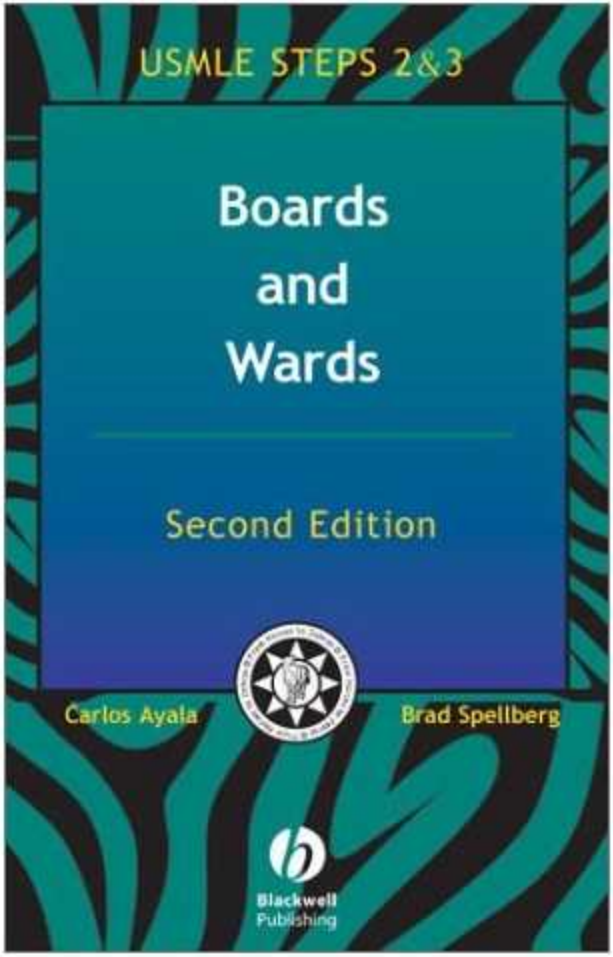
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1 INTERNAL MEDICINE

CARDIOLOGY

HYPERTENSION (HTN)

Definition = BP = 140/90 measured on 3 separate days

CAUSES

1. 95% of all HTN is idiopathic, call "**essential HTN**"
2. Most of 2° HTN causes can be divided into 3 organ systems & drugs

CAUSES OF SECONDARY HYPERTENSION

Cardiovascular	❖ Aortic regurgitation causes **wide pulse pressure** ❖ Aortic coarctation causes HTN in arms with ¯ **BP in legs**
Renal	❖ **Glomerular dz commonly presents with proteinuria** ❖ **Renal artery stenosis causes refractory HTN** in older men (atherosclerosis) or young women (fibromuscular dysplasia) ❖ Polycystic kidneys
Endocrine	❖ Hypersteroidism, typically **Cushing's & Conn's syndromes, which cause HTN with hypokalemia** (↑ aldosterone) ❖ Pheochromocytoma causing episodic autonomic symptoms ❖ Hyperthyroidism causing **isolated systolic HTN**
Drug induced	❖ Oral contraceptives, glucocorticoids, phenylephrine, NSAIDs

MALIGNANT HYPERTENSION

1. Can be hypertensive urgency or emergency
2. Hypertensive urgency
   a. High BP (e.g., systolic > 200 or diastolic >110, but numbers vary depending upon source) **without evidence of end-organ damage**
   b. Tx = oral BP medications with goal of slowly reducing BP over several days
3. Hypertensive emergency

   Defined as severe HTN with evidence of end-organ compromise (e.g., encephalopathy, renal failure, CHF/ischemia)

   Si/Sx = AMS, papilledema, focal neurologic findings, anuria, chest pain, or evidence of CHF (e.g., lower extremity edema, elevated JVP, rales on pulmonary exam)

   This is a medical emergency and immediate therapy is needed

   Tx = IV drip with nitroprusside or nitroglycerin (the latter preferred for ischemia), but **do not lower BP by more than ¾ at first or the patient will stroke out**

HYPERTENSION TREATMENT

Lifestyle modifications first line in pts without comorbid dz

Weight loss, exercise, quitting alcohol & smoking can each significantly lower BP independently—salt restriction may help

↓ fat intake to ↓ risk of coronary artery dz (CAD); HTN is a cofactor

2. Modications

Indications	1. Failure of lifestyle modifications after 6mo to 1yr 2. Immediate use necessary if comorbid organ disease present (e.g., stroke, angina, renal disease) 3. Immediate use in emergent or urgent hypertensive states (e.g., neurologic impairment, ↑ ICP)
First-line drugs	
No comorbid dz	**Diuretic or** b**-blocker** (proven to ↓ mortality)
Diabetes	**ACE inhibitors** (proven to ↓ vascular & renal dz)
↓ ejection fraction	**ACE inhibitors** (proven to ↓ mortality)

Myocardial infarction	b**-blocker & ACE inhibitor** (proven to ↓ mortality)
Osteoporosis	**Thiazide diuretics** (↓ Ca2+ excretion)
Prostatic hypertrophy	a**-blockers** (treat HTN & BPH concurrently)
Contraindications	
β-blockers	**Chronic obstructive pulmonary dz**, due to bronchospasm
β-blockers (relative)	**Diabetes**, due to alteration in insulin/glucose homeostasis & blockade of autonomic response to hypoglycemia
β-blockers	**Hyperkalemia**, due to risk of ↑ serum K levels
ACE inhibitors	**Pregnancy,** due to teratogenicity
ACE inhibitors	**Renal artery stenosis**, due to precipitation of acute renal failure (GFR dependent on angiotensin-mediated constriction of efferent arteriole)
ACE inhibitors	**Renal failure (creatinine >1.5),** due to hyperkalemia morbidity
K+ sparing diuretics	**Renal failure (creatinine >1.5),** due to hyperkalemia morbidity
Diuretics	**Gout**, due to causation of hyperuricemia
Thiazides	**Diabetes,** due to hyperglycemia

ISCHEMIC HEART DISEASE (CORONARY ARTERY DISEASE)

RISK FACTORS FOR CORONARY ARTERY DISEASE

1. **Major risk factors!!!**
    a. Diabetes
    b. Smoking
    c. Hypertension
    d. Hypercholesterolemia (**total cholesterol-HDL ratio >5.0)**
    e. Family history
    f. Age
2. Minor risk factors: obesity, lack of estrogen (males or postmenopausal women not on estrogen replacement), homocystinuria
3. Smoking is the #1 preventable risk factor
4. Diabetes probably imparts the greatest risk of all of them
5. Unlike diabetic microvascular dz (e.g., retinopathy, etc.) **there is no evidence that tight glucose control can diminish onset of CAD**

STABLE ANGINA PECTORIS

Caused by atherosclerotic CAD, supply of blood to heart < demand

Si/Sx = precordial pain radiating to left arm, jaw, back, etc., relieved by rest & nitroglycerin, EKG → **ST depression & T-wave inversion**

Classic Sx often not present in elderly & diabetics (neuropathy)

Dx = clinical, based on Sx, CAD risks, confirm CAD with angiography

ANGINA TREATMENT

Acute	Sublingual NTG ❖ Usually acts in 1-2 min ❖ May be taken up to 3 times q3-5 min intervals ❖ If doesn't relieve pain after 3 doses, pt may be infracting
Chornic prevention	Long-acting nitrates effective in prophylaxis β-blockers ↓ myocardial O2 consumption in stress/exertion Aspirin to prevent platelet aggregation in atherosclerotic plaque Quit smoking (2yrs after quitting, MI risk = nonsmokers) ↓ LDL levels, ↑ HDL with diet (↓ saturated fat intake more important than actual cholesterol intake), ↑ exercise, ↑ fiber intake, stop smoking, lose weight, HMG-CoA reductase inhibitors

	folate lowers homocysteine levels, but there is controversy over role of ↑ homocysteine in MI, so role of folate Tx is unclear
Endovascular intervention	*Percutaneous Transluminal Coronary Angioplasty (PTCA)* Indicated with failure of medical management Morbidity less than surgery but has up to 50% restenosis rate Stent placement reduces restenosis rate to 20-30% Platelet gpIIbIIa antagonists further reduce restenosis rate
Surgery	Procedure is coronary artery bypass graft (CABG) Indications = failure of medical Tx, 3 vessel CAD, or 2 vessel dz in diabetes Comparable mortality rates with PTCA after several years, except in diabetic patients who do better with CABG

UNSTABLE ANGINA (USA)

Sx similar to stable angina but occur more frequently with less exertion and **may occur at rest**

USA is caused by transient clotting of atherosclerotic vessels, clot spontaneously dissolves before infarction occurs

EKG during episode usually shows ST depression or flattening of T wave; if ST segment elevation follows, pt is progressing to infarction

labs = cardiac enzymes (CK-MB, troponins) usually negative

Tx must be aggressive to prevent infarction, hospitalization is indicated

a. Immediate IV heparin, with gpIIbIIa antagonist if labile ST depression on EKG, and aspirin (ASA) to stabilize clotting, pt should continue with ASA after discharge
b. Nitroglycerin increases O2 delivery to myocardium
c. β-blockers decrease myocardial O2 demand
d. Once stabilized, pt should undergo evaluation (e.g., exercise stress testing) for risk stratification, usually followed by medical management, PTCA or CABG

MYOCARDIAL INFARCTION

1. Infarct usually 2^{o} to acute thrombosis in atherosclerotic vessel
2. Si/Sx = crushing substernal pain, as per angina, but not relieved by rest, (+) diaphoresis, N/V, tachycardia or bradycardia, dyspnea
3. Dx
   a. **EKG ® ST elevation & Q waves**
   b. Enzymes: Troponin I or CK-MB—both have similar sensitivities and specificities but CK-MB normalizes at 72hrs after infarction, while Troponin remains elevated for up to 1 week
   c. Appropriate signs & symptoms with risk factors
4. Tx = reestablish vessel patency
   a. Medical Tx = thrombolysis within 6hr of the infarct: by using **TPA + heparin** (first line) or streptokinase
   b. PTCA may be more effective, can open vessels mechanically or with local administration of thrombolytics
   c. CABG is longer-term Tx, rarely used for acute process
5. Adjuvant medical therapies
   a. **#1 priority is aspirin! (proven to ¯ mortality)**
   b. **#2 priority is** b **-blocker (proven to ¯ mortality)**
   c. Statin drugs to lower cholesterol are essential (**LDL must be <100 post-infarct**, proven to ↓ mortality)
   d. Heparin should be given for 48hr post infarct **if tPA was used to lyse the clot** (heparin has no proven benefit if streptokinase was used or if no lysis was performed)
   e. O2 & morphine for pain control
   f. Nitroglycerin to reduce both pre- & afterloads

g. ACE inhibitors are excellent late & long-term therapy, ↓ afterload & prevent remodeling
h. Exercise strengthens hart, develops collateral vessels, ↑ HDL
i. STOP SMOKING!!!!

SELECTED ARRHYTHMIAS

BASIC HEART BLOCKS

Type	**Characteristics**	**Px & Tx**
1^0	❖ **EKG ® PR interval >0.20 secs** ❖ All atrial impulses conducted ❖ May occur in normal individuals due to ↑ vagal tone	Px good, no intervention required
2^o Mobitz type I	Mobitz type I or Wenckebach block **EKG ® PR intervals progressively - from beat to beat** until they become so long the beat is dropped Following the dropped beat, PR interval resets to baseline & begins to progressively lengthen again May also occur in normal people or pts taking drugs (e.g., β-blockers, digoxin, Ca-blockers)	Px good, Tx = stop offending drugs if symptomatic
2^o Mobitz type II	Mobitz type II block **EKG ® PR interval fixed at >0.20 seconds & there is a fixed ratio of dropped beats** Usually due to block with the His bundle system	Px = poor, ↑ risk progression to 3^o Tx = ventricular pacemaker
3^o	Complete heart block **EKG ® absolutely no relationship between P-P intervals & QRS intervals** Si/Sx = dyspnea, syncope, cannon A waves in jugular veins, wide pulse pressure, may b aSx	Tx = permanent ventricular pacemaker

ATRIAL FIBRILLATION (A-fib)

1. Most common chronic arrhythmia
2. Etiologies include ischemia, atrial dilation (often from valve dz), surgery (or any systemic trauma), pulmonary dz, toxicity (e.g., thyrotoxicosis, alcohol intoxication or withdrawal)
3. Pulse is **irregularly irregular, classic descriptor of a-fib**
4. Si/Sx = chest discomfort/palpitations, hypotension/syncope, tachycardia
5. Complications = diffuse embolization, often to brain, of atrial mural thrombi
6. Tx
    a. Rate control with β-blockers, digoxin (not acutely), Ca-blockers (e.g., verapamil & diltiazem)
    b. Convert to normal rhythm (cardioversion) with drugs or electricity
        i. Drug = IV procainamide (first line), sotalol or amiodarone
        ii. Electrical → shocks of 100-200J followed by 360J
        iii. All pts with a-fib lasting >24hr should be anticoagulated with Coumadin for 3wk before electrical cardioversion to prevent embolization during cardioversion
    c. If conversion to sinus rhythm does not work, treat with long-term anticoagulation unless pt has a contraindication—Coumadin is 1^{st} line, aspirin second

MULTIFOCAL ATRIAL TACHYCARDIA (MAT)

1. Multiple concurrent pacemakers in the atria, also an irregularly irregular rhythm, usually found in pts with COPD
2. **EKG ® tachycardia with = 3 distinct P waves present in 1 rhythm strip** (note: if the pt has = 3 distinct P waves but is not tachycardic, rhythm = wandering pacemaker
3. Tx = verapamil also treat underlying condition

SUPRAVENTRICULAR TACHYCARDIA (SVT)

1. SVT is a grab-bag of tachyarrhythmias originating "above the ventricle"
2. Pacer can be in atrium or at AV junction, & multiple pacers can be active at any one time (multifocal atrial tachycardia)
3. It can be very difficult to distinguish ventricular tachycardia from SVT if the pt also has a bundle branch block
4. Tx depends on etiology
    a. Correct electrolyte imbalance, ventricular rate control, digoxin, Ca^{2+}-channel blocker, β-blocker, adenosine & electrical cardioversion in unstable pts
    b. Attempt carotid massage in pts with paroxysmal SVT
    c. Adenosine breaks >90% of SVT, converting it to sinus rhythm, and failure to break a rhythm with adenosine is a potential diagnostic test to rule out SVT

VENTRICULAR TACHYCARDIA (V-TACH)

1. Defined as =3 consecutive premature ventricular contraction (PVCs)
2. Sustained V-tach lasts minimum of 30 sec, requires immediate intervention due to risk of onset of v-fib
3. If hypotension or no pulse is coexistent → defibrillate and treat as V-fib
4. Tx depends on symptomatology
    a. If hypotension or no pulse is coexistent → emergency electrical defibrillation, 200-300-360J
    b. If pt is asymptomatic and not hypotensive, first line medical Tx is amiodarone or lidocaine, which can convert rhythm to normal

VENTRICULAR FIBRILLATION (V-fib)

1. Si/Sx = syncope, severe hypotension, sudden death
2. **Emergent electric countershock is the primary therapy** (very rarely precordial chest thump is effective), converts rhythm 95% of the time (200-300-360J) if done quickly enough
3. Second line Tx is amiodarone or lidocaine
4. Without Tx, natural course = total failure of cardiac output →death

CONGESTIVE HEART FAILURE

ETIOLOGIES & DEFINITION

Causes = valve dz, MI (acute & chronic), HTN, anemia, pulmonary embolism, cardiomyopathy, thyrotoxicosis, endocarditis

Definition = cardiac output insufficient to meet systemic demand, can have right-, left-, or both-sided failure

SIGNS & SYMPTOMS & DIAGNOSIS

Left-sided failure Si/Sx due to ↓ cardiac output & ↑ cardiac pressure = **exertional dyspnea, orthopnea, paroxysmal nocturnal dyspnea**, cardiomegaly, rales, S3 gallop, renal hypoperfusion →↑ aldosterone production → Na retention →↑ total body fluid → worse heart failure

Right-sided failure Si/Sx due to blood pooling "upstream" from R-heart = ↑ jugular venous pressure, dependent edema, hepatic congestion with transaminitis, atrial fibrillation, fatigue, weight loss, cyanosis

Atrial fibrillation common in CHF, ↑ risk of embolization

Dx = echocardiography that reveals ↓ cardiac output

TREATMENT

1. 1st line regimen = ACE inhibitor, β-blocker, diuretics (loop and K-sparing), digoxin
2. If pt intolerant of ACE inhibition, use a combination of hydralazine and isosorbide dinitrate
3. **ACE inhibitors proven to ¯ mortality in CHF**
4. β-blockers
    a. **Proven to ¯ mortality**

   b. However, only metoprolol and carvedilol have been reliably shown to do this, and only carvedilol has been shown to do this in class IV (severe) CHF
   c. Furthermore, β-blockers should NEVER be started while the patient is in active failure, as they can definitely worsen failure
   d. Add the β-blockers once the patient is diuresed to dry weight and on stable doses of other medicines
5. **Spironolactone is proven to ¯ mortality in class IV CHF**, and presumed to also ↓ mortality in milder CHF (but not yet proven to)—mechanism not entirely clear for this
6. Loop diuretics (usually furosemide) are almost always used to maintain dry weight in CHF patients
7. Digoxin does not improve mortality in CHF but does improve symptoms and decrease hospitalizations
8. The combination of hydralazine and isosorbide dinitrate is an excellent 2nd-line therapy for patients intolerant of ACE inhibitors because this combination has AKSI been shown to reduce mortality in CHF, but in head to head trials, the mortality benefit is less than ACE inhibitors.
9. Beware of giving loop diuretics without spironolacotne (a K+-sparing diuretic), because in the presence of hypokalemia, digoxin can become toxic at formerly therapeutic doses—digoxin toxicity presents as **supraventricular tachycardia with AV block and yellow vision**, and can be acutely treated with anti-digitalis Fab antibodies as well as correction of the underlying potassium deficit

CARDIOMYOPATHY

	Dilated	**Hypertrophic**	**Restrictive**
Cause	Ischemic, infectious (HIV, Coxsackie virus, Chagas' disease), metabolic, drugs (alcohol, doxorubicin, AZT)	Genetic myosin disorder	Amyloidosis, scleroderma, hemochromatosis, glycogen storage dz, sarcoidosis
Si/Sx	R & L heart failure, a-fib, S3 gallop, mitral regurgitation **Systolic dz**	Exertional syncope, angina, EKG→LVH **Diastolic dz**	Pulmonary HTN, S4 gallop, EKG→↓QRS voltage **Diastolic dz**
Px	30% survival at 5yr	5% annual mortality usually due to sudden death	30% survival at 5yr
Tx	Stop offending agent, once cardiomyopathy onsets, Tx similar to CHF	β-blockers & Ca blockers Surgical excision of myocardium if Sx severe Dual-chamber pacing with implantable defibrillator	None

VALVULAR DISEASES

MITRAL VALVE PROLAPSE (MVP)

Seen in 7% of population, in vast majority is a benign finding in young people which is aSx & eventually disappears

Murmur: pathologic prolapse ® last systolic murmur with midsystolic click (Barlow's syndrome), predisposing to regurgitation

Dx = clinical, confirm with echocardiography

Tx not required

MITRAL VALVE REGURGITATION (MVR)

1. Seen in severe MVP, rheumatic fever, papillary muscle dysfunction (often 2^o to MI) & endocarditis
2. Results in dilation of left atrium (LA), ↑ in LA pressure, leading to pulmonary edema/dyspnea
3. Dx = clinical, confirm with echocardiography
4. Tx = ACE inhibitors, vasodilators, diuretics, consider surgery in severe dz

MITRAL STENOSIS

1. Almost always due to prior rheumatic fever
2. Decreased flow across the mitral valve leads to left atrial enlargement (LAE) & eventually to right heart failure
3. Si/Sx = dyspnea, orthopnea, hemoptysis, pulmonary edema, a-fib
4. Dx = clinical, confirm with echocardiography
5. Tx
    a. β-blockers to slow HR
    b. Digitalis to slow ventricle in pts with a-fib
    c. Anticoagulants for embolus prophylaxis
    d. Surgical valve replacement for uncontrollable dz
    e. NEVER give (+) inotropic agents for mitral stenosis as are given for other ¯ cardiac output dzs

AORTIC REGURGITATION

1. Seen in endocarditis, rheumatic fever, VS defect (children), congenital bicuspid aorta, 3^o syphilis, aortic dissection, Marfan's syndrome, trauma
2. **There are 3 murmurs in AR**
3. AR has numerous classic signs
    a. Water-Hammer pulse = wide pulse pressure presenting with forceful arterial pulse upswing with rapid fall-off
    b. Traube's sign = pistol-shot bruit over femoral pulse
    c. Corrigan's pulse = unusually large carotid pulsations
    d. Quincke's sign = pulsatile blanching & reddening of fingernails upon light pressure
    e. De Musset's sign = head bobbing caused by carotid pulsations
    f. Muller's sign = pulsatile bobbing of the uvula
    g. Duroziez's sign = to-&-fro murmur over femoral artery heard best with mild pressure applied to the artery
4. Dx = clinical, confirm by echocardiography
5. Tx
    a. ↓ afterload with ACE inhibitors or vasodilators (e.g., hydralazine)
    b. Antibiotic prophylaxis prior to procedures (e.g., dental work)
    c. Consider valve replacement if dz is fulminant or refractory to drugs

AORTIC STENOSIS (AS)

1. Frequently congenital, also seen in rheumatic fever, mild degenerative calcification = aortic sclerosis that is a normal part of aging
2. Obstructive Hypertrophic subaortic stenosis (OHSS)
    a. Also called "Hypertrophic obstructive cardiomyopathy"
    b. Ventricular septum hypertrophies inferior to the valve
    c. Stenosis due to septal wall impinging upon anterior leaflet (rarely posterior leaflet) of mitral valve during systole
3. **Si/Sx = classic triad of syncope, angina, exertional dyspnea**
4. Dx = clinical, confirm by echocardiography
5. Tx is surgery for all symptomatic pts who can tolerate
    a. Either mechanical or bioprosthesis required, pt anticoagulated chronically after surgery

b. Use balloon valvuloplasty of aortic valve for poor surgical candidates
c. Tx with digitalis effective only in mild dz
d. Patients need endocarditis prophylaxis prior to procedures
e. NEVER give AS patients b-blockers or afterload reducers (vasodilators & ACE inhibitors)—peripheral vasculature is maximally constricted to maintain BP, so administration of such agents will cause pt to go into shock.

TRICUSPID & PULMONARY VALVES

Both undergo fibrosis in carcinoid syndrome

Endocarditis prophylaxis required prior to procedures (e.g., dental work)

Tricuspid stenosis → **diastolic rumble easily confused with mitral stenosis, differentiate from MS by - loud with inspiration**

Tricuspid regurgitation → holosystolic murmur, look for jugular & hepatic systolic pulsations

Pulmonary stenosis → dz of children, or in adults with carcinoid syndrome, with midsystolic ejection murmur

Pulmonary regurgitation → develops 2^o to pulmonary HTN, endocarditis, or carcinoid syndrome, due to valve ring widening, **Graham Steell murmur** = diastolic murmur at left sternal border, mimicking AR murmur

Tx for stenosis = balloon valvuloplasty, valve replacement rarely done

ENDOCARITIS

Acute endocarditis is usually caused by *Staphylococcus aureus*

Subacute dz (insidious onset, Sx less severe) usually caused by viridans group, *Streptococcus* (oral flora), *Streptococcus spp.* and *Enterococcus*

marantic endocarditis is due to cancer seeding of heart valves during metastasis, very poor Px, malignant emboli → cerebral infarcts

Culture negative endocarditis is caused by hard-to-culture organisms known as the HACEK group: ***H**aemophilus parainfluenzae, **A**ctinobacillus, **C**ardiobacterium, **E**ikenella, **K**ingela kingai*

SLE cause **Libman-Sack endocarditis**, may be due to autoantibody damage of valves—usually endocarditis is a aSx, but murmur can be heard

Si/Sx = splenomegaly, **splinter hemorrhages** in fingernails, **Osler's nodes** (painful red nodules on digits), **Roth spots** (retinal hemorrhages with clear central areas), **Janeway lesions** (dark macules on palms/soles), conjunctival petechiae, brain/kidney/splenic abscesses → focal neuro findings/hematuria/abdominal or shoulder pain

Dx based upon the Duke Criteria

Major criteria	1. (+) blood cultures (x2) of common organisms 2. (+) echocardiogram or onset of new murmur (transesophageal should be used, as transthoracic only 50-60% sensitive)
Minor criteria	1. Presence of predisposing condition (i.e., valve abnormality) 2. Fever >38^o C 3. Embolic disease (e.g., splenic, renal, hepatic, cerebral) 4. Immunologic phenomena (i.e., Roth spots, Osler's nodes) 5. (+) blood culture x1 or rare organisms cultured

80% specific if 2 major or 1 major +3 minor, or 5 minor criteria are met

Tx = prolonged antibiotics, 4-6wk typically required (new research indicates sometimes 2wk can be sued for certain organisms)

Empiric Tx is often a combination of a β-lactam + aminoglycoside, and therapy is then tailored based upon sensitivities of the organism cultured from blood

Surgery required for severe heart disease or large, expanding abscesses.

RHEUMATIC FEVER/HEART DISEASE

1. Presents usually in 5-15-year-olds after group A Strep infection
2. Dx = Jones criteria (2 major & 1 minor)

3. Major criteria (**mnemonic: JONES**)
    a. Joints (migratory polyarthritis), responds to NSAIDs
    b. Carditis (pancarditis, Carey-Coombs murmur = middiastolic)
    c. Nodules (subcutaneous)
    d. Erythema marginatum (serpiginous skin rash)
    e. Sydenham's chorea (face, tongue, upper-limb chorea)
4. Minor criteria = fever, ↑ ESR, arthralgia, long EKG PR interval
5. In additon to Jones criteria, need evidence of prior strep infection by either culture of (+) antistreptolysin O (ASO) antibody titers
6. Tx = penicillin

PERICARDIAL DISEASE

PERICARDIAL FLUID

Pericardial effusion can result from any disease causing systemic edema

Hemopericardium is blood in the pericardial sac, often 2^o to trauma, metastatic cancer, viral/bacterial infections

Both can lead to cardiac tamponade

Classic Beck's triad: distant heart sounds, distended jugular veins, hypotension

Look for pulsus paradoxus, which is =10mmHg fall in BP during inspiration

EKG shows **electrical alternans,** which is beat-to-beat alternating height of QRS complex

Dx = clinical, confirm with echocardiography

Tx = immediate pericardiocentesis in tamponade, otherwise treat the underlying condition & allow the fluid to resorb

PERICARDITIS

1. Caused by bacterial, viral, or fungal infections, also in generalized serositis 2^o to rheumatoid arthritis (RA), SLE, scleroderma, uremia
2. Si/Sx = retrosternal pain relieved when sitting up, often following URI, not affected by activity or food, listen for pleural friction rub
3. **EKG ® ST elevation in all leads**, also see PR depression
4. Dx = clinical, confirm with echocardiography
5. Tx = NSAIDs for viral, antimicrobial agents for more severe dz, pericardiectomy reserved for recurrent dz

MURM URS

Disease	**Murmur**	**Physical exam**
Mitral stenosis	**Diastolic apical rumble** & opening snap	Feel for RV lift 2^o to RVH
Mitral valve prolapse	**Late systolic murmur with midsystolic click (Barlow's syndrome)**	Valsalva→click earlier in systole, murmur prolonged
Mitral regurgitation	High-pitched **apical blowing holosystolic murmur radiate to axilla**	Laterally displaced PMI< systolic thrill
Tricuspid stenosis	**Diastolic rumble** often confused with MS	**Murmur louder with inspiration**
Tricuspid regurgitation	High-pitched **blowing holosystolic** murmur at left sternal border	**Jugular & hepatic pulsations, murmur louder with inspiration**
Aortic stenosis (AS)	**Midsystolic crescendo-decrescendo murmur at second right interspace, radiates to carotids & apex, with S_4 due to atrial kick**, systolic ejection click	**Pulsus parvus et tardus** = peripheral pulses are weak & late compared to heart sounds, systolic thrill second interspce
Aortic sclerosis	Peaks earlier in systole than AS	None

Aortic regurgitation	**3 murmurs:** **Blowing early diastolic at aorta & LSB** **Austin Flint = apical diastolic rumble** like mitral stenosis but no opening snap Midsystolic flow murmur at base	Laterally displaced PMI, **wide pulse pressure, pulsus bisferiens** (double-peaked arterial pulse)
Hypertrophic subaortic stenosis	Systolic murmur at apex & left sternal border that is poorly transmitted to carotids	**Murmur increases with standing & Valsalva**

Timing	**Possible Disease: Differentiating Characteristics**			
Midsystolic ("Ejection")	**Aortic stenosis/sclerosis**: crescendo-decrescendo, 2nd right interspace	**Pulmonic stenosis**: 2nd left interspace, EKG→RVH	**Any high flow state**→"flow murmur": **aortic regurgitation** (listen for other AR murmurs), **A-S defect** (fixed split S2), **anemia, pregnancy, adolescence**	
Late systolic	**Aortic stenosis**: worse dz→later peak	**Mitral valve prolapse**: apical murmur	**Hypertrophic subaortic stenosis** murmur louder with Valsalva	
Holosystolic	**Mitral regurgitation**: radiates to axilla	**V-S defect**: diffuse across precordium	**Tricuspid regurgitation**: louder with inspiration	
Early diastolic	**Aortic regurgitation**: blowing aortic murmur		**Pulmonic regurgitation**: Graham Steell murmur	
Middiastolic	**Mitral stenosis**: opening snap, no change with inspiration	**Aortic regurgitation** (Austin Flint murmur): apical, resembles MS	**A-S defect**: listen for fixed split S2, diastolic rumble	**Tricuspid stenosis**: louder with inspiration
Continuous	**Patent ductus**: machinery murmur loudest in back	**Mammary soufflé**: harmless, heard in pregnancy due to ↑ flow in mammary artery	**Coarctation of aorta**: upper/lower extremity pulse discrepancy	**A-V fistula**

PULMONARY

HYPOXEMIA

DIFFERENTIAL DIAGNOSIS

Five Mechanisms of Hypoxemia

Cause	**PCO2**	**PA-aO2**	**Effect of O2**	**DLCO**	**Tx**
↓ FIO2	Nml	Nml	+	Nml	O2
Hypoventilation	↑	Nml	+	Nml	O2
Diffusion impairment	Nml	↑	+	↓	O2
V/Q mismatch	↑/Nml	↑	+	Nml	O2
Shunt	↑/Nml	↑	-- (O2 will not correct shunts)	Nml	Reverse cause

PAO2 = FIO2 ($P_{breath} - P_{H2O}$) – (PaCO2/R)
At sea level: FIO2 = .21, P_{H2O} = 47, P_{breath} = 760: **PAO2 = 150 – (PaCO2/R)**
PaCO2 is measured by lab analysis of arterial blood, R = .8

CAUSES

1. Low inspired FIO2 most often caused by high altitude
2. Hypoventilation
    a. Can be due to hypopnea (↓ respiratory rate) or ↓ vital capacity
    b. Hypopnea causes = CNS dz (e.g., narcotics, trauma, infection, etc.)
    c. ↓ vital capacity causes = chest wall neuromuscular dz (e.g., amyotrophic lateral sclerosis, kyphoscoliosis, etc.), airflow obstruction (e.g., sleep apnea), or any parenchymal lung dz
3. Diffusion impairment causes = ↑ diffusion path (fibrosis) or ↓ blood transit time through lung (↑ cardiac output, anemia)
4. V/Q inequality causes = pulmonary embolism, parenchymal lung disease
5. R-L shunt causes = pulmonary edema, pneumonia, atelectasis, atrial & ventricular septal defects, & chronic liver disease

PRESENTATION

1. Symptoms = tachycardia (very sensitive; primary compensation for hypoxia is to increase tissue blood flow), dyspnea/tachypnea, feeling of "inability to breathe enough" (dyspnea) usually precedes increase in breaths per minute
2. Si = crackles & rales present in some pulmonary parenchymal disorders, clubbing/cyanosis (not just in lung dz, but can be correlated to long-term hypoxemic states).

TREATMENT

1. Requires Tx for hypoxemia along with correction of underlying disorder
2. ↑ FIO2 → ↑ PaO2 & ↑ hemoglobin O2 saturation
3. Give O2 by nasal canula (NC), face mask, CPAP, intubation, tracheostomy
    a. General rule, 1L/min O2 ↑ FIO2 by 3% (e.g., giving pt 1L/min O2 → FIO2 = 24%)
    b. Nasal cannula cannot administer >40% FIO2 even if flow rate is >7L/min
    c. Face mask ↑ maximum FIO2 to 50-60%, nonrebreather face mask ↑ maximum FIO2 to >60%
    d. CPAP = tightly-fitting face mask connected to generator that creates continuous positive pressure, can ↑ maximum FIO2 to 80%
    e. Intubation/tracheostomy ↑ maximum FIO2 to 100%
4. **Note that - FIO2 will not improve hypoxemia caused by R-L shunt!** (because alveoli are not ventilated & blood will not come in close contact with O2)
5. Oxygen toxicity seen with FIO2 >50-60% for longer than 28hr, presents with neurologic dz & ARDS-like findings
6. Cannot just rely on O2 supplementation, must also Tx underlying cause
7. High-altitude hypoxemia is self-limiting & stabilizes in weeks to months

CHRONIC OBSTRUCTIVE PULMONARY DISEASE (COPD)

↓ FEV/FVC & Nml/↑ TLC
(Forced expiratory volume at 1min/forced vital capacity & total lung capacity)

Disease	**Characteristics**	**Tx**
Emphysema (Pink puffer)	❖ **Dilation of air spaces with alveolar wall destruction** ❖ **Smoking is by far the most common cause**, α-1-antitrypsin deficiency causes **panacinar** disease ❖ Si/Sx = hypoxia, hyperventilation, barrel chest,	❖ Ambulatory O2 including home O2 ❖ Stop smoking!!! ❖ Bronchodilators ❖ Steroid pulses for

	classic pursed lips breathing, ↓ breath sounds ❖ CXR → loss of lung markings & **lung hyperinflation** ❖ Dx = clinical	acute desaturations
Chronic bronchitis (Blue bloater) (*mucus plugs, inflammation, fibrosis ® narrowing of bronchioles)*	❖ Defined as **expectoration on most days during =3 consecutive months for =2 consecutive years** ❖ Si/Sx = as per emphysema but **hypoxia is more severe**, plus pulmonary hypertension with right ventricular hypertrophy, distended neck veins, hepatomegaly ❖ Dx clinical, confirmed by lung biopsy → ↑ Reid index (gland layer is >50% of total bronchial wall thickness)	As per emphysema, use of antibiotics very controversial
Asthma	❖ Bronchial hyperresponsiveness → **reversible bronchoconstriction** due to smooth mucle contraction ❖ Usually starts in childhood, in which case it often resolves by age 12, can start in adulthood ❖ Acute asthma attacks are the most common cause of pediatric ER visits ❖ Si/Sx = episodic dyspnea & **expiratory wheezing, reversible with bronchodilation** ❖ Dx = =10% ↑ in FEV with bronchodilator therapy ❖ Status asthmaticus (refractory attack lasting for days, can cause death) is a major complication	❖ Albuterol/atrovent inhalers are mainstay ❖ Add inhaled steroids for improved long-term control ❖ Pulse with steroids for acute attacks ❖ Intubate as needed to protect airway
Bronchiectasis (*irreversible dilation, due to bacterial pneumonia*)	❖ Permanent abnormal dilation of bronchioles commonly due to cystic fibrosis, chronic infxn (often tuberculosis, fungal infxn, or lung abscess), or obstruction (e.g., tumor) ❖ Si/Sx = foul breath, purulent sputum, hemoptysis, CXR → **tram-track lung markings**, CT → thickened bronchial walls with dilated airways ❖ Dx = clinical with radiologic support	❖ Ambulatory O2 ❖ Aggressive antibiotic use for frequent infections ❖ Consider lung transplant for long-term cure

RESTRICTIVE LUNG DISEASE

Nml/↑ FEV/FVC & ¯**TLC**

Disease	**Characteristics**	**Tx**
↓ lung tissue	❖ Causes = atelectasis, airway obstruction (tumor, foreign body), surgical excision	❖ Ambulate pt ❖ Incentive spirometer to encourage lung expansion ❖ Remove foreign body/tumor
Parenchymal disease	❖ Causes = inflammatory (e.g., vasculitis & sarcoidosis), idiopathic pulmonary fibrosis, chemotherapy (the **B**'s, **b**usulfan & **b**leomycin), amiodarone, radiation, chronic infection (TB, fungal) & toxic inhalation (e.g., asbestos & silica) ❖ Dx = clinical, biopsy to r/o infxn	❖ Antibiotics for chronic infection ❖ Steroids for vasculitis, sarcoidosis, & toxic inhalations
Interstitial	Chronic injury caused by asbestos, oxygen toxicity, organic	Ambulatory O2

fibrosis	dusts,chonric infection (e.g., TB, fungi, CMV, idiopathic pulmonary fibrosis & collagen-vascular dz) **CXR ® "honeycomb" lung**	Steroids for collagen-vascular dz Add PEEP to reduce FIO2 for O2 toxicity
Extrapulmonary disease	Neuromuscular dz (e.g., multiple sclerosis, kyphoscoliosis, amyotrophic lateral sclerosis, Guillain-Barre, spinal cord trauma) ↑ diaphragm pressure (e.g., pregnancy, obesity, ascites)	Supportive
Pleural effusion	↑ fluid in the pleural space, transudative or exudative Transudate **Low protein content** due to ↓ oncotic pressure Casues = CHF, nephrotic syndrome, hepatic cirrhosis Exudate high protein due to ↑ hydrostatic pressure Causes = malignancy, pneumonia ("parapneumonic effusion"), collagen-vascular dz, pulmonary embolism	Thoracentesis

Effused area: dull/flat on percussion; egophony
Effusion ® do a thoracentesis
Transudate: not enough protein in the blood to hold fluid
Blunting of costophrenic angle
Blurring of posterior diaphragm

LAB ANALYSIS OF PLEURAL EFFUSIONS

Study	**Transudate**	**Exudate**
Effusion protein	=3.0g/dL (=0.5 of serum)	>3.0g/dL (>0.5 of serum)
Effusion LDH	=200IU/L (=0.6 of serum)	>200IU/L (>0.6 of serum)
Specific gravity	=1.015	>1.015
pH	=7.2	<7.2 → parapneumonic effusion
Gram's stain	No organisms	ANY organism → parapneumonic
Cell count	WBC =1000	WBC >1000 (lymphocytes → TB)
Glucose	=50mg/dL	<50mg/dL → infxn, neoplasm, collagen vascular dz (=10 → RA)
Amylase	↑ in pancreatitis, esophageal rupture, malignancy	
RF	Titer > 1:320 → virtually pathognomonic for RA (pH often <7.2)	
ANA	Titer >1:160 → highly indicative for SLE (pH often >7.4)	

PULMONARY VASCULAR DISEASE

PULMONARY EDEMA & ACUTE RESPIRATORY DISTRESS SYNDROME (ARDS)

1. Si/Sx = dyspnea, tachypnea, resistant hypoxia, diffuse alveolar infiltrate
2. Differential for pulmonary edema
    a. **If pulmonary capillary wedge pressure <12 = ARDS**
    b. **If pulmonary capillary wedge pressure >15 = cardiogenic**
3. Tx = O2, diuretics, positive end-expiratory pressure (PEEP) ventilation
4. Purpose of PEEP
    a. Helps prevent airway collapse in a failing lung
    b. ↑ functional residual capacity (maintain lung volume) & ↓ shunting
    c. Expands alveoli for better diffusion

PULMONARY EMBOLISM (PE)

95% of emboli are from leg deep venous thrombi (DVT)

Si/Sx = swollen, painful leg, sudden dyspnea/tachypnea, tachycardia, hemoptysis—**are often no Sx at all, most emboli are clinically silent**

Risk factors = **Virchow's triad = endothelial cell trauma, stasis, hypercoagulable state** (nephrosis, DIC, tumor, postpartum amniotic fluid exposure, antithrombin III deficiency, protein C or S deficiency, factor V Leiden deficiency, oral contraceptives, smoking)

PE can cause lung infarctions

75% occur in lower lobes

Classic CXR findings is "Hampton's hump," a wedge-shaped opacification at distal edges of lung fields

EKG findings

Classically (but rarely) → S wave in I, Q in III, inverted T III

Most common finding is simply sinus tachycardia

Dx = leg Utz to check for DVT, **spiral CT of chest & V/Q scan best to r/o PE**, & pulmonary angiography (gold standard)

Tx = prevention with heparin, IVC filter, or Coumadin, use tPA thrombolysis in massive PE or hemodynamic compromise

PULMONARY HYPERTENSION

1. Defined as pulmonary pressure = ¼ systemic (should be 1/8)
2. Can be active (1^o pulmonary dz) or passive (2^o to heart dz)
   a. 1^o dz includes idiopathic pulmonary HTN (rare, occurs in young women), COPD & interstitial restrictive diseases
   b. 2^o dz seen in any heart disease, **commonly seen in HIV**
3. Si/Sx: loud S_2, tricuspid regurgitation, audible crackles, ↓ breath sounds, pulsatile liver, EKG → right atrial enlargement, CXR → large hilar shadow
4. Dx = clinical, confirm with heart catheterization
5. Tx = home O2 and try prostaglandins

RESPIRATORY TRACT CANCERS

EPIDEMIOLOGY

#1 cause of cancer deaths & second most frequent cancers

Can only be seen on x-rays if >1cm in size, by that time they have usually already metastasized, so **x-rays not a good screening tool**

Si/Sx = cough, hemoptysis, hoarseness (recurrent laryngeal nerve paralysis), weight loss, fatigue, recurrent pneumonia

PARENCHYMAL LUNG CANCERS

1. Diseases & characteristics

Cancer	**Characteristics**
Adenocarcinoma	❖ **Most frequent lung CA in nonsmokers** ❖ **Presents in subpleura & lung periphery** ❖ Presents in preexisting scars, "scar cancer" ❖ Carcinoembryonic antigen (CEA) (+), used to follow Tx, not for screening due to ↓ specificity
Bronchoalveolar carcinoma	❖ Subtype of adenocarcinoma not related to smoking ❖ **Presents in lung periphery** (*spreads along alveolar septa*)
Large cell carcinoma	❖ **Presents in lung periphery** ❖ Highly anaplastic, undifferentiated cancer ❖ Poor prognosis ❖ *Giant-cell; clear-cell*

Squamous cell carcinoma	❖ **Central hilar masses arising from bronchus** ❖ **Strong link to smoking** ❖ *From central airways; keratin pearls*
Bronchogenic carcinoma	❖ **Causes Hypercalcemia due to secretion of PTHrp** (parathyroid hormone related peptide)
Small cell (oat cell) carcinoma	❖ **Usually has central hilar location** ❖ **Often already metastatic at Dx, very poor Px** ❖ **Strong link to smoking (99% are smokers)** ❖ Causes numerous endocrine syndromes o ACTH secretion (cushingoid) o Secretes ADH, causing SIADH
Bronchial carcinoid tumors	❖ Carcinoid syndrome = serotonin (5-HT) secretion ❖ **Si/Sx = recurrent diarrhea, skin flushing, asthmatic wheezing & carcinoid heart dz** ❖ Dx by ↑ 5-HIAA metabolite in urine ❖ Tx = methysergide, a 5-HT antagonist
Lymphagioleiomyomatosis	❖ Neoplasm of lung smooth muscle → cystic obstructions of bronchioles, vessels & lymph ❖ **Almost always seen in menstruating women** ❖ Classic presentation = **pneumothorax** ❖ Tx = progesterone or lung transplant

2. Tx differs from small cell vs. non-small cell lung CA
    a. Small cell → radiation & chemotherapy
    b. Non-small cell CA
        i. Local disease → lung resection +/- radiation
        ii. Metastatic disease → radiation + chemotherapy

OTHER CANCER SYNDROMES

Superior sulcus tumor (Pancoast tumor)

Horner's syndrome (ptosis, miosis, anhydrosis0 by damaging the sympathetic cervical ganglion in the lower neck

Superior vena cava syndrome = obstructed SVC → facial swelling, cyanosis, & dilation of veins of head & neck

Small cell carcinoma can cause a **myasthenia gravis-like condition known as the Lambert-Eaton** syndrome due to induction of Abs to tumor hat cross-reacts with presynaptic Ca channel

Renal cell CA metastatic to lung can cause 2^o polycythemia by ectopic production of erythropoietin

MEDIASTINAL TUMORS

Anterior	**Middle**	**Posterior**
Thymoma	Lymphoma	Neuroblastoma
Thyroid tumor	Pericardial cyst	Schwannoma
Teratoma	Bronchial cyst	Neurofibroma
Terrible lymphoma		
Tx = excision for all, add radiation/chemotherapy as needed		

TUBERCULOSIS

PRIMARY TB

Classically affects lower lobes (bacilli deposited in dependent portion of lung during inspiration)

Usually asymptomatic

Classic radiologic finding is "Ghon Complex" = calcified nodule at primary focus (+) calcified hilar lymph nodes

SECONDARY (REACTIVATION) TB

Reactivates in **apical lung** due to ↑ oxygen tension in upper lobes

Si/Sx = insidious fevers, night sweats, weight loss, cough, hemoptysis, upper lobe infiltration or scarring on CXR

Risk factors = HIV, imprisonment, homelessness, malnourishment

MILIARY (DISSEMINATED) TB

1. Hematogenous **dissemination involving any organ**, often the liver, spleen, bone, kidneys, pericardium, spine, meninges
2. Presents in any patient with immune deficiency
3. Classic syndromes
    a. Pott's dz = TB of spine, presents with multiple compression fractures
    b. Scrofula = TB causing massive cervical lymphadenopathy
    c. Gastroenteritis with profuse diarrhea & colitis

DIAGNOSIS & TREATMENT

1. Latent infection
    a. Latent infection is defined by positive PPD status with no Si/Sx of active disease and no active disease on CXR
    b. PPD test is a **screening test for latent infection**, it is **NOT** a diagnostic test for active tuberculosis
    c. Guidelines for interpretation of PPD
        i. =5mm induration is a positive test for latent infection if the patients:
            1. has HIV
            2. has been in close contact with someone with active TB
            3. has Fibrotic changes on CXR consistent with old TB
            4. is taking immunosuppressive medicine (e.g., >15mg/d of prednisone for >1mo, cyclosporin, etc.)
        ii. =10mm induration is a positive test for a latent infection if the patient:
            1. is a recent immigrant from a high-risk country (most developing countries)
            2. is an injection drug user
            3. works or resides in a prison/jail, nursing home, health care facility (that's you and us!), or a homeless shelter
            4. has a chronic debilitating illness such as renal failure, cancer, or diabetes mellitus
        iii. =15mm induration is a positive test for latent infection if the patient does not meet any of the above categories
    d. Treatment of latent infection (formerly known as "prophylaxis") is isoniazid x9mos (alternate regimens should only be given by specialists)
2. Active infection
    a. To reiterate a point made above: **PPD is not intended as a diagnostic test for active TB**—it is commonly falsely negative in pts with active dz, and a positive test only indicates latent infection, not active disease, thus it is neither sensitive nor specific for active disease
    b. Active infection is diagnosed based on 3 components: clinical assessment, CXR, and sputum (or other body fluid if military disease is considered)
        i. Clinical indicators of active dz include subacute/chronic cough, night sweats, weight loss, hemoptysis, etc.
        ii. CXR indicators of active dz include upper lobe infiltrates or scarring, and cavitary lesions in a patient with symptoms
        iii. Sputum for acid fast staining is the diagnostic study of choice
    c. Treatment
        i. Start regimen with 4 drugs: isoniazid, rifampin, ethambutol, pyrazinamide

ii. Narrow regimen based on sensitivities of culture organism
iii. If culture negative, narrow to 2 drugs at 2 months (isoniazid & rifampin)
iv. Treat for a minimum of 6 months
v. Treatment should be given by specialists in TB care

PNEUMONIA

Organism	Characteristics	Tx
Typical bacterial pneumonia		
Streptococcus pneumonia	Children, elderly, immunosuppressed pts, ↑ frequency in asplenic and AIDS, presents with acute onset cough with shaking rigors, can rapidly progress, #1 cause of CAP (70%)	Ceftriaxone, macrolide, or fluoroquinolones (resistance to all increasing)
Haemophilus	H. influenzae causes 10% CAP, same patients as S. pneumoniae	Ceftriaxone, macrolide, or fluoroquinolones (resistance to all increasing)
Moraxella catarrhalis	Causes 5% CAP, common in COPD & immunosuppressed	Ceftriaxone, macrolide, or fluoroquinolones (resistance to all increasing)
Staphylococcus aureus	2^{o} infects after influenza virus, commonly → pleural effusion	Oxacillin
Gram-negative rods	Often Nosocomial infections	3^{rd} generation cephalosporin or fluoroquinolones
Pseudomonas	Often in cystic fibrosis, commonly Nosocomial, cavitates, rapid antibiotic resistance (use 2 antibiotics!)	3^{rd} generation cephalosporin or fluoroquinolones
Klebsiella	Seen in alcoholics, diabetics, Nosocomial, classically sputum is "currant jelly" bloody red, antibiotic resistant	3^{rd} generation cephalosporin or fluoroquinolones
Anaerobes	Aspiration pneumonia seen in loss of consciousness, dementia, alcoholic → abscess, foul sputum, dz in dependent lung lobes	Metronidazole/clindamycin
Atypical pneumonia		
Mycoplasma pneumonia	Classically young adults (college), causes 10% of CAP, after 2-4wk incubation → tracheobronchitis & nocturnal cough	Doxycycline, macrolide, or quinolones
Legionella pneumophila	Seen in alcoholic, transplant pts, COPD, malignancy, diabetes, water exposure (e.g., air conditioner): 25% lethal with Tx, classic Si/Sx = hyponatremia, CNS changes, LDH >700, diarrhea	Doxycycline, macrolide, or quinolones
Chlamydia pneumoniae	Seen in elderly pts, Sx = sore throat, hoarse voice, sinusitis	Doxycycline, macrolide, or quinolones
Chlamydia psittaci	Contracted from birds (often parrots), bird may show signs of illness also (e.g., ruffled feathers)	Doxycycline, macrolide, or

		quinolones
Coxiella burnetii	Called "Q-fever", contracted from farm animals (e.g., cattle, goats), inhalation or ingestion of milk, etc.	Doxycycline, macrolide, or quinolones
Francisella tularensis	Found in hunters, butchers, etc, classically contracted from rabbits, but other animals & ticks as well	Streptomycin
Actinomyces israelii	50% → empyema, crosses tissue planes (e.g., pericardium, spine), look for sinus tract drainage through anterior chest wall	Penicillin (6-12mos)
Nocardia asteroids	Gram-positive acid fast aerobe, mimics TB, Si/Sx = fever, night sweats, **eosinophilia**, seen in AIDS as opportunistic infection	Bactrim
Fungal pneumonia		
Pneumocystis carinii	Insidious onset of dry cough/dyspnea, bilateral infiltrates, not pleural effusions (very rare), Dx → sputum silver stain, ↑ LDH: AIDS pts with CD4<200 get prophylaxis with Bactrim	Bactrim
Coccidioides immitis	"San Joaquin Valley Fever", major risks = travel to SW desert (e.g., California, Arizona, New Mexico, Texas), imprisonment, ↑ incidence after earthquakes, Filipinos & blacks have ↑ rate disseminated dz, Dx best by sputum cytology → budding yeast	Amphotericin (ampB) or fluconazole (flucon)
Histoplasma	Exposure to Ohio/Mississippi River valleys, bat or bird dung	AmpB/flucon
Aspergillus	Seen in neutropenic pts, CXR → "fungus-ball" with cavitation	AmpB/itracon
Cryptococcus	Seen in AIDS patients or any immunosuppressed	AmpB/flucon
Viral pneumonia		
Influenza	Presents in patients >65yr, can be deadly in them	Amantadine/oseltamivir/zanamivir
Hantavirus	Children/young adults exposed to SW desert rodents, 50% fatal with Tx, 3-6 day prodromal fever & myalgias → acute ARDS	Supportive (intubation)
Other	RSV, adenovirus, Parainfluenza, less severe than influenza	supportive

GASTROENTEROLOGY AND HEPATOLOGY

GASTROESOPHAGEAL DISEASE

CHRONIC (NONEROSIVE) GASTRITIS (ATROPHIC GASTRITIS)

1. Type A (fundal) = autoimmune (pernicious anemia, thyroiditis, etc.)
2. Type B (antral) due to *Helicobacter pylori* (H.p.), NSAIDs, herpes, CMV
3. NSAIDs are #1 cause of chronic gastritis (in antrum, not fundus)
4. Si/Sx = usually aSx, may cause pain, nausea/vomiting, anorexia, upper GI bleeding manifested as coffee grounds emesis or hematemesis
5. Dx = upper endoscopy
6. H.p. infxn Dx by urease breath test, can screen with serum IgG test (less expensive but less sensitive & does not indicate **active** infection), can confirm with endocsopic Bx
7. Tx depends on etiology

a. Tx H.p. gastritis with proton pump inhibitor +2 antibiotics (tetracycline + clarithromycin or metronidazole) + bismuth compound
b. If drug induced, stop offending agent (usually NSAIDs), add sucralfate, H2 blocker, or proton pump inhibitor
c. Pernicious anemia Tx = vitamin B12 replenishment
d. Stress ulcer (especially in ICU setting), Tx with sucralfate or H2 blocker IV infusion

GASTRIC ULCERS (GU)

1. H.p. found in 70% of GU, 10% caused by ulcerating malignancy
2. **As opposed to duodenal ulcers, GUs are NOT caused by acid hypersecretion**—patients with GU have low-to-normal acid secretion, may have ↓ mucosal protection from acid
3. Si/Sx = gnawing/burning pain in midepigastrium, **worse with food intake**, if ulcer erodes into artery can cause hemorrhage & peritonitis, may be guaiac positive
4. Dx = endoscopy with Bx to confirm not malignant, H.p. testing as above
5. Tx = mucosal protectors (e.g., bismuth, sucralfate, misoprostol), H2 blockers or proton pump inhibitors & antibiotics for H.p.

SMALL INTESTINE

DUODENAL ULCER (DU)

1. Almost all DU pts have ↑ acid production, 80% have ↑ nocturnal secretion
2. H.p. found in 90% of duodenal ulcers
3. Smoking & excessive alcohol intake ↑ risk for peptic ulcer
4. Sx/Si = burning or gnawing epigastric pain 1-3hr postprandial, **relieved by food/antacids**, pain typically awakens patient at night, melena
5. Dx = endoscopy, barium swallow if endoscopy unavailable
6. Tx = as for GU above, quit smoking
7. Sequelae
    a. Upper GI bleed
        i. Usually see hematemesis, melena, or (rarely) hematochezia if briskly bleeding ulcer
        ii. Dx with endoscopy
        iii. Tx = Endoscopic coagulation or sclerosant, surgery rarely necessary
    b. Perforation
        i. Change in pain pattern is suspicious for perforation
        ii. Plain abd films may show free air, can perform UGI series with water-soluble contrast (barium contraindicated)
        iii. Tx is emergency surgery

CROHN'S DISEASE (INFLAMMATORY BOWEL DISEASE)

1. A GI inflammatory disease that may be infectious in nature
2. Affects any part of GI from mouth to rectum, but usually the intestines
3. Si/Sx = abdominal pain, diarrhea, malabsorption, fever, stricture causing obstruction, fistulae, see below for extraintestinal manifestations
4. Dx = colonoscopy with biopsy of affected areas → transmural, **noncaseating granulomas, cobblestone mucosal morphology, skip lesions, creeping fat on gross dissection is pathognomonic**
5. Tx
    a. Sulfasalazine (5-ASA), better for colonic dz but also helps in small bowel
    b. Steroids for acute exacerbation, but no effect on underlying dz
    c. Immunotherapy (azathioprine & mercaptopurine)—useful in pts with unresponsive dz
    d. Newest Tx is anti-tumor necrosis factor (TNF) antibody, infliximab

CARCINOID SYNDROME

1. APUDoma (amine precursor uptake & decarboxylate)
2. Occurs most frequently in the appendix
3. Carcinoid results from liver mets that secrete serotonin (5-HT)
4. Si/Sx = flushing, watery diarrhea & abdominal cramps, bronchospasm, right-sided heart valve lesions
5. Dx = ↑ level of urine 5-HIAA (false (+) seen if eat lots of bananas)
6. Tx = somatostatin & methylsergide

LARGE INTESTINE

ULCERATIVE COLITIS (UC) (INFLAMMATORY BOWEL DISEASE)

1. An idiopathic autoinflammatory disorder of the colon
2. Always starts in rectum & spreads proximal
3. If confined to rectum = ulcerative proctitis, a benign subtype
4. Si/Sx = bloody diarrhea, colicky abdominal pain, can progress to generalized peritonitis, watch for toxic megacolon!
5. Dx = colonoscopy with biopsy → crypt abscess with numerous PMNs, friable mucosal patches that bled easily
6. Tx depends on site & severity of dz
    a. Distal colitis → topical mesalamine & corticosteroids
    b. Moderate colitis (above sigmoid) → oral steroids, mesalamine & sulfasalazine
    c. Severe colitis → IV steroids, cyclosporine & surgical resection if unresponsive
    d. Fulminant colitis (rapidly progressive) → broad-spectrum abx
7. comparison of inflammatory bowel disease (IBD)

	Ulcerative colitis	**Crohn's disease**
Location	Isolated to colon	Anywhere in GI tract
Lesions	Contiguously proximal from colon	Skip lesions, disseminated
Inflammation	Limited to mucosa/submucosal	Transmural
Neoplasms	Very high risk fro development	Lower risk for development
Fissures	None	Extend through submucosal
Fistula	None	Frequent: can be enterocutaneous
Granulomas	None	Noncaseating are characteristic
Extraintestinal manifestations	Seen in both: ❖ Arthritis, iritis, erythema nodosum, pyoderma gangrenosum ❖ Sclerosing cholangitis = chronic, fibrosing, inflammation of biliary system leading to cholestasis & portal hypertension	

LIVER

JAUNDICE—VISIBLE WHEN SERUM BILIRUBIN EXCEEDS 2MG/DL

1. Congenital Hyperbilirubinemia

Syndrome	**Characteristics**	**Tx**
Gilbert's	❖ Mild defect of glucuronyl transferase in 5% of population ❖ Si/Sx = ↑ serum **unconjugated bilirubin** → jaundice in stressful situations, completely benign	None required
Crigler-Najjar	❖ Genetic deficiency of glucuronyl transferase → ↑ serum **unconjugated bilirubin** ❖ Type 1 = severe, presents in neonates with markedly ↑ bilirubin levels → death from kernicterus by age 1	Phenobarbitol

	❖ Type 2 = mild, pts suffer no severe clinical deficits	
Dubin-Johnson	❖ ↑ **conjugated bilirubin** due to defective bilirubin excretion ❖ Si/Sx = jaundice, liver turns black, no serious clinical deficits	None required
Rotor	❖ ↑ **conjugated bilirubin** similar to Dubin-Johnson ❖ defect is in bilirubin storage, not excretion	None required

2. Hemolytic Anemias
    a. Excess production → ↑ unconjugated bilirubin
    b. Si/Sx = as per any anemia (weakness, fatigue, etc.), others depend on etiology of hemolytic anemia
    c. Dx = (+) Coombs' test, ↓ haptoglobin, (+) urine hemosiderin
    d. Tx depends on etiology
3. Intrahepatic cholestasis (hepatocellular)
    a. May be due to viral hepatitis or cirrhosis
    b. May be due to drug-induced hepatitis (acetaminophen, methotrexate, oral contraceptives, phenothiazines, INH, fluconazole)
    c. Dx = ↑ transaminases, liver biopsy to confirm hepatitis
    d. Tx = cessation of drugs, or supportive for viral infection
4. Extrahepatic
    a. Myriad causes include choledocholithiasis (but not Cholelithiasis), Ca of biliary system or pancreas, cholangitis, biliary cirrhosis
    b. Primary biliary cirrhosis
        i. An autoimmune disorder usually seen in women
        ii. Si/Sx = jaundice, pruritus, hypercholesterolemia, **antimitochondrial antibody test is 90% sensitive**
        iii. Dx = clinical (+) serology, confirm with biopsy
        iv. Tx = liver transplant, otherwise supportive
    c. Secondary biliary cirrhosis results from long-standing biliary obstruction due to any cause (e.g., cholangitis)
    d. Si/Sx of acquired jaundice = acholic stools (pale), urinary bilirubin, fat malabsorption, pruritus, ↑ serum cholesterol, xanthomas
    e. Dx may required abdominal CT or Endoscopic retrograde cholangiopancreaticoduodenoscopy (ERCP) to rule out malignancy or obstruction of bile pathway
    f. Tx depends on etiology

HEPATITIS

1. General Si/Sx = jaundice, abdominal pain, diarrhea, malaise, fever, ↑ AST & ALT
2. Hepatitis diagnosis and treatment

Type	**Characteristics**	**Tx**
Fulminant	❖ Complication of acute hepatitis, progresses over <4wk ❖ Can be 2^o to viral hepatitis, drugs (INH), toxins & some metabolic disorders like Wilson's dz ❖ Elevated Pt & hepatic encephalopathy	Urgent liver transplant
Viral	❖ Hepatitis A → fecal-oral transmission, transient influenza-like illness ❖ Hepatitis B & C → blood transmission, B also sex & vertical → chronic hepatitis ❖ 5-10% of HBV & >50% of HCV infx → chronic ❖ Dx = serologies & ↑ ALT & AST-ratio = 1:1	Interferon-α +/- lamivudine for HBV Interferon-α +/- Ribavirin for HCV Both ↓ risk of chronic infxn

	○ HBV surface antigen = active infection ○ Anti-HBV surface antibody = immunity ○ Anti-HBV core antibody = immunity ○ HBV e antigen = highly infectious ○ HCV antibody = exposure, not immune	
Granulomatous	❖ Causes = TB, fungal (e.g., *Coccidioides, Candida, Aspergillus*), sarcoidosis, brucella, rickettsial, syphilis, leptospirosis ❖ Dx = liver biopsy	Antibiotics, prednisone for sarcoidosis
Alcoholic	❖ Most common form of liver disease in US ❖ Si/Sx = as per other hepatitis with specific alcohol signs = palmar erythema Dupuyten's contractures, spider angiomas, gynecomastia ❖ Dx = clinical, ↑ AST & ALT, with AST:ALT = 2:1 is highly suggestive	Cessation of alcohol can reverse dz if early in course otherwise → cirrhosis & only Tx is transplant
Autoimmune	❖ Type 1 occurs in young women, (+) ANA, (+) anti-smooth muscle Ab ❖ Type 2 occurs mostly in children, linked to Mediterranean ancestry, (+) anti-liver-kidney=muscle (anti-LKM) antibody ❖ Si/Sx as for any other hepatitis	Tx=prednisone +/- azathioprine

CIRRHOSIS

1. Most commonly due to alcoholism, also to chronic viral hepatitis
2. Si/Sx = purpura & bleeding & ↑ PT/PTT, jaundice, ascites 2^{o} to ↓ albumin & portal hypertension, spontaneous bacterial peritonitis, encephalopathy, asterixis
3. Ascites differential diagnosis

	Portal Hypertension	**No Portal Hypertension**
Serum/ascites albumin gradient	>1.1g/dL	<1.1g/dL
Causes	Cirrhosis, alcoholic hepatitis, Budd-Chiari, CHF	Pancreatic dz, nephrosis, TB, peritoneal mets, idiopathic
Other labs	Ascites total protein >2.5 → heart dz Ascites total protein =2.5 → liver dz	Amylase ↑ in pancreatic dz

   a. Spontaneous bacterial peritonitis
      i. Usually low protein ascites with no Sx of infxn
      ii. Dx = ascitic fluid with absolute neutrophil count of > 250 or (+) Gram's stain/culture of ascitic fluid
      iii. Common organisms include E. coli, Klebsiella, Enterococcus & S. pneumoniae
      iv. Tx = ceftriaxone or cefotaxime, plus IV albumin to maintain renal perfusion pressure
   b. Encephalopathy
      i. Due to ↑ levels of toxins, likely related to ammonia, but ammonia levels do not correlate well with encephalopathy
      ii. Characterized by asterixis (flapping tremor of the wrist upon flexion) & altered mental status
      iii. Tx of encephalopathy is to lower ammonia levels
         1. Lactulose metabolized by bacteria, acidifies the bowel, $NH_3 \rightarrow NH_4+$, which cannot be absorbed
         2. Neomycin kills bacteria making NH_3 in gut

c. Alcohol withdrawal has 4 phases—any given pt can go through any of these phases but does not have to go through all of them, and the phases occurring during a prior withdrawal episode are predictive for what will happen the next time withdrawal occurs
    i. Tremor—occurs within hours of last drink, so it's the 1st sign of withdrawal
    ii. Seizure—occurs at several hours to about 48 hours after the last drink, these can be fatal and are best treated with benzodiazepines, not standard anti-seizure medicines
    iii. Hallucinosis—occurs at 48-72 hours after the last drink, this is NOT delirium tremens (DTs), but rather is simply auditory or tactile hallucinations, also best treated with benzodiazepines
    iv. Delirium tremens—at about 72 hours after the last drink the autonomic instability that defines DTs begins with dangerous tachycardia and hypertension, and can be accompanied by each of the other 3 phases (tremor, seizure, hallucinosis)—the autonomic instability is also best treated with benzodiazepines
d. Treatment of inpatient alcoholics
    i. IV thiamine & B_{12} supplements to correct deficiency (very common), also most **give thiamine before IV glucose or will precipitate Wernicke's encephalopathy**
    ii. Give IV glucose, fluids & electrolytes
    iii. Correct any underlying coagulopathy
    iv. Benzodiazepine for prevention & Tx of delirium tremens

HEPATIC ABSCESS

Caused by (in order of frequency in US) bacteria, parasites (usually amebic) or fungal

Bacterial abscesses usually result from direct extension of infection from gallbladder, hematogenous spread via the portal vein from appendicitis of diverticulitis, or via the hepatic artery from distant sources such as from a pneumonia or bacterial endocarditis

Organisms in pyogenic hepatic abscesses are usually of enteric origin (e.g., E. coli, K. pneumoniae, Bacteroides & Enterococcus)

Si/Sx = high fever, malaise, rigors, jaundice, epigastric or RUQ pain & referred pain to the right shoulder

Labs → leukocytosis, anemia, ↑ alkaline phosphatase

Dx = Utz or CT scan

Tx

IV ampicillin/metronidazole

Percutaneous or surgical drainage

For amebic abscesses (caused by Entamoeba histolytica) use metronidazole

Complications = intrahepatic spread of infxn, sepsis & abscess rupture

Mortality of hepatic abscesses is 15%, higher with coexistent malignancy

PORTAL HYPERTENSION

1. Defined as portal vein pressure >12mmHg (normal = 6-8mmHg)
2. Si/Sx = ascites, hepatosplenomegaly, variceal bleeding, encephalopathy
3. Can be presinusoidal, intrahepatic, or postsinusoidal in nature
4. Causes of portal hypertension

Prehepatic	**Intrahepatic**	**Posthepatic**
❖ Portal vein thrombosis ❖ Splenomegaly ❖ Arteriovenous fistula	❖ Cirrhosis ❖ Schistosomiasis ❖ Massive fatty change ❖ Nodular regenerative hyperplasia ❖ Idiopathic portal hypertension	❖ Severe right-sided heart failure ❖ Hepatic vein thrombois (Budd-Chiari syndrome) ❖ Constrictive pericarditis ❖ Hepatic veno-occlusive

	❖ Granulomatous dz (e.g., tuberculosis, sarcoidosis)	disease

5. Dx = endoscopy & angiography (variceal bleeding)
6. Tx
    a. Acute variceal bleeding controlled by sclerotherapy
    b. If continued bleeding, use Sengstaken-Blakemore tube to tamponade bleeding
    c. Pharmacotherapy = IV infusion of vasopressin or Octeotide
    d. Long term → propranolol once varices are identified (↓ bleeding risk but effect on long-term survival is variable)
    e. Decompressive shunts—most efficacious way of stopping bleeding
    f. Indication for liver transplant is end-stage liver disease, not variceal bleeding
7. **Budd-Chiari syndrome**
    a. Rarely congenital, usually acquired thrombosis occluding hepatic vein or hepatic stretch of inferior vena cava
    b. Associated with hypercoagulability (e.g., polycythemia vera, hepatocellular or other CA, pregnancy, etc.)
    c. Sx = acute onset of abdominal pain, jaundice, ascites
    d. Hepatitis quickly develops, leading to cirrhosis & portal hypertension
    e. Dx = right upper quadrant ultrasound
    f. Tx = clot lysis or hepatic transplant
    g. Px poor, less than 1/3 pts survive at 1yr
8. Veno-occlusive disease (VOD)
    a. Occlusion of hepatic venules (not large veins)
    b. A/w graft vs. host disease, chemotherapy & radiation therapy
    c. Px = 50% mortality at 1yr
    d. Tx = hepatic transplants, sometimes is self-limiting

NEPHROLOGY

RENAL TUBULAR AND INTERSTITIAL DISORDERS

DRUG-INDUCED INTERSTITIAL NEPHRITIS

1. Penicillin, sulfonamides, diuretics & NSAIDs cause hypersensitivity
2. Si/Sx = pyuria, maculopapular rash, eosinophilia, proteinuria, hematuria, oliguria, flank pain, fever, eosinophiluria—**eosinophiluria is rare, but is pathognomonic for hypersensitivity TIN or atheroembolic dz**
3. Dx = clinical, improvement following withdrawal of offending drug can help confirm Dx, but sometimes the dz can be irreversible
4. Tx = removal of underlying cause, consider corticosteroids for allergic dz

ACUTE RENAL FAILURE (ARF)

1. Rapid ↑ azotemia (↑ creatinine & BUN), +/- oliguria (=<500mL/day urine)
2. Causes = 1) prerenal (hypoperfusion), 2) postrenal (obstruction), 3) renal
3. Prerenal failure caused by volume depletion, heart failure, liver failure, sepsis, heat-stroke (myoglobinuria), burns & bilateral renal artery stenosis
4. Postrenal ARF due to obstruction 2^{o} to BPH, bladder/pelvic tumors, calculi
5. Intrinsic renal causes = acute tubular necrosis (most common), others include nephrotoxin exposure & renal ischemia
6. Si/Sx = hyperkalemia → arrhythmias, oliguria, metabolic acidosis
7. Dx
    a. Urinary eosinophils suggest allergic nephriti or atheroembolic dz
    b. **RBC casts virtually pathognomonic for glomerulonephritis**

Test/Index	Prerenal	Postrenal	Renal
Urine osmolality	>500	<350	<350
Urine Na	<20	>40	>20
FE_{Na}	<1%	>4%	>2%
BUN/Creatinine	>20	>15	<15

8. Tx
    a. IV fluids to maintain urine output, diurese to prevent volume overload
    b. Closely monitor electrolyte abnormalities
    c. Indications for dialysis: recalcitrant volume overload status, critical electrolyte abnormalities, unresponsive metabolic acidosis, toxic ingestion, uremia

ACUTE TUBULAR NECROSIS (ATN)

Most common cause of ARF, falls into the intrinsic renal category

ATN causes = renal ischemia 2^o to sepsis, trauma, hemorrhage, crush injury or rhabdomyolysis → myoglobinuria, direct toxins (e.g., amphotericin, aminoglycosides, radiocontrast dyes)

3 phases of injury: 1) prodromal, 2) oliguric, 3) postoliguric

Tx = resolution of precipitating cause, IV fluids to maintain urinary output, monitor electrolytes, diruese as needed to prevent fluid overload

RENAL TUBULE FUNCTIONAL DISORDERS

1. Renal tubular acidosis (RTA)

Type	Characteristic	Urinary pH
Type I	**Distal tubular defect** of urinary H^+ gradient	**Urine pH > 5.5**
Type I	**Proximal tubule failure** to resorb HCO_3	Urine pH >5.5 early, then → <5.5 as acidosis worsens
Type IV	¯ **aldosterone** → hyperkalemia & hyperchloremia Usually due to ↓ secretion (**hyporeninemic hypoaldosteronism**), seen in diabetes, interstitial nephritis, NSAID use, ACE inhibitors & heparin Also due to aldosterone resistance, seen in urinary obstruction & sickle cell dz	**Urine pH <5.5**

2. Diabetes insipidus (DI)
    a. ↓ ADH secretion (central) or ADH resistance (nephrogenic)
    b. Si/Sx = polyuria, polydipsia, nocturia, urine specific gravity <1.010, urine osmolality (U_{osm}) =200, serum osmolality (S_{osm}) =200
    c. Central DI
        i. 1^o (idiopathic) or 2^o (acquired via trauma, infarction, granulomatous infiltration, fungal or TB infection of pituitary)
        ii. Tx = DDAVP (ADH analogue) nasal spray
    d. Nephrogenic DI
        i. 1^o dz is X-linked, seen in infants, may regress with time
        ii. 2^o dz in sickle cell, pyelonephritis, nephrosis, amyloid, multiple myeloma, drugs (aminoglycoside, lithium, demeclocycline)
        iii. Tx = ↑ water intake, sodium restriction
    e. **Dx = water deprivation test**
        i. Hold all water, administer vasopressin
        ii. Central DI: U_{osm} after deprivation no greater than S_{osm} but ↑ =10% after vasopressin given
        iii. Nephrogenic DI: U_{osm} after deprivation no greater than S_{osm} & vasopressin does not ↑ U_{osm}

3. Syndrome of inappropriate antidiuretic hormone (SIADH)
    a. Etiologies
        i. CNS dz: trauma, tumor, Guillain-Barre, hydrocephalus
        ii. Pulmonary dz: pneumonia, tumor, abscess, COPD
        iii. Endocrine dz: hypothyroidism, Conn's syndrome
        iv. Drugs: NSAIDs, antidepressants, chemotherapy, diuretics, phenothiazine, oral hypoglycemis
    b. Dx = hyponatremia with U_{osm} >300mmol/kg
    c. Tx = usually self-limiting, otherwise give normal saline, demeclocycline for resistant cases—**beware of central pontine myelinolysis with rapid correction of hyponatremia**

CHRONIC RENAL FAILURE

1. Always a/w azotemia of renal origin
2. Uremia = biochemical & clinical syndrome of the following characteristics
    a. Azotemia
    b. Acidosis due to accumulation of sulfates, phosphates, organic acids
    c. Hyperkalemia due to inability to excrete K^+ in urine
    d. Fluid volume disorder (early cant' concentrate urine, late can't dilute)
    e. Hypocalcemia due to lack of vitamin D production
    f. Anemia due to lack of EPO production
    g. Hypertension 2^o to activated renin-angiotensin axis
3. Si/Sx = anorexia, nausea/vomit, dementia, convulsions, eventually coma, bleeding due to platelet dysfunction, fibrinous pericarditis
4. Dx = renal Utz → small kidneys in chronic dz, anemia from chronic lack of EPO, diffuse osteopenia
5. Tx = salt & water restriction, diuresis to prevent fluid overload, dialysis to correct acid-base or severe electrolyte disorders

GLOMERULAR DISEASES

NEPHROTIC SYNDROME

1. Si/Sx = proteinuria >3.5g/day, generalized edema (anasarca), lipiduria with hyperlipidemia, marked ↓ albumin, hypercoagulation
2. Dx of type made by renal biopsy
3. General Tx = protein restriction, salt restriction & diuretic therapy for edema, HMG-CoA reductase inhibitor for hyperlipidemia

Disease	**Characteristics**
Minimal change disease (MCD)	❖ Classically seen in young children ❖ Tx = prednisone, disease is very responsive, Px is excellent
Focal segmental glomerulosclerosis	❖ Clinically similar to MCD, but occurs in adults with refractory HTN ❖ Usually idiopathic, but heroin, HIV, diabetes, sickle cell are associated ❖ Idiopathic typically presents in young, hypertensive black males ❖ Tx = prednisone + cyclophosphamide, dz is refractory, Px poor
Membranous glomerulonephritis	❖ Most common primary cause of nephrotic syndrome in adults ❖ Slowly progressive disorder with ↓ response to steroid treatment seen ❖ Causes of this disease are numerous o Infections include HBC, HCV, syphilis, malaria o Drugs include gold salts, penicillamine (note, both used in RA) o SLE (10% of pts develop) o Occult malignancy ❖ Tx = prednisone +/- cyclophosphamide, 50% → ESRD

Membranoproliferative glomerulonephritis	❖ Disease as 2 forms o Type I often slowly progressive o Type II more aggressive, often have an autoantibody against C3 convertase "C3 nephritic factor" → ↓ serum levels of C3 ❖ Tx = prednisone +/- plasmapheresis or interferon-α, Px very poor

Systemic Glomerulonephropathies

Disease	**Characteristic Nephropathy**
Diabetes	Most common cause of ESRD in US Early manifestation is microalbuminuria ACE inhibitors ↓ progression to renal failure if started early Strict glycemic & hypertensive control also ↓ progression Biopsy shows pathognomonic Kimmelstiel-Wilson nodules As dz progresses only Tx is renal transplant
HIV	Usually seen in HIV acquired by intravenous drug abuse Presents with focal segmental glomerulonephritis Early Tx with antiretrovirals may help kidney disease
Renal amyloidosis	Dx → birefringence with Congo Red stain Tx = transplant, dz is refractory & often recurrent
Lupus	
Type I	No renal involvement
Type II	**Mesangial disease** with focal segmental glomerular pattern Tx not typically required for kidney involvement
Type III	**Focal proliferative disease** Tx = aggressive prednisone +/- cyclophosphamide
Type IV	**Diffuse proliferative disease**, the most severe form of lupus nephropathy Presents with a combination of nephrotic/nephritic disease Classic LM → wire-loop abnormality Tx = prednisone + cyclophosphamide, transplant may be required
Type V	**Membranous disease**, indistinguishable from other 1^o membranous GNs Tx = consider prednisone, may not be required

NEPHRITIC SYNDROME

1. Results from diffuse glomerular inflammation
2. Si/Sx = acute onset hematuria (smoky-brown urine), ↓ GFR resulting in azotemia (↑ BUN & creatinine), oliguria, hypertension & edema

Disease	**Characteristics**
Poststreptococcal (postinfecitous) glomerulonephritis (PSGN/PIGN)	❖ Prototype of nephritic syndrome (acute glomerulonephritis) ❖ Classically follows infection with group A β-hemolytic streptococci (S. pyogenes), but can follow infxn by virtually any organism, viral or bacterial ❖ Lab → urine red cells & casts, azotemia, ↓ serum C3, ↑ ASO titer ❖ **Immunofluorescence ® coarse granular IgG or C3 deposits** ❖ Tx typically not needed, dz usually self-limiting
Crescentic (rapidly progressive) glomerulonephritis	❖ Nephritis progresses to renal failure within weeks or months ❖ May be part of PIGN or other systemic diseases ❖ Goodpasture's disease o **Disease causes glomerulonephritis with pneumonitis** o **90% pts present with hemoptysis**, only later get glomerulonephritis o Peak incidence in men in mid-20s

	o **Classic immunofluorescence ® smooth, linear deposition of IgG** ❖ Tx = prednisone & plasmapheresis, minority → ESRD
Berger's disease (IgA nephropathy)	❖ **Most common worldwide nephropathy** ❖ Due to IgA deposition in the mesangium ❖ Si/Sx = recurrent hematuria with low-grade proteinuria ❖ Whereas PIGN presents weeks after infection, **Berger's presents concurrently or within several days of infection** ❖ 25% of pts slowly progress to renal failure, otherwise harmless ❖ Tx = prednisone for acute flares, will not halt dz progression
Henoch-Schonlein purpura (HSP)	❖ Also an IgA nephropathy, but almost always presents in children ❖ Presents with abdominal pain, vomiting, hematuria, & GI bleeding ❖ **Classic physical finding = "palpable purpura" on buttocks & legs in kids** ❖ Often follows respiratory infection ❖ Tx not required, dz is self-limiting
Multiple myeloma	❖ ↑ production of light chains → tubular plugging by Bence-Jones proteins ❖ 2^o Hypercalcemia also contributes to development of "myeloma kidney" ❖ Myeloma cells can directly invade kidney parenchyma ❖ Defect in normal antibody production leaves pt susceptible to chronic infection by encapsulated bacteria (e.g., E. coli) → chronic renal failure ❖ Tx is directed at underlying myeloma

Urinalysis in Primary Glomerular Diseases

	Nephrotic syndrome	**Nephritic syndrome**	**Chronic disease**
Proteinuria	↑↑↑↑	+/-	+/-
Hematuria	+/-	↑↑↑↑	+/-
Cells	----	**(+) RBCs (+) WBCs**	+/-
Casts	**Fatty casts**	**RBC & granular casts**	**Waxy & pigmented granular casts**
Lipids	Free fat droplets, oval fat bodies	----	-----

RENAL ARTERY STENOSIS (RAS)

PRESENTATION

Classic dyad = sudden hypertension with low K^+ (pt not on diuretic)

Causes are atherosclerotic plaques & fibromuscular dysplasia

Screening Dx = oral captopril induces ↑ renin

Dx confirmed with angiography

Tx = surgery vs. angioplasty

URINARY TRACT OBSTRUCTION

GENERAL CHARACTERISTICS

1. Most common causes in children are congenital
2. Most common causes in adults are BPH & stones
3. Obstruction → urinary stasis → ↑ risk of UTI

NEPHROLITHIASIS

1. Calcium pyrophosphate stones
    a. 80-85% stones are **radiopaque**, a/w hypercalciuria

   b. Hypercalciuria can be idiopathic or due to ↑ intestinal calcium absorption, ↑1° renal calcium excretion, or Hypercalcemia
   c. **50% a/w idiopathic hypercalciuria**
   d. Tx = vigorous hydration, loop diuretics if necessary
2. Ammonium magnesium phosphate stones ("struvite stones")
   a. 2nd most common form of stones, are **radiopaque**
   b. Most often due to urease (+) Proteus or Staph. saprophyticus
   c. Can form large staghorn or struvite calculi
   d. Tx = directed at underlying infection
3. Uric acid stones
   a. 50% of pts with stones have hyperuricemia
   b. 2° to gout or ↑ cell turnover (leukemia, myeloproliferative dz)
   c. Stones are **radiolucent**
   d. Tx = alkalinize urine, treat underlying disorder
4. Si/Sx of stones = urinary colic = sharp, 10/10 pain, often described as the worst pain in the pt's life, radiates from back → anterior pelvis/groin
5. Tx = vigorous hydration, loop diuretics as needed

TUMORS OF THE KIDNEY

RENAL CELL CARCINOMA

Most common renal malignancy, occurs in male smokers aged 50-70
Hematogenously disseminates by invading renal veins or the vena cava
Si/Sx = hematuria, palpable mass, flank pain, fever, 2° polycythemia
Tx = resection, systemic interleukin-2 immunotherapy, poor Px

WILMS' TUMOR

1. Most common renal malignancy of childhood, incidence peaks at 2-4yr
2. Si/Sx = palpable flank mass (often huge)
3. Can be part of **WAGR** complex = **W**ilms' tumor, **A**niridia, **G**enitourinary malformations, mental motor **R**etardation
4. **Also a/w hemihypertrophy of the body**
5. Tx = nephrectomy plus chemotherapy &/or radiation

ENDOCRINOLOGY

THE HYPOTHALAMIC PITUITARY AXIS

PROLACTINOMA

Si/Sx = headache, diplopia, CN III palsy, impotence, amenorrhea, gynecomastia, galactorrhea, ↑ androgens in females → virilization
50% cause hypopituitarism, caused by mass effect of the tumor
Dx = MRI/CT confirmation of tumor
Tx
   First-line = dopamine agonist (e.g., bromocriptine)
   Large tumors or refractory → transsphenoidal surgical resection
   Radiation therapy for nonresectable macroadenomas

ACROMEGALY

1. Almost always due to pituitary adenoma secreting growth hormone
2. Childhood secretion prior to skeletal epiphyseal closure → gigantism
3. If secretion begins after epiphyseal closure → acromegaly
4. Si/Sx = adult whose glove, ring, or shoe size acutely ↑, coarsening of skin/facial features, prognathism, voice deepening, joint erosions, peripheral neuropathies due to nerve compression

5. Dx = ↑ insulin-like growth factor 1 &/or MRI/CT confirmation of neoplasm
6. Tx = surgery or radiation to ablate the enlarged pituitary, octreotide (somatostatin analogue) second line for refractory tumors

DIABETES

TYPE I DIABETES

1. Autoinflammatory destruction of pancreas → insulin deficiency
2. Si/Sx = polyphagia, polydipsia, polyuria, weight loss in child or adolescent, can lead to diabetic ketoacidosis (DKA) when pt is stressed (e.g., infection)
3. Dx = see type II below for criteria
4. Tx = **insulin replacement required—oral hypoglycemics will not work!**
5. Complication of type I diabetes = diabetic ketoacidosis (DKA)
6. Sx/Si of DKA = **Kussmaul hyperpnea** (slow & deep breaths), **abdominal pain, dehydration, (+) anion gap**, urine/blood ketones, hyperkalemia, hyperglycemia, Mucor sinusitis = rapidly fatal fungal infxn seen in DKA
7. DKA Tx
    a. **1^{o} Tx = FLUIDS!!!**
    b. **2^{o} = K^{+} & insulin**
    c. **3^{o} = add glucose to insulin drip if pt becomes normoglycemic**—insulin is given to shut down ketogenesis, NOT to ↓ glucose, so insulin must be given until ketones are gone despite normal glucose!

TYPE II DIABETES

1. Peripheral insulin resistance—a metabolic dz, not autoinflammatory!
2. usually adult onset, not ketosis prone, often strong FHx
3. Si/Sx
    a. Acute = dehydration, polydipsia/-phagia/-uria, fatigue, weight loss
    b. Subacute = infections (yeast vaginitis, Mucor, S. aureus boils)
    c. Chronic
        i. Macrovascular = stroke, coronary artery disease
        ii. Microvascular = retinitis, nephritis
        iii. Neuropathy = ↓ sensation, paresthesias, glove-in-hand burning pain, autonomic insufficiency
4. Dx of any diabetes (type I or II)
    a. Random plasma glucose over 200 with symptoms or
    b. Fasting glucose over 125 twice or
    c. 2-hr oral glucose tolerance test glucose >200 with or without Sx
5. Tx
    a. Oral hpoglycemics first line for mild to moderate hyperglycemia
        i. Metformin is first line, unknown mechanism, watch of GI upset and lactic acidosis
        ii. Sulfonylureas (e.g., glyburide, glipizide), ↑ β-cell insulin secretion
        iii. Thiazolidinediones (e.g., pioglitazone & rosiglitazone) increases tissue sensitivity to insulin
    b. Dz refractory to oral hypoglycemics requires insulin
    c. Diet & nutrition education
    d. ACE inhibitors slow progression of nephropathy
6. Monitorin: glycosylated hemoglobin $A1_c$ ($HgA1_c$)
    a. Because of serum half-life of hemoglobin, $HgA1_c$ is a marker of the prior 3mo of therapeutic regimen

b. **Tight glucose control has been shown to reduce complications & mortality in IDDM & NIDDM**, thus $HgA1_c$ is a crucial key tool to follow efficacy & compliance of diabetic Tx regimens
c. $HgA1_c$ of <8 is recommended

7. Complication = hyperosmolar hyperglycemic nonketotic coma (HHNK)
   a. 2^o to hypovolemia, precipitated by acute stress (e.g., infxn, trauma)
   b. Glucose often >1000mg/dL, no acidosis , (+) renal failure & confusion
   c. Tx = rehydrate (may require 10L), mortality approaches 50%

ADRENAL DISORDERS

CUSHING'S SYNDROME

1. Usually iatrogenic (cortisol Tx) or due to pituitary adenoma = Cushing's disease, rarely due to adrenal hyperplasia, ectopic ACTH/CRH production
2. Si/Sx = **buffalo hump, truncal obesity, moon facies, striae**, hirsutism, hyperglycemia, hypertension, purpura, amenorrhea, impotence, acne
3. Dx = 24 hr urine cortisol & high dose dexamethasone suppression test
4. Tx
   a. Excision of tumor with postop glucocorticoid replacement
   b. Mitotane (adrenolytic), ketoconazole (inhibits P450), metyrapone (blocks adrenal enzyme synthesis), or aminoglutethimide (inhibits P450) for nonexcisable tumors

ADRENAL INSUFFICIENCY

1. Can be 1^o (Addison's disease) or 2^o ($\downarrow$ ACTH production by pituitary)
2. Addison's disease
   a. Causes = autoimmune (most common), granulomatous disease, infarction, HIV, DIC (Waterhouse-Friderichsen syndrome)
   b. **Waterhouse-Friderichsen** = hemorrhagic necrosis of adrenal medulla during the course of meningococcemia
   c. Si/Sx = fatigue, anorexia, nausea/vomit, constipation, diarrhea, salt craving (pica), hypotension, **hyponatremia, hyperkalemia**
   d. **Dx = hyperpigmentation, - ACTH, $^-$ cortisol response to ACTH**
3. 2^o Dz $\rightarrow$ **NO hyperpigmentation, $^-$ ACTH**, $\uparrow$ cortisol response to ACTH
4. Acute adrenal crisis
   a. Due to stress (e.g., surgery or trauma), usually in setting of treated chronic insufficiency or withdrawal of Tx
   b. Can occur in pituitary apoplexy (infarction)
5. Tx = cortisol replacement, $\uparrow$ replacement for times of illness or stress—**must taper replacement off slowly to allow HPA axis to restore itself**

ADRENLA CORTICAL HYPERFUNCTION

1. 1^o hyperaldosteronism = Conn's syndrome
   a. Adenoma or hyperplasia of zona glomerulosa
   b. Si/Sx = **HTN, - Na, - Cl, $^-$K, alkalosis,** $\downarrow$ renin (feedback inhibiton)
   c. Dx = $\uparrow$ aldosterone, $\downarrow$ renin, CT $\rightarrow$ adrenal neoplasm
   d. Tx = excision of adenoma—bilateral hyperplasia $\rightarrow$ spironolacotne; bilateral adrenalectomy should NOT be performed
2. 2^o hyperaldosteronism
   a. Due to increased renin production 2^o to renal ischemia (e.g., CHF, shock, renal artery stenosis), cirrhosis, or tumor
   b. Dx = $\uparrow$ renin (renin levels differentiate 1^o vs. 2^o hyperaldosteronism)
   c. Tx = underlying cause, β-blocker or diuretic for hypertension

ADRENAL MEDULLA

1. Pheochromocytoma
    a. Si/Sx = hypertension (episodic or chornic), **diaphoresis, palpitations,** tachycardia, headache, nausea/vomit, flushing, dyspnea, diarrhea
    b. **Rule of 10**: 10% malignant, 10% bilateral, 10% extra-adrenal (occurs in embryologic cells that reactivate outside the adrenal gland)
    c. Dx = ↑ urinary catecholamines, CT scan of adrenal showing neoplasm
    d. Tx
        i. Surgical excision after preop administration of α-blockers
        ii. Ca^{2+} channel blockers for hypertensive crisis
        iii. Phenoxybenzamine or phentolamine (α-blockers) for inoperable disease

GONADAL DISORDERS

MALE GONADAL AXIS

Differential Diagnosis of Male Gonadal Disorders

Disease	**Characteristics**	**Tx**
Klinefelter's syndrome	❖ XXY chromosome inheritance, variable expressivity ❖ Often not Dx until puberty when ↓ virilization is noted ❖ Si/Sx = tall, eunuchoid, with small testes & gynecomastia, ↓ testosterone, ↑LH/FSH from lack of feedback ❖ **Dx = buccal smear analysis for presence of Barr bodies**	Testosterone supplements
XYY syndrome	❖ Si/Sx = may have mild mental retardation, severe acne, ↑ incidence of violence & antisocial behavior ❖ Dx = karyotype analysis	None
Testicular feminization syndrome	❖ Defect in the dihydrotestosterone receptor → female external genitalia with sterile, undescended testes ❖ Si/Sx = appear as females but are sterile & the vagina is blind-ended, testosterone, estrogen & LH are all ↑ ❖ Dx = H&P, genetic testing	None
5-α-reductase deficiency	❖ Si/Sx = ambiguous genitalia until puberty, then a burst in testosterone overcomes lack of dihydrotestosterone → external genitalia become masculinized, **testosterone & estrogen are normal** ❖ Dx = genetic testing	Testosterone supplements

HYPOGONADISM OF EITHER SEX

Genetic Hypogonadism

Disease	**Characteristics**	**Tx**
Congenital adrenal hyperplasia (CAH)	Defects in steroid synthetic pathway causing either virilization of females or failure to virilize males 21-α-hydroxylase deficiency causes 95% of all CAH Severe dz presents in infancy with ambiguous genitalia & salt loss (2^o to ↓↓ aldosterone) Less severe variants → minimal virilization & salt loss, & can have Dx delayed for several years	Tx = replacement of necessary hormones
Prader-Willi syndrome	Paternal imprinting (only gene from dad is expressed) Si/Sx = presents in infancy with floppy baby, **short limbs**, obesity due to gross hyperphagia, nasal speech, retardation, **classic almond-shaped eyes with strabismus** Dx = clinical or genetic analysis	None

Laurence-Moon-Biedl syndrome	Autosomal recessive inheritance Si/Sx = obese children, **normal craiofacies,** may be retarded, **are not short, have polydactyly** Dx = clinical or genetic	None
Kallman's syndrome	Autosomal dominant hypogonadism with anosmia (can't smell) Due to ↓ production/secretion of GnRH by hypothalamus Dx by lack of circulating LH & FSH	Pulsatile GnRH → virilization

THYROID

HYPERTHYROIDISM

1. Causes = Graves' dz, Plummer's dz, adeoma, subacute thyroiditis
2. Si/Sx of hyperthyroidism = tachycardia, **isolated systolic hypertension,** tremor, a-fib, anxiety, diaphoresis, weight loss with increased appetite, insomnia/**fatigue**, diarrhea, **exophthalmos, heat intolerance**
3. Graves' disease
    a. Diffuse toxic goiter, causes 90% of US hyperthyroid cases
    b. Seen in young adults, & is 8x more common in females than males
    c. **Si/Sx include 2 findings only seen in hyperthyroid due to Graves': infiltrative ophthalmopathy & pretibial myxedema**
    d. **Infiltrative ophthalmopathy** = exophthalmos not resolving when thyrotoxicosis is cured, due to autoantibody-mediated damage
    e. **Pretibial myxedema**
        i. Brawny, pruritic, nonpitting edema usually on the sins
        ii. Often spontaneously remits after months to years
    f. Dx confirmed with thyroid stimulating immunoglobulin test
4. Plummer's disease (toxic multinodular goiter)
    a. Due to multiple foci of thyroid tissue that cease responding to T4 feedback inhibition, more common in older people
    b. Dx = multiple thyroid nodules felt in gland, confirm with radioactive iodine uptake tests → hot nodules with cold background
5. Thyroid adenoma due to overproduction of hormone by tumor in the gland
6. Subacute thyroiditis (giant cell or de Quervain's thyroiditis)
    a. Gland inflammation with spilling of hormone from the damaged gland
    b. **Presents with hyperthyroidism, later turns into hypothyroidism**
7. Tx for all
    a. Propylthiouracil or methimazole induces remission in 1mo to 2yr (up to 50% of time), lifelong Tx not necessary unless relapses
    b. Radioiodine is first line for Graves': radioactive iodine is concentrated in the gland & destroys it, resolving the diffuse hyperthyroid state
    c. If the above fail → surgical excision (of adenoma or entire gland)
8. Thyroid storm is the most extreme manifestation of hyperthyroidism
    a. Due to exacerbation of hyperthyroidism by surgery or infection
    b. Si/Sx = high fever, dehydration, cardiac arrhythmias, high output cardiac failure, coma & 25% mortality
    c. Tx
        i. β-blockers and IC fluids are first priority to restore hemodynamic stability
        ii. Give propylthiouracil (PTU) to inhibit iodination of more thyroid hormone
        iii. After PTU on board, give iodine-containing product which will feedback inhibit further thyroid hormone release—make sure the PTU is on board first, or the iodine

can cause an initial INCREASE in hormone release before it feedback suppresses release

HYPOTHYROIDISM

1. Causes include Hashimoto's & subacute thyroiditis
2. Si/Sx = **cold intolerance**, weight gain, **low energy**, husky voice, mental slowness, constipation, thick/coarse hair, puffiness of face/eyelids/hands (**myxedema)**, prolonged relaxation phase of deep tendon reflexes
3. Hashimoto's disease
    a. Autoimmune lymphocytic infiltration of the thyroid gland
    b. **8:1 ratio in women to men**, usually between ages of 30 and 50
    c. **Dx confirmed by antithyroid peroxidase (TPO) antibodies**
    d. Tx = lifelong Synthroid
4. Subacute thyroiditis
    a. Seen following flu-like illness with sore throat & fevers
    b. Si/Sx = **jaw/tooth pain**, can be confused with dental dz, ↑ ESR
    c. Early on looks like hyperthyroidism as damaged gland spills T4
    d. Tx with aspirin, only with cortisol in very severe disease
    e. Usually self-limiting, resolves after weeks to months
5. Myxedema coma
    a. **The only emergent hypothyroid condition**—spontaneous onset or precipitated by cold exposure, infection, analgesia, sedative drug use, respiratory failure, or other severe illness
    b. Si/Sx = stupor, coma, seizures, hypotension, hypoventilation
    c. Tx = IV levothyroxine, cortisone, mechanical ventilation

THYROID MALIGNANCY

1. Terms hot & cold used to describe nodules, refer to whether or not the nodules take up iodine (i.e., are they functionally active or not)
2. Hot nodules are rarely cancerous, usually seen in elderly, soft to palpation, ultrasound (Utz) shows cystic mass, thyroid scan shows autonomously functioning nodule
3. Cold nodule
    a. Has a greater potential of being malignant
    b. More common in women
    c. Nodule is firm to palpation, often accompanied by vocal cord paralysis, Utz shows solid mass
4. Papillary CA
    a. The most common cancer of thyroid
    b. Good Px, 85% 5-yr survival, spread is indolent, via lymph nodes
    c. Pathologically distinguished by ground glass Orphan Annie nucleus & psammoma bodies (other psammoma body dz = serous papillary cystadenocarcinoma of ovary, mesothelioma, meningiomas)
5. Medullary CA
    a. Has intermediate prognosis
    b. Cancer of parafollicular "C" cells that are derived from the ultimobranchial bodies (cells of branchial pouch 5)
    c. Secretes calcitonin, can Dx & follow dz with this blood assay
6. Follicular CA
    a. Good Px, commonly blood-borne metastases to bone & lungs
7. Anaplastic CA has one of the poorest Px of any cancer (0% survival at 5yr)
    a. Note: thyroid nodule—fine needle aspirate, surgical excision

The Multiple endocrine Neoplasia Syndromes

Type I (Wermer's syndrome)	**The 3(4) Ps: P**ituitary, (**P**rolactinoma most common), **P**arathyroid**, P**ancreatoma
Type IIa (Sipple's syndrome)	Pheochromocytoma, medullary thyroid CA, parathyroid hyperplasia or tumor
Type IIb (Type III)	Pheochromocytoma, medullary thyroid CA, mucocutaneous neuromas, particularly of the GI tract

MUSCULOSKELETAL

METABOLIC BONE DISEASES

OSTEOPOROSIS

1. Due to **postmenopausal (¯ estrogen)**, physical inactivity, high cortisol states (e.g., Cushing's, exogenous), hyperthyroidism, Ca^{2+} deficiency
2. Si/Sx = typically aSx until fracture occurs, particularly of hip & vertebrae
3. Dx = **DEXA scan** showing ↓ bone density compared to general population
4. Tx
    a. Estrogens are first line, only Tx shown to stimulate new bone growth
    b. Bisphosphonates are second line, like estrogen proven to ↓ risk of fracture & slow or stop bone degeneration
    c. Calcitonin particularly useful for treating bone pain but its effects wear off after chronic use
    d. Raloxifene & tamoxifen (selective estrogen receptor modulators) ↑ bone density but also ↑ risk for thromboembolism—role unclear currently
5. **Every osteoporosis pt should take Ca to keep dietary intake = 1.5g/day**

RICKETS/OSTEOMALACIA

Vitamin D deficiency in children = rickets, in adults = osteomalacia

Si/Sx in kids (rickets) = **craniotabes** (thinning of skull bones), **rachitic rosary** (costochondral thickening looks like string of beads), **Harrison's groove** (depression along line of diaphragmatic insertion into rib cage), **Pigeon breast** = pectus carinatum (sternum protrusion)

In adults the dz mimics osteoporosis

Dx = x-ray → radiolucent bones, can confirm with vitamin D level

Tx = vitamin D supplementation

SCURVY

Vitamin C deficiency → ↓ osteoid formation

Si/Sx = subperiosteal hemorrhage (painful), **bleeding gums,** multiple ecchymoses, osteoporosis, **"woody leg" from soft tissue hemorrhage**

Dx = clinical

Tx = vitamin C supplementation

PAGET'S BONE DISEASE (OSTEITIS DEFORMANS)

Idiopathic ↑ activity of both osteoblasts & osteoclasts, usually in elderly

Si/Sx = **diffuse fractures & bone pain,** most commonly involves spine, pelvis, skull, femur, tibia, **high output cardiac failure, ¯ hearing**

Dx = **- - alkaline phosphatase**, (+) bone scans, x-rays → sclerotic lesions

Tx = bisphosphonates first line, calcitonin second line

Complications = pathologic fractures, Hypercalcemia & kidney stones, spinal cord compression in vertebral disease, osteosarcomas in long-standing disease

NONNEOPLASTIC BONE DISEASES

FIBROUS DYSPLASIA

Idiopathic replacement of bone with fibrous tissue

3 types = a) monostotic, b) polystotic, c) McCune-Albright's

McCune-Albright's syndrome

Syndrome of hyperparathyroidism, Hyperadrenalism & acromegaly

Dx = polystotic fibrous dysplasia, precocious puberty, café-au-lait spots

Tx = supportive surgical debulking of deforming defects

PYOGENIC OSTEOMYELITIS

S. aureus most common cause, also S. epidermidis & Strep. spp.

Sickle cell patients get Salmonella, IV drug abusers get Pseudomonas

Si/Sx = painful inflammation of bone, striking skin changes include hyperpigmentation, ulceration, erythema

Dx = **x-ray ® periosteal elevation, can lag onset of dz by weeks,** MRI is gold standard, can confirm with cultures of deep bone biopsy

Tx = 6-8 weeks of antibiotics, fluoroquinolones empirically, then narrow as cultures come back, surgical debridement as needed.

BONE TUMORS

Tumor	**Pt Age**	**Characteristics**	**Tx**
Osteochondroma	<25	❖ Benign, usually in males ❖ Seen at distal femur & proximal tibia	Excision
Giant cell	20-40	❖ Benign, epiphyseal ends of long bones (>50% in knee) ❖ X-ray → **soap bubble** sign ❖ Often recurs after excision	Excision & local irradiation
Osteosarcoma	10-20	❖ #1 primary bone malignancy, in males ❖ Seen at distal femur & proximal tibia ❖ 2-3 fold ↑ alkaline phosphatase ❖ **X-ray ® Codman's triangle** = periosteal elevation due to tumor & **"sun-burst" sign** = lytic lesion with surrounding speculated periostitis	Excision & local irradiation
Ewing's sarcoma	<15	❖ Young boys, metastasizes very early ❖ Si/Sx mimic osteomyelitis	Chemotherapy

MULTIPLE MYELOMA

1. Malignant clonal neoplasm of plasma cells producing whole Abs (e.g., IgM, IgG, etc.), light chains only, or very rarely no Abs (just ↑ B cells)
2. Seen in pts >40, African Americans have 2:1 incidence
3. **Si/Sx = bone pain worse with movement, lytic bone lesions on x-ray**, pathologic fractures, **Hypercalcemia**, renal failure, anemia, frequent infection by encapsulated bacteria, ¯ **anion gap** (Abs positively charged, unseen cations make anion gap appear ↓)
4. **Hyperviscosity syndrome** = stroke, retinopathy, CHF, **ESR >100**
5. **Bence-Jones proteinuria**
    a. **Urine dipsticks do NOT detect light chains**, can use sulfosalicyclic acid test in lieu of dipstick to screen
    b. Dx = 24-hr urine collection → protein electorphoresis
    c. Light chain deposition causes renal amyloidosis
6. Dx
    a. Serum/urine protein electrophoresis (SPEP/UPEP)
        i. Both → tall elctrophoretic peak called "M-spike" due to ↑ Ab

ii. SPEP → M-spike if clones make whole Ab
iii. UPEP → spike if clones make light chains only
iv. **Either SPEP or UPEP will almost always be (+)**

b. Dx = (+) SPEP/UPEP & any of 1) ↑ plasma cells in bone marrow, 2) osteolytic bone lesions, 3) Bence-Jones proteinuria

7. Tx
   a. Raidaiton given for isolated lesions, chemotherapy for metastatic dz
   b. Bone marrow transplantation may prolong survival
   c. Palliative care important for pain
8. Px poor despite Tx

ARTHROPATHIES AND CONNECTIVE TISSUE DISORDERS

RHEUMATOID ARTHRITIS (RA)

Autoimmune dz of unknown etiology → **symmetric inflammatory arthritis**

Female-male = 3:1, patients are commonly **HLA-DR4 (+)**

Si/Sx = **symmetric arthritis worse in morning** affecting knees, feet, metacarpophalangeal (**MCP**) & proximal interphalangeal (**PIP**) joints, pleural effusions (Serositis), anemia of chronic dz, flexion contractures → ulnar deviation of digits, subQ nodules (present in <50% of pts)

Labs

Rheumatoid factor (RF) = IgM anti-IgG

Present in >70% of RA pts, but may appear late in dz course

Not specific for RA, can be (+) in any chronic inflammatory state & may be present in 5-10% of healthy geriatric patients

ESR is elevated in >90% cases, but is not specific for RA

Dx = clinical, no single factor is sufficient

Tx

NSAIDs are first line, selective cyclooxygenase-2 inhibitors may be preferable

Hydroxychloroquine second line, refractory pts → prednisone, gold salts, penicillamine, all of which cause severe side effects

TNF antagonists markedly improve symptoms, even in patients refractory to standard therapy

SYSTEMIC LUPUS ERYTHEMATOSUS

Systemic autoimmune disorder, female-male = 9:1

Si/Sx = fever, polyarthritis, skin lesions, splenomegaly, hemolytic anemia, thrombocytopenia, Serositis (e.g., pleuritis & pericarditis), Libman-Sacks endocarditis, renal dz

Labs

Antinuclear antibody (ANA) sensitive (>98%) but not specific

Anti-double-stranded DNA (anti-ds-DNA) antibodies 99% specific

Anti-Smith (anti-Sm) antibodies are highly specific but not sensitive

Anti-Ro antibodies are (+) in 50% of ANA negative lupus

Antiribosomal P & antineuronal antibodies correlate with risk for cerebral involvement of lupus (lupus cerebritis)

Antiphospholipid autoantibodies cause false-positive lab tests in SLE

SLE pts frequently have false (+) RPR/VDRL tests for syphilis

SLE pts frequently have - PTT (lupus anticoagulant antibody)

PTT is falsely ↑ because the lupus anticoagulant antibody bind sot phospholipid that initiates clotting in the test tube

Despite the PTT test & the name lupus anticoagulant antibody, SLE patients are THROMBOGENIC, because antiphospholipid antibodies cause coagulation in vivo

Mnemonic for SLE diagnosis: **DOPAMINE RASH**

Discoid lupus = circular, erythematous macules with scales
Oral aphthous ulcers (can be nasopharyngeal as well)
Photosensitivity
Arthritis (typically hands, wrists, knees)
Malar rash = classic butterfly macule on cheeks
Immunologic criteria = anti-ds-DNA, anti-Sm Ab, anti-Ro Ab, anti-La
Neurologic changes = psychosis, personality change, seizures
ESR rate ↑ (NOT 1 of the 11 criteria, but it is a frequent lab finding)
Renal disease → nephritic or nephrotic syndrome
ANA (+)
Serositis (pleurisy, pericarditis)
Hematologic dz = hemolytic anemia, thrombocytopenic leukopenia

Drug-induced SLE

Drugs = procainamide, hydralazine, Dilantin, sulfonamides, INH
Lab ® antihistone antibodies, differentiating from idiopathic SLE

Tx = NSAIDs, hydroxychloroquine, prednisone, cyclophosphagmide depending on severity of dz
Px = variable, 10-yr survival is excellent, **renal dz is a poor Px indicator**

SJOGREN'S SYNDROME (SS)

1. An autoinflammatory disorder a/w **HLA-DR3**
2. Si/Sx = **classic triad of keratoconjunctivitis sicca** (dry eyes)**, xerostomia** (dry mouth), **arthritis**, usually less severe than pure RA
3. Sytemic Si/Sx = pancreatitis, fibrinous pericarditis, CN V sensory neuropathy, renal tubular acidosis, 40-fold ↑ in lymphoma incidence
4. Dx = Concomitant presence of 2 of the triad is diagnostic
5. Lab → ANA (+), anti-Ro/anti-La Ab(+) ("SSA/SSB Abs"), 70% are RF(+)
6. Tx = steroids, cyclophosphamide for refractory disease

BEHCET'S SYNDROME

1. Multisystem inflammatory disorder that chronically recurs
2. Si/Sx = painful oral & genital ulcers, also arthritis, vasculitis, neurologic dz
3. Tx = prednisone during flare-ups

SERONEGATIVE SPONDYLOARTHROPATHY

Osteoarthritis

A noninflammatory arthritis caused by joint wear & tear
The most common arthritis, results in wearing away of joint cartilage
Si/Sx = pain & crepitation upon joint motion, ↓ range of joint motion, can have radiculopathy due to cord impingement
X-ray ® osteophytes (bone spurs) & asymmetric joint space loss
Physical exam → **Heberden's nodes** (DIP swelling 2^o to osteophytes) & **Bouchard's nodes** (PIP swelling 2^o to osteophytes)
Note: RA affects MCP & PIP joints, osteoarthritis affects PIP & DIP
Tx = NSAIDs, muscle relaxants, joint replacement (third line)
Isometric exercise to strengthen muscles around joint has been shown to improve Sx

Ankylosing spondylitis

Rheumatologic dz usually in **HLA-B27(+)** males (male-female = 3:1)
Si/Sx = sacrolitis, spinal dz → complete fusion of adjacent vertebral bodies causing **"bamboo spine"**, uveitis, heart block

If sacroiliac joint is not affected, it is not ankylosing spondylitis!
Dx = x-ray signs of spinal fusion & negative rheumatoid factor
Tx = NSAIDs & strengthening of back muscles

Reiter's syndrome
Usually seen in males, **about ¾ of these patients are HLA-B27(+)**
Presents as nongonococcal **urethritis** (often Chlamydial), **conjunctivitis, reactive arthritis & uveitis**
Classic dermatolic Sx = **circinate balanitis** (serpiginous, moist plaques on glans penis) **& keratoderma blennorrhagicum** (crusting papules with central erosion, **looks like mollusk shell)**
Tx = erythromycin (for Chlamydia coverage) + NSAIDs for arthritis

Psoriatic arthritis
Presents with **nail-pitting** & **DIP** joint involvement
Occurs in up to 10% of patients with psoriasis
Psoriatic flares may exacerbate arthritis, & vice versa
Tx = UV light for psoriasis & gold/penicillamine for arthritis

Inflammatory bowel disease can cause seronegative arthritis
Disseminated gonococcal infection can cause **monoarticular** arthritis

SCLERODERMA (PROGRESSIVE SYSTEMIC SCLEROSIS = PSS)
Systemic fibrosis affecting virtually every organ, female-male = 4:1
Can be diffuse disease (PSS), or more benign CREST syndrome
Si/Sx of CREST syndrome
Calcinosis = subcutaneous calcifications, often in fingers
Raynaud's phenomenon, often the initial symptom
Esophagitis due to lower esophageal sphincter sclerosis → reflux
Sclerodactyly = fibrosed skin causes immobile digits & rigid facies
Telangiectasias occur in mouth, on digits, face & trunk
Other Sx = flexion contractures, biliary cirrhosis, lung/cardiac/renal fibrosis
Lab = (+) ANA in 95%, anti-Scl-70 has ↓ sensitivity but ↑ specificity, anticentromere is 80% sensitive for CREST syndrome
Dx = clinical
Tx = immunosuppressives for palliation, none are curative

SARCOIDOSIS
Idiopathic, diffuse dz presenting in 20s to 40s, **African Americans are 3x more likely to develop than Caucasians**
Si/Sx = **50% of pts present with incidental finding on CXR & are aSx,** other presentations include fevers, chills, night sweats, weight loss, cough dyspnea, rash, arthralgia, blurry vision (uveitis)
CXR ® bilateral hilar adenopathy
Can affect ANY organ system
CNS → CN palsy, classically CN VII (can be bilateral)
Eye ® uveitis (can be bilateral), requires aggressive Tx
Cardiac → heart blocks, arrhythmias, constrictive pericarditis
Lung → typically a restrictive defect
GI → ↑ AST/ALT, CT → granulomas in liver cholestasis
Renal → nephrolithiasis due to Hypercalcemia
Endocrine → diabetes insipidus
Hematologic → anemia, thrombocytopenia, leukopenia
Skin → various rashes, including erythema nodosum

Dx is clinical, **noncaseating granulomas on biopsy is very suggestive**
Lab → 50% pts have ↑ angiotensin converting enzyme level
Tx = prednisone (first line), but 50% pts spontaneously remit, so only Tx if 1) eye/heart involved, 2) dz does not remit after months
↑ calcitriol (vit D) → produced by macrophages in the granulomas

MIXED CONNECTIVE TISSUE DISEASE (MCTD)

1. Commonly onsets in women in teens & 20s
2. Si/Sx = overlapping SLE, scleroderma & polymyositis, but **characterized by (+) anti-U1 RNP antibody that defines the dz**
3. Dx = anti-U1RNP antibody
4. Tx = steroids, azathioprine

GOUT

1. **Monoarticular arthritis** due to urate crystal deposits in joint
2. **Gout develops after 20-30 yrs of hyperuricemia, often precipitated by sudden changes in serum urate levels** (gout in teens → 20s likely genetic)
3. **Most people with hyperuricemia never get gout**
4. ↑ production of uric acid can be genetic or acquired (e.g., alcohol, hemolysis, neoplasia, psoriasis)
5. Underexcretion of urate via kidney (<800mg/dL urine urate) can be idiopathic or due to kidney dz, drugs (aspirin, diuretics, alcohol)
6. Si/Sx of gout = painful monoarticular arthritis affecting distal joints (often first Metatarsophalangeal joint = **podagra, overlying skin erythema**
7. Dx = **clinical triad of monoarticular arthritis, hyperuricemia, (+) response to colchicine,** confirm with needle tap of joint → crystals
8. Acute Tx = colchicines & NSAIDs (not aspirin!)
9. Px = some people never suffer more than 1 attack, those that do → chronic tophaceous gout, with significant joint deformation (**classic rat-bite appearance to joint on x-ray**) & toothpaste-like discharge from joint
10. Maintenance Tx
    a. Do not star unless patient has more than 1 attack
    b. Over-production → allopurinol (inhibits xanthine oxidase)
    c. Under-excreters → probenecid/sulfinpyrazone
    d. **Always start while pt still taking colchicines, because sudden ¯ in serum urate precipitates an acute attack**
11. Pseudogout
    a. Caused by calcium pyrophosphate dehydrate (CPPD) crystal deposition in joints & articular cartilage (chondrocalcinosis)
    b. Mimics gout very closely, seen in persons age 60 or older, often affects larger, more proximal joints
    c. Can be 1^{o} or 2^{o} to metabolic dz (hyperparathyroidism, Wilson's dz, diabetes, hemochromatosis)
    d. Dx → microscopic analysis of joint aspirate
    e. Tx = colchicines & NSAIDs
12. Microscopy
    a. **Gout ® needle-like negatively birefringent crystals**
    b. **"P" seudogout ® "P"ositively birefringent crystals**

MUSCLE DISEASES

GENERAL

1. Diseases of muscle are divided into 2 groups: neurogenic & myopathic
2. Neurogenic diseases → **distal weakness, no pain, fasciculations present**
3. Myopathic diseases → **proximal weakness, +/- pain, no fasciculations**

DUCHENNE'S MUSCULAR DYSTROPHY

1. **X-linked** lack of dystrophin
2. Si/Sx commence at 1yr of age with **progressive proximal weakness & wasting,** ↑ CPK, **calf hypertrophy**, waddling gait, Gower's maneuver (pts pick themselves off the floor by using arms to help legs)
3. Tx = supportive
4. Px = death occurs in 10s-20s, most often due to pneumonia
5. Becker's dystrophy is similar but less severe disease

POLYMYOSITIS

Autoinflammatory dz of muscles & sometimes skin (dermatomyositis)
Female-male = 2:1, occurs in young children & geriatric populations
Si/Sx = symmetric weakness/atrophy of proximal limb muscles, muscle aches, dysphonia (laryngeal muscle weakness), dysphagia
Dermatomyositis presents with periorbital heliotropic red to purple rash
Dx = ANA (+), ↑ creatine kinase, muscle biopsy → inflammatory changes
Tx = steroids, methotrexate or cyclophosphamide for resistant disease

MYASTHENIA GRAVIS (MG)

1. Autoantibodies block the postsynaptic acetylcholine receptor
2. Most common in women in 20s-30s or men in 50s-60s
3. **Associated with thymomas, thyroid & other autoimmune dz (e.g., lupus)**
4. Sx = **muscle weakness worse with use**, diplopia, dysphagia, proximal limb weakness, can progress to cause respiratory failure
5. Dx = trial of edrophonium → immediate ↑ in strength, confirm with electromyelography → repetitive stimulation ↓ action potential
6. DDx
    a. **Lambert-Eaton syndrome**
        i. AutoAb to **pre**synaptic Ca channels seen with small cell lung CA
        ii. Differs from MG in that Lambert-Eaton → ↓ reflexes, autonomic dysfunction (xerostomia, impotence) & **Sx improve with muscle use (action potential strength - with repeated stimulation)**
    b. Amionglycosides worsen MG, or induce mild MG Sx in normal people
7. Tx = anticholinesterase inhibitors (e.g., pyridostigmine) first line
    a. Steroids, cyclophosphamide, azathioprine for ↑ severe dz
    b. Plasmapheresis temporarily alleviates Sx by removing the Ab
    c. Resection of thymoma can be curative

HEMATOLOGY

ANEMIA

MICROCYTIC ANEMIAS (=MCV <80)

1. **Result from ¯ hemoglobin (Hgb) production or impaired Hgb function**
2. Iron deficiency anemia
    a. **NOT a Dx, must find the cause of iron deficiency!!!**
    b. Epidemiology
        i. #1 anemia in the world, hookworms the #1 cause in the world

ii. ↑ incidence in women of childbearing age 2° to menses
iii. **In elderly it is colon cancer until proven otherwise**
iv. Dietary deficiency **virtually impossible in adults, seen in kids**

c. Si/Sx = tachycardia, fatigue, pallor all from anemia, smooth tongue, brittle nails, esophageal webs & pica all from iron deficiency
d. Dx = ¯ **serum iron**, ↓ serum ferritin, - **total iron binding capacity (TIBC),** peripheral smear → target cells
e. Tx = iron sulfate, should achieve baseline hematocrit within 2 mo

3. Sideroblastic anemia
   a. Ineffective erythropoiesis due to disorder of porphyrin pathway
   b. Etiologies = chronic alcoholism, drugs (commonly isoniazid), genetic
   c. Si/Sx as per any anemia
   d. Labs: - **iron**, N/↑TIBC, ↑ ferritin
   e. Dx = ringed sideroblasts on iron stain of bone marrow
   f. Tx = sometimes responsive to pyridoxine (vitamin B_6 supplements)
4. Lead poisoning
   a. Si/Sx = anemia, encephalopathy (worse in children), seizures, ataxic gait, **wrist/foot drops**, renal tubular acidosis
   b. Classic findings
      i. **Bruton's lines** = blue/gray discoloration at gumlines
      ii. Basophilic stippling of red cells (blue dots in red cells)
   c. Dx = serum lead level
   d. Tx = chelation with dimercaprol (BAL) &/or EDTA
5. Thalassemias
   a. Hereditary dz of ↓ production of globin chains → ↓ Hgb production
   b. Differentiation through gel-electrophoresis of globin proteins
   c. α-thalassemia (↓ α-glbin chain synthesis, there are 4 α alleles)
      i. seen commonly in Asians, less so in Africans & Mediterraneans

# Alleles Affected/Dz	Characteristic	Blood smear
4 Hydrops fetalis	Fetal demise, total body edema	Bart's β, Hgb precipitations
3 Hgb H disease	Precipitation of β-chain tetramers	Intraerythrocytic inclusions
2 α-Thalassemia minor	Usually clinically silent	Mild microcytic anemia
1 Carrier state	No anemia, asymptomatic	No abnormalities

   d. β-Thalassemia (↓ β-globin chain synthesis, there are 2 β alleles)
      i. Usually of Mediterranean or African descent

	Thalassemia major (b -/b -)	Thalassemia Minor (b +/b -)
Si/Sx	Anemia develops at 6mo old (due to switch from fetal γ Hgb to adult β), splenomegaly, frontal bossing due to extramedullary hematopoiesis, iron overload (2° to transfusions)	Typically asymptomatic carriers
Dx	**Electrophoresis** ↓↓↓ Hgb A, ↑ Hgb A2, - **Hgb F**	**Electrophoresis** ↓ Hgb A, ↑Hgb A2(γ), **N Hgb F**
Tx	Folate supplementation, splenectomy for hypersplenism, transfuse only for severe anemia	Avoid oxidative stress

6. Sickle cell anemia
   a. HgS tetramer polymerizes, causing sickling o deoxygenated RBCs
   b. Si/Sx

i. Vaso-occlusion → pain crisis, myocardiopathy, infarcts of bone/CNS/lungs/kidneys & autosplenectomy due to splenic infarct → ↑ susceptible to encapsulated bacteria
ii. **Intravascular hemolysis ® gallstones in children or teens**
iii. ↑ risk of aplastic anemia from parvo virus B19 infections

c. Dx = hemoglobin electrophoresis → HgS phenotype
d. Tx
i. O2 (cells sickle when Hgb desaturates), transfuse as needed
ii. Hydroxyurea → ↓ incidence & severity of pain crises
iii. Pneumococcal vaccination due to ↑ risk of infection

MEGALOBLASTIC ANEMIAS (=MCV >100)

1. **Results from ¯ DNA synthesis with normal RNA/protein synthesis**
2. **Pathognomonic blood smear ® hypersegmented neutrophils**
3. Vitamin B_{12} deficiency
   a. Pernicious anemia is most common cause
      i. Antibody to gastric parietal cells → ↓ production of intrinsic factor (necessary for uptake of B_{12} in the terminal ileum)
      ii. Accompanied by achlorhydria & atrophic gastritis
   b. Other causes = malabsorption due to gastric resection, resection of terminal ileum, or intestinal infection by *Diphyllobothrium latum*
   c. Si/Sx = megaloblastic anemia **with neurologic signs** = peripheral neuropathy, paresthesias, ↓ balance & position sense, **worse in legs**
   d. **Dx = - serum methylmalonic acid & - homocysteine levels**—more sensitive than B_{12} levels, which may or may not be ↓
   e. Tx = Vitamin B_{12}, high-dose oral Tx proven equivalent to parenteral
4. Folic acid deficiency
   a. Folic acid derived from green, leafy vegetables ("foliage")
   b. Causes = dietary deficiency (most common), pregnancy or hemolytic anemia (↑ requirements), methotrexate or prolonged Bactrim Tx (inhibits reduction of folate into tetrahydrofolate)
   c. Si/Sx = megaloblastic anemia, no neurologic signs
   d. Dx = **Nml serum methylmalonic acid but - homocysteine levels**—more sensitive than folate levels, which may or may not be ↓
   e. Tx = oral folic acid supplementation

NORMOCYTIC ANEMIAS

Hypoproliferative Anemias

Disease	**Characteristics**	**Tx**
Anemia of renal failure	❖ ↓ erythropoietin production by kidney ❖ indicates chronic renal failure	Erythropoietin IM 3x per week
Anemia of chronic dz	❖ seen in chronic inflammation (e.g., cancer, TB or fungal infxn, collagen-vascular dz) ❖ Dx = ¯ **serum iron**, Nm./↑ ferritin, ¯ **TIBC**	Tx underlying inflammatory dz, supportive
Aplastic anemia	❖ Bone marrow failure, usually idiopathic, or due to parvovirus B19 (especially in sickle cell, hepatitis virus, radiation, drugs (e.g., chloramphenicol) ❖ Dx = bone marrow Bx → hypocellular marrow	BMT for severe dz, ATG & cyclosporin may help for mild dz

Hemolytic Anemias

Disease	Characteristics	Tx
Intrinsic hemolysis (RBC defects)		
Spherocytosis	❖ Autosomal dominant membrane protein defect (fibrillin) → spherical, stiff RBCs trapped in the spleen ❖ Si/Sx = childhood jaundice & gallstones, indirect hyperbilirubinemia, Coombs negative ❖ Dx = clinical (+) peripheral smear → spherocytes	Folic acid, splenectomy for severe dz
Extrinsic hemolysis		
Autoimmune hemolysis (IgG-mediated)	❖ Etiologies = idiopathic (most common), lupus, drugs (e.g., penicillin, leukemia, lymphoma ❖ Si/Sx = rapid-onset, **spherocytes on blood smear**, ↑ indirect bilirubin, jaundice, ¯ **haptoglobin, - urine hemosiderin** ❖ Dx = (+) direct Coombs' test	First line = prednisone +/- splenectomy, cyclophosphamide for refractory dz
Cold-agglutinin disease (IgM-mediated)	❖ Most commonly idiopathic, can be due to *Mycoplasma pneumoniae* & mononucleosis (CMV, EBV infxns) ❖ Si/Sx = anemia on exposure to cold or following URI ❖ Dx = cold-agglutinin test & indirect Coombs' test	Prednisone for severe dz, supportive for mild
Mechanical destruction	❖ Causes = DIC, Thrombotic thrombocytopenic purpura (TTP), hemolytic-uremic syndrome (HUS) & artificial heart valve ❖ Peripheral smear → schistocytes	Tx directed at underlying disorder

COAGULATION DISORDERS

THROMBOCYTOPENIA

1. Caused by splenic sequestration, stem-cell failure, or ↑ destruction
2. Si/Sx = bleeding time ↑ at counts < 50,000, clinically significant bleeds start at counts <20,000, CNS bleeds occur when counts <10,000
3. ↓ production seen in leukemia, aplastic anemia & alcohol (even minimal)
4. Causes of platelet destruction (thrombocytopenia)

Disease	Characteristics	Tx
Idiopathic thrombocytopenic purpura (ITP)	❖ Autoantibody-mediated platelet destruction ❖ **In children follows URI & is self-limiting, in adults it is chronic**	Steroids (1st line), splenectomy (2nd line) or cyclophosphamide
Thrombotic thrombocytopenic purpura (TTP)	❖ Idiopathic dz, often seen in HIV, can be fatal ❖ **Pentad** = hemolytic anemia, renal failure, thrombocytopenia, fever, neurologic dz	Plasma exchange or IVIG until dz abates, dz is fatal without Tx
Hemolytic-uremia syndrome (HUS)	❖ Usually in kids, often due to E. coli O157:H7 ❖ Si/Sx = acute renal failure, bloody diarrhea & abdominal pain, seizures, **fulminant thrombocytopenia with hemolytic anemia**	Dialysis helps children, but adult Px is much poorer
Disseminated intravascular coagulation (DIC)	❖ Seen in adenocarcinoma, leukemia, sepsis, trauma ❖ ↑ fibrin-split product, ↓ fibrinogen, ↑ PT/PTT	Directed at underlying cause
Drug-induced	❖ Causes = heparin, sulfonamides, valproate ❖ Reverses within days of ceasing drug intake	Stop drug

Labs in platelet destruction

Study	Autoantibody	DIC	TTP/HUS

Blood smear	Microspherocytes	Schistocytes (+)	**Schistocytes (+++)**
Coombs' test	(+)	----	----
PT/PTT	Nml	↑↑↑	Nml/↑

INHERITED DISORDERS

1. von-Willebrand factor (vWF) deficiency
    a. **Most common inherited bleeding dz**
    b. Si/Sx = **episodic - bleeding time & ecchymoses, normal PT/PTT**
    c. Dx = vWF levels & ristocetin-cofactor test
    d. Tx = DDAVP (↑ vWF secretion) or cryoprecipitate for acute bleeding)
2. Hemophilia
    a. X-linked deficiency of factor VIII (hemophilia A) or autosomal recessive defect of factor IX (hemophilia B = Christmas disease)
    b. Si/Sx = hemarthroses (bleeding into joint), ecchymoses with minor trauma, - **PTT, normal PT, normal bleeding time**
    c. Dx = ↓ factor levels
    d. Tx = recombinant factor VIII or factor IX concentrate

HYPERCOAGULABLE DISEASES

Primary (inherited)	**Secondary (acquired)**	
Antithrombin III deficiency	Prolonged immoblinization	L-asparaginase
Protein C deficiency	Pregnancy	Hyperlipidemia
Protein S deficiency	Surgery/Trauma	Anticardiolipin Ab
Factor V Leiden deficiency	Oral contraceptives	Lupus anticoagulant
Dysfibrinogenemia	Homocystinuria	DIC
Plasminogen (activator) deficiency	Malignancy (adenocarcinoma)	Vitamin K deficiency
Heparin cofactor II deficiency	Smoking	
Homocystinemia	Nephrotic syndrome	
Factor II (prothrombin) mutation		

MYELOPROLIFERATIVE DISEASES

1. Caused by clonal proliferation of a myeloid stem cell → excessive production of mature, differentiated myeloid cell lines
2. All can transform into acute leukemias
3. Thrombocytosis
    a. 1^o (essential) versus 2^o (reactive)
    b. 1^o can be Essential Thrombocythemia, but can also see a thrombocytosis in polycythemia rubra vera or chronic myelogenous leukemia
    c. 2^o or reactive thrombocytosis can be seen in any chronic inflammatory disorder, serious infection, acute bleed, iron-deficiency anemia (mechanism unclear), or following splenectomy

Disease	**Characteristics**	**Tx**
Polycythemia vera	Rare, peak onset at 50-60yr, male predominance Si/Sx = headache, diplopia, retinal hemorrhages, stroke, angina, claudication (all due to vascular sludging), early satiety, splenomegaly, gout, **pruritus after showering, plethora, basophilia**	Phlebotomy, hydroxyurea to keep blood counts low

	5% progress to leukemia, 20% to myelofibrosis	
Essential thrombocythemia	Si/Sx = platelet count > $5x10^5$ cell/μL, splenomegaly, ecchymoses Dx = rule out 2^o thrombocytosis (due to iron deficiency, malignancy, etc.) 5% progress to myelofibrosis or acute leukemia	Platelet exchange (apheresis), hydroxyurea or anagrelide
Idiopathic myelofibrosis	Typically affects patients = 50yr Si/Sx = massive hepatosplenomegaly, blood smear → **teardrop cells** Dx = hypercellular marrow on biopsy Poor Px, median 5yr before marrow failure	Supportive (splenectomy, antibiotics, allopurinol for gout)

LEUKEMIAS

ACUTE LYMPHOBLASTIC LEUKEMIA

1. **Peak age 3-4yr**, most common neoplasm in children
2. Si/Sx = fever, fatigue, anemia, pallor, petechiae, infections
3. Lab → leukocytosis, anemia, ↓ platelets, marrow bx → ↑ blasts, peripheral blood blasts are **PAS+, CALLA+, TdT+**
4. Tx = chemotherapy: induction, consolidation, maintenance—CNS radiation or intrathecal chemotherapy during consolidation
5. Px = 80% cure in children (much worse in adults)

ACUTE MYELOGENOUS LEUKEMIA (AML)

1. **Most common leukemia in adults**
2. Si/Sx = fever, fatigue, pallor, petechiae, infections, lymphadenopathy
3. Lab → thrombocytopenia, peripheral blood & marrow bx → myeloblasts that are **myeloperoxidase +, Sudan Black +, Auer Rods +**
4. Tx
    a. Chemotherapy → induction, consolidation (no maintenance)
    b. All-trans retinoic acid used for a subtype of AML, causes differentiation of blasts, beware of onset of DIC in these patients
5. Px = overall 30% cure, bone marrow transplant improves outcomes

CHRONIC MYELOGENOUS LEUKEMIAS

Presents most commonly in the 50s, can be any age

Si/Sx = anorexia, early satiety, diaphoresis, arthritis, bone tenderness, leukostasis (WBC = $1x10^5$) → dyspnea, dizzy, slurred speech, diplopia

Labs → **Philadelphia chromosome** (+), **peripheral blood ® cells of all maturational stages**, ↓ leukocyte alkaline phosphatase

Philadelphia (Ph) chromosome is pathognomonic, seen in >90% of CML pts, due to translocation of abl gene from chromosome 9 to bcr on 22

Tx in chronic phase = reduction of WBC count with hydroxurea or interferon (IFN)-α, or brand new Tx with the drug-designed tyrosine kinase inhibitor, signal transduction inhibitor (STI)-571, which specifically blocks the oncogenic tyrosine kinase protein formed by the bcr:abl translocation

Blast crisis = acute phase, invariably develops causing death in 3-6mo, mean time to onset = 3-4yr, only BMT can prevent

CHRONIC LYMPHOCYTIC LEUKEMIA

1. Increasing incidence with age, causes 30% of leukemias in US

2. Si/Sx = organomegaly, hemolytic anemia, thrombocytopenia, blood smear & marrow, → normal morphology lymphocytosis of blood & marrow, **lymphocytes almost always express CD5 protein**
3. **Tx = palliative, early therapy does NOT prolong life**
4. Other presentations of similar leukemias
    a. Hairy cell leukemia (B-cell subtype)
        i. Si/Sx = characteristic hairy cell morphology, pancytopenia
        ii. Tx = interferon-α, splenectomy
    b. T-cell leukemias tend to involve skin, often present with erythematous rashes, some are due to human T-cell leukemia virus (HTLV)

Most common Leukemias by Age: Up to age 15 = ALL; age 15-39 = AML; age 40-59 = AML & CML 60 & over = CLL

LYMPHOMA

NON-HODGKIN'S LYMPHOMA (NHL)

1. Commonly seen in HIV, often in brain, teenagers, get in head & neck
2. Burkitt's lymphoma
    a. Closely related to Epstein-Barr virus (EBV) infections
    b. African Burkitt involves jaw/neck, US Burkitt's involves abdomen
3. Cutaneous T-cell Lymphoma (CTCL, mycosis fungoides)
    a. Si/Sx = often in elderly, diffuse scaly rash or erythroderma (total body erythema), precedes clinically apparent malignancy by years
    b. **Stained cells have cerebriform nuclei** (looks like cerebral gyri)
    c. Leukemic phase of this disease is called "Sezary syndrome"
    d. Tx = UV light therapy, consider systemic chemotherapy
4. Angiocentric T-cell lymphoma
    a. 2 subtypes = nasal T-cell lymphoma (lethal midline granuloma) & pulmonary angiocentric lymphoma
    b. Si/Sx = large mass, biopsy often non-Dx due to diffuse necrosis
    c. Tx = palliative radiation therapy, Px very poor

HODGKIN'S LYMPHOMA

Occurs in a bimodal age distribution, young men & the elderly

EBV infection is present in up to 50% of cases

Si/Sx = **Pel-Epstein fevers** (fevers wax & wane over weeks), chills, night sweats, weight loss, pruritus, **Sx worsen with alcohol intake**

Reed-Sternberg (RS) cells seen on biopsy, **appear as binucleated giant cells ("owl eyes")** or **mononucleated giant cell (lacunar cell)**

Tx depends on clinical staging

Stage I = 1 lymph node involved → radiation

Stage II = =2 lymph nodes on same side of diaphragm → radiation

Stage III = involvement on both sides of diaphragm → chemo

Stage IV = disseminated to organs or extranodal tissue → chemo

Chemo regimens

MOPP = meclorethamine, oncovin (vincristine), procarbazine, prednisone

ABVD = adriamycin, bleomycin, vincristine, dacarbazine

2 SURGERY

FLUIDS AND ELECTROLYTES

PHYSIOLOGY

1. 50-70% of lean body weight is water, most of it is in skeletal muscle
2. Total body water (TBW) is divided into extracellular (1/3) & intracellular (2/3) compartments
3. Extracellular water
    a. Comprises 20% of lean body weight
    b. 25% intravascular & 75% extravascular (interstitial)
4. Intracellular water comprises 40% of lean body weight

FLUID MANAGEMENT

1. **3 for 1 rule**
    a. By 1-2 hours after a 1L infusion of isotonic saline or lactated Ringer's, only 300mL remains in the intravascular compartment
    b. **Thus 3-4 times the vascular deficit should be administered** if isotonic crystalloid solutions are used for resuscitation
2. Colloid solutions (contain high molecular weight molecules, e.g., albumin, hetastarch & dextrans) stay in the intravascular space longer
3. Colloids are more expensive than crystalloids & are most useful in the edematous patient where, for instance, 100mL of 1% albumin solution will be able to draw about 400mL from the extravascular compartment, thus decreasing edema

HYDRATION OF SURGICAL PATIENTS

1. Pts are commonly NPO (Nothing per Oral) & require IV fluid hydration
2. An uncomplicated pt without oral intake loses =1L of fluid a day from sweat, urine, feces & respiration
3. Adequate fluid hydration is indicated by **urine output = ½ cc/kg/hr (for typical patient =30cc/hr)** & by measuring daily weight changes
4. Electrolytes should be replaced as necessary
    a. Salivary & colon secretions are high in K^+
    b. Stomach, ileum & bile secretions are high in Cl^-
    c. Salivary, ileum, pancreas & bile secretions are high in HCO_3^-

COMMON ELECTROLYTE DISORDERS

Disorder	DDx	Si/Sx	Tx
$\uparrow Na^+$	❖ Fluid loss ❖ Steroid use ❖ Hypertonic fluids	❖ Lethargy, weakness, irritability ❖ Can be severe → seizures & coma	❖ Normal saline IV ❖ Correct ½ the deficit in 1st 24hr & the 2nd ½ over 2-3 days
$\downarrow Na^+$	❖ Copious bladder irrigation s/p TURP ❖ High output ileostomy ❖ Adrenal insufficiency	❖ Severe (<115mmol/L) → seizures, nausea, vomiting, stupor, or coma	❖ Water restriction ❖ Hypertonic saline IV & loop diuretics
$\uparrow K^+$	❖ Acidosis ❖ ↓ insulin ❖ Leukocytosis ❖ Burns ❖ Crush injury	❖ Neuromuscular & cardiac sequelae (heart block, v-fib & asystole) ❖ EKG → peaked T waves, flattened P waves, wide	❖ Stabilize cardiac membranes with IV calcium gluconate ❖ Glucose & insulin infusion ❖ Albuterol & loop diuretics ❖ Biding resins (Kayexalate)

		QRS, eventually a sinusoidal pattern	& dialysis longer term
$\downarrow K^+$	❖ Diarrhea, NG suction & vomiting ❖ Diuretics, met. Alk. ❖ Cushing's, burns, β-agonists, $\downarrow Mg^{++}$	❖ Ectopy, T-wave depression, prominent U waves ❖ Also V-Tach & increased sensitivity to digoxin	❖ Oral supplements unless the patient is NPO ❖ Infusion of K^+ over =10mEq/hr ❖ Correction of hypomagnesemia ❖ K^+ sparing diuretics
$\uparrow Ca^{++}$	❖ Malignancy (#1 cause in inpatients) ❖ Disorders involving bone, parathyroid, or kidneys	❖ Altered mental status, muscle weakness, ileus, constipation, nausea & vomiting ❖ Nephrolithiasis ❖ QT interval shortening	❖ Calcium restriction ❖ Hydration & loop diuretics ❖ Calcitonin, pamidronate ❖ Dialysis
$\downarrow Ca^{++}$	❖ Acute pancreatitis ❖ Blood transfusion ❖ Parathyroid resection ❖ $\downarrow Mg^{++}$ ❖ renal failure	❖ Chvostek's & Trousseau's signs ❖ Paresthesias, tetany, seizures, weakness & mental status changes ❖ QT interval prolonged	❖ Calcium gluconate ❖ Vitamin D supplement
$\uparrow Mg^{++}$	❖ Overzealous Mg^{++} supplements in patients with renal failure	❖ Lethargy, weakness, ↓ deep tendon reflexes ❖ Paralysis, ↓ BP & HR ❖ Prolonged PR & QT intervals	❖ Calcium gluconate ❖ Normal saline infusion with a loop diuretic ❖ Dialysis
$\downarrow Mg^{++}$	❖ Diarrhea, malabsorption ❖ Vomiting ❖ Aggressive diuresis, alcoholism, chemoTx	❖ Torsades des pointes ❖ V-fib, atrial tach & atrial fib ❖ Hyperreflexia & tetany ❖ T wave & QRS widening PR & QT intervals prolonged	❖ $MgSO_4$
↑Phos	❖ Usually iatrogenic ❖ Rhabdomyolysis ❖ Hypoparathyroid ❖ Hypocalcemia ❖ Villous adenoma ❖ Refeeding syndrome	❖ Can cause soft-tissue calcification ❖ Heart block	❖ Decrease dietary phosphorus ❖ Aluminum hydroxide ❖ Hydration & acetazolamide ❖ Dialysis
↓Phos	❖ Excessive IV glucose ❖ Hyperparathyroidism ❖ Osmotic diuresis	❖ Diffuse weakness & flaccid paralysis (all due to decreased ATP production)	❖ Potassium phosphate or sodium phosphate

TURP = transurethral resection of prostate

Note: refeeding syndrome caused by a large glucose load too soon after prolonged NPO status-see decrease in Mg, K, and Phos

BLOOD PRODUCT REPLACEMENT

NORMAL HEMOSTASIS

1. Coagulation involves endothelium, platelets & coagulation factors
2. Endothelial damage allows platelets to bind to subendothelium, inducing platelet release of ADP, 5-HT, PDGF, which promote platelet aggregation

3. Initial thrombus stabilized by fibrin laid down by coagulation factors
4. Coagulation cascades
    a. The two coagulation pathways share factors I, II, V & X
    b. Extrinsic pathway
        i. Tissue thromboplastin (tissue factor), activates factor VII, which then activates factor X
        ii. Measured in vitro by prothrombin time (PT)
    c. Intrinsic pathway
        i. Factor XII $\rightarrow$ XI $\rightarrow$ IX $\rightarrow$ VIII, activated factor VIII causes activation of the common factor X
        ii. Measured in vitro by partial thromboplastin time (PTT)
    d. Factor I = fibrin, which cross-links platelets to provide the tensile strength needed to stabilize the thrombus
5. Vitamin K is fat soluble, derived from leafy vegetables & colonic flora
    a. Cofactor for γ-carboxylation of factors II, VII, IX, X & the anticoagulation factors, proteins C & S, enables them to interact with Ca^{2+}
    b. Deficiency caused by malabsorption, prolonged parenteral feeding, prolonged oral antibiotics, or ingestion of oral anticoagulants
    c. First sign is prolonged PT< due to the short half-life of factor VII

PREOPERATIVE EVALUATION OF BLEEDING DISORDERS

1. Si/Sx = Hx of FHx of ↑ bleeding following minor cuts, dental procedures, menses, or past surgeries, ecchymoses or sequelae of liver dz
2. Ask about NSAID or herbal medicine intake the week of surgery
3. Bleeding time
    a. Evaluates platelet function
    b. ↑ bleeding time indicates quantitative or qualitative platelet dz
    c. Also ↑ in von Willebrand's dz & vasculitis
4. Thrombin time (TT)
    a. Measures the time to clot after the addition of thrombin, which is responsible for conversion of fibrinogen to fibrin
    b. ↑ TT may be due to ↑ fibrin, dysfibrinogenemia, DIC, or heparin
5. **Routine preoperative lab screening is not warranted without Si/Sx suggestive of underlying disorder**

TRANSFUSIONS

1. Packed red blood cells (pRBCs)
    a. Type & screen = pt's RBCs tested for A, B & Rh antigens & donor's serum screened for antibodies to common RBC antigens
    b. Cross-match = when the pt's serum checked for preformed antibodies against the donor's RBCs
    c. In trauma situations, type O negative blood is given while additional units are being typed & crossed
    d. **1 unit pRBCs should - hemoglobin by 1g/dL & - hematocrit 3%**
    e. Complicaitons
        i. Acute rejection
            1. Due to preformed antibodies against the donor RBCs
            2. Si/Sx = anxiety, flushing, tachycardia, renal failure, shock
            3. **The most common cause is clerical error**
            4. Recheck all paperwork & repeat cross-match

5. Tx = stop transfusion, IV fluids to maintain urine output

ii. Infectious diseases
1. HCV is by far the most common cause of hepatitis in pts who received prior transfusions, although risk of new HCV infection is now lower with blood bank screening
2. Current risks

Disease	**Estimated risk**
Hepatitis B	1 case per 50,000 units transfused
Hepatitis C	1 case per 50,000 units transfused
HIV	1 case per 300,000 units transfused

2. Platelet transfusions
   a. Pts do not bleed significantly until platelets <50,000/μL, so transfusion should be given only to maintain this level
   b. If pt is anticipated to experience severe blood loss intraopereatively or the pt is actively bleeding transfuse to maintain even higher
   c. Most common complication is alloimmunization
      i. Platelet counts fail to rise despite continued transfusion
      ii. Caused by induction of antibodies against the donor's MHC type
      iii. Single donor, HLA-matched platelets may overcome problem
3. Plasma component transfusion
   a. Plasma products do not require cross-matching but donor & recipient should be ABO compatible
   b. Fresh frozen plasma (FFP)
      i. Contains all the coagulation factors
      ii. Used to correct all clotting factor deficiencies
   c. Cryoprecipitate is rich in factor VIII, fibrinogen & fibronectin

PERIOPERATIVE CARE

PREOPERATIVE CARE

1. All pts require detailed history & physical
2. Laboratory tests
   a. CBC for pts undergoing procedure that may incur large blood loss
   b. Electrolytes, BUN & creatinine in pts over 60yr or who have illnesses (e.g., diarrhea, liver & renal dz) or take medications (e.g., diuretics) that predispose them to electrolyte disorders
   c. UA in pts with urological Sx or those having urologic procedures
   d. PT & PTT in pts with bleeding diathesis, with liver disease, or who are undergoing neurosurgery or cardiac surgery
   e. Liver function tests in pts with liver disease
   f. CXR in pts with ↑ risk of pulmonary complications (e.g., obesity or thoracic procedures) & those with preexisting pulmonary problems
   g. EKG in males >40, females >50, or young pts with preexisting cardiac dz

PERIOPERATIVE REVIEW OF SYSTEMS

1. Neurological
   a. Cerebrovascular disease
      i. Strokes usually occur postop & are caused by hypotension or emboli from atrial fibrillation

ii. Patients with a recent history of strokes should have their surgical procedure delayed 6wk
iii. Anticoagulation should stop 2 weeks prior to surgery if possible

2. Cardiovascular
    a. Most postop complications are cardiac related
    b. Goldman cardiac risk index stratifies the operative risk of noncardiac surgery pts & helps in the decision of pursuing further Dx testing

Goldman Cardiac Risk Index

Condition	**Points**	**Concern**
S3 gallop, JVD	11	CHF
MI within 6mo	10	Cardiac injury
Abnormal EKG rhythm	7	Diseased cardiac conduction
>5 PVCs/min	7	Cardiac excitability
Age >70	5	Increased comorbidity
General poor health	3	Increased morbidity
Aortic stenosis	3	Left ventricular outflow obstruction
Peritoneal/thoracic/aortic surgery	3	Major surgery
Emergency	3	Emergency surgery
>26 points warrants life-saving procedures only due to ↑↑↑ risk of cardiac-related death		

3. Pulmonary
    a. Pulmonary complications rarely occur in healthy pts
    b. COPD is the most important & significant risk factor to consider
    c. Obesity, abdominal & intrathoracic procedures predispose pts to pulmonary complications in the postoperative period
    d. Smoking Hx, independent of COPD, is also an important risk factor
4. Renal
    a. Postop acute renal failure → =50% mortality despite hemodialysis
    b. Chronic renal failure is a significant risk factor not only because of the ↑ risk of developing acute failure, but because of the associated metabolic disturbances & underlying medical conditions
    c. Azotemia, sepsis, intraoperative hypotension, nephrotoxic drugs & radiocontrast agents are risk factors for postoperative renal failure
    d. Preventive measures include expanding the intravascular volume with IV fluids & use of diuretics after administration of radiocontrast dye
5. Infection/immunity
    a. Infection risk depends upon patient characteristics & surgery
    b. Advanced age, diabetes, immunosuppression, obesity, preexisting infection & preexisting illness all increase risk
    c. Surgical risk factors include GI surgery, prosthetic implantation, preoperative wound contamination & duration of the operation
    d. Prophylaxis
        i. To prevent surgical wound infections, antibiotics should be administered before the skin incision is made
        ii. Appropriate choice of the antibiotics depends on the procedure
        iii. Give all patients with prosthetic heart valves antibiotic prophylaxis to prevent bacterial endocarditis
6. Hematologic

a. Deep venous thrombosis (DVT) prevented by early ambulation & mechanical compression stockings
b. Subcutaneous heparin may be substituted for compression stockings
c. Pulmonary embolus should always be considered as a cause of postop acute onset dyspnea

7. Endocrinology
    a. Adrenal insufficiency
        i. Surgery creates stress for the body, normally the body reacts to stress by secreting more corticosteroids
        ii. Response may be diminished in pts taking corticosteroids for =1wk preoperatively & pts with primary adrenal insufficiency
        iii. Hence, for these patients, steroid replacement is needed, & **hydrocortisone is given before, during & after surgery to approximate the response of the normal adrenal gland.** If these measures are not taken, then adrenal crisis may occur
        iv. Adrenal crisis
            1. A life-threatening complication of adrenal insufficiency
            2. **Si/Sx = unexplained hypotension & tachycardia despite fluid & vasopressor administration**
            3. Tx = corticosteroids dramatically improve BP

FEVER

1. Intraoperative fever
    a. DDx = transfusion reaction, malignant hyperthermia, or prior infxn
    b. Malignant hyperthermia
        i. Triggered by several anesthetic agents, e.g., halothane, isoflurane & succinylcholine
        ii. Tx = dantrolene, cooling measures, ICU monitoring
2. Postoperative fever
    a. **Mnemonic for causes: the 5Ws**
        i. Wind (lungs)
        ii. Water (urinary tract)
        iii. Wound
        iv. Walking (DVT)
        v. Wonder drug (drug reaction)
    b. Immediate postoperative fever includes atelectasis, streptococcus & clostridium wound infections & aspiration pneumonia
    c. 1-2 days postoperatively look for indwelling vascular line infection, aspiration pneumonia & infectious pneumonia
    d. Tx = encourage early postoperative ambulation, incentive spirometry use post-operatively, treat infections with appropriate antibiotics

TRAUMA

GENERAL

1. Trauma is the major cause of death in those under age 40
2. management broken into primary & secondary surveys

PRIMARY SURVEY =ABCDE

1. A = Airway
    a. Al pts immobilized due to ↑ risk of spinal injury
    b. Maintain airway with jaw thrust or mandible/tongue traction, protecting cervical spine

c. If pt is likely to vomit, position them in a slightly lateral & head-down position to prevent aspiration
d. If airway cannot be established, 2 large bone (14-gauge) needles can be inserted into the cricothyroid membrane
e. Do not perform tracheotomy in the field or ambulance
f. Unconscious patients need endotracheal (ET) tube!

2. B = breathing
   a. Assess chest expansion, breath sounds, respiratory rate, rib fractures, sub-Q emphysema & penetrating wounds
   b. Life-threatening injuries to the lungs or thoracic cavity are:
      i. Tension pneumothorax → contralateral mediastinal shift, distended neck veins (↑ CVP), hypotension, ↓ breath sounds on 1 side & hyperresonance on the other side, Tx = immediate chest tube or 14-gauge needle puncture of affected side
      ii. Open pneumothorax → Tx = immediate closure of the wound with dressings & placement of a chest tube
      iii. Flail chest → caused by multiple rib fractures that form a free-floating segment of chest wall that moves paradoxically to the rest of the chest wall, resulting in an inability to generate sufficient inspiratory or expiratory pressure to drive ventilation, Tx = intubation with mechanical ventilation
      iv. Massive hemothorax → injury to the great vessels with subsequent hemorrhage into the thoracic cavity, Tx = chest tube, surgical control of the bleeding site
3. C = Circulation
   a. 2 large bore IVs placed in upper extremities (if possible)
   b. For severe shock, place a central venous line
   c. O-negative blood on stand-by for any suspected significant hemorrhage
4. D = disability
   a. Neurologic disability assessed by history, careful neurologic examination (Glasgow Coma Scale), laboratory tests (blood alcohol level, blood cultures, blood glucose, ammonia, electrolytes & urinalysis) & skull x-rays
   b. Loss of consciousness
      i. DDx = **AEIOUS TIPS** = Alcohol, Epilepsy, Environment (temp), Insulin (+/-), Overdose, uremia (electrolytes), Trauma, Infection, psychogenic, Stroke
      ii. Tx = Coma cocktail, dextrose, thiamine, naloxone & O2
   c. ↑ ICP → HTN, bradycardia & bradypnea = Cushing's triad
   d. Tx = ventilation to keep PaCO2 at 30-40mmHg, controlling fever, administration of osmotic diuretics (mannitol), corticosteroids & even bony decompression (burr hole)
5. E = Exposure
   a. Remove all clothes without moving pt (cut off if necessary)
   b. Examine all skin surfaces & back for possible exit wounds
   c. Ensure patient not at risk for hypothermia (small children)

SECONDARY SURVEY

1. Identify all injuries, examine all body orifices
2. Periorbital & mastoid hematomas ("raccoon eyes" & Battle's sign), hemotympanum & CSF otorrhea/rhinorrhea → basilar skull fractures
3. The Glasgow Coma Scale should be performed

Finding	**Points**	**Finding**	**Points**
Eye opening		***Motor response***	
Spontaneous	4	To command	6
To voice	3	Localizes	5

To stimulation (pain) No response	2 1	Withdraws Abnormal flexion Extension No response	4 3 2 1
Verbal response Oriented Confused Incoherent Incomprehensible No response	 5 4 3 2 1		
GCS < 8 indicates severe neurologic injury, intubation must be performed to secure airway			

4. Deaths from abdominal trauma are usually from sepsis due to hollow viscus perforation or hemorrhage if major vessels are penetrated
5. Diagnostic peritoneal lavage, abdominal Utz, or CT scan (if pt stable) suggests abdominal injury, if pt unstable Dx is by surgical laparotomy, Tx = surgical hemostasis
6. If blood noted at urethra perform retrograde urethrogram before placement of a bladder catheter, hematuria suggests significant retroperitoneal injury & requires CT scan for evaluation, take pt to OR for surgical exploration if unstable
7. Check for compartment syndrome of extremities, Si/Sx = tense, pale, paralyzed, paresthetic & painful extremity, tx = fasciotomy

SHOCK

Type	**Cardiac output**	**Pulmonary capillary wedge pressure**	**Peripheral vascular resistance**
Hypovolemic	↓	↓	↑
Cardiogenic	↓	↑	↑
Septic	↑	↓	↓

Correction of defect in shock

Type	**Defect**	**1st-line treatment**
Hypovolemic	↓ preload	2 large bore IVs, crystalloid or colloid infusions, replace blood losses with the **3 for 1** rule = give 3L of fluid per liter of blood loss
Cardiogenic	Myocardial failure	Pressors-dobutamine first line, can add dopamine &/or norepinephrine, supplemental O2
Septic	↓ peripheral vascular resistance	Norepinephrine to vasoconstrict peripheral arterioles, prevent progression to multiple organ dysfunction syndrome (MODS), give IV antibiotics as indicated, supplemental O2

1. Shock in trauma can be neurogenic or hypovolemic
2. Neurogenic due to blood pooling in splanchnic bed & muscle from loss of autonomic innervation
3. Tx = usually self-limiting, can be managed by placing pt in supine or Trendelenburg position

BURNS

PARTIAL THICKNESS

1. 1^o & 2^o burns are limited to epidermis & superficial dermis
2. Si/Sx = skin is red, blistered, edematous, skin underneath blister is pink or white in appearance, very painful

3. Infection may convert to full-thickness burns

FULL THICKNESS

1. 3^o & 4^o burns affect all layers of skin & subcutaneous tissues
2. Si/Sx = skin is initially painless, dry, white, charred, cracked, insensate
3. 4^o burns also involve muscle & bone
4. All full-thickness burns require surgical treatment
5. % of body surface area (BSA) affected

Palm of hand	1%	Upper extremities	9%
Head and neck	9%	Lower extremities	18%
Anterior trunk	18%	Genital area	1%
Posterior trunk	18%		

In adults

6. Tx = resuscitation, monitor fluid status, remove eschars
    a. Consider any facial burns or burning of nasal hairs as a potential candidate for ARDS & airway compromise
    b. Fluid resuscitation
        i. Parkland formula = % BSA x weight (kg) x 4, formula used to calculate volume of crystalloid needed
        ii. Give ½ of fluid in first 8hr, remainder given over the next 16hr
    c. CXR to r/o inhalation injury
    d. Labs → PT/PTT, CBC, type & cross, ABGs, electrolytes, UA
    e. Irrigate & debride wound, IV & topical antibiotics (silver sulfadiazine, mafenide, Polysporin), tetanus prophylaxis & stress ulcer prophylaxis
    f. Transfer to burn center if pt is very young or old, burns >20% BSA, full-thickness burns >5% BSA, coexisting chemical or electrical injury, facial burns, or preexisting medical problems
    g. Make pt NPO until bowel function returns, pt will have extremely ↑ protein & caloric requirements with vitamin supplementation
    h. Excision of eschar to level of bleeding capillaries & split thickness skin grafts
    i. **Marjolin's ulcer = squamous cell carcinoma arising in an ulcer or burn**

NECK MASS DIFFERENTIAL

Disease	**Characteristics**	**Dx findings**	**Tx**
Congenital			
Torticollis	❖ Lateral deviation of head due to hypertrophy of unilateral sternocleidomastoid ❖ Can be congenital, neoplasm, infection, trauma, degenerative disease, or drug toxicity (particularly D_2 blockers = phenothiazines)	Rock hard knot in the sternocleidomastoid that is easily confused with the hyoid bone upon palpation	Muscle relaxants &/or surgical repair
Thyroglossal duct cyst	❖ **Midline** congenital cysts, which usually present in childhood	**Cysts elevate upon swallowing**	Surgical removal
Branchial cleft cyst	❖ **Lateral** congenital cysts, which usually do not present until adulthood, when they become infected or inflamed	**Do not elevate upon swallowing** Aspirate contains cholesterol crystals	Surgical excision

Cystic hygroma	❖ Occluded lymphatics, which usually present within first 2 years of life ❖ **Lateral or midline**	Translucent, benign mass, painless, soft & compressible	Surgical excision
Dermoid cyst	❖ **Lateral or midline** ❖ Soft fluctuant mass composed of an overgrowth of epithelium	**No elevation with swallowing**	Surgical excision
Carotid body tumor = paraganglioma	❖ Palpable mass at bifurcation of common carotid artery ❖ Not a vascular tumor, but originate from neural crest cell sin the carotid body within the carotid sheath ❖ Rule of 10: 10% malignant, 10% familial, 10% secrete catecholamines	**Pressure on tumor can cause bradycardia & dizziness**	Surgical excision
Acquired-Inflammatory			
Cervical lymphadenitis	❖ Bilateral lymphadenopathy is usually viral ,caused by EBV, CMV, or HIV ❖ Unilateral is usually bacterial, caused by S. aureus, group A & B Strep ❖ Other causes: ❖ Cat scratch fever (bartonella henselae), transmitted via scratch of young cats ❖ Scrofula due to military tuberculosis ❖ Actinomyces israelii → sinuses drain pus containing "sulfur granules" ❖ Kawasaki's syndrome ❖ Hodgkin's lymphoma	Fine-needle aspirate & culture	Per cause Viral → supportive, bacteria → IV antibiotics, Kawasaki's → aspirin, Lymphoma → chemotherapy
Thyroid			
Goiter	❖ Enlargement of thyroid gland ❖ Usually 2^{o} to decreased iodine intake, inflammation or use of goitrogens	Fine-needle aspirate, TSH, T3 levels	Treat underlying condition
Malignancy	❖ Papillary CA o **Most common cancer of thyroid** o Goo Px, 85% 5-yr survival ❖ Medullary CA o Intermediate Px o **Secretes calcitonin**, can use it to Dx & follow dz ❖ Follicular CA o Has good Px o Commonly metastasizes to bone & lungs ❖ Anaplastic CA o Has terrible Px (0% survival at 5yr)	Fine-needle aspirate	Surgical excision

RIGHT UPPER QUADRANT

Disease	**Characteristics**
Biliary colic	❖ Si/Sx = constant RUQ to epigastric pain

	❖ Utz → gallstones but no gallbladder wall thickening or pericholecystic fluid
Cholecystitis	❖ Si/Sx = fever, RUQ tenderness, **Murphy's sign** (inspiratory arrest upon deep palpation of RUQ) ❖ Labs → moderate to severe leukocytosis, ↑ LFTs, ↑ bilirubin
Pneumonia	❖ Si/Sx = pleuritic chest pain & fever ❖ CXR → infiltrate, labs → leukocytosis
Fitz-Hugh-Curtis syndrome	❖ Syndrome of periherpatitis caused by ascending Chlamydia or N. gonorrhoeae salpingitis ❖ Si/Sx = RUQ pain, fever, Hx or Si/Sx of salpingitis ❖ Labs → leukocytosis but normal bilirubin & LFTs ❖ Utz → normal gallbladder & biliary tree but fluid around the liver & gallbladder
Cholangitis	❖ Life threatening ❖ Si/Sx o **Charcot's triad** = fever, jaundice & RUQ pain o **Reynolds' pentad**: add hypotension & mental status change ❖ Labs → leukocytosis, blood Cx → enteric organisms, ↑ LFTs, ↑ bilirubin ❖ UTz & CT → biliary duct dilatation from obstructing gallstones ❖ Dx with ERCP or percutaneous transhepatic cholangiography (PTC)
Hepatitis	❖ Si/Sx = RUQ pain/tenderness, jaundice, fever ❖ Labs → ↑ LFTs, ↑ bilirubin, leukocytosis, (+) hepatitis, virus serologies ❖ Utz rule out other causes of RUQ pain
Appendicitis	❖ Si/Sx = RLQ pain/tenderness originally diffuse & then migrating to **McBurney's point** (1/3 distance from the anterior superior iliac spine to the umbilicus), fever, diarrhea ❖ Perform rectal exam to rule out retroperitoneal appendicitis ❖ Labs → leukocytosis, fecolith on plain film or abdominal CT ❖ Decision to take to OR based mostly on clinical picture
Yersinia enterocolitis	❖ Si/Sx = fever, diarrhea, severe RLQ pain make it hard to distinguish from appendicitis ❖ Labs → leukocytosis, plain films negative for fecolith
Ectopic pregnancy	❖ Si/Sx = crampy to constant lower abdominal pain, vaginal bleeding, tender adnexal mass & menstrual irregularity ❖ Labs → anemia, ↑hCG, culdocentesis reveals blood
Salpingitis/Tubo-ovarian abscess	❖ Si/Sx = lower abdominal/pelvic pain (constant to crampy, sharp to dull), purulent vaginal discharge, cervical motion tenderness, adnexal mass ❖ Labs → leukocytosis, wet smear → WBCs, endocervical Cx (+) for N. gonorrhoeae or Chlamydia ❖ Utz → TOA, CT scan can help r/o appendicitis
Meckel's diverticulum	❖ **1-10-100** rule: 1-2% prevalence, 1-10cm in length, 50-100cm proximal to ileocecal valve, or ruel of 2's: **2% of population, 2% are symptomatic (usually before age 2), remnants are roughly 2 in, found 2ft from ileocecal valve & found 2x as common in males** ❖ Si/Sx = GI bleed (melena, hematochezia), small bowel obstruction (intussusception, Littre's hernia), Meckel's diverticulitis (similar presentiaotn to appendicitis) ❖ Nuclear medicine gastric scan to detect gastric mucosa present in 50% of Meckel's diverticula or tagged RBC scan to detect bleeding source
Ovarian torsion	❖ Si/Sx = acute onset, sharp unilateral lower abdominal/pelvic pain, pain may be intermittent due to incomplete torsion, pain related to change in position, nausea &

	fever present, tender adnexal mass ❖ Utz & laparoscopy confirm Dx
Intussusception	❖ Most common in infants 5-10mo ❖ Si/Sx = infant crying with pulling legs up to abdomen, dark, red stool (**currant jelly**), vomiting, shock ❖ Barium or air contrast enema → diagnostic "coiled sparing" sign

LEFT UPPER QUADRANT (LUQ)

Disease	**Characteristics**
Peptic ulcer	❖ Si/Sx = epigastric pain relieved by food or antacids ❖ Perforated ulcers present with sudden upper abdominal pain, shoulder pain & GI bleed ❖ Labs → endoscopy or upper GI series
Myocardial infarction	❖ Si/Sx = chest pain, dyspnea, diaphoresis, nausea ❖ Labs → EKG, troponins, CK-MB
Splenic rupture	❖ Si/Sx = tachycardia, broken ribs, Hx of trauma, & hypotension ❖ **Kehr's sign** = left upper quadrant pain & referred left shoulder pain ❖ Labs → leukocytosis ❖ X-ray → fractured ribs, medially displaced gastric bubble ❖ CT scan of abdomen preferred method of Dx

LEFT LOWER QUADRANT (LLQ)

Disease	**Characteristics**
Diverticulitis	❖ Si/Sx = LLQ pain & mass, fever, urinary urgency ❖ Labs → leukocytosis ❖ CT scan & Utz → thickened bowel wall, abscess-do not do contrast enema
Sigmoid volvulus	❖ Si/Sx = elderly, chronically constipated patient, abdominal pain, distention, obstipation ❖ X-ray → **inverted-U**, contrast enema → **bird's beak deformity**
Pyelonephritis	❖ Si/Sx = high fever, rigors, costovertebral angle tenderness, Hx of UTI ❖ Labs → pyuria & (+) urine culture
Ovarian torsion	❖ See RLQ above
Ectopic pregnancy	❖ See RLQ above
Salpingitis	❖ See RLQ above

MIDLINE

Disease	**Characteristics**
Pancreatitis	❖ Si/Sx = severe epigastric pain radiating to the back nausea/vomiting, sign of hypovolemia because of "third spacing", ↓ bowel sounds ❖ In hemorrhagic pancreatitis, there are ecchymotic appearing skin findings in the flank (**Grey Turner's** sign) or periumbilical area (**Cullen's signs**) ❖ Labs → leukocytosis, ↑ serum & urine amylase, ↑ lipase ❖ X-ray → dilated small bowel or transverse colon adjacent to the pancreas, called **"sentinel loop"** ❖ CT → phlegmon, pseudocyst, encrosis, or abscess
Pancreatic pseudocyst	❖ Si/Sx = sequelae of pancreatitis, if pancreatitis Sx do not improve, may present with fever or shock in infected or hemorrhagic cases

	❖ CT & Utz → fluid-filled cystic mass
Abdominal aortic aneurysm (AAA)	❖ Si/Sx = usually aSx, rupture presents with back or abdominal pain & shock, compression on duodenum or ureters can cause obstructive Sx, palpable pulsatile periumbilical mass ❖ X-ray (cross-table lateral films), Utz, CT & aortography reveal aneurysm
Gastroesophageal reflux disease	❖ Si/Sx = position dependent (supine worse) substernal or epigastric burning pain, regurgitation, dysphagia, hoarse voice ❖ Dx by barium swallow, manometric or pH testing & esophagoscopy
Myocardial infarction	❖ See LUQ above
Peptic ulcer	❖ See LUQ above
Gastroenteritis	❖ Si/Sx = diarrhea, vomiting, abdominal pain, fever, malaise, headache ❖ Labs → stool studies not usually indicated except in severe cases

TREATMENT

1. Generally all above surgical conditions will require **NPO, NG tube, IV fluids, cardiac monitoring**
2. IV antibiotics as needed
3. Surgery for hemostasis, & life-threatening conditions, consulting appropriate surgical service (O.B., pediatric surgery, etc.) as indicated

ESOPHAGUS

HIATAL HERNIA

1. The majority of patients with reflux have hiatal hernia (80%)
2. Si/Sx = same as GERD
3. Dx = barium swallow to identify anatomic variations
4. There are two types of hiatal hernias
    a. Type I
        i. Sliding hiatal hernia, is more common than the type II hernia
        ii. It is the movement of the gastroesophageal junction & stomach up into the mediastinum
        iii. Tx = medical as per GERD according to the degree of Sx present
    b. Type II
        i. Herniation of the stomach fundus through the diaphragm parallel to the esophagus
        ii. Tx = mandatory surgical repair due to ↑ risk of strangulation

ACHALASIA

1. The most common motility disorder, affects 70% of pts with scleroderma
2. Loss of esophageal motility & failure of lower esophageal sphincter (LES) relaxation, may be caused by ganglionic degeneration or Chagas' disease, results in the dilatation of the proximal esophagus
3. Si/Sx = dysphagia of both solids & liquids, weight loss & repulsion of undigested fooddsuffs that may produce a foul odor
4. May ↑ risk of esophageal CA because stasis promotes development of Barrett's esophagus
5. Dx
    a. Barium swallow → dilatation of the proximal esophagus with subsequent narrowing of the distal esophagus, studies may also reveal esophageal diverticula
    b. Manometry → ↑ LES pressure & diffuse esophageal spasm
6. Tx
    a. Endoscopic dilation of LES with balloon cures 80% of pts

b. Alternative is a myotomy with a modified fundoplication
c. Surgical Tx may be used for palliation in patients with scleroderma, who may experience dysphagia or severe reflux

ESOPHAGEAL DIVERTICULA (ZENKER'S DIVERTICULUM)

1. Proximal diverticula are usually Zenker's
2. Pulsion diverticula involving only the mucosa, located between the thyropharyngeal & cricopharyngeus muscle fibers (condition a/w muscle dysfunction/spasms)
3. Si/Sx = dysphagia, regurgitation of solid foods, choking, left-sided neck mass & bad breath
4. Dx = clinically + barium swallow
5. Tx = myotomy of criocpharyngeus muscle & removal of diverticulum

ESOPHAGEAL TUMORS

1. Squamous cell carcinoma
    a. Most common esophageal cancer, alcohol & tobacco synergistically ↑ risk of development
    b. Most commonly seen in men in the sixth decade of life
2. Adenocarcinoma
    a. Seen in pts with chronic reflux → Barrett's esophagus = squamous to columnar metaplasia
    b. 10% of Barrett's patients will develop adenocarcinoma
3. Si/Sx for both = **dysphagia**, weight loss, hoarseness, tracheoesophageal fistula, recurrent aspiration & may include symptoms of metastatic disease
4. Dx = barium study demonstrates **classic apple-core lesion**, Dx confirmed with endoscopy with biopsy to confirm diagnosis, CT of abdomen & chest is also performed to determine extent of spread
5. Tx = esophagectomy with gastric pull-up or colonic interposition with or without chemotherapy/radiation
6. Px = poor unless resected prior to spread (very rare); however, palliation should be attempted to restore effective swallowing

GASTRIC TUMORS

1. Benign tumors comprise <10% of all gastric tumors, most commonly are polyps & Leiomyoma
2. Stomach CA most common after 50yr, ↑ incidence in men
3. Linked to blood group A (suggesting genetic predisposition), immosuppression & environmental factors
4. Nitrosamines, excess salt intake, low fiber intake, *H. pylori*, achlorhydria, chronic gastritis are all risk factors
5. Almost always adenocarcinoma, usually involves antrum, rarely fundus, aggressive spread to nodes/liver
6. Rarer gastric tumors = lymphoma & leiomyosarcoma
7. Several classic physical findings in metastatic gastric cancers
    a. **Virchow's node= large rock-hard supraclavicular node**
    b. **Krukenberg tumor = mucinous, signet-ring cells that metastasize from gastric CA to bilateral ovaries, so palpate for ovarian masses in women**
    c. **Sister Mary Joseph sign = metastasis to umbilicus, feel fro hard nodule there, a/w poor prognosis**
    d. **Blumer's shelf = palpable nodule superiorly on rectal exam, caused by metastasis of GI cancer**
8. Linitis plastica
    a. Infiltrating, diffuse CA, invariably fatal within months
    b. **This is the most deadly form of gastric cancer**

9. Lymphoma causes 4% of gastric cancers, better Px than adenocarcinoma, a/w *H. pylori* infection
10. Si/Sx for all = weight loss, anemia, anorexia, GI upset
11. Dx = biopsy
12. Tx = mostly palliative, combination surgery & chemotherapy when tolerated
13. Px = about 5% survival at 5yr

HERNIA

INGUINAL HERNIAS

1. Most common hernia, more common in men
2. Direct type = viscera protrudes directly through abdominal wall at Hesselbach's triangle (inferior epigastric artery, rectus sheath & inguinal ligament), medial to inferior epigastric artery
3. Indirect type is more common (2/3 are indirect), pass lateral to inferior epigastric artery into spermatic cord covered by cremasteric muscle
4. Si/Sx = intermittent groin mass with bowel sounds that appear during Valsalva maneuvers
5. DDx = femoral hernias, which protrude below the inguinal ligament
6. Dx = physical exam, some unable to completely differentiate until surgery
7. Tx = surgical repair with mesh placement

FEMORAL HERNIAS

1. More common in women
2. Si/Sx = bulge above or below the inguinal ligament, ↑ risk of incarceration
3. Dx = clinical &/or surgical
4. Tx = surgical repair should not be delayed

VISCERAL HERNIAS

1. Cause intestinal obstruction
2. Si/Sx = as per bowel obstruction (e.g., obstipation, abdominal pain, etc.)
3. X-ray → no gas in rectum, distended bowel, air-fluid levels
4. DDx = other causes of bowel obstruction such as adhesions, external hernia, malignancy, etc.
5. Dx = clinical or surgical
6. Tx = surgical repair if hernia is not reducible

Hernia Definitions

Combined (pantaloon)	Concurrent direct & indirect hernias
Sliding	Part of the hernia sac wall is formed by a visceral organ
Richter's	Part of the bowel is trapped in the hernia sac
Littre's	Meckel's diverticulum contained inside hernia
Reducible	Able to replace herniated tissue to its usual anatomic location
Incarcerated	Hernias that are not reducible
Strangulated	Incarcerated hernia with vascular compromise → ischemia
Incisional	Herniation through surgical incision, commonly 2^o to wound infection

HEPATIC TUMORS

BENIGN TUMORS

1. Hemangioma is most common benign tumor of the liver
2. Hepatic adenoma incidence related to oral contraceptives
3. Adenomas may rupture → severe intraperitoneal bleed
4. Dx = Utz, CT scan

5. Tx =Surgery only indicated if danger of rupture, patient symptomatic, or large amount of liver involved

MALIGNANT TUMORS

1. Metastases are the most common malignant hepatic tumors
2. Hepatocellular CA is the most common 1^{o} hepatic malignancy
    a. Note also called "hepatoma", incorrectly implying benign tumor (historical misnomer)
    b. Most common malignancy in the world, endemic is SEA & sub-Saharan Africa due to vertical transmission of HBV
    c. Associated with cirrhosis, HBV & HCV infection, alcoholism, hemochromatosis, Wilson's disease
    d. Si/Sx = weight loss, jaundice, weakness, dull & constant RUQ or epigastric pain, hepatomegaly, palpable mass or bloody ascites may also be present
    e. Labs $\rightarrow \uparrow$ serum alkaline phosphatase, $\uparrow$ bilirubin, (+) hepatitis B or C virus serologies, commonly causes $\uparrow$ α-fetoprotein (AFP) level
    f. Dx = Utz or CT scan
    g. Tx = surgical resection & its variations is the treatment modality that offer the greatest survival rates
3. Hemangiosarcoma
    a. Associated with toxic exposure to polyvinyl chloride, Thorotrast, & arsenic
    b. Dx = Utz or CT scan
    c. Tx = surgical resection, may be curative if liver function is normal; in presence of cirrhosis, usually not effective.

GALLBLADDER

CHOLELITHIASIS = GALLSTONES

1. Higher incidence in women, multiple pregnancies, obesity (**the 4Fs = female, forty, fertile, fat**)
2. 10% of US population has gallstones, complications of the disorder are what necessitate intervention
3. Pts =20yr with gallstones should be worked up for congenital spherocytosis or hemoglobinopathy
4. Si/Sx = asymptomatic by definition
5. Dx = Utz, often incidental finding that does not require therapy
6. Tx
    a. Asymptomatic pts with gallstones do not require cholecystectomy unless there is an $\uparrow$ risk for developing cancer
    b. Pts with a porcelain gallbladder (calcified gallbladder walls) & those of Native American descent with gallstones are at $\uparrow$ risk of developing gallbladder cancer & should receive a cholecystectomy

BILIARY COLIC

1. Due to gallstone impaction in cystic or common bile duct
2. **The vast majority of people who have asymptomatic gallstones WILL NEVER progress to biliary colic** (2-3% progress per year, lifelong risk = 20%)
3. Sx = sharp colicky pain made worse by eating, particularly fats
4. May have multiple episodes that resolve, but eventually this condition will lead to further complications so surgical resection of the gallbladder is required
5. Dx = Utz, ERCP
6. Tx = cholecystectomy to prevent future complications

CHOLECYSTITIS

1. Cholecystitis is due to 2^{o} infeciton of obstructed gallbladder
    a. The EEEK! Bugs: Escherichia coli, Enterobacter cloacae, Enterococcus, Klebsiella spp.
    b. Si/Sx = sudden onset, severe, steady pain in RIQ/epigastrium; muscle guarding/rebound; **(+) Murphy's sign** (RUQ palpation during inspiration causes sharp pain & sudden cessation of inspiration)
    c. Labs → leukocytosis (may be over 20,000 in emphysematous cholecystitis = presence of gas in gallbladder wall), ↑ AST/ALT, ↑ bilirubin
    d. Dx = Utz ↑ gallstones, pericholecystic fluid & thickened gallbladder wall, if results equivocal can confirm with radionuclide cholescintigraphy (e.g., HIDA scan)—CT scan is usually not the test of choice to diagnose cholecystitis
    e. Tx
        i. NPO, IV hydration & third-generation cephalosporins or mezlocillin +/- aminoglycoside & Flagyl
        ii. Demerol better for pain as morphine causes spasm of the sphincter of Oddi
        iii. Surgical resection if unresponsive or worsening

CHOLEDOCHOLITHIASIS

1. Passage of stone through the cystic duct, can obstruct common bile duct (CBD)
2. Si/Sx = obstructive jaundice, ↑ conjugated bilirubin, hypercholesterolemia, ↑ alkaline phosphatase
3. Dx = ultrasound (Utz) → CBD >9mm diameter (Utz first line for Dx)
4. **Passage of stone to CBD can cause acute pancreatitis if the ampulla of Vater is obstructed by the stone**
5. Tx = laparoscopic cholecystectomy

ASCENDING CHOLANGITIS

1. Results from 2^{o} bacterial infection of obstructed CBD, facilitated by obstructed bile flow
2. Obstruction usually due to choledocholithiasis, but can be 2^{o} to strictures, foreign bodies (e.g., surgical clips form prior abdominal surgery) & parasites
3. **Charcot's triad = jaundice, RUQ pain, fever (85% sensitive for cholangitis)—for Reynold's pentad add altered mental status & hypotension**
4. Dx = Utz or CT → common bile duct dilation, definitive Dx requires Endoscopic retrograde pancreaticoduodenoscopy (ERCP) or percutaneous transhepatic cholangiography (PTC)
5. This is a life-threatening emergency!
6. Tx
    a. NPO, IV hydration, IV amipicillinc/gentamicin/Flagyl or mezlocillin/Flagyl
    b. ERCP or PTC to decompress the biliary tree & remove obstructing stones

CANCER

1. Very rare, usually occurs in seventh decade of life
2. More commonly seen in females, gallstones are risk factors for developing cancer
3. Most common 1^{o} tumor of gallbladder is adenocarcinoma
4. Frequenlty seen in Far East, a/w Clonorchis sinesis (liver fluke) infestation
5. When the tumor occurs at the confluence of the hepatic ducts forming the common duct, the tumor is called "**Klatskin's tumor**" (mean survival = 9-12 mo, no Tx, invariably lethal)
6. **Courvoisier's law** = gallbladder enlarges when CBD is obstructed by pancreatic CA but not enlarged when CBD is obstructed by stone
7. Courvoisier's sing is a palpable gallbladder
8. Si/Sx = as for biliary colic but persistent
9. Dx = Utz or CT to show tumor, but preoperative Dx of gallbladder CA is often incorrect
10. Tx = palliative stenting of bile ducts, can consider surgical resection for palliation only

11. Px = terminal, almost all pts are dead within 1yr of Dx

EXOCRINE PANCREAS

ACUTE PANCREATITIS

1. Pancreatic enzymes autodigest pancreas → hemorrhagic fat necrosis, calcium deposition & sometimes formation of pseudocysts (cysts not lined with ductal epithelium)
2. Most common causes in US = gallstones & alcohol
3. Other causes include infection, trauma, radiation, drug (thiazides, AZT, protease inhibitors), hyperlipidemia, hypercalcemia, vascular events, tumors, scorpion sting
4. Si/Sx = severe abdominal pain, prostration (fetal position opens up retroperitoneal space & allows more room for swollen pancreas), hypotension (due to retroperitoneal fluid sequestration), tachycardia, fever, ↑ serum amylase (90% sensitive)/lipase, hyperglycemia, hypocalcemia
5. Dx = clinically &/or abdominal CT, **classic x-ray finding = sentinel loop or colon cut-off sign** (loop of distended bowel adjacent to pancreas)
6. **Classic physical findings = Grey Turner's sign (discoloration of flank) & Cullen' sign (periumbilical discoloration)**
7. Tx is aimed at decreasing stress to pancreas
    a. NPO until symptoms/amylase subside; TPN if NPO for >7-10 days
    b. Demerol to control pain
    c. IV fluid resuscitation
    d. Alcohol withdrawal prophylaxis
    e. May require ICU admission if severe
8. Complications = abscess, pseudocysts, duodenal obstruction, shock lung & acute renal failure
9. Repeated bouts of pancreatitis cause chronic pancreatitis, resulting in fibrosis & atrophy of the organ with early exocrine & later endocrine insufficiency
10. Prognosis of acute pancreatitis determined by **Ranson's criteria:**

On Admission	**Within 24-48hrs**
Age >55, WBCs >16,000/mL, AST >250IU/dL LDH > 350, blood glucose >200, base deficit >4mEq/L	↓ HCT > 10%, BUN rise > 5mg/dL, serum calcium <8mg/dL, arterial pO2 <60mmHg, fluid sequestration >6L

Risk of mortality: 20% if 3-4 signs, 40% if 5-6 signs, 100% if 7 or more signs

PANCREATIC PSEUDOCYST

1. Collection of fluid in pancreas surrounded by a fibrous capsule, no communication with fibrous ducts
2. **Suspect anytime a patient is readmitted with pancreatitis complaints within several weeks of being discharged after a bout of pancreatitis**
3. 2^o to pancreatitis or trauma as in steering wheel injury
4. Dx = Abd Utz/CT
5. Tx = percutaneous surgical drainage or pancreaticogastrostomy (creation of surgical fistula to drain cyst into the stomach), but small cysts will resorb on their own
6. New cysts contain blood, necrotic debris, leukocytes; old cysts contain straw-colored fluid
7. Can become infected with purulent contents, causing peritonitis, after rupture

PANCREATIC CANCER

1. Epid = 90% are adenocarcinoma with 60% of these arising in the head of pancreas
2. More common in African Americans, cigarette smokers & males, linked to chronic pancreatitis & diabetes mellitus
3. Si/Sx = jaundice, weight loss, abdominal pain, **classic sign is Trousseau's syndrome = migratory thrombophlebitis, occurs in 10% of patients**

4. Frequently invades duodenum, ampulla of Vater, common bile duct & can also cause biliary obstruction
5. Dx = Labs: ↑ bilirubin, ↑ alk phos, ↑ CA 19-9 (not diagnostic), **CT scan**
6. Tx = Whipple's procedure, resection of pancreas, part of small bowel, stomach, gallbladder
7. Site of cancer & extent of disease at time of diagnosis determines Px: usually very poor, 5-yr survival rate after palliative resection is 5%

ENDOCRINE PANCREATIC NEOPLASM

1. Insulinoma due to hyperplasia of insulin producing β-cells
2. Hyperglucagonemia = α cell tumor → hyperglycemia & exfoliative dermatitis
3. Zollinger-Ellison syndrome
    a. Dx = clinically, elevated serum levels of insulin, glucagon, or gastrin
    b. Tx = surgical resection of the tumor

SMALL INTESTINE

SMALL BOWEL OBSTRUCTION (SBO)

1. **Most common surgical condition of the small bowel**
2. Causes = peritoneal adhesions, hernias & neoplasms in order of occurrence in the adult population
3. Other causes include Crohn's, Meckel's, radiation enteritis, gallstone ileus & inflammation
4. Si/Sx = crampy abdominal pain, nausea, vomiting, lack of flatus, abdominal tenderness, abdominal distention & hyperactive, high-pitched bowel sounds
5. DDx= paralytic ileus (similar Si/Sx)
6. Numerous etiologies including abdominal surgery, hypokalemia, narcotics, anticholinergics, acute pancreatitis, gastroenteritis & cholecystitis
7. Dx = abdominal series → distended loops of small bowel proximal to the obstruction upright film → air-fluid levels or free air beneath the diaphragm on a PA chest film
8. Tx
    a. Conservative Tx = IV fluids, NG tube decompression & Foley catheter, partial obstructions may be successfully treated with conservative therapy
    b. Surgical candidates receive antibiotics to include both anaerobic & gram-negative coverage
    c. Objective of surgery is to remove obstruction & resect nonviable bowel

SMALL BOWEL NEOPLASMS

1. Leiomyoma is most common benign tumor of the small bowel
2. Si/Sx = pain, anemia, weight loss, nausea & emesis, common complication is obstruction that is caused primarily by Leiomyomas
3. Carcinoid tumors (small bowel is the second most common location, appendix is first) → cutaneous flushing, diarrhea & respiratory distress
4. Malignant neoplasms in order of decreasing incidence: **adenocarcinoma, carcinoid, lymphoma & sarcomas**
5. Dx = biopsy; not necessarily reliable
6. Tx = surgical resection of primary tumor along with lymph nodes & liver metastases if possible

COLON

COLONIC POLYPS

1. Classified as **neoplastic, hamartomas, inflammatory, or miscellaneous**
2. Neoplastic polyps are most commonly adenomas & can be classified as either tubular adenoma (smallest malignant potential), tubulovillous adenoma, or villous adenoma (greatest malignant potential)

3. The mean age of patients with polyps is 55, incidence ↑ with age
4. 50% of polyps occur in the sigmoid or rectum
5. Si/Sx = intermittent rectal **bleeding** is most common presenting complaint
6. Dx = colonoscopy, sigmoidoscopy, always consider family Hx
7. Tx
    a. Colonoscopic polypectomy or laparotomy
    b. If invasive adenocarcinoma is found, a colectomy is not mandatory if gross & microscopic margins are clear, if tissue is well-differentiated without lymphatic or venous drainage & polyp stalk does not invade

FAMILIAL POLYPOSIS SYNDROMES

1. Familial adenomatous polyposis (FAP)
    a. Si/Sx = autosomal dominant inheritance of APC gene, abundant polyps throughout the colon & rectum beginning at puberty
    b. Gardner's syndrome consists of polyposis, desmoid tumors, osteomas of mandible or skull, & sebaceous cysts
    c. Turcot's syndrome is polyposis with medulloblastoma or glioma
    d. Dx = family Hx, colonoscopy, presence of congenital hypertrophy of retinal pigment epithelium predicts FAP with 97% sensitivity
    e. Tx = colectomy & upper GI endoscopy to rule out gastroduodenal lesions—a favored operation is an abdominal colectomy, mucosal proctectomy & ileoanal anastomosis
2. Peutz-Jeghers syndrome
    a. Si/Sx = autosomal dominant inheritance, nonneoplastic hamartomatous polyps in stomach, small intestine & colon, skin & mucous membrane hyperpigmentation, **particularly freckles on lips**
    b. - **risk of developing CA in other tissues** (e.g., breast, pancreas)
    c. Dx = clinical & family Hx
    d. Tx = careful, regular monitoring for malignancy
3. Juvenile polyposis syndromes
    a. Examples include juvenile polyposis coli, generalized juvenile gastrointestinal polyposis & Cronkhite-Canada syndrome
    b. Si/Sx = hamartomatous polyps & thus carry decreased malignant potential, similar to Peutz-Jeghers, patients with familial juvenile polyposis carry increased risk of gastrointestinal cancer
    c. Dx = clinical & family Hx
    d. Tx = polypecotmy is generally reserved for symptomatic polyps

DIVERTICULAR DISEASE

1. General characteristics
    a. 50% of people will have diverticula, ↑ incidence between fifth & eighth decade of life in Western countries, but **only 10-20% cause Sx**
    b. True diverticula = herniations involving the full bowel wall thickness
    c. True diverticula are rare, often found in cecum & ascending colon
    d. False diverticula = only mucosal herniations through muscular wall
    e. False diverticula are common, >90% found in sigmoid colon
    f. It is believed that ↑ intraluminal pressure (perhaps promoted by ↓ fiber diet) causes herniation
2. Diverticulosis
    a. Presence of multiple false (acquired) diverticula

b. Si/Sx = 80% are aSx & are found incidentally, can cause recurrent abdominal pain in left lower quadrant & changes in bowel habits, 5-10% of pts present with lower GI hemorrhage that can be massive
c. Dx = colonoscopy or barium enema to reveal herniations
d. Tx
    i. aSx pts should ↑ fiber content of diet, ↓ fatty food intake & avoid foods that exacerbate diverticular obstruction (e.g., seeds)
    ii. Surgical therapy for uncomplicated diverticulosis is **rare**
    iii. See below for management of GI hemorrhage

3. Diverticulitis
    a. Diverticular infxn & macroperforation resulting in inflammation
    b. The inflammation may be limited to the bowel, extend to pericolic tissues, form an abscess, or result in peritonitis
    c. Si/Sx
        i. Left lower quadrant pain, diarrhea or constipation, fever, anorexia & leukocytosis—**bleeding is more consistent with diverticulosis, not diverticulitis**
        ii. **Life-threatening complications from diverticulitis include large perforations, abscess or fistula formation & obstruction**
        iii. The most common fistula a/w diverticular dz is colovesicular (presenting with recurrent urinary tract infections)
    d. Dx
        i. CT scan may demonstrate edema of the bowel wall & the presence/location of formed abscesses
        ii. Barium enema & colonoscopy are generally contraindicated for the acute pt, but if the pt's Sx point to obstruction or to the presence of a fistula, a contrast enema is warranted
    e. Tx
        i. Majority of pts respond to conservative Tx with IV hydration, antibiotics with anaerobic coverage & NPO orders
        ii. Abscess requires CT- or Utz-guided percutaneous drainage
        iii. If pt suffers recurrent bouts after acute resolution, a sigmoid colectomy is usually considered on an elective basis
        iv. Perforation or obstruction → resection of affected bowel & construction of a temporary diverting colostomy & a Hartman pouch—reanastomosis performed 2-3 months postop

GI HEMORRHAGE

1. **Bright-red blood per rectum** (BRBPR) usually points to bleeding in the **distal small bowel or colon**, although a proximal bleeding site must be considered
2. Massive lower GI hemorrhage is usually caused by diverticular disease, angiodysplasia, ulcerative colitis, ischemic colitis, or a solitary ulcer
3. Chronic rectal bleed is usually due to hemorrhoids, fissures, CA, or polyps
4. Dx
    a. Digital rectal exam (DRE) & visualization with an anoscope & sigmoidoscope to locate & Tx obvious bleeding site
    b. Endosocpy to evaluate for an upper gastrointestinal bleed
    c. Angiography if pt continues to bleed despite r/o upper GI source
    d. If bleeding is minimal/stopped or angiography is indeterminate & the pt is stable, the bowel should be prepped & colonoscopy performed
    e. Tagged RBC scan or barium enema if colonoscopy is non-Dx
5. Tx

a. IV fluids & transfusions as needed to maintain hemodynamic stability
b. Surgery is fortunately rarely required & should be considered only if bleeding persists (over 90% of bleeding ceases spontaneously) despite intervention

LARGE INTESTINE OBSTRUCTION

1. Accounts for 15% of obstructions—most common site is sigmoid colon
2. 3 most common causes are **adenocarcinoma, scarring 2^{o} to diverticulitis & volvulus—consider adhesions if pt had previous abdominal surgery**
3. Other causes are fecal impaction, inflammatory disorders, foreign bodies & other benign tumors
4. Si/Sx = abdominal distention, crampy abdominal pain, nausea/vomiting
5. **X-ray ® distended proximal colon, air-fluid levels, no gas in rectum**
6. Dx = clinical + x-ray, consider barium enema if x-rays are equivocal—**DO NOT GIVE BARIUM ORALLY WITH SUSPECTED OBSTRUCITON**
7. Tx = emergency laparotomy if cecal diameter >12cm or for severe tenderness, peritonitis, sepsis, free air
8. Pseudo-obstruction (**Ogilvie's syndrome**)
    a. The presence of massive right-sided colon dilatation with no evidence of obstruction
    b. Tx = colonoscopy & rectal tube for decompression

VOLVULUS

1. Rotation of the large intestine along its mesenteric axis—twisting can promote ischemic bowel, gangrene & subsequent perforation
2. Most common site is **sigmoid** (70%) followed by **cecum** (30%)
3. **Commonly occurs in elderly individuals**
4. Si/Sx = obstructive symptoms, including distention, tympany, rushes & high-pitched bowel sounds
5. Dx = clinical, confirmed by radiographic studies
    a. X-ray → dilated loops of bowel with loss of haustra with **a kidney bean appearance**
    b. Barium enema → a narrowing mimicking a **"bird's beak" or "ace of spades"** picture with point of beak pointing to site of bowel rotation
6. Tx
    a. Sigmoidoscopy or colonoscopy for decompression
    b. If not successful, laparotomy with a two-stage resection & anastomosis is necessary
    c. Cecal volvulus is treated with cecopexy (attachment of mobile cecum to peritoneal membrane) or right hemicolectomy

COLON CANCER

1. Epidemiology
    a. Second leading cause of cancer deaths
    b. Low-fiber, high-fat diet may contribute to risk of development—**while this has been classically taught it remains controversial & recent data suggest otherwise**
    c. Genetic influences include tumor suppressor & proto-oncognes
    d. Lynch syndromes I & II or hereditary nonpolyposis colorectal cancer (HNPCC)
        i. **Lynch syndrome I** is an autosomal dominant predisposition to colorectal cancer with right sided predominance (70% proximal to the splenic flexure)
        ii. **Lynch syndrome II** shows all of the features of Lynch syndrome I & also causes extracolonic cancers, particularly endometrial carcinoma, carcinoma of the ovary, small bowel, stomach & pancreas, & transitional cell CA of the ureter & renal pelvis

2. Screening
    a. >40yr of age without risk factors (strong family Hx, ulcerative colitis, etc.) → yearly stool occult blood tests, flexible sigmoidoscopy q3-5yr or colonoscopy q10yr or barium enema q5-10yr
    b. Colonoscopy/barium enema if polyps found
    c. Pts with risk factors require more frequent & full colonoscopies
3. Dx
    a. Endoscopy or barium enema—biopsy not essential
    b. Obtain preoperative carcinoembryonic antigen (CEA) to follow disease, these levels will be elevated before any physical evidence of disease
4. Surgical = resection and regional lymph node dissection
5. Adjuvant Tx for metastatic dz = 5-fluorouracil (+) leucovorin or levamisole → 30% improvement in survival
6. Follow-up
    a. Hx & physical & CEA level q3mo for 3yr then follow up every 6mo for 2yr
    b. Colonoscopy at 6mo, 12mo & yearly for 5yr
    c. CT & MRI for suspected recurrences

RECTUM AND ANUS

HEMORRHOIDS

1. A varicosity in the lower rectum or anus caused by congestion in the veins of the hemorrhoidal plexus
2. Si/Sx = anal mass, bleeding, itching, discomfort
3. The presence or absence of pain depends on the location of the hemorrhoid: internal hemorrhoid is generally not painful whereas an external hemorrhoid can be extremely painful
4. **Thrombosed external hemorrhoid**
    a. Not a true hemorrhoid, but subcutaneous external hemorrhoidal veins of the anal canal
    b. It is classically **painful** tense, bluish elevation beneath the skin or anoderm
5. Hemorrhoids are classified by degrees
    a. 1^o = no prolapse
    b. 2^o = prolapse with defecation, but returns on its own
    c. 3^o = prolapse with defecation or straining, require manual reduction
    d. 4^o = not capable of being reduced
6. Dx = H&P, inspection of the perianal area, digital rectal exam, anoscopy & sigmoidoscopy
7. Tx = conservative therapy consists of a high-fiber diet, Sitz baths, stool bulking agents, stool softeners, cortisone cream, astringent medicated pads
8. Definitive Tx = sclerotherapy, cryosurgery, rubber band ligation & surgical hemorrhoidectomy

FISTULA-IN-ANO

1. Communication between the rectum to the perianal skin, usually secondary to anal crypt infection
2. Infection in the crypt forms abscess then ruptures & a fistulous tract is formed, can be seen in Crohn's disease
3. Si/Sx = intermittent or constant discharge, may exude pus, incontinence
4. Dx = physical exam
5. Tx = fistulotomy
6. factors that predispose to maintenance of fistula patency = **FRIEND** = Foreign body, Radiation, Infeciton, Epithelialization, Neoplasm, Distal obstruction

ANAL FISSURE

1. epithelium in the anal canal denuded 2^o to passage of irritating diarrhea & a tightening of the anal canal related to nervous tension

2. Si/Sx = **classic** presentation, a severely painful bowel movement a/w bright-red bleeding
3. Dx = anoscopy
4. Tx = stool softeners, dietary modifications & bulking agents
5. Surgical Tx = lateral internal sphincterotomy if painis unbearable & fissure persists

RECTAL CANCER
1. More common in males
2. Si/Sx = **rectal bleeding**, obstruction, altered bowel habits & tenesmus
3. Dx = colonoscopy, sigmoidoscopy, biopsy, barium enema
4. Tx = sphincter-saving surgery, adjuvant Tx for rectal cancer with positive nodal metastasis or transmural involvement includes radiation therapy & 5-FU chemotherapy

ANALCANCER
1. Most commonly squamous cell CA, others include transitional cell, adenocarcinoma, melanoma & mucoepidermal
2. Risk factors include fistulas, abscess, infections & Crohn's disease
3. Si/Sx = **anal bleeding**, pain & mucus evacuation
4. Dx = biopsy
5. Tx = chemotherapy & radiation

BREAST
CANCER RISKS
1. Risk increased by
    a. #1 factor is gender (1% of breast cancers are in men)
    b. Age (#1 factor in women)
    c. Young first menarche (<11yr)
    d. Old first pregnancy (>30yr)
    e. Late menopause (>50yr)
    f. Family history defined as 1^{o} relative with cancer at a young age (95% of cancers are not familial)
2. Risk NOT increased by caffeine, sexual orientation (lesbian)
3. Vitamin E does NOT protect against breast cancer
4. While breast cancers can be asymptomatic, others can present with nipple discharge (unilateral), pain, nipple retraction, dimpling & nipple rash
5. Remember, **most breast cancers develop in the upper outer quadrants**
6. Most common types of cancer are invasive ductal carcinoma (majority), invasive lobular CA & inflammatory CA

MASTALGIA
1. Cyclical or noncyclical breast pain NOT due to lumps
2. Pain worse with respiration may be due to Tietze syndrome (costochondritis)
3. Mondor's disease = thoracoepigastric vein phlebitis → skin retraction along vein course
4. Dx = clinical
5. Tx = danazol, works by inducing amenorrhea (hirsutism & weight gain side effects)

FIBROADENOMA (FA)
1. Most common tumor in teens & young women (peak in 20s)
2. FAs grow rapidly, no increased risk for developing CA
3. Dx = clinical
4. Tx NOT required, often will resorb within several weeks, reevaluation after a month is standard

CYSTS

1. Most common tumor in 35-50yr-olds, rarely postmenopausal, arise in terminal ductal lobular unit
2. Cysts can arise overnight.
3. No clinical significance, can be easily drained
4. Si/Sx = pain & tenderness that varies with the menstrual cycle
5. Dx = history, breast exam & aspiration of any suspected cystic lesions, fluid that is drawn from a cyst is usually straw- or green-colored
6. If aspirated fluid is bloody, send for cytology to rule out cystic malignancy
7. Tx = drainage of cyst

DUCTAL CARCINOMA IN SITU (DCIS)

1. Usually nonpalpable, seen as irregularly shaped ductal calcifications on mammography
2. This is a true premalignancy, will lead to invasive ductal CA
3. Dx = core or excisional biopsy
4. Tx = excision of mass, ensure clean margins on excision (if not, excise again with wider margins) & add postop radiation that reduces rate of recurrence

INVASIVE DUCTAL CARCINOMA (IDC)

1. Most common breast cancer, occurs commonly in mid-30s to late 50s, forms solid tumors
2. **Tumor size is the most important Px factor,** node involvement is also important for Px
3. Dx = core or excisional biopsy—all breast masses in women >35yr require a tissue diagnosis, regardless of mammographic findings (i.e., even if mammography is not suspicious)
4. Tx = **either** modified radical mastectomy or lumpectomy with postop radiation, both give equivalent outcomes
5. Adjuvant tamoxifen or raloxifene can be added to reduce the risk of metastasis depending on the size of the primary tumor

INVASIVE LOBULAR CARCINOMA

1. Only 3-5% of invasive CA is lobular, present at age 45-56, vague appearance on mammogram
2. Patients have increased frequency of bilateral cancer
3. Dx = core or excisional biopsy
4. Tx = **either** prophylactic bilateral mastectomy at time of diagnosis, or mastectomy plus very close follow-up

PAGET'S BREAST DISEASE (NOT BONE DISEASE)

1. Presents with dermatitis/macular rash over nipple or areola
2. underlying ductal CA almost always present
3. Dx = biopsy
4. Tx = excision + radiation

INFLAMMATORY CARCINOMA

1. Breast has classic Sx of inflammation: redness, pain & heat
2. Rapidly progressive breast cancer, almost always widely metastatic at presentation
3. Dx = physical exam & biopsy
4. Tx = chemotherapy + radiation, Px poor

MAMOGRAPHY

1. Highly effective screening tool in all but young women
2. Dense breast tissue found in young women interferes with the test's sensitivity & specificity
3. All women over age 50 should have yearly mammograms (proven to ↓ mortality in these patients)

4. Women over age 40 recommended to have yearly or biannual mammograms (efficacy less clear in this group)
5. Women with 1^{o} relatives who have cancer should begin mammogram screening **10yr prior to the age at which the relative developed cancer**

UROLOGY

SCROTAL EMERGENCIES

1. Testicular torsion
    a. Usually peripubertal patient
    b. Si/Sx = acute onset testicular pain & edema, nausea & vomiting, tender, swollen testicle with transverse lie, **absent cremasteric reflex on affected side**
    c. Dx = Doppler Utz to assess testicular artery flow
    d. Tx = emergent surgical decompression, with excision of testicle if it infarcts
2. Epididymitis
    a. Si/Sx = unilateral testicular pain, dysuria, occasional urethral discharge, fever, leukocytosis in severe cases, painful & swollen epididymis
    b. Dx = history & physical, labs → UA can be negative or show pyuria, urine Cx should be obtained, swab for N. gonorrhoeae & Chlamydia
    c. Tx = antibiotics & NSAIDs
3. Appendix testis (torsion of testicular appendage)
    a. Si/Sx = similar to testicular torsion, severe tenderness over superior pole of testicle, **"blue dot" sign** of ischemic appendage, normal position & lie, **cremasteric reflex present**, testicle & epididymis not tender
    b. Dx = Utz, perfusion confirmed with nuclear medicine scan
    c. Tx = supportive, should resolve in 2wk
4. Fournier's gangrene
    a. Necrotizing fasciitis of the genital area
    b. Si/Sx = acute pruritus, rapidly progressing edema, erythema, tenderness, fever, chills, malaise, necrosis of skin & subcutaneous tissues, crepitus caused by gas-forming organisms
    c. Dx = history of diabetes mellitus, or immunocompromised, physical exam, labs → leukocytosis, positive blood & wound cultures (polymicrobial); x-ray → subcutaneous gas
    d. Tx emergently with wide surgical debridement & antibiotics

PROSTATE CANCER

1. Si/Sx = advanced dz causes obstructive Sx, UTI, urinary retention, pts may also present with Sx due to metastases (bone pain, weight loss & anemia), rock-hard nodule in prostate
2. Dx = labs → anemia, azotemia, elevated serum acid phosphatase & PSA—note that use of these tests for screening is controversial due to relatively low sensitivity & specificity
3. Transrectal Utz, CT scan, MRI, plain films for metastatic work-up, biopsy to confirm Dx
4. Bone scan helpful to detect bony metastases
5. Tx
    a. May not require Tx, most are indolent cancers, but note that some are very aggressive & may warrant Tx depending on pt's wishes
    b. Modalities include finasteride, local irradiation, nerve sparing or radical prostatectomy—risks of surgery include impotence & incontinence
    c. Aggressiveness of Tx depends on extend of disease & age of patient

ORTHOPEDICS

WRIST INJURIES

1. Fractures
    a. Distal radius fracture (**Colles'**) occurs after fall on outstretched hand
    b. Ulnar fracture occurs after direct blow, commonly seen in hockey, lacrosse or martial arts
    c. Dx = x-rays, history & physical
    d. Tx for both = cast immobilization for 2-4wk followed by bracing
    e. Scaphoid fracture
        i. Usually 2^{o} to falls, commonly misdiagnosed as a "wrist sprain"
        ii. Dx = clinical (pain in anatomical **snuffbox**), x-rays to confirm, bone scan or MRI for athletes that require early definitive diagnosis
        iii. Tx = thumb splint for 10wk (↑ risk of avascular necrosis)
2. Carpal tunnel syndrome
    a. Si/Sx = pain & paresthesias in fingers worse at night
    b. Dx = **Tinel's sign** (pathognomonic) = tapping median nerve on palmar aspect of wrist producing "shooting" sensation to finger & **Phalen's test** = wrist flexion to 60^{o} for 30-60 sec reproduces pt's Sx
    c. Tx = avoid causative activities, splint wrist in slight extension, consider steroid injection into carpal canal; surgery for refractory dz
    d. Px = may require up to 1yr before Sx resolve even after surgery

SHOULDER INJURIES

1. Rotator cuff injury (impingement syndrome)
    a. Typically develops over time in pts >45yr
    b. Si/Sx = pain/tenderness at deltoid & over anterior humeral head, difficulty lying on shoulder, ↓ internal rotation, crepitation, **Neer's sign** (pain elicited with forcible forward elevation of arm), lidocaine injection into subacromial space alleviates pain
    c. Dx = clinical, confirm with MRI
    d. Tx = NSAIDs & stretching, consider steroid injection for refractory dz, arthroscopic surgery for severe dz refractory to steroids
2. Shoulder dislocation
    a. Subluxation = symptomatic translation of humeral head relative to glenoid articular surface
    b. Dislocaiotn = compete displacement out of the glenoid fossa
    c. Anterior instability (about 95% of cases) usually due to subcoracoid dislocation is the most common form of shoulder dislocation
    d. Si/Sx = pain, joint immobility, arm "goes dead" with overhead motion
    e. Dx = clinical, assess axillary nerve function in neuro exam, look for signs of rotator cuff injury, confirm with x-rays if necessary
    f. Tx = initial reduction of dislocation by various traciotn-countertraciton techniques, 2- to 6wk period of immobilization (longer for younger patients), intense rehabilitation; rarely is surgery required

HIP & THIGH INJURIES

1. Dislocations
    a. Requires significant trauma, usually posterior, occur in children
    b. Sciatic nerve injury may be present—do a careful neurologic exam
    c. Dx = x-rays, consider CT scan to assess any associated fractures
    d. Tx
        i. **Orthopedic emergency requiring reduction under sedation (open reduction may be required)**
        ii. Light traction for 5 days or longer is strongly recommended

iii. No weight bearing for 3wk minimum, followed by 3-4wk of light weight-bearing activities
iv. Follow-up imaging studies required every 3-6mo for 2yr.

e. Major complication is avascular necrosis of femoral head

2. Femoral neck fracture
   a. Like hip dislocation, requires significant force
   b. Si/Sx = severe hip & groin pain worse with movement, leg may be externally rotated
   c. Dx = radiography is definitive diagnosis
   d. Tx = operative reduction with internal fixation

KNEE INJURIES

Injury	**Characteristics**	**Tx**
Anterior cruciate ligament tear (ACL)	❖ Si/Sx = **presents with a "pop" in the knee**, pt may also complain of **knee instability or giving way** ❖ **Lachman test** &/or anterior drawer finds pathologic anterior tibial translation & can Dx without imaging ❖ MRI is most helpful to determine full extent of injury	Conservative or arthroscopic repair of tear
Posterior cruciate ligament tear (PCL)	❖ Tear seen during falls on flexed knee & dashboard injuries in motor vehicle accidents (MVAs) ❖ X-rays to rule out associated injury or fracture ❖ MRI useful to determine full extent of injury	Conservative or arthroscopic repair of tear
Collateral ligament tear	❖ **Medial collateral is the most commonly injured knee ligament** (lateral collateral is least commonly injured) ❖ Seen after direct blow to lateral knee ❖ **Commonly pt also injures ACL or PCL** ❖ X-rays to r/o associated injury or fracture ❖ MRI useful to determine full extent of injury	Hinge brace
Meniscus tear	❖ Acute trauma or more commonly due to degeneration seen with aging ❖ Medial menisci injured 3x more often, male>female ❖ Dx = **McMurray test** = pt supine with hips flexed 90^{o} & knee fully flexed, maneuver foot into abduction-adduction & external-internal rotation while palpating joint line for a click ❖ MRI is standard diagnostic test	Rest (fails >50% of time), consider arthroscopy

NEUROSURGERY

HEAD INJURY

Intracranial Hemorrhage

Type	**Bleeding site**	**Characteristics**	**Treatment**
Epidural	Middle meningeal artery	❖ **Dx = CT ® biconcave disk not crossing sutures** ❖ This is a medical emergency!!!	Evacuate hematoma via burr holes
Subdural	Cortical bridging veins	❖ Causes = trauma, coagulopathy, common in elderly ❖ Sx may start 1-2wks after trauma ❖ **Dx = CT ® crescentic pattern extends across suture lines** ❖ Px worse than epidural due to ↑ risk of	Evacuate hematoma via burr holes

		concurrent brain injury	
Subarachnoid	Circle of Willis, often at MCA branch	❖ Causes = AV malformation, berry aneurysm, trauma ❖ Berry aneurysms → severe sudden headache, **CN III palsy** ❖ CSF xanthochromia (also seen any time CSF protein >150mg/dL or serum bilirubin >6mg/dL) ❖ Dx berry aneurysm with cerebral angiogram	Berry aneurysm = surgical excision or fill with metal coil Nimodipine to prevent vasospasm & resultant 2^o infarcts
Parenchymal	Basal ganglia, internal capsule, thalamus	❖ Causes = hypertension, trauma, AV malformation, coagulopathy ❖ CT/MRI → focal edema, hypodensity	↑ ICP → mannitol, hyperventilate, steroids &/or ventricular shunt

1. General treatment
    a. Establish ABCs, intubate & ventilate unconscious patients
    b. Maintain cervical spine precautions
    c. ↑ ICP → mannitol, hyperventilate, steroids &/or ventricular shunt

FACIAL FRACTURES

1. LeFort fractures are the classic facial trauma fractures
2. Look for mobile palate, fractures always involve the pterygoid plates
3. Dx = clinical + CT
4. Tx = surgical repair & stabilization

BASILAR SKULL FRACTURES

1. **Presents with 4-classic physical findings: "raccoon's eyes" & Battle's sign, hemotympanum, CSF rhinorrhea & otorrhea**
2. "Raccoon's eyes" are dark circles (bruising) about the eyes, signifying orbital fractures
3. Battle's sign is ecchymoses over the mastoid process, indicating a fracture there
4. Dx = clinical + x-ray or CT
5. Tx = supportive

TUMORS

1. Si/Sx
    a. Headache awakening pt at night or is worse in morning after waking
    b. ↑ ICP → nausea/vomit, **bradycardia with hypertension & Cheyne-Stokes respirations (Cushing's triad)** & papilledema
    c. (+) focal deficits, frequently of CN III → fixed, dilated pupil
2. DDx

Type	**Characteristics**
Metastatic	Small circular lesion, often multiple, at gray/white jnxn—**most common CNS neoplasm**: 1^o = lung, breast, melanoma, renal cell, colon, thyroid
Glioblastoma multiforme	Large, irregular, ring enhancing due to central infarction (outgrows blood supply)—**most common 1^o CNS neoplasm**
Meningiomas	Second most common 1^o CNS neoplasm, slow growing & benign
Retinoblastoma	Occurs in children, 60% sporadic, 40% familial (often bilateral)
Craniopharyngioma	Compresses optic chiasm (visual loss) & hypothalamus
Prolactinoma	The most common pituitary tumor, Sx = **bilateral gynecomastia, amenorrhea,**

	galactorrhea, impotence, bilateral hemianopsia
Lymphoma	The most common CNS tumor in AIDS pts (100x ↑ incidence), **MRI ® ring-enhancing lesion difficult to distinguish from toxoplasmosis**
Schwannoma	Usually affects CN VIII (acoustic neuroma) → tinnitus, deafness & ↑ ICP

3. Dx
    a. Bx → definitive diagnosis
    b. Clinical suspicion + CT/MRI can diagnose lymphoma, prolactinoma, meningioma
    c. Demographics important for retinoblastoma
4. Tx = excision for all 1^o tumors except prolactinoma & lymphoma
    a. First-line Tx for prolactinoma = bromocriptine (D_2 agonist inhibits prolactin secretion), 2^{nd} line = surgery
    b. Tx for lymphoma ais radiation therapy, poor Px
    c. Tx for metastases is generally radiation therapy & support

HYDROCEPHALUS

1. Definition = ↑ CSF → enlarged ventricles
2. Si/Sx = ↑ ICP, ↓ cognition, headache, focal findings, in children separation of cranial bones leads to grossly enlarged calvarium
3. **Dx made by finding dilated ventricles on CT/MRI**
4. Lumbar puncture opening pressure & CT appearance are crucial to determine type of hydrocephalus
5. Normal ICP is always communicating
    a. Hydrocephalus ex vacuo
        i. Ventricle dilation after neuron loss (e.g., stroke, CNS dz)
        ii. Sx due to neuron loss, not ventricular dilation in this case
        iii. Tx = none indicated
    b. Normal pressure hydrocephalus
        i. Si/Sx = classic triad: bladder incontinence, dementia, ataxia ("wet, wacky, wobbly")
        ii. Causes: 50% idiopathic, also meningitis, cerebral hemorrhage, trauma, atherosclerosis
        iii. Due to ↓ CSF resorption across arachnoid villi
        iv. Dx = clinically, or radionucleotide CSF studies
        v. Tx = diuretic therapy, repeated spinal taps, consider shunt placement
6. ↑ ICP can be communicating or noncommunicating
    a. Pseudotumor cerebri
        i. Communicating spontaneous ↑ ICP
        ii. **Commonly seen in obsess, young females**, can be idiopathic, massive quantities of vitamin A can cause it
        iii. CT ® no ventricle dilation (may even be shrunken)
        iv. Tx = symptomatic (acetazolamide or surgical lumboperitoneal shunt), dz is typically self-limiting
    b. Noncommunicating
        i. Due to block between ventricles & subarachnoid space → CSF outflow obstruction at fourth ventricle, foramina of Luschka/Magendie/Munro/Magnum
        ii. Causes = congenital (e.g., Arnold-Chiari syndrome), tumor effacing outflow path, or scarring 2^o meningitis or subarachnoid hemorrhage
        iii. Dx = CT
        iv. Tx = treat underlying cause if possible

VASCULAR DISEASES

ANEURYSMS

1. Abnormal dilatation of an artery to **more than twice** its normal diameter
2. Most common cause is atherosclerosis
3. Common sites include abdominal aorta aneurysms (AAAs) & peripheral vessels including femoral & popliteal arteries
4. True aneurysms involve all 3 layers of the vessel wall—caused by atherosclerosis & congenital defects such as Marfan's syndrome
5. False aneurysms are "pulsatile hematomas" covered only by a thickened fibrous capsule (adventitia)—usually caused by traumatic disruption of the vessel wall or at an anastomotic site
6. Si/Sx = mostly asymptomatic; however, patients can present with rupture, thrombosis & embolization, some patients may complain of referred back pain &/or epigastric discomfort
7. Rupture of AAA
    a. **A ruptured AAA is surgical emergency** & the patient maypresent with **classic** abdominal pain, pulsatile abdominal mass & hypotension
    b. The rate of rupture for a 5-cm diameter AAA is 6% per yr, rate for 6-cm diameter AAA is 10% per year
    c. A patient's risk of rupture is increased by large diameter (Laplace's law), recent expansion, hypertension & COPD; as a result, regular follow-up & control of hypertension are critical
8. Dx
    a. Palpation of a pulsatile mass in the abdomen on physical exam, confirmed with abdominal Utz or CT
    b. CT is the best modality to determine the size of the aneurysm in a stable patient
    c. A plain film of the abdomen may demonstrate a calcified wall
    d. Aortogram most definitive diagnosis, also reveals size & extent
9. Tx
    a. BP control & decrease risk factors, or surgical intervention
    b. Surgical intervention usually involves the placement of the synthetic graft within the dilated wall of the AAA; surgery is recommended for **aneurysms > 5cm** in diameter in a good surgical candidate
10. Complications
    a. MI, renal failure (due to proximity of renal vasculature off of aorta) & colonic ischemia (AAAs usually involve the inferior mesenteric artery [IMA])
    b. Be aware of formation of **aortoduodenal fistula** in patients who have had a synthetic graft placed for AAA disease & present with GI bleeding
11. **Peripheral aneurysms**
    a. Most commonly in the popliteal artery
    b. 50% of popliteal aneurysms are bilateral & 33% of patients with a popliteal aneurysm will have an AAA
    c. Si/Sx = rupture is rare, & pts usually present with thrombosis, embolization, or claudication
    d. Tx = surgical if patient is symptomatic

AORTIC DISSECITON

1. An intimal tear through which blood can flow, creating a plane between the intima & remainder of vessel wall
2. Usually confined to thoracic aorta (e.g., syphilis)
3. These planes can progress proximally & distally to disrupt blood supply to intestines, spinal cord, kidneys & even the coronary vessels
4. In general type A affects ascending aorta only, type B can affect both ascending & descending aorta

5. Si/Sx = **Classic severe tearing (ripping) chest pain in hypertensive patients that radiates toward the back**
6. Dx = clinical, confirm with CT or aortogram, but if pt unstable take immediately to OR
7. Tx
    a. Descending aortic dissection is usually medical (e.g., control of HTN) unless life-threatening complications arise
    b. In contrast, ascending dissection → immediate surgical intervention with graft placement

PERIPHERAL VASCULAR DISEASE (PVD)

1. Caused by atherosclerotic dz in the lower extremities
2. Si/Sx = intermittent claudication, rest pain, ulceration, gangrene, reduced femoral, popliteal & pedal pulses, dependent rubor, muscular atrophy, trophic changes & skin blanching on foot elevation
3. Dry gangrene is the result of a chronic ischemic state & necrosis of tissue without signs of active infection
4. Wet gangrene is the superimposition of cellulitis & active infeciotn to necrotic tissue
5. Leriche's syndrome
    a. Aortoiliac disease → claudication in hip, gluteal muscles & impotence
    b. 5% have limb loss at 5yr with rest pain (represents more severe ischemia) & if not treated almost 50% of patients will need amputation 2^o to gangrene
6. Dx
    a. Complete H&P, important to assess risk factors for atherosclerosis & limitations of lifestyle from PVD
    b. Noninvasive testing includes but is not limited to measurement of the ankle brachial index (ABI) & duplex examination
        i. ABI is the ratio of BP in the ankle to the BP in the arm
        ii. Patients without disease have ABIs > 1.0 given the higher absolute pressure in the ankle
        iii. Patients with severe occlusive disease (e.g., rest pain) will generally have indices <0.4; patients with claudication generally have indices <0.7
        iv. The exercise ABI most useful diagnostically; ABI may drop with exercise in a patient with PVD
        v. Duplex (Utz) examination combines ultrasound & Doppler instruments, & can provide information regarding blood flow velocity (related to stenosis) & display blood flow as a waveform; **normal waveform is triphasic, moderate occlusive disease demonstrates biphasic, & severe disease shows a mnophasic pattern**
        vi. Preoperative angiograms are classically done to confirm the Dx & to establish distal vessel run-off, or "road-map" vessels for the surgeon
7. Tx
    a. Lifestyle modifications including smoking cessation & increasing moderate exercise
    b. Pharmacotherapy is pentoxifylline
    c. Minimally invasive therapy include percutaneous balloon angioplasty (PTA) &/or atherectomy—best results for isolated lesions of high grade stenosis in the iliac & superior femoral arteries (SFA) vessels
    d. Treatment of iliac disease now involves PTA plus the placement of endoluminal stents
    e. Indications for surgical intervention are severe **rest pain, tissue necrosis, nonhealing infection & intractable claudication**
    f. Surgical treatment includes local endarterectomy with or without patch angioplasty & bypass procedures

g. Results are better with Autologous vein grafts; common operation for aortoiliac disease is the aortobifemoral bypass graft, while disease of the SFA is commonly treated with a femoral-popliteal bypass graft

8. Potential complication = **thrombosis**, must be addressed with either thrombolytic agents, balloon thrombecotmy, or revision of graft

VESSEL DISEASE

1. Varicose veins
   a. Dilated, prominent tortuous superficial veins in the lower limbs
   b. Commonly seen in pregnancy (progesterone causes dilation of veins) & prolonged stnaidn professions, may have an inherited predisposition
   c. Si/Sx = may be asymptomatic or cause itching, may also have dull aching & heaviness in lega, especially at the end of the day
   d. Dx = clinically
   e. Tx = support hose, elevated limbs, avoid prolonged standing, sclerotherapy or surgical ablation may be indicated
2. Venous ulcers
   a. 2^o to venous hypertension, DVT, or varicose veins, usually located on the medial ankle & calf
   b. Si/Sx = **painless ulcers**, large, shallow & contain bleeding granulation tissue
   c. Phlegmasia alba dolens (milk leg)
      i. Venous thrombosis usually occurring in postpartum women
      ii. Si/Sx = cool, pale swollen leg with impalpable pulses
      iii. Tx = heparin & elevation
   d. Phlegmasia cerulean dolens (venous gangrene)
      i. Venous thrombosis with complete obstruction of arterial inflow
      ii. Si/Sx = sudden intense pain, massive edema & cyanosis
      iii. Tx = heparin, elevation, venous thrombecotmy if unresolved
   e. Dx = clinical, Doppler studies of extremities
   f. Tx = reduction of swelling by elevation, compression stockings & Unna's boots (zinc oxide pste impregnated bandage), skin grafting is rarely indicated
3. Arterial ulcers
   a. 2^o to occlusive arterial disease
   b. Si/Sx = **painful by contrast to venous ulcers**, usually found on lower leg & lateral ankle, particularly on dorsum of the foot, toes & heel, absent pulses, pallor, claudication, & may have "blue toes"
   c. Dx = clinical, work-up of PVD
   d. Tx = conservative management or bypass surgery

CAROTID VASCULAR DISEASE

1. Atherosclerotic plaques in carotid arteries (most commonly at carotid bifurcation)
2. DDx of carotid insufficiency = trauma, anatomic kinking, fibromuscular dysplasia & Takayasu's arteritis
3. Si/Sx = Carotid bruit, TIAs (neurologic changes that reverse in less than 24hr), amaurosis fugax (transient monocular blindness), reversible ischemia neurologic deficits (lasting up to 3 days with no permanent changes) & CVAs that result I permanent neurologic changes
4. Dx = angiography; however, duplex scanning is noninvasive & is able to determine location, percent stenosis & assess the plaque characteristics (e.g., soft vs. calcified)
5. Tx = modification of risk factors important, anticoagulation & use of antiplatelet agents (aspirin, dipyridamole) intended to prevent thrombosis
6. Surgical therapy is carotid endarterectomy (CEA), pts are usually placed on postop aspirin therapy

7. **Surgical indications: symptomatic patient** = 1) carotid stenosis >70%, 2) multiple TIAs (risk of stroke is 10%/yr), 3) patients who have suffered a CVA & have lesion amenable to surgery (stroke recurrence is as high as 50% without surgery); **asymptomatic patient** = endarterectomy is controversial, but stenosis >75% is an accepted indication
8. Mortality rate of operation is very low (1%), & risk of stroke after CEA is reduced to 0.5-2%

SUBCLAVIAN STEAL SYNDROME

1. Caused by occlusive lesion in subclavian artery or innominate artery, causing decreased blood flow distal to the obstruction
2. This results in the "stealing" of blood from vertebral artery via retrograde flow
3. Si/Sx = arm claudication, syncope, vertigo, nausea, confusion & supraclavicular bruits
4. Dx = angiogram, Doppler, MRI
5. Tx = **carotid-subclavian bypass**

RENOVASCULAR HYPERTENSION

1. Caused by renal artery stenosis & subsequent activation of the renin-angiotensin pathway
2. Commonly due to atherosclerotic lesions
3. Can also be 2^o to fibromuscular dysplasia, subintimal dissections & hypoplasia of renal artery
4. Si/Sx = most patients are asymptomatic, some will present with headache, abdominal bruits, or cardiac, cerebrovascular, or renal dysfunction related to hypertension, a sudden onset of hypertension is more consistent with a Dysplastic process when compared to the slower evolving atherosclerosis
5. Surgically correctable HTN = **renal artery stenosis (most common)**, pheochromocytoma, unilateral renal parenchymal disease, Cushing's syndrome, primary hyperaldosteronism, hyperthyroidism, hyperparathyroidism, coarctation of the aorta, cancer & increased ICP
6. Dx = definitive Dx obtained by **angiography (string of beads appearance)**, others include IVP, renal scans & renal vein renin ratios
7. Tx = BP control & consider balloon catheter dilation of stenosis—results better with fibromuscular dysplasia vs. atherosclerotic lesions, surgical correction involves endarterectomy, bypass, or resection

MESENTERIC ISCHEMIA

1. **Chronic intestinal ischemia**
    a. 2^o to atherosclerotic lesions of at least two of the three major vessels supplying the bowel
    b. Si/Sx = **weight loss & postprandial pain & abdominal bruit**
    c. Dx = definitive diagnosis is made with aortogram
    d. Tx = surgical intervention (endarterectomy, bypass from aorta to involved graft) is **indicated** in absence of malignancy (particularly pancreatic cancer must be ruled out)
2. **Acute intestinal ischemia**
    a. Acute thrombosis of a mesenteric vessel secondary to atherosclerotic changes or emboli from the heart
    b. Si/Sx = rapid onset of pain that is out of proportion to exam, vomiting, diarrhea & history of heart condition predisposing to emboli formation (e.g., atrial fibrillation)
    c. Dx = angiogram should be performed immediately to confirm or rule out diagnosis
    d. Tx = embolectomy/thrombectomy, resection of necrotic bowel & bypass .

3OBSTETRICS and GYNECOLOGY

OBSTETRICS

TERMINOLOGY

1. Gravidity = total number of pregnancies
2. Parity = number of pregnancies carried to viability—can also express parity as 4 numbers: term pregnancies, preterm, abortions, & living children (TPAL)
3. Term delivery = delivery of infant after 37-wk gestation
4. Premature delivery = delivery of infant weighing between 500 and 2500g & delivery between 20 and 37wk

PRENATAL CARE

THE FIRST VISIT

1. Pregnancy diagnosis
    a. Si/Sx = amenorrhea, ↑ urinary frequency, breast engorgement & tenderness, nausea, fatigue, **bluish discoloration of vagina due to vascular congestion (Chadwick's sign) & softening of cervix (Hegar's sign)**
    b. Pregnancy test
        i. Detects human chorionic gonadotropin (hCG) or its β subunit
        ii. Rapidly dividing fertilized egg produces hCG even before implantation occurs
        iii. Commercial kits detect pregnancy 12-15 days after conception
        iv. Home tests have low false-positive rate but high false-negative rate
    c. Ultrasound (Utz)
        i. Gestational sac identified at 5wk, fetal image detected by 6-7wk, cardiac activity first noted at 8wk
        ii. Utz is most accurate method to determine gestational age
2. Obstetrical Hx
    a. Duration of previous gestations
    b. Mode of delivery (e.g., normal spontaneous vaginal delivery vs. C-section vs. vacuum assisted)
    c. Duration of labor, maternal, postpartum & neonatal complications, newborn weight, newborn sex
3. Menstrual Hx including last menstrual period (LMP), regularity of cycles, age at menarche
4. Contraceptive Hx (important for risk assessment, oral contraceptive pills [OCPs] have been a/w birth defects
5. Medical Hx
    a. Medicines, consider potential teratogens

Drug	**Birth defect**
Lithium	Ebstein's anomaly (single-chambered right side of heart)
Carbamazepine & valproate	Neural tube defects
Retinoic acid	CNS defects, craniofacial defects, cardiovascular effects
ACE inhibitors	Renal failure in neonates, renal tubules dysgenesis, ↓ skull ossification
Oral hypoglycemics	Neonatal hypoglycemia
Coumadin	Skeletal & CNS defects
NSAIDs	Constriction of ductus arteriosus, necrotizing enterocolitis

    b. FHx, social Hx including tobacco ETOH, drug use, type of work, exposure to animals
    c. Diabetes & hypertension
6. Estimated date of confinement (EDC)
    a. **Nagele's rule = LMP + 7 days – 3 mo + 1yr.**

    b. This calculation depends on regular 28-day cycles (only 20-25% of women), adjustments must be made for longer or shorter cycles
7. Complete physical exam with pelvic examination including PAP smear & cultures for gonorrhea & Chlamydia & estimation of uterine size
8. Labs include CBC, blood type with Rh status, urinalysis with culture, RPR test for syphilis, Rubella titer, TB skin testing, can offer HIV antibody test
9. If pt is not already immune to Rubella, do NOT vaccinate, as the vaccine is live virus
10. Genetic testing as indicated by history (e.g., hemoglobin electorphoresis in African-American pt to determine sickle cell anemia likelihood)
11. Recommend 25-35 pound weight gain during pregnancy
12. Consider folate, iron & multivitamin supplements

FIRST TRIMESTER VISITS
1. Visit every 4wk
2. Assess weight gain/loss, BP, pedal edema, fundal height, urine dip for glucosuria & proteinuria (**trace glucosuria is normal because of - GFR, anything more than trace protein should be evaluated**)
3. Estimation of gestational age by uterine size
    a. Normal uterus is 3x4x7cm
    b. Gravid uterus begins to enlarge & soften by 5-6wk

HEIGHT OF UTERUS BY GESTATIONAL WEEK

12 week	**16 weeks**	**20 weeks**	**20-36 weeks**
At pubic symphysis	Midway from symphysis to umbilicus	At umbilicus	Height (cm) correlates with weeks of gestation

SECOND TRIMESTER VISITS
1. Continue every 4wk
2. After 12 wk, use Doppler Utz to evaluate fetal heartbeat at each visit
3. Offer triple marker screen (hCG, estriol, AFP) at 15-18wk
    a. α-fetoprotein (αFP) ↓ in Down's syndrome
    b. α-fetoprotein ↑ in multiple gestation, neural tube deficit & duodenal atresia
4. At 17-19 wk (quickening) & beyond, document fetal movement
5. Amniocentesis if >35 years old or if history indicates (e.g., recurrent miscarriages, previous child with chromosomal or single gene defect, abnormal triple marker screen)
6. Glucose screening at 24wk (1hr Glucola)
7. Repeat hematocrit at 25-28wk

THIRD TRIMESTER VISITIS
1. Every 4wk until week 32, every 2wk from weeks 32-36, every wk until delivery
2. Inquire about preterm labor Sx: **vaginal bleeding, contractions, rupture of membranes**
3. Inquire about pregnancy-induced hypertension (PIH)
4. Screen for Streptococcus agalactiae (group B strep) at 35-37wk
5. Give RhoGAM at 28-30wk if indicated

PHYSIOLOGIC CHANGES IN PREGNANCY

HEMATOLOGIC
1. Pregnancy is a **hypercoagulable** state
    a. ↑ clotting factor levels
    b. Venous stasis due to uterine pressure on lower extremity great veins
2. Anemia of pregnancy

    a. Plasma volume increases about 50% from sixth wk to week 30-34
    b. Red cell mass increases later & to a smaller degree, causing a relative anemia of about 15% due to dilution
3. Slight leukocytosis due to granulocyte demargination
4. Platelets decrease slightly, but remain within normal limits

CARDIAC

1. Cardiac output increases 50% (increase in both HR & stroke volume)
2. Because of ↑ flow, increased S2 split with inspiration, distended neck veins, systolic ejection murmur & S3 gallop are normal findings
3. **Diastolic murmurs are not normal findings in pregnancy**
4. ↓ peripheral vascular resistance due to progesterone-mediated smooth muscle relaxation
5. BP decreases during first 24wk of pregnancy with gradual return to nonpregnant levels by term

PULMONARY

1. Nasal stuffiness & ↑ nasal secretions due to mucosal hyperemia
2. 4-cm elevation of diaphragm due to expanding uterus
3. Tidal volume & minute ventilation ↑ 30-40% (progesterone mediated)
4. Functional residual capacity & residual volume ↓ 20%
5. Hyperventilation → ↑ PO2, ↓ PCO2—this allows the fetal PCO2 to remain near 40 & still be able to give off CO2 to maternal blood (sets up a CO2 concentration gradient across maternal-fetal circulation & PO2 gradient allowing maternal to fetal O2 transfer)
6. Respiratory rate, vital capacity & inspiratory reserve do not change, total lung capacity decreases about 5%

GASTROINTESTINAL

1. ↓ GI motility due to progesterone
2. ↓ esophageal sphincter tone → gastric reflux also due to progesterone
3. ↑ alkaline phosphatase
4. Hemorrhoids due to constipation & ↑ venous pressure due to enlarging uterus compressing inferior vena cava

RENAL

1. ↓ bladder tone due to progesterone predisposes pregnant women to urinary stasis & UTIs/pyelonephritis
2. GFR increases 50%
    a. ↑ GFR → glucose excretion occurs in nearly all pregnant women
    b. Thus urine dipsticks are not useful in managing pts with diabetes
    c. **However, there should be no significant increase in protein loss**
3. Serum creatinine & blood urea nitrogen decrease

ENDOCRINE

1. ↓ fasting blood glucose in mother due to fetal utilization
2. ↑ postprandial glucose in mother due to ↑ insulin resistance
3. Fetus produces its own insulin starting at 9-11wk
4. ↑ maternal thyroid bonding globulin (TBG) due to ↑ estrogen, ↑ total T3 & T4 due to ↑ TBG
5. Free T3 & T4 remain the same so pregnant women are euthyroid
6. ↑ cortisol & cortisol-binding globulin

SKIN

1. Normal skin changes in pregnancy mimic liver disease due to ↑ estrogen
2. Can see spider angiomas, palmar erythema
3. Hyperpigmentation occurs from ↑ estrogen & melanocytes stimulating hormone, affects umbilicus, perineum, face (chloasma) & linea (nigra)

MEDICAL CONDITIONS IN PREGNANCY

GESTATIONAL DIABETES MELLITUS (GDM)

1. GDM = glucose intolerance or DM first recognized during pregnancy
2. **#1 medical complication of pregnancy, occurs in 2% of pregnancies**
3. GDM risk factors = previous history of GDM, maternal age =30yr, obesity, family history of DM, previous history of infant weighing 4000g at birth, history of repeated spontaneous abortions or unexplained stillbirths
4. GDM caused by placental-released hormone, human placental lactogen (HPL), which antagonizes insulin
5. GDM worsens as pregnancy progresses because increasing amounts of HPL are produced as placenta enlarges.
6. Maternal complications = hyperglycemia, ketoacidosis, ↑ risk of UTIs, **2-fold ↑ in pregnancy induced hypertension (PIH)**, retinopathy (can occur very quickly & dramatically)
7. Fetal complications
    a. Macrosomia (=4500g), neonatal hypoglycemia due to abrupt separation from maternal supply of glucose, hyperbilirubinemia, polycythemia, polyhydramnios (amniotic fluid volume =2000mL)
    b. **Abruption & preterm labor** due to ↑ uterine size & postpartum uterine atony, **3- to 4-fold - in congenital anomalies** (often cardiac & limb deformities), spontaneous abortion & respiratory distress
8. Dx = 1-hr Glucola screening test at 24-28wk or at onset of prenatal care in pt with known risk factors, confirm with 3-hr glucose tolerance test
9. Tx = strict glucose control, which significantly decreases complications
    a. Insulin is not required if the pt can adhere to a proper diet
    b. **Oral hypoglycemics are contraindicated** because they cross the placenta & can result in fetal & neonatal hypoglycemia
10. Delivery
    a. Route of delivery determined by estimated fetal weight
    b. If 4500g consider C-section, if 5000g C-section recommended
    c. Postpartum 95% of GDM patients return to normal glucose levels
    d. Glucose tolerance screening recommended 2-4mo postpartum to pick up those few women who will remain diabetic & require Tx

THROMBOEMBOLIC DISEASE

1. Incidence during pregnancy is 1-2% usually occurs postpartum (80%)
2. Si/Sx for superficial thrombophlebitis = swelling, tenderness, erythema, warmth (4 cardinal signs of inflammation), may be a palpable cord
3. Deep vein thrombosis (DVT) occurs postpartum due to spread of uterine infection to ovarian veins
4. Si/Sx of DVT = persistent fever, uterine tenderness, palpable mass, but often aSx
5. Dx
    a. Doppler ultrasound is first line, sensitivity & specificity >90%
    b. Gold standard is venography but this is invasive
6. Tx
    a. Superficial thrombophlebitis → leg elevation, rest, heat, NSAIDs
    b. DVTs → heparin to maintain PTT 1.5-2.5x baseline

c. **Coumadin contraindicated in pregnancy** because it crosses the placenta, is teratogenic early & causes fetal bleeding later

7. Px
    a. 25% of untreated DVTs progress to pulmonary embolism (PE)
    b. Anticoagulation decreases progression to 5%
    c. PEs in pregnancy are treated identically to DVTs

PREGNANCY-INDUCED HYPERTENSION (PIH)

1. Epidemiology
    a. Develops in 5-10% of pregnancies, 30% of multiple gestations
    b. Causes 15% of maternal deaths
    c. Risk factors = nulliparity, age >40 years, family history of PIH, chronic hypertension, chronic renal disease, diabetes, twin gestation
2. Types of Pregnancy-induced Hypertension

Disease	**Characteristics**
Preeclampsia	❖ Hypertension (>140/90 or ↑ in SBP of >30mmHg or DBP of >15mmHg compared to previous) ❖ New onset proteinuria &/or edema ❖ Generally occurring at =20wk
Severe preeclampsia	❖ SBP > 160mmHg or DBP >110mmHg ❖ Marked proteinuria (>1g/24hr collection or >1+ on dip), oliguria, ↑ creatinine ❖ CNS disturbances (e.g., headaches or scotomata) ❖ Pulmonary edema or cyanosis ❖ Epigastric or RUQ pain, hepatic dysfunction
Eclampsia	❖ **Convulsions** in a woman with preeclampsia ❖ 25% occur before labor, 50% during labor & 25% occur in first 72hr postpartum

3. Other Si/Sx seen in preeclampsia or eclampsia
    a. Pts have rapid weight gain (2^o to edema)
    b. Peripheral lower extremity edema is common in pregnancy; however, persistent edema unresponsive to rest & leg elevation, or edema involving the upper extremities or face is not normal
    c. Hyperreflexia & clonus are also noted
4. Tx
    a. The only cure for PIH is delivery of the baby, decision to do so depends on severeity of preeclampsia & maturity of fetus
    b. Mild preeclampsia + immature fetus → bed rest, preferably in left lateral decubitus position to maximize blood flow to uterus, close monitoring, tell pt to return to ER if preeclampsia worsens
    c. Severe preeclampsia/eclampsia → delivery when possible, magnesium sulfate to prevent seizure, antihypertensives to maintain BP<140/100
5. Complication of severe PIH = HELLP syndrome
    a. **HELLP** = Hemolysis, Elevated Liver enzymes, Low Platelets
    b. Occurs in 5-10% of women with severe preeclampsia or eclampsia, more frequently in multiparous, older pts
    c. Tx = delivery (the only cure), transfuse blood, platelets, fresh frozen plasma as needed, IV fluids & pressors as needed to maintain BP

CARDIAC DISEASE

1. Pts with congenital heart disease have a ↑ risk (1-5%) of having a fetus with a congenital heart disease
2. Pts with pulmonary hypertension & ↑ right-sided pressures (e.g., Eisenmenger's complex) have poor Px with pregnancy
3. Tx of preexisting cardiac disease = supportive, e.g., prevention &/or prompt correction of anemia, aggressive Tx of infections, ↓ physical activity/strenuous work, adherence to a low-sodium diet & proper weight gain
4. Peripartum cardiomyopathy
    a. Rare but severe pregnancy-associated condition
    b. Occurs in last month pregnancy or first 6mo postpartum
    c. Risk factors = African American, multiparous, age >30yr, twin gestation, or preeclampsia
    d. Tx = bed rest, digoxin, diuretics, possible anticoagulation, consider postdelivery heart transplant especially in those whose cardiomegaly has not resolved 6mo after Dx

GROUP B STREPTOCOCCUS (GBS = STREPTOCOCCUS AGALACTIAE)

1. Asymptomatic cervical colonization occurs in up to 30% of women
2. 50% of infants become colonized, clinical infection in <1%
3. Intrapartum prophylaxis with penicillin is reserved for the following situations:
    a. Preterm labor (<37wk) or prolonged rupture of membranes (ROM) (>18hours) or fever in labor regardless of colonization status
    b. Women identified as colonized with GBS through screening at 35-37wk gestation
    c. Women with GBS bacteriuria or with a previous infant with GBS disease

HYPEREMESIS GRAVIDARUM

1. Increased nausea & vomiting that, unlike "morning sickness," persists past the sixteenth week of pregnancy
2. Causes = ↑ hCG levels, thyroid or GI hormones
3. Si/Sx = excessive vomiting, dehydration, hypochloremic metabolic alkalosis
4. Dx = clinical, rule out other cause
5. Tx = fluids, electrolyte repletion, antiemetics (IV, IM, or suppositories)
6. Some pts require feeding tubes & parenteral nutrition

FETAL ASSESSMENT AND INTRAPARTUM SURVEILLANCE

FETAL GROWTH

1. Measure by fundal height, if 2-cm deviation from expected fundal height during weeks 18-36 → repeat measurement &/or Utz
2. Utz is most reliable tool for assessing fetal growth
3. In early pregnancy measurement of gestational sac & crown-rump length correlate very well with gestational age
4. Later in pregnancy 4 measurements are done because of wide deviation in normal range = biparietal diameter of skull, abdominal circumference, femur length & cerebellar diameter

FETAL WELL-BEING

1. =4 fetal movements per hr generally indicate fetal well-being
2. Nonstress test (NST)
    a. Measures response of fetal heart rate to movement
    b. Normal (i.e., reactive) NST occurs when fetal heart rate ↑ by 15 beats/min (bpm) for 15sec following fetal movement
    c. 2 such accelerations with 20min are considered normal

    d. A nonreactive NST → further assessment of fetal well-being
    e. Test has a high false-positive rate (test suggests fetus is in trouble, but fetus is actually healthy), so it must be interpreted in the context of other tests & is often repeated within 24hr to verify results
3. Biophysical profile (BPP)
    a. 5 measures of fetal well-being, each rated on a scale of 0-2
    b. Fetal breathing → =1 fetal breathing movement in 30min lasting at least 30sec
    c. Gross body movement → =3 discrete movements in 30min
    d. Fetal tone → =1 episode of extension with return to flexion of fetal limbs/trunk OR opening/closing of hand
    e. Qualitative amniotic fluid volume → =1 pocket of amniotic fluid at least 1cm in 2 perpendicular planes
    f. Reactive fetal heart rate → reactive NST
    g. Final score of 8-10 is normal, score of 6 is equivocal & requires further evaluation, score of 4 or less is abnormal & usually requires immediate intervention

TESTS OF FETAL MATURITY

1. Respiratory system is last fetal system to mature, so decisions regarding when to deliver a premature infant often depend on tests that assess the maturity of the system
2. Phospholipid production (collectively known as "surfactant") remains low until 32-33wk of gestation, but this is highly variable
3. Lack of surfactant → neonatal respiratory distress syndrome (RDS)
4. Phospholipids enter amniotic fluid from fetal breathing & are obtained by amniocentesis & tested for maturity
5. Tests for fetal maturity
    a. Lecithin-sphingomyelin (L:S) ratio
        i. Lecithin is major phospholipid found in surfactant & increases as fetal lungs become mature
        ii. Sphingomyelin production remains constant throughout pregnancy
        iii. Ratio >2.0 is considered mature
    b. Phosphatidylglycerol (PG) appears late in pregnancy, its presence generally indicates maturity

INTRAPARTUM FETAL ASSESSMENT

1. Causes of nonreassuring fetal status
    a. Uteroplacental insufficiency
        i. Placenta impaired or unable to provide oxygen & nutrients while removing products of metabolism & waste
        ii. Causes = placenta previa or abruption, placental edema from hydrops fetalis or Rh isoimmunizaiton, postterm pregnancy, intrauterine growth retardation (IUGR), uterine hyperstimulation
        iii. Fetal response to hypoxia → shunting of blood to brain, heart & adrenal glands.
        iv. If unrecognized can progress to metabolic acidosis with accumulation of lactic acid & damage to vital organs.
    b. Umbilical cord compression due to oligohydramnios, cord prolapse or knot, anomalous cord, or abnormal cord insertion
    c. Fetal anomalies include IUGR, prematurity, postterm, sepsis, congenital anomalies
2. Fetal heart rate (FHR) monitoring
    a. Normal FHR is 120-160bpm
    b. Tachycardia = FHR >160bpm for 10min or more

        i. Most common cause is maternal fever (which may signal chorioamnionitis)
        ii. Other causes = fetal hypoxia, immaturity, tachyarrhythmias, anemia, infection, or maternal thyrotoxicosis or treatment with sympathomimetics
    c. Bradycardia = FHR <120bpm for 10min or more, caused by congenital heart block, fetal anoxia (e.g., from placental separation) & maternal treatment with β-blockers
    d. FHR variability
        i. A reliable indicator of fetal well-being, suggesting sufficient CNS oxygenation
        ii. ↓ variability a/w fetal hypoxia/acidosis, depressant drugs, fetal tachycardia, CNS or cardiac anomalies, prolonged uterine contractions, prematurity & fetal sleep
3. Accelerations
    a. Types & patterns of accelerations play a role in intrapartum evaluation of the fetus
    b. Accelerations
        i. ↑ FHR of at least 15bpm above baseline for 15-20sec
        ii. This pattern indicates a fetus unstressed by hypoxia or academia → reassuring & suggests fetal well-being
    c. Early decelerations
        i. ↓ FHR (not below 100bpm) that mirrors a uterine contraction (i.e., begins with onset of contraction, dips at peak of contraction, returns to baseline with end of contraction)
        ii. Results from pressure on fetal head → vagus nerve stimulated reflex response to release acetylcholine at fetal SA node
        iii. Considered physiologic & not harmful to fetus
    d. Variable decelerations
        i. Do not necessarily coincide with uterine contraction
        ii. Characterized by rapid dip in FHR, often <100bpm with rapid return to baseline
        iii. Also reflex-mediated, due to umbilical cord compression
        iv. Can be corrected by shifting maternal position, or amnioinfusion if membranes have ruptures & cord compression is secondary to oligohydramnios
    e. Late decelerations
        i. Begin after contraction has already started, dip after peak of contraction, returns to baseline after contraction is over
        ii. Viewed as potentially dangerous, a/w uteroplacental insufficiency
        iii. Causes include placental abruption, PIH, maternal diabetes, maternal anemia, maternal sepsis, postterm pregnancy & hyperstimulated uterus
        iv. Repetitive late decelerations requires intervention

ISOIMMUNIZATION

1. Development of maternal IgG antibodies following exposure to fetal red blood cell antigens
2. Exposure commonly occurs at delivery, but can occur during pregnancy as well
3. in subsequent pregnancies (rarely late in the same pregnancy) these antibodies can cross the placenta → attach to fetal RBC cells & hemolyze them → fetal anemia
4. Can occur with any blood group, but most often occurs when mother is Rh-negative & fetus is Rh-positive
5. Extent to which fetus is affected depends on amount of IgG antibodies crossing placenta & ability of fetus to replenish destroyed RBCs
6. Worst case scenario is hydrops fetalis
    a. Significant transfer of antibodies across placenta → fetal anemia
    b. Liver attempts to make new RBCs (fetal hematopoiesis occur sin liver & bone marrow) at the expense of other necessary protein → ↓ oncotic pressure → fetal ascites & edema
    c. High-output cardiac failure a/w severe anemia

7. Maternal IgG titer = 1:16 is high enough to pose risk to the fetus
8. Tx = RhoGAM
    a. Administration of antibody to the Rh antigen (Rh immune globulin = RhoGAM) within 72hr of delivery prevents active antibody response by the mother in most cases
    b. Risk of subsequent sensitization ↓ from 15% to 2%
    c. When RhoGAM is also given at 28wk of gestation, risk of sensitization is further reduced to 0.2%
9. RhoGAM given to Rh-negative mothers if the father is Rh-positive
    a. At 28wks gestation
    b. Within 72hr of delivery of Rh-positive infant
    c. Other times maternal-fetal blood mixing can occur
        i. At time of amniocentesis
        ii. After an abortion
        iii. After an ectopic pregnancy
        iv. Note: Kleinhauer-Betke test (identifies fetal RBCs in maternal blood)

GENETIC TESTING

1. Chromosomal abnormalities account for 50-60% of spontaneous abortion, 5% of stillbirths, 2-3% of couples with multiple miscarriages
2. 0.6% of all live births have a chromosomal abnormality
3. Indications for prenatal genetic testing
    a. Most common is advanced maternal age (AMA)
        i. Trisomy 21 (Down's syndrome) incidence ↑ 10-fold from age 35 to age 45, other polysomies ↑ similarly
        ii. Amniocentesis routinely offered to all women who will be >35yr old at estimated time of delivery
    b. Prior child with chromosome or single gene abnormality
    c. Known chromosomal abnormality such as a balanced translocation or single gene disorder in parent(s)
    d. Abnormal results from screening tests such as the triple marker screen

LABOR AND DELIVERY

INITIAL PRESENTATION

1. Labor = progressive effacement & dilation of uterine cervix resulting from contractions of uterus
2. **Braxton-Hicks contractions** (false labor) = uterine contractions without effacement & dilation of cervix
3. 85% of patients undergo spontaneous labor & delivery between 37 and 42wk gestation
4. Pts are told to come to hospital for regular contractions q5min for at least 1hr, rupture of membranes, significant bleeding, ↓ fetal movement
5. Initial exam upon arrival
    a. Auscultation of fetal heart tones
    b. Leopold maneuvers help determine fetal lie (relation of long axis of fetus with maternal long axis), determine fetal presentation (i.e., breech vs. cephalic) & position of presenting part with respect to right or left side of maternal pelvis
    c. Vaginal examination
        i. Check for rupture of membranes, cervical effacement & cervical dilation (in cm)
        ii. Fetal station (level of fetal presenting part relative to ischial spines) measured from -3 (presenting part palpable at pelvic inlet) to +3 (presenting part palpable beyond pelvic outlet)

iii. 0 station = presenting part palpable at ischial spines, significance of 0 station is that biparietal diameter (biggest diameter of fetal head) has negotiated pelvic inlet (smallest part of pelvis)

STAGES OF LABOR

1. Labor divided into 3 stages
2. Stage 1
    a. Interval between onset of labor & full cervical dilation (10cm)
    b. Further subdivided into:
        i. Latent phase = cervical effacement & early dilation
        ii. Active phase = more rapid cervical dilation occurs, usually beginning at 3-4cm
3. Stage 2 = interval between complete cervical dilation & delivery of infant
4. Stage 3 = interval between delivery of infant & delivery of placenta
5. Stage 4 = immediate postpartum period lasting 2hr during which pt undergoes significant physiologic changes

MANAGEMENT OF LABOR

1. First stage
    a. Continuous monitoring of fetal heart rate, either external monitoring via Doppler, or internal monitoring via fetal scalp electrode (FSE) that allows for more detailed evaluation of fetal heart rate pattern
    b. Monitoring of uterine activity
        i. External tocodynamometer measures frequency & duration of contractions, but not intensity
        ii. Internal uterine pressure catheter (IUPC) measures intensity by measuring intrauterine pressure
    c. Analgesic (typically meperidine) &/or anesthetic (typically an epidural block that provides both continuous analgesia & anesthesia) can be given—agents usually not given until active stage of labor
2. Second stage
    a. Maternal effort (i.e., pushing) accelerates delivery of fetus (↑ in intra-abdominal pressure assists fetal descent down birth canal)
    b. Delivery should be well controlled with protection of the perineum
    c. If used, episiotomies are usually cut midline
    d. After head is delivered, bulb suction of nose & mouth is performed & neck is evaluated for presence of nuchal cord
    e. Shoulders are delivered by applying gentle downward pressure on head to deliver anterior should followed by easy upward force to deliver posterior shoulder
    f. Delivery of body follows, cord is clamped & cut, & infant given to mother or to warmer
    g. Blood from umbilical cord sent for ABO & Rh testing as well as arterial bloo gases
3. Third stage
    a. 3 signs of placenta separation
        i. Uterus rises in abdomen signaling that placenta has separated
        ii. Gush of blood
        iii. Lengthening of umbilical cord
    b. Excessive pulling on placenta should be avoided because of risk of uterus inversion with associated profound hemorrhage & retained placenta
    c. Gentle traction should be applied at all times
    d. May take up to 30min for placenta to be expulsed
4. Fourth stage
    a. Systemic evaluation of cervix, vagina, vulva, perineum & peiurethral area for lacerations

b. Likelihood of serious postpartum complications is greatest in first 1-2hr postpartum

ABNORMAL LABOR

1. Dystocia = difficult labor
    a. Cause detected by evaluating the 3 **Ps**
        i. **Power**
            1. Refers to strength, duration & frequency of contractions
            2. Measured by using tocodynamometer or IUPC
            3. For cervical dilation to occur =3 contractions in 10min must be generated
            4. During active labor maternal effort comes into play, as maternal exhaustion, effects of analgesia/anesthesia, or underlying disease may prolong labor
        ii. **Passenger**
            1. Refers to estimates of fetal weight + evaluation of fetal lie, presentation & position
            2. Occiput posterior presentation, face presentation & hydrocephalus are a/w dystocia
        iii. **Passage**
            1. Difficult to measure pelvic diameters
            2. Adequacy of pelvis often unknown until progress (or no progress) is made during labor
            3. Distended bladder, adnexal or colon masses & uterine fibroids can all contribute to dystocia
    b. Dystocia divided into prolongation disorders
        i. Prolonged latent phase
            1. Latent phase >20hr in primigravid or >14hr in multigravid patient is prolonged & abnormal
            2. Causes include ineffective uterine contractions, fetopelvic disproportion & excess anesthesia
            3. Prolonged latent phase $\rightarrow$ no harm to mother or fetus
        ii. Prolonged active phase
            1. Active phase > 12hr or rate of cervical dilation <1.2cm/hr in primigravid or <1.5cm/hr in multigravid
            2. Causes include excess anesthesia, ineffective contractions, fetopelvic disproportion, fetal malposition, rupture of membranes before onset of active labor
            3. Prolonged active phase $\rightarrow \uparrow$ risk of intrauterine infection & increased risk of cesarean section
2. Arrest disorders
    a. 2^o arrest occurs when cervical dilation during active phase ceases for =2hr
    b. Suggests either cephalopelvic disproportion or ineffective uterine contractions
3. Management of abnormal labor
    a. Labor induction = stimulation of uterine contractions before spontaneous onset of labor
    b. Augmentation of labor = stimulation of uterine contractions that began spontaneously but have become infrequent, weak, or both
    c. Induction trial should occur only if cervix is prepared or “ripe”
    d. Bishop score used to try to quantify cervical readiness for induction

Bishop Score

Factor	**Points**			
	0	1	2	3
Dilation	Closed	1-2cm	3-4cm	=5cm
Effacement	0-30%	40-50%	60-70%	=80%
Station	-3	-2,-1	0	=+1
Position		Posterior	Mild	Anterior

Score: 9-13 a/w highest likelihood of successful induction
0-4 a/w highest likelihood of failed induction

4. Indications for induction = suspected fetal compromise, fetal death, PIH, premature ROM, chorioamnionitis, postdates pregnancy, maternal medical complication
5. Contraindications for induction include placenta previa, active genital herpes, abnormal fetal lie, cord presentation
6. If cervix not "ripe", prostaglandin E2 gel can be used to attempt to ripen cervix, biggest risk is uterine hyperstimulation → uteroplacental insufficiency
7. Another method is insertion of laminaria or rods inserted into the internal os that absorb moisture & expand, slowly dilating cervix, risks include failure to dilate, laceration, rupture of membranes & infection
8. Prolonged latent phase can be managed with rest, augmentation of labor with oxytocin, &/or amniotomy that may allow for fetal head to provide greater dilating force be considered & may warrant cesarean section vs. augmentation
9. During active phase of labor fetal malposition & cephalopelvic disproportion must be considered & may warrant cesarean section vs. augmentation
10. If fetus has descended far enough, forceps or vacuum can be used, if not cesarean section is carried out
11. Risks of prolonged labor include infection, exhaustion, lacerations, uterine atony with hemorrhage
12. Breech presentation occurs in 2-4% of pregnancies & risk ↑ in cases of multiple gestations, polyhydramnios, hydrocephaly, anencephaly & uterine anomalies

POSTPARTUM HEMORRHAGE

1. Defined as blood loss >500mL a/w delivery
2. Causes = uterine atony (most common), lacerations, retained placenta
3. Uterine atony
    a. Normally uterus quickly contracts following delivery of placenta, muscle contraction compresses down on spiral arteries & prevents excessive bleeding
    b. If contraction does not occur → postpartum hemorrhage
    c. Risk factors for uterine atony = multiple gestations, hydramnios, multiparity, macrosomia, previous history of postpartum hemorrhage, fibroids, magnesium sulfate, general anesthesia, prolonged labor, amnionitis
    d. Dx based on clinical exam of soft, "boggy" uterus
    e. Tx
        i. Start with uterine massage to stimulate contractions
        ii. IV fluids & transfusions as needed, cervix & vagina visualized for lacerations
        iii. Medical Tx = oxytocin, methergine (potent uterotonic always given IM—if given IV cause severe hypertension), or prostaglandins → uterine contractions
        iv. If these measures are unsuccessful, surgical interventions are used & include ligation of uterine arteries, ligation of internal iliac arteries, selective arterial embolization or hysterectomy as last resort
4. Retained placenta

    a. Occurs when separation of placenta from uterine wall or expulsion of placenta is incomplete
    b. Risk factors include previous cesarean section, fibroids & prior uterine curettage
    c. Placental tissue that abnormally implants into uterus can also result in retention
    d. Placenta accrete: placental villi abnormally adhere to superficial lining of uterine wall
    e. Placenta increta: placental villi penetrate into uterine muscle layer
    f. Placenta percreta: placental villi completely invade uterine muscle layer
5. Disseminated intravascular coagulation (DIC)
    a. A rare cause of postpartum hemorrhage
    b. Severe preeclampsia, amniotic fluid embolism & placental abruption are a/w DIC
    c. Tx aimed at correcting coagulopathy

POSTPARTUM CARE

LACTATION & BREAST FEEDING

1. Engorgement occurs about 3 days postpartum
2. 3 causes of tender enlarged breasts postpartum are engorgement, mastitis & plugged duct
3. Tx engorgement with continued breast feeding, mastitis with antibiotics (nursing can be continued) & plugged duct with warm packs
4. Advantages of breast feeding = ↑ bonding between mother & child, convenience, ↓ cost, protection against infection & allergies
5. Breast milk provides all vitamins except vitamin K

CONTRACEPTION

1. Contraception should be discussed with all patients prior to discharge
2. About 15% of women are fertile 6wk postpartum
3. OCPs are not contraindicated in breast-feeding & postpartum tubal ligation should be discussed as well

POSTPARTUM IMMUNIZATIONS

1. Rubella nonimmune women should be immunized (they can continue to breast feed)
2. Rh-negative woman who has given birth to an Rh-positive baby should receive RhoGAM

POSTPARTUM DEPRESSION

1. Recurrence rate for patients with previous postpartum depression is 25%
2. Postpartum depression ranges from the "blues" that affects 50% of women & typically occurs about day 2-3, resolving in 1-2wk, to postpartum depression that affects 10% of women, to suicidal ideation that occurs more rarely
3. Especially worrisome is a mother who has estranged herself from her newborn or has become indifferent
4. Tx depends on severity of Sx & may range from simple telephone contact to psychotherapy & medication to inpatient hospitalization.

POSTPARTUM UTERINE INFECTION

1. Incidence of infection ranges form 10-50% depending on population, mode of delivery (C-section > vaginal delivery) & risk factors
2. Risk factors = maternal obesity, immunosuppression, chronic disease, vaginal infection, amnionitis, prolonged labor, prolonged ROM, multiple pelvic examinations during labor, internal fetal monitoring or intrauterine pressure catheter, C-section
3. **Most common infection post C-section is endometritis** (uterine infection)
4. Si/Sx = fever on first or second postpartum day, uterine tenderness, ↓ bowel sounds, leukocytosis (difficult to interpret because of normal leukocytosis in puerperium)

5. DDx
    a. First day postpartum: think lungs (wind) → atelectasis, especially f general anesthesia was used, or pneumonia
    b. Second day postpartum: think urinary tract (water) → UTI, pyelonephritis
    c. Third day postpartum: think wound
    d. Fourth day postpartum: think extremities (walking) → thrombophlebitis
6. Endometritis usually polymicrobial with aerobic & anaerobic organisms present
7. Dx = clinical
8. Tx = first generation cephalosporin, add coverage (mezlocillin + aminoglycoside) if no response within 48-72hr
9. Prophylactic antibiotic therapy (one-time dose) at time of C-section delivery significantly reduces incidence of postpartum infection

OBSTETRICAL COMPLICATIONS

ABORTION

1. Termination of a pregnancy before viability, usually at 20wk or less, occurs spontaneously in 15% of all pregnancies
2. Risk factors = ↑ parity, advanced maternal age, ↑ paternal age, conception within 3mo of a live birth
3. Single pregnancy loss does not significantly increase risk of future loss
4. Chromosomal abnormalities cause 50% of early spontaneous abortion, mostly trisomies (the longer a pregnancy goes before undergoing spontaneous abortion, the less likely that fetus is chromosomally abnormal)
5. Other causes = endocrine dz (e.g., thyroid), structural abnormalities (e.g., fibroids, incompetent cervix), infection (e.g., Listeria, Mycoplasma, ToRCHS) chronic dz (e.g., DM, SLE, renal or cardiac dz), environmental factors (e.g., toxins, radiation, smoking, alcohol)
6. Vaginal bleeding in first half of any pregnancy is presumed to be a threatened abortion unless another diagnosis such as ectopic pregnancy, cervical polyps, cervicitis, or molar pregnancy can be made

Types of Abortions

Threatened	❖ Si/Sx = vaginal bleeding in first 20wk of pregnancy without passage of tissue or ROM with cervix closed ❖ Occurs in 25% of pregnancies (1/2 go on to spontaneously abort) ❖ ↑ risk preterm labor & delivery, low birth weight perinatal mortality ❖ Dx = Utz to confirm early pregnancy is intact ❖ If no cardiac activity by 9wk → consider D&C procedure ❖ HCG levels are also used to identify viable pregnancies at various stages of development
Inevitable	❖ Si/Sx = threatened abortion with dilated cervical os &/or ROM, usually accompanied by cramping with expulsion of products of conception (POC) ❖ Pregnancy loss is unavoidable ❖ Tx = surgical evacuation of uterine contents & RhoGAM if mother is Rh-negative
Completed	❖ Si/sx = documented pregnancy that spontaneously aborts all POCs ❖ POCs should be grossly examined & submitted to pathology to confirm fetal tissue &/or placental villi, if none is observed must rule out ectopic pregnancy ❖ Pts may require curettage because of ↑ likelihood that abortion was incomplete (suspected if β-hCG levels plateau or fail to decline to zero) ❖ RhoGAM given to Rh-negative women
Incomplete	❖ Si/Sx = cramping, bleeding, passage of tissue, with dilated cervix & visible tissue in vagina or endocervical canal

	❖ Curettage usually needed to remove remaining POCs & to control bleeding ❖ Again Rh-negative patients are given RhoGAM ❖ Hemodynamic stabilization may be required if bleeding is very heavy
Missed	❖ Failure to expel POC ❖ Si/Sx = lack of uterine growth, lack of fetal heart tones & cessation of pregnancy symptoms ❖ Evacuation of uterus required after fetal death has been confirmed, suction curettage recommended for first-trimester pregnancy, dilation & evacuation (D&E) recommended for second-trimester pregnancies ❖ Serious but rare complication is DIC ❖ Rh-negative patients receive RhoGAM
Recurrent	❖ Si/Sx = =2 consecutive or total of 3 spontaneous abortions ❖ If early, often due to chromosomal abnormalities → karyotyping for both parents to determine if they carry a chromosomal abnormality ❖ Examine mother for uterine abnormalities ❖ Incompetent cervix is suspected by history of painless dilation of cervix with delivery of normal fetus between 18 and 32 weeks of gestation ❖ Tx = surgical cerclage procedures to suture cervix closed until labor or rupture of membranes occurs

ECTOPIC PREGNANCY

1. Implantation outside of uterine cavity
2. ↑ incidence recently because of ↑ in PID, second leading cause of maternal mortality
3. Risk factors = previous ectopic pregnancy, previous history of salpigitis (scarring & adhesions impede transport of ovum down tube), age =35yr old, >3prior pregnancies, sterilization failure
4. Si/Sx = abdominal/pelvic pain, referred shoulder pain from hemoperitoneal irritation of diaphragm, amenorrhea, vaginal bleeding, cervical motion or adnexal tenderness, nausea, vomiting, orthostatic changes
5. DDx = surgical abdomen, abortion, salpingitis, endometriosis, ruptured ovarian cyst, ovarian torsion
6. Ectopic pregnancy should be suspected in any reproductive age woman who presents with abdominal/pelvic pain, irregular bleeding & amenorrhea—lag in treatment is a significant cause of mortality
7. Dx
    a. (+) pregnancy test with Utz to determine intrauterine vs. extrauterine pregnancy
    b. Very low progesterone level strongly suggests nonviable pregnancy that may be located outside the uterine cavity while higher levels suggest viable pregnancy
8. Tx
    a. Surgical removal now commonly done via laparoscopy with maximum preservation of reproductive organs
    b. Methotrexate can be used early, especially if pregnancy is <3.5cm in diameter, with no cardiac activity on Utz
    c. Regardless of technique used, posttreatment serial β-hCG levels must be followed to ensure proper falloff in level
    d. Rh-negative women should receive RhoGAM to avoid Rh sensitization

THIRD-TRIMESTER BLEEDING

1. Occurs in about 5% of all pregnancies
2. Half of these are due to placenta previa or placental abruption, others due to vaginal/vulvar lacerations, cervical polyps, cervicitis, cervical cancer

3. In many cases no cause for bleeding is found

	Placenta Previa	**Placental Abruption**
Abnormality	Placenta implanted over internal cervical os (completely or partially)	Premature separation (complete or partial) of normally implanted placenta from decidua
Epidemiology	↑ risk grand multiparas & prior C-section	↑ risk preeclampsia, previous history of abruption, rupture of membranes in a patient with hydramnios, cocaine use, cigarette smoking & trauma
Time of onset	20-30wk	Any time after 20wk
Si/Sx	Sudden, **painless** bleeding	**Painful** bleeding, can be heavy, painful & frequent uterine contractions
Dx	Utz → placenta abnormal location	Clinical, based on presentation of painful vaginal bleeding, frequent contractions & fetal distress, **Utz not useful**
Tx	Hemodynamic support, expectant management, deliver by C-section when fetus mature enough	Hemodynamic support, urgent C-section or vaginal induction if pt is stable & fetus is not in distress
Complications	Associated with 2-fold ↑ in congenital malformations so evaluation for fetal anomalies should be undertaken at Dx	↑ risk of fetal hypoxia/death, DIC may occur as a result of intravascular & retroplacental coagulaiton

PRETERM LABOR (PTL)

1. Regular uterine contractions at =10min intervals, lasting =30 sec, between 20 and 36 wk gestation & accompanied by cervical effacement, dilation &/or descent of fetus into the pelvis
2. It is a major cause of preterm birth → significant perinatal morbidity & mortality
3. Risk factors = premature rupture of membranes (PROM), infection (UTI, vaginal, amniotic), dehydration, incompetent cervix, smoking, fibroids, placenta previa, placental abruption, many cases are idiopathic
4. Si/Sx = cramps, dull low back pain, abdominal/pelvic pressure, vaginal discharge (mucous, water, or bloody) & contractions (often painless)
5. Dx = external fetal monitoring to quantify frequency & duration of contractions, vaginal exam → extent of cervical dilation/effacement
6. Utz to confirm gestational age, amniotic fluid volume (helps to determine if rupture of membranes has occurred), fetal presentation & placental location
7. Tx focused on delaying delivery if possible until fetus is mature
    a. 50% of patients have spontaneous resolution of preterm uterine contractions
    b. IV hydration important because dehydration is well known to cause uterine irritability
    c. Empiric antibiotic therapy is given for suspected chorioamnionitis or vaginal infection
    d. Tocolytic regimens
        i. Magnesium sulfate, β-2 agonists like terbutaline & ritodrine, Ca^{2+}-blockers like nifedipine, or indomethacin may be instituted although they have never been shown to substantially prolong delivery more than several days
        ii. Contraindications to tocolysis = advanced labor (cervical dilation >3cm), mature fetus, chorioamnionitis, significant vaginal bleeding, anomalous fetus, acute fetal distress, severe preeclampsia or eclampsia
    e. From 24-34wk steroids such as betamethasone are generally used to enhance pulmonary maturity

f. Management of infants at 34-37wk is individualized; survival rates for infants born at 34wk is within 1% of the survival rate for infants born at 37wk & beyond; assessment of fetal lung maturity may help decide who to deliver between 34 and 37wk

8. Common complications include death, respiratory distress syndrome & subsequent bronchopulmonary dysplasia, sepsis, intraventricular hemorrhage, necrotizing enterocolitis, developmental delays & seizures

PREMATURE RUPTURE OF MEMBRANES (PROM)

1. Rupture of chorioamniotic membrane before onset of labor, occurs in 10-15% of all pregnancies
2. Labor usually follows PROM; 90% of patients & 50% of preterm patients go into labor within 24hr after rupture
3. Biggest risk is labor & delivery of preterm infant with associated morbidities/mortality, second biggest complication is infection (chorioamnionitis)
4. PROM at 26wk of gestation or less is a/w pulmonary hypoplasia
5. Dx = vaginal exam with testing of nonbloody fluid from the vagina
    a. Nitrazine test: uses pH to distinguish alkaline amniotic fluid (pH >7.0) with more acidic urine & vaginal secretions (note false-positive seen with semen, cervical mucus, *Trichomonas* infection, blood unusually basic urine)
    b. Fern test: amniotic fluid placed on slide that is allowed to dry in room (up to 30min); the branching fern leaf pattern that results when the slide is completely dry is caused from odium chloride precipitates from amniotic fluid
    c. Utz confirms Dx by noting oligohydramnios, labor is less likely to occur if sufficient fluid remains
6. Tx
    a. If intrauterine infection is suspected, empiric broad spectrum antibiotics are started
    b. Otherwise treat as for preterm labor above

MULTIPLE GESTATIONS

1. 1 in 90 incidence in US (slightly higher in black women, slightly lower in white women)
2. **Dizygotic twins occur when 2 separate ova are fertilized by 2 separate sperm, incidence - with - age & parity**
3. Monozygotic twins represent division of the fertilized ovum at various times after conception
4. Multiple gestation are considered high-risk pregnancies because of the disproportionate increase in perinatal morbidity & mortality as compared with a singleton gestation
    a. **Spontaneous abortions & congenital anomalies occur more frequently in multiple pregnancies as compared with singleton pregnancies**
    b. Maternal complications = anemia, hydramnios, eclampsia, PTL, postpartum uterine atony & hemorrhage, increased risk for C-section
    c. Fetal complications: congenital anomalies, spontaneous abortion, IUGR, prematurity, PROM< umbilical cord prolapse, placental abruption, placenta previa & malpresentation
5. Average duration of gestation ↓ with ↑ number of fetuses (twins deliver at 37wk, triplets deliver at 33wk, quadruplets deliver at 29wk)
6. Twin-twin transfusion syndrome
    a. Occurs in 10% of twins sharing a chorionic membrane
    b. Occurs when blood flow is interrupted by a vascular anastomoses such that one twin becomes the donor twin & can have impaired growth, anemia, hypovolemia, & the other twin (recipient twin) can develop hypervolemia, hypertension, polycythemia & congestive heart failure as a result of the increased blood flow from one twin to the other
7. Dx of twins usually suspected when uterine size exceeds calculated gestational age & can be confirmed with ultrasound

8. DDx = incorrect dates, fibroids, polyhydramnios & molar pregnancy
9. Delivery method largely depends on presentation of twins; usually if first fetus is in vertex presentation, vaginal delivery is attempted; if not C-section is often performed
10. Important to watch for uterine atony & postpartum hemorrhage because over-distended uterus may not clamp down normally

GYNECOLOGY

BENIGN GYNECOLOGY

MENSTRUAL CYCLE

1. Due to hypothalamic pulses of gonadotropin releasing hormone (GnRH), pituitary release of follicle stimulating hormone (FSH) & luteinizing hormone (LH), & ovarian sex steroids Estradiol & progesterone
2. ↑ or ↓ of any of these hormones → irregular menses or amenorrhea
3. At birth, the human ovary contains approximately 1 million primordial follicles each with an oocyte arrested in the prophase stage of meiois
4. Process of ovulation begins in puberty = follicular maturation
    a. After ovulation the dominant follicle released becomes the corpus luteum, which secretes progesterone to prepare the endometrium for possible implantation
    b. If the ovum is not fertilized the corpus luteum undergoes involution, menstruation begins & cycle repeats
5. Phases of the menstrual cycle
    a. First day of menstrual bleeding is day 1 of the cycle

Follicular phase (proliferative phase)	**Ovulatory phase**	**Luteal phase (secretory phase)**
Day 1-13 of cycle	*Day 13-17 of cycle*	*Day 15-first day of menses*
Estradio-induced negative feedback on FSH & (+) feedback on LH in anterior pituitary leads to LH surge on day 11-13	Dominant follicle secretion of Estradiol → (+) feedback to anterior pituitary FSH & LH, ovulation occurs 30-36hr after the LH surge, small FSH surge also occurs at time of LH surge	Marked by change from Estradiol to progesterone predominance, corpus luteal progesterone acts on hypothalamus, causing negative feedback on FSH & LH, resulting in ↓ to basal levels prior to next cycle, if fertilization & implantation do not occur → rapid ↓ in progesterone

CONTRACEPTION

1. Oral contraceptive pills (OCPs) = combination estrogen & progestin
    a. Progestin is major contraceptive by suppressing LH & thus ovulation, also thickens cervical mucus so it is less favorable to semen
    b. Estrogen participates by suppressing FH thereby preventing selection & maturation of a dominant follicle
    c. Estrogen & progesterone together inhibit implantation by thinning endometrial lining, also resulting in light or missed menses
    d. Monophasic pills deliver a constant dose of estrogen & progestin
    e. Phasic OCPs alter this ratio (usually by varying the dose of progestin) that slightly ↓ the total dose of hormone per month, but also has slightly ↑ rate of break-through bleeding between periods
    f. Pts usually resume fertility once OCPs are discontinued; however, **3% may have prolonged postpill amenorrhea**

Advantages	Disadvantages
❖ Highly reliable, failure rate <1% (failure usually related to missing pills) ❖ Protect against endometrial % ovarian CA ❖ ↓ incidence of pelvic infections & ectopic pregnancies ❖ Menses are more predictable, lighter, less painful	❖ Requires daily compliance ❖ Does not protect against STDs ❖ 10-30% have breakthrough bleeding ❖ side effects: o Estrogen → bloating, weight gain, breast tenderness, nausea, headaches o Progestin → depression, acne, HTN

g. Absolute contraindications to use of OCPs = pregnancy, DVT or thromboembolic dz, endometrial CA, cerebrovascular or coronary artery dz, breast CA, cigarette smoking in women >35yr old, hepatic dz/neoplasm, abnormal vaginal bleeding, hyperlipidemia

Alternatives to OCPs

Method	Indication	Advantage	Disadvantage
Progestin only pills ("Mini-pills")	**Lactating women**	Can start immediately postpartum No impact on mild production or the baby	↑ failure rate than OCP (ovulation continues in 40%) requires strict compliance—low dose of progesterone requires that pill be taken at same time each day
Depo-Provera (Medroxy-progesterone)	Contraception for =1yr Noncompliance with daily OCPs Breast feeding	**IM injection** maintained for 14wk	Irregular vaginal bleed 50% pts infertile for 10mo after last injection risk of abortion
Norplant	Long-term contraception	Subcutaneous implants provide **contraception for 5yr** Prompt fertility when DC'd	30% of breakthrough pregnancies are ectopic
Intrauterine device	For those at low risk for STDs	Inserted into endometrial cavity, left in place for several years	Contraindicated in cervical or vaginal infxn, Hx of PID or infertility Spontaneous expulsion, menstrual pain, ↑ rat of ectopic pregnancy, septic abortion & pelvic infxns
Postcoital	Emergency contraception	**Progestin/estrogen** taken **within 72hr of intercourse**, repeat in 12hr Allows for early termination of unwanted pregnancy	Follow pt to ensure withdrawal bleeding occurs within 5 days Nausea

Oral estrogen or NSAIDs can ¯ bleeding, bleeding ¯ with each use, 50% pts are amenorrheic in 1yr
Injection given within first 5 days of menses (ensuring pt not pregnant)

PAP SMEAR

1. First Pap smear should be done when woman becomes sexually active or by age 18, then yearly thereafter
2. In pts with 1 sexual partner, 3 consecutive normal Pap smears & onset of sexual activity after age 25, may be able to screen less frequently
3. Reliability depends on presence/absence of cervical inflammation, adequacy of specimen & prompt fixation of specimen to avoid artifact
4. If Pap → mild- or low-grade atypical → repeat Pap—atypia my spontaneously regress
5. Recurrent mild atypia or high-grade atypia → more intensive evaluation
    a. Colpscopy
        i. Allows for magnification of cervix allowing subtle areas of Dysplastic change to be visualized, optimizing selection of biopsy sites
        ii. Cervix washed with acetic acid solution, white areas, abnormally vascularized areas & punctuate lesions are selected for biopsy
    b. Endocervical curettage (ECC) → sample of endocervix obtained at same time of colposcopy so that disease further up in endocervical canal may be detected
    c. Cone biopsy
        i. Cone-shaped specimen encompassing squamocolumnar junction (SC) & any lesions on ectocervix removed from cervix by knife, laser, or wire loop
        ii. Allows for more complete ascertainment of extent of disease & in many cases is therapaeutic as well as diagnostic
        iii. Indications = (+) ECC, unsatisfactory colposcopy meaning that entire squamocolumnar junction was not visualized, & discrepancy between Pap smear & colposcopy biopsy
6. Tx = excision of premalignant or malignant lesions—if cancer

VAGINITIS

1. 50% of cases due to Gardnerella ("bacterial vaginosis"), 25% due to Trichomonas, 25% due to Candida (↑ frequency in diabetics, in pregnancy & in HIV)
2. Most common presenting symptom in vaginitis is discharge
3. Rule out noninfectious causes, including chemical or allergic sources
4. Dx by pelvic examination with microsopic examination of discharge
5. DDx of vaginitis

	Candida	**Trichomonas**	**Gardnerella**
Vaginal pH	4-5	>6	>5
Odor	None	Rancid	"fishy" on KOH prep
Discharge	Cheesy white	Green, frothy	Variable
Si/Sx	Itchy, burning Erythema	Severe itching	Variable to none
Microscopy	Pseudohyphae, more pronounced on 10% KOH prep	Motile organisms	Clue cells (large epithelial cells covered with dozens of small dots)
Treatment	Fluconazole	Metronidazole—treat partner also	metronidazole

ENDOMETRIOSIS

1. Affects 1-2% of women (up to 50% in infertile women), peak age = 20-30s
2. Endometrial tissue in extrauterine locations, most commonly ovaries (60%), but can be anywhere in the peritoneum & rarely extraperitoneal

3. Adenomyosis = endometrial implants within the uterine wall
4. Endometrioma = endometriosis involving an ovary with implants large enough to be considered a tumor, filled with chocolate-appearing fluid (old blood) that gives them their name of "chocolate cysts"
5. Si/Sx = **the 3 D's = dysmenorrheal, dyspareunia, dyschezia** (painful defecation), pelvic pain, infertility, uterosacral nodularity palpable on rectovaginal exam, severity of Sx often do not correlate with extent of dz
6. Dx requires direct visualization via laparoscopy or laparotomy with histologic confirmation
7. Tx
    a. Start with NSAIDs, can add combined estrogen & progestin pills, allowing maintenance without withdrawal bleeding & dysmenorrheal
    b. Can use progestin-only pills, drawback is breakthrough bleeding
    c. GnRH agonists inhibit ovarian function → hypoestrogen state
    d. Danazol inhibits LH & FSH midcycle surges, side effects include hypoestrogenic & androgenic (hirsutism, acne) states
    e. Conservative surgery involves excision, cauterization, or ablation of endometrial implants with preservation of ovaries & uterus
    f. Recurrence after cessation of medical Tx is common, definitive Tx requires hysterectomy, (+) oophorectomy (TAH/BSO), lysis of adhesions & removal of endometrial implants
    g. Pts can take estrogen replacement therapy following definitive surgery, risk of reactivation of endometriosis is very small compared to risk of prolonged estrogen deficiency

REPRODUCTIVE ENDOCRINOLOGY AND INFERTILITY

AMENORRHEA

1. Amenorrhea = absence of menstruation, primary amenorrhea = a woman who has never menstruated, secondary amenorrhea = a menstrual-aged woman who has not menstruated in 6mo
2. Causes of amenorrhea
    a. **Pregnancy = most common cause**, thus every evaluation should begin with an exclusion of pregnancy before any further work-up
    b. Asherman's syndrome
        i. Scarring of the uterine cavity after a D&C procedure
        ii. **The most common anatomic cause of 2^o amenorrhea**
    c. Hypothalamic deficiency due to weight loss, excessive exercise (e.g., marathon runner), obesity, drug induced (e.g., marijuana, tranquilizers), malignancy (prolactinoma, craniopharyngioma), psychogenic (chronic anxiety, anorexia)
    d. Pituitary dysfunction results from either ↓ hypothalamic pulsatile release of GnRH or ↓ pituitary release of FSH or LH
    e. Ovarian dysfunction
        i. Ovarian follicles are either exhausted or resistant to stimulation by FSH & LH
        ii. Si/Sx = those of estrogen deficiency = hot flashes, mood swings, vaginal dryness, dyspareunia, sleep disturbances, skin thinning
        iii. **Note that estrogen deficiency 2^o to hypothalamic-pituitary failure does not cause hot flashes, while ovarian failure does**
        iv. Causes = inherited (e.g., Turner's syndrome), premature natural menopause, autoimmune ovarian failure (Blizzard's syndrome), alkylating chemotherapies
    f. Genital outflow tract alteration, usually the result of congenital abnormalities (e.g., imperforate hymen or agenesis of uterus/vagina)
3. Tx
    a. Hypothalamic → reversal of underlying cause & induction of ovulation with gonadotropins

b. Tumors → excision or bromocriptine for prolactinoma
c. Genital tract obstruction → surgery if possible
d. Ovarian dysfunction → exogenous estrogen replacement

DYSFUNCTIONAL UTERINE BLEEDING

1. Irregular menstruation without anatomic lesions of the uterus
2. **Usually due to chronic estrogen stimulation** (vs. amenorrhea, an estrogen deficient state), more rarely to genital outflow tract obstruction
3. Abnormal bleeding = bleeding at intervals <21 days or >36 days, lasting longer than 7 days, or blood loss >80mL
4. Menorrhagia (excessive bleeding) is usually due to anovulation
5. Dx
    a. Rule out anatomic causes of bleeding including uterine fibroids, cervical or vaginal lesions or infection, cervical & endometrial cancer
    b. Evaluate stress, exercise, weight changes, systemic disease such as thyroid, renal or hepatic disease & coagulopathies, & pregnancy
6. Tx
    a. Convert proliferative endometrium into secretory endometrium by administration of a progestational agent for 10 days
    b. Alternative is to give OCPs that suppress the endometrium & establish regular, predictable cycles
    c. NSAIDs (+) iron used in pts who want to preserve fertility
    d. **Postmenopausal bleeding is cancer until proven otherwise**

HIRSUTISM & VIRILIZATION

1. Hirsutism = excess body hair, usually a/w acne, most commonly due to polycystic ovarian dz or adrenal hyperplasia
2. Virilization = masculinization of a woman, a/w marked ↑ testosterone, clitomegaly, temporal balding, voice deepening, breast involution, limb-shoulder girdle remodeling

Disease	**Characteristics**	**Treatment**
Polycystic ovarian disease	❖ **#1 cause of androgen excess & hirsutism** ❖ etiology likely related to LH overproduction ❖ Si/Sx = oligo- or amenorrhea, anovulation, infertility, hirsutism, acne ❖ Labs → ↑**LH/FSH, - testosterone**	❖ Break feedback cycle with OCPs → ↓ LH production ❖ Weight loss may allow ovulation, sparing fertility ❖ Refractory pts may require clomiphene to (+) ovulation
Sertoli-Leydig cell tumors	❖ Ovarian tumors secreting testosterone, usually in women aged 20-40 ❖ Si/Sx = **rapid onset** of hirsutism, acne, amenorrhea, virilization ❖ Labs → ↓**LH/FSH, - - - Testosterone**	❖ Removal of involved ovary (tumors usually unilateral) ❖ 10-yr survival = 90-95%
Congenital adrenal hyperplasia	❖ Usually due to 21-α-hydroxylase defect ❖ Autosomal recessive, variable penetrance ❖ When severe → virilized newborn, milder forms can present at puberty or later ❖ Labs → ↑**LH/FSH, - DHEA**	❖ Glucocorticoids to suppress adrenal androgen production

MENOPAUSE

1. Defined as the cessation of menses, **average age in US is 51yr**

2. Suspect when menstrual cycles are not regular & predictable & whe cycles are not a/w any premenstrual symptoms
3. Si/Sx = rapid onset hot flashes & sweating with resolution in 3min, mood changes, sleep disturbances, vaginal dryness/atrophy, dyspareunia (painful intercourse) & osteopororsis
4. Dx = irregular menstrual cycles, hot flashes & ↑ FSH level (>30mlU/mL)
5. Depending on clinical scenario other laboratory tests should be conducted to exclude other diagnoses that can cause amenorrhea such as thyroid disease, hyperprolactinemia, pregnancy
6. Tx
    a. **First line is estrogen hormone replacement therapy (HRT)**
    b. HRT can be via continuous estrogen with cyclic progestin to allow controlled withdrawal bleeding or via daily administration of both estrogen & progestin, which does not cause withdrawal bleeding
    c. There are risks & benefits of HRT

Risks	**Benefits**
Endometrial CA ↑ risk with HRT, but risk significantly ↓ by addition of =10 days of progesterone to induce uterine wall sloughing	Relief of menopause Sx
Breast CA Very controversial, studies equivocal, some show that prolonged HRT (=5-10yr) →↑ relative risk of breast CA Regardless, breast CA or heavy risk factors for its development are contraindications to HRT	↓ risk of heart dz or stroke ↑ HDL, ↓LDL
DVT/PE Only seen with oral estrogen (not transdermal)	↓ osteoporosis
Breast pain Due to constant estrogen stimulation	↓ risk of dementia

    d. Raloxifene
        i. Second-generation tamoxifen-like drug = mixed estrogen agonist/antagonist, FDA approved to prevent osteoporosis
        ii. So far raloxifene shown to act like estrogen in bones (good), ↓ serum LDL (good) but does not stimulate endometrial growth (good) unlike tamoxifen & estrogen alone), effects on breast are not yet known
    e. **Calcium supplements are not a substitute for estrogen replacement**

INFERTILITY

1. Defined as failure to conceive after 1yr of unprotected sex
2. Affects 10-15% of reproductive-age couples in the US
3. Causes = abnormal spermatogenesis (40%), anovulation (30%), anatomic defects of the female reproductive tract (20%), unknown (10%)
4. Dx
    a. **Start work-up with male partner not only because it is the most common cause,** but because the work-up is simpler, noninvasive & more cost-effective than work-up of infertility in the female
    b. Normal semen excludes male cause in >90% of couples
    c. Work-up of female partner should include measurement of basal body temperature, which is an excellent screening test for ovulation
        i. Temperature drops at time of menses, then rises 2 days after LH surge at the time of progesterone rise
        ii. Ovulation probably occurs 1 day before first temperature elevation & temperature remains elevated for 13-14 days

iii. A temperature elevation of >16 days suggests pregnancy

d. Anovulation
   i. Hx of regular menses with premenstrual Sx (breast fullness, ↓ vaginal secretions, abdominal bloating, mood changes) strongly suggests ovulation
   ii. Sx such as irregular mesnes, amenorrhea episodes, hirsutism, acne, galactorrhea, suggest anovulation
   iii. FSH measured at day 2-3 is best predictor of fertility potential in women, FSH >25IU/L correlated with a poor prognosis
   iv. Dx confirm with basal body temperature, serum progesterone (↑ postovulation, >10ng/mL → ovulation), endometrial Bx

e. Anatomic disorder
   i. **Most commonly results from an acquired disorder, especially acute salpingitis 2^{o} to N. gonorrhoeae & C. trachomatis**
   ii. Endometriosis, scarring, adhesions from pelvic inflammation or previous surgeries, tumors & trauma can also disrupt normal reproductive tract anatomy
   iii. Less commonly a congenital anomaly such as septate uterus or reduplication of the uterus, cervix, or vagina is responsible
   iv. **Dx with hysterosalpingogram**

5. Tx
   a. Anovulation → restore ovulation with use of ovulation-inducing drugs
      i. First line = clomiphene, an estrogen antagonist that relieves negative feedback on FSH, allowing follicle development
      ii. Anovulatory women who bleed in response to progesterone are candidates for clomiphene, as are women with irregular menses or midluteal progesterone levels <10ng/mL
      iii. 40% get pregnant, 8-10% ↑ rate of multiple births, mostly twins
      iv. If no response, FSH can be given directly → pregnancy rates of 60-80%, multiple births occur at an ↑ rate of 20%
   b. Anatomic abnormalities → surgical lysis of pelvic adhesions
   c. If endosalpinx is not intact & transport of the ovum is not possible, an assisted fertilization technique, such as in vitro fertilization, may be used with 15-25% success

UROGYNECOLOGY

PELVIC RELAXATION & URINARY INCONTINENCE

1. ↑ incidence with age, also with birth trauma, obesity, chronic cough
2. Si/Sx = prolapse of urethra (urethrocele), uterus, bladder (cystocele), or rectum (rectocele), pelvic pressure & pain, dyspareunia, bowel & bladder dysfunction, & urinary incontinence
3. Types of urinary incontinence
   a. Stress incontinence = bladder pressure exceeds urethral pressure briefly at times of strain or stress such as coughing or laughing
   b. Urge incontinence & overflow incontinence result from ↓ innervation & control of bladder function resulting in involuntary bladder contraction (urge0 or bladder atony (overflow)
4. Dx = urodynamic testing, assess for underlying medical conditions such as diabetes, neurologic dz, genitourinary surgery, pelvic irradiation, trauma & medications that may account for Sx
5. Tx = correct underlying cause
   a. Kegel exercises to tone pelvic floor
   b. Insertion of pessary devices to add structural support
   c. Useful drugs = anticholinergics, Ditropan/Detrol, β-agonists
   d. Useful drugs = anticholinergics, Ditropan/Detorl, β-agonists
   e. Surgical repair aimed at restoring structures to original anatomic position

GYNECOLOGY ONCOLOGY

ENDOMETRIAL CANCER

1. Most common reproductive tract caner with approximately 35,000 new cases per year
2. "Estrogen-dependent" cancer
    a. Estrogen source can be glandular from the ovary
    b. Extraglandular from peripheral conversion of androstenedione to estrone or from a granulosa cell tumor
    c. Exogenous from oral estrogen, cutaneous patches, vaginal creams & now tamoxifen (reduces risk of breast cancer by 50%, but a/w 3x ↑ incidence of endometrial cancer)
3. Risk factors
    a. Unopposed postmenopausal estrogen replacement therapy
    b. Menopause after 52yr
    c. Obesity, nulliparity, feminizing ovarian tumors (e.g., ovarian granulosa cell tumors), chronic anovulation, polycystic ovarian syndrome, postmenopausal (75% of patients), diabetes
4. Si/Sx = abnormal uterine bleeding, especially postmenopausal—any woman over age 35yr with abnormal uterine bleeding should have a sample of endometrium taken for histologic evaluation
5. DDx = endometrial hyperplasia
    a. Abnormal proliferation of both glandular & stromal elements, can be simple or complex
    b. Atypical hyperplasia
        i. Significant numbers of glandular elements that exhibit cytological atypia & disordered maturation
        ii. Analogous to carcinoma in situ → 20-30% risk for malignancy
6. Dx
    a. **Pap smear IS NOT reliable in Dx of endometrial cancer; however, if atypical glandular cells of undetermined significance (AGCUS) are found on the smear then endometrial evaluation is mandatory**
    b. Bimanual exam for masses, nodularity, induration & immobility
    c. Endometrial biopsy by endocervical curettage, D&C, hysteroscopy with directed biopsies
7. Tx
    a. Simple or complex hyperplasia → progesterone to reverse hyperplastic process promoted by estrogen (e.g., Provera x 10d)
    b. Atypical hyperplasia → hysterectomy because of likelihood that it will become invasive endometrial carcinoma
    c. Endometrial carcinoma
        i. Total abdominal hysterectomy with bilateral salpingo-oophorectomy (TAH/BSO), lymph node dissection
        ii. Adjuvant Tx may include external-beam radiation
        iii. Tx for recurrence is high-dose progestins (e.g., Depo-Provera)
8. Px
    a. **Most important prognostic factor is histological grade**
    b. GI is highly differentiated, G2 is moderately differentiated, G3 is predominantly solid or entirely undifferentiated carcinoma
    c. Depth of myometrial invasion is second most important Px factor
    d. Pt with G1 tumor that does not invade the myometrium has a 95% 5-yr survival, pt with G3 tumor with deep myometrial invasion has 5-yr survival rate closer to 20%

UTERINE LEIOMYOMAS = FIBROIDS

1. Benign tumors, growth related to estrogen production, usually most rapid growth occurs perimenopausally

2. Most common indication for hysterectomy (30% of cases)
3. Si/Sx = bleeding (usually menorrhagia or ↑ amount & duration of flow), pelvic pressure, pelvic pain often manifested as dysmenorrheal
4. Dx = Utz, confirm with tissue sample by either D&C or biopsy (especially in post-menopausal pts)
5. Tx
    a. If Sx are mild → reassurance & observation
    b. Medical Tx → estrogen inhibitors such as GnRH agonists shrink uterus, resulting in a simpler surgical procedure or can be used as a temporizing measure until natural menopause occurs
    c. Surgery → myomectomy indicated in young pts who want to preserve fertility (risk of intraoperative & postoperative hemorrhage ↑ compared to hysterectomy); hysterectomy is considered definitive treatment, but should be reserved for symptomatic women who have completed childbearing

LEIOMYOSARCOMA

1. Rare malignancy accounting for only 3% of cancers involving uterine corpus
2. ↑ suspicion for postmenopausal uterine enlargement
3. Si/Sx suggestive of sarcoma = postmenopausal bleeding, pelvic pain & →↑ vaginal discharge
4. Tx = hysterectomy with intraoperative lymph node biopsies
5. Surgical staging same as that for endometrial adenocarcinoma
6. Survival rate is much lower than that for endometrial cancer, only 50% of patients survive 5yr
7. Adjunctive therapies are of minimal benefit

CERVICAL CANCER

1. Annual Pap smear is most important screening tool available to detect disease
2. Risk factors = early sexual intercourse, multiple sexual partners, HPV infection (especially type 16, 18), cigarette smoking, early childbearing & immunocompromised patients
3. Average age of Dx = 50yr, but can occur much earlier
4. 85% are of squamous cell origin, 15% are adenocarcinomas arising from endocervical glands
5. Si/Sx = postcoital bleeding, but there is no classic presentation for cervical cnacer
6. Dx = Pap screening, any visible cervical lesion should be biopsied
7. Tx
    a. Local dz → hysterectomy + lymph node dissection—ovaries may remain → survival >70% at 5yr
    b. Extensive or metastatic dz → pelvic irradiation → survival <40% at 5yr

Neoplasm	**Characteristics**	**Tx**
Benign cysts	❖ Functional growth resulting from failure of normal follicle to rupture ❖ Si/Sx = pelvic pain or pressure, rupture of cysts → acute, severe pain & hemorrhage mimicking acute abdomen ❖ Confirm cyst with Utz	❖ Typically self-limiting ❖ Rupture may require laparotomy to stop bleeding
Benign tumors: more common than malignant, but risk of malignancy ↑ with age		
Epithelial	❖ Serous cystadenocarcinoma most common type, almost always benign unless bilateral →↑ risk of malignancy ❖ Other types = mucinous, endometrioid, Brenner tumors, all rarely malignant ❖ Dx = clinical, can see on CT/MRI	❖ Surgical excision

Germ cell	❖ Teratoma is most common (also called "dermoid cyst") ❖ Very rarely malignant, contain differentiated tissue from all 3 embryologic germ layers ❖ Si/Sx = unilateral cystic, mobile, nontender adnexal mass, often aSx ❖ Dx confirmed with Utz	❖ Excision to prevent ovarian torsion or rupture
Stromal cell	❖ Functional tumors secreting hormones ❖ Granulosa tumor makes estrogens → gynecomastia, loss of body hair, etc. ❖ Sertoli-Leydig cells make androgens, virilize females	❖ Excision

Malignant Tumors

❖ Usually occur in women >50yr old
❖ Risk factors = low parity, ↓ fertility, delayed childbearing—**OCP use is a protective factor**
❖ Most lethal gynecologic cancer due to lack of early detection → ↑ rate of metastasis (60% at Dx)
❖ Dz ar typically asymptomatic until extensive metastasis has occurred
❖ Can follow dz with Ca-125 marker, not specific enough for screening
❖ Yearly pelvic exams remain most effective screening tool
❖ Si/Sx = vague abdominal/pelvic complaints, e.g., distension, early satiety, constipation, pelvic pain, urinary frequency—shortness of breath due to pleural effusion may be only presenting Sx

Tx = debulking surgery with chemo- & radiotherapy

Subtypes	**Characteristics**	**Treatment**
Epithelial cell	❖ Cause 90% of all ovarian malignancies ❖ Serous cystadenocarcinoma is most common, often originate from benign precursors ❖ Others = enodmetrioma & mucinous cystadenocarcinoma	❖ Excision
Germ cell	❖ Most common ovarian cancers in women <20 years old ❖ Can produce HCG or α-fetoprotein, useful as tumor markers ❖ Subtypes = dysgerminoma, which is very radiosensitive, & immature teratoma	❖ Radiation first line ❖ Chemotherapy second line ❖ 5-yr survival >80% for both
Stromal	❖ granulosa cell makes estrogen, can result in 2^{o} endometriosis or endometrial carcinoma ❖ Sertoli-Leydig tumor makes androgens	❖ Total hysterectomy with oophorectomy

VULVAR & VAGINAL CANCER

1. Vulvar intraepithelial neoplasia (VIN)
    a. VIN I & II = mild & moderate dysplasia, ↑ risk progressing to advanced stages & then carcinoma
    b. VIN III = carcinoma in situ
    c. Si/Sx = pruritus, irritation, presence of raised lesion
    d. Dx = biopsy for definitive diagnosis
    e. DDx includes Paget's disease, malignant melanoma
    f. Tx = excision, local for VIN I & II & wide for VIN III
2. Vulvar cancer
    a. 90% are squamous
    b. Usually presents postmenopausally
    c. Si/Sx = pruritus, with or without presence of ulcerative lesion
    d. Tx = excision

    e. 5-yr survival rate is 70-90% depending on nodal status, if deep pelvic nodes are involved survival is a dismal 20%
3. Vaginal CIS & carcinoma are very rare
    a. 70% of patients with vaginal CIS have either previous or coexistent genital tract neoplasm
    b. Tx = radiation, surgery reserved for women with extensive dz

GESTATIONAL TROPHOBLASTIC NEOPLASIA (GTN) = HYDATIDIFORM MOLE OR MOLAR PREGNANCY

1. Rare variation of pregnancy in which a neoplasm is derived from abnormal placental tissue (trophoblastic) proliferation
2. Usually a benign disease called a "molar pregnancy" that is further subdivided into complete mole (90%) in which there is no fetus & incomplete mole in which there is a fetus & molar degeneration
3. Persistent or malignant disease develops in 20% of pts (mostly in complete moles)
4. Complete moles are 46XX, do not form fetus
5. Partial moles are 69XXY triploids, often form partial fetus
6. Si/Sx = exaggereated pregnancy Sx, with missing fetal heart tones & enlarged uterus (size > dates), painless bleeding commonly occurs in early second trimester
7. Pts can also present with PIH
8. Utz $\rightarrow$ characteristic "snowstorm" pattern
9. Dz = Utz+ $\uparrow\uparrow\uparrow$ hCG levels
10. Tx = removal of uterine contents by D&C & suction curettage
11. Nonmetastatic persistent GTN is treated with methotrexate
12. Follow-up = check that hCG levels are appropriately dropping
13. Contraception is recommended during first yr of follow-up

4 PEDIATRICS

DEVELOPMENT

DEVELOPMENT MILESTONES

Age	Gross motor	Fine motor	Language	Social/cognition
Newborn	Head side to side Moro & grasp reflex			
2mos	Holds head up	Swipes at object	Coos	Social smile
4mos	Rolls front to back	Grasps object	Orients to voice	Laughs
6mos	Rolls back to front, sits upright	Transfers object	Babbles	Stranger anxiety, sleeps all night
9mos	Crawl, pull to stand	Pincer grasp, eats with fingers	Mama-dada (nonspecific)	Picture book
12mos	Stands	Mature pincer	Mama-dad (specific)	Picture books
15mos	Walks	Uses cup	4-6 words	Temper tantrum
18mos	Throws ball, walks upstairs	Uses spoon for solids	Names common objects	Toilet training may begin
24mos	Runs, up/down stairs	uses spoon for semisolids	2-word sentence (2 word at 2yr)	Follows 2-step command
36mos	Rides tricycle	Eats neatly with utensils	3-word sentence (3 word at 3yr)	Knows first & last name

TANNER STATES

Boys	Girls
Testicular enlargement at 11.5yr	Beast buds at 10.5yr
Increase in genital size	Pubic hair
Pubic hair	Linear growth spurt at 12yr
Peak growth spurt at 13.5yr	Menarche at 12.5yr

THE ToRCHS

Disease	Characteristics
Toxoplasmosis	❖ Acquired in mothers via ingestion of poorly cooked meat or through contact with cat feces ❖ Carriers common (10-30%) in population, only causes neonatal dz if acquired during pregnancy (1%) ❖ 1/3 of women who acquire during pregnancy transmit infection to fetus & 1/3 of fetuses are clinically affected ❖ Sequelae = intracerebral calcifications, hydrocephalus, chorioretinitis, microcephaly, severe mental retardation, epilepsy, intrauterine growth retardation (IUGR), hepatosplenomegaly ❖ Screening is useless since acquisition prior to infection is common & clinically irrelevant ❖ Pregnant women should be told to avoid undercooked meat, wash hands after handling cat, do not change litter box ❖ If fetal infection established → Utz to determine major anomalies & provide counseling regarding termination if indicated
Rubella	❖ 1st trimester maternal Rubella infxn → 80% chance of fetal transmission ❖ 2nd trimester → 50% chance of transmission to fetus, 3rd trimester → 5% ❖ Si/Sx of fetus = IUGR, cataracts, glaucoma, chorioretinitis, patent ductus artiosus, pulmonary stenosis, atrial or ventricular septal defect, myocarditis, microcephaly, **hearing loss, "blueberry muffin rash",** mental retardation ❖ Dx confirmed with IgM Rubella Ab in neonate's serum, or viral culture ❖ Tx = prevention by universal immunization of all children against Rubella, there is no effective therapy for active infection
Cytomegalovirus (CMV)	❖ #1 congenital infection, affecting 1% of births ❖ transmitted through bodily fluids/secretions, infection often asymptomatic ❖ 1° seroconversion during pregnancy → ↑ risk of severely affected infant, but congenital infection can occur if mother reinfected during pregnancy ❖ About 1% risk of transplacental transmission of infection, about 10% of infected infants manifest congenital defects of varying severity ❖ Congenital defects = microcephaly, intracranial calcifications, severe mental retardation, chorioretinitis, IUGR

	❖ 10-15% of asymptomatic but exposed infants will develop later neurologic sequelae
Herpes simplex virus	❖ **C-section delivery for pregnant women with active herpes** ❖ Vaginal → 50% chance that the baby will acquire the infection & is a/w significant morbidity & mortality ❖ Si/Sx = vesicles, seizures, respiratory distress, can cause pneumonia, meningitis, encephalitis → impaired neurologic development after resolution ❖ Tx = acyclovir (markedly decreases mortality)
Syphilis	❖ Transmission from infected mother to infant during pregnancy nearly 100% **occurs after the first trimester in the vast majority of cases** ❖ Fetal/perinatal deaths in 40% of affected infants ❖ Early manifestation in first 2yrs, later manifestations in next 2 decades ❖ Si/Sx of early dz = jaundice, ↑ LFTs, hepatosplenomegaly, hemolytic anemia, rash followed by desquamation of hands & feet, wart-like lesions of mucous membranes, **blood-tinged nasal secretions (snuffles), diffuse osteochondritis, saddle nose (2^o to syphilitic rhinitis)** ❖ Si/Sx of late dz = **Hutchinson teeth** (notching of permanent upper 2 incisors), mulberry molars (both at 6yr), bone thickening (frontal bossing), **anterior bowing of tibia (saber shins)** ❖ Dx = RPR/VDRL & FTA serologies in mother with clinical findings in infant ❖ Tx = procaine penicillin G for 10-14 days

INFANT BOTULISM

1. Acute, flaccid paralysis caused by *Clostridium botulinum* neurotoxin that irreversibly blocks acetylcholine release from peripheral neurons
2. Dz acquired via **ingestion of spores in honey** or via inhalation of spores
3. 95% cases in infants 3wk to 6mo old, peak 2-4 mo
4. Si/Sx = constipation, lethargy, poor feeding, weak cry, ↓ spontaneous movement, hypotonia, drooling, ↓ gag & suck reflexes, as dz progresses → **loss of head control & respiratory arrest**
5. Dx = clinical, **based on acute onset of flaccid descending paralysis with clear sensorium, without fever or paresthesias**, can confirm by demonstrating botulinum toxin in serum or toxin/organism in feces
6. Tx = intubate, supportive care, no antibiotics or antitoxin needed in infants

VIRAL EXANTHEMS

Disease/Virus	**Si/Sx**
Measles (Rubeola) Paramyxovirus	❖ Erythematous maculopapular rash, **erupts 5 days after onset of prodromal Sx, begins on head & spreads to body, lasting 4-5 days**, resolving from head downward ❖ **Koplik spots (white spots on buccal mucosa) are pathognomonic**, but leave before rash starts so often not found when pt presents ❖ **Dx = fever & Hx of the 3C's: cough, coryza, conjunctivitis**
Rubella (German measles) Togavirus	❖ **Suboccipital lymphadenopathy** (very few dzs do this) ❖ Maculopapular rash begins on face then generalizes ❖ Rash lasts 5 days, fever may accompany rash on first day only ❖ May find reddish spots of various sizes on soft palate
Hand, foot & mouth disease Coxsackie A virus	❖ Vesicular rash on hands & feet with ulcerations in mouth ❖ Rash clears in about 1wk ❖ Contagious by contact
Roseola infantum (Exanthem subitum) (HHV6)	❖ **Abrupt high fever persisting for 1-5 days even though child has no physical Sx to account for fever & does not feel ill** ❖ When fever drops, macular or maculopapular rash appears on trunk & then spread peripherally over entire body, lasts 24hr.
Erythema infectiosum (Fifth disease) Parvovirus B-19	❖ **Classic sign = "slapped cheeks,"** erythema of the cheeks ❖ Subsequently an erythematous maculopapular rash spreads from arms to trunk & legs forming a reticular pattern ❖ **Dz is dangerous in sickle cell pts (& other anemias) due to parvovirus B-19's tendency to cause aplastic crises**
Varicella (Chicken pox) Varicella Zoster Virus (VZV)	❖ Highly contagious, pruritic "tear drop" vesicles that break & crust over, start on face or trunk (centripetal) & spread to extremities ❖ New lesions appear for 3-5 days & typically take 3 days to crust over, so rash persists for about 1wk ❖ **Lesions are contagious until they crust over** ❖ Zoster (shingles) = reactivation of old Varicella infxn, painful skin eruptions are seen along the distribution of dermatomes that correspond to the affected dorsal root ganglia

RECOMMENDED CHILDHOOD IMMUNIZATION SCHEDULE

Age	**Vaccine**
Newborn	Hep B (1)
2mo	Hep B (2), DTaP (rotavirus), Hib, Polio
4mo	DTaP (rotavirus), Hib, Polio
6mos	Hep B (3), DTaP (rotavirus), Hib
12mo	MMR, Varicella, Hib, Polio
15mo	DTaP (may combine with Hib at 12mos)
4-6y	MMR, DTaP, Polio
11-12y	MMR (if 2nd dose not given yet), Varicella, Td

RESPIRATORY DISORDERS

OTITIS MEDIA

1. Usually in children, precipitated by a viral URI
2. Congenital disorders (e.g., Down's syndrome, cleft palate) that prevent Eustachian tube drainage ↑ risk of infection
3. Si/Sx = ear pressure, ↓ hearing, fever, **erythema & ¯ mobility of tympanic membrane** (TM), TM bulging & a meniscus of fluid behind the TM (effusion)
4. Caused by S. pneumoniae, H. influenzae, Moraxella, or viral infection such as respiratory syncytial virus (RSV)
5. Tx = amoxicillin, Augmentin (2nd line)
6. Surgical tube placement may be required for chronic effusions to prevent developmental delay secondary to hearing loss

BRONCHIOLITIS

1. Commonly seen in children under 2yr, peak incidence at 6mo
2. **>50% due to RSV**, others include parainfluenzae & adenovirus
3. Si/Sx = mild rhinorrhea & fever progress to cough, wheezing with crackles, tachypnea, nasal flaring, decreased appetite
4. Dx by culture or antigen detection of nasopharyngeal secretions
5. Tx = bronchodilators, oxygen as needed

PEDIATRIC UPPER RESPIRATORY DISORDERS

Disease	**Cause**	**Si/Sx**	**Labs**	**Tx**
Croup (Laryngotrach-eobronchitis)	Parainfluenza, influenza, RSV, Mycoplasma	**Presents in fall & winter, 3mo-3yr old, with barking cough, inspiratory stridor, Sx worse at night**, hoarse voice, preceded by URI	**Neck x-ray ® "steeple sign"**	O2, cool mist, racemic Epi & steroids if sever, Ribavirin may be used for immunocompromised
Epiglottitis	H. influenzae type B	**Medical emergency!!! Fulminant inspiratory stridor, drooling, sits leaning forward**, dysphagia, "hot potato" voice	**"Thumb print" sign on lateral neck film**, cherry-red epiglottitis on endoscopy	**Examine pt in OR**, intubate as needed, ceftriaxone
Bacterial tracheitis	Staph. & Strep. Spp.	Inspiratory stridor, high fever, toxic appearing	Leukocytosis	Nafcillin or ceftriaxone
Foreign body aspiration		**Usually presents after 6mo old** (need to grasp object to inhale it) with **inspiratory stridor** (chronic), wheeze, ↓ breath sounds, dysphagia & unresolved pneumonia	CXR → hyperinflation on affected side, ENT consult	Endoscopic or surgical removal

PNEUMONIA

1. Common etiologies vary with age
    a. Newborns get S. agalactiae (group B Strep), gram-negative rod, Chlamydia trachomatis
    b. Infants get S. pneumoniae, H. influenze, Chlamydia, S. aureus, Listeria monocytogenes & viral
    c. Preschoolers get RSV, other viruses & Mycoplasma
    d. Adolescents get S. pneumoniae, Mycoplasma & Chlmaydia
2. Si/Sx = cough (productive in older children), fever, nausea/vomiting, diarrhea, tachypnea, grunting, retractions, crackles
3. Pertussis presents with 3 stages

a. Catarrhal stage = 1-2 weeks of cough, rhinorrhea, wheezing
b. Paroxysmal stage = 2-4 weeks of paroxysmal cough with "whoops"
c. Convalescent stage = 1-2 weeks of persistent chronic cough

4. Chlamydia causes classic "staccato cough" & conjunctivitis, pts afebrile
5. RSV causes wet cough, often with audible wheezes
6. Staphylococcus infections may be a/w skin lesions as well
7. Dx = rapid antigen detection or culture of secretions, CXR → infiltrates
8. Tx = infants get hospitalized, broncodilators & O2 for RSV, erythromycin for atypical dz (e.g., Chlamydia, Mycoplasma), cefuroxime for bacteria.

MUSCULOSKELETAL

LIMP

1. Painful limp is usually acute onset, may be a/w fever & irritability, toddlers may refuse to walk
2. DDx painful limp
3. Painful limp usually has insidious onset, may be due to weakness or deformity of limb 2^{o} to developmental hip dysplasia, cerebral palsy, or leg length discrepancy

PEDIATRIC PAINFUL LIMP

Disease	**Characteristics**	**Tx**
Septic arthritis	❖ **#1 cause of painful limp in 1-3yr-old** ❖ Usually monoarticular → hip, knee, or ankle ❖ Causes = S. aureus **(most common)**, H. influenzae, N. gonorrhoeae ❖ Si/Sx = **acute onset pain**, arthritis, fever, ↓ ROM, child may lie still & refuse to walk or crawl, - **WBC,** - **ESR** ❖ X-ray → joint space widening, soft tissue swelling ❖ Dx = joint aspiration → turbid gray, **WBC = 10,000 with neutrophil predominance**, low glucose	Tx = drainage, antibiotics appropriate to Gram's stain or cultures
Toxic synovitis	❖ Most common in males 5-10yr old, may precede viral URI ❖ Si/Sx = **insidious onset pain,** low grade fever, **WBC & ESR normal** ❖ **Typically no tenderness, warmth, or joint swelling** ❖ X-ray → usually normal ❖ Dx → technetium scan ® - **uptake of epiphysis**	Rest & analgesics for 3-5 days
Aseptic avascular necrosis	❖ Legg-Calve-Perthes dz = head of femur, Osgood-Schlatter = tibial tubercle, Kohler's bone dz = navicular bone ❖ Legg-Calve-Perthes → usually 4-9yr old (M:F = 5:1), bilateral in 10-20% of cases, ↑ incidence with delayed growth & ↓ birth weight ❖ Si/Sx = **afebrile, insidious onset** hip pain, inner thigh, or knee, ↑ pain with movement, ↓ with rest, antalgic gait, **normal WBC & ESR** ❖ X-ray → **femoral head sclerosis** & ↑ width of femoral neck ❖ Dx → technetium scan → ¯ **uptake in epiphysis**	↓ weight bearing on affected side over long time
Slipped capital femoral epiphysis	❖ Often in **obsess male adolescents** (8-17yr old), 20-30% bilateral ❖ 80% → slow, progressive, 20% → acute a/w trauma ❖ Si/Sx → **dull, aching pain** in hip or knee, ↑ pain with activity ❖ X-ray → lateral movement of femur shaft in relation to femoral head, looks like **"ice-cream scoop falling off cone"** ❖ Dx = clinical	Surgical pinning
Osteomyelitis	❖ Neonates → S. aureus (50%), S. agalactiae, E. coli ❖ Children → Staph & Strep, Salmonella (sickle cell), P. aeruginosa ❖ Si/Sx young infants → fever may be only symptom ❖ Si/Sx older children → fever, malaise, ↓ extremity movement, edema ❖ X-ray lags changes by 3-4 weeks ❖ Dx → neutrophilic leukocytosis, ↑ ESR (50%), blood cultures, bone scan (90% sensitive), **MRI is the gold standard**	IV antibiotics for 4-6wk

COLLAGEN VASCULAR DISEASES

1. Juvenile rheumatoid arthritis
   a. Chronic inflammation of =1 joints in pt =16yr old
   b. Most commonly in children 1-4yr old, females > males
   c. 3 categories = systemic, pauciarticular, polyarticular

d. Dx = Sx persist for 3 consecutive mo with exclusion of other causes of acute/chronic arthritis or collagen vascular diseases
e. Tx= NSAIDs, low-dose methotrexate, prednisone only in acute febrile onset

TYPES OF JUVENILE RHEUMATOID ARTHITIS

Systemic (10-20%)	❖ High, **spiking fevers** with return to normal daily, generalized lymphadenopathy ❖ **Rash of small, pale pink macules with central pallor on trunk & proximal extremities with possible involvement of palms & soles** ❖ Joint involvement may not occur for weeks to months after fever ❖ 1/3 have disabling chronic arthritis
Pauciarticular (40-60%)	❖ Involves =4 joints, large joints primarily affected (knees, ankles, elbows, asymmetric) ❖ Other Si/Sx – fever, malaise, anemia, lymp hadenopathy, **chronic joint dz is unusual** ❖ Divided into 2 types o Type 1 (most common) → females <4yr, ↑ risk for chronic iridocyclitis, 90% ANA+ o Type 2 → males >8yr, ANA-, 75% HLA-B27+, ↑ risk of ankylosing spondylitis or Reiter's later in life
Polyarticular	❖ =5 joints involved, small & large, insidious onset, fever, lethargy, anemia ❖ 2 types depending on if rheumatoid factor is present or not Rheumatoid factor (+) → 80% females, late onset, more severe, rheumatoid nodules present, 75% ANA+ ❖ Rheumatoid factor - →occurs any time during childhood, mild, rarely a/w rheumatoid nodules, 25% ANA+

2. Kawasaki's disease (mucocutaneous lymph node syndrome)
   a. Large & medium vessel vasculitis in children <5yr old, predilection for Japanese children
   b. Dx = fever > 104^{o} for >5days, unresponsive to antibiotics (+) 4 out of 5 of the following criteria (mnemonic: CRASH)
      i. Conjunctivitis
      ii. Rash, primary truncal, protean
      iii. Aneurysms of coronary arteries
      iv. Strawberry tongue, crusting of lips, fissuring of mouth & oropharyngeal erythema
      v. Hands & feet show induration, erythema of palms & soles, desquamation of fingers & toes
   c. Complications = cardiac involvement, 10-40% of untreated cases show evidence of coronary vasculitis (dilation/aneurysm) within first weeks of illness
   d. Tx = immediate IVIG to prevent coronary vasculitis, high-dose aspirin-prednisone is contraindicated & will exacerbate the dz!
   e. Px
      i. Response to IVIG & aspirin is rapid, 2/3 pts afebrile within 24hr
      ii. Evaluate pts one week after discharge, repeat echocardiography 3-6wk after onset of fever, if baseline & repeat echo do not detect any coronary abnormalities, further imaging is unnecessary
3. Henoch-Schonlein purpura
   a. IgA small vessel vasculitis, related to IgA nephropathy (Berger's disease)
   b. Si/Sx = **pathognomonic palpable purpura** on legs & buttocks (in children), abdominal pain, may cause intussusception
   c. Tx = self-limited, rarely progresses to glomerulonephritis

HISTIOCYTOSIS X

1. Proliferation of histiocytic cells resembling Langerhans' skin cells
2. 3 common variants
   a. Letterer-Siwe disease
      i. Acute, aggressive, disseminated variant, usually fatal in infants
      ii. Si/Sx = hepatosplenomegaly, lymphadenopathy, pancytopenia, lung involvement, recurrent infections
   b. Hand-Schuller-Christian
      i. Chronic progressive variant, presents prior to 5yr old
      ii. **Classic triad = skull lesions, diabetes insipidus, exophthalmos**
   c. Eosinophilic granuloma
      i. Extraskeletal involvement generally limited to lung
      ii. Has the best Px, rarely fatal, sometimes spontaneously regresses

METABOLIC

CONGENITAL HYPOTHYROIDISM

1. Due to 2^{o} agenesis of thyroid or defect in enzymes
2. **T4 is crucial during first 2yr of life for normal brain development**
3. Birth Hx → normal Apgars, prolonged jaundice (↑ indirect bilirubin)
4. Si/Sx = presents at 6-12wk old with poor feeding, lethargy, **hypotonia, coarse facial features, large protruding tongue**, hoarse cry, constipation, developmental delay
5. Dx = ↓ T4, ↑TSH
6. Tx = levothyroxine replacement
7. **If Dx delayed beyond 6wk, child will be mentally retarded**
8. Newborn screening is mandatory by law

NEWBORN JAUNDICE

1. Physiologic jaundice is clinically benign, occurs 24-48hr after birth
    a. Characterized by unconjugated hyperbilirubinemia
    b. 50% of neonates have jaundice during first wk of life
    c. Results from increased bilirubin production & relative deficiency in glucuronyl transferase in the immature liver
    d. Requires no Tx
2. Jaundice present AT birth is ALWAYS pathologic
3. Unconjugated hyperbilirubinemia
    a. Caused by hemolytic anemia or congenital deficiency of glucuronyl transferase (e.g., Crigler-Najjar & Gilbert's syndromes)
    b. Hemolytic anemia can be congenital or acquired
        i. Congenital due to spherocytosis, G6PD, pyruvate kinase deficiency
        ii. Acquired due to ABO/Rh isoimmunization, infection, drugs, twin-twin transfusion, chronic fetal hypoxia, delayed cord clamping, maternal diabetes
4. Conjugated hyperbilirubinemia
    a. Infectious causes = sepsis, the ToRCH group, syphilis, Listeria monocytogenes, hepatitis
    b. Metabolic causes = galactosemia, α-1-antitrypsin deficiency
    c. Congenital causes = extrahepatic biliary atresia, Dubin-Johnson & Rotor syndromes
5. Tx = UV light to break down bilirubin pigments & Tx underlying cause
6. complications of UV light = retinal damage, dehydration, dermatitis, diarrhea
7. Tx urgently to prevent mental retardation 2^{o} to kernicterus (biliary precipitation in basal ganglia)

REYE SYNDROME

1. Acute encephalopathy & fatty degeneration of the liver a/w **use of salicylates in children with Varicella or influenza-like illness**
2. Most cases in children 4-12yr old
3. Si/Sx = biphasic course with prodromal fever → aSx interval → abrupt onset vomiting, delirium, stupor, hepatomegaly with abnormal LFTs, may rapidly progress to seizures, coma & death
4. Dx = clinical (+) ↑↑ liver enzymes, normal CSF
5. Tx = control of ↑ intracranial pressure due to cerebral edema (major cause of death) with mannitol, fluid restriction, give glucose because glycogen stores are commonly depleted
6. Px = ↑ chance to progress to coma if =3-fold ↑ in serum ammonia level, ↓ prothrombin not responsive to vitamin K
7. Recovery rapid in mild dz, severe dz may → neuropsychologic defects

FEBRILE SEIZURES

1. Usually occurs between 3mo & 5yr, a/w a fever without evidence of infection (intracranial) or defined cause
2. It is the most common convulsive order in young children, rarely develops into epilepsy
3. Risk = very high fever (=39^{o}C) & family history, seizure occurs during rise in temperature, not at the peak of temperature
4. Si/Sx = commonly tonic-clonic seizure with mot lasting <10min with a drowsy postictal period.
5. **Note:** if seizure lasts >15min, most likely due to infection or toxic process and careful work-up should follow
6. Dx = clinical, routine lab tests should only be performed to evaluate fever source, EEG not indicated unless febrile seizure is atypical (complex febrile seizure)
7. Consider lumbar puncture to r/o meningitis
8. Tx = careful evaluation for source of fever, control of fever with antipyretics, parental counseling & reassurance to decrease anxiety
9. Px = 33-50% of children experience recurrence of seizure

GENETIC AND CONGENITAL DISORDERS

FAILURE TO THRIVE (FTT)

1. Failure of children to grow & develop at an appropriate rate
2. Due to inadequate calorie intake or inadequate calorie absorption

3. Can be idiopathic or due to gastroesophageal reflux, urinary tract infections, cardiac disease, cystic fibrosis, hypothyroidism, congenital syndromes, lead poisoning, malignancy
4. Additional factors include poverty, family discord, neonatal problems, maternal depression
5. Dx requires 3 criteria:
    a. Child <2yr old with weight <3rd to 5th percentile for age on more than one occasion
    b. Child <2yr whose weight is <80% of ideal weight for age
    c. Child <2yr old whose weight crosses 2 major percentiles downward on a standardized growth chart
    d. Exceptions = children of genetically short stature, small-for-gestational-age infants, preterm infants, normally lean infants, "overweight" infants whose rate of height gain increases while rate of weight gain decreases
6. Tx
    a. Organic causes → treat underlying condition & provide sufficient caloric supplementation
    b. Idiopathic → observe the parent feeding the infant & educate parents on appropriate formulas, foods, & liquids that are appropriate for the infant
    c. In older infants & children it is important to offer solid foods before liquids, decrease distractions during meal times, & child should eat with others & not be force-fed
    d. Monitor closely for progressive weight gain in response to adequate calorie feeding
7. Px poor in first year of life due to maximal postnatal brain growth during the first 6mo of life—1/3 of children with nonorganic FTT are developmentally delayed.

CRANIOFACIAL ABNORMALITIES

1. Mildest form is bifid uvula, no clinical significance
2. Cleft lip
    a. Can occur unilaterally or bilaterally, due to failure of fusion of maxillary prominences
    b. **Unilateral cleft lip is the most common malformation of the head & neck**
    c. Does not interfere with feeding
    d. Tx = surgical repair
3. Cleft palate
    a. Can by anterior or posterior (determined by position relative to incisive foramen)
    b. Anterior cleft palate due to failure of palatine shelves to fuse with primary palate
    c. Posterior cleft palate due to failure of palatine shelves to fuse with nasal septum
    d. **Interferes with feeding, requiring a special nipple for the baby to feed**
    e. Tx = surgical repair
4. Macroglossia
    a. Congenitally enlarged tongue seen in Down's syndrome, gigantism, hypothyroidism
    b. Can also be acquired in amyloidosis & acromegaly
    c. This is different from glossitis (redness & swelling, with burning sensation) that is seen in vitamin B deficiencies
    d. Tx is directed at underlying cause

DOWN'S SYNDROME

1. **Invariably caused by trisomy 21, - risk if maternal age >35yr**
2. Si/Sx → cardiac septal defects, psychomotor retardation, classic Down's facies, ↑ risk of leukemia, premature Alzheimer's dz
3. Down's facies = flattened occiput (brachycephaly), **epicanthal folds, up-slanted palpebral fissures, speckled irises (brushfield spots)**, protruding tongue, small ears, redundant skin at posterior neck, **hypotonia, simian crease in palms (50%)**
4. Px = typically death in 30s-40s

TURNER'S SYNDROME

1. **#1 cause of 1° amenorrhea**, due to XO genotype
2. Si/Sx = newborns have ↑ skin at dorsum of neck (**neck webbing**), lymphedema in hands & feet, as develop → short stature, ptosis, **coarctation of aorta, amenorrhea but uterus is present**, juvenile external genitalia, bleeding due to GI telangiectasia, no mental retardation
3. Tx = hormone replacement to allow 2° sex characteristics to develop

FRAGILE X SYNDROME

1. X-linked dominant trinucleotide repeat expansion disorder
2. **#1 cause of mental retardation in boys**
3. Si/Sx = long face, prominent jaw, large ears, enlarged testes (postpubertal), developmental delay, mental retardation
4. Tx = none

ARNOLD-CHIARI MALFORMATION

1. Congenital disorder
2. Si/Sx = caudally displaced cerebellum, elongated medulla passing into foramen magnum, flat skull base, hydrocephalus, meningomyelocele & aqueductal stenosis
3. Px = death as neonate or toddler

NEURAL TUBE DEFECTS

1. A/w ↑ α-fetoprotein levels in maternal serum
2. **Preventable by folic acid supplements during pregnancy**
3. Si/Sx = spina bifida (posterior vertebral arches don't close) & Meningocele (no vertebrae cover lumbar cord)
4. Tx = prevention, neurologic deficits often remain after surgical correction

FETAL ALCOHOL SYNDROME

1. Seen in children born to alcoholic mothers
2. Si/Sx = characterized by facial abnormalities & developmental defects (mental & growth retardation), **smooth filtrum of lip**, microcephaly, atrial septal defect
3. Tx = prevention

CONGENITAL PYLORIC STENOSIS

1. Causes projectile vomiting in first **2wk-2mo of life**
2. More common in males & in first-born children
3. **Pathognomonic physical finding is palpable "olive" nodule in midepigastrium**, representing hypertrophied pyloric sphincter
4. If olive is not present, diagnosis made by ultrasound
5. Tx = longitudinal surgical incision in hypertrophied muscle

CONGENITAL HEART DISEASE

1. Atrial septal defect (ASD)
    a. Usually aSx, often found on routine preschool physicals
    b. Predispose to CHF in 2nd and 3rd decades, also predispose to stroke due to embolus bypass tract (Eisenmenger's complex)
    c. Si/Sx = loud S1, **wide fixed-splite S2**, midsystolic ejection murmur
    d. Dx = echocardiography
    e. Tx = surgical patching of bypass, more important for females due to eventual increased CV stress of pregnancy
2. Ventricular septal defect (VSD)
    a. **Most common congenital heart defect**, 30% of small to medium defects close spontaneously by age 2
    b. Si/Sx = small defects may be completely a aSx throughout entire life, large defects → CHF, ↓ development/growth, frequent pulmonary infections, holosystolic mu rmur over entire precordium, maximally at 4th LICS
    c. Eisenmenger's complex = R→L shunt 2° to pulmonary HTN
        i. RV hypertrophy → flow reversal through the shunt, so that an R→L shunt develops
        ii. Causes cyanosis 2° to lack of blood flow to lung
        iii. Allows venous thrombi (e.g., DVT) to bypass lung, causing systemic paradoxical embolization
    d. Dx = echocardiography
    e. Tx = complete closure for simple defects
3. Tetralogy of Fallot
    a. 4 physical defects comprising the Tetralogy are
        i. Ventricular septal defect
        ii. Pulmonary outflow obstruction
        iii. Right ventricular hypertrophy
        iv. Overriding aorta (aorta inlet spans both ventricles)
    b. Si/Sx = acyanotic at birth, ↑ cyanosis over first 6mo, "**Tet spell"** = acute cyanosis & panic in child, child adopts a squatting posture to improve blood flow to lungs, **CXR shows classic boot-shaped contour** due to RV enlargement
    c. Dx = echocardiography
    d. Tx = surgical repair of VSD, repair of pulmonary outflow tracts
4. Transposition of the great arteries
    a. Aorta comes off right ventricle, pulmonary artery off left ventricle
    b. Must have persistent arteriovenous communication or dz is incompatible with life (can be via patent ductus arteriosus or persistent foramen ovale)
    c. Si/Sx = marked cyanosis at birth, early digital clubbing, often no murmur, **CXR ® enlarged egg-shaped heart** & ↑ pulmonary vasculature
    d. Dx = echocardiography
    e. Tx = surgical switching of arterial roots to normal positions with repair of communication defect
    f. Px = invariably fatal within several months of birth without Tx
5. Coarctation of the aorta
    a. Congenital aortic narrowing, often aSx in young child

   b. Si/Sx = ↓ BP in legs with normal BP in arms, **continuous murmur over collateral vessels in back, classic CXR sign = rib notching**
   c. Dx confirmed with aortogram or CT
   d. Tx = surgical resection of coarctation & reanastomosis
6. Patent ductus arteriosus (PDA)
   a. ↑ incidence with premature births, predisposes pt to endocarditis & pulmonary vascular disease
   b. Si/Sx = **continuous machinery murmur heard best at 2nd left interspace, wide pulse pressure**, hypoxia
   c. Dx = echocardiography or heart catheterization
   d. Tx = indomethacin (block prostaglandins, induces closure) for infants, surgical repair for older children

TRAUMA AND INTOXICATION

CHILD ABUSE

1. Can be physical trauma, emotional, sexual, or neglect
2. Nutritional neglect is the most common etiology for underweight infants
3. most common perpetrator of sexual abuse is family member or family friends, 97% of reported offenders are males
4. **Physicians are required by law to report suspected child abuse or neglect (law provides protection to mandated reporters who report in good faith), clinical & lab evaluations are allowed without parental/guardian permission**
5. Epidemiology
   a. 85% of children reported to children's protective services (CPS) are <5yr, 45% are <1yr old
   b. 10% of injuries to children <5yr old seen in the ER are due to abuse, & 10% of abuse cases involve burns
   c. **High-risk children** = premature infants, children with chronic medical problems, colicky babies, those with behavioral problems, children living in poverty, children of teenage parents, single parents, or substance abusers
6. Si/Sx = injury is unexplainable or not consistent with Hx, bruises are the most common manifestation
   a. Accidental injuries seen on shins, forearms, hips
   b. Less likely to be accidental are bilateral & symmetric, seen on buttocks genitalia, back, back of hands, different color bruises (repeat injuries over time)
   c. Highly suspicious for abuse are fractures due to pulling or wrenching, causing damage to the metaphysic
7. **Classic findings**
   a. Chip fracture, where the corner of metaphysic of long bone is torn off with damage to epiphysis
   b. Periosteum spiral fracture before infant can walk
   c. Rib fractures
8. Dating fracture can be done by a callus formation (callus appears in 10-12 days)
9. Burns
   a. Shape/pattern of burn may be diagnostic
   b. **Cigarette** → circular, punched out lesions of similar size, hands & feet common
   c. Immersion → most common in infants, affecting buttocks & perineum (hold thighs against abdomen), or with scalded line clearly demarcated on thighs or waist without splash marks
   d. Stocking-glove burn on hands or feet
10. Injury to head is the most common cause of death from physical abuse, infants can present with convulsions, apnea, increased intracranial pressure, subdural hemorrhages, retinal hemorrhages (marker for acceleration/deceleration injuries), or in a coma
11. Sexual abuse
    a. Child may talk to mother or teacher, friend, relative about situation
    b. Si/Sx = vaginal, penile, or rectal pain, erythema, discharge, bleeding, chronic dysuria, enuresis, constipation, encopresis
    c. Behavior = sexualized activity with peers or objects, seductive behavior
12. Dx
    a. Labs → PT/PTT & platelets to screen for bleeding diathesis
    b. Consider bone survey in children <2yr old, plain films or MRI for severe injuries or refusal/inability to communicate
    c. For sexual abuse collect specimens of offender's sperm, blood & hair, collect victim's nail clipping & clothing, obtain *Chlamydia & gonorrhea* cultures from mouth, anus & genitalia
    d. Dx is tentatively based on H&P, record all information, photography when appropriate
13. Tx
    a. Medical, surgical, psychiatric treatment for injuries
    b. Report immediately, do not discharge before talking to CPS
    c. Admit pt if injuries are severe enough, if Dx unclear, or if no other safe placement available

POISONINGS

1. Accidental seen in younger children left unsupervised momentarily, usually a single agent ingested or inhaled (plants, household products, medications)
2. Intentional seen in adolescents/adults, toxic substances for recreational purposes or overdose taken with intent to produce self-harm
3. Epidemiology
    a. Nearly 50% of cases occur in children <6yr old, as a result of an accidental event or as abuse
    b. 92% occur at home, 60% with nonpharmacologic agent, 40% with pharmacologic agent
    c. Ingestion occurs in 75% of cases, 8% dermal, 6% ophthalmic, 6% inhalation
4. Hx is crucial during initial contact with patient or guardian
    a. Evaluation of severity (asymptomatic, symptomatic)
    b. Age & weight
    c. Time, type, amount & route of exposure
    d. Past medical history
5. Si/Sx

Si/Sx	**Possible toxin**
Lethargy/coma	Ethanol, sedative-hypnotic, narcotics, antihistamines, antidepressants, neuroleptic
Seizures	Theophyline, cocaine, amphetamines, antidepressants, antipsychotics, pesticides
Hypotension (with bradycardia)	Organophosphate pesticides, beta blockers
Arrhythmia	Tricyclic antidepressants, cocaine, digitalis, quinidine
Hyperthermia	Salicylates, anticholinergics

6. Tx
    a. Syrup of ipecac followed by clear liquid (water) induces vomiting, should not use in children <6mo, those with depressed sensorium, those with seizures or who ingested strong acids or bases
    b. Lavage usually unnecessary in children, may be useful with drugs that decrease gastric motility
    c. Charcoal may be most effective & safest procedure to prevent absorption, repeat doses every 2-6hr with cathartic for first dose, ineffective in heavy metal or volatile hydrocarbon poisoning

ADOLESCENCE

EPIDEMIOLOGY

1. Injuries
    a. 50% of all deaths in adolescents attributed to injuries
    b. Many occur under the influence of alcohol & other drugs
    c. Older adolescents more likely to be killed in motor vehicle accidents while younger adolescents are at risk for drowning & fatal injuries with weapons
    d. Homicide rate is 5x higher for black males than white males
2. Suicide
    a. Second leading cause of adolescent death
    b. Females more likely to attempt than males but males are 5x more likely to succeed than females
    c. Pts with preexisting psychiatric problems or those who abuse alcohol & drugs more likely to attempt suicide
3. Substance abuse
    a. A major cause of morbidity in adolescents
    b. Average age of first use is 12-14yr old
    c. 1 of every 2 adolescents have tried an illicit drug by their high school graduation
    d. Survey of high school seniors (1994-1995) noted that 90% had experience with alcohol & =40% had tried marijuana
4. Sex
    a. 61% of all male & 47% of all female high school students have had sex
    b. Health risks of early sexual activity are unwanted pregnancies, sexually transmitted diseases (STDs) such as gonorrhea, *Chlamydia* & HIV
    c. 86% of all STDs occur among adolescents & young adults 15-29yr old
    d. More than 1 million adolescent females become pregnant yearly, 33% are <15yr old—this is a second major cause of morbidity in adolescents
5. Eating disorders
    a. Anorexia nervosa occurs in 0.5% of adolescent females & bulimia in 1-3%
    b. Si/Sx = cardiovascular symptoms, fluid & electrolyte abnormalities, amenorrhea, decreased bone density, anemia, parotid gland enlargement, tooth decay, constipation (hallmark of anorexia)
    c. Adolescents with anorexia lose 15% of ideal body weight & appear sick, but those with bulimia may look well nourished

d. Anorexia nervosa is seen at 2 peak ages, one at 14.5yr, the next at 18yr, but 25% of females with anorexia may be <13yr old

CONFIDENTIALITY

1. Most issues revealed by adolescents to physicians in an interview are confidential
2. **Exceptions** include suicidal or homicidal behavior, sexual or physical abuse
3. It is strongly encouraged for physicians to inform adolescents about confidentiality at the beginning of the interview to help develop a trusting relationship between adolescent & physician

SCREENING

1. Annual risk behavior screening in every adolescent is strongly recommended
2. **HEADSSS** assessment allows physicians to evaluate critical areas in each adolescent's life that may be detrimental to growth & development
    a. **H**ome environment → who does adolescent live with?, any recent changes?, quality of parental interaction (if applicable)?, has he/she ever run away from home?
    b. **E**mployment & **E**ducation → is child in school?, favorite subjects?, academic performance?, are friends in school?, any recent changes?, does child have a job?, future plans?
    c. **A**ctivities → what does child like to do in spare time? Who does child spend time with?, involved in any sports/exercise?, hobbies?, attends parties or clubs?
    d. **D**rugs → has child ever used tobacco?, alcohol?, marijuana?, other illicit drugs?, if so, when was the child's last use?, how often?, do friends or family members use drugs?, who does the child use these substances with?
    e. **S**exual activity → sexual orientation?, is child sexually active?, number of sexual partners?, does the child use condoms or other forms of contraception?, any history of STDs or pregnancy?
    f. **S**uicide → does the child ever feel sad, tired, or unmotivated?, has the child ever felt that life was not worth living?, any feelings of wanting to harm self?, if so, does the child have a plan?, has the child ever tried to harm self in the past?, does the child know anyone who has attempted suicide?
    g. **S**afety → does the child use a seat belt or bike helmet?, does the child enter into high-risk situations?, does the child have access to a firearm?

5 OUTPATIENT MEDICINE

HEADACHE

SIGNS/SYMPTOMS & DIFFERENTIAL DIAGNOSIS

Type	Epidemiology	Characteristics
Tension	Usually after age 20 (rarely >age50)	❖ Most common headache type ❖ **Bilateral, band-like, dull in quality** ❖ Worse with stress; not aggravated by activity ❖ Chronic HA a/w depression
Cluster	**M**:F = 6:1 Mean age 30yr	❖ **Unilateral,** stabbing peri/retro-orbital pain, lasting 15min-3hr ❖ Seasonal attacks occur in series (6x/day) lasting weeks, follwed by months of remission ❖ **a/w ipsilateral lacrimation (85%), ptosis, nasal congestion & rhinorrhea** ❖ Often occurs within 90min of onset of sleep
Migraine	80% have positive FHx **F**:M = 3:1	❖ Classically, HA is **unilateral (60%)** with **aura (only 15%)**; pt looks for quiet place to rest ❖ Visual aura: **scotoma** (blind spots), **teichopsia** (jagged zigzag lines), **photopsia** (shimmering lights), or **rhodopsins** (colors) ❖ Accompanied by **nausea & photophobia** ❖ Triggered by stress, odors, certain foods, alcohol, menstruation, or sleep deprivation
Temporal arteritis (Giant cell)	**F**:M = 2:1 Age >50	❖ **Unilateral temporal** headache ❖ **a/w jaw claudication, temporal artery tenderness with palpation, ESR =50** ❖ 50% also have polymyalgia rheumatica ❖ If not treated leads to optic neuritis & **blindness** ❖ Screen by ESR; Dx with temporal artery Bx
Trigeminal neuralgia	Peak age at 60	❖ Episodic, severe pain shooting from side of mouth to ipsilateral ear, eye, or nose
Withdrawal headache	Peak age at 60	❖ Common cause of frequent headaches ❖ Can be withdrawl from various drugs
SAH		❖ Head trauma is most common cause ❖ Spontaneous: usually berry aneurysm rupture ❖ Classically the “worst headache of my life”

DX IS MADE BY CLINICAL HISTORY & PHYSICAL EXCEPT:

1. **Temporal arteritis Dx requires temporal artery biopsy**
2. **Trigeminal neuralgia Dx requires head CT or MRI** to r/o sinusitis, cerebellopontine angle neoplasm, multiple sclerosis, herpes zoster
3. **Subarachnoid hemorrhage requires** confirmation by CT scan or lumbar puncture to detect CSF xanthochromia (can be detected hr after onset of HA)
4. Suspect intracranial lesion causing headache **in pts>50 or pts with headaches immediately upon waking up**
5. **Suspect - ICP in pts awakened in middle of night by headache, who have projectile vomiting, or focal neural deficits; obtain head CT**

TREATMENT OF HEADACHE

Headache	Treatment
Tension	Acutely NSAIDs or Midrin Prophylaxis with antidepressants or β-blockers
Cluster	Acutely 100% O2, sumatriptan or dihydroergotamine Prophylaxis with verapminl, lithium, methysergide, or ergotamine
Migraine	Acutely sumatriptan, dihydroergotamine, NSAIDs, antiemetics Prophylaxis with b**-blockers** (first line) or calcium blockers
Temporal arteritis	High-dose prednisone or cytotoxic drug to prevent blindness
Trimgeminal neuraligia	Carbamazepine (1st line) or Phenytoin, clonazepam, valproic acid
Withdrawal	NSAIDs
SAH	Immediate neurosurgical evaluation & nimodipine to reduce incidence of postrupture vasospasm & ischemia

Sumatriptan contraindicated with known coronary dz or ergot drugs taken within 24hr

EARS, NOSE, AND THROAT

OTITIS EXTERNA

1. Si/Sx = **pulling on pinna or pushing on tragus causes pain**
2. Pseudomonas is usual cause in patients with diabetes, can be chronic in pts with seborrhea
3. Tx = antibiotic ear drops
4. DDx = Ramsay Hunt syndrome (herpes zoster otiticus)
    a. Herpes infection of geniculate ganglia (CN VII)
    b. Si/Sx = painful vesicles in external auditory meatus
    c. Tx = urgent acyclovir to prevent extension to meningitis
5. In diabetics, get CT/MRI of temporal bone to r/o osteomyelitis (**malignant otitis externa**), which requires surgical debridement

INNER EAR DISEASE

1. Tinnitus (ringing in the ears)
    a. Objective (heard by observer) or subjective (heard only by patient)
    b. Causes = foreign body in external canal, pulsating vascular tumors, or medications (aspirin), hearing loss
2. Vertigo
    a. Feel as though surroundings are spinning when eyes are open, whereas in dizziness pt feels as if he/she is spinning, not the surroundings

Disease	Characteristics	Tx
Benign positional vertigo	❖ Sudden, episodic vertigo with head movement lasting for seconds	Hallpike maneuver
Meniere's disease	❖ Dilation of membranous labyrinth due to excess endolymph ❖ **Classic triad = hearing loss, tinnitus & episodic vertigo lsting several hours**	Medical (thiazide, anticholinergics, antihistamines) or surgery (labyrinthectomy)
Viral labyrinithitis	❖ Preceded by viral respiratory illness ❖ Vertigo lasting days to weeks	Meclizine
Acoustic neuroma	❖ CN VIII schwannoma, commonly, affects vestibular portion but can also affect cochlea ❖ Si/Sx = vertigo, sudden deafness, tinnitus ❖ Dx = MRI of cerebellopontine angle	Tx = local radiation or surgical excision

EPISTAXIS

1. 90% of bleeds occur at Kiesselbach's plexus (anterior nasal septum)
2. **#1 cause of epistaxis in children is trauma (induced by exploring digits)**
3. Also precipitated by rhinitis, nasal mucosa dryness, septal deviation & bone spurs, alcohol, antiplatelet medication, bleeding diathesis
4. Tx = direct pressure, topical nasal vasoconstrictors (Neo-Synephrine), consider anterior nasal packing if unable to stop, 5% originate in posterior nasal cavity requiring packing to occlude choana

SINUSITIS

1. Maxillary sinuses most commonly involved
2. DDx

	Organisms	**Si/Sx**	**Tx**
Acute bacterial (<4wk)	*S. pneumoniae, H. influenzae*, *Moraxella catarrhalies*	**Purulent rhinorrhea**, headache, **pain on sinus palpation**, fever, **halitosis**, anosmia, **tooth pain**	Bactrim, amoxicillin, decongestants
Chronic bacterial (>3mo)	*Bacteroides, Staph. aureus, Pseudomonas, Streptococcus* spp.	Same as for acute but lasts longer, also otitis media in children	Surgical correction of obstruction, nasal steroids
Fungal	*Aspergillus*—**diabetics get** mucormycosis!	Usually seen in the immunocompromised	Surgery & amphotericin

3. Dx = CT scan showing inflammatory changes or bone destruction
4. Potential complications of sinusitis include meningitis, abscess formation, orbital infection, osteomyelitis

PHARYNGITIS

Disease	**Si/Sx**	**Dx**	**Tx**
Group A Strep throat	High fever, **severe throat pain without cough**, edematous **tonsils with white or yellow exudate, cervical adenopathy**	❖ H&P 50% accurate ❖ Antigen agglutination kit for screening ❖ Throat swab culture is gold standard	Penicillin to prevent acute rheumatic fever
Membranous (diphtheria)	High fever, dysphagia, drooling, **can cause respiratory failure** (airway occlusion)	**Pathognomonic gray membrane on tonsils extending into throat**	**STAT antitoxin**
Fungal (Candida)	Dysphagia, sore throat with white, cheesy patches in oropharynx (oral thrush), **seen in AIDS & small children**	Clinical or endoscopy	Nystatin liquid, swish & swallow
Adenovirus	**Pharyngoconjunctival fever (fever, red eye, sore throat)**	Clinical	Supportive
Mononucleosis (EBV)	Generalized lymphadenopathy, exudative tonsillitis, palatal petechiae & splenomegaly	❖ **(+) heterophile antibody** ❖ **skin rash** occurs in pts given ampicillin	Supportive
Herpangina (coxsackie A)	Fever, pharyngitis, body ache, tender vesicles along tonsils, uvula & soft palate	Clinical	supportive

OUTPATIENT GASTROINTESTINAL COMPLAINTS

DYSPEPSIA

1. Si/Sx = upper abdominal pain, early satiety, postprandial abdominal bloating or distention, nausea, vomiting, often exacerbatd by eating

2. DDx = peptic ulcer, gastroesophageal reflux disease (GERD), cancer, gastoparesis, malabsorption, intestinal parasite, drugs (e.g., NSAIDs), etc.
3. Dx = clinical
4. Tx = empiric for 4 wk, if Sx not relieved → endoscopy
    a. Avoid caffeine, alcohol, cigarettes, NSAIDs, eat frequent small meals, stress reduction, maintain ideal body weight, elevate head of bed
    b. H2 blockers & antacids, or PPI
    c. Antibiotics for H. pylori are NOT indicated for nonulcer dyspepsia

GASTROESOPHAGEAL REFLUX DISEASE (GERD)

1. Causes = obesity, relaxed lower esophageal sphincter, esophageal dysmotility, hiatal hernia
2. Si/Sx = heartburn occurring 30-60min postprandial & upon reclining, usually relieved by antacid self-administration, dyspepsia, postprandial burning sensation in esophagus, also regurgitation of gastric contents into the mouth, cough, hoarseness, and globus sensation
3. Atypical Si/Sx sometimes seen = asthma, chornic cough/laryngitis, atypical chest pain
4. Upper endoscopy → tissue damage but may be normal in 50% of cases
5. Dx = clinical, can confirm with ambulatory pH monitoring
6. Tx
    a. First line = lifestyle modifications: avoid lying down postprandial, avoid spicy foods & foods that delay gastric emptying, reduction of meal size, weight loss
    b. Second line = H2-receptor antagonists—aim to discontinue in 8-12 wk
    c. Promotility agents may be comparable to H2-antagonists
    d. Third line = PPIs, reserve for refractory dz, often will require maintenance Tx since Sx return upon discontinuation
    e. Fourth line = surgical fundoplication, relieves Sx in 90% of pts, may be more cost-effective in younger pts or those with severe dz
7. Sequelae
    a. Barrett's esophagus
        i. Chronic GERD → metaplasia from squamous to columnar epithelia in lower esophagus
        ii. Requires close surveillance with endoscopy & aggressive Tx as 10% progress to adenocarcinoma
    b. Peptic stricture
        i. Results in gradual solid food dysphagia often with concurrent improvement of heartburn symptoms
        ii. Endoscopy establishes diagnosis
        iii. Requires aggressive PPI Tx & surgical opening if unresponsive

DIARRHEA

1. Diarrhea = stool weight >300g/day (normal 100-300g/day)
2. Small bowel dz → stools typically voluminous, watery & fatty
3. Large bowel dz → stools smaller involume but more frequent
4. Prominent vomiting suggests viral enteritis or Staph. aureus food poisoning
5. Malabsorption diarrhea characterized by high fat content
    a. Lose fat soluble vitamins, iron, calcium & B vitamins
    b. Can cause iron deficiency, megaloblastic anemia (B12 loss) & hypocalcemia
6. General Tx = oral rehydration, IV fluids & electrolytes (supportive)
7. Specific diarrheas

Type	Characteristics	Dx	Tx
Infectious	❖ **#1 cause of acute diarrhea** ❖ Si/Sx = vomiting, pain; blood/mucus & fevers/chills suggest invasive dz	❖ Stool leukocytes, Gram's stain & culture, O&P for parasitic ❖ C. difficile toxin test	❖ Ciprofloxacin ❖ Metronidazole for C. difficile
Osmotic	❖ Causes = lactose intolerance, oral Mg, sorbitol/mannitol	❖ ↑ osmotic gap ❖ check fecal fat	❖ withdraw inciting agent
Secretory	❖ Causes = toxins (cholera), enteric viruses, ↑ dietary fat	❖ Normal osmotic gap ❖ Fasting → no change	❖ Supportive
Exudative	❖ Mucosal inflammation → plasma & serum leakage ❖ Causes = enteritis, TB, colon, CA, inflammatory bowel dz	❖ ↑ ESR & CRP ❖ Radiologic imaging or colonoscopy to visualize intestine	❖ Varies by cause
Rapid transit	❖ Cause = laxatives, surgical excision of intestinal tissue	❖ Hx of surgery or laxative use	❖ Supportive
Encopresis	❖ Oozing around fecal impaction in children or sick elderly	❖ History of constipation	❖ Fiber rich diet & laxatives
Celiac sprue	❖ Gluten allergy (wheat, barley, rye, oats contain gluten) ❖ Sx/Si = weakness, FTT, growth retardation ❖ Classic rash = **dermatitis herpetiformis** = pruritic, red papulovesicular lesions on shoulders, elbows & knees ❖ 10-15% of pts develop intestinal lymphoma	**Dx by small bowel biopsy ® pathognomonic blunting of intestinal villi**	❖ Avoid dietary gluten
Tropical sprue	❖ Diarrhea probably caused by a tropical infection ❖ Si/Sx = glossitis, diarrhea, weight loss, steatorrhea	Dx = clinical	❖ Tetracycline (+) folate
Whipple's disease	❖ GI infection by Tropheryma whippelii ❖ Si/Sx = diarrhea, arthritis, rash, anemia	Dx = biopsy → PAS (+) macrophages in intestines	❖ Penicillin or tetracycline
Lactase deficiency	❖ Most of world is lactase deficient as adults, people lose as they emerge from adolescence ❖ Si/Sx = abdominal pain, diarrhea, flatulence after ingestion of any lactose-contianing product	Dx = clinical	❖ Avoid lactose or take exogenous lactase
Intestinal lymphangiectasia	❖ Seen in children, congenital or acquired dilation of intestinal lymphatics leads to marked GI protein loss ❖ Si/Sx = diarrhea, hypoproteinemia, edema	Dx = jejunal biopsy	❖ Supportive
Pancreas dz	❖ Typically seen in pancreatitis & CF due to deficiency of pancreatic digestive enzymes ❖ Si/Sx = foul smelling steatorrhea, megaloblastic anemia (folate deficiency), weight loss	Hx of prior pancreatic disease	❖ Pancrease supplement-ation

Infectious Causes of Diarrhea

	Bacterial	**Viral**	**Parasitic**
Etiology	*E. coli, Shigella, Salmonella, Campylobacter Jejuni, Vibrio parahaemolyticus, Vibrio cholera, Yersinia enterocolitica*	Rotavirus Norwalk virus	*Giardia lamblia, Cryptosporidium, Entamoeba histolytica*
Tx	Ciprofloxacin, Bactrim	Supportive	Metronidazole

UROGENITAL COMPLAINTS

URINARY TRACT INFECTION (UTI)

1. Epidemiology
    a. 40% of females have =1 UTI, 8% have bacteriuria at a given time
    b. Most common in sexually active young women, elderly, posturethral catheter or instrumentation—rare in males (↑ risk with prostate dz)
    c. Due to E. coli (80%), S. saprophyticus (15%), other gram-negative rods
2. Si/Sx = **burning during urination**, urgency, sense of incomplete bladder emptying, hematuria, lwer abdominal pain, nocturia
3. Systemic Sx = fever, chills, **back pain suggest pyelonephritis**
4. Dx = **UA ® pyruia**; (+) bacteria on Gram's stain; positivie culture results
5. Tx
    a. Lower UTI → Bactrim (1st line), fluoroquinolones for refractory dz
    b. Uncomplicated pyelonephritis →same antibiotics given IV or PO depending on severity of pt's illness
    c. Men cured within 7 days of Tx do not warrant further work-up, but **adolescents & men with pyelonephritis or recurrent infxn require renal Utz & intravenous pyelogram to r/o anatomic etiology**
    d. UTI 2° to bacterial prostatitis requires 6-12wk of antibiotics
    e. Asymptomatic bacteriuria
        i. Defined as urine culture > 100,000CFU/mL but no Sx
        ii. Only Tx in (1) pregnancy (use penicillins or nitrofurantoin), or pts with (2) renal transplant, (3) about to undergo GU procedure, (4) severe vesicular-ureteral reflux & (5) struvite calculi

SEXUALLY TRANSMITTED DISEASES (STDs)

Disease	**Characteristics**	**Tx**
Herpes simplex virus (HSV)	❖ Most common cause of genital ulcers (causes 60-70% of cases) ❖ Si/Sx = **painful vesicular & ulcerated** lesions 1-3mm diameter, onsets 3-7 days after exposure ❖ Lesions generally resolve over 7 days ❖ Primary infection also characterized by malaise, low grade fever & inguinal adenopathy in 40% of patients ❖ Recurrent lesions are similar appearing, but milder in severity & shorter in duration, lasting about 2-5 days ❖ Dx confirmed with direct fluorescent antigen (DFA) staining, Tzanck prep, serology, HSV, PCR< or culture	❖ Tx = acyclovir, famciclovir, or valacyclovir to ↓ duration of viral shedding & shorten initial course
Pelvic inflammatory disease	❖ Chlamydia trachomatis & Neisseria gonorrhoeae are primary pathogens, but PID is polymicrobial involving both aerobic & anaerobic bacteria ❖ PID includes endometritis, salpingitis, tubovarian abscess (TOA) & pelvic peritonitis ❖ Infertility occurs in 15% of pts after 1 episode of	❖ Toxic pts, ↓ immunity & noncompliant should be Tx as inpatients with IV antibiotics ❖ Use fluoroquinolones

	salpingitis, ↑ to 75% after =3 episodes ❖ Risk of ectopic pregnancy ↑ 7-10 times in women with history of salpingitis ❖ Dx = abdominal, adnexal & cervical motion tenderness + at least 1 of the following: (+) Gram's stain, temp>38°C, WBC>10,000, pus on culdocentesis or laparoscopy, tubovarian abscess on bimanual or Utz	+ metronidazole or cephalosporin + doxycycline ❖ Start antibiotic as soon as PID is suspected, even before culture results are available
Human papillomavirus (HPV)	I. Serotypes 16, 18 most commonly a/w cervical cancer II. Incubation period varies from 6wk to 3mo, spread by direct skin-to-skin contact III. Infection after single contact with an infected individual results in 65% transmission rate IV. Si/Sx = condyloma acuminate (genital warts) = soft, fleshy growths on vulva, vagina, cervix, perineum & anus V. Dx = clinical, confirmed with biopsy	I. Topical podophyllin or trichloracetic acid, if refractory → cryosurgery or excision II. If pregnant, C-section recommended to avoid vaginal lacerations
Syphilis (Treponema pallidum)	III. Si/Sx = **painless ulcer** with bilateral inguinal adenopathy, chancre heals in 3-9wk IV. Because of lack of Sx, Dx of primary syphilis is often missed V. 4-8wk after appearance of chancre, 2° dz → fever, lymphadenopathy, maculopapular rash affecting palms & soles, condyloma lata in intertriginous areas VI. Dx = serologies, VDRL & RPR for screening, FTA-ABS to confirm	VII. Benzathine penicillin G

ACQUIRED IMMUNODEFICIENCY SYNDROEM (AIDS)

1. Epidemiology
    a. AIDS is a global pandemic (currently the fastest spread is in SE Asia & central Europe)
    b. Heterosexual transmission is the most common mode worldwide
    c. In the US, IV drug users & their sex partners are the fastest growing population of HIV (+) pts
    d. Homosexual transmission is slowing dramatically
2. HIV biology
    a. Retrovirus with the usual gag, pol & env genes
    b. p24 is a core protein encoded by gag gene, can be used clinically to follow disease progression
    c. gp120 & gp41 are envelope glycoproteins that are produced on cleavage of gp160, coded by env
    d. Reverse transcriptase (coded by pol) converts viral RNA to DNA so it can integrate into the host's DNA
    e. Cellular entry is by binding to both CD4 & an additional ligand (can be CCR4, CCR5, others) that typically is a cytokine receptor
    f. HIV can infect CD4(+) T cells, macrophages, thymic cells, astrocytes, dendritic cells & others
    g. The mechanisms of T-cell destruction are not well understood but probably include direct cell lysis, induction of CTL responses against infected CD4(+) cells & exhaustion of bone marrow production (suppression of production of T cells)
    h. In addition, the virus induces alterations in host cytokine patterns rendering surviving lymphocytes ineffective

3. Disease course
    a. In most patients AIDS is relentlessly progressive & death occurs within 10-15yr of HIV infection
    b. Long-term survivors
        i. Up to 5% of patients are "long-term survivors," meaning the disease does not progress even after 15-20yr without Tx
        ii. This may be due to infection with defective virus, a potent host immune response, or genetic resistance of the host
        iii. People with homozygous deletions of CCR5 or other viral coreceptors are highly resistant to infection with HIV, while heterozygotes are less resistant
    c. Although patients can have no clinical evidence of disease for many years, HIV has no latent phase in its life cycle; clinical silence in those patients who eventually progress is due to daily, temporarily successful host repopulation of T cells
    d. Death is usually caused by opportunistic infections (OIs)
        i. OIs typically onset after CD4 counts fall below 200
        ii. Below 200 CD4 cells, all pts should be on permanent Bactrim prophylaxis against P. carinii pneumonia (PCP) & Toxoplasma encephalitis
        iii. Below 50 CD4 cells, all patients should receive azithromycin prophylaxis against M. avium-intracellulare complex (MAC)
        iv. Kaposi's sarcoma = common skin cancer found in homosexual HIV patients, thought to be caused by cotransmission of human herpes virus 8 (HHV8)
        v. Other diseases found in AIDS patients include generalized wasting & dementia
4. Treatment
    a. Triple combination therapy is now the cornerstone
        i. Cocktail includes 2 nucleoside analogues (e.g., AZT, ddI, d4T) (+) a protease inhibitor
        ii. Protease inhibitors block the splicing of the large gag precursor protein into its final components, p24 &p7
        iii. Newest addition to arsenal is hydroxyurea
            1. Inhibits host ribonucleotide reductase → decreased concentration of purines
            2. ddI is a purine analogue (competitor), so hydroxyurea ↑ efficacy of ddI
            3. In theory, virus should not be able to become resistant to hydroxyurea, since it acts on a host enzyme & not on the virus
    b. No patient should ever be on any single drug regimen for HIV—resistance is invariable in monotherapy
    c. Current Tx is able to suppress viral replication to below detectable limits in the majority of patients, but **up to 50% of patients end up "failing" therapy (viral loads rebound)**
    d. Failure of the regimen is a/w poor compliance (missed doses lead to resistance) & **prior exposure to one or more drugs in the regimen** (the virus is already resistant to the agent).
    e. The long-term significance of viral suppression is unclear, but **it is known that the virus is NOT cleared from the body at up to 2yr after it ceases to be detectable in the blood** (it can be found latent in lymph nodes)

HEMATURIA

1. Red/brown urine discoloration 2^o to RBCs, correlates with presence of >5 RBCs/high-powered field on microanalysis
2. Can be painful or painless
    a. Painless = 1^o renal dz (tumor, glomerulonephritis), TB infection, vesicular dz (bladder tumor), prostatic dz
    b. Painful = nephrolithiasis, renal infarction, UTI

3. DDx = myoglobinuria or hemoglobinuria, where hemoglobin dipstick is positive but no RBCs are seen on microanalysis
4. Dx = finding of RBCs in urinary sediment
    a. Urinalysis → WBCs (infection) or RBC casts (glomerulonephritis)
    b. CBC → anemia (renal failure), polycythemia (renal cell CA)
    c. Urogram will show nephrolithiasis & tumors (Utz → cystic vs. solid)
    d. Cystoscopy only after UA & IVP; best for lower urinary tract
5. Tx varies by cause

PROSTATE

1. Benign prostatic hyperplasia
    a. Hyperplasia of the periurethral prostate causing bladder outlet obstruction
    b. Common after age 45 (autopsy shows that 90% of men over 70 have BPH)
    c. Does not predispose to prostate cancer
    d. Si/Sx urinary frequency, urgency, nocturia, ↓ size & force of urinary stream leading to hesitancy & intermittency, sensation of incomplete emptying worsening to continuous overflow incontinence or urinary retention, rectal exam → enlarged prostate (classically a rubbery vs. firm, hard gland that may suggest prostate cancer) with loss of median furrow
    e. Labs → PSA elevated in up to 50% of pts, not specific—not useful marker for BPH
    f. Dx based on symptomatic scoring system, i.e., prostate size >30mL (determined by Utz or exam), maximum urinary flow rate (<10mL/sec) & postvoid residual urine volume (>50mL)
    g. Tx = α-blocker (e.g., terazosin), 5-α-reductase inhibitor (e.g., Finasteride); avoid anticholinergics, antihistaminergics, or narcotics
    h. Refractory dz requires surgery = transurethral resection of prostate (TURP); open prostatectomy recommended for larger glands (>75g)
2. Prostatitis
    a. Si/Sx = fever, chills, low back pain, urinary frequency & urgency, tender, possible fluctuant & swollen prostate
    b. Labs → leukocytosis, pyuria, bacteriuria
    c. Dx = clinical
    d. Tx = systemic antibiotics

IMPOTENCE

1. Affects 30 million menin US, strongly a/w age (about 40% among 40yr-olds & 70% among 70-yr-olds)
2. Causes
    a. 1^{o} erectile dysfunction = never been able to sustain erections
        i. Psychological (sexual guilt, fear of intimacy, depression, anxiety)
        ii. ↓ testosterone 2^{o} to hypothalamic-pituitary-gonadal disorder
        iii. Hypo- or hyperthyroidism, Cushing's syndrome, ↑ prolactin
    b. 2^{o} erectile dysfunction = acquired, **>90% due to organic cause**
        i. Vascular dz = atherosclerosis of penile arteries &/or venous leaks causing inadequate impedance of venous outflow
        ii. Drugs = diuretics, clonidine, CNS depressants, tricyclic antidepressants, high-dose anticholinergics, antipsychotics
        iii. Neurologic dz = stroke, temporal lobe seizures, multiple sclerosis, spinal cord injury, autonomic dysfunction 2^{o} to diabetes, post-TURP or open prostatic surgery
3. Dx
    a. Clinical, r/o above organic causes
    b. Nocturnal penile tumescence testing differentiates psychogenic from organic-nocturnal tumescence is involuntary, (+) in psychogenic but not in organic dz

4. Tx
    a. Sildenafil (Viagra)
        i. Selective inhibitor of cGMP specific phosphodiesterase type 5a → improves relaxation of smooth muscles in corpora cavernosa
        ii. Side effects = transient headache, flushing, dyspepsia & rhinitis, transient visual disturbances (blue hue) is very rare, drug may lower blood pressure → **use of nitrates is an absolute contraindication,** deaths have resulted from combo
    b. Vacuum-constriction devices use negative pressure to draw blood into penis with band placed at base of penis to retain erection
    c. Intracavernosal prostaglandin injection has mean duration about 60min; risks = penile bruising/bleeding & priapism
    d. Surgery = penile prostheses implantation; venous or arterial surgery
    e. Testosterone therapy for hypogonadism
    f. Behavioral therapy & counseling for depression & anxiety

COMMON SPORTS MEDICINE COMPLAINTS

LOW BACK PAIN

1. 80% of people experience low back pain—2nd most common complaint in 1° care (next to common cold)
2. **50% of cases will recur within the subsequent 3yr**
3. **Majority cases attributed to muscle strains**, but always consider disk herniation
4. Si/Sx of disk herniation = shooting pain down leg (sciatica), **pain on straight leg raise (>90% sensitive)** & pain on **crossed straight leg raise (>90% specific, not sensitive)**
5. Dx
    a. **Always rule out RED FLAGS** with Hx and physical exam
    b. If no red flags detected, presume Dx is muscle strain & not serious—**no radiologic testing is warranted**
    c. Dz not remitting after 4wk of conservative Tx should be further evaluated with repeat Hx & physical; consider radiologic studies
    d. Red flags

Diagnosis	**Si/Sx**	**Dx**
Fracture	❖ Hx of trauma (fall, car accident) ❖ Minor trauma in elderly (e.g., strenuous lifting)	❖ Spine x-rays
Tumor	❖ **Pt>50yr old** (accounts for >80% of cancer cases) or <20yr old ❖ Prior Hx of CA ❖ **Constitutional Sx** (fever/chills, weight loss) ❖ Pain worse when supine or at night	❖ Spinal MRI is gold standard, can get CT also
Infection	❖ Immunosuppressed pts ❖ Constitutional Sx ❖ Recent bacterial infection or IV drug abuse	❖ Blood cultures, spinal MRI to r/o abscess
Cauda equine syndrome	❖ Acute urinary retention, **saddle anesthesia**, lower extremity weakness or paresthesias & ↓ reflexes, ↓ anal sphincter tone	❖ Spinal MRI
Spinal stenosis	❖ Si/Sx = **pseudoclaudication** (neurogenic) with pain ↑ with walking **& standing**; relieved by sitting or leaning forward	❖ Spinal MRI
Radiculopathy (herniation compressing	❖ Sensory loss: (**L**5→**L**arge toe/medial foot, **S**1→**s**mall toe/lateral foot) ❖ Weakness: (L1-L4→quadriceps, L5→foot	❖ **Clinical**—MRI may confirm clinical Dx but false positive are

spinal nerves)	dorsiflexion, S1→plantar flexion) ❖ ↓ reflexes (L4→patellar, S1→achilles)	common (clinically insignificant disk herniation)

Radiculopathy ? herniation; radiculopathy indicates evolving spinal nerve impingement & is a more serious Dx than simple herniation indicated by straight leg testing & sciatica.

6. Tx
    a. No red flags → conservative with acetaminophen (safer) or NSAIDSs, **muscle relaxants have not been shown to help**; avoid narcotics
    b. **Strict bed rest is NOT warranted** (extended rest shown to be debilitating, especially inolder patients)—encourage return to normal activity, low-stress aerobic & back exercises
    c. 90% of cases resolve within 4wk with conservative Tx
    d. Red flags:
        i. Fracture → surgical consult
        ii. Tumor → urgent radiation/steroid (↓ compression), then excise
        iii. Infection → abscess drainage & antibiotics per pathogen
        iv. Cauda equine syndrome → emergent surgical decompression
        v. Spinal stenosis → complete laminectomy
        vi. Radiculopathy → anti-inflammatories, nerve root decompression with laminectomy or microdiscectomy only if (1) sciatica is severe & disabling, (2) Sx persist for 4wk or worsening progression & (3) strong evidence of specific nerve root damage with MRI correlation of level of disk herniation

SHOULDER DISLOCATION

1. Subluxation = symptomatic translation of humeral head relative to glenoid articular surface
2. Dislocation = complete displacement out of the glenoid
3. Anterior instability (about 95% of cases) usually due to subcoracoid dislocation is the most common form of shoulder dislocation
4. Si/Sx = pain, joint immobility, arm "goes dead" with overhead motion
5. Dx = clinical, assess axillary nerve function in neuro exam, look for signs of rotator cuff injury, confirm with x-rays if necessary
6. Tx = initial reduction of dislocation by various traction-countertraction techniques, 2-6wk period of immobilization (longer for younger patients), intense rehabilitation; rarely is surgery required

CLAVICLE FRACTURE

1. Occurs primarily due to contact sports in adults
2. Si/Sx = pain & deformity at clavicle
3. Dx = clinical, confirm fracture with standard AP view x-ray
4. Must rule out subclavian artery injury by checking pulses, brachial plexus injury with neuro examination & pneumothorax by checking breath sounds
5. Tx = sling until range of motion is painless (usually 2-4 wk)

ELBOW INJURIES

1. Epicondylitis (tendonitis)
    a. Lateral epicondylitis (**tennis elbow**)
        i. Usually in tennis player (50%), or racquetball, squash, fencing
        ii. Si/Sx = pain 2-5cm distal & anterior to lateral epicondyle reproduced with wrist extension while elbow is extended
    b. Medial epicondylitis (**golfer's elbow**)
        i. Commonly in golf, racquet sports, bowling, baseball, swimming
        ii. Si/Sx = acute onset of medial elbow pain & swelling localized 1 or 2cm area distal to medial epicondyle, pain usually reproduced with wrist flexion & Pronation against resistance

c. Tx for both = ice, rest, NSAIDs, counterforce bracing, rehabilitation
d. Px for both varies, can become chronic condition; surgery sometimes indicated (debridement & tendon reapproximation)

2. Olecranon fracture
    a. Usually direct blow to elbow with triceps contraction after fall on flexed upper extremity
    b. Tx = long arm cast or splint in 45-90^{o} flexion for =3wk
    c. Displaced fracture requires open reduction & internal fixation
3. Dislocation
    a. Elbow joint most commonly dislocated joint in children, 2nd most in adults (next to shoulder)
    b. Fall onto outstretched hand with fully extended elbow (posterolateral dislocation) or direct blow to posterior elbow (anterior dislocation)
    c. May also be seen after jerking child's arm by hurried parent or guardian (**nursemaid's elbow**)
    d. Key is associated nerve injury (ulnar, median, radial or anterior interosseous nerve), vascular injury (brachial artery) or other structural injury (associated coronoid process fracture common)
    e. Tx = reduce elbow by gently flexing supinated arm, long arm splint or bivalved cast applied at 90^{o} flexion
4. Olecranon bursitis
    a. Inflammation of bursa under olecranon process
    b. Seen with direct blow to elbow by collision or fall on artificial turf
    c. Si/Sx = swollen & painful posterior elbow with restricted motion
    d. Dx = clinical, confirm with bursa aspiration to r/o septic bursitis
    e. Tx = bursa aspiration, compression dressing & pad

ANKLE INJURIES

1. Achilles tendonitis
    a. 2^{o} to overuse, commonly seen in runners, gymnasts, cyclists & volleyball players
    b. Si/Sx = swelling or erythema along area of Achilles tendon with tenderness 2-5cm proximal to calcaneus
    c. Evaluate for rupture = Thompson test (squeezing leg with passive plantar flexion) positive only with complete tear
    d. Tx = rest, ice, NSAIDs, taping or splinting to ↓ stress & ↑ support
    e. Rupture requires long leg casting x 4wk, short leg walking cast x 4wk, short leg walking cast x 4wk, then wear hell lift x 4wk
    f. Open repair speeds recovery & is recommended with complete tears in younger patients
2. Ankle sprains
    a. Lateral sprain occurs when ankle is plantar-flexed (90% of sprains)
    b. Anterior drawer sign is done with foot in 10-15^{o} plantar flexion
    c. Medial sprain is rare (10%) because ligament is stronger
    d. Dx = multiple view x-rays both free & weight bearing
    e. Tx = **RICE** = **R**est (limit activity +/- crutches), **I**ce, **C**ompression (ACE bandage), **E**levation above level of heart to decrease swelling
    f. Severe sprains may benefit from casting, open repair rarely indicated

PREVENTIVE MEDICINE

CANCER SCREENING

Disease	**Intervention**
Cervical CA	❖ Annual PS in women = 18yr or sexually active (ACS) ❖ Perform less often if =3 consecutive Paps are nl & pt is monogamous
Breast CA	❖ Exam & mammogram every 1-2yr women 50-69yr (AAFP, USPTF) ❖ Self exams, annual exam & mammogram in women >40yr (ACS)
Colorectal CA	❖ Hemoccult annually >50yr (screen earlier with positive family Hx) ❖ Pt >50yr → sigmoidoscopy q5yr or colonoscopy q10yr (ACS)
Prostate CA	❖ Annual digital exam & PSA should be offered to all men >50yr (ACS
Endometrial CA	❖ High-risk patients should have biopsy shortly after menopause (ACS)
Other CA	❖ Annual physical exam for signs of thyroid, skin, oral, testicular or ovarian CA (ACS)

ADULT IMMUNIZATION

Tetanus	All require primary series & periodic boosters q 10yr (A)
MMR	All require vaccination if born after 1956 without immunity (A)
Hepatitis B	Recommended for all young adults & ↑ risk pts (A)
Pneumococcal	Give once in immunocompetent pts =65yr or to any pt with ↑ risk (B)
Influenza	Annually for all pts =50yr or high-risk pts (B)
Hepatitis A	Only for high-risk patients like travelers (B)
Varicella	Adults without Hx of disease or previous vaccination (B)
In HIV pts avoid live preparations, but MMR should be given if CD4 count >500	
In pregnant pts lvie vaccinations are not recommended (MMR, OPV, VZV)	

(A) = proven benefit, (B) = probably benefit

TRAVEL PROPHYLAXIS

Traveler's diarrhea	Prevent w/Pepto-Bismol; Tx w/ciprofloxacin & loperamide
Malaria	Chloroquine; mefloquine (endemic chloroquine-resistant areas)
Hepatitis A	Most travelers; vaccine requires 4wk; give IVIG for short-term
Typhoid	Endemic in India, Pakistan, Peru, Chile, Mexico; oral or inject
Yellow fever	Endemic parts of South America & Africa
Meningococcus	Endemic in meningococcal belt (sub-Saharan Africa)
Ensure all other routine immunizations are up to date (MMR, polio, Hep B)	

SMOKING CESSATION

1. 20-50million US smokers attempt to quit; 6% long-term success rate
2. **Nicotine replacement (gum or patch) increases success about twofold**
3. Support from weekly counseling session, telephone calls, family & other support groups shown ↑ success
4. For best success, set a precise quit date to begin complete abstinence
5. Pts with negative affect (e.g., depression) have more difficulty quitting
6. **Bupropion +/- nicotine replacement** has 12 mo abstinence rate of >30%, **2x better than nicotine replacement alone**
7. On average, pts who quit successfully will gain weight (mean = 5lb)

OTHER PERIODIC HEALTH EXAMINATION CONCERNS

1. Adolescence (11-24yr)
    a. Leading cause of death are MVA & injuries & homicide/suicide
    b. BP check, Pap smears, rubella status, drug & STD education, safety

2. HTN: check BP every 2yr in normotensive pts 21+yr (USPTF)
3. hyperlipidemia: check cholesterol & lipids in normal population about every 5yr in men 35-65yr & women 45-65yr (USPTF)
4. Endocarditis antibiotic prophylaxis (amoxicillin or erythromycin) given before & after dental procedures & certain surgeries; consider prophylaxis for (1) prosthetic values, (2) mitral or aortic valvular dz, (3) congenital heart dz & (4) prior Hx of infectious endocarditis

BIOSTATISTICS

Term	**Definition**
Sensitivity	Probability that test results will be positive in pts with disease
Specificity	Probability that test results will be negative in pts without disease
False-positive	Pt without disease who has a positive test result
False-negative	Pt with disease who has a negative test result
PPV	Positive predictive value: probability pt with positive test actually has disease
NPV	Negative predictive value: probability pt with negative test actually has no disease
Incidence	# of newly reported case of disease divided by total population
Prevalence	# of existing cases of disease divided by total population at a given time
Relative risk	From cohort study (prospective)—risk of developing dz for people with known exposure compared to risk of developing dz without exposure
Odds ratio	From case control study (retrospective)—approximates relative risk by comparing odds of developing dz in exposed pts to odds of developing dz in unexposed pts (if dz is rare, odds ratio approaches true relative risk)
Variance	An estimate of the variability of each individual data point from the mean
Std deviation	Square root of the variance
Type I error (α error)	Null hypothesis is rejected even though it is true—e.g., the study says the intervention works but it only appears to work because of random chance
Type II error (β error)	Null hypothesis is not rejected even though it is false—e.g., the study fails to detect a true effect of the intervention
Power (1-β)	An estimate of the probability a study will be able to detect a true effect of the intervention—e.g., power of 80% means that if the intervention works, the study has an 80% chance of detecting this but a 20% chance of randomly missing it

STUDY TYPE

Prospective is more powerful than retrospective

Interventional is more powerful than observational

1. Clinical trial: **Prospective interventional trial** in which pts are randomized into an intervention group & a control group. **Randomization blunts effect of confounding factors. Blinding both clinician & patient (double-blind) further decreases bias**
2. Cohort study: Population is divided by exposure status. Requires large population (cannot study rare disease). Can study multiple effects by exposure. Gives **relative risk if prospective**. Can be prospective or retrospective.
3. Case control study: Pts divided by those with dz (cases) & those without dz (controls). Fewer patients are needed (good for rare disease). Can study correlation of multiple exposures. Gives **odds ratio. Always retrospective**.

CALCULATION OF STATISTICAL VALUES

	Pt has dz	**Pt does not have dz**
Positive test	A = true-positive	B = false-positive
Negative test	C = false-negative	D = true-negative

PPV = a / (a+b) sensitivity = a / (a+c)

NPV = d / (c+d) specificity = d / (b+d)

Sensitivity & specificity are inherent characteristics of the test—they must be given in the question. **Predictive values vary with the prevalence of the disease**. They are NOT inherent characteristics of the test, but rather reflect an interaction of sensitivity & specificity with the frequency of the disease in the population.

Example 1 : for disease X, a theoretical screening test is 90% sensitive & 80% specific. In Africa, where the disease has a prevalence of 50%, the test's PPV = 82% (a / (a+b) = 45/55), & the NPV is 89% (d / (c+d) = 40/45).

	Pt has dz	**Pt does not have dz**
Positive test	45	10
Negative test	5	40

Always fill the table in assuming 100 patients—it's easier to do the math this way. The prevalence of the disease (50%) tells you that 50 patients should be in the first column, because 50% of 100 patients have the disease. Therefore, 50 patients should also be in the second column (if 50 of 100 patients have the disease, 50 patients also do NOT have the disease). The sensitivity tells you that 45 of the patients in the first column should be in the top row because the test will find 90% of the 50 patients who have the disease. The specificity tells you that 40 of the patients in the second column should be in the bottom row because the test will correctly describe 80% of the 50 people who truly don't have the disease (& incorrectly claims that 20% of the 50 patients who truly don't have the disease do have the disease).

6 PSYCHIATRY

INTRODUCTION

DSM-IV (DIAGNOSTIC & STATISTICAL MANUAL)

1. The DSM-IV lists current US diagnostic criteria for psychiatric conditions
2. **The USMLE will rely on DSM-IV diagnostic criteria**
3. **Do not try memorizing all the possible Sx mentioned by the DSM** to define a given condition. It is impossible and not a good use of time. This review will focus on the Sx you are **most likely to see on the exam.**

PRINCIPES OF PSYCHIATRY FOR THE USMLE (MOR ECOMPLEX IN REAL LIFE)

1. Major psychiatric Dx requires **significant impairment in the pt's life**
2. **Always r/o drug abuse** (frequent comorbidity in psychiatric dz)
3. **Combination Tx** (pharmacology & psychotherapy) **is superior** to either alone but **pharmacologic Tx is first line for severe dz in acute setting**
4. **Criteria for hospitalization (any single criterion is acceptable)**
    a. Danger to self (suicide)
    b. Danger to others
    c. Unable to provide food, clothing, shelter (grave disability)
5. Psychiatric dz is chronic—if asked about dz course, **"cures" are rare**
6. Prognosis depends on symptom onset, insight & premorbid function

Prognosis	**Symptom onset**	**Insight**	**Premorbid function**
Favorable	Acute	Good	High
Unfavorable	Subacute/Chronic	Poor	Low

Insight = pt recognizes symptom as abnormalitites & is distressed by them.

MOOD DISORDERS

MAJOR DEPRESSIVE DISORDER (MDD)

1. A syndrome of repeated major depressive episodes
2. One of the most common psychiatric disorders, with lifetime prevalence of 15-25%, with a greater incidence in women & elderly (often overlooked)
3. Si/Sx for depression in general
    a. Major Si/Sx = ¯ **mood** &/or **anhedonia** (inability to experience pleasure)
    b. Others = insomnia (less commonly hypersomnia), ↓ appetite/weight loss (less commonly ↑ appetites/weight gain, fatigue), ↓ concentration, guilt or feeling worthless, recurrent thoughts of death & suicide
    c. **Commonly presents with various somatic complaints & ¯ energy level rather than complaints of depression**—beware of clinical scenarios in which pts have multiple unrelated physical complaints
4. DDx = dysthymic disorder, bipolay disorder, medical dz (**classically hypothyroidism**), bereavement
5. Dx requires depressive episode to continue for =2wk, with =2 episodes separarted by =2mo (**2 episodes of 2wk, 2mo apart**)
6. Tx

Drug	**Examples**	**Side effects**
SSRIs	Fluoxetine, paroxetine	Favorable profile: rare impotence
TCAs	Amitriptyline, desipramine, imipramine, nortriptyline	More sever: confusion, sedation, **orthostatic hypotension**, **prolonged QRS duration** (think autonomic/cholinergic)
MAO inhibitors	Phenelzine, tranylcypromine	Very severe: class syndromes ❖ **Serotonin syndrome** = caused by **MAO inhibitor**

		interaction with SSRIs, Demerol, or pseudoephedrine & others, presents with hyperthermia, muscle rigidity, AMS ❖ **Hypertensive crisis** = malignant hypertension when ingested with foods rich in **tyramine** (wine & cheese)

   a. Psychotherapy = **psychodynamic** (understanding self/inner conflicts), **cognitive-behavioral** (recognizing negative thought or behavior & altering thinking/behavior accordingly), **interpersonal** (examines relation of Sx to negative/absent relationships with others)
   b. **Electroconvulsive therapy (ECT)** is effective for refractory cases, main side effect is short-term memory loss

DYSTHYMIC DISORDER

1. Si/Sx = as per major depressive episodes but is continuous
2. Dx = **steady Sx duration for minimum of 2yr**—dysthymic disorder is longer but less acute than MDD
3. If major depressive episode takes place during the initial 2yr of dysthymia, then by definition the Dx is MDD rather than dysthymic disorder
   a. If after initial 2yrs = "double depression" (code for both MDD & dysthymia)
4. Tx as per MDD

BEREAVEMENT

1. **Bereavement** is a commonly asked test question!
2. Si/Sx = an older adult whose partner has died & who has been feeling sad, losing weight & sleeping poorly (depression symptoms)
3. Dx: key is **how much time** has elapsed since the partner died—**if Sx persist for >2mo, Dx is MDD rather than normal bereavement**
4. Although bereavement is normal behavior, grief management may be helpful.

BIPOLAR DISORDER (MANIC-DEPRESSION)

1. Seen in 1% of population, genders equally affected but **often presents in young people while major depression is a dz of middle age (40s)**
2. Si/Sx = abrupt onset of - **energy, ¯ need to sleep, pressured speech** (speaks quickly to the point of making no sense), ↓ attention span, **hypersexuality, spending large amounts of money**, engaging in outrageous activities (e.g., directing traffic at an intersection while naked)
3. DDx = cocaine & amphetamine use, personality disorders (cluster B), schizophrenia, hypomania
4. Dx
   a. **Manic episode causes significant disability**, whereas hypomania presents with identical Sx but no significant disability
   b. Episodes **must last =1wk & should be abrupt, not continuous**, which would suggest personality disorder or schizophrenia
   c. **Bipolar I** = manic episode with or without depressive episodes (pts often have depressive episodes before experiencing mania)
   d. Bipolar II = depressive episodes **with hypomanic episodes** but, by definition, **the absence of manic episodes**
   e. **Rapid cycling** = 4 episodes (depressive, manic, or mixed) in 12mo, can be precipitated by antidepressants
5. Tx
   a. Hospitalizaiton, often involuntary since manic pts rarely see the need
   b. **Valproate** or **carbamazepine** are 1st line, **lithium** 2nd line
   c. Valproate & carbamazepine cause **blood dyscrasias** (thrombocytopenia, hepatotoxicity)

d. Lithium blood levels must be checked due to frequent toxicity, including **tremor** & polyuria due to **nephrogenic diabetes insipidus**

6. Px worse than major depression, episodes more frequent with age

DRUG-INDUCED MANIA

1. Cocaine & amphetamine are major culprits
2. Si/Sx = mania as above, also tachycardia, hypertension, dilated pupils, **EKG arrhythmia or ischemia in young people is highly suggestive**
3. Dx = urine or serum toxicology screen
4. Tx = calcium-channel blockers for acute autonomic Sx, drug Tx programs longer term

PSYCHOSIS

SI/SX

1. **Hallucinations & delusions** are hallmark
   a. Hallucination = false sensory perception not based on real stimulus
   b. Delusion = false interpretation of external reality
   c. Can be paranoid, grandiose (thinking one possesses special powers), religious (God is talking to the pt), or ideas of reference (every event in the world somehow involves the pt)

DDx

Disease	**Characteristics**
Schizophrenia	❖ **Presents in the late teens-20s (slightly later in women), very strong genetic predisposition** ❖ Often accompanied by **premorbid** sign, including poor school performance, poor emotional expression & lack of friends ❖ Positive Sx = hallucinations (**more often auditory than visual**) & delusions ❖ Negative Sx = lack of affect, alogia ❖ Other Sx = disorganized behavior &/or speech ❖ **Schizophrenia lasts =6 continuous mo** ❖ **Schizophreniform disorder lasts 1-6mo** ❖ **Brief psychotic disorder lasts 1day-1mo**, with full recovery of baseline functioning—look for acute stressor, e.g., the death of a loved one
Other psychoses	❖ Schizoaffective disorder = meets criteria for mood disorders & schizophrenia ❖ Delusional disorder = **nonbizarre delusions** (they could happen, e.g., pt's spouse is unfaithful, a person ho is trying to kill the pt, etc), without hallucinations, disorganized speech or disorganized behavior
Mood disorderds	❖ Major depression & bipolar disorder can cause delusions & in extreme case, hallucinations—can be difficult to differentiate from schizophrenia
Delirium	❖ Seen in pts with underlying illnesses, often in ICU (ICU psychosis) ❖ **Patients are not oriented to person, place, time** ❖ **Severity waves & wanes even during the course of 1 day** ❖ Resolves with treatment of underlying dz
Drugs	❖ LSD & PCP → predominantly visual, taste, touch, or olfactory hallucination ❖ Cocaine & amphetamines → paranoid delusions & **classic sensation of bugs crawling on the skin (formication)** ❖ Anabolic steroids → body-builder with bad temper, acne, shrunken testicles ❖ Corticosteroids → psychosis/mood disturbances early in course of therapy
Medical	❖ Metabolic, endocrine, neoplastic & seizure dz can all cause psychosis ❖ **Look for associated Si/Sx not explained by psychosis**, including local neurologic findings, seizure, sensory/motor deficits, abnormal lab values

TX

1. Hospitalization if voices tell pts to hurt themselves or others, or if condition is disabling to the point that pts cannot care for themselves
2. Pharmacologic therapy
    a. All antipsychotics act as dopamine-blockers
    b. Difference among agents relate to side-effect profile
    c. Compliance to drugs can be improved with **depot** form of haloperidol, which administers a month's supply of drug in 1 IM injection
3. Psychotherapy can improve social functioning
    a. Behavioral Tx teaches social skills that allow pts to deal more comfortably with other people
    b. Family oriented Tx teaches family members to act in more appropriate, positive fashion

PX

1. Schizophrenia is a chronic, episodic dz, recovery from each relapse typically leaves pt below former baseline function
2. Presence of negative Sx (e.g., flat affect) marks poor Px
3. High-functioning prior to psychotic break marks better Px

ANTIPSYCHOTIC DRUGS

Drug		**Adverse effects**
Typical antipsychotics		
Chlorpromazine	Low potency	↑ anticholinergic effects, ↓ movement disorders
Haloperidol	High potency	↓ anticholinergic effects, ↑ movement disorders
Atypical antipsychotics		
Clozapine	For refractory dz	1% incidence of agranulocytosis mandates weekly CBC
Risperidone	1st line	Minimal
Olanzapine	1st line	Minimal

Atypical agents have much lower incidence of movement disorders

ANTIPSYCHOTIC-ASSOCIATED MOVEMENT DISORDERS

Disorder	**Time course**	**Characteristics**
Acute dystonia	4hr → 4 days	❖ Sustained muscle spasm anywhere in the body but often in neck (torticolis), jaw, or back (opisthotonos) ❖ Tx = immediate IV diphenhydramine
Parkinsonism	4days → 4 mo	❖ Cog-wheel rigidity, shuffling gait, resting tremor ❖ Tx = benztropine (anticholinergic)
Tardive dyskinesia	4mo → 4yr	❖ Involuntary, irregular movements of the head, tongue, lips, limbs & trunk ❖ Tx = immediately change medication or ↓ doses because effects are often permanent
Akathisia	Any time	❖ Subjective sens of discomfort → restlessness: pacing, sitting down & getting up ❖ Tx = lower medication doses
Neuroleptic malignant syndrome	Any time	❖ Life-threatening muscle rigidity → fever, ↑BP/HR, rhabdomyolysis appearing over 1-3days ❖ Can be easily misdiagnosed as ↑ psychotic Sx ❖ Labs → ↑ WBC, ↑ creatine kinase, ↑ transaminases, ↑ plasma myoglobin, as well as myoglobinuria ❖ Tx = supportive immediately stop durg, give dantrolene (inhibits Ca

		release into cells), cool pt to prevent hyperpyrexia

ANXIETY DISORDERS

PANIC DISORDER

1. Si/Sx = mimic MI: chest pain, palpitations, diaphoresis, nausea, marked anxiety, escalate for 10min, remain for about 30min (rarely longer than an hour)
2. Occurs in younger pts (average age 25)—good way to distinguish from MI
3. DDx = MI, drug abuse (e.g., cocaine, amphetamines), phobias
4. Dx is by exclusion of true medical condition & drug abuse
5. Panic attacks are unexpected, so if pt consistently describes panic Sx in a specific setting, phobia is more likely diagnosis
6. Tx
    a. TCAs (clomipramine & imipramine) are best studied
    b. More recently SSRIs have been shown to have efficacy
    c. Benzodiazepines work (immediately, have ↑ risk of addiction
    d. Therefore, start benzodiazepine for immediate effects, add a TCA or SSRI, taper off the benzodiazepine as the other drugs kick in
    e. Cognitive/behavior TX & **respiratory training** (to help patients recognize & overcome desire to hyperventilate) are helpful

AGORAPHOBIA

1. Sx = fear of being in situations where it would be very difficult to get out of should a panic attack arise
2. Theorized that pts develop panic disorder because (they've had enough unexpected attacks to know that it can come at any time--& wouldn't it be embarrassing if it happened while sitting in the mezzanine watching a sold-out performance of Tosca? (it would certainly be more interesting).
3. Dx = clinical, look for evidence of social/occupational dysfunction
4. Tx (for phobias in general)
    a. β-blockers useful for prophylaxis in phobias related to performance
    b. **Exposure desensitization** = exposure to noxious stimulus in increments, while undergoing concurrent relaxation Tx

OBSESSIVE COMPULSIVE DISORDER (OCD)

1. **Obsessions = recurrent thought; compulsions = recurrent act**
2. Sx = obsessive thought causes anxiety & the compulsion is a way of temporarily relieving that anxiety (e.g., pt worries whether he/she locked the door & going back to see it's locked relieves the anxiety), but because relief is only temporary the pt performs compulsion repeatedly
3. Obsessions commonly involve **cleanliness/contamination** (washing hands), doubt, symmetry (elaborate rituals for entering doorways, arranging books, etc.) & sex
4. Dx = pt should be disturbed by their obsessions & **should recognize their absurdity** in contrast to obsessive compulsive personality disorder, where pt sees nothing wrong with compulsion
5. Tx = SSRIs (first line) or clomipramine, psychotherapy in which the pt is literally forced to overcome their behavior

POSTTRAUMATIC STRESS DISORDER (PTSD)

1. Dx requires a traumatic, violent incident that effectively scars the person involved; the experiences of Vietnam vets are emblematic of this disorder
2. Sx
    a. Pt relives the initial incident via conscious thoughts or dreams
    b. Due to resultant subjective & physiologic distress, the pt avoids any precipitating stimuli & **hence often avoid public places & activities**
    c. Pt may suffer restricted emotional involvement/responses & may experience a detachment from others

    d. **Depression is common, look for moodiness, diminished interest in activities & difficulties with sleeping & concentrating**
3. DDx = **acute stress disorder**
    a. Dx also requires a traumatic incident, but Sx are more immediate (within 4wk of the event) & limited in time (<4wk)
    b. The Sx are different; imagine being so traumatized that you are in a daze, where nothing seems real & you have trouble remembering what has happened (commonly seen in victims of sexual assault)
4. Tx
    a. Use of tricyclics (imipramine & amitriptyline) is well-supported by clinical trials, SSRIs have also been used
    b. **Beware of giving benzodiazepines due to a high association of substance abuse with PTSD!**
    c. Psychotherapy takes two approaches
        i. Exposure therapy, the idea being to confront one's demons by "reliving" the experience (either step-wise or abruptly)
        ii. Relaxation techniques, think of the 2 modalities as attacking the source vs. controlling the symptoms
5. Px = variable, but the predictive factors are similar to schizophrenia: abrupt Sx & strong premorbid functioning lead to better outcomes

GENERALIZED ANXIETY DISORDER

1. Sx = worry for most days for at least 6mo, irritability, inability to concentrate, insomnia, fatigue, restlessness (just think of a medical student or intern preparing for the USMLE!)
2. DDx = specific anxieties, including separation anxiety disorder, anorexia nervosa, hypochondriasis
3. **Dx requires evidence of social dysfunction** (e.g., poor school grades, job stagnation, or marital strains) to r/o "normal" anxiety
4. Tx = psychotherapy due to chronicity of the problem
    a. Cognitive-behavioral tx = teaching pt to recognize his/her worrying & find ways to respond to it through behavior & thought patterns
    b. **Biofeedback & relaxation** techniques, in particular, can help the pt deal with physical manifestations of anxiety, e.g., heart rate
    c. Pharmacotherapy includes buspirone or β-blockers (works for peripher Sx, e.g., tachycardia, but not worry itself)

PERSONALITY DISORDERS

GENERAL CHARACTERISTICS

1. Sx = pervasive pattern of maladaptive behavior causing functional impairment, consistne behavior can often be traced back to childhood
2. Typically present to psychiatrists because behavior is causing significant problems for other, e.g., colleagues at work, spouse at home, **or for the medical staff in the inpatient or clinic setting (typical USMLE question)**
3. **Pts usually see nothing wrong with their behavior (ego-syntonic),** contrast with pts who recognize their hallucinations as abnormal (ego-dystonic)
4. Ego defenses
    a. Unconscious mental process that individuals resort to in order to quell inner conflicts & anxiety that are unacceptable to the ego
    b. Examples include "splitting" & "projection"
5. Tx = psychotherapy, medication used for peripheral Sx (e.g., anxiety)

CLUSTERS

1. **Cluster A** = paranoid, schizoid & schzotypal personalities, often thought of as **"weird" or "eccentric"**
2. **Cluster B** = borderline, antisocial, histrionic & narcissistic personalities, **"dramatic" & "aggressive"** personalities
3. **Cluster C** = avoidant, dependent & obsessive-compulsive personalities, **"shy" & "nervous"** personalities

SPECIFIC PERSONALITY DISORDERS

Disorder	**Characteristics**
Paranoid (Cluster A)	❖ Negatively misinterpret the action, words, intentions of others ❖ Often utilize **projection** as ego defense (attributing to other people impulses & thoughts that are unacceptable to their own selves) ❖ **Do not hold fixed delusions** (delusional disorder), **nor do they experience hallucinations** (schizophrenia)
Schizoid (Cluster A)	❖ Socially withdrawn, introverted, with little external affect ❖ Do not form close emotional ties with others (often feel no need) ❖ Are, however, able to recognize reality
Schizotypal (Cluster A)	❖ **Believe in concepts not considered real by the rest of society (magic, clairvoyance)**, display the prototypical ego defense: **fantasy** ❖ Not necessarily psychotic (can have brief psychotic episodes) ❖ Like schizoids, they are often quite isolated socially ❖ **Often related to schizophrenics (unlike other cluster A disorders)**
Antisocial (Cluster B)	❖ Violate the rights of others, break the law (e.g., theft, substance abuse) ❖ Can also be quite seductive (particularly with the opposite sex) ❖ **For Dx the pt must have exhibited the behavior by a certain age (15—think truancy) but must be a certain age (at least 18—adult)** ❖ **A popular USMLE topic; you may have to differentiate it from conduct disorder (bad behavior, but Dx of children/adolescents)**
Borderline (Cluster B)	❖ Volatile emotional lives, swing wildly between idealizing & devaluing other people: (**splitting** ego defense = people are very good or bad) ❖ **Also commonly asked on USMLE**, typical scenario is a highly disruptive hospitalized pt; on interview, he (but usually she) says some nurses are incompetent & cruel but wildly praises others (including you) ❖ **Exhibit self-destructive behavior (scratching or cutting themselves)** ❖ Ability to **disassociate**: they simply "forget" negative affects/experiences by covering them with overly exuberant, seemingly positive behavior.
Histrionic (Cluster B)	❖ Require the attention of everyone, use sexuality & physical appearance to get it, exaggerate their thoughts with dramatic but vague language ❖ Utilize disassociation & **repression** (block feelings unconsciously)—don't confuse with **suppression** (feeling put aside consciously)
Narcissistic (Cluster B)	❖ Feel entitled—strikingly so—because they are the best & everyone else is inferior, handle criticism very poorly
Dependent (Cluster C)	❖ Can do little on their own, nor can they be alone
Avoidant (Cluster C)	❖ Feel inadequate & are extremely sensitive to negative comments ❖ Reluctant to try new things (e.g., making friends) for fear of embarrassment
Obsessive-compulsive (Cluster C)	❖ Preoccupied with detail: rules, regulations, neatness ❖ Isolation is a common ego-defense: putting up walls of self-restraint & detail-orientation that keep away any sign of emotional affect

OTHER EGO DEFENSES

1. Acting out = transforming unacceptable feeling into actions, often loud ones (tantrums)
2. Identification = patterning behavior after someone else's
3. Intellectualization = explaining away the unreasonable in the form of logic
4. Rationalization = making the unreasonable seem acceptable (e.g., upon being fired, you say you wanted to quit anyway)
5. Reaction formation = set aside unconscious feelings & express exact opposite feelings (show extra affection for someone you hate)
6. Regression = resorting to child-like behavior (often seen in the hospital)
7. Sublimation = taking instinctual drives (sex) & funneling that energy into a socially acceptable action (studying)

SOMATOFORM AND FACTITIOUS DISORDERS

DEFINITIONS

1. Somatoform disorder = **lack of conscious manipulation of somatic Sx**
2. Factitious disorder = **consciously faking** or manipulating Sx for purpose of "assuming the sick role," **but not for material gain**

FACTITIOUS DISORDER

1. Pt may mimic any Sx, physical or psychological, to assume the sick role
2. **The patient is not trying to avoid work or win a compensation claim**
3. Munchausen syndrome = factitious disorder with predominantly physical (not psychologic) symptoms
4. Munchausen by proxy = pt claiming nonexistent symptoms in someone else under their care, e.g., parents bringing in their "sick" children
5. DDx = malingering
6. **HINT: the USMLE will very likely present a scenario involving nurses or other health care workers as the pts (often involving an episode of apparent hypoglycemia), look for evidence of factitious disorder (e.g., low C-peptide levels suggesting insulin self-injection)**
7. Dx is by exclusion of real medical condition
8. Tx is nearly impossible; when confronted pts often become angry, deny everything, tell you how horrible you are & move on to someone else

SOMATOFORM DISORDERS

1. Somatization disorder
    a. Often female pts with problems starting before age 30, with history of frequent visits to the doctor for countless procedures & operations (often exploratory) & often history of abusive/failed relationships
    b. Sx = somatic complaints involving different systems, particularly gastrointestinal (nausea, diarrhea), neurologic (weakness) & sexual (irregular menses), with no adequate medical explanation on the basis of exam/lab findings
    c. Dx = r/o medical condition & material or psychologic gain
    d. Tx = continuity of care
        i. Schedule regular appointments so pt can express his or her Sx
        ii. Perform physical exam but do not order laboratory tests
        iii. As the therapeutic bond strengthens, strive to establish awareness in the pt that psychologic factors are involved & if successful in doing so, arrange a psychiatric consult—but if done too early or aggressively, pt may be reluctant or resentful
2. Conversion disorder
    a. Sx are neurologic, not multisystem, & are not consciously faked
    b. Sensory deficits often fail to correspond to any known pathway, e.g., a stocking-&-glove sensory deficit that begins precisely at the wrist, studies will reveal intact neurologic

pathways, & pts rarely get hurt, e.g., patients who are "blind" will not be colliding into the wall
    c. Dx requires identification of a stressor that precipitated the Sx as well as exclusion of any adequate medical explanation (**NOTE**: in some studies 50% of pts who received this Dx were eventually found to have nonpsychiatric causes of illness, e.g., brain tumors & multiple sclerosis.)
    d. Tx = supportive, Sx resolve within days (less than a month), **do not tell pt that they are imagining their Sx, but suggest that psychotherapy may help with their distress**
    e. Px = the more abrupt the symptoms, the more easily identified the stressor & the higher the premorbid function, the better the outcome
3. Hypochondriasis
    a. Sx = preoccupation with disease, pt does not complain of a large number of Sx but misinterprets them as evidence of something serious
    b. Tx = regular visits to MD with every effort not to order lab tests or procedures, psychotherapy should be presented as a way of coping with stress, **again, do not tell patients that they are imagining their Sx**
4. Body dysmorphic disorder
    a. Sx = concern with body, **pt usually picks 1 feature, often on the face & imagines deficits that other people do not see;** if there are slight imperfections, the pt exaggerates them excessively
    b. Look for a significant amount of emotional & functional impairment
    c. Tx = SSRIs may be helpful in some cases, surgery is not recommended

CHILD AND ADOLESCENT PSYCHIATRY

AUTISM & ASPERGER'S SYNDROME

1. Autism is the prototypic **pervasive developmental disorder**, pervasive because the disorder encompasses so many areas of development: language, social interaction, emotional reactivity
2. The expression "living in his own world" captures this tragic disorder; the autistic child fails to develop normal interactions with others & seems to be responding to internal stimuli
3. Si/Sx
    a. Becomes evident before 3yr old, often much earlier
    b. The baby does not seem to be concerned with the mother's presence or absence & makes no eye contact, as the baby becomes older, deficiencies in language (including repetitive phrases & made-up vocabulary) & abnormal behavior become more obvious
    c. Look for the behavioral aspects; the child often has a strange, persistent fascination with specific, seemingly mundane objects (vacuum cleaners, sprinklers) & may show stereotyped, ritualistic movements (e.g., spinning around)
    d. Autistic children have an inordinate need for constancy
4. Think of Asperger's syndrome as autism **without** the language impairment
5. **Contrary to older thought, poor parenting/bonding is not a cause of autism!—parents need reassurance about this**

DEPRESSION

1. Depression may present slightly differently depending on the age group
    a. Preschool children may be hyperactive & aggressive
    b. Adolescents show boredom, irritability, or openly antisocial behaviors
2. One should still look for the same symptoms as described for adult depression: depressed mood, anhedonia, neurovegetative changes, etc.
3. Tx
    a. Unlike adult depression, the use of antidepressants is much more controversial, with far less data supporting its effectiveness

b. **Note:** children's mood disorders are especially sensitive to psychosocial stressors, so family therapy is a major consideration

SEPARATION ANXIETY

1. Look for a child that seems a bit too attached to his parents or any other figures in his life; the child is worried that something will happen to these beloved figures or that some terrible event will separate them.
2. Si/Sx = sleep disturbances (nightmares, inability to fall asleep alone) & somatic Sx during times of separation (headaches, stomach upset at school)
3. Tx = desensitizing therapy (gradually increasing the hours spent away from Mon & Dad), in some cases imipramine is used

OPPOSITIONAL DEFIANT/CONDUCT DISORDER

1. Differentiate the 2 by words & action
2. Oppositional defiant disorder Si/Sx ("bark")
    a. Pts are argumentative, temperamental & defiant, more so with people they know well (they may seem harmless to you)
    b. Big surprise that they are often friendless & perform poorly inschool
3. Conduct disorder Si/Sx ("bite")
    a. Pts bully others, start fights, may show physical cruelty to animals, violate/destroy other people's property (fire-setting), steal things & stay out past curfews or run away
    b. They do not feel guilty for any of this
    c. A glimpse into the child's family life often reveals pathology in the form of substance abuse or negligence
4. Oppositional defiant disorder may lead to conduct disorder, but the two are not synonymous
5. Tx = providing a setting with strict rules & expected consequence for violation of them

ATTENTION-DEFICIT HYPERACTIVITY DISORDER (ADHD)

1. Si/Sx can be divided into the components suggested by their name
    a. Attention-deficit Sx = inability to focus or carry out tasks completely & being easily distracted by random stimuli
    b. Hyperactivity Sx are more outwardly motor: the child is unable to sit still, talks excessively & can never "wait his turn" in group games
2. Dx requires that Sx have been present since before 7yr old
3. Tx = methylphenidate, an amphetamine
    a. Parents & teachers notice improvement in the child's behavior
    b. Because of concerns about impeding the child's growth, drug holidays are often taken (e.g., no meds over weekends or vacations)
    c. Children with ADHD also do better with an extremely structured environment featuring consistent rules & punishments
    d. Px is variable some children show remissions of their hyperactivity, but quite a few continue to show Sx through adolescence & adulthood; children with ADHD have a higher likelihood of developing conduct disorders or antisocial personalities

TOURETTE'S DISORDER

1. Tics are involuntary, stereotyped, repetitive movements or vocalizations
2. **Tourette's Dx requires both a motor tic & a vocal tic present for =1yr**
3. **The vocal tics are often obscene or socially unacceptable (coprlalia)**, which is a cause of extreme embarrassment to the patient
4. Tx = haloperidol, effective, but not required in mild cases
5. Psychotherapy is unhelpful in treating the tics per se, but can be helpful in dealing with the emotional stress caused by the disorder

ANOREXIA & BULIMIA NERVOSA

1. Eating disorders are by no means limited to children—but because they often start in adolescence, they are worth mentioning here

2. In both disorders exists a profound disturbance in body image & its role in the person's sense of self-worth
3. Anorexia Si/Sx
    a. **By definition anorexic patients are below their expected body weight** because they do not eat enough, often creating elaborate rituals for disposing of food in meal settings, e.g., cutting meat into tiny pieces & rearranging them constantly on the plate
    b. **Amenorrhea occurs 2^{o} to weight loss**
4. Bulimia Si/Sx
    a. More common than anorexia, **characterized by binge eating**: consuming huge amounts of food over a short period, with a perceived lack of control
    b. This may be accompanied by active purging (vomiting, laxative use)
    c. **Unlike anorexics, who by definition have decreased body weight, bulimics often have a normal appearance**
    d. **Abrasion over the knuckles** (from jamming the fingers into the mouth to induce vomiting) & **dental erosion** suggest the Dx
5. Tx
    a. Hospitalization may be required for anorexia to restore the pt's weight to a safe level, which the pt will often resist
    b. Because of vomiting, monitoring serum electrolytes is essential; the most worrisome consequence is cardiac dysfunction.
    c. Psychotherapy is the mainstay of Tx for both diseases
6. Overall, anorexia nervosa has a relatively poor prognosis, with persistent preoccupation with food & weight; bulimics far slightly better

DRUGS OF ABUSE

INTRODUCTION

1. Always consider drug abuse when a pt's life seems to be going down the tubes, e.g., deteriorating family relations, work performance, financial stability
2. Generally (with many exceptions), withdrawal Sx are the opposite of intoxication, dysphoria is characteristic of all of them—**withdrawal is a sign of physiologic dependence**
3. Individual drugs

Drug	**Intoxication Si/Sx**	**Withdrawal**
Alcohol	Disinhibition, ↓ cognition Screen for alcoholism with CAGE ❖ C-feeling the need to cut down ❖ A-feeling annoyed when asked about drinking ❖ G-feeling guilty for drinking ❖ E-need a drink in the morning (eye-opener)	Tremor, seizures, delirium tremens (high mortality! → present with benzo's)
Cocaine/ Amphetamine	Agitation, irritability, ↓ appetite, formication, ↑ or ↓ BP & HR, cardiac arrhythmia or infarction, stroke, seizure, nosebleeds	Hypersomnolence, dysphoria ↑ appetite
Heroin (opioids)	Intense, fleeting euphoria, drowsy, slurred speech, ↓ memory, pupillary constriction, ↓ respiration **The triad of ¯ consciousness, pinpoint pupils & respiratory depression should always lead to a suspicion of opioids**	Nausea/vomiting, pupillary dilation & insomnia
Benzodiaz-epine & barbiturates	Respiratory & cardiac depression	Agitation, anxiety, delirium
PCP	Intense psychosis, violence, rhabdomyolysis, hyperthermia	
LSD	Sensation is enhanced, colors are richer, music more profound, tastes heightened	

MISCELLANEOUS DISORDERS

DISORDERS OF SEXUALITY & GENDER IDENTITY

1. Sexual identity is based on biology, e.g., men have testes
2. Gender identity is based on self-perception, e.g., biological male perceives himself as a male
3. **Children have a firm conception of their gender identity very early (before age 3)**
4. Sexual orientation is who the person is attracted to; **remember that homosexuality is not a psychiatric disorder** (it used to be, until taken off the DSM in the 1970s) & that treating crises of sexual orientation should focus on accepting one's orientation, not changing it to conform to social "norms"

DISASSOCIATIVE DISORDER (MULTIPLE PERSONALITY DISORDER)

1. The older name says it all: a patient seemingly possesses different personalities that can each take control at a given time. A patient's history may give some history of childhood trauma, e.g., abuse. Treatment focuses on gradual integration of these personalities
2. The main differentials are **dissociative amnesia & dissociative fugue**. Amnesia is a syndrome of forgetting a great deal of personal information; fugue refers to the syndrome of sudden travel to another place, with inability to remember the past & confusion of present identity. Neither case involves shifting between different identities.

ADJUSTMENT DISORDER

1. This refers to any behavioral or emotional Sx that occur in response to stressful life events in the excess of what is normal.
2. Obviously has a catch-all quality to it; **this will be a frequent answer option on the USMLE**
3. **Dx requires the Sx to come within 3mo of the stressor** (so they do not have to be immediate) & **they must disappear within 6mo of the disappearance of the stressor.**
4. Bereavement may seem to be a type of adjustment disorder (the stressor being death), but they are separate diagnoses
5. Depending on the setting, adjustment disorder may appear as depression or anxiety—so how to tell the difference? It isn't easy, but remember: **axis I disorders such as major depression & generalized anxiety take precedence.**

IMPULSIVE-CONTROL DISORDERS

1. Pt is unable to resist the drive to perform certain actions **harmful to themselves or others**.
2. Note the emotional response: these individuals **feel anxiety before the action & gratification afterward**
3. *Intermittent explosive disorder*
    a. Discrete episodes of aggressive behavior far in excess of any possible stressor
    b. The key term is **episodic**; antisocial personalities also commit aggressive behaviors, but their aggression is present between outbursts of such behavior
4. *Kleptomania:* the impulse to steal
    a. The object of theft is not needed for any reason (monetary or otherwise)
    b. The kleptomaniac often feels guilty after stealing
5. *Pyromania:* purposeful fire-setting
    a. There is often a fascination with fire itself that distinguishes this from the antisocial personality/conduct disorders, where the fire-setting is purposeful, e.g., revenge, & not the failure to resist an impulse
6. *Trichotillomania:* hair-pulling, resulting in observable hair loss

DSM-IV Classification	
AXIS I	Clinical disorders
AXIS II	Personality disorders/mental retardation
AXIS III	Medical conditions
AXIS IV	Social and environmental factors
AXIS V	Level of functioning

7 NEUROLOGY

INFARCT

TERMINOLOGY

1. Stroke = a sudden, nonconvulsive focal neurologic deficit
2. TIAs = deficit lasting =24 hr (usually <1hr) & resolve completely
3. Emboli sources = **carotid atheromas (most common)**, cardiac & fat emboli, marantic endocarditis (metastasizing cancer cells)
4. Lacunar infarct = small infarct in deep gray matter, strongly a/w hypertension & atherosclerosis
5. Watershed infarcts occur at border of areas supplied by different arteries (e.g., MCA-ACA), often following prolonged hypotension

PRESENTATION

Sign/Symptom	**Artery**	**Region (lobe)**
Amaurosis fugax (monocular blind)	Carotid (emboli)	Ophthalmic artery
Drop attack/vertigo/CN palsy/coma	Vertebrobasilar (emboli)	Brain stem
Aphasia	Middle cerebral	Dominant frontal or temporal
Sensory neglect & apraxia	Middle cerebral	Nondominant frontal or temporal
Hemiplegia	Middle or anterior cerebral	Contralateral parietal
Urinary incontinence & grasp reflex	Middle or anterior cerebral	Frontal
Homonymous hemianopsia	Middle or posterior cerebral	Temporal or occipital

Dominant = left in 99% of right-handers & 50% of left-handers
Apraxia = patient cannot follow command even if it is understood & the pt is physically capable of it.

1. Wernicke's aphasia (temporal lobe lesion) = receptive, pt speaks fluently but words do not make sense: **Wernicke's is wordy**
2. Broca's aphasia (frontal lobe lesion) = expressive, pt is unable to verbalize: **Broca's is broken**
3. Edema occurs 2-4 days postinfarct, watch for this clinically (e.g., ↓ consciousness, projective vomiting, pupillary changes)
4. Decorticate (cortical lesion) posturing → flexion of arms
5. Decerebrate (midbrain or lower lesion) posturing → arm extension

DIFFERENTIAL DIAGNOSIS

1. Stroke, seizure, neoplasm, encephalitis, multiple sclerosis
2. Stroke causes = 35% local atheroembolic, 30% cardiac, 15% lacunar, 10% parenchymal hemorrhage, 10% subarachnoid hemorrhage, =1% other (e.g., vasculitis, temporal arteritis, etc.)
3. Dx = CT for acute, MRI for subacute infarct &/or hemorrhage
4. Rule out seizure → EEG, loss of bowel/bladder control & tongue injury
5. Lumbar puncture to rule out encephalitis & rule in intracranial bleed

TREATMENT

1. tPA within 3-6 hours of onset (preferably 1hr) for occlusive dz only!
2. **Intracranial bleeding is an absolute contraindication to tPA use!**
3. Correct underlying disorder, e.g., hyperlipidemia, hypertension, diabetes, valve abnormality, coagulopathy, atrial fibrillation
4. For embolic strokes give aspirin/warfarin anticoagulation for prophyalxis
5. If carotid is 70% occluded & patient has Sx → endarterectomy

PROGNOSIS

1. 20-40% mortality at 30days (20% atheroemboli, 40% bleed)
2. Less than 1/3 patients achieve full recovery of lifestyle
3. Atheroembolic strokes recur at 10%/yr

INFECTION & INFLAMMATION

MENINGITIS

1. 50% due to *Streptococcus pneumonia*, 25% due to *Neisseria meningitis, Hemophilus influenza* is rare now due to vaccination, *Listeria* seen in neonates, elderly and immunocompromised pts, and Group B Strep (*S. agalactiae)* and *E. coli* are the #1 and #2 causes of neonatal meningitis
2. Si = **meningismus** (pt cannot touch chin to chest), (+) **Kernig's sign** (pt is supine with hip and knees flexed at 90^{o}, examiner cannot extend knee), (+) **Brudzinski's sign** (pt is supine, when examiner flexes neck, pt involuntarily flexes hip and knees).
3. CSF differential for meningitis

	Cells	**Protein**	**Glucose**
Bacterial	↑ **neutrophils**	↑↑	↓↓ (=2/3 serum)
Viral	↑ mononuclear	+/- ↑	**Nml**
Subacute	↑ mononuclear	↑	↓

4. Can be acute, subacute, chronic presentation
5. Acute
    a. Send CSF for Gram's stain, bacterial cultures, HSV PCR
    b. Treat all patients empirically by age until specific tests return

Age	**Regimen**	**Common etiologies**
Neonates (=1mo)	**Ampicillin + cefotaxime**	*Streptococcus agalactiae, Listeria, Escherichia coli*
Children to teens	**Cefotaxime + vancomycin**	*Streptococcus pneumonia, Neisseria meningitidis*
Adults	**Cefotaxime + vancomycin**	*S. pneumonia* by far most common

    c. Of viral causes, only HSV (acyclovir) & HIV (AZT) can be treated—otherwise treatment is supportive

Organism	**Patients**	**Characteristics**	**Treatment**
Streptococcus pneumoniae	**#1 cause in adults:** old age, asplenia, poor health predispose	Can progress from otitis media, sinusitis, or bacteremia	Pen G (if susceptible) 2nd line = cefotaxime, 3rd line = vancomycin
Neisseria meningitidis	=1yr old or in adults in epidemics in close populations (military barracks)	**Petechiae on trunk, legs, conjunctivae**—beware o Waterhouse-Friderichsen syndrome (adrenal infarct)	Pen G Rifampin or fluoroquinolones prophylaxis for close contacts
Hemophilus influenzae type B	Formerly #1 cause in children, until vaccine	Now rare, but can cause epiglottitis	Cefotaxime
Streptococcus agalactiae	**#1 cause in neonates**	Acquired at birth	Ampicillin
Escherichia coli	Common in neonates	Acquired at birth	Cefotaxime
Listeria monocytogenes	Elderly/neonates, AIDS, diabetes, steroids	Difficult CSF Gram's stain/Cx, DX → blood Cx	Ampicillin
Staphylococcus aureus	Trauma/neurosurgery	Wound infxn from skin	Oxacillin/vancomycin

6. Subacute/chronic meningitis
    a. Si/Sx = per acute but evolves over wk→mo, +/- fever
    b. DDx = fungal, mycobacterial, noninfectious, other rae dzs
    c. Send CSF for fungal Cx, cytology, India Ink, TB PCR
    d. Fungal meningitis
        i. DDx = *Cryptococcus, Coccidioides*, other more rare dz
        ii. **Cryptococcus commonly seen in AIDS**
            1. **India Ink stain will show Cryptococcus in CSF**
            2. **opening pressure is commonly elevate**

iii. **Coccidioides blastocysts seen on CSF cytology**
iv. Tx = IV amphotericin B (intrathecal may be necessary)

e. TB meningitis
   i. Usually occurs in elderly by reactivation, grave Px
   ii. Dx is made by TB PCR of the CSF
   iii. Tx = **RIPE**: **R**ifampin + **I**NH + **P**yrazinamide + **E**thambutol

f. Other causes = sarcoid, cancer, collagen-vascular dz, drug reactions

ENCEPHALITIS

1. Si/Sx = similar to meningitis, but focal findings are evident

Etiology	**Disease**	**Si/Sx**	**Tx/Px**
Toxoplasmosis	1. Transplacental congenital dz → hydrocephalus / mental retardation 2. Adults exposed via cat feces get dz if immunosuppressed —**Toxo is the #1 CNS lesion in AIDS**	**Multiple ring enhancing lesions ® focal neurologic deficits** Toxoplasmosis antibody test very sensitive	Bactrim Prophylaxis if CD4 =200/µL
HSV	**#1 cause of viral encephalitis**	**Olfactory hallucinations, bloody CSF, personality changes** EEG/MRI → temporal lobe dz	Acyclovir
Syphilis	**Meningovascular disease** **Parenchymal disease:** 1. Tabes dorsalis = bilateral spinal cord demyelination 2. Dementia paralytica = cortical atrophy, neuron loss gliosis	**Argyll-Robertson pupil** Pain, hypotonia, ↓ tone, ↓ DTRs, ↓ proprioception, incontinence Sx = psychosis, dementia, personality change	IV penicillin
PML	Usually in AIDS, caused by JC virus	Diffuse neurologic dz	Non, death inevitable

ABSCESS

1. Si/Sx = headache, fever, ↑ ICP, focal neurologic findings
2. Risk factors = congenital R-L shunt (lung filtration bypassed), otitis, paranasla sinusitis, metastases, trauma & immunosuppression
3. Anaerobes & aerobes, gram-positive cocci & gram-negative rods
4. Tx = antibiotics (+) **surgical drainage if >3cm or if persists**
5. **Brain abscesses are invariably fatal if untreated**
6. Helminthic infections
   a. Cysticercosis (*Taenia solium)*
      i. Eggs transmitted by fecal-oral route
      ii. **Encephalitis in Latin American immigrant is due to neurocysticercosis until proven otherwise**
      iii. Tx = praziquantel (+) steroids (dead cyst → inflammation)
   b. Hydatid cysts (*Echinococcus)*
      i. Acquired by dog feces, can cause focal Sx & seizure
      ii. If cysts rupture they can cause fatal anaphylaxis
      iii. Tx = careful surgical excystation, mebendazole

DEMYELINATING DISEASES

MULTIPLE SCLEROSIS (MS)

1. Unknown etiology, but (+) genetic & environmental predispositions, ↑ common in pts who lived first decade of life in northern latitudes
2. Si/Sx = relapsing asymmetric limb weakness, ↑ DTRs, nystagmus, tremor, scanning speech, paresthesias, optic neuritis, (+) Babinskin sign
3. Dx = history, MRI, lumbar puncture
4. MRI → periventricular plaques, multiple focal demyelination scattered in brain & spinal cord (**lesion disseminated in space & time)**
5. **Lumbar puncture ® - CSF immunoglobulins manifested as multiple oligoclonal bands on electrophoresis**
6. Tx = interferon-β, may induce prolonged remissions in some pts
7. Px
    a. Variable types of disease, long remissions sometimes seen
    b. But can progressively decline → death in only a few years

GUILLAIN-BARRE SYNDROME

1. Acute autoimmune demyelinating dz involving peripheral nerves
2. **Si/Sx = muscle weakness & paralysis ascending up from lower limbs, ¯ reflexes, can cause bilateral facial nerve palsy**
3. **Most often preceded by gastroenteririts (classically *Campylobacter jejuni*)**. Mycoplasma or viral infection, immunization, or allergic reactions
4. Dx = Hx of antecedent stimuli, CSF → **albumin-cytologic dissociation** (CSF protein ↑↑↑ without ↑ in cells seen)
5. Tx = plasmapheresis, IVIG< intubation for respiratory failure
6. Px is excellent for 80-90% of patients, will spontaneously regress
7. Respiratory failure & death can occur in remainder

CENTRAL PONTINE MYELINOLYSIS

1. Diamond-shaped region of demyelination in basis pontis
2. **Due to rapid correction of hyponatremia & in liver dz**
3. No Tx once condition has begun
4. Coma or death is a common outcome

METABOLIC & NUTRITIONAL DISORDERS

CARBON MONOXIDE POISONING

1. Seen in pts enclosed in burned areas, or during the start of a cold winter (people are using their new gas heaters) → bilateral pallidal necrosis
2. Si/Sx = headache, nausea, vomiting, delirium, cherry-red color of lips
3. Dx = elevated carboxyhemoglobin levels
4. Tx = hyperbaric oxygen (1^{st} line) or 100% O2.

THIAMINE DEFICIENCY

1. Usually 2^{o} to alcoholism
2. Beriberi peripheral neuropathy due to Wallerian degeneration
3. Wernicke's encephalopathy: **Wernicke's triad = confusion (confabulation), ophthalmoplegia, ataxia**
4. Wernicke's is related to lesions of mamillary bodies
5. Tx: give thiamine prior to glucose (e.g., thiamine should be run in IV fluid without glucose) or will exacerbate mamillary body damage

B12 DEFICIENCY

1. Subacute degeneration of posterior columns & lateral corticospinal tract

2. Si/Sx = weakness & ↓ vibration sense (both worse in legs), paresthesias, hyperreflexia, ataxia, personality change, dementia—**note, neurological deficits can occur even if no hematologic abnormalities are present!**
3. Tx = B12 replacemtn (can use high-dose oral in lieu of injection)

WILSON'S DISEASE (HEPATOLENTICULAR DEGENERATION)

1. Defect in copper metabolism → lesions in basal ganglia
2. Si/Sx = extrapyramidal tremors & rigidity, psychosis, & manic-depression
3. **Pathognomonic ® Kayser-Fleischer ring around the cornea**
4. Dx = ↓ serum ceruloplasmin
5. Tx = penicillamine or liver transplant if drug fails

HEPATIC ENCEPHALOPATHY

1. Seen in cirrhosis, may be due to brain toxicity 2^o to excess ammonia & other toxins not degraded by malfunctioning liver
2. Sx = hyperreflexia, **asterixis** (flapping of extended wrists), dementia, seizures, obtundation/coma
3. Tx = lactulose, neomycin & protein restriction to ↓ ammonia-related toxins

TAY-SACHS DISEASE

1. Hexosaminidase A defect → ↑ ganglioside GM2
2. Si/Sx = **cherry-red spot on macula**, retardation, paralysis, blind
3. Dx by biopsy of rectum, or enzymatic assay, no Tx

SEIZURES (Sz)

TERMINOLOGY

1. Complex sz → loss of consciousness (LOC), simple sz does not
2. Generalized sz = entire brain involved, partial sz = focal area
3. Tonic sz → prolonged contraction, clonic sz → twitches
4. Absence = complex generalized sz → brief LOC
5. Grand mal = complex generalized tonic-clonic sz

PRESENTATION

1. Hx of prior head trauma, stroke, or other CNS disease ↑ risk for sz
2. Si/Sx = loss of bowel/bladder control, tongue, maceration, postictal confusion/lethargy, focal findings indicate epileptogenic foci
3. If pt has Hx of seizures, always check blood level of medication

TREATMENT

1. Tx seizures if they recur or if pt has known epileptic focus

Partial	**Grand mal**	**Absence**	**Myoclonic**
Phenytoin	Valproate	Ethosuximide	Valproate
Carbamazepine	Carbamazepine	Valproate	Clonazepam
Valproate	Phenytoin	Clonazepam	

2. Tx underlying cause: electrolyte, infxn, toxic ingestion, trauma, azotemia, stroke/bleed, delirium tremens, hypoglycemia, hypoxia
3. **Phenytoin causes gingival hyperplasia, hirsutism**
4. Carbamazepine causes leukpenia/aplastic anemia, hepatotoxic
5. Valproate causes neutropenia, thrombocytopenia, hepatotoxic
6. Stop Tx if no seizures for 2yr & normal EEG

STATUS EPILEPTICUS

1. Continuous seizing lasting >5min
2. Tx with benzodiazepines for immediate control, followed by Phenytoin loading & pehnobarbitol for refractory cases
3. This is a medical emergency!

DEGENERATIVE DISEASES

DEMENTIA VS. DELIRIUM DIFFERENTIAL

	Dementia	**Delirium**
Definition	Both cause global decline in cognition, memory, personality, motor, or sensory function	
Course	Constant, progressive	Sudden onset, waxing/waning daily
Reversible?	Usually not	Almost always
Circadian?	Constant, no daily pattern	Usually worse at night (sun-downing)
Consciousness	Normal	Altered (obtunded)
Hallucination	Usually not	Often, classically visual
Tremor	Often not	Often present (i.e., asterixis)
Causes	Alzheimer's, multi-infarct, Pick's dz, alcohol, brain infxn/tumors, malnutrition (thiamine/B12 deficiency)	Systemic infection/neoplasm, drugs (**particularly narcotics & benzodiazepines**), stroke, heart dz, alcoholism, uremia, electrolyte imbalance, hyper/hypoglycemia
Treatment	Supportive	Treat underlying cause, **control Sx with haloperidol instead of sedatives**—due to agitation pts are often given benzodiazepines or sedatives, but these drugs often exacerbate the delirium as they disorient the pt even more

ALZEHEIMER'S DISEASE (SENILE DEMENTIA OF ALZHEIMER TYPE)

1. Most common cause of dementia—affects 5% of people over 70
2. Si/Sx = dementia, anxiety, hallucination/delusion, tremor
3. Occurs in Down's syndrome pts at younger ages (age 30-40)
4. Dx = clinical, with definitive diagnosis only possible at autopsy
5. Tx = anticholinesterase inhibitor can slow dementia, antidepressants & antipsychotics can be used for psychosis
6. Px = inevitable decline in function usually over about 10yr

MULTI-INFARCT DEMENTIA

1. Si/Sx = acute, step-wise ↓ in neurologic function, multiple focal deficits on exam, hypertension, old infarcts by CT or MRI
2. Dx = clinical, radiographic
3. Tx = prevent future infarcts by ↓ cardiovascular risks

PICK'S DISEASE

1. Clinically resembles Alzheimer's more in women, younger age onset (50s)
2. Predominates in frontal (more personality changes seen) & temporal lobes
3. Dx = MRI → symmetrical frontal or temporal atrophy, confirm by autopsy
4. Tx/Px = as per Alzheimer's

PARKINSON'S DISEASE

1. Parkinson's disease = idiopathic parkinsonism, mid- to late-age onset
2. Parkinsonism
    a. **Syndrome of tremor, cog-wheel rigidity, bradykinesia, classic shuffling gait, mask-like facies** +/- dementia due to loss of dopaminergic neurons in substantia nigra
    b. DDx = Parkinson's disease, severe depression (bradykinesia & flat affect), intoxication (e.g., manganese, synthetic heroin), phenothiazine side effects, rare neurodegenerative diseases
3. Dx = clinical, r/o other causes

4. Tx
    a. Sinemet (levodopa = carbidopa) best for bradykinesia
    b. Anticholinergics (benztropine/trihexyphenidyl) for tremor
    c. Amantadine $\rightarrow\uparrow$ dopamine release, effective for mild dz
    d. Surgical pallidotomy for refractory cases
5. Px = typically progresses over years despite treatment

HUNTINGTON'S CHOREA

1. Si/Sx = progressive choreiform movements of all limbs, ataxic gait, grimacing $\rightarrow$ dementia, usually in 30s-50s (can be earlier or later)
2. Autosomal CAG triplet repeat expansion in HD gene $\rightarrow$ atrophy of striatum (especially caudate nucleus), with neuronal loss & gliosis
3. Dx = MRI $\rightarrow$ atrophy of caudate, (+) family history
4. Tx/Px = supportive, death inevitable

AMYOTROPHIC LATERAL SCLEROSIS (LOU GEHRIG'S DISEASE, MOTOR NEURON DISEASE)

1. Si/Sx = **upper & lower motor neuron dz** ® muscle weakness with fasciculations (anterior motor neurons) progressing to denervation atrophy, hyperreflexia, spasticity, difficulty speaking/swallowing
2. Dx = clinical Hx & physical findings
3. Tx/Px = supportive, death inevitable, usually from respiratory failure

8 DERMATOLOGY

TERMINOLOGY

1. Macule = flat discoloration <1cm in diameter
2. Papule = elevated skin lesion, <1cm diameter
3. Plaque = elevated skin lesion, >1cm in diameter
4. Vesicle = small fluid-containing lesion <0.5cm in diameter
5. Wheal = like a vesicle but occur transiently as in urticaria (hives)
6. Bulla = large fluid-containing lesion, >0.5cm in diameter
7. Lichenification = accentuated skin markings in thick epidermis due to scratching
8. Keloid = an irregular raised lesion resulting from scar tissue hypertrophy
9. Petechiae = flat, pinhead, nonblanching, red-purple lesion caused by hemorrhage into the skin: seen in any cause of thrombocytopenia
10. Purpura = larger than petechiae
11. Cyst = closed epithelium-lined cavity or sac containing liquid or semi-solid material
12. Hyperkeratosis = ↑ thickness of stratum corneum (seen in chronic dermatitis)
13. Parakeratosis = hyperkeratosis with retention of nuclei in stratum corneum & thinning of stratum granulosum (usually seen in psoriasis)
14. Steroids

Potency	**Drug**	**Use for disease on…**
Low	1% hydrocortisone	Face, genitals, skin folds (prevent atrophy/striae),also use in children for dz on body
Moderate	0.1% triamcinolone	Body/extremities, or ↑ dz on face, genitals, skin folds
High	Fluocinonide (Lidex)	Thick skin (palms/soles), or ↑ body dz, **do not use on face**
Very high	Diflorasone	Thick skin, or if very severe on body

INFECTIONS

ACNE

1. Inflammation of pilosebaceous unit caused by secondary *Propionibacterium acnes* infection of blocked pore
2. Si/Sx = open comedones (blackheads) & closed comedones (whiteheads) onface, neck, chest, back & buttocks, can become inflamed & pustular
3. Tx = typical antibiotics, Retin-A, benzoyl peroxide, systemic antibiotics, if acne is scarring consider Acutane

IMPETIGO

1. Superficial skin infection of epidermis
2. Si/Sx = honey-crusted lesions or vesicles occurring most often in children around the nose & mouth, can be bullous or nonbullous
3. Common organisms include *Staphylococcus aureus & S. pyogenes*
4. Tx = Keflex or oxacillin for 7-10 days

FOLLICULITIS

1. Si/Sx = erythematous pustules commonly noted around beard area
2. *S. aureus* most common, *Pseudomonas aeruginosa* caused "hot tub" folliculitis (organism lives in warm water), also fungi & viruses
3. Tx = local wound care, Keflex only if severe

SUBCUTANEOUS INFECTIONS

1. Cellulitis
    a. Si/Sx = spreading subcutaneous infxn with classic signs of inflammation: *rubor* (red), *calor* (hot), *dolor* (pain), & *tumor* (swelling)

    b. *Staphylococcus & Streptococcus* most common etiologies
    c. Tx = oxacillin or Keflex
2. Abscess
    a. Local collection of pus, often with fever, ↑ white count
    b. Tx = incision & drainage (I&D), can add Keflex
3. Furuncle (boil) & carbuncle
    a. Furuncle = pus collection in 1 hair follicle, often caused by *S. aureus*
    b. Carbuncle = pus collection involving many hair follicles
    c. Tx = I&D, add Keflex or oxacillin if severe
4. Paronychia
    a. Infxn of skin surrounding nail margin that can extend into surrounding skin & into tendons within hand
    b. Commonly caused by *S. aureus*, also *Candida*
    c. Tx = warm compress, I&D if area is purulent, add Keflex if severe
5. Necrotizing fasciitis
    a. Infxn along fascial planes with severe pain, fever, ↑ WBC, local inflammation may be deceptively absent but pt will appear very ill
    b. Caused by *S. pyogenes* (group A Strep) or *Clostridium perfringens*
    c. Tx = **Immediate, extensive surgical debridement, add penicillin & clindamycin to help prevent further spread**
    d. Px = ↑↑↑ mortality unless debridement is rapid & extensive

SCARLET FEVER

1. *S. pyogenes* (group A Strep = GAS) is the cause
2. Si/Sx
    a. "**Sunburn with goose bumps**" rash, finely punctuate, erythematous but blanches with pressure, initially on trunk, generalizes within hours
    b. Sandpaper rough skin, **strawberry tongue**, beefy-red pharynx, circumoral pallor
    c. **Pastia's lines = rash, most intense in creases of axillae & groin**
    d. Eventual desquamation of hands & feet as rash resolves
    e. Systemic Sx include fever, chills, delirium, sore throat, cervical adenopathy, all of which appear at same time as rash
3. Complications include rheumatic fever & glomerulonephritis
4. Tx = penicillin

HIDRADENITIS SUPPURATIVA

1. Si/Sx = plugged apocrine glands presenting as inflamed masses in groin/axilla, become secondarily infected
2. Tx = surgical debridement & antibiotics

ROSE SPOTS

1. **Rose spots** = small pink papules in groups of 1-2 dozen on trunk, found in 30% of pts with typhoid fever (*Salmonella typhi*)
2. Typhoid fever Si/Sx
    a. High fever, myalgias, abdominal tenderness, splenomegaly
    b. **Classic pulse-fever dissociation** = high fever with relative bradycardia (also seen in brucellosis)
3. **Tx for chronic aSx typhoid fever (carrier state like "Typhoid Mary") is cholecystectomy because S. typhi resides in the gallbladder**

ERYTHRASMA

1. Si/Sx = irregular erythematous rash found along major skin folds (axilla, groin, fingers, toes, & breasts)
2. Commonly seen in adult diabetics, caused by *Corynebacterium spp.*

3. Dx = Wood's lamp of skin → **coral-red fluorescence, KOH prep negative**
4. Tx = erythromycin

COMMON DISORDERS

PSORIASIS

1. Si/Sx = pink plaques with silvery-white scaling **occurring on extensor surfaces such as elbows & knees** (also scalp, lumbosacral, glans penis, intergluteal cleft), **& fingernail pitting** can be a/w arthritis
2. Classic finding = **Auspitz sign** → removal of overlying scale causes pinpoint bleeding due to thin epidermis above dermal papillae
3. Classic finding = **Koebner's phenomenon** → psoriatic lesions appear at sites of cutaneous physical trauma (skin scratching, rubbing, or wound)
4. Dx = clinical, biopsy is gold standard
5. Tx = topical steroids (1st line), PUVA (2nd line) = **P**soralens + **UVA** light, methotrexate & cyclosporin (3rd line)

ECZEMA (ECZEMATOUS DERMATITIS)

1. Family of superficial, intensely pruritic, erythematous skin lesions
2. Atopic dermatitis
    a. Si/Sx = **an "itch that rashes,"** rash 2° to scratching chronic pruritus, commonly found on the face in infancy, later in childhood can present on the flexor surfaces such as antecubital & popliteal foassa
    b. Atopy = inherited predisposition to asthma, allergies & dermatitis
    c. Dx is clinical
    d. Tx = avoid irritants or triggers, keep skin moist with lotions, use steroids & antihistamines for Sx relief of itching & inflammation
3. Contact dermatitis
    a. Si/Sx = linear pruritic rash at site of contact
    b. Caused by delayed type hypersensitivity reaction after exposure to poison ivy, poison oak, nickel, or chemicals
    c. Dx is clinical, history of exposure crucial
    d. Tx = as per atopic dermatitis
4. Seborrheic dermatitis
    a. Si/Sx = erythema, scaling, white flaking (dandruff) in areas of sebaceous glands (face, scalp, groin, axilla, & external ear)
    b. Called "cradle cap" in infants
    c. Dx = clinical & KOH prep to rule out fungal infection
    d. Tx = selenium shampoo on face & trunk, steroids for severe dz

URTICARIA (HIVES)

1. Common disorder caused by mast cell degranulation & histamine release
2. Si/Sx = transient papular wheals, intensely pruritic, surrounded by erythema, **dermographism** (write word on the skin & it remains imprinted as erythematous wheals)
3. Most lesions are IgE-mediated (type I hypersensitivity) but exercise, certain chemicals in sensitive pts & inhibitors of prostaglandin synthesis (e.g., aspirin) can also cause IgE-independent reactions
4. Dx = skin testing or aspirin or exercise challenge
5. Tx = avoidance of triggers, antihistamines, steroids, epinephrine
6. Can cause respiratory emergency requiring intubation

HYPOPIGMENTATION

1. Vitiligo
    a. Loss of melanocytes in discrete areas of skin, appearing as sharply demarcated depigmented patches

b. Occurs in all races but most apparent in darkly pigmented pts
c. Chronic condition that may be autoimmune in nature
d. a/w thyroid dz in 30% of pts, especially women
e. Tx = mini-grafting or total depigmentation
f. Px = some pts remit over long tem, others never do

2. Albinism
   a. **Melanocytes are present** but fail to produce pigment due to tyrosinase deficiency
   b. Si/Sx = white skin & eyelashes, nystagmus, iris translucency, ↓ visual acuity, decreased retinal pigment & strabismus
   c. Tx = avoid sun exposure, sunscreens
   d. Px = the oculocutaneous form predisposes to skin cancer
3. Pityriasis alba
   a. Nonpathological areas of hypopigmentation on face or upper extremities
   b. Can be 2^o to prior infection or inflammation, often regress over time
   c. Differentiated from tinea versicolor by KOH prep

HYPERPIGMENTATION

1. Freckle (ephelis) is caused by normal melanocytes number but ↑ melanin within basal keratinocytes, darkens with sun exposure
2. Lentigo is pigmented macules caused by melanocytes hyperplasia that, unlike freckles, do not darken with sun exposure
3. Nevocellular nevus
   a. Common mole, benign tumor derived from melanocytes
   b. Variations of nevi
      i. Blue nevus = black-blue nodule present at birth, often mistaken for melanoma
      ii. Spitz nevus = red-pink nodule, often seen in children, confused with hemangioma or melanoma
      iii. Dyplastic nevus = atypical, irregularly pigmented lesion with ↑ risk of transformation into malignant melanoma
      iv. Dysplastic nevus syndrome is autosomal dominant inherited dz
   c. Dx = biopsy, Tx = full excision
4. Melasma (chloasma)
   a. A mask-like hyperpigmentation on face seen in pregnancy
   b. Sunlight accentuates pigmentation, which typically fades postpartum
   c. Tx = minimize facial exposure to sun, or hydroquinone cream (works for any hyperpigmentation)
5. Hemangioma
   a. Group of "birthmarks," capillary hemangiomas present at birth
   b. Port-wine stains (purple-red on face or neck)
      i. Can be a/w Sturge-Weber syndrome
      ii. Must screen for glaucoma & CNS dz (CT scan)
      iii. Tx = laser therapy, will not regress spontaneously
   c. Strawberry hemangiomas (bright raised red lesions) are benign, most disappear on their own
   d. Cherry hemangiomas (benign small red papule) Tx with laser therapy
6. Xanthoma
   a. Yellowish papules, often accumulations of foamy histiocytes
   b. Can be idiopathic or a/w familial hyperlipidemia
   c. If seen on eyelids they are called "xanthelasma"
   d. Tx = ↓ hyperlipidemia, surgically excise papules as needed
7. Pityriasis rosea

a. Erythematous maculopapular rash with scale apparent in center
b. Often preceded by a "herald patch" on trunk
c. **Can appear on back in a Christmas tree distribution**
d. Tx = sunlight, otherwise spontaneously remits in 6-12wk

8. Erythema nodosum
    a. Inflammation of subcutaneous fat (panniculits) & adjacent vessels
    b. Characteristic lesions are **tender red nodules occurring on the lower legs** & sometimes forearms
    c. Usually resolves in 6-8wk, Tx directed at underlying cause
    d. Common causes
        i. Infections = *Mycoplasma, Chlamydia, Coccidioides immitis, Mycobacterium leprae* & others
        ii. Drugs = sulfonamides & contraceptive pills
        iii. Inflammatory Bowel Disease, sarcoidosis, rheumatic fever
        iv. Pregnancy
9. Dermatomyositis
    a. An autoimmune disorder sometimes seen with polymyositis
    b. Presents with **heliotropic (reddish-purple) patches on eyelids** & erythematous scally rash on hands
    c. Tx = high-dose steroids
10. Seborrheic keratosis
    a. Black or brown benign plaques, appear to be stuck onto skin surface
    b. Commonly seen in elderly & runs in families
    c. Can be mistaken for melanoma
    d. Tx = liquid nitrogen freezing, usually too many to treat
11. Acanthosis nigricans
    a. Black velvety plaques on flexor surfaces & intertriginous areas
    b. Seen in obesity & endocrine disorders (e.g., diabetes)
    c. Can mark underlying malignancy (e.g., GI/GU, lymphoma)
12. bronze diabetes = 1^{o} hemochromatosis
    a. Familial defect causing intestinal hyperabsorption of iron
    b. **Classic triad: - skin pigmentation, cirrhosis, diabetes mellitus**
    c. Other Sx = cardiomyopathy, pituitary failure & arthropathies
    d. **Clinical pearl: hemochromatosis is the likely Dx in any patient with osteoarthritis involving the MCP joints**
    e. Dx = transferring saturation (iron/TIBC) = 50%
    f. Tx = phlebotomy, which improves survival if started early

VERRUCAE (WARTS)

1. Verruca vulgaris = hand wart
2. Verruca plana (flat wart) smaller than vulgaris, seen on hands & face
3. Humna papilloma virus (HPV) types 1-4 cause skin & plantar warts
4. HPV 6 & 11 cause anorectal & genital warts (condyloma acuminatum)
5. HPV 16, 18, 31, 33, 35 cause cervical cancer
6. Condylomata lata are flat warts caused by *Treponema pallidum* (syphilis)

CANCER

Disease	**Si/Sx**	**Tx**	**Px**
Basal cell carcinoma	Most common skin cancer, classic "**rodent ulcer**" seen on face, with **pearly translucent borders & fine telangiectasias**, not usually found on lips	Excision	Excellent—almost never metastasize

Squamous cell carcinoma	Common in elderly, appears as erythematous nodules on sun-exposed areas that eventually ulcerate & crust, **frequently preceded by actinic keratosis = rough epidermal lesions on sun-exposed areas such as lower lip, ears & nose**	Excision, radiation	Metastasize more than basal cell but not as much as melanoma
Malignant melanoma	Seen in lightly pigmented individual with ↑ sun exposure—diagnose with **ABCDEs** **A**symmetry = malignant, benign = symmetrical **B**order = irregular, benign = smooth **C**olor = multicolored, benign = 1 color **D**iameter >6mm, benign = <6mm **E**levation = raised above skin, benign = flat **E**nlargement = growing, benign = not growing	Excision, chemo if mets likely	High rate of metastasis → **#1 skin cancer killer, risk of mets - with depth of invasion on biopsy**
Kaposi's sarcoma	Connective tissue cancer caused by human herpes virus 8, appears as red/purple plaques or nodules on skin & GI viscera, almost exclusively seen in AIDS patients	HIV drugs, chemo	Benign unless damages internal organs
Cutaneous T-cell lymphoma	**"Mycosis fungoides," presents with erytheroderma (total body erythematous & pruritic rash), rash can precede malignancy by years**, leukemic phase of disease call "Sezary syndrome"	PUVA, topical chemo, radiation	7-10yr life expectancy without Tx

NEUROCUTANEOUS SYNDROMES (PHAKOMATOSES)

1. Tx is supportive depending upon individual signs & symptoms
2. Neurocutaneous Syndrome (Phakomatoses)

Disease	**Characteristics**
Tuberous sclerosis	Ash leaf patches (hypopigmented macules), Shagreen spots (leathery cutaneous thickening), adenoma sebaceum of the face, **Seizures, mental retardation**
Neurofibromatosis (NF)	Si/Sx = **café-au-lait**, neurofibromas, meningiomas, acoustic neuromas, kyphoscoliosis—NF 2 causes bilateral acoustic neuromas
Sturge-Weber syndrome	Si/Sx = **port-wine hemangioma of face** in CN V distribution, mental retardation, seizures
Von Hippel-Lindau syndrome	Si/Sx = multiple hemangiomas in various organs, ↑ frequency of renal cell CA & polycythemia (↑erythropoietin secretion)

BLISTERING DISORDERS

PEMPHIGUS VULGARIS (PG)

1. PG is a rare autoimmune disorder, **affecting 20-40yr-olds**
2. Si/Sx = **flaccid epidermal bullae** that easily slough off leaving large denuded areas of skin (Nikolsky's sign), ↑ risk of 2^o infxn
3. DDx = bullous pemphigoid
4. Dx = skin biopsy → **immunofluorescence surrounding epidermal cells** showing "tombstone" fluorescent pattern
5. Tx = high-dose oral steroids, antibiotics for infection
6. Px = **often fatal if not treated**

BULLOUS PEMPHIGOID (BP)

1. Common autoimmune disease affecting **mostly the elderly**
2. Resembles PG but much less severe clinically
3. Si/Sx = **Hard, tense bullae** that do not rupture easily & usually heal without scarring if uninfected
4. Dx = skin biopsy → immunofluorescence as a **linear band along the basement membrane, with - eosinophils** in dermis

5. Tx = oral steroids
6. Px = much better than PG

ERYTHEMA MULTIFORME

1. A hypersensitivity reaction to drugs, infections, or systemic disorders such as malignancy or collagen vascular disease
2. Si/Sx = **diffuse, erythematous target-like lesions** in many shapes (hence name "multiforme"), often accompanying a herpes eruption
3. **Stevens-Johnson syndrome = a severe febrile form (sometimes fatal) ® hemorrhagic crusting also affects lips & oral mucosa**
4. Dx = clinical, hx of herpes infection or drug exposure
5. Tx = stop offending drug, prevent eruption of herpes with acyclovir

PORPHYRIA CUTANEA TARDA

1. Autosomal dominant defect in heme synthesis (50% ↓ in uroporphyrinogen decarboxylase activity in RBC & liver)
2. Si/Sx = blisters on sun-exposed areas of face & hands, ↑ hair on temples & cheeks, **no abdominal pain** (differentiates from other porphyrias)
3. Dx = Wood's lamp of urine → **urine fluoresces with distinctive orange-pink color due to levels of uroporphyrins**
4. Tx = sunscreen, phlebotomy, chloroquine, no alcohol
5. Px = remitting/relapsing, exacerbations due to viral hepatitis, hepatoma, alcohol abuse, estrogen, sunlight

VECTOR BORNE DISEASES

BACILLARY ANGIOMATOSIS (PELIOSIS HEPATIS)

1. Si/Sx = weight loss, abdominal pain, **rash = red or purple vascular lesions,** from papule to hemangioma-sized, located anywhere on skin & disseminated to any range
2. DDx = kaposi's sarcoma, cherry hemangioma
3. **Almonst always seen in HIV (+) patients or homeless population**
4. Caused by *Bartonella* spp. Leading to dysregulated angiogenesis
5. **Cat-scratch disease caused by *B. henselae* transmitted by kitten scratches, trench fever cause by *B. Quintana* spread by lice**
6. Dx = histopathology with silver stain, visualization of organisms in lesion, blood culture & PCR can also be done
7. Tx = erythromycin
8. Px = excellent with Tx, some pts require lifelong suppressive Tx

LYME DISEASE

1. Si/Sx = fever, chills, headaches, lethargy, photophobia, meningitis, myocarditis, arthralgia & myalgias
2. **Classic rash = erythema chronicum migrans ® erythematous annular plaques with a red migrating border & central clearing & induration**
3. Dx = PCR for *Borrelia burgdorferi* DNA, or skin biopsy of migrating edge looking for causative spirochete
4. Tx = spray skin & clothes with DEET or permethrin, wear long pants in woods to prevent tick bite (*Ixodes dammini & Ixodes pacificus*)
5. Once infected → high-dose penicillin or ceftriaxone for 2-4wk

ROCKY MOUNTAIN SPOTTED FEVER

1. Si/Sx = acute onset fever, headache, myalgias, classic rash
2. Rash = **erythematous maculopapular, starting on wrists & ankles then moving toward palms, soles & trunk**

3. Rash may lead to cutaneous necrosis due to DIC-induced occlusion of small cutaneous vessels with thrombi
4. Dx = by Hx (exposure to outdoors or tick bite, *Dermacentor spp.*), serologies for *Rickettsia rickettsii*, skin biopsy
5. Doxycycline or chloramphenicol

PARASITIC INFECTIONS

SCABIES

1. Si/Sx = erythematous, **markedly pruritic papules & burrows located intertriginous areas** (e.g., finger & toe webs, groin), lesions contagious
2. Dx = microscopic identification of *Sarcoptes scabiei* mite in skin scrapings
3. Tx = pt & all close contacts apply Permethrin 5% cream to entire body for 8-10hr then repeat in 1wk, wash all bedding in hot water the same day
4. Lindane cream is less effective, a/w adverse effects in kids
5. Symptomatic relief of hypersensitivity reaction to dead mites may be treated with antihistamines & topical steroids

PEDICULOSIS CAPITIS (HEAD LOUSE)

1. Si/Sx = can be asymptomatic, or pruritus & erythema of scalp may be noted, common in school-aged children
2. Dx = microscope exam of hair shaft, nits may fluoresce with Wood's lamp
3. Permethrin shampoo or gel to scalp, may need to repeat

PEDICULOSIS PUBIS ("CRABS")

1. Si/Sx = very **pruritic papules in pubic area**, axilla, periumbilically in males, along eyelashes, eyebrows & buttocks
2. Dx = microscopic identification of lice, rule out other STDs
3. Tx = apply Permethrin 5% shampoo for 10min then repeat in 1wk

CUTANEOUS LARVA MIGRANS (CREEPING ERUPTION)

1. Si/Sx = erythematous, pruritic, **serpiginous thread-like lesion** marking burrow of migrating nematode larvae, often on back, hands, feet, buttocks
2. Organism = hookworms: *Ancylostoma, Necator & Strongyloides*
3. Dx = Hx of unprotected skin lying in moist soil or sand, Bx of lesion
4. Tx = ivermectin orally or thiabendazole topically

FUNGAL CUTANEOUS DISORDERS

Disease	**Si/Sx**	**Dx**	**Tx**
Tinea	❖ Erythematous, pruritic, scaly, well-demarcated plaques ❖ Black dots may be seen on scalp of patients with tinea capitis	Clinical or KOH prep	Topical antifungal (oral needed for tinea capitis)
Onycho-mycosis	❖ Fingernails or toenails appear thickened, yellow, degenerating	Clinical or KOH prep	PO itraconazole or fluconazole
Tinea versicolor	❖ Caused by *Pityrosporum ovale* ❖ Multiple sharply marginated hypopigmented macules on face & trunk noticed in summer because macules will not tan	KOH prep → yeast & hyphae with classic **spaghetti & meatball appearance**	Selenium sulfide shampoo daily on affected areas for 7d

Candida	❖ Erythematous scaling plaques, often in intertriginous areas (groin, breast, buttocks, web of hands) ❖ Oral thrush → cottage-cheese-like white plaques ❖ Dysphagia & odynophagia	KOH prep → budding yeast & pseudohyphae	Topical Nystatin or oral fluconazole

9 OPHTHALMOLOGY

EYES

CLASSIC SYNDROMES OR SYMPTOMS

1. Amblyopia
    a. Decreased vision secondary to failure of development of the pathway between the retina & visual cortex before age 7
    b. Usually affects one eye, can be secondary to cataract, severe refractive error, or strabismus
    c. Si/Sx = estropia (inwardly rotated "crossed eyes") or exotropia (outwardly rotated "walled eyes"), diplopia & refractive error not correctable with lenses
    d. Tx = early correction of cause of visual acuity disturbance
2. Bitemporal hemianopsia
    a. Unable to see in bilateral temporal fields
    b. Usually caused by a pituitary tumor
3. Internuclear ophthalmoplegia
    a. **Classically found in multiple sclerosis**
    b. Lesion of median longitudinal fasciculus (MLF)
    c. Si/Sx = inability to adduct the ipsilateral eye past midline on lateral gaze (inability to perform conjugate gaze)
    d. Caused by lack of communication between contralateral CN VI nucleus & the ipsilateral CN III nucleus
4. Parinaud's syndrome
    a. Midbrain tectum lesion → bilateral paralysis of upward gaze
    b. Commonly a/w pineal tumor
5. Marcus-Gunn pupil
    a. Due to afferent defect of CN II, pupil will not react to direct light but will react consensually when light is directed at the normal contralateral eye
    b. **Characterized by (+) swinging flashlight test**
        i. Swing penlight quickly back & forth between eyes
        ii. Denervated pupil will not constrict to direct stimulation & **instead will actually appear to dilate when light is shone in it** because it is dilating back to baseline when consensual light is removed form other eye
6. Argyll-Robertson pupil
    a. **Pathognomonic for 3^o syphilis (neurosyphilis)**
    b. Pupils constrict with accommodation but do not constrict to direct light stimulation (pupils accommodate but do not react)
7. Lens dislocation
    a. Occurs in homocystinuria, Marfan's & Alport's syndromes
    b. Lens **dislocates superiorly in Marfan's** (**mnemonic:** Marfan's patients are tall, their lenses dislocate upward), inferiorly in homocystinuria & variably in Alport's syndrome
8. Kayser-Fleischer ring
    a. **Pathognomonic for Wilson's disease**
    b. Finding is a ring of golden pigment around the iris
9. Pterygium
    a. Fleshy growth from conjunctiva onto nasal side of cornea
    b. a/w exposure to wind, sand, sun & dust
    c. Tx = cosmetic removal unless impairing vision
10. Pinguecula
    a. Benign yellowish nodules on either side of the cornea
    b. Commonly seen in patients >35
    c. Rarely grows & requires no treatment

11. Subconjunctival hemorrhage
    a. Spontaneous onset of a painless, bright red patch on sclera
    b. Benign, self-limited condition usually seen after overexertion
12. Retrobulbar neuritis
    a. Caused by inflammation of the optic nerve usually unilateral
    b. **Seen in multiple sclerosis, often is the initial sign**
    c. Si/Sx = rapid loss of vision & pain upon moving eye, spontaneously remitting within 2-8wk, each relapse damages the nerve more, until eventually blindness results
    d. Funduscopic exam is nonrevealing
    e. Tx = corticosteroids
13. Optic neuritis
    a. Inflammation of optic nerve within the eye
    b. Causes include viral infection, multiple sclerosis, vasculitis, methanol, meningitis, syphilis, tumor metastases
    c. Si/Sx = variable vision loss & ↓ pupillary light reflex
    d. **Funduscopic exam reveals disk hyperemia**
    e. If pt is >60yr, biopsy temporal artery to r/o temporal arteritis
    f. Tx = corticosteroids

PALPEBRAL INFLAMMATION

Disease	**Si/Sx**	**Tx**
Chalazion	❖ Inflammation of internal meibomian sebaceous gland ❖ Presents with swelling on conjunctival surface of eyelid	None, self-limiting
Hordeolum (stye)	❖ Infection of external sebaceous glands of Zeiss or Mol ❖ Presents with tender red swelling at lid margin	Hot compress, can add antibiotics
Blepharitis	❖ Inflammation of eyelids & eyelashes due to infection (*S. aureus*) or secondary to seborrhea ❖ Presents with red, swollen eyelid margins, with dry flakes noted on lashes ❖ **Without Tx can extend along eyelid (cellulitis)**	Wash lid margins daily with baby shampoo, control scalp seborrhea with shampoo
Orbital cellulitis	❖ Can occur if blepharitis is left untreated ❖ Also seen as compolication of paranasal sinus infection ❖ **Can spread to cavernous sinus leading to deadly thrombosis & meningitis**	Treat emergently with IV nafcillin or cephalosporin

RED EYE

1. **Assess pain, visual acuity, type of eye discharge, upillary abnormalities in all patients**
2. DDx

Disease	**Si/Sx**	**Cause**	**Tx**
Bacterial conjunctivitis	❖ Minimal pain, no vision changes ❖ **Purulent** discharge ❖ No pupillary changes ❖ **Rarely** preauricular adenopathy (only *N. gonorrhoeae*)	*S. pneumoniae, Staph. spp., N. gonorrhoeae, Chlamydia trachomatis* (in neonates, sexually active adults)	Topical sulfacetamide or erythromycin
Viral conjunctivitis	❖ Minimal pain, no vision changes ❖ **Watery** discharge	Adenovirus most common, others = HSV, Varicella,	No treatment required, self-

	❖ No pupillary changes ❖ **Often preauricular adenopathy** ❖ **Often pharyngitis** (adenovirus)	EBV, influenza, echovirus, coxsackie virus	limiting dz
Allergic conjunctivitis	❖ No pain, vision, or pupil changes ❖ **Marked pruritus** ❖ **Bilateral** watery eyes	Allergy/Hay fever	Antihistamine or steroid drops
Hyphema	❖ Pain, no vision changes ❖ No discharge, no pupil changes ❖ **Blood in anterior chamber of eye, fluid level noted**	Blunt ocular trauma	Eye patch to ↓ movement
Xerophthalmia	❖ Minimal pain, vision blurry, no pupillary changes, no discharge ❖ **Bitot's spots** visible on exam (desquamated, keratinized conjunctival cells) ❖ **Keratoconjunctivitis sicca** (Sjogren's disease) **Dx by Schirmer test** (place filter paper over eyelid, if not wet in 15min → Dx)	Sjogren's disease or vitamin A deficiency	Artificial tears, vitamin A
Corneal abrasiona	❖ **Painful, with photophobia** ❖ No pupil changes ❖ Watery discharge ❖ Dx by fluorescein stain to detect areas of corneal defect	Direct trauma to eye (finger, stick, etc.)	Antibiotis, eye patch, examine daily
Keratitis	❖ **Pain**, photophobia, tearing ❖ **Decreased vision** ❖ **Herpes shows classic dendritic branching on fluorescein stain** ❖ **Pus in anterior chamber (hypopyon) is a grave sign**	Adenovirus, HSV, *Pseudomonas, S. pneumoniae, Staph., Moraxella* (often in contact lesn wearers)	**Emergency, immediate Ophtho consult** Tx = topical vidarabine for herpes
Uveitis	❖ Inflammation of the iris, ciliary body, &/or choroid ❖ **Pain, miosis,** photophobia ❖ **Flare & cells** seen in aqueous humor **on slit lamp examination**	Seen in seronegative spondyloarthropathy, inflammatory bowel disease, sarcoidosis, or infxn (CMV, syphilis)	Tx underlying dz
Angle closure glaucoma	❖ **Severe pain** ❖ ¯ **vision**, halos around lights ❖ **Fixed mid-dilated pupil** ❖ eyeball firm to pressure	↓ aquesou humor outflow via canal of Schlemm—mydriatics can also cause	**Emergency,** IV mannitol & acetazolamide, laser iridotomy for cure

DACRYOCYSTITIS (TEAR CUDT INFLAMMATION)

1. Infection of lacrimal sac, usually caused by *Staphylococcus aureus, Streptococcus pneumoniae, Hemophilus influenzae, or S. pyogenes*
2. Si/Sx = inflammation & tenderness of nasal aspect of lower lid, purulent discharge may be noted or expressed
3. Tx = Keflex

EYE COLORS

1. **Yellow eye** (icterus) from bilirubin staining of sclera (jaundice)

2. **Yellow vision** seen in digoxin toxicity
3. **Blue sclera** classically found in osteogenesis imperfecta & Marfan's disease
4. **Opaque eye** due to cataract
    a. Opacity of lens severe enough to interfere with vision
    b. Causes = congenital, diabetes (sorbitol precipitation in lens), galactosemia (galactitol precipitation in lens), Hurler's disease

RETINA

1. Diabetic retinopathy
    a. Occurs after about 10yr of diabetes
        i. Background type
            1. Flame hemorrhages microaneurysms & soft exudates (cotton-wool spots) on retina
            2. Tx is strit glucose & hypertension control
        ii. Proliferative type
            1. More advanced dz, with neovascularization easily visible around fundus (hyperemia) & hard exudates
            2. Tx is photocoagulation (laser ablation of blood vessels in the retina) that slows disease progression but is not curative
2. Age-related macular degeneration (AMD)
    a. AMD causes painless loss of visual acuity
    b. Dx by altered pigmentation in macula
    c. Pts often retain adequate peripheral vision
    d. Tx = antioxidants and laser therapy
3. Retinal detachment
    a. Presents with painless, dark vitreaous floaters, flashes of light (photopsias), blurry vision, eventually progressing to a curtain of blindness in vision as detachment worsens
    b. Tx = urgent surgical reattachment
4. Retinitis pigmentosa
    a. Slowly progressive defect in night vision (often starts in young children) with ring-shaped scotoma (blind-spot) that gradually increases in size to obscure more vision
    b. Disease is hereditary with unclear transmission mode
    c. May be part of the Laurence-Moon-Biedl syndrome
    d. There is no treatment
5. Classic physical findings of retina
    a. **Leukocoria** = absent red reflex, actually appears white, seen in retinoblastoma
    b. **Roth spots** = small hemorrhagic spots with central clearing in retina a/w endocarditis
    c. **Copper wiring, flame hemorrhages A-V nicking** seen in subacute hypertension &/or atherosclerosis
    d. **Cotton-wool spots** (soft exudates) seen in chronic HTN
    e. Papilledema appears as disk hyperemia, blurring & elevation, a/w ↑ intracranial pressure
    f. "Sea fan" neovascularization in sickle cell anemia
    g. Wrinkles on retina seen in retinal detachment
    h. **Cherry-red spot on macula** seen in Tay-Sachs, Niemann-Pick disease, central retinal artery occlusion
    i. Hollenhorst plaque = yellow cholesterol emboli in retinal artery
    j. Brown macule on retina = malignant melanoma (most common intraocular tumor in adults).

10 RADIOLOGY

INTRODUCTION

This section will cover common causes for radiologic findings presented in the clinical vignettes on the USMLE as well as on rounds. Where useful, the causes will be divided into categories using the mnemonic **VINDICATE**

V = Vascular
I = Inflammatory/Infectious
N = Neoplastic
D = Degenerative
I = Idiopathic/Intoxication
C = Congenital
A = Autoimmune
T = Trauma
E = Endocrine

HELPFUL TERMS AND CONCEPTS

LUCENT vs. SCLEROTIC LESIONS

On plain film, a lucency is a focal area of bone or tissue that has a decreased density, usually resulting form a pathological process. A lucent bone lesion may appear like a dark, punched-out hole in the surrounding, normal bone. In contrast, sclerotic bone lesions appear denser than the surrounding bone. Thus, a sclerotic mass presents as whiter and more intense than its surroundings.

HYPODENSE vs. HYPERDENSE

Similar to that on plain films, tissue density on CT can be characterized by how light or dark it appears relative to surrounding, normal parenchyma. Hypodense lesions appear darker than normal tissue and hyperdense lesions are brighter. Air- or fluid-filled lesions such as cysts and abscesses are common hypodense lesions.

RING-ENHANCEMENT

This refers to a bright intensity that can be observed surrounding many lesions on both CT and MRI. This usually indicates local edema around a mass lesion and in the brain it can indicate breakdown of the blood-brain barrier.

RADIOPAQUE

The more radiopaque an object is, the brighter it appears on plain film. Dental fillings, bullets, and metal prostheses are very radiopaque so they appear white on plain film.

RADIOLUCENT

The more radiolucent an object is, the darker it appears on plain film.

COMMON RADIOLOGIC STUDIES

Study	**Indications**
CT vs. MRI	CT → faster, less expensive, greater sensitivity for acute head trauma, better for detection of spinal cord compression MRI → better visualization of soft tissue, allows multiplanar imaging (axial, coronal, sagittal & obliques), no ionizing radiation

Endoscopic retrograde cholangiopancreatography (ERCP)	Pancreatitis 2^{o} to choledocholithiasis, cholestatic jaundice
Ultrasound (Utz)	Abdominal aortic aneurysm, gallbladder disease, renal & adrenal masses, ectopic pregnancy, kidney stones
Carotid Doppler Utz	Carotid artery stenosis, assessing flow dynamics
Intravenous pyelogram (IVP)	GU obstruction
Kidney, ureter, bladder (KUB) x-ray	Kidney stones, solid abdominal masses, abdominal free air
Lateral decubitus chest plain film	To determine whether a suspected pleural effusion will layer

Note 80/20 rule: gallstones diagnosed 80% of the time & kidney stones 20% of the time by Utz. Kidney stones diagnosed 80% of the time & gallstones only 20% of the time by x-ray.

AN APPROACH TO A CHEST X-RAY

A = **A**irway—is trachea midline? & **A**lignment—symmetry of clavicles
B = **B**ones—look for fractures, lytic lesions, or defects
C = **C**ardiac silhouette—normally occupies < ½ chest width
D = **D**iaphragms—flattened (e.g., COPD)?, blunted angles (effusion)?, elevated (airspace consolidation)?
E = **E**xternal soft tissues—lymph nodes (especially axilla), subQ emphysema, other lesions
F = **F**ields of the lung—opacities, nodules, vascularity, bronchial cuffing, etc.

COMMON RADIOLOGIC FINDINGS

Finding/description	**Differential Diagnosis**	
Hair-on-end skull sign on plain film Caused by new bone formation that occurs perpendicular to the skull table, resulting in a thin, spiked appearance, as if bony hairs growing out of skull	Congenital Sickle cell anemia Osteosarcoma	
Hypodense cerebral masses on CT	**Neoplastic:** Glioma Prolactinoma Craniopharyngiomas	**Infectious:** Pyogenic abscess Tuberculoma Hydatid cyst
Multiple contrast-enhancing lesions on CT or MRI	**Neoplastic:** Metastases Breast CA & bronchogenic lung CA most common Also malignant melanoma, prostate, lymphoma	**Infectious:** Bacterial abscess Toxoplasmosis Cysticercosis **Vascular**: Infarct **Degenerative:** Demyelinating disease
Nonsclerotic skull lucency	**Infectious:** TB Syphilis Osteomyelitis **Neoplastic** Multiple myeloma	**Trauma** Burr hole **Endocrine** Hyperparathyroidism

	Metastases	
Sclerotic bone lesions	**Infectious:** Osteomyelitis (presents with periosteal reaction) Syphilis **Congenital:** Fibrous dysplasia Tubersou sclerosis **Vascular:** Helaing fracture callus	**Noeplastic:** Metastases—primarily prostate & breast Lymphoma Multiple myeloma—usually presents with multiple lesions Osteosarcoma
"Bone within bone" sign	**Endocrine:** Growth arrest & recovery Paget's disease Osteopetrosis	**Intoxication** Heavy metal poisoning
Inferior surface rib notching	**Vascular:** Coarctation of the aorta—classic finding Superior vena cava obstruction	**Congenital:** Chest wall A-V malformation
Ivory vertebral body Sclerotic change in a single vertebra	**Neoplastic:** Sclerotic metastases Lymphoma	**Endocrine:** Paget's disease
Honeycomb lung Fibrotic replacement of lung parenchyma with thick-walled cysts	**Idiopathic:** Idiopathic interstitial fibrosis Histiocytosis X Sarcoidosis **Congenital:** Cystic fibrosis Tuberous sclerosis Neurofibromatosis	**Autoimmune:** Scleroderma Rheumatoid arthritis **Intoxication:** Allergic alveolitis Asbestosis Bleomycin Nitrofurantoin Cyclophosphamide
Ground glass opacities on lung CT Hazy, granular increase in density of lung parenchyma that usually implies an acute inflammatory process	**Inflammation:** Interstitial pneumonia Hypersensitivity pneumonitis *Pneumocystic carinii* pneumonia Alveolar proteinosis	
Water-bottle-shaped heart on PA plain film	Pericardial effusions with more than 250mL of fluid	
Pulmonary edema Classically, severe pulmonary edema appears as a **bat's wing shadow**	**Vascular:** CHF **Inflammatory**: ARDS Mendelson's syndrome	**Intoxication:** Smoke inhalation **Trauma:** Near drowning
Blunting of costophrenic angles 300-500mL of fluid is needed before blunting of the lateral costophrenic angles becomes apparent	Pleural effusion	
Kerley B lines	**Vascular:**	**Inflammatory:**

Interlobar septa on the peripheral aspects of the lungs that become thickened by disease or fluid accumulation	Left ventricular failure Lymphatic obstruction	Sarcoidosis lymphangitis carcinomatosa
Multiple lung small soft tissue Densities <2mm	**Inflammatory** Sarcoidosis Military TB Fungal infection Parasites Extrinsic allergic alveolitis	**Neoplastic:** Metastases **Endocrine:** Hemosiderosis
Lung nodules >2cm Ghon complex—calcified granuloma classic for TB, found at lung base along hilum	**Neoplastic:** Metastases Primary lung CA Benign hamartoma **Intoxication:** Silicosis **Idiopathic:** Histiocytosis X	**Inflammatory**: Sarcoidosis TB Wegener's Fungal infections Abscess
Hilar adenopathy	**Inflammatory:** Sarcoidosis (bilateral, eggshell calcification) Amyloidosis **Intoxication:** Silicosis	**Neoplastic:** Bronchogenic CA (unilateral) Lymphoma
Ring shadow Annular opacity with central lucency	**Infectious:** TB (apex) Lung abscess Fungal Amebiasis	**Neoplastic:** Bronchogenic carcinoma Metastases Lymphoma **Autoimmune:** Rheumatoid lung dz
Unilaterally elevated diaphragm	**Trauma:** Phrenic nerve palsy **Congenital:** Pulmonary hypoplasia scoliosis	**Vascular:** Pulmonary embolism
Bilaterally elevated diaphragm	Obesity Pregnancy Fibrotic lung dz	
Steeple sign Narrowed area of subglottic trachea	Parainfluenza virus (croup)	
Thumb sign	Epiglottitis classically caused by *Haemophilus influenzae*	
Pneumoperitoneum Free air under the diaphragm on an upright chest film or upright abdomen Double wall sign on abdominal plain film The appearance of the outer & inner walls of bowel is almost	**Inflammatory**: Perforation Ulcer Diverticulitis Appendicitis Toxic megacolon Infracted bowel	Also can be: Peritoneal dialysis Pneumomediastinum that has tracked inferiorly Diaphragmatic rupture

pathognomonic for pneumoperitoneum		
Gasless abdomen on abdominal plain film	Obstruction Severe ascites Pancreatitis	
Filling defects in stomach on upper GI series	Gastric ulcer Gastric cancer	
Dilated small bowel	**Mechanical obstruction** Postsurgical Incarcerated hernia Intussusception	Paralytic ileus **Inflammatory:** Celiac sprue Scleroderma
Coffee bean sigmoid volvulus	Large bowel obstruction Paralytic ileus	
String sign on barium swallow Narrowing of the terminal ileum caused by thickening of the bowel wall	Crohn's disease	
Lead pipe sign on barium enema Smooth, narrowed colon without haustra	Inflammatory bowel dz	
Apple core lesion Circumferential growth in the bowel lumen	Colon cancer	
Liver calcifications	**Inflammatory:** Granuloma Hydatid cyst	**Neoplastic:** Hepatoma
Gas in portal vein Linear lucencies that reach within 2cm of liver capsule	**Vascular (seen in adults**): Mesenteric infarct Air embolism	**Inflammatory (children):** Necrotizing enteroclitis
Unilateral cystic renal mass Hypodensities with thin walls	**Inflammatory:** Renal abscess Hemodialysis-induced cyst Hydatid cyst	**Congenital:** Bilateral renal cysts Polycystic kidney dz Neoplastic: Renal cell carcinoma
String of beads on renal arteiogram Multiple dilatations alternating with strictures of both renal arteries	Fibromuscular dysplasia	

BOARDS & WARDS APPENDICES

ZEBRAS AND SYNDROMES

Disease	Description/Sx
Achondroplasia	Autosomal dominant dwarfism due to early epiphyseal closure → shortening & thickening of bones. Si/Sx = leg bowing, hearing loss, sciatica, infantile hydrocephalus. Patients can live normal lifespans.
Adrenoleukodystrophy	X-linked recessive defect in long-chain fatty acid metabolism due to a peroxisomal enzyme deficiency. Causes rapidly progressing central demyelination, adrenal insufficiency, hyperpigmentation of skin, spasticity, seizures & death by age 12
Albers-Schonberg disease (osteopetrosis)	↑↑ Skeletal density due to osteoclastic failure → multiple fractures due to ↓ perfusion of thick bone, also causes anemia due to ↓ marrow space & blindness, deafness & cranial nerve dysfunction due to narrowing & impingement of neural foramina.
Alkaptonuria	Defect of phenylalanine metabolism causing accumulation of homogentisic acid. Presents with black urine, ochronosis (blue-black pigmentation of ear, nose, and cheeks) & arthropathy due to cartilage binding homogentisic acid.
Alport's syndrome	X-linked hereditary collagen defect causing sensorineural hearing loss, lens dislocation, hematuria (glomerulonephritis).
Ataxia-Telangiectasia	DNA repair defect affects B & T lymphocytes. Autosomal recessive disease usually appears by age 2. physical signs include ataxia of gait, telangiectasias of skin & conjuctiva, & recurrent sinus infections.
Banti's syndrome	"Idiopathic portal HTN." Splenomegaly & portal HTN following subclinical portal vein occlusion. Insidious onset, occurring years after initial occlusive event
Bartter's syndrome	Kidney disease that causes Na, K & Cl wasting. Despite increased levels of renin, the blood pressure remains low.
Beckwith-Wiedemann syndrome	Autosomal dominant fetal overgrowth syndrome of macrosomia, microcephaly, macroglossia, organomegaly, omphalocele, distinctive lateral earlobe fissures, hypoglycemia a/w hyperinsulinemia, ↑ incidence of Wilms' tumor.
Bernard-Soulier syndrome	Autosomal recessive defect of platelet GpIb receptor (binds to vWF), presents with chronic, severe mucosal bleeds & giant platelets on blood smear
Binswanger's disease	Subacute subcortical dementia caused by small artery infarcts in periventricular white matter. Usually seen in long-standing hypertension, but is rare.
Bruton's agammaglobulinemia	X-linked block of B-cell maturation, causing ↓ B cell levels & immunoglobulin levels. Presents with recurrent bacterial infections in infants >6mo of age
Caisson's disease	Decompression sickness ("the bends") caused by rapid ascent from deep-se diving. Sx occur from 30min to 1hr = joint pain, cough, skin burning/mottling.
Caroli's disease	Segmental cystic dilation of intrahepatic bile ducts complicated by stones & cholangitis, can be cancer precursor.
Charcot-Marie-Tooth disease	Autosomal dominant peroneal muscular atrophy causing foot drop & stocking-glove decrease in vibration/pain/temperature sense & DTRs in lower extremities. Histologically → repeated demyelination & remyelination of segmental areas of the nerve. Patients may present as children (type 1) or adults (type 2)
Chediak-Higashi syndrome	Autosomal recessive defect of microtubule function of neutrophils, leads to decreased lysosomal fusion to phagosomes. Presents with recurrent *Staphylococcus* & *Streptococcus* infections, albinism, peripheral & cranial

	neuropathies.
Cheyne-Stokes respirations	A central apnea seen in CHR, ↑ ICP, or cerebral infection/inflammation/trauma: cycles of central apena followed by regular crescendo-decrescendo breathing (amplitude first waxes & then wanes back to apnea): Biot's is an uncommon variant seen in meningitis in which the cycles consist of central apnea followed by steady amplitude breathing that then shuts back off to apnea.
Chronic granulomatous disease	Phagocytes lack respiratory burst or NADPH oxidase, so can engulf bacteria but are unable to kill them. Presents with recurrent infections with *Aspergillus & S. aureus* infections. Tx = recombinant interferon-γ.
Cystinuria	Autosomal recessive failure of tubular resorption of cystine & dibasic amino acids (lysine, ornithine, arginine), clinically see cystine stones. Tx = hydration to ↑ urine volume, alkalinizaiton of urine with bicarbonate & acetazolamide
De Quervain's tenosynovitis	Tenosynovitis causing pain on flexion of thumb (motion of abductor pollicis longus).
Diamond-Blackfan syndrome	"Pure red cell aplasia," a congenital or acquired deficiency in the RBC stem cell. Congenital disorder is sometimes a/w abnormal facies, cardiac & renal abnormalities. Tx = steroids.
DiGeorge's syndrome	Embryologic defect in development of pharyngeal pouches 3 & 4 → thymic aplasia that causes T-cell deficiency, & parathyroid aplasia. Most commonly presents with tetany due to hypocalcemia secondary to hypoparathyrdoiism, & recurrent severe viral, fungal, or protozoal infections.
Dressler's syndrome	Acute pericarditis, develops within 2-4wk after acute MI or heart surgery, may be due to autoimmune reaction to myocardial antigens.
Ehlers-Danlos syndrome	Autosomal dominant defect in collagen synthesis, variable expressivity. Si/Sx = loose joints, pathognomonic ↓ skin elasticity, mitral regurgitation, genu recurvatum of knee (fixed in hyperextension), aortic dilation.
Ehrlichiosis	Rickettsial family member, *Ehrlichiosis canis*, causes acute febrile illness, malaise, myalgia, severe headache but with no rash. The protracted illness presents with leukopenia, thrombocytopenia & renal failure. It is contracted by tick bites.
Ellis-van Creveld	Syndrome of polydactyly + single atrium
Erb's paralysis	Waiter's tip—upper brachial plexopathy (C5,6).
Evan's syndrome	IgG autoantibody-mediated hemolytic anemia & thrombocytopenia, a/w collagen-vascular dz, TTP, hepatic cirrhosis, leukemia, sarcoidosis, Hashimoto's thyroiditis. Tx = prednisone & intravenous immunoglobulin.
Fabry's disease	X-linked defect in galactosidase, Sx = lower trunk sin lesions, corneal opacity, renal/cardiac/cerebral disease that are invariably lethal in infancy or childhood
Fanconi's anemia	Autosomal recessive disorder of DNA repair. Presents with pancytopenia, ↑ risk of malignancy, short stature, bird-like facies, café-au-lait spots, congenital urogenital defects, retardation, absent thumb.
Fanconi's syndrome	Dysfunction of proximal renal tubules, congenital or acquired (drugs, multiple myeloma, toxic metals), presenting with ↓ reabsorption of glucose, amino acids, phosphate, & bicarbonate. A/w RTA type II, clinically see glycosuria, hyperphosphaturia, hypophosphatemia (vitamin D-resistant rickets), aminoaciduria (generalized, not cystine specific), systemic acidosis, polyuria, polydipsia.
Farber's disease	Auto recessive defect in ceramidase, causing ceramide accumulation in nerves, onset within months of birth, death occurs by age 2.
Felty's syndrome	Rheumatoid arthritis plus splenomegaly & neutropenia, often with

	thrombocytopenia.
Fibrolamellar carcinoma	Variant of hepatocellular carcinoma. Occur sin young people (20-40yr), is not a/w viral hepatitis or cirrhosis. Has a good Px. Histologically shows nests & cords of malignant hepatocytes separated by dense collagen bundles.
Fitz-Hugh-Curtis syndrome	Chlamydia or gonorrhea perihepatitis as a complication of pelvic inflammatory disease. Presents with right upper quadrant pain & sepsis.
Galactosemia	Deficient galactose-1-phosphate uridyl transferase blocks galactose conversion to glucose for further metabolism, leading to accumulation of galactose in many tissues. Sx = failure to thrive, infantile cataracts, mental retardation, cirrhosis. Rarely due to galactokinase deficiency, blocking the same path at a different step.
Gardner's syndrome	Familial polyposis syndrome with classic triad of desmoid tumors, osteomas of mandible or skull & sebaceous cysts.
Gaucher's disease	The most frequent cause of lysosomal enzyme deficiency in Ashkenazi Jews. Autosomal recessive deficiency in β-glucocerebrosidase. Accumulation of sphingolipids in liver, spleen & bone marrow. Can be fatal if very expensive enzyme substitute (alglucerase) not administered.
Glanzmann's thrombasthenia	Autosomal recessive defect in GpIIbIIIa platelet receptor that binds fibrinogen, inhibiting platelet aggregation, presents with chronic, severe mucosal bleeds.
Glycogenoses	Genetic defects in metabolic enzymes causing glycogen accumulation. Si/Sx = hepatosplenomegaly, general organomegaly, exertional fatigue, hypoglycemia. Type I = von Gierke's disease, type II = Pompe's disease, type III = Cori's disease, type V = McCardle's disease
Hartnup's disease	Autosomal recessive defect in tryptophan absorption at renal tubule. Sx mimic pellagra = the 3 D's: Dermatitis, Dementia, Diarrhea (tryptophan is niacin precursor). Rash is on sun-exposed areas, can see cerebellar ataxia, mental retardation & psychosis. Tx = niacin supplements.
Hepatorenal syndrome	Renal failure without intrinsic renal dz, occurring during fulminant hepatitis or cirrhosis, presents with acute oliguria & azotemia, typically progressive & fatal.
Holt-Oram syndrome	Autosomal dominant atrial septal defect in association with finger-like thumb or absent thumb, & cardiac conduction abnormalities & other skeletal defects
Homocystinuria	Deficiency in cystine metabolism. Sx mimic Marfan's = lens dislocation (downward in homocystinuria as opposed to upward in Marfan's), thin bones, mental retardation, hypercoagulability & premature atherosclerosis → strokes & MIs
Hunter's disease	X-linked lysosomal iduronidase deficiency, less severe than Hurler's syndrome. Sx = mild mental retardation, cardiac problems, micrognathia, etc.
Hurler's disease	Defect in iduronidase, causing multiorgan mucopolysaccharide accumulation, dwarfism, hepatosplenomegaly, corneal clouding, progressive mental retardation & death by age 10.
Isovalinic academia	"Sweaty-foot odor" disease. Caused by a defect in Leucine metabolism, leads to buildup of isovaline in the bloodstream, producing characteristic odor.
Job's syndrome	B-cell defect causing hyper-IgE levels but defects in other immunoglobulin & immune functions. Presents with recurrent pulmonary infections, dermatitis, excess teeth (pts unable to shed their baby teeth), frequent bone fractures, classic "gargoyle facies," IgE levels 10- to 100-fold higher than normal
Kasabach-Merritt	An expanding hemangioma trapping platelets, leading to systemic thrombocytopenia
Keshan's disease	Childhood cardiomyopathy 2^{o} to selenium deficiency, very common in China.
Klippel-Trenaunay-	Autosomal dominant chromosomal translocation → prematurity, hydrops fetalis,

Weber syndrome	Hypertrophic hemangioma of leg & Kasabach-Merritt thrombocytopenia.
Klumpke's paralysis	Clawed-hand-lower brachial-plexopathy (C8, T1) affecting ulnar nerve distributions, often presents with Horner's syndrome as well
Leigh's disease	Mitochondrially inherited dz → absent or ↓↓ thiamine pyrophosphate. Infants or children present with seizures, ataxia, optic atrophy, ophthalmoplegia, tremor.
Lesch-Nyhan syndrome	Congenital defect in HPRT → gout, urate nephrolithiasis, retardation, choreiform spasticity & self-mutilation (patients bite off their own fingers & lips). Mild deficiency → Kelley-Seegmiller syndrome = gout without nervous system Si/Sx
Leukocyte adhesion deficiency	Type I due to lack of β_2-integrins (LFA-1), type II due to lack of fucosylated glycoprotein (selectin receptors). Both have plenty of neutrophils in blood but can't enter tissues due to problems with adhesion & transmigration. Both present with recurrent bacterial infections, **gingivitis, poor wound healing & delayed umbilical cord separation**
Lhermitte sign	Tingling down the back during neck flexion, occurs in any craniocervical disorder
Liddle's disease	Disease mimics hyperaldosteronism. Defect is in the renal epithelial transporters. Si/Sx = HTN, hypokalemic metabolic alkalosis.
Li-Fraumeni's syndrome	Autosomal dominant inherited defect of p53 leading to primary cancers of a variety of organ systems presenting at an early age.
Maple syrup urine disease	Disorder of branched chain amino acid metabolism (Valine, Leucine, Isoleucine). Sx include vomiting, acidosis & pathognomonic maple-like odor of urine.
Marchiafava-Bignami syndrome	Overconsumption of red wine → demyelination of corpus callosum, anterior commissure & middle cerebellar peduncles. Possible anoxic/ischemic phenomenon
Marfan's disease	Genetic collage defect → tall, thin body habitus, long & slender digits, pectus excavatum, scoliosis, aortic valve dilation → regurgitation, aortic dissection, mitral valve prolapse, joint laxity, optic lens dislocations & blue sclera.
Melanosis coli	Overzealous use of laxatives cuasing darkening of colon, but no significant dz
Mendelson's syndrome	Chemical pneumonitis following aspiration of acidic gastric juice, patient presents with acute dyspnea, tachypnea & tachycardia, with pink & frothy sputum.
Meralgia paresthetica	A condition common to truckers, hikers & overweight individuals who wear heavy backpacks or very tight-fitting belts compressing inguinal area. This causes patients to have a diffuse unilateral pain & paresthesias along anterior portion of upper thigh, corresponding to lateral femoral cutaneous nerve. Typically self-limiting, but can treat with steroids for refractory disease
Minamata disease	Toxic encephalopathy from mercury poisoning, classically described from fish eaten near Japanese mercury dumping site.
Molluscum contagiosum	Poxvirus skin infection causing umbilicated papules, transmitted by direct contact, often venereal. The central umbilication is filled with semi-solid white material that contains inclusion bodies & is highly characteristic for the disease
Monckeberg's arteriosclerosis	Calcific sclerosis of the media of medium-sized arteries, usually radial & ulnar. Occurs in people over 50, but it does NOT obstruct arterial flow since intima is not involved. It is unrelated to other atherosclerosis & does not cause dz.
Muchausen's syndrome	A factitious disorder in which the pt derives gratification form feigning a serious or dramatic illness. Munchausen's by proxy is when the pt derives gratification from making someone else ill (often a mother injures her child for attention).

Niemann-Pick's disease	Autosomal recessive defect in sphingomyelinase with variable age onset (↑ severe dz in younger pt) → demyelination/neurologic Sx, hepatosplenomegaly, xanthoma, pancytopenia.
Noonan's syndrome	Autosomal dominant with Sx similar to Turner's syndrome → hyperelastic skin, neck webbing, ptosis, low-set ears, short stature, pulmonary stenosis, AS defect coarctation of aorta, small testes. Presents in males, X & Y are both present.
Ortner's syndrome	Impingement of recurrent laryngeal nerve by the enlarging atrium in mitral regurgitation, leading to hoarseness.
Osteogenesis imperfecta	Genetic disorder of diffuse bone weakness due to mutations resulting in defective collagen synthesis. Multiple fractures 2^o to minimal trauma = brittle bone disease. Classic sign = blue sclera, due to translucent connective tissue over choroid.
Peliosis hepatic	Rare primary dilation of hepatic sinusoids. A/w exposure to anabolic steroids, oral contraceptives & danazol. Irregular cystic spaces filled with blood develop in the liver. Cessation of drug intake causes reversal of the lesions.
Plummer-Vinson syndrome	Iron deficiency syndrome with classic triad of esophageal web, spoon nail & iron deficiency anemia. Web produce dysphagia, will regress with iron replacement.
Polycystic kidney disease	Autosomal dominant bilateral dz, Si/Sx = onset in early or middle adult life with hematuria, nephrolithiasis, uremia, 33% of cases have cysts in liver, 10-20% of cases have intracranial aneurysms, hypertension is present in 50% of pts at Dx. Juvenile version is autosomal recessive, much rarer than adult type; almost all cases have cysts in liver & portal bile duct proliferation = "congenital hepatic fibrosis."
Poncet's disease	Polyarthritis that occurs DURING active TB infection but no organisms can be isolated from the affected joints, is thought to b autoimmune-mediated disease
Pott's disease	Tubercular infection of vertebrae (vertebral osteomyelitis) leading to kyphoscoliosis secondary to pathologic fractures.
Prinzmeteal's angina	Variant angina occurring at rest due to vasospasm, EKG → ST elevation instead of depression, Tx = calcium channel blockers.
Refsum's disease	Autosomal recessive defect in phytanic acid metabolism → peripheral neuropathy, cerebellar ataxia, retinitis pigmentosa, bone disease & ichthyosis (scaly skin).
Rett's syndrome	Congenital retardation secondary to ↑ serum ammonia levels, more common in females. Sx = autism, dementia, ataxia, tremors.
Schafer's disease	Effect in hexosaminidase B, in contrast to the A component of the enzyme that is defective in Tay-Sachs. Px is better for Schafer's.
Schindler's disease	Defect in N-acetylgalactosaminidase.
Schmidt's syndrome	Hashimoto's thyroiditis with diabetes &/or Addison's disease (autoimmune syndrome)
Sweet's syndrome	Recurrent painful reddish-purple plaques & papules a/w fever, arthralgia & neutrophilia. Occurs more commonly in women, possibly due to hypersensitivity reaction a/w Yersinia infection. Can also be seen in following URI or along with leukemia. Tx = prednisone, antibiotics if a/w yersinia infection.
Syndrome X	Angina relieved by rest (typical) with a normal angiogram. Caused by vasospasm of small arterioles, unlike Prinzmetal's angina, which is vasospasm of large arteries.
Tay-Sachs disease	Autosomal recessive defect in hexosaminidase A, causing very early onset, progressive retardation, paralysis, dementia, blindness, cherry-red spot on

	macula & death by 3-4yr. Common in Ashkenazi Jews.
Tropical spastic paraparesis	Insidious lower extremity paresis caused by HTLV, which is endemic to Japan & the Caribbean, transmitted like HIV, via placenta, body fluids & sex. Presents with mild sensory deficits, marked lower extremity hyperreflexia, paralysis, urinary incontinence.
Turcot's syndrome	Familial adenomatous polyposis with CNS medulloblastoma or glioma
Usher syndrome	Most common condition involving both hearing & vision impairment. Autosomal recessive dz → deafness & retinitis pigmentosa (a form of night blindness)
Verner-Morrison syndrome	VIPoma = vasoactive intestinal polypeptide overproduction. Leads to pancreatic cholera, increased watery diarrhea, dehydration, hypokalemia, hypo/achlorhydria.
Von Recklinghausen's disease	Diffuse osteolytic lesions caused by hyperparathyroidism causing characteristic "brown tumor" of bone due to hemorrhage. Can mimic osteoporosis on x-rays
Wiskott-Aldrich syndrome	X-linked recessive defect in IgM response to capsular polysaccharides like those of *S. pneumoniae*, but pts have ↑ IgA levels. Classic triad = recurrent pyogenic bacteria infections, eczema, thrombocytopenia. Bloody diarrhea is often first Sx, then URIs; leukemia & lymphoma are common in children who survive to age 10.
Xeroderma pigmentosa	Defect in reparif of DNA damage caused by UV light (pyrimidine dimmers). Patients highly likely to develop skin cancers. Only Tx is avoidance of sunlight.

TOXICOLOGY

Toxin	**Si/Sx**	**Dx**	**Antidote**
Acetaminophen	N/V within 2hr, ↑ liver enzymes, ↑ prothrombin time at 24-48hr	Blood level	N-acetylcysteine within 8-10hr
Alkali agents	Derived from batteries, dishwasher detergent, drain cleaners, ingestion causes mucosal burns → dysphagia & drooling	Clinical	Milk or water, then NPO
Anticholinergic	**Dry as a bone, mad as a hatter, blind as a bat, hot as a hare** (delirium, miosis, fever)	Clinical	physostigmine
Arsenic	**Mees lines** (white horizontal stripes on fingernails), capillary leak, seizures	Blood level	Gastric lavage & dimercaprol
Aspirin	Tinnitus, respiratory alkalosis, **anion gap metabolic acidosis with normal S_{osm}**	Blood level	Bicarbonate, dialysis
Benzodiazepine	Rapid onset of weakness, ataxia, drowsiness	Blood level	Flumazenil
β-blockers	Bradycardia, heart block, obtundaiton, **hyperkalemia, hypoglycemia**	Clinical	Glucagon, IV calcium
Carbon monoxide	Dyspnea, confusion, coma, **cherry-red color of skin**, mucosal cyanosis	Carboxy-Hgb	100% O2 or hyperbaric O2
Cyanide	In seconds to minutes → trismus, **almond-scented breath**, coma	Blood level	Amyl nitrite (+) Na thiosulfate
Digoxin	**Change in color vision, supraventricular tachycardia with heart block**, vomiting	Blood level	Anti-digoxin Fab-antibodies
Ethylene glycol	**Calcium oxalate crystals in urine, anion gap metabolic acidosis with high S_{osm}**	Blood level	Ethanol drip, fomepizole
Heparin	Bleeding, thrombocytopenia	Clinical	Protamine

Iron	Vomiting, bloody diarrhea, acidosis, CXR → radiopaque tablets	Blood level	Deferoxamine
Isoniazid	Confusion, peripheral neuropathy	Blood level	Pyridoxine
Lead	**Microcytic anemia with basophilic stippling**, ataxia, retardation, peripheral neuropathy, **purple lines on gums**	Blood level	EDTA, penicillamine
Mercury	**"Erethism" = ¯ memory, insomnia, timidity, delirium (mad as a hatter)**	Blood level	Ipecac, dimercaprol
Methanol	**Anion gap metabolic acidosis with high S_{osm},** blindness, **optic disk hyperemia**	Blood level	Ethanol drip, bicarbonate
Opioids	CNS/respiratory depression, miosis	Blood level	Narcan
Organophosphate	Incontinence, cough, wheezing, dyspnea, miosis, bradycardia, heart block, tremor	Blood level	Atropine, pralidoxime
Phenobarbital	CNS depression, hypothermia, miosis, hypotensions	Blood level	Charcoal, bicarbonate
Quinidine	Torsades des pointes (ventricular tachycardia)	Blood level	IV magnesium
Theophylline	First Sx = hematemesis, then CNS → seizures or coma, cardiac → arrhythmias, hypotension	Blood level	Ipecac, charcoal, cardiac monitor
Tricyclics	Anticholinergic Sx, QRS > 100ms, torsades des pointes	Blood level	Bicarbonate drip
Warfarin	Bleeding	↑ PT	Vitamin K

VITAMINS AND NUTRITION

Nutrient	**Deficiency**	**Excess**
B_1 (thiamine)	Dry beriberi → neuropathy Wet beriberi → high-output cardiac failure Either → Wernicke-Korsakoff's syndrome	
B_2 (riboflavin)	Cheilosis (mouth fissures)	
B_3 (niacin)	Pellagra → dementia, diarrhea, dermatitis Also seen in Hartnup's disease (dz of tryptophan metabolism)	
B_5 (pantothenate)	Enteritis, dermatitis	
B_6 (pyridoxine)	Neuropathy (frequently caused by isoniazid therapy for TB)	
B_{12} (cyanocobalamin)	Pernicious anemia (lack of intrinsic factor) → neuropathy, megaloblastic anemia, glossitis	
Biotin	Dermatitis, enteritis (caused by ↑ consumption of raw eggs, due to the avidin in the raw eggs blocking biotin absorption)	
Chromium	Glucose intolerance (cofactor for insulin)	
Copper	Leukopenia, bone demineralization	
Folic acid	Neural tube defects, megaloblastic anemia	
Iodine	Hypothyroidism, cretinism, goiter	
Iron	Plummer-Vinson syndrome = esophageal webs, spoon nails	Hemochromatosis → multiorgan failure (bronze diabetes)
Selenium	Myopathy (Keshan's disease)	
Vitamin A	Metaplasia of respiratory epithelia (seen in cystic fibrosis due to failure of fat-soluble vitamin absorption), xerophthalmia, night blindness (lack of retinal in rod cells),	Pseudotumor cerebri (can be caused by consuming polar bear

	acne, Bitot's spots, frequent respiratory infections (respiratory epithelial defects)	livers), headache, nausea, vomiting, skin peeling
Vitamin C	Scurvy: poor healing, Hypertrophic bleeding gums, easy bruising, deficient osteoid mimicking rickets	
Vitamin D	Rickets in kids, osteomalacia in adults	Kidney stones, dementia, constipation, abdominal pain, depression
Vitamin E	Fragile RBCs, sensory & motor peripheral neuropathy	
Vitamin K	Clotting deficiency	
Zinc	Poor wound healing, decreased taste & smell, alopecia, diarrhea, dermatitis, depression (similar to pellagra)	
Calories	**Marasmus** = total calorie malnutrition → pts look deceptively well, but immunosuppressed, poor wound healing, impaired growth	
Protein	**Kwashiorkor** = protein malnutrition → edema/ascites, immunosuppression, poor wound healing, impaired growth & development	