annular tubules)
   3. Sclerosing stromal tumor

PARANEOPLASTIC SYNDROME OF OVARIAN TUMOR

Cause: autoantibodies, circulating immune complexes

A. NERVOUS SYSTEM DISORDERS
    1. Cerebellar degeneration
    2. Polyneuritis
B. CONNECTIVE TISSUE DISORDERS
    1. Dermatomyositis
C. HEMATOLOGIC DISORDERS
    1. Hemolytic anemia
    2. Disseminated intravascular coagulation
D. CUTANEOUS DISORDERS
    1. Acanthosis
E. NEPHROTIC SYNDROME

Secondary Ovarian Tumor (5–15%)

Metastases from: pelvic organs, upper GI tract, breast, bronchus, reticuloendothelial tumors, leukemia

Solid Ovarian Tumor

1. Ovarian fibroma
2. Theca cell tumor of ovary
3. Granulosa cell tumor
4. Sertoli-Leydig cell tumor
5. Brenner tumor
6. Sarcoma
7. Dysgerminoma
8. Yolk sac tumor of ovary
9. Teratoma of ovary
10. Metastasis
11. Endometrioma
12. Massive ovarian edema
13. Leiomyoma

Functioning Ovarian Tumor

◊ ⅔ of gonadal stromal tumors produce steroids

◊ The most common functioning ovarian tumor is the sex cord-stromal tumor (= 8% of ovarian neoplasms)

OVARIAN TUMOR WITH HYPERANDROGENISM

- male-pattern baldness, loss of female body contour
- hirsutism, elevated serum testosterone
- ± elevated serum dehydroepiandrosterone

Causes of Hyperandrogenism and Hyperestrogenism		
Cause	*Hyper-androgenism*	*Hyper-estrogenism*
Ovarian Disorder		
Sex cord-stromal tumor		
Sertoli stromal tumor		
Sertoli-Leydig cell tumor	+	(+)
Steroid cell tumor		
Leydig cell tumor	+	(+)
Stromal luteoma	+	+
Steroid cell tumor NOS	+	(+)
Granulosa stromal tumor		
Granulosa cell tumor	(+)	+
Thecoma	(+)	+
Sclerosing stromal tumor	–	+
Sex cord tumor with annular tubules	–	+
Gynandroblastoma	+	–
Germ cell tumor		
Carcinoid (monodermal teratoma)	+	–
Gonadoblastoma		
Surface epithelial tumor		
Serous tumor	–	+
Mucinous tumor	–	+
Endometrioid tumor	–	+
Brenner tumor	+	+

Secondary (metastatic) tumor	+	+
Tumorlike lesion		
Polycystic ovary syndrome	+	–
Stromal hyperplasia	+	–
Stromal hyperthecosis	+	–
Hyperreactio luteinalis	+	–
Pregnant luteoma	+	–
Pituitary Disorder		
Cushing disease	+	–
Adrenal Disorder		
Cushing syndrome	+	–
Adult-onset congenital adrenal hyperplasia	+	–
Hyperfunction of adrenal gland	+	–
Drugs		
Testosterone	+	–
Danazol	+	–
Anabolic steroids	+	–
Synthetic progestins	+	–
Estrogen	–	+
Tamoxifen	–	+
Other Disorder		
Idiopathic hirsutism	+	–

A. SOLID ± CYSTIC
   1. Sertoli-Leydig cell tumor

B. SOLID
   2. Leydig cell tumor

uncommon: metastasis, teratoma, choriocarcinoma, Sertoli cell tumor

OVARIAN TUMOR WITH HYPERESTROGENISM

- sexual precocity in premenarchal girls
- irregular excessive uterine bleeding

A. CYSTIC
   1. Granulosa cell tumor
   2. Mucinous cystadenoma

B. SOLID
   3. Thecoma

uncommon: stromal luteoma, choriocarcinoma, teratoma, Brenner tumor

OTHER FUNCTIONING OVARIAN TUMORS

- increased hCG levels: choriocarcinoma
- hyperthyroidism: struma ovarii
- carcinoid syndrome: carcinoid tumor
- Cushing syndrome: steroid cell tumor

- hypoglycemia: fibroma, dysgerminoma, carcinoid

FALLOPIAN TUBE

Fallopian Tube Disease outside Pregnancy

1. Pelvic inflammatory disease
2. Atypical tubal infection: tuberculosis, actinomycosis
3. Torsion of fallopian tube
4. Endometriosis
5. Primary fallopian tube tumor
   - › hydatid cyst of Morgagni
   - › leiomyoma
   - › fallopian tube cancer

Proximal Fallopian Tube Obstruction

1. Extensive fibrosis / salpingitis isthmica nodosa (40%)
2. Amorphous debris / minimal adhesions (40%)
3. Tubal spasm (20%)

UTERUS

Prepubertal Vaginal Bleeding

1. Vaginal foreign body
   Prevalence: in 18% of children with vaginal bleeding + discharge; in 50% of children with vaginal bleeding + no discharge
2. Vaginal rhabdomyosarcoma
3. Precocious puberty
4. Hemangioma
5. Vascular malformation

Postmenopausal Uterine Bleeding

1. Endometrial atrophy (in 60–75%)
   - thin atrophic endometrium prone to superficial ulceration
   - √ in 75% endometrial thickness < 4–5 mm
     - ◊ Patient may forego endometrial biopsy!
   - √ in 25% endometrial thickness of 6–15 mm
2. Endometrial hyperplasia
3. **Endometrial polyp**
4. Submucosal fibroid
   - √ hypoechoic mass with an overlying normal echogenic endometrium
   - √ ± acoustic attenuation
   - √ ± prolapse into endometrial cavity

   Rx: can be removed at hysteroscopy if > 50% of mass projects into endometrial cavity
5. Adenomyoma
   - √ indistinguishable from submucosal fibroid

6. Endometrial carcinoma (in 7–20%)
7. Estrogen withdrawal

Optimal time of imaging:
immediately after cessation of bleeding when endometrium is presumed to be thinnest

Rx: any focal / generalized thickness > 5 mm at transvaginal US requires further investigation (sonohysterography, guided biopsy, hysteroscopy)

Postpartum Hemorrhage (PPH)

= blood loss sufficient to cause symptoms of hypovolemia
- tachycardia, hypotension, oliguria

= blood loss > 500 mL after vaginal birth / > 1,000 mL after cesarean delivery

Physiology: bleeding decreases over 1st postpartum week

Incidence: 3.3% in developed countries

Classification:

(a) **Primary PPH** = early postpartum hemorrhage > 500 mL within 24 hours in 4–6% of all deliveries

Cause: uterine atony (75%–90%), laceration of lower genital tract, bladder flap hematoma, uterine rupture, acute uterine inversion

(b) **Secondary PPH** = late postpartum hemorrhage between 24 hours and 6 weeks in 1–2% of all deliveries

Cause: endometritis, retained products

DDx: endometritis, uterine dehiscence / perforation, subinvolution of placental implantation site

Increased risk: maternal age > 35 years, primipara, previous C-section, previous postpartum hemorrhage, prolonged labor, multiple pregnancy, fibroids, placental abruption, placenta previa / accreta, instrument delivery, prophylactic uterorelaxant drug therapy

mnemonic: 4 Ts **T**onus, **T**issue, **T**rauma, **T**hrombin

1. **Uterine atony** (75–90% of 1° PPH)

= generalized ineffective contraction of uterine corpus with bleeding at placental site

Risk factors: uterine overdistension (multiple pregnancy, macrosomia, polyhydramnios), labor related factors (prolonged labor, precipitate labor, induction of labor, forceps delivery, prolonged use of oxytocin, use of uterorelaxant drug)

- hemorrhage in immediate postpartum period
- pliable uncontracted uterus

√ normal uterus

DDx: normal postpartum findings
- √ small amount of fluid / blood in uterine cavity
- √ intrauterine gas (up to 3 weeks post partum)
- √ prominent intramural + parametrial vessels
- √ focal thinning of myometrial wall (after C-section) + small hematoma / seroma

Rx: medical Rx; internal uterine balloon tamponade; selective embolization of uterine arteries (gelatin sponge particles); uterine compression sutures; vascular ligation

2. Retained products of conception (most frequent cause of secondary PPH)
3. Lower genital tract trauma (2–4% of all PPH)

√ paravaginal hematoma (coronal reconstruction!)
Risk factors: primipara, macrosomia, multiple pregnancy, prolonged dilatation, vulvovaginal varices, preclampsia, coagulation disorder, instrumental vaginal delivery
Bleeding source: episiotomy (cervical, vulvar, perineal tear), vaginal laceration
(a) infralevator extension: spread to vulva, perineum, ischiorectal fossa
• diagnosis by inspection + vaginal bleeding
Rx: transvaginal drainage
(b) supralevator extension: upward spread through broad ligament + retroperitoneal space
• NO obvious vaginal bleeding → delay in diagnosis
• abdominal pain, hypovolemic shock
√ bladder flap hematoma
= fluid-attenuation collection in extraperitoneal space between posterior bladder wall + anterior wall of lower uterine segment
bladder flap = dissection of urinary bladder from lower uterine segment during cesarean section to allow spontaneous descent of bladder

4. Coagulation disorder (acquired / congenital)

Diffusely Thickened Irregular Endometrium

Normal endometrial thickness:
Sensitivity for detection of endometrial abnormalities: 80% for transvaginal US; 30% for endometrial biopsy
Time of sonohysterography: day 4, 5, or 6 of menstrual cycle

1. **Endometrial hyperplasia**
Age: peri- / postmenopausal women
Cause: prolonged endogenous / exogenous unopposed estrogen stimulation
√ focal / diffuse endometrial thickening > 5–6 mm
√ formation of polyps of up to 5 cm
Types:
(a) glandular-cystic hyperplasia (most common)
Histo: dilated glands lined by tall columnar / cuboidal epithelium
√ small cysts within evenly echogenic endometrium
Prognosis: NO premalignant condition
(b) adenomatous hyperplasia
√ endometrium with irregular hypoechoic areas
Prognosis: precursor of endometrial cancer
2. Secretory endometrium
◊ Improve timing of the examination!
3. Endometrial cancer
4. Endometritis
5. **Tamoxifen-related endometrial changes**
= nonsteroidal antiestrogen in breast acts as a weak estrogen agonist → proliferative effects on endometrium
Increased prevalence of: endometrial hyperplasia, polyps, carcinoma

◊ 50% of women treated with tamoxifen will develop endometrial abnormalities within 6–36 months

Histo:

(a) endometrial thickness increased to 10.4 mm; 4.2 mm in control subjects
(b) polyps (36%); 10% in control subjects
(c) atrophic changes (28%); 87% in control subjects

• hemorrhage (requires further evaluation)

√ endometrial thickening > 5–9 mm:

√ endometrial hyperplasia
√ endometrial polyp
√ subendometrial cystic changes (= glandular distension within a polyp / reactivated adenomyosis within inner myometrium)

MR:

√ endometrial-myometrial interface ← endometrial atrophy / proliferative changes:

√ homogeneously hyperintense on T2WI
√ signal void + enhancement on T1WI

√ polyps:

√ heterogeneous intensity on T2WI
√ latticelike enhancement traversing endometrial canal on T1WI

Focally Thickened Endometrium

1. **Endometrial polyp**

= focal hyperplasia of stratum basale; in 20% multiple

Age: mainly 30–60 years

Histo: projections of endometrial glands + stroma into uterine cavity

(a) hyperplastic polyp resembling endometrial hyperplasia
(b) functional polyp resembling surrounding endometrium (least frequent)
(c) atrophic polyp

Frequently associated with: tamoxifen therapy

US:

√ sessile broad-based / pedunculated well-defined smooth hyperechoic homogeneous intracavitary mass (79%) / of variable echogenicity (best seen on sonohysterography):

√ cystic spaces (in 59%) ← enlarged dilated glands filled with proteinaceous fluid
√ heterogeneous texture ← suggestive of infarction, inflammation, hemorrhage
√ vessel visualized within stalk on color Doppler

Malignant transformation: in 0.4–3.7%

2. Primary carcinoma of the endometrium

Risk factors: exposure to unopposed estrogen, obesity, nulliparity, hypertension, diabetes

Location: predominantly in uterine fundus; 24% in isthmic portion)

◊ 10% cancer rate with endometrial thickness of 6–15 mm
◊ 50% cancer rate with endometrial thickness of > 15 mm

√ irregular heterogeneous endometrium > 5 mm in thickness
√ focal / diffuse endometrial thickening (mean thickness of 18.2 mm)
√ irregular poorly defined endometrial-myometrial interface

√ increased echogenicity in myometrium (= invasive endometrial cancer)
√ Doppler waveforms with resistive index < 0.7 suggest malignancy

3. Metastatic carcinoma: ovary, cervix, fallopian tube, leukemia
4. Hydatidiform mole
   √ echogenic mass with irregular sonolucent areas
5. Incomplete abortion
6. Submucosal leiomyoma
   √ mass hypo- / hyperechoic relative to myometrium
   √ wide attachment to myometrium
   √ intracavitary margin outlined by echogenic rim of endometrium
   √ ± acoustic attenuation
   Rx: hysteroscopic removal if > 50% of mass projects into endometrial cavity
7. Focal adenomyoma
   √ hypoechoic mass with an overlying echogenic endometrium
   DDx: indistinguishable from submucosal fibroid
8. Intrauterine synechiae
   √ echogenic bands extending from one endometrial surface to the other

DDx: adherent blood clots

Fluid Collection within Endometrial Canal

Types: blood, mucus, purulent material

A. PREMENOPAUSAL
   1. Infection: endometritis, pyometrium
   2. Congenital obstructive lesion: imperforate hymen, vaginal septum, vaginal / cervical atresia
   3. Acquired obstructive lesion: cervical stenosis (following instrumentation / cone biopsy / radiation), cervical carcinoma
   4. Spontaneous hematometra in bleeding disorders
   5. Pregnancy: intrauterine, ectopic, incomplete abortion
   6. Endometrial cancer
   7. Endometrial polyp, submucosal fibroid
   8. Functional: during menstruation

B. POSTMENOPAUSAL
   1. Endometrial / cervical cancer
   2. Cervical stenosis
   3. Normal if amount small

Endometrial Cysts

1. Endometrial cystic atrophy
   Histo: cystically dilated atrophic glands lined by single layer of flattened / low cuboidal epithelium
   √ very thin endometrium of < 4–5 mm
2. Endometrial cystic hyperplasia

Diffuse Uterine Enlargement

1. Diffuse leiomyomatosis
2. Adenomyosis
3. Endometrial carcinoma (15%)

Uterine Mass

A. BENIGN
   1. Uterine fibroids (99%)
   2. Pyometra
   3. Hemato- / hydrocolpos
   4. Transient uterine contraction: during pregnancy
   5. Bicornuate uterus
   6. Adenomyosis
   7. Intrauterine pregnancy
   8. Lipoleiomyoma (< 50 cases in world literature)

B. MALIGNANT
   1. Cervical carcinoma
   2. Endometrial carcinoma
   3. Leiomyosarcoma
   4. Invasive trophoblastic disease

CERVIX

Congenital Cervical Anomaly

1. Septate uterus (34–55%)
2. Duplication of cervix: uterus didelphys, septate uterus, bicornuate uterus
   √ 2 endocervical canals usually divided by thicker plane of tissue than with a cervical septum
3. Cervical agenesis = blind-ending vagina often with complete absence of uterus / rudimentary uterine tissue
   √ evaluate for concurrent renal anomalies (30–50%)

Cervical Mass

1. Fibroid
2. Cervical carcinoma
3. Endocervical polyp
4. Nabothian cyst
5. Cervical leiomyoma
6. Endometriosis

Use of transducer pressure may show lesion mobility if a lesion is in the endocervical canal (pedunculated intracavitary myoma / polyp). Lesions arising from the cervical stroma will remain fixed in position with transducer pressure.

Cervical Stenosis

= obliteration + obstruction of endocervical canal
= inability to insert a 2.5-mm wide dilator

A. CONGENITAL
   1. Transverse vaginal septum in uterus didelphys
   2. Congenital absence of cervix
B. ACQUIRED
   1. Cervical carcinoma: postmenopausal
   2. Endometrial cancer: premenopausal
   3. Benign masses: polyp, fibroid
   4. S/P radiation treatment
   5. S/P surgery, endocervical curettage, cone biopsy

• obstruction to menstrual flow → amenorrhea, dysmenorrhea
√ distension of endometrial cavity by secretions + blood products
√ narrowing of endocervical canal < 5 mm by HSG preventing insertion of HSG catheter
Cx: reflux endometriosis

VAGINA

Vaginal Cyst

1. Gartner duct cyst (above pubic symphysis)
2. Bartholin gland cyst (below pubic symphysis)
3. Skene duct cyst
4. **Müllerian / paramesonephric duct cyst**
   = aberrant embryologic remnant of paramesonephric duct
   Histo: mucinous pseudostratified columnar epithelium
   Location: anterolateral wall of vagina near cervix
5. **Epithelial inclusion cyst**
   = arise from urogenital sinus
   Histo: lined by transitional epithelium containing thick caseous material
6. **Epidermal / vaginal inclusion cyst**
   Cause: prior trauma / surgery
   Histo: stratified squamous epithelium
   Location: posterior / lateral wall of vagina

Vaginal Fistula

1. Enterovaginal fistula:
   (a) rectovaginal: incomplete healing of perineal laceration ← obstetric trauma, radiation therapy
   (b) anovaginal: inflammatory bowel disease (10% of patients with Crohn disease)
   (c) colovaginal: diverticulitis
2. Vesicovaginal fistula: hysterectomy, radiation therapy
3. Ureterovaginal fistula: vaginal hysterectomy

Vaginal & Paravaginal Neoplasm

A. PRIMARY benign
   1. Cavernous hemangioma of vulva
   2. Pedunculated submucosal leiomyoma prolapsed into vagina

B. Primary malignant
Frequency: 1–2% of all gynecologic malignancies; 20% of all vaginal malignancies

Cystic Lesions of Female Lower Genitourinary Tract			
Lesion	*Location*		*relative to pubic symphysis*
Skene duct cyst	urethral orifice	anterior vaginal introitus	inferior
Bartholin cyst	vaginal introitus	medial to labia minora	inferior
Gartner duct cyst	upper vagina	anterolateral wall	superior
Urethral diverticulum	midurethra	posterolateral margin	superior

1. Vaginal carcinoma
   (a) squamous cell carcinoma (90%)
   Associated with: human papilloma virus
   (b) adenocarcinoma (9%)
2. Melanoma (3%)
3. Sarcoma (1%): rhabdomyosarcoma
4. Adenoid cystic carcinoma of Bartholin gland

C. SECONDARY MALIGNANT
Frequency: 80% of all vaginal malignancies
← direct extension from bladder, rectum, cervix, uterus

HYSTEROSALPINGOGRAPHY

Fundic Depression on HSG

A. with normal outer contour
   1. Septate uterus
   2. Arcuate uterus
B. with abnormal outer contour
   1. Bicornuate uterus
   2. Fundal myoma

Filling Defect on HSG

1. Synechia
2. Endometrial polyp
3. Submucosal myoma
4. Uterine folds = parallel to long axis of uterus
5. Air bubbles

Abnormal Uterine Contour on HSG

1. Submucosal myoma
2. Adenomyosis

3. Trauma: cesarean section, myomectomy

GAS IN GENITAL TRACT

A. UTERUS
   1. Endometritis
   2. Superinfection of leiomyoma: more common in submucosal leiomyoma (insufficient blood supply)
   3. Bacterial metabolism of necrotic neoplastic tissue
   4. Fistula to GI tract: uterine cancer
   5. Pyometra ← obstruction by cervical cancer
   6. Gas gangrene ← clostridial infection from septic abortion

B. OVARY
   1. Superinfected ovarian neoplasm

C. VAGINA
   1. **Vaginitis emphysematosa**
      = nonbacterial self-limiting process mostly occurring during pregnancy characterized by numerous gas-filled spaces in submucosa of vagina + exocervix

ANATOMY AND PHYSIOLOGY OF THE FEMALE REPRO DUCTIVE SYSTEM

HUMAN CHORIONIC GONADOTROPIN

= hCG = glycoprotein elaborated by placental trophoblastic cells beginning the 8th day after conception

Immunologic Pregnancy Test

= indirect agglutination test for hCG in urine; cross-reaction with other hormones / medications possible

• becomes positive at 5 weeks MA

Advantages: readily available, easily + rapidly performed

Disadvantages: frequently false-positive + false-negative results

Sensitivity:

(a) slide: 400–15,000 mIU/mL (2-minute test time)

(b) test tube: 1,000–3,000 mIU/mL (2-hour test time)

Radioimmunoassay (RIA) Pregnancy Test

= measures beta subunit of hCG in serum with a sensitivity as low as 1–2 mIU/mL

◊ Serum β-hCG becomes positive at 3–4 weeks MA / 7–10 days following conception!

Standards:

(1) Second International Standard (SIS)

(2) International Reference Preparation (IRP)

(3) Third International Standard (TIS)

1 mIU/mL (SIS) = 2 mIU/mL (IRP) = 2 mIU/mL (TIS)

1 ng/mL = 5–6 mIU/mL (SIS)

= 10–12 mIU/mL (IRP or TIS)

◊ Variations of lab values of up to 50% can occur among different laboratories!

◊ 6–15% between-run precision!

Advantages: specific for hCG, sensitive

◊ Highly specific + sensitive for pregnancy

Disadvantages: requires specialized lab and 3–24 hours for completion

Sensitivity:

(a) qualitative: 25–30 mIU/mL (3-hour test time)

(b) quantitative: 3–4 mIU/mL (24-hour test time)

Rise:

> 66% increase of initial β-hCG level over 48 hours in 86% of NORMAL pregnancies

< 66% increase of initial β-hCG level over 48 hours in 87% of ECTOPIC pregnancies

◊ β-hCG levels double every 2 days during first 60 days of a NORMAL pregnancy!

"1–7–11 Rule"		
β–*hCG (IRP)*	*US Landmarks*	*Gestational Age*
1,000 mIU/mL	gestational sac	32 d (4.5 weeks)
7,200 mIU/mL	yolk sac	36 d (5.0 weeks)
10,800 mIU/mL	embryo + heart motion	40 d (6.0 weeks)

FOLLICLE-STIMULATING HORMONE (FSH)

Action: influence on (1) number of follicles, (2) development of ovarian cysts, (3) size of ovaries

Physiology: rises abruptly at birth ← decrease in estrogen + progesterone after loss of placenta; falls to low levels after 3 months of age; remains low until puberty

ANATOMY OF GESTATION

Choriodecidua

Chorion

[*chorion*, Greek = skin, leather]

= trophoblast + fetal mesenchyme with villous stems protruding into decidua; provides nutrition for developing embryo

(a) chorion **frondosum** = part adjacent to decidua basalis, forms primordial placenta [*frondosus* , Latin = foliage]

(b) chorion **laeve** = smooth portion of chorion with atrophied villi

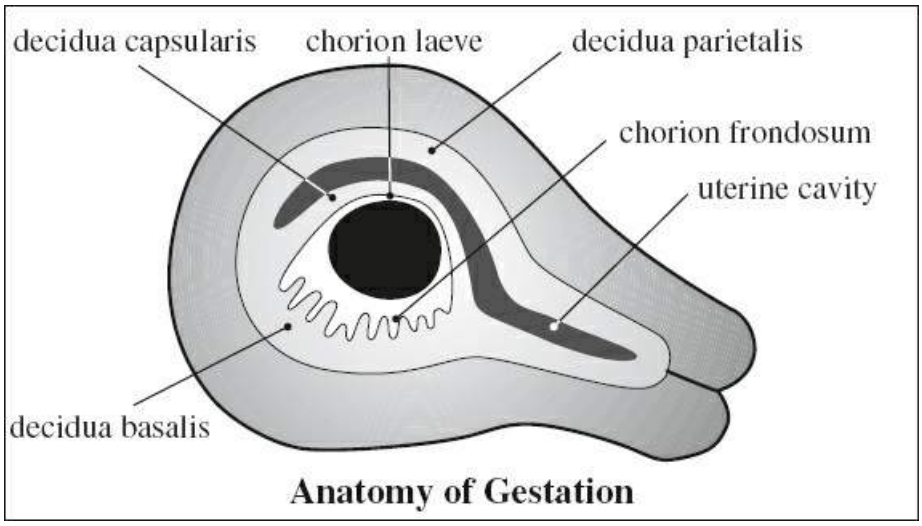
(c) "chorionic plate" = amnionic membrane covering the chorionic plate of the placenta

Decidua

(a) decidua basalis = between chorion frondosum + myometrium

(b) decidua capsularis = portion protruding into uterine cavity

(c) decidua parietalis = decidua vera = portion lining the uterine cavity elsewhere



Anatomy of Gestation

Gestational Sac (GS)

Origin: arises from blastocyst, which implants into secretory endometrium 6–9 days after ovulation (= 20–23 days of MA), surrounded by echogenic trophoblast

◊ GS measures 0.1 mm at time of implantation

√ **"intradecidual" sign** (earliest sign: 48% sensitive, 66% specific, 45% accurate at < 5 weeks GA) = eccentrically located fluid collection corresponding to gestational sac completely embedded within an echogenic decidua adjacent to a thin echogenic line (= collapsed uterine cavity) = highly suggestive for IUP

A nonspecific fluid collection with a smooth spherical / oval contour represents an IUP until proven otherwise!

√ **"double (decidual) sac" sign** (DDS) [most useful > 5 weeks GA with a mean sac diameter of 10 mm / 40 days GA] = 2 concentric hyperechoic rings surrounding a portion of the gestational sac + bulging into uterine cavity (delineated by a thin crescent of endometrial fluid) = ***definitive IUP***

(a) outer echogenic ring (= decidua parietalis)

(b) inner echogenic ring (= decidua capsularis)

√ GS surrounded by endometrial thickening > 12 mm

√ continuous hyperechoic inner rim > 2 mm thick

√ GS of spherical / ovoid shape without angulations

√ interposed hypoechoic line (apposed endometrial walls)

√ DDS present with a mean sac diameter of 10 mm (= 40 days GA)

◊ A "double decidual sac" sign correlates with the presence of a pregnancy in 98%!

◊ Absence of these 2 signs (in 35%) does not exclude an IUP

Gestational Sac Size

= average of 2–3 diameters (craniocaudad, AP, TRV) of rounded intrauterine anechoic (fluid) space within sac walls

◊ Used for dating between 6 and 12 weeks MA (identified as early as 4.5–5.0 weeks MA on transabdominal scan)

EGA [in wk] = (GS [in mm] + 25.43) ÷ 7.02

Accuracy: ± 7 days

Growth rate of mean sac diameter (MSD):

1.13 (range 0.71–1.75) mm per day (often variable)

Linear growth: 10 mm by 5th week MA

60 mm by 12th week MA

fills chorionic cavity by 11th–12th week MA

An MSD cutoff of 25 mm WITHOUT an embryo is a criterion for definitive pregnancy failure;
An MSD range of 16–24 mm WITHOUT an embryo is an indicator of suspicion of pregnancy failure.

Visualization of Gestational Sac

Earliest visualization: mean sac diameter of 2–3 mm

A. GS VISUALIZATION VERSUS β-hCG LEVEL (2nd International Standard):

(a) on transabdominal scan:

in 100% with β-hCG levels of > 1,800 IU/L

(b) on transvaginal scan:

in 20% with β-hCG levels of < 500 IU/L

in 80% with β-hCG levels of 500–1,000 IU/L

in 100% with β-hCG levels of > 1,000 IU/L

B. GS VISUALIZATION VERSUS MENSTRUAL AGE

5.0 ± 1 weeks = 10 mm

5.5 ± 1 weeks = 13 mm

6.0 ± 1 weeks = 17 mm

6.5 ± 1 weeks = 20 mm

C. GS VISUALIZATION VERSUS EMBRYO

Secondary Yolk Sac

= rounded sonolucent structure (outside amniotic cavity) within chorionic sac (= extracoelomic cavity) connected to umbilicus via a narrow stalk; formed by proliferation of endodermal cells; part of yolk sac is incorporated into fetal gut; the rest persists as sac connected to fetus by vitelline duct

Function:

(a) transfer of nutrients from trophoblast to embryo prior to functioning placental circulation

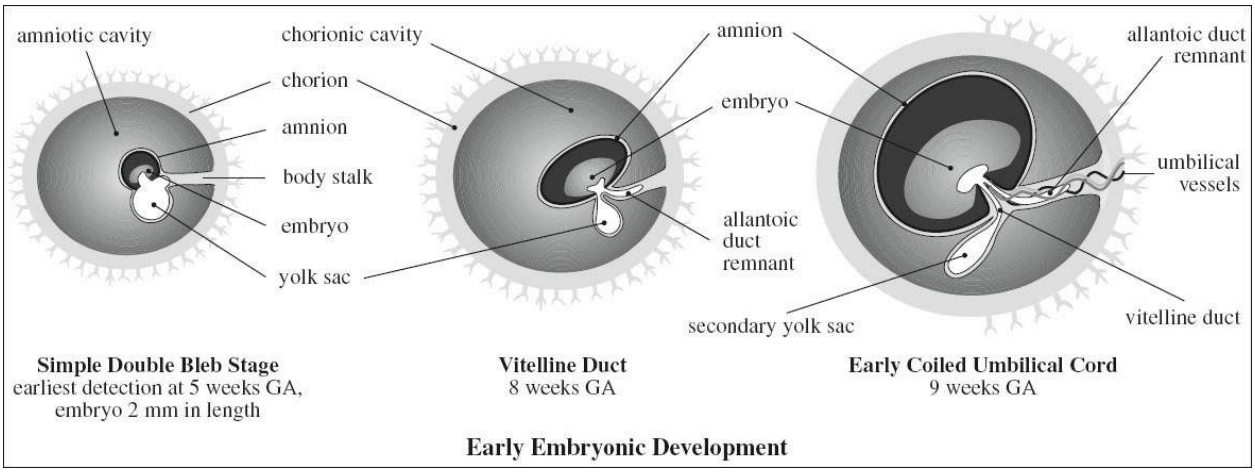
(b) early formation of blood vessels + blood precursors on sac wall

(c) formation of primitive gut

(d) source of primordial germ cells

Time of formation: at around 28 days MA

Mean size: 1.0 mm by 4.7 weeks MA; 2.0 mm by 5.6 weeks MA; 3.0 mm by 7.1 weeks MA; 4.0 (2.2–5.3) mm by 10 weeks MA; disappears around 12 weeks MA



Early Embryonic Development

◊ First visible structure within gestational sac = ***confirms IUP***

√ eccentrically located within gestational sac (inside chorionic cavity)

Definite visualization on transvaginal scan:

√ at 5.5 weeks MA

√ inside GS with a mean sac diameter of ≥ 8 mm

Definite visualization on transabdominal scan:

√ at 7 weeks MA

√ inside GS with a mean diameter of ≥ 20 mm

Embryo

Developmental stages:

Preembryonic period: 2nd–4th week MA

Trilaminar embryonic disk: during 5th week MA

Embryonic period: 6th–10th week MA

Physiologic umbilical herniation: 8th–12th week MA

Fetal period: early 11th week MA

Average growth rate:

0.7 mm per day / 1.5 mm every 2 days

√ curvilinear growth from 7 mm at 6.3 weeks MA → to 50 mm at 12.0 weeks MA

Earliest visualization (on endovaginal scan):

at 5.4 weeks MA at CRL of 1.2 mm

√ eccentrically located at periphery of yolk sac (inside amniotic cavity)

◊ Most accurate measurement of GA in 1st trimester!

VISUALIZATION OF EMBRYO VERSUS GS

(a) on transabdominal scan
100% visualization if gestational sac ≥ 27 mm

(b) on transvaginal scan
100% visualization if gestational sac ≥ 12 mm

◊ Transvaginal scan not necessary if on transabdominal scan gestational sac > 27 mm without evidence of embryo!

Failed pregnancy: nonvisualization of embryo with mean gestational sac size of ≥ 18 mm

Cardiac Activity of Embryo

◊ Heart begins to contract at a CRL of 1.5–3.0 mm = 22 days GA = 36 days MA

√ absence of cardiac activity in embryos < 4 mm may be normal

Definite visualization on endovaginal scan:

(a) at 46 days GA

(b) at mean sac diameter of 16 mm

(c) with CRL ≥ 5 mm = 6.2 weeks

A 7-mm CRL is necessary to yield a specificity and positive predictive value of **100%** → decreasing false-positive diagnosis associated with a 5-mm CRL cutoff.

Definite visualization on transabdominal scan:

(a) at 55 days GA

(b) mean sac diameter of 25 mm

Heart rate:

at 5-6 weeks GA 101 bpm

at 8-9 weeks GA 143 bpm

Gastrulation (2nd–4th week GA)

[*gaster*, Latin = stomach; *-ula*, Latin = diminutive suffix]

= transformation of bilaminar disk into trilaminar embryo

Stages:

› bilaminar embryo develops an **epiblast** (= layer facing amniotic cavity) + **hypoblast** (= layer facing yolk sac)

› disk forms a **mesoderm** "sandwich" bordered above by **ectoderm** + below by **endoderm**

› at both ends where embryonic ectoderm and endoderm meet are cranially the **oropharyngeal membrane** (= future mouth) + caudally the **cloacal membrane** (= future urogenital and anal orifices)

› craniocaudal + lateral folding converts the flat trilaminar embryonic disk into a **gut tube** within a **body tube**

› lateral edges of somatic mesoderm move ventrally toward each other creating a **coelomic space** (= future peritoneal cavity) that separates gut from body tube (GI tract from **primary abdominal wall**)

› myoblasts migrate into primary abdominal wall forming muscles and connective tissue

› the **cloaca** (= common chamber at caudal end) forms as precursor to the intestinal + urinary + genital tracts

› a ventral diverticulum (= allantois) projects from the cloaca into the connecting stalk (= **body stalk**) attaching the embryo to the chorionic mesoderm

Amnionic Membrane

= curvilinear echogenic line within chorionic sac; fills chorionic cavity by 11–12 weeks MA ← onset of fetal urine production at about 10 weeks

Fusion:

› fuses with chorionic membrane at 14–16 weeks MA to form the chorionic plate

› incomplete fusion with chorion frequent
(DDx: subchorionic hemorrhage, twin abortion, coexistent with limb-body wall complex)

Umbilical Cord

Function: communication between placenta and fetus allowing exchange of gas and nutrients

Embryology:

› cord forms between 7th–8th week post conception with contributions from body stalk, omphalomesenteric or vitelline duct, yolk sac, allantois

› junction of the amnion with ventral surface of embryo forms umbilicus

› allantoic vessels establish continuity with placental villi and form the vessels of the umbilical cord

› allantois / urachus develops as 2nd outpouching from primitive gut 12–16 weeks GA and projects into connecting stalk

› physiologic midgut herniation into base of umbilical cord at ~ 7–12 weeks (returns by end of 11th week GA)

› cord grows until end of 2nd trimester: average diameter of 17 mm, length of 50–60 cm

Anatomy:

› 2 umbilical arteries (= branches of the 2 internal iliac arteries) + 2 umbilical veins by 6 weeks GA
Function: deoxygenated blood from fetus to placenta
› one umbilical vein (remains after regression of right umbilical vein by 8 weeks GA) → connects to left portal vein → fissure for ligamentum venosum after birth
Function: oxygenated blood from placenta to fetus
› covered with unique compressible matrix of mucopolysaccharide-rich substance = Wharton jelly
› covered by amnion
› spiraling of cord with 0–40 helical turns (L > R) by 9 weeks
◊ coiling adds strength + resists compression of vessels
◊ normal cord length + coiling requires adequate fluid space and fetal activity

Cord thickness: 1–2 cm in diameter

(a) "lean" umbilical cord = cross-sectional area of cord measuring below 10th percentile for GA
Associated with: increased prevalence of fetal IUGR, oligohydramnios, fetal distress during delivery

(b) "fat" umbilical cord
Associated with: mothers with diabetes, fetus with aneuploidy

Umbilical coiling index (UCI):
= number of cord spirals completed per cm of cord length

(a) hypocoiled cord (UCI ≤ 0.29 / < 10th percentile)
Associated with:
increased rate of IUGR, fetal demise, intrapartum fetal heart rate decelerations, fetal distress at delivery, karyotype abnormalities, higher rate of abnormal cord insertion

(b) hypercoiled cord (UCI ≥ 0.6 / > 90th percentile)
Associated with:
increased rate of fetal IUGR, intrapartum fetal cardiac decelerations, vascular thrombosis, cord stenosis

PLACENTA

[*plakuos* , Greek = flat cake]

(a) fetal portion
1. Villi of chorion frondosum
contain arterial plexuses supplied by umbilical artery and protrude into intervillous space bathing in maternal blood

(b) maternal portion
2. Decidua placentalis: lines intervillous space

Imaging of Normal Placenta

CT:
@ 1st trimester
√ placenta indistinguishable from myometrium
@ 2nd trimester

√ hyperattenuating relative to subjacent myometrium following enhancement
√ rounded hypoattenuating foci surrounded by enhancing placenta = placental cotyledons

@ 3rd trimester
√ increased heterogeneity of normal placenta and visualization of venous lakes

Variant Morphology of Placenta

A. Additional lobes

1. **Succenturiate lobe of placenta**
   = ACCESSORY LOBE
   = single / multiple separate additional lobe(s) separate from but connected to main placenta by fetal blood vessels within membrane
   Prevalence: 0.14–3.00%
   Cause: placental villi atrophy in area of inadequate blood supply → proliferate in two opposite directions (**trophotropism**) with fetal vessels remaining at the site of villous atrophy
   Cx: (1) Retention of accessory lobe in utero → postpartum hemorrhage
   (2) Placenta previa (= implantation over cervical os) → intrapartum hemorrhage
   (3) Vasa previa (= connecting succenturiate vessels traversing internal os) may rupture → fetal blood loss
2. **Bilobed placenta**
   = 2 placentas of relative same size connected by a thin bridge of placental tissue
   Risk: none

B. **Placenta extrachorialis**
   = chorionic plate smaller than basal plate; ie, the transition of membranous to villous chorion occurs at a distance from the placental edge that is smaller than the basal plate radius

1. **Circummarginate placenta**
   Frequency: up to 20% of placentas
   Risk: no clinical significance
   √ fetal membranes form a flat ring at site of attachment to chorionic plate
   √ placental margin not deformed
2. **Circumvallate placenta**
   = attachment of fetal membranes form a folded thickened ring with underlying fibrin + often hemorrhage
   Prevalence: 1–2% of pregnancies
   Risk: premature labor, threatened abortion, increased perinatal mortality, abruption, marginal hemorrhage

C. **Placenta membranacea**
   = thin membranous placenta circumferentially occupying the entire periphery of chorion + presence of well-vascularized placental villi in the peripheral membranes ← failure of regression
   Cause: ? endometritis, endometrial hyperplasia, extensive vascularization of decidua

capsularis, previous endometrial damage by curettage

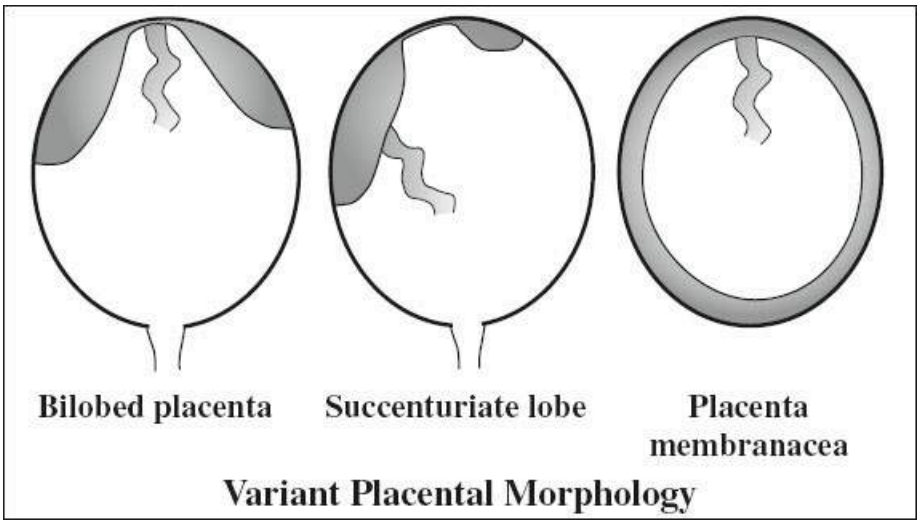
Risk: repeated vaginal bleeding extending into 2nd trimester; abortion at 20–30 weeks; postpartum hemorrhage

√ thickened outline over whole gestational sac (0.2–3.0 cm)

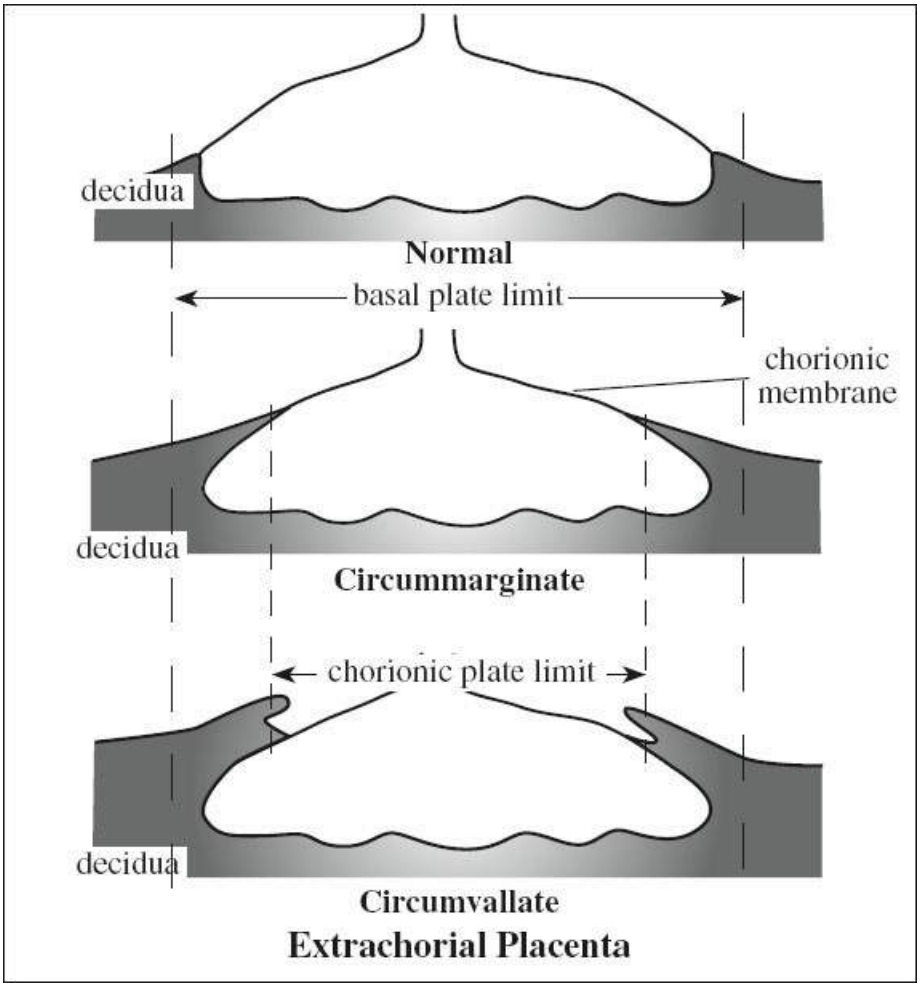
√ may show additional distinct disk of placenta

Placental Grading

= grading according to echo appearance of basal zone, chorionic plate, placental substance



Variant Placental Morphology



◊ Premature placental calcifications are associated with cigarette smoking, hypertension, IUGR!

◊ Not considered useful because placental grading is imprecise for fetal dating or for fetal lung maturity!

GRADE 0

√ homogeneous placenta + straight line of chorionic plate

Time: < 30 weeks MA

GRADE 1

√ undulated chorionic plate + scattered bright placental echoes

Time: seen at any time during pregnancy; in 40% at term

◊ in 68% L/S (lecithin-sphingomyelin) ratio > 2.0

GRADE 2

√ linear bright echoes parallel to basal plate

√ confluent stippled echoes within placenta ± indentations of chorionic plate

Time: rarely seen in gestations < 32 weeks MA and in 40% at term

◊ in 87% L/S ratio > 2.0

GRADE 3

√ calcified intercotyledonary septa, often surrounding sonolucent center

Time: rarely seen in gestations < 34 weeks MA;
in 15–20% at term

◊ in 100% L/S ratio > 2.0 (= strongly correlated with lung maturity)

Premature Placental Senescence

= grade 3 placenta seen in gestation < 34 weeks MA

◊ In 50% suggestive of maternal hypertension / IUGR

Uteroplacental Circulation

By 20 weeks MA trophoblast invades maternal vessels and transforms spiral arteries into distended tortuous vessels = uteroplacental arteries

Physiology: maintains fetal pulmonary, hepatic, renal function by exchange of gas, metabolites, nutrients and indirect vascular interaction of fetal with maternal blood

Histo:

(a) in decidual segments of spiral arteries: proliferating trophoblast from anchoring villi invades lumen of spiral arteries + partially replaces endothelium

(b) in myometrial segments of spiral arteries: disintegration of smooth muscle elements → loss of elastic lamina → easily distensible vascular system of low resistance

Uterine Blood Volume Flow

› 50 mL/min shortly after conception

› 500–900 mL/min by term

Intervillous blood flow: 140 ± 53 mL/min (by 133Xe washout)

Umbilical Artery Doppler

Variables affecting Doppler measurements:
site of Doppler (close to placenta preferred), fetal heart rate, fetal breathing, drugs (eg, ritodrine hydrochloride decreases S/D ratio)

√ degree of diastolic flow increases as gestation progresses

› high-resistance flow @ < 20 weeks

› S/D ratio between 3.3 and 4.3 @ ≥ 20 weeks

› S/D ratio between 1.7 and 2.4 @ term

√ highly turbulent flow

IUGR Lesions

= narrowing of vascular lumen through

(a) thrombosis of decidual segments of uteroplacental aa.

(b) failure of development of myometrial segments of uteroplacental arteries

FETAL MENSURATION

◊ US is more reliable than LMP / physical examination!

Ultrasound Milestones

√ gestational sac w/o embryo or yolk sac = 5.0 weeks

√ gestational sac + yolk sac w/o embryo = 5.5 weeks

√ heartbeat ± embryo < 5 mm = 6.0 weeks
Accuracy: ± 0.5 week

Fetal Age

= GESTATIONAL AGE (GA) = "MENSTRUAL AGE" (MA)
= age of pregnancy based on woman's regular last menstrual period (LMP) projecting the estimated date of confinement (EDC) at 40 weeks
◊ Note the inaccurate clinical usage of "gestational age," which strictly speaking refers to the true (histologic) age of the pregnancy counting from the day of conception, whereas "menstrual age" refers to the (clinical) age of the pregnancy accounting for the ~ +2 weeks discrepancy!
◊ On subsequent US scans GA = GA assigned at 1st ultrasound + number of intervening weeks!

Timeline of Normal Early Pregnancy

Time Period [weeks]	*Developmental Milestone*
0	last menstrual period
2	conception
4.5–5.0	gestational sac appears
5.0–5.5	yolk sac appears
6.0	embryo appears, cardiac pulsation > 100 bpm
6.5–7.0	amniotic membrane appears, cardiac pulsation > 120 bpm
7–8	spine develops
8	head curvature separated from body, 4 limb buds appear
8.0–8.5	intrinsic motion of embryo occurs
8–10	rhombencephalon develops

Accuracy of Biometry (95% confidence range)

Stage	*Based on*	*Accuracy [weeks]*
1st trimester		
5–6 weeks	US milestones	±0.5
6–13 weeks	CRL	±0.7
2nd trimester		
14–20 weeks	cBPD / HC	±1.2
	BPD / FL	±1.4
20–26 weeks	cBPD / HC	±1.9
	BPD / FL	±2.1–2.5
3rd trimester		
26–32 weeks	cBPD / HC / FL	±3.1–3.4
	FL	±3.1
32–42 weeks	cBPD / HC / FL	±3.5–3.8
	FL	±3.5

ACCURACY OF CLINICAL ASSESSMENT:
menstrual history ±2–3 weeks
1st-trimester exam ±2 weeks
fundal height ±4 weeks

Early Embryonic Size

= length of embryo < 25 mm on transvaginal scan performed at < 11 weeks MA
Gestational age (days) = embryonic size (mm) + 42
Accuracy: ± 3 days

Crown-Rump Length (CRL)

= length of fetus; useful up to 12 weeks MA (usually identified by 7 weeks MA on transabdominal scan)
Rule of thumb: MA (in weeks) = CRL (in cm) + 6
Accuracy: ± 5–7 days

Biparietal Diameter (BPD)

= measured from leading edge to leading edge of calvarial table at widest transaxial plane of skull = level of thalami + cavum septi pellucidi + sylvian fissures with middle cerebral arteries

◊ Excellent means of estimating GA in 2nd trimester > 12 weeks MA

Accuracy: 2 mm for "between occasion error"
◊ Most accurate for dating if combined with HC, AC, FL provided body ratios are normal!
◊ Less reliable for dating in 3rd trimester because of increasing biologic variability!

Discordant Estimated Date of Confinement (EDC) by LMP and BPD

1. Methodological error in measurement
   (a) wrong axial section
   (b) cranial compression (multiple gestation, breech presentation, oligohydramnios, dolichocephaly)
2. Erroneous LMP
   other measurements (AC, FL) correlate with BPD
3. Abnormal head growth
   (a) BPD < AC: microcephaly, fetal macrosomia
   (b) BPD > AC: intracranial abnormality, asymmetric IUGR

Cephalic Index (CI)

= BPD / OFD; measurements of BPD and occipitofrontal diameter (OFD) both from outer to outer edge of calvarium
◊ Confirms appropriate use of BPD if ratio is between 0.70 and 0.86 (2 SD)

Corrected BPD (cBPD)

= BPD and OFD are used to adjust for variations in head shape

$$cBPD = \sqrt{BPD \times OFD} \div 1.26$$

Head Circumference (HC)

Used if ratio of BPD/OFD outside 0.70–0.86

HC = ([BPD + OFD]/2) x π

= ([BPD + OFD] x 1.62) x 3.1417

Accuracy: slightly less than for BPD

HC too large: hydrocephalus, hydranencephalus, intracranial hemorrhage, short limb dystrophies, tumor

HC too small: anencephaly, cerebral infarction, synostosis, microcephaly vera

Abdominal Circumference (AC)

= measured at level of vascular junction of umbilical vein with left portal vein ("hockey-stick" appearance) where it is equidistant from the lateral walls in a plane perpendicular to long axis of fetus; measured from outer edge to outer edge of soft tissues

◊ Allows evaluation of head-to-body disproportion

◊ Better predictor of fetal weight than BPD

AC too large: GI tract obstructions, obstructive uropathy, ascites, hepatosplenomegaly, congenital nephrosis, abdominal tumor

AC too small: diaphragmatic hernia, omphalocele, gastroschisis, renal agenesis

Femur Length (FL)

= measurement of ossified femoral diaphysis

Error: "flare" at distal end included in measurement (= reflection from cartilaginous condyle)

Thoracic Circumference (TC)

= measured in axial plane of chest, which includes four-chamber view of heart without inclusion of SQ tissue

◊ Linear growth between 16 and 40 weeks similar to AC

Useful age-independent parameter: TC÷AC > 0.80

Estimated Fetal Weight (EFW)

based on measurements of head size (BPD / HC), abdominal size (AD / AC), and femur length (FL)

Accuracy:

body part used	*95% confidence range*
abdomen	± 22%
head + abdomen	± 17–20%
head + abdomen + femur	± 15%

Appearance of Epiphyseal Bone Centers

in 95% of all cases

› distal femoral epiphysis (DFE): > 33 weeks GA

› distal femoral epiphysis (DFE) > 5 mm: > 35 weeks

› proximal tibial epiphysis (PTE): > 35 weeks GA

› proximal humeral epiphysis (PHE): > 38 weeks GA

CNS Ventricles

width of 3rd ventricle: < 3.5 mm (any gestational age)

Diameter of Cisterna Magna

measured from inner margin of occiput to vermis cerebelli: 2–10 mm

ASSESSMENT OF FETAL WELL-BEING

Amniotic Fluid Index

= sum of vertical depths of largest clear amniotic fluid pockets in the 4 uterine quadrants measured in mm

Method: patient supine, uterus viewed as 4 equal quadrants, transducer perpendicular to plane of floor + aligned longitudinally with patient's spine

Variation: 3.1% intraobserver, 6.7% interobserver

Result:

- › 95th percentile: 185 mm at 16 weeks GA, rising to 280 mm at 35 weeks, declining to 190 mm at 42 weeks
- › 5th percentile: 80 mm at 16 weeks GA, rising to 100 mm at 23 weeks, declining to 70 mm at 42 weeks

Biophysical Profile (Platt and Manning) = BPP

= in utero Apgar score = assessment of fetal well-being

Gestational age at entry: 25 weeks MA

Observation period: 30 (occasionally 60) min; ordinarily < 8 min needed; in 2% full 30 min required

A. ACUTE BIOPHYSICAL VARIABLES

◊ Subject to rhythmic variation coincident with sleep-wake cycle!

1. **Fetal breathing movement** (FBM):

   √ ≥ 1 episode of chest + abdominal wall movement for at least 30 seconds (time is arbitrary to avoid confusion with general body movements / maternal respiration)

   stimulated by: glucose, catecholamine, caffeine, prostaglandin synthetase inhibitor

   suppressed by: barbiturates, benzodiazepine, labor, hypoxia, asphyxia, prostaglandin E2

2. **Fetal body movement**:

   √ ≥ 3 discrete movements of limbs / trunk

   Influenced by: glucose, gestational age, time of day, maternal drugs, intrinsic rhythm, labor

3. **Fetal tone**

   upper + lower limbs usually fully flexed with head on chest; least sensitive test parameter

   √ ≥ 1 episode of opening + closing of hand / extension + flexion of limb

B. CHRONIC FETAL CONDITION

4. **Amniotic fluid volume**

   √ at least one pocket ≥ 2 cm in vertical diameter in two perpendicular planes

◊ Avoid inclusion of loops of cord!

BPP Score

for each test: 2 points if normal; 0 points if abnormal

False-negative rate: 0.7÷1,000

◊ The probability of fetal death within a week of a BPP score of 8/8 is 1÷1,000!

Stress Tests

Nonstress Test (NST)

◊ Test needed in less than 5% of cases!

√ reactive fetal heart rate tracing (normal) = at least 4 fetal heart accelerations (> 15 bpm over baseline lasting > 15 seconds) in a 20-minute period subsequent to fetal movement > 34 weeks GA

√ nonreactive (abnormal) fetal heart rate tracing = absence of acceleration in a continuous 40-min observation period

N.B.: no heart accelerations in immaturity, during sleep cycle, with maternal sedative use

Accuracy: false-negative rate of 3.2÷1,000 (if done weekly) or 1.6÷1,000 (if done biweekly); 50% false-positive rate for neonatal morbidity + 80% for neonatal mortality

Results of Biophysical Profile Score
(including NST for a maximum of 10 points)

Score	*Fluid*	*Interpretation*	*Perinatal Mortality*
10		asphyxia rare	0.0%
8	normal	asphyxia rare	<0.1%
8	abnormal	chronic compromise	8.9%
6	normal	equivocal	variable
6	abnormal	asphyxia probable	8.9%
4		asphyxia highly probable	9.1%
2		asphyxia almost certain	12.5%
0		asphyxia certain	60.0%

Contraction Stress Test (CST)

= external monitoring after injection of oxytocin / maternal breast stimulation

√ > 3 uterine contractions in 10-minute period

Accuracy: false-negative rate of 0.4÷1000; 50% false-positive rate

INVASIVE FETAL ASSESSMENT

Amniocentesis

Indications:

(1) Inadequate sonographic fetal anatomic survey ← fetal position / maternal body habitus

(2) Equivocal sonographic findings: eg, abnormal posterior fossa but spinal defect not seen

(3) Experienced sonographer not available
(4) Nonlethal anomaly detected on level I sonogram for which karyotype testing is appropriate

Risk: fetal loss rate generally quoted as 1÷200 (0.5%)

A. FETAL RISK
   1. Spontaneous abortion (0.3–1.5%)
   2. Amniotic fluid leak
   3. Chorioamnionitis
   4. Fetal injury: skin dimple, limb gangrene, porencephalic cyst, hemothorax, spleen laceration, orthopedic abnormality, amniotic band syndrome

B. MATERNAL RISK (rare)
   1. Bowel perforation
   2. Hemorrhage
   3. Isoimmunization

Diagnostic Amniocentesis

1. Genetic studies: karyotype, DNA analysis, biochemical assay
   Timing: early (11–15 weeks), late (15–18 weeks)
2. Neural tube defect: α-fetoprotein, acetylcholinesterase
3. Isoimmunization: Δ-OD 450
4. Fetal lung maturity
5. Intraamniotic infection
6. Confirmation of ruptured membranes

Advantage over CVS:

1. Error rate (< 1% versus 2%)
2. Culture failure rate (0.6% versus 2.2%)
3. Fetal loss rate (0.6–0.8% less)

Therapeutic Amniocentesis

1. Polyhydramnios
2. Twin-twin transfusion syndrome

Technique:

√ avoid fetus, placenta, umbilical cord, uterine contraction, fibroid, large uterine vessel
√ use continuous ultrasound guidance
√ inject 2–5 mL of indigo carmine dye in first sac of twin (colorless fluid assures that second sac has been entered)

Chorionic Villus Sampling (CVS)

= aspiration of cells from chorion frondosum for genetic studies (karyotype, DNA analysis, biochemical assay)

◊ Transabdominal CVS for rapid karyotyping in 2nd + 3rd trimester = placental biopsy

Advantage: > 2 weeks earlier results compared with amniocentesis

Timing: 9–11 weeks

Approach:

(a) transcervical route = catheter introduced through cervix into chorion frondosum, easier for posterior placenta; contamination by cervical flora possible
◊ CONTRAINDICATED in cervical infections!
(b) transabdominal route = 20–22-gauge needle inserted through anterior abdominal wall; easier for anterior / fundal placenta; sterile technique

Chromosome analysis:
(a) direct preparation = analysis of cytotrophoblasts (may have different karyotype than fetus) → analysis can be performed immediately
(b) villus culture = cells from central mesenchymal core (same karyotype as fetus) → cultured for several days before analysis

Errors (2%):
1. **Mosaicism** = cell line forming cytotrophoblast may develop abnormal karyotype while fetal cell line is normal
2. Maternal contamination = cells from maternal decidua may overgrow mesenchymal core cells

Risks:
1. Spontaneous abortion (1%)
2. Perforation of amniotic sac
3. Infection
4. Teratogenesis: limb reduction defect

Cordocentesis

= PERCUTANEOUS UMBILICAL BLOOD SAMPLING (PUBS)

A. DIAGNOSTIC CORDOCENTESIS
1. Hematocrit
2. Karyotype
3. Immunodeficiency: chronic granulomatous disease, severe combined immunodeficiency
4. Coagulopathy: von Willebrand syndrome, factor deficiency
5. Platelet disorder: alloimmune / idiopathic thrombocytopenic purpura
6. Hemoglobinopathy: sickle cell anemia, thalassemia
7. Infection: toxoplasmosis, rubella, parvovirus, varicella, cytomegalovirus
8. Hypoxia / acidosis

B. THERAPEUTIC CORDOCENTESIS
1. Intravascular fetal transfusion (fresh rh-negative CMV-negative leukodepleted irradiated packed cells compatible with mother infused at 10–15 mL/min)
2. Direct delivery of medication to fetus

Cx:
1. Chorioamnionitis
2. Rupture of membranes
3. Umbilical cord hematoma
4. Umbilical cord thrombosis
5. Bleeding from insertion site
6. Fetal bradycardia

MULTIPLE GESTATIONS

Prevalence: 1.2% of all births; in 5–50% clinically undiagnosed at term
Occurrence (Hellin rule):

twins	in	1÷85 pregnancies (= 85^1)
triplets	in	1÷7,225 pregnancies (= 85^2)
quadruplets	in	1÷614,125 pregnancies (= 85^3)
quintuplets	in	1÷52,200,625 pregnancies (= 85^4)

- uterus large for dates
- may have ↑ hCG, HPL (human placental lactogen), AFP levels

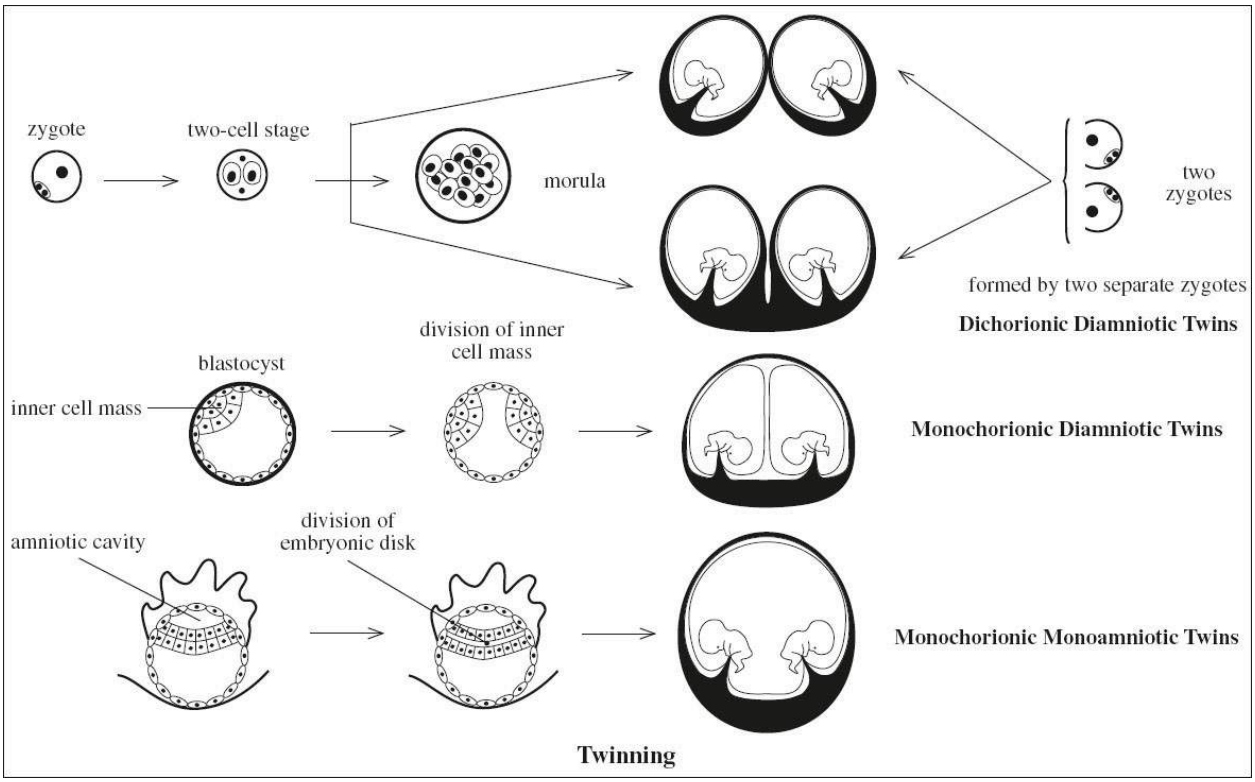
Perinatal morbidity & mortality compared with singletons:
twins: up to 5-fold increase
triplets: up to 18-fold increase

Twin Pregnancy

Zygote = fertilized egg
Prevalence: in up to 2.5% of all pregnancies

Monozygotic Twins (⅓)

= identical TWINS
= division of a single fertilized ovum fertilized by one sperm during earliest stages of embryogenesis (chorion differentiates 4 days and amnion 8 days after fertilization)
Prevalence: 1:250 birth (constant around the world)
Predisposing factors: (1) Advanced maternal age
(2) In vitro fertilization
√ same sex + identical genotype
Cx: (1) perinatal mortality 2.5 times greater than for dizygotic twins
(2) Fetal anomalies 3–7 times higher than in dizygotic twins / singletons (often only affecting one twin): anencephaly, hydrocephalus, holoprosencephaly, cloacal exstrophy, VATER syndrome, sirenomelia, sacrococcygeal teratoma



Embryologic Events in Monozygotic Twinning			
Days after Fertilization	*Embryologic Event*	*Cleavage results in*	
		Chorion	*Amnion*
1–2	cell divisions → morula	di~	di~
3–4	chorionic differentiation		
6	blastocyst implants in endometrium	mono~	di~
8	amnionic differentiation	mono~	mono~
>13	division of embryonic disk	mono~	mono~
		but conjoined	

DICHORIONIC DIAMNIOTIC TWINS (30%)

= separation at two-cell stage (= blastomere) ~ 60 hours / < 4 days after fertilization
√ 2 separate fused / unfused placentas
√ membrane > 2 mm ← 2 separate chorionic sacs + 2 separate amniotic sacs (92% accurate for dichorionic diamniotic twins)
√ "twin peak" sign = triangular projection of placental tissue insinuated between layers of intertwin membrane

MONOCHORIONIC DIAMNIOTIC TWINS (69–80%)

= separation in blastocyst stage between 4th and 7th day after fertilization (chorion already developed and separated from embryo)
√ 2 separate amniotic sacs in single chorionic sac

◊ Common monochorionic placenta has vascular communications in 100%!

Cx: (1) Twin-twin transfusion syndrome
(2) Twin embolization syndrome
(3) Acardiac parabiotic twin

MONOCHORIONIC MONOAMNIOTIC TWINS (1%)

= division of embryonic disk between 8th and 12th day after fertilization (amniotic cavity already developed)

√ common amniotic + chorionic sac without separating membrane

√ entanglement of cords = the only definitive positive sonographic sign of monoamnionicity

Cx: double perinatal mortality up to 45%
(1) Entangled umbilical cord (70%)
(2) True knot of cord
(3) Conjoined twins: umbilical cord with > 3 vessels, shared fetal organs, continuous fetal skin contour

Prognosis: 40% survival rate

Dizygotic Twins (⅔)

= FRATERNAL TWINS

(a) fertilization of 2 ova by 2 separate spermatozoa during 2 simultaneous ovulations (occurring either in both ovaries or in one ovary)

(b) **superfetation** = fertilization of 2 ova by 2 separate spermatozoa during 2 subsequent ovulations (? frequency)

(c) **superfecundation** = 2 ova fertilized by 2 different fathers (very rare)

Prevalence: 1÷80 to 1÷90 births

Predisposing factors:
(1) Advanced maternal age (increased up to age 35): ↓ gonadal-hypothalamic feedback + ↑ FSH levels
(2) Ovulation-inducing agents (multiple pregnancies in 6–17% with clomiphene, in 18–53% with Pergonal®)
(3) Maternal history of twinning (3 times as frequent compared with normal population)
(4) Increased parity
(5) Maternal obesity
(6) Race with inherited predisposition for multiple ovulations (Blacks > Whites > Asians)

√ different phenotypes; same / opposite sex

√ always dichorionic diamniotic

Growth Rates of Twins

◊ Twins should be scanned every 3–4 weeks > 26–28 weeks GA!

A. Below 30–32 weeks GA
√ normal individual twins grow at same rate as singletons
√ BPD growth rates similar to singleton fetuses

B. Beyond 30–32 weeks GA
√ combined weight gain of both twins equals that of a singleton pregnancy (AC of

twins < AC of singleton)
◊ Weight of twin fetus falls below that of singleton when combined weight of twins > 4,000 g!
√ BPD + HC growth may / may not be affected (controversial)
√ FL not affected

DISCORDANT GROWTH

= weight difference at birth > 25%
Cause: (1) Twin-twin transfusion syndrome
(2) IUGR of one fetus
√ BPD difference > 5 mm (discordant growth in 20–30%)
√ discordant HC increases probability of IUGR
√ AC is single most sensitive parameter for IUGR
√ EFW is the most sensitive set of combined parameters for IUGR
√ > 15% S/D ratio difference of umbilical artery Doppler waveforms between twins

Amnionicity & Chorionicity

Rules:
◊ Only monozygotic twins can give rise to monochorionic monoamniotic pregnancies!
◊ All monoamniotic twins must also be monochorionic!
◊ All dizygotic twins must be dichorionic and diamniotic!
◊ 77% of all twin pregnancies are dichorionic
› 67% of all dizygotics (⅔ of all twins)
› 10% of all monozygotics (⅓ of all twins)

1. GESTATIONAL SACS (< 10 weeks MA)
Accuracy: 100% in 1st trimester, 80–90% in 2nd trimester
√ 2 gestational sacs, each with a live fetus, indicates dichorionic twinning
√ single gestational sac with 2 live fetuses indicates monochorionic twins
√ single extraembryonic coelom indicates monochorionic twins
2. YOLK SAC
√ number of yolk sacs = number of amnions
3. FETAL GENDER
√ different genders (in 25% of twin pregnancies) must be dizygotic twins and thus dichorionic!
(DDx: testicular feminization demonstrates female external genitalia with a 46,XY karyotype)
√ identical sex twins with a monochorionic placenta must be monozygotic
√ identical sex twins with a dichorionic placenta require further analysis to determine zygosity
4. PLACENTAL SITES
√ 2 placentas (in 45% of twin pregnancies) indicate dichorionic diamniotic pregnancy
√ 1 placenta indicates
(a) monochorionic pregnancy OR
(b) dichorionic pregnancy with fused placenta (occurs in 50% of dichorionic twin

pregnancies)

5. CHORIONIC PEAK
   - √ "**twin peak**" sign in late 1st and early 2nd trimester (= triangular projection of placental tissue extending beyond chorionic surface of placenta + insinuated between layers of intertwin membrane + wider at chorionic surface with tapering to a point some distance inward from surface) indicates dichorionic pregnancy
6. MEMBRANE
   - √ separating membrane confirms diamniotic pregnancy, but does not distinguish between mono- or dichorionic pregnancy
   - √ dichorionic membrane (2 layers of chorion + 2 layers of amnion) is thicker (> 2 mm) than monochorionic membrane (2 layers of amnion < 1 mm): 88–92% accuracy in 1st trimester, 39–83% accuracy in 2nd + 3rd trimester
     - ◊ All membranes appear to be thin in 3rd trimester!
   - √ absence of membrane suggests a monoamniotic monochorionic twin pregnancy
     - ◊ Nonvisualization of membrane is not sufficient evidence of monoamnionicity due to technical factors!
7. CORD
   - √ entanglement of cords is the only definitive positive sonographic sign of monoamnionicity
   - √ simultaneous recording of fetal arterial signals at nonsynchronous rates within wide Doppler gate
8. AMNIOGRAPHY
   - √ detection of imbibed intestinal contrast in both twins by CT following single sac contrast injection proves monoamniotic monochorionic twin pregnancy

Risks of Multiple Gestations

1. Placental abruption 3-fold
2. Anemia 2.5-fold
3. Hypertension 2.5-fold
4. Congenital anomaly 2–3-fold
5. Preterm delivery 12-fold
6. Perinatal mortality 4–6-fold

◊ Risk increases with number of fetuses, monozygosity, monochorionicity

Risk for IUGR in Multiple Gestations

monochorionic-monoamniotic > monochorionic-diamniotic > dichorionic-diamniotic

Risk for Perinatal Mortality in Multiple Gestations

1% for singletons, 9% for diamniotic dichorionic twins,
26% for diamniotic monochorionic twins,
50% for monoamniotic monochorionic twins

Prognosis:

(1) Perinatal mortality 5–10 times that of singleton pregnancy (91–124÷1,000 births)
   - › 9% for dichorionic diamniotic twins
   - › 26% for monochorionic diamniotic twins

› 50% for monochorionic monoamniotic twins
(a) preterm delivery with birth weight < 2,500 g
(b) IUGR (25–32%; 2nd most common cause of perinatal mortality + morbidity)
(c) amniotic fluid infection (60%)
(d) premature rupture of membranes (11%)
(e) twin-twin transfusion syndrome (8%)
(f) large placental infarct (8%)
(g) placenta previa
(h) abruptio placentae
(i) preeclampsia
(j) cord accidents
(k) malpresentations
(l) velamentous cord insertion (7-fold increase compared with singleton pregnancy)

(2) Fetal death in utero: 0.5–6.8%; 3 times as often in monochorionic than in dichorionic gestations
◊ 50% of twin gestations seen at 10 weeks GA will be singletons at birth!

(3) Increased risk of congenital anomalies: 23÷1,000 births = twice as frequent as in singletons; 3–7 times more frequent in mono- than in dizygotic twins

UTERUS

Uterine Size

◊ Overfilling of urinary bladder can modify uterine shape!

A. PREPUBERTAL UTERUS

(a) neonate

√ uterine size:
› length of 2.3–4.6 (mean, 3.4) cm
› fundal width of 0.8–2.1 (mean, 1.2) cm
› cervical width of 0.8–2.2 (mean, 1.4) cm
◊ becomes smaller by 4th month of life (2.6–3.0 cm)

√ uterine shape:
› **spade**-shaped uterus (58%) with cervix often twice as thick as fundus
› **tube**-shaped uterus (32%) with cervical + fundal AP measurements identical
› adult **pear**-shaped uterus (10%) with fundus wider than cervix

Uterine Size and Shape

Stage	*Uterine Length [cm]*	*Fundal Width [cm]*	*Uterine Body-to-Cervix Ratio*
Neonatal	3.5	1.2	2÷1
Pediatric	1–3	0.4–1.0	1÷1
Prepubertal	3–4.5	0.8–2.1	1–1.5÷1
Pubertal	5–8	1.6–3.0	1.5–2÷1
Reproductive	8–9	3–5	2÷1
Postmenopausal	3.5–7.5	1.2–1.8	1–1.5÷1

√ endometrium:
√ thin echogenic endometrium ± surrounding hypoechoic halo
√ endometrial fluid (in 23%) ← maternal hormonal stimulation
◊ Best time to evaluate uterus in child with ambiguous genitalia is first few months of life!

(b) infant

Age: infancy to 7 years of age

√ uterine size:
› length of 2.5–4.5 (mean, 3.3) cm
› fundal width of 0.4–1.0 cm
› cervical width of 0.6–1.0 cm
√ cervix occupies ²/₃ of uterine length
√ thin echogenic line of endometrium visible in 50%

(c) prepuberty

√ uterine size:
› mean length of 4.3 cm
› fundal width of 0.8–2.1 (mean, 1.2) cm
› cervical width of 0.8–2.2 (mean, 1.4) cm
√ usually tubular configuration with fundocervical ratio of 1÷1

B. PUBERTY

√ pear-shaped uterus with thick and round body
√ uterine body-to-cervix ratio 1.5÷1

C. POSTPUBERTAL UTERUS

› nulliparous: 5–8 cm (L); 3 cm (AP); 1.6–3.0 cm (TRV)
› multiparous: 6–11 cm (L); 3–4 cm (AP); 3–5 cm (TRV)
√ fundocervical ratio of 2÷1 to 3÷1
√ mean uterine volume of 90 cm^3

D. POSTMENOPAUSAL UTERUS

• most rapid decline in size within first 10 years

> 65 years: 3.5–7.5 cm (L); 1.2–3.3 cm (AP); 1.2–1.8 cm (TRV)

√ fundocervical ratio of 2÷1 to 1÷1
√ calcified uterine arcuate vessels, especially with diabetes / vascular disease / hypertension / hypercalcemia

Uterine Position

Flexion = angle of long axis of uterine body to that of cervix
Version = angle of long axis of cervix to long axis of vagina
mnemonic: **V** for **V**agina and **V**ersion!
Anteversion + anteflexion = most common position
Cave: Retroversion can be mistaken for a pelvic mass!

Trilaminar Uterine Zonal Anatomy (on T2WI)

◊ Premenarchal uterus has indistinct zonal anatomy
◊ Thickness of zones depends on menstrual cycle + hormonal medication!

1. ENDOMETRIUM

√ high signal intensity ← mucin-rich endometrial glands

2. JUNCTIONAL ZONE = INNER MYOMETRIUM
   Mean thickness: < 12 mm
   Histo: compact smooth muscle fibers with 3-fold increase in number + size of nuclei compared with outer myometrium
   √ low SI (= compact smooth muscle with lower water content); seen in 40–60%, may not be visible in premenarchal + postmenopausal women
3. OUTER MYOMETRIUM
   Histo: 65–70% smooth muscle
   √ intermediate SI (= less compact muscle with greater water content + blood vessels); → increases during secretory phase
4. OUTER SURFACE OF UTERUS
   √ thin low-signal intensity line

Uterine Enhancement Pattern

1. Myometrium
   demarcates level of internal cervical os
2. Inner mucosal + outer stromal layers of cervix
   √ hypoattenuating on CECT
3. Inner stromal layer of cervix

Cervix

= lower cylindrical portion of uterus
Size: 2.5–3.0 cm (L) x 2.5 cm (W)
Stroma: primarily collagenous tissue + smooth muscle (15%)
Portions:
(1) Supravaginal upper portion = **endocervix**
• not palpable / visible by pelvic exam
(2) Lower portion protruding into vagina = **ectocervix** encircled by vagina (higher posteriorly and laterally) forming **fornices** (= vaginal recesses)
• palpable during pelvic exam + visible with speculum

US:
√ ovoid / round on short-axis (coronal endovaginal) view
√ cylindrical on long-axis (sagittal)
√ little / NO vascularity on color Doppler

Ectocervix

Histo: mucosa composed of stratified squamous epithelium similar to vaginal epithelium
Transformation zone = **squamocolumnar junction**
= region where glandular tissue (columnar epithelium) is replaced by squamous epithelium
Location: (a) on ectocervix in 94% of women < 25 years (b) on ectocervix in 2% of women > 65 years
√ not discernible at imaging
N.B.: most cervical cancers arise in transformation zone

Endocervical Canal

~ 8 mm wide fusiform canal connecting uterus with vagina, tapering at both ends into
(a) **external cervical os** = opening into vaginal canal
(b) **internal cervical os** = opening into uterine cavity

Size of internal cervical os: 10 mm (L) x 1–12 mm (W)

Histo: endocervical mucosa
› characterized by villi lined with a single layer of mucus-secreting columnar epithelial cells + separated by crypts (= endocervical glands) extending 3–10 mm deep into stroma of cervix
› arranged into longitudinal ridges with interdigitating branching folds (plicae palmatae of arbor vitae = irregular branched mucosal pattern of cervical canal

√ best visualized on HSG

US:
√ endocervical canal = echogenic line (best on SAG view) delineating interface between anterior + posterior mucosa
√ thin central an- / hypoechoic region ← fluid / mucus during periovulatory period

MR: (see below)

Cervical Isthmus

= junction of supravaginal cervix and uterine body
√ slight external tapering of outer contour of uterus
√ slight internal narrowing forming internal cervical os

Cervical Zones (on T2WI = best soft-tissue contrast)

= distinctive trilaminar appearance
(1) Central stripe of high signal intensity
Histo: secretions in endocervical canal + cervical mucosa + plicae palmatae
√ 3–8 mm hyperintense layer of mucosa + secretions
(2) Middle layer of low SI continuous with junctional zone
Histo: inner zone of fibromuscular stroma with percentage of nuclear area 2.5 times greater than in outer zone
√ 3–8 mm hypointense layer of inner cervical stroma
(3) Outer layer of intermediate signal intensity
Histo: outer zone of fibromuscular stroma with greater number of fibroblasts + smooth muscle cells and less vascularized connective tissue
√ 2–8 mm intermediate-SI layer of outer cervical stroma
(4) Outermost thin low-intensity serosal layer continuous with uterine serosa

Postpartum Uterus

Puerperium = period 6–8 weeks after delivery
[*puer* = Latin, boy + *parere* , Latin = to bear; *puerpera* = a woman in childbed]

• after childbirth weight of uterus = 1 kg decreasing by 50% during following 24–48 hours

√ length of uterus: › 20.0 cm after birth
› 11.2 cm at 3 weeks
› 8.7 cm at 6 weeks

◊ Timing of uterine involution
› prolonged in multiparous women
› foreshortened in preterm delivery
› not affected by birth weight / breast feeding

√ heterogeneous myometrium of higher echogenicity compared to nongravid uterus

√ increased diffuse / focal myometrial vascularity at site of placental insertion

Endometrium by US

Measurements refer to
› AP diameter of both apposed endometrial layers (= bilayer thickness) excluding intrauterine fluid
› the level of the uterine fundus
› midline long-axis image of uterus

◊ Measurements increase by 1–2 mm in patients with large body habitus

◊ If there is a discrepancy between concomitant endometrial + ovarian findings bleeding is usually associated with anovulatory cycles

1. MENSTRUAL PHASE (usually days 1–4)
Thickness: 1–5 (mean, 4.6) mm
√ interrupted thin echogenic line of central interface
2. PROLIFERATIVE PHASE (days 5–13)
Thickness: 6–12 mm
√ bright echogenic central line (= apposed borders of endometrial canal)
√ thickened mildly echogenic endometrium compared with myometrium ← development of glands, blood vessels, stroma
3. LATE PROLIFERATIVE + OVULATORY PHASE (days 13–16)
Thickness: mean of 12.4 mm on the day of luteinizing hormone surge
√ "triple ring" sign = multilayered endometrium:
√ echogenic basal layer
√ hypoechoic inner functional layer
√ thin echogenic median layer arising from the central interface
√ concomitant with mature preovulatory follicle
√ disappears within 12–48 hours after ovulation
4. PERIOVULATORY PHASE (days 8–20)
= uncertain days defined relative to day of ovulation
N.B.: day of luteinizing hormone surge extremely variable = ovulation occurs between day 8 and 20 of menstrual cycle
5. SECRETORY PHASE (days 16–28)
Thickness: 7–12–16 mm
√ bright central line
√ markedly echogenic thick endometrium of more homogeneous echotexture ← stromal edema + distended glands filled with mucus + glycogen:
√ ± posterior acoustic enhancement
√ maximum thickness during midsecretory phase
√ concomitant with a corpus luteum
√ thin hypoechoic halo of inner myometrial zone

6. HORMONAL CONTRACEPTIVES
   √ endometrium thin throughout menstrual cycle

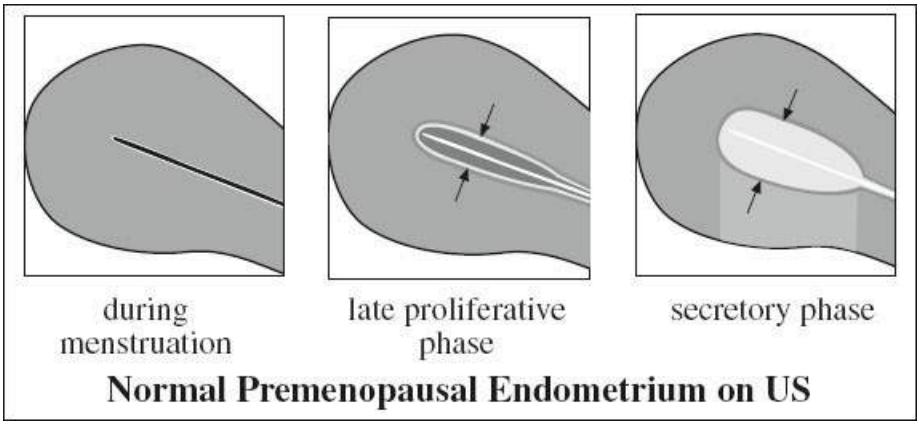
Postmenopausal Endometrium

Menopause = permanent cessation of menstruation with an intact uterus
[men, *ancient Greek* = month + pausis, *Greek* = cessation]
Definition: amenorrhea for 12 months
Onset: 51–53 (range, 40–60) years (Western countries)
Affected by: smoking, race, ethnicity, body mass index

Perimenopause = menstrual cycles of variable lengths + volume with frequent skipping of cycles

A. NO HORMONAL REPLACEMENT THERAPY
   √ bilayer thickness of usually 1–2 mm (max. 5 mm) with a homogeneous echogenic endometrium = 99% NPV for endometrial cancer
   Histo: consistently associated with atrophic inactive endometrium

B. WITH HORMONE REPLACEMENT THERAPY
   (a) cyclic estrogen + progestin therapy
      √ endometrial thickness may increase to 8 mm:
         √ thickest prior to progestin exposure
         √ thinnest after progestin phase (imaging should be done at beginning / end of a treatment cycle)



Normal Premenopausal Endometrium on US

   (b) continuous estrogen + progesterone regimen
      √ normal endometrial thickness
      Histo: endometrial atrophy
   (c) unopposed estrogen therapy usually prescribed for posthysterectomy patients
      Associated with: increased risk of endometrial hyperplasia / carcinoma
   (d) tamoxifen (= estrogenic effect on uterus) usually prescribed for breast cancer patients
      √ endometrial thickness > 8 mm in 50% (notably beyond 3 years of therapy)
      √ endometrial thickness may increase to 15 mm
      Rx: biopsy / D&C recommended (?) if endometrial thickness > 8 mm

Normal Postpartum Endometrium

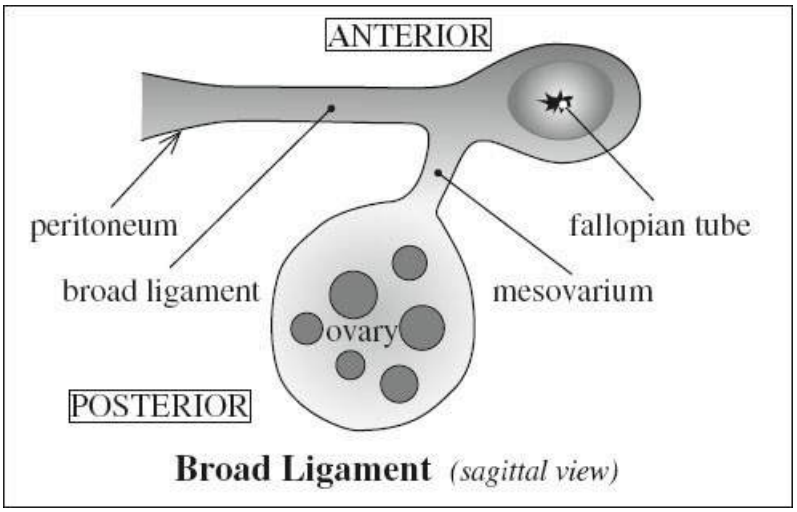
√ endometrial cavity < 20 mm in diameter:
  √ small echogenic foci of retained membranes / remaining superficial decidua / clot / debris
    › normal in up to 24% in first few days post partum
    › normal in up to 50% at 1 week post partum
    › normal in up to 6% at 3 weeks post partum
  √ intrauterine air (as late as 3 weeks after vaginal / cesarean delivery)
√ cavity wall:
  √ smooth well-defined border
  √ irregular heterogeneous lining
  √ endometrial stripe thickness decreases with uterine involution
√ endometrium restored by 3–6 weeks post partum

Pelvic Spaces

1. Rectouterine pouch = cul-de-sac
   Anterior boundary: broad ligaments + uterus
   ◊ Most dependent portion of pelvis in women!
2. Rectovesical recess
   ◊ Most dependent portion of pelvis in men!
3. Vesicouterine recess
4. Inguinal fossa
   located between lateral + medial umbilical folds

Pelvic Ligaments

1. **Broad ligament**
   Histo: double fold of peritoneum covering anterior + posterior surfaces of uterus
   Origin: uterine peritoneum
   Location: lateral uterine margin to pelvic sidewall incompletely dividing true pelvis into anterior + posterior compartments
   Attachment: pelvic sidewall
   › medial superior free edge (= point where peritoneal layers are continuous): encloses fallopian tube
   › lateral superior free edge: suspensory ligament of ovary
   › lower margin: cardinal ligament
   Contents (= parametrium):
   extraperitoneal connective tissue, smooth muscle, fat, fallopian tube, round ligament, ovarian ligament, uterine + ovarian blood vessels, nerves, lymphatics, mesonephric remnants
   √ usually not seen on CT, unless surrounded by ascites
2. **Round ligament**
   = anterior suspensory ligament of uterus
   Histo: band of fibromuscular tissue + lymphatic channels
   Origin: anterolateral uterine fundus, just below + anterior to ovarian ligament



Attachment: through internal inguinal canal (lateral to deep inferior epigastric vessels) to labia majora

3. **Cardinal ligament** = transverse cervical ligament = Mackenrodt ligament
   Origin: cervix + upper vagina
   Attachment: fascia of obturator internus muscle
   Relationship:
   › uterine artery runs along its superior aspect
   › forms the base of the broad ligament
4. **Uterosacral ligament**
   Origin: posterolateral cervix + vagina
   Attachment: anterior body of sacrum at S2 / S3
5. **Ovarian ligament** = utero-ovarian lig. = round ligament of the ovary
   = round fibromuscular band just inferior + posterior to fallopian tube + round ligament enclosed between 2 layers of broad ligament
   Origin: medial aspect of ovary
   Attachment: uterine cornu
   Contents: ovarian branches of uterine artery + vein
   √ short narrow soft-tissue band between uterus and ovary on CT
6. **Suspensory ligament of ovary** = infundibulopelvic lig.
   = peritoneal fold (= superolateral part of broad ligament) suspending ovary from posterolateral pelvic wall
   Origin: anterolateral tubal end of ovary
   Attachment: connective tissue covering psoas muscle
   Contents: ovarian artery + veins (= major component due to gradual arterial atrophy); lymphatics
   Length: up to 4–5 cm
   ◊ Good anatomic landmark to localize ovary!
   √ extends from ovary in direction of iliac vessels on CT
7. **Lateral umbilical fold** / ligament
   = reflection of peritoneum over deep inferior epigastric vessels
8. **Medial umbilical fold** / ligament

= reflection of peritoneum over obliterated umbilical arteries

9. **Median umbilical ligament**
   = reflection of peritoneum over obliterated urachus
   Origin: dome of urinary bladder
   Attachment: umbilicus

FALLOPIAN TUBE

[Gabriele Falloppio *aka* Fallopius (1523-1562), chair of anatomy at University of Padua]
Location: superior aspect of broad ligament
Length: 10–12 cm
Segments:

(1) **Interstitial** / intramural / cornual portion
    = short segment that traverses muscular wall of the uterus
(2) **Isthmic** portion
    = long narrow segment between interstitial + ampullary end
    Diameter: up to 4 mm
(3) **Ampullary** portion
    = widened region near ovary accounting for > 50% of the entire tubal length
    Diameter: up to 8 mm
(4) **Infundibular** portion
    = most lateral funnel-shaped segment
    Diameter: up to 10 mm

Free edge: 25 fingerlike projections / fimbriae
Wall:

(a) mucosa: folds form fingerlike projections (= plicae) → plicae coalesce at infundibulum contiguous with fimbriae
(b) muscularis
(c) serosa

√ usually not visualized unless abnormal / surrounded by fluid

OVARY

Origin: thickening of mesothelial layer of peritoneum → gonadal ridge → primitive gonad; part of mesonephros remains connected to genital ridge = mesovarium
Fixation: *gubernaculum* connects ovary to uterine fundus = **ovarian ligament**; part of gubernaculum between uterus and labia = **round ligament** that is accompanied by peritoneum analogous to processus vaginalis of testis (= **canal of Nuck**)

The ovary is fairly mobile with attachments to

anterior pelvic wall	by broad ligament
uterine body	by uteroovarian ligament
fallopian tube	by tuboovarian ligament
lateral pelvic wall	by infundibulopelvic ligament

Ovarian descent: inhibited by gubernaculum → NO further than level of uterine fundus
N.B.: failure of gubernaculum to contract → ovary may descend through inguinal canal into labium majus

Mesovarium: short double-layered peritoneal fold extending posteriorly from broad ligament attaching anteriorly to ovary; contains ovarian blood vessels (= anastomotic branches of ovarian + uterine arteries and venous plexus)

◊ Lax supporting ligaments + shallow fetal and infantile pelvis make fetal ovary more susceptible to torsion than postpubertal ovary!

Embryology of ovary:

(a) coelomic (surface) epithelium (*gonadal cortex)* migrates from near the allantois and invaginates into

(b) mesenchymal substance of central part = *medulla of ovary* (= primary sex cords) and incorporates primordial germ cells that develop into primordial follicles

(c) germinal epithelium eventually loses connection with central mass; an additional layer develops between medulla and cortex = *tunica albuginea*

Oocytogenesis:

› cells from dorsal endoderm of yolk sac migrate along hindgut to gonadal ridge (**primordial germ cells**) which multiply by mitosis

› after reaching gonadal ridge they are named **oogonia** (= diploid stem cells of ovary)

› oogonia become fully surrounded by a layer of connective tissue (= pre-granulosa cells of **primary oocyte**)

› primary oocyte formation completed by end of 3rd trimester

› most primary oocytes degenerate + only a small portion of primary oocytes undergo ovulation after onset of puberty

Histo:

A. Stromal cells
   › form cortex, medulla, hilus
   › surround all developing follicles
   › cell surface has estrogen-, progesterone-, testosterone-binding sites
   › major source of androgens in postmenopause

B. Cells derived from stroma cells
   1. Fibroblasts
   2. Luteinizing stromal cells containing lipid
   3. Hilus cells
      morphologically similar to Leydig cells in testis;
      contain intracellular crystalline structures (= crystals of Reinke)
   4. Theca cells
      › surround granulosa cells
      › produce estradiol under control of FSH
      › stimulated by LH after ovulation into theca-lutein cells, which develop lipid-laden cytoplasm involved in steroidogenesis

C. Cells derived from sex cords
   1. Granulosa cells
      › surround each primordial oocyte
      › form lining of developing follicle
      › granulosa cell layer contains small cystic cavities lined by basal lamina (= Call-Exner bodies)
      › produce estradiol under control of FSH

› stimulated by LH after ovulation into granulosa-lutein cells, which develop lipid-laden cytoplasm involved in steroidogenesis

2. Sertoli cells
not seen in normal ovary

Ovarian Size

Ovarian volume = length x height x width x 0.523

fetus: > 28 weeks GA
< 3 months: 1.06–3.56 cm^3
4–12 months: up to 2.71 cm^3
1 year: 1.05 ± 0.7 (S.D.) cm^3
2–6 years: ≤ 1.0 ± 0.4 (S.D.) cm^3
6–10 years: 1.2–2.3 cm^3
11–12 years: 2–4 cm^3
after puberty: 2.5–5 cm (L), 0.6–1.5 cm (H), 1.5–3 cm (W) = 8 (range 2.5–20) cm^3
premenopausal: < 6 cm^3
postmenopausal: < 2.5 cm^3
< 30 years: mean volume of 6.6 cm^3
30–39 years: mean volume of 6.1 cm^3
40–49 years: mean volume of 4.8 cm^3
50–59 years: mean volume of 2.6 cm^3

◊ An ovary > 20 cm^3 is enlarged!
◊ An ovary between 15 and 20 cm^3 requires follow-up!
◊ An ovarian volume > 4 cm^3 + > 6 follicles in girls < 7 years suggests premature sexual development!

Ovarian Morphology

neonate:
√ follicles occasionally fail to involute + undergo growth
< 8 years:
√ solid ovoid structures with homogeneous / finely heterogeneous texture
√ up to 68–80% of ovaries contain cystic follicles (in 95% < 9 mm, in 5% > 9 mm)
premenopausal:
√ changes in size, morphology, blood flow with menstrual cycle

Ovarian Volume and Appearance

Stage	*Ovarian Volume [cm^3]*	*Ovarian Appearance*
Neonatal	1.0–3.5	follicles + cysts common
Pediatric	0.5–1.5	< 6 follicles; cysts uncommon
Prepubertal	1.0–4.0	follicles + cysts common
Pubertal	2.0–6.0	follicles + cysts common
Reproductive	4.0–16.0	follicles + cysts common
Postmenopausal	1.2–5.8	follicles + cysts in 15–20%

Visualization of Ovaries by US

(a) after menopause (average onset at age 50):
< 5 years after menopause: in 78%
> 10 years after menopause: in 64%
› both ovaries: in 85%
› one ovary: in 60%
(b) following hysterectomy: in 43%

Location of Ovaries

Influenced by: › size of uterus + ovary
› distension of bladder + rectosigmoid
› presence of pelvic mass

(a) in neonates: located above level of true pelvis (visualized by transabdominal US)
(b) older child: located adjacent to uterus deep within pelvis
Location: ovarian fossa (= fossa of Waldeyer) bounded posteriorly by ureter + internal iliac artery, superiorly by external iliac vein, anteriorly by obliterated umbilical artery
(c) during 1st pregnancy: pulled into abdomen by enlarging uterus + stretched broad ligament
(d) after 1st pregnancy: greater ovarian mobility ← enlarged redundant broad ligament
Potential locations: › adnexal region lateral to uterus
› posterior cul-de-sac
› superior / posterior to uterine fundus

◊ In retroverted uterus ovaries may be ventral / lateral to uterus

Ovarian Blood Supply

= dual arterial supply

Ovarian Artery

Origin: abdominal aorta slightly below renal artery
Course: (a) descends caudally + laterally ventral to psoas major muscle
(b) crosses over external / common iliac vessels
(c) passes through suspensory ligament of ovary near pelvic brim
(d) descends inferiorly + medially between 2 layers of broad lig. near mesovarian border
Terminus: multiple branches within ovarian hilum

Adnexal Branch of Uterine Artery

Ovarian Vein

◊ Tracking the ovarian vein caudally is most helpful to identify ovary!
Origin: pampiniform plexus in mesovarium that merges to form one vein
Course: alongside ovarian artery
Terminus: left ovarian vein → left renal vein; right ovarian vein → inferior vena cava below level of renal vessel

RELATIONSHIP OF OVARIAN VESSELS TO URETER

@ lower renal pole medial to ureter
@ middle to lower lumbar region crossover
@ lower abdomen + pelvis lateral to ureter
√ location of ureter relative to a pelvic mass can be a most helpful hint to the ovarian origin on CT

Ovarian Doppler Signals

A. NONFUNCTIONING OVARY
√ high-impedance waveform
B. FUNCTIONING OVARY
› days 1–6:
√ high-impedance waveform with RI close to 1.0
› days 7–22 = midfollicular to midluteal phase
= developing dominant follicle + ovulation + corpus luteal phase:
√ continuous diastolic flow with RI close to 0.5
› days 23–28 = late luteal phase:
√ high-impedance waveform with RI close to 1.0

Ovarian Cycle

1. FOLLICULAR PHASE = days 1–14 (of a 28-day cycle)
• a number of immature primordial follicles begin to mature in response to FSH
√ multiple small cysts:
(a) unstimulated follicles are < 2 mm in size
(b) stimulated follicles grow > 2 mm in size
√ 2–3 follicles in each ovary of day 4 enlarge subsequently to ~ 10 mm
• 2–3 follicles capture the most FSH and aromatize the most estradiol from their granulosa cells
√ follicles may be seen by 5–7 days
√ single more ascendant / **dominant / graafian follicle** appears by day 8–10–12 (*see below*):
√ progressively increasing diastolic flow on the side of maturing follicle
2. OVULATORY PHASE = day 14
• "**Mittelschmerz**" = pain just prior to ovulation (pressure of graafian follicle distending ovarian capsule)
√ sudden decrease in follicular size over minutes / hours (= rupture of mature graafian follicle with extrusion of oocyte)
√ fluid in cul-de-sac detectable in up to 40%
3. LUTEAL PHASE = days 15–28
= remnant dominant follicle transforms into **corpus luteum hemorrhagicum**
√ irregular cyst with scalloped margins
◊ All corpora lutea evolve over days and change size and texture constantly
◊ All corpora lutea contain hemorrhage: → uncontrolled bleeding into center frequently at time of ovulation + on day 8 when regression begins
√ round / ovoid bulging protrusion on one side of ovary = **corpus luteum of**

menstruation:
√ mean diameter of 10–25 mm (typically < 3 cm)
√ hyperechoic 1–4-mm thick wall
√ hyperechoic central blood clot gradually transforming into weblike fibrin net
√ color Doppler US:
√ corpus luteum surrounded by circumferential wreath-like color flow = "**ring of fire**"
√ blood flow in main arteriole supplying the corpus luteum is ~ 100 cm/sec
√ arterial flow differences between active + inactive ovary:
√ inactive (nondominant) ovary: steady high-resistance pattern of ovarian arterial flow
√ active (dominant) ovary: low-resistance arterial pattern with its nadir in early luteal phase
√ involution + atrophy of corpus luteum on about 24th day of cycle = **corpus luteum atreticum**
Prognosis: large painful corpora lutea resolve in a week

Postmenopausal Ovary

√ less echogenic, fewer follicles than normal
√ small atrophic organ with mean size of 1.2–5.8 cm^3
◊ Ovarian volume > 8 cm^3 is abnormal!
√ may contain simple cyst up to 3 cm (in 15%)
Rx: serial follow-up to document spontaneous regression
√ may contain simple cyst < 1 cm (in 21%)
Rx: no follow-up necessary
√ peripheral 1–3 mm punctate echogenic foci without associated soft-tissue mass
Cause: (a) dystrophic calcifications in atretic follicles
(b) dystrophic calcifications in surface epithelial inclusion cysts
(c) tiny cystic spaces with reverberation artifacts

Graafian Follicle

[Reinier de Graaf (1641-1673), Dutch physician and anatomist]
= DOMINANT FOLLICLE
Time of onset: day 8–10–12 of 28-day menstrual cycle
Size of mature graafian follicle: 17–29 mm
• rapidly rising estradiol production triggers the hypothalamic arcuate nucleus to increase GnRH secretion → prompts anterior pituitary to disgorge the stored LH over 24 hr
• LH binds to ovarian receptors → releases cAMP from granulosa cells → halting granulosa cell mitosis + increasing peptidase, collagenase, growth factor, angiotensin, prostaglandin as the cause for follicular rupture + conversion to corpus luteum
√ > 14 mm in diameter:
√ growth rate 2–3 mm/day until the last preovulatory 24 hours followed by a sudden increase in diameter
√ subsequent enlargement to 21 (range 17–24) mm by day 14
√ **cumulus oophorus** = 1-mm mural echogenic focus projecting into antrum of follicle +

containing oocyte, followed by ovulation within next 36 hours
√ 2 dominant follicles may develop in 5–11% of cycles BUT NOT within same ovary

Signs of Ovulation

√ development of solid echoes within graafian follicle
√ decrease in diameter / sudden collapse of dominant follicle 28–35 hours after LH peak
√ "ring" structure within uterine fundus
√ free fluid appearing in pouch of Douglas

Signs of Ovulatory Failure

√ development of internal echoes prior to 18 mm size
√ continuous cystic enlargement up to 30–40 mm

Hormonal Status

Thelarche = onset and progress of breast development
Mean age: 8 years

Adrenarche = onset and progress of pubic (pubarche) + axillary hair development
Mean age: 9.8 years

Menarche = first episode of vaginal bleeding originating from the uterus
Mean age: 12.7 years in USA

RADIOLOGY CONSIDERATIONS FOR MOTHER & FETUS & NEONATE

CONTRAST MEDIA DURING PREGNANCY

No well-controlled studies available on the use of oral / IV iodinated / IV gadolinium contrast material!

Oral Contrast Material

◊ Not considered a threat to pregnant patients due to intraluminal administration + excretion!
◊ Intraluminal barium can act as internal shielding

IV Iodinated Contrast Medium

= FDA category B drug: NO fetal risk in animal reproduction studies
◊ Considered generally inert + safe in pregnancy!
Physiology: IV iodinated contrast material crosses placenta + enters the fetus
Risk: depression of fetal thyroid function ← uptake of free iodine; NO mutagenic / teratogenic effects of lower-osmolality contrast media (in lab animals)
Recommendation: evaluate thyroid function of newborn in first few days of life (already standard practice in U.S. for all newborns)

IV Gadolinium-based Contrast Medium

Physiology: IV gadolinium-based contrast material crosses placenta + enters the fetus
Risk: toxic effects of high doses in lab animals (doses 2–7 x higher than used in humans); NO direct toxic effects of gadolinium in humans
Theoretical risk: gadolinium chelates may accumulate in amniotic fluid → dissociate over time → release toxic free gadolinium ions (of no known clinical significance)
Recommendation: well documented thoughtful risk-benefit analysis based on potential benefit outweighing theoretical risks

FETAL EXPOSURE TO RADIATION

Counseling for necessary exposure to radiation while pregnant:

- Have written policy for screening + management of pregnant women:
  - › last menstrual period (LMP > 14 days): reliable, regular?
  - › checking of b-hCG level needed?
  - › imaging protocol adjustment possible?
- Expeditious consultation with medical physicist to evaluate required fetal dose and associated risk
- Discussion of risk with parents to make informed decision

Potential Radiation Effects on Fetus by Gestational Age			
Gestational Period	*Gestational Age (wk)*	*Effects (theoretical risk for < 100 mGy unlikely)*	*Estimated Threshold Dose (mGy)*
Before implantation	0–2	**All** (death of embryo) **or None**	50–100
	3–4	Spontaneous abortion possible	
Organogenesis	2–8	Congenital anomalies: skeleton, eyes, genitals	200
		Growth retardation	200–250
Fetal Period	8–15	Severe mental retardation	60–310
		Intellectual deficit	25 IQ point loss per Gray
		Microcephaly	200
	16–25	Severe mental retardation (low risk)	250–280
	18–27	IQ deficit not detectable at diagnostic doses	
	> 27	None applicable to diagnostic medicine	

  - › for most diagnostic procedures the risk of congenital anomalies, miscarriage, birth defects, or mental retardation is negligible
  - › the risk of childhood cancer and leukemia is real but small compared to other spontaneous risks
  - › available imaging options should be described
  - › consequences of delaying / refusing imaging must be explained

    MR: inform patient that there are no known risks to the fetus. However, MR's safety has not been proved and cannot be guaranteed
- Calculation of precise dose delivered to fetus with consideration of gestational age, maternal body habitus and acquisition parameters
  - › not performed after head scan (insignificant scatter radiation to fetus)
  - › not performed during first 2 weeks of pregnancy (all-or-nothing response)
- Thermoluminescent dosimeter (TLD) on skin of patient to determine surface dose if medical physicist not on staff:
  - › fetal dose estimate = ⅓ of entrance dose of average patient
  - › if estimated dose > 50 mGy a consulting physicist is needed for detailed dosimetry report
- Modify CT scans to use the lowest dose possible: ⇓ z-axis coverage, ⇑ pitch, ⇓ tube potential (kilovolt peak), ⇓ tube current–time product (milliampere-second)

Effect of Ionizing Radiation on Fetus

= biologic effect of ionizing radiation on physical and chemical processes result in
(1) cell death OR
(2) morphologic effects (via alteration of nuclear DNA) → genetic mutation (teratogenesis) / carcinogenesis

Deterministic Effects

= NONSTOCHASTIC EFFECT = THRESHOLD EFFECT
[*terminus* , Latin = end, limit; *determinare* , Latin = setting limits]
= dose threshold before damage occurs to a number of cells (= multicellular damage) caused by radiation at high doses
Effect: malformation, growth + mental retardation, death
Risk: increasing with increasing dose

Dose threshold: 100 mGy to fetus (dependent on time of exposure to gestation)
- 3% chance of cancer (leukemia, breast, thyroid, brain)
- 6% chance of mental retardation
- 15% chance of microcephaly
- loss of 30 IQ points per 100 mGy

◊ NO risk to embryo / fetus from any diagnostic procedure!

Vulnerable stage: 8th–15th (range, 2nd–20th) week GA

Recommendation: assess for pregnancy termination at 150 mGy exposure to fetus

Stochastic Effects

[*stokhastikos* , Greek = capable of guessing, conjecture]

= damage to a single cell with exposure to any amount of ionizing radiation increasing with radiation dose

Effect: carcinogenesis, other germ cell mutation

Dose threshold: none

Incremental risk of cancer:

fetal dose up to 1 mGy: < 1÷10,000

fetal dose of 20–50 mGy: < 1÷250

(general population without radiation: 1÷500)

Effect of Diagnostic Imaging on Fetus

Natural background radiation: 1 mGy to fetus during pregnancy

◊ Most radiologic studies use ionizing radiation of < 0.05 Gy (50 mGy) resulting in a negligible risk compared to natural risks of pregnancy

Natural risks of pregnancy:
- › 15% risk of spontaneous abortion
- › 4% risk of prematurity
- › 4% risk of growth retardation
- › 3% risk of spontaneous birth defect
- › 1% risk of mental retardation

A fetal radiation dose of 50 mGy increases the overall lifetime risk for cancer by 2%!

Fetal radiation doses of < 50 mGy are not associated with increased fetal malformation or fetal loss throughout pregnancy!

A fetal radiation dose of < 100 mGy also should not be considered a reason to terminate pregnancy.

CT during Pregnancy

(a) head / cervical spine / extremities: little concern during any trimester of pregnancy

(b) Chest = low-dose examination when fetus is excluded from primary beam

(c) renal stones, appendicitis, pulmonary emboli: no fetal neurologic deficits

(d) appendicitis: may double risk for childhood cancer

◊ US and MR should be considered whenever possible!

During pregnancy CT is the first-line imaging modality for trauma and suspected pulmonary emboli.

Trauma is the leading cause of nonobstetric maternal mortality worldwide.

In developing countries, venous thromboembolism is the leading cause of maternal mortality.

MR during Pregnancy

Concern: heating effects of RF pulses and acoustic noise

◊ No known harmful effects to date at ≤ 1.5 T

> MR imaging can be used in pregnant patients regardless of gestational age (1) when the information gained is likely to alter treatment, (2) when it cannot be obtained through other nonionizing means, and (3) when MR imaging cannot be delayed until completion of the pregnancy.

Recommendation: written informed consent to document patient's understanding of risk-benefit ratio + any alternative diagnostic options

US during Pregnancy

◊ No documented adverse effects on fetus from US

Estimated Radiation Doses to Fetus	
Type of Exam	*Fetal Dose (mGy)*
Annual background radiation	*1.1–2.5*
High Dose (10–50 mGy)	
Abdominal CT	1.3–35
Pelvic CT	10–50
CT abdomen & pelvis	25
CT angio of aorta	34
PET/CT	10–50
Moderate Dose (0.1–10.0 mGy)	
Radiography	
Abdomen (AP) 21-cm patient thickness	1.0
Abdomen (AP) 33-cm patient thickness	3.0
L spine (2 views)	1.0–10
IVP	5–10
DC barium enema	1.0–2.0
CT	
Head & neck CT	0–10
Chest CT / angio CT of chest	0.01–0.66
CT pelvimetry (single section)	<1
CT of coronaries	0.1
NucMed	
Perfusion scintigram (low dose)	0.1–0.5
^{99m}Tc bone scintigram	4–5
Pulmonary DSA	0.5
Low Dose (< 0.1 mGy)	
C-spine (2 views)	< 0.001
Extremity radiography	< 0.001
Mammography (2 views)	0.001–0.010
T-spine	0.003
CXR (2 views)	0.0005–0.0100

Estimated Radiation Doses to Fetus from a Single Acquisition with a 64-Row CT Scanner					
		CT Protocol		*Imaging Parameters*	
Type of CT Exam	*Fetal Dose (mGy)*	*Section Thickness (mm)*	*Noise Index*	*Tube Current-Time Product (mAs)*	*Pitch*
Chest	0.02	2.5	30	80	1.375
Pulmonary angio	0.02	1.25	30	88	0.984
	0.24–0.66 in anthropomorphic phantom with 16-row CT				
Abdomen	1.3	2.5	36	110	1.375
Urinary tract	11	2.5	36	110	1.375
	4–12 in anthropomorphic phantom with 16-row CT				
Pelvis	13	2.5	36	130	1.375
Abdomen & Pelvis	13	2.5	36	130	1.375
	15–40 in anthropomorphic phantom with 16-row CT				
Angio	13	2.5	30	130	1.375

Upper exposure limit: 720 mW/cm^2 for spatial-peak temporal average intensity
Doppler US: can produce high intensities
◊ Keep exposure time + acoustic output at lowest level possible

Clinical Scenarios

Abdominal Pain in Pregnancy

Imaging sequence: US → low-dose CECT / MR (if US nondiagnostic)

Acute Appendicitis in Pregnancy

◊ Most common nonobstetric emergency requiring surgery during pregnancy!
Associated with: premature labor, fetal morbidity + mortality, high rate of perforation
• limited use of clinical signs in pregnancy
Imaging sequence: US with graded compression → MR / CECT (if US nondiagnostic)
› Graded Compression US: 66–100% sensitive, 95–96%specific
› MR: 100% sensitive, 94% specific, 94% accurate, PPV of 1.4%, NPV of 100%
› CT: 92% sensitive, 99% specific, NPV of 99%
Associated cancer risk: 1÷500 fetuses exposed to 30 mGy

Pulmonary Embolism in Pregnancy

Prevalence: 0.5–3.0÷1,000 pregnancies
Risk of DVT: 5 x increase compared to nonpregnant state ← ↑ venous stasis + hypercoagulability
Mortality: up to 15%

• progressive ↑ in D-dimer levels during normal pregnancy

Imaging sequence: PA chest → Doppler US → CT angio chest OR V/Q scan (if allergic to iodine)

› Compression US
  » for thigh veins: 95% sensitive, 98% specific
  » for iliac veins: low sensitivity

N.B.: 10% of patients have PE angiographically

› CT angiography: 81–91% sensitive, 93–97% specific

› High-probability V/Q scan: 41% sensitive

Benefit of CT (with abdominal shielding):
  » radiation exposure comparable to V/Q scan
  » allows identification of other causes of chest pain (pulmonary edema, pneumonia, pleural effusion)

Trauma in Pregnancy

◊ Leading nonobstetric cause of maternal death!

Prevalence: 6–7% of pregnant women (MVA)

Fetal mortality: 3–38% after blunt trauma ← placental abruption or maternal death / shock

(a) low-level trauma: US

(b) serious trauma: tailored CT of head, chest, abdomen, pelvis; MR for neural axis; angio for extravasation
  ◊ Concerns about fetal radiation exposure should neither deter nor delay radiologic evaluation!

(c) uterine / fetal injury: US ± CT / MR

Urolithiasis in Pregnancy

◊ Most common painful nonobstetric condition for hospitalization in pregnant patients!

• admitting diagnosis in 28% incorrect

Prevalence: 0.4–5.0÷1,000 pregnancies

Prognosis: 70–80% of ureteral calculi pass spontaneously

Cx: pyelonephritis, premature labor induced by renal colic

Imaging sequence: US → low-dose NECT (if US nondiagnostic)

› US: 34–95% sensitive

› MR urography

› low-dose CT: > 95% sensitive, > 98% specific

NEONATAL EXPOSURE TO IV CONTRAST MEDIA

◊ *Interruption of **breast feeding** is NOT recommended! (*not even for 24–48 hours)!

› breast feeding is recommended as the only source of feeding for full-term healthy infants during first 6 months of life (WHO)

› should be continued during first 2 years / longer if desired

› temporary cessation can lead to complete weaning

It is not necessary to stop breast-feeding. Some mothers may prefer to express and discard breast milk for 12–24 hours after they are given contrast agents.

Pharmacokinetics:
nonionized and water-soluble iodinated + Gd-based contrast media have high molecular weight → minimal binding to breast milk → low concentration of injected dose in breast milk (0.01% for gadopentetate and 0.5% for iohexol) → contrast in milk peaks at 5 hours; undetectable after 12 hours

Only a small percentage of iodinated or Gd-based contrast material is excreted in breast milk and absorbed by the infant. There have been no reported cases of direct toxicity, allergic sensitivity, or reaction to these agents.

Ingested Dose: 0.2% of maximum dose allowed for urography

IV CONTRAST MATERIAL IN PEDIATRICS

Conventional dose: 1 mL÷pound up to 150 mL
Maximum dose: 280–300 mg I/mL
Recommended Pediatric Dose for Urography:
for babies < 6.5 kg: 900 mg I/kg body weight
for babies > 7.0 kg: 600 mg I/kg body weight

OBSTETRIC AND GYNECOLOGIC DISORDERS

ABORTION

= loss of products of conception < 20 weeks of MA (definitions may vary)

A. INDUCED ABORTION
   (a) medical / therapeutic abortion
   (b) nonmedical abortion

B. SPONTANEOUS ABORTION

Spontaneous Abortion

= FAILED PREGNANCY = PREGNANCY LOSS = MISCARRIAGE

Frequency:

› > 50% of all fertilized ova (estimate)
› 31–43% of all implantations (estimate)
› 10–25% of clinically diagnosed pregnancies
› 2–4% with normal cardiac activity
› decreases with increasing gestational age

Time of loss: < 8–10 weeks MA; majority before 7th week MA

Etiology (usually due to abnormal karyotype):
autosomal trisomy (52%), triploidy (20%), monosomy (15%)

◊ Spontaneous pregnancy loss at < 8 weeks gestation occurs in 10–17% of embryos with cardiac activity!

Signs of Abnormal Pregnancy
√ thin decidual reaction of < 2 mm
√ abnormally shaped sac
√ gestational sac low in uterus

Impending / Inevitable Abortion

= ABORTION IN PROGRESS
= gestational sac with embryo having become detached from implantation site → spontaneous abortion within next few hours

• Clinical triad: (1) bleeding > 7 days, (2) persistent painful uterine contractions, (3) rupture of membranes
• cervix moderately effaced / dilated > 3 cm
√ sac located low within uterus (DDx: cervical ectopic with closed internal os)
√ progressive migration of sac toward / into cervical canal (on rescanning a short time later)
√ dilated cervix
√ sac surrounded by anechoic zone of blood

Threatened Abortion

= 1st trimester bleeding (after period of implantation bleed at 3–4 weeks MA) with a live

embryo

Frequency: 20–25% of all pregnancies

- Clinical triad: (1) mild bleeding, (2) cramping, (3) closed cervix

NONVIABILITY DIAGNOSIS WITH CERTAINTY

on transvaginal ultrasound

@ Cardiac activity:
- √ no cardiac activity with a CRL ≥ 5 mm
- √ no cardiac activity with certain GA ≥ 6.5 weeks
- √ no cardiac activity with a GS diameter > 16 mm

@ Yolk sac:
- √ no yolk sac with a GS diameter ≥ 20 mm
- √ embryo visualized without demonstrable yolk sac
- √ yolk sac diameter > 5.6 mm at < 10 weeks MA

@ GS contents:
- √ fibrinous strands / residual embryonic debris (in 25%)

NONVIABILITY DIAGNOSIS WITH HIGH PROBABILITY

on transvaginal ultrasound

@ Ultrasound milestones not met as expected:
- √ ≥ 5.0 weeks gestational sac first identifiable
- √ ≥ 5.5 weeks yolk sac first identifiable
- √ ≥ 6.0 weeks embryo and FHM first identifiable

@ Yolk sac:
- √ no yolk sac with GS of 6–9 mm
- √ distorted sac configuration

@ Choriodecidua
- √ thinning of choriodecidual reaction with hypoechoic clefts

@ Cardiac activity:
- √ no cardiac activity with GS of ≥ 9 mm
- √ slow embryonic heart rate (=bradycardia):

≤ 6.2 Weeks	*≤ 7.0 Weeks*	*Mortality Rate*
> 100 bpm	> 120 bpm	11%
90–99 bpm	110–119 bpm	32%
80–89 bpm	100–109 bpm	64%
< 80 bpm	< 100 bpm	100%

Predictors of poor outcome:

@ Bradycardia
- √ < 85 bpm during 5–8 weeks EGA

@ Small sac size = "first-trimester oligohydramnios"

[misnomer: amnionic cavity is not diminished in size but rather the chorionic cavity]

= MSD (mean sac diameter) – CRL ≤ 5 mm (with a live embryo at 5.5–9.0 weeks)

Prognosis: miscarriage in 94%

@ Abnormal yolk sac

√ failure to visualize yolk sac at 5.5 weeks MA = mean diameter of GS ≥ 8 mm
√ yolk sac size > 5 mm
√ calcification / debris within yolk sac
√ double appearance of yolk sac

@ Abnormal amnion
√ mean diameter of amniotic cavity > CRL

@ Subchorionic hemorrhage
Frequency: in up to 18% of pregnancies during first half of pregnancy
N.B.: significance controversial

Prognosis: 50% develop normally; 15–39% blighted ovum, 4% mole, 4–13% ectopic pregnancy, 0–15% incomplete abortion, 17–57% missed abortion

Complete Abortion

- absence of transvaginal bleeding, cervix closed
- abrupt decline of serum β-hCG

√ IUP no longer visualized although documented previously
√ thin regular endometrium (< 10–15 mm) with apposed surfaces
√ absence of central / eccentric fluid-filled sac

DDx: nongravid state, very early IUP, ectopic pregnancy
Rx: dilatation & curettage may be avoided if IUP was documented previously

Incomplete Abortion

= RETAINED PRODUCTS OF CONCEPTION (RPOC)
= portion of chorionic villi (placental tissue) / trophoblastic tissue (fetal tissue) remaining within uterus after spontaneous abortion (= miscarriage) / planned termination / preterm or term delivery
= most frequent cause of secondary postpartum hemorrhage (2°PPH)

Incidence: › 1st trimester: 40%
› 2nd trimester 17%
› 3rd trimester: 3%

- incomplete placenta at delivery, patulous cervix
- continued (occasionally massive) genital bleeding (may occur months / years after last abortion / delivery)
- normal / low levels of β-hCG

US:
√ fetal parts / embryo / echogenic mass within uterine cavity (MOST ACCURATE SIGNS)
√ irregular / angulated small gestational sac containing amorphous echogenic material
√ ragged disrupted choriodecidual reaction
√ subchorionic fluid ± hemorrhage
√ intracavitary heterogeneously echogenic mass separate from endometrium
√ > 8–10–13 mm thickened endometrial echo complex
◊ Measurement of endometrial thickness alone is a poor test for diagnosing an incomplete miscarriage!
√ calcification of retained products (late finding)

Incomplete Miscarriage versus Endometrial Thickness on US				
Endometrial Thickness	*Sensitivity*	*Specificity*	*PPV*	*NPV*
> 5 mm	0.94	0.05	**0.85**	0.13
> 8 mm	0.87	0.21	**0.86**	0.22
> 12 mm	0.75	0.37	**0.87**	0.80
> 15 mm	0.56	0.53	**0.87**	0.17
> 25 mm	0.10	0.32	**0.88**	0.33

Sawyer E, Ofuasia E, Ofili-Yebovi D et al.: The value of measuring endometrial thickness and volume on transvaginal ultrasound scan for the diagnosis of incomplete miscarriage. Ultrasound Obstet Gynecol 2007; 29:205-209

Doppler US (x 2 improvement in diagnosis):

√ ± increased vascularity in endometrial echo complex / intracavitary mass (compared to myometrium)

√ flow velocity > 21 cm/sec (supplying residual trophoblastic tissue)

√ ± low-resistance internal blood flow often at endometrial-myometrial interface

Pitfalls: uterine AVM (involves myometrium only), endometrial polyp, submucosal fibroid

MR:

√ partially / delayed enhancing heterogeneous mass on T1WI + T2WI (DDx: gestational trophoblastic disease)

Dx: presence of chorionic villi in curettage exhibiting variable vascularity

Cx: endometritis, myometritis, peritonitis, septic shock, diffuse intravascular coagulation (with retention > 1 month)

Rx: expectant management, uterotonic medication (prostaglandin E1 analogs), suction D&C after IV oxytocin, hysteroscopic removal

DDx: intraluminal blood clot, mole, blighted ovum, embryonic demise, intrauterine fetal death

Placental Polyp

= intrauterine polypoid mass formed by a retained fragment of placental tissue after an abortion / term pregnancy

Predilection: placenta accreta

MR:

√ hyperintense polypoid mass on T2WI

DDx: arteriovenous malformation, trophoblastic disease, endometrial polyp, submucosal myoma

Subinvolution of Placental Implantation Site

= exceptionally rare postpartum condition characterized by failure of uterine vessels to involute following delivery

Risk factors: atony, multiparity, cesarean section, uterine prolapse, uterine fibroids, endometritis, coagulopathy, RPOC

√ unusually large postpartum uterus

√ dilated myometrial vessels

Missed Abortion

= dead conceptus within uterine cavity for ≥ 8 weeks occurring prior to 28 weeks MA

Time of diagnosis: not before 13 weeks MA

• brownish vaginal discharge, closed firm cervix

√ no cardiac activity in a well-defined embryo with CRL > 9 mm (on abdominal scan) / CRL > 5 mm (on TV scan)

√ gestation not in correspondence with menstrual age

√ sac > 25 mm in diameter without an embryo (DDx: anembryonic pregnancy)

√ sac > 20 mm without yolk sac

√ crenated irregular / distorted angular sac configuration

√ stringlike debris within gestational sac (in 25%)

√ discontinuous / irregular / thin (2 mm) choriodecidual reaction

√ no double decidual sac

√ low sac position

√ subchorionic collection

Cx: coagulopathy ← low plasma fibrinogen (after 4 weeks in 2nd trimester pregnancy)

Rx: suction D&C (in 1st trimester); prostaglandin E suppositories (in 2nd trimester)

DDx: blighted ovum

ACARDIA

= ACARDIAC MONSTER = TWIN REVERSED ARTERIAL PERFUSION SEQUENCE (TRAP)

= rare developmental anomaly of monochorionic twinning in which one twin develops without a functioning heart

Prevalence: 1÷30,000–35,000 births; in 1% of monozygotic twins

Pathophysiology:

normal twin perfuses acardiac twin through artery-to-artery + vein-to-vein anastomoses in shared placenta → reversed circulation alters hemodynamic forces → abnormal cardiac morphogenesis

Spectrum:

(1) **Holoacardia** = no heart at all

(2) **Pseudoacardia** = rudimentary cardiac tissue

√ proximity of the 2 cord insertions on placental surface linked by an arterioarterial anastomosis

√ reversed arterial flow in cord toward acardiac twin

√ fused placentas

√ polyhydramnios

A. PUMP TWIN

Risk: increased for fetal demise + preterm labor

√ morphologically normal

√ cardiac overload signs: hydrops, IUGR, hypertrophy of right ventricle, increased cardiothoracic ratio, hepatosplenomegaly, ascites

B. PERFUSED TWIN = ACARDIAC TWIN

Pathophysiology: vascular anastomosis sustains life of acardiac monster
Associated with: monochorial placenta (= same gender); wide range of abnormalities
√ absent / rudimentary heart ("acardius")
√ tiny / absent cranium (acephalus)
√ small upper torso ± absent / deformed upper extremities
√ marked integumentary edema + cystic hygroma
Prognosis: mortality of 100% for perfused twin, 50% for pump twin (increased with increased size of acardiac twin)
Rx: laser ablation of umbilical cord to acardiac twin (up to 20–22 weeks)

ADENOMYOSIS

= ENDOMETRIOSIS INTERNA (term no longer used)
= focal / diffuse benign invasion of myometrium by endometrium (heterotopic "endometrial islands") inciting reactive myometrial (smooth muscle) hyperplasia
Cause: ? uterine trauma (parturition, myomectomy, curettage), chronic endometritis, hyperestrogenemia
Prevalence: 5–70% of hysterectomy specimens
Hormonal dependency:
ectopic endometrial glands of adenomyosis (= generally of basalis type of endometrium) do NOT respond to cyclic ovarian hormones (largely nonfunctioning ← resistance to hormonal stimulation unlike endometriosis); some degree of proliferative + secretory changes occur during menstrual cycle; tamoxifen (= nonsteroidal antiestrogen) increases incidence of adenomyosis in postmenopausal women
Path: endometrial glands deeper than ¼ of thickness of junctional zone = 2–3 mm below endometrial-myometrial junction
Histo: endometrial glands + stroma within myometrium surrounded by smooth muscle hyperplasia
Age: multiparous premenopausal women > 30 years during menstrual life (later reproductive years)
Associated with: endometriosis (in 36–40%)
Types: diffuse form / focal (localized circumscribed) form
• asymptomatic in 5–70%; pelvic pain, menorrhagia, dysmenorrhea (abates after menopause)
√ globular uterine enlargement
HSG:
√ multiple small linear / saccular diverticula extending into myometrium
√ uterine cavity may be enlarged / distorted
√ irregular masslike filling defect in uterine fundus in focal adenomyosis
US (53–89% sensitive, 67–98% specific, 68–86% accurate):
√ poorly marginated hypoechoic heterogeneous areas within myometrium + myometrial cysts
√ globular / asymmetrically enlarged uterus
MR (78–93% sensitive, 66–93% specific, 85–90% accurate):
√ diffuse / focal thickening of junctional zone forming an ill-defined area of low SI ± embedded bright foci on T2WI
Cx: infertility

Rx: conservative medical treatment (analgesics + minimally effective menstrual suppression Rx with danazol / GnRH agonist); surgical treatment (endometrial ablation, laparoscopy, lesion excision; alternatively uterine artery embolization; hysterectomy (the only definitive cure for debilitating adenomyosis)

Cystic Adenomyosis

= very rare well-circumscribed cystic myometrial lesion of hemorrhage in different stages of organization (in 40% of diffuse adenomyosis, in 100% of focal adenomyosis)

Path: extensive menstrual bleeding into ectopic endometrium ← unusual response to cyclical ovarian hormones

Location: uterine origin confirmed by (a) myometrial splaying around lesion, (b) "bridging vessel" sign (c) separate distinct identification of ovaries

√ "Swiss cheese" appearance of myometrium on US

√ miniature uterus:

- √ fluid content of high SI ← hemorrhage at different stages of organization similar to endometriotic cyst
- √ surrounding wall of inner zone of low SI on T1WI (= junctional zone)
- √ relatively bright outer myometrium

DDx: (1) Leiomyoma with hemorrhagic degeneration
(2) Hematometra

Diffuse Adenomyosis (67%)

In 90% associated with: pelvic endometriosis (in women < 36 years of age)

• infertility ← impaired uterine contractility for directed sperm transport

US:

- √ smooth uterine enlargement (DDx: diffuse leiomyomatosis)
- √ asymmetric thickening of anterior and posterior myometrial walls
- √ diffuse heterogeneous myometrial echotexture (in 75%):
  - √ nodular / linear areas of increased myometrial echogenicity (= heterotopic endometrial tissue)
  - √ area of decreased myometrial echogenicity (= smooth muscle hyperplasia)
- √ HIGHLY SPECIFIC < 5 mm small subendometrial cysts (in 50%) ← dilated cystic glands / hemorrhagic foci
- √ widening of junctional zone > 12 mm on T2WI
- √ poor definition of endomyometrial junctional zone (= endometrial tissue extending into myometrium)
- √ pseudowidening of endometrium ← increased myometrial echogenicity
- √ lack of uterine contour abnormality / mass effect

MR:

- √ enlargement of the uterus
- √ widening of junctional zone (= inner myometrium) ≥ 12 mm hypointense on T2WI, T2-weighted SE images, contrast-enhanced T1WI ← hyperplasia of smooth muscle
- √ bright foci on T2WI (50%) ← islands of ectopic endometrial tissue + cystic dilatation of glands:

√ pseudowidening of endometrium (= indistinct foci of endometrial invasion of myometrium)
√ myometrial cysts + nodules, linear striations
√ foci of high SI on T1WI ← hemorrhage within ectopic endometrial tissue
√ variable degrees of enhancement always less than adjacent myometrium

DDx: (1) Marked physiologic thickening of junctional zone during menstruation (esp. cycle days 1 + 2)
◊ Avoid imaging during menstrual phase
(2) Myometrial contraction (ill-defined hypointense area on T2WI in up to 75%, transient nature, distortion of endometrial lining)
(3) Muscular hypertrophy (hypoechoic inner myometrium, diffuse junctional zone thickening)
(4) Endometrial carcinoma (error in staging if adenomyosis coexists)

Focal Adenomyosis (33%)

= "ADENOMYOMA"
√ polypoid mass (= polypoid adenomyoma / adenomyomatous polyp) protruding into uterine cavity (less commonly in myometrial / subserosal location)

US:
√ focal echogenic myometrial mass of 2–7 cm in diameter:
√ mass of oval / elongated shape with ill-defined margins
√ contiguity with junctional zone
√ penetrating vascular pattern

MR:
√ oval myometrial mass with indistinct margins of primarily low SI on all sequences ← surrounding reactive dense smooth muscle hypertrophy
√ widening of the junctional zone from 8 mm up to 12 mm
√ focal thickening of junctional zone > 12 mm
√ linear / round foci of high SI on T1WI within mass ← T1 shortening effect of methemoglobin in hemorrhagic foci
√ spotty signal voids on GRE ← T2*-shortening effect of hemosiderin in old hemorrhagic foci
√ foci of central high-intensity spots / linear striations on T2WI (= dilated endometrial glands in secretory phase / endometrial cyst, hemorrhagic focus) in 50%
√ low to intermediate SI on DWI ← benign neoplastic nature

Rx: polypectomy / myomectomy

DDx:
(1) Fibroid = leiomyoma (round hypoechoic mass anywhere in myometrium, well-defined margins, separate from junctional zone, calcifications, edge shadowing, whorled appearance, draping pattern of dilated vessels in periphery of mass, low SI on T1WI + T2WI, no small foci of high SI on T2WI)
(2) Adenomatoid tumor of uterus
= rare benign mesothelial tumor difficult to distinguish from leiomyoma / adenomyoma
(3) Metastatic myometrial involvement by cancer of breast, stomach, malignant lymphoma

(4) Low-grade endometrial stromal sarcoma (rare, young woman, extensive myometrial invasion)

AMNIOTIC BAND SYNDROME

= CONGENITAL CONSTRICTION BAND SEQUENCE = EARLY AMNION RUPTURE SYNDROME
= "slash defects" in nonanatomic distribution

Pathogenesis:
(a) early amniotic rupture exposing the fetus to the injurious environment of constrictive fibrous mesodermic bands that emanate from the chorionic side of the amnion
(b) vascular disruption events

Prevalence: 0.5–1.0÷10,000 live births

√ very thin sheet / band attached to fetus:
√ fine linear echoes that extend from fetal defect to uterine wall but are difficult to see
√ membrane that flaps with fetal movement
√ restriction of fetal motion ← entrapment of fetal parts by bands

Associated with fetal deformities in 77%:

1. Limb defects (multiple + characteristically asymmetric)
   √ simple grooves / constriction rings of limbs / digits
   √ amputation of limbs / digits
   √ distal syndactyly
   √ clubbed feet (30%)
   √ gibbus deformity of spine
2. Craniofacial defects
   = asymmetric nonanatomic defects of skull + brain
   √ pterygium, facial cleft
   √ anencephaly
   √ asymmetric lateral encephalocele
   √ facial clefting of lip / palate
   √ asymmetric microphthalmia
   √ incomplete / absent cranial calcification
   √ ± attachment of head to uterine wall
3. Visceral defects
   √ thoracoschisis
   √ **abdominoschisis** ± exteriorization of liver
   √ normal umbilical cord

> DDx of abdominoschisis due to bands from body stalk anomaly depends on demonstration of a normal umbilical cord.

√ abdominal contents floating in amniotic fluid without clear visualization of encasing membrane

DDx: (1) Chorioamnionic separation ← subchorionic hemorrhage
(2) Intrauterine synechiae
(3) **Adams-Oliver syndrome** (aplasia cutis, limb defects), scalp and skull defects at vertex associated with often asymmetric transverse limb defects

(4) Body stalk anomaly

ANEMBRYONIC PREGNANCY

= BLIGHTED OVUM

= abnormal intrauterine pregnancy with developmental arrest prior to formation of embryo; may occur as a blighted twin

Cause: early arrest of embryonic development related to chromosomal abnormality

• ± vaginal bleeding

√ empty gestational sac (> 6.5 weeks MA)

√ yolk sac identified without embryo:

√ vanishing (passed) yolk sac on serial scans

√ gestational sac small / appropriate / large for dates:

√ decrease in gestational sac (GS) size

√ GS fails to grow by > 0.6 mm/day on serial scans

√ irregular weakly echogenic decidual reaction of < 2 mm

√ distorted sac shape

(a) by transabdominal scan:

GS usually not visualized before 5.0–5.5 weeks MA; yolk sac forms at 4 weeks MA when GS is 3 mm; embryo usually visualized by 6 weeks MA

√ GS size ≥ 10 mm of mean diameter without DDS

√ GS size ≥ 20 mm of mean diameter without yolk sac

√ GS size ≥ 25 mm of mean diameter without embryo

(b) by transvaginal scan

normal intradecidual GS routinely detected at 4–5 weeks with a mean sac diameter of 5 mm

√ GS size ≥ 8 mm of mean diameter without yolk sac

√ GS size ≥ 16 mm of mean diameter without cardiac activity

Cx: first trimester bleeding

ARTERIOVENOUS MALFORMATION OF UTERUS

= UTERINE ARTERIOVENOUS FISTULA = UTERINE CIRSOID ANEURYSM

Associated with: dilatation & curettage, endometrial carcinoma, gestational trophoblastic disease

• genital bleeding, often requiring blood transfusions

MR:

√ tortuous tubular signal voids in myometrium / parametrium / protruding into endometrial cavity on T1WI + T2WI

√ vascular lake with sluggish flow hyperintense on T2WI

√ intensely enhancing lesion isointense to vessels on contrast-enhanced dynamic subtraction MR

ASHERMAN SYNDROME

[Joseph G. Asherman (1889–?), Czech-Israeli gynecologist in Tel Aviv]

= association of multiple intrauterine synechiae (= adhesions consisting of fibrous tissue or smooth muscle) with menstrual dysfunction + infertility

Cause: sequelae of endometrial trauma (vigorous instrumentation during dilatation & curettage) usually during postpartum or postabortion period / severe endometritis

Path: scars / bands of fibrous tissue (synechiae) connect opposing sides of the endometrium by crossing the endometrial cavity; scars cause the endometrial cavity to contract resulting in an irregular surface

• hypomenorrhea / amenorrhea; habitual abortion / sterility

HSG:

√ solitary / multiple filling defects

√ bands of tissue traversing endometrial cavity

√ irregular surface contour of uterine cavity

√ small uterine cavity partially / near completely obliterated (DDx: DES exposure)

Sonohysterography:

√ echogenic bands bridging the uterine cavity

◊ Thick fibrotic bands may prevent complete uterine distension

MR:

√ small thin irregular endometrial cavity

BARTHOLIN GLAND CYST

[Caspar Bartholin the Younger (1655–1738), Danish anatomist and physician]

= retention cyst

Origin: derived from urogenital sinus, female homologue of male (bulbourethral) Cowper glands

Cause: chronic inflammation / infection of gland → ductal obstruction from purulent material / thick mucus

Histo: lined by <u>mucinous</u> transitional cell / columnar epithelium

Location: posterolateral inferior ⅓ of vaginal introitus medial to labia minora <u>at / below</u> level of pubic symphysis

Size: 1–4 cm

√ unilocular cyst hyperintense on T2WI

√ variable T1 hyperintensity depending on proteinaceous / mucinous contents

Rx: administration of silver nitrate; marsupialization; surgical excision

BECKWITH-WIEDEMANN SYNDROME

[John Bruce Beckwith (1933–?), pediatric pathologist at Children's Orthopedic Hospital in Seattle, WA]

[Hans Rudolf Wiedemann (1915–2006), chair of pediatrics at the University of Kiel, Germany]

= EMG SYNDROME (**E**xomphalos = omphalocele, **M**acroglossia, **G**igantism)

= common autosomal dominant overgrowth syndrome with reduced penetrance + variable expressivity related to short arm of chromosome 11; sporadic in 85%

Prevalence: 1÷13,700 to 1÷14,300 live births; M÷F = 1÷1

4% risk for developing embryonal tumors:

nephro-, hepato-, pancreatoblastoma, rhabdomyosarcoma

• neonatal polycythemia

√ advanced bone age

Constellation:

(1) Hemihypertrophy 13–33%
(2) Hyperplastic visceromegaly: 57%
kidney, liver (hepatomegaly), spleen, pancreas, clitoris, penis, ovaries, uterus, bladder
(3) Abdominal wall defects
(a) Omphalocele 76%
(b) Umbilical hernia 49%
(c) Diastasis recti 33%
(4) Macroglossia 98%
(5) Facial nevus flammeus 63%
(6) Ear lobe creases and pits 66%
(7) Prominent eyes with intraorbital creases
(8) Infraorbital hypoplasia 81%
(9) Gastrointestinal malrotation 83%
(10) Pancreatic islet hyperplasia → hyperglycemia
(11) Cardiac anomalies
(12) Natal / postnatal gigantism 77%

@ Adrenal gland
Histo: adrenocortical hyperplasia, hyperplastic adrenal medulla, cystic adrenal cortex, bilateral adrenal cytomegaly (= enlargement of fetal cortical cells)

@ Kidney
Histo: disordered lobar arrangement, medullary dysplasia
√ nephromegaly
√ increased cortical echogenicity ← glomeruloneogenesis
√ accentuation of corticomedullary definition
√ medullary sponge kidney
√ pyelocalyceal diverticula

OB-US:
√ LGA fetus with growth along 95th percentile
√ polyhydramnios (51%)
√ thickened placenta
√ long umbilical cord

Cx: (1) Development of malignant tumors (in 4%)
(2) Neonatal hypoglycemia (50–61%)

BRENNER TUMOR

[Fritz Brenner (1877–1969), German physician and pathologist practicing in German South West Africa and Johannesburg]
= almost always benign uncommon epithelial-stromal ovarian tumor
Frequency: 1.5–2.5%
Histo: transitional epithelial cells (similar to urothelium) within prominent fibrous connective tissue stroma
Associated with: mucinous cystadenoma / other epithelial tumor in 20–30%
Peak age: 40–70 years

• may have estrogenic activity
Size: most 1–2 cm (up to 30 cm) in diameter; bilateral in 5–7%
√ ± extensive calcifications
US:
√ usually hypoechoic solid homogeneous tumor with well-defined back wall
MR:
√ markedly hypointense tumor component on T2WI (fibrous component + calcifications)
√ moderate enhancement (DDx: hypovascular fibrothecoma)

CERVICAL CARCINOMA

◊ Most common gynecologic malignancy in developing countries; 3rd most common gynecologic malignancy (after endometrial + ovarian cancer) in USA; 6th most common cause of death from cancer in women
Highest prevalence: Central + South America > South Central Asia > parts of Africa
Incidence: 12÷100,000 women annually; 12,990 new cases + 4,120 deaths in USA (2016)
Peak age: 45–55 years
Histo: squamous cell carcinoma (80–95%) arising low in endocervical canal, adenocarcinoma (5–20%) arising from endocervical columnar epithelium, clear cell adeno-carcinoma (unusual) in women exposed to DES in utero
Risk factors: lower socioeconomic standing, Black race, early marriage, multiparity, early age at first intercourse, multiple sexual partners, cigarette smoking, immuno-suppressed state, use of oral contraceptives, human papilloma virus infection (HPV serotypes 16, 18, 31, 33, 56 → > 80% of all invasive cervical carcinomas)
Significance of tumor size:
> 4 cm: nodal metastases (80%), local recurrence (40%), distant metastases (28%)
< 4 cm: nodal metastases (16%), local recurrence (5%), distant metastases (0%)
Spread:
(a) direct extension to lower uterine segment + vagina + paracervical space along uterosacral and broad ligaments
(b) lymphatic: paracervical > parametrial > hypogastric + obturator > external iliac > common iliac + presacral > para-aortic nodes
(c) hematogenous: lung, liver, bone
• leukorrhea ± abnormal vaginal bleeding (< 30%)
• intermenstrual / postcoital bleeding / metrorrhagia
Clinical staging: limited accuracy of 66% stage I (78%), stage III (25%)
Location:
arises almost exclusively from transformation zone (= squamo- columnar junction)
(a) on cervix (in young woman)
(b) in endocervical canal (older woman)
with protrusion into vagina / invasion of lower myometrium

Tumors tend to be exophytic in younger patients + endophytic in older patients ← variable location of transformation zone with advancing age

US:
@ Primary tumor

√ small tumor isoechoic to mucosa difficult to detect
√ altered echotexture + distortion of normal cervical morphology + lack of compressibility with increasing size
√ color Doppler US may facilitate visualization and delineation of tumor ← hypervascular tumor (in 95%)

CT:

@ Primary tumor

Staging of Cervical Cancer (2009)
Fédération Internationale de Gynécologie et d'Obstétrique (FIGO)

FIGO Stage	*Description*	*Nodal Metastases*
0	Carcinoma in situ (before invasion)	0.3%
I	Confined to cervix	
IA	preclinical microscopic invasion	
IA1	microinvasion of stroma (≤ 3 mm deep and ≤ 7 mm wide)	0.3%
IA2	tumor > 3 mm and ≤ 5 mm deep and ≤ 7 mm horizontal spread	14%
IB	tumor larger than IA	16%
IB-1	clinically visible lesion ≤ 4 cm	
IB-2	clinically visible lesion > 4 cm	
II	Extension beyond cervix but not to pelvic wall / lower 1/3 of vagina	
IIA	no parametrial invasion	33%
IIA1	clinically visible lesion ≤ 4 cm in diameter	
IIA2	clinically visible > 4 cm in diameter	
IIB	parametrial invasion excepting pelvic sidewall	37%
III	Extension to pelvic wall or lower 1/3 of vagina or hydronephrotic / nonfunctioning kidney	
IIIA	invasion of lower 1/3 of vagina	
IIIB	pelvic side wall invasion + hydronephrosis	
IV	Located outside true pelvis or invasion of bladder or rectal mucosa	55%
IVA	invasion of bladder / rectal mucosa	
IVB	spread to distant organs (paraaortic / inguinal nodes, intraperitoneal metastasis)	

√ growth pattern: exophytic, infiltrating, endocervical
√ bulky enlargement of cervix > 3.5 cm (DDx: cervical fibroid)
√ iso- (50%) / hypoattenuating after IV contrast ← necrosis, ulceration, reduced vascularity
√ gas within tumor (necrosis / prior biopsy)
√ fluid-filled uterus (blood, serous fluid, pus) ← obstruction
√ hypoattenuating lesion of myometrium / with vaginal distension

@ Parametrial spread (30–58% accuracy):

- √ parametrial soft-tissue mass
- √ ureteral encasement
- √ thickening of ureterosacral ligaments
- √ > 4-mm soft-tissue strands of increased attenuation extending from cervix into parametria, cardinal / sacrouterine ligaments
- √ obliteration of fat planes
- √ ill-defined irregular cervical margins
- √ eccentric parametrial enlargement

DDx: parametrial inflammation ← instrumentation, ulceration, infection, prior pelvic surgery, endometriosis

@ Pelvic side wall disease
- √ tumor < 3 mm from side wall
- √ enlarged piriform / obturator internus muscles
- √ encasement of iliac vessels
- √ destruction of pelvic bones

@ Pelvic visceral disease (60% PPV)
- √ loss of perivesical / perirectal fat plane
- √ asymmetric nodular thickening of bladder / rectal wall
- √ intraluminal mass
- √ air in bladder ← fistula

@ Lymphatic spread (65–77–80% accuracy)
- √ nodes > 1 cm in diameter (> 7 mm for internal iliac nodes, > 9 mm for common iliac nodes, > 10 mm for external iliac nodes) with 44% sensitivity
- √ lymph node necrosis (100% PPV)

DDx: adenopathy from secondary tumor infection

MR (76–78–91% accuracy for staging, 82–94% accuracy for parametrial involvement):

@ Primary tumor
- √ focal bulge / mass in cervix:
  - √ mass isointense on T1WI
  - √ hyperintense on T2WI compared with fibrous stroma (DDx: postbiopsy changes, inflammation, nabothian cysts)
  - √ size of tumor accurately depicted (on T2WI rarely overestimated due to inflammation / edema)
    - ◊ Tumor diameter and probability of recurrence + metastases are related; tumor diameter > 4 cm (stage IB2) means no surgical treatment
  - √ early contrast enhancement on fat-saturated T1WI
- √ blurring + widening of junctional zone (retained secretions in uterine cavity) ← obstruction of cervical os
- √ disruption of hypointense vaginal wall by hyperintense thickening on T2WI
- √ disruption of hypointense cervical fibrous stromal ring on T2WI by nodular / irregular tumor SI

@ Parametrial invasion (best seen on T1WI):
- √ low-intensity spiculated areas of soft tissue radiating from periphery of cervical mass
- √ irregular lateral margins of cervix = linear stranding around cervical mass
- √ thickening of uterosacral ligament

@ Pelvic sidewall invasion
√ tumor involves obturator internus, piriform, levator ani m.
√ dilatation of ureter + hydronephrosis
@ Pelvic visceral disease
√ disruption of hypointense walls of bladder / rectum (DDx: hyperintense thickening of bladder wall on T2WI ← bullous edema)
@ Lymphatic spread
√ lymphadenopathy > 10 mm, hyperintense compared with muscle / blood vessels on T2WI

PET/CT:

Indication: staging, restaging, evaluation of response to therapy

Pitfalls:

(1) Cyclical endometrial uptake during ovulatory + menstrual phases
(2) Attenuation correction artifact with metallic prosthetic implants, IUD, surgical clips
(3) Physiologic ovarian uptake in premenopausal women by corpus luteum
(4) Uptake by uterine leiomyoma
(5) Uptake by postsurgical healing, radiation fibrosis, infection

Prognosis: depending on tumor stage + volume of primary mass + histologic grade + lymph node metastases; in 30% recurrent / persistent disease (usually within 2 years)

5-year survival rate: tumor diameter ≤ 1 cm 84%
tumor diameter > 4 cm 67%
stage IIB 65%
stage III 40%
stage IVA < 20%

Cx: stenosis + obstruction of cervical canal → hydrometra, hematometra, pyometra

Rx: (1) Surgery for stages < IIA / tumor < 4 cm
(2) Radiation therapy ± chemotherapy for stages > IIB

Prevention: human papillomavirus vaccine

DDx: (1) Endometrial polyp / adenocarcinoma (centered in endometrial cavity protruding into endocervical canal)
(2) Prolapsed submucosal fibroid (more hypointense on T2WI)

Recurrent Cervical Carcinoma

= local tumor growth / development of distant metastasis ≥ 6 months after complete regression

@ Pelvic recurrence

Prevalence: varies with stage, histologic type, adequacy of therapy, host response; 11% in stage IB

Site: cervix, uterus, vagina / vaginal cuff, parametria, ovaries, bladder, ureters, rectum, anterior abdominal wall, pelvic side wall

• lower extremity swelling ← lymphatic obstruction
• pain ← nerve compression, ureteral obstruction

√ hydrometra ← obstruction by preserved cervix

√ rectovaginal fistula
√ hydronephrosis (70% by autopsy)
√ vesicovaginal fistula
√ pelvic side wall mass
DDx: radiation fibrosis (82% MR accuracy)

@ Nodal recurrence
◊ Prognosis worsens as nodal involvement progresses!
(a) primary: paracervical, parametrial, internal + external iliac, obturator nodes (= medial group of the external iliac nodes)
Frequency: in 75% of adenocarcinoma, in 61% of squamous cell carcinoma (autopsy)
(b) secondary: sacral, common iliac, inguinal, paraaortic nodes
Frequency: in 62% of adenocarcinoma, in 30% of squamous cell carcinoma (autopsy)

@ Solid abdominal organ recurrence
Location: liver (33%) > adrenal gland (15%) > spleen, pancreas, kidney

@ Peritoneal recurrence
1. Peritoneal carcinomatosis (5–27% by autopsy)
2. Tumor deposits in mesentery + omentum

• **Sister Joseph nodule** = umbilical metastasis developing from anterior peritoneal surface

@ GI tract recurrence
Location: rectosigmoid junction (17%), colon, small bowel
√ fistula formation
√ focal bowel wall thickening + tethering
√ intestinal obstruction (12% by autopsy)
Prognosis: immediate cause of death in 7%

@ Chest recurrence
1. Lung metastases (33–38% by autopsy)
2. Pleural metastases associated with hydrothorax
3. Pericardial metastasis
4. Lymphangitic carcinomatosis (< 5%)
5. Mediastinal / hilar adenopathy + pleural lesions / effusion

@ Osseous recurrence
Prevalence: 15–29% by autopsy
Location: vertebra > pelvis > rib > extremity
Mechanism: direct extension from paraaortic nodes (most common) / lymphatic / hematogenous spread

@ Skin + subcutaneous tissue recurrence (in up to 10%)

CHORIOAMNIONIC SEPARATION

(a) normally seen < 16 weeks MA
Cause: incomplete fusion of amniotic membrane with chorionic plate
(b) abnormal > 17 weeks MA

Cause: hemorrhage / amniocentesis (10%)
√ membrane extends over fetal surface + stops at origin of umbilical cord
√ elevated membrane thinner than chorionic membrane
Cx: rupture of amniotic membrane → may lead to amniotic band syndrome
DDx: amniotic band syndrome, uterine synechia, fibrin strand after amniocentesis, cystic hygroma (moves with embryo)

CHORIOANGIOMA

= benign vascular malformation of proliferating capillaries (= hamartoma) without malignant potential
Prevalence: 0.5–1.0% of pregnancies; > 5 cm in 1÷3,500 to 1÷16,000 births
◊ Most common tumor of the placenta
Histo: angiomatous (capillary), cellular, degenerative subtypes
Location: usually near the umbilical cord insertion site supplied by fetal circulation
• elevated maternal serum α-fetoprotein level (rare)
US:
√ well-circumscribed hypo- / hyperechoic rounded intraplacental mass protruding from the fetal surface of the placenta into amniotic cavity
√ contains anechoic cystic areas (= vessels)
√ arterial signal on Doppler ultrasound in angiomatous chorioangioma
MR:
√ placental mass with high T2 SI (similar to hemangioma)
√ heterogeneous SI ← acute infarction + degenerative changes
Prognosis: regression after infarction
Maternal Cx: preterm labor, toxemia, placental abruption, preeclampsia, hemorrhage
Fetal Cx (30–50%):
polyhydramnios (in ⅓), fetal hydrops, fetal hemolytic anemia, fetal thrombocytopenia, cardiomegaly, IUGR, congenital anomalies, fetal demise (with large / multiple lesion)
Rx: expectant management with serial US imaging (6–8 week intervals for small tumors, 1–2 week intervals for large tumors); serial fetal transfusion, fetoscopic laser coagulation, chemosclerosis with absolute alcohol, endoscopic surgical devascularization
DDx: partial hydatidiform mole, placental hematoma, teratoma, metastasis, leiomyoma

CHORIOCARCINOMA

= remarkably aggressive
Frequency: < 1%

Primary Ovarian Choriocarcinoma

= NONGESTATIONAL CHORIOCARCINOMA
Prevalence: extremely rare; 50 cases in world literature
Age: < 20 years
Associated with: germ cell tumor / epithelial neoplasm
• ↑ serum hCG (100% sensitive, 100% specific)
• isosexual precocity (50%)

√ usually unilateral
√ vascular predominantly solid tumor with areas of hemorrhage + necrosis + cyst formation
Prognosis: 90% 5-year survival in spite of typically late diagnosis at advanced stage
DDx: ectopic pregnancy (frequently mistaken diagnosis!), metastasis to ovary from gestational choriocarcinoma (reproductive age)

Gestational Ovarian Choriocarcinoma

Cause: metastasis from uterine choriocarcinoma (frequently bilateral ovarian masses); arising from ectopic ovarian pregnancy (extremely rare)
Age: reproductive age

Gestational Uterine Choriocarcinoma

Prevalence: 5% of gestational trophoblastic diseases
Age: child-bearing age
Histo: biphasic pattern including syncytiotrophoblastic + cytotrophoblastic proliferation without villous structures; extensive necrosis + hemorrhage; early + extensive vascular invasion
Preceded by: *mnemonic:* MEAN
Mole (hydatidiform) in 50.0%
Ectopic pregnancy in 2.5%
Abortion, spontaneous in 25.0%
Normal pregnancy in 22.5%
• continued elevation of hCG after expulsion of molar / normal pregnancy (25%); continued vaginal bleeding
US:
√ mass enlarging the uterus
√ mixed hyperechoic pattern (hemorrhage, necrosis)
CT (useful for staging):
√ heterogeneous predominantly hypoattenuating intrauterine tissue
√ detection of distant metastases
MR:
√ heterogeneous hyperintense mass on T2WI
√ focal signal voids (= vessels) on T1WI + T2WI
√ disruption of hypointense myometrium (= local invasion)
√ marked enhancement ← high vascularity
√ enhancing parametrial tissue (= local spread)
Metastases:
(a) hematogenous (usually): lung, kidney (10–50%), brain
√ radiodense pulmonary masses with hazy borders ← hemorrhage + necrosis
√ hyperechoic hepatic foci
(b) lymphatic: pelvic lymph nodes
(c) direct extension (occasionally): vagina
Prognosis: 85% cure rate (even with metastases); fatal with spread to kidneys + brain
Rx: (1) Chemotherapy: methotrexate, actinomycin D ± cyclophosphamide
(2) Hysterectomy (if at risk for uterine rupture)

DDx: *mnemonic:* THE CLIP
True mole
Hydropic degeneration of placenta
Endometrial proliferation
Coexistent mole and fetus
Leiomyoma (degenerated)
Incomplete abortion
Products of conception (retained)

CLEAR CELL NEOPLASM OF OVARY

= MESONEPHROID TUMOR
= almost always invasive carcinoma
Frequency: 2–5–10% of all ovarian cancers
Histo: clear cells (cuboidal cells with clear cytoplasm) + hobnail cells (columnar cells with large nuclei projecting into the lumina of glandular elements); identical to clear cell carcinoma of endometrium, cervix, vagina, kidney; ~ 100% malignant
Not associated with: in utero DES exposure (like lesions of the vagina + cervix)
• 75% of patients present with stage I disease
√ frequently unilocular cyst + mural nodule(s)
Prognosis: 50% 5-year survival rate (better than for other ovarian cancers)

CLOACAL EXSTROPHY

= exstrophy of all structures forming cloaca (rectum, bladder, lower GU tract) similar to bladder exstrophy
Prevalence: 1÷200,000–400,000 live births; M < F
Cause: ? premature rupture of cloacal membrane; ? abnormal overdevelopment of lower cloaca preventing mesenchymal tissue migration: ? abnormal fusion of genital tubercle below cloacal membrane; ? abnormal caudal position of body stalk; ? failure of mesenchymal ingrowth

Associated abnormalities: OEIS
(a) lumbosacral (common): vertebral column / spinal cord abnormalities, tethered cord, lipomeningocele, lipomyelocystocele
(b) genitourinary (in up to 60%): hydronephrosis, renal developmental variants, abnormal genitalia, oligohydramnios ← renal obstruction
•absent anal dimple ← anal atresia

√ low abdominal wall defect
√ absence of visible bladder
√ omphalocele (initial observation) as craniad part of large complex anterior wall defect extending inferiorly to pubis
√ "elephant trunk" = bowel herniation between everted bladder halves

CONJOINED TWINS

= incomplete division of embryonic cell mass in monozygotic twins occurring at 13–16 days but before the 3rd week of GA

Prevalence: 1÷50,000 to 1÷200,000 deliveries; 1÷14,000 to 1÷25,000 in Southeast Asia + Africa; 1÷600 twin births; M÷F = 1÷3

OB-US (diagnosed as early as 12 weeks GA):

- √ single placenta without separating amniotic membrane (monochorionic, monoamniotic = HALLMARK OF MONOZYGOTIC TWINNING)
- √ inseparable fetal bodies + skin contours:
  - √ fetuses commonly face each other
  - √ both fetal heads persistently at same level
  - √ no change in relative position of fetuses
  - √ bibreech (more common) / bicephalic presentation (cephalic-breech presentation is most common presentation for omphalopagus)
  - √ backward flexion of cervical spine (in anterior fusion)
  - √ single cardiac motion (if heart shared)
- √ polyhydramnios (in almost 50%)
- √ single umbilical cord with > 3 vessels
- √ fewer limbs than expected

Associated malformations:

- √ omphalocele
- √ congenital heart disease (high frequency in all types of conjoined twinning)

Prognosis: 40–60% stillborn; 35% die within 24 hours of life

Craniopagus

- = united at any part of the skull except face / foramen magnum (usually vertical / parietal in > 60%)
- √ shared cranium, meninges, dural venous sinuses (brains commonly remain separate ± connecting bridge of neural tissue)

Ischiopagus

- = united from umbilicus to large conjoined pelvis: face to face / end to end

Types: tetrapus (4 legs), tripus (3 legs), bipus (2 legs)

- √ usually two sacra ± single symphysis pubis
- √ varying degrees of renal fusion + ectopia
- √ one / two urinary bladders
- √ single external urethral orifice (usually)
- √ shared sex organs (frequently born as females)
- √ lower GI tract usually shared with anal atresia + colovesical fistulas
- √ large pelvic vessel connecting both aortas

Omphalopagus

- = joined ventrally in umbilical region, often with inclusion of lower thorax
- √ liver fusion (80%)
- √ shared terminal ileum (joined Meckel diverticulum) + proximal colon (33%)

Parapagus

- = side-to-side position with ventrolateral fusion sharing umbilicus, abdomen, pelvis

Types: dithoracic (= separate thoraces), dicephalic (= separate heads)
√ conjoined pelvis with single symphysis pubis
√ one / two sacra
√ multiple other anomalies

Pygopagus

[*pegos*, Greek = fixed, pegged]
= united dorsally sharing sacrococcygeal + perineal region
√ fusion of sacral vertebrae (spinal cords usually separate)
√ single anus ± single rectum
√ single urinary bladder + urethra (15%)

Conjoined Twins *classified according to most prominent site of connection*	
Superior Conjunction	
Dipygus (<1%)	single head, thorax, abdomen + two pelves and four legs
Syncephalus (<1%)	facial fusion ± thoracic fusion
Craniopagus (2%)	joined between homologous portions of cranial vault
Middle Conjunction	
Thoracopagus (40%)	between thoracic walls; conjoined hearts (75%)
Omphalopagus (33%)	joined between umbilicus + xiphoid
Xiphopagus	joined at xiphoid
Rachipagus	joined at any level of spinal column above sacrum
Thoracoomphalopagus	
Inferior Conjunction	
Diprosopus (<1%)	two faces + one head and body
Dicephalus (<1%)	two heads + one body
Ischiopagus (6%)	joined by inferior sacrum and coccyx
Pygopagus (19%)	joined by posterolateral sacrum and coccyx
Incomplete Duplication (10%)	*duplication of only one part of body*
◊ The more fused twins are usually joined laterally, whereas the more separate twins are joined anteriorly, posteriorly, cranially, and caudally!	

Thoracopagus

= united from upper thorax to umbilicus
√ common sternum, diaphragm, upper abdominal wall
√ common pericardial sac (90%) + some degree of cardiac fusion
√ fusion of liver (invariably):
  √ shared biliary system (in 25%)
  √ ± absent / anomalous hepatic venous drainage
√ common small intestine (in 50%): joined at duodenum + separated at distal ileum

Prognosis: cardiac fusion precludes successful surgical separation in 75%

CORD PROLAPSE

= prolapse / descent of cord into endocervical canal after rupture

Prevalence: 0.5% at delivery, 2–3% prenatally

Predisposing factors:

low birth weight, breech presentation, nonvertex fetal lie, polyhydramnios, cephalopelvic disproportion, multiparity, abnormal placentation, increased length of umbilical cord, velamentous cord insertion, spontaneous rupture of membranes

- prolonged fetal bradycardia
- severe and repetitive fetal heart rate decelerations

May be associated with: fetal hypoxia, perinatal death, fetal neurologic sequelae

Cx: cord compression with high perinatal mortality

N.B.: MEDICAL EMERGENCY! Alert obstetrician immediately!

OB management:

(1) Patient immediately placed into Trendelenburg / knee-elbow position in radiology department (!)
(2) Cesarean section for term infants
(3) Expectant management for preterm infants

DDx: Cord / funic presentation (= normal looping of umbilical cord between fetal presenting part and cervix)

DERMOID

= DERMOID CYST = MATURE CYSTIC TERATOMA

= congenital benign slow-growing germ cell tumor containing mature tissues from all 3 germ cell layers with predominance of ectodermal component

Frequency: 96% of germ-cell tumors; 5–11–25% of all ovarian neoplasms; 20% of ovarian tumors in adults; 50–80% of pediatric ovarian tumors

◊ Most common ovarian neoplasm!

Origin: self-fertilization of a single germ cell after the first meiotic division (= random error in meiosis)

Path: unilocular thin-walled cyst lined by an opaque gray-white wrinkled epidermis from which hair shafts protrude; lumen of cyst filled with sebaceous secretions mixed with hair strands

Histo: composed primarily of mature ectodermal components (skin, hair follicles, sebaceous glands, teeth, desquamated epithelium); cartilage; bone; muscle; bronchus; fat; salivary gland; neuronal tissue; pancreas; retina; may contain struma ovarii, carcinoid tumor

◊ 15% of mature cystic teratomas may not show a fat component on imaging!

Mean age: 36 years (range, 4 months to 74 years); age peak 20–40 years; in 80% during reproductive life; M>F

- relatively soft pelvic mass ($^2/_3$) difficult to palpate
- pelvic pressure / pain ← torsion / hemorrhage
- paraneoplastic syndrome (rare): autoimmune hemolytic anemia refractory to conventional therapy, virilization, hyperestrogenism; asymptomatic (mostly)

Location: ovaries and testes (common); also anywhere along path of germ cell migration during embryogenesis, usually along midline of body; "misplaced" in head and neck, mediastinum, abdomen, omentum, retroperitoneum, abdominal viscera, sacrococcygeal region; bilateral in 8–15–25%

Mean diameter: 7–10 cm

√ well-defined thin-walled heterogeneous mass = mixture of solid and cystic components (appearance dependent on composition)

√ fat, fat-fluid level, calcium within the same lesion is considered PATHOGNOMONIC (albeit present in only a minority of cases)

√ cystic mass with macroscopic fat (93%):

- √ fat-fluid / hair-fluid level
- √ "**dermoid plug**" = Rokitansky nodule = 10–65 mm oval / round mural solid tissue protuberance / tubercle / nipple (mamilla) projecting into cyst lumen; often containing hair, calcific, dental, adipose or sebaceous components
- √ calcification (56%)

Plain film (diagnostic in 40%):

- √ tooth / bone
- √ fat density (SPECIFIC)

US (77–87% sensitive):

- √ variable presentation *(see table)*:
  - √ complex mass containing echogenic components (66%)
  - √ predominantly solid mass (10–31%)
  - √ well-defined purely cystic mass (9–15%)
  - √ thin capsule + NO septa
- √ mixture of sebum + hair strands:
  - √ clump of hair = hyperechoic focus with multiple tissue interfaces that absorbs + reflects sound → gradual "dirty" acoustic shadowing
  - √ sebum (liquefied at body temperature) = background of anechoic fluid with variable internal echoes
  - √ "**tip of the iceberg**" sign → hair ball floating in sebum in 25–44% (DDx: stool-filled rectosigmoid)

Sonographic Features of Dermoids

Feature	*Incidence [%]*	*PPV [%]*
√ shadowing echogenic focus	s	96
√ hyperechoic lines and dots	61	98
√ regional / diffuse bright echoes	58	98
√ fluid-fluid level	8	60
√ cyst with wall nodularity	53	
√ solid mass without cystic features	42	

  - √ dermoid mesh = bright undulating hyperechoic fine lines and dots = hair dispersing into surrounding fluid (DDx: fibrous strands in hemorrhagic cyst)
- √ hyperechoic focus with acoustic shadowing ← calcification (in 86%; 96% PPV)

√ NO central vascularity on color Doppler

CT:

√ round well-circumscribed thin-walled uni- or multilocular cystic mass with solid components of fat floating in interface between two water-density components (93%)

√ Rokitansky nodule = dermoid plug (81%) of adipose tissue; usually single, may be multiple

√ sebum-rich fat-fluid level in cyst cavity (12%)

√ globular calcifications (tooth) / rim of calcification (56%)

√ Hounsfield unit values of −20 to −140 ← fat within dermoid cyst (highly suggestive of Dx)

MR:

√ cyst with fluid-fluid level:

√ hyperintense lipid-laden nondependent cyst fluid (above fluid of low SI) on T1WI + of intermediate intensity on T2WI

√ hyperintense mass (= fat + serous fluid both with high SI) on T2WI

√ chemical shift artifact of bright / dark bands (along frequency-encoding gradient)

√ signal drop at chemical-selective fat-saturated T1WI in 97% (mandatory sequence!)

√ chemical shift imaging for identification of microscopic fat:

√ in-phase GRE image:

√ dependent fluid hypointense compared with muscle

√ nondependent fluid slightly hypointense compared with surrounding fat

√ opposed-phase GRE image:

√ dependent fluid still hypointense compared with muscle

√ slightly hypointense compared with surrounding fat

√ thin black outline at interface between water and fat ← phase cancellation of water + lipid in same voxel

Dx: fat + calcification are PATHOGNOMONIC

Cx: (1) Malignant degeneration in 1–2% (usually within dermoid plug of tumors > 10 cm in diameter in postmenopausal women) into squamous cell carcinoma (most common)

(2) Torsion (4–16%)

(3) Rupture with chemical peritonitis (1–4%)

(4) Hydronephrosis

Rx: surgery (to avoid torsion / rupture)

DDx: tuboovarian abscess, acute hemorrhagic cyst, atypical endometrioma, bowel gas

Rupture of Ovarian Cystic Teratoma

Cause: torsion, infarction, trauma, infection, malignant change, prolonged pressure during labor, idiopathic

• acute abdomen (due to severe chemical peritonitis) → shock

√ discontinuity of tumor wall + ascites

√ distorted / flattened shape of tumor

√ spilled sebaceous material / hair ball on T1WI + fat-suppressed T1WI (DDx to fluid)

√ calcifications outside confines of cyst

√ thickened peritoneum / intraperitoneal adhesions on contrast-enhanced fat-suppressed T1WI

Cx: chronic recurrent leakage → chronic granulomatous peritonitis (= gliomatosis) →

peritoneal adhesions → bowel obstruction
DDx: tubercular peritonitis, carcinomatosis

DIETHYLSTILBESTROL (DES) EXPOSURE

= first reported transplacental carcinogen
@ Vagina: adenosis, septa, ridges, clear-cell adenocarcinoma (1÷1,000 females exposed in utero to DES, by age 35)
@ Cervix: hypoplasia, stenosis, mucosal displacement, pseudopolyps, hooded / "cockscomb" appearance
@ Uterus: hypoplasia, bands, contour irregularity, "T- shaped" uterus
@ Tubes: deformity, irregularity, obstruction

ECLAMPSIA

= coma ± pre-, intra-, or postpartum convulsions not related to a coincidental neurologic disorder in a preeclamptic patient

Pathophysiology:

A. VASOSPASM THEORY
overregulation of cerebral vasoconstrictive response to acute + severe hypertension → progresses to vasospasm; prolonged vasospasm → local ischemia, increased brain capillary permeability, disruption of blood-brain barrier, arteriolar necrosis → cerebral edema + hemorrhage

B. FORCED-DILATATION THEORY
with severe arterial hypertension upper limit of cerebral autoregulation is reached → cerebral vasodilatation starts disrupting blood-brain barrier → cerebral edema

Time of onset: 2nd half of pregnancy in primigravida; < 20th week GA with trophoblastic disease

- severe throbbing frontal headache; seizures (usually tonic-clonic)
- retinal / cortical blindness: scotomata, amaurosis, blurred vision
- hyperreflexia, hemi- / quadriparesis, confusion, coma

CT (positive in up to 50%):
√ bilateral rather symmetric white matter hypodensities without contrast enhancement
√ ± cerebral edema → compression of lateral ventricles
√ usually transient + completely reversible cerebral-cortical + basal ganglia hypodensities (= reversible ischemic lesions)
√ cerebral infarction in prolonged ischemia
√ intracerebral hemorrhage (major cause of mortality in 10–60%)

MR:
√ transiently increased T2-SI in cerebral cortex + subcortical white matter frequently in watershed areas of posterior hemispheres

ECTOPIA CORDIS

= fusion defect of anterior thoracic wall / sternum / septum transversum prior to 9th week of gestation

A. THORACIC TYPE (60%)

= heart outside thoracic cavity protruding through defect in sternum

B. ABDOMINAL TYPE (30%)
= heart protruding into abdomen through gap in diaphragm

C. THORACOABDOMINAL TYPE (7%)
= in pentalogy of Cantrell

D. CERVICAL TYPE (3%)
= displacement of heart into cervical region

Associated with:
(1) Facial deformities
(2) Skeletal deformities
(3) Ventral wall defects
(4) CNS malformations: meningocele, encephalocele
(5) Intracardiac anomalies: tetralogy of Fallot, TGA
(6) Amniotic band syndrome

Prognosis: stillbirth / death within first hour / death within first days of life in most case

ECTOPIC PREGNANCY

= implantation of blastocyst outside the endometrial cavity

Incidence: 2% of all pregnancies in USA (1992); higher for in vitro fertilization; 73,700 cases in USA (1986)

Risk of recurrence: 10–15%

Cause: delayed transit of fertilized zygote (formed on day 14 MA) secondary to
(a) abnormal angulation of oviduct
(b) adhesions or scarring from inflammation
(c) slowed tubal transit from ciliary abnormalities

Risk factors:
(1) Previous tubal surgery: tubal ligation / tuboplasty
(2) Previous PID (30–50%): esp. Chlamydia
(3) Assisted reproductive technology (ART): in vitro fertilization / gamete intrafallopian tube transfer (GIFT)
(4) Endometriosis
(5) Previous ectopic pregnancy (prevalence up to 1.1%, 10-fold increase in risk, 25% chance of recurrence)
(6) Current use of IUD
(7) Advanced maternal age > 40 years
(8) In utero exposure to diethylstilbestrol
(9) Documented tubal anomaly: salpingitis, prior surgery

Time of manifestation: usually by 7th week of MA

- asymptomatic (50%); cervical motion tenderness
- CLASSIC CLINICAL TRIAD (< 50%):
  - abnormal vaginal bleeding (75–86%)
  - mild pelvic pain (97%): pain decreases with tubal rupture!
  - palpable adnexal mass (23–41%)
- 5–9 week history of secondary amenorrhea (61%)

- positive urinary pregnancy test (50%)
- progesterone level < 25 mg/mL
- β-hCG does not rise > 66% within 48 hours (lower levels + slower rise and decline compared with IUP)
  - ◊ Most ectopic pregnancies do not exhibit a β-hCG of > 6,500 mIU/mL (1st IRP) prior to symptomatology!
  - ◊ A β-hCG level above the discriminatory zone with absence of IUP suggests ectopic pregnancy!

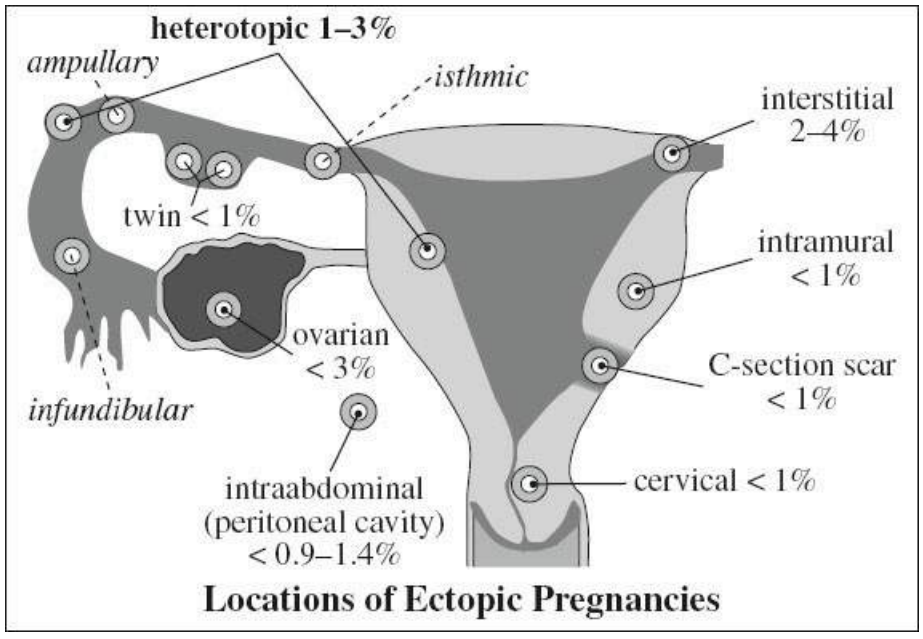
Discriminatory zone of β-hCG (at which a normal IUP should be visualized):
- › by endovaginal scan: ≥ 2,000–3,000 mIU/mL (IRP) ≥ 2000 mIU/mL (TIS)
- › by transabdominal scan: ≥ 6,500 mIU/mL (IRP)

Caveats: technical quality of exam, multiple gestations, distortion of uterine cavity (leiomyoma), lab error, assay variation

Dx: diagnostic laparoscopy (3–4% false negative, 5% FP)

Location: bilateral (0.1%)

» 95% 1. Tubal
» < 5% 2. Interstitial
3. Cervical
4. Cesarean scar in anterior lower uterine segment
5. Ovarian
6. Intraabdominal (peritoneal cavity)



Locations of Ectopic Pregnancies

Probability of Ectopic Pregnancy *without IUP or clinical symptoms of an ectopic pregnancy*	
√ normal scan / simple cyst in adnexa	5%
√ complex adnexal mass	92%
√ tubal ring	95%
√ live embryo outside uterus	100%

» even less common

7. Intramural
8. Heterotopic
9. Ectopic twin pregnancy

Spectrum:

Type 1: unruptured live ectopic + heartbeat
Type 2: early embryonic demise without rupture / embryonic structures / heartbeat
Type 3: ruptured ectopic with blood in pelvis
Type 4: no sonographic signs of ectopic

Prognosis: leading cause of 1st trimester maternal death

Transvaginal US (6–20% false-negative rate):

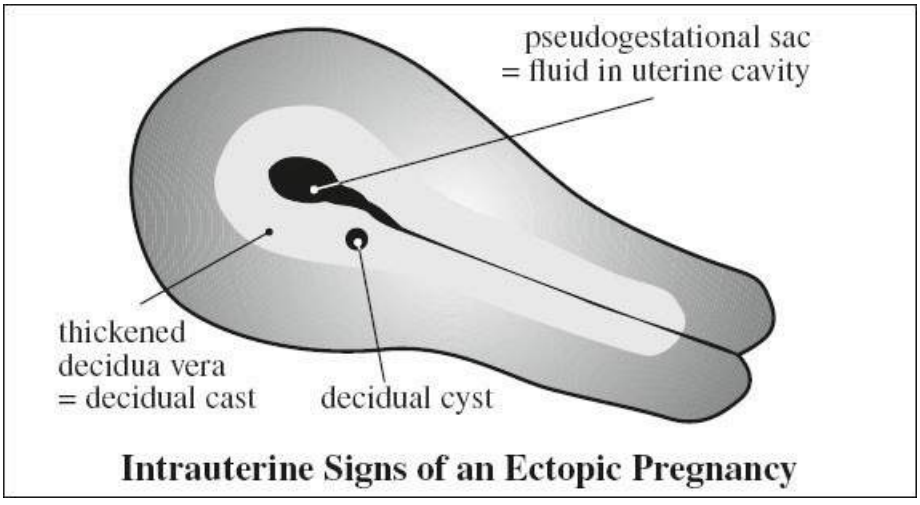
◊ Detected 1 week sooner than by transabdominal US!

@ Uterus

√ absence of intrauterine pregnancy (beyond 6 weeks MA / with β-hCG level > 1,000 mIU/mL [2nd IRP])
◊ If pregnancy not documented as intrauterine, the patient must be considered at risk!
◊ No IUP by endovaginal (transvesical) US means ectopic pregnancy in 67% (45%)

√ normal endometrium

√ thickening of endometrium:
√ trilaminar endometrium
√ hyperechoic endometrial thickening (50%) ← hormonal stimulation from ectopic pregnancy
√ sloughing of endometrium = decidual cast (21%)



Intrauterine Signs of an Ectopic Pregnancy

√ decidual endometrium lacks low-impedance blood flow

√ **decidual cyst** = thin-walled 1–5-mm cyst at junction of endometrium and myometrium (14%); may be seen in normal pregnancy

√ **pseudogestational sac** (10–20%) = thick single parietal decidual layer surrounding a centrally located anechoic fluid collection in uterine cavity ← bleeding (DDx: true gestational sac)

Tubal Ectopic Pregnancy (95%)

Location:

(1) Ampullary ectopic (75–80%)
(2) Isthmic ectopic (10–12–15%)
(3) Fimbrial / infundibular ectopic (5–11%)

Transvaginal US:

@ Adnexa

◊ Up to 35% of ectopic pregnancies may not display any adnexal abnormality!

√ adnexal mass separate from ovary:

√ echogenic "tubal mass" (89–100%)

√ extrauterine gestational sac WITHOUT live embryo / yolk sac (35%)

√ yolk sac

√ embryonic heartbeat (6–28%) = PATHOGNOMONIC

√ "tubal ring" = extrauterine hypoechoic saclike structure (20–65%) 1–3 cm in diameter surrounded by a 2–4-mm concentric echogenic ring

√ varying flow pattern depending on viability

√ corpus luteum within ovary in > 50% on side of ectopic pregnancy (DDx: ectopic pregnancy)

@ Cul-de-sac

√ clotted blood free in peritoneal cavity / hematosalpinx (36%)

√ free fluid (40–83%): echogenic / particulate fluid (= hemoperitoneum) with a 93% positive predictive value for an ectopic pregnancy

DDx: anechoic fluid in 10–27% of IUP

@ Abdominal cavity

√ echogenic fluid in posterior subhepatic space (Morison pouch) = ruptured ectopic probable

Doppler-US (low diagnostic impact):

√ "**ring-of-fire**" sign = high-velocity low-impedance flow in hyperechoic rim of extrauterine gestation in 54% (up to 4 kHz shift with 3 MHz transducer, Pourcelot index of 0.38 ± 0.2, RI between 0.18 and 0.58) [DDx: normal maturing follicle / corpus luteal cyst within ovary]

√ absence of peritrophoblastic flow after 36 days (< 0.8 kHz shift with 3 MHz transducer or < 1.3 kHz shift with 5 MHz transducer)

DDx of low-impedance flow:

corpus luteum cyst, tuboovarian abscess, fibroid

MR:

√ hematosalpinx:

√ slightly hyperintense relative to urine on fat-suppressed T1WI

√ low signal intensity on T2WI

√ hemoperitoneum:

√ iso- (acute) to hyperintense (subacute) free fluid with SI greater than that of urine on T1WI

√ heterogeneous appearance on T2WI

√ heterogeneous paraovarian adnexal mass of mixed SI on fat-suppressed T1WI + T2WI

√ extravasation of contrast material (= bleeding site) on contrast-enhanced dynamic subtraction MR

Prognosis:

(1) 3.8÷10,000 mortality rate (4% of all maternal deaths)

◊ Leading cause of death during 1st trimester with a mortality rate of 9–14%!

(2) Infertility (in 40%)

Dx: (1) Laparoscopy (almost 100% accurate)

(2) Culdocentesis: aspiration of nonclotting blood with a hematocrit > 15 = high probability for ectopic

Cx: tubal rupture (10–15%)

Rx: (1) Surgery

(2) Methotrexate (> 90% success rate)

Contraindications to methotrexate therapy:

(1) β-hCG level of > 5000 IU/L

(2) Documented fetal cardiac activity on US

(3) Ectopic mass of ≥ 3.5 cm

(4) Hemodynamic instability

(5) Unreliable patient who may not comply with serial β-hCG testing

Complications of methotrexate therapy:

(1) Selflimiting posttreatment pain

(2) Treatment failure: severe pain, hemodynamic instability, tubal rupture, hemoperitoneum

(3) Increase in size of gestational mass (in up to 56%) up to 8 cm in diameter

(4) Slow resolution of ectopic (up to 108 days)

DDx: (1) Hemorrhagic corpus luteum / hematoma

(2) Adnexal mass: hydrosalpinx, endometrioma, ovarian cyst

(3) Fluid-containing small bowel loop

(4) Eccentrically placed GS in bicornuate / retroflexed / fibroid uterus

Interstitial Ectopic Pregnancy (2–4%)

= ectopic pregnancy in an eccentric location relative to endometrium + close to uterine serosa

Location: implantation of blastocyst in upper lateral aspect of uterus BUT outside the endometrial cavity in intramyometrial portion of fallopian tube

Interstitial segment of fallopian tube:

√ thin echogenic line that extends from lateral aspect of uterine cavity through myometrium to uterine serosa (best evaluated in TRV plane)

◊ Often late rupture ← greater myometrial distensibility compared with other parts of tube!

◊ High likelihood of catastrophic hemorrhage from intramyometrial arcuate vasculature supplied by both ovarian + uterine arteries!

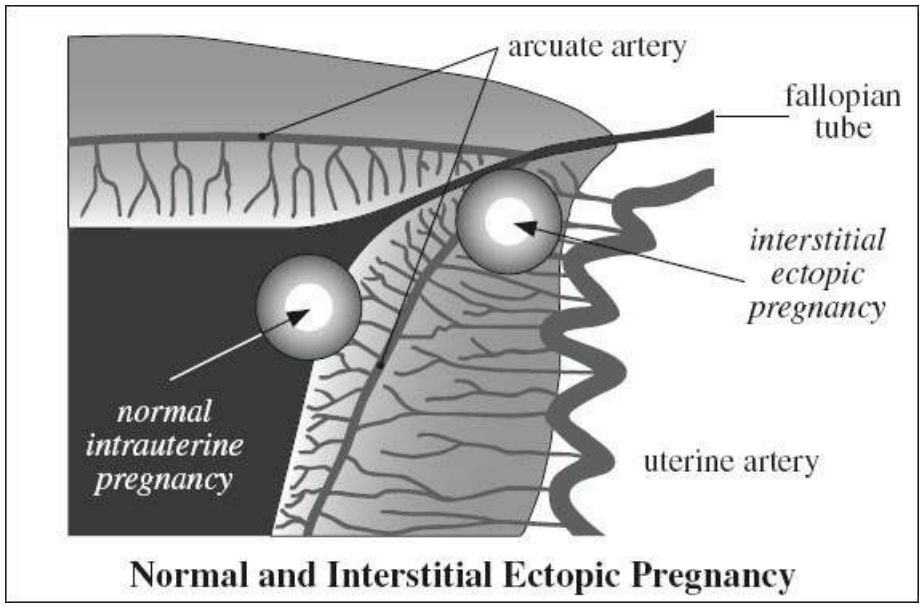
Increased risk: previous ipsilateral salpingectomy, in-vitro fertilization (IVF)

- Baart de la Faille sign = broad-based palpable mass extending outward from uterine angle
- Ruge-Simon syndrome = fundus displaced to contralateral side with rotation of uterus + elevation of affected cornu

√ "**interstitial line**" sign = thin echogenic line extending from endometrium directly up to center of ectopic pregnancy (= endometrial canal / interstitial portion of fallopian tube) in 92% (80% sensitive, 98% specific)

√ eccentric heterogeneous mass in cornual region (66%):
- √ eccentrically placed gestational sac (25%)
- √ "**bulging sign**" = CHARACTERISTIC bulging of uterine contour

√ "myometrial mantle sign" = ectopic pregnancy surrounded by myometrium on all sides:
- √ myometrium between sac and uterine cavity
- √ thinning of myometrial mantle to < 5 mm (33%) with enlargement of pregnancy



Normal and Interstitial Ectopic Pregnancy

√ large vascular channels + peritrophoblastic blood flow

√ absence of "double decidual" sign

√ empty endometrial cavity

MR:
- √ intact junctional zone between uterine cavity + mass

Cx: rupture of an interstitial pregnancy → profuse bleed from erosion of uterine arteries + veins due to close proximity of gestational sac to intramyometrial arcuate vasculature (pregnancy may survive up to 12 weeks GA)

Maternal mortality: up to 2.5%; 15 x that of other tubal ectopic pregnancies

DDx: eccentrically located normal pregnancy ←distortion from uterine fibroids / myometrial contraction; cornual pregnancy; angular pregnancy ; hydatidiform mole; degenerating uterine fibroid

Ovarian Ectopic Pregnancy (3%)

= ovum fertilized + retained within ovary

Increased risk: presence of intrauterine device, assisted reproductive technology, endometriosis, pelvic inflammatory disease

• adnexal mass moves with ovary (DDx: corpus luteum cyst)

√ gestational sac / atypical cyst with thick hyperechoic ring inside ovary / inseparable from ovary

√ empty endometrial cavity + normal fallopian tubes

√ "ring of fire" sign = peritrophoblastic flow on color Doppler (DDx: corpus luteum cyst)

√ interval growth + gradually recognizable GS contents

DDx: corpus luteum cyst (progressive involution and increasing crenulation of its margins)

Perform serial measurements of β-hCG serum levels and follow-up US in 2–3 days in any suspected intraovarian ectopic of a clinically stable patient.

Abdominal Ectopic Pregnancy (0.9–1.4%)

= implantation within peritoneal cavity excluding tubal + ovarian + intraligamentous locations

Pathophysiology: nutrient supply via omentum + abdominal organs (bowel, liver, spleen, urinary bladder)

Frequency: 1÷6,000 ectopic pregnancies

Increased risk: assisted reproduction

Classification:

(1) primary (rare) = fertilization of ovum within abdominal cavity

(2) secondary (common) = ruptured tubal / ovarian pregnancy with extrusion into peritoneal cavity

◊ > 25% may be missed sonographically!

• bloating, abdominal pain (fetal movement / peritoneal irritation ← adhesions); bleeding, hypotension, shock

√ absence of GS in endometrium / cervix / tube / ovary

√ intraperitoneal GS with surrounding echogenic margin

√ placenta outside confines of uterine cavity

√ peritrophoblastic flow on color Doppler

√ uterus compressed with visible endometrial cavity line

√ absence of uterine wall between gestation + bladder / abdominal wall

√ anhydramnios

√ free echogenic fluid (= hemoperitoneum)

Mortality: up to 20% ← hemorrhage; 7.7 x that of other ectopic pregnancies

Cx: bowel obstruction / perforation; erosion of pregnancy through abdominal wall; massive blood loss ← incomplete / complete placental separation

Lithopedion

= "stone child" = very rare obstetric complication consisting of a dehydrated + calcified demised fetus in an extrauterine pregnancy existing for > 3 months without infection

Types:

(1) Lithokelyphosis = fetal membranes calcified

(2) Lithokelyphopedion = fetus + membranes calcified
(3) True lithopedion = only fetus calcified

Maternal age at discovery: 23–100 years of age; within 4–20 years of fetal demise

Location: most common in adnexa

√ large densely calcified mass in lower abdomen / upper pelvis

√ CT scan reveals fetal skeleton

DDx: uterine fibroid, calcified ovarian malignancy / cyst, sarcoma

Cervical Ectopic Pregnancy (< 1%)

= implantation of blastocyst within the endocervical canal and subsequently fibrous wall of cervix

Risk factors: IUD; in-vitro fertilization; repeated endometrial curettage; Asherman syndrome

• vaginal bleeding, vague abdominal pain

√ uterus shape: hourglass-like / figure of 8 ← ballooned cervix

√ cardiac activity inferior to internal os

√ absent "sliding" sign (= nonadherent gestational sac can be manipulated by gentle pressure with transvaginal transducer)

√ ± peritrophoblastic flow around ectopic gestational sac

Dx: embryonic heartbeat in a gestational sac within the endocervical canal caudad to cervical internal os

DDx of Cervical Ectopic versus Abortion in Progress

Cervical Ectopic	*Abortion in Progress*
implantation of GS in cervix	GS not attached
round gestational sac	irregular deformed GS
surrounding echogenic ring	no echogenic margins
peritrophoblastic color flow	no peritrophoblastic color flow
hourglass / figure-of-8 uterus	globular uterus
closed internal cervical os	open internal cervical os
negative sliding sign	positive sliding sign
fetal heartbeat inferior to cervical os	absent fetal cardiac activity
well-formed yolk sac / fetal pole	poor visualization of fetal parts
no blood products in endometrium	blood products in endometrium
interval growth / rise in hCG	NO interval growth / rise in hCG

A misdiagnosis of a cervical ectopic pregnancy as abortion in progress can be deleterious because a D&C can cause massive life-threatening hemorrhage secondary to trophoblastic invasion of the cervix.

DDx: low-lying gestational sac with abortion in progress

Cesarean Scar Ectopic Pregnancy (< 1%)

= implantation within a scar of a prior cesarean section in the anterior lower uterine segment

Path: blastocyst surrounded by myometrium + fibrous tissue

• vaginal bleeding between 5 weeks and 16 weeks

A high degree of suspicion for cesarean scar pregnancy is necessary because up to 40% of patients will not present with specific clinical symptoms.

√ gestational sac in anterior lower uterine segment
√ thinned / absent anterior myometrium between sac and bladder (best assessed in SAG plane)
√ empty uterus + empty cervical canal
√ gestational sac with echogenic margins + peritrophoblastic flow at scar site
√ enlarging sac → exerts increasing mass effect on bladder
Cx: uterine rupture with catastrophic hemorrhage

Cornual Ectopic Pregnancy (< 1%)

= implantation of blastocyst within one horn (= cornua) of a bicornuate / septate uterus
√ eccentric position of gestational sac > 1 cm from lateral wall of endometrial cavity
√ < 5 mm thin rim of myometrium (identical to interstitial ectopic pregnancy)
Cx: rupture with catastrophic hemorrhage

Heterotopic Pregnancy

= simultaneous occurrence of intra- + extrauterine pregnancy
Prevalence: 1÷21,000–30,000 pregnancies; 1–3% in patients undergoing ovulation induction + in-vitro fertilization
• persistent adnexal pain + abnormal β-hCG levels after abortion of intrauterine pregnancy
◊ An IUP should not preclude a complete pelvic ultrasound evaluation, although depiction of an IUP virtually excludes the diagnosis of an ectopic pregnancy!
√ enlarged uterus with visible intrauterine GS
√ concurrent heterogeneous extrauterine GS
√ free echogenic fluid (= hemoperitoneum) after termination of intrauterine pregnancy
√ enlarged ovaries from ovarian hyperstimulation
Rx: laparoscopic removal of extrauterine embryo
Mortality: delayed diagnosis of missed ectopic pregnancy → catastrophic hemoperitoneum + hypovolemic shock

Intramural Ectopic Pregnancy (< 1%)

= gestational sac completely surrounded by myometrium
Increased risk: adenomyosis, in vitro fertilization, defective trophoblastic activity, previous uterine trauma (D&C, myomectomy)
• abdominal pain, vaginal bleeding, positive pregnancy test
√ nonvisualization of GS in endometrium / tubes
√ peritrophoblastic flow at color Doppler
Cx: uterine rupture
Rx: hysterectomy

Angular Pregnancy

= implantation within lateral angle of uterus medial to uterotubal junction

Prognosis: high rate of spontaneous abortion, uterine rupture, (23%), placenta accreta
√ completely surrounded by myometrium ± focal thinning
√ ± placental invasion of myometrium (placenta accreta)
√ ± intramural hemorrhage
√ ± myometrial discontinuity

EMBRYONIC DEMISE

Frequency: 20–71% loss rate of one twin < 10 weeks

Early Embryonic Demise / Failing Pregnancy

• β-hCG level < 2–3 standard deviations below the mean for given MA / GS size / CRL
√ on endovaginal scan:
A. DEFINITE DEMISE
√ absence of cardiac activity with CRL of ≥ 5 mm / ≥ 6.5 weeks GA (repeat scan in 3 days for confirmation)
B. PROBABLY FAILING PREGNANCY
√ mean sac diameter of ≥ 16 mm without embryo
√ mean sac size of ≥ 8 mm without yolk sac (repeat scan in 3 days for confirmation)
√ > 1,000 mIU/mL (1st IRP) without gestational sac
√ > 7,200 mIU/mL (1st IRP) without yolk sac
√ > 10,800 mIU/mL (1st IRP) without embryo
C. MODERATELY HIGH RISK OF DEMISE
√ bradycardia of 80–90 bpm
√ large subchorionic hematoma lifting much of placenta
√ yolk sac > 6 mm / abnormal shape
D. HIGH RISK OF SUBSEQUENT DEMISE
√ severe bradycardia < 80 bpm
√ small mean gestational sac size

◊ Difference between mean sac size and CRL of < 5 mm is predictive of miscarriage in 94%!

√ mean gestational sac size too small for good clinical dates
√ gestational sac growth ≤ 0.7 mm/day (normal growth rate of daily 1.13 mm determines appropriate time interval for follow-up scan, ie, when sac is expected to be 27 mm)
√ sac position in lower uterine segment / cervix
√ stringlike / granular debris / fluid-fluid level within gestational sac ← intrasac bleeding

Late Embryonic Demise

√ on endovaginal scan:
√ wrinkled collapsing amniotic membrane
√ irregular distorted shape of gestational sac
(DDx: compression by bladder, myoma, contraction)
√ absence of double decidual sac = thin weakly hyperechoic / irregular choriodecidual reaction of < 2 mm

ENDOMETRIAL CANCER

Most common invasive gynecologic malignancy in industrialized countries; 4th most prevalent female cancer in USA women

Incidence: 60,050 new cases with 10,470 deaths annually (2016)

Histo: adenocarcinoma (90–95%), sarcoma (1–3%)

Peak age: 55–62 years; 74% > age 50

Risk factors: nulliparity, late menopause, exposure to unopposed estrogen therapy, polycystic ovaries, obesity, hypertension, diabetes mellitus

Histo:

(a) endometrioid carcinoma (75% of all cancers)
(b) serous, mucinous, clear cell carcinoma (less common): similar to ovarian counterpart
(c) squamous (rare): associated with cervical stenosis, pyometra, chronic inflammation
(d) mixed mesodermal tumor: contains elements of epithelial + mesenchymal differentiation

2009 FIGO Staging for Endometrial Carcinoma

FIGO Stage	*Description*
0	In situ
I	Tumor confined to uterus
IA	< 50% invasion of myometrium
IB	≥ 50% of myometrium
II	Cervical stromal invasion
IIIA	Invasion of serosa / adnexa / peritoneal metastases
IIIB	Vaginal / parametrial involvement
IIIC1	Pelvic lymph node involvement
IIIC2	Paraaortic lymph node involvement
IV	Extension to pelvic wall, lower 1/3 of vagina, hydronephrotic / nonfunctioning kidney
IVA	Invasion of bladder / bowel mucosa
IVB	Distant metastases (lung, brain, bone) including metastases to pelvic / paraaortic lymph nodes intraabdominal / inguinal lymph nodes

◊ Clinical staging with dilatation & curettage inaccurate in up to 51%!

Lymph node metastases: 3% with superficial invasion; 40% with deep invasion

• postmenopausal bleeding without hormonal therapy

Location: predominantly in uterine fundus; 24% in isthmic portion

US:

√ normal-sized / enlarged uterus
√ focal / diffuse endometrial thickening (mean anteroposterior bilayer thickness of 18.2 mm)
◊ Any endometrial thickness > 5 mm is suspicious (100% negative predictive value, not very specific):
◊ 10% cancer rate with endometrial thickness of 6–15 mm
◊ 50% cancer rate with endometrial thickness of > 15 mm
√ irregular heterogeneous echogenic texture with hypoechoic areas (= signs of invasive endometrial cancer):
√ irregular poorly defined endometrial-myometrial interface

√ increased echogenicity in myometrium
√ intrauterine fluid collection (DDx: cervical stenosis)

Transvaginal US:
√ apparent distension of endometrial lumen with extrinsic thinning of the myometrium (= polypoid tumor)
√ Doppler pulsatility index of < 1.5 or resistive index < 0.7 suggests malignancy (DDx: endometritis, benign endometrial polyp)
√ areas of venous flow (DDx: endometrial hyperplasia)

MR (82–92% accuracy for staging, 74–87% accuracy for depth of invasion):
√ endometrial cancer has a slightly lower SI than endometrium but higher SI than myometrium on T2WI
√ endometrial thickness abnormal if > 3 mm (postmenopausal woman) / > 10 mm (under estrogen replacement)
DDx: blood clot, uterine secretions, adenomatous hyperplasia, submucosal leiomyoma
√ disruption / absence of junctional zone ← myometrial invasion
√ hyperintense areas penetrating into myometrium (= deep muscle invasion; 74–87% accuracy with CEMR / DWI)

ENDOCERVICAL POLYP

= most common benign cervical growth

Incidence: up to 4%

Age: multiparous women in their 30s and 40s

Histo: connective-tissue stalk with focal hyperplasia of glandular columnar epithelium ± squamous metaplasia (frequent)

Types: adenomatous (mostly), cystic, fibrous, vascular, inflammatory, fibromyomatous

Often associated with: endometrial hyperplasia ← ? link to estrogen exposure

• common cause of intermenstrual bleeding
• metrorrhagia, menorrhagia, postmenopausal bleeding, contact bleeding, vaginal discharge

√ typically slightly hyperechoic polyp compared with normal mucosa
√ may undergo cystic change → confusion with nabothian cyst
√ may be mobile at dynamic imaging with transducer pressure
√ ± vascular stalk arising from endocervical mucosa (Doppler US)

Visualization of the origin of the endocervical polyp is critical to differentiate it from a lesion arising in the uterine body with extension into the endocervical canal (eg, prolapsed intracavitary leiomyoma / endometrial polyp).

Rx: management of prolapsed lesions tends to be more complicated ← more extensive blood supply

√ coexisting endometrial polyp (in 25%)

Cx: malignancy / dysplasia (in 0.2–1.5%)

ENDOMETRIOID CARCINOMA OF OVARY

Frequency: 8–15% of all ovarian cancers; 2nd most common malignant ovarian neoplasm (after serous adenocarcinoma)

Associated with: hyperplasia / carcinoma of the uterine endometrium in 20–33%

Path: malignant mixed mesodermal tumor = carcinoma-sarcoma is grouped with endometrioid

cancer

Histo: tubular glandular pattern with a pseudostratified epithelium resembling endometrial adenocarcinoma / metastatic colon carcinoma; ~ 100% malignant

√ solid / complex (= cystic + solid) tumor

√ bilateral in 15% of stage I cases

Prognosis: better than serous / mucinous carcinomas

ENDOMETRIOSIS

= ENDOMETRIOSIS EXTERNA

= encysted functional endometrial epithelium + stroma in an ectopic site <u>outside</u> myometrium

N.B.: internal endometriosis within myometrium = adenomyosis

Prevalence: 5–10% of menstruating women; in 5% of post-menopausal women on estrogen replacement therapy

Etiology:

(1) Metastatic / implantation theory
= "shedding" of endometrial cells during retrograde menstruation via fallopian tubes onto peritoneum
◊ Up to 90% of women have bloody peritoneal fluid during perimenstrual period
◊ Obstructive müllerian duct anomalies are the most common cause in girls < 17 years of age

(2) Dissemination theory = vascular + lymphatic spread

(3) Direct theory = intraoperative implantation (uterine surgery, amniocentesis, needle biopsy)

(4) Coelomic metaplasia theory = conversion of peritoneal epithelium into functioning endometrial tissue

(5) Induction theory = combination of metastatic + metaplastic theory

Mean age: 25–29 years

Histo: endometrial glands, stroma, rare smooth muscle fibers; secretory changes during 2nd half of menstrual cycle; stromal decidualization during pregnancy

- infertility:
  ◊ 20–50% of infertile women have endometriosis
  ◊ 30–50% of women with endometriosis are infertile
  Cause: involvement of tubes + ovaries → peritubal adhesions → anatomic distortion, impaired tubal mobility to capture ovum, tubal destruction / occlusion
- pelvic pain:
  - cyclic pelvic pain: estrogen-sensitive ectopic endometrial implants proliferate and bleed synchronously with uterine endometrium
  ◊ 24–33% of women with pelvic pain have endometriosis: NO correlation between amount of pelvic pain + extent of disease
  - dysmenorrhea, perimenstrual diarrhea, dyspareunia
  - sacral back ache with menses, rectal discomfort
  - chronic pelvic pain ← peritoneal adhesions
    ◊ Endometriosis is found in 90% of women with chronic pelvic pain!
- abnormal menstrual bleeding

- fixed pelvic organs during bimanual exam
- localized tenderness along uterosacral ligaments + cul-de-sac + adnexa; thickened nodular ligaments + rectovaginal masses

Location:

(1) Ovaries (20–40%): cysts with hemorrhagic content
(2) Ligaments: uterosacral ligament; round ligament (= painful inguinal mass in the canal of Nuck, R > L)
(3) Rectouterine pouch = pouch of Douglas = posterior cul-de-sac); anterior rectosigmoid
(4) Vesicouterine pouch = posterior wall of urinary bladder = anterior cul-de-sac
(5) Uterine serosal surface / wall: posterior > anterior
(6) Fallopian tube (6%): (sub)serosal / mucosal
(7) Bladder dome
(8) Cesarean section / other abdominal surgical scars (< 1%)

Depth:

1. Deeply infiltrating endometriosis = > 5 mm from peritoneal surface
   Associated with: fibrosis + muscular hyperplasia

Morphologic types:

1. Diffuse endometriosis
2. Discrete pelvic mass = endometrioma (in up to 10%)

Dx: laparoscopy / surgery ← limitations of imaging

Rx: (1) Expectant with NSAID

(2) Hormonal therapy (for pelvic pain / dyspareunia) to create a state of pseudopregnancy / pseudo-menopause / chronic anovulation: danocrine (Danazol®), GnRH agonist (Lupron®), oral contraceptive pills

(3) Surgery (for infertility / intractable pain):
implant recurrence in 28% by 18 months + in 40% by 9 years; adhesion recurrence in 40–50%

Diffuse Endometriosis

Path: punctate small foci / stellate patches of < 2 cm initiating inflammatory response → organizing hemorrhage, fibrosis, adhesions

US (low sensitivity):

√ in 70% normal = often no detectable abnormality (when lesions small + scattered)

MR (71% sensitive, 82% specific):

√ frequently hyperintense multiple cysts bilaterally with thick walls on T1WI
√ foci of elevated signal intensity on T1WI (only 13% sensitive) ← peritoneal implants
√ hypointense masses on T2WI
√ loss of interface between lesion + adjacent organs
√ hydrosalpinx hyperintense on T1WI ← blood products as luminal content

Endometrioma

= the only form of endometriosis that is readily imaged

Path: endometriotic cyst in ovary containing thick dark degenerated blood products = "**chocolate cyst**"← repeated cyclic hemorrhage, in up to 50% bilateral

over time: iron overload, high concentration of protein, increased viscosity

Histo: obliterated mostly endometrial gland lining; initially thin wall that becomes fibrotic + thickened with irregular external border

◊ Multiplicity favors the diagnosis of endometrioma

US (83% sensitive, 89% specific for endometrioma):

√ unilocular endometrioma = nonspecific cyst of usually 2–5 cm (up to 20 cm) in diameter:

Location: within ovary, often bilateral

√ variable appearance of cyst cavity:

√ diffuse homogeneous internal low-level echoes / ground-glass appearance (in 95%) ← hemorrhagic debris

√ fine reticular appearance ← interdigitating septations without blood flow

√ ± fluid-fluid / fluid-debris level ← layering of debris

√ ± echogenic material floating in dependent portion of cyst cavity ← fresh blood clot

√ ± triangular / curvilinear soft-tissue component / often attached to cyst wall ← retracting blood clot

√ anechoic cyst (rare)

√ posterior acoustic enhancement

√ echogenic wall nodularity / irregularity (in 20–35%) ← cholesterol deposits

√ blood flow in thick septations ← revascularization of chronic hematoma

√ multilocular endometrioma = multiple separate cysts:

√ thin / thick septations between loculi

√ hematosalpinx (in 28%)

√ change in size + appearance on 6-week follow-up

DDx:

(1) Hemorrhagic ovarian cyst (acute symptoms, more complex cyst with clot retraction, thin fibrin stranding, resolution in 4–6 weeks)

(2) Dermoid cyst (calcification, fat-fluid level, hyperechoic areas)

(3) Cystic neoplasm

(4) Tuboovarian abscess

CT:

√ solid and cystic heterogeneous masses (varied findings)

√ irregular margins

MR (91–96% accurate, 90–92% sensitive, 91–98% specific with fat suppression):

√ typically homogeneously hyperintense **"light bulb"** SI of cyst(s) on T1WI similar to fat ← intra- and extracellular methemoglobin shortens T1 of fluids:

√ hyperintensity on fat-suppressed T1WI (effectively excludes fat in a dermoid)

√ ± "**T2 shading**" sign = faint / complete loss of signal of entire cyst (lower than that of simple cyst fluid) / in dependent fluid-debris layer on T2WI ← high concentration of cross-linked proteins of high viscosity + iron ← recurrent hemorrhage (usually mixed with areas of high SI) in cyst that exhibits high SI on T1WI

DDx: hemorrhagic functional ovarian cyst (solitary, thin-walled, SI lower on T1WI + higher on T2WI); mature cystic teratoma

The presence of blood is more conclusively established on the basis of the MRI appearance (> 90% specific)!

√ atypically hypointense on all pulse sequences in 27%
√ restricted diffusion
√ multilocularity + multiplicity

◊ CEMR NOT needed to evaluate for endometriosis

√ ancillary insensitive findings:
√ hypointense peripheral ring ← hemosiderin staining of thick fibrous wall in chronic lesion (DDx: PID)
√ adhesion to surrounding organs = bowel tethering and sharp angulations
√ peritoneal implants
√ ± obliteration of posterior cul-de-sac

Cx: (1) Adhesions (after rupture of endometrioma)
• fixed pelvic organs (during bimanual US)
√ obscuration of organ interfaces
√ posterior displacement of uterus (retroverted uterus) and ovaries
√ angulation of bowel loops
√ elevation of posterior vaginal fornix
√ loculated fluid collection
√ dilated fallopian tube: hydrosalpinx (in up to 30%); hydrosalpinx÷hematosalpinx = 6÷4
◊ Suggestive of endometriosis if hydrosalpinx exhibits T1-hyperintensity!

(2) Malignant transformation to ovarian cancer (1–2.5%)
Histo: endometrioid ca. > clear cell carcinoma
• in women > 45 years of age
√ typically for endometriomas > 9 cm
√ enhancing mural nodules

DDx: hemorrhagic functional cyst (most often solitary, brighter than endometrioma on T2WI, generally no shading), mature cystic teratoma, pelvic inflammatory disease, cystic ovarian neoplasm, pedunculated myoma

Ruptured Ovarian Endometrioma

= uncommon acute complication
• acute abdomen ← chemical peritonitis
√ distorted shape of endometrioma
√ thinned irregular wall component = rupture site
√ markedly hyperintense fluid in free intraperitoneal space on fat-suppressed T1WI
Rx: EMERGENCY SURGERY

Atypical Sites of Endometrial Implantation

@ GI tract (12–37%)
• catamenial diarrhea, constipation
• rectal pain / hematochezia [*khezein*, Greek = defecate]
Path: initially serosal endometriotic deposits → that erode into bowel wall → hypertrophy + fibrosis of muscularis propria
Location: inferior margin of sigmoid colon + anterior wall of rectosigmoid (72%) >

rectovaginal septum (14%) > ileum (7%) usually within 10 cm of ileocecal valve > jejunum > cecum (4%) > appendix (3%, almost always associated with ovarian endometriosis); occasionally multiple

√ single extramucosal mass with crenulated / spiculated mucosal pattern (DDx: drop metastasis)

√ polypoid intraluminal mass / annular constricting lesion (rare appearance)

Cx: adhesion, bowel stricture, GI obstruction

DDx: invasive malignancy (in deeply penetrating lesion)

@ GU tract (3–20–37%)

• dysuria, urgency, frequency, cyclical hematuria

• urinary obstruction, flank pain

Path: initially serosal endometriotic deposits that may infiltrate into bladder / ureteral wall

√ mass projecting into bladder lumen typically at dome of bladder posteriorly (DDx: bladder cancer)

√ smooth / tapered / angulated short to medium-length ureteral stricture near inferior aspect of sacroiliac joint

@ Chest

= THORACIC ENDOMETRIOSIS SYNDROME

• pleuritic chest pain, cyclic hemoptysis

Cause: microembolization (via lymphatics or vascular channels), peritoneal-pleural migration (through diaphragmatic defects)

Time of onset: 5 years after pelvic endometriosis

• presenting symptoms:

  • pneumothorax (73%), hemothorax (14%)

  • hemoptysis (7%), lung nodules (6%)

√ almost exclusively right-sided pleural lesions

√ bilateral lung nodules

√ catamenial pneumothorax

√ pleural effusion

@ Cutaneous Tissue

• palpable mass ± catamenial bleeding

• focal pain / tenderness associated with menses

Location: laparotomy scar, cervical biopsy / electrocautery, episiotomy scar, umbilicus

√ well-defined hypoechoic / cystic / solid mass

√ hyperechoic border / tissue stranding ← inflammatory reaction

DDx: abscess, hematoma, hernia, sebaceous cyst, lipoma, hemangioma, malignant tumor

@ CNS

• cyclic headaches, seizures

√ subarachnoid hemorrhage

FACIAL CLEFTING

Prevalence: 0.5÷1,000 in blacks; 1÷1,000 live births in white population; 1.5÷1,000 in Asians; 3.6÷1,000 in American Indians; 13% of all congenital anomalies; 2nd most common

congenital malformation; most common craniofacial malformation

Normal embryology:

1st branchial arch develops into maxillary + mandibular prominences; by 5th week the stomadeum is surrounded by 5 prominences: frontal-nasal, paired maxillary, paired mandibular prominences; nasal pits are formed by invagination of nasal placodes on each side of frontal-nasal prominence; the 2 maxillary prominences grow medially to fuse with the 2 medial nasal prominences forming the upper lip; the lateral nasal prominences form the nasal alae

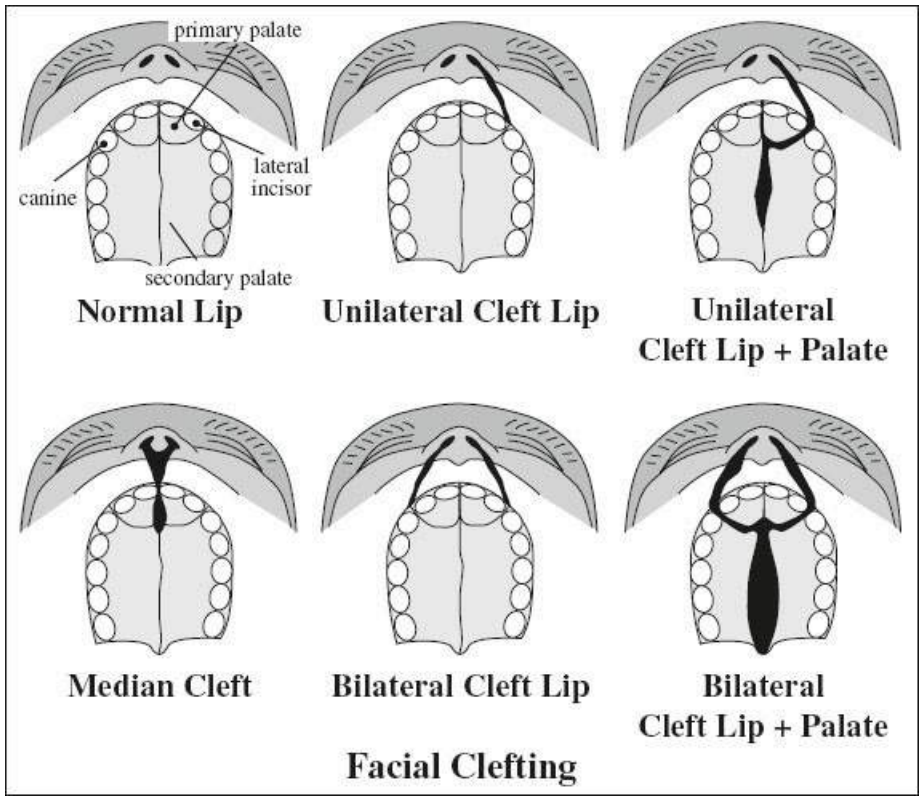
Risk of recurrence: 4% with one affected sibling, 17% with one affected sibling + parent

Cleft lip ± palate and isolated cleft palate are distinct entities with different implications for underlying genetic syndromes, associated anomalies, and prognosis.

Median Facial Cleft

= failure of fusion of the 2 medial nasal prominences

Prevalence: rare



Cause:

1. Median cleft face syndrome = frontonasal dysplasia
   √ brain anomalies rare
2. Holoprosencephaly
3. Majewski syndrome (short rib, polydactyly, median cleft)

Lateral Facial Cleft

Cleft Lip *(25%)*

Cause: lack of fusion of maxillary prominence with medial nasal prominence (= intermaxillary segment) around 7th week MA

Associated with: anomalies in 20% (most frequently clubfoot); NO chromosomal anomalies

Site: isolated in 8%, bilateral in 20%

√ linear echo-poor region extending from one side of fetal upper lip into nostril

Prognosis: excellent

Cleft Lip & Palate *(50%)*

Cause: incomplete fusion of lip + primary palate with secondary palate

Associated with: 72 abnormalities in 56–80%: most frequently polydactyly; chromosomal anomalies in 20–33%

Location: L > R

Site: unilateral in 23%, bilateral in 30%

√ linear defect extending through alveolar ridge + hard palate reaching the floor of the nasal cavity / orbit (often deeper + longer cleft than in isolated cleft lip)

√ paranasal echogenic mass inferior to nose (= premaxillary protrusion of soft tissue + alveolar process + dental structures) in bilateral cleft lip + palate

Cleft Palate *(25%)*

= lack of fusion of mesenchymal masses of lateral palatine processes around 8th–9th weeks MA

Associated with: anomalies in 50% (most frequently clubfoot + polydactyly)

Stickler syndrome = ocular abnormalities, maxillary hypoplasia, isolated cleft palate

√ often missed on prenatal sonograms

√ small fetal stomach + polyhydramnios ← impaired fetal swallowing

FIGO and TNM Staging of Fallopian Tube Cancer (1993)		
FIGO	*TNM*	*Description*
I	T1	Limited to fallopian tube
IA	T1a	limited to one fallopian tube without serosa
IB	T1b	limited to both fallopian tubes without serosa
IC	T1c	+ extension onto / through serosa + positive peritoneal lavage / ascites
II	T2	Limited to pelvis
IIA	T2a	involvement of one / both fallopian tubes
IIB	T2b	extension to other pelvic structures
IIC	T2c	+ positive peritoneal lavage / ascites
III	T3	Peritoneal implants outside pelvis
IIIA	T3a	microscopic abdominal peritoneal seeding
IIIB	T3b	≤2 cm implants of abdominal peritoneum
IIIC	T3c	>2 cm implants of abdominal peritoneum
	N1	Regional lymph node metastasis
IV	M1	Distant metastasis
◊ 50–70–75% of patients have stage III / IV disease at time of diagnosis!		

FALLOPIAN TUBE CANCER

= PRIMARY FALLOPIAN TUBE CARCINOMA

Prevalence: 3.72÷1,000,000 women (likely underestimated); 0.9–17% of prophylactic salpingo-oophorectomies

Age: 6th–7th decade

Path: tumor produces large amount of serous secretions → painful distension of fallopian tube → palpable pelvic mass → passage of fluid from either end of patent tube → shrinkage of pelvic mass

Histo: papillary serous carcinoma (most common)

- often insidious nonspecific presentation
- hydrops tubae profluens [profluo, Latin = discharging]
  = intermittent discharge of clear / bloody fluid ← spontaneous / caused by pressure, followed by shrinkage of adnexal mass
- Latzko triad (in 15%):
  (1) intermittent profuse serosanguinous vaginal discharge
  (2) colicky lower abdominal pain relieved by discharge
  (3) adnexal mass

Growth pattern: nodular, papillary, infiltrative, masslike

Location: ampulla of tube; bilateral in 20%

√ fluid-filled tubular adnexal structure containing nodular / papillary solid components
√ multilocular cystic mass with spoke-wheel appearance
√ contrast enhancement of solid component
√ intrauterine fluid collection, peritumoral ascites
√ low vascular impedance (= resistive index of 0.29–0.40) in solid component on Doppler

ultrasound
√ increased adnexal metabolic activity on PET
Dx: at least one of following histologic criteria
(1) tumor arises from endosalpinx
(2) tumor resembles epithelium of mucosa
(3) demonstrable transition from benign to malignant
(4) normal ovaries or endometrium / foci of metastasis

FETAL AKINESIA DEFORMATION SEQUENCE (FADS)

Cause: neurogenic diseases, myogenic anomalies, restrictive dermopathies
Location: generalized + symmetric; lower > upper limbs
√ abnormal limb position, craniofacial deformation
√ growth restriction, polyhydramnios
√ abnormally short umbilical cord
Dx: fixed abnormal position (flexion deformities, multiple camptodactylies) in association with restricted fetal movements / complete akinesia
DDx: trisomy 18
Prognosis: usually lethal ← lung hypoplasia

FETAL CARDIAC DYSRHYTHMIAS

Normal heart rate: 120–160 bpm

Premature Atrial Contractions

= PAC = most common benign rhythm abnormality
√ transient tachycardia
√ transient bradycardia ← atrial bigeminy if every other beat is nonconducted
Cx: supraventricular tachycardia (unusual)
Rx: discontinue smoking, alcohol, caffeine
Follow-up: biweekly auscultation until arrhythmia resolves

Supraventricular Tachyarrhythmia

Prevalence: 1÷25,000; most frequent tachyarrhythmia in children
Etiology: viral infection, hypoplasia of sinoatrial tract
Pathogenesis:
(1) Automaticity = irritable ectopic focus discharges at high frequency
(2) Reentry = electric pulse reentering atria + inciting new discharges
Types:
1. Supraventricular tachyarrhythmia (SVT)
(a) paroxysmal supraventricular tachycardia
(b) paroxysmal atrial tachycardia
√ atrial rate of 180–300 bpm
√ ventricular response of 1÷1
2. Atrial flutter
√ atrial rate of 300–460 bpm
√ ventricular rate of 60–200 bpm

3. Atrial fibrillation
   √ atrial rate of 400–700 bpm
   √ ventricular rate of 120–200 bpm

Hemodynamics: fast ventricular rate results in suboptimal filling of heart chambers → decreased cardiac output, overload of RA, CHF

Associated with:

(1) cardiac anomalies (5–10%): ASD, congenital mitral valve disease, cardiac tumors, WPW syndrome, cardiomyopathy
(2) thyrotoxicosis

OB-US:

√ M-mode echocardiography with simultaneous visualization of atrial + ventricular contractions → allows inference of atrioventricular activation sequence

Cx: congestive heart failure + nonimmune hydrops

Rx: intrauterine pharmacologic cardioversion (digoxin, verapamil, propranolol, procainamide, quinidine)

Atrioventricular Block

Prevalence: 1÷20,000 live births; in 4–9% of all infants with CHD

Etiology: (1) Immaturity of conduction system
(2) Absent connection to AV node
(3) Abnormal anatomic position of AV node

Associated with:

(1) Cardiac structural anomalies (45–50%): corrected transposition, univentricular heart, cardiac tumor, cardiomyopathy
(2) Maternal connective tissue disease: lupus erythematosus

Types:

1. **First-degree heart block** = simple conduction delay
   √ normal heart rate + rhythm (not reportedly diagnosed in utero)
2. Second-degree heart block
   (a) **Mobitz type I**
   = progressive prolongation of PR interval → finally leading to the block of one atrial impulse (Luciani-Wenckebach phenomenon)
   √ a few atrial contractions → NOT followed by a ventricular contraction
   (b) **Mobitz type II**
   = intermittent conduction with a ventricular rate as a submultiple of the atrial rate (eg, 2÷1 / 3÷1 block)
   √ atrial contraction NOT followed by a ventricular contraction in a constant relationship
3. **Third-degree heart block** = complete heart block
   = complete dissociation of atria + ventricles
   √ slow atrial + ventricular contractions independent from each other

Cx: decreased cardiac output + CHF

FETAL DEATH IN UTERO

= INTRAUTERINE DEMISE
= fetal death during 2nd + 3rd trimesters
Specific signs:
√ absent cardiac / somatic motion
Nonspecific signs seen not before 48 hours after death:
√ same / decreased BPD measurement compared to prior exam
√ development of dolichocephaly
√ "**Spalding**" sign = overlapping fetal skull bones
√ distorted fetus without recognizable structures
√ skin edema (epidermolysis) = fetal maceration
√ increased amount of echoes in amniotic fluid (= fetal tissue fragments)
√ gas in fetal vascular system

"Vanishing Twin"

= disappearance of one twin in utero ← complete resorption / anembryonic pregnancy
Prevalence: 21% (range, 13–78%) before 14 weeks GA
Time: < 13 weeks MA
√ NO sonographic evidence of twin pregnancy later in pregnancy

"Fetus Papyraceus"

= compression + mummification of fetus
Time: in 2nd trimester
Path: resorption of fluid resulting in paperlike fetal body + compression into adjacent membranes
√ compressed mummified fetus plastered against uterine wall
Risk to surviving twin:
A. Dichorionic gestation (minimal risk)
(1) Premature labor
(2) Obstruction of labor by macerated fetus
B. Monochorionic gestation
DIC ← release of thromboplastin from degenerating fetus
(a) into maternal circulation
(b) into twin fetus through shared circulation (= **twin embolization syndrome**)

FETAL HYDROPS

Nonimmune Hydrops

= excess of total body water → extracellular accumulation of fluid in tissues + serous cavities without antibodies against RBC
Prevalence: 1÷1,500 to 1÷4,000 deliveries
Cause:
1. Cardiac anomalies (40%):
(a) structural heart disease (25%): AV septal defect, hypoplastic left heart, rhabdomyoma
(b) tachyarrhythmia (15%)

2. Hematologic causes: thalassemia, hemolysis, fetal blood loss
3. Idiopathic (25–44%)
4. Twin-twin transfusion (20%)
5. Chromosomal abnormalities (6%): Turner syndrome
6. Skeletal dysplasias: achondroplasia, achondrogenesis, osteogenesis imperfecta, thanatophoric dwarfism, asphyxiating thoracic dysplasia
7. Renal disease (4%): congenital nephrotic syndrome
8. Infections: toxoplasmosis, CMV, syphilis, Coxsackie virus, parvovirus
9. Cervical tumors: teratoma
10. Chest masses: cystic adenomatoid malformation, extralobar sequestration, mediastinal tumor, rhabdomyoma of heart, diaphragmatic hernia
11. Abdominal masses: neuroblastoma, hemangioendothelioma of liver
12. Placental tumors: chorioangioma

Prognosis: 46% death in utero; 17% neonatal death

Immune Hydrops

= ERYTHROBLASTOSIS FETALIS

= lysis of fetal RBCs by maternal IgG antibodies

Prevalence: 35÷10,000 live births at risk

Pathophysiology:

rh-negative women (= no D antigen) may become isoimmunized (= alloimmunization) if exposed to paternally derived fetal Rh-positive blood inherited from the father (= D allotype present); maternal IgM antibodies develop initially, later IgG antibodies with ability to cross placenta (= transplacental passage)

Cause of isoimmunization:

fetomaternal hemorrhage during pregnancy / delivery / spontaneous or elective abortion if fetus is D-positive; fetus has a 50% chance of being rh-negative as 56% of Rh D-positive fathers are heterozygous for D antigen

At risk:

Caucasians (15%), Blacks (6%), Orientals (1%); absence of D antigen originates in Basques

Determination of extent of disease by:

(1) Optical density shift at 450 nm (= delta OD 450) reflects amount of bilirubin in amniotic fluid; reasonably reliable only > 25 weeks MA; unreliable in alloimmunization due to Kell antibodies
(2) Percutaneous umbilical cord sampling (PUBS) with direct determination of Hct and Hb

• hemolysis + anemia
√ anasarca (= skin edema)
√ fetal ascites in 2nd trimester (present in only 66%) → indicates severe anemia with Hct < 15%, Hb < 4 g/dL
√ pleural effusion
√ increased diameter of umbilical vein
√ subcutaneous edema (skin thickness > 5 mm)
√ polyhydramnios (75%)
√ placentomegaly > 6 cm

√ pericardial effusion
√ hepatosplenomegaly
√ increased blood flow in middle cerebral artery ← increased cardiac output + decline in blood viscosity

Prophylaxis:
Rh immune globulin (RhoGAM® = antibody against D antigen) given at 28 weeks to all rh-negative women → blocks antigen sites on Rh-positive cells in maternal circulation → prevents initiation of maternal antibody production

OB management:
regular monitoring from 18 weeks on when maternal anti-D concentration exceeds 4 IU/mL → severe anemia unlikely if maternal antibodies < 15 IU/mL

Prognosis: (if untreated) in 45–50% mild anemia, in 25–30% moderate anemia (with neonatal problems only), in 20–25% hydrops (death in utero / neonatally)

Rx: umbilical vein transfusion during PUBS (necessary in only 10% before 34 weeks GA)

FETUS IN FETO

= one monozygotic twin encompasses body of other twin

Location: mostly retroperitoneum

√ well-circumscribed complex mass with internal calcifications + mixed fluid and solid components

√ vertebral bodies within mass (DIAGNOSTIC)

DDx: teratoma

FETAL TRAUMA

Prevalence: 7% of pregnant patients sustain accidental injury (greatest frequency during 3rd trimester); 0.3–0.4% are admitted to a hospital

Cause: motor vehicle accident (66%), physical abuse (10%)

Type of injury to pregnancy:
1. Uterine rupture (0.6%)
2. Complete (6–66%) / incomplete (30–80%) placental separation

US:
√ evaluate fetal motion, breathing, heart rate, placenta

◊ The major cause of fetal death is maternal death!

GARTNER DUCT CYST

= secretory retention cyst of remnant mesonephric duct

Frequency: 1–2%

Origin: remnant of vaginal portion of mesonephric / wolffian duct ← incomplete involution with gradual enlargement ← persistent glandular secretion

Histo: lined by nonmucinous flat cuboidal / low columnar epithelium

May be associated with: complex renal + urogenital malformations
(1) Herlyn-Werner-Wunderlich syndrome = ipsilateral renal agenesis + ipsilateral blind vagina
(2) Ectopic ureteral insertion into Gartner duct cyst

• usually asymptomatic
Location: anterolateral aspect of proximal third of vaginal wall above level of most inferior aspect of pubic symphysis extending into ischiorectal fossa
Size: usually < 2 cm
√ well-defined round lesion with fluid contents:
√ T2-hyperintense + T1-hypointense fluid
√ hemorrhagic / proteinaceous contents hypointense on T2WI + hyperintense on T1WI
√ may contain septa
√ large cyst may displace ureter upward / protrude through introitus
Cx: dyspareunia; interference with vaginal delivery
Rx: cyst aspiration; tetracycline sclerotherapy; surgical excision
DDx: urethral diverticulum (urethral displacement)

GASTROSCHISIS

= paramedian full-thickness abdominal fusion defect usually on right side of umbilical cord; may involve thorax; nonrotated bowel lacking secondary fixation to dorsal abdominal wall
Prevalence: 4÷10,000 live births (in 2005), sporadic
Cause: deficient mesenchyme during lateral body wall folding
former theory: abnormal involution of right umbilical vein / premature interruption of right omphalomesenteric artery with ischemic damage to abdominal wall
Risk factor: young maternal age (teenage mother÷mother aged > 25 years = 7÷1); more common in non-Hispanic white mothers; NO sex predilection
Age of occurrence: 37 days (5 weeks) of embryonic life
Age of detection: as early as 12 weeks GA; difficult < 20 weeks GA ← small size of defect (1–3 cm) and lack of bowel dilatation
Associated anomalies (5–14%):
intestinal atresia / stenosis (25%; small size of opening → compression / torsion of vessels; ectopia cordis (rare)
• MS-AFP ≥ 2.5 MoM in 77–100%
√ exteriorized bowel = thick-walled edematous freely floating loops outside fetal abdomen ← inflammation + direct trauma ← lack of peritoneal covering
√ dilated intra- / extraperitoneal bowel ← intestinal atresia
√ gastric fundus pulled toward defect
√ < 2–5 cm paraumbilical defect, usually on right side of cord insertion
√ normal insertion of umbilical cord
√ no fetal ascites
√ polyhydramnios may be present
√ liver / spleen may herniate infrequently
√ malrotation / nonrotation of bowel
Cx before birth:
(1) Bowel obstruction
(2) Peritonitis (exposure of bowel to fetal urine / meconium)
(3) Perforation ← peritonitis

(4) Fetal growth restriction (38–77%) ← nutritional loss from exposed bowel

Cx after birth:

malrotation, jejunal / ileal atresia (18%), bowel necrosis, necrotizing enterocolitis, hyperalimentation hepatitis, prolonged intestinal motility dysfunction, chronic short-gut syndrome

Mortality rate: 17%

Survival rate: 91–94% after surgical treatment (during 1st day of life, not influenced by mode of delivery); death from premature delivery / sepsis / bowel ischemia

GESTATIONAL TROPHOBLASTIC DISEASE

= group of disorders characterized by abnormal proliferation of trophoblastic tissue with invasive tendency originating from the developing blastocyst

Cause: aberrant fertilization

Components of trophoblast:

1. Cytotrophoblast = stem cell with high mitotic activity
2. Syncytiotrophoblast = synthesis of β-hCG
3. Intermediate trophoblast = responsible for endometrial invasion + implantation

- 1st trimester bleeding; increased levels of β-hCG
- rapid uterine enlargement / excessive size for EGA
- hyperemesis gravidarum / preeclampsia (in 2nd trimester)

Frequency: < 1% of all gynecologic malignancies

Associated with: molar pregnancy (most), post abortion, ectopic pregnancy, term pregnancy

Spectrum:

1. Benign hydatidiform mole (80–90%)
2. Invasive mole (5–8–10%)
3. Choriocarcinoma (1–2–5%)
4. Placental site trophoblastic tumor (rare)

Cytogenesis:

= fertilization of one egg by two sperm = chromosomes completely / predominantly of paternal origin

1. Diploid karyotype
   - › 46,XX = from fertilization of ovum by two <u>23,X sperm</u> after loss of maternal haploid chromosomes
   - › 46,XY = from fertilization of a chromosomally empty ovum by <u>two different sperm:</u>
     - complete hydatidiform mole (almost 100%), invasive mole (almost 100%), choriocarcinoma (50%)
2. Triploid karyotype (69,XXX; 69 XXY; 69,XYY)
   = fertilization of a normal ovum (23,X) by <u>two different sperm</u> thus containing $^{2}/_{3}$ paternal chromosomes
   - occurs in partial hydatidiform mole

At risk: maternal age > 35 years and < 20 years, previous molar gestation, previous spontaneous abortions

GRANULOSA CELL TUMOR

◊ Most common hormone-active estrogenic tumor of ovary
◊ Most common malignant sex cord-stromal tumor (70%)
Frequency: 2–3% of all ovarian neoplasms
Origin: from cells surrounding developing follicles
Age: puberty (5%), reproductive age (45%), postmenopausal (50%)
Path:
(a) large encapsulated smooth / lobulated multicystic mass with thick irregular septa + solid components; multiple blood-filled cysts ← hemorrhage / cystic degeneration with increase in tumor size
(b) unilocular cyst (rare) apt to manifest with virilization
• abdominal pain (acute hemorrhage into tumor / rupture into peritoneal cavity); palpable adnexal mass
Location: unilateral in 95%; bilateral in 2–5%
Size: average size of 12.5 cm (up to 40 cm) in diameter
US:
√ large complex multilocular cystic mass with fluid / blood (most frequently) + solid components:
√ thick irregular septations but NO intracystic papillary projections
√ solid component isoechoic to myometrium with Doppler flow
√ predominantly solid small heterogeneous hypoechoic mass simulating fibroid (uncommon)
√ calcifications (rare)
CT:
√ iso- to hyperattenuating enhancing solid component
√ hyperattenuating hemorrhage within cystic component
MR:
√ intermediate SI of solid component + multiple cystic spaces on T2WI = "spongelike" appearance
√ hyperintense on T1WI ← hemorrhage within tumor cysts
√ enhancement of solid component
√ ascites
Estrogenic effects:
√ uterine enlargement
√ endometrial thickening / hemorrhage
√ endometrial polyps / hyperplasia (80%) / carcinoma (10%)
N.B.: Androgenic effect with virilization extremely rare
Pattern of dissemination (extraovarian spread uncommon):
√ local extension
√ peritoneum-based metastases similar to epithelial neoplasm (rare)
√ cystic liver metastases
Prognosis: low malignant potential; late recurrence following surgery after > 3 decades
Rx: uni- / bilateral salpingo-oophorectomy ± postoperative chemotherapy
DDx: serous / mucinous ovarian tumor (intracystic papillary projections); metastasis

Adult Granulosa Cell Tumor (95%)
◊ Most common estrogenic ovarian tumor!

(rarely produces androgen)

Frequency: 95% of all GCT; 5–10% of solid ovarian tumors

Age: in middle-aged peri- and postmenopausal (50%) women; peak prevalence at 50–55 years

Histo: macrofollicular (multiple cysts resembling follicles), microfollicular (with Call-Exner bodies), insular, trabecular, cylindromatous, watered silk, diffuse type; frequently accompanied by theca cells + fibroblasts

- irregular menstruation cycles, menorrhagia ← endometrial hyperplasia; postmenopausal bleeding; amenorrhea
- 90% present at stage I (confined to ovary)

Cx: (1) Malignant transformation (5–25%)
(2) Low-grade endometrial carcinoma (3–25%)
(3) Recurrence → raised serum aromatase + estradiol levels

Recurrence: common even decades after resection with slow growth

Juvenile Granulosa Cell Tumor (5%)

Frequency: 5% of all GCT; 90% of GCT in patients < 30 years old

Mean age: 13 years; 80% of GCT occur in first 2 decades; only in 3% in women > 30 years of age

Path: solid component of granulosa + theca cells; follicles lined by granulosa cells staining positive for α-inhibin

Histo: larger cells with hyperchromatic nuclei + lack of characteristic nuclear groves (compared with adult GCT); NO Call-Exner bodies

Associated with: Ollier disease, Maffucci syndrome

- hyperestrogenism (in 80%):
  - ◊ 10% of all cases of precocious precocity
  - isosexual pseudoprecocity in 70% ← estrogen effect without ovulation / production of progesterone
  - premature breast development; low gonadotropin levels
  - pubic-axillary hair formation
  - clear vaginal discharge ← stimulated endocervical glands
  - atypical irregular uterine bleeding
  - accelerated somatic + skeletal development

Cx: malignant degeneration (rare)

Prognosis: 80–93% cure rate after surgery
◊ Juvenile tumors have a better prognosis (most diagnosed in stage I) but tend to recur after a shorter interval than adult tumors
◊ Increased risk of endometrial + breast cancer

Recurrence: unusual after simple resection for stage Ia / Ib tumors; as late as 25 years after treatment
- serum inhibin → useful marker to monitor

DDx: malignant germ cell tumors (yolk sac tumor, embryonal ca.), cystic teratoma, thecoma (hyperestrogenism in 50%, postmenopausal in 80%), Sertoli-Leydig cell tumor

HELLP SYNDROME

= **H**emolysis, **E**levated **L**iver enzymes, **L**ow **P**latelets

◊ Most common cause of severe liver disease in pregnancy!

Prevalence: 4–12% of patients with severe preeclampsia / eclampsia; higher in White women (24%), with delayed diagnosis of preeclampsia / delayed delivery (57%), in multiparous patients (14%)

Time of onset: before / immediately after birth (usually within 48 hours after delivery)

Histo: portal areas surrounded by deposited fibrin + hemorrhage + hepatocellular necrosis

- nonspecific epigastric / RUQ pain (90%)
- nausea + vomiting (45%), occasionally jaundice
- headache (50%); demonstrable edema (55%)
- abnormal liver function tests, low platelet count

√ hepatomegaly

√ fatty infiltration of liver (peak at 35th week)

√ intraparenchymal hemorrhage of liver ← subcapsular hematoma / rupture into peritoneal cavity

√ hepatic edema ← early ischemia ← necrosis

√ ascites + pleural effusions

√ subcapsular hematoma of kidney

√ vitreous hemorrhage

Cx: (1) Perinatal mortality (8–60%)

(2) Maternal death (3–24%) ← hepatic necrosis, hemorrhagic liver infarction, liver rupture, DIC, abruptio placentae, acute renal failure, sepsis

HYDATIDIFORM MOLE

= MOLAR PREGNANCY

[*hydatisia*, Greek = a drop of water; *mola*, Latin = false conception]

Frequency: 1÷1,200 to 1÷2,000 pregnancies; < 5% of abortions

Prognosis: noninvasive in 85%, locally invasive in 13%, metastasizing in 2%

Complete / Classic Mole (common)

= pregnancy failure ← implantation of nonviable fertilized egg

Cause: fertilization of an "empty egg" (= ovum with no active chromosomal material after loss of its maternal haploid chromosome)

(a) by single 23,X sperm (in 90%) → followed by sperm mitosis to form 46,XX chromosome set

(b) by two different sperms of 23,X and 23,Y (in 10%) → to form 46,XY chromosome set

◊ 46,YY diploid karyotype is not observed!

Path: complex multicystic mass = "cluster of grapes"

Histo: generalized hydropic swelling of all chorionic villi with prominent acellular space centrally; pronounced tropho- blastic proliferation of syncytio- and cytotrophoblast

- severe eclampsia prior to 24 weeks
- uterus too large for dates (in 50%); 1st trimester bleeding

- marked elevation of β-hCG with hyperemesis
- passing of grapelike vesicles per vagina
- hyperthyroidism ← thyroid-stimulating properties of β-hCG
- anemia ← plasma volume expansion + vaginal bleeding

US:

√ hyperechoic to moderately echogenic central uterine mass interspersed with punctate hypoechoic areas

√ numerous discrete cystic spaces (= hydropic villi) within a central area of heterogeneous echotexture = "snowstorm"

√ no identifiable fetal tissue

√ increased vascularity with low-resistance waveforms in spiral arteries of uterus

√ in 25% atypical appearance:

√ large hyperechoic areas (= blood clot) + areas of cystic degeneration resembling incomplete abortion

√ single large central fluid collection with hyperechoic rim mimicking an anembryonic gestation / abortion

√ no fetal parts / no chorionic membrane

√ bilateral theca lutein cysts (18–37–50%) → may take 4 months to regress after evacuation of a molar pregnancy ← hyperstimulation of ovaries by excessive β-hCG production

√ ± ascites

MR:

√ predominantly hypointense heterogeneous mass distending uterine cavity on T1WI

√ hyperintense mass on T2WI

√ ± focal areas of hemorrhage + cystic spaces

√ avid enhancement

√ hypointense myometrium (without invasion)

Prognosis: in 80–85% benign, in 15–20% invasive mole / choriocarcinoma

Rx: dilatation + suction curettage (curative in 85%)

DDx: (1) Hydropic degeneration of the placenta (associated with incomplete / missed abortions)

(2) Degenerated uterine leiomyoma

(3) Incomplete abortion = retained products with hemorrhage

(4) Choriocarcinoma

(5) Loculated abruptio placentae

(6) Hydropic changes of the placenta

Complete Mole with Coexistent Fetus (1–2%)

= molar degeneration of one conceptus of a dizygotic twin pregnancy with same risk of malignant degeneration as in classic mole

- vaginal bleeding in 2nd trimester; uterus large for dates
- abnormally elevated serum β-hCG
- amniocentesis with normal diploid karyotype excludes diagnosis of partial mole

√ normal gestation with placenta + separate typical echogenic material of a hydatidiform

mole
√ ovarian theca lutein cysts
Prognosis: fetal survival unlikely ← maternal complications from coexistent mole

Invasive Mole

= CHORIOADENOMA DESTRUENS
= locally invasive nonmetastasizing neoplasm
Histo: excessive trophoblastic proliferation with presence of villous structure + invasion of myometrium
Preexisting condition: complete / partial hydatidiform mole
• history of previous molar gestation / missed abortion (75%)
• continued uterine bleeding
• persistently elevated β-hCG levels ← failure of β-hCG to return to undetectable levels after treatment of a complete hydatidiform mole
Spread: lung, vagina
√ hyperechoic tissue with punctate lucencies
√ irregular focal hyperechoic region within myometrium
√ bilateral theca lutein cysts, 4–8 cm in size
√ myometrial invasion occasionally demonstrable
Rx: chemotherapy, hysterectomy (if at risk for uterine perforation)
DDx: choriocarcinoma (same imaging features)

Partial Hydatidiform Mole

= areas of molar change alternating with normal villi + nonviable fetus with significant congenital anomalies
Cause: fertilization of an egg by two sperm → triploid genotype of 69,XXY (66%) or 69,XXX (33%)
Histo: moderate focal proliferations of syncytiotrophoblast; normal villi interspersed with hydropic villi
• early onset of preeclampsia
√ nearly always coexistent fetus with severe abnormalities + IUGR
√ placenta with numerous cystic spaces
√ oligohydramnios
Prognosis:
(1) frequently spontaneous abortion (unrecognized as mole for lack of karyotyping of the abortus)
(2) no survival of triploid fetus
(3) 3% risk of persistent gestational trophoblastic neoplasia

HYDRO- / HEMATOMETROCOLPOS

= accumulation of sterile fluid (hydro-) / blood (hemato-) / pus (pyo-) within uterus (-metria) + vagina (-colpos);
(a) premenarcheally = secretions + mucus
(b) postmenarcheally = blood
Prevalence: 1÷16,000 female births

• asymptomatic; vague pelvic discomfort
• pain during defecation / urination
√ smooth symmetric enlargement resulting in pear-shaped uterus ± distended vagina
√ varying amounts of low-level internal echoes centrally within uterus continuous with vaginal canal
√ hematosalpinx ± endometriosis
OB-US:
√ cystic / midlevel echogenic retrovesical mass ← mucous secretions ← stimulation by maternal estrogens during fetal life
√ cystic mass ± fluid-debris level (= distended vagina)
√ bladder often not identified (compressed by distended vagina)
MR:
√ endometrial cavity + upper part of vagina distended by blood products:
√ fluid of hyperintense SI on T1WI
√ less hyperintense than urine on T2WI
DDx: ovarian cyst, duplication cyst, meconium cyst, mesenteric cyst, rectovesical fistula, anterior meningocele, cystic tumor, trophoblastic disease, degenerating leiomyoma / leiomyosarcoma
Cx: endometritis, myometritis, parametritis (= pelvic lymphangitis), pelvic abscess, septic pelvic thrombophlebitis, urinary tract infection

Acquired Hydro- / Hematometra

Cause: neoplastic obstruction of endocervical canal / vagina; postpartum infection; attempted abortion; cervical stenosis after radiotherapy; postsurgical scarring (eg, dilatation & curettage, traumatic delivery); senile contraction

Congenital Hematometra / Hematometrocolpos

Age: puberty
Cause:
(a) persistent urogenital sinus = single exit chamber for bladder + vagina; separate orifice for anus; caused by virilization of female fetus / intersex anomaly / arrest of normal vaginal development
Frequently associated with: ambiguous genitalia
Age: newborn period
(b) cloacal malformation = single perineal orifice for bladder + vagina + rectum; caused by early embryologic arrest
Frequently associated with: duplicated genital tract
Age: newborn period
(c) imperforate hymen, transverse vaginal septum, segmental vaginal atresia, imperforate cervix, blind horn of bicornuate uterus, Mayer-Rokitansky-Küster-Hauser syndrome (= agenesis of uterus + vagina with active uterine anlage)
◊ Hematometrocolpos / hematocolpos ← imperforate hymen / transverse vaginal septum
◊ Hematometra ← cervical dysgenesis + vaginal agenesis / Mayer-Rokitansky-Küster-Hauser syndrome / obstructed uterine horn
• primary amenorrhea = "delayed menarche"

- cyclical abdominal pain; interlabial mass

May be associated with:

imperforate anus, hydronephrosis, renal agenesis / dysplasia, polycystic kidneys, duplication of vagina + uterus, sacral hypoplasia, esophageal atresia

INCOMPETENT CERVIX

= gaping cervix usually develops during 2nd trimester / early 3rd trimester

Predisposed: cervical trauma (D & C, cauterization), DES exposure in utero with cervical hypoplasia, estrogen medication

• physical examination tends to underestimate the true length of the cervix

◊ Appearance of cervix may change during course of sonographic examination!

Cause: uterine contraction / manual pressure on fundus / patient erect (stress test of cervix) / degree of bladder distention

Normal Cervical Length		
	Transabdominal	*Transvaginal*
1st trimester (< 14 wks)	53 ± 17 mm	40 ± 8 mm
2nd trimester (14–28 wks)	44 ± 14 mm	42 ± 10 mm
3rd trimester (≥ 28 wks)	40 ± 10 mm	32 ± 12 mm
◊ Distended bladder improves visualization but increases cervical length on transabdominal US!		
◊ Difference between nulli- and multiparous women 10%!		

√ dilatation of cervical canal beginning at internal os + extending toward external os:

√ beaking / funneling of cervical canal

√ bulging of membranes through external os ← amniotic fluid within dilated endocervical canal

√ visualization of fetal parts within dilated endocervical canal

√ shortening of cervix to < 25 mm

Prognosis: 14th–18th week best time for Rx prior to significant cervical dilatation

CONTRACEPTIVE DEVICES

Intrauterine Devices (IUD) *approved in USA*

• retrieval string protrudes 2–3 cm from external cervical os

√ double echogenic line with plastic IUD

√ reverberation echoes with metal IUD

1. **Mirena®**

   Function: barium-impregnated T-shaped polyethylene frame with collar of a synthetic progesterone (levonorgestrel); discharges a small amount of the drug for up to 5 years → thickens cervical mucus + thins uterine lining

2. **ParaGard®**

   Function: polyethylene frame wound with copper wire slowly releasing spermicidal copper ions for up to 10 years

3. 1st generation devices:

   (a) Lippes loop

   √ 4–5 echogenic dots on SAG view

   √ horizontal line / dot on TRV view

   (b) Saf-T-coil

√ echogenic solid line on SAG view
√ series of echoes / dot on TRV view

(c) Copper 7 / Copper T / Progestasert®
√ dot in fundus + solid line in corpus on SAG view
√ solid line in fundus + dot in corpus on TRV view

(d) Dalkon shield (pulled from market in 1974)
Cx: PID, sepsis, 17 deaths

Cx:

(1) Pelvic inflammatory disease (2–3-fold risk compared with that of non-IUD users) in 35%; actinomycosis with IUD in place for > 6 years
(2) Perforation (0.1%) into / through myometrium during placement
(3) Migration by tracking into surgical scar

"Lost IUD"

= locator device missing; string not visible / not palpated

Cause: 1. Migration (displacement) / detachment of string
2. Expulsion of IUD
4. Uterine perforation of IUD

◊ Abdominopelvic radiograph is indicated if IUD not identified by US!

EXPULSION OF IUD

Frequency: 10%
Risk factors: insertion early in menstrual cycle / immediate postpartum period, nulliparity, menorrhagia, severe uterine distortion
Location: cervix, vagina

DISPLACEMENT OF IUD

= improper position within uterine cavity
Frequency: 25%

PERFORATION OF IUD

Frequency: up to 1÷1,000 cases
Risk factors: lactation, birth within past 6 months, uterine abnormality, clinician inexperience
√ embedment in endometrium / myometrium (18%)
√ migration into peritoneal cavity → freely floating / encased in adhesions / adherent to bowel or omentum

IUD & Pregnancy

Prevalence: 2÷100 women annually
√ IUD may not be visualized after 1st trimester → as uterus grows IUD is drawn into cavity
√ ± ectopic pregnancy
Prognosis: high risk of spontaneous (40–50%) / septic abortion, premature labor, chorioamnionitis, low birth weight
Rx: early removal of IUD during 1st trimester using IUD hook / alligator forceps unless removal of IUD could disrupt pregnancy

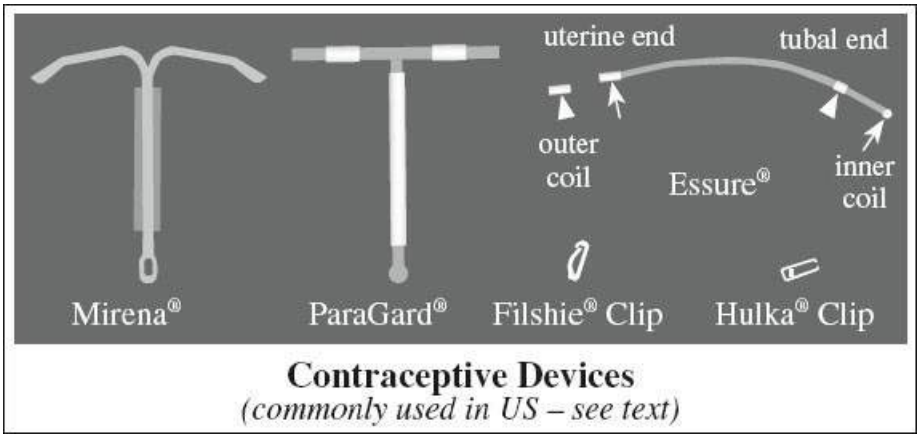
Tubal Occlusion Devices

› external occlusion by minilaparotomy:

(a) hinged clips

1. **Filshie® Clip**
   Cx: 0.51% failure rate at 1 year; dislodgement; migration
2. **Hulka® Clip**
   Cx: 3.56% failure rate at 10 year

(b) rings / loops
Falope ring, Yoon ring, Lay loop



Contraceptive Devices
(commonly used in US – see text)

› internal occlusion:

◊ Occlusion must be verified 3 months after placement with adequate HSG pressure of 150–200 mmHg!

(1) **Essure® Permanent Birth Control System**

inner coil: stainless steel + polyethylene terephthalate fibers; tubal end with ball; uterine end with connected rectangle

outer coil: radiographically invisible nitinol (= alloy of titanium + nickel): uterine end with isolated rectangle; tubal end with square

HSG: √ peripheral tubal end of inner coil (arrow ↑ in drawing) within fallopian tube
√ < 50% of inner coil within uterine cavity
√ central tubal end of inner coil (arrow ↑ in drawing) extends < 30 mm into tube from contrast-filled cornu

Cx:

(1) Tubal patency after 3 months (3%) → follow-up in another 3 months
(2) Expulsion into uterine cavity (0.6–3%)
(3) Partial / complete extrusion into peritoneal cavity (1–2%) ± adhesions with small bowel obstruction

(1) **Adiana® Permanent Contraception System**

= nonabsorbable nonradiopaque silicone elastomer matrix inserted into fallopian tube after focal radiofrequency thermocoagulation

HSG: √ tubal opacification of < 10 mm

Cx: Tubal patency after 3 months (8.8%) → follow up in another 3 months (4.3–5.6%)

INTRAUTERINE GROWTH RESTRICTION

= FETAL GROWTH RETARDATION

= perinate with a weight at / below the 10th percentile for gestational age occurring as a result of a pathologic process inhibiting expression of normal intrinsic growth potential
for twin pregnancy: discordant weight > 25%

◊ Fetal weight at / below 10th percentile for age will classify 7% of normal fetuses as growth retarded!

Prevalence: 3–7% of all deliveries; in 12–47% of all twin pregnancies; in 25% of fetuses following birth of a growth-retarded sibling / stillborn

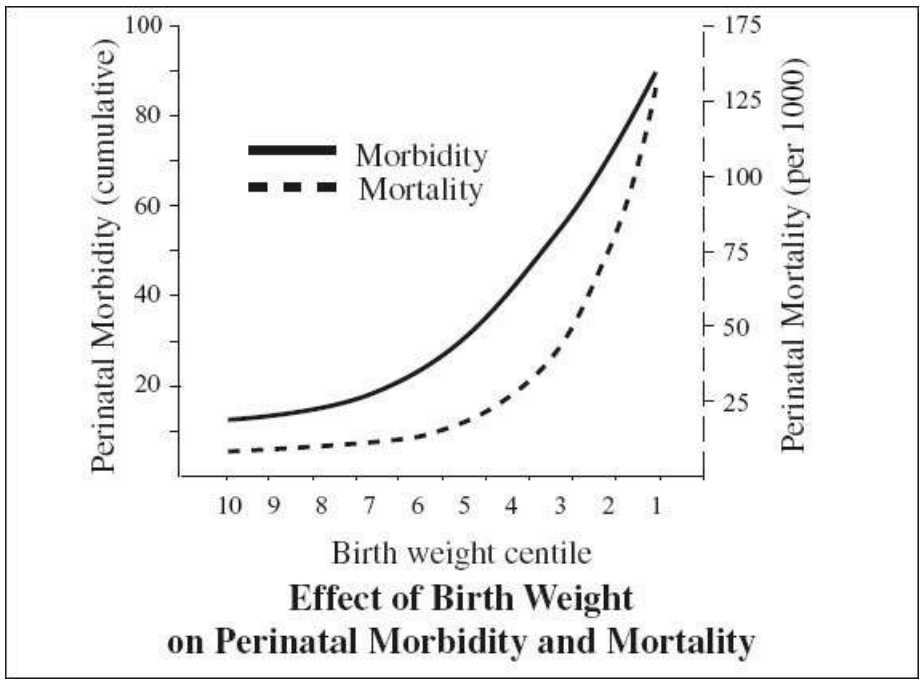
- fundal height as screening test (37–60% true positive, 40–55% false negative; 26–60% false positive)

◊ IUGR is primarily an ultrasound diagnosis!

Sequence of events in fetal hypoxia:
nonreactive CST > absence of fetal breathing > nonreactive NST > diminished fetal movements > absence of fetal movements > absence of fetal tone

Etiology:

A. UTEROPLACENTAL INSUFFICIENCY (80%)
= injury during period of cell hypertrophy → decreased cell size with features of intrauterine starvation + protective cardiac output redistribution reflex



Effect of Birth Weight on Perinatal Morbidity and Mortality

- absence of body fat; diminished liver and muscle glycogen

1. Maternal causes:
√ asymmetric IUGR / symmetric IUGR (in severe cases)
(a) deficient supply of nutrients:
cyanotic heart disease, severe anemia (in 10–25% of sickle cell anemia), maternal starvation, life in high altitudes, drugs (anticonvulsants, methotrexate,

warfarin), alcohol abuse (dose related), illicit drugs (up to 50% with heroine addiction, 30% with cocaine abuse), uterine anomaly, multiple gestation (in 15–20%)

(b) maternal vascular disease resulting in inadequate placental perfusion:
nicotine-induced release of catecholamines, preconceptual diabetes, preeclampsia, chronic renal disease, collagen vascular disease (SLE)

(c) maternal demographics:
maternal age (adolescence / advanced), nulliparous mother, small short habitus, racial influence (Asians)

2. Primary placental causes:
extensive placental infarctions, chronic partial separation (abruption), partial mole, Breus mole, chorioangioma, placenta previa, low implantation, placental metastases (breast, melanoma), placentitis (luetic, malaria)
Histo: reduction in placental villous surface area + in number of capillary vessels
√ asymmetric growth failure

B. PRIMARY FETAL CAUSES (20%)
= injury during the period of cell hyperplasia (= embryogenesis) producing profound reduction in cell number across all cell lines
√ symmetric IUGR (globally decreased intrinsic growth)
√ normal / increased amniotic fluid volume

1. Chromosomal abnormalities (in 2–6%): triploidy, tetraploidy, trisomy 13 + 18 + 21, aneuploidy (Turner syndrome), partial deletion (4p, 5p [cri-du-chat], 13q), partial trisomy (4p, 18p, 10q, 18q), unbalanced translocation (chromosomes 4 + 15), balanced translocation (chromosomes 5 + 11)
2. Structural anomalies: CHD, genitourinary anomalies, CNS anomalies, dwarfism
3. Viral infection: rubella (in 40–60%), CMV, varicella (in 40%)

◊ All fetuses with IUGR need to have a detailed and often repeated search for structural anomalies!

Diagnostic Ultrasound Methods in IUGR:

◊ An accurate fix on fetal age dictates the accuracy of diagnosis of IUGR (early US exam, clinical dates, early physical exam, pregnancy test)!

◊ Every effort needs to be made to determine the underlying cause for growth failure as it effects management + perinatal morbidity and mortality!

1. **Fetal morphometric indices**
The 3 key parameters for diagnosing IUGR are
(1) Low estimated fetal weight (EFW),
(2) Low amniotic fluid volume (AFV),
(3) Maternal hypertension (HBP)!

(a) intrafetal proportions
√ elevated HC÷AC ratio for dysmature IUGR (overall 36% sensitive, 90% specific, 67% PPV, 72% NPV; 93% sensitive in fetus > 28 weeks MA with severe dysmature IUGR)
◊ Early-onset dysmature IUGR not detectable!
◊ May not be used in anomalous fetuses!

(b) rate of growth = growth velocity
√ HC, AC, FL measurements allow DDx between erroneous dates + normal small fetus + fetus with intrinsic abnormality
√ plot growth curves
◊ Minimum time interval of 2 weeks necessary!

2. **Amniotic fluid volume**
◊ Screening for decreased amniotic fluid is of value in the fetus with dysmature IUGR (60–84% sensitive, 79–100% accurate)!
√ normal amniotic fluid does not exclude IUGR
√ oligohydramnios means dysmature IUGR in a fetus with normal GU tract until proven otherwise (DDx: trisomy 13 + 18)
3. **Fetal morphologic assessment + fat distribution**
√ diminished thigh circumference
√ absent paraspinal fat pad (posterior neck)
√ reduced / absent malar fat pads
√ disproportionately small liver size
√ increased small bowel echogenicity ← absent omental fat
4. **Placental assessment**
√ increased placental calcium deposition
5. **Biophysical profile**
Accuracy: false-negative fetal death rate of 0.645 per 1000 fetuses within 1 week of the last normal BPP; 33% sensitive, 17% positive predictive value
6. **Invasive fetal testing**: fetal blood analysis for karyotyping, hypoxemia, hyper-capnia, acidemia, hypoglycemia, hypertriglyceridemia
7. **Nonstress test** (NST)
8. **Contraction stress test** (CST)

Sonographic Criteria for IUGR

Sonographic Finding	*PPV [%]*	*NPV [%]*
Advanced placental grade	16	94
Elevated FL÷AC ratio	18–20	92–93
Abnormal UA waveform	17–37	
Low total intrauterine volume	21–24	92–97
Small BPD	21–44	92–98
Slow BPD growth rate	35	97
Low EFW	45	99
Oligohydramnios	55	92
Elevated HC÷AC ratio	62	98

Diagnostic Doppler Methods in IUGR:

A. PLACENTAL PERFUSION
1. Umbilical artery velocimetry (UA)
◊ Not useful with unknown dates / for screening!
◊ Better predictor of adverse perinatal outcome than MCA or RA pulsatility index

Pathophysiology: fewer terminal villi ← develop-mental defect / villous infarction
√ elevated systolic÷diastolic ratio (S/D ratio > 3.0 beyond 30–34 weeks GA) ← increase in vascular resistance within placental circulation
√ absent diastolic flow ← villous obliteration > 50% (50–90% mortality rate)
√ reverse diastolic flow ← villous obliteration > 50% (= impending fetal collapse)
Note: S/D ratio increases with sampling site closer to fetus + increasing fetal heart rate; ↓ of S/D ratio with advancing gestational age; S/D ratio may decrease in lateral recumbent position

2. Uterine artery waveform
Method: sample volume at point of overlap of uterine artery with external iliac artery
√ S/D ratio > 2.6 after 26 weeks GA
√ persistence of early diastolic notch
Pathophysiology: lack of trophoblastic invasion of spiral arteries
Rules:
› Trophoblastic invasion may not occur until 20–22 weeks GA in some patients
› An abnormal waveform at 24 weeks GA will never become normal
› A normal waveform will never revert to a high resistive waveform
› Both / one uterine artery may be abnormal

B. FETAL CIRCULATION
Pathophysiology: preferential shunting of blood to brain ("brain sparing") + myocardium in response to hypoxemia

1. Fetal middle cerebral artery (MCA)
◊ Significant correlation between hypoxemia at cordocentesis and MCA pulsatility index
◊ If the MCA pulsatility index is normal the fetus is unlikely to have a major adverse outcome
Method: sample volume in MCA of near field 1 cm distal to its origin
√ ↓ in S/D ratio to 2.5 to 3.0 (normal is about 6.0)

2. Renal artery waveform (RA)
Method: sample volume in proximal renal artery on coronal image that visualizes entire renal a.
√ increase of pulsatility index

3. Fetal aortic flow volume (no proven usefulness)
√ decrease in blood flow to < 185–246 mL/kg/min

Cx: increased risk for perinatal asphyxia, meconium aspiration, electrolyte imbalance from metabolic acidosis, polycythemia
Neonatal Cx: pulmonary hemorrhage + vasoconstriction, persistent fetal circulation, intracranial hemorrhage, bowel ischemia, necrotizing enterocolitis, acute renal failure
Prognosis: 6–8-fold risk increase for intrapartum + neonatal death
◊ 20% of all stillborn fetuses are growth retarded!

DDx of fetus small for gestational age (SGA):
Definition: fetus measures less than expected for GA age but grows normally throughout pregnancy

(1) Small normal fetus (80–85%)
(2) Small abnormal fetus (5–10%)
(3) Dysmature fetus (10–15%)

Pure Symmetric IUGR

= DECREASED–CELL-NUMBER IUGR = EARLY-INSULT IUGR = LOW-PROFILE IUGR
= proportionate reduction of all fetal measurements due to
(a) intrinsic alteration in growth potential (usually due to chromosomal abnormalities)
(b) severe nutritional deprivation overwhelming protective brain-sparing mechanism occurring < 26 weeks MA and persisting until delivery
√ proportionate decrease in HC and AC with maintenance of normal HC÷AC ratios
√ estimated fetal weight < 10th percentile for age by middle of 2nd trimester

Mixed IUGR

= onset of IUGR during period of mixed hyperplasia / hypertrophy with near normal inherent fetal growth potential but decreased size + impaired function of placenta
√ impaired fetal growth ± asymmetry
√ abnormal Doppler umbilical artery flow velocity ← increased placental vascular resistance
√ progressive oligohydramnios

Asymmetric IUGR

= DECREASED–CELL-SIZE IUGR
= LATE-ONSET IUGR = LATE-FLATTENING IUGR (75%)
= disproportionate reduction of fetal measurements ← uteroplacental insufficiency with preferential shunting of blood to fetal brain occurring after 26 weeks GA
◊ IUGR usually not detectable before 32–34 weeks GA (time of maximal fetal growth)!
Effective time for screening: 34 weeks MA
Routine surveillance: every 4 weeks from 26 weeks MA on
√ AC > 2 SD below the mean for age = highly suspicious; AC > 3 SD below mean for age = DIAGNOSTIC

◊ The abdominal circumference is the single most effective fetal parameter for the detection of asymmetric IUGR!

√ high HC÷AC and FL÷AC ratios (head size + femur length less affected)
√ fetal weight percentile useful for follow-up
√ accelerated placental maturity
√ decreased amniotic fluid volume
√ elevated umbilical artery S/D ratio
◊ FL÷AC ratio + umbilical artery S/D ratio are the only effective techniques to screen for IUGR on a single exam with late prenatal care in 3rd trimester!

KRUKENBERG TUMOR

= metastatic ovarian adenocarcinoma most commonly originating in GI tract
Origin: stomach > breast > colon > appendix > pancreas > biliary primary; ? colon÷stomach =

2÷1
◊ 2% of females with gastric cancer develop Krukenberg tumor
◊ Krukenberg tumors antedate the discovery of the primary lesion in up to 20%!

Age: any age, most common in 5th–6th decade
√ solid mass + intratumoral cysts; in 60–80% bilateral
√ hypo- / hyperechoic mass ± cystic degeneration
MR:
√ variable hypointensity on T2WI ← mucin-filled signet-ring cells + abundant collagen formation
√ moderate to marked enhancement of solid components

LIMB-BODY WALL COMPLEX

= BODY STALK ANOMALY
= characterized by attachment of visceral organs to placenta with short / absent umbilical cord
Prevalence: 0.12÷10,000 live and still births
Cause: ? abnormal lateral body folding; ? severe form of amniotic band syndrome; ? early vascular disruption; ? embryonic dysplasia due to malformation of ectodermal placodes

A. EXTERNAL DEFECTS
1. Ventral wall anomaly
√ large eccentric defect
Location: L÷R = 3÷1 (DDx: gastroschisis)
2. Craniofacial defects: anencephaly, cephalocele, facial cleft
3. Limb anomalies: clubfoot, absent limbs
4. Spinal defects: dysraphism, scoliosis

B. INTERNAL DEFECTS (in 95%)
1. Cardiac defects
2. Diaphragmatic absence
3. Bowel atresia
4. Renal abnormalities: agenesis, hydronephrosis, dysplasia

US (confusing appearance):
√ fetus usually in a fixed position
√ cord insertion site not identifiable
√ NO free-floating loops of cord
√ severe kyphoscoliosis (frequent)
√ ± oligohydramnios → MRI
√ complete evisceration of abdominal contents with adherence to placental surface
√ persistence of extraembryonic coelom (= separation of amnion + chorion)

Prognosis: invariably fatal shortly after birth

MACROSOMIA

= FETAL GROWTH ACCELERATION
= fetus large for gestational age (LGA) with EFW > 90th percentile for age / > 4,000 g at term
√ AC > 3 SD above the mean for age (most reliable + largest measurement)
√ estimated fetal weight (EFW) including fetal head, abdomen, femur length > 90th percentile (±

15% accuracy)
√ low FL÷AC ratio
√ low HC÷AC ratio
√ enlarged thigh circumference
√ low FL÷thigh circumference ratio
√ greater than expected interval growth
√ polyhydramnios
Risk: shoulder dystocia, prolonged labor, meconium aspiration

MASSIVE OVARIAN EDEMA

= tumorlike condition with marked enlargement of one / both (occasionally) ovaries ← accumulation of edema fluid in stroma
Prevalence: rare; common in young woman during ovulation induction / pregnancy
Location: right > left ovary
Age: 6–33 (average 21) years
Cause:
(1) partial / intermittent torsion → obstruction to ovarian lymphatic + venous drainage
(2) ovarian stromal proliferation with enlargement of ovary susceptible to torsion
Histo: edematous ovarian stroma + extensive fibromatosis surrounding primordial follicles, luteinized cells
• acute / intermittent lower abdominal pain for months
• masculinization (in chronic phase)
√ solid / multicystic adnexal mass
√ ovarian diameter of 5–40 (mean 11.5) cm
Rx: oophorectomy / salpingo-oophorectomy / wedge resection with ovarian suspension

MEIGS SYNDROME

[Joe Vincent Meigs, 1892–1963, obstetrician and gynecologist at Harvard University and Massachusetts General Hospital]
= characterized by
(1) Ascites (in 15–40% of tumors > 10 cm):
(2) Pleural effusion (rare)
(3) Benign ovarian tumor: fibroma / fibrothecoma (91%), granulosa cell tumor (5%), Brenner tumor (2%)]
Pseudo-Meigs syndrome
(4) Mature teratoma / leiomyoma / cystadenoma / ovarian malignancy
Pathogenesis: ? vasoendothelial and fibroblast growth factors + cytokines; pressure of tumor on lymph vessels
• CA-125 may be elevated
◊ Ascites + pleural effusion resolve after removal of tumor

MUCINOUS OVARIAN TUMOR

Frequency: 20% of all ovarian tumors; 2nd most common benign epithelial neoplasm of ovary (after serous ovarian neoplasm)

Histo: single layer of nonciliated tall columnar epithelium with clear cytoplasm of high mucin content (similar to endocervix + intestinal epithelium)
Age: middle adult life, rare before puberty + after menopause
Cx: (1) Rupture may lead to pseudomyxoma peritonei
(2) Torsion
DDx: serous ovarian tumor (smaller, unilocular)

Mucinous Cystadenoma (80%)
Prevalence: 20% of all benign ovarian neoplasms
Age: 3rd–5th decade of life
√ multilocular cyst with numerous thin septa
√ cysts frequently have high protein content:
√ low-level echoes in cysts
√ high attenuation on CT
√ hyperintense on T1WI
√ usually unilateral, bilateral in 5%

Borderline Malignant Mucinous Cystadenoma (10%)

Mucinous Cystadenocarcinoma (10%)
Histo: mucoid material in cysts, sometimes accompanied by hemorrhagic / cellular debris; difficult to differentiate from benign variety + metastasis from intestinal primary
√ multilocular with numerous smooth thin-walled cysts
√ solid tissue areas: thick septa + other soft-tissue elements within septated cyst
√ usually unilateral; bilateral in 5–10% of stage I cases
√ capsular infiltration with loss of definition + fixation
CT:
√ multiseptated tumor of low attenuation
√ high-attenuation proteinaceous material (20–30 HU) in some loculi
MR:
√ variable signal intensity in different loculi ← proteinaceous / mucinous content, hemorrhage

NABOTHIAN CYST
= most common benign masslike lesion of cervix
Incidence: in women during reproductive years
Cause: mucus-retention / epithelial-inclusion cyst ← obstruction of endocervical gland by proliferating squamous epithelium ← chronic cervicitis / after childbirth
Size: < 1 cm (majority); may enlarge to become symptomatic
√ simple anechoic cyst without vascularity (incidentally detected at imaging)
√ may increase in echogenicity ← proteinaceous / hemorrhagic content
√ "tunnel cluster" (in up to 8%) = multicystic dilatation of endocervical glands mimicking adenoma malignum
Rx: none (unless symptomatic)

DDx: adenoma malignum = minimal deviation adenocarcinoma (solid components, marked hypervascularity)

NUCHAL CORD

= umbilical cord encircling fetal neck: single loop (96%) > 2 loops (2–3%) > 3 or more loops (< 1%)

Prevalence: 5–29% of pregnancies; increases with fetal age; frequently transient

Associated with: increased cord length, small fetus, vertex presentation, polyhydramnios

• generally not of clinical significance: no difference in 5-min Apgar score, no increase in infant mortality

√ umbilical cord loop > 360° around fetal neck

√ two adjacent cross sections of cord on longitudinal view of neck (diagnosis facilitated by color Doppler flow)

√ "**divot**" sign = indentation of skin by nuchal cord suggests tight loop

√ NO effect on fetal MCA + umbilical artery flow velocimetry

Cx: (1) Fetal distress: fetal bradycardia + intrapartum deceleration + depressed 1-min Apgar score

(2) Umbilical artery acidemia

(3) Passage of meconium

(4) Fetal demise

OB management:

1. Assess fetal well-being (biophysical profile biweekly, NST, fetal growth)
2. Vaginal delivery permissible if without evidence of fetal compromise
3. Intervention only for signs of fetal distress

OMPHALOCELE

= herniation of abdominal viscera through an enlarged umbilical ring into base of umbilical cord during 3rd–4th week of GA

Prevalence: 1÷4,000–5,500 pregnancies; 2–3÷10,000 live births

Cause:

(a) migration failure of lateral mesodermal body folds:
√ omphalocele contains liver

(b) persistence of primitive body stalk beyond 12th week MA

Age: earliest detection at 12 weeks menstrual age; diagnosis < 11–12 weeks' gestation should be made with caution

Normal physiologic herniation should be < 1 cm into cord and never involve the liver. At 14 weeks follow-up bowel should have returned into abdominal cavity.

High incidence of ASSOCIATED ANOMALIES (45–88%):

1. Chromosomal (10–25–58%): trisomy 13, 18, 21; Turner syndrome (13% with liver in omphalocele, 77% with bowel in omphalocele)
2. Genitourinary (40%)
   mnemonic: OEIS complex (= aide-mémoire acronym)
   Omphalocele

Exstrophy of bladder
Imperforate anus
Spinal defect

3. Cardiac (16–30–47%): VSD; ASD; tetralogy of Fallot; ectopia cordis in pentalogy of Cantrell; DORV
4. Neural tube defects (4–39%): holoprosencephaly; encephalocele; cerebellar hypoplasia
5. IUGR (20%)
6. Beckwith-Wiedemann syndrome (5–10%)
7. GI tract:
   intestinal atresia (vascular compromise); malrotation; abnormal fixation of liver; esophageal atresia; facial cleft; diaphragmatic hernia
8. Limb-body wall deficiency; cystic hygroma

• MS-AFP ≥ 2.5 in 40–70%

Sac contents: primarily bowel, liver, other viscera (variable)

√ herniation of abdominal viscera at base of umbilical cord:
liver (27%) ± stomach ± bowel

√ midline central defect at base of umbilical cord insertion:
√ defect over entire ventral abdominal wall of variable size (mean, 2.5–5 cm)
√ widened cord where it joins the skin of the abdomen

√ covering amnioperitoneal membrane:
√ inner layer = peritoneum; outer layer = amnion
√ cord inserts at apex of defect on covering membrane, NOT directly on abdominal wall

√ hypoechoic loose mesenchymal tissue (= Wharton jelly) between layers of membrane

√ ascites within herniated sac (common)

√ polyhydramnios (occasionally oligohydramnios)

mnemonic: OMPHALOCele
Other anomalies (common)
Membrane surrounding viscera
Perfectly midline
Heart anomalies
Ascites
Liver commonly herniated
O for "zero" bowel complications
Chromosomal abnormalities (common)

Cx: (1) Infection, inanition
(2) Immaturity (23%)
(3) Rupture of hernia sac (in up to 15%)
(4) Intestinal obstruction

Mortality rate: 10% mortality if isolated abnormality; 80% with one / more concurrent malformations; ~ 100% with chromosomal + cardiovascular abnormalities

DDx: (1) Congenital umbilical hernia (covered by intact skin and subcutaneous tissue)
(2) Gastroschisis (usually right-sided defect)
(3) Limb-body wall complex (usually left-sided defect)

Pseudo-omphalocele

(1) Deformation of fetal abdomen by pressure with transducer coupled with an oblique scan orientation may give the appearance of an omphalocele
√ obtuse angle between pseudomass + fetal abdominal wall

(2) Physiologic herniation of midgut into umbilical cord between 8th and 12th week of gestation
√ herniated sac never contains liver
√ herniated sac usually < 7 mm
√ disappears by 12th week GA

OMPHALOMESENTERIC DUCT CYST

Etiology: persistence + dilatation of an omphalomesenteric / vitelline duct segment → joining embryonic midgut and primary yolk sac → which is formed during the 3rd week and → closed by the 16th week of gestation

Histo: cyst lined by columnar mucin-secreting GI epithelium

M÷F = 3÷5

Location: usually in close proximity to fetus
√ umbilical cord cyst up to 6 cm in diameter
√ beneath amniotic surface of cord (= eccentric)

Cx: (1) Compression of umbilical vessels by expanding cyst
(2) Erosion of umbilical vein from acid-producing gastric mucosal lining

DDx: allantoic cyst, umbilical cord hematoma

OVARIAN CANCER

= 7th leading cause of cancer in women (4% of all cancers among women); 2nd most common gynecologic malignancy; 5th leading cause of cancer deaths in USA women after lung, breast, colon, pancreas (leading cause of cancer deaths of all female cancers); accounts for 50% of cancer deaths of female genital tract (67% of patients present with advanced stage III disease)

◊ 1÷75 women will develop ovarian cancer (lifetime risk)
◊ 1÷100 women will die of ovarian cancer

Incidence: 50÷100,000 women annually (33÷100,000 women > age 50 annually); in USA 22,280 new cases + 14,240 deaths (2016)

Etiology: ovarian surface epithelium proliferates temporarily to repair defect after rupture of ovum, which may result in an "inclusion body" / "cystoma"; an error in DNA replication within inclusion body may occur resulting in inactivation / loss of a tumor-suppressor gene

Epidemiology:

(1) sporadic: "ovulation hypothesis" = risk of ovarian cancer is a direct function of the number of ovulatory cycles during a woman's life span

(2) hereditary (1–5%) = defined as ovarian cancer occurring in at least two 1st-degree relatives
◊ 50% lifetime probability to develop ovarian cancer
(a) breast cancer-ovarian cancer syndrome
(b) ovarian cancer only syndrome

(c) Lynch type II cancer family syndrome
= inheritance of nonpolyposis colorectal cancer, endometrial cancer and (rarer) ovarian cancer

Increased risk:
nulliparity, early menarche, late menopause, Caucasian race, higher socioeconomic group, positive family history for ovarian cancer (risk factor of 3 with one close relative, risk factor of 30 with two close relatives affected with ovarian cancer), history of breast cancer (risk factor of 2) / early colorectal cancer (risk factor of 3.5)

Decreased risk = protective effect:
multiparity, use of oral contraceptives, breast-feeding

Age: increasing with age; peaking at 55–59 years (80% of cases in women > 50 years)

Spread:

(1) direct extension through subperitoneal space (sigmoid mesocolon on left, cecum + distal ileum on right), uterus, fallopian tubes, broad ligament

(2) intraperitoneal implantation = exfoliation of tumor cells from ovarian capsule into peritoneal space (often microscopic):
with frequent seeding to:
› posterior cul-de-sac in pouch of Douglas
› infundibulopelvic ligaments
› omentum
› superior aspect of sigmoid
› right paracolic gutter
› termination of small bowel mesentery
› undersurface of right hemidiaphragm
with less frequent seeding to:

FIGO and TNM Staging of Ovarian Cancer (2010)		
FIGO	*TNM*	*based on staging laparotomy*
I	T1	Limited to ovary
IA	T1a	limited to one ovary
IB	T1b	limited to both ovaries
IC	T1c	+ positive peritoneal lavage / ascites
II	T2	Limited to pelvis
IIA	T2a	involvement of uterus / fallopian tubes
IIB	T2b	extension to other pelvic tissues
IIC	T2c	+ positive peritoneal lavage / ascites
III	T3±N1	Limited to abdomen = intraabdominal extension outside pelvis / retroperitoneal or inguinal nodes / extension to small bowel / omentum
IIIA	T3a	microscopic abdominal peritoneal seeding
IIIB	T3b	≤2 cm implants of abdominal peritoneum
IIIC	T3c±N1	>2 cm implants of abdominal peritoneum
IV	M1	Hematogenous disease (liver parenchyma) / spread beyond abdomen / positive Lnn
◊ 50–70–75% of patients have stage III / IV disease at time of diagnosis!		

› Morison pouch
› liver surface
› porta hepatis
› intrahepatic fissure

(3) lymphatic spread
› craniad parallel to gonadal veins in infundibulopelvic ligament terminating at level of renal vessels
› laterally through broad ligament terminating at pelvic side wall: external iliac, obturator, hypogastric chains

Size: short-axis diameter of > 1 cm (in 88% positive for ovarian cancer)
√ hydronephrosis (2nd most common form of tumor-related morbidity after bowel obstruction)
√ thoracic adenopathy: paracardiac lymph nodes > 5 mm in 28% of stage II/III disease; mediastinal lymphadeno-pathy (29% at autopsy)

(4) hematogenous dissemination (% at autopsy):
liver (45–48%), lung (34–39%), adrenal gland (15–21%), pancreas (11–21%), spleen (15–20%), bone (11%), kidney (7–10%), skin (5%), brain (3–6%)
√ malignant pleural effusion (pleural metastases in 28–60%, lung parenchymal metastases in 7%, pericardial metastases in 5%)

Staging laparotomy:
= abdominal hysterectomy + bilateral salpingo-oophorectomy + omentectomy + random peritoneal biopsy + lymph node biopsy

Limitations of imaging:
◊ Microscopic peritoneal disease not detectable!

Benefit of imaging:

◊ Second-look surgery can be avoided if there is evidence for residual / recurrent tumor!

Cave: NO biopsy in the absence of peritoneal disease as it may cause spillage and upstaging of the cancer!

- often "silent" without obvious signs / symptoms
- occasional pelvic-abdominal pain
- constipation, urinary frequency; early satiety; ascites
- paraneoplastic hypercalcemia
- Human epididymal protein 4 (HE4)

Accuracy: 89% sensitive, 92% specific during premenopause

- CA-125 level (= cancer-associated marker = high-molecular-weight glycoprotein) > 35 kU/L:

Accuracy: (a) premenopausal (83% sensitive, 60% specific)
(b) postmenopausal (94% sensitive, 82% specific)

Levels: > 35 (> 65) kU/L in 29–50 (21) % of stage I disease

◊ ↑ CA-125 levels in 80% of ovarian cancers (60% of mucinous + 20% of nonmucinous tumors) and in 40% of patients with advanced intraabdominal nonovarian malignancy!

◊ ↑ CA-125 levels in 30% of benign processes (in 1% of healthy individuals, fibroid, first-trimester pregnancy, menstruation, endometriosis, PID, benign ovarian tumors, liver cirrhosis, pancreatitis)!

US:

◊ Screening finds adnexal cysts in 1–15% of postmenopausal women; only 3% of ovarian cysts < 5 cm are malignant!

@ Morphologic tumor criteria (85–97% sensitive, 56–95% specific, 99% NPV):

√ thick irregular walls and thick septations
(DDx: endometrioma, abscess, peritoneal cyst, cystadenofibroma, mucinous cystadenoma)

√ papillary projections ≥ 3 mm: in 67% [38%] {9%} of borderline [malignant] {benign} neoplasm

√ solid / moderately echogenic loculi

√ postmenopausal ovarian volume > 9 cm^3

@ Doppler tumor criteria (50–100% sensitive, 46–100% specific, 49% PPV; more sensitive + specific in postmenopausal women):

√ presence of color flow (in 93% of malignant + 35% of benign tumors) usually within thick wall, septa, papillary projections, solid inhomogeneous areas

√ low-resistance Doppler waveform ← lack of muscular layer of arterial wall + presence of arteriovenous shunts in neoplasm: RI < 0.40, PI < 1.0 (37–47% PPV)

False positive: physiologic alteration of ovarian blood flow during menstrual cycle, benign tumor, acute inflammatory disease, endometriosis

@ Metastatic disease

√ omental / peritoneal masses ("omental cake")

√ pseudomyxoma peritonei (with tumor rupture)

√ liver metastases

√ ascites

CT (70–90% preoperative staging accuracy):

@ Primary tumor:
- √ lesion diameter > 4 cm
- √ enhancing papillary projections
- √ septa and walls > 3 mm thick
- √ partially solid, partially cystic mass
- √ lobulated solid mass
- √ tumor vessels on contrast-enhanced images

@ Local extension:
- √ localized distortion of uterine contour
- √ irregular interface between tumor and myometrium
- √ loss of tissue plane between tumor and wall of sigmoid colon / bladder
- √ encasement of sigmoid colon
- √ tumor distance from pelvic side wall < 3 mm
- √ iliac vessels surrounded / displaced by tumor

@ Secondary findings:
- √ ascites:
  - √ often lesser sac ascites with displacement of fundus and posterior wall of stomach anteriorly (DDx to benign ascites) + gastrosplenic ligament laterally
  - √ loculated ascites ← adhesions
- √ > 10-mm nodular / plaquelike peritoneal implants:
  - √ indentation of hepatic / splenic surface
  - √ ± calcifications
- √ lymphadenopathy, may be calcified
- √ omental implants:
  - √ small nodules / strands of hyperdense soft tissue → increased attenuation of omental fat / marked omental thickening ("omental cake")
  - √ fat plane obscured between anterior abdominal wall + intestinal wall
- √ mesenteric deposits:
  - √ round / irregular ill-defined masses / stellate lesions of small bowel mesentery
  - √ tethering of small bowel loops
- √ invasion of bowel:
  - √ bowel obstruction (most common form of ovarian-cancer associated morbidity)
  - √ nodular / plaquelike lesions along / projecting from peritoneal surfaces
  - √ bowel wall thickening
- √ pseudomyxoma peritonei

MR:
- ◊ Useful for lesions that are indeterminate by US (with 89% highest accuracy of all modalities)
- √ papillary projections from wall / septum of a cystic lesion
- √ mass with solid + cystic components
- √ necrosis within a solid lesion
- √ multiple > 3 mm thick septations; irregular septum / wall
- √ large size > 6 cm
- √ bilateral adnexal lesions
- √ ascites; peritoneal disease; lymphadenopathy

√ strong early enhancement with high wash-in rate > 9.5 L/s
◊ Note clearly benign features:
√ high SI on T1WI = fat / blood
√ subsequent loss of SI on fat-suppressed T1WI = blood
√ low SI on T2WI = fibrous tissue / hemosiderin
√ lack of enhancement

PET: √ ovarian carcinoma is FDG avid requiring a size of 6–10 mm of spatial resolution
DDx: endometrioma, benign cystic teratoma, inflammatory mass (PID), physiologic change
√ may be useful for staging and recurrence

BE:
√ serosal spiculation / tethering
√ annular constriction / complete obstruction

Rx:
stage I: total abdominal hysterectomy (TAH) + bilateral salpingo-oophorectomy (BSO) ± melphalan / intraperitoneal Phosphorus-32
stage > I: TAH-BSO + surgical cytoreduction (debulking) + 6 cycles of chemotherapy (cyclophosphamide + cisplatin)

Prognosis (without change in past 60 years):
46% overall 5-year survival rate, 10–25% for stage IV, 37% for stage III, 50% for stage II, 80–90% for stage I

DDx: tuboovarian abscess, dermoid cyst, endometrioma

OVARIAN CYST

Definition: any ovarian cyst > 2.5 cm
◊ Fetal ovarian cysts > 4 cm may be at risk of in utero torsion!

Dominant Follicle

Cause: physiologic (estrogen sensitive)
• pelvic pain from
(a) stretching of ovarian capsule
(b) ovulation (Mittelschmerz) triggered by surge in LH
(c) cyst rupture / hemorrhage

Number: 1 or 2 dominant follicles
√ follicular enlargement at a rate of 2 mm per day during first half of menstrual cycle ← under influence of FSH
√ 18–25 mm Graafian follicle at time of ovulation
√ conversion into corpus luteum after ovulation
DDx: nonovulatory follicle (< 10 mm); ovarian cyst
Cx: ovarian torsion

Functional / Retention Cyst

◊ Functional cysts are commonly unilateral!
Cause:
(a) failure of involution of follicle / corpus luteum with changes in the menstrual cycle

(b) excessive hormonal stimulation of follicles preventing normal follicular regression (eg, theca-lutein cysts)

Prognosis: spontaneous regression is common but unpredictable; typically resolve within 2 menstrual cycles (less likely if cyst > 5 cm)

Cx: torsion

Rx: (1) Hormonal manipulation
(2) Surgery → absolutely indicated if cyst enlarges
(3) Percutaneous aspiration (if chance of malignancy is nil as in infants)

DDx: cystic teratoma, simple benign epithelial neoplasm, endometrioma in resolution, paraovarian cyst, quiescent hydrosalpinx

Follicular Cyst (from preovulatory follicle)

Cause:
(a) unruptured Graafian follicle from failure to ovulate
(b) Graafian follicle with failure to regress / involute
(c) ruptured Graafian follicle that sealed immediately (after continued stimulation)

- pain ← rapid cystic enlargement / rupture / hemorrhage
- may elaborate estrogen (extremely common)
- sign of anovulatory cycle

Predisposed: patients during puberty + menopause; status post salpingectomy

Size: usually 3–8 cm; occasionally up to 10 cm (if cyst remains hormonally sensitive); up to 25 cm (under influence of placental gonadotropin in pregnancy)

√ thin-walled unilocular cyst
√ located within ovary → compressing adjacent ovarian follicle-containing parenchyma
√ usually multiple / may be single

US:
√ contains anechoic fluid → posterior through-transmission
√ ± minimal mobile low-level internal echoes

CT:
√ well-defined round simple fluid collection
√ thin nonenhancing wall
√ internal attenuation of < 15 HU

Prognosis: usually resolves after 1–2 menstrual cycles (follow-up best performed on days 5–10 of subsequent menstrual cycle)

DDx: cystadenoma (larger, persistent, in older woman)

Corpus Luteum Cyst (from postovulatory follicle)

= hemorrhage into mature corpus luteum

Physiology: grows under the influence of LH; granulosa cells undergo marked neoangiogenesis → frequently causing hemorrhage

Types:

1. **Corpus luteum of menstruation**
   = formed after rupture of follicle + increasing in size until 22nd day of menstrual cycle

   Size: usually > 12–17 mm

• elaborates progesterone → release into maternal circulation → delayed menstruation / persistent bleeding

Prognosis: resolves within 1–2 menstrual cycles

2. **Corpus luteum of pregnancy**

= maintained by circulating β-hCG during pregnancy with similar effect as LH

• may be temporarily painful

Size: usually 30–40 mm, may grow up to 15 cm in diameter

◊ Excessively large cyst with thin wall suggests poor function ← low progesterone level

√ reaches maximum size after 8–10 weeks

√ occurs on same side as ectopic in 85%

Prognosis:

normally resolved by 12–16 weeks (as placenta becomes dominant source of progesterone); occasionally persists past 1st trimester with failure to involute

US:

√ increased peripheral vascularity with high diastolic flow component

√ irregular thick-walled usually unilateral cyst

√ echogenic (= organized clot) / isoechoic with low-level internal echoes (= hemorrhage) / sonolucent (= serum)

√ posterior through-transmission

CT:

√ unilocular cyst with thick crenulated enhancing wall

√ intracystic blood products with high attenuation

√ fluid surrounding adnexa (after rupture)

Cx:

(1) Enlarging hemorrhagic corpus luteum with

› severe pelvic adhesions preventing ovulation of luteinized follicles

› NSAIDs which may cause luteinized unruptured follicle syndrome

› excessive anticoagulation

› endometriosis

(2) Rupture with intraperitoneal life-threatening hemorrhage at ovulation

DDx: endometrioma, ovarian tumor, organized clot in any enclosed space

Corpus Albicans Cyst

= from corpus luteum following regression of luteal tissue; no hormone production

Theca Lutein Cyst

= multiple bilateral corpus luteum cysts ← ovarian hyperstimulation ← abnormally high levels of β-hCG

Cause: (a) multiple gestations (twins)

(b) gestational trophoblastic disease (in 40%)

(c) fetal hydrops

(d) pharmacologic stimulation of ovaries with β-hCG

(e) normal pregnancy (uncommon)

• elaborates estrogen
√ multiloculated cysts, often bilateral
√ ovaries several cm in size
√ involution within a few months after source of gonadotropin removed

Surface Epithelial Inclusion Cyst

common in postmenopausal women
Age: any; in newborns (influence of maternal estrogen)
Prevalence: 3–5–17% in postmenopausal women
• usually asymptomatic
• acute unilateral pelvic pain ← hemorrhage / pressure
√ up to 8–10 cm in diameter

Imaging Classification of Ovarian Cysts

Simple Ovarian Cyst

Location: uni- > bilateral; intra-abdominal > intrapelvic
Size: < 20 mm in diameter = maturing / physiologic follicle

√ round smooth cyst + thin sharply defined wall of < 3 mm
√ unilocular = NO internal septations / mural nodules

N.B.: may occasionally contain single avascular septation

√ contents anechoic
√ posterior acoustic enhancement

√ "**daughter cyst**" = small round anechoic structure within a cyst is PATHOGNOMONIC for an ovarian cyst (82%)

√ Doppler flow in cyst wall (detected in 19–61%) with a pulsatility index of > 1.0 / RI > 0.4 (unreliable!)
√ isointense to urine on T1WI + T2WI
DDx: serous cystadenoma

Management of Premenopausal Asymptomatic Adnexal Cyst
(Society of Radiologists in Ultrasound, 2010)

Cyst Size [cm]	*Cyst Content*	*Recommendation*
≤ 3	simple / hemorrhagic	no follow-up; may be omitted from report
3 – 5	simple / hemorrhagic	no follow-up; mention in report
> 5 and ≤ 7	simple	sonographic follow-up annually
	hemorrhagic	follow-up in 6–12 weeks to ensure resolution
> 7	simple	MR imaging / surgery

Postmenopausal (> 5 years) Asymptomatic Adnexal Cyst (Society of Radiologists in Ultrasound, 2010)		
Cyst Size [cm]	*Cyst Content*	*Recommendation*
≤ 1	simple	no follow-up; may be omitted from report
> 1 and ≤ 7	simple	sonographic follow-up annually
> 7	simple	MR imaging / CA-125 / surgery

Risk of Malignancy Index (RMI)	
Score	*Description*
U-score	Number of malignant features at **ultrasound**: multilocular cyst, solid component, bilateral, metastases, ascites
0	no features of malignancy
1	one feature of malignancy
3	≥ 2 features of malignancy
M score	Patient's **menopausal** status: no menstruation > 1 year / > 50 years old with hysterectomy
1	premenopausal
3	postmenopausal
RMI	**RMI** = U x M x CA-125 level
> 200	high risk (84–85% sensitive, 77–97% specific); staging CT + referral to gynecologic oncology
25–200	intermediate risk; MRI for further characterization
< 25	low risk; clinical reevaluation

Complex / Complicated Ovarian Cyst

= does not satisfy criteria for hemorrhagic cyst / endometrioma

Cause: ovarian torsion

√ thick-walled cyst of heterogeneous echogenicity
√ multiple septations, mobile internal echoes, solid appearance, fluid-fluid level

√ internal septations / mural nodules / internal echoes
√ ± polyhydramnios, ascites ← transudate / cyst rupture

Cx: obstruction of bowel / kidneys

Hemorrhagic Ovarian Cyst

= functional cyst (follicular cyst / corpus luteum) that developed internal hemorrhage → resolves partially / completely over time

◊ Common cause of RLQ pain ← rupture into peritoneal cavity

Path: functional cyst + corpus luteum cyst

US:

√ hematocrit level in acute bleed
√ "ground-glass" pattern = diffuse low-level echoes
√ whirled / spongy pattern of mixed echogenicity
√ "fishnet weave" pattern = fine interdigitating septations / lacelike reticular pattern for

first 24 hours (SPECIFIC)
- √ gelatinous echogenic mass (= retracting clot) jiggling during transducer ballottement with triangular / curvilinear echogenic regions at cyst wall
- √ fluid-debris level
- √ NO color Doppler signals inside cyst
- √ posterior through-transmission

CT:
- √ unilocular cyst with an attenuation of 25–100 HU
- √ fluid-fluid level + hemoperitoneum (after cyst rupture)

MR:
- √ SI varies depending on age of hemorrhage:
  - √ intermediate SI on T1WI + low SI on T2WI ← deoxyhemoglobin of subacute hemorrhage
  - √ increased SI on T1WI + decreased SI on T2WI ← intracellular methemoglobin
- √ hematocrit effect of layering blood products
- √ intermediate to high intensity on fat-suppressed T1WI
- √ hyperintense / intermediate intensity with distinct central area of hypointensity on T2WI
- √ heterogeneous mild signal loss with NO shading on T2WI
- √ pelvic peritoneal fluid of elevated T1 signal ← hemorrhage

DDx: endometrioma ("light bulb" T1-hyperintensity, T2 shading, stable over time)

Cx: rupture into intraperitoneal space

Ovarian Cyst concerning for Neoplasm
- √ irregular solid / multilocular cystic mass
- √ solid component / papillary projections on cyst wall
- √ absence of thin septations
- √ presence of thick septations > 3 mm
- √ central vascularity with high flow in echogenic component / septation / focal wall thickening
- √ low resistance flow (RI < 0.5, PI ≤ 1.0)
- √ ascites
- √ omental / peritoneal nodules

Management of Asymptomatic Adnexal Cyst

A. NEONATAL
- √ change in position between exams suggests pedunculated lesion → potential for torsion
- √ fluid-debris level / low-level echoes / retracting clot suggest torsion

B. PREMENOPAUSAL

Risk of malignancy: < 1% for simple cyst < 5 cm, 0.8% for lesion > 7.5 cm
- ◊ Adnexal cysts up to 10 cm are highly likely benign (in 84% serous cystadenoma)!
- ◊ Hemorrhage WITHOUT a vascular soft-tissue component is a reliable indicator of a benign lesions

N.B.: All follow-up scans should take place in the immediate postmenstrual period (= early proliferative phase), when follicular cysts should not be present!

C. POSTMENOPAUSAL (< 5 years after LMP)
= ovulation + hemorrhagic cysts may occasionally occur
Risk of malignancy: 1.6% for simple cyst < 5 cm
Rx: follow-up in 6–12 weeks to ensure resolution

C. POSTMENOPAUSAL (> 5 years after LMP)
Risk of malignancy: 1.0–9.6%
◊ A hemorrhagic cyst in an anovulatory woman is likely neoplastic! 18% of complex cysts are malignant!

OVARIAN FIBROMA

Frequency: 3–4% of all ovarian tumors; bilateral in < 10%
◊ Most common of the sex cord-stromal tumors!
Age: 4th– 6th decade
Path: solid firm white mass
Histo: pure mesenchymal tumor consisting of intersecting whorled bundles of spindle-shaped fibroblasts + collagen; varying degrees of edema often separate cells

- usually asymptomatic (pure fibromas are not estrogenic, admixture of theca cells causes estrogenic effect)
- Meigs syndrome (in only 1%)
- elevated carcinogenic antigen levels

Associated with: basal cell nevus (Gorlin) syndrome in commonly bilateral calcified fibromas
◊ Fibromas occur in 17% of patients with basal cell nevus syndrome
Location: unilateral (common); bilateral in 4–8%
√ ± cystic degeneration and edema in larger lesions
√ calcification + hemorrhage (< 10%)
US:
√ solid hypoechoic mass with marked sound attenuation
√ occasionally hyperechoic / with increased through-transmission
MR:
√ well-circumscribed mass with nonspecific hypo- to isointensity on T1WI
√ low-SI mass on T2WI less than or equal to myometrium ← abundant collagen content (FAIRLY DIAGNOSTIC)
√ scattered high-signal-intensity areas on T2WI (= edema / cystic degeneration)
√ delayed mild enhancement with gadolinium
CT:
√ well-defined solid homogeneous / slightly heterogeneous mildly hypoattenuating mass
√ poor delayed contrast enhancement
Rx: may be managed conservatively; rarely recurs after excision
DDx: fibrothecoma; pedunculated uterine leiomyoma; Brenner tumor; adenofibroma; malignant ovarian neoplasm

OVARIAN FIBROMATOSIS

= rare benign condition causing tumorlike enlargement of ovaries related to massive ovarian edema

Cause: ?

Average age: 25 years

- pelvic pain, menstrual abnormalities, occasional virilization

Histo: proliferation of collagen-producing spindle cells surrounding normal ovarian structures with collagenous thickening of superficial cortex; partial preservation of normal ovarian structures within the fibrous mass, which allows differentiation of ovarian fibromatosis from similar conditions.

√ nonspecific enlargement of ovaries

√ at least partial preservation of ovarian anatomy

US:

√ enlarged heterogeneously echogenic ovary with areas of acoustic shadowing

√ low flow at Doppler imaging

MR:

√ hypointense areas on T1WI + T2WI

√ "**black garland**" on T2WI ← fibrous tissue encasing peripheral aspect of ovary

DDx: (1) Pelvic aggressive fibromatosis (desmoid) involving ovary
(2) Brenner tumor (calcifications)
(3) Ovarian sex-cord stromal tumors: fibroma, fibrothecoma
(4) Krukenberg tumor (bilateral, avid enhancement)

OVARIAN HYPERSTIMULATION SYNDROME

= potentially life-threatening iatrogenic complication of ovulation induction / ovarian stimulation

Incidence: (a) Clomid®: mild in 13%, moderate in 8%
(b) Pergonal®: mild in 20–33%, moderate in 3–6%, severe in 0.1–2%

Etiology:

(1) Induced by hCG therapy with human menopausal gonado-tropin (Pergonal®), occasionally with clomiphene (Clomid®)
(2) Hydatidiform mole
(3) Chorioepithelioma
(4) Multiple pregnancies

Path: enlarged ovaries with multiple follicular + theca lutein cysts, edematous stroma

Pathophysiology:

secretion of ovarian vasoactive angiogenic substances → increased capillary permeability → fluid shift out of intravascular space → ascites → hemoconcentration

- abdominal pain (100%) + distension (100%)
- nausea (100%), vomiting (36%), acute abdomen (17%)
- dyspnea (16%), thrombophlebitis (11%), fainting (11%)
- marked hemoconcentration, blurred vision (5%)
- anasarca (5%), hydrothorax, enhanced fertility

√ "**spoke-wheel**" appearance of ovaries = bilateral symmetrically enlarged ovaries > 5 cm in longest dimension containing large geometrically packed follicles:

√ cysts separated by thin septa

Modified Golan Classification of Hyperstimulation Syndrome			
Category	*Grade*	*Ovarian size [cm]*	*Signs and symptoms*
Mild (65%)	I	< 6	Abdominal distension
	II		+ nausea, vomiting, diarrhea
Moderate	III	6–12	+ ascites at US; weight gain
Severe	IV	> 12	Clinical ascites / pleural effusion
	V		+ hypovolemia, hemoconcentration, hypercoagulability, renal failure, hepatic dysfunction, thrombo-embolism, shock

√ cysts usually anechoic, unless complicated by hemorrhage
√ resolution on follow-up

√ ovarian cyst > 10 cm (100%): usually disappears after 20–40 days; may persist for 12–16 weeks during pregnancy
√ ascites (33%)
√ pleural effusion (5%)
√ hydroureter (11%)

MR:
√ cysts with increased SI on T1WI (common) ← hemorrhage
√ ↑ SI of ovarian stroma on T2WI ← edema

Cx of volume depletion:
(1) Hypovolemia + hemoconcentration
(2) Oliguria, electrolyte imbalance, azotemia
(3) Death from intraabdominal hemorrhage / thromboembolic event

Other Cx:
(1) Ovarian torsion (7%)
(2) Ectopic pregnancy (in 2.1–8.6%)

OVARIAN MALIGNANT GERM CELL TUMOR

= OMGCT = heterogeneous group of tumors sharing the primitive germ cell of the embryonic gonad as a common origin

Incidence: 2.6% of all malignant ovarian neoplasms
◊ 60–75% of ovarian cancers seen in 1st–2nd decade

Age-adjusted incidence: 0.34–0.41÷100,000 women-years

Types and Incidence of each OMGCT:
1. Dysgerminoma 37%
2. Immature teratoma 36%
3. Yolk sac tumor 15%
4. Choriocarcinoma 3%
5. Malignant mixed germ cell tumor < 1%
6. Embryonal carcinoma < 1%
7. Malignant degeneration of mature cystic teratoma 3%

Mean age: highest incidence at age 14 (range, 15–19) years
- abdominal distension / pain (in 87%) of 2–4 weeks duration
- pelvic pain ← torsion / hemorrhage / tumor rupture
- vaginal bleeding, fever, large mass at presentation (in 85%)
- elevated a-fetoprotein ← component of yolk sac tumor: 60% in immature teratoma; 100% in endodermal sinus tumor:
- elevated β-hCG ← component of choriocarcinoma: 30% of endodermal sinus tumors

⇑ α-fetoprotein / β-hCG are virtually diagnostic of OMGCTs

Spread: most commonly lymphatic
Average size: 15 cm in diameter
√ unilateral, rarely bilateral
√ calcifications (40%)
√ homogeneously solid (3%), predominantly solid (85%), predominantly cystic (12%)

Dysgerminoma (37%)
= malignant germ cell tumor of ovary homologous to testicular seminoma
◊ Second most common ovarian germ cell tumor
◊ Most common ovarian malignant germ cell tumor (OMGCT)
Frequency: 1–2% of all primary ovarian neoplasms; 35% of all ovarian malignant germ cell tumors
Age-adjusted incidence: 0.109÷100,000 women-years
Path: solid well encapsulated lobulated tumor ± coagulative necrosis / hemorrhage
Histo: uniform population of round cells with clear to eosinophilic cytoplasm + central large round / flattened nucleus resembling primordial germ cells in well-defined nests, separated by fibrous strands, infiltrated by T lymphocytes; numerous mitoses
Peak age: 2nd–3rd decade (range, 7 months – 70 years)
- pain, bloating, menstrual disorder
- often nonspecific elevation of serum lactic dehydrogenase + alkaline phosphatase
- typically NO elevation of a-fetoprotein / b-hCG

Cave: elevation of a-fetoprotein / b-hCG in 5% ← presence of multinucleated syncytiotrophoblastic giant cells

Location: usually unilateral; bilateral in 7–10%
Mean diameter: 15 cm
√ multilobulated well-defined solid mass divided by fibrovascular enhancing septa
√ ± areas of hemorrhage and necrosis
√ speckled pattern of calcifications (rare)
MR:
√ mass of low signal intensity relative to muscle on T1WI
√ isointense / slightly hyperintense mass on T2WI
√ hypo- / isointense septa on T2WI with contrast enhancement on T1WI
US:
√ heterogeneous hyperechoic solid mass
√ prominent arterial color Doppler flow within septa
Rx: highly radiosensitive

DDx: fibrothecoma (predominantly low SI on T2WI), Brenner tumor (extensive low SI on T2WI), granulosa cell tumor (associated with uterine enlargement, most common estrogenic ovarian tumor), epithelial ovarian carcinoma, metastasis

Embryonal Carcinoma of Ovary (< 1%)

Laterality: unilateral

Path: predominantly solid mass with cystic spaces containing mucoid material, smooth outer surface, extensive areas of hemorrhage + necrosis

Histo: solid sheets + nests of large primitive cells in pseudo- glandular pattern + occasional papillae; large crowded pleomorphic vesicular nuclei with prominent nucleoli

Average size: 17 cm

Immature Teratoma of Ovary (36%)

= EMBRYONAL TERATOMA = MALIGNANT TERATOMA

= SOLID TERATOMA

Frequency: 1.3% of all ovarian malignancies; 36% (= 2nd most common) of all malignant germ cell tumors

Path: predominantly solid encapsulated mass ± small cysts; frequently with areas of necrosis + hemorrhage; ± fat + hair + sebaceous material

Histo: immature embryonic tissue derived from the 3 germ cell layers; grades 0–3 reflect amount of immature neuroectodermal tissue

May be associated with: gliomatosis peritonei = multiple peritoneal implants of mature glial tissue; dermoid cyst in up to 26%

Peak age: 15–19 years

• ↑ AFP levels (50%); no elevation of serum hCG levels

Laterality: dermoid cyst in contralateral ovary in 10%

Mean tumor size: 12–25 cm in diameter

√ predominantly solid tumor with numerous cysts of varying size + intratumoral fat

√ scattered small calcifications ← invariable association with mature teratoma

US:

√ heterogeneous solid mass + scattered small calcifications

√ areas of increased echogenicity = larger fat components

CT / MR:

√ predominantly solid mass + fatty elements

√ numerous cysts of variable sizes

√ coarse irregular calcifications

MR:

√ wide variety of signal intensities on T2WI

√ ± fatty fluid within cystic compartments

Prognosis: responsible for 30% of deaths from ovarian cancer in women < 20 years

Growing Teratoma Syndrome

= enlarging teratoma of mature elements arising during / after chemotherapy for treatment of a nonseminomatous germ cell tumor in male / female patients with normal serum α-fetoprotein and b-hCG levels

Mechanism: (a) ? chemotherapeutic retroconversion = induction of somatic maturation in malignant cells by chemotherapy
(b) selective destruction of immature elements by chemotherapy, which leaves behind resistant mature elements

Malignant Mixed Germ Cell Tumor (< 1%)

= composed of > 1 germ cell element (mainly dysgerminoma, teratoma, and yolk sac tumor)
√ solid mass + areas of cystic change ← hemorrhage / necrosis / cystic lesion with solid components

Nongestational Choriocarcinoma (3%)

Frequency: with 2.1–3.4% among rarest of all OMGCTs
Histo: plexiform arrangement of syncytiotrophoblast cells with mononucleated (mostly cytotrophoblast) cells around foci of hemorrhage
US:
√ well-defined adnexal mass of mixed echogenicity
√ NO uterine / ectopic pregnancy
CT:
√ enhancing highly vascular solid mass
MR:
√ abnormal large signal voids on T2WI ← vascular structures + small cystic cavities
√ high-signal-intensity foci in solid portions on T1WI ← hemorrhage
√ substantial uptake of contrast material in solid portions ← highly vascularized tumor
DDx: gestational choriocarcinoma (concomitant / proximate gestation, no other germ cell tumor component)

Polyembryoma

= usually component of mixed OMGCT (immature teratoma + yolk sac tumor), extremely rare
Histo: small embryo-like bodies with central "germ disks" composed of embryonal carcinoma epithelia and 2 cavities (dorsal cavity resembling amniotic cavity + ventral cavity resembling yolk sac cavity); embryoid bodies lie in an edematous to myxoid stroma with prominent blood vessels
Mean age: 24.5 (range, 3–44) years
• ± elevation of a-fetoprotein + b-hCG
√ large unilateral mass

Yolk Sac Tumor of Ovary (15%)

= ENDODERMAL SINUS TUMOR OF OVARY
Frequency: 1% of all ovarian malignancies; 15% (= 3rd most common) of all malignant germ cell tumor
Path: large encapsulated mass with admixed solid + cystic components ← up to 2-cm large cysts +hemorrhage + necrosis; capsular tears in 27% ← rapid growth
Histo: resembles endodermal sinuses of primitive yolk sac
(a) papillary pattern (most common): contains glomerular structures with central vessel + peripheral sleeve of embryonic epithelial cells (= Schiller-Duval bodies)

(b) others: solid, reticular, endodermal sinus, alveolar -glandular, polyvesicular vitelline, myxomatous, microcystic, macrocystic papillary, hepatoid
› periodic acid-Schiff reaction
› α-fetoprotein–positive hyaline globules

Age: 2nd–3rd decade; rare in women > 40 years

May be associated with: teratoma, dermoid cyst, chorioca.

- frequently abdominal enlargement + pain ← rapid growth
- elevated serum AFP (common)

Laterality: bilateral in < 5%; contralateral ovary with dermoid cyst in 10%

Mean size: 15 cm in diameter

√ unilateral smoothly contoured enhancing mixed solid + cystic mass

√ "**bright dot**" sign = enhancing foci in wall / solid component of tumor (common) ← dilated vessels

√ cystic areas ← epithelial-lined cysts / cysts of coexisting mature teratoma / hemorrhage / necrosis

√ capsular tears

US:

√ predominantly heterogeneous echogenic solid tumor

√ cystic spaces divided by septa

MR:

√ foci of high signal intensity on T1WI ← hemorrhage

Rx: surgery + combination chemotherapy

Prognosis: poor

OVARIAN VEIN THROMBOSIS

Etiology:

(1) Bacterial seeding from puerperal endometritis with secondary thrombosis (pregnancy + puerperium are hypercoagulable states) = **puerperal ovarian vein thrombophlebitis**
(2) Pelvic inflammatory disease
(3) Gynecologic surgery
(4) Malignant tumors
(5) Chemotherapy

Prevalence: 1÷600–1÷2,000 deliveries

- presents on 2nd / 3rd postpartum day
- lower abdominal / flank pain (> 90%)
- palpable ropelike tender abdominal mass (50%)
- fever + chills if diagnosis delayed

Location: right [left] {both} ovarian veins in 80% [6%] {14%}

CT:

√ tubular structure in location of ovarian vein with low-density center + peripheral enhancement

Cx: IVC thrombosis; pulmonary embolism (25%); septicemia; metastatic abscess formation
Mortality: 5%

Rx: IV antibiotics + heparin; ligation of involved vessel at most proximal point of thrombosis

after failure to improve after 3–5 days

DDx: appendicitis, broad-ligament phlegmon / hematoma, torsion of ovarian cyst, urolithiasis, pyelonephritis, degenerated pedunculated leiomyoma, pelvic cellulitis, pelvic / abdominal abscess

PARAOVARIAN CYST

= vestigial remnant of wolffian duct in mesovarium

Frequency: 10–20% of all adnexal masses

Mean age: 3rd–4th decade

Embryology: wolffian body (= mesonephros) consists of

(a) mesonephric duct (= wolffian duct)
→ degenerates in female into vestigial structures of epithelial-lined cysts (= canals / ducts of Gartner)
Location: at lateral edge of uterus and vagina extending from broad ligament to vestibule of vagina

(b) mesonephric tubules
→ in female degenerate into vestigial structures of
1. Epoöphoron (at lateral part of fallopian tube)
2. Paroöphoron (at medial part of fallopian tube)
Location: between the tube and hilum of the ovary within the 2 peritoneal layers of broad ligament

Size: mean diameter of 8 cm → up to 18 cm

- usually incidental
- symptomatic due to large size (> 5 cm) / torsion

1. **Gartner duct cyst**:
inclusion cyst lateral to vagina + uterine wall
2. **Paroöphoron**: [*oion*, Greek = egg + *pherein*, Greek = bearing]
medial location between tube + hilum of ovary
3. **Epoöphoron**:
lateral location between tube + hilum of ovary
4. **Hydatid** Cyst **of Morgagni** (= appendices vesiculosae = **fimbrial cyst**): most lateral + outer end of Gartner duct within longest fimbria of fallopian tube
√ ≥ 1 vesicle(s) attached to fringes of tube + filled with clear serous fluid

√ thin-walled unilocular cyst separate from ovary WITHOUT change over time

√ may indent ovary mimicking exophytic ovarian cyst
N.B.: separable by pressure exerted by transvaginal transducer

√ may arise out of pelvis (if pedunculated + mobile)

√ ± low-level internal echoes ← hemorrhage

√ occasionally multiple; rarely bilateral

Cx: torsion (2–16%), hemorrhage, rupture, infection, neoplastic transformation (3%)

DDx: ovarian cyst (functional, cystic teratoma, benign epithelial neoplasm), peritoneal inclusion cyst, hydrosalpinx

PARAOVARIAN CYSTADENOMA

May be associated with: Von Hippel-Lindau disease
Location: typically unilateral
√ simple cyst
√ one / more small nodules along a smooth inner wall (86%)
√ ± septations
Cx: malignant degeneration in 2–3%
DDx: (1) Hydrosalpinx (tubular shape, folds / short echogenic lines protruding into lumen)
(2) Peritoneal inclusion cyst (surrounding much of the ovary, history of surgery / PID)
(3) Cystic neoplasm of fallopian tube (more solid components)
(4) Paraovarian cyst with blood clot (resolution of clot on follow-up sonogram)
(5) Exophytic complex ovarian mass

PELVIC CONGESTION SYNDROME

= chronic (> 6 months) noncyclical pelvic pain associated with pelvic venous distension + valvular ovarian vein insufficiency
Prevalence: ovarian varices in 10% in general population
◊ Closely related to frequency of ovarian varices; 60% may develop pelvic congestion syndrome
Pathophysiology:
venous obstruction ← retroaortic left renal vein, compression of left renal vein by SMA = nutcracker phenomenon; right common iliac vein compression; valvular incompetence; portal hypertension; acquired vena cava syndrome
Risk factors: hereditary factors, hormonal influence, pelvic surgery, retroverted uterus, history of varicose veins, multiple pregnancies
• uni- / bilateral chronic dull deep pelvic ache, pressure, heaviness often associated with movement / posture / activities that increase abdominal pressure
• dyspareunia (71%), dysmenorrhea (66%), postcoital ache (65%)
• rectal discomfort, urinary frequency
• varicose veins in vulva, buttocks, legs
• ovarian point tenderness (94% sensitive, 77% specific)
US:
√ multiple tortuous pelvic veins > 4–6 mm in diameter around uterus + ovaries
√ slow (≤ 3 cm/s) / reversed (caudal) flow
√ dilated arcuate vein in myometrium
√ polycystic changes of ovaries
CT / MR:
√ dilated tortuous enhancing tubular structures
Location: around uterus, ovary, broad ligament, pelvic sidewall, paravaginal plexus
Angio (standard nearly replaced by US, CT, MRI):
Technique: selective catheterization of ovarian veins, transuterine injection of contrast material, direct injection into vulval varices
√ ovarian vein diameter > 10 mm
√ retrograde flow in ovarian / pelvic veins
√ tortuous collateral pelvic venous pathways

√ delayed / stagnant clearance of injected contrast from veins

Rx: hormone analogues (medroxyprogestrone, GnRH analog goserelin) + analgesics; laparoscopic transperitoneal ligation of ovarian veins; hysterectomy ± salpingo-oophorectomy; percutaneous coil embolization of the gonadal vein (70–85% successful)

DDx: asymptomatic pelvic varicosities

Ovarian Vein Syndrome

= obstructive uropathy ← ureteral compression at pelvic brim by dilated / aberrant / thrombosed ovarian vein

Anatomy: ovarian vein crosses ureter obliquely in retroperitoneum at L3

Site: R÷L = 95÷5

Time of onset: during (2nd–3rd trimester) / after pregnancy

IVP:

√ oblique extrinsic impression on ureter:

√ proximal hydroureteronephrosis + normal pelvic ureter

√ medial deviation of obstructed segment (with retrocaval ureter) = characteristic reverse J configuration

CT / coronal MR urography:

√ concurrent evaluation of cause of compression, implicated vessel + proximal dilatation

Cx: spontaneous rupture with life-threatening hemorrhage (rare)

PELVIC INFLAMMATORY DISEASE (PID)

= acute clinical syndrome usually associated with ascending spread of microorganisms ("canalicular spread") from vagina / cervix to uterus, fallopian tubes, and adjacent pelvic structures; not related to surgery / pregnancy

Frequency: 24% of visits to emergency department for gynecologic pain; 10% of women in reproductive age (17% in Blacks); 106,000 outpatient visits and 60,000 hospitalizations annually in USA (2015)

Risk factors: early age at sexual debut, multiple sexual partners, high coital frequency, history of sexually transmitted disease, douching

Predisposed: formerly married > married > never married; intrauterine contraceptive device (1.5–4-fold increase in risk)

Etiology: (a) bilateral: venereal disease, IUD, S/P abortion

(b) unilateral (= nongynecologic): rupture of appendix, diverticulum, S/P pelvic surgery

Organism:

(1) Chlamydia trachomatis + Neisseria gonorrhoeae (> 50% with high prevalence of coinfection) → damage protective barrier of endocervical canal → spread to tubes (30–50%) producing fibrosis + adhesions

(2) Aerobes: Streptococcus, Escherichia coli, H. influenzae

(3) Anaerobes: Bacteroides, Peptostreptococcus, Peptococcus

(4) Mycobacterium tuberculosis (hematogenous)

(5) Actinomycosis in IUD users

= chronic suppurative infection characterized by multiple abscesses, abundant granulation

tissue, fibrosis

(6) Herpesvirus hominis type 2, Mycoplasma

◊ Polymicrobial infection in 30–40%

May be associated with: Fitz-Hugh-Curtis syndrome (*see below*)

- usually bilateral dull aching lower abdominal pain 7–10 days after menstruation ← peritoneal irritation
- adnexal + cervical motion tenderness:
  - "chandelier" sign = patient reaching for the chandelier ← intense pain during pelvic examination
- purulent vaginal discharge / uterine bleeding
- dysuria, dyspareunia, nausea, vomiting
- fever, leukocytosis, ↑ ESR; ↑ serum C-reactive protein

US:

√ No findings
√ thickened tubular adnexal structures ± central fluid
√ increased adnexal volume
√ periadnexal inflammatory hyperemia
√ loss of normal tissue planes + ill-defined uterus:
  √ echogenic periovarian fat
√ ± free fluid

CT:

√ nonspecific stranding of parapelvic fat
√ thickening of uterosacral ligaments

MR:

√ ill-defined hyperintense parametrial area on fat-suppressed T2WI + intense enhancement on contrast-enhanced fat-suppressed MR (= extent of inflammation)

Dx: clinically, laparoscopically

◊ Imaging employed only to differentiate between medical + surgical condition and if
(a) symptoms nonspecific
(b) expected response to treatment absent
(c) complication suspected (eg, abscess)
(d) percutaneous treatment a possible option

Cx: (1) Infertility: 8% [20%] {40%} after single [2] {≥ 3} episodes of PID ← tubal occlusion (in 25%)

(2) Tubo-ovarian abscess

(3) Ectopic pregnancy (6 x as frequent)

(4) Chronic pelvic pain ← pelvic adhesions

Sexually Transmitted Diseases (STD)			
Chlamydia	33%	Human papilloma virus (warts)	6.0%
Trichomoniasis	25%	Genital herpes simplex	4.0%
Nonspecific urethritis	10%	Hepatitis B virus	1.2%
Gonorrhea	9%	Syphilis	1.0%
Mucopurulent cervicitis	8%	HIV	0.3%

Cervicitis

= generic term describing cervical inflammation

Cause: (a) noninfectious: trauma, pelvic irradiation, chemical irritation, malignancy
(b) infectious: Trichomonas vaginalis, Candida albicans, herpes simplex virus (esp. type 2), Neisseria gonorrhoeae, Chlamydia trachomatis

- purulent / mucopurulent cervical + vaginal discharge
- pelvic pressure / discomfort

US:
√ diffusely heterogeneous echotexture of cervical mucosa and stroma
√ nonspecific markedly increased vascularity without mass

Endometritis

√ endometrial prominence
√ small amount of fluid within uterine lumen
√ gas reflection within uterine cavity (most specific)
√ pain over uterus

Postpartum Endometritis

Frequency: 2–3% of vaginal deliveries; in up to 85% of cesarean sections
Associated with: prolonged labor, premature rupture of membranes, retained clots, retained products of conception

- fever (most common cause of postpartum fever)

√ normal ultrasound
√ thickened heterogeneous endometrium
√ intracavitary fluid
√ intrauterine air

Fitz-Hugh–Curtis Syndrome

= GONORRHEAL PERIHEPATITIS

[Thomas Fitz-Hugh, Jr (1894–1963), American physician; Arthur Hale Curtis (1881–1955) American gynecologist]

= inflammation of peritoneal capsule of liver ← peritoneal spread of infection via right paracolic gutter

Frequency: up to 15% in women with PID

- right upper quadrant pain ← ascending pelvic infection

Path: inflammation of liver capsule / diaphragm

Organism: chlamydia÷gonorrhea = 5÷1
US:
√ perihepatic and pericholecystic ascites ± loculations
Location: anterior to liver (original description), hepatorenal fossa (= Morison space), gallbladder (mimicking acute cholecystitis)
√ ± peritoneal septations (= "violin string" adhesions extending from anterior surface of liver to peritoneum)
CT:
√ thickening + intense enhancement of anterior liver capsule and gallbladder wall ± loculations
√ periportal edema
√ ± transient subcapsular + periportal hepatic perfusion abnormalities

Salpingitis

• often beginning during / immediately after menstruation ← mucus barrier of cervix less effective
MR:
√ thickened wall of dilated fallopian tube + tubal contents of low signal intensity on T2WI
√ debris / hemorrhage in fluid component most conspicuously hypointense to urine on heavily T2WI
Cx: tubo-ovaritis = salpingo-oophoritis = tubal fimbriae adhere to ovary

Salpingitis Isthmica Nodosa
Etiology: unknown; commonly associated with pelvic inflammatory disease, infertility, ectopic pregnancy
Location: uni- / bilateral
• nodular thickening of isthmic portion of tube
√ irregularity + multiple 2–3 mm diverticula / obstruction of isthmic portion of fallopian tube on HSG

Fallopian Tube Cyst

Cause: pelvic inflammatory disease, endometriosis, adhesions, microtubal surgery, total abdominal hysterectomy without salpingo-oophorectomy, ectopic pregnancy, tumor (rare)
Prevalence: in 8% of women with PID / endometriosis
Location: between uterus + adnexa; often bilateral
Site of obstruction: ampullary / infundibular portion of tube
√ undulating / folded tubular structure in extraovarian location filled with sterile fluid / debris / pus
√ "**kissing ovary**" sign = adhesions pull ovaries and tubes toward the midline
√ serpentine C- or S-shaped complex cystic solid adnexal mass ← encasement of ovary by fallopian tube
◊ Find ipsilateral ovary!
Cx: tubal torsion
DDx: dilated uterine / ovarian vein, TOA, cystic ovarian neoplasm, endometrioma,

developing follicle, fluid-filled small bowel (peristalsis)

Hydrosalpinx = Chronic PID

= accumulation of continued secretion of tubal epithelium (sterile fluid) into lumen of a fallopian tube obstructed at two sites

◊ A simple hydrosalpinx is not accompanied by pelvic inflammation!

Cause:

1. Adhesions from prior episodes of PID
2. Tubal ligation
3. Hysterectomy without salpingo-oophorectomy
4. Endometriosis
5. Tubal malignancy

• asymptomatic / recurrent lower abdominal pain, infertility

US (sensitivity of 34%):

√ thin- / thick-walled C- / S-shaped tubular / corkscrew-like structure separate from ovaries

√ "waist" sign = indentations of its opposing walls

√ incomplete septation ← infolding of tube on itself

√ PATHOGNOMONIC longitudinal folds:

√ "**cogwheel**" sign = short linear / small round projections of mucosal folds protruding into lumen of fluid-filled tube similar to spokes of a cogwheel on short-axis images

√ "beads-on-a-string" sign = flat nodular submucosal folds in chronic dilatation

MR:

√ T2-hyperintense + T1-hypointense dilated fallopian tube interposed between ovary and uterus

√ high-SI of fluid on T1WI ← proteinaceous fluid (DDx: hemorrhage)

√ incomplete longitudinal folds = partially effaced mucosal / submucosal plicae (SPECIFIC)

HSG:

√ absence of peritoneal spill

√ dilated ampullary portion of tube (visualization of mucosal folds confirm intratubal contrast accumulation) (DDx: contrast collection adjacent to tubes ← peritubal adhesions)

N.B.: prescribe postprocedural antibiotic prophylaxis (eg, doxycycline) to prevent procedure-related infection!

DDx: tortuous pelvic veins (blood flow at Doppler imaging), dilated fluid-filled bowel (lack of peristalsis), cystic ovarian neoplasm

Pyosalpinx

= infection + superimposed obstruction of fallopian tube

• acute pelvic pain, fever, leukocytosis

• cervical motion tenderness

Path: fallopian tube filled with pus

Location: more likely bilateral than hydrosalpinx

√ enhancing thickened wall and septa of fallopian tube
√ thickened uterosacral ligaments
√ edema of presacral fat
√ small-bowel ileus
MR:
√ T2-hyperintense cystic tubule
√ T1-variointense depending on protein content of fluid
√ pelvic fat stranding
Prognosis: pus undergoing proteolysis transforming a pyosalpinx into a hydrosalpinx

Hematosalpinx
= fallopian tube filled with blood
Cause: pelvic endometriosis, tubal ectopic pregnancy, pelvic inflammatory disease, adnexal torsion, malignancy, trauma
◊ A hematosalpinx is an invitation to search for endometrial deposits + endometriomas!
√ tubular / corkscrew-shaped structure centered in fallopian tube
√ "waist" sign = tubular cystic structure with a folded configuration
√ tubal contents of homogeneous low-level echoes on US
√ tubal contents of high attenuation on CT
√ tubal contents of low signal on T2WI with small round projections in a tubular shape (MOST SPECIFIC)
√ tubal contents of high signal on T1WI fat-suppressed image

Tubo-ovarian abscess (TOA)
= inflammatory mass encompassing ovary + fallopian tube
Cause: sexually transmitted disease, IUD (20%), diverticulitis, appendicitis, pelvic surgery, gynecologic malignancy
Organism: anaerobic bacteria become dominant, Actinomyces israelii associated with IUD
Location: usually in posterior cul-de-sac extending bilaterally
√ multilocular complex mass often with debris, septations, irregular thick wall:
√ ± fluid-debris level
√ intense contrast enhancement of abscess wall
√ nonspecific free pelvic fluid
√ anterior displacement of broad ligament ← posterior position of mesovarium (DDx from other pelvic abscess)
US:
√ surrounding edema / inflammation = increased echogenicity of pelvic fat
CT:
√ pelvic fat stranding
√ thickening + enhancement of peritoneum and uterine ligg.
√ gas is SPECIFIC but rare
MR:
√ T1WI:
√ abscess usually hypointense ± mildly hyperintense areas ← hemorrhagic /

proteinaceous material
√ hyperintense rim along inner abscess wall ← granulation tissue and hemorrhage
√ T2WI:
√ heterogeneous hyperintense mass with septa of low SI
√ meshlike hypointense linear stranding in adjacent pelvic fat ← adhesions + fibrosis
√ hyperintense edema of parametrial fat
CEMR:
√ enhancement of septa + thick abscess wall
√ enhancement of surrounding inflammatory stranding
Cx: (1) rupture → life-threatening peritonitis → intraperitoneal abscess
(2) secondary involvement of adjacent structures (eg, ileus, hydroureteronephrosis)
DDx: endometrioma, ovarian tumor, infected cyst, abscess from other sources (eg, Crohn disease, appendicitis)

PENA-SHOKEIR PHENOTYPE

= autosomal recessive syndrome (45% sporadic, 55% familial) characterized by fetal akinesia
Cause: decreased / absent fetal motion ← abnormalities of fetal muscle / nerves / connective tissue ("fetal akinesia deformation sequence")
Time of first detection: 16–18 weeks MA
@ Spine: scoliosis, kyphosis, lordosis
@ Thorax: pulmonary hypoplasia, cardiac anomalies
@ Kidney: renal dysplasia
@ Limbs: limited movement, knee + hip ankylosis (arthrogryposis), abnormal shape + position, demineralization, camptodactyly, clubfeet
√ craniofacial anomalies
√ polyhydramnios
√ IUGR
√ short umbilical cord
Prognosis: still birth
DDx: multiple pterygium syndrome, Neu-Laxova syndrome, restrictive dermopathy, Larsen syndrome, trisomies 13 + 18

PENTALOGY OF CANTRELL

= sporadic very rare abnormality
Prevalence: 5.5÷1,000,000 live births; M÷F = 2.7÷1
Cause: failure of fusion of lateral thoracic folds + transverse diaphragmatic septum with variable extension inferiorly during days 14–18 of embryonic life
1. Omphalocele (63%) = defect of supraumbilical abdominal wall and sternum
2. Ectopia cordis
3. Deficiency of anterior diaphragm → herniation of intraabdominal organs into thoracic cavity is rare
4. Deficiency of diaphragmatic pericardium
5. Congenital cardiovascular malformation: atrioventricular septal defect (50%), VSD (18%), tetralogy of Fallot (11%), left ventricular diverticulum, Ebstein malformation

Associated with:
(a) chromosomal anomalies: trisomies 13, 18, Turner syndrome
(b) facial defects: cleft lip or palate
(c) CNS anomalies: exencephaly, encephalocele, spina bifida, hydrocephalus
(d) musculoskeletal anomalies: clubfoot, absent radius

√ exteriorization of heart

Prognosis: death within a few days after birth

PERLMAN SYNDROME

= rare fetal overgrowth disorder characterized by visceromegaly, renal lesions, distinctive facial features, high neonatal mortality

Cause: ? autosomal recessive with reported abnormalities of chromosome 11

• generalized muscle hypotonia, pancreatic islet cell hyperplasia
• hypertrophy of islets of Langerhans

√ cystic hygroma
√ fetal macrosomia
√ macrocephaly
√ agenesis of corpus callosum
√ choroid plexus cyst
√ nephromegaly + hydronephrosis
√ hepatomegaly
√ cryptorchidism
√ polyhydramnios

Prognosis: death within first few days of life

PLACENTAL ABRUPTION

= PLACENTAL HEMORRHAGE
= premature separation of placenta from myometrium ← maternal hemorrhage into decidua basalis after 20th week EGA

Frequency: 0.5–1.3% of gestations

Risk factors: *mnemonic:* VASCULAR
Vascular disease + hypertension
Abruption (previous history)
Smoking
Cocaine
Unknown: idiopathic
Leiomyoma
Anomaly: fetal malformation
Reckless driving: trauma

Associated with: intraplacental infarction / hematoma

• vaginal bleeding (80%): bright red (acute), brownish red (chronic); abdominal pain (50%)
• consumptive coagulopathy = DIC (30%); uterine rigidity (15%)

US:
◊ A normal ultrasound (50%) does NOT rule out abruption if

(a) separation occurs WITHOUT hematoma
(b) hematoma is isoechoic to placenta

Echogenicity of hemorrhage:

√ hyperechoic / isoechoic hematoma (initially difficult to distinguish from placenta):
√ abnormally thick + heterogeneous placenta (if blood isoechoic)
√ hypoechoic / complex collection between uterine wall + placenta in 50% within 1 week ← hematoma / placental infarction
√ anechoic collection within 2 weeks

NECT:

◊ NECT & CECT are 43–100% sensitive & 80–98% specific.
√ lenticular high-attenuating collection = retroplacental hematoma
√ high-attenuation blood products in dependent portions of the amniotic sac

CECT:

√ nonenhancing placenta
√ contiguous retroplacental area of decreased enhancement forming acute angles with myometrium = retroplacental hematoma
√ areas of contrast extravasation in infarcted placenta (occasionally)

Falsely positives:

(1) Myometrial contraction = bulging areas hypoattenuating relative to placenta forming obtuse angles with adjacentx myometrium
(2) Venous lake = pooled maternal blood on maternal side of the placenta
(3) Chorionic villous plate indentations
(4) Small wedge-shaped placental infarcts of no clinical significance
(5) Small subchorionic hemorrhages + preplacental hemorrhages of no clinical significance

MR (modality of choice):

√ increased intrauterine T1 signal at site of bleeding

Prognosis:

(1) Only large hematomas (occupying > 30–40% of the maternal surface) result in fetal hypoxia
(2) Abruptions with contained hematoma have worse prognosis
(3) Responsible for up to 15–25% of all perinatal deaths
(4) Normal term deliveries in 27% with hematomas that were detected > 20 weeks GA
(5) Normal delivery in 80% of intrauterine hematomas detected < 20 weeks GA

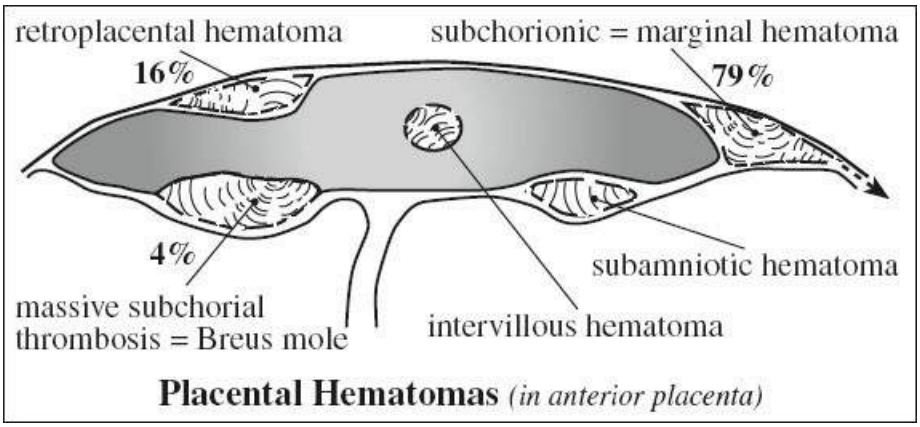
Cx:
(1) Perinatal mortality (20–60%)
(2) Fetal distress / demise (15–27% of all perinatal deaths)
(3) Premature labor + premature delivery (23–52%) (3-fold increase)
(4) Threatened abortion during first 20 weeks
(5) Infant small-for-gestational age (6–7%)

DDx:
(1) Normal draining basal veins
(2) Normal uterine tissue
(3) Retroplacental myoma
(4) Focal contraction

(5) Chorioangioma
(6) Coexistent mole

Retroplacental Hemorrhage (16%)

= ABRUPTIO PLACENTAE
= accumulation of blood beneath placenta separating placenta from myometrium
Pathophysiology: hypertension + vascular disease → rupture of spiral arteries → high-pressure bleed (hemorrhage may dissect into placenta / myometrium)
Frequency: 4.5%; 16% of all placental abruptions
• external bleeding
√ thickened heterogeneous appearing placenta (hematoma of similar echogenicity as placenta)
√ becomes anechoic in 1–2 weeks
√ rounded placental margins + intraplacental sonolucencies
Prognosis: clinically significant if 30–40% of maternal surface of placenta involved
Cx: (1) Precipitous delivery
(2) Coagulopathy
(3) Fetal demise (15–25% of all perinatal deaths)
Risk for fetal demise with hematomas > 60 mL: 6% before [29% after] 20 weeks GA



Placental Hematomas *(in anterior placenta)*

Signal Intensities of Intrauterine Hematoma				
Stage	*T1WI*	*T2WI*	*DWI*	*Hemoglobin (Hb)*
Hyperacute	↔ to ↓	↑	↑ to ↓	intracell oxyHb
Acute	↔ to ↓	↓	↓	intracell deoxyHb
Early subacute	↑	↓	↓	intracell metHb
Late subacute	↑	↑	↑	extracell metHb
Chronic	↓	↓	↔ to ↓	intracell hemosiderin

DDx: myometrial contraction, fibroid, subplacental venous network

Subchorionic Hemorrhage (79%)

= MARGINAL PLACENTAL HEMORRHAGE

= SUBMEMBRANOUS PLACENTAL HEMORRHAGE
= separation of chorionic membrane from decidua with accumulation of blood in subchorionic space
N.B.: placental membranes are more easily stripped from myometrium than from placenta
Pathophysiology: low-pressure bleed ← tears of marginal veins; associated with cigarette smoking
Frequency: 79% of all placental abruptions; in 91% before 20 weeks MA
• may lead to vaginal hemorrhage after dissection through decidua (= 18% of all causes of 1st-trimester bleeding)
√ placental margin detached from adjacent myometrium (60%):
√ separation / rounding of placental margin
√ elevation of chorioamnionic membrane
(DDx: incomplete chorioamnionic fusion during 2nd trimester, blighted twin)
√ hematoma contiguous with placental margin (100%) = **marginal hematoma**
√ predominant hemorrhage often separate from placenta, even on opposite side of placenta
Prognosis: worsens with (1) increased maternal age, (2) earlier gestational age, (3) size of hematoma (> 60 mL); 9% overall miscarriage rate; risk of fetal demise doubles once hematoma reaches ²/₃ of circumference of chorion

Preplacental Hemorrhage

= BREUS MOLE = SUBCHORIAL HEMORRHAGE = MASSIVE SUBCHORIAL THROMBOSIS
= variant of placental abruption with progressive slow intracotyledonary bleeding
Frequency: in 4% of all placental abruptions
Etiology: massive pooling + stasis ← extensive venous obstruction
Time of onset: 18 weeks MA
√ total loss of normal placental architecture
√ gelatinous character of placenta elicited by fetal movement / abdominal jostling
√ hematoma bulging into amniotic fluid
√ severe symmetric IUGR
Risk for fetal demise: 67% overall; 100% for hematomas > 60 mL
DDx: subamniotic hematoma

Intraplacental Hemorrhage

= massive retroplacental hematoma dissecting into placenta; related to placental infarcts
√ focal mass of varying echogenicity within placenta

Intraamniotic hematoma

√ internal echoes in amniotic fluid

PLACENTA ACCRETA

= defect in normal decidua basalis from prior trauma allows abnormal adherence + penetration of chorionic villi to / into myometrium
Prevalence: 1÷2,500–7,000 deliveries related to increase in uterine surgery; in 5% of placenta previa patients
Risk of placenta accreta versus cesarean section:

in 10% of placenta previa; in 24% of placenta previa + 1 cesarean section; in 48% of placenta previa + 2 cesarean sections; in 67% of placenta previa + 4 cesarean sections

Predisposed: areas of uterine scarring with deficient decidua: previous dilatation + curettage, endometritis, submucosal leiomyoma, Asherman syndrome, manual removal of placenta, adenomyosis, increasing parity

Associated with: placenta previa (in 20%)

Types:

1. Placenta accreta (76%)
   = chorionic villi in direct contact with myometrium
2. Placenta increta (18%)
   = villi invade myometrium
3. Placenta percreta (6%)
   = villi penetrate through uterine serosa

US (77–93% sensitive, 71–96% specific):

√ loss of normal retroplacental clear space

√ thinning to < 1 mm / absence of hypoechoic myometrial zone between placenta + echodense uterine serosa / posterior bladder wall (normally, retroplacental hypoechoic zone of decidua + myometrium + dilated periuterine venous channels measures 9.5 mm thick > 18 weeks GA)

√ thinning / irregularity / focal disruption of linear hyperechoic boundary echo (= uterine serosa-bladder wall interface)

√ focal masslike elevations / extensions of echogenic placental tissue beyond uterine serosa

√ > 6 irregular intraplacental lacunae (= poorly marginated irregular vascular spaces with turbulent flow) → highest positive predictive value

MR (80–88% sensitive, 65–100% specific):

√ heterogeneous hyperintense placenta on T2WI

√ dark intraplacental bands (= lacunae) on T2WI

√ interruption of junctional zone

√ focal thinning of hypointense myometrium

√ abnormal uterine bulging

Cx: (1) Life-threatening hemorrhage in 3rd stage of labor necessitating emergent hysterectomy

(2) Maternal death

(3) Retention of placental tissue

(4) Persistent postpartum bleeding

Rx: (1) Hysterectomy

(2) Conservative measures: curettage, oversewing of placental bed, ligation of uterine arteries

PLACENTA PREVIA

= abnormally low implantation of ovum with the placenta covering all / part of internal cervical os > 15 weeks GA

Frequency: 0.5% of all deliveries; 3–5% of all pregnancies complicated by 3rd trimester bleeding (of these 7–11% are due to placenta previa); in 0.26% with unscarred

uterus

Risk for placenta previa versus cesarean section:

0.65% after 1 section, 1.8% after 2 sections, 3% after 3 sections, 10% after 4 sections

Cause: defective decidual vascularization in areas of endometrial scarring → compensatory placental thinning → placenta occupies a greater surface of the uterus with increased probability for encroachment upon internal os

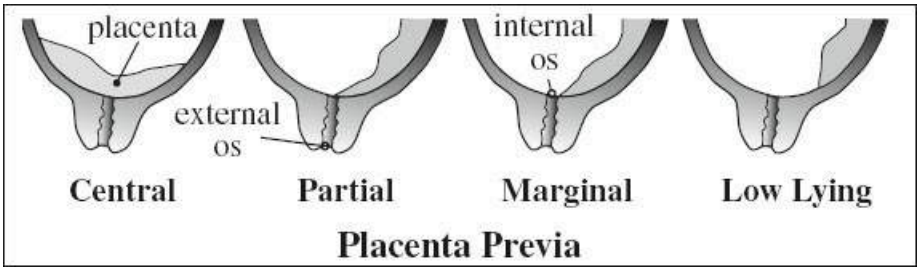
Predisposed:

(1) Previous uterine incision: cesarean section, myomectomy
(2) Older woman
(3) Multiparous woman

• painless vaginal bleeding in 93%: usually 3rd trimester / as early as 20 weeks

Types on clinical examination:

1. Normal placental implantation = lower placental edge > 2 cm away from margin of internal os
2. Complete / total previa (⅓) = complete covering of internal os
3. Central previa = placenta implanted directly over internal os
4. Partial previa = internal os partially but not fully covered by placenta
5. Marginal previa = placenta extends to edge of internal os
6. Low-lying placenta = low placental edge within 2 cm of internal os without covering it; palpable by examining finger



US - False Positives (5–7%):

1. **Placental "migration"** / rotation
   = differential growth rates between lower uterine segment + placenta
   ◊ 63–93% will have normal implantation at term!
   › conversion to normal position: anterior wall > posterior wall of uterus
   › NO conversion if placenta attaches to both posterior + anterior walls
2. Overfilled urinary bladder
   bladder-induced compression leads to apposition of the lower anterior + posterior uterine walls simulating a placenta previa → cervical length > 3.5–4 cm
3. Focal myometrial contraction in the region of the lower uterine segment → myometrial thickness > 1.5 cm

mnemonic: ABCD and F

Abruption (may mimic placenta previa)
Bladder (must be empty)
Contraction (may have to wait 15–20 min)
Dates (be wary in 1st half of pregnancy)

Fibroid

US - False Negatives (2%):

1. Obscuring fetal head
   → remedied by Trendelenburg position / gentle upward traction on fetal head
2. Lateral position of placenta previa
   → remedied by obtaining oblique scans
3. Blood in region of internal os: mistaken for amniotic fluid

MR:

√ abnormal position of placenta infringing on cervical os

Cx: secondary to premature detachment of placenta from lower uterine segment

(1) Maternal hemorrhage (blood from intervillous space)
(2) Premature delivery
(3) IUGR
(4) Perinatal death (5%)

Rx: precludes vaginal delivery + pelvic examination

PLACENTAL SITE TROPHOBLASTIC DISEASE

= very rare neoplasm (? type of choriocarcinoma)

Path: microscopic tumor / diffuse nodular replacement of myometrium

Histo: proliferation of predominantly intermediate trophoblasts but no syncytio- or cytotrophoblasts

- abnormal bleeding / amenorrhea
- low β-hCG levels ← lack of syncytiotrophoblastic proliferation

√ cystic / solid lesions ± central component

√ myometrium usually invaded

Prognosis: benign / highly malignant course

Rx: hysterectomy

POSTMATURITY SYNDROME

= inability of aging placenta to support demands of fetus

Prevalence: in 15% of all postterm gravidas

• meconium-stained amniotic fluid

√ grade 3 placenta (in 85%), grade 2 (in 15%), grade 1 (in 0%)

√ decreased subcutaneous fat + wrinkling of skin

√ long fingernails

√ decreased vernix

Cx: meconium aspiration, perinatal asphyxia, thermal instability

Postterm Fetus

= fetus undelivered by 42nd week MA

Prevalence: 7–12% of all pregnancies

Risk of perinatal mortality: 2-fold at 43 weeks MA; 4–6-fold at 44 weeks MA

PREECLAMPSIA

= TOXEMIA OF PREGNANCY = EPH GESTOSIS

Prevalence: 5% of pregnancies, typically during 3rd trimester

• Clinical triad: [EPH = **E**dema, **P**roteinuria, **H**ypertension]

(1) Peripheral edema + weight gain

(2) Proteinuria

(3) Pregnancy-induced / -aggravated hypertension

Histo: blunted invasion of vasa media of spiral arterioles + focal vasculitis + atheromatous degeneration + fibrin deposits in intima of maternal placental arterioles

√ heavy calcium deposition (in areas of placental degeneration)

√ IUGR (6% with late-onset preeclampsia, 18% with early-onset preeclampsia)

Cx:

@ CNS: convulsive eclampsia, stroke

@ Liver: hematoma, infarction

@ Kidney: glomerular endotheliosis = variant of thrombotic microangiopathy → decreased GFR

Eclampsia

• convulsions + coma

PREMATURE RUPTURE OF MEMBRANES

= spontaneous rupture of chorioamnionic membranes before the onset of labor

Types:

(a) Preterm premature rupture of membranes (PPROM) < 37 weeks GA

(b) Term premature rupture of membranes (TPROM) > 37 weeks GA

Prevalence: overall 2.1–17.1%; PPROM 0.9–4.4%;
in 29% of all preterm deliveries;
in 18% of all term deliveries

Risk of recurrence: 21% of women with PPROM
Cause: ? infection of membranes
√ decrease in the amount of amniotic fluid
CT:
√ products of conception low-lying / in cervix
√ blood in cervix / vagina ←signs of impending / ongoing spontaneous abortion
Cx:
(a) TPROM:
> 24 hours may result in intrapartum fever
> 72 hours may result in chorioamnionitis + still-birth
(b) PPROM: respiratory distress syndrome (9–43%), neonatal sepsis (2–19%)

SCLEROSING STROMAL TUMOR OF OVARY

= benign sex cord-stromal tumor
Age: < 30 years
• irregular menses
Histo: pseudolobular pattern = cellular areas separated by edema + collagenous hypocellular tissue
√ hypointense nodules set against hyperintense stroma on T2WI
√ peripheral enhancement with centripetal progression

SECKEL SYNDROME

= BIRD-HEADED DWARFISM
= rare autosomal recessive disorder (44 cases)
• proportionate postnatal short stature
• characteristic stance: slight flexion of hips and knees
• mental retardation, simian crease, cryptorchidism
@ Skull
√ severe microcephaly
√ receding forehead, large beaked nose, micrognathia
@ Skeleton
√ dislocation of radial head + hypoplasia of proximal end of radius
√ absence of phalangeal epiphysis
√ clinodactyly of 5th digit
√ gap between 1st and 2nd toe
√ hip dislocation
√ hypoplasia of proximal fibula
√ absence of patella
√ 11 pairs of ribs
OB-US:
√ severe IUGR
√ oligohydramnios
√ decreased bone length: femur, tibia, fibula
√ decreased AC, HC

SEROUS OVARIAN TUMOR

◊ Most common neoplasm in benign + malignant category

Frequency: 30% of all ovarian tumors 60–80% of all malignant ovarian neoplasms

Path: areas of solid tissue components + hemorrhage and necrosis (more common in malignant tumors)

Histo: lined by tall columnar epithelial cells (as in fallopian tubes), filled with serous fluid, psammoma bodies (= microscopic calcifications in up to 30% of malignant tumors)

Age: 20–50 years (malignant variety later)

Serous Cystadenoma (60%)

◊ Second most common benign tumor of the ovary (after dermoid cyst); 20% of all benign ovarian neoplasms

√ usually unilocular (occasionally multilocular) thin-walled cyst up to 20 cm in diameter

√ only small amount of solid tissue: occasional septum / mural nodule (papillary projections in 9%)

√ bilateral in 7–20–30%

Cystadenofibroma

= variant of serous cystadenoma, rarely malignant

Prevalence: nearly 50% of all benign ovarian cystic serous tumors; bilateral in 6%

Mean age: 31 (range, 15–65) years

• may produce estrogen excess

√ small multilocular cystic tumor

√ clusters of short rounded papillary processes

MR:

√ multiloculated cystic mass

√ solid fibrous component:

√ low SI on T2WI

√ mild enhancement on T1WI

Borderline Malignant Serous Cystadenoma (15%)

Histo: identical to peritoneal serous micropapillomatosis

√ papillary projections within cyst (in 67%)

Serous Cystadenocarcinoma (25%)

= SEROUS PAPILLARY CARCINOMA OF OVARY

Prevalence: 60–80% of all ovarian carcinomas

Origin: peritoneal mesothelial cells with müllerian differentiation / nests of ovarian tissue remnants within peritoneum

Age: postmenopausal woman

Histo: identical to primary peritoneal serous papillary ca.

√ multilocular cyst with large amount of solid tissue: papillomatous excrescences within cyst (= papillary serous carcinoma) in 38%

√ may have calcifications

√ bilateral in 50–70%

√ loss of capsular definition + tumor fixation
√ ascites ← peritoneal surface implantation
√ lymph node enlargement: periaortic, mediastinal, supra- clavicular
CT:
√ psammomatous calcifications (12%)

SERTOLI-STROMAL CELL TUMOR OF OVARY

= ANDROBLASTOMA = ARRHENOBLASTOMA
Origin: from hilar cells of ovary
Prevalence: < 0.5%
Age: any age; most common in 2nd–3rd decade
Histo: components of Sertoli cells, Leydig cells, fibroblasts; tissues are so varied that it is frequently confused with other tumors
Classification:
(1) Sertoli cell tumor (4%) - usually nonfunctioning
(2) Leydig cell tumor
(3) Sertoli-Leydig cell tumor
• androgenic
√ hypoechoic mass simulating fibroid
√ may have cystic / hemorrhagic degeneration

Sertoli-Leydig Cell Tumor

◊ Most common virilizing tumor of ovary!
Frequency: 0.5% of all ovarian neoplasms
Mean age: 25 (range, 15–66) years; 75% occur in patients < 30 years of age
Path: solid ± cystic areas; hemorrhage is rare
Histo: well differentiated / intermediately differentiated / poorly differentiated / retiform (4 subtypes)
• nonfunctioning (50%); abdominal mass ± pain
• virilization (30%): amenorrhea, male secondary sexual characteristics
◊ Virilizing tumor often small and difficult to detect!
• estrogenic (20%); no hormonal manifestations (50%)
Location: unilateral in 98%
√ small mass often difficult to visualize by US / CT
√ maximally 5–27 cm in diameter
√ solid mass ± cystic components ← hemorrhage and necrosis
√ well-defined hypoechoic mass + (rarely) intratumoral cysts
√ calcifications are unusual
√ contrast enhancement
MR:
√ predominantly low SI (= fibroblasts) + scattered areas of high SI on T2WI
Cx: malignant transformation in 10–18%
Prognosis: good when detected at stage I (in 92%)
Recurrence: soon after initial diagnosis (in 20%)

DDx: granulosa cell tumor (spongelike multicystic with areas of hemorrhage)

SINGLE UMBILICAL ARTERY

= TWO-VESSEL CORD

Etiology:

(1) Primary agenesis of one umbilical artery (usually first appears in 5th menstrual week)
(2) Secondary atrophy / atresia of one umbilical artery
(3) Persistence of original single allantoic artery of body stalk

Prevalence: 0.2–1% of singleton births; 5% in dizygotic twins; 2.5% in abortuses; increased incidence in trisomy D / E, diabetic mothers, White patients, spontaneous abortions

Associated with:

(a) congenital anomalies (21–33%):
1. CHD (most frequent): VSD, conotruncal anomalies
2. GU: hydronephrosis, dysplastic kidney
3. Abdomen: ventral wall defect, diaphragmatic hernia
4. Esophageal atresia, cystic hygroma, cleft lip
5. CNS: hydrocephalus, holoprosencephaly, spina bifida
6. Polydactyly, syndactyly

(b) IUGR & small for gestational age
(c) premature delivery
(d) perinatal mortality (20%): stillbirth (66%)
(e) marginal (18%) / velamentous (9%) cord insertion
(f) chromosomal anomalies (10–67%): trisomy 18 (in 40%) > trisomy 13 > Turner syndrome > triploidy

◊ Detailed anatomic survey & close follow-up evaluation of fetal growth strongly recommended!

Maternal risk factors:

advanced maternal age, white ethnicity, multiparity (3–7 x higher than for singleton pregnancy), smoking, diabetes, hypertension, preeclampsia, maternal drug use, epilepsy

Site: left artery slightly more often absent than right

√ axial view of cord shows 2 vessels
√ single umbilical artery nearly as large as umbilical vein → umbilical vein-to-umbilical artery ratio < 2
√ incurvation of distal aorta toward common iliac artery on the side of patent umbilical artery
√ ipsilateral hypoplastic / absent common iliac artery in fetus
√ color flow imaging permits earlier (15–16 weeks) + more confident diagnosis

Prognosis:

(1) 4-fold increase in perinatal mortality (14%) with concurrent major abnormality
(2) Isolated single umbilical artery does not affect clinical outcome

DDx:

(1) Normal variant = 2 arteries at fetal end may fuse near placental end into single umbilical artery (umbilical arteries normally unite with allantoic artery near placental insertion)
(2) Arterial convergence of 2 into 1 umbilical artery

STEIN-LEVENTHAL SYNDROME

= POLYCYSTIC OVARY SYNDROME

[Irving Freiler Stein (1887–1976), American gynecologist in Chicago]

[Michael Leo Leventhal (1901-1971), American gynecologist in Chicago]

= functional NOT imaging diagnosis

Prevalence: 2.5–8% of women in reproductive age; affects 4–5 million women in USA

Etiology: deficient aromatase activity (= catalyst for conversion of androgen into estrogen) → androgen excess (= hyperandrogenism); exaggerated pulsatile release of LH stimulates continued ovarian androgen secretion at the expense of estradiol; reduction of local estrogen impairs FSH activity → accumulation of small- and medium-sized atretic follicles without final maturation into graafian follicles (= incomplete ovulatory cycles)

Path: pearly white ovaries with multiple cysts below the capsule → lined by a hyperplastic theca interna layer showing pronounced luteinization; granulosa cells are absent / degenerating; corpora lutea are absent

Age: late 2nd decade

Associated with: Cushing syndrome, basophilic pituitary adenoma, postpill amenorrhea, virilizing ovarian / adrenal tumor

- OB/GYN symptoms:
  - ⇓ fertility / sterility
  - recurrent spontaneous abortion
  - secondary amenorrhea (most common cause)
    - ◊ Women with PCOS are frequently ovulatory!
  - menstrual irregularities / oligomenorrhea
- metabolic symptoms:
  - obesity (30–70%) with body mass index ≥ 30 kg/m2
  - periodic abdominal discomfort
  - glucose intolerance (16%) + type 2 diabetes mellitus (10%)
  - dyslipidemia (↑ triglycerides, ↑ LDL (low-density lipoproteins), ↑ VLDL (very-low-density lipoproteins), ↓ HDL (high-density lipoproteins)
- cardiovascular symptoms:
  - hypertension; coronary + carotid atherosclerosis
  - myocardial infarct + cerebrovascular accidents
- cephalic symptoms:
  - cystic acne; cephalic hair loss
  - mild facial / severe generalized hirsutism (70% in USA)
- laboratory findings:
  - ↑ LH levels without LH surge with ↔ / ↓ FSH = ↑ LH/FSH ratio ← preferential production of androgen
    LH: regulates synthesis of androgens from cholesterol in ovarian theca cells
    FSH: regulates aromatase activity of granulosa cells = how much estrogen is synthesized from androgenic precursors
  - elevated androstenedione / testosterone levels
  - elevated estrone / estradiol

√ at least one enlarged ovary > 10 cm^3
  √ normal ovarian size (in 30%), polycystic ovaries have a volume of 6–30 cm^3
√ excessive number of developing follicles:
  √ multiple (> 12) follicles of 2–9 mm in subcapsular location
    ◊ 20–30% of normal young women may have ovaries of a similar appearance!
Cx: endometrial cancer < 40 years of age ← unopposed chronic estrogen stimulation
DDx: ovaries in congenital adrenal hyperplasia, normal ovaries
Rx: (1) Ovulation induction with clomiphene (Clomid®) / menotropins (Pergonal®)
(2) Wedge resection (transient effect only)

STEROID CELL TUMOR

= LIPID / LIPOID CELL TUMOR
= characterized by cells resembling typical steroid hormone-secreting cells (lutein cells, Leydig cells, adrenocortical cells)
Frequency: 0.1–0.2% of all ovarian tumors
Age: wide range of ages; usually 5^{th}–6^{th} decade
Types: (1) **Stromal luteoma** (60% estrogenic, 12% androgenic)
(2) **Leydig / hilus cell tumor** (75% androgenic)
(3) Steroid tumor not otherwise specified
Path: usually < 3 cm yellow nodule with rich vascularity; rarely cystic
Histo: abundant clear cytoplasm + varying amounts of lipid resembling adrenocortical cells
• virilizing (majority): amenorrhea, hirsutism
• Cushing syndrome (rare)
√ unilateral < 3 cm small solid tumor
√ cystic change / necrosis (rare)
CT:
  √ areas of low attenuation (= abundant lipid content)
MR:
  √ NO high-signal intensity on T1WI ← lipid content obscured by fibrous stroma
  √ various signal intensities on T2WI
  √ intense contrast enhancement ← high tumor vascularity
Prognosis: clinically malignant (33%)

STRUMA OVARII

= rare highly specialized form of ovarian teratoma
Terminology: (a) pure form = tumor composed entirely of thyroid tissue
(b) impure form = component of mature cystic teratoma occupying > 50% of its volume
Prevalence: 0.30–0.65% of ovarian tumors; 5–20% of all mature cystic ovarian teratomas
Age: premenopausal women
Path: unilateral; often < 10 cm in size
Histo: mature thyroid tissue of variably sized acini filled with colloid: lined by single layer of columnar / flattened epithelium

- asymptomatic / pelvic mass
- hyperthyroidism / thyrotoxicosis (5%)
- pseudo-Meigs syndrome = abdominal ascites / hydrothorax

√ multilocular cystic mass with smooth margins + large cystic spaces = dilated thyroid follicles filled with thyroglobulin and thyroid hormones

US:

√ nonspecific solid + cystic tumor

√ characteristic struma pearls = well circumscribed round vascularized echogenic solid areas with smooth contour

CT:

√ high-attenuation loculi = iodinated thyroid hormone and calcifications

√ intense enhancement

√ ± loculi of fat attenuation = sebaceous material

MR:

√ multilobulated complex mass with thick septa + multiple cysts of variable SI + enhancing solid components

√ cystic spaces with marked hypointensity on T2WI + intermediate intensity on T1WI (= thick gelatinous colloid)

√ T1-hyperintense locules ← hemorrhage

√ SI drop-off with surrounding chemical shift artifact on opposed-phase T1WI ← microscopic fat

√ strong enhancement of solid component / thickened septa / cyst walls

Prognosis: benign in 95%

Cx: malignancy (in 5–10%)

Dx: usually by pathologic analysis

DDx: mature cystic teratoma without fatty tissue, cystadenoma, cystadenocarcinoma, endometriosis, tuboovarian abscess, metastatic tumor

TERATOMA OF OVARY

= immature derivatives of all 3 germ cell layers

Prevalence: most common germ cell neoplasm; 20% of adult + 50% of pediatric ovarian tumors

Types: (1) Mature cystic teratoma

(2) Immature teratoma

(3) Monodermal teratoma

(4) Combination tumor = intermixed varying histologic components without definite interface

(5) Collision tumor = two adjacent histologically distinct tumors without histologic admixture at interface

Age: usually childhood / adolescence

√ variably from purely cystic to mainly solid masses

US:

√ cystic / complex mass (most frequently)

√ usually large solid mass with internal echoes

Dx: identification of intratumoral fat on US, CT, MR imaging

Cx: 1. Torsion (16%)

2. **Ruptured teratoma** (1–4%)
   - √ discontinuity of tumor wall
   - √ fatty implants within peritoneal cavity
   - √ chronic granulomatous peritonitis:
     - √ ascites, hazy omental infiltration
     - √ inflammatory omental mass
3. Malignant transformation (1–2%)
4. Infection (1%)
5. Autoimmune hemolytic anemia (< 1%)

Malignant Transformation of Ovarian Teratoma

Prevalence: 1–2% of ovarian teratomas; 1% of all ovarian malignancies

Path: squamous cell carcinoma arising from squamous lining of the cyst (in 80%); adenocarcinoma

Age: > 45 years

- serum squamous carcinoma antigen level > 2 ng/mL
- elevated CA-125 level > 35 U/mL (in 67%)
- elevated CA 19-9 level > 37 U/mL (in 75%)

Location: in any of 3 germ cell layers

Common site: Rokitansky nodule

Size of tumor: > 10 cm

√ transmural growth of Rokitansky nodule

√ contrast enhancement of Rokitansky nodule

CT / MR:

√ invasive growth of large irregularly marginated soft-tissue component through tumor wall

√ irregular soft-tissue components within tumor

√ obtuse angle between soft tissue and inner cyst wall

√ enhancing soft-tissue component

Malignant Carcinoid of Ovary

= rare neoplasm of monodermal teratoma with differentiation toward argentaffin cells

Prevalence: 0.5 of all carcinoid tumors; 0.1% of all malignant ovarian tumors

Path: usually component of mature cystic teratoma

Histo: insular (= composed of islet cells); trabecular; mucinous (= composed of goblet cells); stromal; mixed (= combination of the 4 pure types)

- carcinoid syndrome (⅓) in the absence of metastases ← NO inactivation of serotonin ← tumor drains directly into systemic circulation bypassing the liver

Laterality: unilateral

Size of tumor: up to 20 cm

√ multilocular cystic mass with soft-tissue component

√ solid enhancing component may appear as sponge-like mass

√ low SI on T2WI + intermediate SI on T1WI

THECA CELL TUMOR OF OVARY

= THECOMA = FIBROSED THECOMA = FIBROTHECOMA
= benign sex cord-stromal tumor similar to fibroma
Path: solid mass, occasionally with cystic changes
Histo: spectrum of tumors with varying amounts of theca cells (= swollen lipid-rich stromal cells with estrogenic activity) + fibroblasts
Frequency: 0.5–1% of all ovarian neoplasms; 50% of all gonadal-stromal tumors
Mean age: 59 years; > 30 years (30%); postmenopausal (> 80%)
• estrogenic activity with uterine bleeding (60%)
May be associated with: endometrial hyperplasia; endometrial carcinoma (> 20%)
Laterality: unilateral
US:
√ echogenic mass with sound attenuation / well-defined hypoechoic mass / anechoic lesion with sound through-transmission
√ endometrial thickening
MR:
√ hypointense ovarian mass on T2WI ← fibrotic component
√ high SI on T2WI for components with little / no fibrosis ← edema / cystic degeneration of larger masses
√ low signal intensity on T1WI
√ variable degree of contrast enhancement governed by amount of nonenhancing fibrous tissue
√ widening of endometrial stripe (= thickened endometrium)
√ endometrial polyps
Prognosis: almost always benign with low malignant potential

Luteinized Thecoma

= rare subtype of fibrothecoma containing steroid type cells
• hormonal activity: estrogenic (50%), nonfunctioning (39%), androgenic (11%)
Age: younger

TORSION OF FALLOPIAN TUBE

Frequency: 1÷1.5 million women (exceedingly rare)
Age: adolescent girls + women of reproductive age
Risk factors: long / congested mesosalpinx, prior tubal ligation, hydatid cyst of Morgagni, hydrosalpinx, PID, hypermotility of fallopian tube, trauma
Location: R >> L ← fixation by sigmoid colon
Mechanism: adnexal venous + lymphatic obstruction → enlargement of fimbrial end as lead point
• acute onset of crampy / constant dull lower abdominal pain
• nausea, vomiting, peritoneal signs
US:
√ fusiform tubal dilatation with tapered ends
√ thickened echogenic wall ± internal debris
√ central solid component (= edematous mesosalpinx) surrounded by dilated tube

CT:
√ dilated fluid-filled structure separate from ovary:
√ tubular shape with tapered ends (= "beak" sign)
√ twisted configuration of dilated tubular cystic mass
√ intraluminal attenuation > 50 HU (= hemorrhage)
√ thick enhancing fallopian tube wall
√ free fluid + peritubal fat stranding
√ thickening + enhancement of broad ligaments
√ focal reactive ileus

TORSION OF OVARY

= OVARIAN TORSION
= twisting of ovary on its axis around suspensory ligament
Adnexal torsion: torsion of ovary / fallopian tube / both (67%)
Predisposing condition:
(1) Enlarged ovary (in 50–81%):
(a) physiologic: large hemorrhagic cyst, paraovarian cyst, multicystic ovary from hyperstimulation, abscess
(b) neoplastic: benign mature cystic teratoma (= "dermoid"), serous cystadenoma, malignancy
◊ Benign mature cystic teratoma is the most common neoplasm causing torsion!
◊ Ovarian torsion is rare with ovarian cysts < 5 cm
(2) Hypermobility of normal adnexa ← markedly mobile fallopian tube, excessively long mesosalpinx, elongated pelvic ligaments, fallopian tube spasm, strenuous exercise, abrupt changes in intraabdominal pressure
◊ Most frequent in prepubertal girls + during 1st trimester of pregnancy
At risk: 1st trimester of pregnancy (8–16 weeks EGA) responsible for 14% of all ovarian torsions
◊ Uncommon after PID / endometriosis / malignant neoplasm ← immobile ovaries ← presence of adhesions
Prevalence: 2.7% of gynecologic emergencies
Associated with: ipsilateral ovarian lesion (in 50–81%)
Path: hemorrhagic necrosis
Pathophysiology:
(a) early stage of partial torsion: arteries with thick muscular walls are less collapsible so that circulatory stasis affects initially lymphatics + veins → massive ovarian edema + distention of peripheral follicles → diffuse ovarian enlargement + capsular stretch
(b) later stage of progressive complete torsion: arterial obstruction (= arterial stasis + thrombosis) → ovarian ischemia / necrosis / hemorrhagic infarction → severe peritonitis → systemic inflammation + death
Age: any; usually affects women of reproductive age (17–20% during pregnancy) in first 3 decades of life; may occur prenatally
◊ Torsion of a normal ovary is unusual and more common in adolescents!
• gradual / sudden onset of severe lower abdominal / pelvic pain:

- sharp localized right / left lower abdominal pain + tenderness with peritoneal signs
- intermittent pain / resolving pain

• waves of nausea, vomiting, pyrexia; palpable mass in 50%

Location: R÷L = 3÷2 (? protective effect of sigmoid mesentery); frequently one ovary with corresponding fallopian tube

US (87% PPV, 93% specific):

√ enlarged ovary > 4 cm in diameter (28 x normal size):
  √ ovarian stromal heterogeneity with solid + cystic components ← hemorrhage and edema
  √ good sound transmission ← vascular engorgement and stromal edema
  √ ± coexistent complex (cystic / solid) pelvoabdominal /adnexal mass

√ "string of pearls" = multiple peripherally aligned displaced follicles measuring 8–25 mm in diameter (64–74%) ← transudation of fluid into nonovulatory follicles

√ small amount of free fluid in cul-de-sac (in up to 87%):
  √ clear ascites (70%) / hemorrhagic ascites (10%)

√ ± local tenderness of ovary at transvaginal US

√ "**whirlpool**" sign = ellipsoid / tubular mass abutting ovarian mass = twisted vascular pedicle (88%)

Color Doppler:

√ engorgement of blood vessels on side of torsion

√ "**corkscrew**" appearance = twisted circular / coiled arterial + venous vessels within vascular pedicle

√ diminished / absent venous flow (in 93%) ← early collapse of compliant venous walls

√ absent / high-resistance arterial Doppler waveforms (in 73%) = SPECIFIC but NOT SENSITIVE
  ◊ Normal arterial waveforms do NOT rule out torsion! Some color Doppler flow in up to 60% of surgically proved cases ← dual blood supply by ovarian + uterine arteries / symptoms secondary to venous thrombosis

Utility: Nonviable ovary shows NO central venous flow! Viable twisted ovary shows central venous flow!

CT:

√ unilateral ovarian enlargement (100%) with cortical follicles

√ displacement of torsed ovary toward pelvic midline / contralateral side + superior to fundus

√ deviation of uterus toward side of torsed ovary (36%)

√ amorphous targetlike / tubular mass (84%) between adnexal mass + uterus ← tubal thickening > 10 mm

N.B.: the diameter of the normal tube measures up to 4 mm at isthmic, 8 mm at ampullary, 10 mm at infundibular portion

√ cystic ovarian mass with smooth wall thickening (76%) converging on a thickened fallopian tube:
  √ eccentric > 10 mm ← suggests hemorrhagic infarction
  √ attenuation > 50 HU on NECT = hemorrhagic infarction

√ small uniform peripheral hypoattenuating cysts surrounding an edematous ovarian stroma

√ obliteration of fat planes / fat stranding around torsed ovary

√ twisted vascular ovarian pedicle (PATHOGNOMONIC)
√ enlarged veins
√ lack of enhancement of solid component (= infarction)
√ hematoma / gas within torsed mass
√ ascites

MR:

@ ovary:
√ imaging findings vary with stage:
√ initially ovarian enlargement with diffuse high SI on T2WI ← stromal edema = frequently viable ovary
√ variable SI ← hemorrhage + necrosis
√ ↓ SI on T1WI and T2WI ← hemorrhagic infarction
√ high SI on fat-suppressed T1WI ← blood products
√ smooth thickening of cyst wall / mural nodule
√ no enhancement of solid component on contrast-enhanced dynamic subtraction MR = chronic stage
√ enlarged follicles along periphery of ovary
√ twisted vascular pedicle
√ beaked protrusion at periphery of torsed ovary ← engorged blood vessels
√ obliteration of fat planes

@ tube:
√ tubal thickening (SAG image improves detection)
√ increased tubal SI on T2WI ← edema
√ hemorrhage into thickened tube

@ uterus:
√ deviation of uterus to side of torsion

√ pelvic ascites / hemoperitoneum

Prognosis:

(1) Spontaneous detorsion is common (history of prior similar episodes = intermittent torsion)
(2) Infection of torsed ovary with local peritonitis ± bowel obstruction

Cx: infarction, necrosis, infection, peritonitis

Rx: immediate surgery (most ovaries NOT salvageable)

DDx: (1) Hemorrhagic ovarian cyst (fishnet appearance, retracting blood clot, fluid-fluid / fluid-debris level

(2) Serous cystadenoma (large unilocular thin-walled cystic lesions ± thin septations / papillary projection)

(3) Ovarian hyperstimulation syndrome (bilaterally enlarged ovaries due to multiple distended peripherally located corpora lutea cysts)

TRIPLOIDY

= 69 chromosomes (= 3 haploid sets of 23 chromosomes)

Prevalence: 1% of conceptions; 0.04% of 20-week fetuses

NO obvious pattern!

√ early severe asymmetric IUGR (MOST PROMINENT FEATURE); cephalocorporal disproportion

√ oligohydramnios
√ large hydropic placenta with scattered vesicular spaces (partial hydatidiform mole)
√ congenital heart disease: ASD, VSD
√ brain anomalies: hydrocephalus, holoprosencephaly, neural tube defect
√ cleft lip / palate
√ syndactyly of fingers
√ omphalocele
√ renal abnormalities
Prognosis: most ending in spontaneous abortion

TRISOMY 13

= PATAU SYNDROME

Cause: nondisjunction of chromosome 13 during meiosis
Prevalence: 1÷5,000 live births
@ OB: severe IUGR, hydramnios
@ CNS: alobar holoprosencephaly, posterior encephalocele, neural tube defect
@ Face: midline labial cleft, proboscis, hypotelorism, cyclopia, anophthalmia
@ Skeleton: postaxial polydactyly, rocker-bottom foot
@ Heart: (CHD in 90%) VSD, echogenic chordae tendineae, hypoplastic ventricle, tetralogy of Fallot, transposition
@ Kidney: polycystic kidney, horseshoe kidney
@ GI: omphalocele (occasionally)
Prognosis: few infants live more than a few days / hours; death by 3 months of age
DDx: Meckel-Gruber syndrome

TRISOMY 18

= EDWARDS SYNDROME

Prevalence: 1÷3,000–5,000 live births
• triple-marker screening test:
(1) ↓ maternal alpha-fetoprotein
(2) ↓ hCG (DDx: increased in Down syndrome)
(3) ↓ estriol
√ no anomalies (14%) on initial 2nd-trimester sonogram only ← incomplete / early gestational age
@ OB: severe symmetric IUGR (28% < 24 weeks MA), single umbilical artery (30%), polyhydramnios (occasionally)
@ Face: micrognathia, hypotelorism, facial cleft (10–40%)
@ Head: strawberry-shaped head (50%), cystic hygroma
@ CNS: holoprosencephaly, choroid plexus cyst (30–51–75%), cerebellum ≤ 10th percentile with prominent cisterna magna (45%), myelomeningocele
@ Hand: clenched hand with overlapping of index finger (33%, HIGHLY CHARACTERISTIC), abnormal wrist position (27%)
@ Arm: shortened radial ray, clubbed forearm

@ Foot: clubbed foot, rocker-bottom foot
@ Heart: CHD in 90%: VSD (82%), ASD (8%), complete AV canal, DORV
@ GI: diaphragmatic hernia, omphalocele (30–40%), tracheoesophageal fistula
@ Kidney: polycystic kidney, horseshoe kidney, UPJ obstruction

Prognosis: usually delivered by emergency cesarean section ← IUGR + fetal distress, if not detected prenatally; death by 1 year of age

TWIN EMBOLIZATION SYNDROME

= rare complication of monochorionic pregnancy following the death of one twin whose blood pressure falls to zero

Pathophysiology:

1. Acute reversal of transfusion to co-twin at time of intra-uterine demise of one twin with ischemic changes in survivor
2. Embolization (= transfer of thromboplastin-enriched blood / detritus) from the dead to the living twin through vascular anastomoses in placenta
   • DIC (disseminated intravascular coagulation)

Embolized organs: CNS (72%), GI tract (19%), kidneys (15%), lungs

√ ventriculomegaly, cortical atrophy, porencephalic cyst, cystic encephalomalacia within 2 weeks of death of co-twin

Morbidity / mortality: 17%

TWIN-TWIN TRANSFUSION SYNDROME

= FETOFETAL TRANSFUSION SYNDROME = MONOVULAR TWIN TRANSFUSION = INTRAUTERINE PARABIOTIC SYNDROME

= complication of monozygotic twinning with one placenta or one fused placenta of mono- / dizygotic twins

Prevalence: 5–18% of twin pregnancies; 5–15% of monozygotic multiple pregnancies; 15–30% of monochorionic twin gestations

Cause: unbalanced intrauterine shunting of blood through shared placental vessels

Time of onset: 2nd trimester with discordant amniotic fluid volumes

Path: large communication between arterial circulation of one twin + venous circulation of the other twin through arteriovenous shunt (= common villous district) deep within placenta

√ discrepant amniotic fluid volume (75%)
√ discordant BPD by > 5 mm (57%)
√ discordant estimated fetal weight > 25% (67–100%)

A. DONOR TWIN

= twin that transfuses the recipient twin + remains itself underperfused residing in an oligo- / anhydramniotic sac
• anemia + hypovolemia
• high output cardiac failure + hydrops (rare)
√ oligohydramnios (75–80%)
√ "**stuck twin**" ← severe oligohydramnios (60%) ← oliguria
√ amnion invisible ← close contact with fetal parts
√ fetus fixed relative to the uterine wall → without change during shift in maternal position

√ diminished / absent active fetal motion
√ absence of intermingling of fetal parts between twins
√ IUGR (= intrauterine growth restriction, common) diagnosed by discordant EFW of > 25%
√ morphologically normal

Prognosis: fetal death in utero

B. RECIPIENT TWIN

• polycythemia (higher hemoglobin)
• plethora = hypervolemia (volume overload)
√ polyhydramnios (70–75%) ← increased fetal urination
√ fetal hydrops (10–25%): pericardial + pleural effusions, ascites, skin thickening
√ organomegaly
√ fetus papyraceus = macerated dead fetus
√ velamentous cord insertion (64%)

Prognosis: 80–100% perinatal mortality if presenting < 28 weeks MA and left untreated

Cx: amniorrhexis, preterm labor

Rx: elective termination, volume-reduction amniocentesis of polyhydramniotic sac (decreases mortality rate to 34%), selective feticide, laser ablation of vascular anastomoses

DDx: IUGR of one dizygotic twin (two separate placentas, two different sexes)

UTERINE ANOMALIES

= MÜLLERIAN DUCT ANOMALIES

= anomalies of fusion of paramesonephric duct (= MÜLLERIAN DUCT) completed by 18th week of fetal life

Prevalence: 0.1–3%

◊ Uterine anomalies are found in 9% of women with infertility / repeated spontaneous abortions!

◊ 25% of women with uterine abnormalities have fertility problems

Associated with: urinary tract anomalies in 20–50%; possibly increased familial occurrence of limb reduction

Embryology:

(a) müllerian ducts develop at 5–6 weeks GA from coelomic epithelium and form uterovaginal canal by **lateral fusion** at 7–9 weeks GA

(b) by 8 weeks the uterovaginal canal reaches the urogenital sinus at the müllerian tubercle while a vaginal plate develops distally resulting in **vertical fusion** (upper $^{2}/_{3}$ to $\mathbf{4}/_{5}$ of vagina are of müllerian duct origin, lower ⅓ or $^{1}/_{5}$ of vagina originate from urogenital sinus)

Risk: spontaneous abortion, prematurity, IUGR, abnormal fetal lie, dystocia

Classification:

[classes in parenthesis refer to the classification of the American Fertility Society]

A. ARRESTED MÜLLERIAN DUCT DEVELOPMENT

1. bilateral: **Uterovaginal agenesis / hypoplasia** (class I)

I-A = Vaginal I-D = Tubal
I-B = Cervical I-E = Combination

I-C = Fundal

Prevalence: 1÷5,000; 5–10% of uterine anomalies

Often associated with: vaginal agenesis / hypoplasia

Age of detection: menarche

• primary amenorrhea

• normal secondary sex characteristics

√ small / absent uterus with small endometrial canal

√ ± endometrial layer

√ poor zonal differentiation + abnormal T2-hypointense myometrium

2. unilateral: **Unicornuate uterus** = Uterus unicornis unicollis (class II)

II-A = Communicating II-D = No cavity

II-B = Noncommunicating II-E = No horn

= failure of one müllerian duct to elongate / reach the urogenital sinus during 9th week of gestation

(a) with contralateral rudimentary horn

› cavitary = functioning endometrial tissue ("functional rudimentary horn")

» communicating with contralateral cavity (10%)

» noncommunicating (22%)

› noncavitary (33%) = no endometrial tissue

› noncavitary with endometrial strip (32%)

(b) without rudimentary horn

Frequency: 3–6–20% of uterine anomalies

May be associated with: ipsilateral renal agenesis

• infertility in 5–20%

√ reduced uterine volume

√ asymmetric ellipsoidal uterine configuration located in lateral aspect of pelvis

√ solitary fusiform "**banana-shaped**" uterine cavity with lateral deviation within pelvis terminating in a single fallopian tube on HSG

√ nonfunctional rudimentary horn of low SI on T2WI with loss of normal zonal anatomy

√ large high-signal-intensity cavity on T1WI + T2WI in functional rudimentary horn (= hematometra)

Cx: endometriosis ← cryptomenorrhea within endometrium-containing rudimentary horn; ectopic pregnancy ← transperitoneal sperm migration; abnormal fetal lie, IUGR; preterm delivery

3. **Mayer-Rokitansky-Küster-Hauser syndrome**

(1) vaginal agenesis / hypoplasia of proximal + middle segments

(2) intact normal ovaries + fallopian tubes

(3) variable anomalies of uterus (agenesis / hypoplasia, uni- or bicornuate)

(4) variable anomalies of urinary tract (renal agenesis, pelvic kidney in 40–50%) + skeletal system (12%)

mnemonic: MURCS complex

MÜllerian duct aplasia

Renal aplasia

Cervicothoracic **S**omite dysplasia

Frequency: 1÷4,000–1÷5,000

Cause: lack of müllerian development

- normal external genitalia; amenorrhea
- shallow distal vaginal pouch (derived from urogenital sinus)
- cyclic pelvic pain in 6–10% ← functioning endometrium within rudimentary uterine tissue

◊ 2nd most common cause of primary infertility

Rx: neovaginoplasty

B. TOTAL / PARTIAL FAILURE OF MÜLLERIAN DUCT FUSION = duplication defects = disorders of lateral fusion (75% of uterine anomalies)

1. **Uterus didelphys** (class III)

= failure of fusion of paramesonephric ducts at 9 weeks of gestation → complete duplication with 2 vaginas + 2 cervices + 2 uterine horns

Frequency: 11% of uterine anomalies

May be associated with: renal agenesis

- usually asymptomatic; frequently first diagnosed during routine obstetric sonography

√ two widely spaced uterine corpora with normal zonal anatomy and volume, each with a single fallopian tube

√ separate widely divergent uterine horns

√ large fundal cleft

√ cervical duplication

√ longitudinal vaginal septum (in 75%)

√ unilateral hemivaginal septum:

√ obstructing transverse vaginal septum between upper ⅓ and lower ⅔ of vagina connecting to longitudinal septum (commonly with ipsilateral renal agenesis)

√ opacification of single deviated horn on HSG

DDx: bicornuate bicollis uterus (communication between uterine horns maintained)

Cx: unilateral hydro- / hematocolpos (if transverse vaginal septum present) with reflux endometriosis

Rx: metroplasty is rarely performed

2. **Bicornuate uterus** = uterus bicornis (class IV)

IV-A = Complete IV-B = Partial

= lack of fusion of corpus

(a) bicornis bicollis = complete division down to external os

(b) bicornis unicollis = division down to internal os

Frequency: 10% of all uterine anomalies

√ external uterine fundal contour (MR):

√ concave heart-shaped surface depression > 1–2 cm deep

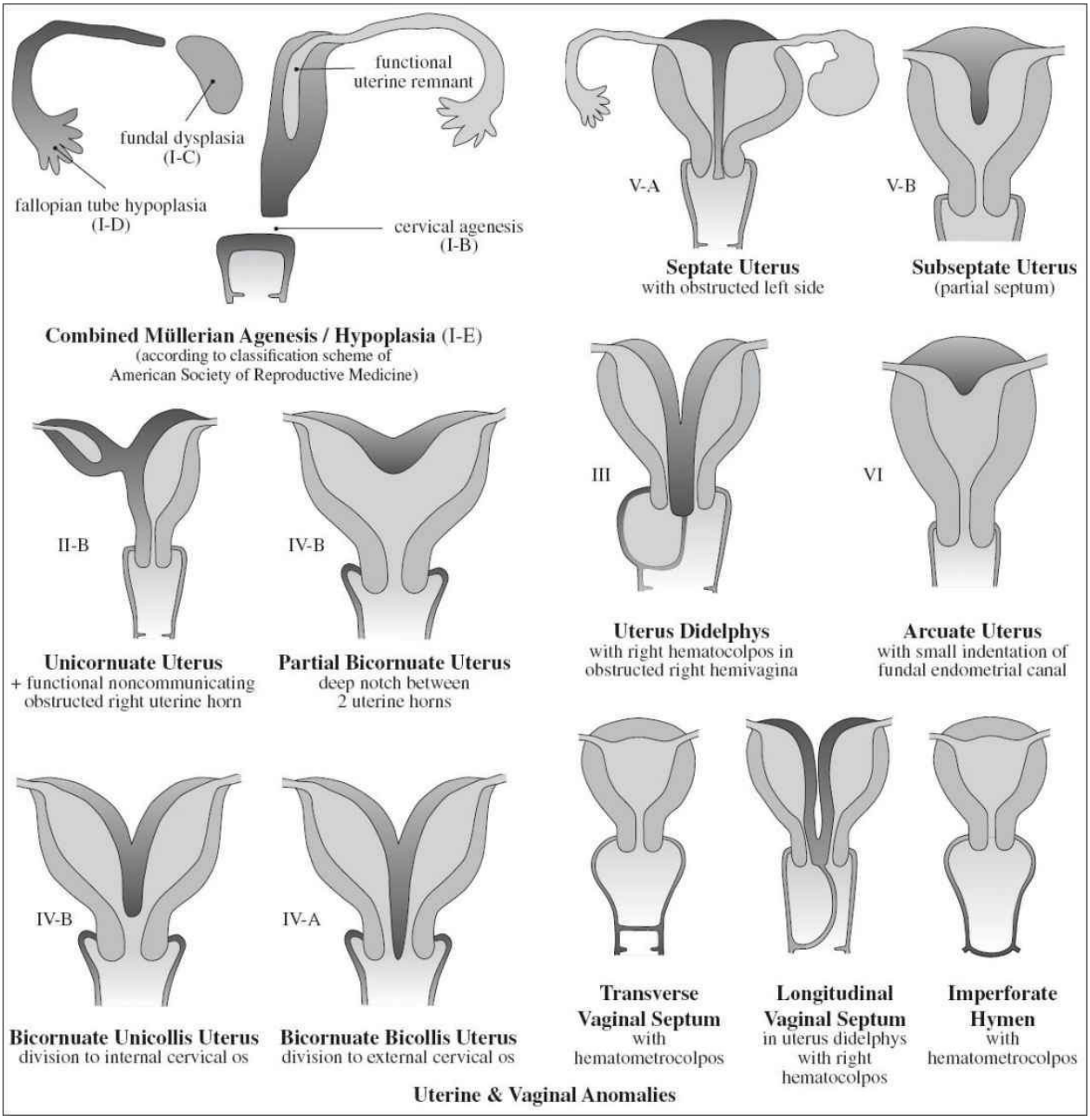
√ large fundal cleft

√ separation of uterine horns

√ intercornual angle of > 75–105° (demonstrated on luteal-phase US in conjunction with HSG)

√ intercornual distance (= distance between maximum lateral extent of hyperintense

endometrium on transaxial image) > 4 cm



√ divider between cornua comprised of myometrium / fibrous tissue / both
√ fusiform shape of each uterine horn with lateral convex margins
√ discrepancy in size of the 2 uterine horns
√ elongation + widening of cervical canal + isthmus

Laparoscopy: typical external fundal indentation

Cx: repeated spontaneous abortions in 30% (frequently in 2nd–3rd trimester), premature rupture of membranes, premature labor (20%), SGA infant, persistent malpresentations (transverse lie)

DDx: septate uterus (convex external contour)
◊ HSG is unreliable to distinguish bicornuate from septate uterus!

◊ 3-dimensional US is 90–92% accurate!
◊ MR is nearly 100% accurate!

Rx: transabdominal surgery to fuse uterine horns (abdominal / open metroplasty)

C. NONRESORPTION OF SAGITTAL UTERINE SEPTUM

1. **Septate uterus** (class V)

V-A = Complete V-B = Partial

= failure of resorption of septum by 12th week EGA

◊ Most common anomaly (55%) associated with reproductive failure in 26–65–94% unrelated to length of septum

Path: septum may be composed of fibrous tissue (low SI), myometrium (intermediate SI), or both

• generally asymptomatic ± unilateral obstruction, dysmenorrhea, normal menses, endometriosis

√ convex / flat / minimally indented (≤ 1 cm) external fundal contour

√ intercornual angle of ≤ 75° (MR more accurate than HSG with its projectional problems)

√ duplication of uterine horns on HSG (DDx to bicornuate uterus unreliable)

√ distal portion of septum hypoechoic to myometrium / of low SI on T2WI (= fibrous tissue)

Types:

(a) **Uterus septus**

= complete septum extending to internal os

√ endometrial canals completely separated by tissue isoechoic to myometrium extending into endocervical canal

(b) **Uterus subseptus**

= partial septum involving endometrial canal

Cx: 90% abortion rate (poor septal vascularity)

Rx: hysteroscopic metroplasty (= excision of septum)

2. **Uterus arcuatus** (class VI)

= nearly completely resorbed uterovaginal septum

◊ Most common anomaly unassociated with reproductive failure = normal variant

√ NO division of uterine horns

√ normal fundal contour

√ smooth indentation of fundal endometrial canal

√ increased transverse diameter of uterine cavity

√ single uterine canal with saddle-shaped fundus on HSG

D. INADEQUATE HORMONAL STIMULATION DURING FETAL DEVELOPMENT

= DES (= diethylstilbestrol)-related abnormalities (class VII)

• synthetic hormone used until 1971 to prevent miscarriage; rarely seen today

• may cause abnormal uterine morphology (with decreased fertility)

• increased risk of vaginal clear cell carcinoma

1. **Uterine hypoplasia**

associated with DES exposure in utero

√ mean uterine volume = 50 cm^3

2. **T-shaped uterus**
   Prevalence: 15% of women exposed to DES in utero
   √ low uterine volume
   √ uterine fundus thinner than cervix
   √ greater width than depth of corpus + fundus over cervix
   √ T-shaped lumen on hysterosalpingogram

E. VAGINAL SEPTUM ANOMALY

1. **Transverse vaginal septum**
   = failure of vertical fusion between vaginal plate (from urogenital sinus) + müllerian ducts around 5th month of gestation
   Path: fibrous membrane of connective tissue with vascular + muscular components
   • NO transillumination (DDx to imperforate hymen)
   Location: upper vagina (46%), mid-vagina (40%), lower vagina (14%)
   √ hematocolpos (balloon sonocolpography)
   √ thickness measurement of septum is needed
   DDx: congenital absence of cervix versus high septum (identification of cervix is crucial)
2. **Longitudinal vaginal septum**
   Cause: (a) failure of fusion of lateral müllerian ducts resulting in duplication of uterus, cervix (uterus didelphys), vagina
   (b) incomplete resorption of vaginal septum
   • difficulties with sexual intercourse / vaginal delivery
   √ low-signal-intensity septum distinct from surrounding high-signal-intensity of vaginal mucosa + secretions on T2WI
3. **Imperforate hymen**
   = failure at very end of vaginal recanalization process
   Prevalence: 0.1%; usually isolated finding; most common anomaly of female genital tract
   • primary amenorrhea + cyclic pelvic pain
   • ± bulging introitus in infancy (from vaginal mucus)
   • positive transillumination of bluish membrane
   Location: junction between urogenital sinus + sinovaginal bulb
   √ distended vagina bulging at introitus ← hydro- / hematocolpos
   √ hematocolpos with high-SI on T1WI + T2WI ← subacute bleeding episodes

UTERINE LEIOMYOMA

= FIBROID = MYOMA
= benign overgrowth of smooth muscle + connective tissue
◊ Most common gynecologic neoplasm! Commonest cause for uterine enlargement after pregnancy!
Prevalence: in 20–25% of White women; in 50% of Black women; Black÷White women = 3÷1 to 9÷1; 0.3–2.6% during pregnancy; account for 30% of all hysterectomies in USA
Path: whorl-like trabeculated mesenchymal tumor surrounded by pseudocapsule; may outgrow its blood supply resulting in:

(a) hyaline degeneration / fibrosis (> 60%)
= homogeneous eosinophilic bands / plaques of proteinaceous material in extracellular space
(b) myxoid degeneration (50%)
= gelatinous intratumoral foci of hyaluronic acid-rich mucopolysaccharides
(c) red / hemorrhagic / carneous degeneration (10%)
= massive hemorrhagic infarction ← venous thrombosis / rupture of intratumoral arteries; often during pregnancy / during use of oral contraceptives
• painful
(d) cystic degeneration (4%)
= extreme sequelae of edema
(e) calcification (4%)
= dense amorphous calcifications of hyalinized tissue

Specific types:
(1) **Lipoleiomyoma** (0.8%)
(2) **Myxoid leiomyoma** = rare soft translucent mass ← abundant myxoid material between smooth muscle cells, may be clinically malignant
(3) **Intravenous leiomyomatosis** = wormlike masses growing within pelvic veins
(4) Benign metastasizing leiomyoma
(5) **Diffuse leiomyomatosis** = development of innumerable small leiomyomas
√ symmetric enlargement of uterus
(6) **Peritoneal disseminated leiomyomatosis**
• frequently associated with pregnancy
√ multiple nodules on peritoneal surface

Histo: monoclonal proliferation of smooth muscle cells (NOT myometrial hyperplasia) separated by variable amounts of fibrous connective tissue

Hormonal dependency:
◊ Higher estrogen÷progesterone receptor ratio than in normal myometrium!
(1) Growth during pregnancy in 15–32% by a mean volume of 12 ± 6% within the 1st trimester (NOT during remainder of pregnancy)
◊ The larger the myoma, the greater the likelihood of growth
(2) Growth under estrogen therapy
(3) Shrinkage in puerperium + after menopause

Age: usually > 30 years; rare in girls < 18 years + in postmenopausal women

• asymptomatic in 70–75%; palpable abdominopelvic mass
• pelvic pressure:
  • urinary frequency ← compression of bladder
  • constipation ← impingement on rectosigmoid
• pain (in up to 30%) ← acute hemorrhagic infarction and necrosis, torsion of pedunculated subserosal fibroid, prolapse of pedunculated submucosal fibroid, compression of adjacent structures
• dysmenorrhea = colicky pelvic pain with menstruation
• abnormal uterine bleeding:
  • menorrhagia / hypermenorrhea = heavy + prolonged menstrual flow

- metrorrhagia = uterine bleeding outside time of menstruation
- infertility + early spontaneous fetal loss ← interference with embryo transfer + implantation in submucosal / intracavitary leiomyoma

Location: mostly in fundus + corpus; cervix (3–8%); fallopian tube; broad ligament; ovary

Classification by location in uterus:

1. **Intramural fibroid** (95%)
   = within confines of uterine outline
   - asymptomatic (mostly)
   - occasionally menorrhagia ← interference with normal uterine contractility
   - occasionally infertility ← compression of interstitial portion of fallopian tube / distortion of endometrial cavity
2. **Subserosal / exophytic / pedunculated fibroid**
   - usually asymptomatic; pain from infarction ← torsion

   √ "bridging vascular" sign = multiple feeding vessels arising from the uterine arteries + bridging the interface between uterus and any > 3 cm juxtauterine leiomyoma

   (a) **intraligamentous fibroid** (lateral growth between folds of broad ligament)
   - simulates ovarian mass
   - occasionally infertility ← compression of isthmic / ampullary portion of fallopian tube

   Cx: hydroureteronephrosis ← compression of ureter

   (b) **parasitic fibroid** = subserosal fibroid, which has become detached ← circulatory occlusion of vessels in pedicle; revitalized through omental / mesenteric blood supply

   √ may grow after hysterectomy
3. **Submucosal fibroid** (4–5–18%)
   = projecting into endometrial canal

   ◊ Most frequent symptomatic type of fibroid:
   - dysmenorrhea, menorrhagia, infertility
   - increased prevalence of early abortion

   Cx: hemorrhage, ulceration

   (a) fibroid polyp (2.5%) = partial / complete extrusion of pedunculated submucosal fibroid into cervical canal / vagina

Cystic, fatty, and calcific degeneration within a leiomyoma may lead to a heterogeneous imaging appearance internally, but a smooth outer contour, preserved mucosa, and negative Pap test are important features for differentiation from cervical carcinoma.

√ uterine enlargement
√ lobulated / nodular distortion of uterine outline (subserosal leiomyoma) + indentation of urinary bladder
√ distortion / obliteration of the contour of the uterine cavity (submucosal leiomyoma)
√ intramural soft-tissue mass (most frequent), usually multiple, solitary in 2%
√ speckled / ringlike / popcorn calcification

HSG:
√ mass effect on endometrial cavity
√ lack of tubal opacification with cornual leiomyoma

US (60% sensitivity, 99% specificity, 87% accuracy):

• point tenderness elicited with probe pushing on fibroid
√ hypoechoic solid concentric mass (< 33%) ← prevailing muscle component
√ echogenic attenuating mass ← prevailing dense fibrosis
√ sharp discrete refractory shadows (from borders between fibrous tissue and smooth muscle, margins of leiomyoma with normal myometrium, edges of whorls, bundles of smooth muscle)
√ anechoic features ← internal degeneration: atrophic, hyaline, cystic, myxomatous, lipomatous, calcareous, carneous, necrobiotic, hemorrhagic, proteolytic degeneration
√ acoustic shadowing (= calcifications)
◊ Presence of a prominent artery by color Doppler suggests potential for growth during pregnancy

CT:
√ hypo- / iso- (usually) / hyperdense mass
√ deformed uterine contour
√ calcifications (common)
@ Degenerated leiomyoma
√ central region of low attenuation
√ heterogeneous enhancement

MR (86–92% sensitive, 100% specific, 97% accurate; most accurate + desirable for planning myomectomy):
N.B.: subserosal, intramural and submucosal classification enabled by uterine zonal anatomy
√ hyperintense rim on T2WI in 33% (= pseudocapsule of dilated lymphatics / veins / edema)
√ enhancement pattern (usually later than for myometrium): 65% hypointense, 23% isointense, 12% hyperintense to myometrium
@ **Nondegenerated leiomyoma**
√ well-circumscribed mass of:
√ homogeneously low SI on T2WI compared with myometrium (for leiomyoma with variable amounts of collagen)
√ low to intermediate SI on T1WI = isointense to surrounding uterus
√ slightly higher SI + contrast enhancement on T2WI (for cellular leiomyoma with little / no collagen)
@ **Degenerated leiomyoma**
• localized pain + tenderness + fever + leukocytosis lasting for a few days
• enlargement of the uterus during pregnancy may interfere with blood supply to fibroids
√ low SI on T2WI ← hyaline / calcific degeneration)
√ low SI on T2WI + variable SI on T1WI ← hyaline / coagulative necrosis
√ high SI on T2WI ← cystic degeneration without enhancement of cystic areas
√ very high SI on T2WI ← myxoid degeneration with minimal enhancement
√ variable SI on T2WI ← red degeneration
√ peripheral / diffuse high SI on T1WI ← proteinaceous content of blood

Hysterosalpingography (9% sensitive, 97% specific, 76% accurate)

Cx:
(1) Infertility in 35%
(a) narrowing of isthmic portion of tube

(b) impingement on endometrium interfering with implantation; infertility rates highest for submucosal leiomyomas

(2) Complications during pregnancy

◊ Significantly increased for myomas > 6 cm in size / multiple in number / myomas > 200 cm^3 and when fibroid is retroplacental

(a) increased frequency of spontaneous abortions
(b) increased frequency of ectopic pregnancies
(c) increased frequency of IUGR
(d) preterm labor in 7% + premature rupture of membranes
(e) placental abruption
(f) uterine dyskinesia, uterine inertia during labor
(g) dystocia, obstruction of birth canal during vaginal delivery (if near internal os)
(h) abnormal presentation
(i) postpartum hemorrhage
(j) retained products of conception

(3) Hydroureteronephrosis
(4) Leg edema ← compression of pelvic vessels
(5) Sarcomatous transformation (in < 0.1%)

Rx: (1) Hysterectomy for pain, menorrhagia, visceral compression (after childbearing completed)

(2) Myomectomy for 2nd trimester fetal loss / anemia due to hypermenorrhea / pelvic pain

◊ Submucosal leiomyomas may be treated with hysteroscopic myomectomy

(3) Uterine artery embolization for symptomatic fibroids

DDx of necrotic leiomyoma:

(1) Ovarian mass: ovarian cyst, hemorrhagic cyst, endometrioma, cystic dermoid, cystadenoma, malignancy
(2) Ectopic interstitial pregnancy
(3) Intrauterine gestational sac
(4) Intrauterine fluid collection
(5) Hydatidiform mole
(6) Myometrial contraction (lasting for 15–30 minutes)
(7) Cervical tumor
(8) Hematoma of broad ligament

DDx of pedunculated subserosal leiomyoma:

(1) Ovary: use transvaginal US / MR to identify follicles!

DDx of leiomyoma by MR:

(1) Adenomyosis
(2) Solid adnexal mass: Brenner tumor, fibroma
(3) Focal myometrial contraction (transient)
(4) Uterine leiomyosarcoma

Uterine Lipoleiomyoma (0.8%)

= uncommon benign uterine neoplasm with substantial amount of fat due to fatty

metamorphosis
Cause: fatty metamorphosis of smooth muscle cells
Histo: smooth muscle + fat + connective tissue
Associated with: leiomyomas
Location: corpus; predominantly intramurally, endophytic or exophytic
US:
√ well-defined hyperechoic mass surrounded by hypoechoic ring of myometrium
CT:
√ predominantly fatty mass + areas of nonfat soft-tissue density tissue arising from uterus
MR:
√ hyperintense fat on T1WI + T2WI with chemical shift artifact

Benign Metastasizing Leiomyoma

= smooth muscle tumors in lung, lymph nodes, abdomen
Prevalence: < 60 cases
Classification:
(1) Benign metastasizing leiomyoma
Origin: uterus in mature women; progression with estrogen + regression with progesterone
• benign uterine leiomyoma removed many years earlier
Rx: hysterectomy, bilateral oophorectomy, long-term hormone therapy; good prognosis
(2) Metastatic leiomyoma
Origin: extrauterine primary in men + children (? slow-growing sarcoma)
Rx: surgical resection with mixed success
(3) Multiple fibroleiomyomatous hamartomas
Origin: lung; totally benign behavior
Spread: lymph nodes outside of pelvis, peritoneal surface, venous channels, lung, heart
• asymptomatic in most cases, fever, mild nonproductive cough
Histo: well-differentiated benign-appearing smooth muscle cells
√ multiple pulmonary nodules
√ miliary pattern
√ pedunculated pulmonary leiomyoma with cyst formation
√ giant cyst

UTERINE LEIOMYOSARCOMA

Prevalence: 0.67÷100,000; 25% of all uterine sarcomas
Cause: (a) de novo growth independent of leiomyoma!
(b) sarcomatous transformation of preexisting leiomyoma (in < 1% of leiomyomas)
Histo: infiltrative margins, nuclear atypia, increased mitotic figures
• rapidly enlarging uterus (< 3%)
√ mass with irregular margin
√ rapid change in size + appearance
√ extensive degeneration
√ loss of well-defined outer capsule

Dx: often first established by pathologist

UTERINE RUPTURE IN PREGNANCY

= disruption of all layers surrounding the fetus (membranes, decidua, myometrium, serosa)

Prevalence: 3–5% for classic cesarean sections; 1–2% for lower segment operations; 1% of pregnant trauma patients

Classification:

1. Spontaneous rupture during labor
2. Traumatic rupture during delivery
3. Rupture ← myometrial scars / disease
4. Rupture during blunt trauma

Predisposed: previous uterine surgery, previously excessively long / difficult labor

• pain, shock, absent fetal heart tones

Location:

(a) corpus with rupture before onset of labor

(b) lower uterine segment during labor, L > R

√ full-thickness defect of uterine wall

√ extrusion of fetus into the abdomen

√ hemoperitoneum

Cx: hypofibrinogenemia (triggered by excessive blood loss, trauma, amniotic fluid embolism)

Mortality: 2–20% maternal mortality; 10–25% fetal mortality

DDx: **Uterine dehiscence** = rupture of only myometrium

UTERINE TRAUMA DURING PREGNANCY

Prevalence: 6–7%

Cause: motor vehicle accident (70%), physical abuse (10%)

During pregnancy at increased risk for:

› serious abdominal injury ← enlarged spleen, displacement of spleen and liver closer to rib cage

› complex multiple intestinal injuries ← bowel displacement superiorly

› bladder injury ← compression of bladder

› collecting-system injury ← hydronephrosis of pregnancy

› pelvic hemorrhage ← engorged ovarian + pelvic veins

1. Placental abruption
   complete (6–66%) / incomplete (30–80%)
   • more common > 16 weeks of gestation
   Prognosis: 67–75% rate of fetal mortality
2. Uterine rupture (0.6%)
   Prognosis: nearly 100% fetal mortality; up to 10% maternal mortality
3. Premature rupture of membranes
4. Fetal injury: eg, cerebral injury
5. Fetal death

The major cause of fetal death is maternal death!

US: evaluate fetal motion, breathing, heart rate, placenta

Essentially all **diagnostic ionizing** imaging examinations for evaluation of traumatic injury are well below 50 mGy and NOT associated with an increased risk of fetal anomalies or fetal loss throughout pregnancy!

VAGINAL AGENESIS

◊ 2nd most common cause of primary amenorrhea

Prevalence: 1÷4,000–5,000 women

• cyclic abdominal pain

May be associated with:

(1) Uterine + partial tubal agenesis (90%)
(2) Unilateral renal agenesis / ectopia (34%)
(3) Skeletal malformations (12%)
(4) McKusick-Kaufman syndrome (hydrometrocolpos + polydactyly + heart defects)
(5) Ellis-van Creveld syndrome

VASA PREVIA

= presence of abnormal fetal vessels within amniotic membranes that are unsupported by Wharton jelly / placental tissue and cross internal cervical os / lower uterine segment in advance of fetal parts

Prevalence: 0.04%

At risk: 2nd-trimester low-lying placenta / placenta previa, velamentous cord insertion, succenturiate placenta, in vitro fertilization, and multiple gestation

Cause:

(a) cord vessels of velamentous (membranous) cord insertion from low-lying placenta connecting to main body of placenta
(b) vessels connecting portions of a bilobed placenta
(c) vessels connecting succenturiate lobe to main portion of placenta

√ Doppler ultrasound demonstrates flow within aberrant vessels overlying the internal os

Cx: (1) tear of fetal vessels after rupture of membranes / due to direct injury during labor → fetal exsanguination
(2) Cord compression by presenting part during labor
(3) Cord prolapse

Rx: cesarean delivery

Prognosis: 50–100% fetal mortality; fetal survival rate improves from 44% to 97% if recognized

DDx: prominent maternal sinus vessels at edge of marginal previa (= marginal sinus previa)

VELAMENTOUS CORD INSERTION

= umbilical cord insertion into membranes outside placental margin = attachment of cord to chorion laeve

Prevalence: 0.09–1.8%, more frequent in multiple gestations

• low Apgar scores
• abnormal intrapartum fetal heart rate patterns

√ segments of umbilical cord course between amnion + chorion unprotected by Wharton jelly / placenta
√ splayed umbilical vessels at periphery of placenta

Associated with:

(a) multiple gestation, uterine anomaly, IUD
(b) congenital anomalies (in 5.9–8.5%):
asymmetric head shape, spina bifida, esophageal atresia, obstructive uropathy, VSD, cleft palate

Cx:
(1) IUGR
(2) Preterm labor
(3) Placental abruption

Risk:
(1) Cord compression
(2) Rupture of cord with traction during delivery
(3) Vasa previa
(4) Neonatal demise

Table of Dose, Energy, Half-Life, Radiation Dose					
Organ	*Pharmaceutical*	*Dose*	*keV*	$T_{½}$ *phys*	$T_{½}$ *bio*
Brain	^{99m}Tc-pertechnetate	10–30 mCi	140	6 hr	
	^{99m}Tc-DTPA	10 mCi	140	6 hr	
	^{99m}Tc-glucoheptonate	10 mCi	140	6 hr	
	^{99m}Tc-Ceretec®	20 mCi	140	6 hr	
	^{123}I Spectamine®	3–6 mCi	159	13.6 hr	
CSF	^{111}In-DTPA	500 µCi	173, 247	2.8 d	
	^{99m}Tc-DTPA	1 mCi	140	6 hr	
Cardiac	^{201}Tl	1–2 mCi	72, 135, 167	73 hr	
	^{99m}Tc-pyrophosphate	15 mCi	140	6 hr	
	^{99m}Tc-pertechnetate	15–25 mCi	140	6 hr	
	^{99m}Tc–labeled RBCs	10–20 mCi	140	6 hr	
	^{99m}Tc-sestamibi	25 mCi	140	6 hr	
	^{99m}Tc-teboroxime	30 mCi	140	6 hr	
Liver	^{99m}Tc-sulfur colloid	3–5 mCi	140	6 hr	
	^{99m}Tc-DISIDA	4–5 mCi	140	6 hr	
Lung	^{127}Xe	5–10 mCi	172, 203, 375	36.4 d	13 sec
	^{133}Xe	10–20 mCi	81, 161	5.3 d	20 sec

	^{81m}Kr	20 mCi	176, 188, 190	13 sec	
	^{99m}Tc-MAA aerosol	3 mCi	140	6 hr	8 hr
Kidney	^{99m}Tc-DTPA	15–20 mCi	140	6 hr	
	^{99m}Tc-DMSA	2–5 mCi	140	6 hr	
	99mTc-glucoheptonate	15–20 mCi	140	6 hr	
	99mTc-mercapto-acetyltriglycine	10 mCi	140	6 hr	
	131I-Hippuran	250 µCi	365*	8 d	18 min
	123I-Hippuran	1 mCi	159	13.2 hr	
Thyroid	99mTc-pertechnetate	5–10 mCi	140	6 hr	
	123I	50–200 µCi	159	13.2 hr	
	125I	30–100 µCi	27, 35	60 d	
	131I	30–100 µCi	365*	8 d	
Testes	99mTc-pertechnetate	10 mCi	140	6 hr	
Gastric mucosa	^{99m}Tc-pertechnetate	50 µCi / kg	140	6 hr	
Gallium	^{67}Ga-citrate	3–5 mCi	93, 184, 296, 388	3.3 d	
WBC	^{111}In-oxine	550 µCi	173, 247	2.8 d	
	$^{9^{9m}}$Tc-Ceretec	10–20 mCi	140	6 hr	
mnemonic:	* = as many days as in a year				

Radiation Dose to Critical Organs		
Radiopharmaceutical	*Critical Organ*	*rad/mCi*
^{131}I	Thyroid	1,000
^{125}I	Thyroid	900
^{111}In-oxine WBC	Spleen	26
^{123}I	Thyroid	15
^{111}In-DTPA	Spinal cord	12
^{201}Tl	Kidney	1.5
^{67}Ga-citrate	Colon	1.0
^{99m}Tc-MAA	Lung	0.4
^{99m}Tc-albumin microspheres	Lung	0.4
^{99m}Tc-DISIDA	Large bowel	0.39
^{99m}Tc-sulfur colloid	Liver	0.33
^{99m}Tc-pertechnetate	Intestine	0.3
	Thyroid	0.15
^{99m}Tc-glucoheptonate	Kidney	0.2
^{99m}Tc-pertechnetate (+ perchlorate)	Colon	0.2
^{99m}Tc-pyrophosphate	Bladder	0.13
^{99m}Tc-phosphate	Bladder	0.13
^{99m}Tc DTPA	Bladder	0.12
^{99m}Tc–tagged RBCs	Spleen	0.11
^{99m}Tc-albumin	Blood	0.015
^{133}Xe	Trachea	

Pediatric Dose

Actual doses for pediatric patients may vary in different institutions based on empirical data. As rough guidelines use:

1. Clark's rule (body weight):
   $Dose_{Ped} = Body\ weight\ [in\ lbs]\ /\ 150 \times Dose_{Adult}$
2. Young's rule (child up to age 12):
   $Dose_{Ped} = Age\ of\ child\ /\ (Age\ of\ child + 12) \times Dose_{Adult}$
3. Surface area:
   $Dose_{Ped} = (weight\ [in\ kg]^{0.7}\ /\ 11)\ /\ 1.73 \times Dose_{Adult}$

Lactating Patients

1. Nursing mothers must be counseled about the need to interrupt / discontinue breast feeding
2. Pumped milk may be refrigerated and used after the radioactivity has decayed

Complete cessation of breast feeding:

^{67}Ga-citrate

^{131}I-sodium iodide therapy

Interruption of breast feeding for 12 hours:

^{99m}Tc-macroaggregated albumin

^{99m}Tc-labeled RBCs (in vivo labeling)
^{111}In-labeled WBCs

Interruption of breast feeding for 24 hours:

^{99m}Tc-pertechnetate
^{123}I-metaiodobenzylguanidine
^{99m}Tc-labeled WBCs

Interruption of breast feeding for 168 hours:

^{210}Tl-chloride

QUALITY CONTROL OF RADIOPHARMACEUTICALS

◊ Quality control logs should be kept for 3 years!

Production of Radionuclides

Reactor-produced Radionuclides

◊ Not carrier free = contamination with other forms
» Thermal neutrons captured by stable nuclides
» Used to produce standard generators

(1) ^{99}Mo/^{99m}Tc generator

(parent) (daughter)

^{99}Mo → ^{99m}Tc → ^{99}Tc → ^{99}Ru

67 hours 6 hours 2.1 x 105 years stable

glass column filled with aluminum (Al_2O_3); parent and daughter isotopes are firmly absorbed onto aluminum at top of column; daughter isotope can be separated / eluted by passing isotonic oxidant-free NaCl through the column

(2) ^{81m}Kr generator

(parent) (daughter)

^{81}Rb → ^{81m}Kr → ^{81}Kr

4.7 hours 13 seconds stable

Accelerator / Cyclotron-produced Radionuclides

◊ Generally carrier-free product
• collision of charged particles (protons, deuterons, helium, alpha particles) with target nuclide
• used to produce ^{67}Ga, ^{123}I, ^{201}Tl

Fission-produced Radionuclides

◊ Carrier-free product
• splitting of a heavy nucleus into smaller nuclei
• used to produce ^{131}I, ^{99}Mo

Radionuclide Impurity

= amount (µCi) of radiocontaminant per amount (µCi/mCi) of desired radionuclide

^{99}Mo Breakthrough Test

Test frequency: with every elution

(a) NRC allowable contamination of 1÷1,000
= 1 μCi ^{99}Mo per 1 mCi of ^{99m}Tc
(b) USP limit of 0.15 μCi ^{99}Mo per 1 mCi ^{99m}Tc
(c) < 5 μCi ^{99}Mo per administered dose (NRC dropped this requirement, but nonagreement states may still require this)
(d) chemical evaluation: ^{99}Mo contaminated eluate forms colored complexes with phenylhydrazine (for reactor product generators)

- measured in dose calibrator with lead shielding of vial (filters 140 keV but permits 740 and 780 keV of ^{99}Mo to pass through)

Effect of impurity: increased radiation dose, poor image quality

Radiochemical Impurity

Test frequency: with every elution

Precise registration of different compounds of ^{99m}Tc, eg,

› hydrolyzed reduced technetium (HR Tc) a radiocolloid [$TcO(OH)2 \bullet H_2O$]
Limit: < 2% (presently no legal limit)
› free pertechnetate $[TcO^4]^{-1}$

- can be monitored by paper chromatography

Effect of impurity with hydrolyzed reduced Tc:
RES uptake, poor image quality, increased radiation dose

Chemical Impurity

Chemicals from elution process are restricted in their amount (NRC limit):

^{99m}Tc: < 10 μg Al^{3+} per 1 mL eluate if radionuclide from fission generator; < 20 μg Al^{3+} per 1 mL eluate if radionuclide from thermal activation generator

Aluminum Ion Breakthrough Test:

Test frequency: with every elution

- one drop of generator eluate placed on one end of special test paper containing aluminum reagent
- equal-sized drop of a standard solution of Al^{3+} (10 ppm) is placed on other end of strip
- if color at center of drop eluate is lighter than that of standard solution, the eluate has passed the colorimetric test

Effect of impurity: degradation of image quality

Radiopharmaceutical Sterility and Pyrogenicity

USP XX Test

Monitor rectal temperature of 3 suitable rabbits after injection of material via ear vein

Acceptable results: no rabbit shows a rise of > 0.6°C; total rise for all three rabbits < 1.4°C

Limulus Amoebocyte Lysate Test (LAL)

◊ Highly specific for Gram-negative bacterial endotoxins, sensitivity 10 x greater than USP XX test

Amoebocyte = primitive blood cell of horseshoe crab (Limulus polyphebus); lysate

	formed by hydrolysis of amoebocyte
Positive result:	in the presence of minute amounts of endotoxin LAL forms an opaque gel; response to other pyrogens (particulate contaminations, chemicals) doubtful

QUALITY CONTROL OF CALIBRATORS

Quality Control for Dose Calibrators

Test	*When*	*Limit*	*Test Isotopes*
Constancy	daily,*	< ±5%	^{137}Cs
Channel check	daily,*	< ±5%	^{137}Cs
Linearity	quarterly,*	< ±5%	^{99m}Tc
Accuracy	annually,*	< ±5%	^{137}Cs, ^{57}Co, ^{133}Ba
Geometry	*	< ±1.6%	^{99m}Tc
* = after install / repair			

Dose Calibrator

= gas ionization chamber → transforms photon flux into current with digital readout

Disadvantages:

(1) open top geometry

(2) nonlinearity between photon energy and measured current (corrected with a calibration factor)

Constancy = Precision

= reproducibility over time

Test frequency: daily

Method: measurement of a long-lived source, usually 137Cs standard

Evaluation: measurement must fall within ± 5% of the calculated activity

Linearity

= accurate measurement over large range of activity levels

Test frequency: 4 x per year

Method: 1 mCi source activity is measured every 4 hours for 10 / more measurements (down to 10–100 μCi)

Evaluation: measurements must fall within ± 5% of the calculated physical decay curve

Accuracy

Test frequency: annually

Method: measurements of three different activity standards whose amount is certified by the National Bureau of Standards (NBS); standard values are decayed mathematically to calibrator date

^{99m}Tc: 140 keV, half-life of 6.01 hr

^{57}Co: 123 keV, half-life of 270 d

^{133}Ba: 356 keV, half-life of 10.5 yr

^{137}Cs: 662 keV, half-life of 30.1 yr

Evaluation: measurements must fall within expected range

Geometry

= to ensure that measurement is not dependent upon location of tracer within ionization chamber (usually done by manufacturer)

Test frequency: at installation / after factory repair / recalibration

Method: 0.5 mL of ^{99m}Tc (activity 25 mCi) is measured in a 3-mL syringe; syringe contents are then diluted with water to 1.0 mL, 1.5 mL, and 2.0 mL and each level remeasured; test is repeated with a 10-mL glass vial

QUALITY CONTROL FOR SCINTILLATION CAMERA

Quality Control for Gamma Cameras

Test	*When*	Test Result
Peaking	daily	^{99m}Tc and ^{57}Co
Energy resolution	daily	< 14% at FWHM
Extrinsic field uniformity	daily	< 5% RMS variation
Bar phantom	weekly	visual assessment
Field uniformity	monthly	visual assessment
Center of rotation	monthly	visual assessment
Jaczak phantom	quarterly	visual assessment

Peaking

= ensures that window of pulse height selector is correctly set to desired photopeak

(a) for ^{99m}Tc source: between 137 and 143 keV

(b) for ^{57}Co source: between 117 and 123 keV

Frequency of quality control: daily

Field Uniformity

= ability of camera to reproduce a uniform radioactive distribution = variability of observed count density with a homogeneous flux

(a) Integral uniformity = maximum deviation

(b) Differential uniformity = maximum rate of change over a specified distance (5 pixels)

Causes for nonuniformity:

(1) High kilovoltage drift of photomultiplier tubes
(2) Physical damage to collimator
(3) Improper photopeak setting
(4) Contamination

Frequency of quality control: daily

Evaluation:

(1) Compare uncorrected with corrected images. Note acquisition time!
(2) Store correction flood
(3) Rerecord image with corrected flood + check for uniformity

(4) Variation in image should be < 5% RMS

Intrinsic Field Uniformity Test

(without collimator)

1. Remove collimator + replace with lead ring (to eliminate edge packing)
2. Place a point source at a distance of at least 5 crystal diameters from detector (4–5 feet for small, 7–9 feet for large crystals)
3. Point source contains 200–400 μCi of ^{99m}Tc for minimal personnel exposure (avoid contamination of crystal)
4. Set count rate below limit of instrument (< 30,000 counts)
5. Adjust the pulse height selector to normal window settings by centering at 140 keV with a window of 15% (for ^{99m}Tc studies only)
6. Use the same photographic device
7. Acquire 1.25 million counts for a 10" field of view, 2.5 million counts for a 15" field of view
8. Register counts, time, CRT intensity, analyzer settings, initials of controller

Extrinsic Field Uniformity Test

(with collimator on)

1. Collimator is kept in place
   - ◊ Only 1 of 2,000 gamma rays that reach the collimator are transmitted to the sodium iodide crystal!
2. Sheet source / flood of 2–10 mCi activity is placed on collimator
   (a) fillable floods: mix thoroughly, avoid air bubbles, check for flat surface
   (b) nonfillable: commercially available ^{57}Co source
3. Other steps as described above

Spatial Resolution / Linearity

A. SPATIAL RESOLUTION

= parameter of scintillation camera that characterizes its ability to accurately determine the original location of a gamma ray on an X,Y plane; measured in both X and Y directions; expressed as full width at half maximum (FWHM) of the line spread function in mm

(a) intrinsic spatial resolution
(b) system spatial resolution

B. INTRINSIC SPATIAL LINEARITY

= parameter of a scintillation camera that characterizes the amount of positional distortion caused by the camera with respect to incident gamma events entering the detector

(a) differential linearity = standard deviation of line spread function peak separation (in mm)
(b) absolute linearity = maximum amount of spatial displacement (in mm)

Frequency of quality control: every week

Method:

1. Mask detector to collimated field of view (lead ring)
2. Lead phantom is attached to front of crystal

(a) Four-quadrant bar pattern (3 pictures each after 90° rotation to test entire crystal)
(b) Parallel-line equal-spacing (PLES) bar pattern [2 pictures]
◊ Change bar direction angles weekly
(c) Smith orthogonal hole test pattern (OHP) [one picture only]
(d) Hine-Duley phantom [2 pictures]

3. Set symmetric analyzer window to width normally used
4. Place a point source (1–3 mCi) at a fixed distance of at least 5 crystal diameters from detector on central axis (remove all sources from immediate area so that background count rate is low)
5. Acquire 1.25 million counts for a small field, 2.5 million counts for a large field on the same media used for clinical studies
6. Record counts, time, CRT intensity, analyzer setting, initials of controller

(All new cameras are equipped with a spatial distortion correction circuit)

Evaluation:
visual assessment of (1) Spatial resolution over entire field (2) Linearity

Intrinsic Energy Resolution

= ability to distinguish between primary gamma events and scattered events; performed without collimator; expressed as ratio of photopeak FWHM to photopeak energy (in %)

Limit: 11% for SPECT, 14% for some planar cameras

Frequency of quality control: daily (may be weekly for some cameras)

CRT-output / Photographic Device

(1) Check for dirt, scratches, burnt spots on CRT face plates
(2) Adjust gray scale + contrast settings to suit film

SPECT QUALITY CONTROL

= SINGLE PHOTON EMISSION COMPUTED TOMOGRAPHY

= gamma cameras rotating about a pallet supporting the patient obtain 60–120 views over 180° / 360° rotation with typically a field of view of 40–50 cm across the patient and 30–40 cm in axial direction

Spatial resolution: ~8 mm for high-count study

SPECT Uniformity

1. 64 x 64 word matrix = 30 million count flood with collimator, orientation and magnification same as patient study
2. ^{57}Co sheet source with < 1% uniformity variance is necessary
3. 128 x 128 word matrix = 120 million count flood with collimator, orientation, magnification same as patient study

Frequency of quality control: weekly

Center of Rotation (COR)

1. ^{99m}Tc-filled line source (5–8 mCi) positioned 3–5 cm off the center of rotation while keeping scanning palette out of field of view
2. Direction of rotation to be the same as in patient study

3. Number of steps (32, 64, or 128) to be the same as in patient study
4. Time per step such that at least 100K counts are acquired
5. COR must be done with same collimator, orientation, and magnification as patient study

Frequency of quality control: weekly

Jaczak Phantom SPECT Study

tests multiple camera systems with a final image

- phantom contains multiple objects of various sizes (hot and cold rods and cold balls)
- final reconstructed image is visually assessed

SPECT Sources of Artifacts

1. Scanning palette in field of view
2. Collimator shifting + rotation on camera face
3. Noncircular orbit of camera head
4. PMT failure
5. PMT uncoupling
6. Cracked crystal
7. Improper peaking of camera

SOURCES OF ARTIFACTS

A. Attenuator between source and detector

Materials: cable, lead marker, solder dropped into collimator during repair, belt buckle / watch / key on patient, defective collimator

(a) at time of correction flood procedure:
√ hot spot

(b) after correction flood procedure:
√ cold spot

B. Cracked crystal
√ white band with hot edges

C. PMT failure + loss of optical coupling between PMT + crystal
√ cold defect

D. Problems during film exposure + processing
1. Double exposed film
2. Light leak in multiformat camera
3. Water lines from film processing
4. Frozen shutter:
√ part of film cut off
5. Variations in film processing

E. Improper window setting
1. Photopeak window set too high:
√ hot tubes
2. Photopeak window set too low:
√ cold tubes

F. Administration of wrong isotope
√ atypically imaged organs

G. Excessive amounts of free ^{99m}Tc-pertechnetate
√ too much uptake in choroid plexus, salivary glands, thyroid, stomach

H. Faulty Injection Technique
eg, inadvertently labeled blood clot in syringe leading to iatrogenic pulmonary emboli

I. Contamination with radiotracer
on patient's skin, stretcher, collimator, crystal

J. CRT problems
1. Burnt spot on CRT phosphor
2. Dirty / scratched CRT face plates

POSITRON EMISSION TOMOGRAPHY

= PET = technique that permits noninvasive in vivo examination of metabolism, blood flow, electrical activity, neurochemistry

Concept: measurement of distribution of a biocompound as a function of time after radiolabeling and injection into patient

Labeling: PET compounds are radiolabeled with positron-emitting radionuclides

Physics:

^{18}F = positron-emitting (β+) radionuclide → positron matter-antimatter annihilation reaction with an electron (β–) → formation of **annihilation photons** (511 keV each) emitted in exactly opposite directions

Detection of positron annihilation photons:

simultaneous arrival of dual photons at detectors (bismuth germanate-68) on opposite sides of the patient (= electronic collimation through **coincidence circuitry**)

N.B.: lead collimators not necessary (= advantages in resolution + sensitivity over SPECT); spatial reconstruction similar to transmission CT

Radionuclide Production in PET

in nuclide generator / particle accelerator (positive / negative ion cyclotron; linear accelerator)

Expected amount of radionuclide: 500–2,000 mCi

Generator characteristics:

beam energy (radionuclide production rate increases monotonically with beam energy), beam current (production rate directly proportional to beam current), accelerated particle, shielding requirement, size, cost

Radiopharmaceutical Production in PET

(1) Initialize accelerator, setup
(2) Irradiation
(3) Synthesis
(4) Sterility test, compounding

Sensitivity of PET

= fraction of radioactive decays within the patient that are detected by the scanner as true events (measured in counts per sec per microcurie per milliliter)

◊ 30–100 times more sensitive than SPECT ← electronic collimation as opposed to lead

collimation!

Resolution of PET

= resolving power = smallest side-by-side objects that can be distinguished as separate objects in images with an infinite number of counts (measured in mm); determined by
- › distance a positron travels before annihilation occurs (usually 0.5–2 mm depending on energy)
- › angle variation from 180° (±5° = 0.5 mm)
- › physical size of detector (1–3 mm)

◊ Typical spatial resolution: 4–7 mm (reconstructed spatial resolution = 5–6 mm full width at half maximum in phantom measurements)

◊ In clinical practice spatial resolution is about 10 mm

Detection dependent on:

(1) Tumor size
(2) FDG activity
(3) Tumor-to-background ratio
(4) Effect of motion

◊ A smaller than 1 cm lesion can be detected when conditions are favorable

Radioactivity Distribution in PET

Pixel values proportional to radioactivity per volume

Unit: mg of glucose per minute per 100 g tissue

Imaging time: 1–10 min

Common Radiopharmaceuticals in Positron Emission Tomography

Isotope		*Use*	*Half-life (min)*	*Average Positron Energy (keV)*	*Typical Reaction*	*Yield at 10 MeV (mCi/μA EOSB)*
Rubidium	^{82}Rb		1.23	1,409	Sr/Rb generator	—
Fluorine	^{18}F	glucose metabolism	110.00	242	$^{18}O(p,n)^{18}F$	120
Oxygen	^{15}O	O_2, H_2O, CO_2, CO	2.1	735	$^{15}N(p,n)^{15}O$	70
Nitrogen	^{13}N	perfusion of NH_3	10.00	491	$^{13}C(p,n)^{13}N$	110
Carbon	^{11}C	carbon metabolism	20.3	385	$^{14}N(p,\alpha)^{11}C$	85

p = proton injected; n = neutron ejected; = alpha particle; EOSB = end of saturated bombardment (infinitely long irradiation at which time the numbers of radionuclides produced equals the number of radionuclides that are decaying) per microampere of beam current (= number of particles per sec emerging from accelerator and impinging on target material)

Organ-specific Concentration

(a) heart, brain: contain little glucose-6-phosphatase → resulting in high concentrations of ^{18}F-fluorodeoxyglucose
- › metabolic rate of glucose is proportional to phosphorylation rate of FDG

(b) liver: abundance of glucose-6-phosphatase + low levels of hexokinase resulting in rapid clearing of FDG

(c) urine: 50% of injected activity excreted unmetabolized in urine

(c) neoplasm: enhanced glycolysis with increased activity of hexokinase + other enzymes

FDG Distribution

Intense accumulation in: brain, myocardium, intrarenal collecting system + ureter + bladder

Moderate accumulation in: liver, spleen, bone marrow, renal cortex, mediastinal blood pool

Sites of variable physiologic uptake:

@ **Brown (baby) fat**
= highly specialized heat producing tissue in response to cold exposure / ingestion of food (= nonshivering / diet-induced thermogenesis)
Histo: increased vascularity + high density of mitochondria → generation of heat
Location:
suboccipital cervical and supraclavicular region; paraspinal region of neck and chest; intercostal spaces at costovertebral junction; lipomatous hypertrophy of the interatrial septum, axilla; retrocrural; mediastinum adjacent to thoracic vessels; perinephric fat
◊ Keep uptake room warm; use warm blankets

@ Brain & spinal cord intense uptake in cerebral > cerebellar cortex, basal ganglia, thalamus; moderate uptake in cervical + upper thoracic spine
◊ Often used as a reference for semiquantification

@ Bone marrow usually mild uptake with homogeneous distribution; moderate to intense uptake after chemotherapy + treatment with GCsF (granulocyte colony-stimulating factor) + in anemic patients

@ Nasopharynx Waldeyer ring (negative correlation between age and uptake intensity); sublingual glands (mucous gland with inverted V-shaped uptake at floor of mouth)

@ Thyroid gland moderate / intense uptake in ⅓ of euthyroid patients; consistent with chronic thyroiditis, Graves disease

@ Thymus mild to moderate intensity; rebound hyperplasia + increased uptake for 3 months to 1 year

@ Digestive tract
Cause: metabolically active smooth muscle + mucosa, swallowed secretions, microbial uptake
› esophagus: more intense at GE junction
› stomach: SUV usually < 3.8, may be as high as 5.6
› small bowel: isolated foci with SUV < 4
› colon: right colon may have an SUV as high as 10 (lymphatic cells); moderate to intense uptake in rectum
◊ Enemas do not reduce uptake!

@ Liver hepatocytes have a higher concentration of phosphatase enzymes → resulting in dephosphorylation of FDG-6-phosphate + a faster FDG washout
◊ Delayed imaging for indeterminate liver lesion

@ Spleen diffuse uptake as physiologic reaction to extrasplenic infection, granulocyte colony-stimulating factor therapy, anemia (extramedullary hematopoiesis)

@ Skeletal muscle Major energy sources: fat and glucose (at rest 9÷1, at low exercise 6÷4, at high exercise 1÷9);
› Diabetics take medication, have morning meal within 4 hours prior to imaging
◊ No muscle effort for 24 hours before PET imaging
◊ No chewing gum / tobacco, reading, talking during uptake phase
Location: extraocular muscles; paravertebral muscles in neck + thorax (stress-

induced, patient anxiety); intrinsic laryngeal muscles (speech); diaphragm (hyperventilation, forced respiration)

@ Myocardium free fatty acids are predominant metabolic substrate (50–70%); insulin → increases glucose transporters (GLUT-1 + GLUT-2) → glucose utilization increases after carbohydrate (glucose, lactate) intake
  ◊ Fasting (≥ 4 hours since last meal) switches to predominantly fatty acid metabolism:
    › fall of plasma insulin levels → ⇑ in lipolysis in peripheral tissue + ⇑ fatty acid levels in plasma
    › decrease of glucose transport into myocytes

@ Genitourinary tract pooling in upper pole calix, dilated redundant ureter, bladder diverticulum, endometrial uptake, testes (young patients)
  ◊ Catheterization of bladder to reduce activity + filling with 200 mL of saline just before pelvic imaging

Sites of benign pathologic uptake:

@ Healing bone (for months)

@ Lymph nodes active granulomatous disease (TB, sarcoidosis), infection, recent instrumentation

@ Joints degenerative / inflammatory joint disease (often in sternoclavicular + acromioclavicular + shoulder joints), tendinopathy, enthesopathy, bursitis

@ Infection / inflammation leukocytic infiltration in abscess, pneumonia, sinusitis, granulomatous infection, talc pleurodesis, acute pancreatitis, healing by secondary intention, wound repair, resorption of necrotic debris, hematoma, fistula

Effect of Blood Glucose Level on FDG-Uptake	
Blood Glucose Level [mg/dL]	*Maximum SUV Uptake in Brain*
< 80	13,3 ± 3.7
80–110	12.1 ± 3.2
110–150	9.8 ± 2.4
150–200	7.8 ± 3.1
> 200	4.8 ± 1.8

Focal areas of abnormally increased FDG uptake are suspicious for malignant disease secondary to metabolic alterations that precede morphologic changes.

PET Imaging in Oncology

FDG = glucose analogue tracer 2-[^{18}fluorine]-fluoro-2-deoxy-D-glucose

Pathophysiology:

serum glucose competes with FDG for entry into tumor cells → FDG becomes phosphorylated by hexokinase (malignant cells have increased hexokinase activity → high rate of glycolysis) → FDG-6-phosphate does NOT enter glycolysis pathway → ^{18}FDG trapped intracellularly

Preparation:

(1) fasting for 6 (–18) hours

(2) in diabetics blood glucose level < 200 mg/dL

Reason: FDG tumor uptake is diminished by a competitively elevated serum glucose level

FDG PET scanning should be delayed for 8–12 weeks after surgery / radiation therapy to reduce FDG-avid postsurgical changes / radiation effects that can interfere with scan interpretation!

Dose: 15 (range, 13.5–16.5) mCi
Physical half-life: 110 min
Imaging time: 45–60–70 min after administration (trade-off between decreasing background activity and declining counting statistics)
Distortion correction in whole-body imaging:
attenuation correction can be achieved with a transmission scan before / after emission image acquisition at each corresponding bed position

Standardized Uptake Value (SUV):

= target-to-background measure to allow comparison within and between different patients and diseases normalized to body mass

$SUV = A_{mea}$ [mCi/mL] / (A_{inj} [mCi] / W [kg])

A_{mea}	=	decay-corrected regional radiotracer concentration in volume of interest
A_{inj}	=	injected radiotracer activity
W	=	body weight in kilograms

N.B.: SUV calculations may alternatively be based on body surface area / lean body mass (corrected for body fat as it elevates SUV spuriously)

Typical values:
soft tissue 0.8
blood pool (at 1 hour) 1.5–2.0
liver 2.5
renal cortex 3.5
malignant neoplasm 2–20
non-small cell lung cancer 8.2
breast cancer 3.2
PET - visual assessment: 98% sensitive, 69% specific
PET - SUV measurement: 92% sensitive, 90% specific

FDG Uptake in Benign Tumors / Tumorlike Conditions	
Neck	
Thyroid adenoma	Hyperplastic thyroid nodule
Pleomorphic adenoma	Warthin tumor
Abdomen	
Adrenal hyperplasia	Adrenal adenoma
Pheochromocytoma	Myelolipoma
Bone	
Fibrous dysplasia	Giant cell tumor
Paget disease	Nonossifying fibroma
Eosinophilic granuloma	Aneurysmal bone cyst
Enchondroma	Myositis ossificans

Low FDG Uptake in Malignant Tumors	
Bronchoalveolar cell ca.	Carcinoid
Marginal zone lymphoma (eg, MALToma)	Low-grade HCC
Low-grade sarcoma	Chondrosarcoma
Renal cell carcinoma	Necrotic tumor
Sclerotic bone metastasis	Mucinous tumor

Response Evaluation in PET Imaging

(1) Reproduce the same time delay between injection and imaging as used at baseline imaging
(2) Consider partial volume effect in small residual tumor = risk of underestimation of SUV values
(3) Time delay after last chemotherapy use might influence response assessment

HYBRID PET/CT IMAGING

= combination of high-resolution PET scanner + CT scanner allows acquisition of 3-dimensional images

Indications:

1. Lung cancer
2. Breast cancer
3. Colon cancer recurrence
4. Head and neck cancer
5. Brain tumor

Lymphoma

= histologically heterogeneous group of cancers derived from cells of immune system
Prevalence: 5% of all cancers in USA
Prognosis: 6.0÷100,000 (= 20,150) deaths annually in 2013
√ enlargement of lymph nodes / secondary lymphoid tissues
√ may arise from almost any organ = extranodal lymphoma
Factors in FDG uptake:

› histologic features (Hodgkin disease versus NHL)
› grade (indolent versus aggressive NHL)

PET/CT Artifacts	
Misregistration = located to inappropriate anatomic structure	
Respiration	Patient motion
Bowel motility	Bladder distention
Attenuation-correction Artifact = artificial activity increase	
Metallic objects	Vertebroplasty cement
Contrast media	

› viable tumor cell fraction
› tumor cell proliferation
› upregulation of glucose metabolism
› salvage pathways and tumor-specific pathways
› local perfusion → substrate delivery to the cancer cell
› presence of hypoxia

Extranodal Lymphoma

Prevalence: ⅓ of all lymphomas
Location: skin, stomach, small intestine (most common)
(a) primary extranodal lymphoma = early stage I (65%), stage II (74%) disease
(b) secondary extranodal lymphoma = sign of more advanced stage III or IV disease

Malignant Lymphoma / NHL

Malignancy grade:
√ uptake lower for indolent compared to aggressive lymphoma (SUV > 10 likely to have aggressive disease)
√ aggressive transformation (= change from low-grade to high-grade lymphoma) in 5–10%; requires repeat biopsy

Staging: PET/CT tends to upstage tumors
√ splenic > hepatic uptake indicates splenic involvement
√ heterogeneous scattered uptake in bone marrow involvement

Pitfalls:
(a) gastric + cerebral lymphoma difficult to detect ← physiologic accumulation
(b) increased uptake after treatment with granulocyte colony-stimulating factor (GCSF)
(c) uptake in brown fat of mediastinum
(d) uptake in Lnn with sarcoid involvement
(e) physiologic colonic uptake may be mistaken for lymphoma
(f) small-volume lesions may be undetectable

Response to Rx:
(1) Early response assessment after one cycle of chemotherapy has high prognostic value
(2) Residual abnormal FDG uptake after therapy suggests poor prognosis!

Hodgkin Lymphoma

97% of disease sites identified by FDG PET
◊ Lesion contiguity is CHARACTERISTIC!

IMMUNOSCINTIGRAPHY

= imaging with monoclonal antibodies ([= homogeneous antibody population directed against a single antigen [eg, cancer cell]) and labeled with a radiotracer

Hybridoma technique:
antibody-producing B lymphocytes are extracted from the spleen of mice that were immunized with a specific type of cancer cell; B lymphocytes are fused with immortal myeloma cells (= hybridoma)

Agents:
^{111}Indium-satumomab pendetide = ^{111}In-CYT-103 (OncoScint™ CR/OV) = murine monoclonal antibody product derived by site-specific radiolabeling of the antibody B27.3-GYK-DTPA conjugate with ^{111}In

Use: detection + staging of colorectal + ovarian cancers

Dose: 1 mg of antibody radiolabeled with 5 mCi of ^{111}In injected IV

Biodistribution: liver, spleen, bone marrow, salivary glands, male genitalia, blood pool, kidneys, bladder

Imaging: 2 sets of images 2–5 days post injection + 48 hours apart

LYMPHANGIOSCINTIGRAPHY

Lymphangioscintigraphy Technique

^{99m}Tc-albumin solution injected intradermally to raise a wheal in 1st interdigital web space of both feet / hands

Dose: 500 µCi (18.5 MBq); 92–98% of albumin are tightly bound to ^{99m}Tc

Volume: 0.05 mL; > 98% of albumin macromolecules (molecular weight of 60 kDa) enter lymphatic vessels

Imaging: at 1 min, 10–40 min and 3–5 hr with parallel-hole collimator passing over patient

Transport Index Score (TIS)

= semiquantitative measurement of objective + subjective criteria of peripheral lymphatic radiotracer transport

TIS = K + D + 0.04•T + N + V
K = transport kinetics = degree of transport delay
D = radionuclide distribution pattern = degree of dermal backflow
T = timing of radionuclide appearance in regional lymph nodes (in minutes normalized for 200 min as maximal delay)
N = demonstration + intensity of lymph nodes
V = demonstration + intensity of lymphatic collectors

BRAIN SCINTIGRAPHY

Blood-Brain Barrier (BBB) Agents

= old-style agents require a disruption of blood-brain barrier to diffuse into brain

A. ^{99m}Tc-glucoheptonate
   15–20 mCi bolus injection in < 2 mL saline; 30 flow images of 2-second duration; static image of 1 million counts after 4 hours; delayed image after 24 hours (higher target-to-background ratio than DTPA)
B. ^{99m}Tc DTPA
C. ^{201}Thallium: best predictor for tumor burden

Brain Perfusion Agents

= lipophilic agents rapidly crossing blood-brain barrier with accumulation in brain

Applications: any disease in- / decreasing regional perfusion

1. Brain death (most common)
2. Refractory seizure disorder
3. Dementia

potentially: stroke, receptor imaging, activation studies, tumor recurrence

^{99m}Tc HMPAO

= hexamethylpropylene amine oxime = exametazime

Product: Ceretec®

Dose: 10–30 mCi

Imaging: as early as 15 min post injection

Pharmacokinetics: lipophilic radiopharmaceutical distributes across a functioning blood-brain barrier proportional to cerebral blood flow; no redistribution

Indication: acute cerebral infarct imaging before evidence of CT / MR pathology; positive findings within 1 hour of event

^{99m}Tc-ECD

= ethyl cysteinate dimer = bicisate

Product: NEUROLITE®

Dose: 10–30 mCi

Imaging: 30–60 min post injection

^{123}I-Iofetamine

= N-isopropyl-p[^{123}I]iodoamphetamine iodine = ^{123}I-IMP

Product: Spectamine®

Pharmacokinetics:
initially distributes proportional to regional cerebral blood flow with increased flow to basal ganglia and cerebellum; homogeneous uptake in gray matter; ↓ activity in white matter; redistribution over time

√ activity in an area of initial deficit on reimaging (after 4 hours) implies improved prognosis

Increased Perfusion in Radionuclide Angiography

1. Primary / metastatic brain tumor
2. AVM, large aneurysm, tumor shunting

3. Luxury perfusion after infarction
4. Infection: eg, herpes simplex encephalitis
5. Extracranial lesions: bone metastasis, fibrous dysplasia, Paget disease, eosinophilic granuloma, fractures, burr holes, craniotomy defects

Decreased Perfusion in Radionuclide Angiography

1. Arterial stenosis
2. Alzheimer disease:
   √ bilateral temporoparietal hypoperfusion
3. Most tumors
4. Hemorrhage
5. Subdural hematoma

Indications for Radionuclide Angiography of Brain

Seizures

Abnormal cerebral radionuclide angiography within 1 week of seizure activity even without underlying organic lesion

Etiology:

(1) 35% cerebral tumors: meningioma in 34%, metastases in 17%
(2) Cerebrovascular disease (more common in > 50 years of age)
(3) Trauma, inflammation, CNS effects of systemic disease

√ transient hyperperfusion of involved hemisphere

SEIZURE FOCUS IMAGING

for localizing intractable seizures

√ focal hypoperfusion during interictal injection of tracer (less sensitive)
√ focal hyperperfusion during ictal injection of tracer (better detection)

Brain Tumor

Etiology:

√ good correlation between hyperperfusion and enlarged supplying vessels:

(1) Meningioma (increased activity in 60–80%);
(2) Metastases (increased activity in 11–23%);
(3) Vascular metastases: thyroid, renal cell, melanoma, anaplastic tumors from lung / breast

Arterial Stenosis

◊ Radionuclide angiography of limited value!

√ asymmetric decreased perfusion in acute / chronic cerebrovascular disease:

(1) Complete occlusion / > 80% stenosis of ICA: 53–80% sensitivity
(2) 50–80% stenosis of ICA: 50% sensitivity
(3) < 50% stenosis of ICA: 10% sensitivity

Problematic lesions:

(1) Bilaterally similar degree of stenosis

(2) Occlusion of MCA + unilateral ACA
(3) Vertebrobasilar occlusive disease (20% sensitivity)

Stroke

√ "flip-flop" phenomenon (= ⇓ perfusion in arterial phase, equalization of activity in capillary phase, ⇑ activity in venous phase) ← late arrival of blood via collaterals and slow washout

PET IN BRAIN IMAGING

A. REGIONAL CEREBRAL BLOOD FLOW

(a) breathing of carbon monoxide (11C and 15O), which concentrates in RBCs

(b) 133Xe inhalation / injection into ICA / IV injection after dissolution in saline: volume distribution within cerebral water space; no correction for recirculation necessary because all Xe is exhaled during lung passage, but correction for scalp + calvarial activity is required

√ washout rate of gray matter÷white matter = 4–5÷1

B. GLUCOSE METABOLISM

for measurements of metabolic rate + mapping of functional activity

(a) 11C glucose: rapid uptake, metabolization, and excretion by brain

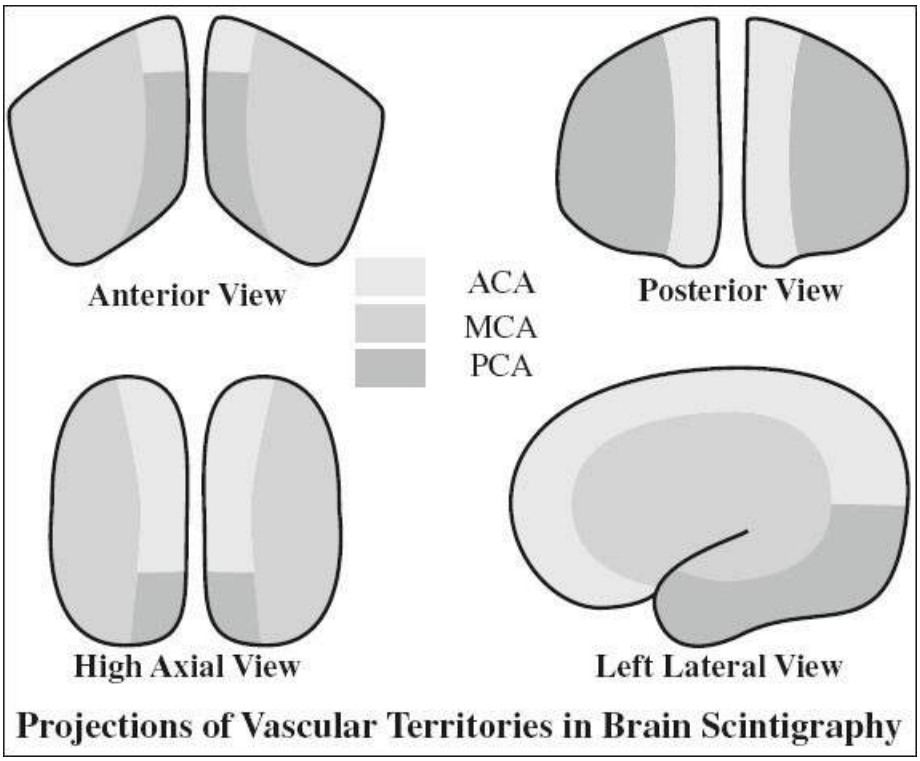
(b) ^{18}F-fluorodeoxyglucose (FDG): diffuses across blood-brain barrier + competes with glucose for phosphorylation by hexokinase → traps FDG-6-phosphate within mitochondria; FDG-6-phosphate cannot enter most metabolic pathways (eg, glycolysis, storage as glycogen) and accumulates proportional to intracellular glycolytic activity; FDG-6-phosphate is dephosphorylated slowly by glucose-6-phosphatase and then escapes cell

Indications:

1. **Focal epilepsy** prior to seizure surgery
   - √ interictal ⇓ uptake of FDG of > 20% at seizure focus (70% sensitivity, 90% for temporal lobe hypometabolism)
   - √ hypermetabolism within 30 minutes of seizure
   - √ measurement of opiate receptor density with 11C-labeled carfentanil (= high-affinity opium agonist) uptake by μ receptors (found in thalamus, striatum, periaqueductal gray matter, amygdala), which mediate analgesia and respiratory depression
2. **Alzheimer disease**

   Prevalence: 5.4 million persons in USA in 2016

   - clinical diagnosis false positive in 35% ← challenging diagnosis in earlier milder forms of the disease



Projections of Vascular Territories in Brain Scintigraphy

Histo: amyloid plaques + neurofibrillary angles (autopsy)
√ bilateral temporoparietal hypoperfusion + hypometabolism → decreased FDG uptake (92–100% sensitive)
√ sparing of sensory and motor cortex + basal ganglia + thalamus
√ atrophy of entire brain with predilection for hippocampus
DDx: frontal lobe dementia, primary progressive aphasia without dementia, normal-pressure hydrocephalus, multi-infarct dementia

3. **Parkinson disease**
= deficient presynaptic terminals with normal postsynaptic dopaminergic receptors
• clinical diagnosis in 50–70% accurate
DDx: drug-induced chorea, Huntington disease, tardive dyskinesia, progressive supranuclear palsy, Shy-Drager syndrome, striatonigral degeneration, alcohol-related cerebellar dysfunction, olivopontocerebellar atrophy
4. **Huntington disease**, senile chorea
√ hypometabolism of basal ganglia
5. **Schizophrenia**
√ abnormally reduced glucose activity in frontal lobes
√ dopamine receptors in caudate / putamen elevated to 3 x that of normal levels
6. **Stroke**, cerebral vasospasm
√ disassociated oxygen metabolism + brain blood flow

PET in Brain Tumor

Indications:
(1) Tumor grading + estimation of prognosis

◊ Apparently low-grade gliomas without contrast enhancement by CT/MR are malignant in 30%

(2) Localization of optimal biopsy site

◊ The most malignant area shows maximum of uptake

Grading and Prognosis for Gliomas			
Grade	*Uptake Ratio*	*Pathology*	*Median Survival*
0	no uptake	in 86% grade I / II	2.3 years
1	tumor ≤ normal white matter		
2	tumor > white matter and < normal cortex	in 94% grade III / IV	11 months
3	tumor ≥ normal cortex		

Unproven:

(3) Detection of recurrence versus radionecrosis

◊ Plagued by low specificity of 22% (cut-off greater than WM) and 56% (cut-off greater than cortex)

(4) Assessment of response to therapy

◊ SUV increases within weeks following radiation / chemotherapy ← ⇑ in metabolically active inflamma- tory elements + energy consumption for apoptosis

(5) Defining target volume for radiotherapy (?)

Assessment: 35–50 min post injection

› SUV

› tumor-to-white matter ratio (T/WM): 1.5

› tumor-to-cortex ratio (T/C): > 0.6

◊ Activity in tumor + reference area steadily increases with time after injection

RADIONUCLIDE CISTERNOGRAPHY

Indications:

1. Suspected normal pressure hydrocephalus
2. Occult CSF rhinorrhea / otorrhea
3. Suspected ventricular shunt malfunction

4 Porencephalic cyst, leptomeningeal cyst, posterior fossa cyst

Technique:

1. Measurement of spinal subarachnoid pressure
2. Sample of CSF for analysis
3. Subarachnoid injection of radiotracer

Normal study (completed within 48 hours):

symmetric activity sequentially from basal cisterns → up the sylvian fissures + anterior commissure → eventual ascent over cortices with parasagittal concentration

√ image lumbar region immediately after injection to ensure subarachnoid injection

√ activity in basal cistern by 2–4 hours

√ activity at vertex by 24–48 hours

√ no / minimal lateral ventricular activity (may be transient in older patients)

Agents:

1. **^{111} Indium-DTPA**
   Physical half-life: 2.8 days
   Gamma photons: 173 keV (90%), 247 keV (94%) detected with dual pulse height analyzer
   Dose: 250–500 μCi
   Radiation dose: 9 rad/500 μCi for brain + spinal cord (in normal patients)
   Imaging: at 10-minute intervals / 500,000 counts up to 4–6 hours; repeat scans at 24, 48, 72 hours
2. **^{99m} Technetium-DTPA**
   Not entirely suitable for imaging up to 48–72 hours; DTPA tends to have faster flow rate than CSF; used for shunt evaluation + CSF leak study since leak increases CSF flow
   Dose: 4–10 mCi
   Radiation dose: 4 rad for brain + spinal cord
3. **131 Iodine-serum albumin (RISA)**
   prototype agent; beta emitter
   Physical half-life: 8 days; high radiation dose of 7.1 rad/100 μCi; no longer used secondary to pyrogenic reactions
4. **169 Ytterbium-DTPA**
   Physical half-life: 32 days
   Gamma decay: 63 keV; 177 keV (17%); 198 keV (25%); 308 keV; dual pulse height analyzer set for 177 + 198 keV
   Dose: 500 μCi
   Radiation dose: 9 rad/500 mCi for brain + spinal cord (in normal patients)

CSF Leak Study

Purpose: localization of origin of CSF leak in patient with CSF rhinorrhea / otorrhea
Causes of dural fistula:
(a) traumatic: in 30% of basilar skull fractures
(b) nontraumatic: brain, pituitary and skull tumors; skull infections; congenital defects
Location of dural fistula:
cribriform plate > ethmoid cells > frontal sinus
Method:

- » Weigh cotton pledgets
- » Pledgets placed by ENT surgeon in the anterior and posterior turbinates bilaterally
- » Radiopharmaceutical injected intrathecally via lumbar puncture; immediate postinjection view of lumbar region to ensure intrathecal placement
  - ◊ Contraindicated in active meningitis / elevated intracranial pressure!
- » Pledgets removed and weighed 4–6 hours after lumbar injection
- » Pledget activity counted + indexed to weight
- » Results compared with 0.5-mL serum specimens drawn at the time of pledget removal
- » Pledget to serum count ratio of > 1.5 = evidence of CSF leak
- » With active leak patient should be placed in various positions with various maneuvers to accentuate leak

Disadvantage: low sensitivity + high FN in intermittent leak

THYROID SCINTIGRAPHY

Indications:

(1) Classification of hyperthyroidism
(2) Evaluation of solitary / dominant nodule
(3) Detection and staging of postoperative thyroid cancer
(4) Evaluation of upper mediastinal mass
(5) Evaluation of neonatal hypothyroidism
(6) Evaluation of developmental anomalies

A. SUPPRESSION SCAN
= to define autonomy of a nodule
√ suppression of a hot nodule following T3 / T4 administration is proof that autonomy does not exist

B. STIMULATION SCAN
= to demonstrate thyroid tissue suppression by hyperfunctioning nodule
√ administration of TSH documents functioning thyroid tissue (rarely done)

C. PERCHLORATE WASHOUT TEST
= to demonstrate organification defect
√ repeat measurement of radioiodine uptake following oral potassium perchlorate shows lower values if organification defect present

◊ Best interpreted by direct comparison with sonography!

^{99m}Tc-Pertechnetate in Thyroid Imaging ($^{99m}TcO_4^-$)

Physical half-life (for gamma emission): 6.03 hours
Biologic half-life: 1 day (94% decays to ^{99}Tc in 24 hours)
Decay: by photon emission of 140 keV
Quality control:
(1) < 0.1% ^{99}Mo (= 1 µCi/mCi), maximum of ^{99}Mo at 5 µCi
(2) < 0.5 mg aluminum/10 mCi ^{99m}Tc
(3) < 0.01% radionuclide impurities
Administration: oral / IV
Dose: 3–5 mCi administered IV 20 min prior to imaging (100–300 mrad/mCi)
Pharmacokinetics:
Uptake by: thyroid, salivary glands, gastric mucosa, choroid plexus
Excretion: mostly in feces, some in urine
Uptake in thyroid: 0.5–3.7% at 20 minutes (time of maximum uptake); assessment of trapping function only; NO organification; may be almost completely discharged by perchlorate
Imaging:
(a) Collimator: usually with pinhole collimator for image magnification (5-mm hole)
(b) Distance: selected so that organ makes up $^2/_3$ of field of view; significant distortion of organ periphery occurs if detector too close
(c) Counts: 200,000–300,000 counts are usually acquired within 5 min after a dose of 5–10 mCi of ^{99m}Tc-pertechnetate
(d) Image must include markers for scale + anatomic landmarks + palpatory findings

Advantages:

(1) Low cost
(2) Reduced radiation exposure
(3) Greater photon flux than iodine = detectability of small thyroid lesions (> 8 mm) is improved
(4) Excellent physical characteristics

Disadvantages:

(1) High neck background (target-to-background ratio less favorable than with iodine)
(2) Lesions with pertechnetate-iodine discordance (= hot on ^{99m}Tc-pertechnetate + cold on radio-iodine) are very rare + due to ^{99m}Tc-avid cancer
(3) Poor for substernal evaluation

^{123}Iodine

◊ Agent of choice for thyroid imaging!

Production: in accelerator; contamination with ^{124}I dependent on source (^{122}Te in ~ 5%, 123Xe in ~ 0.5%); contamination with ^{125}I increases with time elapsed after production

Physical half-life: 13.3 hours

Decay: by electron capture with photon emission at 159 keV (83% abundance) + x-ray of 28 keV (87% abundance)

Dose: 200–400 µCi orally 24 hours prior to imaging (radiation dose of 7.5 mrad/µCi)

Uptake: iodine readily absorbed from GI tract (10–30% by 24 hours), distributed primarily in extracellular fluid spaces; trapped + organified by thyroid gland; trapped by stomach + salivary glands

Excretion: via kidneys in 35–75% during first 24 hours + GI tract

Advantages:

(1) Low-radiation exposure
(2) Excellent physical characteristics
(3) Uptake + scan with one agent (organified)

Disadvantages compared with ^{99m}Tc-pertechnetate:

(1) More expensive
(2) Less available with short shelf-life
(3) More time-consuming
(4) Radionuclide impurities
(5) Higher dose to thyroid (but less to whole body)

^{131}Iodine

Indication: thyroid uptake study, thyroid imaging, treatment of hyperthyroidism, treatment of functioning thyroid cancer, imaging of functioning metastases

Production: by fission decay

Physical half-life: 8.05 days (allows storing for long periods)

Decay: principal gamma energy of 364 keV (82% abundance) + significant beta decay fraction of a mean energy of 192 keV (92% abundance)

Dose: 30–50 µCi (1.2 rad/µCi = 50 rad for thyroid)

Radiation dose: (90% from beta decay, 10% from gamma radiation) 0.6 mrad/mCi for whole body; 1.2 mrad/μCi for thyroid (critical organ)

Pharmacokinetics: identical to ^{123}I

Thyroid Agents			
	^{131}I	^{123}I	^{99m}Tc
Physical half-life	8 d	13 hr	6 hr
Main photopeak	364 keV	159 keV	140 keV
Usual dose	50–100 μCi	100–300 μCi	2–10 mCi
Absorbed dose	50–100 rad	2–5 rad	0.2–1.8 rad
Administration	PO	PO	IV
Interval to image	24 hr	6 hr	20 min

Advantages:

(1) Low cost
(2) Ectopic tissue search
(3) Uptake and scan at same time

Disadvantages:

(1) Too energetic for gamma camera, well suited for rectilinear scanner with limited resolution
(2) High radiation exposure (← beta decay) → PROHIBITS USE FOR DIAGNOSTIC PURPOSES
(3) Ectopic thyroid tissue just as well detectable with ^{123}I or ^{99m}Tc-pertechnetate

^{131}Iodine SPECT/CT

Advantage: precise localization of foci of radioactivity to anatomic structures (incremental value over planar imaging in 40%)

Indication: distinction of benign mimics from true metastatic disease

PHYSIOLOGIC ^{131}IODINE ACTIVITY

NIS = sodium (**N**) / iodide (**I**) symporter (**S**) transports 2 sodium cations (Na+) for each iodide anion (I−) into the cell

A. Thyroidal tissue
   1. after total thyroidectomy: thyroglossal duct, thyroid bed remnant
   2. Ectopic thyroid: lingual thyroid, lateral aberrant thyroid, intracardiac thyroid (struma cordis), ovarian thyroid (struma ovarii)

B. Orthotopic / ectopic extrathyroidal tissue with NIS expression
   1. Extrathyroidal tissue with NIS expression: salivary gland (parotid, submandibular), choroid plexus, lacrimal gland, nasal mucosa, thymus, breast, gastric mucosa, colon
      ◊ Breast feeding must be terminated after administration of ^{131}I.
   2. Ectopic extrathyroidal tissue with NIS expression: Barrett esophagus, Meckel diverticulum, GI duplication cyst, supernumerary breast tissue

C. Physiologic
   1. Intravascular space: cardiac blood pool, carotid ectasia

2. Hepatic metabolism: diffuse hepatic activity ← ^{131}I–labeled thyroxine ← produced by carcinoma metabolized in liver
3. Secretions of saliva, sweat, tears, nose: oropharynx, esophagus, Zenker diverticulum, poorly dissolved ^{131}I capsule, chewing gum / tobacco, external contamination
4. GI and GU excretion: colon, bladder

D. Benign disease
1. Cyst with passive diffusion: lactational duct, renal, ovarian, pleuropericardial, bronchogenic
2. Inflammation: lung, pericardium, joint, sinus, wound healing, etc.
3. Third spacing: pericardial effusion, pleural effusion, ascites, scrotal hydrocele

E. Neoplasm: meningioma, non-small cell lung carcinoma, teratoma, salivary gland + ovarian + gastric adenocarcinoma

F. Contamination: urine, feces, drooling

Iodine Fluorescence Imaging

Technique: collimated beam of 60 keV gamma photons from an 241Am source is directed at thyroid, which results in production of K-characteristic x-rays of 28.5 keV; x-rays are detected by semiconductor detector

Advantages:

(1) No interference with flooded iodine pool / thyroid meds
(2) Measures total iodine content
(3) Low radiation exposure (15 mrad) acceptable for children + pregnant women

Disadvantage: dedicated equipment necessary

PARATHYROID SCINTIGRAPHY

for the evaluation of primary hyperparathyroidism after other causes for hypercalcemia have been excluded

[Technetium-thallium Subtraction Imaging]

*** superceded by ^{99m}Tc-MIBI at most centers ***

= DUAL ISOTOPE SCINTIGRAPHY

Sensitivity: 72–92% (depending on size, smallest adenoma was 60 mg)

Specificity: 43% (benign thyroid adenomas, focal goitrous changes, Hashimoto thyroiditis, parathyroid ca., cancer metastatic to neck, lymphoma, sarcoidosis, lymph nodes also concentrate thallium)

Method:

» IV injection of 1–3.5 mCi ^{201}Tl chloride; images recorded for 15 minutes with 2-mm pinhole collimator
√ concentrates in normal thyroid + enlarged parathyroid glands (extraction proportional to regional blood flow + tissue cellularity)

» IV injection of 1–10 mCi ^{99m}Tc-pertechnetate; images recorded at 1-min intervals for 20 min
√ pertechnetate concentrates only in thyroid

» Computerized subtraction

√ focal / multifocal excess ^{201}Tl

Limitations:

(1) Unfavorable dosimetry + poor quality images of ^{201}Tl (up to 3.5 mCi, 80 keV photons)
(2) Prolonged patient immobilization (motion artifact)
(3) Processing artifacts (eg, over- / undersubtraction)
(4) Poor ^{99m}Tc thyroid uptake from interfering medications / recent iodinated contrast media
(5) Parathyroid pathology may be mimicked by coexisting thyroid disease (eg, nonfunctioning adenoma, multinodular goiter)

Indication: localization of one / more parathyroid adenomas (hyperplasia not visualized), may be more sensitive than CT / MR in detection of ectopic mediastinal parathyroid tissue and in postoperative context

^{99m}Technetium-Sestamibi (^{99m}Tc-MIBI)

Indication: recurrent hypercalcemia following previous parathyroid surgery

Sensitivity: 79–100% (smallest adenoma weighed 150 mg); 79% for early pinhole, 85% for late pinhole, 86% for subtraction, 83% for SPECT imaging

◊ adversely affected by multigland disease

◊ For unknown reasons even large tumors (2 g) may not accumulate sufficient MIBI for detection!

Pharmacokinetics:

after IV injection lipophilic cationic molecules of MIBI distribute according to blood flow → cross cell membrane by passive diffusion → concentrate intracellularly in region of mitochondria proportional to regional blood flow and cellular metabolic activity (eg, in myocardium and mitochondria-rich oxyphil cells of parathyroid gland); MIBI washes out of thyroid quickly, but is retained in abnormal parathyroids → need for dual-phase study

Physiologic distribution:

(1) Parotid gland
(2) Submandibular salivary glands (uptake in oral cavity)
(3) Thyroid gland
(4) Heart
(5) Liver
(6) Bone marrow: mild generalized uptake
(7) Thymus: mild uptake in young individuals
(8) Brown fat

( ) NO uptake in normal parathyroid glands

Advantages (over thallium):

A. Physical properties:
   › optimal gamma emission (140 keV)
   › abundant photons (high dose of 20 mCi)
   › favorable dosimetry
   › high parathyroid-to-thyroid ratio
   › unaffected by medications / iodinated contrast
B. Technical features:

› single readily available radiopharmaceutical
› simple protocol of early + delayed images
› no prolonged patient immobilization
› no subtraction study / computer processing
› SPECT / multiple projections possible

C. Scan interpretation
› sharp images
› clear visualization of abnormal parathyroid glands
› ectopic sites surveyed
› improved detection sensitivity

Method:

» IV injection of 20–30 mCi ^{99m}Tc-MIBI
» 1st set of images: 10–15–30 minutes after injection
» 2nd set of images: at 1.5–3–4 hours post injection
» Adjunctive dual phase imaging with
(a) optional dual-isotope thyroid-selective agent (^{123}I, ^{99m}Tc) for computer-aided subtractions
Disadvantages:
(1) Necessity of 2 radionuclide injections
(2) Requires cooperative + immobile patient identically positioned for 2 studies
(3) Increased likelihood of artifacts
(b) single isotope early – and delayed phase technique ← ^{99m}Tc sestamibi washes out more rapidly from thyroid gland than from hyperfunctioning parathyroid glands
» Image acquisition: of cervicothoracic region from submandibular glands to basal ⅓ of heart
(1) 2-D planar imaging: anterior, anterior oblique, lateral views with large-field-of-view camera equipped with low-energy high-resolution parallel-hole collimator acquiring 5 minutes/view for 1st set of images and 10 minutes/view for 2nd set of images
(2) 3-D SPECT imaging with improved contrast resolution (⇑ target to background)
(a) software program
(b) hybrid SPECT/CT imaging system with anatomic information from CT
Advantage: more precise anatomic localization of ectopic mediastinal parathyroid adenomas

False positive scintigraphic findings:

1. Solitary thyroid adenoma
2. Nodule in multinodular goiter
3. Tumor: breast, lung, head & neck carcinoma, bronchial carcinoid
4. Metastasis to lymph node and bone

Delayed wash-out in neck region:

1. Differentiated thyroid malignancy
2. Primary thyroid lymphoma
3. Lymph node metastasis from papillary thyroid ca.
4. Reactive lymph node
5. Remnant thymus

6. PTH-secreting paraganglioma
7. Enlarged submandibular gland

False negative scintigraphic findings:

1. Double parathyroid adenomas
2. Four-gland hyperplasia

◊ Small gland less likely detected than large gland!

LUNG SCINTIGRAPHY

Perfusion Agents

^{99m}Tc-Macroaggregated Albumin (MAA)

Preparation:

heat-denatured + pH-adjusted human serum albumin (HSA); added stannous chloride → precipitates albumin into tin- containing macroaggregates; lyophilization prolongs stability; added ^{99m}Tc-pertechnetate is reduced by SnCl2 and tagged onto the MAA particles

Quality control (USP guidelines):

(1) 90% of particles should have a diameter of 10–90 μm
(2) No particle should exceed 150 μm
(3) Should ≥ 90% pure ← ascending chromatography
(4) ^{99m}Tc-MAA batch should be used < 8 hr post preparation
(5) Preparation should not be backflushed with blood into syringe → "hot spots" in lung images

Physical half-life: 6 hr

Biologic half-life: 6 hr

Dose: ~ 2–4–6 mCi + 0.14 μg/kg albumin corresponding to > 60,000 particles (200,000–700,000 particles recommended for even spatial distribution + good image quality)

N.B.: ↓ number of particles to 50,000–80,000 in

(a) critically ill patients with severe COPD, on mechanical ventilator support, documented pulmonary arterial hypertension, significant left-to-right cardiac shunts → NO reduction in tagged activity!
(b) children up to age 5 need reduction in number of particles + tagged activity!

» IV injection in supine position to give an even distribution between base + apex of lung (ventral to posterior gradient persists)
» imaging in upright position to allow maximum expansion of lung, especially at lung bases

Radiation dose (rad/mCi): 0.013 for whole body, 0.25 for lung (critical organ), 0.01 for gonads

Physiology:

90% of MAA particles act as microemboli → trapped in an estimated 600 million pulmonary arterioles small enough to trap the particles on 1st pass; physiologically insignificant effect → only 500,000 particles are injected per study; 0.22% (2÷1,000) of capillaries become occluded; protein is lysed within 6–8 hours and taken up by RES; particles < 1 μm are phagocytized by RES in liver + spleen

Imaging: Large-field-of-view scintillation camera + parallel-hole low-energy collimator with identical recording times for corresponding views

Views:

› anterior, posterior

› posterior oblique (LPO, RPO): additional information in 50% ← segmental delineation of basal segments and ← separation of both lungs

› anterior oblique (LAO, RAO): oblique views reduce equivocal findings from 30% to 15%

› lateral: "shine through" from contralateral lung

Counts: 750,000–1,000,000 counts for each image

^{99m}Tc-Human Albumin Microspheres (HAM)

Particle size: 20–30 µm

Biologic half-life: 8 hours

Ventilation agents

^{133}Xe, ^{127}Xe, ^{125}Xe, ^{81m}Kr, ^{13}N, $^{1}{}_{5}O_{2}$, $^{11}CO_{2}$, ^{11}CO, radioactive aerosol (^{99m}Tc–DTPA, ^{99m}Tc-PYP, ^{99m}Tc-labeled ultrafine dry dispersion of carbon "soot")

133Xenon

Fission product of 235U

Decay: to stable 133Cs under emission of beta particle (374 keV), gamma ray (81 keV), x-ray (31 keV); beta-component responsible for high radiation dose of 1 rad to lung)

Physical half-life: 5.24 days

Biologic half-life: 2–3 min

Physical properties: highly soluble in oil + grease, absorbed by plastic syringe

Administration: injection into mouth piece of a disposable breathing unit at the beginning of a maximal inspiration

Dose: 15–20 mCi

Technique:

Ventilation study preferably done <u>before</u> perfusion scan to avoid interference with higher-energy ^{99m}Tc (Compton scatter from ^{99m}Tc into lower 133Xe photopeak); [may be feasible after perfusion scan if dose of ^{99m}Tc-MAA is kept below 2 mCi + concentration of 133Xe is above 10 mCi/L of air and if 133Xe acquisition times for washing, equilibrium, washout images are kept to about 30 sec]

◊ Posterior imaging routine, ideally in upright position

<u>Phase 1 = single-breath image</u>:

= inhalation of 10–20 mCi 133Xe to vital capacity with breath-holding over 10–30 seconds (65% sensitivity for abnormalities)

√ cold spot is abnormal

<u>Phase 2 = equilibrium phase</u>:

= tidal breathing = closed-loop rebreathing of 133Xe + oxygen for 3–5 minutes for tracer to enter poorly ventilated areas; also functions as internal control for air leaks

» posterior oblique + posterior images are obtained to improve correlation with perfusion scan

√ activity distribution corresponds to aerated lung

Phase 3 = washout phase:

= clearance phase after readjusting intake valves of spirometer permits patient to inhale ambient air and to exhale 133Xe into shielded charcoal trap

» washout phase should last > 5 minutes

» images taken at 30–60-second intervals for > 5 min

√ rapid clearance within 90 seconds yields slight normal retention in upper zones

√ tracer retention (hot spot) at 3 minutes reveals areas of air-trapping

√ poor image quality secondary to significant scatter

√ abnormal scan:

(a) COPD / acute obstructive disease:

√ delayed wash-in (during initial 30 seconds of tidal breathing)

√ tracer accumulation on equilibrium views ← partial obstruction with collateral air drift + diffusion into affected area via bloodstream

√ delayed washout = retention > 3 minutes ← air trapping

√ tracer retention in regions not seen on initial single-breath view ← collateral airdrift into abnormal lung zones

(b) consolidated lung disease

√ no tracer uptake throughout imaging sequence

127Xenon

cyclotron-produced with high cost

Physical half-life: 36.4 days

Photon energies: 172 keV (22%), 203 keV (65%)

Advantages:

(1) High photon energy allows ventilation study following perfusion study

(2) Decreased radiation dose (0.3 rad)

(3) Storage capability because of long physical half-life

^{81m}Krypton

insoluble inert gas; eluted from 81Rb generator (half-life of 4.7 hr); decays to 81Kr by isomeric transition

Physical half-life: 13 sec

Biologic half-life: < 1 min

Principal photon energy: 190 keV (65% abundance)

Advantages:

(1) Higher photon energy than ^{99m}Tc so that ventilation scan can be performed following perfusion study

(2) Each ventilation scan can be matched to perfusion scan without moving patient

(3) Can be used in patients on respirator (no contamination due to short half-life)

(4) Low radiation dose (during continuous inhalation for 6–8 views 100 mrad are delivered)

Disadvantages:

(1) High cost
(2) Limited availability (generator good only for one day, so weekend availability may not be possible
(3) No washout images possible ← short half-life
(4) Decreased resolution ← septal penetration with low-energy collimators

√ lack of activity = abnormal area (tracer activity is proportional to regional distribution of tidal volume

^{99m}Tc-DTPA Aerosol

= ^{99m}Tc-diethylenetriaminepentaacetic radioaerosol
= UltraVent®
Biological half-life: 55 min
Administration: delivery through a nebulizer during inspiration
Dose: 30–50 mCi in 2–3 mL of saline added to nebulizer unit and connected to wall oxygen at a flow rate of 8–10 L/min
Physiology:
radioaerosols are small particles that become impacted in central airways, sediment in more distal airways, experience random contact with alveolar walls during diffusion in alveoli; cross respiratory epithelium with rapid removal by bloodstream
◊ Less physiologic indicator of ventilation + subject to nebulization technique
◊ Erect position preferable for basilar perfusion defects (dependent lung region receives more ventilation + radiotracer)
Technique:
» breathing from nebulizer for 3–5 minutes
» images recorded in multiple projections, each for 100,000 counts
◊ Aerosol applied ideally before perfusion; however postperfusion aerosol imaging is possible to assess for "fill-in" of aerosol in region of perfusion defect
◊ The count rate of ^{99m}Tc-MAA activity must be > 4 times the count rate of the ventilation activity!

√ abnormal scan:
(a) COPD
√ decreased activity in peripheral lung (slow and turbulent airflow prevents a normal amount of aerosol to reach the involved lung)
√ central airway deposition (aerosol sticks to trachea + bronchial walls)
(b) consolidated lung disease
√ absent tracer

^{99m}Tc-labeled Ultrafine Carbon Particles (Technegas)
preferred in pulmonary obstructive disease

Carbon Dioxide Tracer

^{15}O-labeled carbon dioxide
Physical half-life: 2 min (requires on-site cyclotron)
Physiology: inhalation of carbon dioxide; rapid diffusion across alveolar-capillary membrane; clearance from lung within sec

√ cold spot ← failure of tracer entry into airway = airway disease
√ hot spot ← delayed / absent tracer clearance = perfusion defect (87% sensitive, 92% specific)

Indications:

1. Emboli can be detected in preexisting cardiopulmonary disease
2. Equivocal / indeterminate V/Q studies

Positron Emission Tomography for Lung Tumor

Dose: 10 mCi FDG

Technique:

» patient fasts for 4 hours
◊ ↑ serum glucose may cause a decrease in FDG uptake!
◊ Blood glucose level of diabetic should be < 200 mg/dL
» imaging 30–45–60 minutes after IV injection in 30–45 image planes (15 cm axial field of view; resolution of 5 mm)
» calculation of maximum standardized uptake ratio (SUV) in region of interest
◊ SUV > 2.5 indicates malignant disease

Indications:

(1) Evaluation of solitary pulmonary nodule
(2) Staging (PET-CT better than any other technique)
(3) Recurrent disease

HEART SCINTIGRAPHY

Cardiac Imaging Choices

1. PLANAR imaging
2. SPECT imaging
3. QUANTITATIVE analysis
= circumferential profiles = plotting of average counts along equally spaced radii emanating from center of LV makes interpretation more objective + reproducible

Planar Imaging

√ tracer defect may be visible on only one image projection
√ 15–20% regional tracer intensity variation is normal

Left Ventricular Anatomy and Projections

A. AP
√ displays anterolateral wall, apex, inferior wall
√ decreased activity at apex of LV ← thinning in 50%
B. LEFT LATERAL
√ displays inferior + anterior wall
C. LAO 40° / LAO 70°
◊ Most often used projection; for all exercise studies
√ displays interventricular septum, posterior wall, inferior wall
√ best projection to separate right + left ventricles

√ best projection to evaluate septal + posterior LV wall motion

D. RAO 45°
√ displays anterior + inferior ventricular wall
√ useful during 1st-pass studies with temporal separation of ventricles

E. LPO 45° (rarely used)
10° caudal tilt minimizes LA contamination of LV region
√ displays anterior + inferior ventricular wall
√ preferred over RAO 45° because LV is closer to camera

F. Angled LAO (slant-hole collimator / caudal tilt)
√ separates ventricular from atrial activity
√ highlights apical dyskinesis

Location of Perfusion Defects on Planar Images

(1) Right coronary artery (RCA) best seen on left LAT / AP projections
√ inferior + posteroseptal segments

(2) Circumflex branch of left coronary artery (LCX) best seen on LAO projection
√ posterolateral segment

(3) Anterior descending branch of left coronary artery (LAD)
√ anteroseptal, anterior, anterolateral segments

N.B.: decreased activity in apical + posterior segments is not reliably correlated with disease of any vessel!

SPECT Myocardial Perfusion Imaging (MPI)

improves object contrast by removing overlying tissues; cinematic display of wall motion; EF calculation

√ tracer defect should be visible on more than one image set
√ up to 30% regional tracer intensity reduction compared with peak activity is normal

(a) Standard SPECT 180° acquisition extending from 45° RAO to 45° LPO for single-head camera

(b) ECG-gated SPECT
√ viable although hypoperfused myocardium may demonstrate systolic contraction + wall thickening
√ geometric EF calculation based on ROIs drawn on end-systolic + end-diastolic frames (different from blood pool scans)

Display of SPECT Images

SPECT = single photon emission tomography

- stress study = top row
- resting study = second row

1. Short-axis views (SA): apex → base
2. Horizontal long axis (HLA): inferior → superior (anterior)
3. Vertical long axis (VLA): septum → lateral

Rotating (Cine) Planar Images

= rotating (cine loop) of stress + rest planar images for a review of unprocessed raw data to recognize artifacts

Analysis of Tomographic Slices

Quality control:

1. Assess count statistics: poor, fair, good, excellent
   → peak pixel activity in LV myocardium should exceed 100 counts for ^{201}Tl and 200 counts for ^{99m}Tc
2. Review raw data sets in cinematic display to determine if any artifact is present due to
   (a) patient movement
   (b) respiratory motion
   (c) extracardiac uptake (eg, lymphoma, breast cancer)
3. Review sinogram of cardiac (horizontal) motion for extracardiac uptake (eg, in lungs or esophagus) and motion-related artifact

Cavity Size:

› cavity-to-wall thickness ratio
› poststress images with larger cavity than rest images = **stress -induced transient ischemic dilatation** (TID) > 1.22 ← stress-induced subendocardial ischemia indicative of severe and extensive multivessel coronary artery disease + high risk for a hard cardiac event
› dilatation on rest + stress images indicates LV dysfunction / volume overload

ECG-gated SPECT

displayed as individual tomographic slices / 3-D cine loop (8 frames per cardiac cycle); spatial + temporal changes in tracer activity reflect regional myocardial wall motion + thickening

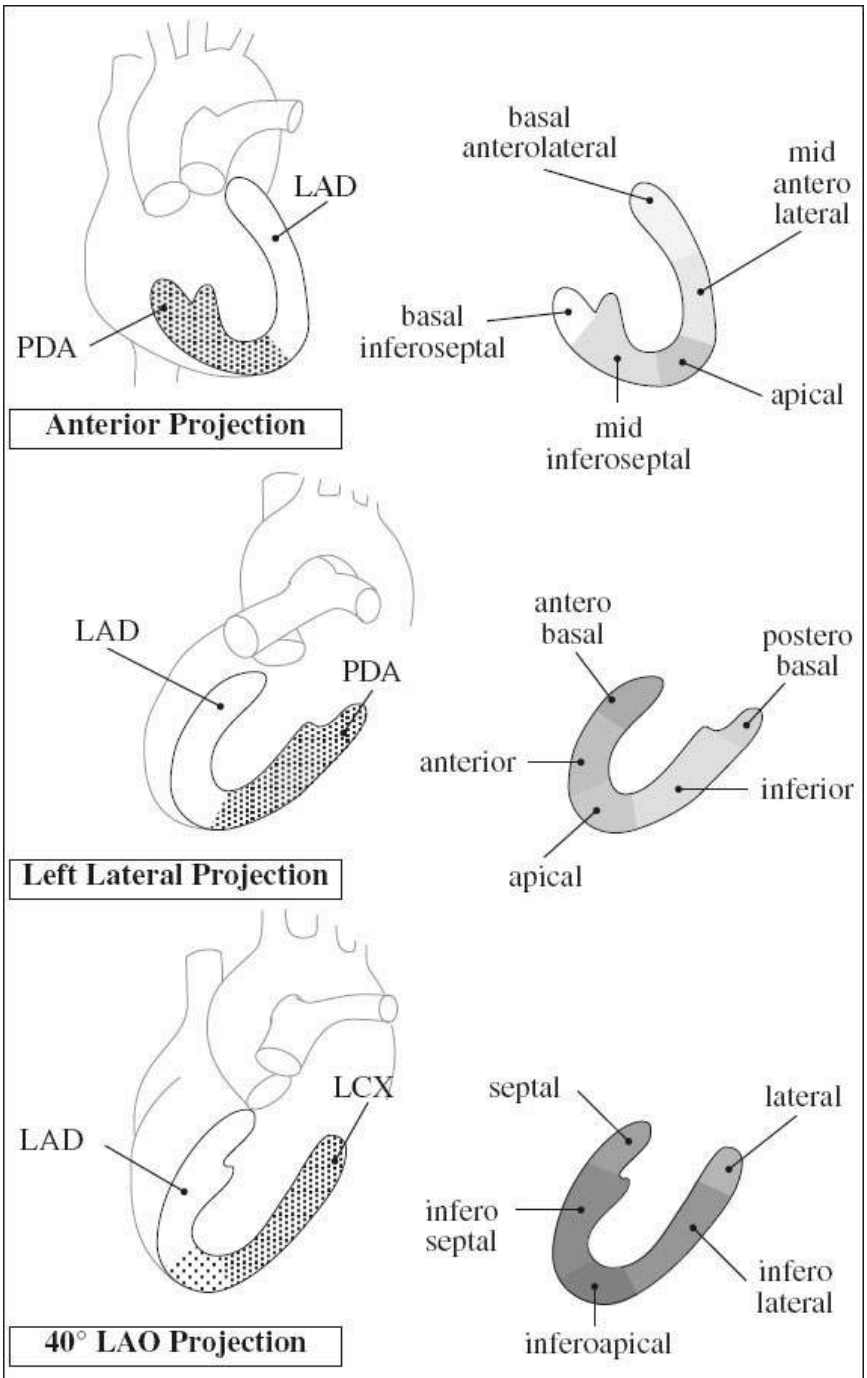
Evaluation for:

› global function
√ LV ejection fraction normal / ≥ 60%
√ end-diastolic + end-systolic LV volumes
normal EDV: 95 ± 27 mL (M), 64 ± 19 mL (F)
normal ESV: 41 ± 17 mL (M), 22±12 mL (F)
› endocardial surface
› motion of endocardial + epicardial surfaces
› myocardial thickening (brightening)
› regional LV wall motion abnormalities graphically depicted as 3-D plot
0= normal
1 = mildly hypokinetic
2 = moderately hypokinetic
3 = severely hypokinetic
4 = akinetic
5 = dyskinetic
› RV size + perfusion + wall motion

Calculated automated algorithm (QPS, Cedars-Sinai):

(a) Myocardial contour of endo- and epicardial surfaces overlying end-diastolic + end-systolic frames displayed on 3 short-axis images (apical, midventricular, basal) on midcavity horizontal and midcavity vertical long-axis image

(b) Quantitative polar plots measuring regional myocardial perfusion at end diastole and end systole (in %), motion (in 10 mm), and wall thickening (in %)
(c) Three-dimensional display of endocardial (solid) and epicardial (grid) LV surfaces
(d) Endocardial time-volume curve during R-R interval, endsystolic and end- diastolic volumes, and LVEF



Planar Reconstruction Planes

LAD supplies:	upper ²/₃ of interventricular septum, anterior wall + part of lateral wall, apex of left ventricle (in most patients)
LCX supplies:	posterior portion of left ventricle (in 10%) lateral portion of left ventricle
RCA supplies:	lower ¹/₃ of interventricular septum, inferior wall of LV + entire RV
PDA supplies:	(through RCA) posterior wall (in 90%)

Interpretation:

√ reversible defect (perfusion defect on stress + no defect on rest images) = myocardial ischemia

√ nonreversible (fixed) defect from stress to rest →

(a) myocardial infarct

(b) attenuation artifact if associated with normal regional wall thickening / wall motion

Value of review of gated SPECT images:

› reduction in number of borderline interpretations

› increase in "definitely normal" from 74% to 93%

Technique:

» patient supine with arms raised above head

» nylon belt wrapped snugly around abdomen to minimize respiratory motion

1. Low-dose (0.2–0.4-mSv) end-tidal expiratory breath-hold CT to obtain an attenuation map
2. ECG-gated SPECT with a frame rate of 8–16 per cardiac cycle with forward-backward gating to allow rejection of premature and postpremature heartbeats by using an acceptance window of 20–30% R-R variation

» symmetric 15% energy window centered at 140 keV = photopeak energy of ^{99m}Tc sestamibi

» low-energy high-resolution parallel hole collimators

» acquisition parameters include 90° rotation (with use of two camera heads) + noncircular orbit with step-and-shoot acquisitions

2. Reconstruction of SPECT images (for 128 x 128 matrix)

(a) without attenuation by filtered back projection method

(b) with attenuation correction by iterative ordered subset expectation maximum algorithm and filtering

(c) careful coregistration of myocardial perfusion imaging data set with CT attenuation map

(d) display in traditional cardiac planes + as polar maps normalized to myocardial region with highest counts

(e) compare normalized map with database of normalized polar maps from subjects with verified normal left ventricular perfusion

Ejection Fraction

Ejection fraction (EF) = stroke volume (SV) divided by end-diastolic volume (EDV)

stroke volume = <u>end-diastolic volume (EDV) minus end-systolic volume (ESV)</u>

EF = [EDV - ESV] / [EDV]

= [EDcounts - EScounts] / [EDcounts - BKGcounts]

sensitive indicator of left ventricular function

@ <u>Left ventricle</u>

› calculated on shallow LAO view

Normal value 50–65% (5% variation)

Definitely abnormal < 50%

Hypertrophic myocardium > 65%

◊ Peak exercise LVEF is an independent predictor of coronary artery disease

@ Right ventricle

mean normal value > 45%

(RV ejection fraction is smaller than for LV because RV has greater EDV than LV but the same stroke volume)

Variability of EF:

LVEF is not a fixed number for any patient but varies with: heart rate, blood pressure, level of circulating catecholamines, patient position, medications

Accuracy in detection of coronary artery disease:

(a) Exercise EF: 87% sensitive; 92% specific

(b) Exercise ECG: 60% sensitive; 81% specific

Interpretation:

◊ Ventricular function at rest is insensitive to CAD!

(1) at rest

√ EF may be decreased in CAD

DDx: cardiomyopathy, valvular disease

√ correlates well with clinical severity + regional distribution of myocardial infarction

(2) during exercise

√ reduced (hypokinetic) / absent (akinetic) / paradoxical (dyskinetic) wall motion indicate varying degrees of CAD / myocardial infarction

√ focal akinetic / dyskinetic area = aneurysm

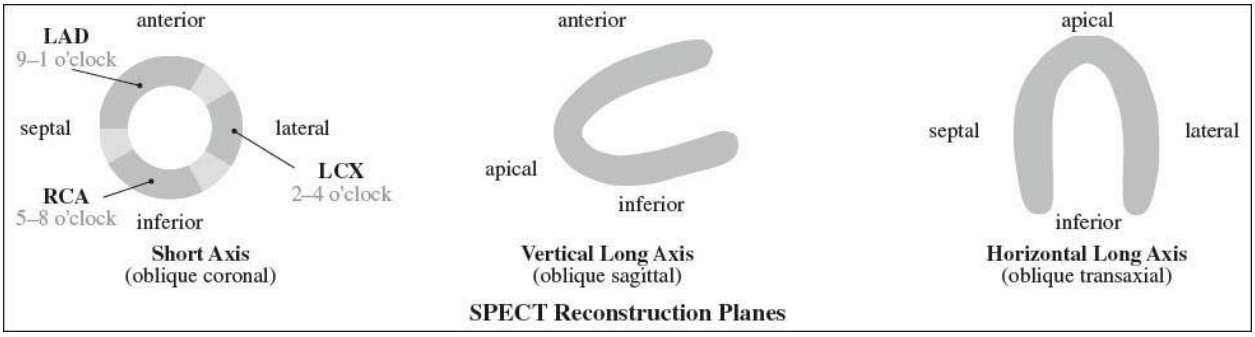
√ paradoxical septal motion (= septal movement to right in systole) may reflect septal infarction, left bundle branch block, S/P bypass surgery

Shortcoming:

poor study in patients with atrial fibrillation because of inability to achieve adequate cardiac gating (exercise MUGA can yield more sensitive assessment of coronary artery disease)

False-positive with (a) inadequate exercise

(b) recent ingestion of meal



Blood Pool Agents

^{99m}Tc-DTPA / ^{99m}Tc-Sulfur Colloid

preferred for cardiac first-pass studies as they allow multiple studies with little residual from any preceding study

^{99m}Tc-labeled Autologous RBCs

= agent of choice because of good heart-to-lung ratio

(1) IN VIVO LABELING

» IV injection of reducing agent stannous pyrophosphate (1 vial PYP diluted with 2 mL sterile saline = 15 mg sodium pyrophosphate containing 3.4 mg anhydrous stannous chloride)

» 15–20–30 min later injection of ^{99m}Tc-pertechnetate (+7), which binds to "pretinned" RBCs (reduction to ^{99m}Tc[+4])

◊ Least time-consuming + easiest method!

◊ Worst labeling efficiency (30% not tagged to RBCs + excreted in urine)!

(2) IN VIVTRO LABELING

= MODIFIED IN VIVO METHOD

◊ Preferred over in vivo because of high labeling efficiency within syringe, which reduces exposure to plasma constituents + creates little free pertechnetate!

» IV injection of 1 mg stannous pyrophosphate

» 10 min later 2–5–10 mL of blood are drawn into a heparinized syringe

» 10–20-min incubation period with ^{99m}Tc-pertechnetate

» reinjection of preparation in 3-way stopcock technique

N.B.: poor tagging in

(a) heparinized patient

(b) injection through IV line (adherence to wall)

(c) syringe flushed with dextrose instead of saline

(3) IN VITRO LABELING

◊ Most reliable labeling method!

» 50 mL drawn blood incubated with ^{99m}Tc reduced by stannous ion; RBCs washed and reinjected

N.B.: Labeling kit (with chelating + oxidizing substances) allows excellent in vitro labeling with only 3 mL of blood and 15-min incubation period!

Dose: 15–20–30 mCi (larger dose required for stress MUGA + obese patients);
for children: 200 µCi/kg; minimum dose of 2–3 mCi

Radiation dose: 1.5 rad for heart, 1.0 rad for blood, 0.4 rad for whole body

^{99m}Tc-HSA

HSA = human serum albumin

Indication: drug interference with RBC labeling (eg, heparinized patient)

Physiology:

(a) albumin slowly equilibrates in extracellular space

(b) poorer heart-to-lung ratio than with labeled RBCs

Ventricular Function

First-pass Ventriculography

= FIRST-PASS RADIONUCLIDE ANGIOGRAPHY = FIRST TRANSIT

= recording of initial transit time of an intravenously administered tight ^{99m}Tc bolus through heart + lungs; limited number of cardiac cycles available for interpretation;

additional projections / serial studies require additional bolus injection

Accuracy: good correlation with contrast ventriculography

Agents: pertechnetate, pyrophosphate, albumin, DTPA, sulfur colloid (almost any ^{99m}Tc-labeled compound except lung scanning particles), ^{99m}Tc-labeled autologous RBCs

Indications:

(1) Only 15 seconds of patient cooperation required
(2) Calculation of cardiac output + ejection fraction (RBCs)
(3) Subsequent first-pass studies within 15–20 minutes of initial study possible (DTPA)
(4) Separate assessment of individual cardiac chambers in RAO projection (temporal separation without overlying atria, pulmonary artery, aortic outflow tract), eg, for right ventricular EF and intracardiac shunts

Minimal dose: 10 mCi

Technique:

» cannulation of antecubital / external jugular vein with ≥ 20 ga needle attached to 3-way stopcock and two syringes:
  » syringe 1 contains ≤ 1 mL of radiotracer
  » syringe 2 contains a saline flush (10–20 mL)
» injection of radiotracer → followed by a strong flush of saline

Gating:

improved images obtained by selection of time interval corresponding only to RV passage of bolus averaged over several (3–5) individual beats; gating may be done intrinsically or with ECG guidance

Imaging: region of interest (ROI) over RV silhouette in RAO projection; background activity taken over horseshoe-shaped ventricular wall; counts in ROI displayed as function of time; 25 frames/second for 20–30 seconds

Quality Control:

(a) Bolus Adequacy:
  › good = FWHM of time activity curve < 1 second
  › adequate = FWHM of 1–1.5 seconds
  › delayed = FWHM of > 1.5 seconds
  › split = more than one discrete peak
  Problem: delayed bolus may cause oversubtraction of background resulting in spurious ↑ in LVEF, ↓ in LV volume, overestimation of regional wall motion
(b) Count Statistics
  > 4000–5000 cps (counts per second) of LV end-diastolic counts in the representative cycle
(c) Tracer Transit Time
  visual examination of bolus transiting the central circulation
(d) Beat Selection
  only beats with end-diastolic counts of ≥ 70% of peak end-diastolic counts
(e) Background Selection
  a frame close to the beginning of the LV phase

Normal passage of bolus: SVC, RA, RV, lungs, LA, LV, aorta

R-to-L shunt: tracer appears in left side of heart before passage through lungs

Evaluation of:

1. Obstruction in SVC region
2. Reflux from RA into IVC / jugular vein
3. Stenosis in pulmonary outflow tract
4. R-L shunt
5. Contractility of RV
6. Sequential beating of RA and RV
7. Ejection fraction of RV and LV

Cardiac Rhythm & Conduction:

Regional wall motion + LVEF may be effected by:

(1) Frequent premature ventricular contractions (PVCs)
(2) Ventricular bigeminy
(3) Very irregular atrial fibrillation
(4) Pacemaker rhythm: from apex → to base
(5) Left bundle branch block (LBBB)
√ infero- / anteroapical wall motion abnormalities
N.B.: paradoxical septal motion not detectable in RAO projection

Equilibrium Images

= "blood pool" radionuclide cardioangiography

Agents: ^{99m}Tc-labeled autologous RBCs (most commonly) / human serum albumin

Imaging: after thorough mixing of radiotracer throughout vascular space

» acquisition of images during selected portions of cardiac cycle triggered by R-wave; each image is composed of > 200,000 counts (2–10 minutes) obtained over 500–1,000 beats after equilibrium has been reached; high-quality images can be obtained in different projections

» gated acquisition from 16–32 equal subdivisions of the R-R cycle (electronic bins) allows display of synchronized cinematic images (assembled to composite single-image sequence) of an "average" cardiac cycle

√ may be displayed as time activity curves reflecting changes in ventricular counts throughout R-R interval

› measured functional indices: preejection period (PEP), left ventricular ejection time (LVET), left ventricular fast filling time (LVFT1), left ventricular slow filling time (LVFT2), PEP/LVET ratio, rate of ejection + filling of LV

» at rest: count density of 200–250 counts/pixel requires generally 7–10 minutes acquisition time for 200,000–250,000 counts/frame

» during exercise: 100,000–150,000 counts/frame requires an acquisition time of 2 minutes

Evaluation of:

1. LV ejection fraction
2. Regional wall motion
3. Valvular regurgitation

Interpretation:

1. Heart failure: decreased EF, prolongation of PEP, shortening of LVET, decreased rate

of ejection

2. Hypertensive heart: normal systolic indices, normal EF, prolonged LVFT1
3. Hypothyroidism: prolonged PEP, normal EF
4. Aortic stenosis: mild reduction of EF, prolonged LV emptying time, decreased rate of ejection, normal rate of filling

√ area of decreased periventricular uptake secondary to

(a) pleural effusion > 100 mL

(b) ventricular hypertrophy

Gated Blood Pool Imaging

= MULTIPLE GATED ACQUISITION (MUGA)

= gated equilibrium images depict average cardiac contraction by summation over several minutes

Recording of:

(1) Ejection fraction (EF) of left ventricle before + after exercise (> 6 million counts, 32 frames)

(2) Regional wall motion of ventricular chambers (> 4.5 million counts, 24 frames)

(a) at rest: myocardial infarction, aneurysm, contusion

(b) *during exercise:* ischemic dyskinesia (detectable in 63%)

(3) Regurgitant index

Projection:

(a) septal view (usually LAO 45°) best for EF; often requires some cephalad tilting of detector head

(b) two additional views for evaluation of wall motion (usually anterior + left lateral views)

Imaging:

physiologic trigger provided by R-R interval of ECG ("bad beat" rejection program desirable); R-R interval divided into typically about 20 frames; several hundred cardiac contractions are summed (depending on count density) for each planar projection

(a) gated images obtained for 5 minutes

(b) 2-min image acquisition time for each stage of exercise

PROs: (1) Higher information density than 1st-pass method

(2) Assessment of pharmacologic effect possible

(3) "Bad beat" rejection possible

CONs: (1) Significant background activity

(2) Inability to monitor individual chambers in other than LAO 45° projection

(3) Plane of AV valve difficult to identify

Radiation dose: 1.5 rad for heart; 1.0 rad for blood; 0.4 rad for whole body

Qualitative evaluation:

(1) Chamber size

(2) Wall thickness

(3) Regional wall motion

Myocardial Perfusion Imaging Agents

Most commonly used: ^{99m}Tc sestamibi + ^{99m}Tc tetrofosmin
Preparation: » NPO for 4 hours before perfusion imaging
» NO caffeine for 12–24 hours before exam
At discretion of referring physician:
» withhold consumption of β- and calcium channel blockers for 24 hours before imaging
» long-acting nitrates should be withheld the day of the exam

43Potassium

Not suitable for clinical use because of its high energy

^{201}Thallium-chloride

= cation produced in cyclotron from stable ^{203}Tl
= image agent of choice to assess myocardial viability
Cyclotron: by (p,3n) reaction to radioactive 201Pb (half-life of 9.4 hours) → decays by electron capture to ^{201}Tl
Decay: by electron capture to ^{201}Hg
Energy spectrum: 69–83 keV of Hg-K x-rays (98% abundance); 135 keV (2%) + 167 keV (8% abundance) gamma photons
Physical half-life: 74 hours
Biologic half-life: 10 ± 2.5 days
Dose: low dose of 3–4 mCi (the larger dose for SPECT) because of long half-life and slow body clearance
Radiation dose:
3 rad for kidneys (critical organ) (= 1.2 rad/mCi); 1.2 rad for gonads (= 0.6 rad/mCi); 0.7 rad for heart + marrow (= 0.34 rad/mCi); 0.5 rad for whole body (= 0.24 rad/mCi)
Quality control: should contain < 0.25% 203Pb; < 0.5% ^{202}Tl (439 keV)
Indications:
1. Acute myocardial infarction
2. Coronary artery disease
» particularly useful over ECG in:
(a) conduction disturbances: eg, bundle branch block, preexitation syndrome
(b) previous infarction
(c) under drug influence: eg, digitalis
(d) left ventricular hypertrophy
(e) hyperventilation
(f) ST depression without symptoms
(g) if stress ECG impossible to obtain

Thallium uptake & distribution:
› intracellular uptake via Na/K-ATPase (analogue to ionic potassium), but less readily released from cells than K+
› distribution is proportional to regional blood flow
› uptake depends on
(1) quality of regional perfusion
(2) viable cells with integrity of Na/K pump
@ Blood pool < 5% remain in blood pool 15 minutes post injection

@ Myocardial uptake depends on
(a) myocardial perfusion
(b) myocardial mass
(c) myocardial cellular integrity
◊ First-pass extraction efficiency is 88%!
REMEMBER: 90% in 90 seconds!
› 4% of total dose localizes in myocardium at rest (myocardial blood flow = 4% of cardiac output)
› peak myocardial activity occurs at 5–15 minutes after injection
› uptake can be increased to 8–10% with dipyridamole stress
› clearance from myocardium is proportional to regional perfusion + begins within a few min after injection ("wash out"); zones of initially higher uptake wash out more rapidly than areas of low uptake (= "redistribution")

@ Skeletal muscle + splanchnicus: first-pass extraction efficiency is 65%
› accumulate 40% of injected dose
› 4–6 hour fast + exercise → ↓ flow to splanchnicus and ↑ cardiac uptake

@ Lung: 10% of total dose localizes in lung
› augmented pulmonary extraction with LV dysfunc-tion, bronchogenic carcinoma, lymphoma of lung
√ < 5% activity over lung is normal
√ ↓ heart-to-lung ratio with triple-vessel disease

@ Kidney: accumulates 4% of injected dose
› excretion of 4–8% within 24 hours

@ Thyroid:
√ increased uptake > 1% in Graves disease + thyroid ca.

@ Brain:
√ uptake only if blood-brain barrier disrupted

Technique:

A. **Single dose method**
» 3 mCi injected at peak exercise for exercise image immediately + rest image 3 hours later

B. **Split dose method**
» 2 mCi injected for exercise image
» 1 mCi reinjected at rest after 3 hours with rest image taken 30 minutes later

C. **Booster reinjection technique**
» reinjection of thallium followed by imaging after 18–24–72 hours ↑ blood concentration of isotope
= late reversibility provides evidence of regional myocardial ischemia + viability not appreciated even on very delayed (24–72 hour) redistribution images; predicts scintigraphic improvement post intervention
Reasoning: 50% of irreversible persistent defects improve significantly after booster reinjection

Imaging:

1. EXERCISE IMAGE = DISTRIBUTION IMAGE
= stress thallium image

= map of regional perfusion obtained within minutes after injection at peak exercise; initial distribution proportional to myocardial blood flow + arterial concentration of radioisotope + muscle mass; 300,000–400,000 counts / view (~ 5–8 minutes sampling time), should be completed by 30 minutes

2. REDISTRIBUTION IMAGE
   = equilibrium between tracer uptake and efflux dependent on blood flow + mass of viable tissue + concentration gradient
   = map of hypoperfused ischemic but viable myocardium obtained at rest after 2–3–4–6 hours; washout half-life from normal myocardium is 54 min
3. DELAYED IMAGE (optional)
   = viability study at 24 hours

Interpretation:

√ "apical thinning" = less myocardial mass of cardiac apex as a normal finding
√ normally diminished tracer uptake at basal portions of ventricle (near plane of mitral valve) ← more fibrous tissue + less muscle mass
√ variation in tracer intensity by 15–20% between regions on planar images may be normal ← soft-tissue attenuation artifacts from subdiaphragmatic abdominal contents or breast tissue

Interpretation of Stress Thallium Images

Immediate Image	*Delayed Image*	*Diagnosis*
normal	normal	normal
defect	fill-in	exertional ischemia
defect	persistent	myocardial scar
defect	partial fill-in	scar + ischemia / persistent ischemia

1. Initial phase = first-pass extraction
   √ temporary defect accentuated by exercise
   √ defect > 15% of ventricular surface suggests > 50% stenosis of coronary artery
   √ right heart well seen during stress test, tachycardia, volume / pressure overload
   √ dilated heart cavity on stress images (but not on rest images) ← exercise-induced LV dysfunction
2. Redistribution phase (on 2–4-hour images)
   √ washout in normal areas
   √ slow continued accumulation of tracer for areas of greatly ⇓ perfusion
   √ ↑ uptake in viable ischemic zones ("redistribution")
   √ permanent defect = nonviable myocardium as in myocardial infarction / fibrosis
   √ ↑ lung activity (ie, > 50% of myocardial count) indicative of
   (a) left ventricular failure ← severe LCA disease / myocardial infarction
   (b) pulmonary venous hypertension ← cardiomyopathy / mitral valve disease
   √ right heart faintly visualized during rest (15% of perfusion to right side); ⇑ activity in RV ←
   (a) ↑ in ventricular systolic pressure
   (b) ↑ in mean pulmonary artery pressure

(c) ↑ in total pulmonary vascular resistance

Sensitivity: overall 82–84% for stress ^{201}Tl (60–62% for exercise ECG)

(a) <u>increased with:</u>
  (1) Severity of stenosis (86% + 67% sensitive with stenosis > 75% + < 75%)
  (2) Greater number of involved arteries
  (3) Stenosis of left main > LAD > RCA > LCX
  (4) Prior infarction
  (5) High work load during exercise testing in patients with single-vessel disease

(b) <u>decreased with:</u>
  (1) Presence of collaterals
  (2) Beta blockers
  (3) Time delay for poststress images

Specificity: overall 91–94% for stress ^{201}Tl (81–83% for exercise ECG)

False-positive thallium test (37–58%):

A. Infiltrating myocardial disease
  1. Sarcoidosis
  2. Amyloidosis

B. Cardiac dysfunction
  1. Cardiomyopathy
  2. IHSS
  3. Valvular aortic stenosis
  4. Mitral valve prolapse (rare)

C. Decreased cardiac perfusion other than myocardial infarction
  1. Cardiac contusion
  2. Myocardial fibrosis
  3. Coronary artery spasm: severe unstable angina may cause defect after stress + on redistribution images, but will be normal at rest!

D. Normal variant
  1. Apical myocardial thinning
  2. Attenuation by diaphragm, breast, implant, pacemaker

mnemonic: I'M SIC

Idiopathic hypertrophic subaortic stenosis
Myocardial infarct without coronary artery disease
Scarring, **S**pasm, **S**arcoidosis
Infiltrative / metastatic lesion
Cardiomyopathy

False-negative thallium test:

1. Under influence of beta-blocker: eg, propranolol
2. "Balanced ischemia" = symmetric 3-vessel disease
3. Insignificant obstruction
4. Inadequate stress
5. Failure to perform delayed imaging
6. Poor technique

mnemonic: 3NMRS COR

3-vessel disease (rare)

Noncritical stenosis
Medications interfering
Right coronary lesion (isolated)
Submaximal exercise
Collateral (coronary) blood vessels
Overestimation of stenosis on angiography
Redistribution (early / delayed)

Advantages compared with ^{99m}Tc compounds:

(1) Higher total accumulation in myocardium
(2) Provides redistribution information

Disadvantages:

(1) Low energy x-rays result in poor resolution → improved with SPECT
(2) Dose is limited by its long half-life
(3) Half-value thickness of 3 cm results in less avid appearing myocardium: inferior wall (deeper part of myocardium) / anterolateral wall (overlain by breast)
(4) Imaging must be completed by 45 minutes post injection or redistribution occurs

^{99m}Tc-MIBI (Sestamibi)

= cationic lipophilic isonitrile complex, which binds to myocyte intramitochondrial proteins

Pharmacokinetics:

› relatively rapid clearance from circulation (40% first- pass extraction) ← passive diffusion across cell membranes
› high myocardial accumulation (4%) with nonlinear uptake proportional to regional perfusion (fall-off in extraction at higher rates of flow)
› slow washout with long retention time in myocardium and little recirculation
› significant hepatic + gallbladder activity

Excretion: through biliary tree (give milk after injection and before imaging to decrease GB activity)

Dose: 25–30 mCi (Cardiolite®)

Imaging: optimum images 1 hour after injection (may be imaged up until 3 hours)

Technique: separate injections for stress and rest studies because of slow washout

A. 1-DAY PROTOCOL (rest-stress protocol)
Improved detection of reversibility compared with stress-rest protocol
» inject 5–8 mCi ^{99m}Tc-sestamibi
» take rest images 60–90 min after injection
» wait 0–4 hours
» stress patient followed by injection with 15–25 mCi ^{99m}Tc-sestamibi at peak stress (↑ myocardial blood flow means ↑ myocardial uptake)
» image 30–60 minutes later (optimum imaging time of stress-induced defects)

B. 2-DAY PROTOCOL (impractical stress-rest protocol):
» stress images on 1st day: ^{99m}Tc-sestamibi given at peak stress; imaging after 30–60-minute delay → to allow some clearing of liver activity
» repeat on 2nd day ONLY if stress views abnormal

C. DUAL TRACER STRATEGY

» ^{201}Tl for initial injection
» ^{99m}Tc-sestamibi as 2nd injection immediately afterwards → its higher energy photons are unaffected by residual ^{201}Tl

Advantages over thallium:

(1) Low radiation dose ← shorter half-life allowing larger doses with less patient radiation
(2) Excellent imaging characteristics due to
  (a) improved photon flux → faster imaging + ability for cardiac gating
  (b) higher photon energy → less attenuation artifact from breast tissue / diaphragm + less scatter
(3) NO redistribution
(4) Temporal separation of injection and imaging allows injection during acute myocardial infarct when patient may not be stable for imaging; after stabilization + intervention (angioplasty / urokinase) imaging can demonstrate the pre-intervention defect
(5) Low cost
(6) Easy availability
(7) Flexible scheduling
(8) Increased patient throughput

Disadvantage: less well suited to assess viability

^{99m}Tc-Teboroxime

= neutral boronic acid oxime complex

Pharmacokinetics:

› very rapid clearance time from circulation ← rapid uptake by myocardium = high extraction efficiency
› distribution proportional to cardiac blood flow EVEN at high blood flow levels (sestamibi + thallium plateau at high levels of flow)
› biexponential washout from myocardium + little recirculation
› high background from lung + liver (cleared earlier and more rapidly from the liver)

Dose: 25–30 mCi (CardioTec®)

Imaging: must begin immediately post injection ← rapid washout; rest image can immediately follow stress image

^{99m}Tc-Tetrofosmin

= diphosphine complex (Myoview™)

Related compounds: ^{99m}Tc-Q12 (furifosmin), Q3

Pharmacokinetics:

› lower first-pass extraction + accumulation than thallium
› slow myocardial washout
› rapid background clearance
› quicker liver excretion than sestamibi

Positron Emission Tomography

Perfusion agents: ^{13}N-ammonia, ^{15}O water, ^{82}Rb

Metabolic agents: ^{18}Fluorine-deoxyglucose = FDG (glycolysis), ^{11}carbon-palmitate (beta-oxidation), ^{11}carbon-acetate (tricarboxylic acid cycle)

MYOCARDIAL METABOLIC PET

Pathophysiology: in myocardial ischemia glycolysis (utilization of glucose) increases while mitochondrial β-oxidation of fatty acids decreases!

Sensitivity: > 95%

Technique:

» give oral glucose load
» inject 10 mCi FDG
» image after 30 min

Variation: simultaneous injection of perfusion tracer

Interpretation:

√ mismatched defect (= decreased perfusion but enhanced metabolism indicated by FDG uptake) indicates → viable (but dysfunctional) myocardium salvageable by revascularization procedure

√ matched defect (= flow + FDG accumulation both decreased) → nonviable myocardium

◊ 80–90% of matching defects do NOT improve after bypass

√ 11C-acetate superior to FDG (accurately reflects overall oxidation metabolism ← not influenced by myocardial substrate utilization)

Comparison with thallium:

accuracy for fixed lesions similar; higher for reversible ischemia

MYOCARDIAL PERFUSION PET

Ability to detect obstructive CAD in > 1 coronary artery with > 50% stenosis: 83%–100% sensitive, 73%–100% specific, 80%–100% PPV, 36%–100% NPV, 84%–98% accurate

Advantages of PET over SPECT:

1. Improved accuracy ← increased specificity + marginally improved sensitivity
2. Capacity to quantify left ventricular function at rest + during peak stress and coronary flow reserve
3. Better definition of extent of anatomic CAD
4. Lower radiation dose than SPECT
5. Integration of PET + CT for anatomic extent of CAD

Stress test

Rationale:

◊ Rest-injected images can separate viable from nonviable myocardium + detect very severe ischemia (with stenosis of > 90–95%), but cannot detect most coronary artery disease (CAD)!

Exercise increases myocardial work and oxygen requirement: at peak exercise blood flow may rise 5-fold from baseline through coronary artery dilatation + increase in heart rate; exercise will unveil CAD-related regional hypoperfusion relative to normal regions, if coronary artery stenosis > 50%

Physical / Physiologic / Exercise Stress Test

◊ Exercise in erect position (peak heart rate lower if supine) on treadmill or bicycle; isometric handgrip exercise raises blood pressure less (but adequate for evaluation)

◊ Starting point of workload selected according to preliminary exercise results (at an average of 200 kilowatt pounds)

Bruce treadmill protocol:

» grade of exercise incrementally increased by inclination + belt speed (200 kilowatt pounds)

» graded exercise in 3-min stages of increasing workload

» endpoints for discontinuing exercise:

(1) attainment of 85% of predicted maximal heart rate = 220 – age in years
(2) Inability to continue ← fatigue, dyspnea, leg cramps, dizziness, chest pain
(3) Severe angina / hypotension
(4) Severe ECG ischemic changes / arrhythmia
(5) Fall in BP > 10 mmHg below previous stage
(6) Ventricular tachycardia
(7) Run of 3 successive premature ventricular beats

◊ Cardiologist with crash cart should be available!

Problems with exercise imaging:

(1) Sensitivity to detect ischemic lesions decreases with suboptimal exercise (in particular for older population)
(2) Higher false-positive tests in women (artifacts from overlying breast tissue)
(3) Propranolol (beta blocker) interferes with stress test, should be discontinued 24–48 hr prior to testing

Pharmacologic Stress Test

Advantages:

(1) Reproducibility
(2) Independent from patient motivation
(3) Freedom from patient infirmities: eg, severe peripheral vascular disease, arthritis, pain

Vasoactive drugs:

A. Primary coronary vasodilators

Action: binding to A_2 receptors affects the intracellular cyclic AMP, GMP, and calcium levels → coronary hyperemia

N.B.: Discontinue use of caffeine, tea, chocolate, cola drinks for 24 hours prior to test

◊ Cannot be used in patients on theophylline!

(1) IV infusion of 140 µg/kg/min dipyridamole (= Persantine®) → 3–5-fold increase in coronary artery blood flow

Total dose: 0.84 mg/kg

Drug action: 30 minutes

Side effects: flushing, nausea, bronchospasm (reversible with aminophylline)

» dipyridamole injection over 4 min

» wait 10 min for maximum effect
» inject radiotracer
◊ Prolonged supervision after test necessary!

(2) IV infusion of 140 µg/kg/min adenosine (= Adenocard®, Adenoscan®)

Radiopharmaceuticals for Myocardial Perfusion PET				
Radiotracer	*Physical Half-Life*	*Availability*	*Advantage*	*Disadvantage*
Rubidium 82 (^{82}Rb)	76 sec	Strontium 82 (^{82}Sr)/^{82}Rb generator	simplicity of use	relatively poor resolution
Nitrogen 13 (^{13}N) ammonia	10 min	Cyclotron	high extraction simplifies quantitation	requires cyclotron, heterogeneous uptake
Copper 62 (^{62}Cu)–pyruvaldehyde-bis (N4-methylthiosemicarbazone (PTMS)	10 min	^{62}Zn/^{62}Cu generator	rapid blood pool clearance, long myocardial retention	short parent isotope half-life
Oxygen 15 (^{15}O)–water	2 min	Cyclotron	diffusible with high extraction	requires cyclotron, not suitable for clinical imaging
Fluorine 18 (^{18}F) flurpiridaz	110 min	Cyclotron	long half-life allows exercise studies	higher radiation dose for same-day stress-rest studies

Drug action: 2–3 minutes (half life of 15 seconds)
Side effects: flushing, nausea, transient AV block, bronchospasm
Drug reversal: theophylline
» continuous IV infusion for 3 minutes
» radiotracer injection
» continue infusion for additional 3 minutes
◊ Supervision after test not needed
Contraindication: significant pulmonary disease requiring use of inhalers

(3) IV injection of 0.4 mg Regadenoson (Lexiscan®) followed by saline flush = highly specific adenosine A2A receptor agonist acting as coronary vasodilator with very low affinity for A1 (→ AV node block), A2B (→ severe peripheral vasodilation and hypotension), A3 (→ bronchoconstriction)
Advantages: weight-unadjusted single bolus dose, fast onset + short duration of action, fewer side effects than adenosine
» radiotracer injection 10–20 sec after saline flush
» 150 mg of IV aminophylline > 3–4 minutes after radiotracer injection
» complete limited exercise protocol tailored to patient's physical ability

B. Chronotropic inotropes
Drug action: β-1 agonist → ↑ myocardial contractility + work = ↑ oxygen demand
Candidates: patients with COPD, asthma, allergy to vasodilators, patients on theophylline preparations

(1) IV infusion of 5 µg/kg/min dobutamine for 5 minutes, increased in steps of 5 µg/kg every 5 minutes to a maximum infusion rate of 30–40 µg/kg/min titrated to patient's response
» radiotracer injected at onset of significant symptoms / ECG changes / achievement of maximal rate of infusion or heart rate
» infusion maintained for an additional 2 minutes with dose adjusted to patient's condition

(2) IV infusion of arbutamine with its own computerized delivery system titrating

dose rate automatically

Contraindication: severe hypertension, atrial flutter / fibrillation

Precautions:

1. Monitoring devices: electrocardiographic and blood pressure monitors
2. Emergency resuscitation equipment: defibrillator
3. Emergency cart: drugs + pharmacologic antidotes (epinephrine, β-blocker, atropine, bronchodilator, antiarrhythmic medication)

Applied to:

1. THALLIUM IMAGING (redistribution images after stress test):
   - » injection of 1.5–2 mCi of ^{201}Tl during peak exercise, continuation of exercise for additional 60 seconds before imaging commences

   Clues for stress images:
   - √ RV myocardium well visualized
   - √ little pulmonary background activity
   - √ little activity in liver, stomach, spleen
   - √ distribution more uniform after stress than during rest
   - ◊ Degree of liver uptake useful as direct measure of level of exercise!

   Sources of technical errors:

   mnemonic: ABCDE PS

   Attenuation from overlying breast / diaphragm
   Background oversubtraction
   Camera field nonuniformity
   Drugs, **D**elayed (excessively) imaging, **D**ose infiltration
   Eating / **E**xercising between stress + delayed images
   Positioning variation between stress + delayed images
   Submaximal exercise
2. GATED BLOOD POOL IMAGING (response of EF)
   - √ ↑ in ejection fraction from 63–93% in normals
   - √ ↑ in ventricular wall motion (anterolateral > posterolateral > septal)
3. MR MYOCARDIAL PERFUSION IMAGING

Infarct-avid Imaging

= hot spot imaging

Agent: ^{99m}Tc-pyrophosphate (standard), 203Hg chlormerodrin, ^{99m}Tc-tetracycline, ^{99m}Tc-glucoheptonate, ^{18}F-sodium fluoride, ^{111}Indium-antimyosin (murine monoclonal antibodies to myosin), ^{99m}Tc-antimyosin Fab fragment

^{99m}Tc-Pyrophosphate

Pathophysiology in MYOCARDIAL INFARCTION:

Pharmacologic Stress Agents				
Stress Agent	*Dose*	*Administration*	*Mechanism of Action*	*Contraindication, Side Effects*
Dobutamine	40 µg/kg/min (max)	infusion	direct B_1 + B_2 receptor stimulation with dose-related increase in heart rate + blood pressure + myocardial contractility	Systemic hypertension Complex arrhythmia HOCM Uncontrolled CHF
Atropine	0.25-mg fractions typical (max 2 mg)	fractional injections	nonselective muscarinic acetylcholinergic antagonist	Narrow-angle glaucoma Myasthenia gravis Obstructive uropathy
Adenosine (Adenocard®, Adenoscan®)	140 mg/kg/min	4–6 min infusion	Activation of A_1, A_{2B} and A_3 receptors Activation of A_{2A} receptors Half-life = 10 sec	2nd / 3rd-degree AV block Systolic BP < 90 mmHg Active airway disease Hypersensitivity
Regadenoson (Lexiscan®)	0.4 mg	single injection	A_{2A} receptor agonist inducing direct coronary arteriolar vasodilatation Weak affinity fr A_{2B} + A_3 receptors Initial phase half-life = 2–4 min followed by elimination phase of 2–4 h	Similar but reduced side effects as adenosine (→ suitable for patients with mild reactive airway + obstructive lung disease)

pyrophosphate is taken up by myocardial necrosis through complexation with calcium deposits > 10–12 hours post infarction

- › requires presence of residual collateral blood flow
- › 30–40% maximum accumulation in hypoxic cells with a 60–70% reduction in blood flow (greater levels of occlusion reduce uptake)

Uptake post infarction:

- › earliest uptake by 6–12–24 hours;
- › peak uptake by 48–72 hours;
- › persistent uptake seen up to 5–7 days with return to normal by 10–14 days

Sensitivity: 90% for transmural infarction, 40–50% for subendocardial (nontransmural) infarction

Specificity: as low as 64%

Dose: 15–20 mCi IV (minimal count requirement of 500,000/view)

Imaging: at 3–6 hr (60% absorbed by skeleton within 3 hr)

Indications:

1. Lost enzyme pattern = patient admitted 24–48 hr after infarction
2. Equivocal ECG + atypical angina:
   (a) left ventricular bundle branch block
   (b) left ventricular hypertrophy
   (c) impossibility to perform stress test
   (d) patient on digitalis
3. ST depression without symptoms
4. Equivocal enzyme pattern + equivocal symptoms
5. S/P cardiac surgery (perioperative infarction in 10%, enzymes routinely elevated, ECG always abnormal), requires preoperative baseline study as 40% are preoperatively abnormal
6. For detection of right ventricular infarction

NOT HELPFUL:

1. In differentiating multiple- from single-vessel disease
2. Typical angina

3. Normal ECG stress test + NO symptoms

Scan interpretation:

[Grade 2+ and above are positive]

Grade 0 no activity

Grade 1+ faint uptake

Grade 2+ slightly less than sternum, equal to ribs

Grade 3+ equal to sternum

Grade 4+ greater than sternum

√ "doughnut" pattern = central cold defect (necrosis in large infarct) usually in cases of large anterior + anterolateral wall infarctions

√ uptake in inferior wall extending behind sternum (anterior projection) suggests RV infarction

◊ SPECT imaging improves sensitivity (← eliminates rib overlap)

√ diffuse uptake can be seen in angina, cardiomyopathy, subendocardial infarct, pericarditis and normal blood pool (normal blood pool can be eliminated with delayed imaging)

FALSE POSITIVES (10%):

A. Cardiac causes:

1. Recent injury: myocardial contusion, resuscitation, cardioversion, radiation injury, Adriamycin® cardiotoxicity, myocarditis, acute pericarditis
2. Previous injury: left ventricular aneurysm, mural thrombus, unstable angina, previous infarct with persistent uptake
3. Calcified heart valves / calcified coronary arteries (rare) / chronic pericarditis
4. Cardiomyopathy: eg, amyloidosis

B. Extracardiac causes:

1. Soft-tissue uptake: breast tumor / inflammation, chest wall injury, paddle burns from cardioversion, surgical drain, lung tumor
2. Osseous: calcified costal cartilage (most common), lesions in rib / sternum
3. Increased blood pool activity secondary to renal dysfunction / poor labeling technique (improvement on delayed images)

mnemonic: SCUBA

Subendocardial infarction (extensive)
Cardiomyopathy / myocarditis
Unstable angina
Blood pool activity
Amyloidosis

FALSE NEGATIVES (5%)

Myocardial metastasis

PERSISTENTLY POSITIVE SCAN (> 2 weeks)

= ongoing myocardial necrosis indicating poor prognosis, may continue on to cardiac aneurysm, repeat infarction, cardiac death

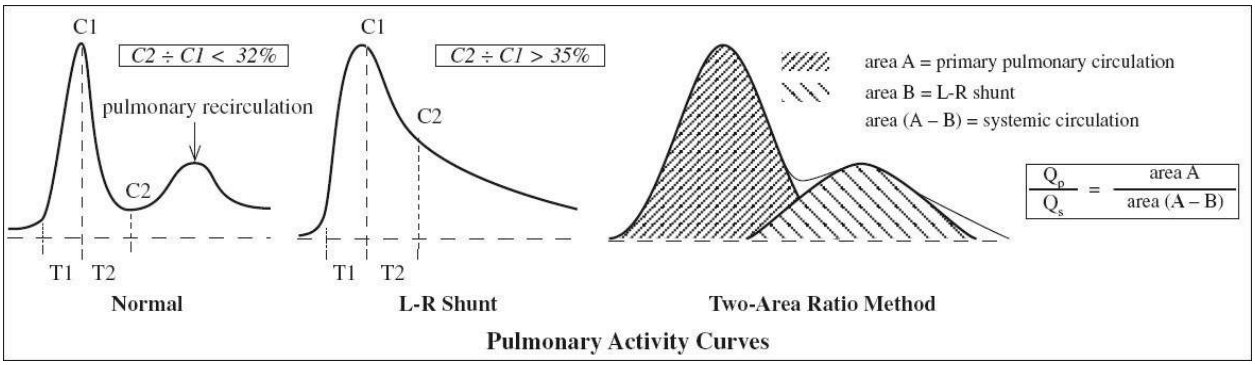
› in 77% of persistent / unstable angina pectoris

› in 41% of compensated congestive heart failure

› in 51% of ECG evidence of ventricular dyssynergy

Prognosis: the larger the area, the worse the mortality + morbidity

^{99m}Tc-Antimyosin Fab Fragments



= specific marker for myocyte damage
= Fab fragments of an antibody raised against water-insoluble heavy chains of cardiac myosin exposed due to necrosis
Sensitivity: 95%
√ uptake ONLY in acute infarct with decreasing intensity as the infarct heals

Nonavid Infarct Imaging

= COLD SPOT IMAGING
= myocardial perfusion study for acute myocardial infarct
Agent: ^{201}Tl (at rest)
Sensitivity after onset of symptoms:
96% within 6–12 hours, 79% after 48 hours, 59% in remote infarction; sensitivity for SPECT (seven pinhole tomography) 94% > planar scintigraphy 75%
√ fixed permanent defect in acute infarction
√ fixed permanent defect at rest + on stress thallium + redistribution images in old infarction
√ "cold defect" at rest may represent transient ischemia in unstable angina
N.B.: ^{201}Tl cannot distinguish between recent + remote infarction!

Intracardiac Shunts

Blood-pool agents administered by peripheral IV injection:
^{99m}Tc-pertechnetate, DTPA, sulfur colloid, macroaggregated albumin, labeled RBCs
Method:
C2÷C1-method measures hemodynamic significance of a shunt; raw data obtained from pulmonary activity curve (gamma variate method, Qp÷Qs ratio = two-area ratio method, count method); accuracy depends on the shape of the input bolus (single peak of < 2 second duration); measuring C1, C2, T1, T2

A. Normal
C2÷C1 is < 32%
B. L-R shunt
Indication: ASD, VSD, AV canal, aortopulmonic window, rupture of sinus of Valsalva aneurysm

√ C2÷C1 > 35% (area A = primary pulmonary circulation; area B = L-R shunt; area (A – B) = systemic circulation; QP ÷ QS = area A / area (A – B) > 1.2

C. R-L shunt

Indication: Tetralogy of Fallot, transposition, truncus, Ebstein anomaly

√ early arrival of tracer in left side of heart + aorta (first-pass method) prior to arrival of activity from lungs to LV

√ quantification possible only by registration of sum of activity of trapped macroaggregate / microspheres in brain + kidneys

Causes of abnormal nonshunt-related activity:

(1) Radiopharmaceutical breakdown

√ free pertechnetate activity in salivary glands, gastric mucosa, thyroid, kidney

(2) Hepatic cirrhosis abnormal pulmonary vascular channels bypassing the lung (in 10–70%)

(3) Pulmonary AVM

BILIARY SCINTIGRAPHY

Application:

1. Acute cholecystitis
2. Congenital biliary atresia
3. Evaluation of bile leak
4. Choledochal cyst
5. Biliary-enteric fistula
6. Chronic GB dysfunction

^{99m}Tc-IDA analogs = HIDA agents

= ^{99m}Tc-acetanilide iminodiacetic acid analogs (IDA)

Dependent on the substance's lipophility, there is a trade-off between renal excretion + hepatic uptake (BIDA is the most lipophilic, HIDA the least lipophilic)

1. HIDA (2,6-dimethyl derivative): [H = hepatic] bilirubin threshold of < 18 mg/dL; 15% renal excretion
2. BIDA (parabutyl derivative): bilirubin threshold of < 20 mg/dL
3. PIPIDA (paraisopropyl derivative): 2% renal excretion
4. DIDA (diethyl derivative)

most often used:

5. DISIDA (diisopropyl derivative) = Disida®, Disofenin®, Hepatolite®: bilirubin threshold of < 30 mg/dL
6. TMB-IDA (m-bromotrimethyl IDA) = Mebrofenin®, Choletec®: T1/2 uptake is 6 min, T1/2 excretion is 14 min in normals; bilirubin levels may be as high as 30 mg/dL

Quality control: the final compound should contain

› 90–100% ^{99m}Tc-IDA
› < 10% ^{99m}Tc-tin colloid
› < 10% ^{99m}Tc-sodium pertechnetate

Pharmacokinetics:

@ Bloodstream
tracer binds predominantly to albumin → decreasing renal excretion (renal excretion seen in most normals); dissociation of albumin + ^{99m}Tc-IDA takes place in space of Disse

@ Liver
peak liver activity 5–15 minutes post injection
= hepatic phase; 85% extracted by hepatocytes tracer enters anion pathway of bilirubin
◊ Delayed liver uptake implies hepatocyte dysfunction / CHF (less likely)
◊ Look for liver lesions on early images

@ Bile
secretion by hepatocytes without conjugation; CBD + cystic duct visualized within 10–30 min (not always visualized in normals); GB visualized by 20–60 min
◊ Activity in right paracolic gutter / intraperitoneal space implies postoperative bile leak

@ Bowel
excretion into duodenum by 30 minutes; bowel visualized within 1 hour; no

enterohepatic recirculation

Dose: 2–8 mCi for adults

Radiation dose: 2 rad for upper large bowel; 0.55 rad for gallbladder; 3 rad/mCi for small bowel; 0.01 rad/mCi for whole body

Patient preparation:

» Fasting for at least (2–)4 hours to avoid a contracted gallbladder (because endogenous cholecystokinin contracts gallbladder)

» Injection of 0.02 µg/kg Kinevac® over > 3 minutes to empty gallbladder about 30 minutes before tracer injection in patients on prolonged fasting (fasting > 24 hours causes an overdistended GB)

» Narcotics (opiates) + sedatives → increase tone of sphincter of Oddi and have to be stopped 6–12 hours before exam

Equipment:

Large field-of-view scintillation camera fitted with LEAP collimator; spectrometer set at 140 keV with 20% window

Computer software for deconvolutional analysis allows determination of percent of hepatic arterial and of portal venous blood flow to liver (helpful in assessment of liver transplants)

Imaging: at 5–10-minute intervals for 60 min; if gallbladder not visualized for at least up to 4 hrs; RLAT, RAO, LAO projections to confirm gallbladder position

◊ Look for enterogastric reflux as a cause of biliary gastritis!

IV morphine sulfate (0.04 mg/kg or up to 3 mg):

contracts sphincter of Oddi + raises intrabiliary pressure → retrograde filling of gallbladder

Effect: maximum 5 minutes post injection → shortens study time in cases of nonvisualization of gallbladder → increases accuracy from 88% to 98% and specificity from 83% to 100%

» redose patient with a small amount of radiotracer

» inject morphine at 45–60 minutes if tracer in bowel

» image for 45 minutes after injection

Normals: (excludes diagnosis of acute cholecystitis)

√ gallbladder appearance within 60 minutes

√ gallbladder visualization within 30 minutes in 90%

√ small bowel activity within 90 min (80% within 60 min)

LIVER SCINTIGRAPHY

^{99m}Technetium Sulfur Colloid

= LIVER-SPLEEN SCAN

Indications: liver, spleen, bone marrow, acute rejection in renal transplant, lower GI bleeding, gastric emptying

Physiology: small colloid particles are phagocytized by reticuloendothelial system (RES); 90% of RES function lies within liver + spleen, 10% primarily within bone marrow

Preparation:

^{99m}Tc-pertechnetate and sodium trisulfate are heated in a water bath (95 ± 5°C) for 10 ± 2 minutes; sulfur atoms aggregate to form a "colloid" (average particle size 0.1–1 μm with a range of 0.001–1 μm; true colloid has a particle size of 0.001–0.5 μm); gelatin is added to prevent further growth of particles

Quality control:

(a) > 92% remain at origin of ascending chromatography

(b) upper limit for particle size is 1 μm

› Usual cause for poor preparation is excessive / prolonged heating or a pH > 7

› Preparation should not be used > 6 hours (agglomeration of particles with aging)

Dose: usually 3–6 mCi (8 mCi for SPECT)

Radiation dose: 0.3 rad/mCi for liver (critical organ); 0.02 rad/mCi for whole body; 0.025 rad/mCi for bone marrow

Imaging: 15–30 min post IV injection

Pharmacokinetics: accumulation in liver (85%), spleen (10%), bone marrow (5%); lung localization is rare (presumably secondary to circulating endotoxins + macrophage infiltration)

A. RETICULOENDOTHELIAL LOCALIZATION

√ colloid shift away from liver in diffuse hepatic dysfunction / decreased hepatic perfusion

√ ↑ bone marrow activity in hemolytic anemia

√ ↑ splenic activity in hypersplenism of splenomegaly / cancer / systemic illness

B. BONE MARROW LOCALIZATION

Hematopoietic system extends into long bones in children; recedes to axial skeleton, femora, and humeri with age

◊ Bone marrow distribution cannot be used to determine sites of erythropoiesis!

C. ABSCESS LOCALIZATION Sulfur colloid phagocytized by PMNs + monocytes

Labeling:

(a) in vivo: small labeling yield

(b) in vitro: 40% labeling efficiency, but difficult + time-consuming preparation

SPLENIC SCINTIGRAPHY

1. ^{99m}Tc-sulfur colloid: 3–5 mCi
2. ^{99m}Tc-heat–denatured erythrocytes

Indication:

(1) Splenic trauma

(2) Accessory + ectopic spleen

Technique to make heat–denatured erythrocytes:

» 20–30 minutes after injection of pyrophosphate IV 15–20 mL of blood are drawn

» drawn blood is incubated with 2 mCi of pertechnetate → heated to 49.5°C for 35 minutes and → reinjected

◊ Fragmentation of RBCs from overheating increases hepatic uptake!

Imaging: 20 minutes post injection

GASTROINTESTINAL SCINTIGRAPHY

Radionuclide Esophagram

Preparation: 4–12 hours fasting; imaging in supine / erect position
Dose: 250–500 μCi ^{99m}Tc-sulfur colloid in 10 mL of water taken through straw
Imaging: when swallowing begins
Normal transit time: 15 seconds with 3 distinct sequential peaks progressing aborally
Prolonged transit time:
achalasia, progressive systemic sclerosis, diffuse esophageal spasm, nonspecific motor disorders, "nutcracker" esophagus, Zenker diverticulum, esophageal stricture + obstruction
Difficult interpretation in: hiatal hernia, GE reflux, Nissen fundoplication

Levine / Denver Shunt Patency

Technique: sterile injection of 0.5–1 mCi ^{99m}Tc-MAA / sulfur colloid via paracentesis
Imaging: over abdomen (or chest) to detect uptake in liver (or lung) → confirms patency

RENAL SCINTIGRAPHY

Renal Agents

1. Agents for renal function: ^{99m}Tc-DTPA, ^{131}I-Hippuran
2. Renal cortical agent: ^{99m}Tc-DMSA
3. Renal combination agent: ^{99m}Tc-glucoheptonate

^{99m}Tc-DTPA

= ^{99m}Tc-diethylenetriamine pentaacetic acid
= agent of choice for assessment of
(1) Perfusion
(2) Glomerular filtration = relative GFR
(3) Obstructive uropathy
(4) Vesicoureteral reflux

Pharmacokinetics:
glomerular agent excreted exclusively by glomerular filtration (similar to inulin) without reabsorption / tubular excretion / metabolism; chelating agent in 5–10% bound to plasma protein; extracted with 20% efficiency on each pass through kidney (= filtration fraction)
◊ May be used only in patients with normal / mildly impaired renal function!

Time-activity behavior:
› abdominal aorta (15–20 seconds)
› kidneys + spleen (17–24 seconds); liver appears later because of portal venous supply
› renal cortical activity (2–4 min): mean transit time of 3.0 ± 0.5 min; static images of cortex taken at 3–5 min
› renal pelvic activity (3–5 min): peak at 10 minutes; asymmetric clearance of renal pelvis in 50%; accelerated by furosemide

Biologic half-life: 20 minutes
Dose: 10–20 mCi
Radiation dose: 0.85 rad/mCi for renal cortex; 0.6 rad/mCi for kidney; 0.5 rad/mCi for bladder; 0.15 rad/mCi for gonads; 0.15 rad/mCi for whole body

Adjunct: Lasix administration (20–40 mg IV) 20 minutes into exam allows assessment of renal pelvic clearance with accuracy equal to Whitaker test (DDx of obstructed from dilated but nonobstructed pelvicalyceal system)

[^{99m}Tc-Glucoheptonate]

◊ ^{99m}Tc-GHA is largely replaced by ^{99m}Tc-MAG_3

Pharmacokinetics:

rapid plasma clearance + urinary excretion with excellent definition of pelvicalyceal system during 1st hour; extracted by

(a) glomerular filtration and

(b) tubular excretion (30–45% within 1st hour); 5–15% of dose accumulates in tubular cells by 1 hour, 15–25% by 3 hours; cortical accumulation remains for 24 hours

Imaging:

(a) collecting system within first 30 minutes

(b) renal parenchyma after 1–2 hours (interfering activity in collecting system)

Biologic half-life: 2 hours

Dose: 15 (range 10–20) mCi

Radiation dose: 0.17 rad/mCi for kidney; 0.008 rad/mCi for whole body; 0.015 rad/mCi for gonads

^{99m}Tc-DMSA

= ^{99m}Tc-dimercaptosuccinic acid

= suitable for imaging of functioning cortical mass: pseudotumor versus lesion

Pharmacokinetics:

high protein-binding + slow plasma clearance; 4% extracted per renal passage; 4–8% glomerular filtration within 1 hour and 30% by 14 hours; 50% of dose accumulates in proximal + distal renal tubular cells by 3 hours (= cortical agent)

Imaging: after 1– 3–24 hours (optimal at 34 hours); ↑ sensitivity to structural defects with SPECT

Biologic half-life: > 30 hours

Dose: 5–10 mCi

Radiation dose: 0.014 rad/mCi for gonads; 0.015 rad/mCi for whole body

[^{131}I-OIH]

largely replaced by ^{99m}Tc-MAG_3

= ^{131}I-orthoiodohippurate (Hippuran®)

= good for evaluation of renal tubular function / effective renal plasma flow; agent with highest extraction ratio without binding to renal parenchyma; visualizes kidney even in severe renal failure

Pharmacokinetics:

80% secreted by proximal tubules; 20% filtered by glomeruli; maximal renal concentration within 5 minutes; normal transit time of 2–3 minutes; ~ 2% free iodine

◊ Lugol's solution is administered to protect thyroid!

Imaging: in 15–60-second intervals for 20 minutes; renal uptake determined from images obtained by 1–2 minutes (patient in supine position → equidistance of kidneys

to camera)

Biologic half-life: 10 minutes (with normal renal function)

Dose: 200 (range 150–300) µCi

Radiation dose: 0.06 rad/200 µCi for bladder; 0.02 rad/ 200 µCi for kidney; 0.02 rad/200 µCi for whole body; 0.02 rad/200 µCi for gonads

^{99m}Tc-Mertiatide = ^{99m}Tc-Mercaptoacetyltriglycine (MAG_3)

= renal plasma flow agent similar to OIH but with imaging benefits of ^{99m}Tc label (improved dosimetry)

Pharmacokinetics:

tubular agent → cleared primarily by active secretion in proximal tubules + only minimal glomerular filtration; clearance is less than Hippuran; surrogate measure for effective renal plasma flow

Dose: 10 mCi

Evaluation: true renal plasma flow = MAG3 flow (obtained off renogram curve) multiplied by a constant (varies between 1.4 and 1.8)

Enalaprilat (Vasotec®)-enhanced Renography

Technique:

Renal Scintigraphic Agents

Agent	*Dose*	*Pharmacokinetics*	*Imaging Characteristics*
MORPHOLOGIC AGENTS			
^{99m}Tc-GHA	5 mCi	proximal tubular uptake + glomerular filtration	collecting system visualized on delayed images
^{99m}Tc-DMSA	2–5 mCi	proximal + distal tubular uptake	limited availability, relatively high radiation dose, collecting system not visualized on delayed images
FUNCTIONAL AGENTS			
^{131}I-OIH	200–400 µCi	80% secreted, 20% filtered	routinely used for ERPF measurement, analog of PAH, highest renal extraction fraction, poor image detail, high radiation dose, requires high-energy collimator
^{99m}Tc-DTPA	10–15 mCi	nearly 100% filtered	GFR calculation, delayed time-to-peak with slow clearance
^{99m}Tc-MAG_3	2–10 mCi	99% secreted	ERPF estimate, good cortical detail, high target-to background ratio

» Blood pressure check → to prevent testing excessively hypertensive patients
» Discontinue captopril / lisinopril 3 days before study
» Discontinue enalaprilat
» Stop any other antihypertensive medications overnight (except for β-blockers)
» Fasting: liquids acceptable
» Bladder catheterization to monitor urinary output
» ½ normal saline IV drip at 75 mL/hour at a dose of 10 mL fluid/kg body weight → to ensure adequate hydration
» Furosemide (= Lasix®) IV
20 mg if serum creatinine < 1.5 mg/dL
40 mg if serum creatinine > 1.5 mg/dL
60 mg if serum creatinine > 3.0 mg/dL
(not to exceed 1.0 mg/kg)

» 2.5–5 mCi ^{99m}Tc-MAG$_3$ IV for baseline study
(a) flow phase with 1 sec/frame for 60 frames
(b) tracer kinetic (dynamic) phase with 15 sec/frame for 120 frames
» Rehydration with ½ normal saline keeping a 250–300 mL negative fluid balance
» Postvoid image (or Foley catheter with PVR)
» 0.04 mg/kg enalaprilat IV (up to a maximum of 2.5 mg) infused over 5 min + blood pressure and heart rate checks q 5 minutes
» Repeat furosemide (= Lasix®) IV
» 5–7.5 mCi ^{99m}Tc-MAG$_3$ IV [or 10 mCi ^{99m}Tc-MAG$_3$ IV single post-enalaprilat study for patients already on ACEI therapy]
» Image acquisition:
› 1–3 seconds / frame for first 60 seconds
› 10–30 seconds / frame thereafter
› image display at 1–3-minute intervals
› total acquisition time of 20–30 minutes
» whole-kidney ROI (better count statistics) / cortical ROI (for unusual retention in renal pelvis)

2-day protocol:
› ACEI renography on day 1
› if test abnormal patient has to return on day 2 for a baseline study to maximize specificity

Captopril (Capoten®)-enhanced Renography

Dose: 1 mg/kg PO for pediatric patient; 25 or 50 mg PO for adult patient (crush tablets + dissolve in 200 mL of water)

Technique:
» no solids for 4 hours prior to study
» moderate hydration with 7 mL water / kg BW ingested 30–60 minutes before study
» radiopharmaceutical injected 60 minutes after ingestion of captopril
» at the same time 20 mg furosemide IV → to wash out radiopharmaceutical from distal nephron + calices + pelvis → improving detection of cortical retention

Differential Renal Function

Agents:
(1) ^{99m} Tc-DTPA: measurements prior to excretion within first 1–3 minutes; images taken at 1.5-second intervals for 30 seconds followed by serial images for next 30 minutes
(2) ^{131}I-Hippuran: measurements prior to excretion within first 1–2 minutes

Evaluation: generation of time-activity curves
√ upslope (= accretion phase)
√ peak activity (maximum uptake phase)
√ downslope (excretion phase)
√ increased hepatic + soft-tissue uptake with impaired renal function
√ measurements usually not significantly affected with differences in renal depth
√ measurements are accurate in renal obstruction if obtained within 1–3 minutes
√ prediction about functional recovery not possible following surgical relief of obstruction

Diuretic Renal Scintigraphy

Indication: differentiation of obstructed from nonobstructed chronically dilated collecting system ± ureter in patients with history of surgery / obstruction

Agents: tubular agent ^{99m}Tc mertiatide (eg, ^{99m}Tc-MAG_3); glomerular agent ^{99m}Tc pentetic acid (ie, ^{99m}Tc-DTPA)

Time activity curve of urinary tract obstruction:

(a) moderate obstruction
- √ ↓ radiotracer activity (= perfusion) in affected kidney during angiographic phase
- √ delayed cortical concentration (= delayed uptake) before administration of diuretic
- √ delayed clearance of activity after administration of diuretic with half-time > 20 minutes

(b) high-grade obstruction:
- √ failed clearance of radiotracer from kidney
- √ no excretion of tracer into renal collecting system

False positives:

attenuated effectiveness of furosemide, reservoir effect in severe dilatation of nonobstructed collecting system, poor hydration, high filling pressure of bladder

Radionuclide Cystogram

Use: evaluation of bladder volume at reflux, volume of refluxed urine, residual urine volume, ureteral reflux drainage time

Technique:

(a) indirect: IV injection of ^{99m}Tc-DTPA

(b) direct: instillation of 0.5–1 mCi ^{99m}Tc-pertechnetate-saline mixture into bladder (more sensitive for reflux during filling phase, which occurs in 20%)

Imaging:

posterior upright views throughout filling and voiding phases; review on cinematic loop helpful; residual bladder volume can be calculated

Advantage:

lower radiation dose to gonads than fluoroscopic contrast cystography (5 mrad)!

ADRENOCORTICAL SCINTIGRAPHY

1. NP-59
2. Selenium-75 6-β-selenomethylnorcholesterol (Scintadrin®)

Iodocholesterol

Agent: ^{131}I-6-β-iodomethyl-19-norcholesterol (NP-59); no FDA approval (available as investigational new drug)

Indications: adrenocortical imaging

(1) ACTH-independent Cushing syndrome: adenoma, cortical nodular hyperplasia

(2) Adrenocortical carcinoma
- √ spectrum from nonfunctioning to functioning

(3) Primary aldosteronism: adenoma, bilateral adrenal hyperplasia → improved scintigraphic discrimination requires dexamethasone suppression before + during imaging

(4) Hyperandrogenism: adrenal adenoma, zona reticularis hyperplasia, polycystic ovary disease, ovarian stromal hyperplasia, androgen-secreting ovarian neoplasm
(5) Incidentaloma (= adrenal mass)
√ localization to side of CT-depicted adrenal mass (= concordant uptake) suggests hyperfunctioning adenoma
√ markedly diminished / absent uptake (= discordant uptake) or symmetric uptake (= nonlateralization) suggests space-occupying mass (eg, cyst) / malignant adrenal mass

Pharmacokinetics:
NP-59 is incorporated into low-density lipoproteins (LDL) → circulates to adrenal cortex → absorbed from LDL complex by low-density lipoprotein receptors → esterified in adrenal cortex; adrenocortical uptake affected by adrenocortical secretagogues (corticotropin, angiotensin II); enterohepatic excretion may obscure adrenals (prior laxative administration beneficial)

Dose: 1 mCi (37 MBq) with slow IV injection

Radiation dose: 26 rad/mCi for adrenals, 8.0 rad/mCi for ovaries, 2.4 rad/mCi for liver, 2.3 rad/mCi for testes, 1.2 rad/mCi for whole body

Method: Lugol solution administered orally (50 mg of iodine per day) for 4–5 days starting the day before injection → to block thyroid uptake of free iodine; mild laxative → to decrease bowel activity

Imaging:
(a) 5–7-days interval between injection + imaging
(b) 3–5-days interval between injection + imaging in case of dexamethasone suppression (1 mg four times daily for 7 days prior to and throughout 4–5 days of postinjection imaging interval)

SCINTIGRAPHY OF NEUROENDOCRINE TUMORS

Origin: embryonic neural crest tissue forming neuroendocrine cells + neuroendocrine tumors

Location: hypothalamus, pituitary gland, thyroid gland, adrenal medulla, GI tract

Function: neuroendocrine cells synthesize amines from precursor molecules → decarboxylate amines → polypeptides (= neurotransmitters + hormones); former name: APUD (amine precursor uptake and decarboxylose) cells + APUDomas

Radiopharmaceuticals:
similar in molecular structure to hormones that tumor synthesizes / incorporates into metabolic + cellular processes

Somatostatin Analogs

= 14-amino acid peptide that inhibits peptide + hormone synthesis by neuroendocrine cells ("antigrowth hormone") in the anterior pituitary (ACTH, prolactin, TSH) and in pancreas + GI tract (insulin, glucagon, gastrin, VIP, secretin, motilin, cholecystokinin)

Biologic half-life: 2–4 minutes (molecule disrupted by various plasma enzymes in circulation)

Octreotide = Sandostatin®
= 8-amino acid analog of somatostatin
Plasma half-life: 2 hours

^{111}INDIUM-PENTETREOTIDE = OCTREOSCAN®

Indication: pituitary tumor, gastrinoma, paraganglioma, carcinoid, neuroblastoma, small cell lung cancer, pheochromocytoma
Physical half-life: 68 hours
Emission: 171 and 245 keV
Chelating agent: diethylenetriaminepentaacetic acid
Sensitive to: somatostatin receptor subtypes 2 (80% of enteropancreatic neuroendocrine tumors) and 5
Distribution: kidneys, spleen, gallbladder, liver, urinary bladder, intestines, thyroid, pituitary gland
Dose: 3–5–6 mCi
Preparation: oral laxative (in patient without diarrhea); cessation of octreotide therapy 72 hours before administration
Advantage: superior to MIBG
Imaging protocol:
» SPECT of area of interest after 4 hours (to avoid superimposed physiologic biliary excretion into small + large bowel)
» delayed SPECT imaging at 18–24 hours
» planar whole-body imaging

Guanethidine Analogs

Indications:
catecholamine-producing adrenal medullary tumor (intrarenal pheochromocytoma + extraadrenal paraganglioma) and chromaffin cell tumor (C cells of thyroid, melanocytes of skin, chromaffin cells of adrenal medulla, pancreatic cells, Kulchitsky cells)
(1) Pheochromocytoma (80–90% sensitive, > 90% specific) tumors as small as 0.2 g have been detected
(2) Neuroblastoma, carcinoid, medullary thyroid carcinoma, nonfunctioning retroperitoneal neuroendocrine tumor, middle mediastinal paraganglioma, adrenal metastasis of choriocarcinoma, Merkel (skin) tumor

Pharmacokinetics:
active transport into cell membrane (= type I uptake mechanism) of sympathomedullary system, which have neurosecretory granules capable of accumulating MIBG; not metabolized to any appreciable extent
Normal activity is seen in liver, spleen, bladder, salivary glands, myocardium, lungs; 85% of injected dose is excreted unchanged by kidneys

Preparation:
(1) Lugol solution administered orally (50 mg of iodine per day) for 4–5 days starting the day before injection → to block thyroid uptake of free iodine
(2) To avoid false-negative scan → cessation of sympatho- mimetics, reserpine, calcium channel blockers, tricyclic antidepressants, labetalol for 3–4 days before administration

^{131}I-METAIODOBENZYLGUANIDINE (MIBG)

Sensitivity: 77–100%

Emission: 159 keV (for ^{123}I); 364 keV (for ^{131}I)
Dose: 0.5–1.0 mCi
Radiation dose: 35 rad/mCi for adrenal medulla, 1.0 rad/mCi for ovaries, 0.4 rad/mCi for liver, 0.22 rad/mCi for whole body
Imaging: planar static whole body imaging at 48–72 hours (target-to-background ratio improved at 72 hours) of thorax, abdomen, pelvis with 100,000 counts / 20 minutes per image at each location ± SPECT

^{123}I-METAIODOBENZYLGUANIDINE (MIBG)

agent of choice ← higher quality images + lower radiation burden + quicker results, allows SPECT imaging
Dose: 5–10 mCi
Radiation dose: 2.76 rad/mCi for adrenals, 0.07 rad/mCi for ovaries, 0.05 rad/mCi for liver, 0.02 rad/mCi for whole body
Imaging: at 6 hours and 24 hours

Glucose Analogs

2-(^{18}FLUORINE)FLUORO-2-DEOXY-D-GLUCOSE (FDG)

Uptake: accumulation in cells of rapidly growing tumor ← accelerated glucose metabolism (phosphorylation to FDG-6-phosphatase)
FDG-positive: aggressive neuroendocrine tumor
FDG-negative: slow tumor growth in 50% of neuroendocrine tumors

BONE AGENTS

A. POLYPHOSPHATES = LINEAR PHOSPHATES = CONDENSED PHOSPHATES
First agents described; contain up to 46 phosphate residues; simplest form contains 2 phosphates = pyrophosphate (PYP)
B. DIPHOSPHONATES Organic analogs of pyrophosphate characterized by P-C-P bond; chemically more stable; not susceptible to hydrolysis in vivo; most widely used agents:
1. Ethylene hydroxydiphosphonate (EHDP)
= ethane-1-hydroxy-1,1-diphosphonate
2. Methyl diphosphonate (MDP)
Synonym: Methylene diphosphonate / Medronate
C. Imidodiphosphonates (IDP) Characterized by P-N-P bond

Physiologic Uptake of Bone Agents

(a) rapid distribution into ECF (78% of injected dose with biologic half-life of 2.4 minutes) directly related to blood flow + vascularity; blood clearance rate determines ECF (= background) activity (at 4 hours 1% for diphosphonates, 5% for pyrophosphate / polyphosphate secondary to greater degree of protein binding)
(b) chemisorbs on hydroxyapatite crystals in bone + in calcium crystals in mitochondria; MDP concentration at 3 hours is directly proportional to calcium contents of tissues (14–24% calcium in bone, 0.005% calcium in muscle); 50–60% (58% for MDP, 48% for EHDP, 47% for PYP) are localized in bone by ~ 3 hours depending on blood flow + osteoblastic activity; 2–10% of the dose are present within soft tissues; myocardial uptake depends on

at least some revascularization of infarcted muscle

Excretion of Bone Agents

via urinary tract by 6 hours in 68% of MDP / EHDP, in 50% of PYP, in 46% of polyphosphates

◊ Forcing fluids + frequent voiding reduces radiation dose to bladder!

Indications for Bone Imaging

1. Imaging of bone, myocardial / cerebral infarct, ectopic calcifications, some tumors (neuroblastoma)
2. Rx for Paget disease, myositis ossificans progressiva, calcinosis universalis → inhibits formation + dissolution of hydroxyapatite crystals

Pediatric Indications for Bone Scan

A. Back pain
   1. Diskitis
   2. Pars interarticularis defect: SPECT imaging adds sensitivity
   3. Osteoid osteoma: can be used intraoperatively to ensure removal of nidus
   4. Sacroiliac infection

B. Nonaccidental trauma

Pediatric Dose Formula: 0.25 mCi/kg ^{99m}Tc-medronate; (minimum dose of 1 mCi)
or dose range: [(age + 1)/(age + 7)] × [lowest adult range]

Imaging with Bone Agents

@ Bone: 2–3 hours post injection
   ◊ Fractures may not show positive uptake until 3–10 days depending on age of patient

@ Myocardium: 90–120 min post injection
   ◊ Ideal imaging time is 1–3 days post infarction

Usual dose: 20 mCi (740 MBq)

Radiation dose: 0.13 rad/mCi for bladder (critical organ), 0.04 rad/mCi for bone, 0.01 rad/mCi for whole body

Labeling: Tc (VII) is eluted as a pertechnetate ion; chemical reduction with Sn (II) chloride; chelated into a complex of ^{99m}Tc(IV)-tin-phosphate

Quality Control:
(1) < 10% ^{99m}Tc-tin colloid / free ^{99m}Tc-pertechnetate (a good preparation is 95% bound)
(2) Agent should not be used prior to 30 min after preparation
(3) Avoid injection of air in preparation of multidose vials (oxidation results in poor Tc bond)
(4) Kit life is 4–5 hours after preparation

Three-Phase Bone Scanning

over area of interest

1. Rapid sequence flow study (2–5 sec/frame) = early arterial flow = 1st phase
2. Immediate postflow images (1 million counts for central body + 0.5 million counts for extremities) = blood pool = tissue phase = 2nd phase
3. Delayed images (0.5–1.0 million counts) between 3–4 hours following injection = 3rd

phase

BONE MARROW AGENTS

for assessment of hematopoiesis / phagocytosis by RES

1. ^{99m}Tc-sulfur colloid (10% uptake in bone marrow)
2. ^{111}In chloride
3. ^{99m}Tc-MMAA
   = mini-microaggregated albumin colloid for liver, spleen, hematopoietic marrow
   Particle size: 30–100 μm
   Dose: 10 mCi
   Marrow dose: 0.55 rad
   Marrow accumulation at 1 hour:
   6 x higher than for sulfur colloid
   3 x higher than for antimony-sulfur colloid

Indications for Bone Marrow Imaging:

A. EXPANSION of hematopoietically active bone marrow
   1. Hematologic disorders to reveal presence of peripheral expansion of functional marrow
B. FOCAL DEFECT from displacement by infiltrating disease
   1. Marrow replacement disorders: eg, Gaucher disease
   2. Bone infarction: eg, sickle cell anemia (DDx from osteomyelitis)
   3. Avascular necrosis in children

Indications for Non-organ–specific Whole Body Imaging

1. Tumor
   Agents: ^{67}Ga citrate, ^{131}I MIBG,
   ^{111}In pentetreotide (OctreoScan™),
   ^{111}In antiprostate antibody (ProstaScint®),
   ^{111}In OncoScint™,
   ^{99m}Tc anti-CEA antibody (CEA-Scan®),
   ^{18}F deoxyglucose
2. Inflammation / infection
   Agents: ^{67}Ga citrate, ^{111}In oxime labeled WBC, ^{99m}Tc HMPAO labeled WBC

AGENTS FOR INFLAMMATION

^{67}Ga-citrate Scintigraphy

overall 58–100% sensitivity; 75–100% specificity (lower for abdominal inflammation because of problematic abdominal activity)
Indication: ^{67}Ga mostly limited to
(a) chest: interstitial pneumonia, opportunistic infection, sarcoidosis, drug toxicity
(b) bone: osteomyelitis
Pathophysiology:
leakage of protein-bound ^{67}Ga into extracellular space ← hyperemia + increased

capillary permeability; ^{67}Ga is preferentially bound to nonviable PMNs + macrophages

1. Leukocyte incorporation (rich in lactiferous)
2. Bacterial uptake (iron-chelating siderophores)
3. Inflammatory tissue stimulates lactoferrin production

Gallium in Chronic Abdominal Inflammation

67% sensitivity, 64% specificity, 13% false-negative rate, 5% false-positive rate

Dose: 5 mCi

Imaging: routine at 48–72 hours (after clearance of high background activity); optional at 6–24 hours (prior to renal + gastrointestinal excretion); delayed images as needed

√ diffuse uptake in peritonitis

√ localized uptake in acute pyogenic abscess, phlegmon, acute cholecystitis, acute pancreatitis, acute gastritis, diverticulitis, inflammatory bowel disease, surgical wound, pyelonephritis, perinephric abscess

Labeled Leukocyte Scintigraphy

= primary imaging method for inflammation / infection

Indication:

(1) Fever of unknown origin / bacteremia
(2) Abdominal infection / abscess
(3) Osteomyelitis
(4) Inflammatory bowel disease
(5) Vascular graft infection

Preparation (3-hour time):

» 30–40 mL of whole blood drawn into syringe containing an anticoagulant

» syringe stands in upright position for 1–2 hr with addition of hydroxyethyl starch (for sedimentation of RBCs)

» under centrifugation leukocytes form a pellet at bottom of tube (allows separation of leukocytes from platelets)

Requirements:

1. WBC count > 2,000/mm3
2. Neutrophil-mediated inflammatory process

Biodistribution: closely parallels hematopoietically active marrow

Physiologic uptake:

@ Granulation wounds = healing by secondary intention (eg, ostomies, skin graft)

◊ Leukocytes do NOT accumulate in normally healing wounds

@ Lung

√ physiologic diffuse lung uptake up to 4 hours

◊ Lung uptake > 24 hours due to pneumonia / ARDS

√ physiologic diffuse lung uptake in severely septic patient ← cytokine release at site of infection + subsequent activation of pulmonary vascular endothelium

^{111}In-labeled WBC

= ^{111}In-oxime–labeled autologous leukocytes with 80% sensitivity; 97% specificity, 91%

accuracy (superior to ^{67}Ga citrate); no activity in intestinal contents / urine

Indication:

occult sepsis (postoperative fever), acute pyogenic infection, abdominal + renal abscess, inflammatory bowel disease, nonpulmonary infection with HIV positivity, prosthetic graft infection (bone / cardiovascular graft), acute + chronic + complicated bone / joint infection

Technique:

chelating agents (oxime = 8-hydroxyquinoline / tropolone) used for labeling of leukocytes; lipophilic oxime-indium complex penetrates cell membrane of white cells; intracellular proteins scavenge the indium from oxime; oxime diffuses out from cell; requires 2 hr of preparation time

Recovery rate: 30% at 1–4 hours after injection

Limitations: 19 gauge IV access, leukopenia, impaired chemotaxis, abnormal WBCs, children

Dose: 0.5 mCi

Half-life: 67 hours

Useful photopeaks: 173 keV (89%), 247 keV (94%)

Radiation dose:

13–18 rad/mCi for spleen; 3.8 rad/mCi for liver; 0.65 rad/mCi for red marrow; 0.45 rad/mCi for whole body; 0.29 rad/mCi for testes; 0.14 rad/mCi for ovaries (compared with ^{67}Ga higher dose to spleen, but lower dose to all other organs)

Biodistribution: spleen, liver, bone marrow; blood clearance halftime of 6–7 hours; NO bowel activity

Imaging:

best at 18–24 hours following injection of cell preparation; optional at 2–6 hours (eg, in inflammatory bowel disease); delayed images as needed; bone marrow uptake provides useful landmarks

- SPECT imaging >> standard planar imaging

√ focal activity greater than in spleen is typical for abscess (comparison based on liver, spleen, bone marrow activity)

√ activity equal to liver (significant inflammatory focus)

√ abdominal activity is always abnormal (eg, pseudomembranous / ischemic colitis, inflammatory bowel disease, GI bleeding)

False positives:

@ Chest: CHF, RDS, embolized cells, cystic fibrosis, vascular access lines, dialysis catheter

@ Abdomen: accessory spleen, colonic accumulation, renal transplant rejection, active GI hemorrhage, vasculitis, ischemic bowel disease, following CPR, uremia, postradiation therapy, Wegener granulomatosis, ALL, lumbar puncture

@ Miscellaneous: IM injection, histiocytic lymphoma, cerebral infarction, arthritis, skeletal metastases, thrombophlebitis, hematoma, hip prosthesis, cecal carcinoma, postsurgical pseudoaneurysm, necrotic tumors that harvest WBCs

False negatives:

chronic infection, aortofemoral graft, LUQ abscess, infected pelvic hematoma,

splenic abscess, hepatic abscess (occasionally)

Disadvantages:

2-day procedure, low-quality images especially of extremities

Advantages:

no activity in normal GI / GU tract (preferred in postoperative patient + vascular grafts); simultaneous WBC + sulfur colloid bone marrow scan possible

^{99m}Tc-HMPAO Labeled WBC

Optimal use: osteomyelitis in extremities

Biodistribution: bone marrow, little soft tissue, spleen > liver, renal + bladder activity

Excretion: in bile + urine

Advantages over ^{111}In WBC imaging:

(a) improved photon flux with lower dose

(b) earlier imaging (same day)

Disadvantages:

(1) Biliary excretion leads to bowel activity, which may obscure abdominal / graft abscess if not imaged early

(2) Heart and blood pool activity

(3) Nonspecific accumulation in lung may obscure lung disease

Technique:

chelating agents (exametazime oxime) used for labeling of leukocytes; ^{99m}Tc-Ceretec binds with autologous WBCs and is reinjected

Dose: up to 10 mCi

Imaging:

30 min (optimum for use in abdomen), 60 min, 3–4 hours, 4–8 hours (optimum outside abdomen); 24 hr (optional)

False positives:

may be due to unusual marrow distribution, correlation with bone marrow (sulfur colloid) scan may be necessary

^{67}GA-CITRATE

^{67}Ga acts as an analogue of ferric ion; used as gallium citrate (water-soluble form)

Production: bombardment of zinc targets (67Zn, 68Zn) with protons (cyclotron); virtually carrier-free after separation process

Decay: by electron capture to ground state of 67Zn

Energy levels:

(a) used: 93 keV (38%), 184 keV (24%), 296 keV (16%), 388 keV (8%)

(b) unused: 91 keV (2%), 206 keV (2%)

Physical half-life: 3.3 days (= 78 hours)

Biologic half-life: 2–3 weeks

Adult dose: 3–6 mCi or 50 μCi/kg

Radiation dose:

0.3 rad/mCi for whole body; 0.9 rad/mCi for distal colon (= critical organ); 0.58 rad/mCi for red marrow; 0.56 rad/mCi for proximal colon; 0.46 rad/mCi for liver; 0.41 rad/mCi for

kidney; 0.24 rad/mCi for gonads

Binding Sites of ^{67}Ga-citrate

Physiology:

^{67}Ga is bound to iron-binding sites of various proteins (strongest bond with transferrin in plasma, lactoferrin in tissue); multiexponential + slow plasma disappearance; competitive iron administration (Fe-citrate) enhances target-to-background ratio by increasing ^{67}Ga excretion

A. Fluid spaces
   1. Transferrin, haptoglobin, albumin, globulins in blood serum (90%)
   2. Interstitial fluid space (increased capillary permeability and hyperemia in inflammation + tumor)
   3. Lactoferrin in tissue

B. Cellular binding
   1. Viable PMNs incorporate 10% of ^{67}Ga (bound to lactoferrin in intracytoplasmic granules)
   2. Nonviable PMNs + their protein exudate (iron-binding proteins are deposited at sites of inflammation; these remove iron from the extracellular space; iron is no longer available for bacterial growth)
   3. Lymphocytes have lactoferrin-binding surface receptors
   4. Phagocytic macrophages engulf protein-iron complexes
   5. Bacteria + fungi (siderophores = lysosomes = low-molecular–weight chelates produced by bacteria) have iron-transporting protein mechanism
   6. Tumor cell-associated transferrin receptor + transportation into cells (lymphocytes bind ^{67}Ga less avidly than PMNs; RBCs do NOT bind ^{67}Ga)

mnemonic: LFT'S

Lactoferrin (WBCs)
Ferritin
Transferrin
Siderophores (bacteria)

Uptake of ^{67}Ga-citrate

at 24 hr: most intense in RES, liver, spleen (4%), bone marrow (lumbar spine, sacroiliac joints), bowel wall (chiefly colonic activity on delayed images), renal cortex, nasal mucosa, lacrimal + salivary glands, blood pool (20%), lung (< 3% = equivalent to background activity), breasts

at 72 hr: 75% of dose remains in body its activity equally distributed among soft tissue (orbit, nasal mucosa, large bowel), liver, bone or bone marrow (occiput); kidney activity no longer detectable; lacrimal + salivary glands may still be prominent

Excretion of ^{67}Ga- citrate

(a) via urinary tract (10–25% within 24 hours) no activity in kidneys + urinary bladder after 24 hours

(b) via GI tract (10–20%) hepatobiliary pathway + colonic mucosal excretion

◊ Enemas + laxatives promote clearing of bowel activity!
◊ Bowel cleansing not optimal as gallium lies also within colonic wall
(c) via various body fluids eg, human milk (mandates to stop nursing for 2 weeks)

Imaging of ^{67}Ga-citrate

usually [6, 24], 48–72 hours (up to 7 days)

◊ Best target-to-background ratio generally at 72 hours
◊ Optimal target-to-background ratio at 6–24 hours for abscess
◊ Optimal target-to-background ratio at 24–48 hours for tumor
• 500,000 count spot views / whole body
• SPECT useful

Degrading Factors of Gallium Imaging

√ lesions < 2 cm are not detectable
√ photon scatter within overlying tissues
√ physiologic high activity of liver, spleen, bones, kidney, GI tract may obscure lesion

Normal Variants of Gallium Uptake

1. Breasts: increased uptake under stimulus of menarche, estrogens, pregnancy, lactation, phenothiazine medication, renal failure, hypothalamic lesion
2. Liver: suppressed uptake by chemotherapeutic agents / high levels of circulating iron / irradiation / severe acute liver disease
3. Lung: prominent uptake after lymphangiography
4. Spleen: increased uptake in splenomegaly
5. Thymus: uptake in children
6. Salivary glands: uptake within first 6 months after radiation therapy to neck (may persist for years)
7. Epiphyseal plates in children
8. Previous steroid therapy, chemotherapy, and radiation therapy may decrease Ga uptake
9. Healing surgical incision

No Gallium Uptake

most benign neoplasms; hemangioma; cirrhosis; cystic disease of the breast, liver, thyroid; reactive lymphadenopathy; inactive granulomatous disease

Indications for Gallium Imaging

A. Infection Gallium has been largely replaced with WBC imaging but can be used in chronic infection
   1. Inflamed / infarcted bowel (eg, Crohn disease)
      DDx: normal bowel excretions (must be cleared by enema; bowel pathology shows persistent activity)
   2. Diffuse lung uptake sarcoidosis, diffuse infections (TB, CMV, PCP), lymphangitic metastases, pneumoconioses (asbestosis, silicosis), diffuse interstitial fibrosis (UIP), drug-induced pneumonitis (bleomycin, cyclophosphamide, busulfan), acute radiation pneumonitis, recent lymphangiographic contrast
   3. Lymph node involvement sarcoidosis, TB, MAI, Hodgkin disease

DDx: NOT seen in Kaposi sarcoma, a useful distinction in AIDS patients with hilar nodes

B. Tumor Neoplastic uptake is variable; prominent uptake is usually seen in:
   1. Non-Hodgkin lymphoma (especially Burkitt)
   2. Hodgkin disease
   3. Hepatoma
   4. Melanoma

   Useful in:
   › detection of tumor recurrence
   › DDx of focal cold liver lesions on Tc-^{99m} sulfur colloid scan

Gallium in Bone Imaging

Increased activity in:

1. Active osteomyelitis (90% sensitivity is higher than for ^{99m}Tc-MDP)
2. Sarcoma
3. Cellulitis (bone scan followed by gallium scan)
4. Septic arthritis, rheumatoid arthritis
5. Paget disease
6. Metastases (65% sensitivity, less than for bone agents)

Gallium in Tumor Imaging

Particularly useful in evaluating extent of known tumor disease + in detection of tumor recurrence

A. USEFUL CATEGORY
   1. Lymphoma
      a: Hodgkin disease: 74–88% sensitivity
      b: NHL: sensitivity varies
         › histiocytic form: 85–90% sensitivity
         › lymphocytic well-diff.: 55–70% sensitivity
         95% sensitivity for mediastinal disease,
         80% sensitivity for cervical + superficial lesions; poor sensitivity below diaphragm
   2. Burkitt lymphoma: almost 100% sensitivity
   3. Rhabdomyosarcoma: >95% sensitivity
   4. Hepatoma: 85–95% sensitivity
   5. Melanoma: 69–79% sensitivity

B. POSSIBLY USEFUL
   1. NHL: good for large + mediastinal lesions
   2. Nodal metastases from seminoma + embryonal cell carcinoma: 87% sensitivity
   3. Non-small cell lung cancer: 85% sensitivity for primary of any histologic type, 90% probability for uptake in mediastinal nodes, 67% probability for uptake in normal mediastinal nodes, 90% probability for uptake in extrathoracic metastases

C. NOT USEFUL head & neck tumors, GI tumors (especially adenocarcinomas; 35–40% sensitivity), breast tumor (52–65% sensitivity), gynecologic tumors (<26% sensitivity), pediatric tumors

Gallium in Lung Imaging

◊ Scans obtained at 48 hours, because 50% of normals show activity at 24 hours

A. FOCAL UPTAKE
   1. Primary pulmonary malignancy (>90% sensitivity)
   2. Benign disorders: granuloma, abscess, pneumonia, silicosis

B. MULTIFOCAL / DIFFUSE UPTAKE
   (a) Infection
      1. Tuberculosis
         √ intense uptake in active lesions (97%)
           = parameter of activity
         √ diffuse uptake in miliary TB + rapidly progressive TB pneumonia
      2. Pneumocystis carinii
         √ increased uptake at time when physical signs, symptoms, and roentgenographic changes are unimpressive
      3. Cytomegalovirus
   (b) Inflammation
      1. Sarcoidosis 70% sensitivity for active parenchymal disease, 94% sensitivity for hilar adenopathy
         = indicator of therapeutic response to steroids
      2. Interstitial lung disease pneumoconiosis, idiopathic pulmonary fibrosis, lymphangitic carcinomatosis
      3. Exudative stage of radiation pneumonitis
   (c) Drugs
      1. Bleomycin toxicity
      2. Amiodarone
   (d) Contrast lymphangiography (in 50%)

C. GALLIUM UPTAKE + NORMAL CHEST FILM
   1. Pulmonary drug toxicity
   2. Tumor infiltration
   3. Sarcoidosis
   4. Pneumocystis carinii

Panda Sign

= facial uptake of ^{67}Ga in both parotid glands + both lacrimal glands + nose

1. Sarcoidosis
   ◊ 100% specific for sarcoidosis if lung infiltrates are present!
2. Treated lymphoma
3. Systemic lupus erythematosus
4. Sjögren syndrome

Gallium in Renal Imaging

Abnormal uptake on delayed images at 48–72 hours

A. Renal tumor
   1. Primary renal tumor (variable uptake)
   2. Lymphoma / leukemia

3. Metastases (eg, melanoma)

B. Renal inflammation
   1. Acute pyelonephritis (88% sensitivity)
      √ diffuse / focal uptake
   2. Lobar nephronia
   3. Renal abscess

C. Others
   1. Collagen-vascular disease, vasculitis, Wegener granulomatosis
   2. Amyloidosis, hemochromatosis
   3. Hepatic failure
   4. Administration of antineoplastic drugs

D. Transplant
   1. Acute / chronic rejection
   2. Acute tubular necrosis

E. Urinary bladder
   1. Cystitis
   2. Tumor

mnemonic: CHANT An OLD PSALM

Chemotherapy
Hemochromatosis, **H**epatorenal failure
Acute tubular necrosis, **A**cute lobar nephronia
Neoplasm
Transfusion, **T**uberous sclerosis
Abscess
Obstruction
Lymphoma
Drugs (Fe, drugs causing ATN)
Pyelonephritis, **P**olyarteritis nodosa
Sarcoidosis
Amyloidosis, **A**llograft
Leukemia
Metastasis, **M**yeloma

Gallium Imaging in Lymphoma

= chief use of gallium in tumor imaging before + after chemo- / radiation therapy:
√ persisting ^{67}Ga uptake indicates residual tumor
√ reversion to normal of a previously ^{67}Ga avid mass indicates fibrosis
√ new ^{67}Ga uptake during therapy indicates tumor progression

A. Hodgkin disease
   50–70% average sensitivity dependent on size, location, technique

B. Non-Hodgkin lymphoma
   30% sensitivity for lymphocytic subtype,
   70% sensitivity for histiocytic subtype

Sensitivity:
   90% for mediastinal nodes

80% for neck nodes
48% for periaortic nodes
47% for iliac nodes
36% for axillary nodes

Gallium Imaging in Malignant Melanoma

Types:

1. Lentigo maligna: low invasiveness, low metastatic potential
2. Superficial spreading melanoma: intermediate prognosis
3. Nodular melanoma: most lethal

Prognosis (level of invasion versus 5-year survival):

Level I (in situ) 100%
Level II (within papillary dermis) 100%
Level III (extending to reticular dermis) 88%
Level IV (invading reticular dermis) 66%
Level V (subcutaneous infiltration) 15%

Ga-67:

> 50% sensitivity for primary + metastatic sites
Detectability versus tumor size:
73% sensitivity > 2 cm; 17% sensitivity < 2 cm

Bone, brain, liver scintigraphy:

show very low yield in detecting metastases at time of preoperative assessment and are not indicated

STATISTICS

Decision Matrix				
GOLD STANDARD				
	normal	*abnormal*	*subtotal*	
TN	FN	T-	NPV	
abnormal	FP	TP	T+	PPV
subtotal	D-	D+	total	preval
	specificity	sensitivity		accuracy

TP = test positive in diseased subjects
FP = test positive in nondiseased subjects
FN = test negative in diseased subjects
TN = test negative in nondiseased subjects
T+ = abnormal test results
T- = normal test results
D+ = diseased subjects
D- = nondiseased subjects

STATISTICS

Incidence = number of diseased people per 100,000 population annually
Prevalence = number of existing cases per 100,000 population at a target date
Frequency = number of times an event occurred; often graphically represented in histograms
Mortality = number of deaths per 100,000 population annually
Fatality = number of deaths per number of diseased

Sensitivity

= ability to detect disease
= probability of having an abnormal test given disease
= number of correct positive tests / number with disease
= true positive ratio = TP / (TP + FN) = TP / D+
• D+ column in decision matrix
◊ Independent of prevalence

Specificity

= ability to identify absence of disease
= probability of having a negative test given no disease
= number of correct negative tests / number without disease
= true negative ratio = TN / (TN + FP) = TN / D-
• D- column in decision matrix

◊ Independent of prevalence

Accuracy

= number of correct results in all tests
= number of correct tests / total number of tests
= (TP + TN) / (TP + TN + FP + FN) = (TP + TN) / total
◊ Depends much on the proportion of diseased + nondiseased subjects in studied population
◊ Not valuable for comparison of tests
Example: same test accuracy of 90% for two tests A and B

Positive Predictive Value

= positive test accuracy
= likelihood that a positive test result identifies disease
= number of correct positive tests / number of positive tests
= TP / (TP + FP) = TP / T+
• T+ row in decision matrix
◊ Dependent on prevalence
◊ PPV ↑ with ↑ prevalence for given sensitivity + specificity
◊ PPV ↑ with ↑ specificity for given prevalence

Test A: 90% Accuracy
(**equal** number of diseased and nondiseased diseased)

Decision Matrix

	normal	*abnormal*	*subtotal*	
normal	90	10	100	90%
abnormal	10	90	100	90%
subtotal	100	100	200	50%
	90%	90%		90%

Test B: 90% Accuracy
(**unequal** number of diseased and nondiseased diseased)

Decision Matrix

	normal	*abnormal*	*subtotal*	
normal	170	20	190	89%
abnormal	0	10	10	100%
subtotal	170	30	200	15%
	90%	90%		90%

Negative Predictive Value

= negative test accuracy
= likelihood that a negative test result identifies absence of disease
= number of correct negative tests / number of negative tests
= TN / (TN + FN) = TN / T-
• T- row in decision matrix

◊ Dependent on prevalence
◊ NPV ↑ with ↑ prevalence for given sensitivity + specificity
◊ NPV ↑ with ↑ sensitivity for given prevalence

False-positive Ratio

= proportion of nondiseased patients with abnormal test result
• D- column in decision matrix
= FP / (FP + TN) = FP / D-
= 1 – specificity = (TN + FP - TN) / (TN + FP)

False-negative Ratio

= proportion of diseased patients with a normal test result
• D+ column in decision matrix
= FN / (TP + FN) = FN / D+
= 1 – sensitivity = (TP + FN - TP) / (TP + FN)

Disease Prevalence

= proportion of diseased subjects to total population
= (TP + FN) / (TP + TN + FP + FN) = D+ / total

◊ Sensitivity + specificity are independent of prevalence!

◊ Affects predictive values + accuracy of a test result

Example:

Test A, C, D: 90% sensitivity + 90% specificity

Bayes Theorem

= the predictive accuracy of any test outcome that is less than a perfect diagnostic test is influenced by
(a) pretest likelihood of disease
(b) criteria used to define a test result

Receiver Operating Characteristics (ROC)

= degree of discrimination between diseased + nondiseased patients using varying diagnostic criteria instead of a single value for the TP + TN fraction
= curvilinear graph generated by plotting TP ratio as a function of FP ratio for a number of different diagnostic criteria (ranging from definitely normal to definitely abnormal)

Y-axis: true-positive ratio = sensitivity

X-axis: false-positive ratio = 1 – specificity; reversing the values on the X-axis results in an identical "sensitivity-specificity curve"

Use: variations in diagnostic criteria → reported as a continuum of responses → ranging from definitely abnormal to equivocal to definitely normal ← based on subjectivity + bias of individual radiologists

◊ A minimum of 4–5 data points of diagnostic criteria are needed!

Difficulty: subjective evaluation of image features; subjective diagnostic interpretation; data must be ordinal (= discrete rating scale from definitely negative to definitely positive)

Interpretation:

- ◊ ↑ in sensitivity leads to ↓ in specificity!
- ◊ ↑ in specificity leads to ↓ in sensitivity!
- ◊ Most sensitive point is the point with the highest TP ratio
  → equivalent to "overreading" by using less stringent diagnostic criteria (all findings read as abnormal)
- ◊ Most specific point is the point with the lowest FP ratio
  → equivalent to "underreading" by using more strict diagnostic criteria (all findings read as normal)
- ◊ Does not consider disease prevalence in the population
- ◊ The ROC curve closest to the Y-axis represents the best diagnostic test

Test C_1: 10% prevalence, 90% sensitivity, 90% specificity

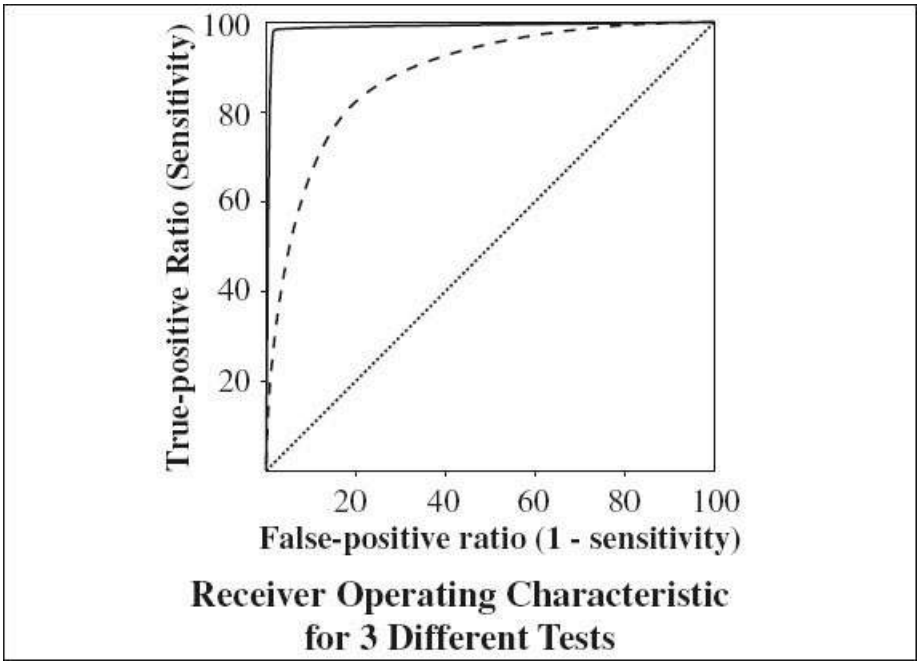
Decision Matrix

	normal	*abnormal*	*subtotal*	
normal	162	2	164	99%
abnormal	18	18	36	50%
subtotal	180	**20**	**200**	10%
	90%	90%		90%

Test C_2: 90% prevalence, 90% sensitivity, 90% specificity

Decision Matrix

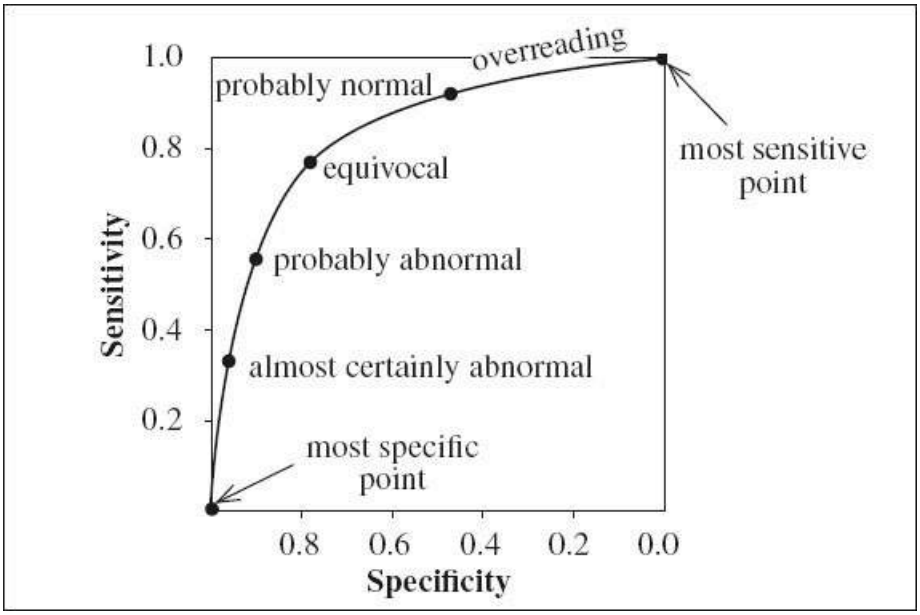
	normal	*abnormal*	*subtotal*	
normal	18	18	36	50%
abnormal	2	162	164	99%
subtotal	20	**180**	**200**	90%
	90%	90%		90%

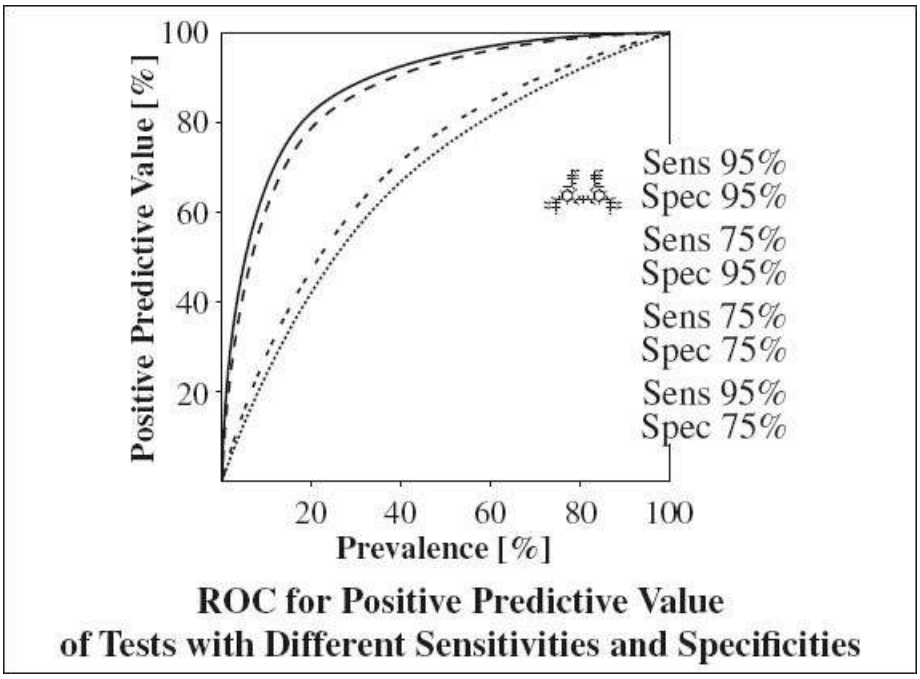


Confidence Limit

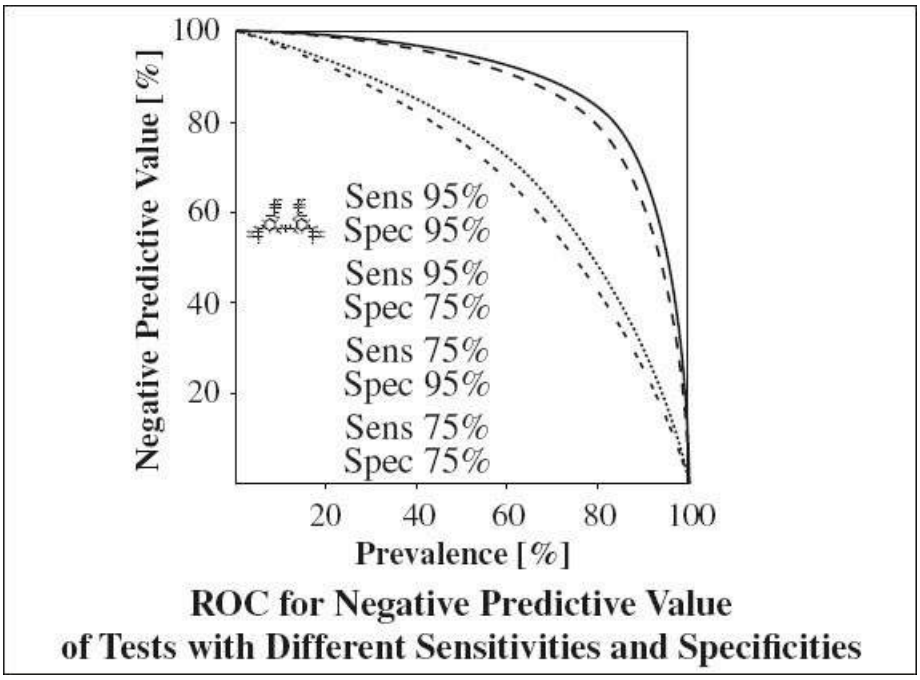
= degree of certainty that the proportion calculated from a sample of a particular size lies within a specific range (binomial theorem)

◊ Analogous to the mean ± 2 SD





ROC for Positive Predictive Value of Tests with Different Sensitivities and Specificities



ROC for Negative Predictive Value of Tests with Different Sensitivities and Specificities

Clinical Epidemiology

= application of epidemiologic principles + methods to problems encountered in clinical medicine with the purpose of developing + applying methods of clinical observation that will lead to valid clinical conclusions

Epidemiology = branch of medical science dealing with incidence, distribution, determinants in control of disease within a defined population

Screening Techniques

Principle question: Can early detection influence the natural history of the disease in a positive manner?

Outcome measure: Early detection + effective therapy should reduce morbidity + mortality → ↑ survival rates (observational study)!

Biases:

Lead time = interval between disease detection at screening + the usual time of clinical manifestation; early diagnosis always appears to improve survival by at least this interval, even when treatment is ineffective

Length time = differences in growth rates of tumors:

(a) slow-growing tumors exist for a long time before manifestation → enhancing opportunity for detection

(b) fast-growing tumors exist for a short time before manifestation → less opportunity for detection at screening = "interval cancers" = clinically detected between scheduled screening exams are likely fast-growing tumors; patients with tumors detected by means of screening tests will have a better prognosis than those with interval cancers

Self-selection bias = decision to participate in screening program usually made by patients better educated + more knowledgeable + more health-conscious; mortality rates from noncancerous causes can be expected to be lower than in general population

Solution: randomization

Overdiagnosis = detection of lesions of questionable malignancy, eg, in situ cancers, which might never have been diagnosed without screening + have an excellent prognosis

Selection Bias

1. Define target population (for whom study is intended)
2. Define accessible population (inclusion + exclusion criteria)
3. Devise sampling scheme (for intended sample population)
4. Study population (= enrolled population)

Sample Bias = intended sample does not adequately reflect the spectrum of characteristics in target population / poor choice of control group volunteers

Consequence: overestimation of diagnostic accuracy → test in question appears more specific

Loss-to-Follow-up Bias = subjects in cohort study lost to follow up differ from those who remain in study until study termination / endpoint

Disease Spectrum Bias = only cases with a limited range of disease spectrum are included

Consequence: overestimation of sensitivity

Referral Bias = individual preferences (eg, distinct clinical groups use different indications for ordering a test) / local practices (eg, tertiary care center) determine which subjects are referred

Participation Bias = factors that affect final enrollment of the intended sample (eg, some subjects refuse to participate, certain records unavailable for review, participants inadvertently excluded)

Image-based Selection Bias = subjects participation depends on having undergone a certain

imaging study

Study Examination Bias = exclusion of technically limited / incomplete studies or prospective inclusion of only patients who are deemed competent to produce a technically adequate examination

Consequence: overestimation of sensitivity + specificity by excluding uninterpretable imaging results

Observation Bias

= methodologic differences in which information is collected about / from study subjects

Consequence: misclassification

Recall Bias = exposure information misclassified for subjects with and without disease (eg, patients with positive results and subsequent treatment will recall better and may exaggerate presentation symptoms)

Interviewer Bias = interviewer may inadvertently coach subjects

Solution: use interviewer not involved / interested in study result

Verification / Work-up Bias = differences in the manner in which disease status is determined

Follow-up / Medical Surveillance Bias = subjects differentially undergo follow-up of disease status

Response Bias = missing data are present nonrandomly for study subjects who are still included in analysis

Reviewer Bias = person collecting / reviewing data is inappropriately blinded

Diagnostic-Review Bias = reference test results are not definite + study test results affect how final diagnosis is established

Test-Review Bias = knowledge of diagnosis may affect test interpretation in a retrospective study if subjective study test is performed after diagnosis has been established

Solution: adequate control group

Incorporation Bias = results of test are incorporated as evidence for final diagnosis if reference test cannot be performed

Imperfect-Standard Bias = reference standard not 100% accurate or use of surrogate reference test ← cost / ethical considerations

Reader-Order Bias = retained knowledge of results of one study influences interpretation of second study

Solution: randomization

Measurement Bias = discrepancy in measurements obtained with a new technique compared to the reference technique on the same subjects under same conditions

Clustering / Repeated-Measurement Bias = multiple measurements / observations obtained from the same subject

Consequence: distortion of standard deviation

Context Bias = effect of altered disease prevalence on estimates of given parameters such as sensitivity, specificity and ROC

Publication Bias = in metaanalysis if journals reviewed favor publication of studies with positive results

Consequence: overly optimistic results

Confounding = in epidemiologic and observational studies additional factors / variables are

associated with exposure and disease status (eg, age, sex)
Solution: randomization, restriction, matching, stratification

Randomized Trials

Design: two arms consisting of (a) study group and (b) control group with patients assigned to each arm on randomized basis
Endpoint: difference in mortality rates of both groups
Power: study must be of sufficient size + duration to detect a difference, if one exists; analogous to sensitivity of a diagnostic test
Impact on effective size of groups:
Compliance = proportion of women allocated to screening arm of trial who undergo screening
Contamination = proportion of women allocated to control group of trial who do undergo screening

Case-control Studies

Retrospective inquiry, which is less expensive, takes less time, is easier to perform:
(a) determine the number of women who died from breast cancer
(b) chose same number of women of comparable age who have not died from breast cancer
(c) ascertain the number of women who were screened
(d) number of women who were not screened in both arms
Calculation of odds ratio = ad / bc

KAPPA COEFFICIENT

= statistical measure of agreement between 2 observers (= interobserver concordance) for categorical items accounting for chance
P_o = proportion of observed agreement
P_c = hypothetical proportion of chance agreement

$$K = \frac{P_o - P_c}{1 - P_c}$$

Predictive value of K (Strength of Agreement):
< 0.00 poor
0.00 – 0.20 slight
0.20 – 0.40 fair
0.40 – 0.60 moderate
0.60 – 0.80 substantial
0.80 – 1.00 almost perfect

CONTRAST MEDIA, NEPHROTOXICITY, PREMEDICATION, CONTROL OF HEART RATE

Ionic = dissociation in water

Nonionic = soluble in water (hydrophilic); no dissociation in solution

Iodine-to-particle ratio:

= quotient of iodine atoms (attenuation of x rays) and number of particles (osmotoxic effect)

ratio 1.5 agents = high-osmolar contrast media (HOCM)

ratio 3.0 agents = low-osmolar contrast media (LOCM)

ratio 6.0 agents = isotonic contrast media (IOCM)

N.B.: Organic iodine is an essential element, so individuals cannot be allergic to it. An **allergy to shellfish** is not a predictor of increased risk to contrast media!

IONIC MONOMERS

= monoacidic salts composed of benzoic acid derivatives, with 3 hydrogen atoms replaced by iodine atoms + 3 hydrogen atoms replaced by simple amide chains

In solution: strong organic acid completely dissociated (ionized) into negatively charged ions / anions

Conjugated cations: (1) sodium
(2) methylglucamine (meglumine)
(3) combination of both

Iodine concentration: up to 400 mg/mL

Iodine-to-particle ratio: 3÷2 or 1.5÷1

Osmolality: 1,400–2,100 mOsm/kg = HOCM

IONIC DIMERS

Construction: 2 iodinated benzene rings containing 6 iodine atoms, one of which contains an ionizing carboxyl group; benzene rings are connected by a common amide side chain

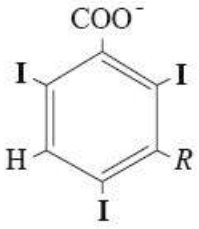
Conjugation with: sodium + meglumine

Compound: ioxaglate (the only available)

Iodine concentration: 320 mg/mL

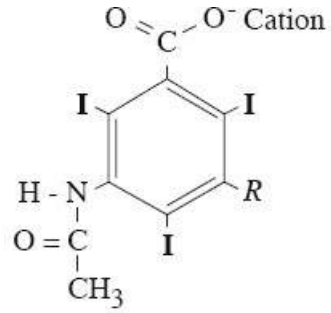
Iodine-to-particle ratio: 6÷2 or 3÷1

Osmolality: 600 mOsm/kg = LOCM



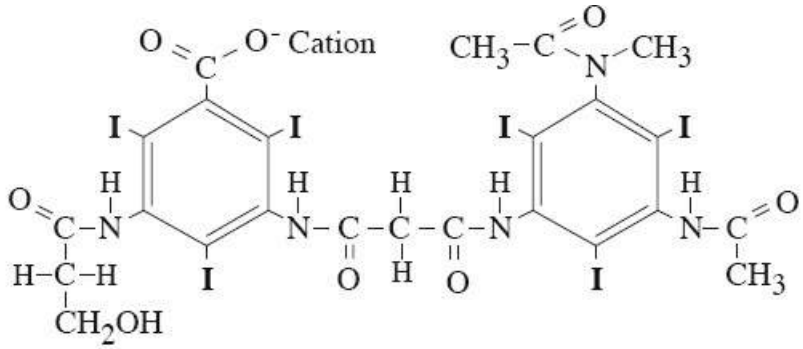
Acetrizoate

The parent triiodinated contrast medium in 1st clinical use; the benzene ring is attached to a carboxyl (COO-) group at the 1-carbon position and conjugated with sodium / meglumine



Diatrizoate

The unsubstituted hydrogen of acetrizoate has been exchanged for another acetamido unit leading to higher biologic tolerance through higher degree of protein binding



Ioxaglate (Hexabrix®)

Sodium and meglumine are conjugated with the carboxyl group

NONIONIC MONOMERS

Construction: benzoic acid carboxyl group replaced by amide; side chains have been modified by adding 4–6 hydroxyl (OH) groups → allows solubility in water

Iodine concentration: up to 350 mg/mL

Iodine-to-particle ratio: 3÷1

Compounds: iohexol, iopamidol, ioversol, iopental, iopromide (Ultravist®), iobitridol (Xenetix®), ioxilan (Oxilan®)

Osmolality: 616–796 mOsm/kg

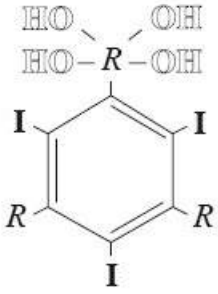
NONIONIC DIMERS

Construction: contain up to 12 hydroxyl groups → eliminates ionicity, ↑ hydrophilicity, ↓ osmotoxicity, ↑ iodine atoms per molecule

Compounds: iodecol, iotrolan (Isovist®), iodixanol (Visipaque®)

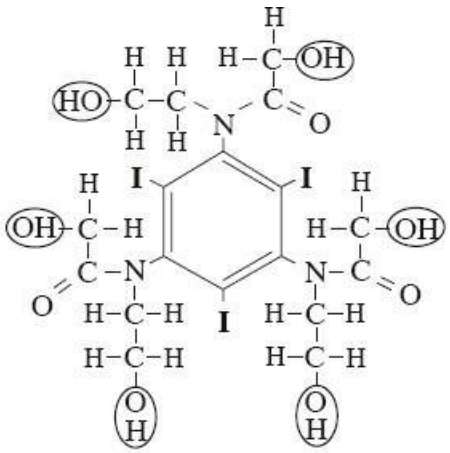
Iodine-to-particle ratio: 6÷1

Osmolality: hypo- / isoosmolar



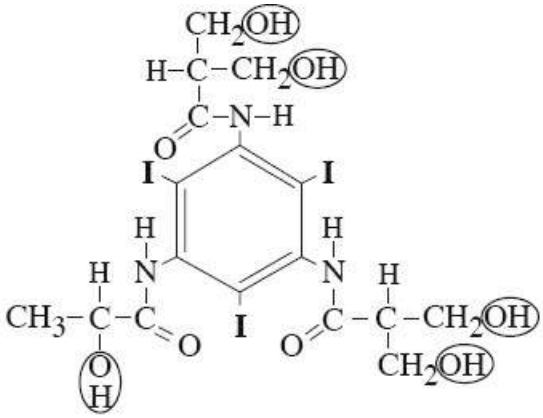
Metrizamide

The 1st compound with 4 hydroxyl groups positioned at one end of the molecule on the glucosamide moiety



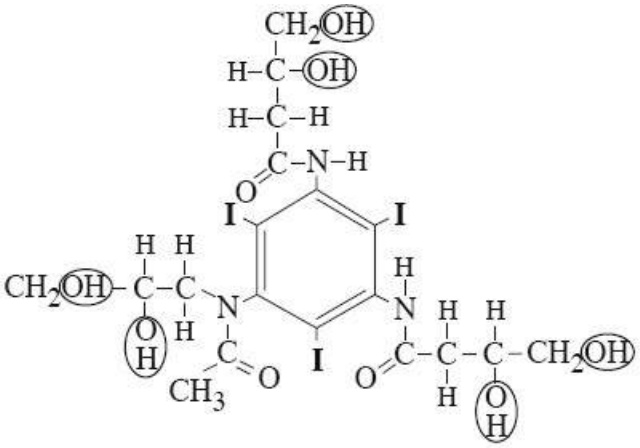
Iohexol (Omnipaque®)

contains 6 hydroxyl (OH) groups more evenly distributed around the molecule improving subarachnoid toxicity



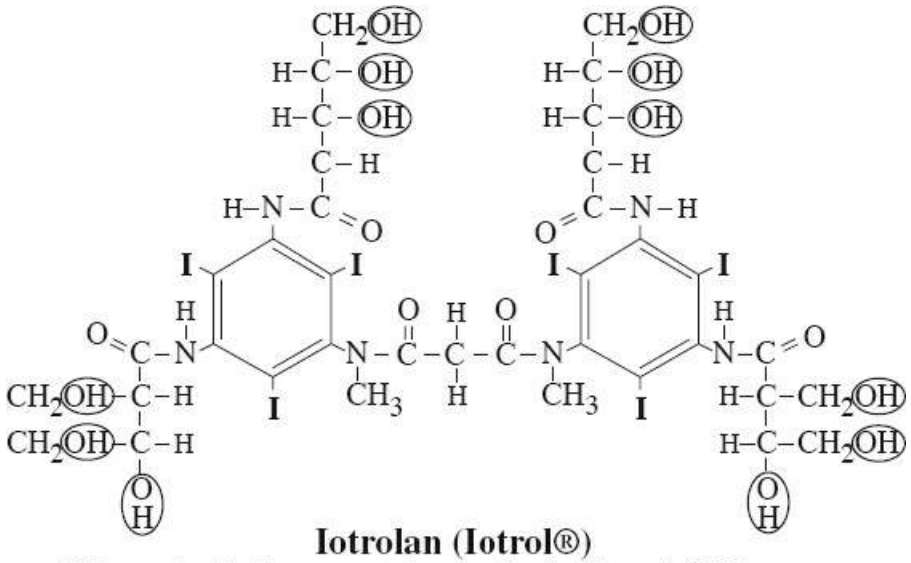
Iopamidol (Isovue®)

This nonionic monomer contains five hydroxyl (OH) groups



Ioversol (Optiray®)

This nonionic monomer contains six hydroxyl (OH) groups



Iotrolan (Iotrol®)
This nonionic dimer contains twelve hydroxyl (OH) groups

Excretory Urography

Clearance: > 99% of contrast material eliminated through kidney (< 1% through liver, bile, small and large intestines, sweat, tears, saliva); vicarious excretion with renal insult / failure (may be unilateral as in obstructive uropathy)

Halftime: 1–2 hours (doubled in dialysis patients)

Concentration: 60% by weight

(a) Sodium-containing HOCM
√ less distension of collecting system

(b) Meglumine-only HOCM
√ improved distension of collecting system ← decreased tubular resorption of water

(c) LOCM
√ denser nephrogram + slightly denser pyelogram than HOCM ← higher tubular concentration

Angiography

Burning sensation:

(a) intense with concentration of 60–76% HOCM
(b) reduced with concentration of ≤ 30% HOCM / LOCM

◊ Overall incidence of adverse allergic-type reactions is (for unknown reasons) much less with intraarterial than with intravenous use of contrast media!

Venography

(1) Foot / calf discomfort or pressure or burning
(a) ~ 24% with 60% HOCM
(b) ~ 5% with 40% HOCM / 300 mg iodine/mL LOCM
◊ The addition of 10–40 mg lidocaine/50 mL of contrast media decreases patient discomfort!

(2) Postphlebography deep vein thrombosis
(a) 26–48% with 60% HOCM

(b) 0–9% with dilute HOCM / LOCM

◊ Infusion of 150–200 mL of 5% dextrose in water / 5% dextrose in 0.45% saline / heparinized saline through injection site immediately after examination reduces likelihood of DVT!

Physicochemical Properties of Commonly Used Radiographic Contrast Media

Contrast Media	*Compound*	*mOsm/kg H2O*	*Viscosity (cps) at 37• C*	*Iodine mg/mL*
Ionic monomers				
URORADIOLOGICAL				
Cysto-Conray® II (Mallinckrodt)	Meglumine-iothalamate	1,300	4.0	202
GASTROINTESTINAL				
Hypaque® Sodium Oral Solution (Nycomed Amersham)	Na diatrizoate	1,300	4.0	249
Gastrografin® (Bracco)	Na-meglumine diatrizoate	1,940	8.4	370
INTRAVASCULAR				
Renovue®-Dip (Bracco)	Meglumine iodamide	433	1.8	111
Conray®-60 (Mallinckrodt)	Meglumine-iothalamate	1,400	4.0	282
Renografin®60 (Bracco)	Na-meglumine diatrizoate	1,450	4.0	292
Ionic dimers				
Hexabrix® (Mallinckrodt)	Na-meglumine ioxaglate	600	7.5	320
Nonionic monomers				
Oxilan® 300 (Cook)	ioxilan	585	5.1	300
Ultravist® 300 (Berlex)	iopromide	607	4.9	300
Isovue® 300 (Bracco)	iopamidol	616	4.7	300
Optiray® 300 (Mallinckrodt)	ioversol	651	5.5	300
Omnipaque® 300 (Nycomed Amersham)	iohexol	672	6.3	300
Omnipaque® 140 (Nycomed Amersham)	iohexol	322	1.5	140
Omnipaque® 240 (Nycomed Amersham)	iohexol	520	3.4	240
Omnipaque® 350 (Nycomed Amersham)	iohexol	844	10.4	350
Nonionic dimers				
Iotrol® 300 (Schering AG)	iotrolan	~310	9.1	300
Visipaque®-320 (Nycomed Amersham)	iodixanol	290	11.8	320

Osmolality of human serum is 290 mOsm/kg!
The higher the number of hydroxyl groups → the larger the size of the molecule + the higher the viscosity + hydrophilicity; responsible for a decrease in protein- and tissue-binding properties → making the compound biologically more inert

Gadolinium-based Contrast Agents					
Contrast Media	*Compound*	*Excess Ligand (%)*	*T1-Relaxivity Plasma [L/(mmol•sec)] at 37• C, 1.5 T*	*Log K_{cond} (pH 7.4)*	*Excretion*
Linear Nonionic					
Omniscan (GE)	Gadodiamide (Gd-DTPA-BMA)	5.0	4.6	14.9	renal (R)
Optimark™ (Mallinckrodt)	Gadoversetamide (Gd-DTPA-BMEA)	10.0	5.2	15.0	renal
Linear Ionic					
MultiHance® (Bracco)	Gadobenate (Gd-BOPTA)	0.1	6.7	18.4	96% renal, 4% biliary
Magnevist® (Bayer)	Gadopentetate (Gd-DTPA)	0.1	4.3	17.9	renal
Eovist® (Bayer)	Gadoxetate (Gd-EOB-DTPA)	0.6	6.9	18.7	50% renal, 50% biliary
Vasovist® (Bayer)	Gadofosveset	0.1	19.0	18.9	95% renal, 5% biliary
Macrocyclic nonionic					
ProHance® (Bracco)	Gadoteridol (Gd-HP-DO3A)	0.1	4.4	17.1	renal
Macrocyclic ionic					
Dotarem® (Guerbet)	Gadoterate (Gd-DOTA)	0.0	3.6	18.0	renal
Gadovist® (Bayer)	Gadobutrol (Gd-BT-DO3A)	0.1	5.2	15.5	renal

◊ The greater the relaxivity (proportional to magnitude of magnetic moment, its tumbling frequency, its electron spin relaxation time) the smaller the dose needed to achieve a given level of enhancement

◊ The higher the dissociation constants (Log K) the greater the stability of an agent

Abbreviations: BMA = bis-methylamide; BMEA = bis-methoxyethylamide; BOPTA = benzyloxypropionictetraacetate; BT = butrol; DOPTA = tetraazacyclododecanetetraacetic acid; DOTA = dodecane-tetraacetic acid; DO3A = 1,4,7,10-tetraazacyclododecane 1,4,7-triacetic acid; DTPA = diethylenetriaminepentaacetic acid; EOB = ethoxybenzyl; Gs = gadolinium (free Gd^{3+} is toxic); HP = hydroxypropyl

◊ Distribution is intra- and extravascular in all with the exception of Vasovist, which is predominantly intravascular.

◊ Dissociation $T_{1/2}$ = > 1000 years for all macrocyclic compounds

Evaluation of Intravenous Access

1. Chose a catheter appropriate for injection:
   - › antecubital / large forearm vein ≥ 20-gauge for 3 mL/sec
   - › peripherally placed 22-gauge for < 1.5 mL/sec
2. Confirm venous return
3. Perform a saline flush
4. Perform a test injection with the power injector esp. for power-injector compatible central venous / peripherally inserted central catheters by observing manufacturer-recommended pressure limits

Contrast Extravasation

= escape of contrast material from vascular lumen + infiltration of interstitial tissue during injection

Incidence: < 1%; no direct correlation with injection flow rate

- may be asymptomatic; edema, erythema
- swelling, tightness, tenderness, stinging, burning pain

Dx: (1) Palpate catheter venipuncture site during initial seconds of injection
(2) Ask patient to report any sensation of pain / swelling at injection site

Severe Cx (uncommon): compartment syndrome, skin ulceration, tissue necrosis

Rx: (1) Elevate affected extremity / site
(2) Apply a warm / cold compress

(3) Monitor for a sufficiently long period

(4) Discharge with instructions to watch for symptoms that indicate a need for surgical evaluation

(5) Initiate surgical consultation for progressive pain / swelling, decreased capillary refill, paresthesia, skin ulceration / blistering

ADVERSE CONTRAST REACTIONS

Risk factors:

1. A history of a previous severe reaction to iodinated contrast agent increases the overall risk of a subsequent reaction by about 5- to 6-fold.
2. All severe allergies and reactions (to medications and food)

   There is NO specific link between shellfish allergy and allergy to contrast agents.
3. History of asthma / bronchospasm / atopy
4. History of cardiac / renal disease
5. Age > 60 years OR < 5 years

A. Nonidiosyncratic (= dose-related) reactions

Cause: direct chemotoxic / hyperosmolar effect

- nausea, vomiting; cardiac arrhythmia; renal failure
- pulmonary edema; cardiovascular collapse

B. Idiosyncratic (= anaphylactoid) reactions

= reactions occurring unpredictably + independently of dose / concentration = not a true antigen-IgE antibody-mediated reaction nor a reaction to iodine / iodide

Cause: unknown

- hives, itching; facial / laryngeal edema
- bronchospasm, respiratory collapse; circulatory collapse

C. Delayed reactions

- erythematous rashes, pruritus, fever, chills, flulike symptoms
- joint pain, loss of appetite, taste disturbance, headache
- fatigue, depression, abdominal pain, constipation, diarrhea

Significant underlying medical conditions

(a) renal disease
(b) cardiac disease
(c) blood dyscrasias
(d) pheochromocytoma
(e) ↑ symptoms with COPD plus pulmonary hypertension
(f) ↑ sickling in patients with sickle-cell disease

◊ Approximately 20–40% of population are at increased risk for adverse reaction to contrast media!

◊ In patients with adverse reactions to HOCM repeated reactions will be lowered to 5% by using LOCM

◊ No direct correlation / association to povidone-iodine skin cleansing solution (Betadine®)

Assessment of Patients before Contrast Injection

A. General status
Assess hemodynamic, neurologic, general nutritional, anxiety status
B. History of significant allergies
1. Prior anaphylactic response to any allergen
2. Asthma
C. Renal disease
1. Renal dysfunction: obtain baseline BUN + creatinine
2. Diabetes mellitus
3. Multiple myeloma
◊ Hydrate patients and limit contrast dose!
D. Cardiac disease
1. Angina
2. CHF with minimal exertion
3. Severe aortic stenosis
4. Primary pulmonary hypertension
5. Severe cardiomyopathy
◊ Limit contrast dose!

NEPHROTOXICITY

= CONTRAST-INDUCED NEPHROTOXICITY (CIN)
= sudden deterioration of renal function after recent IV administration of contrast media in the absence of another nephrotoxic event

Indications for Obtaining Creatinine Levels

A. IODINATED CONTRAST AGENTS

Prevalence of Adverse Contrast Reactions		
	High-osmolar Ionic	*Low-osmolar Nonionic*
Non–life-threatening reaction	1–2%	0.2–04%
Life-threatening reaction	0.2%	0.04%
Mortality	1÷100,000	1÷100,000
Late reaction		6%

Risk Factors and Incidence of Adverse Reactions for High- and Low-Osmolality Contrast Media		
Type of Reaction	*HOCM [%]*	*LOCM [%]*
Overall incidence		
Australia (Palmer et al.)	3.80	1.20
USA (Wolf et al.)	4.20	0.70
Japan (Katayama et al.)	12.70	3.10
Severe adverse reaction	0.22	0.04
Severe allergies to drugs, foods, etc.	23.40	6.90
Asthma	19.70	7.80
Repeat reaction to contrast media	16–44	4.1–11.2

1. Age > 60 years
2. History of kidney disease as an adult, including tumor / transplant
3. Family history of kidney failure
4. Diabetes treated with insulin / other prescribed meds
5. Hypertension
6. Paraproteinemia syndromes / diseases (eg, myeloma)
7. Current use of nephrotoxic medications (eg, chemotherapeutic agents, chronic use of NSAIDs)

B. GADOLINIUM-BASED CONTRAST AGENTS

1. Age > 60 years
2. History of kidney disease as an adult, including tumor / transplant
3. Single kidney / kidney surgery
4. Diabetes treated with insulin / other prescribed meds
5. Hypertension requiring medical therapy

Nonoliguric Transient Renal Dysfunction

= transient decline of renal function

- serum creatinine level peaks on days 3–5
- serum creatinine returns to baseline values within 14–21 days
- fractional excretion of sodium < 0.01 (DISTINCTIVE CHARACTERISTIC compared with other causes)

Acute Renal Failure

= sudden + rapid deterioration of renal function

= increase in serum creatinine of > 25% or to > 2 mg/dL within 2 days of receiving contrast material

Frequency: 1–30%; 3rd most common cause of in-hospital renal failure after hypotension and surgery

Risk factors:

Contrast agent–independent acute kidney injury is NOT significantly different and may be clinically indistinguishable when adjusted for patient risk factors.

1. Preexisting renal insufficiency (serum creatinine > 1.5 mg/dL)

2. Diabetes mellitus with renal insufficiency (possibly related to dehydration / hyperuricemia)
   ◊ Ratio 3 nonionic LOCM appear to be 50% less nephrotoxic than ratio 1.5 ionic HOCM
   ◊ Diabetics with normal renal function are not at ↑ risk!
3. Dehydration
4. Cardiovascular disease
5. Use of diuretics
6. Advanced age > 70 years
7. Multiple myeloma (in dehydrated patients)
8. Hypertension
9. Hyperuricemia / uricosuria
10. High dose of contrast material

CAVE:

◊ Small decreases in renal function may greatly exacerbate the mortality caused by the underlying condition!

◊ Metformin (Glucophage®) should be discontinued for 48 hours after contrast medium administration (accumulation of metformin may result in lactic acidosis → fatal in 50%)!

◊ It is not necessary to stop metformin after gadolinium administration because gadolinium is not nephrotoxic!

◊ Avoid concomitant use of nephrotoxic drugs (eg, gentamicin, NSAIDs)

Proposed mechanisms:

› contrast agents are concentrated in nephrons + collecting tubules

1. Vasoconstriction
   (a) ↑ in intrarenal pressure induced by hypertonicity
   (b) intrarenal smooth muscle contraction ← hypertonic substances
2. RBC aggregation in medullary circulation
3. Direct tubular cell injury

Potential antidotes:

Hydration (0.9% saline at 100 mL/hr) 12 hours before + 12 hours after angiography

◊ Extracellular volume expansion is the most effective + widely recommended measure!

√ immediate dense nephrogram persisting for up to 24 hours (in 75%)

√ gradually increasing dense nephrogram resembling bilateral acute ureteral obstruction (in 25%):

√ bilaterally enlarged smooth kidneys

√ poor opacification of urine-conducting structures

√ effacement of collecting system (interstitial edema)

Cx: 34% mortality (0.4% of all patients)

Rx: 0.1% require renal replacement therapy

NEPHROGENIC SYSTEMIC FIBROSIS

= NEPHROGENIC FIBROSING DERMOPATHY

= rare potentially debilitating chronic fibrosing condition involving multiple organ systems

initially described in 2006 without specific imaging findings

Cause: gadolinium-based contrast agents

Pathophysiology: unclear

Risk factors:

(1) High dose gadolinium-based contrast agent
   › highest risk: Omniscan®, Magnevist®, OptiMARK™
   › medium risk: MultiHance®, Ablavar®, Eovist®
   › low risk: Gadavist®, Dotarem®, ProHance®
(2) Acute / chronic renal failure: especially dialysis, hepatorenal syndrome, perioperative liver transplantation period, renal transplant failure
(3) Venous thrombosis
(4) Vascular surgery

Age: any; most commonly middle-aged; M÷F=1÷1

Organ involvement: skin, subcutaneous tissue, lung, pleura, skeletal muscle, bone, heart, pericardium, testis, esophagus, kidney

Onset: days to months (average time, 2–10 weeks) after administration of GBCA, up to 8 years after exposure

@ Skin

Location: distal lower extremities → (subsequent) extension to thighs → lower abdomen → upper extremities

- patterned skin plaques, cobblestone, marked induration
- erythematous papules coalescing into plaques of peau d'orange appearance
- thickening of dermis developing a woody texture similar to scleromyxedema / scleroderma with sparing of face

Cx: pain + decreased range of motion → contractures and joint immobility

Histo: thick collagen bundles ← proliferation of dermal fibroblasts + dendritic cells (CD-68, factor XIIIa-positive) with variable amounts of mucin + elastic fibers

DDx: cellulitis, fasciitis, scleroderma, cutaneous lymphoma, lymphatic / venous obstruction, dermatopolymyositis

Risk reducing strategy:

(1) Consider CT in anuric patient
(2) Use low-risk Gd-based contrast agent
(3) Initiate dialysis within 2 hours of exposure + schedule several prolonged dialysis treatments for those patients who are already on dialysis

TREATMENT OF CONTRAST REACTIONS

◊ 94–100% of severe + fatal anaphylactoid reactions occur within 20 minutes of contrast medium injection
   ⇒ use a plastic cannula for IV access
   ⇒ maintain IV access for 30 min
   ⇒ have emergency drugs close to the room where contrast injections are done
   ⇒ post a listing of available medications + their common doses in the room

Oral Steroid Premedication Protocol (see table)

Indication: previous respiratory adverse contrast reaction, history of significant allergies /

severe asthma

Caution in patients with: active tuberculosis, diabetes mellitus, peptic ulcer disease

◊ Antihistamines alone have not proved to be effective!

Treatment of Premedicated Patients

A. Patient on β-blocker

if response to epinephrine inadequate

⇒ 1–5 mg glucagon IV + subsequent slow drip of 5 mg glucagon over 60 minutes

Classification of Acute Nonrenal Adverse Reactions to Contrast Agents

Severity	*General*	*Cardiovascular*	*Gastrointestinal*	*Central Nervous System*
Physiologic type	***Patients do NOT require premedication in the future.***			
Mild	flushing, warmth / chills, sneezing, rhinorrhea / nasal congestion	mild hypertension	mild nausea / vomiting	anxiety, self-limited syncope / vasovagal reaction, dizziness, headache
Moderate	...	chest pain without other symptoms / EKG changes, hypertensive urgency	moderate nausea / vomiting	vasovagal reaction requiring treatment
Severe	seizures	hypertensive crisis / arrhythmia / EKG changes	...	unresponsiveness / unconsciousness
Allergic type	***Patients MAY need premedication with steroids.***			
Mild	limited urticaria, pruritus, skin edema, sneezing, rhinorrhea / nasal congestion	mild hypertension	nausea, mild vomiting	...
Moderate	generalized edema, urticaria, pruritus / edema	hoarseness / throat tightness ± mild hypoxia, wheezing with mild hypoxia	...	...
Severe	severe edema (including facial and laryngeal edema)	hypotension / hypoxia	...	...

Premedication Protocols

Protocol	*Option 1 (best)*	*Option 2 (less desirable)*	*Option 3 (least)*
Elective			
Steroid	Prednisone: 50 mg PO at 13 + 7 + 1 hours prior to injection of nonionic low-osmolality contrast agent	Methylprednisolone (Medrol®): 32 mg PO 12 + 2 h prior to injection of nonionic low-osmolality contrast agent	...
Antihistamine	Diphenhydramine (Benadryl®): 50 mg IV, IM, oral 1 h prior to injection of low-osmolality contrast agent	Diphenhydramine: 50 mg IV, IM, oral 1 h prior to injection of nonionic low-osmolality contrast agent	...
Emergent			
Indication	*most desirable in emergency*	may be used with allergies to methylprednisolone / aspirin / NSAIDs	used when there is inadequate time to achieve corticosteroid effect
Steroid	IV methylprednisolone sodium succinate 40 mg	IV dexamethasone sodium sulfate 7.5 mg	**omit steroids**: steroids not effective when given < 4–6 h prior to injection of contrast material
or	IV hydrocortisone sodium succinate 200 mg every 4 h until study	betamethasone 6.0 mg every 4 h until study performed	
Antihistamine	diphenhydramine 50 mg IV 1 h before injection of contrast material	diphenhydramine 50 mg IV 1 h before injection of contrast material	diphenhydramine 50 mg IV 1 h prior to injection of contrast

Treatment for Reactions to Contrast Agents in Adults		
Reaction	*Treatment*	*Dosage*
Bronchospasm		
Mild	β-agonist inhaler = albuterol	2 puffs (= 180 µg); repeat up to 3 times
Moderate	β-agonist inhaler = albuterol	2 puffs (= 180 µg); repeat up to 3 times
	epinephrine	IM: 0.3 mg (0.3 mL of 1÷1000 dilution) → repeat to total dose of 1 mg or IV: 0.3 mg (1–3 mL of 1÷10,000 dilution) → repeat to total dose of 1 mg
Severe	epinephrine	IM: 0.3 mg (0.3 mL of 1÷1000 dilution) → repeat to total dose of 1 mg or IV: 0.3 mg (1–3 mL of 1÷10,000 dilution) → repeat to total dose of 1 mg
Laryngeal edema	Epinephrine	IM: 0.3 mg (0.3 mL of 1÷1000 dilution) → repeat to total dose of 1 mg or IV: 0.3 mg (1–3 mL of 1÷10,000 dilution) → repeat to total dose of 1 mg
Hypotension < 90 mmHg, < 100 bpm	Elevate legs > 60°	Consider 1000-mL bolus of 0.9% normal saline / lactated Ringer
Vasovagal reaction		
Mild	None	...
Moderate to severe	Atropine	IV: 0.6–1.0 mg slowly infused followed by saline flush → repeat to total dose of 3 mg
Anaphylactoid reaction < 90 mmHg, > 100 bpm	Epinephrine	IM: 0.3 mg (0.3 mL of 1÷1000 dilution) → repeat to total dose of 1 mg or IV: 0.3 mg (1–3 mL of 1÷10,000 dilution) → repeat to total dose of 1 mg
Hypertensive crisis	Labetalol	IV: 20-mg slow in fusion over 2 min (double dose every 10 min)
	or Nitroglycerin	sublingual tablet of 0.4 mg - repeat very 5–10 min
	or Furosemide (Lasix)	IV: 20–40 mg slowly infused over 2 min

B. Patient on calcium channel blocker (eg, nifedipine, nicardipine)
   ⇒ calcium IV
C. Excessive vasoconstriction on epinephrine IV
   ⇒ infusion of 0.5–10 µg/kg/min of reconstituted sodium nitroprusside (Nipride®) (50 mg in 500–1000 mL of 5% dextrose wrapped in metal foil during use to protect solution from light)
D. Metformin (Glucophage®)
   ⇒ Stop metformin medication at time of contrast injection + for subsequent 48 hours
   ⇒ Reinstate medication if renal function remains normal
   ◊ Contrast material is contraindicated if patient is in renal failure because of risk of lactic acidosis!

Useful Medications

1. Alpha- and β-adrenergic agents:
   Action: vasoconstriction, increased cardiac output
   ♦ **Epinephrine**
      ⇒ 1 mL glass vial of epinephrine 1:1,000
         Adult dose: 0.1–0.2 mL epinephrine (1:1,000 = 0.1–0.2 mg) SQ
         Pediatric dose: 0.01 mL/kg up to 0.3 mL/dose
      ⇒ repeat in 15–30 minutes if needed
         Indications: bronchospasm, facial edema, severe urticaria, laryngospasm
      ⇒ 10-mL syringe of epinephrine 1÷10,000 (prepackaged)
         Adult dose: 1–3 mL epinephrine (1÷10,000)
         (= 0.1 mg) slowly IV
         Pediatric dose: 0.1 mL/kg slowly IV
      ⇒ repeat every 5–15 minutes if needed
         Indications: bronchospasm / laryngospasm with peripheral vascular collapse

Maximum dose: 1.0 mg

♦ **Dopamine** (Inotropin®)

Adult dose: 2–5 pg/kg/min IV; rarely need to exceed 20 pg/kg/min

Indications: hypotension

Cx: arrhythmia, myocardial ischemia, nausea, vomiting, tremulousness, headache

2. **Atropine sulfate**

Adult dose: 0.6–1.0 mg slowly IV

Pediatric dose: 0.02 mg/kg slowly IV (0.2 mg/kg of the 0.1 mg/mL solution); minimum dose of 0.1 mg (children) + 1.0 mg (adolescents)

Repeat after 5 min

Maximum dose: 0.04 mg/kg (2–3 mg) in adults

Indications: bradycardia, hypotension

Cx: angina, myocardial infarction

3. **Metered-dose inhalers** of β-adrenergic bronchodilators

♦ Metaproterenol (Alupent®)

♦ Terbutaline (Brethaire®)

♦ Albuterol (Proventil®, Ventolin®)

Dose: 2 puffs every 20–30 minutes, as needed

4. **H_1 antagonists** = antihistamines

♦ Diphenhydramine (Benadryl®)

Adult dose: 25–50 mg PO/IM/IV

Pediatric dose: 1–2 mg/kg IV, up to 50 mg

♦ Hydroxyzine (Vistaril®)

Dose: 25–50 mg PO/IM/IV

Indications: hives, rash, itching

Cx: hypotension, sedation

5. **H_2 receptor blockers**

♦ Cimetidine (Tagamet®)

Dose: 300 mg PO / slowly IV (diluted in 10 mL D5W solution)

♦ Ranitidine (Zantac®)

Dose: 50 mg PO / slowly IV (diluted in 10 mL D5W solution)

Indications: hypotension; bronchospasm

6. **Aminophylline**

• 250 mg in 250 mL of 5% dextrose

Dose: 6 mg/kg IV in D5W over 15–20 minutes (loading dose); then 0.4–1.0 mg/kg/hour

Indications: bronchospasm, pulmonary edema

Cx: hypotension, cardiac arrhythmia

7. **Terbutaline**

• 0.25–0.50 mg IM/SQ

8. Sedatives

♦ **Midazolam** (Versed®)

Dose: 1–2.5 mg IV over 2 minutes; titrate to effect q 2 minutes; maximum 5 mg

Indications: sedation

♦ **Diazepam** (Valium®)

Dose: 2–10 mg IM/IV q 3–4 hours; maximum 30 mg
Indications: seizures

♦ **Pentobarbital** (Nembutal®)
Dose: < 50 mg/min IV; 150–200 mg IM
Indications: toxic convulsions
Cx: respiratory depression, apnea, laryngospasm, hypotension

9. Pain
♦ **Fentanyl**
Dose: 25–50 mg IV; short acting
♦ **Morphine**
Dose: 1–3 mg IV
Indications: pain; pulmonary edema
♦ **Demerol**
Cx: respiratory depression
10. **Volume expander**
♦ **Crystalloid solution** as 0.9% saline
♦ **Hydroxylethyl starch** (high-molecular-weight colloid)
11. **Furosemide** (Lasix®)
Adult dose: 20–40 mg IV slow push / PO
Pediatric dose: 1 mg/kg/dose IV up to 40 mg
Effect: 5–15 minutes after IV; 60 min after PO
Indications: acute pulmonary edema, CHF, hypertensive emergency
12. Corticosteroids
♦ **Methylprednisolone** (Solu-Medrol®)
Dose: (a) 32 mg PO; 12 hours & 2 hours prior
(b) 100–1,000 mg (anaphylaxis with shock)

REDUCTION OF HEART RATE FOR IMAGING

Purpose: Cardiac anatomic imaging
Pharmacology: ↓ frequency of sinus node, ↓ spontaneous rate of depolarization of ectopic pacemakers, slowing conduction in atria + AV node, ↑ functional refractory period of AV node
Target: < 60 beats per minute
Drugs: cardioselective (β1) β-blocker

♦ **Metoprolol**
Dose: 2.5–5 mg IV administered over 1–2 minutes; may be repeated at 2–5-minute intervals
Maximum dose: 30 mg
Oral bioavailability: 40% (high interindividual differences)
Biologic half-life: 3–4 hours
♦ **Atenolol**
Dose: 5–10 mg IV
Oral bioavailability: 50%
Biologic half-life: 5–8 hours

♦ **Esmolol**

Dose: 1–2 mg/kg bolus / continuous titrated infusion

Biologic half-life: 9 min

Protocol: (1) Oral premedication 1 hour prior to scan: 100 mg Metoprolol / 100–200 mg Atenolol

(2) IV supplement as needed: 5 mg Metoprolol at arrival to scanner; additional 2–5 mg each 5 minute (max 30 mg) or 1–2 mg/kg body weight Esmolol

Side effects:

(a) β1-selective intrinsic sympathomimetic activity:
- hypotension, bradycardia, widening of QRS complex
- prolonged AV conduction times

(b) binding on noncardiac β2 receptors → compensatory sympathetic reflexes → activation of vascular α-adrenergic receptors:
- peripheral vasoconstriction sparing brain

Contraindications (in 5–10%):

1. (Allergic) asthma bronchiale / severe chronic obstructive pulmonary disease
2. AV block Mobitz type II or type III
3. Severe bradycardia of < 50 bpm
4. Severe hypotension of < 100 mmHg
5. Acute congestive heart failure
6. Allergy to β-blockers

SEDATION, ANALGESIA, LOCAL ANESTHESIA

Classification and Effects of Levels of Sedation				
Level	*Response to stimuli*	*Airway*	*Spontaneous ventilation*	*Cardiovascular function*
minimal*	normal	unaffected	unaffected	unaffected
moderate	purposeful	no intervention required	adequate	usually maintained
deep	purposeful after repeated / painful stimuli	intervention may be required	may be inadequate	usually maintained
general anesthesia	unarousable	intervention often required	frequently inadequate	may be impaired

SEDATION

= administration of medication to calm the nervous system: ⇓ awareness; ⇓ responsiveness to external stimuli; ⇓ anxiety; ⇓ spontaneous movements; may produce amnesia

Phases of sedation protocol: 1. Preprocedural assessment
2. Intraprocedural monitoring
3. Postprocedural monitoring

Presedation Assessment

1. Evaluate patient (within 30 days of procedure + update within 24 hours)
   (a) personal history:
      › cardiovascular: hypertension, myocardial infarction within prior 6 months, CHF, arrhythmia → pose an increased risk
      › respiratory: asthma, COPD, other lung disease
      › gastrointestinal: GERD, peptic ulcer, nil per os (NPO) status
      › fasting status: predictor of aspiration
         ◊ In an emergent procedure administer 10 mg IV **metoclopramide** (Reglan®) + 10 mg IV **famotidine** (Pepcid®) / other H_2 blocker!
   (b) medication history
      › continue cardiovascular medication
      › monitor blood sugar in diabetics
   (c) physical examination
2. Classify physical status of patient *(see table)*

Classification of Patient's Physical Status	
Class	*Status*
I	normal healthy patient without systemic disease
II	mild–moderate systemic disease (ie, controlled hypertension, diabetes) / elderly
III	severe systemic disease (ie, limited activity but not incapacitating)
IV	severe incapacitating systemic disease
V	moribund = without intervention death anticipated within 24 hours
VI	brain dead organ donor
E	emergency modifier

3. Document discussion with patient concerning risks and benefits + obtain consent
4. Document plan for sedation

   Dose adjustment:
   - › in elderly 30–50% dose reduction + more frequent dose intervals
   - › decrease dose with impaired kidney / liver function
   - › habitual users of opioids / benzodiazepines require higher doses

   Convert to monitored anesthesia (= supervision by anesthesiologist) if:
   (a) sedation cannot be administered safely (eg, Pickwickian syndrome, sleep apnea)
   (b) deep sedation is required
5. Assure presence of appropriate personnel + equipment
6. Identify correct patient immediately before onset of procedure

Intraprocedural Monitoring

1. Respiratory rate: continuous monitoring with pulse oximetry
2. ECG: continuous monitoring
3. Blood pressure: every 5 min + before every dose
4. Assessment of Alertness
5. Pain assessment: verbal descriptor, linear numeric, face-pain scale

Assessment of Alertness during Sedation	
Level	*Description*
V	ready response to name calling; normal speech
IV	lethargic response to name calling; mild slowing of speech
III	response to repeated name calling; slurred speech
II	response only after mild prodding
I	no response to mild prodding / shaking

Postprocedural Monitoring

= monitoring for postprocedural complications as drugs are unopposed by anxiety and pain related to procedure → deepening of sedation + respiratory depression

Frequency: in 15-minute intervals for ≥ 30 minutes after last dose; for ≥ 2 hours after use of

reversal agent

Sedatives

A. Benzodiazepines

Action: facilitate actions of g-aminobutyric acid (= main inhibitory neurotransmitter) in CNS; synergistic with opioids

Properties: anxiolytic, amnestic

1. **Midazolam** (Versed®)
   Administration: IM, IV (rapid onset of action)
   Elimination half-life: 1–4 hours (short)
2. **Lorazepam** (Ativan®)
   Administration: PO, IM, IV (variable peak effect)
   Elimination half-life: mean of 15 hours
3. **Diazepam** (Valium®): also anticonvulsant
   Elimination half-life: 20–100 hours
   Administration: PO, IM, IV (painful)

B. **Diphenhydramine** (Benadryl®)

Action: blocks histamine-1 receptors (H1 blocker); anticholinergic

Contraindication: asthma, narrow-angle glaucoma, urinary retention

Side effect: dry mouth, dizziness, sedation

Reversal Agents

= drugs counteracting effects of drugs used for anesthesia

Assessment: patient difficult to arouse, cardiorespiratory depression (= oxygen desaturation, drop in blood pressure)

Adult Parenteral Dosing for Sedatives

Brand	*Supplied*	*Dosing*
Versed®	1 mg/mL or 5 mg/mL	1–2.5 mg IV over 2 min; titrate to effect q 2 min; maximum 5 mg
Ativan®	2 mg/mL or 4 mg/mL	0.05 mg/kg IM 2 hrs prior; 2 mg or 0.0444 mg/kg IV
Valium®	5 mg/mL	2–10 mg IM/IV q 3–4 hours; maximum 30 mg
Benadryl®	50 mg/mL	10–50 mg IV / ≤ 100 mg IM

(1) reversing effects of opioids (reverse first)

1. **Naloxone** (NARCAN®)
   Onset: within 1–2 minutes
   Duration: 45 minutes; may be needed repeatedly

(2) reversing effects of benzodiazepines (reverse second)

1. **Flumazenil** (Romazicon®)
   Onset: within 1–2 minutes
   Duration: 30–60 minutes; may be needed repeatedly

ANALGESIA

= symptomatic relief of pain with use of pharmacologic agents
◊ Pain is more resistant to analgesics in an anxious patient!

A. Opioids = drugs with opium- / morphin-like action augmented when administered with benzodiazepines
› titrated to effect (no maximal dose)
Action: analgesic, sedative, antitussive, antirigor properties
Side effects: nausea, constipation, CNS depression, respiratory depression
Long-term side effects: tolerance, addiction

(a) natural alkaloids

1. **Morphine**
Administration: IM, IV, suppository, PO (immediate / sustained release tablet, solution)
Dose: 1–3 mg IV
Indications: pain; pulmonary edema
Elimination: metabolized to active morphine-6-glucoronide + eliminated by kidneys; releases histamine
Contraindication: renal failure, asthma, hypotension

Aldrete Postanesthesia Discharge Score

Variable	*Parameter*	*Score*
Activity	4 extremities	2
	2 extremities	1
	0 extremities	0
Respiration	breathing deeply / coughing freely	2
	dyspneic / shallow breathing / tachypneic	1
	apneic	0
Circulation	BP ± 20% of presedation level	2
	BP ± 20–49% of presedation level	1
	BP ± 50% of presedation level	0
Consciousness	fully awake	2
	arousable on calling	1
	not responding	0
Oxygen saturation	> 92% on room air	2
	needs O_2 to remain > 90%	1
	< 90% with O_2	0

(b) synthetic derivatives

2. **Fentanyl**
Administration: transdermal, buccal, nasal spray, PO (tablet, lozenge), IM, IV
Action: 50–100 x potency of morphine
Dose: 25–50 mg IV; short acting
Side effect: few; stiff chest syndrome (= rigidity of skeletal muscles caused by rapid IV administration) treated with intubation + succinylcholine

3. **Meperidine** (Demerol®)

Administration: IM, IV
Action: 0.1 x potency of morphine; antirigor property
Elimination: metabolized to CNS stimulant normeperidine → seizure risk with high dose + renal insufficiency
Side effect:
itching; atropine-like (dry mouth, tachycardia, pupil dilatation); myocardial depression; interactions with nonprescription drugs (eg, Prozac®, St John's wort); coadministration of serotonin uptake inhibitor causes life-threatening serotonin syndrome (autonomic instability with hypertension, tachycardia, diaphoresis, hyperreflexia, hyperthermia, agitation)

Adult Dosing of Analgesics

Brand Name	*Component*	*Admin*	*Available Dose*	*Recommended Dose (p.r.n.)*	*Max Dose*
Tylenol	Acetaminophen	Tablet	325, 500, 650 mg	500–1000 mg PO q 4–6 hr	4000 mg/d
Tylenol	Acetaminophen	Solution	500 mg/15 mL	500–1000 mg PO q 4–6 hr	4000 mg/d
Aspirin (extra strength)	ASA	Tablet	500 mg	1–2 tabs PO q 4–6 hrs	4000 mg/d
Celebrex	Celecoxib	Tablet	50, 100, 200, 400 mg	400 mg PO 1st day then 200 mg PO b.i.d.	
Dolobid	Diflunisal	Tablet	500 mg	1000 mg PO initially then 500 mg PO q 8–12 hr	1500 mg/d
Motrin IB	Ibuprofen	Tablet	200 mg	200 mg PO q 4–6 hr.	1200 mg/d
Indocin	Indomethacin	Capsule	25, 50 mg	25–50 mg PO q 8–12 hr.	150–200 mg/d
Indocin	Indomethacin	Solution	25 mg/5 mL	25–50 mg PO q 8–12 hr	150–200 mg/d
Toradol	Ketorolac	Tablet	10 mg	transition from IV to PO: 20 mg PO then 10 mg PO q 4–6 hr	40 mg/d < 5 d
Toradol	Ketorolac	Injectable	15, 30 mg/mL	30 mg IV/IM q 6 hr	120 mg/d < 5 d
Aleve	Naproxen	Caplet	220 mg	440 mg PO in 1st hr then 220 mg PO q 8–12 hr	660 mg/d or 440 mg in 8–12-hr period
Naprosyn	Naproxen	Tablet	250, 375, 500 mg	500 mg initially then 250 mg PO q 6–8 hr or 500 mg q 12 hr	1500 mg/d
Naprosyn	Naproxen	Solution	125 mg/5 mL	500 mg initially then 250 mg PO q 6–8 hr or 500 mg q 12 hr	1500 mg/d

Drugs for Pain-controlled Analgesia in 70-kg Adult

Name	*Intermittent Dose*	*Frequency*	*Basal Infusion Rate*
Hydromorphone	0.2–0.5 mg	6–10 min	0.2–0.5 mg/hr
Meperidine	10–15 mg	6–10 min	15–50 mg/hr
Morphine	1–2 mg	6–10 min	0.5–1 mg/hr
Fentanyl	10–25 µg	2–5 min	25–50 µg/hr
Alfentanil	0.01–0.03 mg	1–3 min	none

(c) semisynthetic derivatives

4. **Hydromorphone** (Dilaudid®)
Administration: suppository, PO (tablet, liquid), IM, IV
Action: 4–8 x potency of morphine; antitussive
Side effect: few

B. Nonopioids reserved for less severe pain in outpatients, not used in a procedure, not associated with dependency

1. **Acetaminophen**
Side effect: liver toxicity with dose excess of 4 g per day

2. Nonsteroidal anti-inflammatory drug (**NSAID)**
Administration: PO; limit to maximally 2 months of Rx
Action: more effective against inflammation
Side effect: depression of platelet function
(a) selective COX-2 inhibitor
3. **Celecoxib** (Celebrex®)
Side effect: less GI irritation + bleeding
(a) nonselective COX-2 inhibitor
› acetylated carboxylic acid derivative
4. **Aspirin**
Side effect: GI irritation + bleeding
› nonacetylated carboxylic acid derivative
5. **Diflunisal** (Dolobid®)
Side effect: better gastric tolerance
› acetic acid derivative
6. **Indomethacin** (Indocin®)
Side effect: CNS, GI
7. **Ketorolac** (Toradol®) excellent pain relief, parenteral administration possible, limit use to 5 days
Side effect: renal toxicity + liver injury
› propionic acid derivative
8. **Ibuprofen** (Advil®, Motrin®)
Side effect: hypertension, fluid retention
9. **Naproxen** (Aleve®, Naprosyn®)
Side effect: hypertension, fluid retention

Pain-controlled Analgesia

= self-administration of small doses of opioid analgesic by means of computer-controlled IV infusion
Benefit: enhances patient satisfaction, reduction of required total dose
Indication: solid-organ embolization in patients with good neurologic, pulmonary and renal function
Control setting: dose delivered, lock-out interval (= time between doses), background continuous infusion

LOCAL ANESTHESIA

= pharmacologic blocking of pain signal reception by CNS
Administration: topical (cream, ointment, aerosol, lotion, jelly) / infiltrative (subcutaneous injection)
Action: reversible binding to sodium channels → stabilizing nerve membranes
Risk: too large dose / intravascular injection result in Local Anesthetic Systemic Toxicity (LAST)
› early signs: metallic taste sensation, mouth numbness, ringing in ears, light-headedness
› late signs: nervousness, blurred vision, tremor, seizure, cardiovascular collapse

Allergy: to preservative para-aminobenzoic acid used in all local anesthetics

Side effect: pain with infiltration (managed with reassurance, pinching of skin, warming of anesthetic, slow injection, sedation, use of topical anesthetic prior to injection, alkalinization with 8.4% sodium bicarbonate in 1÷10 ratio for lidocaine + 1÷35 ratio for bupivacaine)

(a) amides (more potent + more common)

1. **Lidocaine** (Xylocaine®)
2. **Emla® Cream** (2.5% prilocaine + 2,5% lidocaine) applied with occlusive dressing for ≥ 1 hour before minor dermal procedure

› longer acting

3. **Mepivacaine** (Polocaine®)
4. **Bupivacaine** (Marcaine®, Sensorcaine®)
   Side effect: more cardiotoxic
5. **Ropivacaine** less toxic alternative to bupivacaine

(b) esters

1. **Procaine** (Novocain®)
2. **Chloroprocaine** (Nesacaine®)

Local Anesthetics

Name	*Concentration*	*Max. Dose*	*Max. Volume*	*Onset + Duration*
Procaine	0.25–0.5%	350–600 mg	140–240 mL + 70–120 mL	2–5 min + 15–60 min
Chloroprocaine	1–2%	<800 mg	80–40 mL	6–12 min + 30 min
Lidocaine, plain	1–2%	3–5 mg/kg < 300 mg	30–15 mL	1–2 min + 30–60 min
Lidocaine + epinephrine	1–2% 1÷100,000 or 1÷200,000	5–7 mg/kg < 500 mg	50–25 mL	1–2 min + 60–240 min
Bupivacaine	0.25–0.5%	2.5 mg/kg < 175 mg	70–35 mL	5 min + 120–240 min
Bupivacaine + epinephrine	0.25–0.5% 1÷200,000	< 225 mg	90–45 mL	5 min + 180–360 min
Mepivacaine	1%	< 400 mg	40 mL	3–5 min + 45–90 min

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