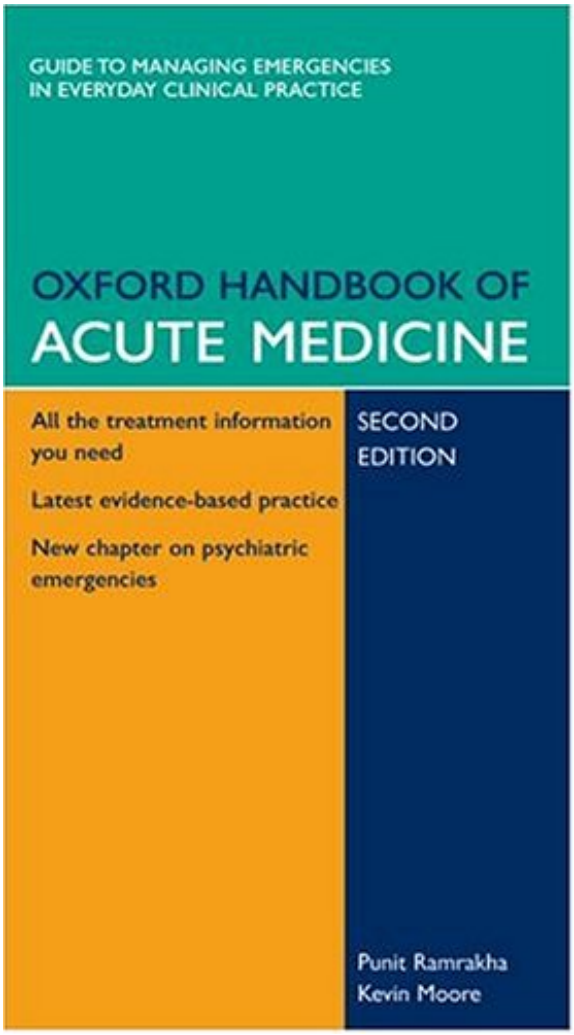
GUIDE TO MANAGING EMERGENCIES
IN EVERYDAY CLINICAL PRACTICE
OXFORD HANDBOOK OF
ACUTE MEDICINE
All the treatment information you need
Latest evidence-based practice
New chapter on psychiatric emergencies
SECOND EDITION
Punit Ramrakha
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Editors: Ramrakha, Punit S.; Moore, Kevin P.
Title: *Oxford Handbook of Acute Medicine, 2nd Edition*

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Preface to the second edition

There has been a rapid expansion and change of clinical practice over the last 5â€“6 years, and the need for a detailed handbook that educates, reassures, and helps in the management of acutely ill people has not diminished. The task of updating the text for this new edition would not have been possible without the help of colleagues and specialists who have taken the time to read, advise and in some cases revise large sections of this book to ensure that it is in line with modern management. We thank them most sincerely.

The most obvious changes include a new chapter on psychiatric emergencies, initially drafted by Dr Ed Beveridge. Managing patients who are confused or psychiatrically disturbed is frightening to many junior doctors, and this chapter includes straightforward advice on management, the law and the restraint of patients. Although no chapter has escaped revision, we have radically revised the chapters on cardiac emergencies, HIV disease and infectious diseases. We have added a new section of colour Plates showing eye and skin conditions. The text now incorporates all the major advances in medical care since the first edition was published, and we hope that readers will continue find this book useful and informative.

P S R

K P M

June 2004

Editors: Ramrakha, Punit S.; Moore, Kevin P.
Title: *Oxford Handbook of Acute Medicine, 2nd Edition*

Foreword to the first edition by Professor John Ledingham

A professor of medicine at Edinburgh in the more leisurely days of 1862 taught that an acute illness was â€˜one that ran its course in 14 daysâ€™. A student courageously inclined to dispute this definition retorted that an omnibus ran from Edinburgh to Leith in 20 minutes, but that was not a definition of an omnibus. Acute in the context of this book suggests rather more urgency than was the concept in 1862! There is a need for junior doctors (and senior ones too) to have at their finger tips the essentials of management of all acute emergencies. This book will surely be a great help in achieving that aim. The authors have succeeded in producing an admirably succint and yet comprehensive account of the management of a huge variety of conditions requiring urgent treatment and have done so without being too tiresomely didactic.

Handbooks in the series from Oxford University Press are already in the pockets of most clinical students all over the world. This one is sure to be there too and will, I suspect, also be in the pockets of junior doctors and even (perhaps covertly) readily available to more senior physicians. Such a practical book as this needs to have been written by authors thoroughly and recently familiar with the whole field of acute medicine. It has been and has been done very well. I am delighted to provide a Foreword to an excellent book which really does fill

an important gap.

Editors: Ramrakha, Punit S.; Moore, Kevin P.
Title: *Oxford Handbook of Acute Medicine, 2nd Edition*

Preface to the first edition

As every doctor soon discovers, the management of acute medical emergencies is the most demanding and stressful aspect of medical training. Most handbooks of clinical medicine can only go into general detail about the management of medical problems and the specific advice needed to manage acutely ill patients is usually insufficient in these texts.

The aim of this handbook is to give confidence to doctors to manage acute medical problems effectively and safely, and is intended to complement the *Oxford Handbook of Clinical Medicine*. Many books on acute medicine are written by senior staff, who have not been at the frontline for some time, and certain aspects of care are assumed or overlooked. This book was written by junior doctors with first-hand experience of the practical problems and dilemmas faced in casualty.

The layout of the book reflects clinical practice: assessment, differential diagnosis, immediate management, and some aspects of long-term therapy. We have included an extensive section on practical procedure as well as a section on pharmacotherapy to provide information on the use of certain common and unusual drugs to complement that provided the *British National Formulary* (BNF).

Throughout the book the text commonly exceeds that required for the management of specialist problems by the generalist. We make no apology for this. This is intended to provide the doctor with an understanding of specialist interventions so that

they are more conversant with what is possible and what is happening to their patient.

Acknowledgements

We would like to thank all of the contributors and particularly Masud Husain (Neurology), Bill Lynn (Infectious Diseases), and Amanda Perry (Haematology) for being prompt, comprehensive, and adhering to the format of the book. Thanks also go to Jan Foster and Katie Darling for their artwork. We would also like to thank OUP for their encouragement during their inception and writing of this book. PSR is indebted to Vandana and his parents for their support and motivation. KPM is indebted to Janet, Alice, and Thomas for their continued patience when the portable computer accompanied family holidays. Finally, we would like to acknowledge the environment at the Hammersmith Hospital where acute medicine is both interesting and fun.

P S R

K P M

October, 1997

Editors: Ramrakha, Punit S.; Moore, Kevin P.
Title: *Oxford Handbook of Acute Medicine, 2nd Edition*

Oxford Handbook List

- Oxford Handbook of Psychiatry (OHPS) - 1st Edition
- Oxford Handbook of Tropical Medicine (OHTM) - Second Edition
- Oxford Handbook of Accident and Emergency Medicine (OHAE) - Second Edition
- Oxford Handbook of Palliative Care (OHPC) - First Edition
- Oxford Handbook of Clinical Dentistry (OHCD) - Fourth Edition
- Oxford Textbook of Psychotherapy (OTPT) - First Edition
- Oxford Handbook of Acute Medicine (OHAM) - Second Edition
- Oxford Handbook of Critical Care (OHCC) - 2nd edition

Editors: Ramrakha, Punit S.; Moore, Kevin P.
Title: *Oxford Handbook of Acute Medicine, 2nd Edition*

Symbols and abbreviations

Abbreviations

~

approximately

-ve

negative

+ve

positive

â†“

decreased

â†‘

increased

â†”

normal

Â°

degrees

A&E

accident and emergency

AAA

abdominal aortic aneurysm

Ab

antibody

ABC

airway, breathing, and circulation

ABG

arterial blood gases

ACE

angiotensin-converting enzyme

ACEI

angiotensin-converting enzyme inhibitors

AChR

acetylcholine receptor

ACLS

advanced cardiac life support

ACS

acute coronary syndrome

ACTH

adrenocortico stimulating hormone

AD

adrenaline

ADH

anti-diuretic hormone

AF

atrial fibrillation

AIDS

acquired immunodeficiency syndrome

ALI

acute lung injury

ALL

acute lymphoblastic leukaemia

ALP

alkaline phosphatase

ALT

alanine transaminase

AMA

anti-mitochondrial antibody

AMI

acute myocardial infarction

AML

acute myeloid leukaemia

ANA

anti-nuclear antibody

ANCA

anti-neutrophil cytoplasmic antibody

AP

anteroposterior

aPC

activated protein C

APSAC

anistreplase

APTT

activated partial thromboplastin time

AR

aortic regurgitation

ARDS

adult respiratory distress syndrome

ARF

acute renal failure

AS

aortic sterosis

ASA

acetyl salicylic acid

ASD

atrial septal defect

ASOT

anti-streptococcal titre

AST

asparate transaminase

ATN

acute tabular necrosis

ATP

aderosine triphosphate

AV

atrioventricular

AVNRT

atrioventricular-nodal re-entry tachycardia

AVR

aortic valve replacement

AVRT

accessory pathway tachycardia

AXR

abdominal X-ray

AZT

zidovudine

BAL

bronchoalveolar

BBB

bundle branch block

BC

blood cultures

BLS

basic life support

BM

bone marrow

BMT

bone marrow transplant

BNF

British National Formulary

BOOP

bronchiolitis obliterans organizing pneumonia

BP

blood pressure

Ca

carcinoma

CABG

coronary artery bypass graft

CAD

coronary artery disease

cAMP

cyclic AMP

CAVM

continuous arteriovenous haemofiltration

CAVHD

Haemodiafiltration

CBD

Common bile duct

CCDC

Consultant in Communicable Disease Control

CCF

Congestive cardiac failure

CCHF

Crimean-Congo haemorrhagic fever

CCU

Coronary care unit

CEA

Carcinoembryonic antigen

CI

cardiac index

CK

creatine phosphokinase

CMV

cytomegalovirus

CNS

central nervous system

CO

cardiac output

COP

cryptogenic organizing pneumonia

COPD

chronic obstructive pulmonary disease

CPAP

continuous positive airways pressure

CPK

creatinine phosphokinase

CPR

cardiopulmonary resuscitation

CrAg

cryptococcal antigen

CRF

Chronic renal failure

CRP

C-reative protein

CSF

cerebrospinal fluid

CSM

carotid sinus message

CT

computerised tomography

CTPA

CT pulmonary angiography

CVA

cerebrovascular accident

CVP

central venous pressure

CVVH or CVVHD

continuous venovenous haemofiltration

CVS

cardiovascular system

CXR

chest X-ray

D&V

diarrhoea and vomiting

DA

dopamine

DAT

direct antigen test

DBP

diastolic blood pressure

DC

direct current

DDAVP

desmopressin

DI

diabetes insipidus

DIC

disseminated intravascular coagulation

DKA

diabetic ketoacidosis

DM

diabetes mellitus

DNA

deoxyribose nucleic acid

DSH

deliberate self-harm

DT

delerium tremens

DTPA

diethylenetriaminepentaacetic acid

DU

duodenal ulcer

DVT

deep vein thrombosis

E

ecstasy

EBV

Ebstein Barr Virus

EC

extracellular

ECG

electrocardiogram

Echo

echocardiogram
ECV
extracellular volume
EEG
electroencephalogram
EF
ejection fraction
EG
ethylene glycol
EM
electron microscopy
EMD
electromechanical dissociation
EMG
electromyogram
ENT
ear nose and throat
EP
electrophysiological
EPS
electrophysiological studies
ERCP
endoscopic retrograde cholangiopancreatography
ESR
erythrocyte sedimentation rate
ET
endo tracheal
FBC
full blood count
FDP

fibrinogen degredation products

FEIBA

Factor VIII inhibitor bypassing activity

FEV1

forced expiratory volume (1 minute)

FFP

fresh frozen plasma

FH

family history

FSH

folliculer stimulating hormone

FVC

forced vital capacity

G6PD

glucose-6-phosphate dehydrogenase

G&S

group and save

GB

gall bladder

GBM

glomerular basement membrane

GBS

Guillainâ€“BarrÃ© syndrome

GCS

Glasgow coma scale

GCSF

granulocyte colony-stimulating factor

GFR

glomerular filtration rate

GH

growth hormone

GHB

gammahydroxybutyric acid

GI

gastrointestinal

GIT

gastrointestinal track

glc

glucose

GP

general practitioner

GP

glycoprotein

GTN

glyceryl trinitrate

GU

genitourinary

GUM

genitourinary medicine

GVHD

graft vs. host disease

HAART

highly active anti-retroviral therapy

HACEK

Haemophilus, Acintobacillus, cardiobacterium, Eikenella and Kingella spp. (causes of culture negative endocarditis)

HAIgM

Hepatitis A Ig M

HAPO

high-altitude pulmonary oedema

HAV

Hepatitis A Virus

HBc

Hepatitis B core

HbS

Hepatitis B Surface

HBsAg

Hepatitis B Surface Antigen

HBV

Hepatitis B Virus

HCG

Human chorionic ganadotrophin

HCV

Hepatitis C Virus

HDL

high-density lipoprotein

HDU

high dependency unit

HIV

human immunodefeciency virus

HLA

human lymphocyte antigen

HMG-CoA

hydroxy methyl glutaryl-Coenzyme A

HOCM

hypertrophic obstructive cardiomyopathy

HONC

hyperosmolar non-ketotic coma

HR

heart rate

HRT

hormone replacement theraphy

HSV

Herpes Simplex virus

HT

hypertension

HTLV

human-T-lymphotropic virus

HUS

haemolyticâ€“uraemic syndrome

(I:E)

inspiratory:exporatory ratio

IABP

intra aortic balloon pump

IBD

inflammatory bowel disease

ICD

implantable cardioverter defibrillator

ICP

intracranial pressure

ICU

intensive care unit

ID

infectious disease

IE

infective endocarditis

IgA

immunoglobulin A

IgE

immunoglobulin E

IgG

immunoglobulin G

IgM

immunoglobulin M

IHD

ischaemic heart disease

IJV

internal jugular vein

INR

international normalized ratio (prothrombin ratio)

IPPV

intermittent positive pressure ventilation

ITP

idiopathic thrombocytopanic purpura

ITU

intensive therapy unit

IVC

inferior vena cava

IVI

intravenous infusion

IVU

intravenous urogran

JPS

joint position sense

JVP

jugular venous pressure

KS

kaposi's sarcoma

LA

left atrium

LAD

left anterior descending coronary artery

LBBB

left bundle branch block

LDH

lactate dehydrogenase

LDL

low-density lipoprotein

LFT

liver function test

LH

leutinizing harmone

LHRH

leutinizing harmone releasing harmone

LMN

lower motor neurone

LMS

left main stem

LMWH

low-molecular-weight heparin

LP

lumbar puncture

LSD

lysergic acid diethylamide

LV

left ventricular

LVEDP

left ventricular end diastolic pressure

LVF

left ventricular failure

LVH

left ventricular hypertrophy

MACE

major cardiac events

MAI

Mycobacterium avium intracellulare

MAOI

monoamine oxidase-inhibitor

MAP

mean arterial pressure

MAT

multifocal atrial tachycardia

MC&S

microscopy, culture and sensitivity

MCA

middle cerebral artery

MCTD

mixed connective tissue disease

MCV

mean corpuscular volume

MDMA

â€˜ecstacyâ€™

MI

myocardial infarction

MOF

multiple organ failure

MR

magnetic resonance

MR

mitral regurgitation

MRA

magnetic resonance angiography

MRCP

magnetic resonance cholangio-pancreatography

MRI

magnetic resonance imaging

MRSA

methicillin resistant *Staphylococcus aureus*

MS

multiple sclerosis

MSU

midstream urine

MV

mitral valve

MVP

mitral valve prolapse

MVR

mitral valve replacement

MVT

monomorphic ventricular tachycardia

N&V

nausea and vomiting

NA

noradrenaline

NABQI

N-acetyl-benzoquinoneimine

NAC

N-acetyl-cysteine

NANB

non-A, non-B

NBM

nil by mouth

NBTV

non-bacterial thrombotic vegetation

NCS

nerve conduction studies

NG

nasogastric

NIV

non-invasive ventilation

NPV

negative pressure ventilation

NQ-MI

non-Q-wave MI

NR

normal range

NSAID

non-steroidal anti-inflammatory drug

NSTEMI/UA

non-ST elevation myocardial infarction

OCP

oral contraceptive pill

OD

overdose

OER

oxygen extraction ratio

OPG

orthopentamogram

PA

pulmonary artery

PACI

partial anterior circulation infarct

PAN

polyarterists nodosa

pANCA

anti neutrophil cytoplasmic antibody type-p

P_aO_2

partial pressure of oxygen in arterial blood

PAWP

pulmonary artery wedge pressure

PBC

primary biliary cirrhosis

PCA

patient-controlled analgesia

PCI

percutaneous coronary intervention

PCP

Pneumocystitis carinii pneumonia

PCR

polymerase chain reaction

PCV

packed cell volume

PCWP

pulmonary capillary wedge pressure

PDA

patent ductus arteriosus

PE

phenytoin equivalent

PE

pulmonary embolism

PEA

pulseless electrical activity

PEEP

positive end expiratory pressure

PEF

peak expiratory flow

PEFR

peak expiratory flow rate

PEG

percutaneous endoscopic gastrostony

PEP

post-exposure prophylaxis

PET

positron emission tomography

PFO

patent foramen ovele

PHI

primary HIV infection

PMH

past medical history

PML

progressive multi-focal leucoencephalopathy

PMN

polymarphonuclear cells (neutrophils)

PMR

polymyalgia rheumatica

PPI

proton pump inhibitor

PR

per rectum

PSA

prostate-specific antigen

PSC

primary sclerosing cholargitis

PT

prothrombin time

PTH

parathyroid harmone

PUO

pyrexia of unknown origin

PVE

prosthetic valve endocarditis

PVR

pulmonary vascular resistance

PVT

polymorphic ventricular tachycardia

Qw-MI

Q-wave MI

RA

right atrium

RAD

right axis deviation

rAPC

recombinant activated protein C

RAS

renin angiotensin system

RBBB

right bundle branch block

RBC

red blood cell

RCA

right coronary artery

RCP

Royal College of Physicians

RF

rheumatic fever

RNA

ribose nucleic acid

RNP

ribo nucleic protein

RR

respiratory rate

RS

respiratory system

RSV

respiratory syncytial virus

r t - P A

recombinant tissue plasminogen activator

RTA

road traffic accident

RUQ

right upper quadrant

RV

right ventricular

RVDP

right ventricular end diastolic pressure

RVF

right ventricular failure

RVOT

right ventricular outflow tract

SAH

sub arachnoid haemorrhage

SARS

severe acute respiratory syndrome

SBE

subacute bacterial endocarditis

SBP

systolic blood pressure

SCU

subclaview vein

SIADH

syndrome of inappropriate ADH secretion

SK

streptokinase

SL

sublingual

SLE

systemic lupus erythematosus

SOB

short of breath

SOL

space-occupying lesion

SR

slow release

SSRI

selective serotonin reuptake inhibitor

SSS

staphylococcal scalded skin syndrome

STEMI

ST elevation myocardial infarction

STS

serological tests for syphilis

SVC

superior vena cava

SVR

systemic vascular resistance

SVT

supraventricular tachycardia

SXR

skull X-ray

TB

tuberculosis

TBG

thyroid-binding

TEN

toxic epidermal necrolysis

TFT

thyroid function test

TIA

transient ischaemic attack

TIBC

total iron binding capacity

TIPS

transvenous intrahepatic portosystemic shunting

TnI

troponin I

TnT

troponin T

TOE

trans oesophageal echocardiogram

tPA

tissue plasminogen activator

TPHA

Treponema Pallidum haemagglutination

TPN

total parentral nutrition

TPR

temperature, pulse and respirations

TR

tricuspid regurgitation

TRALI

transfusion-related acute lung injury

TRH

thyrotropin releasing hormone

TSH

thyroid stimulating harmone

TT

thrombin tiare

TTP

thrombotic thrombocytopenic purpura

TURBT

transurethral resection of bladder tumour

TURP

transurethral resection of prostate

U&Es

urea and electrolytes

UA

unstable angina

UC

ulcerative colitis

UFH

unfractionated heparin

UMN

upper motor neuron

URTI

upper respiratory tract injection

US

ultrasound

USS

ultrasound scan

UTI

urinary tract infection

UV

ultraviolet

VC

vital capacity

VE

ventricular extrasystole

VF

ventricular fibrillation

VMA

vanillyl mandellic acid

VOR

vestibulo-ocular reflex

VPB

ventricular premature beats

VQ

ventilation (v)-perfusion (Q)

VSD

ventriculo-septal defect

VT

ventricular tachycardia

vW

von Willebrand

VZIG

varicella zoster immunoglobulin

VZV

varicella zoster virus

WBC

white blood cell

WCC

white cell count

WPW

Wolffâ€“Parkinsonâ€“White

ZN

Ziehlâ€“Nieelson syndrome

â†‘

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Coma: clues from examination 1

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Coma: clues from examination 2

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Coma: management

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Limb weakness: assessment

-

Limb weakness: localizing the lesion

[+]

Acute dizziness: assessment

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Acute dizziness: management

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Acute loss of vision

[+]

Approach to acute/sub-acute visual loss

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Painful red eye: assessment

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Painful red eye: management

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Acute bacterial meningitis: assessment

[+]

Acute bacterial meningitis: immediate management

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Acute bacterial meningitis: continuing therapy

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Acute bacterial meningitis: complications and their treatment

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Meningitis with lymphocytic CSF

[+]

Acute viral encephalitis

[+]

Head injury: presentation

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Head injury: assessment

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Head injury: immediate management

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Head injury: further management

[+]

Raised intracranial pressure (

[+]

Raised intracranial pressure: immediate management

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Raised intracranial pressure: further management

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Intracranial space-occupying lesion

[+]

Extradural haemorrhage

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Intracerebral haemorrhage

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Subdural haematoma

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Subarachnoid haemorrhage: assessment

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Subarachnoid haemorrhage: immediate management

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Subarachnoid haemorrhage: further management

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Status epilepticus (tonicâ€“clonic) 1

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Status epilepticus (tonicâ€“clonic) 2

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Status epilepticus (tonicâ€“clonic) 3

[+]

Stroke: overview

[+]

Stroke: haemorrhage or infarct?

-

Stroke: other investigations

[+]

Stroke: complications

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Stroke: secondary prevention

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Cerebellar stroke

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Confusional states and delirium 1

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Confusional states and delirium 2

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Neuromuscular respiratory failure 2

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Spinal cord compression: management

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[+]

Guillainâ€“BarrÃ© syndrome 2

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Botulism

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Tetanus

[+]

Glasgow Coma Scale (

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Examination of brainstem function 1

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Examination of brainstem function 2

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Examination of brainstem function 3

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Examination of brainstem function 4

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Oculocephalic and oculovestibular responses

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Brain death

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Diabetic ketoacidosis: management

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Diabetic ketoacidosis: complications

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[+]

Hypoglycaemic coma: assessment

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Hypoglycaemic coma: management

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Urgent surgery in patients with diabetes

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Hyponatraemia: management

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Hypernatraemia

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Acute hypocalcaemia

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Hypercalcaemia

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Hypophosphataemia

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Addisonian crisis: assessment

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Addisonian crisis: management

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Myxoedema coma

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Thyrotoxic crisis: assessment

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Thyrotoxic crisis: management

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Pituitary apoplexy

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Hypopituitary coma

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Phaeochromocytomas: assessment

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Phaeochromocytomas: management

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Polyuria

[+]

Malignant hyperthermia

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Neurolepetic malignant syndrome

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Chapter 10 - Gastroenterological emergencies

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Acute upper gastrointestinal bleeding 1

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Acute upper gastrointestinal bleeding 2

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Acute upper gastrointestinal bleeding 3

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Peptic ulcer disease

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Erosive gastritis/oesophagitis

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Variceal haemorrhage: medical management

[+]

Variceal haemorrhage: further management

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Malloryâ€“Weiss tear

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Acute gastroenteritis: assessment

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Bacterial gastroenteritis

-

Viral gastroenteritis

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Pseudomembranous colitis

-

Giardiasis

[+]

Travellers' diarrhoea

[+]

Bloody diarrhoea

[+]

Bacterial dysentery

[+]

Amoebic dysentery

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Inflammatory bowel disease (

[+]

Inflammatory bowel disease 2

[+]

Inflammatory bowel disease 3

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Jaundice: assessment

-

Viral hepatitis

[+]

Alcoholic hepatitis

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Drug-induced hepatitis

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Autoimmune hepatitis

-

Acholuric jaundice

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Sepsis

[+]

Ischaemic hepatitis

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Obstructive jaundice

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Gallstone disease

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Acute cholecystitis

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Biliary obstruction

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Ascites

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Acute liver failure: assessment

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Acute liver failure: investigations

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Acute liver failure: management

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â€˜Acute-on-chronicâ€™ liver failure

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Hepatic encephalopathy

[+]

Liver abscesses

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Acute pancreatitis: assessment

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Acute pancreatitis: management

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Blood transfusion reactions: management

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Sickle cell crisis: management

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[+]

Circulating inhibitors of coagulation

[+]

Abnormal platelets 1

[+]

Abnormal platelets 2

[+]

Anti-coagulant therapy

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Bleeding with fibrinolytic therapy

[+]

Bleeding in liver disease

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Bleeding in uraemia

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Massive transfusion/cardiopulmonary bypass

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Haemophilia and related disorders 1

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Haemophilia and related disorders 2

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Combined thrombotic and haemorrhagic disorders

[+]

Disseminated intravascular coagulation (

[+]

Thrombotic thrombocytopenic purpura (

[+]

Microangiopathic haemolytic anaemia

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Heparin-associated thrombocytopenia

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Acute leukaemias: presentation

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Acute leukaemias: management

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Acute leukaemias: treatment

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Early complications of bone marrow transplantation (

[+]

Complications of bone marrow transplantation

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The febrile neutropenic patient 1

[+]

The febrile neutropenic patient 2

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The febrile neutropenic patient 3

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Infections in the transplant patient

[+]

Cytomegalovirus (

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Hyperviscosity syndrome

[+]

Tumour lysis syndrome

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Hypercalcaemia of malignancy

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Superior vena cava obstruction

[+]

Massive mediastinal mass

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Chapter 13 - Dermatological emergencies

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Change in names of certain medicinal substances

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ECG Ruler

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Color Plates

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Adult basic life support

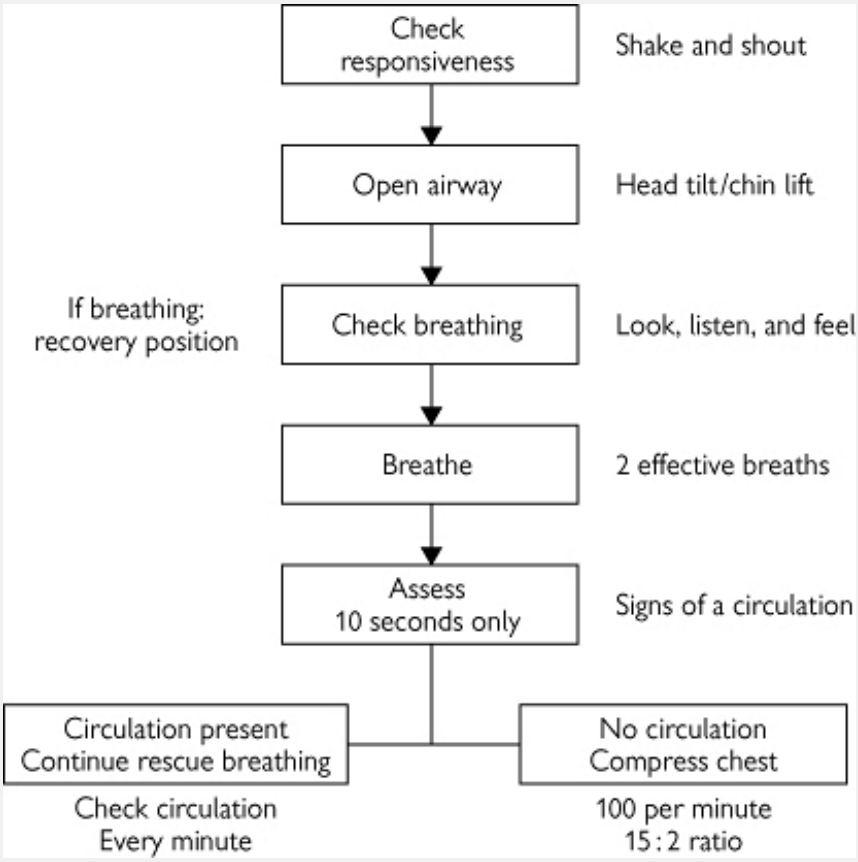
Basic life support is the backbone of effective resuscitation following a cardiorespiratory arrest. The aim is to maintain adequate ventilation and circulation until the underlying cause for the arrest can be reversed. 3â€“4 minutes without adequate perfusion (less if the patient is hypoxic) will lead to irreversible cerebral damage. The usual scenario is an unresponsive patient found by staff who alert the cardiac arrest team. The initial assessment described below should have already been performed by the person finding the patient. The same person should have also started CPR. Occasionally you will be the first to discover the patient and it is important to rapidly assess the patient and begin CPR. The various stages in basic life support are described below and summarized in the algorithm opposite.

- Assessment of the patient
    - Ensure safety of rescuer and victim
    - Check whether the patient is responsive. Gently shake victim and ask loudly â€˜are you all right?â€™
        - If victim responds place them in the recovery position and get help.
        - If victim is unresponsive shout for help and move on to assess airway (see below).

- Airway assessment
    - Open the airway. With two fingertips under the point of the chin, tilt the head up. If this fails place your fingers behind the angles of the lower jaw and apply steady pressure upwards and forwards. Remove ill-fitting dentures and any obvious obstruction. If the patient starts breathing, roll the patient over into the recovery position and try to keep the airway open until an orophyrangeal airway can be inserted (see P6).
    - Keep airway open, look, listen, and feel for breathing. Look for chest movements, listen at the victim's mouth for breathing sounds and feel for air on your cheek (for no more than 10 seconds).
        - If patient is breathing turn patient into the recovery position, check for continued breathing and get help.
        - If patient is not breathing or making occasional gasps or weak attempts at breathing send someone for help (or go for help if alone). (On return) Start rescue breaths by giving two slow effective breaths each resulting in a visible rise and fall in the chest wall.
- Assessment of circulation
    - Assess signs of circulation by feeling the carotid pulse for no more than 10 seconds.
        - If there are signs of circulation but no breathing continue rescue breaths and check for signs of breathing every 10 breaths (approximately 1 breath a minute).
        - If there are no signs of circulation start chest compression at a rate of 100 times per minute.

Combine rescue breaths and compression at a rate of 15 compressions to two effective breaths.

- The ratio of compressions to lung inflation remains the same for resuscitation with two persons.



Send or go for help as soon as possible to guidelines For further information see the Resuscitation Council (UK) website (http://www.resus.org.uk/pages/bls.htm)

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Adult advanced life support

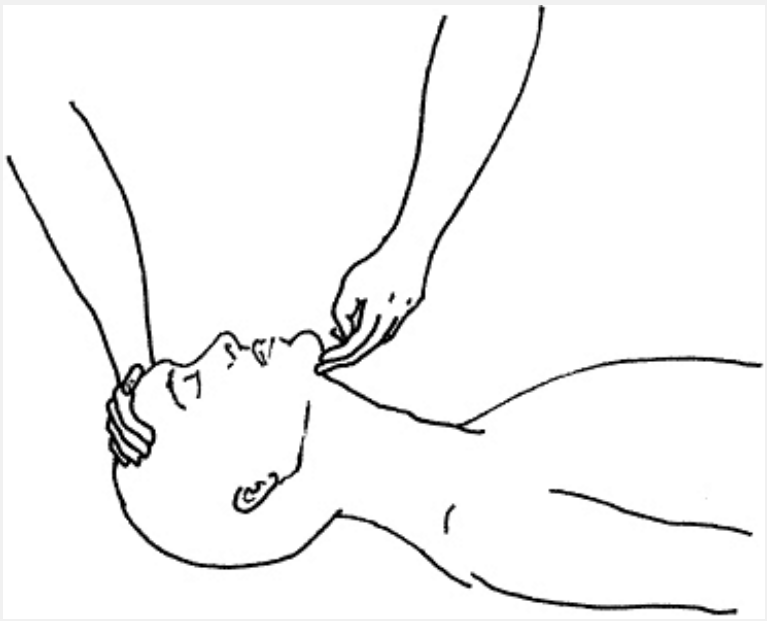
- It is unlikely that an effective spontaneous cardiac activity will be restored by basic life support without more advanced techniques (intubation for effective ventilation, drugs, defibrillation, etc.). Do not waste time. As soon as help arrives, delegate CPR to someone less experienced in ACLS, so that you are able to continue.
- Attach the patient to a cardiac monitor as soon as possible to determine the cardiac rhythm and treat appropriately (see P8 for universal treatment algorithm).
- Oropharyngeal (Guedel) or nasopharyngeal airways help maintain the patency of the airway by keeping the tongue out of the way. They can cause vomiting if the patient is not comatose. ET intubation is the best method of securing the airway (P5). *Do not attempt this if you are inexperienced*.
- Establish venous access. Central vein cannulation (internal jugular or subclavian) is ideal but requires more training and practice and is not for the inexperienced. If venous access fails, drugs may be given via an ET-tube into the lungs (except for bicarbonate and calcium salts). Double the doses of drugs if using this route, as absorption is less efficient than iv.

Post resuscitation care

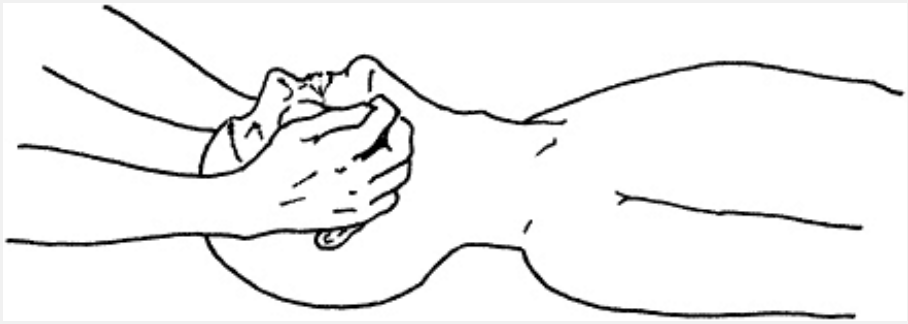
- Try to establish the events that precipitated the arrest from the history, staff, witnesses, and the hospital notes of the patient. Is there an obvious cause (MI, hypoxia, hypoglycaemia, stroke, drug overdose or interaction, electrolyte abnormality, etc.)? Record the duration of the arrest in the notes with the interventions and drugs (and doses) in chronological order.
- Examine the patient to check both lung fields are being ventilated. Check for ribs that may have broken during CPR. Listen for any cardiac murmurs. Check the neck veins. Examine the abdomen for an aneurysm or signs of peritonism. Insert a urinary catheter. Consider an NG-tube if the patient remains unconscious. Record the Glasgow Coma Score (P520) and perform a brief neurological assessment (see P406).
- Investigations: *ECG* [looking for MI, ischaemia, tall T-waves (â†‘K^+)]; *ABG* [mixed metabolic and respiratory acidosis is common and usually responds to adequate oxygenation and ventilation once the circulation is restored. If severe, consider bicarbonate]; *CXR* (check position of ET-tube, look for pneumothorax); *U&Es; and glucose*.
- After early and successful resuscitation from a primary cardiac arrest, the patient may rapidly recover completely. The patient must be transferred to HDU or CCU for monitoring for 12â€“24h. Commonly the patient is unconscious post arrest and should be transferred to ITU for mechanical ventilation and haemodynamic monitoring and support for â‰¥24 hours.
- Change any venous lines that were inserted at the time of arrest for central lines inserted with sterile technique. Insert an arterial line and consider PA catheter (Swanâ€“Ganz) if requiring inotropes.
- Remember to talk to the relatives. Keep them informed of

events and give a realistic (if bleak) picture of the arrest and possible outcomes.

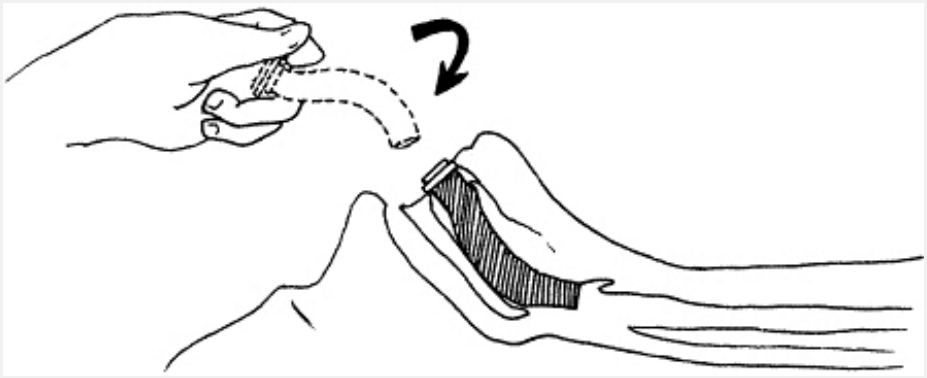
- When appropriate consider the possibility of organ donation and do not be frightened to discuss this with the relatives. Even if discussion with the relatives is delayed, remember corneas and heart valves may be used up to 24 hours after death. Brain stem death (see P532).



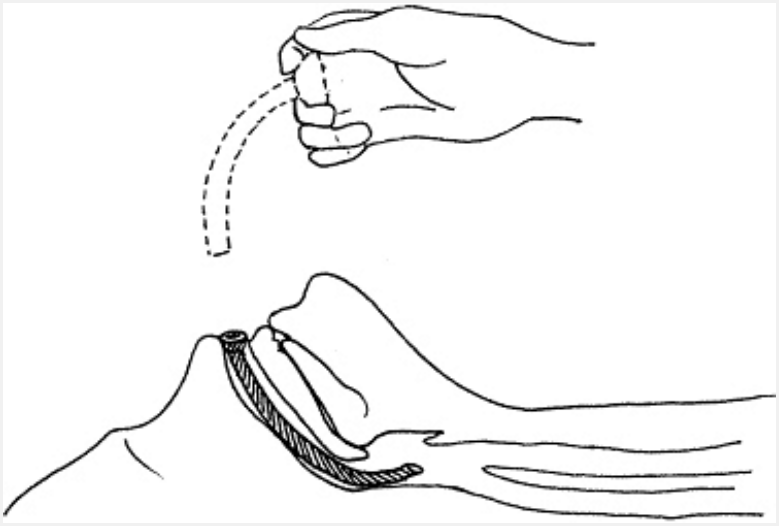
Jaw lift to open the airway



Jaw thrust (thrust the angle of the mandible upwards)



Insertion of oropharyngeal airway



Insertion of nasopharyngeal airway

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Universal treatment algorithm

- Cardiac rhythms of cardiac arrest can be divided into two groups:
    - (VF/VT)
    - Other cardiac rhythms, which include asystole and PEA.
- The principle difference in treatment of the two groups of arrhythmias is the need for attempted defibrillation in the VF/VT group of patients.
- The figure opposite summarizes the algorithm for management of both groups of patients.

VF/VT

- VF/VT are the most common rhythms at the time of cardiac arrest.
- Success in treatment of VF/VT is dependent on the delivery of prompt defibrillation. With each minute the chance of successful defibrillation declines by 7â€“10%.
- Precordial thump. If arrest is witnessed or monitored a sharp blow with a closed fist on the patient's sternum may convert VF/VT back to a perfusing rhythm. It is particularly effective if delivered within 30 seconds after cardiac arrest.

- Shock cycles are generally in groups of three. Initially 200J, 200J, and 360J, with subsequent cycles at 360J.
- After each shock (or sequence) the carotid pulse should be palpated only if the waveform changes to one usually capable of providing a cardiac output.
- Shock cycle is repeated every minute if VF/VT persists.
- Myocardial and cerebral viability must be maintained after each shock cycle with chest compressions and ventilation of lungs as described on P2.
- In between cycles of defibrillation reversible factors must be identified and corrected, the patient intubated (if possible) and venous access obtained.
- Adrenaline should be given every 3 minutes (1mg iv and 2â€“3mg via endotracheal route).

Non-VF/VT rhythms

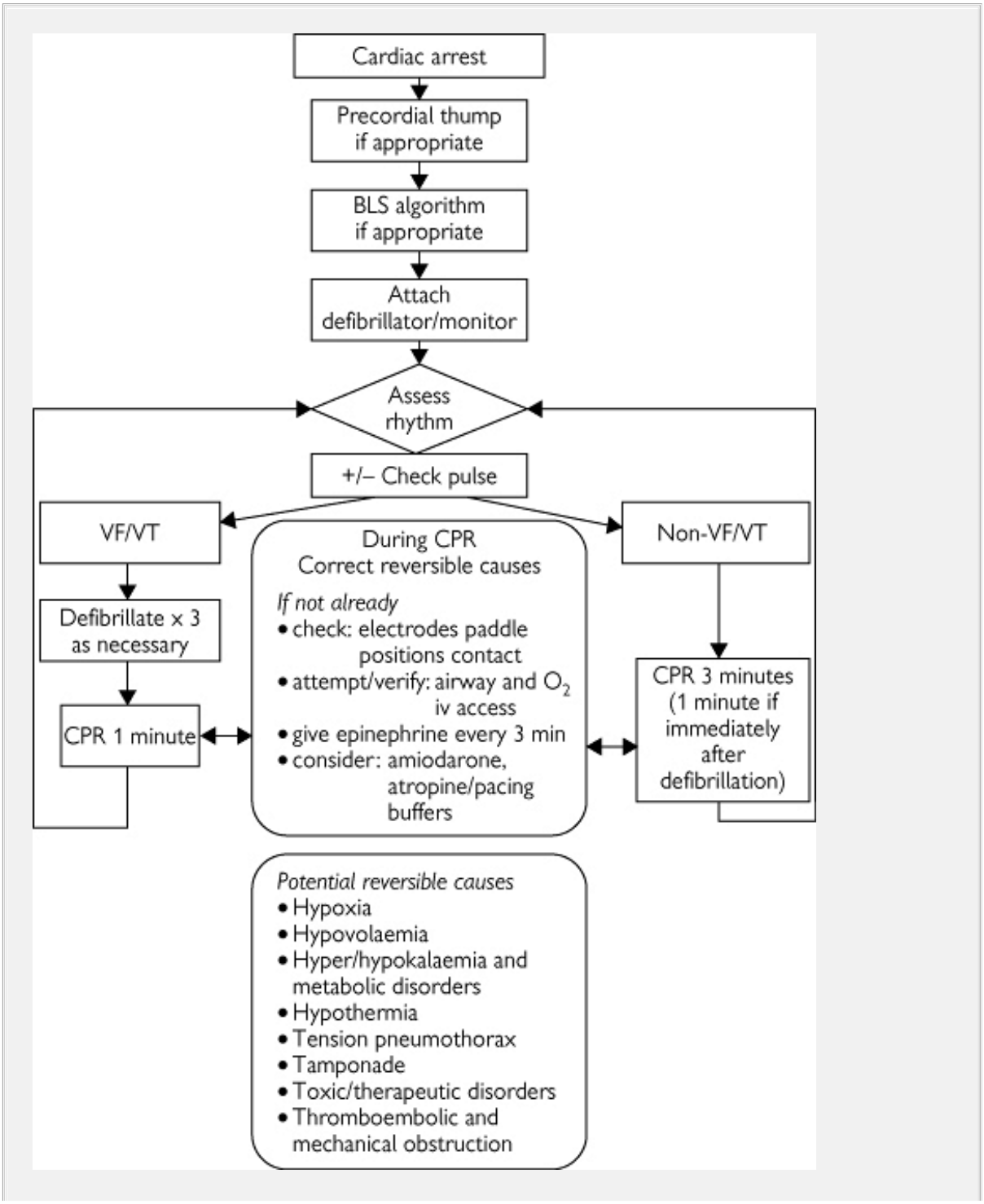
- The outcome from these rhythms is generally worse than for VF/VT unless a reversible cause can be identified and treated promptly.
- Chest compressions and ventilation should be undertaken for 3 minutes with each loop of the algorithm (1 minute if directly after a shock).
- With each cycle attempts must be made to intubate the patient, gain iv access, and give adrenaline.

Asystole

- Atropine 3mg iv should be given to block all vagal output.
- In the presence of P-waves on the strip/monitor, pacing (external or transvenous) must be considered.

PEA

- Identification of the underlying cause (see P 9) and its correction are both vital for successful resuscitation. Resuscitation must be continued whilst reversible causes are being sought.



(for further details see the Resuscitation Council (UK) website http://www.resus.org.uk/pages/als.htm)

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Acute coronary syndrome (ACS)

ACS is an operational term used to describe a constellation of symptoms resulting from acute myocardial ischaemia. An ACS resulting in myocardial injury is termed MI. ACS includes the diagnosis of UA, NSTEMI, and STEMI. The term ACS is generally assigned by ancillary/triage personnel on initial contact with the patient. Guidelines for identification of ACS are summarized on P46.

Definition

The current nomenclature divides ACS into two major groups, on the basis of delivered treatment modalities (see figure).

- STEMI. An ACS where patients present with ischaemic chest discomfort and ST-segment elevation on ECG. This group of patients must undergo reperfusion therapy on presentation.
- NSTEMI and UA. ACS where patients present with ischaemic chest discomfort associated with transient or permanent non ST-elevation ischaemic ECG changes. If there is biochemical evidence of myocardial injury the condition is termed NSTEMI and in the absence if biochemical myocardial injury the condition is termed UA (see P11). This group of patients is not treated with thrombolysis.

Initial management of ACS

- All patients with suspected ACS should be placed in an environment with continuous ECG monitoring and defibrillation capacity.
- The referring doctor should be instructed to give aspirin (300mg po if no contraindications) and *not* to give any im injections (causes a rise in total CK and risk of bleeding with thrombolysis/anticoagulation).

Immediate assessment should include

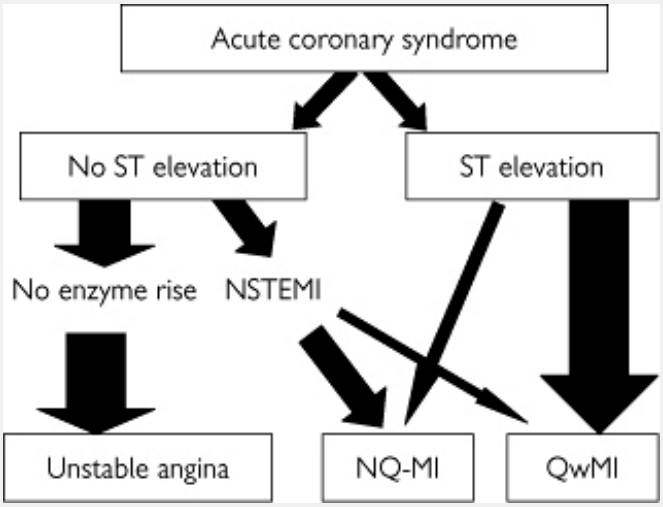
â€¢ Rapid examination to exclude hypotension and note the presence of murmurs and to identify and treat acute pulmonary oedema.	
â€¢ Secure iv access.	
â€¢ 12-lead ECG should be obtained and reported within 10 minutes.	
â€¢ Give	*Oxygen* (initially only 28% if history of COPD)
	Diamorphine 2.5â€“10mg iv prn for pain relief
	Metoclopramide 10mg iv for nausea
	GTN spray 2 puffs (unless hypotensive)
â€¢ Take blood for:	Supplement K^+ to keep it at 4â€“5mmol/L.

FBC/U&Es	
Glucose	May be â†‘acutely post MI, even in non-diabetics, and reflects a stress-catecholamine response, which may resolve without treatment.
Biochemical markers of cardiac injury.	
Lipid profile	Total cholesterol, LDL, HDL, triglycerides Serum cholesterol and HDL remain close to baseline for 24â€“48 hours but fall thereafter and take â‰¥8 weeks to return to baseline.
â€¢ Portable CXR to assess cardiac size, pulmonary oedema and toexclude mediastinal enlargement.	
â€¢ General examination should include peripheral pulses, fundoscopy, abdominal examination for organomegaly, and aortic aneurysm.	

Conditions mimicking pain in ACS

- Pericarditis
- Dissecting aortic aneurysm
- Pulmonary embolism
- Oesophageal reflux, spasm, or rupture
- Biliary tract disease
- Perforated peptic ulcer

- Pancreatitis



Nomenclature of ACS: Patients with ACS may present with or without ST elevation on the ECG. The majority of patients with ST elevation (large arrows) ultimately develop QwMI whereas a minority (small arrow) develop a NQ-MI. Patients without ST-elevation are experiencing either UA or an NSTEMI depending on the absence or presence of cardiac enzymes (e.g. troponin) detected in the blood.[1]

Footnote

1

Adapted from Antman, EM (1997) Acute myocardial infarction. In Braunwald EB, ed. *Heart Disease: A Textbook of cardiovascular medicine*; Saunders, Philadelphia.

Editors: Ramrakha, Punit S.; Moore, Kevin P.
Title: *Oxford Handbook of Acute Medicine, 2nd Edition*

ST elevation myocardial infarction (STEMI)

Patients with an ACS who have ST-segment elevation/LBBB on their presenting ECG benefit significantly from immediate reperfusion and are treated as one group under the term STEMI.

Presentation

- Chest pain usually similar in nature to angina, but of greater severity, longer duration and not relieved by SL GTN. Associated features include nausea and vomiting, sweating, breathlessness, and extreme distress.
- The pains may be atypical such as epigastric or radiate through to the back.
- Diabetics, the elderly, and hypertensives may suffer painless (â€˜silentâ€™) infarcts and/or atypical infarction. Presenting features include breathlessness from acute pulmonary oedema, syncope or coma from dysrrhythmias, acute confusional states (mania/psychosis), diabetic hyperglycaemic crises, hypotension/cardiogenic shock, CNS manifestations resembling stroke secondary to sudden reduction in cardiac output, and peripheral embolization.

Management

Diagnosis is normally made on presentation followed by rapid stabilization to ensure institution of reperfusion therapy without delay. This is in contrast to NSTEMI/UA where diagnosis may evolve over period of 24â€“72 hours (see P46). The management principles of the various stages are outlined below and expanded on subsequently.

- Stabilizing measures are generally similar for all ACS patients (see P10)
    - All patients with suspected STEMI should have continuous ECG monitoring in an area with full resuscitation facilities.
    - Patients should receive immediate aspirin 300mg po (if no contraindications), analgesia, and oxygen. Secure iv access.
    - Rapid examination to exclude hypotension and note the presence of murmurs and to identify and treat acute pulmonary oedema. RVF out of proportion to LVF suggests RV infarction (see P28).
    - Blood for FBC, biochemical profile, markers of cardiac injury, lipid profile, glucose and portable CXR.
- Diagnosis must be made on the basis of history, ECG (ST elevation/new LBBB), and biochemical markers of myocardial injury (NB if ECG changes diagnostic, reperfusion must not be delayed to wait for biochemical markers) (P16).
- Treatment:
    - General medical measures (P18)
    - Reperfusion (pp20â€“25).
- All patients with STEMI should be admitted to CCU.

- Discharge and risk prevention (P30).

Factors associated with a poor prognosis

- Age >70 years
- Previous MI or chronic stable angina
- Anterior MI or right ventricular infarction
- Left ventricular failure at presentation
- Hypotension (and sinus tachycardia) at presentation
- Diabetes mellitus
- Mitral regurgitation (acute)
- Ventricular septal defect

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STEMI: diagnosis 1

This is based on a combination of history, ECG, and biochemical markers of cardiac injury. In practice history and ECG changes are normally diagnostic resulting in immediate reperfusion/medical treatment. Biochemical markers of cardiac injury usually become available later and help reconfirm diagnosis as well as provide prognostic information (magnitude of rise).

ECG changes

- ST-segment elevation occurs within minutes and may last for up to 2 weeks. ST elevation of â‰¥2mm in adjacent chest leads and â‰¥1mm in adjacent limb leads is necessary to fulfil thrombolysis criteria. Persisting ST elevation after 1 month suggests formation of LV aneurysm. Infarction site can be localized from ECG changes as indicated in the table opposite.
- Pathological Q-waves indicate significant abnormal electrical conduction, but are not synonymous with irreversible myocardial damage. In the context of a â€˜transmural infarctionâ€™ they may take hours or days to develop and usually remain indefinitely. In the standard leads the Q-wave should be â‰¥25% of the R-wave, 0.04s in duration, with negative T-waves. In the precordial leads, Q-waves in V4 should be >0.4mV (4 small sq) and in V6

>0.2mV (2 small sq), in the absence of LBBB (QRS width <0.1s or 3 small sq).

- ST-segment depression (ischaemia at distance) in a second territory (in patients with ST-segment elevation) is secondary to ischaemia in a territory other than the area of infarction (often indicative of multivessel disease) or reciprocal electrical phenomena. Overall it implies a poorer prognosis.
- PR-segment elevation/depression and alterations in the contour of the P-wave are generally indicative of atrial infarction. Most patients will also have abnormal atrial rhythms such as AF/flutter and wandering atrial pacemaker and AV nodal rhythms.
- T-wave inversion may be immediate or delayed and generally persists after the ST elevation has resolved.
- Non-diagnostic changes, but ones that may be ischaemic, include new LBBB or RBBB, tachyarrhythmias, transient tall peaked T-waves or T-wave inversion, axis shift (extreme left or right), or AV block.

Conditions that may mimic ECG changes of a STEMI

- Left or right ventricular hypertrophy
- LBBB or left anterior fasciculatar block
- Wolffâ€“Parkinsonâ€“White syndrome
- Pericarditis or myocarditis
- Cardiomyopathy (hypertrophic or dilated)
- Trauma to myocardium
- Cardiac tumours (primary and metastatic)

- Pulmonary embolus
- Pneumothorax
- Intra-cranial haemorrhage
- Hyperkalaemia
- Cardiac sarcoid or amyloid
- Pancreatitis

Localization of infarcts from ECG changes

Anterior	ST elevation and/or Q-waves in V1â€“V4/V5
Anteroseptal	ST elevation and/or Q-waves in V1â€“V3
Anterolateral	ST elevation and/or Q-waves in V1â€“V6, I, and aVL.
Lateral	ST elevation and/or Q-waves in V5â€“V6 and T-wave inversion/ST elevation/Q-waves in I and aVL
Inferolateral	ST elevation and/or Q-waves in II, III, aVF, and V5â€“V6 (sometimes I and aVL)
Inferior	ST elevation and/or Q-waves in II, III, and aVF

Inferoseptal	ST elevation and/or Q-waves in II, III, aVF, and V1â€“V3
True posterior	Tall R-waves in V1â€“V2 with ST depression in V1â€“V3 T-waves remain upright in V1â€“V2. This can be confirmed with an oesophageal lead if available (method similar to an NG tube). Usually occurs in conjunction with an inferior or lateral infarct
RV infarction	ST-segment elevation in the right precordial leads (V3Râ€“V4R). Usually found in conjunction with inferior infarction. This may only be present in the early hours of infarction

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STEMI: diagnosis 2

Biochemical markers of cardiac injury

Serial measurements evaluating a temporal rise and fall should be obtained to allow a more accurate diagnosis. CK and CK-MB from a skeletal muscle source tend to remain elevated for a greater time period in comparison to a cardiac source.

CK

- Levels twice upper limit of normal are taken as being abnormal.
- Serum levels rise within 4â€“8 hours post STEMI and fall to normal within 3â€“4 days. The peak level occurs at about 24 hours but may be earlier (12 hours) and higher in patients who have had reperfusion (thrombolysis or PCI).
- False positive rates of ~15% occur in patients with alcohol intoxication, muscle disease or trauma, vigorous exercise, convulsions, im injections, hypothyroidism, PE, and thoracic outlet syndrome.

CK-MB isoenzyme is more specific for myocardial disease. Levels may be elevated despite a normal total CK. However, CK-MB is also present in small quantities in other tissues (skeletal muscle, tongue, diaphragm, uterus, and prostate) and trauma or surgery may lead to false positive results. If there is

doubt about myocardial injury with CK-MB levels obtained a cardiac troponin must be measured.

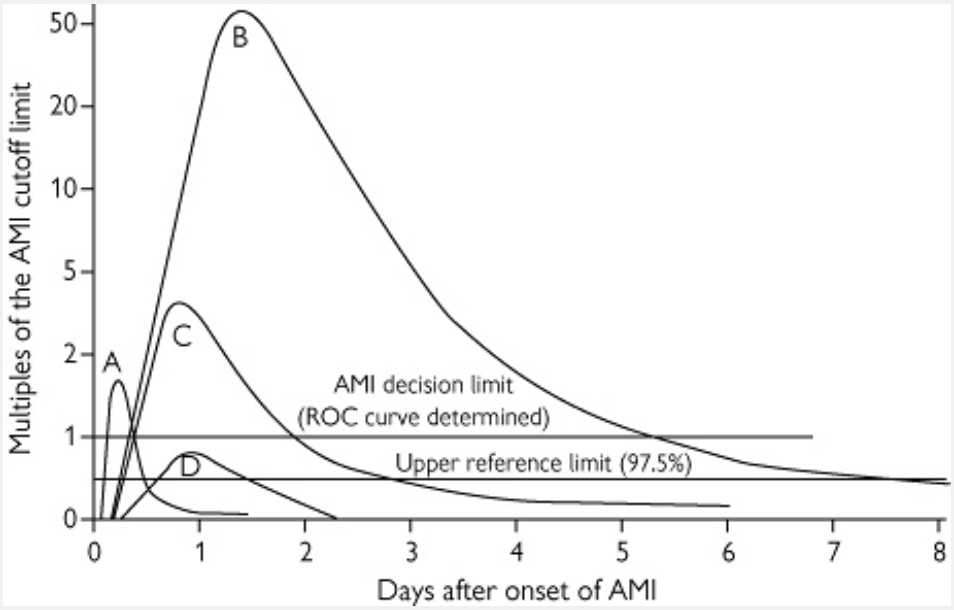
Cardiac troponins (TnT, TnI)

- Both TnI and TnT are highly sensitive and specific markers of cardiac injury.
- Serum levels start to rise by 3 hours post MI and elevation may persist up to 7â€“14 days. This is advantageous for diagnosis of late MI.
- In most STEMI cases the diagnosis can be made using a combination of the clinical picture and serial CK/CK-MB levels. In the event of normal CK-MB levels and suspected non-cardiac sources of CK, troponins can be used.
- Troponins can also be elevated in non-ischaemic myocyte damage such as myocarditis, cardiomyopathy, and pericarditis.

Other markers

There are multiple other markers, but with increasing clinical availability of troponins, measurements are not recommended. These include AST (rise 18â€“36 hours post MI) and LDH (rise 24â€“36 hours post MI).

The time course of the various markers is seen in the figure opposite.



Graph of the appearance of cardiac markers in the blood versus time of onset of symptoms

Peak A: early release of myoglobin or CK-MB isoforms after AMI. *Peak B*: cardiac troponin after AMI. *Peak C*: CK-MB after AMI. *Peak D*: cardiac troponin after unstable angina.[1]

Footnote

1

Adapted from Wu AH *et al.* (1999) *Clin Chem* 45: 1104â€“1121.

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STEMI: general measures

- Immediate stabilizing measures are as outlined on P10
- Control of cardiac pain
    - Diamorphine 2.5â€“10mg iv is the drug of choice and may be repeated to ensure adequate pain relief, unless evidence of emerging toxicity (hypotension, respiratory depression). Nausea and vomiting should be treated with metoclopramide (10mg iv) or a phenothiazine.
    - Oxygen to be administered at 2â€“5L/min for at least 2â€“3 hours. Hypoxaemia is frequently seen post MI due to ventilationâ€“perfusion abnormalities secondary to LVF. In patients with refractory pulmonary oedema, CPAP, or via formal endotracheal intubation may be necessary. Beware of CO_2 retention in patients with COPD.
    - Nitrates may lessen pain and can be given providing that patient is not hypotensive (sublingual or intravenous). They need to be used cautiously in inferior STEMI, especially with right ventricular infarction, as venodilation may impair RV filling and precipitate hypotension. Nitrate therapy has no effect on mortality (ISIS-4).
- Correction of electrolytes

Both low potassium and magnesium may be arrhythmogenic and must be supplemented especially in the context of arrhythmias.

- Strategies to limit infarct size (Î²-blockade, ACE-I, and reperfusion)

Î²-blockade

- Early Î²-blockade in limiting infarct size, reducing mortality, and early malignant arrhythmias. All patients (including primary PCI and thrombolysis patients) should have early Î²-blockade, but those with the following features will benefit most:
    - Hyperdynamic state (sinus tachycardia, â†‘BP)
    - Ongoing or recurrent pain/reinfarction
    - Tachyarrhythmias such as AF.
- Absolute contraindications: HR <60, SBP <100mmHg, moderate to severe heart failure, AV conduction defect, severe airways disease.
- Relative contraindications: asthma, current use of calcium channel blocker and/or Î²-blocker, severe peripheral vascular Î²disease with critical limb ishaemia, large inferior MI involving the right ventricle.
- Use short-acting agent iv initially (metoprolol 1â€“2mg at a time repeated at 1â€“2 minute intervals to a maximum dose of 15â€“20mg) under continuous ECG and BP monitoring. Aim for a pulse rate of 60 and SBP of 100â€“110mmHg. If haemodynamic stability continues 15â€–30 minutes after last iv dose start metoprolol 50mg tds. Esmolol is an ultra-short-acting iv Î²-blocker, which may be tried if there is concern whether the patient will tolerate Î²-blockers.

ACE inhibitors

After receiving aspirin, Î²-blockade (if appropriate), and reperfusion, all patients with STEMI/LBBB infarction should receive an ACE inhibitor within the first 24 hours of presentation.

- Patients with high-risk/large infarcts particularly with an anterior STEMI, a previous MI, heart failure, or impaired LV function on imaging (ECHO) or those who are elderly will benefit most.
- The effect of ACE-I appears to be a class effect: use the drug you are familiar with (e.g. ramipril 1.25mg od).

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STEMI: reperfusion therapy (thrombolysis) 1

Rapid reperfusion is the cornerstone of current management of STEMI and is marked by normalization of ST segments on ECG. Primary PCI and thrombolysis are the main reperfusion modalities. The best long-term outcome is achieved with primary PCI.

Reperfusion occurs in 50â€“70% of patients who receive thrombolysis within 4 hours of onset of pain (cf. ~20% of controls). As with primary PCI, thrombolysis also results in reduced mortality, LV dysfunction, heart failure, cardiogenic shock, and arrhythmias. However, the magnitude of the benefits obtained are smaller. Furthermore, patients must undergo cardiac catheterization to delineate their coronary anatomy before revascularization (achieved at the same time with primary PCI). Time is once again of paramount importance and thrombolysis should be administered as soon as possible.

Indications for thrombolysis

- Typical history of cardiac pain within previous 12 hours and ST elevation in 2 contiguous ECG leads (>1mm in limb leads or >2mm in V1â€“V6).
- Cardiac pain with new/presumed new LBBB on ECG.

- If ECG is equivocal on arrival, repeat at 15â€“30 minute intervals to monitor progression.
- Thrombolysis should not be given if the ECG is normal, or if there is isolated ST depression (must exclude true posterior infarct) or ST elevation with no preceding history of pain.

Timing of thrombolysis

- Greatest benefit is achieved with early thrombolysis (especially if given within 4 hours of onset of first pain).
- Patients presenting between 12â€“24 hours from onset of pain should be thrombolysed only with persisting symptoms and ST-segment elevation.
- Elderly patients (>65 years) presenting within the 12â€“24 hour time period with symptoms are best managed by primary PCI as thrombolysis has demonstrated increased cardiac rupture.
- Patients presenting within 12â€“24 hours from the onset of pain whose clinical picture appears to have settled should be managed initially as an NSTEMI followed by early catheterization.

Choice of thrombolytic agent

- This is partly determined by local thrombolysis strategy.
- Allergic reactions and episodes of hypotension are greater with SK.
- Bolus agents are easier and quicker to administer with a decrease in drug errors in comparison to first-generation infusions.
- rtPA has a greater reperfusion capacity and a marginally higher 30-day survival benefit than SK, but an increased

risk of haemorrhage.

- More recent rPA derivatives have a higher 90-minute TIMI-III flow rate, but similar 30-day mortality benefit to rtPA.

- An rtPA derivative should be considered for any patient with
    - Large anterior MI especially if within 4 hours of onset
    - Previous SK therapy or recent streptococcal infection
    - Hypotension (systolic BP <100mmHg)
    - Low risk of stroke (age <55 years, systolic BP <144mmHg).
    - Reinfarction during hospitalization where immediate PCI facilities are not available.

The characteristics of the major thrombolytic agents are given on P23.

Patients who gain greatest benefit from thrombolysis

- Anterior infarct
- Marked ST elevation
- Age >75 years
- Impaired LV function or LBBB, hypotensive
- Systolic BP <100mmHg
- Patients presenting within 1 hour of onset of pain

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STEMI: thrombolysis 2

Complications of thrombolysis

- Bleeding is seen in up to 10% of patients. Most are minor at sites of vascular puncture. Local pressure is sufficient but occasionally transfusion may be required. In extreme cases, SK may be reversed by tranexamic acid (10mg/kg slow iv infusion).
- Hypotension during the infusion is common with SK. Lay patient supine and slow/stop infusion until the blood pressure rises. Treatment with cautious (100â€“500ml) fluid challenges may be required especially in inferior/RV infarction. Hypotension is not an allergic reaction and does not warrant treatment as such.
- Allergic reactions are common with SK and include a low-grade fever, rash, nausea, headaches, and flushing. Give hydrocortisone 100mg iv with chlorpheniramine 10mg iv.
- Intracranial haemorrhage is seen in ~0.3% of patients treated with SK and ~0.6% of those with rt-PA.
- Reperfusion arrhythmias (most commonly a short, self-limiting run of idioventricular rhythm) may occur as the metabolites are washed out of the ischaemia tissue. See pp40â€“42 for management.
- Systemic embolization may occur from lysis of thrombus

within the left atrium, left ventricle, or aortic aneurysm.

Absolute contraindications to thrombolysis

- Active internal bleeding
- Suspected aortic dissection
- Recent head trauma and/or intracranial neoplasm
- Previous haemorrhagic stroke at any time
- Previous ischaemic stroke within the past 1 year
- Previous allergic reaction to fibrinolytic agent
- Trauma and/or surgery within past 2 weeks at risk of bleeding

Relative contraindications to thrombolysis

- Trauma and/or surgery more than 2 weeks previously
- Severe uncontrolled hypertension (BP >180/110) with/without treatment
- Non-haemorrhagic stroke over 1 year ago
- Known bleeding diathesis or current use of anticoagulation within therapeutic range (INR 2 or over)
- Significant liver or renal dysfunction
- Prolonged (>10 min) of cardiopulmonary resuscitation
- Prior exposure to SK (especially previous 6â€“9 months)
- Pregnancy or post partum
- Lumbar puncture within previous 1 month

- Menstrual bleeding or lactation
- History of chronic severe hypertension
- Noncompressible vascular punctures (e.g. subclavian central venous lines)

Doses and administration of thrombolytic agents

SK

- Give as 1.5 million units in 100ml normal saline iv over 1 hour
- There is no indication for routine heparinization after SK as there is no clear mortality benefit and there is a small increase in risk of haemorrhage

rtPA (alteplase)

- The GUSTO trial suggested that â€˜front-loadedâ€™ or accelerated rtPA is the most effective dosage regimen
- Give 15mg bolus iv then 0.75mg/kg over 30 minutes (not to exceed 50mg), then 0.5mg/kg over 60 minutes (not to exceed 35mg).
- This should be followed by iv heparin (see text)

Reteplase

- Give two iv bolus doses of 10 units 10 minutes apart

Tenecteplase

- Give as injection over 10 seconds at 30â€“50mg according to body weight (500â€“600Âµg/kg)
- Maximum dose is 50mg

APSAC (anistreplase)

- Give as an iv bolus of 30mg over 2â€–5 minutes

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STEMI: reperfusion by primary percutaneous coronary intervention (PCI)

Time is of the essence for reperfusion and each institution should have its recommended protocol. It is imperative that there are no delays in both the decision-making and implementation processes for reperfusion. If primary PCI is chosen one telephone call should ensure a rapid response.

Primary PCI

- Primary PCI is the current gold standard reperfusion strategy for treatment of STEMI.
- Primary PCI requires significant coordination between the emergency services, community hospitals, and invasive centres. It must only be performed if (1) a primary PCI programme is available and (2) the patient presents to an invasive centre and can undergo catheterization without delay.

Indications for primary PCI

- All patients with chest pain and ST-segment elevation or

new LBBB fulfil primary PCI criteria (compare with indications for thrombolysis).

- This will include a group of patients where ST-segment elevation may not fulfil thrombolysis criteria.
- In general patients in whom thrombolysis is contraindicated should be managed by primary PCI. Cases where there is significant risk of bleeding must be managed individually.

Outcome in primary PCI

- Data from over 10 large randomized trials demonstrate a superior outcome in patients with STEMI who are treated with primary PCI in comparison to thrombolysis.
- There is a significant short-term, as well as long-term reduction in mortality and major cardiac events (MACE) (death, non-fatal reinfarction, and non-fatal stroke) in STEMI patients treated with primary PCI. Furthermore, primary PCI patients have overall better LV function, a higher vessel patency rate, and less recurrent myocardial ischaemia.
- Multiple studies (including PRAGUE-2 and DANAMI-2) have also demonstrated that interhospital transportation for primary PCI (community hospital to invasive centre) is safe and primary PCI continues to remain superior to thrombolysis despite the time delays involved.

Complications

- These include bleeding from arterial puncture site, stroke, recurrent infarction, need for emergency CABG, and death, which are similar to high-risk PCI cases (~1%).
- The best results are obtained from high-volume centres with experience of primary PCI.

- Each primary PCI centre will have its own policy for management of cases including the use of LMWH/UFH, and anti-platelet agents

(e.g. IIb/IIIa). It is generally accepted that in the acute phase only the â€˜culpritâ€™ lesion(s)/vessel(s) will be treated. The pattern of disease in the remainder of the vessels will determine whether total revascularization should be performed on the person as an in-patient or as an elective case in the future.

- STEMI patients treated with primary PCI can be discharged safely within 72 hours of admission without the need for further risk stratification.
- Primary PCI is more cost effective in the long term with significant savings from fewer days in hospital, a lower need for readmission, and less heart failure.
- Post-discharge care, secondary prevention, and rehabilitation remain identical to other MI cases.

Rescue PCI

As an adjunct to thrombolysis, PCI should be reserved for patients who remain symptomatic post thrombolysis (failure to reperfuse) or develop cardiogenic shock (see P44). We recommend all patients who do not settle post thrombolysis (on-going symptoms and on-going ST-elevation with/without symptoms) should be discussed with the local cardiac centre for urgent catheterization and revascularization.

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Surgery for acute STEMI

Emergency surgical revascularization (CABG) cannot be widely applied to patients who suffer a MI outside of the hospital. CABG in uncomplicated STEMI patients after 6 hours from presentation is contraindicated secondary to significant haemorrhage into areas of infarction. Unstable patients have a very high peri-operative mortality.

CABG in the context of an acute STEMI is of value in the following situations

- Persistent or recurrent chest pain despite thrombolysis/primary PCI
- High-risk coronary anatomy on catheterization (LMS, LAD ostial disease)
- Complicated STEMI (acute MR, VSD)
- Patients who have undergone successful thrombolysis but with surgical coronary anatomy on catheterization
- Patients known to have surgical coronary anatomy on catheterization performed prior to admission with STEMI.

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STEMI: additional measures

- Low molecular weight and unfractionated heparin
  - UFH
    - There is no indication for â€˜routineâ€™ iv heparin following SK
    - iv heparin (4000U/max iv bolus followed by 1000U/h max adjusted for an aPTT ratio of 1.5â€“2.0 times control) should be used routinely following rt-PA and its derivatives for 24â€“48 hours.
  - LMWH
    - There are trial data for the use of LMWH and thrombolysis (e.g. enoxaparin 30mg iv bolus, then 1mg/kg sc q12h)
    - LMWH can be used at a prophylactic dose to prevent thromboembolic events in patients slow to mobilize as an alternative to UFH.
- Clopidogrel
  - Should be administered to all patients undergoing primary PCI (loading dose 300mg po followed by 75mg od)

- If coronary stents are deployed patient should remain on clopidogrel for at least 1 month for bare metal stents and 3 months for coated stents
- More data are required to see whether longer-term treatment may be of benefit following thrombolysis alone.

- Glycoprotein IIb/IIIa inhibitors
  - There are multiple on-going trials to evaluate their role in combination with thrombolysis and/or LMWH
  - Are recommended routinely in the context of STEMI patients treated with primary PCI. Lower doses of LMWH/UFH should be used (consult manufacturer's information sheet for individual agents)
  - They can also be used in the context of rescue PCI subsequent to failed thrombolysis although there is a greater risk of bleeding. Each case must be judged on its merits.
- Magnesium
  - Earlier trials giving Mg^{2+} before or with thrombolytics showed some benefit in mortality. ISIS-4 showed no benefit from the routine useof iv magnesium post MI. However Mg^{2+} was given late (6 hours) after thrombolysis by which time the protective effect of Mg^{2+} on reperfusion injury may have been lost. Trials are on-going
  - Current accepted role for Mg^{2+} is confined to Mg^{2+}-deplete patients and patients with reperfusion, supraventricular, and ventricular arrhythmias
  - Dose: 8mmol in 20ml 5% dextrose over 20 minutes followed by 65mmol in 100ml 5% dextrose over 24 hours (contraindications: serum Cr >300Âµmol/L, 3Â° AV block).

- Calcium antagonists
    - Best avoided, especially in the presence of LV impairment
    - Diltiazem and verapamil started after day 4â€“5 in post-MI patients with normal LV function have a small beneficial effect
    - Amlodipine is safe to be used in patients with poor LV post MI
    - Nifedipine has been shown to increase mortality and should be avoided.
- Digoxin
    - Has little role in management of an acute STEMI and heart failure complicating an acute MI
    - Can be used safely in management of arrhythmias and HR.

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Right ventricular (RV) infarction

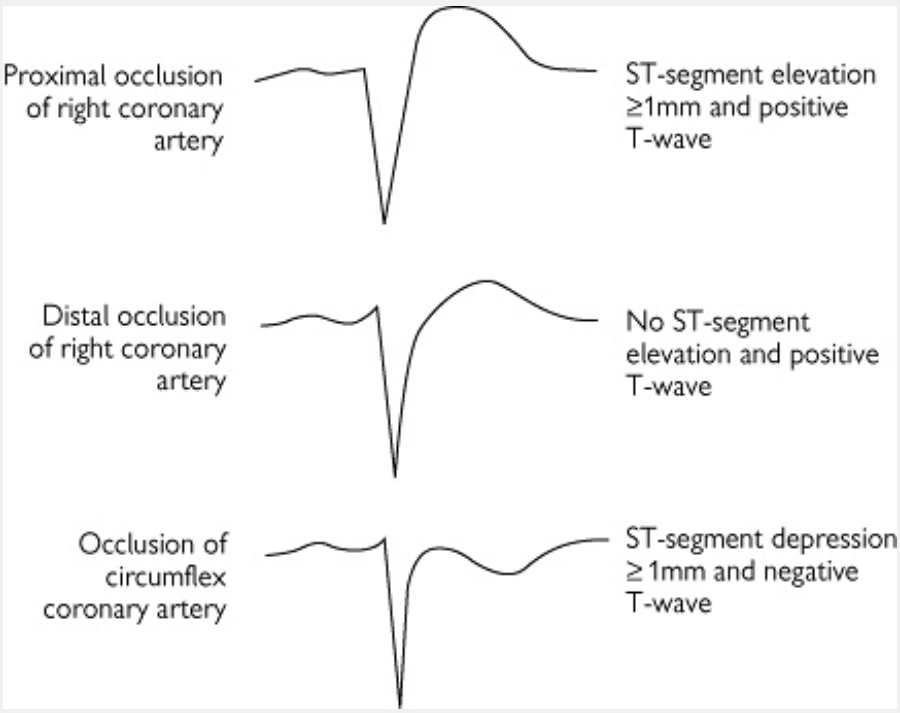
- RV infarction results in elevated right-sided pressures (RA, RVEDP) and low left-sided pressures (BP, CO).
- It is common in inferior STEMI.

Diagnosis

- Clinical: signs of right heart failure (â†‘JVP, Kussmaul's sign, pulsus paradoxus) with absence of pulmonary oedema in the context of a low output state (â†“BP, cold peripheries).
- ECG: in patients with inferior STEMI a 0.1mV (>1mm) ST-segment elevation in any one of leads V4Râ€“V6R is highly sensitive and specific for RV infarction. See figure for different ECG patterns identified in right-sided precordial leads. Changes may be transient and present in the early stages only.
- Echo: looking for RV dilation and wall-motion abnormalities.

Management

- Aim to maintain a high RV preload
    - Initially give 1â€“2L of colloid rapidly
    - Avoid use of nitrates and diuretics as they reduce pre-load and can worsen hypotension
    - In patients requiring pacing AV synchrony must be maintained to ensure maximal CO (atrial and ventricular wires)
    - Cardiovert any arrhythmias (SVT, AF/flutter, or ventricular rhythms).
- Reduce afterload
    - This is particularly important if there is concomitant LV dysfunction
    - Insert IABP
    - Arterial vasodilators (Na nitroprusside, hydralazine) or ACE inhibitors can be used with caution.
- Inotropic support should ideally be avoided and used only if all other measures fail to restore haemodynamic status.
- Reperfusion of the RCA (PCI and thrombolysis) has been demonstrated to improve RV function and reduce mortality.



ST elevation and T-wave configuration in lead V4R in inferoposterior AMI. Proximal occlusion of the RCA produces ST elevation â‰¥1mm and a positive T-wave. Distal occlusion is characterized by a positive T-wave but no ST elevation. Occlusion of the circumflex artery produces a negative T-wave and ST depression of at least 1mm.[1]

Footnote

1

Adapted from Wellens HJ (1999) *N Engl J Med* 340: 1383.

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STEMI: predischarge risk stratification

It is important to identify the subgroup of patients who have a high risk of re-infarction or sudden death. They should undergo coronary angiography with a view to revascularization prior to discharge (if not treated with primary PCI) and/or electrophysiological investigations as necessary.

Primary PCI group

- STEMI patients treated with primary PCI are at a much lower risk of developing post MI complications.
- There is on-going debate whether patients treated with primary PCI should have total revascularization as an in-patient or whether this can be achieved after functional testing on an out-patient basis. Follow your local policy.
- Patients who should have electrophysiological assessment prior to discharge are listed below.

Thrombolysis group

- Patients treated with thrombolysis should be risk stratified prior to discharge and high-risk patients should have in-patient (or early out-patient) angiography. High-risk

patients include those with

- Significant post-infarct angina or unstable angina
- Positive exercise test (modified Bruce protocol) with angina, >1mm ST depression or fall in BP
- Cardiomegaly on CXR, poor LV function on Echo (EF <40%)
- Documented episodes of regular VEs and VT 24 hours post infarction
- Frequent episodes of silent ischaemia on Holter monitoring.

Electrophysiological study

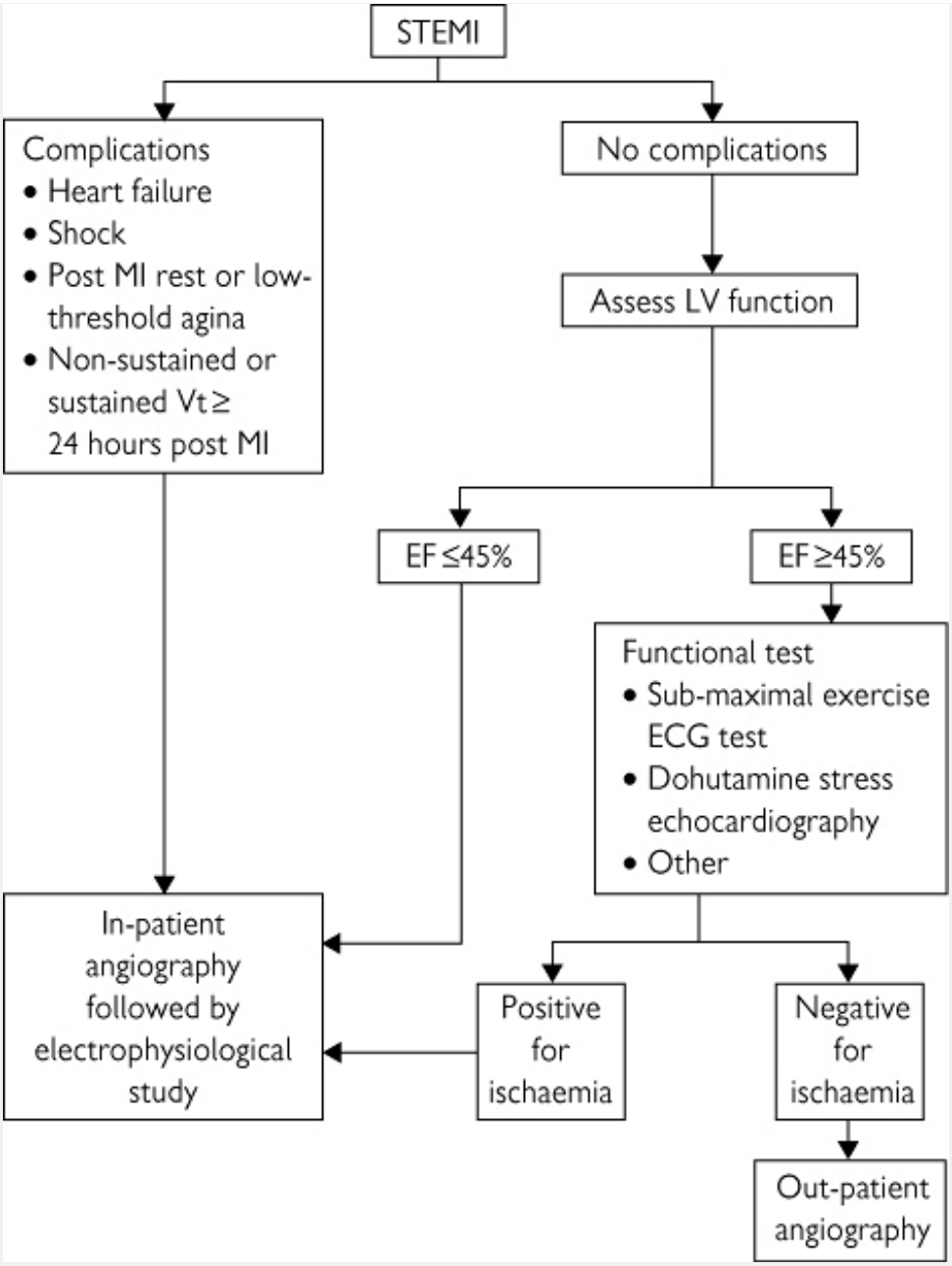
- All STEMI patients with (1) non-sustained VT and documented EF <40% or (2) sustained/pulseless VT/VF (regardless of EF) should undergo electrophysiological testing prior to discharge (MADIT and MUSTT trials) with a view to defibrillator implantation.

Discharge and secondary prevention

- Length of hospital stay in uncomplicated patients. The thrombolysis group need to undergo risk stratification prior to discharge and tend to have a mean hospital stay of 5â€“7 days. The primary PCI group have a shorter hospital stay between 3â€“4 days.
- Prior to discharge an agreed plan between patient (patient's family) and physician is necessary to address modifiable risk factors, beneficial medication, and rehabilitation programme.
- Modifiable risk factors include

- Management of lipids and use of statins
- Detection and treatment of diabetes
- Ensuring blood pressure is adequately controlled
- Counselling to discontinue smoking
- Advice on a healthy diet and weight loss.

- It is vital patients understand the medical regime and in particular the importance of long-term â€˜prognostic medicationâ€™. Unless there are contraindications all patients should be on a minimum of
  - Aspirin 75mg od (if true allergy, use clopidogrel 75mg od)
  - ACE inhibitor at the recommended dosage
  - Statin at the recommended dosage
  - The role of long-term formal anti-coagulation is controversial.
- All patients must be plugged into a rehabilitation programme.



Suggested strategy post STEMI in patients who have undergone thrombolysis to determine the need for in-patient angiography/EPS.[1]

Footnote

[1]Adapted from
Antman EM (2000) Cardiovascular Therapeutics 2nd edition.

Saunders, Philadelphia.

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STEMI: complications

Complications include

- Continuing chest pain
- Fever
- A new systolic murmur: VSD, acute MR, or pericarditis
- Dysrrhythmia (VT, AV block ectopics, and bradycardia)
- Pump failure: hypotension, cardiac failure, and cardiogenic shock.

Complications are encountered more commonly in patients post STEMI, but can also be found in NSTEMI patients (see next section). In NSTEMI patients complications are more common where multiple cardiac events have occurred.

Further chest pain

- Chest pain post MI is not necessarily angina. Careful history is needed to characterize pain. If there is doubt about the aetiology of pain in the absence of ECG changes stress/thallium imaging may aid diagnosis.
- A bruised sensation and musculoskeletal pains are common in the first 24â€“48 hours, especially in patients who have received CPR or repeated DC shock. Use topical agents for

skin burns.

- Recurrent infarction is an umbrella term including both extension of infarction in the original territory and repeated infarct in a second territory.
    - Usually associated with recurrent ST elevation
    - If cardiac enzymes not yet back to normal, a significant change is a two-fold rise above the previous nadir
    - Patients should ideally undergo immediate PCI. Thrombolysis is an alternative, but a less attractive approach. Standard thrombolysis criteria must be met (see P20). Bleeding is a risk (NB: SK should not be used on a second occasion).
- Post infarction angina (angina developing within 10 days of MI) should be treated with standard medical therapy. All patients with angina prior to discharge should undergo cardiac catheterizationand revascularization as an in-patient.
- Pericarditis presents as sharp, pleuritic, and positional chest pain, usually 1â€“3 days post infarct. It is more common with STEMI. A pericardial friction rub may be audible. ECG changes are rarely seen. Treat with high-dose aspirin (600mg qds po) covering with a proton pump inhibitor (e.g. lansoprazole 30mg od po). Other NSAIDs have been associated with higher incidence of LV rupture and increased coronary vascular resistance and are probably best avoided.
- Pericardial effusion is more common with anterior MI especially if complicated by cardiac failure. Tamponade is rare and the result of ventricular rupture and/or haemorrhagic effusions. Detection is with a combination of clinical features and echocardiography. Most resolve gradually over a few months with no active intervention.
- Pulmonary thromboembolism can occur in patients with

heart failure and prolonged bed rest. Routine use of prophylactic LMWH and UFH combined with early mobilization have reduced incidence of PE. Sources include lower limb veins and/or RV (see P146).

Fever

- Often seen and peaks 3â€“4 days post MI
- Associated with elevated WCC and raised CRP
- Other causes of fever should be considered (infection, thrombophlebitis, venous thrombosis, drug reaction, pericarditis).

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Ventricular septal defect post myocardial infarction (MI)

- Classically seen 24 hours (highest risk) to 10 days post MI and affects 2â€“4% of cases.
- Clinical features include rapid deterioration with a harsh pan-systolic murmur (maximal at the lower left sternal edge), poor perfusion, and pulmonary oedema. The absence of a murmur in the context of a low output state does not rule out a VSD.

Diagnosis

- Echocardiography: the defect may be visualized on 2D-Echo and colour flow Doppler shows the presence of left-to-right shunt. Anterior infarction is associated with apical VSD and inferior MI with basal VSD. Failure to demonstrate a shunt on Echo does not exclude a VSD.
- PA catheter (especially in absence of Echo or inconclusive Echo results): a step-up in oxygen saturation from RA to RV confirms the presence of a shunt, which may be calculated by

$$Qp:Qs = \frac{(\text{Art sat} - \text{RA sat})}{(\text{Art sat} - \text{PA sat})} \quad \text{where} \quad \begin{array}{l} Qp = \text{pulmonary blood flow} \\ Qs = \text{systemic blood flow} \end{array}$$

Management

Stabalization measures are all temporizing until definitive repair can take place. Hypotension (see P42) and pulmonary oedema (P112) should be managed as described elsewhere. Important principles are given below.

- Invasive monitoring (PA catheter and arterial line) to dictate haemodynamic management. RA and PCWP dictate fluid administration or diuretic use. Cardiac output, mean arterial pressure, and arterial resistance determine the need for vasodilator therapy.
- If SBP >100mmHg, cautious use of vasodilator therapy, generally with nitroprusside, will lower the systemic vascular resistance and reduce the magnitude of the shunt. Nitrates will cause venodilatation and increase the shunt and should be avoided. Not be used with renal impairment.
- Inotropes if severely hypotensive (initially dobutamine but adrenaline may be required depending on haemodynamic response). Increasing systemic pressure will worsen shunt.
- In most cases intra-aortic balloon should be inserted rapidly for counter pulsation.
- Liaise with surgeons early for possible repair. Operative mortality is high (20â€“70%) especially in the context of peri-operative shock, infero-posterior MI, and RV infarction. Current recommendations are for high-risk early surgical repair combined with CABG Â± MV repair/replacement.
- If patient has been weaned off pharmacological and/or mechanical support it may be possible to postpone surgery for 2â€“4 weeks to allow for some level of infarct healing.

- Patients should ideally undergo catheterization prior to surgical repair to ensure culprit vessel(s) are grafted.
- Closure of the VSD with catheter placement of an umbrella-shaped device has been reported to stabilize critically ill patients until definitive repair is possible.

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Acute mitral regurgitation post MI

- MR due to ischaemic papillary muscle dysfunction or partial rupture is seen 2â€“10 days post MI. Complete rupture causes torrential MR and is usually fatal.
- More commonly associated with inferior MI (postero-medial papillary muscle) than anterior MI (anterolateral papillary muscle).
- â€˜Silent MRâ€™ is quite frequent and must be suspected in any post MI patient with unexplained haemodynamic deterioration.
- Diagnosis is by Echo. In severe MR, PA catheterization will show a raised pressure with a large *v* wave.

Management (P140)

- Treatment with vasodilators, generally nitroprusside, should be started as early as possible once haemodynamic monitoring is available.
- Mechanical ventilation may be necessary.
- Liaise with surgeons early for possible repair.

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Pseudoaneurysm and free wall rupture

- Demonstrated in up to 6% of STEMI patients and leads to sudden death in two-thirds.
- A proportion present sub-acutely with cardiogenic shock allowing time for intervention.
- Diagnosis of sub-acute cases can be made on a combination of clinical features of pericardial effusion, tamponade, and Echo.
- Patients who have undergone early thrombolysis have a lower chance of wall rupture.
- Stabilization of the patient follows similar lines to cardiogenic shock (P44). Case must be discussed with surgeons immediately with view to repair.

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Cocaine-induced MI

- The incidence of cocaine-induced MI, LV dysfunction, and arrhythmias are on the increase.
- It has been estimated that 14â€“25% of young patients presenting to urban emergency departments with non-traumatic chest pain may have detectable levels of cocaine and its metabolites in their circulation. Of this group 6% have enzymatic evidence of MI (figures are from the USA).
- Most patients are young, non-white, male cigarette smokers without other risk factors for ischaemic heart disease.

Diagnosis

- Can be difficult and must be suspected in any young individual with chest discomfort at low-risk of developing ischaemic heart disease.
- Chest pain occurs most commonly within 12 hours of cocaine use. Effects can return up to 24â€“36 hours later secondary to long-lasting active metabolites.
- ECG is abnormal with multiple non-specific repolarization changes in up to 80% of cases and approximately 40% may have diagnostic changes of STEMI qualifying for reperfusion therapy (see P14).
- Biochemical markers of cardiac injury can be

misleading, as most patients will have elevated CK levels secondary to rhabdomyolysis. TnT and TnI are vital to confirm myocardial injury.

Management

- General measures
    - These are the same as for anyone presenting with an MI. Oxygen: high-flow 5â€“10L unless there is a contraindication; analgesia; aspirin 75mg od
    - GTN: to be given at high doses as iv infusion (>10mg/h final levels) and dose titrated to symptoms and haemodynamic response (see STEMI)
    - Benzodiazepines: to reduce anxiety.
- Second-line agents
    - Verapamil is given in high doses and has the dual function of reducing cardiac workload, hence restoring oxygen supply and demand, as well as reversing coronary vasoconstriction. Should be given cautiously as 1â€“2mg iv bolus at a time (up to 10mg total) with continuous haemodynamic monitoring. This should be followed by a high-dose oral preparation to cover the 24-hour period for at least 72 hours post last dose of cocaine (80â€“120mg po tds).
    - Phentolamine is an Î±-adrenergic antagonist and readily reverses cocaine-induced vasoconstriction (2â€“5mg iv and repeated if necessary). It can be used in conjunction with verapamil.
    - Labetalol has both Î±- and Î²-adrenergic activity and can be used after verapamil and phentolamine if patient remains hypertensive. It is effective in lowering cocaine-induced hypertension, but has no effect on

coronary vasoconstriction.

- Reperfusion therapy evidence for use of thrombolysis is limited and generally associated with poor outcome secondary to

hypertension-induced haemorrhagic complications. If patient fails to settle after implementing first-line measures, verapamil, and phentolamine they should undergo immediate coronary angiography followed by PCI if appropriate (evidence of thrombus/vessel occlusion). In the event that angiography is not available thrombolytic therapy can be considered.

- *Caution*: Î²-blockers must be avoided (e.g. propranolol). They exacerbate coronary vasoconstriction by allowing unopposed action of the Î±-adrenergic receptors.

Cocaine-induced MI

Pathogenesis

- The cause of myocardial injury is multifactorial including an increase in oxygen demand (â†‘HR, â†‘BP, â†‘contractility) in the context of decrease in supply caused by a combination of inappropriate vasoconstriction (in areas of minor atheroma), enhanced platelet aggregation, and thrombus formation
- The effects can be delayed as the metabolites of cocaine are potent active vasoconstrictors and can remain in the circulation for up to 36 hours (or longer) resulting in a recurrent wave of symptoms

Other complications

- Cocaine-induced myocardial dysfunction is multifactorial and includes MI, chronic damage secondary to repetitive sympathetic stimulation (as in pheochromocytoma), myocarditis secondary to cocaine impurities/infection, and unfavourable changes in myocardial/endothelial gene expression
- Cocaine-induced dysrrhythmias include both atrial and ventricular tachyarrhythmias, as well as asystole and heart block [see post-MI arrhythmias (P40) and cardiopulmonary resuscitation (P4)]
- Aortic dissection (see P170)

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Ventricular tachyarrhythmia post MI

- Accelerated idioventricular rhythm
  - Common (up to 20%) in patients with early reperfusion in first 48 hours.
  - Usually self limiting and short lasting with no haemodynamic effects
  - If symptomatic, accelerating sinus rate with atrial pacing or atropine may be of value. Suppressive anti-arrhythmic therapy (lignocaine, amiodarone) is only recommended with degeneration into malignant ventricular tachyarrhythmias.
- VPB
  - Common and not related to incidence of sustained VT/VF
  - Generally treated conservatively. Aim to correct acid-base and electrolyte abnormalities (aim K^+ >4.0mmol/L and Mg^{2+} >1.0mmol/L)
  - Peri-infarction Î²-blockade reduces VPB.
- Non-sustained and monomorphic VT
  - Associated with a worse clinical outcome

- Correct reversible features such as electrolyte abnormalities and acid-base balance
- DC cardioversion for haemodynamic instability
- Non-sustained VT and haemodynamically stable VT (slow HR <100bpm) can be treated with amiodarone (300mg bolus iv over 30 minutes, followed by 1.2g infusion over 24 hours). Lignocaine is no longer recommended as fist line. Procainamide is an effective alternative, but is arrhythmogenic
- For incessant VT on amiodarone consider overdrive pacing.

- Ventricular fibrillation and polymorphic VT
  - *A medical emergency* and requires immediate defibrillation
  - In refractory VF consider vasopressin 40U iv bolus
  - Amiodarone 300mg iv bolus to be continued as an infusion (see above) if output restored.

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Atrial tachyarrhythmia post MI

- Includes SVT, AF, and atrial flutter
- If patient is haemodynamically unstable must undergo immediate synchronized DC cardioversion
- Haemodynamically stable patients can be treated with digoxin, Î²-blockers, and/or calcium channel blockers (see P82)
- Amiodarone can be used to restore sinus rhythm. However, it is not very effective in controlling rate. Class I agents should generally be avoided as they increase mortality
- In AF and flutter patients should undergo anti-coagulation to reduce embolic complications if there are no contraindications.

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Bradyarrhythmias and indications for pacing

Alternating or isolated RBBB/LBBB do not need pacing (unless haemodynamically unstable or progression to higher levels of block). New bifasicular block (RBBB with either LAD or RAD) or BBB with first-degree AV block may require prophylactic pacing depending on the clinical picture. Indications for pacing should not delay reperfusion therapy. Venous access (femoral or internal jugular vein) should be obtained first and pacing wire inserted later. External temporary cardiac pacing, atropine (300Âµg to 3mg iv bolus), and isoprenaline can be used to buy time.

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Bradyarrhythmias post MI

- First-degree AV block
  - Common and no treatment required
  - Significant PR prolongation (>0.20s) is a contraindication to Î²-blockade.
- Second-degree AV block

  This indicates a large infarction affecting conducting systems and mortality is generally increased in this group of patients
  - Mobitz type I is self-limiting with no symptoms. Generally, requires no specific treatment. If symptomatic or progression to complete heart block will need temporary pacing
  - Mobitz type II, 2 : 1, 3 : 1 should be treated with temporary pacing regardless of whether it progresses to complete heart block.
- Third-degree AV block
  - In the context of an inferior MI can be transient and does not require temporary pacing unless there is haemodynamic instability or an escape rhythm of <40bpm

- Temporary pacing is required with anterior MI and unstable inferior MI.

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Hypotension and shock post MI

(See cardiogenic shock P44).

The important principles in managing hypotensive patients with myocardial infarction are

- If the patient is well perfused peripherally, no pharmacological intervention is required. Consider lying the patient flat with legs elevated if necessary, provided there is no pulmonary oedema
- Try to correct any arrhythmia, hypoxia, or acidosis
- Arrange for an urgent Echo to exclude a mechanical cause for hypotension (e.g. mitral regurgitation, VSD, ventricular aneurysm) that may require urgent surgery.

Patients may be divided into two sub-groups

- Hypotension with pulmonary oedema (also see P108)
    - Secure central venous access: internal jugular lines are preferable if the patient may have received thrombolytic therapy.

- Commence inotropes (see P44, cardiogenic shock).
- Further invasive haemodynamic monitoring as available (PA pressures and wedge pressure monitoring, arterial line).
- Ensure optimal filling pressures, guided by physical signs and PA diastolic or wedge pressure. Significant mitral regurgitation will produce large *v* waves on the wedge trace and give spuriously high estimates of LVEDP.
- Ensure rapid coronary reperfusion (if not already done), either with thrombolytic therapy or primary PCI where available.
- Intra-aortic balloon counter pulsation (see P898) may allow stabilization until PCI can be performed.

- Hypotension without pulmonary oedema

  This may be due either to RV infarction or hypovolaemia.

Diagnosis

- Check the JVP and right atrial pressure. This will be low in hypovolaemia and high in RV infarction.
- RV infarction on ECG is seen in the setting of inferior MI and ST elevation in right-sided chest leads (V3Râ€“V4R).

Management

- In either case cardiac output will be improved by cautious plasma expansion. Give 100â€“200ml of colloid over 10 minutes and reassess.
- Repeat once if there is some improvement in blood pressure and the patient has not developed pulmonary oedema.
- Invasive haemodynamic monitoring with a PA catheter

(Swanâ€“Ganz) is necessary to ensure hypotension is not due to low left-sided filling pressures. Aim to keep PCWP 12â€“15mmHg.

- Start inotropes if blood pressure remains low despite adequate filling pressures.
- Use iv nitrates and diuretics with caution as venodilatation will compromise RV and LV filling and exacerbate hypotension.
- See P28 for management of RV infarction.

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Cardiogenic shock

- Effects between 5â€“20% of patients and up to 15% of MI patients can present with cardiogenic shock.
- Management involves a complex interaction between many medical, surgical, and intensive care teams with multiple invasive and non-invasive measures. Despite significant advances prognosis remains poor. Therefore, the absolute wishes of the patient with regard to such an invasive strategy should be respected from the outset.

Diagnosis

A combination of clinical and physiological measures:

- *Clinical*: marked, persistent (>30min) hypotension with SBP <80â€“90mmHg.
- *Physiological*: low cardiac index (<1.8L/mm/m^2) with elevated LV filling pressure (PCWP >18mmHg).

Management

- Complex and must be quick.
- Correct reversible factors including

    - Arrhythmias and aim to restore sinus rhythm
    - Acidâ€“base, electrolyte abnormalities
    - Ventilation abnormalities: intubate if necessary.
- Rapid haemodynamic, echocardiographic, and angiographic evaluation
    - Haemodynamic: to ensure adequate monitoring and access including central venous lines, Swanâ€“Ganz, arterial line insertion, urinary catheter
    - Echocardiographic: to assess ventricular systolic function and exclude mechanical lesions, which may need to be dealt with by emergency cardiac surgery including mitral regurgitation (NB: tall *v* waves on PCWP trace), VSD, and ventricular aneurysm/psuedoanuerysm
    - Angiographic: with a view to PCI or CABG if appropriate.
- Aim to improve haemodynamic status achieving a SBP â‰¥90mmHg guided by physical signs and LV filling pressures. As a general guide:
    - PCWP <15 mmHg: cautious of iv fluids (colloids) in 100â€“200ml aliquots
    - PCWP >15 mmHg: inotropic support Â± diuretics (if pulmonary oedema).
- Inotropes should be avoided if at all possible in acutely ischaemic patients. The aim should be to rapidly restore/maximize coronary flow and off-load LV. Early revascularization is vital and has been shown to decrease mortality. IABP will partially help achieve aforementioned goals.
- If haemodynamic status does not improve post revascularization and IABP insertion, inotropes should be

used. Choice of agent can be

difficult and should partly be guided by local protocols and expertise. Generally accepted choices depend on the clinical picture and include

- If patient is hypotensive (Â± pulmonary oedema): start with dopamine (up to 15Âµg/kg/min) and if ineffective substitute with epinephrine and/or norepinephrine
- If patient has adequate blood pressure (Â± pulmonary oedema): dobutamine to increase cardiac output (starting at 2.5â€“5Âµg/kg/min and increasing to 20Âµg/kg/min) titrating to HR and haemodynamics. Phosphodiesterase inhibitors can be used as an alternative. If hypotension and tachycardia complicate dobutamine/PDI inhibitor treatment, (nor)epinephrine can be added as a second agent to achieve desired haemodynamic effect.

- Use of diuretics, thrombolysis, GP IIb/IIIa antagonists, and LMWH/UFH should follow normal principles and be based on the clinical picture.

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Non-ST elevation myocardial infarction (NSTEMI)/unstable angina (UA)

UA and NSTEMI are closely related conditions with similar clinical presentation, treatment, and pathogenesis but of varying severity. If there is biochemical evidence of myocardial damage the condition is termed NSTEMI and in the absence of damage, UA.

Unlike patients with a STEMI where diagnosis is generally made on presentation in the emergency department, diagnosis of NSTEMI/UA may not be definitive on presentation and evolves over the subsequent hours to days. Therefore, management of patients with NSTEMI/UA is a progression through a number of risk-stratification processes dependent on history, clinical features, and investigative results, which in turn determine choice and timing of a number of medical and/or invasive treatment strategies.

The figure opposite is a summary of a recommended *integrated care pathway* illustrating a management plan for diagnosis and risk-directed treatment of a patient with STEMI/UA.

Clinical presentation

There are 3 distinct presentations

- Rest angina (angina when patient is at rest)
- New-onset severe angina
- Increasing angina (previously diagnosed angina which has become more frequent, longer in duration, or lower in threshold).

General examination (as indicated for all ACS (see P10) must be undertaken in particular to rule out pulmonary oedema, and assess haemodynamic stability, cardiac valve abnormalities, and diaphoresis.

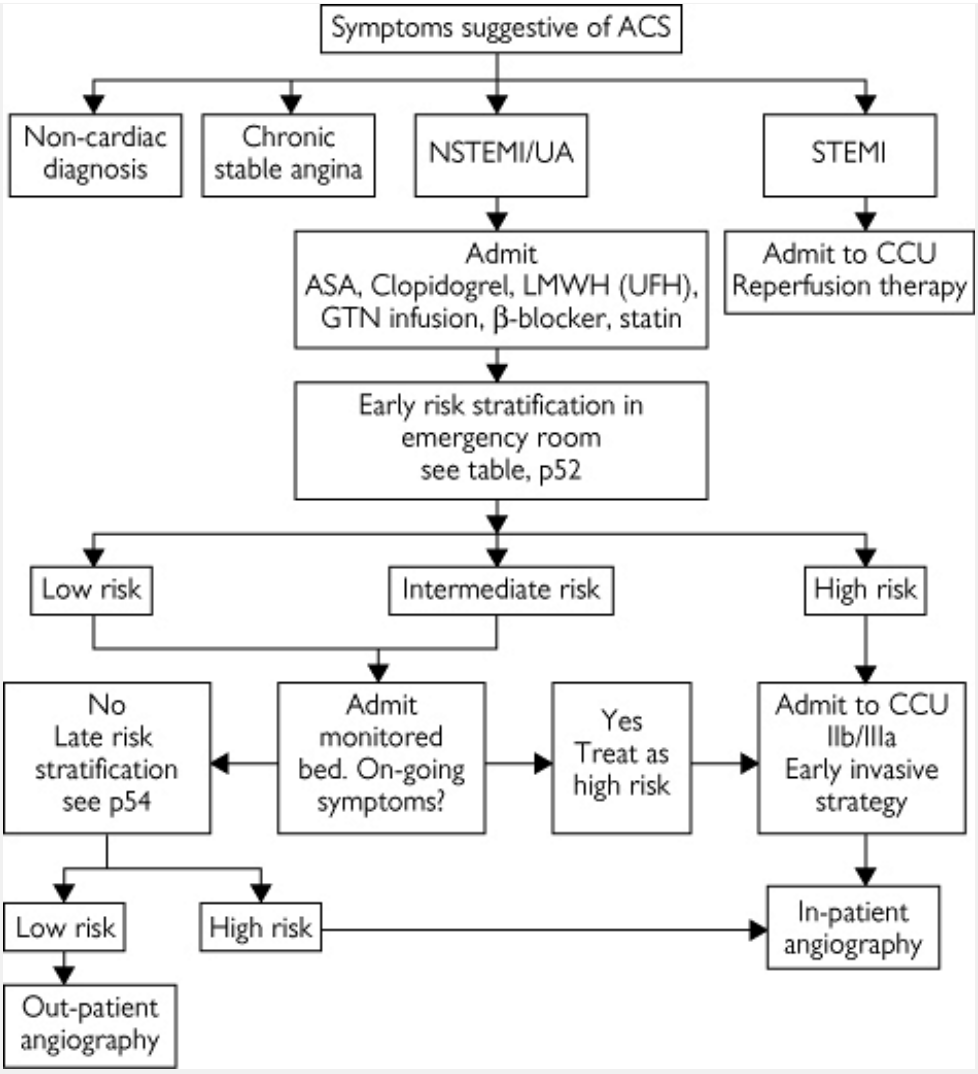
Integrated management plan

We recommend that all patients follow a local integrated care pathway on presentation. The various stages are broadly outlined below. See relevant pages for further information.

- Initial stabilization (see also ACS P10)
    - Transfer patient to area with continuous ECG monitoring and defibrillator facility
    - Strict bed rest
    - Give oxygen, aspirin 300mg po, SL nitrate and mild sedation if required
    - If pain persists give diamorphine 2.5â€“5mg iv prn with metoclopramide 10mg iv.
- General investigations: similar to STEMI patients (see P12â€“17) including blood for FBC, biochemical profile and markers of myocardial injury, lipid profile, as well as CRP and TFT (if persistent tachycardia). Arrange portable CXR (rule out LVF, mediastinal abnormalities).
- Confirm diagnosis (see P48).
- Risk stratification (see P50) in order to determine appropriate medical and invasive treatment strategies.

High-risk patients should be admitted to CCU and low/intermediate patients to monitored beds in step-down unit.

- Treatment is based on patient's risk and includes
  - Medical Strategies
    - anti-ischaemic (P56)
    - antiplatelet (P58)
    - anti-thrombic (P58)
  - Invasive strategies (P60).
- Secondary prevention and discharge.



NSTEMI/UAâ€”integrated care pathway

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NSTEMI/UA: diagnosis

Diagnosis in NSTEMI/UA is an evolving process and may not be clear on presentation. *A combination of history, serial changes in ECG, and biochemical markers of myocardial injury* (usually over a 24â€“48 hour period) *determine the diagnosis*. Once a patient has been designated a diagnosis of ACS with probable/possible NSTEMI/UA they will require the following.

- Serial ECGs: changes can be transient and/or fixed especially if a diagnosis of NSTEMI is made. See P15 for localization of ischaemic areas.
    - ST-segment depression of â‰¥0.05mV is highly specific of myocardial ischaemia (unless isolated in V1â€“V3 suggesting a posterior STEMI).
    - T-wave inversion is sensitive but non-specific for acute ischaemia unless very deep (â‰¥0.3mV).
    - Rarely Q-waves may evolve or there may be transient/new LBBB.
- Serial biochemical markers of cardiac injury are used to differentiate between NSTEMI and UA, as well as determine prognosis. We recommend levels at 6, 12, 24, and 48 hours after last episode of pain. A positive biochemical marker (CK, CK-MB, or troponin) in the context of one or more of the aforementioned ECG changes is diagnostic of NSTEMI. If

serial markers over a 24â€“72 hour period from the last episode of chest pain remain negative, UA is diagnozed.

- Cardiac troponin T and I: are both are highly cardiac specific and sensitive, can detect â€˜microinfarctionâ€™ in the presence of normal CK-MB, are not affected by skeletal muscle injury, and convey prognostic information (worse prognosis if positive). Troponins can be raised in non-atherosclerotic myocardial damage (cardiomyopathy, myocarditis, pericarditis) and should therefore be interpreted in the context of the clinical picture. Both TnT and TnI rise within 3 hours of infarction. TnT may persist up to 10â€“14 days and TnI up to 7â€“10 days. Results must be interpreted with caution in patients with chronic renal failure. See figure on P17.
- CK levels do not always reach the diagnostic twice upper limit of normal and generally have little value in diagnosis of NSTEMI.
- CK-MB has low sensitivity and specificity CK-MB isoforms improve sensitivity (CK-MB2 >1U/L or CK-MB2/CK-MB1 ratio >1.5), but isoform assays are not widely available clinically.
- Myoglobin is non-cardiac specific, but levels can be detected as early as 2 hours after onset of symptoms. A negative test is useful in ruling out myocardial necrosis.

- Continuous ECG monitoring can detect episodes of silent ischaemia and arrhythmia. Both have been shown to be more prolonged in NSTEMI than in UA.

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NSTEMI/UA: risk stratification

NSTEMI/UA are a heterogeneous group of conditions with variable outcomes. An assessment of risk for adverse outcome is vital to ensure formation of an adequate management plan.

Risk stratification should begin on initial evaluation and continue throughout the hospital stay . At each stage patients with a high chance of a poor outcome should be identified and managed appropriately.

We recommend at least two formal risk-stratification processes.

- Early risk stratification (see table, P52): this should take place on presentation and forms part of the initial assessment used to make a diagnosis. It involves a combination of clinical features, ECG changes, and biochemical markers of cardiac injury as demonstrated on P52 . Patients are divided into high risk and intermediate/low risk.
    - High-risk patients should be *admitted to CCU, follow an early invasive strategy* , and be managed with a combination of
        - ASA, clopidogrel, LMWH (UFH), IIb/IIIa
        - Anti-ischaemic therapy (first-line Î²-blocker, GTN)
        - Early invasive strategy (in-patient catheterization

and PCI within 48 hours of admission).

- Intermediate/low-risk patients should be admitted to *a monitored bed on a step-down unit* and *undergo a second in-patient risk stratification* once their symptoms have settled to determine timing of invasive investigations. Initial management should include

  - ASA, clopidogrel, LMWH (UFH)
  - Anti-ischaemic therapy (first-line Î²-blocker, GTN)
  - Undergoing a *late risk stratification in 48â€“72 hours* from admission.

- Late risk stratification : (P54) involves a number of non-invasive tests to determine the optimal timing for invasive investigations in intermediate/low-risk patients. Suggested guidelines are summarized on P54 . It is generally performed if there have been no further episodes of pain/ischaemia at 24â€“48 hours after admission.

  - Intermediate/low-risk patients who develop recurrent pain and/or ischaemic ECG changes at any point during their admission, heart failure, or haemodynamic instability in the absence of a non-cardiac cause should be managed as a high-risk patient (IIb/IIIa and early invasive strategy).
  - The figure on P47 is a summary of a recommended integrated care pathway combining diagnosis, risk stratification, and treatment.
  - There are other risk-stratification assessment scores including Braunwald and TIMI. As recommended above, high-risk patients from these assessments should also follow an early invasive strategy and intermediate/low-risk patients a more conservative strategy.

History
Accelerating tempo of ischaemic symptoms in preceding 48 hours
Prior MI , peripheral or cerebrovascular disease, or CABG , prior aspirin use

Character of pain
Prolonged ongoing (> 20 minutes) rest pain
Prolonged (>20 minutes) rest angina, now resolved, with moderate or high likelihood of CAD
New-onset or progressive CCS Class III or IV angina the past 2 weeks without prolonged (>20 minutes) rest pain but with moderate or high likelihood of CAD
Rest angina (<20 minutes) or relieved with rest or sublingual NTG
Clinical findings
Pulmonary oedema, most likely due to ischaemia
Age>70 years
New or worsening MR murmur S_3 or new/worsening rales
Hypotension, bradycardia, tachycardia
Age >75 years
ECG
Angina at rest with transient
T-wave inversions >0.2mV
Normal or unchanged ECG during an episode of chest discomfort
ST-segment changes >0.05mV
Pathological Q-waves
Bundle-branch block, new or presumed new
Sustained ventricular tachycardia
Cardiac markers
Elevated (e.g. TnT or TnI >0.1ng/mL)
Slightly elevated (e.g. TnT >0.01 but <0.1ng/mL)
Normal
[1] Adapted from American College of Cardiology Practice Guidelines.

Feature	High risk (At least 1 of the following features must be present)	Intermediate risk (No high-risk feature but must have 1 of the following)	Low risk (No high- or intermediate-risk feature but may have any of the following features)
Short-term risk of death non-fatal MI in patients with UA[1]			

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NSTEMI/UA: late risk stratification

The highest risk of adverse outcome in patients who are designated as intermediate/low risk on presentation is during the early phase of admission. Therefore, it is important that the second risk-stratification process occurs within 24â€“48 hours of admission if the patient is stable.

Late risk stratification is based on one of the following non-invasive investigations.

A patient is regarded as being at high risk of adverse outcome if they fulfil one of the features listed below. These patients should have in-patient cardiac catheterization.

- Exercise ECG test
    - Horizontal/down-sloping ST depression with
    - Onset at HR <120bpm or <6.5 METS
    - Magnitude of >2.0mm
    - Post-exercise duration of changes >6 minutes
    - Depression in multiple leads reflecting multiple coronary distributions.
- Abnormal systolic BP response

    - Sustained decrease of >10mmHg or flat BP response with abnormal ECG.
- Other
    - Exercise induced ST-segment elevation
    - VT
    - Prolonged elevation of HR.
- 2 Stress radionuclide myocardial perfusion imaging
    - Abnormal tracer distribution in more than one territory
    - Cardiac enlargement.
- 3 LV imaging
- Stress echocardiography
    - Rest EF <35%
    - Wall motion score index >1.
- Stress radionuclide ventriculography
    - Rest EF <35%
    - Fall in EF >10%.

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NSTEMI/UA: medical management 1

Anti-ischaemic therapy

All patients should be treated with a combination of the below agents to ensure adequate symptom control and a favourable haemodynamic status (SBP â‰ˆ 100â€“110mmHg, PR â‰ˆ 60). *All patients should be treated with adequate analgesia, iv nitrates, Î²-blockers, and statins* (if no contraindications). Other agents can also be added depending on the clinical picture.

- Analgesia: diamorphine 2.5â€“5mg iv (with metoclopramide 10mg iv). Acts as anxiolytic. Reduces pain and systolic blood pressure through venodilatation and reduction in sympathetic arteriolar constriction. Can result in hypotension (responsive to volume therapy) and respiratory depression (reversal with naloxone 400Âµg to 2mg iv).
- Nitrates: GTN infusion (50mg in 50ml nitrate saline at 1â€“10ml/h) titrated to pain and keeping SBP >100mmHg. Tolerance to continuous infusion develops within 24 hours and the lowest efficacious dose should be used. Common side-effects are headache and hypotension, both of which are reversible on withdrawal of medication. *Absolute contraindication* is use of sildenafil (Viagra) in the previous

24 hours. This can result in exaggerated and prolonged hypotension.

- Î²-blockers: should be started on presentation. Initially use a short-acting agent (e.g. metoprolol 12.5â€“100mg po tds), which if tolerated, may be converted to a longer-acting agent (e.g. atenolol 25â€“1000mg od). Rapid Î²-blockade may be achieved using short-acting iv agents such as metoprolol (see Î²-blockade for STEMI). Aim for HR of ~50â€“60bpm. Mild LVF is not an absolute contraindication to Î²-blocker therapy. Pulmonary congestion may be secondary to ischaemic LV systolic dysfunction and/or reduced compliance. If there is overt heart failure Î²-blockade is contraindicated and a calcium antagonist (amlodipine 5â€“10mg od) can be used. By reducing heart rate and blood pressure, Î²-blockers reduce myocardial oxygen demand and thus angina. When either used alone or in combination with nitrates and/or calcium antagonists, Î²-blockers are effective in reducing the frequency and duration of both symptomatic and silent ischaemic episodes.
- Calcium antagonists: diltiazem 60â€“360mg po, verapamil 40â€“120mg po tds. Their use aims to reduce HR and BP and is a useful adjunct to treatments 1â€“3 above. Amlodipine/felodipine 5â€“10mg po od can be used with pulmonary oedema and in poor LV function. Calcium antagonists alone do not appear to reduce mortality or risk of MI in patients with UA. However when combined with nitrates and/or Î²-blockers they are effective in reducing symptomatic and silent ischaemic episodes, non-fatal MI, and the need for revascularization.
- Statins (HMG-CoA reductase inhibitors): high-dose statins (atorvastatin 80mg od) have been shown to reduce mortality and recurrent MI in the acute setting. The role of statins in primary and secondary prevention of culture cardiovascular events is well documented.

- ACE inhibitors: unlike patients with STEMI where early introduction of an ACE inhibitor has significant prognostic benefits, specific trails in the NSTEMI/UA setting are lacking. However, there is good evidence that both patients with low and high risk of cardiovascular disease will benefit from long-term ACE inhibition (HOPE and EUROPA Trials).

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NSTEMI/UA: medical management 2

Anti-platelet therapy

All patients should be given aspirin and clopidogrel (unless contraindications). IIb/IIIa antagonists to high-risk patients only.

- Aspirin (75â€“300mg po) should be administered immediately in the emergency department and continued indefinitely (unless contraindications). It has been shown to consistently reduce mortality and recurrent ischaemic events in many trials. In patients with aspirin hypersensitivity or major gastrointestinal intolerance clopidogrel 75mg od should be used.
- Thienopyidines. Clopidogrel (75mg od) should be given on admission to all patients with proven NSTEMI/UA, regardless of risk and be continued for at least 1 month, ideally for 9 months. Clopidogrel should be withheld in patients requiring CABG for 5â€“7 days to reduce haemorrhagic complications. Clopidogrel is preferred over ticlopidine because of its rapid onset of action and better safety profile.
- Glycoprotein IIb/IIIa antagonists. There are multiple short- and long-acting commercially available molecules. These agents should be used in conjunction with aspirin,

clopidogrel, and LMWH (or UFH). Eptifibatide and tirofiban should be used in high-risk patients with on-going ischaemia and elevated troponin in whom an early invasive management strategy is not planned/available (<24 hours). In patients with an early invasive strategy all IIb/IIIa antagonists can be used. Infusion is generally continued for 12 hours post PCI. Taken as a group these agents protect NSTEMI/UA patients from death and non-fatal MI during the acute phase of their presentation and 24 hours post intervention. See table for doses and administration regime.

Anti-thrombotic therapy

All patients should be given a LMWH (UFH).

- LMWHs have been shown to be as good as or superior to UFH in short-term reduction of death, MI, and revascularization in patients with NSTEMI/UA. They should be used in conjunction with aspirin and clopidogrel in all patients on presentation and be continued for 2â€“5 days after the last episode of pain and ischaemic ECG changes. Other advantages over UFH include subcutaneous administration, lack of monitoring, and reduced resistance and thrombocytopaenia. The table opposite lists the doses of various agents in use for treating NSTEMI/UA.
- UFH. Multiple trials have demonstrated the reduction of risk of death and MI in patients with UA/NSTEMI. UFH should be started on presentation as an alternative to LMWH in conjunction with aspirin and clopidogrel. Infusion should be continued for 2â€“5 days subsequent to the last episode of pain and/or ischaemic ECG changes. An Initial bolus of 60â€“70U/kg (maximum 5000U) should be followed by an infusion of 12â€“15U/kg/h (â‰ˆ1000U/h). The infusion rate should be altered to achieve an aPTT value of 1.5â€“2.0 times control. Coagulation should be checked

initially every 6 hours followed by once every 24 hours after 2 consistent values have been obtained.

Thrombolysis

There is no evidence to suggest that combing thrombolytic agents with aspirin, LMWH, and conventional anti-ischaemic therapy is of benefit. In the TIMI IIIB trial the rt-PA group had a worse outcome at 6 weeks and risk of bleeding was also greater with the thrombolyis group.

Doses of LMWH and GP IIb/IIIa antagonists for treating NSTEMI/UA

LMWH

â€¢ Dalteparin	120U/kg bd (max 10 000U twice daily)
â€¢ Enoxaparin	1mg/kg bd (100U/kg twice daily)

GP IIb/IIIa antagonists

- Abciximab (ReoproÂ®)

  Bolus 250mcg/kg over 1 minute followed by iv infusion 125ng/kg/min

- Tirofiban (AggrastatÂ®)

400ng/kg/min for 30 minutes followed by iv infusion 100ng/kg/min

- Eptifibatide (IntegrilinÂ®)

  Bolus 180mcg/kg followed by iv infusion 2mcg/kg/min

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NSTEMI/UA: invasive versus non-invasive strategies

The current evidence supports early angiography and revascularization in patients who present with either high-risk features or intermediate- low-risk features with on-going symptoms. Furthermore, low- and intermediate-risk patients who settle on medical therapy should undergo symptom-limited, non-invasive stress testing to identify a cohort of patients with an increased risk of adverse outcome. This second group will also benefit from an early invasive management.

Patients managed with an early conservative strategy tend to have an increased need for anti-anginal therapy and rehospitalizataion for angina and many undergo coronary angiography within the year.

The following groups are recommended to benefit from an early invasive strategy (in-patient cardiac catheterization and PCI).

- Patients with high-risk features of NSTEMI/UA
    - Recurrent angina/ischaemic ECG changes despite optimal medical therapy
    - Elevated troponin
    - New/presumed new ST-segment depression
    - Chest pain with clinical features of heart failure

(pulmonary oedema, new/worsening MR, S3 gallop)

  - Haemodynamic instability
  - Sustained ventricular tachycardia
- Poor LV systolic function (EF <40%)
- Patients allocated to low/medium risk in whom subsequent non-invasive testing demonstrates high-risk features
- PCI in previous 6 months
- Previous CABG
- Patients with other comorbidities (e.g. malignancy, liver failure, renal disease) in whom risks of revascularization are not likely to outweigh benefits.

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Discharge and secondary prevention

Length of hospital stay will be determined by symptoms and the rate of progression through the NSTEMI/UA pathway. Generally patients are hospitalized for 3â€“7 days.

Secondary prevention remains of paramount importance and is similar in principle to STEMI patients (see P30).

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Arrhythmias: general approach

Both tachyarrhythmias and bradyarrhythmias may present with significant symptoms and haemodynamic compromise. The approach to patients with arrhythmias depends upon

- The effects of the rhythm on the patient
- The diagnosis from the ECG and the rhythm
- Any underlying cardiac abnormality or identifiable precipitant.

Effects of the rhythm on the patient

- Patients with signs of severe haemodynamic compromise
    - Impending cardiac arrest
    - Severe pulmonary oedema
    - Shock: systolic BP <90mmHg
    - Depressed consciousness.

Treat immediately with unsynchronized external defibrillation for tacharrhythmia and temporary pacing for bradyarrhythmia (see P100).

- Patients with mildâ€“moderate compromise
    - Mild pulmonary oedema
    - Low cardiac output with cool peripheries and oliguria
    - Angina at rest.

Try to record an ECG and long rhythm strip before giving any pharmacological agents and/or defibrillation. This will be invaluable for long-term management. If they deteriorate, treat as above.

Diagnosing the arrhythmia

The main distinctions to make are

- Tachy- (>120/min) versus brady- (<60/min) arrhythmia
- Narrow (â‰¤120ms or 3 small sq.) versus broad QRS complex
- Regular versus irregular rhythm.

Multiple, common precipitating factors

Underlying cardiac disease

- Ischaemic heart disease
- Acute or recent MI
- Angina
- Mitral valve disease
- LV aneurysm
- Congenital heart disease
- Abnormalities of resting ECG

- Pre excitation (short PR interval)
- Long QT (congenital or acquired)

Drugs

- Anti-arrhythmics
- Sympathomimetics (Î²2 agonists, cocaine)
- Anti-depressants (tricyclic)
- Adenylate cyclase inhibitors (aminophylline, caffeine)
- Alcohol

Metabolic abnormalities

- â†“ or â†‘K^+
- â†“ or â†‘Ca^{2+}
- â†“Mg^{2+}
- â†“P_aO_2
- â†‘P_aCO_2
- Acidosis

Endocrine abnormalities

- Thyrotoxicosis
- Phaeochromocytoma

Miscellaneous

- Febrile illness
- Emotional stress
- Smoking
- Fatigue

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Tachyarrhythmias heart rate (HR) >120bpm

- History: Previous cardiac disease, palpitations, dizziness, chest pain, symptoms of heart failure and recent medication. Ask specifically about conditions known to be associated with certain cardiac arrhythmias (e.g. AF: alcohol, thyrotoxicosis, mitral valve disease, IHD, pericarditis; VT: previous MI, LV aneurysm).
- Examination: BP, heart sounds and murmurs, signs of heart failure, carotid bruits.
- Investigations (if patient is haemodynamically stable, before treatment in unstable patients, after restoration of a stable rhythm):

â€¢ 12 lead ECG and rhythm strip â€¢ Blood tests â€¢ Where appropriate â€¢ Chest X-ray	• Regular versus irregular rhythm • Narrow versus broad QRS complex. • FBC, biochemistry, glucose (urgently) • Ca^{2+}, Mg^{2+} (especially if on diuretics) • Biochemical markers of myocardial injury. • Blood cultures, CRP, ESR • Thyroid function tests • Drug levels • Arterial blood gases. • Heart size • Evidence of pulmonary oedema • Other pathology (e.g. Ca bronchus â†' AF, pericardial effusion â†' sinus tachycardia, hypotension Â± AF).

Management

- Haemodynamically unstable patients

  Arrhythmias causing severe haemodynamic compromise (cardiac arrest, systolic BP <90mmHg, severe pulmonary oedema, evidence of cerebral hypoperfusion) require urgent correction, usually with external defibrillation. Drug therapy requires time and haemodynamic stability.

- The only exception is a patient in chronic AF with an uncontrolled ventricular rate: defibrillation is unlikely to cardiovert to SR. Rate control and treatment of precipitant is first line.

- Sedate awake patients with midazolam (2.5â€“10mg iv) Â±

diamorphine (2.5â€“5mg iv + metoclopramide 10mg iv) for analgesia. Beware respiratory depression and have an anaesthetist, flumazenil, and naloxone to hand.

- Formal anaesthesia with propofol is preferred, but remember the patient may not have an empty stomach and precautions should be taken to prevent aspiration (e.g. cricoid pressure, ET intubation).
- Start at 200 J. synchronized shock and increase as required.
- If tachyarrhythmia recurs or is unresponsive try to correct â†“P_aO_2, â†‘P_aCO_2, acidosis, or â†“K^+. Give Mg^{2+} (8mmol iv stat) and shock again. Amiodarone 150â€“300mg bolus iv may also be used.
- Give specific antiarrhythmic therapy (see P66).

- Haemodynamically stable patients
    - Admit and arrange for continuous ECG monitoring and 12-lead ECG.
    - Try vagotonic manoeuvres (e.g. Valsalva or carotid sinus massage P78).
    - If diagnosis is clear introduce appropriate treatment.
    - If there is doubt regarding diagnosis, give *adenosine* 6mg as fast iv bolus followed by 5 ml saline flush. If no response, try 9, 12, and 18mg in succession with continuous ECG rhythm strip.
    - Definitive treatment should start as soon as diagnosis is known (pp66â€“99).

- Narrow complex tachycardias originate in the atria or AV node (i.e. SVT; see figure, P79).
- Irregular, narrow-complex tachycardia is most

commonly AF or atrial flutter with varying AV block.

- Broad complex tachyarrhythmias may originate from either the ventricles (VT) or from the atria or AV node (SVT) with aberrant conduction to the ventricles (RBBB or LBBB configuration).
- If the patient has previous documented arrhythmias, compare the morphology of the current arrhythmia to old ECGs. The diagnosis of VT versus SVT and therapy may be evident from the last admission.

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Treatment options in tachyarrhythmias

Sinus tachycardia

- Look for cause. Î²-blockade if anxious

Atrial fibrillation Atrial flutter SVT (P78)

- Rate control (AV node)
  - Digoxin
  - Î²-blockade
  - Calcium blocker (e.g. verapamil

Version to SR
  - Flecainide
  - Amiodarone
  - Sotalol
  - Disopyramide
  - Synchronized DC shock

Prevention
  - Amiodarone
  - Sotalol
  - Quindine

- Procainamide

Junctional tachycardias (AVNRT) (P98)

- Adenosine
- Î²-blockade
- Verapamil
- (Vagal stimulation)
- Digoxin
- Flecainide
- Synchronized DC shock

Accessory pathway tachycardias (i.e. AVRT) (P96)

- At AV node
  - Adenosine
  - Î²-blockade
- At accessory pathway
  - Sotalol
  - Flecainide
  - Disopyramide
  - Quinidine
  - Amiodarone
- Termination only
  - Synchronized
  - DC Shock

Ventricular tachycardia (P68)

- Termination and prevention
  - Lignocaine
  - Procainamide

- Amoidarone
- Magnesium
- DC shock
- Flecainide
- Disopyramide
- Propafenone
- Î²-blockade

Termination only

- Bretylium

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Broad complex tachycardia: diagnosis

(QRS width >120ms or >3 small sq.)

Diagnostic approach

The following principles can be used to distinguish between different forms of broad complex tachyarrhythmia.

- Examine the rhythm strip. Is it regular or irregular?

  Regular
  - VT (mono/polymorphic)
  - SVT or atrial flutter with bundle branch block
  - Atrial flutter or SVT with pre-excitation (e.g. WPW)

  Irregular
  - AF, atrial flutter, or multifocal atrial tachycardia with bundle branch block
  - Pre-excited AF (e.g. WPW)
  - Torsades de pointes (PVT)
- Are there any features on the 12-lead ECG that help distinguish VT from SVT with aberrancy?

  Factors favouring SVT
  - A grossly irregular broad complex tachycardia with rates

â‰¥200/min suggests AF with conduction over an accessory pathway

- Slowing or termination by vagotonic manoeuvres
- Evidence of atrial and ventricular coupling (e.g. with 1 : 2 AV block).

Factors favouring or diagnostic of VT

- Cycle length stability (< 40ms R-R variation)
- QRS >140ms (3.5 small sq.) especially with normal duration when compared with previous ECG in sinus rhythm
- Marked left axis deviation (negative in lead II)
- QRS concordance in chest leads. If the predominant deflection of the QRS is positive this is highly suggestive of VT
- In patients with previous LBBB or RBBB, it is difficult to distinguish VT from SVT with aberrancy. A different QRS morphology in tachycardia suggests VT (other clues are given in the table opposite)
- Fusion or capture beats
- Independent atrial activity (seen in ~25%).

- What are the effects of adenosine?
  - The transient AV block produces one of three results:
  - The tachycardia terminates. This suggests an SVT with aberrancy or RVOT tachycardia (technically a form of VT).
  - The ventricular rate slows unmasking atrial activity. Either â€˜flutterâ€™ waves (atrial flutter with block or intra-atrial tachycardia) or AF. The tachycardia typically continues after a few seconds once the adenosine wears off.

- No effect on the rhythm. Check that the patient received a therapeutic dose of adenosine (and experienced chest tightness with the injection). Higher doses are required in patients on theophyllines. The diagnosis is most likely to be VT.

If there is any doubt about diagnosis in the acute setting the patient must be treated as VT until proven otherwise.

Morphologic rules

For any broad complex tachycardia with â€˜bundle branch blockâ€™ morphology, assume it is VT unless

	RBBB	LBBB
Lead V1	rSR' with R' > r	rS or QS with time to S-wave nadir <70ms
	RS with R >S	
Lead V6	If a Q-wave is present, it must be 40ms and <0.2mV	R-wave with no Q-wave
Sensitivity 90%, Specificity 67â€“85%.[1]		

[1] Griffith *et al.* (1994) Lancet 343: 386â€“388.

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Monomorphic ventricular tachycardia (MVT)

Management

- Assess airway, breathing, and circulation immediately
- If patient is haemodynamically unstable
    - Deliver precordial thump: this can induce a mechanical premature ventricular complex interrupting VT circuit and terminating arrhythmia.
    - Immediate unsynchronized external defibrillation (200J, 200J, 360J). Patient is often unconscious and if so, no sedation is required.
- If patient is haemodynamically stable
    - Patient should initially be treated with iv pharmacological agents. If this is unsuccessful they can be electrically cardioverted under sedation/anaesthesia.
    - *Chemical cardioversion* is empiric and the choice of agent depends on local policy and expertise. We recommend iv *sotolol, procainamide, or amiodarone* as first-line agents. Amiodarone is the agent of choice in the context of poor LV function. Second-line agents include *lignocaine and Î²-blockers* (the latter is

particularly valuable in the setting of MI/acute ischaemia).

- Give IV *magnesium* (8mmol bolus over 2â€“5 minutes followed by 60mmol in 50ml dextrose over 24 hours) for all patients, especially if there is a risk of hypomagnesaemia (e.g. diuretics, excessive ethanol intake). With recurrent VT bolus dose can be repeated safely. Save a serum sample for analysis later.

- Correct reversible factors

  - *Ischaemia* must be treated especially in the context of post-infarction VT. This can initially be achieved with Î²-blockers. Patients should undergo revascularization at the earliest opportunity (see STEMI, P24).

  - *Electrolyte* abnormalities must be corrected (aim K^+ â‰¥4.0â€“4.5, Mg^{2+} â‰¥1.0).

  - *Acidosis*: if severe (pH â‰¤7.1) give bicarbonate (8.4% sodiumâ€“bicarbonate 50ml via a central line over 20 minutes).

- If there is recurrent or persistent VT

  - *Synchronized DC shock* under sedation or anaesthesia, with an anaesthetist present in case of sudden deterioration.

  - *Overdrive pacing* using a temporary transvenous wire may be used to terminate VT. The combination of prolonged temporary pacing and antiarrhythmics for recurrent VT is particularly effective in situations where the VT is provoked by bradycardia. If possible rhythm strips of *onset* of runs of VT must be analysed looking for bradycardia, heart block, or sick sinus syndrome. Dual-chamber temporary pacing may improve cardiac output by restoring AV synchrony.

- Maintenance therapy is usually oral and depends on

aetiology of VT. Patient must be discussed with cardiac electrophysiologist early and options for electrophysiological study, radiofrequency ablation of VT focus, and/or ICD implantation explored. Patient will need Holter monitor, exercise testing, or more invasive stimulation tests to monitor effectiveness of therapy.

Monomorphic VT: Teaching points

- Defined as â‰¥3 consecutive ventricular ectopics at a rate â‰¥100/min
- Common early post MI (up to 40%). If self-limiting, without haemodynamic compromise, does not require treatment
- Sustained VT in the setting of acute MI (Â± LV dysfunction) is associated with a poor prognosis (short and long term) and requires urgent treatment. Patients should undergo electrophysiological assessment Â± ICD insertion
- Accelerated idioventricular rhythm or â€˜slow VTâ€™ (rate 50â€“100/min) requires treatment if hypotensive (from loss of atrial contribution)

Investigation of ventricular tachycardia

â€¢ ECG	Acute MI, prolonged QT interval
â€¢ CXR	Cardiomegaly, pulmonary oedema
â€¢ U&Es	Hypokalaemia, renal impairment
â€¢ Mg^{2+}, Ca^{2+}	?deficiency
â€¢ Cardiac enzymes	Small rises common after DC shock
â€¢ ABG	?Hypoxia, acidosis
â€¢ Echo	For LV function and to exclude structural abnormality (e.g. aneurysm)

Once acute episode is over, consider referral to cardiologist for

- Holter monitoring
- Exercise testing
- Coronary angiography
- VT stimulation (provocation) testing

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Polymorphic ventricular tachycardia (PVT) 1

General management principles are identical as for monomorphic VT. Most patients will be haemodynamically unstable and must undergo external defibrillation. PVT occurring in the following circumstances requires specific therapy:

- Ischaemic PVT in the context of MI
- Non-ischaemic PVT with QT prolongation (Torsades de Pointes)
- PVT associated with Brugada syndrome.

Ischaemic PVT

- Occurs in conjunction with acute MI and chronic myocardial ischaemia
- MVT in the context of MI can convert to PVT
- Primary treatment is complete revascularization. This must be followed by Holter, exercise ECG, and EP evaluation to determine arrhythmia threshold
- A sub-set of patients especially with poor LV function, or where MVT degenerates into PVT, may require ICD

implantation.

Non-ischaemic PVT with prolonged QT interval (Torsades de Pointes)

This is an irregular polymorphic VT (often self-limiting), which appears to â€˜twistâ€™ about the isoelectric line. It occurs in the setting of prolongation of the QT interval (QTc >500ms) but the relationship between degree of prolongation and risk of serious arrhythmias is unpredictable. It may present as recurrent syncope or dizziness. Quite often patients are mistaken as having seizures.

Brugada syndrome[1]

- Brugada syndrome is characterized by the triad of
    - ST elevation in V1â€“V3
    - RBBB
    - Sudden death (or family history of sudden death) from VF.
- It is common in Japan and in SE Asia. Men are affected more than women.
- The inheritance pattern is autosomal dominant and some families have a mutation in the cardiac sodium channel SCN5A.
- Must obtain specialist advice from cardiac electrophysiologist. Patients will require EP studies with view to ICD implantation.
- Diagnosis is made by serial ECGs after administration of flecanide 2mg/kg body weight iv in 10 minutes or procanamide 10mg/kg iv in 10 minutes. The test is positive if an additional 1mm ST elevation appears in leads V1, V2,

and V3. All positive individuals should undergo EP studies and further specialist evaluation.

Footnote

1

Ramon Brugada Senior Foundation. http://www.crtia.be

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Polymorphic VT 2

Causes of prolonged QT interval

Acquired

â€¢ Drugs	Anti-arrhythmics	(quinidine, procainamide, disopyramide amiodarone, sotalol)
	Anti-psychotics	(pimozide, thioridazine)
	Anti-histamines	(terfenadine, astemizole, especially if other prescribed drugs interact with them (e.g. ketoconazole, erythromycin)
	Anti-malarials	(especially halofantrine)

	Organophosphate poisoning	

- Electrolyte abnormalities (â†“K^+, â†“Mg^{2+}, and â†“Ca^{2+})
- Severe bradycardia (complete heart block or sinus bradycardia)
- Intrinsic heart disease (IHD, myocarditis)
- Intracranial haemorrhage (especially sub-arachnoid)

Congenital long QT syndromes

Jervell, Langeâ€“Neilsen syndrome (AR, with deafness)

Romanoâ€“Ward syndrome (AD, normal hearing)

NB: Although amiodarone and sotalol prolong QT interval, polymorphic VT from these drugs is rare.

$$\text{Normal Qtc} = \frac{\text{QT}}{\sqrt{(\text{RR interval})}} = 0.38\text{-}0.46\text{s} \quad (9\text{-}11 \text{ small sq.})$$

Management

Congenital long QT

- PVT in congenital QT prolongation is adrenergically driven and treatment must include long-term Î²-blockade (e.g. propanolol).
- Other adjunctive treatment includes pacemaker implantation and left stellate ganglionectomy.
- Patients should be considered for ICD therapy. On occasions decisions may be difficult because of the young age of patients.

Acquired long QT

- The primary principle is to correct QT prolongation.
- Offending agent(s) must be identified and discontinued immediately.
- PVT in acquired QT prolongation is often secondary to prolonged pauses, which must be avoided.
- All patients should receive iv magnesium (8mmol as a bolus over 2â€“5 minutes followed by a 60mmol infusion over 24 hours)
- Overdrive temporary pacing [either ventricular or atrial] terminates the arrhythmia. Continued pacing prevents recurrence of PVT.
- Isoprenaline may be used while preparations are being made for pacing. This accelerates the atrial rate and captures the ventricles. Aim for rate of 110â€“120bpm.

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Ventricular tachycardia: drugs

Dosages of selected anti-arrhythmics for the acute treatment of VT

Drug	Dosage
Magnesium sulphate	Loading dose
	8mmol (2g) iv over 2â€“15 minutes (repeat once if necessary)
	Maintenance dose
	60mmol/48ml saline at 2â€“3 ml/h
Lignocaine	Loading dose
	100mg iv over 2 minutes (repeat once if necessary)
	Maintenance dose

	4mg/min for 30 minutes
	2mg/min for 2 hours
	1â€“2mg/min for 12â€“24 hours
Procainamide	Loading dose
	100mg iv over 2 minutes. Repeat every 5 minutes to max of 1g
	Maintenance dose
	2â€“4mg/min iv infusion
	250mg q6h po
Amiodarone	Loading dose
	300mg iv over 60 minutes via central line followed by 900mg iv over 23 hours 200mg po tds Ã— 1 week then 200mg po bd Ã— 1 week
	Maintenance dose
	200â€“400mg od iv or po
Disopyramide	Loading dose

	50mg iv over 5 minutes repeated up to maximum of 150mg iv 200mg po
	Maintenance dose
	2â€“5mg/min iv infusion 100â€“200mg q6h po
Flecainide	Loading dose
	2mg/kg iv over 10 minutes (max 150mg)
	Maintenance dose
	1.5mg/kg iv over 1 hour then 100â€“250Âµg/kg/h iv for 24 hours or 100â€“200mg po bd
Bretylium	Loading dose
	5â€“10mg/kg (~500mg) iv over 10â€“15 minutes
	Maintenance dose
	1â€“2mg/min iv infusion

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Narrow complex tachyarrhythmias (SVT)

These originate within the atrium or the conduction system above the bundle of His. The important distinction to make is between regular and irregular tachyarrhythmias (see table on facing page). Features of the different arrhythmias are shown on P80 . The diagnosis not to miss is AVRT (tachycardias involving an accessory pathway) as digoxin and verapamil are contraindicated.

Making the diagnosis

This can be done by careful examination of the 12-lead tachycardia ECG rhythm strip and the effect of inducing AV block.

- Examination of ECG. Important features to demonstrate are whether rhythm is regular or irregular and to examine for presence/absence and morphology of P-waves.
    - Irregular rhythm
        - No P-waves visible
            - Irregular rhythm with no discernible P-wave (chaotic base line with *f* -waves): treat as *atrial*

fibrillation (P84).

- Irregular rhythm with no discernible P-wave and â€˜saw-toothâ€™ flutter waves (especially in inferior leads and V1): treat as *atrial flutter with variable block* (P92).

- P-waves visible

- Irregular rhythm with multiple P-wave morphologies (>3) and varying PR intervals: treat as multifocal atrial tachycardia (P94).

- Regular rhythm

- No P-waves visible

- No discernible P-wave and â€˜saw-toothâ€™ flutter waves (especially in inferior leads and V1): treat as *atrial flutter with block* (P92).

- P-waves visible

- P-waves with normal morphology: treat as *sinus tachycardia* or *sinus node re-entry tachycardia* .
- P-waves within or distorting the start or end of QRS complex: treat as *AVNRT* (see P98).
- QRS complex may/may not be followed by P-waves with different morphology to sinus P-waves: treat as *AVRT* (see P96).

- Induce AV block by vagotonic manoeuvres (e.g. valsalva, carotid sinus massage) and if unsuccessful, with adenosine. [Adenosine 6mg fast iv bolus (3mg if via central line) followed by 5ml saline flush. If no response try 9, 12mg, and then 18mg]. Check that the patient has received a therapeutic dose of adenosine (and experienced chest tightness with the injection). Higher doses are required in patients on theophyllines.

- AVNRT and AVRT may terminate with adenosine.
- Transient AV block will unmask AF, flutter, and atrial tachycardia, but will not terminate.
- The exact diagnosis may be left to an experienced cardiologist.

P.79

- *If there is degenration of the rhythm into a broad complex tachyarrhythmia and/or haemodynamic compromise patient must be electrically cardioverted immediately* .

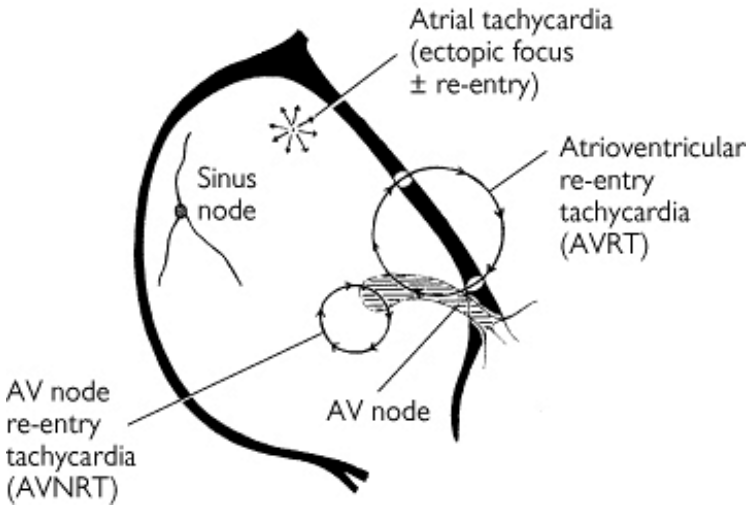
It is important to remember that SVT with previous BBB/aberrancy or AVRT with pre-excitation can present with a broad complex tachycardia. Differentiation from VT may be difficult and if in doubt patient must be treated as VT until proven otherwise. ECG features to distinguish between the two are outlined on P68 .

Regular tachycardia

- Sinus tachycardia
- Atrial flutter (with 2 : 1 or greater block)
- AVRT (i.e. with accessory path, e.g. WPW)
- AVNRT
- Intra-atrial re-entry tachycardia

Irregular tachycardia

- AF
- Atrial flutter with variable block
- Multi-focal atrial tachycardia



Types of supraventricular tachycardia

Sinus tachycardia (100â€“200/min)
Normal P waves
Transient AV block

Atrial fibrillation (<200/min)
f -waves. Chaotic
Transient AV block
Irregular rhythm. Adenosine causes rate to slow briefly.
Fast AF with broad QRS seen in AVRT (e.g. WPW)
Atrial flutter (75â€“175/min)
Flutter waves (saw-tooth) (II, III, aVF and VI)
Transient AV block
Adenosine may convert to AF
AVNRT (140â€“200/min)
Inverted, buried in QRS (usually not seen)
Terminates
Most common recurrent SVT in adults
AVRT (e.g. WPW or accessory pathway) (150â€“250/min)
Inverted, after QRS (inferior leads, RP > PR interval)
Terminates
Normal QRS if antegrade down AV node; broad QRS if antegrade down pathway
Atrial tachycardia (intraatrial re-entry) (100â€“200/min)
Abnormal P wave (PR < RP) 2 : 1 AV block may be seen

Transient AV block
Dig toxicity, lung disease organic heart disease
Multifocal atrial tachycardia) (100â€“130/min
Multiple P morhologies
Transient AV block
Assoc. with lung disease and hypoxaemia
Note: Any of these may be associated with broad QRS complexes either from pre-existing bundle branch block, or rate-related intraventricular conduction abnormality.

Arrhythmia	P wave configuration	Effect of adenosine	Comment

Differential diagnosis of SVT

Digoxin
Loading dose
iv 0.75â€“1mg in 50ml saline over 1â€“2 hours
po 0.5mg q12h for 2 doses
then 0.25mg q12h for 2 days
Maintenance dose
0.0625â€“0.25mg daily (iv or po)
Propranolol
iv 1mg over 1min, repeated every 2 minutes
up to maximum 10mg
po 10â€“40mg 3â€“4 times a day
Atenolol
iv 5â€“10mg by slow injection
po 25â€“100mg daily
Sotalol
iv 20â€–60mg by slow injection
po 80â€–160mg bd
Verapamil

iv 5mg over 2minutes; repeated every 5 minutes
up to maximum 20mg
po 40â€“120mg tds
Procainamide
iv 100mg over 2min; repeated every 5 minutes
up to maximum 1g
po 250mg q6h
Amiodarone
Loading dose
iv 300mg over 60min via central line
followed by 900mg iv over 23 hours
OR
po 200mg tds Ã— 1 week
then 200mg po bd Ã— 1 week
Maintenance dose
200â€“400mg od iv or po
Disopyramide
iv 50mg over 5min; repeated every 5 minutes
up to maximum 150mg iv
100â€“200mg q6h po
Flecainide
2mg/kg iv over 10min (max 150mg)
or 100â€“200mg po bd

Drug Dosage

Dosages of selected anti-arrhythmics for SVT

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Atrial fibrillation: assessment

Presentation

- This may present with palpitations, chest pain, breathlessness, collapse, or hypotension. Less commonly, it may present with an embolic event (stroke, peripheral embolus) or be asymptomatic. It occurs in 10â€“15% of patients post MI.
- Look for signs of an underlying cause (see table).
- Try to establish the duration of the AF: this will determine the subsequent management (see below).

Investigations

These should be directed at looking for a precipitant and underlying heart disease. All patients should have

â€¢ ECG	Broad QRS if aberrant conduction; ST-T-wave changes may be due to rapid rate, digoxin, or underlying cardiac disease
â€¢ CXR	Cardiomegaly, pulmonary oedema, intrathoracic precipitant, valve calcification (MS)
â€¢ U&Es	Hypokalaemia, renal impairment
â€¢ Cardiac enzymes	?MI. Small rise after DC shock
â€¢ Thyroid function	Thyrotoxicosis may present as AF only
â€¢ Drug levels	Especially if taking digoxin
â€¢ Mg^{2+}, Ca^{2+}	
â€¢ ABG	If hypoxic, shocked, or ?acidotic
â€¢ Echo Â± TOE	For LV function and valve lesions and to exclude intracardiac thrombus prior to version to SR
â€¢ Other investigations depend on suspected precipitant.	

Immediate management

Stabilize the patient

- General measures (P64) are as for any patient with an arrhythmia. Obtain venous access. Send bloods (P64) and if possible check the K^+ immediately on an ITU machine.
- Correct any *electrolyte* abnormality.
- If severe *acidosis* (pH â‰¤7.1) give sodium bicarbonate 50ml of 8.4% slowly iv over 20 minutes.
- *CSM* or *iv adenosine* may help confirm the diagnosis, revealing chaotic atrial activity. This is particularly helpful in patients with a rate of 150/min where atrial flutter should always be considered. CSM or adenosine will slow the ventricular rate and reveal flutter waves.
- Does the ECG in AF show intermittent or constant delta waves? This suggests WPW and digoxin and verapamil are contraindicated.

Further management

- Cardiovert to sinus rhythm if appropriate.
- Control the ventricular response rate.
- Try to prevent further episodes of AF.

Causes of atrial fibrillation

Underlying cardiac disease pathology

- Ischaemic heart disease
- Mitral valve disease

- Hypertension
- Heart failure
- Cardiomyopathy
- Pericarditis
- Endocarditis
- Myocarditis
- Atrial myxoma
- Post cardiac surgery

Separate intrathoracic

- Pneumonia
- Malignancy (1Â° or 2Â°)
- Pulmonary embolus
- Trauma

Metabolic disturbance

- Electrolytes (â†“K^+, â†“Mg^{2+})
- Acidosis
- Thyrotoxicosis
- Drugs (alcohol, sympathomimetics)

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Atrial fibrillation: management 1

Rate control versus cardioversion

- Important principles required to make a decision are
    - Are there advantages in immediate cardioversion? (e.g. on-going ischaemia with fast ventricular rhythm, pulmonary oedema, haemodynamic instability).
    - If the patient is cardioverted will they remain in sinus rhythm? (e.g. underlying sepsis/thyroid disease, large LA, poor LV, MV disease).
    - What are the risks of thromboembolic complications and is anti-coagulation required?
- Cardioversion can be achieved chemically or with external defibrillation.

Haemodynamically unstable patients

- All hypotensive patients should undergo external defibrillation using a synchronized shock of initially 200J (see P894).
- Do not attempt to defibrillate hypotensive patients with

known chronic AF or a known underlying cause driving a fast ventricular response. Chances of success are very low (e.g. mitral stenosis, severe LV dysfunction, hyperthyroid, septic).

- Relative contraindications to defibrillation need to be weighed against the patient's clinical condition. If possible, aim to optimize clinical picture before cardioversion:
    - Hypokalaemia may be quickly corrected by giving 20mmol over 1 hour in 100ml nitrate saline via a central line.
    - If digitoxicity is a possibility, ensure K^+ is 4.5â€“5mmol/L and give magnesium sulphate 8mmol in 50ml nitrate saline over 15minutes, before attempting defibrillation at low energies initially (e.g. 20â€“50J).
    - AF >48 hours duration carries a significant risk of thromboembolic complications unless patient is on long-term anti-coagulation and INR has been therapeutic. Consider performing a TOE first.
- The procedure is detailed on P894.
- If DC shock fails initially
    - Give iv amiodarone 300mg over 30 minutes via a central line (followed by iv infusion of 900â€“1200mg over 24 hours)
    - Correct hypokalaemia (aim for K^+ 4.5â€“5.0mmol/L)
    - Attempt further DC shock.

Haemodynamically stable patients

- The initial aim should be rapid pharmacological rate control followed by a decision regarding restoration of sinus rhythm if appropriate.

- When making a decision regarding restoration of sinus rhythm current evidence must be taken into account:
    - Management of AF with a rhythm-control strategy alone has no survival benefit over a rate-control strategy as long as high-risk patients are anti-coagulated.
    - Rate control is not inferior to rhythm control for prevention of death and cardiovascular morbidity in patients with persistent AF after electrical cardioversion.

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Atrial fibrillation: management 2

AF >2 days duration

- *Control ventricular rate* using one of or a combination of digoxin and class II, III, and IV agents (including: Î²-blockers, verapamil, diltiazem, or amiodarone). Can be given as iv preparation to achieve rapid rate control followed by oral preparations (see table, P82 for doses).
- If patient not anti-coagulated *start LMWH/UFH* (UFH: give bolus of 5000U followed by infusion aiming for an aPTT ratio of 2â€“3) until warfarinization is adequate (aim INR 2â€“3).
- Sinus rhythm may be restored by class Ia, Ic, and III agents (we recommend amiodarone, sotalol, quinidine, disopyramide, and flecainide).
- If patient needs to be electrically cardioverted, must perform *TOE* to look for intra-cardiac thrombus or spontaneous contrast (a marker of very sluggish flow). If negative, DC cardioversion may be performed safely. Give bolus of LMWH/UFH before cardioversion if not already on LMWH/UFH.
- Discharge when stable. Consider readmission following 4â€“6 weeks of warfarin for DC cardioversion.

AF <2 days duration

- Although risk of embolism in new onset AF is low, we recommend anti-coagulation at presentation with LMWH/UFH and subsequently warfarin (see above).
- Attempt chemical cardioversion if there are no contraindications to potential agents. Chances of success are much higher with shorter duration of AF. Possible agents include
    - Flecainide 2mg/kg iv over 10 minutes (maximum dose, 150mg). Must be avoided in patients with known IHD and/or poor LV function.
    - Disopyramide 50â€“100mg iv. Ventricular rate may increase and fibrillatory waves coarsen before reverting to sinus rhythm, so load with digoxin/Î²-blocker/verapamil before giving this.
    - Amiodarone may be used iv/po. Dosing requires central line and it may take 24â€“48 hours for sinus rhythm to be achieved. Amiodarone has relatively poor rate-control properties and may need to be combined with Î²-blocker or verapamil initially.
- If cardioversion inappropriate or unsuccessful, achieve rate control as indicated above.
- DC cardioversion can be attempted if rate control is difficult.
- Discharge when stable. Anti-coagulation may be achieved on an out-patient basis if appropriate.

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Atrial fibrillation: rate control

Controlling the ventricular response rate

- Check that there is no history of WPW and that no delta waves are visible on the ECG.
- We recommend Î²-*blockers* and *calcium channel blockers* (verapamil and diltiazem) as first-line agents for rate control. They both have the advantage of maintaining ventricular rate during exertion. If single agent is not adequate either (1) combine Î²-blockers and calcium channel blockers (if BP adequate) or (2) add digoxin or amiodarone.
- *Digoxin* is an alternative drug and can equally be used as first-line agent. Patients should initially be given a full loading dose. The maintenance dose varies (0.0625â€“0.25mg od) depending on body mass, renal function, age, etc. Digoxin is poor at controlling ventricular rate during exertion.
- In patients with poor LV function, Î²-blockers and calcium channel blockers may not be appropriate, inducing heart failure and hypotension. Digoxin with or without amiodarone is a good combination (amiodarone will increase the plasma digoxin level so halve the maintenance

digoxin dose).

- Other drugs that may be tried to control the ventricular rate are listed in the table on P82.
- If controlling ventricular rate is difficult, consider alternative diagnosis, in particular MAT. Digoxin may make the arrhythmia worse (see P94).

Long-term management

- Look for causes (see table on P85) and arrange an Echo.
- Patients successfully cardioverted acutely should be commenced on a prophylaxis regime using class Ia, Ic, or III agents (e.g. sotalol, amiodarone, flecainide, propafenone). The choice of agent must be individualized:
    - Lone AF: use class Ic agents first, followed by class III or Ia if it fails.
    - Poor LV function: amiodarone is the agent of choice.
    - IHD: class III agents and Î²-blockers (prevent ischaemia and as a result ischaemia-driven AF) are agents of choice.

  If subsequently considered to be at low risk, treatment may be stopped at 1 month. Seek cardiac opinion if in doubt.
- Patients cardioverted electively should remain on warfarin and rhythm prophylaxis for 1 month pending out-patient review.
- Patients with paroxysmal AF require long-term therapy to try to maintain sinus rhythm (class III, class Ic, and class Ia). Digoxin only controls the ventricular rate and does not prevent AF. These patients may need long-term anti-coagulation depending on (1) frequency and length of AF paroxysms, (2) presence of underlying structural, cardiac abnormalities, and (3) other systemic risk factors of

thromboembolic complications.

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Atrial flutter

- This is rarely seen in the absence of underlying coronary disease, valve disease, primary myocardial disease, pericarditis, or thyrotoxicosis.
- The atrial rate is 280â€“320/min and atrial activity is seen as flutter waves in the inferior leads and V1 on the ECG.
- The AV node conduction is slower (most commonly 2 : 1 block, sometimes 3 : 1 or 4 : 1) and this determines the ventricular rate.
- Vagotonic manoeuvres and adenosine increase the AV block and reveal the flutter waves but only very rarely terminate the arrhythmia.

Management

- *DC cardioversion is the therapy of choice* as flutter can be resistant to pharmacological therapy.
    - Lower energies are needed (20â€“100J).
    - If flutter has been present >48 hours perform TOE and then cardiovert with LMWH/UFH cover (as for AF).
- *Medical management*
    - Pharmacological agents recommended are similar to AF.

Rate control and reversion rates can be low.

- *Digoxin, verapamil, and Î²-blockers* can all be used to slow ventricular response. iv preparations can be used for more rapid action. The overall response can be poor. iv verapamil (2.5â€“5mg over 1â€“2 minutes repeated every 5 minutes to a maximum dose of 20mg) will slow the response rate and occasionally restore sinus rhythm in 15â€“20% of patients.
- *Ibutilide and dofetilide* have been reported to have reversion rates of 50% and 70% respectively. Alternative agents are *amiodarone, flecainide, quinidine, and procainamide*.
- NB: Class Ia drugs can enhance AV conduction and must always be used after rate control has been achieved (see above).

- *Flutter ablation* can be performed in resistant and/or recurrent atrial flutter. Discuss with cardiac electrophysiologist.

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Multi-focal atrial tachycardia (MAT)

- Commonly occurs in critically ill patients especially with obstructive airways disease who may be hypoxaemic and hypercapnic. Theophylline toxicity is an important factor.
- Characterized by at least 3 different P-wave morphologies with varying PP and PR intervals. Atrial nodal rate is 120â€“180 with 1 : 1 conduction.
- Rapid regular rhythm may be difficult to differentiate from atrial fibrillation. However, differentiation is very important as MAT is not responsive to DC cardioversion and is exacerbated by digoxin.

Management

- The only true *effective treatment is to treat the underlying illness*. If associated with lung disease aim to improve P_aO_2 and P_aCO_2.
- Electrolyte abnormalities must be corrected. High-dose Mg^{2+} iv may restore sinus rhythm (15g over 5 hours).
- There is increasing evidence from small trials that metoprolol is the most effective therapy. Use cautiously iv. However, most patients with MAT and COPD may not

tolerate even a cardio-selective Î²-blocker.

- Verapamil is an alternative agent (5mg iv over 2 minutes and repeated every 5 minutes up to a maximum of 20mg; then 40â€“120mg po tds) if the ventricular rate is consistently over >100/min and the patient is symptomatic.
- DC shock and digoxin are ineffective.

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Accessory pathway tachycardia (A-V re-entrant tachycardia, AVRT)

- The three most common accessory pathways that produce paroxysmal tachycardias are listed below.
- During re-entry tachycardia, the delta wave is lost as the accessory pathway is only conducting retrogradely.
- AF may produce very rapid ventricular rates as the accessory path has rapid antegrade conduction (unlike the AV node). The ECG will show the delta wave in some or all of the QRS complexes.

Management

- DC cardioversion should be used early if the tachycardia is poorly tolerated.
- Class Ia, Ic, and II agents are suitable for chemical cardioversion. We recommend iv flecainide or disopyramide. Î²-blocker may also be given especially if other agents are contraindicated (see table, P82).
- Digoxin and verapamil should be avoided as they may accelerate conduction down the accessory pathway. Amiodarone is dangerous unless given very slowly (e.g.

300mg iv over 2â€“4 hours).

- If recurrent symptoms, patient should be referred for electrophysiological assessment and RF ablation. Seek specialist advice for long-term medical management.

Types of accessory pathways

Kent bundle (Wolffâ€“Parkinsonâ€“White syndrome)

â€¢ ECG	Short PR interval and delta wave	
	Type A	Positive Î´-wave in V1â€“V6
		Negative in lead I
		(Posterior left atrial pathway)
	Type B	Biphasic or negative Î´ wave in V1â€“V3
		Positive in lead I
		(Lateral right atrial pathway)
	Concealed	No Î´-wave visible as pathway only, conducts retrogradely.

Associated with	Ebstein's, HOCM, mitral valve prolapse.

Mahaim pathway (rare)

- Pathway connects AV node to right bundle resulting in a tachycardia with LBBB morphology.

James pathway (Lownâ€“Ganongâ€“Levine syndrome) (rare)

- Short PR interval but no delta wave.
- Pathway connects atria to AV node, His, or fascicles.

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Atrioventricular-nodal re-entry tachycardia (AVNRT)

- AVNRT occurs secondary to a micro re-enterrant circuit in the AV node.
- General principles as outlined on P64 apply.
- Rate control can be achieved with (iv and po) digoxin, Î²-blockers, and calcium channel blockers. Î²-blockers and calcium channel blockers can also promote reversion into sinus rhythm.
- Class Ic and Ia agents (we recommend flecainide) can also be used for chemical cardioversion and maintainance of sinus rhythm long term.
- If arrhythmia is resistent to treatment consider electrical cardioversion.
- Patients with recurrent symptoms should be referred for electrophysiological assessment and possible RF ablation.

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Bradyarrhythmias: general approach

- Ask specifically about previous cardiac disease, palpitations, blackouts, dizziness, chest pain, symptoms of heart failure, and recent drugs.
- Examine carefully, noting the BP, JVP waveform (?cannon waves), heart sounds and murmurs, and signs of heart failure.

Investigations

â€¢ 12-lead ECG & rhythm strip	Look specifically for the relationship between P-waves and QRS complex.
	A long rhythm strip is sometimes necessary to detect complete heart block if atrial and ventricular rates are similar
â€¢ Blood tests	FBC, biochemistry, glucose (urgently)
	Ca^{2+}, Mg^{2+} (especially if on diuretics)

	Biochemical markers of cardiac injury
	Blood cultures, CRP, ESR
	Thyroid function tests
	Drug levels
	Arterial blood gases
â€¢ Chest X-ray	Heart size,
	?signs of pulmonary oedema

Management

Haemodynamically unstable patients

- Give *oxygen* via facemask if the patient is hypoxic on air.
- *Keep NBM* until definitive therapy has been started to reduce the risk of aspiration in case of cardiac arrest or when the patient lies supine for temporary wire insertion.
- Secure peripheral venous access.
- Bradyarrhythmias causing *severe haemodynamic compromise* (cardiac arrest, asystole, SBP <90mmHg, severe pulmonary oedema, evidence of cerebral hypoperfusion) require immediate treatment and temporary pacing (the technique is described on P882).
    - Give *atropine 1mg iv* (Min-I-JetÂ®) bolus; repeat if necessary up to a maximum of 3mg.

- Give *isoprenaline 0.2mg iv* (Min-I-JetÂ®) if there is a delay in pacing and the patient remains unstable. Set up an infusion (1mg in 100ml bag nitrate saline starting at 1ml/min titrating to HR).
- Set up *external pacing system* if available and arrange for transfer to a screening room for trans-venous pacing. If fluoroscopy is not available, â€˜blindâ€™ trans-venous pacing using a balloon-tipped pacing wire may be attempted.

- Bradycardia in shock is a poor prognostic sign. Look for a source of blood loss and begin aggressive resuscitation with fluids and inotropes.

Haemodynamically stable patients

- Admit to CCU with continuous ECG monitoring.
- Keep atropine drawn up and ready in case of acute deterioration.
- Does the patient require a temporary wire immediately? It may be of value to have appropriate central venous access (femoral or internal jugular vein) in place in case of the need for emergency temporary wire insertion.
- Refer the patient to a cardiologist.

External cardiac pacing

- In emergencies, external cardiac pacing may be used first but this is painful for the patient and is only a temporary measure until a more â€˜definitiveâ€™ trans-venous pacing wire can be inserted.
- External cardiac pacing is useful as a standby in patients post myocardial infarction when the risks of prophylactic

trans-venous pacing after thrombolysis are high.

- Haemodynamically stable patients with anterior myocardial infarction and bifasicular block may be managed simply by application of the external pacing electrodes and having the pulse generator ready if necessary.
- Familiarize yourself with the machine in your hospital when you have some time: a cardiac arrest is not the time to read the manual for the apparatus!

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Sinus bradycardia or junctional rhythm

(Heart rate <50/min)

Causes

- Young athletic individual
- Drugs (Î²-blockers, morphine)
- Hypothyroidism
- Hypothermia
- Increased vagal tone
    - vasovagal attack
    - nausea or vomiting
    - carotid sinus hypersensitivity
    - acute MI (especially inferior)
- Ischaemia or infarction of the sinus node
- Chronic degeneration of sinus or AV nodes or atria
- Cholestatic jaundice
- Raised intracranial pressure

Management

- If hypotensive or pre-syncopal treat as on P100:
    - Atropine 600Âµgâ€“3mg iv bolus repeating as necessary.
    - Isoprenaline 0.5â€“10Âµg/min iv infusion.
    - Temporary pacing.
    - Avoid and take steps to correct precipitants (see above).
    - Stop any drugs that may suppress the sinus or AV nodes.
- Long-term treatment:
    - If all possible underlying causes removed and if symptomatic bradycardia remains, refer for permanent pacing.
    - Consider Holter monitoring in patients with possible episodic bradycardia. R-R intervals >2.5 seconds may require permanent pacing, especially if associated with symptoms.

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Intraventricular conduction disturbances

Common causes of bundle branch block

- Ischaemic heart disease
- Hypertensive heart disease
- Valve disease (especially aortic stenosis)
- Conduction system fibrosis (Lev and Lenegre syndromes)
- Myocarditis or endocarditis
- Cardiomyopathies
- Cor pulmonale (RBBB) (acute or chronic)
- Trauma or post-cardiac surgery
- Neuromuscular disorders (myotonic dystrophy)
- Polymyositis.

Management

- General principles (P100) apply.
- Interventricular conduction disturbances on their own do

not require temporary pacing. However, when associated with haemodynamic disturbance or progression to higher levels of block (even if intermittent), must consider insertion of a transvenous pacing wire. The need for longer-term pacing is dependent on the persistence of symptoms and underlying cause. Consult a cardiologist. See P882 for situations where temporary pacing is indicated.

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Types of atrioventricular (AV) conduction block

- First-degree heart block
  - Prolongation of the PR interval (>0.22s, >5 small sq.)
- Second-degree heart block
  - Mobitz type 1 (Wenckebach): progressive increase in PR interval with intermittent complete AV block (P-wave not conducted).
  - Mobitz type 2: The PR interval is constant but there is intermittent failure to conduct the P-wave. Often occurs in the presence of broad QRS complex.
  - 2 : 1, 3 : 1 etc.: As in mobitz type 2, PR interval is constant but every second (in 2 : 1) or third (in 3 : 1) P-wave is not conducted on a regular basis.
- Third-degree (complete) heart block
  - Complete AV dissociation. If the P and QRS rates are similar, a long rhythm strip or exercise (to speed up the atrial rate) will help demonstrate dissociation.

Causes

- Associated with acute infarction or ischaemia
- Drugs (Î²-blockers, digitalis, Ca^{2+}-blockers)
- Conduction system fibrosis (Lev and Lenegre syndromes)
- Increased vagal tone
- Trauma or following cardiac surgery
- Hypothyroidism (rarely thyrotoxicosis)
- Hypothermia
- Hyperkalaemia
- Hypoxia
- Valvular disease (aortic stenosis, incompetence, endocarditis)
- Myocarditis (diphtheria, rheumatic fever, viral, Chagas' disease)
- Associated with neuromuscular disease, i.e. myotonic dystrophy
- Collagen vascular disease (SLE, RA, scleroderma)
- Cardiomyopathies (haemochromotosis, amyloidosis)
- Granulomatous disease (sarcoid)
- Congenital heart block
- Congenital heart disease (ASD, Ebstein's, PDA).

Management

- Principles are listed on P100.
- In summary all symptomatic patients must have temporary pacing. The higher the level of block (irrespective of symptoms) the greater the progression to complete heart block and/or chances of asystole.
- See P882 for situations when temporary pacing is indicated.

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Pulmonary oedema: assessment

Presentation

- Acute breathlessness, cough, frothy blood-stained (pink) sputum.
- Collapse, cardiac arrest, or shock.
- Associated features may reflect underlying cause:
    - Chest pain or palpitations: ?IHD/MI, arrhythmia
    - Preceding history of dyspnoea on exertion: ?IHD, poor LV
    - Oliguria, haematuria: ?acute renal failure (P378)
    - Seizures, signs of intracranial bleed.

Causes

A diagnosis of pulmonary oedema or â€˜heart failureâ€™ is not adequate. An underlying cause must be sought in order to direct treatment appropriately. These may be divided into

- Increased pulmonary capillary pressure (hydrostatic).
- Increased pulmonary capillary permeability.
- Decreased intravascular oncotic pressure.

Often a combination of factors are involved (e.g. pneumonia, hypoxia, cardiac ischaemia) see table on P110.

The main differential diagnosis is acute (infective) exacerbation of COPD (previous history, quiet breath sounds Â± wheeze, fewer crackles). It may be difficult to differentiate the two clinically.

Principles of management

- Stabilize the patient: relieve distress and begin definitive treatment.
- Look for an underlying cause.
- Address haemodynamic and respiratory issues.
- Optimize and introduce long-term therapy.

Initial rapid assessment

- If the patient very unwell (e. g. unable to speak, hypoxic, systolic BP <100mmHg), introduce stabilizing measures and begin treatment immediately before detailed examination and investigations (P109).
- If the patient is stable and/or if there is doubt as to the diagnosis, give oxygen and diuretic, but await the outcome of clinical examination and CXR before deciding on definitive treatment.

Urgent investigations for all patients

â€¢ ECG	Sinus tachycardia most common
	?any cardiac arrhythmia (AF, SVT, VT)
	?evidence of acute ST change (STEMI, NSTEMI, UA)
	?evidence of underlying heart disease (LVH, p mitrale).
â€¢ CXR	To confirm the diagnosis, look for interstitial shadowing, enlarged hila, prominent upper lobe vessels, pleural effusion, and Kerley B lines. Cardiomegaly may or may not be present. Also exclude pneumothorax, pulmonary embolus (oligaemic lung fields), and consolidation.
â€¢ ABG	Typically â†“ P_aO_2. P_aCO_2 levels may be â†“(hyperventilation) or â†‘ depending on severity of pulmonary oedema. Pulse oximetry may be inaccurate if peripherally shut down.
â€¢ U&Es	?pre-existing renal impairment. Regular K^+ measurements (once on iv diuretics).
â€¢ FBC	?anaemia or leukocytosis indicating the precipitant.
â€¢ Echo	As soon as practical to assess LV function, valve abnormalities, VSD, or pericardial effusion.

Investigations for patients with pulmonary oedema

All patients should have

- FBC, U&Es, CRP
- Serial biochemical markers of myocardial injury (CK, CK-MB, troponins)
- LFTs, albumin, total protein
- ECG
- CXR
- Echo (Â± TOE)
- Arterial blood gases

Where appropriate consider

- Septic screen (sputum, urine, blood cultures)
- Holter monitor (?arrhythmias)
- Coronary angiography (?IHD)
- Right and left heart catheter (if Echo unable to provide adequate information on pressures, shunts, valve disease)
- Endomyocardial biopsy (myocarditis, infiltration)
- MUGA scan
- Cardiopulmonary exercise test with an assessment of peak oxygen consumption

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Pulmonary oedema: causes

Look for an underlying cause for pulmonary oedema

Increased pulmonary capillary pressure (hydrostatic)

â†‘Left atrial pressure	• Mitral valve disease • Arrhythmia (e.g. AF) with pre-existing mitral valve disease • Left atrial myxoma
â†‘LVEDP	• Ischaemia • Arrhythmia • Aortic valve disease • Cardiomyopathy • Uncontrolled hypertension • Pericardial constriction • Fluid overload • High output states (anaemia, thyrotoxicosis, Paget's, AV fistula, beri-beri) • Reno-vascular disease

â†‘Pulmonary venous pressure	• L â†’ R shunt (e.g. VSD) • Veno-occlusive disease
Neurogenic	• Intracranial haemorrhage • Cerebral oedema • Post ictal
High-altitude pulmonary oedema	• See P858

Increased pulmonary capillary permeability

Acute lung injury	• ARDS, see P230

Decreased intravascular oncotic pressure

Hypoalbuminaemia	• â†‘losses (e.g. nephrotic syndrome, liver failure) • â†“production (e.g. sepsis) • Dilution (e.g. crystalloid transfusion)

NB: The critical LA pressure for hydrostatic oedema = serum albumin (g/L) Ã— 0.57.

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Title: *Oxford Handbook of Acute Medicine, 2nd Edition*

Pulmonary oedema: management 1

Stabilize the patient

- Patients with acute pulmonary oedema should initially be continuously monitored and managed where full resuscitation facilities are available.
- Sit the patient up in bed.
- Give 60â€“100% oxygen by facemask (unless contraindicated, COPD).
- If the patient is severely distressed, summon the â€˜on-callâ€™ anaesthetist and inform ITU. If dyspnoea cannot be significantly improved by acute measures (below) the patient may require CPAP or mechanical ventilation.
- Treat any haemodynamically unstable arrhythmia [urgent synchronized DC shock may be required.
- Give
    - Diamorphine 2.5â€“5mg iv (caution abnormal ABGs)
    - Metoclopramide 10mg iv
    - Frusemide 40â€“120mg slow iv injection.
- Secure venous access and send blood for urgent U&Es, FBC,

and cardiac enzymes (including troponin).

- Unless thrombolysis is indicated take ABG.
- If the systolic blood pressure is â‰¥90mmHg and the patient does not have aortic stenosis
    - Give sublingual GTN spray (2 puffs)
    - Start iv GTN infusion 1â€“10mg/h, increase the infusion rate every 15â€“20 minutes, titrating against blood pressure (aiming to keep systolic BP ~100mmHg).
- If the systolic blood pressure is <90mmHg treat patient as cardiogenic shock (P44).
- Insert a urinary catheter to monitor urine output.
- Repeat ABG and K^+ if the clinical condition deteriorates/fails to improve, or after 2 hours if there is improvement and the original sample was abnormal.
- Monitor pulse, BP, respiratory rate, O_2 saturation with a pulse oximeter (if an accurate reading can be obtained) and urine output.

Further management

The subsequent management of the patient is aimed at ensuring adequate ventilation/gas exchange, ensuring haemodynamic stability, and correcting any reversible precipitins of acute pulmonary oedema.

â€¢ Assess the patient's respiratory function	
â€¢ Does the patient require respiratory support?	P902
â€¢ Assess the patient's haemodynamic status	
â€¢ Is the patient in shock?	P258
â€¢ Look for an underlying cause	P118
â€¢ Conditions that require specific treatment	
â€¢ Acute aortic and mitral regurgitation	pp138â€“141
â€¢ Diastolic left ventricular dysfunction	P118
â€¢ Fluid overload	P118
â€¢ Renal failure	P118
â€¢ Severe anaemia	P118
â€¢ Hypoproteinaemia	P118.

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Pulmonary oedema: management 2

If the patient remains unstable and/or deteriorates take the following steps.

Assess the patient's respiratory function

- Wheeze may be caused by interstitial pulmonary oedema. If there is a history of asthma, give nebulized salbutamol (2.5â€“5mg), nebulized ipratropium bromide (500Âµg), and hydrocortisone (200mg) iv. Consider commencing aminophylline infusion. This will relieve bronchospasm, as well as â€˜off-loadâ€™ by systemic vasodilatation (P213). However, it may worsen tachycardia and it can be arrhythmogenic and lower K^+ (supplement to ensure K^+ 4â€“5mmol/L).
- *Indications for further respiratory support include*
    - Patient exhaustion or continuing severe breathlessness
    - Persistent P_aO_2 <8kPa
    - Rising P_aCO_2
    - Persistent or worsening acidosis (pH <7.2).

- *CPAP*: This may be tried for co-operative patients, who can protect their airway, have adequate respiratory muscle strength, and are not hypotensive. The positive pressure reduces venous return to the heart and may compromise BP.
- *Endotracheal intubation and mechanical ventilation* may be required and some positive end expiratory pressure (PEEP) should be used (P902).
- Discuss the patient with the on-call anaesthetist or ITU team early.

Assess the patient's haemodynamic status

It is important to distinguish between cardiogenic and non-cardiogenic pulmonary oedema, as further treatment is different between the two groups. This may be difficult clinically. A PA (Swanâ€“Ganz) catheter must be inserted if the patient's condition will allow.

- *Non-cardiogenic pulmonary oedema* occurs when the hydrostatic pressure within the capillary system overcomes the plasma oncotic pressure. In patients with hypoalbuminaemia this will occur at PCWP less than 15mmHg. The critical PCWP may be estimated by serum albumin (g/L) Ã— 0.57. Thus a patient with a serum albumin of 15g/L will develop hydrostatic pulmonary oedema at a LA pressure of 8mmHg; a serum albumin of 30g/L will require an LA pressure of >17mmHg, etc.
- *Cardiogenic pulmonary oedema* is often associated with significant systemic hypotension or low output states. Contributing factors include conditions where there is â€˜mechanicalâ€™ impairment to forward flow [e.g. valvular heart disease (especially if acute), VSD] or severe myocardial disease (large MI, myocarditis,

cardiomyopathy).

- The gradient between PA diastolic pressure and PCWP (PADâ€“PCWP) is generally <5mmHg in cardiogenic and >5mmHg in non-cardiogenic pulmonary oedema (e.g. ARDS).
- The pulse and BP are most commonly elevated due to circulating catecholamines and over activity of the reninâ€“angiotensin system. Examination reveals sweating, cool â€˜shut-downâ€™ peripheries, high pulse volume (assess carotid or femoral pulses).

Management

The general approach involves combination of diuretics, vasodilators Â± inotropes. Patients may be divided into two groups:

- Patients in shock (with systolic BP <100mmHg) (see P116)
- Haemodynamically stable patients with systolic BP >100mmHg (see P117).

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Pulmonary oedema: management 3

Patients with systolic BP <100mmHg

- The patient is in incipient (or overt) shock. The most common aetiology is cardiogenic shock but remember non-cardiogenic causes (e.g. ARDS, septic shock, P258).
- *Optimal monitoring and access*: central line Â± PA catheter (Swanâ€“Ganz), urinary catheter, arterial line (monitoring BP and ABGs). Internal jugular lines are preferable as the risk of pneumothorax is lower.
- Ensure patient is not under filled using PCWP as a guide (<10mmHg) (mistaken diagnosis, e.g. septic shock from bilateral pneumonia).
- *Is there a mechanical cause that may require emergency surgery?*
    - Arrange an urgent Echo to rule out
        - VSD and acute MR in all patients with recent MI with/without new murmur (P32)
        - Prosthetic heart valve dysfunction (e.g. dehiscence, infection) or pre-existing native aortic or mitral disease that may require surgery.

- Discuss patient early on with cardiologist/cardiac surgeon.

The *choice of inotropic agent* depends on the clinical condition of the patient and to some extent, the underlying diagnosis.

- Treatment of septic shock is discussed elsewhere (P270).
- *Systolic BP 80â€“100mmHg* and cool peripheries: start *dobutamine infusion* at 5Âµg/kg/min, increasing by 2.5Âµg/kg/min every 10â€“15 minutes to a maximum of 20Âµg/kg/min until BP >100mmHg. This may be combined with dopamine (2.5â€“5Âµg/kg/min). However, tachycardia and/or hyoptension secondary to peripheral vasodilation may limit its effectiveness. *Phosphodiesterase inhibitors* (enoximone or milrinone) should be considered where dobutamine fails.
- *Systolic BP <80mmHg*: give a slow iv *bolus of epinephrine* (2â€“5ml of 1 in 1000 solution Min-I-JetÂ®) and repeat if necessary.
    - *Dopamine* at doses of >2.5Âµg/kg/min has a pressor action in addition to direct and indirect inotropic effects and may be used at higher doses (10â€“20Âµg/kg/min) if the blood pressure remains low. However it tends to raise the pulmonary capillary filling pressure further and should be combined with vasodilators (e.g. nitroprusside or hydralazine) once the blood pressure is restored (see below). Beware of arrhythmias at these doses.
    - *Epinephrine* infusion may be preferred to high-dose dopamine as an alternative inotrope. Once the blood pressure is restored (>100mmHg), vasodilators such as nitroprusside/hydralazine or GTN infusion should be added to counteract the pressor effects. Epinephrine can be combined with dobutamine and/or a phosphodiesterase inhibitor, especially in the context of

a poor ventricle.

- *Intra-aortic balloon counter pulsation* should also be used with/without inotropes in the context of a potentially reversible cause for the pulmonary oedema and shock (e.g. on-going myocardial ischaemia, VSD, acute MR) (see P34).
- Further doses of diuretic may be given.

Patients with systolic BP â ‰ ¥100mmHg

- Further doses of diuretic may be given [frusemide 40â€“80mg iv q3â€“4h or as a continuous infusion (20â€“80mg/h)].
- Continue the GTN infusion, increasing the infusion rate every 15â€–20 minutes up to 10mg/h, titrating against blood pressure (aiming to keep systolic BP ~100mmHg).
- ACE inhibitors can be used if BP is adequate and there are no other known contraindications (e.g. RAS, renal failure). Arteriolar vasodilators (nitroprusside or hydralazine) may also be added in or used instead of GTN (Â±ACE inhibitor) in patients with adequate BP. Arterial pressure should be monitored continuously via an arterial line to prevent inadvertent hypotension.

Long-term management

- Unless a contraindication exists, start an ACE inhibitor, increasing the dose to as near the recommended maximal dose as possible. In the context of LV impairment, ACE inhibitors have significant prognostic benefit.
- If ACE inhibitors are contraindicated or not tolerated, consider the use of hydralazine and long-acting oral nitrate

in combination.

- If the patient is already on high doses of diuretics and ACE inhibitors consider the addition of spironolactone (25â€“50mg) (NB: monitor renal function and serum potassium).
- In the context of stable patients (no clinical features of failure) and poor LV function Î²-blockers have significant mortality and some symptomatic benefit (NB: start at a very small dose and increase gradually every 2 weeks with regular monitoring). Bisoprolol, carvedilol, and metoprolol can all be used.
- Ensure all arrhythmias are treated (see P64).
- Digoxin can be used for symptomatic improvement.
- Consider multi-site pacing (biventricular) in the context of severe LV dysfunction, broad QRS complex Â± MR on Echo.
- Patients with AF or poor LV function should be considered for long-term anti-coagulation.
- Patients <60 years with severe irreversible LV dysfunction and debilitating symptoms must be considered for cardiac transplantation.

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Pulmonary oedema: specific conditions

Diastolic LV dysfunction

- This typically occurs in elderly hypertensive patients with LV hypertrophy, where there is impaired relaxation of the ventricle in diastole. There is marked hypertension, pulmonary oedema, and normal or only mild systolic LV impairment.
- With tachycardia, diastolic filling time shortens. As the ventricle is â€˜stiffâ€™ in diastole, LA pressure is increased and pulmonary oedema occurs (exacerbated by AF as filling by atrial systole is lost).
- Treatment involves control of hypertension with iv nitrates (and/or nitroprusside), calcium blockers (verapamil or nifedipine), and even selective Î²-blockers (e.g. carvedilol).

Fluid overload

- Standard measures are usually effective.
- In extreme circumstances venesection may be necessary.
- Check the patient is not anaemic (Hb â‰¥10g/dl). Remove 500ml blood via a cannula in a large vein and repeat if

necessary.

- If anaemic (e.g. renal failure) and acutely unwell, consider dialysis (P378).

Known (or unknown) renal failure

- Unless the patient is permanently anuric, large doses of iv frusemide may be required (up to 1g given at 4mg/min) in addition to standard treatment.
- If such treatment fails, or the patient is known to be anuric, dialysis will be required.
- In patients not known to have renal failure, an underlying cause should be sought (P378).

Anaemia

- Cardiac failure may be worsened or precipitated by the presence of significant anaemia. Symptoms may be improved in the long term by correcting this anaemia.
- Generally transfusion is unnecessary with Hb >9g/dl unless there is a risk of an acute bleed. Treatment of pulmonary oedema will result in haemoconcentration and a â€˜riseâ€™ in the Hb.
- If the anaemia is thought to be exacerbating pulmonary oedema, ensure that an adequate diuresis is obtained prior to transfusion. Give slow transfusion (3â€“4 hours per unit) of packed cells, with iv frusemide 20â€“40mg before each unit.

Hypoproteinaemia

- The critical LA pressure at which hydrostatic pulmonary

oedema occurs is influenced by the serum albumin and approximates to [serum albumin concentration (g/L) Ã— 0.57] (see P282).

- Treatment involves diuretics, cautious albumin replacement, spironolactone (if there is secondary hyperaldosteronism), and treatment of the underlying cause for hypoproteinaemia.

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Infective endocarditis (IE)

Clinical presentation of IE is highly variable and dependent on a combination of intra-cardiac pathology, evolution of the infection, and possible extra cardiac involvement. Presentation can be insidious as in streptococcal infections with striking constitutional symptoms, such as *S. aureus*.

Presenting features can include the following.

- Symptoms and signs of the infection. These include malaise, anorexia, weight loss, fever, rigors, and night sweats. Long-standing infection produces anaemia, clubbing, and splenomegaly
- Cardiac manifestations of the infection. Congestive cardiac failure, palpitations, tachycardia, new murmur, pericarditis, or AV block.
- Symptoms and signs due to immune complex deposition

â€¢ Skin	Petechiae (most common), splinter haemorrhages Osler's nodes [small tender nodules (pulp infarcts) on hands and feet, which persist for hours to days] Janeway lesions (non-tender eryhthematous and/or haemorrhagic areas on the palms and soles)
â€¢ Eye	Roth spots (oval retinal haemorrhages with a pale centre located near the optic disc), conjunctival splinter haemorrhages, retinal flame haemorrhages
â€¢ Renal	Microscopic haematuria, glomerulonephritis, and renal impairement
â€¢ Cerebral	Toxic encephalopathy
â€¢ Musculoskeletal	Arthralgia or arthritis

- Complications of the infection

  Local effects
  - Valve destruction results in a new or changing murmur. This may result in progressive heart failure and pulmonary oedema.
  - A new harsh pansystolic murmur and acute deterioration may be due to perforation of the

interventricular septum or rupture of a sinus of Valsalva aneurysm into the right ventricle.

- High degree AV block (2â€“4% of IE) occurs with intra-cardiac extension of infection into the interventricular septum (e.g. from aortic valve endocarditis).
- Intra-cardiac abscess may be seen with any valve infection (25â€“50% of aortic endocarditis, 1â€“5% of mitral but rarely with tricuspid) and is most common in prosthetic valve endocarditis.

Embolic events

- Septic emboli are seen in 20â€“45% of patients and may involve any circulation [(brain, limbs, coronary, kidney, or spleen; pulmonary emboli with tricuspid endocarditis.
- 40â€“45% of patients who have had an embolic event will have another.
- The risk depends on the organism (most common with G - ve infections, *S. aureus* or *candida*) and the presence and size of vegetations (emboli in 30% of patients with no vegetation on Echo, 40% with vegetations <5mm, and 65% with vegetations >5mm).

Ask specifically for a history of dental work, infections, surgery, iv drug use, or instrumentation, which may have led to a bacteraemia. Examine for any potential sources of infection, especially teeth or skin lesions. Risk factors for endocarditis are shown in the table below.

Risk factors for infective endocarditis

â€¢ High risk	Prosthetic valves

risk	
	Previous bacterial endocarditis
	Aortic valve disease
	Mitral regurgitation or mixed mitral disease
	Cyanotic congenital heart disease
	Patent ductus arteriosis
	Uncorrected L â†’ R shunt
	Intra-cardiac and systemicâ€“pulmonary shunts
â€¢ Moderate risk	MVP with regurgitation or valve thickening
	Isolated mitral stenosis
	Tricuspid valve disease
	Pulmonary stenosis
	Hypertrophic cardiomyopathy
	Bicuspid aortic valve disease
	Degenerative valve disease in the elderly

	Mural thrombus (e.g. post infarction)
â€¢ Low risk	MVP without regurgitation
	Tricuspid regurgitation without structural valve abnormality
	Isolated ASD
	Surgically corrected L â†’ R shunt with no residual shunt
	Calcification of MV annulus
	Ischaemic heart disease and/or previous CABG
	Permanent pacemaker
	Atrial myxoma

Other predisposing factors

- Arterial prostheses or arteriovenous fistulae
- Recurrent bacteraemia (e.g. iv drug users, severe periodontal disease, colon carcinoma)
- Conditions predisposing to infections (e.g. diabetes, renal failure, alcoholism, immunosuppression)
- Recent central line

In many cases no obvious risk factor is identified

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Infective endocarditis: diagnosis

Clinical features can be non-specific and diagnosis difficult. A high index of suspicion must be maintained if patients present with unexplained fever, a predisposing cardiac lesion, bacteraemia, and embolic phenomenon.

The *Duke* classification has been devised to help diagnosis:

Definite endocarditis	2 major criteria, or 1 major and 3 minor criteria, or 5 minor criteria.
Possible endocarditis	Findings which fall short of definite endocarditis but are not rejected.
Rejected diagnosis	Firm alternative diagnosis, or sustained resolution of clinical features with <4 days of antibiotic therapy.

Major criteria

- Positive blood culture

Typical microorganism for IE from two separate blood cultures[1]

Persistently positive blood culture.[2]

- Evidence of endocardial involvement

  Positive echocardiogram

  - Oscillating intra-cardiac mass (vegetation)
  - Abscess
  - New partial dehiscence of prosthetic valve
  - New valve regurgitation.

Minor criteria

- Predisposing condition or drug use
- Fever >38Â°C
- Vascular phenomena: arterial emboli, septic pulmonary infarcts, mycotic aneurysm, intracranial and conjunctival haemhorrhage, Janeway lesions
- Immunologic phenomena: glomerulonephritis, Osler's nodes, Roth spots, rheumatoid factor
- Microbiological evidence: positive blood cultures but not meeting major criteria or serological evidence of organism consistent with IE
- Echo: positive for IE but not meeting major criteria.

Common organisms in IE

50â€“60%	Streptococci (especially *Strep. viridans* group)
10%	Enterococci
25%	Staphylococci
	S. aureus = coagulase +ve
	S. epidermidis = coagulase -ve
5â€“10%	Culture negative
<1%	Gram negative bacilli
<1%	Multiple organisms
<1%	Diptheroids
<1%	Fungi

Footnote

[1]*Strep. viridans, Strep. bovis*, HACEK group, community-acquired *Staph. aureus* or *enterococci* in the absence of primary focus.

[2]Blood cultures drawn 12 hours apart or 3 more cultures with first and last drawn 1 hour apart.

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Infective endocarditis: investigations

â€¢ Blood cultures	Take 3â€“4 sets of cultures from different sites at least an hour apart and inoculate a minimum of 10ml/bottle for the optimal pick-up rate. Both aerobic and anaerobic bottles must be used. Lab should be advised that IE is a possibility especially if unusual organisms are suspected. In stable patients on antibiotic therapy doses must be delayed to allow culture on successive days. Ask for prolonged (fungal) cultures in iv drug users.
â€¢ FBC	May show normochromic, normocytic anaemia (exclude haematinic deficiency), neutrophil leukocytosis, and perhaps thrombocytopenia.
â€¢ U&Es	May be deranged (this should be monitored throughout treatment).

â€¢ LFTs	May be deranged, especially with an increase in ALP and Î³-GT.
â€¢ ESR/CRP	Acute phase reaction.
â€¢ Urinalysis	Microscopic haematuria Â± proteinuria.
â€¢ Immunology	Polyclonal elevation in serum Igs, complement levels.
â€¢ ECG	May have changes associated with any underlying cause. There may be AV block or conduction defects (especially aortic root abscess) and rarely (embolic) acute MI.
â€¢ CXR	May be normal. Look for pulmonary oedema or multiple infected or infarcted areas from septic emboli (tricuspid endocarditis).
â€¢ Echo	Transthoracic Echo may confirm the presence of valve lesions and/or demonstrate vegetations if >2mm in size. TOE is more sensitive for aortic root and mitral leaflet involvement. A normal Echo does not exclude the diagnosis.
â€¢ MRI	Useful in investigation of paravalvular extension, aortic root aneurysm, and fistulas.

â€¢ Dentition	All patients should have an OPG (orthopentamogramâ€”a panoramic dental X-ray) and a dental opinion.
â€¢ Swabs	Any potential sites of infection (skin lesions).
â€¢ V/Q scan	In cases where right-sided endocarditis is suspected this may show multiple mismatched defects.
â€¢ Save serum for	*Aspergillus* precipitins *Candida* antibodies (rise in titre) Q fever (*Coxiella burnetti*) complement fixation test *Chlamydia* complement fixation test *Brucella* agglutinins *Legionella* antibodies *Bartonella* sp.

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Infective endocarditis: antibiotics

â€˜Blindâ€™ treatment for endocarditis

- Infective endocarditis is usually a clinical diagnosis and must be considered in any patient with a typical history, fever, and a murmur with no other explanation. Often antibiotics need to be started before the culture results are available. Be guided by the clinical setting (see table[1]).

Presentation	Choice of antibiotic
Gradual onset (weeks)	Benzyl-penicillin + Gentamicin
Acute onset (days) or history of skin trauma	Flucloxacillin + Gentamicin
Recent valve prosthesis (possible MRSA, diptheroid, *Kelbsiella*, corynebacterium or	Vancomycin (or teicoplanin) + Gentamicin +

nosocomial staphylococci)	Rifampicin
iv drug user	Vancomycin

Suggested antibiotic doses

Benzylpenecillin	4MU (2.4g) q4h iv
Flucloxacillin	2g qds iv
Vancomycin	15mg/kg q12h iv over 60 minutes, guided by levels
Gentamicin	3mg/kg divided in 1â€“3 doses guided by levels
Rifampicin	300mg q12h po
Ciprofloxacin	300mg q12h iv for 1 week, then 750mg q12h po for 3 weeks

- Identification of an organism is invaluable for further management and blood cultures should be taken before antibiotics with meticulous attention to detail.
- Antibiotics should be administered iv, preferably via a tunnelled central (Hickman) line.
- If an organism is isolated, antibiotic therapy may be modified when sensitivities are known.
- Suggested antibiotic combinations are shown in the table

above; however individual units may have specific policies. Patients should be discussed with your local microbiologist.

Footnote

1

Oakley CM (1995) *Eur Heart J* 16(*suppl. B*): 90â€“93.

Duration of treatment

- This is controversial with a trend toward shorter courses. Microbiology and ID opinion is important especially in resistant and/or uncommon organisms. The box below shows one suggested protocol.
- The duration of treatment varies depending on the severity of infection and the infecting organism. iv therapy is usually for at least 2 weeks and total antibiotic therapy is for 4â€“6 weeks.
- If the patient is well following this period, antibiotic treatment may be stopped. Provided no surgery is indicated (P134), patient may be discharged and followed up in out-patient clinic.
- Patients should be advised of the need for endocarditis prophylaxis in the future (see table, P136).
- Patients with valvular damage following infection should be followed long term and patients with ventricular septal defects should be considered for closure.

- Viridans streptococci and *Streptococcus bovis* (penicillin sensitive)
    - Benzyl penicillin only (4 weeks)

    - Vancomycin or teicoplanin (4 weeks)
    - Penicillin + aminoglycoside (2 weeks)
    - Ceftriaxone 2g (4 weeks)
- Group B, C, G streptococci, *Strep. pyogenes, Strep. Pneumoniae*
    - Penicillin (4 weeks) + aminoglycoside (2 weeks)
    - Vancomycin (4 weeks) + aminoglycoside (2 weeks)
- Group A streptococci
    - Penicillin (4 weeks)
    - Vancomycin (4 weeks)
- Enterococci
    - Penicillin + aminoglycoside (4â€“6 weeks)
    - Vancomycin + aminoglycoside (4â€“6weeks)
- Extra-cardiac infection from septic emboli
    - Penicillin (4 weeks) + aminoglycoside (2 weeks)
    - Vancomycin (4 weeks) + aminoglycoside (2 weeks)
- *Staphylococcus aureus* and coagulase negative staphylococci
    - Left-sided endocarditis
    - Flucloxacillin (4â€“6 weeks) + aminoglycoside (2 weeks)
    - If MRSA: Vancomycin + rifampicin (6 weeks) Â± aminoglycoside (2 weeks)
    - Right-sided endocarditis
    - Flucloxacillin (2 weeks) + aminoglycoside (2 weeks)

    - Ciprofloxacin (4 weeks) + rifampicin (3 weeks)
    - If MRSA: Vancomycin (4 weeks) + rifampicin (4 weeks)
- Fungi
    - Amphotericin B iv to a total dose of 2.5â€“3g

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Infective endocarditis: monitoring treatment

Patients need careful clinical monitoring both during and for several months after the infection. Re-appearance of features suggestive of IE must be investigated thoroughly to rule out recurrent infection or resistance to treatment regime.

Clinical features

- Signs of continued infection, persistent pyrexia, and the persistence of systemic symptoms.
- Persistent fever may be due to drug resistance, concomitant infection (central line, urine, chest, septic emboli to lungs or abdomen) or allergy (?eosinophilia, ?leukopenia, ? proteinuria: common with penicillin but may be due to any antibiotic; consider changing or stopping antibiotics for 2â€“3 days).
- Changes in any cardiac murmurs or signs of cardiac failure.
- The development of any new embolic phenomena.
- Inspect venous access sites daily. Change peripheral cannulae every 3â€“4 days.

Echo

- Regular (weekly) transthoracic echocardiograms may identify clinically silent, but progressive valve destruction and development of intra-cardiac abscesses or vegetations.
- The tips of long-standing central lines may develop sterile fibrinous â€˜frondsâ€™, which may be visible on TOE: change the line and send the tip for culture.
- â€˜Vegetationsâ€™ need not be due to infection (see table on P131).

ECG

- Looking specifically for AV block or conduction abnormalities suggesting intra-cardiac extension of the infection. A daily ECG must be performed.

Microbiology

- Repeated blood cultures (especially if there is continued fever).
- Regular aminoglycoside and vancomycin levels (ensuring the absence of toxic levels and the presence of therapeutic levels). Gentamicin ototoxicity may develop with prolonged use even in the absence of toxic levels.
- Back titration to ensure that minimum inhibitory and bactericidal concentrations are being achieved.

Laboratory indices

- Regular (daily) urinalysis
- Regular U&Es and liver function tests
- Regular CRP (ESR every 2 weeks)

- FBC: rising Hb and falling WCC suggests successful treatment; watch for Î²-lactam associated neutropenia.
- Serum magnesium (if on gentamicin).

Causes of culture-negative endocarditis[1]

- Previous antibiotic therapy
- Fastidious organism

  Nutritionally deficient variants of *Strep. viridans*

  Brucella, Neisseria, Legionella

  Nocardia

  Mycobacteria

  The HACEK group of oropharyngeal flora

  Cell-wall deficient bacteria and anaerobes
- Cell-dependent organisms

  Chlamydia, rickettsiae (*Coxiella*)
- Fungi

HACEK = *Haemophilus, Acintobacillus, Cardiobacterium, Eikenella*, and *Kingella* sp.

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Culture-negative endocarditis

- The commonest reason for persistently negative blood cultures is prior antibiotic therapy and this effects up to 15% of patients with a diagnosis of IE.
- If the clinical response to the antibiotics is good these should be continued.
- For a persisting fever
    - Withhold antibiotics if not already started
    - Consider other investigations for a â€˜PUOâ€™ (see P296)
    - If clinical suspicion of IE is high, it warrants further investigation
    - Repeated physical examination for any new signs
    - Regular Echo and TOE. â€˜Vegetationsâ€™ need not be due to infection (see table)
    - Repeated blood cultures, especially when the temperature is raised. Discuss with microbiology about prolonged culturing times (4+ weeks) and special culturing and sub-culturing techniques. Most HACEK group organisms can be detected.
- Consider unusual causes of endocarditis

- Q-fever (*Coxiella burnetii*). Complement fixation tests identify antibodies to phase 1 and 2 antigens. Phase 2 antigens raised in the acute illness, phase 1 antigens raised in chronic illnesses such as endocarditis. PCR can be performed on operative specimens. Treat with indefinite (life-long) oral doxycycline Â± co-trimoxazole, rifampicin, or quinolone.
- *Chlamydia psittaci*. Commonly there is a history of exposure to birds and there may be an associated atypical pneumonia. Diagnosis is confirmed using complement fixation tests to detect raised antibody titres.
- Brucellosis. Blood cultures may be positive though organisms may take up to 8 weeks to grow. Serology usually confirms the diagnosis.
- Fungi. *Candida* is the most common species and may be cultured. The detection of antibodies may be helpful though levels may be raised in normals. The detection of a rising titre is of more use. Other fungal infections (e.g. histoplasmosis, aspergillosis) are rare but may be diagnosed with culture or serology, though these are commonly negative. Antigen assays may be positive, or the organism may be isolated from biopsy material. Fungal IE is more common in patients with prosthetic valves and iv drug users. Bulky vegetations are common. Treatment is with amphotericin B Â± flucytosine. Prosthetic valves must be removed. Mortality is >50%.

Causes of â€˜vegetationsâ€™ on Echo[1]

- Infective endocarditis

- Sterile thrombotic vegetations
    - Libman Sacks endocarditis (SLE)
    - Primary anti-phospholipid syndrome
    - Marantic endocarditis (adenocarcinoma)
- Myxomatous degeneration of valve (commonly mitral)
- Ruptured mitral chordae
- Exuberant rheumatic vegetations (black Africans)
- Thrombus (â€˜pannusâ€™) on a prosthetic valve
- A stitch or residual calcium after valve replacement

Footnote

1

Michel PL & Acar J (1995) *Eur Heart J* 16(*suppl B*): 2â€“6.

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Right-sided endocarditis

- Always consider this diagnosis in iv drug users (or patients with venous access).
- Endocarditis on endocardial permanent pacemaker leads is a rare but recognized cause.
- Patients most commonly have staphylococcal infection and are unwell, requiring immediate treatment and often early surgery.
- Lesions may be sterilized with iv antibiotics.
- Surgery may be required for
    - Resistant organisms (*Staph. aureus, Pseudomonas, Candida*, and infection with multiple organisms)
    - Increasing vegetation size in spite of therapy
    - Infections on pacemaker leads (surgical removal of lead and repair or excision of tricuspid valve)
    - Recurrent mycotic emboli

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Prosthetic valve endocarditis (PVE)

- Conventionally divided into early (<2 months post operatively) and late (>2 months post operatively).
- Early prosthetic valve endocarditis
    - Most commonly due to staphylococci, gram negative bacilli, diptheroids, or fungi.
    - Generally infection has begun either per-operatively or in the immediate post-operative period.
    - Often a highly destructive, fulminant infection with valve dehiscence, abscess formation, and rapid haemodynamic deterioration.
    - Discuss with the surgeons early. They commonly require re-operation. Mortality is high (45â€“75%).
- Late prosthetic valve endocarditis
    - The pathogenesis is different. Abnormal flow around the prosthetic valve ring produces microthrombi and non-bacterial thrombotic vegetations (NBTVs), which may be infected during transient bacteraemia. The source is commonly dental or urological sepsis or indwelling venous lines.
    - Common organisms are coagulase negative

staphylococci, *Staph. aureus, Strep. viridans*, or enterococci.

- Frequently needs surgical intervention and this carries a high mortality, but less than for early PVE.

- It may be possible to sterilize infections on bioprostheses with iv antibiotics only. Surgery (see P134) may then be deferred.

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Surgery for infective endocarditis

Discuss early with the regional cardiothoracic centre: immediate intervention may be appropriate.

- Surgical intervention may be necessary either during active infection or later because of degree of valve destruction. Optimal timing depends on a number of factors:
    - Haemodynamic tolerance of lesion
    - Outcome of the infection
    - Presence of complications.
- Choice of anti-microbial therapy should be modified depending on microbiological results from intraoperative specimens. Samples should be sent for culture, staining, immunological testing, and PCR depending on suspected organism.
- Duration of anti-microbial treatment is dependent on the clinical picture:
    - Culture-negative operative specimens: 2â€“3 weeks for valve infection and 3â€“4 weeks for abscess.
    - Culture-positive operative specimens: 3â€“4 weeks for valve infection and 4â€“6 weeks for abscess.

- Timing is dictated by clinical picture. Indications for urgent surgery are listed below. In patients with neurological injury surgery should be delayed to avoid intracranial haemhorrage if cardiac function permits (embolic infarct: delay 10â€“14 days, haemorrhage: 21â€“28 days and when ruptured mycotic aneurysms have been repaired).
- Table opposite summarizes the absolute and relative indications for surgery.

Haemodynamic tolerance of lesion

- If the patient is haemodynamically stable, surgery may be delayed until after antibiotic course is completed. The final management depends on the valve affected, the degree of destruction, and its effect on ventricular function. Severe aortic and mitral regurgitation usually require surgery; tricuspid regurgitation, if well tolerated, is managed medically.
- Decompensation (severe congestive cardiac failure or low cardiac output syndrome with functional renal failure) may respond to surgery but the mortality is high.
- â€˜Metastableâ€™ patients who have been successfully treated after an episode of acute decompensation should be considered for early operation after 2â€“3 weeks antibiotic therapy.

Outcome of the infection

- Persistence or relapse of infection (clinical and laboratory indices) despite appropriate antibiotics at an adequate dose may either be due to a resistant organism or an abscess (paravalvular, extra-cardiac). Consider valve replacement if no extra-cardiac focus found.
- The organism may influence the decision: consider early

surgery for fungal endocarditis or prosthetic endocarditis with *E. coli* or *Staph. aureus*.

Presence of complications

Urgent surgery indications comprise

- High degree AV block
- Perforation of interventricular septum
- Rupture of sinus of Valsalva aneurysm into RV
- Intracardiac abscess
- Recurrent septic emboli
- Prosthetic endocarditis especially associated with an unstable prosthesis.

Indications for surgery in infective endocarditis

Absolute indications

- Moderate to severe heart failure secondary to valve regurgitation
- Unstable prosthesis
- Uncontrolled infection: persistent bacteraemia, ineffective antimicrobial therapy [IE secondary to fungi, *Brucella*, *Pseudomonas aeroginosa* (especially aortic and mitral valve)]
- *Staph. aureus* prosthetic infection with an intracardiac complication

Relative indications

- Perivalvular extension of infection
- Poor response to *Staph. aureus* native valve infection
- Relapse after adequate treatment
- Large (>10mm) hypermobile vegetations
- Persistent unexplained fever in culture-negative endocarditis
- Endocarditis secondary to antibiotic-resistant enterococci

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Endocarditis prophylaxis[1]

Procedures that require antibiotic prophylaxis

Dental	â€¢ All procedures
Upper respiratory tract	â€¢ Tonsillectomy, adenoidectomy
Gastrointestinal	â€¢ Oesophageal dilatation or laser therapy
	â€¢ Oesophageal surgery
	â€¢ Sclerosis of oesophageal varicies
	â€¢ ERCP
	â€¢ Abdominal surgery

	â€¢ Barium enema
	â€¢ Sigmoidoscopy Â± biopsy
Urological	â€¢ Instrumentation of ureter or kidney
	â€¢ Biopsy or surgery of prostate or bladder

Procedures for which the risk of IE is controversial

Upper respiratory tract	â€¢ Bronchoscopy
	â€¢ Endotracheal intubation
Gastrointestinal	â€¢ Upper GI endoscopy Â± biopsy
Genital	â€¢ Vaginal hysterectomy or delivery

- The table on P121 shows cardiac conditions at risk of IE. High and moderate risk requires prophylaxis; â€˜lowâ€™ risk does not.
- The regimen may be modified depending on the â€˜degree of riskâ€™ (both patient and procedure related) as in table below.

Antibiotic prophylaxis

Minimal regimen

	1h before	6h after
No penicillin allergy	Amoxycillin 3g po	No 2nd dose
Allergy to penicillin	Clindamycin 300â€“600mg po	No 2nd dose

Flexible modifications depending on the â€˜degree of riskâ€™

- Additional doses after procedure
- Additional aminoglycosides
- Parenteral administration

Maximal regimen

	1h before	6h after
No penicillin allergy	Amoxycillin 2g iv + Gentamicin 1.5mg/kg im/iv	1â€“1.5g po
	Vancomycin 1g iv over 1 hour	No 2nd dose 1g iv at 12h
Allergy to penicillin	+ Gentamicin 1.5mg/kg im/iv	No 2nd dose

Footnote

1

This is one regime [after Leport C *et al.* (1995) *Eur Heart J* 16 (*suppl. B*): 126â€“131]. Refer to your local policy.

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Acute aortic regurgitation

Presentation

- Sudden, severe aortic regurgitation presents as cardiogenic shock and acute pulmonary oedema.
- The haemodynamic changes are markedly different from those seen in chronic AR. The previous normal-sized LV results in a smaller effective forward flow and higher LVEDP for the same degree of aortic regurgitation.
- Patients are often extremely unwell, tachycardic, peripherally shut down, and often have pulmonary oedema. Unlike chronic AR, pulse pressure may be near normal.
- If available, ask for a history of previous valvular heart disease, hypertension, features of Marfan's syndrome, and risk factors for infective endocarditis (P121).
- Physical signs of severe AR include a quiet aortic closure sound (S2); an ejection systolic murmur over aortic valve (turbulent flow); high-pitched and short early diastolic murmur (AR); quiet S1 (premature closure of the mitral valve).
- Examine specifically for signs of an underlying cause.
- Where there is no obvious underlying cause (e.g. acute MI), assume infective endocarditis until proven otherwise.

Causes

- Infective endocarditis
- Ascending aortic dissection
- Collagen vascular disorders (e.g. Marfan's)
- Connective tissue diseases (large- and medium-vessel arteritis)
- Trauma
- Dehiscence of a prosthetic valve.

Diagnosis

Based on a combination of clinical features and transthoracic and/or transoesophageal Echo.

Management

Acute AR is a surgical emergency and all other management measures are only aimed at stabalizing patient until urgent AVR can take place. Patient's clinical condition will determine the urgency of surgery (and mortality). Liaise immediately with local cardiologists.

General measures

- Admit the patient to intensive care or medical HDU.
- Give oxygen, begin treating any pulmonary oedema with diuretics.
- Monitor blood gases; mechanical ventilation may be necessary.
- Blood cultures Ã— 3 are essential. Other investigations as on P124.

- Serial ECG: watch for developing AV block or conduction defects.

Specific measures

- Every patient must be discussed with the regional cardiothoracic centre.
- In the context of good systemic BP, vasodilators such as sodium nitroprusside or hydralazine may temporarily improve forward flow and relieve pulmonary oedema.
- Inotropic support may be necessary if hypotensive. However, inotropes are best avoided as any increase in systemic pressures may worsen AR.
- All patients with haemodynamic compromise should have immediate or urgent aortic valve replacement.
- Infective endocarditis: indications for surgery are given on P134.
- IABP must be avoided as it will worsen AR.

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Acute mitral regurgitation

Presentation

- Patients most commonly present with acute breathlessness and severe pulmonary oedema. Symptoms may be less severe, or spontaneously improve, as left atrial compliance increases. There may be a history of previous murmur, angina, or myocardial infarction.
- The signs are different to those seen in chronic MR because of the presence of a non-dilated and relatively non-compliant LA. Acute MR results in a large LA systolic pressure wave (*v*-wave) and hence pulmonary oedema.
- Patients may be acutely unwell with tachycardia, hypotension, peripheral vasoconstriction, and pulmonary oedema and a pan-systolic murmur of MR.
- Later in the illness, probably because of sustained high left atrial and pulmonary venous pressures, right heart failure develops.
- Examine for signs of any underlying conditions (see table).
- The important differential diagnosis is a VSD. Transthoracic Echo and Doppler studies can readily differentiate between the two conditions. Alternatively, if Echo is not available, pulmonary artery catheterization in acute MR will exclude the presence of a left to right shunt and the PCWP trace will

demonstrate a large *v*-wave.

- Where there is no obvious underlying cause (e.g. acute MI), assume the patient has infective endocarditis until proven otherwise.

Diagnosis

Based on a combination of clinical features and Echo. Transthoracic Echo can readily diagnose and quantify MR. It also provides information on LV status (in particular regional wall-motion abnormalities which can give rise to MR). TOE can provide specific information about aetiology of valve dysfunction including papillary muscle rupture and MV leaflet (anterior and posterior) structural abnormalities. This information will be vital for a decision regarding definitive management.

General measures

- Admit the patient to intensive care or medical HDU.
- Give oxygen, begin treating any pulmonary oedema with diuretics.
- Monitor blood gases; mechanical ventilation may be necessary.
- Blood cultures Ã— 3 are essential. Other investigations as on P124.
- If present, MI should be treated in the standard manner.

Specific measures

- Pulmonary oedema may be very resistant to treatment.
- In the presence of good BP, reduction in preload [GTN infusion] and afterload especially with ACE inhibitors is

important. Systemic vasodilators such as hydralazine (12.5â€“100mg tds) can also be added in.

- An IABP will help decrease LVEDP and also increase coronary blood flow.

- Patients may require inotropic support. There are multiple combinations and aetiology of MR, haemodynamic status, and local policy/expertise should dictate choice of agent.
- CPAP and intubation and positive pressure ventilation are extremely useful and must be considered in all severe and/or resistant cases.
- Haemodynamic disturbance and severe pulmonary oedema in the context of acute MR is a surgical emergency.
- Infective endocarditis. Indications for surgery are given on P134.
- Post-infarct MR. Management depends upon the patient's condition following resuscitation. Patients who are stabilized may have MVR deferred because of the risks of surgery in the post-infarct patient. Their pre-operative management should consist of diuretics and vasodilators, including ACE inhibitors if tolerated. Advise patients regarding endocarditis prophylaxis.

Causes of acute mitral regurgitation

- Infective endocarditis
- Papillary muscle dysfunction or rupture (post MI, P36)
- Rupture of chordae tendinae (e.g. infection, myxomatous degeneration, SLE)
- Trauma (to leaflets, papillary muscle or chordae)
- Prosthetic valve malfunction (e.g. secondary to infection)
- Left atrial myxoma

- Acute rheumatic fever
- Collagen vascular disorders (e.g. Marfan's)
- Connective tissue diseases (large- and medium-vessel arteritis)

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Deep vein thrombosis (DVT): assessment

Presentation

- Most commonly asymptomatic. Minor leg discomfort or isolated swelling (>65%) in the effected limb are the most common clinical features. Breathlessness or chest pain may be secondary to pulmonary embolism.
- Signs include erythema and swelling of the leg, dilated superficial veins, and calf discomfort on dorsiflexion of the foot (Homan's sign). The thrombus may be palpable as a fibrous cord in the popliteal fossa. Confirm the presence of swelling (>2cm) by measuring the limb circumference 15cm above and 10cm below the tibial tuberosity.
- In all cases of leg swelling, abdominal and rectal (and pelvic in women) examination must be carried out to exclude an abdominal cause.

Risk factors for DVT

Pro-coagulant states	

Congenital	*Acquired*
Factor V_{Leiden}	Malignant disease (~5%)
Antithrombin III deficiency	Antiphospholipid syndrome
Protein C deficiency	Myeloproliferative disorders
Protein S deficiency	Oral contraceptive pill (especially with Factor V_{Leiden} mutation)
	Nephrotic syndrome (via renal AT III losses)
	Homocystinuria
	Paroxysmal nocturnal haemoglobinuria
Venous stasis	Immobility (e.g. long journeys)
	Recent surgery
	Pelvic mass
	Pregnancy or recent childbirth
	Severe obesity
Miscellaneous	Hyperviscosity syndromes (P728)

	Previous DVT or PE
	Family history of DVT/PE

Investigations

- Real time B-mode venous compression ultrasonography of leg veins is largely replacing venography as the initial investigation of choice. It is quick, and non-invasive, with sensitivity and specificity of over 90% and does not carry the risk of contrast allergy or phlebitis. It can simultaneously assess extent of proximal progression of the thrombus in particular extension into pelvic vessels.
- D-Dimers have a high negative predictive value for DVT. A low clinical probability of DVT and a negative D-Dimer does not require further investigation. A positive D-Dimer result should be followed by ultrasonography.
- Venography: Use if results uncertain and clinical suspicion is high.

- Consider baseline investigations [FBC, U&Es, ECG, CXR, urinalysis, and pulse oximetry (Â± ABG)] on all patients.
- If appropriate, look for an underlying cause (see above).
    - Coagulation screen
    - Pro-coagulant screen: refer to local screening policy and get haematology advice (e.g. CRP, ESR, Protein C and S, Antithrombin III levels, Factor V_{Leiden} mutation, auto-Ab screen, immunoglobulins and immunoelectrophoretic strip, anticardiolipin antibody, Ham test, etc.).
    - Screen for malignancy: ultrasound Â± CT (abdomen and

pelvis), CXR, LFTs, PSA, CEA, CA-125, CA-19.9, Î²-HCG, etc.

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Deep vein thrombosis: management

- If there is a high clinical suspicion of DVT (the presence of risk factors and absence of an alternative diagnosis), start empiric anti-coagulation with LMWH. This may be stopped if subsequent investigations are negative.
- Below-knee DVT: thrombi limited to the calf have a lower risk of embolization and may be treated with compression stockings and sub-cutaneous prophylactic doses of LMWH until mobile to deter proximal propagation of thrombus. A brief period of systemic anti-coagulation with LMWH may lessen the pain from below-knee DVT.
- Above-knee DVT: thrombi within the thigh veins warrant full anti-coagulation with LMWH/UFH and subsequently warfarin.

Anti-coagulation

- Heparin
  - LMWHs have now superseded UFH for management of both DVT and PE. They require no monitoring on a daily basis and also allow out-patient treatment.
  - There must be period of overlap between LMWH/UFH

therapy and anti-coagulation with warfarin until INR is within therapeutic range and stable.

- LMWH are administered primarily as a once-daily sc injection and dosage is determined by patient weight.

- Warfarin

  - Always anti-coagulate with LMWH/UFH before starting warfarin. Protein C (a vitamin K-dependent anti-coagulant) has a shorter half-life than the other coagulation factors and levels fall sooner resulting in a transient pro-coagulant tendency.
  - If DVT is confirmed commence warfarin and maintain on LMWH/UFH until INR >2.
  - Anti-coagulate (INR 2â€“2.5) for 3 months.
  - If recurrent DVT, or patient at high-risk of recurrence, consider lifelong anti-coagulation.

Thrombolysis

- This should be considered for recurrent, extensive, proximal venous thrombosis (e.g. femoral or iliac veins), as it is more effective than anti-coagulation alone in promoting clot dissolution and produces a better clinical outcome.
- Catheter-directed thrombolytic therapy (rt-PA or SK) is superior to systemic thrombolysis.
- One approach is streptokinase 250 000U over 30 minutes then 100 000U every hour for 24â€“72 hours (see data sheet). See P22 for contraindications to thrombolysis.

Further management

- Women taking the combined OCP should be advised to stop

this.

- If there are contraindications to anti-coagulation, consider the insertion of a caval filter to prevent PE.
- All patients should be treated with thigh-high compression stockings to try to reduce symptomatic venous distension when mobilizing.

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Pulmonary embolism (PE): assessment

Symptoms

- Classically presents with sudden onset, pleuritic chest pain, associated with breathlessness and haemoptysis. Additional symptoms include postural dizziness or syncope.
- Massive PE may present as cardiac arrest (particularly with electromechanical dissociation) or shock.
- Presentation may be atypical, i.e. unexplained breathlessness or unexplained hypotension or syncope only.
- Pulmonary emboli should be suspected in all breathless patients with risk factors for deep vein thrombosis (DVT) or with clinically proven DVT (P144).
- Recurrent PEs may present with chronic pulmonary hypertension and progressive right heart failure.

Signs

- Examination may reveal tachycardia and tachypnoea only. Look for postural hypotension (in the presence of raised JVP).
- Look for signs of raised right heart pressures and cor

pulmonale (raised JVP with prominent â€˜aâ€™ wave, tricuspid regurgitation, parasternal heave, right ventricular S3, loud pulmonary closure sound with wide splitting of S2, pulmonary regurgitation).

- Cyanosis suggests a large pulmonary embolism.
- Examine for a pleural rub (may be transient) or effusion.
- Examine lower limbs for obvious thrombophlebitis.
- Mild fever (>37.5Â°C) may be present. There may be signs of co-existing COPD.

Causes

- Most frequently secondary to DVT (leg >> arm; see P144).
- Other causes
    - Rarely secondary to right ventricular thrombus (post MI)
    - Septic emboli (e.g. tricuspid endocarditis)
    - Fat embolism (post fracture)
    - Air embolism (venous lines, diving, see P850)
    - Amniotic fluid
    - Parasites
    - Neoplastic cells
    - Foreign materials (e.g. venous catheters).

Prognostic features

The prognosis in patients with pulmonary emboli varies greatly, associated in part with any underlying condition. Generally worse prognosis is associated with larger pulmonary emboli; poor prognostic indicators include

- Hypotension
- Hypoxia
- ECG changes (other than non-specific T-wave changes).

Practice point

- A normal D-dimer excludes pulmonary embolus with ~95% accuracy, but a positive D-dimer can be secondary to other disorders.

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Pulmonary embolism: investigations 1

General investigations

â€¢ ABG	Normal ABG *does not* exclude a PE.
	â†“P_aO_2 is invariable with larger PEs. Other changes include mild respiratory alkalosis and â†“P_aCO_2 (due to tachypnoea) and metabolic acidosis (2Â° to shock).
â€¢ ECG	Commonly shows sinus tachycardia Â± non-specific ST- and T-wave changes in the anterior chest leads. The classical changes of acute cor pulmonale such as $S_1Q_3T_3$, right axis deviation, or RBBB are only seen with massive PE. Less common findings include AF.
â€¢ CXR	May be normal and a near-normal chest film in the context of severe respiratory compromise is highly suggestive of a PE. Less commonly may show focal pulmonary

	oligaemia (Westermark's sign), a raised hemidiaphragm, small pleural effusion, wedge-shaped shadows based on the pleura, sub-segmental atelectasis, or dilated proximal pulmonary arteries.
â€¢ Blood tests	There is no specific test. FBC may show neutrophil leukocytosis; mildly elevated CK, troponin, and bilirubin may be seen.
â€¢ Echo/TOE	Insensitive for diagnosis but can exclude other causes of hypotension and raised right-sided pressures (e.g. tamponade, RV infarction, P28). In PE it will show RV dilatation and global hypokinesia [with sparing of apex (McConnell's sign)] and pulmonary artery dilation. Doppler may show tricuspid/pulmonary regurgitation allowing estimation of RV systolic pressure. Rarely, the thrombus in the pulmonary artery may be visible.

Specific investigations

D-dimer

- A highly sensitive, but non-specific test.
- Useful in ruling out PE in patients with low or intermediate probability.
- Results can be affected by advancing age, pregnancy, trauma, surgery, malignancy, and inflammatory states.

Ventilation/perfusion (V/Q) lung scanning

A perfusion lung scan (with iv Technetium-99 labelled albumin) should be performed in all suspected cases of PE. A ventilation scan (inhaled Xenon-133) in conjunction increases the specificity by assessing whether the defects in the ventilation and perfusion scans â€˜matchâ€™ or â€˜mismatchâ€™. Pre-existing lung disease makes interpretation difficult.

- A normal perfusion scan rules out significant-sized PE.
- Abnormal scans are reported as low, medium, or high probability:
    - A high probility scan is strongly associated with a PE, but there is a significant minority of false positives

    - A low probability scan with a low clinical suspicion of PE should prompt a search for another cause for the patient's symptoms
    - If the clinical suspicion of PE is high and the scan is of low or medium probability, alternative investigations are required.

Investigations for an underlying cause for PEs

- Ultrasound deep veins of legs
- USS abdomen and pelvis (?occult malignancy/pelvic mass)
- CT abdomen/pelvis
- Screen for inherited pro-coagulant tendency (e.g. Protein C, S, antithrombin III, Factor V_{Leiden})
- Autoimmune screen (anticardiolipin antibody, ANA)

- Biopsy of suspicious lymph nodes/masses

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Pulmonary embolism: investigations 2

CTPA

- This is the recommended initial lung imaging modality in patients with non-massive PE.
- Allows direct visualization of emboli as well as other potential parenchymal disease, which may explain alternative explanation for symptoms.
- Sensitivity and specificity are high (>90%) for lobar pulmonary arteries but not so high for segmental and sub-segmental pulmonary arteries.
- A patient with a positive CTPA does not require further investigation for PE.
- A patient with a negative CTPA in the context of a high/intermediate probability of a PE should undergo further investigation.

Evaluation of leg veins with ultrasound

- Not very reliable. Almost half of patients with PE do not have evidence of a DVT and therefore a negative result

cannot rule out a PE.

- Useful second-line investigation as an adjunct to CTPA/V/Q scan.
- Outcome studies have demonstrated that it would be safe not to anti-coagulate patients with a negative CTPA and lower limb US who have an intermediate/low probability of a PE.

Pulmonary angiography

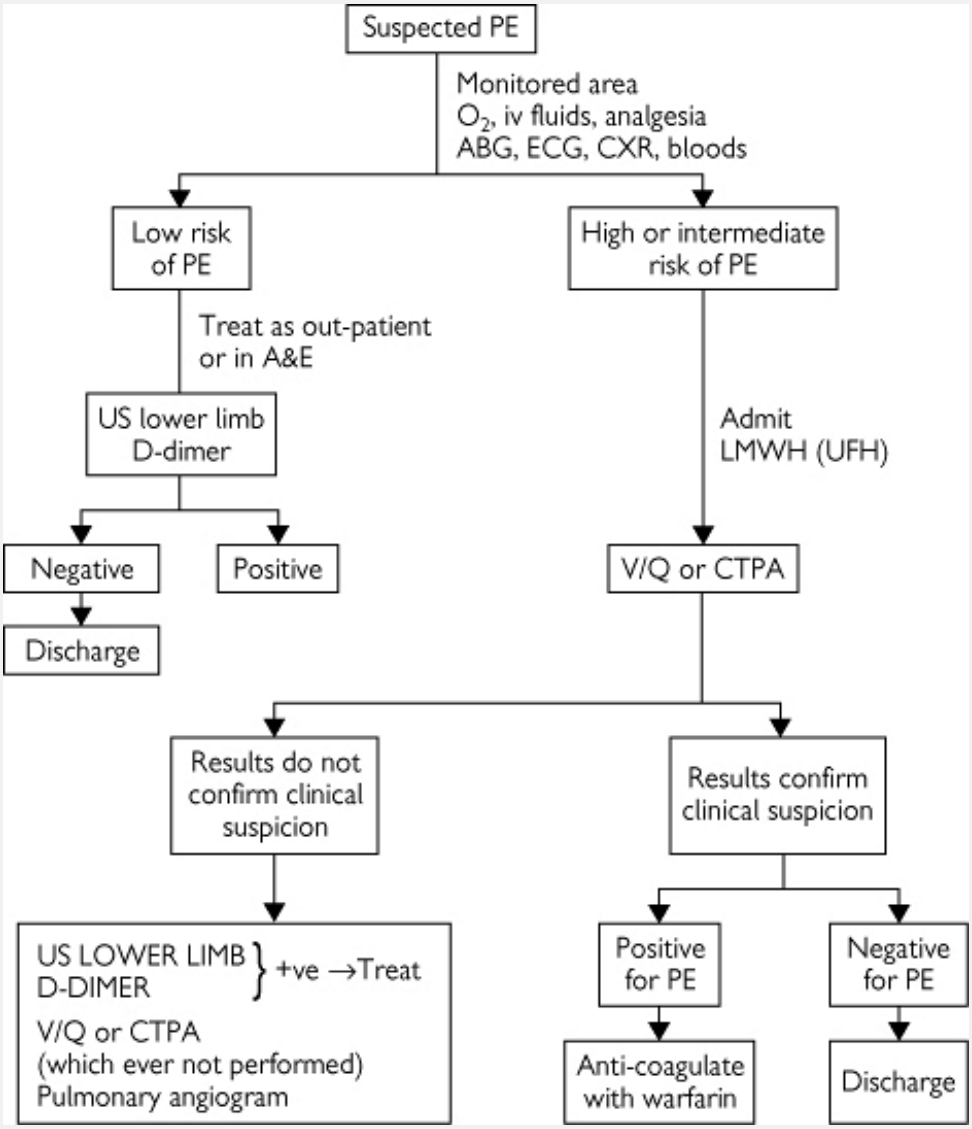
- Is the â€˜gold standardâ€™ investigation.
- It is indicated in patients in whom diagnosis of embolism cannot be established by non-invasive means. Look for sharp cut-off of vessels or obvious filling defects.
- Invasive investigation and can be associated with 0.5% mortality.
- If there is an obvious filling defect, the catheter or a guide wire passed through the catheter may be used to disobliterate the thrombus.
- After angiography, the catheter may be used to give thrombolysis directly into the affected pulmonary artery (see P152).
- The contrast can cause systemic vasodilatation and haemodynamic collapse in hypotensive patients.

MR pulmonary angiography

- Results are comparable to pulmonary angiography in preliminary studies.
- It can simultaneously assess ventricular function.

The Flow diagram opposite summarizes one proposed pathway

for investigation on potential PE patients.



Proposed pathway for investigation of patients with suspected PE

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Pulmonary embolism: management 1

- Stabilize the patient
  - Unless an alternative diagnosis is made the patient should be treated as for a pulmonary embolus until this can be excluded.
  - Monitor cardiac rhythm, pulse, BP, respiration rate every 15 minutes with continuous pulse oximetry and cardiac monitor. Ensure full resuscitation facilities are available.
  - Obtain venous access and start iv fluids (crystalloid or colloid).
  - Give maximal inspired oxygen via facemask to correct hypoxia. Mechanical ventilation may be necessary if the patient is tiring (beware of cardiovascular collapse when sedation is given for endotracheal intubation).
  - *Give LMWH or UFH to all patients with high or intermediate risk of PE until diagnosis is confirmed*. Meta-analysis of multiple trials has shown LMWH to be superior to UFH with a reduction in mortality and bleeding complications. For doses consult local formulary.
  - If there is evidence of haemodynamic instability

(systemic hypotension, features of right heart failure) or cardiac arrest, patients may benefit from thrombolysis with rtPA or streptokinase [same doses used for treatment of STEMI (see below].

- Analgesia
    - Patients may respond to oral NSAIDs.
    - Opiate analgesia to be used with caution. The vasodilatation caused by these drugs may precipitate or worsen hypotension. Give small doses (1â€“2mg diamorphine iv) slowly. Hypotension should respond to iv colloid.
    - Avoid im injections (anti-coagulation and possible thrombolysis).
- Investigations with a view to a definite diagnosis (see previous section)
- Anti-coagulate
    - Patients with a positive diagnosis must undergo anti-coagulation with warfarin. There should be period of overlap with LMWH/UFH until INR values are therapeutic. Target INR is 2â€“3 for most cases (see below).
    - Standard duration of anti-coagulation is
        - 4â€“6 weeks for temporary risk factor
        - 3 months for first idiopathic cases
        - At least 6 months for other cases
        - With recurrent events and underlying predisposition to thromboembolic events (e.g. anti-phospholipid antibody syndrome), lifelong anti-coagulation may be needed (as well as higher target INR >3).

Dosage of thrombolytic agents for pulmonary embolus

rtPA	100mg over 2 hours or 0.6mg/kg over 15 minutes (maximum of 50mg) followed by heparin
Streptokinase	250 000U over 30 minutes followed by 100 000U/h infusion for 24 hours

NB: contraindications for thrombolysis identical to those for STEMI (P22)

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Pulmonary embolism: management 2

Cardiac arrest (also see P8)

- Massive PE may present as cardiac arrest with EMD. Exclude the other causes of EMD (see P8).
- Chest compressions may help break up the thrombus and allow it to progress more distally, thereby restoring some cardiac output.
- If clinical suspicion of PE is high and there is no absolute contraindication to thrombolysis, give rt-PA [similar in dose to STEMI with a maximum of 50mg (see P152) followed by heparin].
- If cardiac output returns, consider pulmonary angiography or inserting a PA catheter to try to mechanically disrupt the embolus.

Hypotension

The acute increase in pulmonary vascular resistance results in right ventricular dilatation and pressure overload, which mechanically impairs LV filling and function. Patients require a higher than normal right-sided filling pressure, but may be worsened by fluid overload.

- Insert an internal jugular sheath prior to anti-coagulation. This can be used for access, later if necessary.
- If hypotensive, give colloid (e.g. 500ml HaemacellÂ® stat).
- If hypotension, persists invasive monitoring and/or inotropic support is required. The JVP is a poor indicator of the left-sided filling pressures in such cases. Adrenaline is the inotrope of choice.
- Femoro-femoral cardiopulmonary bypass may be used to support the circulation until thrombolysis or surgical embolectomy can be performed.
- Pulmonary angiography in a hypotensive patient is hazardous as the contrast may cause systemic vasodilatation and cardiovascular collapse.

Pulmonary embolectomy

- In patients who have contraindications to thrombolysis and are in shock requiring inotropic support, there may be a role for embolectomy if appropriate skills are on site.
- This can be performed percutaneously in the catheterization laboratory using a number of devices or surgically on cardiopulmonary bypass.
- Percutaneous procedures may be combined with peripheral or central thrombolysis.
- Seek specialist advice early. Best results are obtained before onset of cardiogenic shock.
- Radiological confirmation of extent and site of embolism is preferable before thoracotomy.
- Mortality is ~25â€“30%.

IVC filter

- Infrequently used as little to suggest improved short- or long-term mortality.
- Filters are positioned percutaneously and if possible patients must remain anti-coagulated to prevent further thrombus formation.

- Most are positioned infra-renally (bird's nest filter), but can also be supra-renal (Greenfield filter).
- Indications for IVC filter use include
    - Anti-coagulation contraindicated: e.g. active bleeding, heparin-induced thrombocytopenia, planned intensive chemotherapy
    - Anti-coagulation failure despite adequate therapy
    - Prophylaxis in high-risk patients: e.g. progressive venous thrombosis, severe pulmonary hypertension.

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Fat embolism

Commonly seen in patients with major trauma. There is embolization of fat and micro-aggregates of platelets, RBCs, and fibrin in systemic and pulmonary circulation. Pulmonary damage may result directly from the emboli (infarction) or by a chemical pneumonitis and ARDS (see P230).

Clinical features

- There may be a history of fractures, followed (24â€“48 hours later) by breathlessness, cough, haemoptysis, confusion, and rash.
- Examination reveals fever (38â€“39Â°C), widespread petechial rash (25â€–50%), cyanosis, and tachypnoea. There may be scattered crepitations in the chest, though examination may be normal. Changes in mental state may be the first sign with confusion, drowsiness, seizures, and coma. Examine the eyes for conjunctival and retinal haemorrhages; occasionally fat globules may be seen in the retinal vessels. Severe fat embolism may present as shock.

Investigations

â€¢ ABG	Hypoxia and a respiratory alkalosis (with low P_aCO_2) as for thromboembolic PE
â€¢ FBC	Thrombocytopenia, acute intravascular haemolysis
â€¢ Coagulation	Disseminated intravascular coagulation
â€¢ U&Es and glucose	Renal failure, hypoglycaemia
â€¢ Ca^{2+}	May be low
â€¢ Urine	Microscopy for fat and dipstick for haemoglobin
â€¢ ECG	Usually non-specific (sinus tachycardia; occasionally signs of right heart strain
â€¢ CXR	Usually lags behind the clinical course. There may be patchy, bilateral, air space opacification. Effusions are rare
â€¢ CT head	Consider if there is a possibility of head injury with expanding subdural or epidural bleed.

Differential diagnosis

- Pulmonary thromboembolism, other causes of ARDS (P231), septic shock, hypovolaemia, cardiac or pulmonary contusion, head injury, aspiration pneumonia, transfusion reaction.

Management

- Treat respiratory failure (P228). Give oxygen (maximal via facemask; CPAP and mechanical ventilation if necessary).
- Ensure adequate circulating volume and cardiac output. CVP is not a good guide to left-sided filling pressures and a PA catheter (Swanâ€“Ganz) should be used to guide fluid replacement. Try to keep PCWP 12â€“15mmHg and give diuretics if necessary. Use inotropes to support circulation as required (P234).
- Aspirin, heparin and Dextran 40 (500ml over 4â€–6 hours) are of some benefit in the acute stages, but may exacerbate bleeding from sites of trauma.
- High-dose steroids (methylprednisolone 30mg/kg q8h for 3 doses) have been shown to improve hypoxaemia[1] but steroids are probably most effective if given prophylactically.

Footnote

1

Lindeque BG *et al.* (1987) *J Bone Joint Surg* 69: 128â€“131.

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Title: *Oxford Handbook of Acute Medicine, 2nd Edition*

Hypertensive emergencies

Hypertensive crisis

Hypertensive crisis is defined as a severe elevation in blood pressure (SBP >200mmHg, DBP >120mmHg). Rate of change in BP is important. A rapid rise is poorly tolerated and leads to end-organ damage, whereas a gradual rise in a patient with existent poor BP control is tolerated better. Hypertensive crisis is classified as

- Hypertensive emergency, where a high BP is complicated by acute target-organ dysfunction (see table) and includes
    - Hypertensive emergency with retinopathy, where there is marked elevation in BP (classically DBP >140mmHg) with retinal haemorrhages and exudates (previously called accelerated hypertension) and
    - Hypertensive emergency with papilloedema, with a similarly high BP and papilloedema (previously called malignant hypertension).
- Hypertensive urgency, where there is a similar rise in BP, but without target organ damage.

Conditions which may present with

hypertensive emergency

- Essential hypertension
- Renovascular hypertension: atheroma, fibromuscular dysplasia, acute renal occlusion
- Renal parenchymal disease: acute glomerulonephritis, vasculitis, scleroderma
- Endocrine disorders: phechromocytoma, Cushing's syndrome, primary hyperaldosteronism, thyrotoxicosis, hyperparathyroidism, acromegaly, adrenal carcinoma
- Eclampsia and pre-eclampsia
- Vasculitis
- Drugs: cocaine, amphetamines, MAOI interactions, cyclosporine, Î²-blocker and clonidine withdrawal
- Autonomic hyperactivity in presence of spinal cord injury
- Coarctation of the aorta.

Presentation

- Occasionally minimal non-specific symptoms such as mild headache and nose bleed.
- A small group of patients present with symptoms resulting from BP-induced microvascular damage:
    - Neurological symptoms: severe headache, nausea, vomiting, visual loss, focal neurological deficits, fits, confusion, intracerebral haemorrhage, coma.
    - Chest pain (hypertensive heart disease, MI, or aortic dissection) and congestive cardiac failure.
    - Symptoms of renal failure: renal impairment may be chronic (secondary to long-standing hypertension) or

acute (from the necrotizing vasculitis of malignant hypertension).

- Patients may present with hypertension as one manifestation of an underlying â€˜diseaseâ€™ (renovascular hypertension, chronic renal failure, CREST syndrome, phaeochromocytoma, pregnancy).
- Examination should be directed at looking for evidence of end-organ damage even if the patient is asymptomatic (heart failure, retinopathy, papilloedema, focal neurology).

Hypertensive emergencies

- Hypertensive emergency with retinopathy/papilloedema
- Hypertensive encephalopathy
- Hypertension-induced intracranial haemorrhage/stroke
- Hypertension with cardiovascular complications
    - Aortic dissection (P170)
    - MI
    - Pulmonary oedema (P108)
- Pheochromocytoma (P598)
- Pregnancy-associated hypertensive complications

  Eclampsia and pre-eclampsia
- Acute renal insufficiency
- Hypertensive emergency secondary to acute withdrawal syndromes (e.g. Î²-blockers, centrally acting anti-hypertensives)

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Hypertensive emergencies: management 1

Priorities in management

- Confirm the diagnosis and assess the severity.
- Identify those patients needing specific emergency treatment.
- Plan long-term treatment.

Diagnosis and severity

- Ask about previous BP recordings, previous and current treatment, sympathomimetics, anti-depressants, non-prescription drugs, recreational drugs.
- Check the blood pressure yourself, in both arms, after a period of rest and if possible on standing. Monitor the patient's blood pressure regularly while they are in A&E.
- Examine carefully for clinical evidence of cardiac enlargement or heart failure, peripheral pulses, renal masses or focal neurological deficit. Always examine the fundi: dilate if necessary.

Investigations

All patients should have

â€¢ FBC	Microangiopathic haemolytic anaemia with malignant HT
â€¢ U&E	Renal impairment and/or â†“K^+ (diffuse intra-renal ischaemia and 2Â° hyperaldosteronism)
â€¢ Coag. screen	DIC with malignant HT
â€¢ CXR	Cardiac enlargement
	Aortic contour (dissection?)
	Pulmonary oedema
â€¢ Urinalysis	Protein and red cells Â± casts.

Other investigations, depending on clinical picture and possible aetiology include

â€¢ 24-hour urine collection	Creatinine clearance
	Free catecholamines, metanephrines, or VMA
â€¢ Echo	LVH, aortic dissection
â€¢ Renal USS and Doppler	Size of kidneys and renal artery stenosis
â€¢ MR renal angiogram	Renal artery stenosis
â€¢ CT/MR brain	Intracranial bleed
â€¢ Drug screen	Cocaine, amphetamine, others.

Indications for admission

- Diastolic blood pressure persistently â‰¥120mmHg
- Retinal haemorrhages, exudates or papilloedema
- Renal impairment.

Voltage criteria for LVH

- Tallest R (V4â€“V6) + deepest S (V1â€“V3) >40mm
- Tallest R (V4â€“V6) >27mm
- Deepest S (V1â€“V3) >30mm

- R in aVL >13mm
- R in aVF >20 mm
- QRS complex >0.08s (2 small sq.)
- Abnormal ST depression or T inversion in V4â€“V6

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Hypertensive emergencies: management 2

Treatment principles

- *Rapid reduction in BP is unnecessary, must be avoided, and can be very dangerous* . This can result in cerebral and cardiac hypoperfusion (an abrupt change of >25% in BP will exceed cerebral BP autoregulation).
- Initial BP reduction of 25% to be achieved over 1â€“4 hours with a less rapid reduction over 24 hours to a DBP of 100mmHg.
- The only two situations where BP must be lowered rapidly are in the context of aortic dissection and MI.

Treatment

- The majority of patients who are alert and otherwise well may be treated with oral therapy to lower BP gradually.
- First-line treatment should be with a Î²-blocker (unless contraindicated) with a thiazide diuretic, or a low-dose calcium antagonist.
- Urgent invasive monitoring (arterial line) prior to drug therapy is indicated for patients with

    - Evidence of hypertensive encephalopathy
    - Complications of hypertension (e.g. aortic dissection, acute pulmonary oedema, or renal failure)
    - Treatment of an underlying condition (e.g. glomerulonephritis, phaeochromocytoma, CREST crisis)
    - Patients with persistent diastolic BP â‰¥140mmHg
    - Eclampsia.
- Sublingual nifedipine must be avoided.

Conditions requiring specific treatment are listed in table below.

Long-term management

- Investigate as appropriate for an underlying causes.
- Select a treatment regime that is tolerated and effective. Tell the patient why long-term therapy is important.
- Try to reduce all cardiovascular risk factors by advising the patient to stop smoking, appropriate dietary advice (cholesterol), and aim for optimal diabetic control.
- Monitor long-term control and look for end-organ damage (regular fundoscopy, ECG, U&Es). Even poor control is better than no control.

Conditions requiring specific treatment

- Accelerated and malignant hypertension (P166)
- Hypertensive encephalopathy (P168)
- Eclampsia

- Phaeochromocytoma (P598)
- Hypertensive patients undergoing anaesthesia

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Drugs for the treatment of hypertensive emergencies: IV therapy

Labetalol
20â€“80mg iv bolus q10min
2â€“5 minutes
Drug of choice in suspected phaeochromocytoma (P598) or aortic dissection (P170). Avoid if there is LVF
20â€“200mg/min by iv infusion increasing every 15 min.
May be continued orally (see below)
Nitroprusside
0.25â€“10Âµg/kg/min iv infusion (P698)
Seconds
Drug of choice in LVF and/or encephalopathy.
GTN
1â€“10mg/hr iv infusion
2â€“5 minutes
Mainly venodilatation. Useful in patients with LVF or angina.
Hydralazine
5â€“10mg iv over 20 min
10â€“15 minutes
May provoke angina
50â€“300Âµg/min iv infusion
Esmolol HCl
500Âµg/kg/min iv loading dose
Seconds
Short acting Î²-blocker also used for SVTs
50â€“200Âµg/kg/min iv infusion
Phentolamine

2â€“5mg iv over 2â€“5 minutes prn
Seconds
Drug of choice in phaeochromocytoma (P598) followed by labetalol (po) when BP controlled
NB: It is dangerous to reduce the blood pressure quickly. Aim to reduce the diatolic BP to 100â€“110mmHg within 2â€“4 hours. Unless there are good reasons to commence iv therapy, always use oral medicines

Drug	Dosage	Onset of action	Comments

Drugs for the treatment of hypertensive emergencies: Oral therapy

Atendol
50â€“100mg po od
30â€“60 minutes
There are numerous alternative Î²-blockersâ€”see BNF
Nifedipine
10â€“20mg po q8h (q12h if slow release)
15â€“20 minutes
Avoid sublingual as the fall in bp is very rapid.
Labetalol
100â€“400mg po q12h
30â€“60 minutes
Use if phaeochromocytoma suspected. Safe in pregnancy
Hydralazine
25â€“50mg po q8h
20â€“40 minutes
Safe in pregnancy
Minoxidil
5â€“10mg po od
30â€“60 minutes

May cause marked salt and water retention Combine with a loop diuretic (e.g. frusemide 40â€“240mg daily)
Clonidine
0.2mg po followed by 0.1 mg hourly max. 30â€“60 minutes Sedation common. Do not stop abruptly as here is a high incidence of rebound hypertensive crisis
0.8mg total for urgent therapy, or 0.05â€“0.1mg
po q8h increasing every 2 days
NB: Aim to reduce diastolic bp to 100â€“110mmHg in 2â€“4 hours and normalize bp in 2â€“3 days

Drug Dosage Onset of action Comment

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Hypertensive emergency with retinopathy (accelerated and malignant hypertension)

This is part of a continuum of disorders characterized by hypertension (DBP often >120mmHg) and acute microvascular damage (seen best in the retina but present in all organs). It may be difficult to decide whether the damage in some vascular beds is the cause or effect of hypertension. An example is in the context of an acute glomerulonephritis.

- Accelerated hypertension (Grade 3 retinopathy) may progress to malignant hypertension, with widespread necrotizing vasculitis of the arterioles (and papilloedema).
- Presentation is commonly with headache or visual loss and varying degrees of confusion. More severe cases present with renal failure, heart failure, microangiopathic haemolytic anaemia, and DIC.

Management

- Transfer the patient to medical HDU/ITU.
- Insert an arterial line and consider central venous line if there is evidence of necrotizing vasculitis and DIC.

Catheterize the bladder.

- Monitor neurological state, ECG, fluid balance.
- Aim to lower the DBP to 100mmHg or by 15â€“20mmHg, whichever is higher, over the first 24 hours.
- Those with early features may be treated successfully with oral therapy (Î²-blockers, calcium channel blockers).
- Patients with late symptoms or who deteriorate should be given parenteral therapy aiming for more rapid lowering of BP.
- If there is evidence of pulmonary oedema or encephalopathy give frusemide 40â€“80mg iv.
- If there is no LVF, give a bolus of labetalol followed by an infusion. For patients with LVF, nitroprusside or hydralazine are preferable.
- Consult renal team for patients with acute renal failure or evidence of acute glomerulonephritis (>2+ proteinuria, red cell casts). ARF is managed as on P378. Dopamine should be avoided as it may worsen hypertension.
- Consider giving an ACE inhibitor. High circulating renin levels may not allow control of hypertension, which in turn causes progressive renal failure. ACE inhibitors will block this vicious circle. There may be marked first-dose hypotension so start cautiously.
- Haemolysis and DIC should recover with control of BP.

Hypertension in the context of acute stroke/intracranial bleed

- Stroke/bleed may be the result of hypertension or vice versa.
- In the acute setting there is impaired autoregulation of cerebral blood flow and autonomic function. Small changes

in systemic BP may result in catastrophic falls in cerebral blood flow.

- Systemic BP should not be treated unless DBP >130mmHg and/or presence of severe cerebral oedema (with clinical manifestations).

- In most cases BP tends to settle over 24â€“36 hours. If treatment is indicated, above BP reduction principles must be adhered to and a combination of nitroprusside, labetalol, and calcium channel blockers can be used.
- Centrally acting agents must be avoided as they cause sedation.
- In patients with SAH, a cerebroselective calcium channel blocker, such as nimodipine, is used to decrease cerebral vasospasm.
- Systemic BP must also be treated if it qualifies with the above principles and/or if it remains elevated after 24 hours. There is no evidence that this reduces further events in the acute phase.

Hypertensive retinopathy

Grade 1	Tortuous retinal arteries, silver wiring
Grade 2	AV nipping
Grade 3	Flame-shaped haemorrhages and cotton
Grade 4	Papilloedema

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Hypertensive encephalopathy

- Caused by cerebral oedema secondary to loss of cerebral autoregulatory function.
- Usually gradual onset and may occur in previously normotensive patients at blood pressures as low as 150/100. It is rare in patients with chronic hypertension and pressures are also much higher.

Symptoms

- Headache, nausea and vomiting, confusion, grade III and IV hypertensive retinopathy.
- Late features consist of focal neurological signs, fits, and coma.

Diagnosis

- A diagnosis of exclusion and other differential diagnosis must be ruled out (e.g. stroke, encephalitis, tumours, bleeding, vasculitis).
- History is helpful, particularly of previous seizures, SAH usually being sudden in onset and strokes being associated with focal neurological deficit.

- Always exclude hypoglycaemia.
- Starting hypotensive treatment for hypertension associated with a stroke can cause extension of the stroke.
- *An urgent MRI or CT brain must be obtained* to rule out some of the differential diagnosis.

Management

- The primary principle of blood pressure control is *to reduce DBP by 25% or reduce DBP to 100mmHg, whichever is higher, over a period of 1â€“2 hours*.
- Transfer the patient to ITU for invasive monitoring (see previous section).
- Monitor neurological state, ECG, fluid balance.
- Correct electrolyte abnormalities (K^+, Mg^{2+}, Ca^{2+}).
- Give frusemide 40â€“80mg iv.
- Nitroprusside is the first-line agent as it allows easy control of BP changes, despite its tendency to increase cerebral blood flow.
- Labetolol and calcium channel blockers are second-line agents and should be added in if necessary.
- It is vital to avoid agents with potential sedative action such as Î²-blockers, clonidine, and methyldopa.
- In selected patients who are stable and present at the very early stages, oral therapy with a combination of Î²-blockers and calcium blockers may be sufficient.

Editors: Ramrakha, Punit S.; Moore, Kevin P.
Title: *Oxford Handbook of Acute Medicine, 2nd Edition*

Aortic dissection: assessment

Aortic dissection is a surgical/medical emergency and untreated has a >90% 1-year mortality. Dissection begins with formation of a tear in the intima and the force of the blood cleaves the media longitudinally to various lengths. Predisposing factors are summarized in table opposite.

Classification

There are three classifications as illustrated in figure on P173 (DeBakey, Stanford, and Descriptive). Dissections involving the ascending and/or aortic arch are surgical emergencies and those exclusive to the descending aorta are treated medically.

Presentation

- Chest pain. Classically abrupt onset of very severe, most commonly anterior chest pain radiating to the interscapular region. Usually tearing in nature and unlike the pain of myocardial infarction most severe at its onset. Pain felt maximally in the anterior chest is associated with ascending aortic dissection, whereas interscapular pain suggests dissection of the descending aorta. Patients often use adjectives such as â€˜tearingâ€™, â€˜rippingâ€™, â€˜sharpâ€™, and â€˜stabbingâ€™ to describe the pain.
- Sudden death or shock. Usually due to aortic rupture or

cardiac tamponade.

- Congestive cardiac failure. Due to acute aortic incompetence and/or myocardial infarction.
- Patients may also present with symptoms and signs of occlusion of one of the branches of the aorta. Examples include
    - Stroke or acute limb ischaemia: due to compression or dissection
    - Paraplegia with sensory deficits: spinal artery occlusion
    - Myocardial infarction: usually the right coronary artery
    - Renal failure and renovascular hypertension
    - Abdominal pain: coeliac axis or mesenteric artery occlusion.
- Aortic dissection may be painless.
- Ask specifically about history of hypertension, previous heart murmurs or aortic valve disease, and previous chest X-rays that may be useful for comparison.

Examination

- This may be normal.
- Most patients are hypertensive on presentation. Hypotension is more common in dissections of the ascending aorta (20â€“25%) and may be due to blood loss, acute aortic incompetence (which may be accompanied by heart failure), or tamponade (distended neck veins, tachycardia, pulsus paradoxus).
- Pseudohypotension may be seen if flow to either or both subclavian arteries is compromised. Look for unequal blood pressure in the arms and document the presence of peripheral pulses carefully. Absent or changing pulses

suggest extension of the dissection.

- Auscultation may reveal aortic valve regurgitation and occasionally a pericardial friction rub. Descending aortic dissections may rupture or leak into the left pleural space and the effusion results in dullness in the left base.
- Neurologic deficits may be due to carotid artery dissection or compression (hemiplegia) or spinal artery occlusion (paraplegia with sensory loss).

Conditions associated with aortic dissection

Hypertension	Smoking, dyslipidaemia, cocaine/crack
Connective tissue disorders	Marfan's syndrome[1]
	Ehlersâ€“Danlos syndrome
Hereditary vascular disorders	Bicuspid aortic valve
Vascular inflammation	Coarctaion
	Giant cell arteritis
	Takayasu arteritis
	BehÃ§et's disease

	Syphillis
Decceleration trauma	Car accident
Chest trauma	Falls
Pregnancy	
Iatrogenic	Catheterization
	Cardiac surgery

[1] Marfan's syndrome [arm span > height, pubis to sole > pubis to vertex, depressed sternum, scoliosis, high-arched palate, upward lens dislocation, thoracic aortic dilation/aortic regurgitation, increased urinary hydroxyprolene (some)].

Differential diagnosis

- The chest pain may be mistaken for acute MI and acute MI may complicate aortic dissection. Always look for other signs of dissection (see above), as thrombolysis will be fatal.
- Severe chest pain and collapse may also be due to pulmonary embolism, spontaneous pneumothorax, acute pancreatitis, and penetrating duodenal ulcer.
- Pulse deficits without backache should suggest other diagnoses: atherosclerotic peripheral vascular disease, arterial embolism, Takayasu's arteritis, etc.
- Acute cardiac tamponade with chest pain is also seen in

acute viral or idiopathic pericarditis and acute myocardial infarction with external rupture.

Practice point

- Unilateral tongue weakness after a car crash with whiplash injury suggests carotid artery dissection.

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Aortic dissection: investigations

General

- ECG. May be normal or non-specific (LVH, ST/T abnormalities). Look specifically for evidence of acute MI (inferior MI is seen if the dissection compromises the right coronary artery ostium).
- Chest X-ray. May appear normal, but with hindsight is almost always abnormal. Look for widened upper mediastinum, haziness or enlargement of the aortic knuckle, irregular aortic contour, separation (>5mm) of intimal calcium from outer aortic contour, displacement of trachea to the right, enlarged cardiac silhouette (pericardial effusion), pleural effusion (usually on left). Compare with previous films if available.
- Bloods. Base FBC, U&E, cardiac enzymes as well as cross match. A novel monoclonal antibody assay to smooth muscle myosin heavy chains can accurately differentiate an acute dissection from a MI.

Diagnostic

- Echocardiography. *Transthoracic Echo* may be useful in

diagnosing aortic root dilatation, aortic regurgitation, and pericardial effusion/tamponade. *Transoesophageal Echo* (TOE) is the investigation of choice as it allows better evaluation of both ascending aorta and descending aorta, may identify origin of intimal tear, allows evaluation of the origins of the coronary arteries in relation to the dissection flap, and provides information on aortic insufficiency. It is not good at imaging the distal ascending aorta and proximal arch.

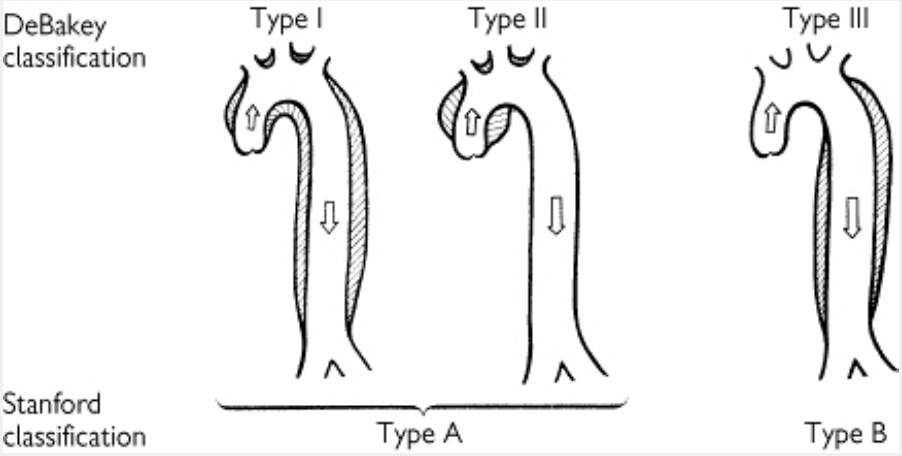
- MRI angiography. Is the gold standard for diagnosing aortic dissection. It has all the positive features of TOE and in particular also provides accurate information on all segments of ascending/arch/descending aorta, entry/exit sites, and branch vessels. Images can be displayed in multiple views as well as reconstructed in three dimensions. However, there are a number of disadvantages including (1) availability of service out of hours and cost, (2) presence of metallic valves or pacemakers may preclude patient from having an MRI, (3) monitoring of unstable patients in the scanner can be difficult and unsafe.
- Spiral (helical) CT with contrast. Allows three-dimensional display of all segments of aorta and adjacent structures. True and false lumen are identified by differential contrast flow, enter and exit site of intimal flap, as well as pleural and pericardial fluid. However it cannot demonstrate disruption of the aortic valve, which may be associated with ascending aortic dissection.
- Angiography. Using the femoral or axillary approach may demonstrate altered flow in the two lumens, aortic valve incompetence, involvement of the branches, and the site of the intimal tear. It is invasive and associated with a higher risk of complications in an already high-risk patient. It has largely been superseded by CT/MRI and TOE.

Selecting a diagnostic modality

- Confirm or refute a diagnosis of dissection.
- Is the dissection confined to the descending aorta or does it involve the ascending/arch?
- Identify extent, sites of enter and exit, and presence and absence of thrombus.
- To see whether there is aortic regurgitation, coronary involvement or pericardial effusions.

Selecting a diagnostic modality

- Where available, TOE should be the first-line investigation. It is safe and can provide all the information necessary to take the patient to the operating theatre
- If TOE is not available or if it fails to provide the necessary information a spiral contrast CT should be performed
- MRI should generally be reserved for follow-up images
- Angiography is rarely used, but is of value if other modalities have failed to provide a diagnosis and/or extensive information is needed on branch vessels



Classification of aortic dissection

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Aortic dissection: management 1

Stabilize the patient

- If the diagnosis is suspected, transfer the patient to an area where full resuscitation facilities are readily available.
- Secure *venous access* with large-bore cannulas (e.g. grey venflon).
- *Take blood* for FBC, U&Es, and cross match (10 units).
- When the diagnosis is confirmed or in cases with cardiovascular complications, *transfer to ITU*, insert an *arterial line* (radial unless the subclavian artery is compromised when a femoral line is preferred), *central venous line*, and *urinary catheter*.
- Immediate measures should be taken to correct blood pressure (see below).
- Adequate analgesia (diamorphine 2.5â€“10mg iv and metoclopramide 10mg iv).

Plan the definitive treatment

This depends on the type of dissection (see figure on P173) and its effects on the patient. General principles are

- Patients with involvement of the ascending aorta should have *emergency surgical repair and BP control*
- Patients with dissection limited to the descending aorta are managed initially medically with aggressive blood pressure control.

However, this may change in the near future with emerging encouraging data from deployment of endovascular stent-grafts.

Indications and principles for surgery

- Involvement of the ascending aorta
- External rupture (haemopericardium, haemothorax, effusions)
- Arterial compromise (limb ischaemia, renal failure, stroke)
- Contraindications to medical therapy (AR, LVF)
- Progression (continued pain, expansion of haematoma on further imaging, loss of pulses, pericardial rub, or aortic insufficiency).

The aim of surgical therapy is to replace the ascending aorta, thereby preventing retrograde dissection and cardiac tamponade (main cause of death). The aortic valve may need reconstruction and resuspension unless it is structurally abnormal (bicuspid or Marfan's), where it is replaced.

Indications and principles for medical management

Medical therapy is the treatment of choice for

- Uncomplicated type B dissection
- Stable isolated arch dissection

- Chronic (>2 weeks' duration) stable Type B dissection.

In all but those patients who are hypotensive, initial management is aimed at reducing systemic blood pressure and myocardial contractility. The goal is to stop the spread of the intramural haematoma and to prevent rupture. The best guide is control of pain. Strict bed rest in a quiet room is essential.

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Aortic dissection: management 2

Control blood pressure. Reduce systolic BP to 100â€“120mmHg.

- Start on iv Î²-blocker (if no contraindications) aiming to reduce the heart rate to 60â€“70/min (see table).
- Once this is achieved, if blood pressure remains high, add a vasodilator such as sodium nitroprusside (see table). Vasodilators in the absence of Î²-blockade may increase myocardial contractility and the rate of rise of pressure (d*P*/d*t*). Theoretically this may promote extension of the dissection.
- Further anti-hypertensive therapy may be necessary and other conventional agents such as calcium channel blockers, Î±-blockers, and ACE inhibitors can be used.
- In patients with aortic regurgitation and congestive cardiac failure, myocardial depressants should not be given. Aim to control blood pressure with vasodilators only.

Hypotension. May be due to haemorrhage or cardiac tamponade.

- Resuscitate with rapid intravenous volume (ideally colloid or blood, but crystalloid may be used also). A pulmonary

artery wedge catheter (Swanâ€“Ganz) should be used to monitor the wedge pressure and guide fluid replacement.

- If there are signs of aortic regurgitation or tamponade, arrange for an urgent Echo and discuss with the surgeons.

Emerging indications and principles for interventional therapy. There are increasing reports and short case series demonstrating favourable outcome (prognostic as well as symptomatic) data on using endovascular stent-grafts in management of primarily Type B and also to a lesser extent Type A aortic dissections.

On the basis of the current evidence endovascular stent-grafts should be considered to seal entry to false lumen and to enlarge compressed true lumen in the following situations:

- Unstable Type B dissection
- Malperfusion syndrome (proximal aortic stent-graft and/or distal fenestration/stenting of branch arteries)
- Routine management of Type B dissection (under evaluation).

Cardiac tamponade. If the patient is relatively stable pericardiocentesis may precipitate haemodynamic collapse and should be avoided. The patient should be transferred to the operating theatre for direct repair as urgently as possible. In the context of tamponade and EMD or marked hypotension pericardiocentesis is warranted.

Long-term treatment. Must involve strict blood pressure control.

Prognosis

- The mortality for untreated aortic dissection is roughly 20â€“30% at 24 hours and 65â€“75% at 2 weeks.

- For dissections confined to the descending aorta, short-term survival is better (up to 80%) but ~30â€“50% will have progression of dissection despite aggressive medical therapy and will require surgery.
- Operative mortality is of the order of 10â€“25% and depends on the condition of the patient pre-operatively. Post-operative 5-year actuarial survival of up to 75% may be expected.

Medical therapy of aortic dissection

Î²-blockade (aim for HR â‰¤60â€“70/min)

Labetalol	20â€“80mg slow iv injection over 10 minutes then 20â€“200mg/h iv, increasing every 15 minutes 100â€–400mg po q12h
Atenolol	5â€–10mg slow iv injection then 50mg po after 15 minutes and at 12 hours, then 100mg po daily
Propranolol	0.5mg iv (test dose), then 1 mg every 2â€–5 minutes up to max. 10 mg; repeat every 2â€–3 hours 10â€–40mg po 3â€–4 times daily

When HR 60â€–70/min (or if Î²-blocker contraindicated) add

Nitroprusside	0.25â€“10Âµg/kg/min iv infusion
Hydralazine	5â€“10mg iv over 20 minutes
	50â€“300Âµg/min iv infusion
	25â€“50mg po q8h
GTN	1â€“10mg/h iv infusion
Amlodipine	5â€“10mg po od

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Acute pericarditis: assessment

Presentation

- Typically presents as central chest pain, often pleuritic, relieved by sitting forward and can be associated with breathlessness.
- Other symptoms (e.g. fever, cough, arthralgia, rash, faintness/dizziness secondary to pain/â†‘HR) may reflect the underlying disease (see below).
- A pericardial friction rub is pathognomonic. This may be positional and transient and may be confused with the murmur of TR or MR.
- Venous pressure rises if an effusion develops. Look for signs of cardiac tamponade (P184).

Investigations

ECG

- May be normal in up to 10%.
- *â€˜Saddle-shapedâ€™ ST-segment elevation* (concave upwards), with variable T inversion (usually late stages) and *PR-segment depression* (opposite to P-wave polarity).

Minimal lead involvement to be considered, typically including I, II, aVL, aVF, and V3â€“V6.

- ST segment is always depressed in aVR, frequently depressed or isoelectric in V1, and sometimes in depressed in V2.
- May be difficult to distinguish from acute MI. Features suggesting pericarditis are
    - Concave ST elevation (versus convex)
    - All leads involved (versus a territory, e.g. inferior)
    - Failure of usual ST evolution and no Q-waves
    - No AV block, BBB, or QT prolongation.
- Early repolarization (a normal variant) may be mistaken for pericarditis. In the former, ST elevation occurs in pre-cordial and rarely in V6 or the limb leads and is unlikely to show ST depression in V1 or PR segment depression.
- Usually not helpful in diagnosing pericarditis post MI.
- The voltage drops as an effusion develops and in tamponade there is electrical alternans, best seen in QRS complexes.

Echo

- May demonstrate a pericardial collection.
- Useful to monitor LV function in case of deterioration due to associated myopericarditis.
- We recommend every patient has an Echo prior to discharge to assess LV function.

Other investigations depend on the

suspected aetiology

All patients should have

- FBC and biochemical profile
- ESR and CRP (levels rise proportionate to intensity of disease)
- Serial cardiac enzymes (CK, CK-MB, troponin). Elevations indicate sub-pericardial myocarditis
- CXR (heart size, pulmonary oedema, infection).

Where appropriate

- Viral titres (acute + 2 weeks later) and obtain virology opinion

- Blood cultures
- Autoantibody screen (RF, ANA, anti-DNA, complement levels)
- Thyroid function tests
- Fungal precipitins (if immunosuppressed), Mantoux test
- Sputum culture and cytology
- Diagnostic pericardial tap (culture, cytology).

Causes of acute pericarditis

- Idiopathic
- Infection (viral, bacterial, TB, and fungal)
- Acute myocardial infarction
- Dressler's syndrome, post-cardiotomy syndrome
- Malignancy (e.g. breast, bronchus, lymphoma)

- Uraemia
- Autoimmune disease (e.g. SLE, RA, Wegner's, scleroderma, PAN)
- Granulomatous diseases (e.g. sarcoid)
- Hypothyroidism
- Drugs (hydralazine, procainamide, isoniazid)
- Trauma (chest trauma, iatrogenic)
- Radiotherapy

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Acute pericarditis: management

General measures

- Admit? Depends on clinical picture. We recommend admission of most patients for observation for complications especially effusions, tamponade, and myocarditis. Patients should be discharged when pain free.
- Bed rest
- Analgesia. NSAIDs are the mainstay. Ibuprofen is well tolerated and increases coronary flow (200â€“800mg qds). Aspirin is an alternative (600mg qds po). Indomethacin should be avoided in adults as it reduces coronary flow and has marked side-effects. Use PPI (lansoprazole 30mg od) to minimize GI side-effects. Opoid analgesia may be required. Colchicine used as monotherapy or in addition to NSAIDs may help settle pain acutely and prevent recurrence.
- Steroids. These may be used if the pain does not settle within 48 hours (e.g. prednisolone EC 40â€“60mg po od for up to 2 weeks, tapering down when pain settles). Use in conjunction with NSAID and taper steroids first before stopping NSAID. It is also of value if pericarditis secondary to autoimmune disorders.
- Colchicine. Anecdotal evidence suggests that either used as monotherpay or in conjunction with NSAIDs it may help to settle pain acutely and prevent relapses (1mg/day

divided doses). Stop if patient develops diarrhoea, nausea. (1mg stat, 500mcg q6h for 48 hour).

- Pericardiocentesis. This should be considered for significant effusion or if there are signs of tamponade (P184).
- Antibiotics. These should be given only if bacterial infection is suspected.
- Oral anticoagulants. Should be discontinued (risk of haemo-pericardium). Patient should be given iv UFH, which is easier to reverse (iv protamine) if complications arise.

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Bacterial pericarditis

- The commonest pathogens are pneumococcus, staphylococci, streptococci, Gram -ve rods, and *Neisseria* species.
- Risk factors include pre-existing pericardial effusion (e.g. uraemic pericarditis) and immunosuppression (iatrogenic, lymphoma, leukaemia, HIV).
- The infection may have spread from mediastinitis, infective endocarditis, pneumonia, or sub-diaphragmatic abscess.
- Suspect in patients with high fever, night sweats, dyspnoea, and raised JVP (chest pain may be mild or absent); there may be other intra-thoracic infection (e.g. pneumonia).
- If suspected, take blood cultures and start iv flucloxacillin (2g qds) and iv gentamicin or iv cefotaxime (2g tds). Adjust treatment when sensitivities known.
- Significant-sized pericardial collections should be drained to dryness if possible. Send fluid for Gram and ZN stain, fungal smear, and culture. Surgical drainage may be required for recurrent effusions.
- Patients with TB pericarditis are very prone to developing cardiac constriction. Steroids have not been shown to prevent this but they do prevent progression once constrictive symptoms develop. Surgical pericardectomy

may be required. Take advice from cardiologists and infectious diseases team.

Viral pericarditis

- Pathogens include Coxsackie A + B, echovirus, adenovirus, mumps, EBV, VZV, CMV, hepatitis B, and HIV.
- Usually a self-limiting illness (1â€“3 weeks) and can be seasonal. Common in young individuals with no associated cardiac history.
- 20â€“30% develop recurrent pericarditis.
- Complications include recurrent pericarditis (20â€“30%), myocarditis, dilated cardiomyopathy, pericardial effusion and tamponade, and late pericardial constriction.
- Treatment is supportive (see above).

Uraemic pericarditis

- This is an indication for urgent dialysis (P385).

Dressler's syndrome, post-cardiotomy syndrome

- Complicates ~1% of acute MI and 10â€“15% patients following cardiac surgery presenting 2â€“4 weeks later (up to 3 months later).
- Consists of recurrent pericarditis, fever, anaemia, high ESR, neutrophil leukocytosis, pleural effusions, and transient pulmonary infiltrates on CXR.
- Treat with bed rest, NSAIDs (aspirin 600mg po qds) and steroids for persisting symptoms (see above).

- Pericarditis following acute MI (see P32).

Neoplastic pericarditis

- The 1-year survival of patients with malignant effusive pericarditis is â‰¤25%. The approach to treatment depends on the underlying malignancy and symptoms.

- Asymptomatic pericardial effusions do not require drainage. Treat the underlying malignancy (Â± mediastinal radiotherapy). Recurrent effusions may need formation of surgical pericardial window.
- Drainage is indicated for cardiac tamponade.

Myopericarditis

- Although it can occur with all cases of pericarditis it is more common in the context of AIDS, vasculitis/connective tissue disorders, rheumatic fever, and TB infection.
- Clinical suspicion should be higher in the context of pericarditis accompanied by significant arrhythmia (especially ventricular) and features of LV dysfunction and sinus tachycardia out of proportion to clinical picture (fever, pain, persistence >5â€“6 days).
- Biochemical markers of myocardial injury are often positive (specially TnT or TnI).
- In the absence of heart failure, treatment is as uncomplicated pericarditis. Steroids should be avoided unless indicated as part of treatment for underlying cause. Heart failure should be treated conventionally. Interferon can be used to treat enteroviral infections and globulins for CMV.
- Pericardial effusions must be drained with care as the

effusion may be â€˜splintingâ€™ a dilated/myocarditic heart. Drainage can lead to rapid dilation and cardiovascular collapse.

- Prognosis is generally good and most recover unless there is severe LV impairment.

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Cardiac tamponade: presentation

Cardiac tamponade occurs when a pericardial effusion causes haemodynamically significant cardiac compression. The presentation depends on the speed with which fluid accumulates within the pericardium. Acute tamponade may occur with 100â€“200ml in a relatively restricted pericardial sac. Chronic pericardial collections may contain up to 1000ml of fluid without clinical tamponade.

Causes

Acute tamponade

- Cardiac trauma
- Iatrogenic
    - Post cardiac surgery
    - Post cardiac catheterization
    - Post pacing/EP study
- Aortic dissection
- Spontaneous bleed
    - Anti-coagulation

    - Uraemia
    - Thrombocytopenia
- Cardiac rupture post MI

â€˜Sub-acuteâ€™ tamponade

- Malignant disease
- Idiopathic pericarditis
    - Uraemia
- Infections
    - Bacterial
    - Tuberculosis
- Radiation
- Hypothyroidism
- Post pericardotomy
- SLE

Presentation

- Patients commonly present either with cardiac arrest (commonly electrical mechanical dissociation) or with hypotension, confusion, stupor, and shock.
- Patients who develop cardiac tamponade slowly are usually acutely unwell, but not *in extremis*. Their main symptoms include
    - Breathlessness, leading to air hunger at rest
    - There may be a preceding history of chest discomfort
    - Symptoms resulting from compression of adjacent structures by a large effusion (i.e. dysphagia, cough,

hoarseness, or hiccough)

- There may be symptoms due to the underlying cause
- Insidious development may present with complications of tamponade including renal failure, liver and/or mesenteric ischaemia, and abdominal plethora.

Important physical signs

Most physical findings are non-specific. They include

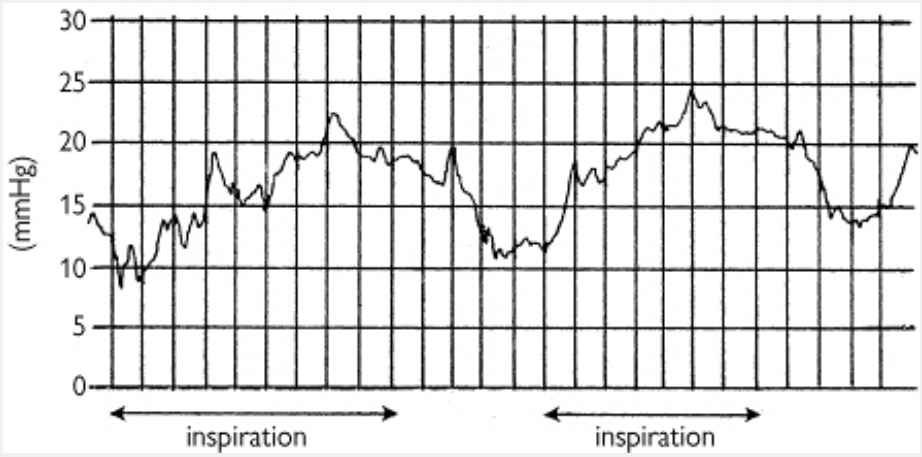
- Tachycardia (except in hypothyroidism and uraemia).
- Hypotension (Â± shock) with postural hypotension.
- Raised JVP (often >10cm) with a prominent systolic *x* descent and absent diastolic *y* descent (see figure). If the JVP is visible and either remains static or rises with inspiration it indicates concomitant pericardial constriction (Kussmaul's sign).
- Auscultation may reveal diminished heart sounds. Pericardial rub may be present and suggests a small pericardial collection.
- Look for pulsus paradoxus (a decrease in the palpable pulse and systolic BP of >10mmHg on inspiration). This may be so marked that the pulse and Korotkoff sounds may be completely lost during

inspiration. This can be measured using a BP cuff[1] or arterial catheter if *in situ* already. Other conditions that can cause a pulsus paradoxus include: acute hypotension, obstructive airways disease, and pulmonary embolus.

- Other physical signs include cool extremities (ears, nose) tachypnoea, hepatomegaly, and signs of the underlying cause for the pericardial effusion.

Causes of hypotension with a raised JVP

- Cardiac tamponade
- Constrictive pericarditis
- Restrictive pericarditis
- Severe biventricular failure
- Right ventricular infarction
- Pulmonary embolism
- Tension pneumothorax
- Acute severe asthma
- Malignant SVC obstruction and sepsis (e.g. lymphoma)



Right atrial pressure (RAP) tracing in tamponade. There is a paradoxical rise in RAP during inspiration

Footnote

[1]Teaching point. To establish presence of pulsus paradoxus non-invasively, inflate BP cuff to 15mmHg above highest

systolic pressure. Deflate cuff gradually until first beats are heard and hold pressure at that level concentrating on disappearance and reappearance of sounds with respiration (bumpâ€“bump, silenceâ€“silence, bumpâ€“bump, where noise reflects expiration). Continue to deflate slowly, paying attention to same pattern until all beats are audible. The difference between the initial and final pressure should be greater than 10mmHg.

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Cardiac tamponade: management

Tamponade should be suspected in patients with hypotension, elevated venous pressure, falling BP, â†‘HR and â†‘RR (with clear chest), pulsus paradoxus especially if predisposing factors are present.

Investigations

- Chest X-ray. The heart size may be normal (e.g. in acute haemopericardium following cardiac trauma). With slower accumulation of pericardial fluid (>250ml) the cardiac silhouette will enlarge with a globular appearance. The size of the effusion is unrelated to its haemodynamic significance. Look for signs of pulmonary oedema.
- ECG. Usually shows a sinus tachycardia, with low voltage complexes and variable ST-segment changes. With large effusions â€˜electrical alternansâ€™ may be present with beat-to-beat variation in the QRS morphology resulting from the movement of the heart within the pericardial effusion.
- Echocardiography. Confirms the presence of a pericardial effusion. The diagnosis of tamponade is a clinical one. Echo signs highly suggestive of tamponade include (1) chamber collapse during diastole (RA, RV, RV outflow tract), (2)

marked variation in transvalvular flow, (3) dilated IVC with little or no diameter change on respiration.

- If available, examine the central venous pressure trace for the characteristic exaggerated *x* descent and absent *y* descent.

Management

Following confirmation of the diagnosis:

- While preparing for drainage of the pericardial fluid, the patient's circulation may temporarily be supported by loading with iv colloid (500â€“1000ml stat) and starting inotropes (i.e. adrenaline).
- In patients with an adequate blood pressure, cautious systemic vasodilatation with hydralazine or nitroprusside in conjunction with volume loading may increase forward cardiac output. This is not to be recommended routinely as it may cause acute deterioration.
- The effusion should be urgently drained (see P890 for pericardiocentesis) guided by Echo or fluoroscopy. *In the event of circulatory collapse drainage must happen immediately without imaging*.
- Surgical drainage is indicated if the effusion is secondary to trauma.
- Avoid intubation and positive pressure ventilation as this reduces CO.
- In patients with cardiac arrest chest compression has little or no value, as there is no room for additional filling.
- Uraemic patients will also need dialysis.
- The cause of the effusion should be established (see P179). Pericardial fluid should be sent for cytology, microbiology including TB, and if appropriate Hb, glucose, and amylase.

Further management is of the underlying cause.

Special cases

Recurrent pericardial effusion

In some cases pericardial effusion recurs. This requires either a change in the treatment of the underlying cause or a formal surgical drainage procedure such as a surgical pericardial window or pericardiectomy.

Low pressure tamponade

Seen in the setting of dehydration. The JVP is not raised, right atrial pressure is normal, and tamponade occurs even with small volumes of pericardial fluid.

- The patient may respond well to iv fluids.
- If there is a significant pericardial collection this should be drained.

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Congenital heart disease in adults 1

Extra-cardiac complications

- Polycythaemia. Chronic hypoxia stimulates erythropoietin production and erythrocytosis. The â€˜idealâ€™ Hb level is ~17â€“18g/dl; some centres advocate venesection to control the haematocrit and prevent hyperviscosity syndrome (P728). Follow local guidelines. Generally consider phlebotomy only if moderate or severe symptoms of hyperviscosity are present and haematocrit >65%. Remove 500ml of blood over 30â€“45 minutes and replace volume simultaneously with 500â€“1000ml saline, or salt-free dextran (if heart failure). Avoid abrupt changes in circulating volume. If hyperviscosity symptoms are the result of acute dehydration or iron deficiency venesection is not required and patient must be rehydrated and/or treated with iron.
- Renal disease and gout. Hypoxia affects glomerular and tubular function resulting in proteinuria, reduced urate excretion, increased urate reabsorption and reduced creatinine clearance. Overt renal failure is uncommon. Try to avoid dehydration, diuretics, radiographic contrast. Asymptomatic hyperuricaemia does not need treatment. Colchicine and steroids are first-line agents for treatment of

acute gout. NSAIDs should be avoided.

- Sepsis. Patients are more prone to infection. Skin acne is common with poor healing of scars. Skin stitches for operative procedures should be left in for 7â€“10 days longer than normal. Dental hygiene is very important due to the risk of endocarditis. Any site of sepsis may result in cerebral abscesses from metastatic infection or septic emboli.
- Thrombosis and bleeding. Multifactorial and caused by a combination of abnormal platelet function, coagulation abnormalities, and polycythaemia. PT and aPTT values may be elevated and secondary to a fall in Factors V, VII, VIII, and X. Both arterial Â± venous thromboses and haemorrhagic complications (e.g. petechiae, epistaxes, haemoptyses) can occur. Dehydration or oral contraceptives are risk factors for thrombotic events. Spontaneous bleeding is generally self-limiting. In the context of severe bleeding general measures are effective including platalet transfusion, FFP, cryoprecipitate, and Vit K. Aspirin and other NSAIDs should generally be avoided to decrease chances of spontaneous bruising/bleeding.
- Primary pulmonary problems. Include infection, infarction, and haemorrhage from ruptured arterioles or capillaries.
- Stroke. Can be both thrombotic as well as haemorrhagic. Arterial thrombosis, embolic events (paradoxical emboli in R â†’L shunt) and injudicious phlebotomy lead to spontaneous thrombosis. Haemostasis problems (as indicated above) especially when combined with NSAIDs or formal anti-coagulation can lead to haemorrhagic stroke. Any injured brain tissue is also a nidus for intracranial infection/abscess formation.
- Complications secondary to drugs, investigations, surgery. Avoid abrupt changes in blood pressure or systemic resistance (see above). Contrast agents may

provoke systemic vasodilatation and cause acute decompensation. They may also precipitate renal failure. Before non-cardiac surgery, try to optimize haematocrit and haemostasis

by controlled phlebotomy and replacement with dextran. High-flow oxygen is important before and after surgery. Extreme precaution with iv lines (see below).

- Arthralgia. Mainly due to hypertrophic osteoarthropathy. In patients with R â†' L shunt megakaryocytes bypass the pulmonary circulation and become trapped in systemic vascular beds, promoting new bone formation.

Cardiac complications

- Congestive cardiac failure. The aetiology can be complex and is often directly dependent on the underlying abnormality. Possibilities include valve dysfunction (calcification of an abnormal valve or secondary to supra- or sub-valvular fibrosis and stenosis), ventricular dysfunction (hypertrophy, fibrosis, and failure), dysfunctioning surgical shunt, or pulmonary arteriolar disease and shunt reversal. Treat as usual taking special care not to dehydrate the patient or precipitate acute changes in blood pressure (see below).
- Endocarditis. The risk depends on the cardiac lesion and the pathogen. See table, P121. The recommended antibiotic prophylaxis regimen is given on P136. Patients should be advised on careful skin care (e.g. acne) and antibiotic prophylaxis to prevent local infections that may â€˜metastasizeâ€™ to heart or brain.
- Arrhythmias. Treat in the standard way (pp64â€“106).

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Congenital heart disease in adults 2

Management

Patients can be very complex and must be discussed with their regular cardiologist and/or local congenital adult heart centre.

General measures

- Contact and take advice from the cardiologist normally involved in the patient's care.
- iv lines are potentially very hazardous due to the risk of sepsis and systemic embolization (air and particulate matter). Use an air filter if available. Remove iv cannulae if there are any local signs of thrombophlebitis.
- Avoid sudden changes in circulating volume (e.g. vomiting, diarrhoea, haemorrhage, venesection). Any acute fall in SVR may precipitate intense cyanosis and death and an acute rise in SVR may abruptly reduce systemic blood flow and cause collapse.
- Monitor for neurological signs and symptoms from cerebral thromboembolism or septic embolism.

Specific measures

- Haemoptysis. Common. Most episodes are self-limiting and precipitated by infection. Differentiation from pulmonary embolism may be difficult. Try to keep the patient calm and ensure adequate BP control. Give high-flow oxygen by mask. If there is clinical suspicion of infection (fever, sputum production, leukocytosis, raised CRP, etc.) start broad-spectrum antibiotics. VQ scan may help in the diagnosis of pulmonary embolism (P146) but is often equivocal. Avoid aspirin and NSAIDs as these exacerbate the intrinsic platelet abnormalities. There is anecdotal evidence for the use of low-dose iv heparin, Dextran 40 (500ml iv infusion q4â€“6h), acrid (ArvinÂ®, reduces plasma fibrinogen by cleaving fibrin), or low-dose warfarin therapy for reducing thrombotic tendency in these patients. Severe pulmonary haemorrhage may respond to aprotinin or tranexamic acid.
- Breathlessness. May be due to pulmonary oedema or hypoxia (increased shunt) secondary to chest infection or pulmonary infarction. Do not give large doses of diuretics or nitrates as this will drop systemic pressures and may precipitate acute collapse. Compare chest X-ray to previous films to try to assess if there is radiological evidence of pulmonary oedema. The JVP in patients with cyanotic CHD is typically high and should not be used as a sole marker of heart failure. Overall patients need a higher filling pressure to maintain pulmonary blood flow. Give high-flow oxygen by mask. Start antibiotics if there is a clinical suspicion of infection (P198). Give oral diuretics if there is evidence of pulmonary oedema or severe right heart failure. Monitor haematocrit and renal function closely for signs of over-diuresis.
- Effort syncope. Should prompt a search for arrhythmias, in particular VT (Holter monitor), severe valve disease, or signs of overt heart failure. Treat as appropriate.

- Chest pain. May be secondary to pulmonary embolism or infarction (spontaneous thrombosis), pneumonia, ischaemic heart disease, or musculoskeletal causes. It requires careful evaluation with the conventional diagnostic modalities already described.

Congenital defects with survival to adulthood

Common

- Bicuspid aortic valve
- Coarctation of the aorta
- Pulmonary stenosis
- Ostium secundum ASD
- Patent ductus arteriosus
- Aneurysm of Sinus of Valsalva

Rarer

- Dextrocardia (situs solitus or invertus)
- Congenital complete heart block
- Congenitally corrected transposition
- Ebstein's anomaly

Congenital defects with good prognosis after surgery

- Ventricular septal defect
- Fallot's tetralogy

Causes of cyanosis in adults with congenital heart disease

- â€˜Eisenmenger reactionâ€™: R â† L shunt through VSD, ASD or patent foramen ovale with pulmonary hypertension (pulmonary hypertension may be secondary to pulmonary vascular disease, pulmonary artery stenosis or banding, pulmonary valve stenosis, tricuspid atresia)
- Abnormal connection: transpositions, IVC or SVC to left atrium, total anomalous pulmonary venous drainage
- Pulmonary AV fistulae

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Acute pneumonia: assessment

Presentation

- Classically cough (productive or non-productive), fever, breathlessness, chest pain, abnormal CXR. There may be prodromal symptoms of coryza, headache, and muscle aches.
- The aetiological agent cannot be predicted from the clinical features.
- Immunocompromised patients may present with agitation, fever, tachypnoea, decreased routine oximetry readings. CXR abnormalities may be subtle.
- Patients with right-sided endocarditis (e.g. iv drug users) may present with haemoptysis, fever, patchy consolidation Â± cavitation.

Adverse prognostic features in acute pneumonia[1]

Pre-existing

- Age â‰¥50 years
- Co-existing disease (IHD, cancer, etc.).

Core clinical features

- Confusion
- Urea >7mmol/L
- Respiratory rate >30/min
- SBP <90mmHg and/or DBP â‰¤60mmHg.

Additional features

- Hypoxia (Sats <92%; P_aO_2 <8kPa) regardless of FiO_2
- WCC <4 or >20 Ã— 10^9
- Bilateral or multi-lobar involvement on CXR â‰¥2 â€˜coreâ€™ features carries a high mortality: consider admission to ITU.

Management

General resuscitation and investigations

- *Check â€˜ABCâ€™ (airway, breathing, and circulation)*. Arrange for *urgent CXR*.
- *Secure venous access:* if there are signs of dehydration, start iv crystalloids; examine regularly for signs of fluid overload.
- *Send bloods*: FBC, U&Es, LFT, CRP.
- *Check ABG*: Correct hypoxia (P_aO_2 â‰¤10kPa) with *oxygen*, at least 35%. If hypoxia fails to correct despite maximum inspired O_2 or there is hypercapnoea (P_aCO_2 â‰¥6kPa) the patient is likely to require ventilation.
- Arrange for *urgent CXR*.
- *Culture blood and sputum*: Urgent sputum microscopy with

Gram-stain is occasionally useful but should not be relied upon routinely.

- *Pain relief*: Paracetamol or a NSAID usually suffice. Morphine may be required; respiratory depression is unlikely to be a problem if the P_aCO_2 is low or normal and it may be reversed with naloxone.

Footnote

1

From BTS Guidelines for the management of community acquired pneumonia in adults (2001) *Thorax* 56 (suppl. IV):

Indications for intensive care

- >2 â€˜coreâ€™ features from table above.
- Signs of hypoperfusion (SBP <90mmHg, oliguria, confusion) not responding to therapy.
- Respiratory failure (P_aO_2 â‰¤8kPa Â± P_aCO_2 â‰¥6kPa).
- Significant acidosis (pH â‰¤7.25, base excess < -8).
- Progressive exhaustion.

Causes of acute pneumonia in-patients admitted to hospital

Community acquired

- *Strep. pneumoniae* (40%)
- *H. influenzae* (5%)
- *Staph. aureus* (2%)
- *Moraxhella catarrhalis* (2%)

- Gram -ve bacteria/anaerobes 1%
- Influenza A&B (11%)
- Other viruses (2%)
- Mixed pathogens (14%)
- No organism identified (30%)

Atypicals

- *Mycoplasma* (11%)
- *Legionella pneumophila* (4%)
- *Chlamydia pneumoniae* (13%)
- Other *Chlamydia* species (4%)

Hospital acquired

- All of the above

Immunocompromised

- All of the above

Who may be discharged from A&E?

- Have a low threshold for admission.
- If patient is young, with no adverse prognostic features, a single lobe involved on CXR, and no complications (e.g. cavitation or effusion) then consider discharge from A&E. Arrange for early out-patient review (2â€“3 days).

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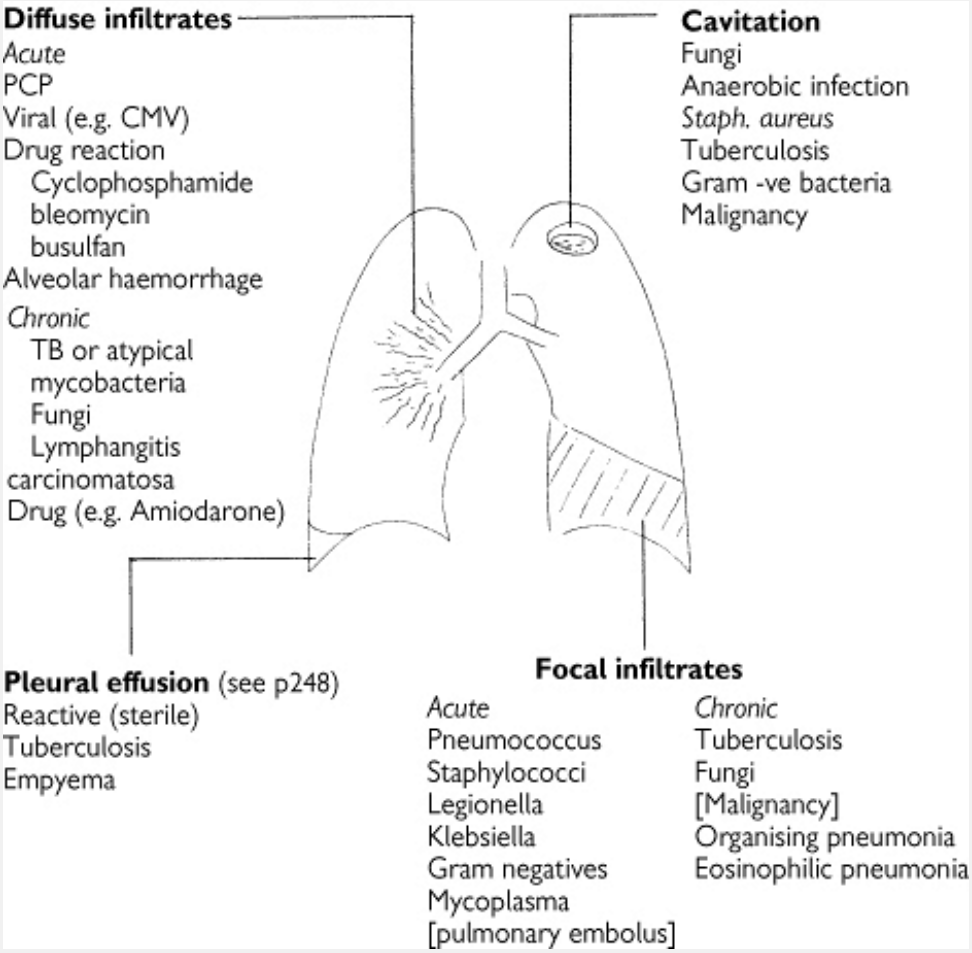
Acute pneumonia: investigations

Investigations

All patients should have

- Arterial blood gases (on air and oxygen)
- FBC, U&Es, liver function tests, ESR, CRP
- ECG
- Chest X-ray (see figure below)
- Blood cultures
- Sputum culture, Gram stain, ZN stain (if suspicious of TB), cytology
- Pleural fluid aspiration (if present) for MC&S, protein, and pH
- *Pneumococcal* antigen: urine, sputum, or blood
- Serology (acute and convalescent)
- Cold agglutinins (*Mycoplasma* day 7â€“14)
- Urine for *Legionella* antigen, sputum for *Legionella* culture, and direct immunofluorescence.



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Where appropriate consider

- Bronchoscopy (Â±BAL) (if immunocompromised, or if fails to respond to first-line antibiotics and no organism identified)
- Echo (?right heart endocarditis, P122)
- VQ scan (to exclude infected pulmonary infarct)
- Trans-bronchial or open lung biopsy
- Aspiration of pleural fluid for MC&S
- Viral titres.

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Acute pneumonia: management

Treatment

- â€˜Blindâ€™ treatment should be started as soon as appropriate cultures have been sent (table, opposite). Modify therapy in the light of subsequent investigations or positive cultures.
- Start on iv therapy for at least 48 hours; adjust according to clinical condition and response (see table).
- In patients with COPD or asthma, consider treatment with salbutamol (2.5â€“5mg nebulized q4â€“6h) to relieve bronchospasm. This may also â€˜loosen secretionsâ€™ and improve mucocilliary action.
- Continue iv fluids as necessary to keep the patient well hydrated.
- Monitor response to therapy with
    - FBC, CRP
    - Pulse oximetry or blood gases
    - CXR at day 3â€“5 (sooner if deteriorating).
- Total duration of therapy usually 10 days.
- Follow-up CXR 4â€“6 weeks after discharge mandatory to exclude an underlying endobronchial lesion.

Choice of antibiotics

In severely ill patients, the history may point to a likely pathogen:

â€¢ COPD	*S. pneumoniae, H. influenzae, M. catarrhalis*
â€¢ Alcoholism	*S. pneumoniae, S. aureus, H. influenzae*, *Klebsiella*, TB, anaerobes, Gram -ve bacteria
â€¢ Recent â€˜fluâ€™	*S. aureus, S. pneumoniae, H. influenzae*
â€¢ Risk of aspiration	Anaerobes, Gram -ve bacteria
â€¢ Contact with birds	*C. psittaci*
â€¢ Haemoptysis	Streptococci, *S. aureus*, lung abscess, necrotizing Gram -ve bacteria, invasive aspergillosis
â€¢ Diarrhoea, abdominal pain	*Legionella*
â€¢ Pharyngitis/otits media	Mycoplasma, anaemia/cold agglutinins

â€¢ Risk factors for HIV	*S. pneumoniae, H. influenzae*, CMV, PCP, *Cryptococcus*
â€¢ Hospital acquired	Gram -ve bacteria, *S. aureus*
â€¢ Neutropenia	*P. aeruginosa*, Gram -ve bacteria, *Aspergillus*
â€¢ Drug addicts	*S. aureus, Candida*
â€¢ Nursing home patients	Higher risk of aspiration: anaerobes, Gram -ve bacteria

â€˜Blindâ€™ treatment of pneumonia[1]

- Most patients can be adequately treated with oral antibiotics.
- Consider iv antibiotics if adverse prognostic features (see P194) present.

Community-acquired pneumonia Â± â€˜atypicalâ€™ features	Amoxycillin + Erythromycin[2],[3]
Hospital-acquired pneumonia	Cefotaxime (or Ceftazidime) Â± Metronidazole
Post-influenza pneumonia (*Staph. aureus* possible)	Cefuroxime (or Amoxycillin + Erythromycin[2] + Flucloxacillin
If MRSA isolated or suspected	Switch Flucloxacillin to Vancomycin
Aspiration pneumonia	Cefuroxime + Metronidazole or Benzyl penicillin + Gentamicin + Metronidazole
Patient with risk factors for HIV and suspicion of PCP	As for CAP + high-dose iv Co-trimoxazole
[2] Alternatively clarithromycin.	
[3] If intolerant of Î²-lactam or macrolide, use fluoroquinolone with activity against *S. pneumoniae* (e.g. levofloxacin).	

Suggested antibiotic dosages

Amoxycillin	500mgâ€“1g iv tds
Benzyl penicillin	1.2â€“2.4g iv qds
Cefuroxime	750mgâ€“1.5g iv tds
Cefotaxime	1â€“2g iv tds
Ceftazidime	1â€“2g iv tds
Co-amoxiclav	1.2g iv tds
Co-trimoxazole	5mg/kg q6h of trimethoprim component
Erythromycin	500mgâ€“1g iv (or po) qds
Flucloxacillin	1â€“2g iv qds
Gentamicin	loading dose (120mg iv) then 1-2.5mg/kg q8â€“12h guided by levels
Metronidazole	500mg iv tds
Vancomycin	200â€“400mg od iv for MRSA 1g iv bd guided by levels
Teicoplanin	200â€“400mg od iv for MRSA

NB: iv erythromycin causes severe phlebitis. Use central line if

available or change to oral preparation after 2â€“3 days. Clarithromycin is an alternative to erythromycin.

Footnote

[1]In patients with a good history of *penicillin allergy* (anaphylaxis, urticaria) alternatives include erythromycin, clarithromycin, levofloxacin (NB: ciprofloxacin is not very active against *S. pneumoniae*). Alternatives for flucloxacillin include vancomycin, teicoplanin, or rifampicin: consult BNF for dosages.

[2]Alternatively clarithromycin.

[3]If intolerant of Î²-lactam or macrolide, use fluoroquinolone with activity against *S. pneumoniae* (e.g. levofloxacin).

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Acute pneumonia: specific situations

Community-acquired pneumonia

- Either *amoxycillin* 1g iv q8h or *cefuroxime* 750mgâ€“1.5g iv q8h plus *erythromycin* 500mgâ€“1g po/iv q6h to cover atypicals plus *flucloxacillin* 1â€“2g iv q6h if *Staph. aureus* is suspected.
- *Penicillin allergy:* cephalosporins are usually safe where there is a history of rashes with penicillin. If there is history of anaphylaxis consider clarithromycin 500mg bd po as sole therapy, or if unwell seek respiratory/microbiological advice.

Aspiration pneumonia

- Risk factors include seizures, reduced conscious level, stroke, dysphagia, periodontal disease, â€˜down-and-outâ€™, general anaesthesia. Always admit.
- Clinical features include wheeze and frothy non-purulent sputum (as soon as 2â€“4 hours after aspiration), tachypnoea, cyanosis, and respiratory distress.
- Gastric acid destroys alveoli resulting in increased capillary permeability and pulmonary oedema. Haemorrhage is

common. Severe necrotizing pneumonia may result.

- *Treatment:* *Cefuroxime* (as above) + *metronidazole* (500mg iv q8h). Amoxycillin + metronidazole + gentamicin.

Hospital-acquired pneumonia

- Most likely organisms are enteric Gram negative Â± anaerobes.
- *Treatment*: broad-spectrum cephalosporin (e.g. *cefotaxime* 2g tds iv) Â± *metronidazole* (500mg iv tds). If intubated â‰¥48 hours use anti-pseudomonal antibiotic (e.g. *ceftazidime* 2g tds, modify dose in renal failure).

Pneumonia in the immunocompromised

- All â€˜routineâ€™ pathogens are possible; other infections depend on the nature of immunosuppression. TB and atypical mycobacteria are more common.
- Since the introduction of combination anti-retroviral treatment opportunistic infections are less common and pulmonary Kaposi's sarcoma or lymphoma rarely seen. However, pulmonary opportunistic infection may be the first manifestation of HIV before it is diagnosed, the most common being *Pneumocystis carinii*. Fungal and viral (CMV) pneumonitis may also occur. Desaturation on exercise in the presence of a normal CXR or one with a diffuse interstitial shadowing is highly suggestive of PCP.
- Recipients of *organ transplants* have depressed cell-mediated immunity due to anti-rejection immunosuppressive therapy. Additional pathogens to which they are susceptible include PCP, viruses (e.g. CMV, RSV, influenza and parainfluenza, adenovirus), and fungi

(*Aspergillus* spp., *Candida* spp.). The CXR abnormalities tend not to be specific for the pathogen and treatment should cover all possible pathogens.

- In general early bronchoscopy and bronchoalveolar lavage is indicated for diagnosis; management should be discussed early with a respiratory/infectious disease/microbiology team.

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Acute pneumonia: complications

Community-acquired pneumonia that fails to respond

- Review the diagnosis (?PE, pulmonary oedema, pulmonary vasculitis, alveolar haemorrhage, cavitation, organizing pneumonia, eosinophilic pneumonia, bronchiectasis).
- Repeat CXR and arrange for CT chest to look for cavitation or empyema. Repeat culture of relevant specimens (e.g. sputum, blood). Consider possible resistant organism or underlying disease, e.g. bronchial carcinoma.
- Consider bronchoscopy to exclude TB, PCP, or an obstructing lesion.
- Review antibiotic dosages and intensify (e.g. inadequate oral erythromycin for *Mycoplasma* pneumonia).

Parapneumonic pleural effusion or empyema

- Parapneumonic pleural effusions develop in up to 50% of patients with bacterial pneumonia admitted to hospital.

- Diagnostic tap should be performed on all parapneumonic effusions to exclude an empyema. Sent pleural fluid for MC&S, urgent Gram stain, and pH analysis.
- Empyema (visibly cloudy fluid, pus, or organisms on Gram stain) or complicated parapneumonic effusion (visibly clear fluid with pH <7.2) should be removed with pleural space drainage. Discuss with respiratory physicians.
- Ultrasound may help look at the level of the effusion and demonstrate loculation with an empyema.
- If an empyema fails resolve with pleural space drainage, arrange chest CT and discuss with cardiothoracic surgeons (P249).

Cavitation or abscess

- Any severe pneumonia may cavitate, but particularly *Staph. aureus, Klebsiella* spp., TB, aspiration pneumonia, bronchial obstruction (foreign body, tumour) or pulmonary emboli (thrombus or septic emboli, e.g. from DVT with super-added infection or tricuspid endocarditis, P132).

Treatment

- Seek advice from respiratory team. Most respond to appropriate antibiotics but may require more prolonged course. Surgical drainage or CT-guided percutaneous aspiration may be necessary.
- â€˜Blindâ€™ treatment: *cefuroxime* 1.5g tds iv (or *cefotaxime* 2g tds iv) + *flucloxacillin* 1â€“2g qds iv + *gentamicin* loading dose (100â€“120mg iv) then 6â€“7mg/kg od (according to renal function and levels) Â± *metronidazole* 500mg iv tds.
- Long-term antibiotics (4â€“6 weeks) likely to be required.

Other complications

â€¢ Respiratory failure	P224
â€¢ Rhabdomyolysis	P392
â€¢ DIC (especially *Legionella*)	P702.

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Mycoplasma pneumonia

- Disease of young adults. Low-grade fever, dry cough, headache, and myalgia. Erythema multiforme may be seen in ~25%. ~5% have a meningoencephalitis.
- WCC is often normal, ESR is high, specific IgM is seen early then levels decline. ~50% develop cold agglutinins (also seen in measles, EBV) which may cause haemolysis. CXR may show reticulonodular shadowing (lower lobe > upper lobe) which may take over 6 weeks to resolve (unlike bacterial pneumonia).
- Treatment is with *erythromycin* 500mg qds po/iv, *clarithromycin* 500mg bd po/iv, or *tetracycline* 500mg qds po/iv.

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Legionella pneumonia

- Illness of middle-aged men; more severe in smokers. Incubation 2â€“10 days followed by high fever, rigors, headache, myalgia, dry cough, progressive respiratory distress, and confusion. Abdominal pain, diarrhoea, nausea and vomiting, and palpable hepatomegaly are seen in ~30%. Complications include pericarditis (Â± effusion), encephalopathy (CSF is usually normal) and rarely renal failure.
- Moderate leukocytosis (â‰¤20 Ã— 10^9/L, neutrophilia, lymphopenia), hyponatraemia, deranged LFTs, proteinuria, haematuria, and myoglobinuria. Diagnosis: rise in specific IgM and IgG titres (urine, blood, sputum).
- CXR may show anything from diffuse patchy infiltrates to lobar or segmental changes and usually deteriorates in spite of treatment. Pleural effusions are seen in ~50%.
- Treatment is with *clarithromycin* 500mg bd po/iv. Continue therapy for 14â€“21 days. Add *rifampicin* (600mg bd po/iv) if symptoms do not settle within 72 hours.
- Pontiac fever is self-limiting (2â€“5 days) acute non-pneumonic *Legionella* infection with high fever, rigors, myalgia, headache, and tracheo-bronchitis.

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Viral pneumonia

- Clinical features resemble *Mycoplasma* pneumonia (see P204). Diagnosis is by 4 Ã— increase in specific antibody titres.
- CMV. Commonest viral infection in AIDS and following solid organ or bone marrow transplantation, presenting as fever, dry cough, and progressive respiratory distress with hypoxia and bilateral crackles. CXR shows diffuse infiltrates; a miliary pattern is associated with rapid progression and poor outcome whereas an interstitial pattern has a better prognosis (see figure, P196). Treat with ganciclovir 5mg/kg iv q12h for 2â€“3 weeks.
- Coxsackie and Echovirus. Titres often rise in â€˜epidemic pleurodyniaâ€™ (Bornholm's disease), a self-limiting illness with chest pain exacerbated by coughing and deep breathing, myalgia, and muscle tenderness. Treatment: analgesia (paracetamol, NSAIDs).
- Varicella pneumonia. More common in smokers and immunosuppressed patients. All patients with varicella pneumonitis should be treated with acyclovir 10mg/kg iv 8 hourly.

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Chlamydia pneumonia

- *Chlamydia pneumoniae* presents in older adults with headaches and longer duration of symptoms before hospital admission. Extra-pulmonary manifestations may include meningoencephalitis, Guillianâ€“Barre syndrome, arthritis, and myocarditis.
- Treatment: *erythromycin* 500mg qds po/iv, *clarithromycin* 500mg bd po/iv, or *tetracycline* 500mg qds po/iv.

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Psittacosis

- *Chlamydia psittaci* produces fever, cough, myalgia, and in severe cases, delirium (psittacosis). Complications include pericarditis, myocarditis, and hepatosplenomegaly. Diagnosis is by serology.
- Treat with tetracycline 500mg po qds for 2â€“3 weeks.

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Miscellaneous conditions

- Extrinsic allergic alveolitis may mimic viral pneumonia and present as breathlessness, dry cough, myalgia, and fever with neutrophilia (eosinophils usually normal acutely) and patchy radiographic changes. There is usually history of exposure to the allergen and serum precipitins are detectable. BAL shows predominance of mast cells and lymphocytes. Treatment is with steroids.
- Pulmonary eosinophilia: this is a heterogenous group of disorders characterized by eosinophilic pulmonary infiltrates producing respiratory symptoms, CXR shadowing, and blood and sputum eosinophilia. The cause may be unknown as in cryptogenic eosinophilic pneumonia, or it may be due to drugs (e.g. nitrofurantoin, phenytoin, and ampicillin), helminth infections (e.g. *Ascaris lumbrocoides*, hookworms, *Strongyloides stercoralis*), tropical pulmonary eosinophilia (lymphatic filarial infection), or the small-vessel systemic vasculitis (Churgâ€“Strauss).
- Allergic bronchopulmonary aspergillosis is a hypersensitivity reaction of airways colonized by *Aspergillus* sp. producing pulmonary eosinophilia. It typically occurs in asthmatics with repeated episodes of bronchial obstruction, inflammation, and mucus impaction resulting in bronchiectasis and upper lobe fibrosis. Such patients are usually aspergillus skin-prick test (IgE) and serum precipitins (IgG) positive. Treatment depends on the

underlying condition.

- COP may present with fever, malaise, cough, breathlessness, and pulmonary shadows on CXR. Characterized by excessive proliferation of granulation tissue within small airways and alveoli, COP is the idiopathic form of bronchiolitis obliterans organizing pneumonia (BOOP). Organizing pneumonia can also be associated with collagen vascular diseases (rheumatoid arthritis, lupus, dermatomyositis), chronic infection (*Legionella*, CMV, *Mycoplasma*), and drugs (amiodarone, bleomycin). Treatment is with steroids.
- Alveolar haemorrhage: intrapulmonary haemorrhage may present with cough, fever, and breathlessness. Haemoptysis may be absent in 30%. The CXR may show diffuse alveolar opacities. BAL shows predominantly RBCs. Causes include systemic vasculitis (e.g. Wegener's granulomatosis, microscopic polyangiitis), collagen vascular diseases (e.g. SLE), Goodpasture's syndrome, ARDS, and idiopathic pulmonary haemosiderosis. Treatment depends on the cause.
- Bronchoalveolar cell carcinoma may mimic an acute pneumonia radiologically although typical symptoms of pneumonia are usually not present unless there is superadded infection. Diagnosis is made by lung biopsy.

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Acute asthma: assessment

Presentation

- The classical triad is *wheeze, breathlessness*, and *cough*. Pleuritic pain may be due to diaphragmatic stretch, pneumothorax, or acute infection.
- Acute attacks may build up over minutes, hours, or days and the patients may deteriorate very rapidly and present as respiratory or cardio-respiratory arrest.
- Factors increasing the risk of severe life-threatening asthma include previous ventilation, hospital admission for asthma in the last year, heavy rescue medication use, >3 classes of asthma medication, repeated attendances at A&E for asthma care, brittle asthma.

Precipitants

- No clear precipitating cause can be identified in over 30% of patients
- Exposure to known allergen or irritant (e.g. pollens, animals, dusts, cigarette smoke)
- Upper respiratory tract infection (commonly viral)
- Chest infection: viral or bacterial

- Neglect or poor compliance with regular inhaled or oral steroids
- Emotional stress
- Cold air or exercise-induced asthma.

Markers of severity

- For assessment of the severity of asthma, see table.
- The severity of an attack may be easily underestimated. Assess
    - The degree of airflow obstruction
    - The effect of increased work of breathing on the patient
    - The extent of ventilationâ€“perfusion mismatch
    - Any evidence of ventilatory failure.

(Patients with marked â€˜morning dipsâ€™ in PEF are at risk of sudden severe attacks.)

Investigations

â€¢ *ABG*	Hypoxaemia on room air is almost invariable. In attempting to maintain alveolar ventilation initially there is hypocapnoea and respiratory alkalosis. â†'P_aCO_2 suggests incipient respiratory failure due to exhaustion; contact ITU immediately.
	Poorly controlled asthma over several days may be recognized by a mild â€˜non-anion gapâ€™ acidosis (serum bicarbonate 20â€“24mmol/L).
	A lactic acidosis seen with severe asthma.
â€¢ Pulse oximetry	Continuous oximetry is essential; aim for â‰¥92%.
â€¢ Chest X-ray	Exclude pneumothorax and to diagnose any parenchymal infection.
â€¢ ECG	Usually normal; in severe asthmatics, signs of right heart strain may be present.
â€¢ FBC, U&E, CRP	Assess for signs of infection; K^+ may be lowered by high doses of Î²-agonists.

Assessment of severity of acute asthma[1]

- Near-fatal asthma
    - Raised P_aCO_2 or immediate requirement for ventilation with raised inflation pressures
- Life-threatening asthma
    - Severe airways obstruction
        - PEF <33% best or predicted
        - Soft breath sounds or â€˜silent chestâ€™
        - Feeble respiratory effort
    - Increased work of breathing and haemodynamic stress
        - Exhaustion
        - Hypotension (systolic BP <100mmHg)
        - Bradycardia or arrhythmia
    - Ventilation-perfusion mismatch
        - Cyanosis
        - Hypoxia (SpO_2 <92% and/or P_aO_2 <8kPa irrespective of inspired O_2 concentration)
    - Ventilatory failure
        - Rising P_aCO_2 suggests â€˜near-fatalâ€™ asthma
        - Confusion or coma
- Acute severe asthma
    - PEF 30â€“50% best or predicted
    - Respiratory rate >25/min
    - Tachycardia: heart rate >100/min
    - Inability to complete sentences in one breath

- Brittle asthma
    - Type 1: wide PEF variation despite intensive and regular therapy
    - Type 2: sudden severe asthma attacks on background of apparently well-controlled asthma

Admission is mandatory if *any* of the markers of severe, life-threatening, or near-fatal asthma are present.

Footnote

1

Adapted from BTS/SIGN British guidelines on management of asthma (2003) *Thorax* 38 (suppl. 1)

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Acute severe asthma: immediate therapy

Priorities

- Treat hypoxia
- Treat bronchospasm and inflammation
- Assess the need for intensive care
- Treat any underlying cause if present (e.g. infection, pneumothorax).
    - Patients may deteriorate rapidly and should not be left unattended.
    - *Remain calm:* reassurance is important in reducing the patient's anxiety which may further increase respiratory effort.

Severe or life-threatening attack

- Initial treatment
    - Sit the patient up in bed.
    - *Oxygen*: the highest percentage available, ideally at least 60% or 15L/min with a high-flow mask. CO_2

retention is not a problem in asthmatic patients. Maintain O_2 sats >92%.

- *Nebulized bronchodilators*: give nebulized salbutamol 5mg or terbutaline 10mg, administered via O_2 and repeat up to every 15â€“30 minutes if required. Consider continuous nebulization of salbutamol 5â€“10mg/h if inadequate response to initial treatment.
- Add *ipratropium bromide* 0.5mg 4â€“6 hourly if initial response to $Î²_2$-agonists is poor.
- Obtain *iv access*.
- Start *steroids*: 200mg of hydrocortisone intravenously (steroids should still be used in pregnant women as the risk of foetal anoxia from the asthma is high). Continue either hydrocortisone 100mg qds iv or prednisolone 30â€“50mg od po.
- *Antibiotics* should be given if there is evidence of chest infection (purulent sputum, abnormal CXR, raised WCC, fever). Yellow sputum may just be due to eosinophils and a raised WCC may be due to steroids. See P199 for choice of antibiotics.
- *Adequate hydration* is essential and may help prevent mucus plugging. Ensure an intake (iv or po) of 2â€“3L/day, taking care to avoid overload. Supplement potassium as required.

- Monitoring progress
  - Pre- and post-nebulizer peak flows.
  - Repeated arterial blood gases 1â€“2 hourly or according to response especially if SaO_2 <93%.
- If response to above treatment not brisk or if the patient's condition is deteriorating
  - Continue oxygen and nebulized $Î²_2$-agonist every 15

minutes.

- Give a single dose of iv magnesium sulphate (see table).
- Consider starting an *iv aminophylline infusion* (see table).
- Consider starting an *iv salbutamol infusion* (see table).
- *Summon anaesthetic help*.

Intravenous bronchodilators for asthma

Magnesium sulphate	1.2â€“2g if infused over 20 minutes

Give as a single dose only. Repeated doses may lead to hypermagnesaemia with muscle weakness and respiratory failure.

Salbutamol	*Loading dose*: 100â€“300Âµg over 10 minutes *Maintenance infusion*: 5â€“20Âµg/min (5mg in 500ml saline at 1â€“3ml/min)

Side Effects: tremor, tachycardia, hypokalaemia, hyperglycaemia common. Lactic acidosis may occur and responds within hours to reduction in salbutamol infusion rate.

Aminophylline	*Loading dose*: 250mg (4â€“5mg/kg) iv over 20 minutes
	Maintenance infusion: 0.5â€“0.7mg/kg/h (250mg in 1 litre N saline at 2â€“4 ml/kg/h)

Do *not* give the loading dose if the patient is on oral theophylines without checking a level. Halve the dose in patients with cirrhosis or CCF, or in those receiving erythromycin, cimetidine, or ciprofloxacin. Monitor levels every 24 hours (aim for levels of 10â€“20mg/L).

Indications for admission to intensive care unit

- Hypoxia (P_aO_2 <8kPa (60mmHg) despite FiO_2 of 60%

- Rising P_aCO_2 or P_aCO_2 >6kPa (45mmHg)
- Exhaustion, drowsiness, or coma
- Respiratory arrest
- Failure to improve despite adequate therapy

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Acute severe asthma: further management

- Cautious CPAP may help reduce the work of breathing in patients with respiratory muscle fatigue but may not increase the functional residual capacity further.
- Ketamine (a dissociative anaesthetic agent) may be useful in ventilated patients (1â€“3mg/min) probably by increasing circulatingcatecholamines by blocking uptake into adrenergic nerve endings.
- Inhalational anaesthetic agents (e.g. halothane, enflurane, isoflurane) have been reported to improve bronchospasm and may be useful when initiating ventilation.
- Mechanical ventilation may be life saving but has a high risk of complications and an overall mortality of ~13%. Barotrauma is seen in ~14% (e.g. pneumothorax, pneumo-mediastinum, or subcutaneous emphysema) and hypotension in ~38% (usually a combination of increased intrathoracic pressure, intravascular fluid depletion due to dehydration, and dilating effect of anaesthetic agents). Seek expert advice from your intensive care physician for the practical management of ventilation of the asthmatic patient.

General principles

- Adequate humidification and warming of inspired gases
- Low frequency ventilation (6â€“10 breaths/min)
- Low tidal volumes (6â€“10ml/kg)
- Long expiratory phase of the cycle (I : E ratio 1 : 3 or longer)
- Minimize airway pressures (aim for <50cm H_2O, normal <25)
- Maintain P_aO_2 >8.0 kPa; allow P_aCO_2 to rise provided pH >7.2
- Adequate sedation and paralysis to overcome respiratory drive
- Avoid opiates and atacurium (may release histamine)
- Consider benzodiazepine, ketamine, vecuronium, isoflurane, etc.

On-going therapy

- Once improvement established continue nebulized $Î²_2$-agonist, reducing this to 4-hourly and prn after 24â€“48 hours
- Peak flow rate should be measured before and after each nebulizer
- Maintain O_2 sats >92%
- Continue nebulized ipratropium bromide 6-hourly until the condition is improving
- Continue steroids, hydrocortisone 100mg q6h iv switching to 30â€“60mg od oral prednisolone when able to swallow, and continue for 10â€“14 days
- Monitor intravenous aminophylline levels every 24 hours
- Monitor serum K^+ daily whilst unwell and supplement as

necessary.

Discharge after hospital admission

- The PEF should be â‰¥75% of best without significant morning dipping (diurnal variability â‰¤25%) and with no nocturnal symptoms
- The patient should be established on inhalers with no requirement for nebulizers for 24â€“48 hours prior to discharge. Check inhaler technique
- Discharge drugs:
    - *Prednisolone* po â‰¥30mg od for 1â€“3 weeks (plan gradual dose reductionif treatment >14 days)
    - *Inhaled corticosteroids* at high dose (usually 1000â€“1500Âµg beclomethasone via spacer) or equivalent
    - Restart inhaled *long-acting* Î²$_2$*-agonists* if prescribed prior to admission
    - Inhaled prn Î²$_2$*-agonist*
    - *Oral theophyllines* if required (confirm drug levels before discharge)
- Provide PEFR meter and chart and arrange follow-up with GP or practice nurse (within 2 days) and chest clinic (within 1 month)

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Mildâ€“moderate asthmatic attacks

Mild asthmatic attack

No severe features, PEF â‰¥75% of predicted (or of best when well).

- Administer the patient's usual bronchodilator (e.g. 2 puffs salbutamol by metered dose inhaler).
- Observe for 60 minutes. If PEF remains â‰¥75% of predicted value, then discharge.
- Ensure patient is on at least 1000Âµg inhaled beclomethasone or equivalent per day.
- Advise the patient to get early GP follow-up, monitor PEF, and return to hospital early if the asthma deteriorates.

Moderate asthmatic attack

No acute severe features, PEF 51â€“75% of predicted (or of best when well)

- Administer nebulized Î²-agonist (salbutamol 5mg or terbutaline 10mg) and oral prednisolone 30â€“60mg.
- Re-assess after 30 minutes. If worse or PEF â‰¤50% of

predicted then admit and assess as below for severe asthma.

- If PEF 51â€“75% predicted then repeat nebulizer and observe for a further 60 minutes.
- The patient may be discharged from A&E if stable after 1â€“2 nebulizers and PEFR â‰¥75%.
- If after second nebulizer and a further 60 minutes' observation thepatient is clearly improving and PEFR â‰¥50%, then discharge may be considered.
- Discharge on
    - Oral prednisolone (usual dose 30â€“40mg od for 7 days)
    - Inhaled corticosteroid (â‰¥1000Âµg/day inhaled beclomethasone)
    - Inhaled Î²-agonist.
- Advise the patient to seek GP follow-up within 48 hours and to return early to A&E if there is any deterioration.
- Consider referral to chest clinic.

Sending people home from A&E

- Mild-moderate exacerbations may be fit to be discharged from A&E.
- If there are any features of acute severe asthma (see table, P211) then admission is mandatory.
- A history of brittle asthma or previous attacks requiring mechanical ventilation is always a requirement for admission.

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Acute exacerbation of chronic obstructive pulmonary disease (COPD): assessment

Presentation

- Deterioration of pre-existing symptoms of exertional breathlessness, cough (sometimes with daily sputum production) and wheeze.
- Respiratory failure (see P224): May be Type 1 (normal P_aCO_2, low P_aO_2) or Type 2 (high P_aCO_2, low P_aO_2 reflecting severe bronchospasm and/or alveolar hypoventilation).
- Wheeze unrelieved or partially relieved by inhalers.
- Increased production of purulent sputum (i.e. infection as a precipitant).
- Positive smoking history (if not then late-onset asthma is likely).
- Confusion/impaired consciousness (exhaustion, CO_2 retention).

Causes

- *Infective exacerbation* (No new CXR changes): Typically *H. influenzae, S. pneumoniae, Moraxella catarrhalis*. Commonly viral.
- Community acquired pneumonia (new CXR changes): See P196.
- *Exposure to known allergen:* COPD may co-exist with allergic asthma.
- *Pneumothorax* (see P236, differentiate from large bullae).
- *Expansion of large bullae.*
- *Sputum retention* with lobar or segmental collapse (atelectasis): pneumonia, excessive sedation or opioid analgesia (trauma, post-surgery), impaired consciousness.
- *Confounding or contributing factors:* myocardial ischaemia, pulmonary oedema, cor pulmonale, pulmonary embolism.

Investigations

All patients should have:

â€¢ U&Es	Look for dehydration, renal failure. Monitor K^+.
â€¢ FBC	Look for leukocytosis or anaemia (chronic respiratory failure may produce a secondary polycythaemia).
â€¢ Pulse oximetry and ABG	To assess degree of respiratory failure and pH. And guide appropriate oxygen treatment.
â€¢ Septic screen	Sputum should be sent for culture. Blood cultures if febrile or CXR

	changes suggest pneumonia.
â€¢ Peak flows	Ask what is normal for patient.
â€¢ Chest X-ray	Focal changes suggest pneumonia (see P196).
â€¢ ECG	Myocardial ischaemia or arrhythmia.

Assessment of severity

- *History:* Assess the severity of COPD when stable and compare with current exacerbation. Ask about symptoms and functional capacity when well (distance walked on flat, stairs climbed, frequency of exacerbations, previous admissions, ever ventilated?). Assess level of usual treatment (regular nebulized bronchodilators or oral steroids, home O_2) and concurrent illnesses (IHD, renal impairment). Any previous documentation (PFTs, ABG).
- *Examination:* Assess for severity of respiratory distress (RR >25/min, use of accessory muscles or paradoxical chest wall movements), hypoxia (cyanosis), hypercapnoea (CO_2 retention flap, confusion), cor pulmonale (peripheral oedema).

Criteria for hospital admission[1]

- Marked increase in symptoms
- Baseline of severe COPD
- New physical signs, e.g. cyanosis, peripheral oedema

- Failure to respond to initial management at home
- Significant co-morbidities
- Diagnostic uncertainty
- Age >70 years
- Insufficient home support

Footnote

[1]Adapted from â€˜Global initiative for chronic obstructive pulmonary diseaseâ€™ 1993.

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Acute exacerbation of COPD: management

- Treat hypoxia and respiratory failure
    - The distinction between â€˜pink puffersâ€™ (breathless to maintain P_aO_2 and so keep P_aCO_2 down) and â€˜blue bloatersâ€™ (lose breathless drive to maintain P_aO_2 and so P_aCO_2 rises) is unhelpful as most patients have features of both.
    - Commence oxygen therapy. Uncontrolled O_2 therapy may worsen CO_2 retention in some patients. While awaiting ABGs give controlled 24â€“28% O_2 via a venture mask. Nasal canulae give unreliable inspired O_2 concentration and may be dangerous. Once ABG results available, adjust FiO_2 accordingly.
    - Arterial blood gases
        - If patient is not retaining CO_2 (P_aCO_2 < 6kPa) and is hypoxic (P_aO_2 <10kPa) then give oxygen 28â€“40%. Repeat ABGs 30 minutes later (sooner if conscious level deteriorates) to ensure correction of hypoxia and exclude rising P_aCO_2. Aim to maintain sats â‰¥92%.
        - If CO_2 retention is present then use 24â€“28% oxygen and repeat blood gases after 15â€“30

minutes. Aim to keep P_aO_2 â‰¥7.3kPa and P_aCO_2 â‰¤7.5kPa, but these limits may not be achievable. Balance hypoxia (which may be fatal) against conscious level, arterial pH, and respiratory effort. Consider non-invasive ventilation, mechanical ventilation, or doxapram.

- NIV. This is the first-line treatment of choice for COPD exacerbations with type 2 respiratory failure in patients who fail to respond to initial therapy. It allows the administration of higher O_2 concentrations without an uncontrolled rise in P_aCO_2. NIV reduces the need for intubation, decreases mortality and hospital stay, and should be considered in all patients with COPD exacerbations with P_aCO_2 â‰¥6.0kPa and pH â‰¤7.35 who have failed to respond to initial bronchodilator therapy.
- Mechanical ventilation. This should be considered in patients unlikely or unable to tolerate NIV (see P906).
- Respiratory stimulants. These have generally been superseded by NIV. However where NIV is not available or has not been successful and mechanical ventilation is not considered appropriate, a trial of doxapram may be worthwhile. It is not beneficial in type 2 respiratory failure due to poor respiratory effort.

- Treat bronchospasm and obstruction
  - *Nebulized Î²-agonists* (salbutamol 5mg or terbutaline 10mg q4h and prn) via oxygen or air if CO_2 retaining. (If patient is very hypoxic, give 2L/min oxygen via nasal cannulae whilst nebulizer in progress.)
  - Patients with COPD may have relatively fixed bronchospasm, but where the patient is very unwell then consider iv aminophylline and/or iv Î²-agonists as for severe asthma (P213).
  - Include *nebulized ipratropium bromide* 500ÂÂµg 6 hourly.

- Give *steroids:* 200mg hydrocortisone iv or 30â€“40mg prednisolone po.
- Urgent physiotherapy may help clearing bronchial secretions.

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Acute exacerbation of COPD

Mechanical ventilation

- COPD *per se* is not a contraindication to ventilation in appropriately selected patients. Ventilation should be considered where respiratory failure is present (P_aO_2 â‰¤7.3kPa) regardless of CO_2 levels and in those patients who have failed to respond to first-line treatment (including NIV), or who are very severely unwell and unlikely to respond to any other intervention.
- Discuss with a senior colleague or ITU staff prior to intubation.

In favour of a good outcome from ventilation

- Acute respiratory failure (normal bicarbonate, acute history)
- Relatively young patient
- Obvious remediable cause (e.g. pneumonia)
- Good recent exercise tolerance and quality of life
- Not previously known to retain CO_2 when well.

Against a good outcome from ventilation

- Relatively old
- Other co-morbid conditions (e.g. IHD, renal failure)
- Previous difficulty weaning from ventilator
- On maximal therapy at home (home nebulizer, long-term oxygen therapy)
- Poor quality of life or poor exercise tolerance.

Management of gas exchange during ventilation

- Patients who are chronically hypoxic or CO_2 retainers will tolerate poor blood gases better than those patients with other causes of respiratory failure.
- When ventilating patients with COPD, achieving a â€˜normalâ€™ P_aCO_2 and P_aO_2 may not be appropriate. Those who are chronically hypoxic or who chronically retain CO_2 (as evidenced by previous abnormal gases or a raised bicarbonate with a normal or near-normal pH) are unlikely to breath spontaneously or wean from the ventilator unless their blood gases are allowed to mirror what is probably their chronic state. Thus a patient with chronic type 2 respiratory failure may need a P_aCO_2 of 6â€“7.5kPa Â± mild hypoxia even on the ventilator to achieve successful weaning.

Treat cause of exacerbation

Infective exacerbation

- Suggested by purulent sputum or increase in sputum

production.

- For lobar consolidation or bronchial pneumonia follow guidelines on pP198â€“200. Otherwise treat with *amoxycillin* 500mgâ€“1g tds po/iv; if unwell or failure to respond treat *cefuroxime* 750mg tds iv for improved cover of resistant *Haemophilus* sp.
- Follow local protocols.

Pneumothorax. Unless very small, consider aspiration Â± drain, P236.

Pulmonary oedema. P108.

Pulmonary embolism. P146.

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Respiratory failure: assessment

Respiratory failure is present when gas exchange becomes significantly impaired. Clinically, it is not possible to predict the P_aO_2 or P_aCO_2 and so this diagnosis relies on ABG analysis. There are two types:

Type 1. Hypoxia P_aO_2 â‰¤8kPa on air or oxygen with normal or low P_aCO_2 (i.e. mainly ventilationâ€“perfusion mismatch).

Type 2. Hypoxia P_aO_2 â‰¤8kPa on air or oxygen with raised P_aCO_2 (>6kPa) (i.e. predominantly alveolar hypoventilation).

In practice, both types may co-exist.

Presentation

- *Shortness of breath* is the commonest presentation. Ask about the speed of onset (sudden onset may suggest pneumothorax, pulmonary embolus, or cardiac failure).
- Respiratory failure may present without dyspnoea, particularly exacerbations of COAD with hypoventilation (â€™blue bloatersâ€™), and non-respiratory causes such as Guillainâ€“BarrÃ© syndrome (P572) or drug overdose. Neuromuscular respiratory failure is discussed on P502.
- *Confusion* may be the sole presentation in the elderly.

The history may point to the cause of respiratory failure:

- History of asthma/chronic bronchitis and smoking.
- History of other chronic lung disease (e.g. fibrosing alveolitis, sarcoidosis).
- Sputum production and fevers (pneumonia).
- Swollen legs due to the development of cor pulmonale or hypoxic/hypercapnic renal fluid retention in patients with chronic lung disease.
- Haemoptysis (pneumonia, PE).
- Cardiac history including palpitations and/or chest pain.
- Drug and/or overdose history.
- Neurological symptoms including painful legs and paraesthesiae (Guillainâ€“BarrÃ© syndrome).
- Allergies.
- Try to assess the functional capacity when well, e.g. distance walked on flat, stairs climbed without stopping, frequency of attacks, previous admissions, ever ventilated?, concurrent illnesses (heart disease, renal impairment, liver impairment), etc.

Physical examination

- Listen to the breathing (stridor, wheeze, coarse crackles).
- Look for wheeze (airflow limitation, either localized (local obstruction) or generalized (e.g. asthma, COPD, pulmonary oedema), coarse crackles (infection, pulmonary oedema, or fibrosis), bronchial breathing (indicates consolidation or collapse, but may also occur with fibrosis or above a pleural effusion), signs of pneumothorax (hyper-resonance, decreased breath sounds), or pleural effusion (stony dull, decreased breath sounds).
- Palpate the upper chest and neck for crepitus

(pneumothorax or pneumomediastinum).

- Look for signs of a DVT (swollen hot leg Â± pain, see P142).

Causes of respiratory failure

Common

- Acute asthma (P210)
- Exacerbation of COPD (P218)
- Pneumonia (P194)
- Pulmonary oedema (P108)
- Pulmonary embolus (P146)
- Infection complicating kyphoscoliosis or other chronic lung disease
- Pleural effusion (P248)
- Pneumothorax (P236)
- ARDS/ALI (P230)
- Respiratory depression
- Drugs e.g. opiates

Rarer

- Lung collapse/atelectasis (tumour, foreign body, sputum plug, infection)
- Acute respiratory muscle weakness [Guillainâ€“BarrÃ© syndrome (P512), myasthenia gravis (P506), poliomyelitis]
- Upper airway obstruction (foreign body, tumour, epiglottitis) (P256)
- Chest trauma

- Anaphylaxis (P264)

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Respiratory failure: investigations

Urgent investigations

â€¢ ABG	On air immediately, or if very unwell whilst on oxygen (note FiO_2)
â€¢ Chest X ray	(see figure, P196)
â€¢ ECG	Look for signs of PE (tachycardia, RBBB, anterior T-wave changes, RAD, rarely $S_1Q_3T_3$, P146), tachyarrhythmias, or myocardial ischaemia
â€¢ Blood tests	FBC (anaemia, leukocytosis), U&Es, glucose
â€¢ Inspect sputum	Yellow, green, mucoid, streaky, or frank blood

â€¢ FEV_1 and FVC	If suspected muscle weakness (e.g. Guillainâ€“BarrÃ©)
â€¢ Septic screen	Sputum culture, blood cultures if febrile or if CXR suggests infection.

Where indicated consider

- Aspirin and paracetamol levels
- Plasma and urine for toxicology
- Urinalysis for glucose and ketones
- Examine the CXR systematically for any abnormality.

CXR assessment

- Consolidation/alveolar shadowing: may be lobar or patchy. Presence of an air bronchogram suggests pneumonia.
- Pulmonary oedema due to left ventricular failure (cardiogenic): typically perihilar (â€™bats-wingâ€™), upper lobe venous congestion, Kerley B lines in peripheral lung fields, Â± pleural effusions, Â± cardiomegaly.
- Non-cardiogenic pulmonary oedema (ARDS/ALI): typically peripheral alveolar shadowing Â± air bronchogram, *no* upper lobe venous congestion, Kerley B lines, pleural effusions, or cardiomegaly.
- Pleural effusions.
- Masses suggesting *bronchogenic carcinoma*.
- Pulmonary embolism: wedge-shaped peripheral opacities, small pleural effusions, localized areas of oligaemia,

enlarged pulmonary artery.

- Pneumothorax (distinguish from large bullae).
- Trauma/rib fractures.
- Diffuse lung disease (e.g. fibrosing alveolitis): small lung fields, interstitial reticulo-nodular shadowing, peripherally and basally.

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Respiratory failure: management

See P502 for neuromuscular respiratory failure.

The severity of respiratory failure depends upon response to oxygen. Failure of hypoxia to correct on 40â€“60% oxygen or progressive hypercapnoea implies that non-invasive or mechanical ventilation may be necessary depending on the clinical condition and underlying cause.

Poor prognostic signs on presentation include

- Inability to speak due to dyspnoea
- Respiratory rate (>40)
- Peak flow â‰¤33% of predicted in acute asthma
- Tachycardia HR â‰¥100 or bradycardia HR â‰¤60
- Exhaustion or coma (ventilatory support is required urgently)
- Stridor (this indicates upper airway obstruction, see P254)
- Pulse oximetry saturation of <90%
- Shock (tachycardia + hypotension). May indicate tension pneumothorax (P242), severe LVF (P108), severe

pneumonia (P198), or large PE (P146).

Hypercapnoea is the end result of many causes of respiratory failure (including asthma and pneumonia), not just COPD, and indicates a tiring patient. Even if relatively elderly the patient may respond well to ventilation with a satisfactory final outcome depending on the disease and premorbid condition.

General resuscitation (ABC)

- Ensure the airway is patent and the mouth is clear.
- If stridor is present request anaesthetic and/or ENT assistance urgently (P254).
- Sit the patient up (unless hypotensive) and administer oxygen at 60% unless there is a history of COPD (use 24â€“28% oxygen).
- Ensure that respiratory effort is adequate and effective (measure respiratory rate and assess depth of respiration), use pulse oximetry to monitor the PaO_2.
- If the patient is exhausted with a failing respiratory drive, call for anaesthetic assistance and consider urgent transfer to ITU.
- In comatose patients with poor respiratory effort consider drug overdose with opiates (pinpoint pupils) or benzodiazepines. Give naloxone 200â€“400Âµg (2â€“4Âµg/kg) iv bolus followed by infusion depending on response and/or iv flumazenil (200Âµg over 15 seconds then 100Âµg at 60-second intervals if required [max. total dose 1mg (2mg if on ITU)].
- Methods of respiratory support are discussed on P902.
- Secure iv access.
- Measure the BP and heart rate, look for signs of cardiac failure (raised JVP, inspiratory crackles, oedema) or signs

of pulmonary embolism (raised JVP, tachycardia, hypotension, normal breath sounds Â± pleural rub).

Indications for intensive care

- Progressive exhaustion or impaired conscious level
- Shock not responding rapidly to initial resuscitation
- Respiratory failure not responding rapidly to initial therapy

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Adult Respiratory Distress Syndrome 1

ALI and its more severe sub-set, ARDS, is a common clinical disorder characterized by injury to the alveolar epithelial and endothelial barriers of the lung, acute inflammation, and protein-rich pulmonary oedema leading to acute respiratory failure. Often occurs in the setting of MOF.

Diagnostic criteria

- Acute onset of respiratory failure with one or more risk factors (table, opposite)
- Hypoxaemia
    - ALI: Ratio P_aO_2 (kPa) : FiO_2 <40
    - ARDS: Ratio P_aO_2 (kPa) : FiO_2 <27
- Bilateral infiltrates on CXR
- Pulmonary capillary wedge pressure <19mmHg, with normal colloid oncotic pressure (in patients with hypoalbuminaemia, the critical PCWP is approx. serum albumin (g/l) Ã— 0.57, see P282) or clinical exclusion of cardiac failure.

Investigations

- CXR
- ABG (consider arterial line as regular samples may be required)
- Take blood for FBC, U&Es, LFTs and albumin, coagulation, X-match, and CRP
- Septic screen (culture blood, urine, sputum)
- ECG
- Consider drug screen, amylase if history suggestive
- Pulmonary artery catheter to measure PCWP, cardiac output, mixed venous oxygen saturation and to allow calculation of haemodynamic parameters
- Other investigations if appropriate
    - CT chest
    - Bronchoâ€“alveolar lavage for microbiology and cell count (?eosinophils)
    - Carboxy-haemoglobin estimation.

Management

- *Almost all cases of ALI alone will require HDU/ICU care: liaise early*
- The main aim is to identify and treat the underlying cause whilst providing support for organ failure:
    - Respiratory support to improve gas exchange and correct hypoxia
    - Cardiovascular support to optimize oxygen delivery to tissues

- Reverse or treat the underlying cause.

Disorders associated with the development of ARDS

Direct lung injury

- Aspiration
  - Gastric contents
  - Near drowning
- Inhalation injury
  - Noxious gases
  - Smoke
- Pneumonia
  - Any organism
  - PCP
- Pulmonary vasculitides
- Pulmonary contusion
- Drug toxicity or overdose
  - Oxygen
  - Opiate overdose
  - Bleomycin
  - Salicylates

Indirect (non-pulmonary) injury

- Shock

- Septicaemia
- Amniotic or fat embolism
- Acute pancreatitis
- Massive haemorrhage
- Multiple transfusions
- DIC
- Massive burns
- Major trauma
- Head injury
    - Raised ICP
    - Intracranial bleed
- Cardio-pulmonary bypass
- Acute liver failure

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Adult Respiratory Distress Syndrome 2

Respiratory support

Spontaneously breathing patient

- In very mild ALI, hypoxia can be corrected with increased inspired oxygen concentrations (FiO_2 40â€“60%). However, such patients are rarely recognized as having ALI as a cause of their respiratory failure.
- Patients invariably require higher oxygen concentrations (non-rebreather masks with reservoir FiO_2 ~60â€“80%) or CPAP (see P904). Consider transfer to HDU/ICU.
- Indications for mechanical ventilation
    - Inadequate oxygenation (P_aO_2 <8kPa on FiO_2 >0.6)
    - Rising or elevated P_aCO_2 (>6kPa)
    - Clinical signs of incipient respiratory/cardiovascular failure.

Mechanical ventilation

This is the realm of the ICU physician. Main aim is to improve

oxygenation/ ventilation while minimizing the risk of further ventilator-induced lung injury; termed lung protective ventilation.

General principles

- Controlled mechanical ventilation with sedation (Â± neuromuscular blockade).
- Aim for tidal volume ~6ml/kg. Recent evidence has confirmed that ventilation with smaller tidal volumes is associated with improved outcome compared to the traditional approach (~10â€“12ml/kg).
- Start with FiO_2 = 1.0. Subsequent adjustments are made to achieve oxygen saturation >90% with FiO_2 < 0.6.
- Positive end expiratory pressure (PEEP) improves oxygenation in most patients and allows reduction in FiO_2. Usual starting level, 5â€“10cm H_2O, with optimal levels in the range 10â€“15cm H_2O. Beware hypotension due to reduction in venous return.
- The use of smaller tidal volumes may impair CO_2 clearance with resulting acidosis despite high ventilatory rates (20â€“25 breaths/minute). Further increases in rate or tidal volume risk worsening ventilator-induced lung injury. Gradual increases in pCO_2 (up to ~13kPa) are well tolerated in most patients and acidosis (pH <7.25) can be treated with intravenous bicarbonate, so-called permissive hypercapnia.
- If oxygenation/ventilation cannot be improved despite these measures, the following can be considered;
    - Inverse ratio ventilation (P906): may improve oxygenation, but pCO_2 may rise further
    - Prone positioning: improves oxygenation in ~70% of patients with ARDS

    - Inhaled vasodilators (nitric oxide, nebulized prostacyclin): may improve oxygenation
- High-frequency ventilation: only available in specialist centers.

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Adult Respiratory Distress Syndrome 3

Cardiovascular support

- Arterial line essential for continuous blood pressure measurements. Other invasive monitoring is invariably used (PA catheter, PiCCO, oesophageal Doppler), but their individual roles and effects on outcome are unclear.
- Most patients are haemodynamically compromised due to the underlying condition and/or ventilatory management, and benefit from fluid resuscitation. This may risk worsening capillary leak in the lung and compromise oxygenation/ventilation. Aim for a low-normal intravascular volume whilst maintaining cardiac index and mean arterial pressure.
- Inotrope and/or vasopressor support is commonly required and the choice of agent is usually decided on a combination of clinical evaluation and invasive haemodynamic monitoring (cardiac index, oxygen delivery, mixed venous/central venous saturation, lactate). Agents commonly employed include dobutamine, dopamine, epinephrine, norepinepherine.
- Repeated assessment is essential.

On-going management

- Look for and treat a precipitant (see table, P231)
- Sepsis
    - Fever, neutrophilia, and raised inflammatory markers are common in ALI/ARDS and do not always imply sepsis
    - A trial of empiric antibiotics guided by possible pathogens, and following an appropriate septic screen (consider bronchoalveolar lavage once intubated and stable), should be considered. Antibiotics should be modified or discontinued in light of microbiological results
    - Indwelling CVP catheters are a common source of sepsis
    - Consider low-dose steroid infusion if (see below)
    - Consider activated protein C, which has been shown to improve survival in patients with septic shock with multi-organ failure.
- Renal failure. Common and may require renal replacement therapy to control fluid balance and blood biochemistry.
- Enteral feeding. Helps maintain integrity of the gut mucosa and is associated with a lower risk of systemic sepsis when compared to parenteral feeding (TPN). Delayed gastric emptying and reduced gut motility is common in ICU patients and may respond to pro-kinetic drugs (metoclopramide, erythromycin) or may require nasojejunal feeding. Stress ulcer prophylaxis (H_2-blockers) should be considered if mechanical ventilation >48 hours, or multi-organ failure.
- Coagulopathy. Common and if mild does not require therapy. If severe/DIC, expert advice should be sought.
- Steroid therapy

- ALI/ARDS: no benefit in the acute stage. Treatment (2mg/kg/day of methylprednisolone) later in the course of the disease (7â€“10 days) may improve prognosis but further studies are awaited.

- Sepsis: evidence suggests that some patients with refractory septic shock (ongoing/increasing vasopressor requirements) may have â€˜relativeâ€™ or â€˜functionalâ€™ adrenal insufficiency and may benefit from â€˜supraphysiologicalâ€™ steroid replacement (200â€“300mg/day hydrocortisone). Identification of patients likely to benefit unclear at present, but ACTH stimulation test may help discriminate.

Causes of sudden deterioration in ARDS

Respiratory

- Pneumothorax
- Bronchial plugging
- Displaced ET tube
- Pleural effusion (haemothorax)
- Aspiration (e.g. NG feed)

Cardiovascular

- Arrhythmia
- Cardiac tamponade
- Myocardial infarction
- GI bleed (â€™stressâ€™ ulcer)
- Septicaemia

Outcome

- The outcome for ALI/ARDS has improved in recent years, with overall mortality rates of ~40%.
- Patients with ALI/ARDS and sepsis, liver disease, non-pulmonary organ dysfunction, or advanced age have higher mortality rates.
- In survivors, although formal lung function tests are abnormal, respiratory compromise at 1â€“2 years is unusual.
- There is increasing evidence that survivors suffer considerable neuromuscular and psychological disability. This may reflect the period of prolonged critical illness rather than be specific for ALI/ARDS.

Footnote

1

The pulmonary physician in critical care (2002) Thorax 5 7.

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Pneumothorax: assessment

Presentation

Most individuals presenting to hospital with a spontaneous pneumothorax have no recognized underlying lung disease. The commonest presenting symptoms are

- Breathlessness: usually abrupt in onset (young, fit patients may have very little, but patients with COPD or asthma may present with a sudden deterioration)
- Chest pain: dull, central, heavy; or there may be a pleuritic element
- In an in-patient, consider the diagnosis in anyone who is
    - Breathless after an invasive thoracic procedure (e.g. subclavian vein cannulation)
    - Increasingly hypoxic or has rising inflation pressures on mechanical ventilation.

Causes

â€¢ Primary/spontaneous	Healthy subjects, no known underlying lung disease.
	More common in tall, young, smoking men aged 20â€“40 years. Probably due to rupture of apical subpleural blebs/bullae
â€¢ Secondary/spontaneous	Pleural rupture due to underlying lung disease: emphysema, fibrosing alveolitis, cystic fibrosis, sarcoidosis
â€¢ Infection	Cavitating pneumonia, e.g. staphylococcal, lung abscess, tuberculosis, PCP
â€¢ Trauma	Particularly chest trauma in RTA
â€¢ Iatrogenic	After pleural biopsy or aspiration, transbronchial biopsy, percutaneous lung biopsy, subclavian vein cannulation, mechanical ventilation with high airway pressures.

Investigations: the chest radiograph

- The classical clinical signs may not always be present.
- In a supine patient a pneumothorax mot not be easy to see. Look for hyperlucency of one lungfield, and usually clear heart border, or a line parallel to the chest wall (caused by retraction of the R middle lobe).
- If a patient has COPD and marked bullous disease, take care that the suspected pneumothorax is not a large thin-walled bullus: with a pneumothorax the pleural line is usually convex to the lateral chest wall; with a bullus, the apparent pleural line is usually concave to the lateral chest wall. If there is any doubt, CT chest will be able to distinguish between the two.

Signs of a significant pneumothorax

- Tension pneumothorax: mid-line shift away from the pneumothorax, raised or obstructed JVP, hypotension, tachycardia, shock.
- Size of pneumothorax: percentages of pneumothorax are hard to estimate; classify according to the size of the visible rim between the lung margin and the chest wall on CXR:
    - Small pneumothorax: visible rim <2cm
    - Large pneumothorax: visible rim >2cm

      (NB: a large pneumothorax approximates to a 50% loss of lung volume).
- Hypoxia: P_aO_2 â‰¤10kPa on air (may simply reflect underlying lung disease).
- Severe dyspnoea.

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Pneumothorax: management

See algorithm, P240.

- Who to discharge from A&E
    - Small spontaneous primary pneumothorax, rim pf air <2cm on CXR, no significant dyspnoea, and no underlying chronic lung disease.
    - Large spontaneous primary pneumothorax following successful aspiration (<2cm rim of air on repeat CXR), no significant dyspnoea or underlying lung disease.
    - Follow up in chest clinic in 10â€“14 days with a repeat CXR.
    - Advise the patient to return to A&E if breathless or increasing chest pain.
- Who to admit for observation
    - All patients with pneumothorax secondary to trauma or with underlying lung disease even if aspiration has been successful: discharge after 24 hours if follow-up CXR shows no recurrence.
    - Patients in whom aspiration has failed to re-expand the lung fully.
    - Give oxygen (>35% unless there is clinical evidence of

COPD, in which case start with 24â€“28% and check ABGs). This accelerates the reabsorption of the pneumothorax up to 4 fold. Most of the pneumothorax is N_2 (air) and supplemental O_2 decreases the partial pressure of N_2 in the blood, increasing the gradient for its reabsorption.

  - Once the air leak is sealed, the pneumothorax reabsorbs at a rate of ~1.25% of the volume of the hemithorax per day. A 15% pneumothorax will take approx. 3 weeks to reabsorb.

- Attempt chest aspiration in patients with

  - Primary pneumothorax: all large primary pneumothoraces, whether symptomatic or not. Repeat aspiration is successful in up to 50%.
  - Secondary pneumothorax: all small secondary pneumothoraces, only if asymptomatic and <50 years. Admit for observation and if there is minimal or no pneumothorax on CXR after 24 hours, discharge with follow-up in chest clinic in 10â€“14 days with CXR.

- Proceed to intercostal chest tube drainage in patients with

  - Primary pneumothorax: failed aspiration after 1â€“2 attempts.
  - Secondary pneumothorax: small pneumothorax if symptomatic or >50 years; failed aspiration after 1 attempt.
  - Miscellaneous: Associated hydro- or haemopneumothorax, all mechanically ventilated patients with a pneumothorax, all patients with a pneumothorax requiring inter-hospital transfer.
  - The technique for insertion of an intercostals drain is described on P920.

- If the lung has re-expanded and the drain is not bubbling, wait 24 hours and repeat CXR to exclude recurrence, and remove the drain.
- A collapsed lung and bubbling drain suggests persistent air leakand suction may be required. Use low-pressure suction (2â€“5kPa)

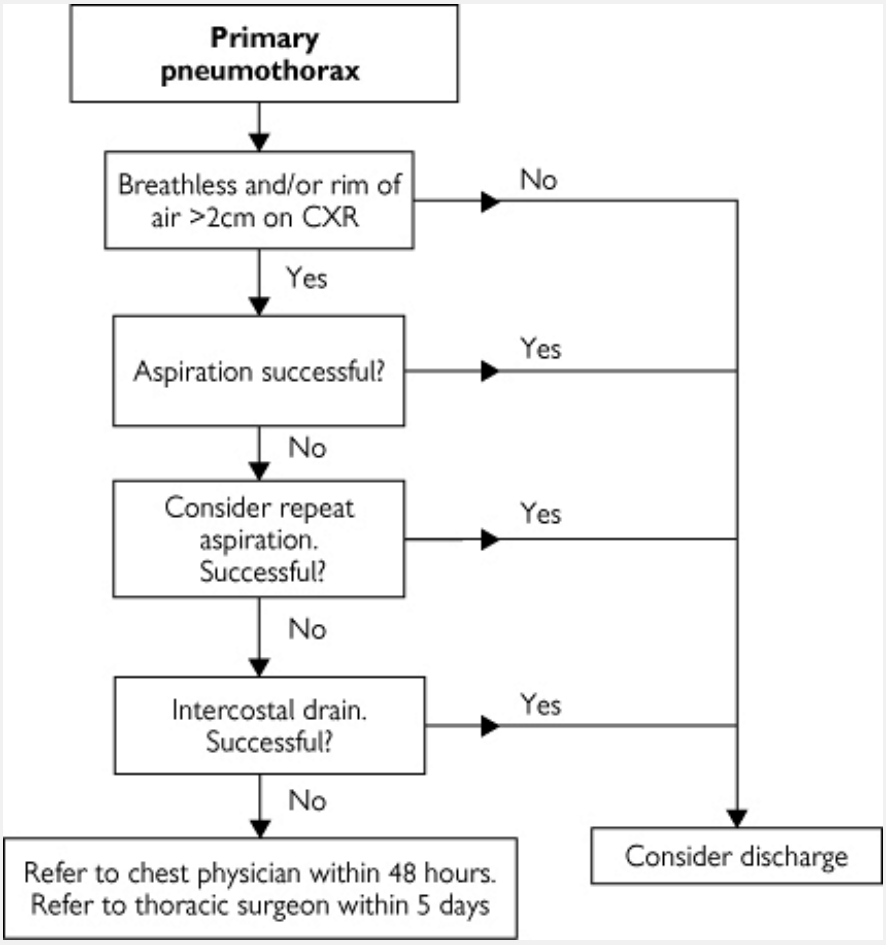
  via appropriate pump or modified wall suction: discuss with chest team.
- A collapsed lung and no bubbling suggests the drain is blocked, displaced, or clamped. If a new drain is required it should be through a new incision.
- If there is a persistent air leak or failure of the lung to re-expand after 3â€“5days consider surgical pleurodesis (consult the chest team and/or cardiothoracic team). Open thoracotomy and pleurectomy, or surgical talc pleurodesis, are more effective than medical pleurodesis (with talc, bleomycin, or tetracycline), which should only be considered for those unwilling or unable to undergo surgery.

Practice points

- There are NO indications in the standard management for a pneumothorax for clamping chest drains. If patients are to be moved, keep the drain bottle below chest height but DO NOT CLAMP
- NEVER clamp a chest drain unless you know what you are doing

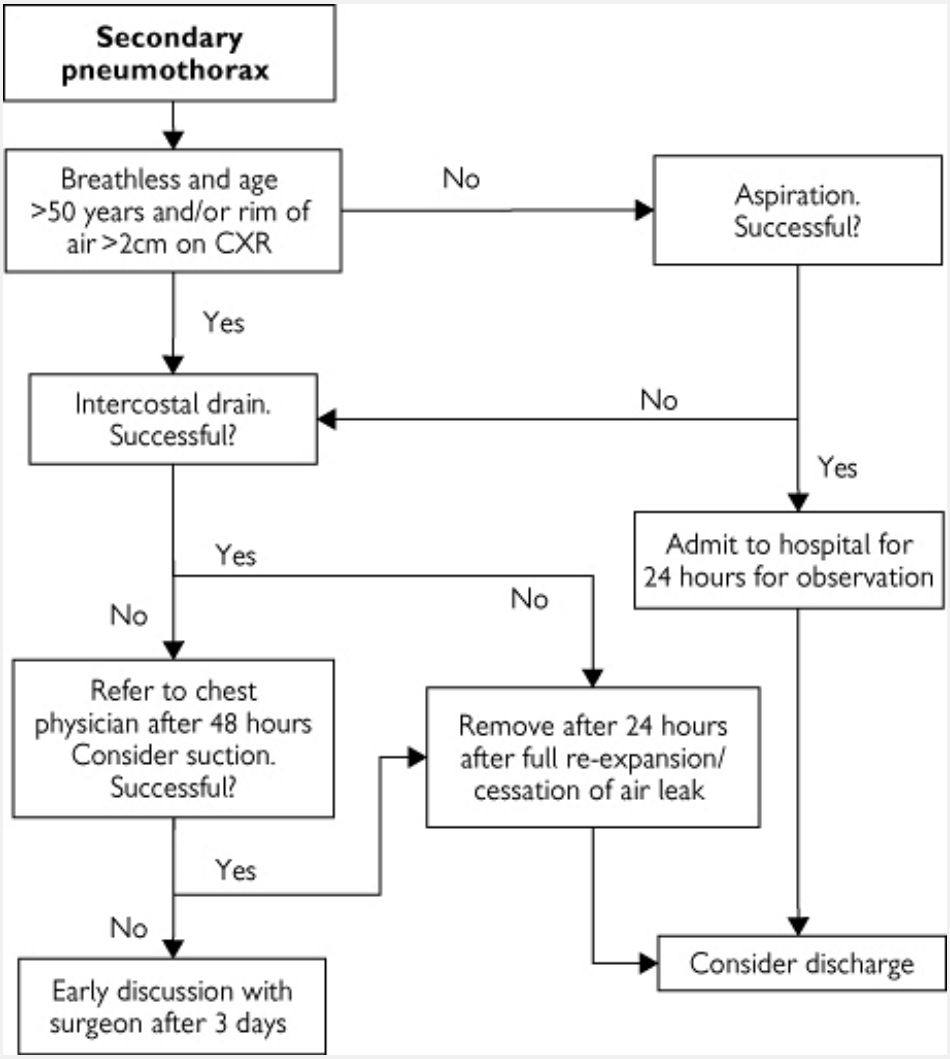
Editors: Ramrakha, Punit S.; Moore, Kevin P.
Title: *Oxford Handbook of Acute Medicine, 2nd Edition*

Acute pneumothorax: management



Adapted from BTS guidelines for the management of spontaneous pneumothorax, (2003) *Thorax* 58 (suppl. 11):

1139â€“1152.



Secondary pneumothorax: Management

Editors: Ramrakha, Punit S.; Moore, Kevin P.
Title: *Oxford Handbook of Acute Medicine, 2nd Edition*

Tension pneumothorax

- Usually seen in patients receiving mechanical ventilation or post CPR
- Patient is usually distressed, tachypnoeic with cyanosis, profuse sweating, and marked tachycardia and hypotension
- This requires immediate attention.

Management

- Do not leave the patient unattended. Give maximal inspired oxygen to reverse hypoxia.
- Insert an 18G (green) cannula (or the largest available) perpendicular to the chest wall into the second intercostal space in the mid-clavicular line on the side with the pneumothorax on clinical examination (reduced breath sounds and trachea deviated away). Relief should be almost immediate. Leave the cannula in place until the air ceases to rush out.
- Improvize an underwater seal using an iv line attached to the cannula with the free end held under a bowl of water, until a formal intercostal drain can be set up.
- Insert a chest drain as soon as possible.
- If no air rushes out when the cannula is inserted, the

patient does not have a tension pneumothorax and the cannula should be removed.

Editors: Ramrakha, Punit S.; Moore, Kevin P.
Title: *Oxford Handbook of Acute Medicine, 2nd Edition*

Haemoptysis: assessment

Presentation

- Haemoptysis is the coughing up of blood from the lungs or tracheobronchial tree (see table).
- Massive haemoptysis is defined as â‰¥400ml over 3 hours or â‰¥600ml over 24 hours. The common causes of *massive* haemoptysis are bronchiectasis, bronchial carcinoma, infection (e.g. TB, lung abscess, or aspergilloma), or trauma.
- Often the cause is obvious from the history. Patients with large bleeds may be able to locate the site of bleeding by a â€˜gurglingâ€™ within the chest. Ask specifically for smoking and drug history.
- Examine for an underlying cause (see table) and to assess the haemodynamic and respiratory effects of the bleed.
- Consider that the blood may be coming from somewhere other than the lungs: upper respiratory tract, GI tract, nasopharynx.

Poor prognostic factors

These include

- Increasing age
- Pre-existing lung or cardiac disease
- Respiratory compromise (rate, cyanosis)
- Hypoxia (P_aO_2 â‰¤10kPa on air)
- On-going haemoptysis of large amounts of fresh blood
- Shock (postural or supine hypotensionâ€”rare).

Initial management

Stabilize the patient

- Massive haemoptysis should usually be managed at a hospital with cardiothoracic surgical back-up, and urgent transfer should be considered if this is not available.
- Give high inspired oxygen.
- Place patient in the recovery position, with the bleeding lung down (if it is known which side the bleeding is from) to try to keep the unaffected lung free of blood.
- If aspiration of blood is threatened, get anaesthetic help urgently; anaesthetize, intubate, and ventilate. A double-lumen endotracheal tube may be used to isolate the lungs but the narrow lumen may make subsequent flexible bronchoscopy difficult.
- Insert a large-bore peripheral cannula, followed by a central line if indicated; internal jugular route is preferred to minimize the risk of pneumothorax.
- Support the circulation: haemoptyses are rarely severe enough to warrant transfusion. If the patient has postural or supine hypotension use intravenous colloid until blood is available.
- Monitor the urine output, pulse, BP, and if appropriate CVP.

Investigations

All patients should have the following

- Blood for FBC, U&Es, coagulation studies, X-match
- Arterial blood gases
- ECG
- CXR (Â± lateral)
- Sputum (microscopy and culture, cytology)
- Flexible bronchoscopy.

Common causes of haemoptysis

Lung disease

- Bronchiectasis(Â± infection)
- Bronchogenic carcinoma
- Infection
    - Tuberculosis
    - Pneumonia
    - Lung abscess
    - Aspergilloma
- Bronchitis
- Trauma
- AV malformation

Cardiovascular

- Pulmonary embolus

- Left ventricular failure
- Mitral stenosis
- Congenital heart disease with pulmonary hypertension
- Aortic aneurysm

Systemic vasculitis

- SLE
- Wegner's
- Goodpasture's
- Microscopic polyangiitis

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Haemoptysis: further management

Diagnose the source of bleeding

- CXR. This should be examined systematically for a mass lesion Â±hilar nodes, bronchiectasis (tram-line shadows), old or new cavities which may suggest aspergillomas. Look for causes of minor haemoptysis, if this is the current problem.
- Fibre-optic or rigid bronchoscopy. This should be performed urgently in all cases of massive haemoptysis. This is unlikely to localize the exact source, but may help localize the lung or lobe affected to guide surgeons or radiologists. Bleeding may be arrested by endoscopically administered adrenaline (1ml 1 : 10 000) or, in massive haemoptysis, a balloon catheter may be inflated for 24â€“48 hours within a segmental or sub-segmental bronchus.
- Selective pulmonary angiography. Can identify the bleeding source in 90% of patients and, when combined with embolization, is effective in controlling bleeding in up to 90%. Multiple procedures may be necessary.
- High resolution CT chest. May help identify parenchymal lesions and peripheral endobronchial lesions.

Specific therapeutic interventions

- Correct coagulopathy: If the haemoptysis is relatively minor it may be sufficient to correct an excessively elevated INR to a therapeutic range (INR 1.5â€“2.0) with FFP. In patients with a prosthetic valve and massive haemoptysis, the clotting must be normalized as best as possible. Discuss with your local haematologists or cardiologists. Support platelets if <50 Ã— 10^9/L.
- Consider nebulized Î²-agonist and/or iv aminophylline as a mucocilliary stimulant and to relieve bronchospasm in patients with asthma and COPD.
- Patients with minor haemoptysis should be fully investigated (see table). No cause is found in ~10%.
- Patients with massive haemoptysis should undergo urgent fibre-optic bronchoscopy to locate the bleeding source.
- Angiography and embolization should be considered for all patients with massive haemoptysis prior to surgery.
- If angiography is not available, patients who continue to bleed >600ml/day or who have an identifiable lesion (e.g. lung abscess, aspergilloma, trauma) should have definitive surgery.
- Discuss all cases of haemoptysis with the chest team. Patients with massive haemoptysis should be managed in a specialist centre with appropriate cardiothoracic and radiological back-up. Transfer the patient (ventilated if unstable) if the patient is fit enough.
- Infection is a common precipitant (e.g. in bronchiectasis). Consider antibiotics (e.g. co-amoxiclav 1g iv q6â€“8h or cefotaxime 2g iv q8h) after appropriate cultures. TB or lung parasites will require specific antimicrobial therapy.

Further investigation of haemoptysis

- Autoantibodies (ANA, ANCA, anti-GBM antibody)
- Serum for *Legionella* serology
- *Aspergillus* precipitins
- CT chest
- VQ scan
- Echo
- Pulmonary and bronchial artery angiogram
- Lung biopsy
- Pulmonary function tests with transfer factor

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Pleural effusions

Presentation

- Dyspnoea
- Chest discomfort or sensation of heaviness
- Symptoms of malignancy: loss of appetite, weight, energy
- Symptoms of infection: fever, cough, sputum, night sweats.

Severity depends on

- Speed of onset (e.g. traumatic or post-procedural)
- Haemodynamic compromise (hypotension, tachycardia)
- Hypoxia or respiratory failure
- Presence of underlying disease (e.g. heart failure, COPD).

Causes

Transudate (protein <30g/L)	Exudate (protein <30g/L)

â€¢ *Raised venous pressure*	â€¢ *Infection*
Cardiac failure	Pneumonia
Constrictive pericarditis	Empyema (bacterial or TB)
Fluid overload	Sub-phrenic abscess
â€¢ *Hypoproteinaemia*	â€¢ *Malignancy*
Nephrotic syndrome	Primary bronchial
Cirrhosis with ascites	Mesothelioma
Protein-losing enteropathy	Secondary (and lymphoma)
	Lymphangitis carcinomatosa
â€¢ *Miscellaneous*	â€¢ *Miscellaneous*
Hypothyroidism	Haemothorax (trauma, iatrogenic)
Meigsâ€™ syndrome	Chylothorax (thoracic duct trauma)
Yellow nail syndrome	Autoimmune (RA, SLE, Dressler's)

	Pancreatitis

Management

- If acute then stabilize the patient and insert a chest drain.
- If effusion is chronic then reach a diagnosis and treat accordingly.

Acute massive effusion

- Give oxygen.
- iv access: via a wide-bore cannula or internal jugular central line. If central access is difficult then avoid attempting unless peripheral access is clearly inadequate. Attempt to cannulate (internal jugular veins only) on the normal side. A bilateral pulmonary problem will be a disaster.
- Take blood: for FBC, clotting, and urgent cross-match (6 units).
- Correct coagulopathies.
- Restore circulating volume: if BP low or tachycardic, then give a plasma expander 500ml stat., according to size of effusion drained and response.
- Insert a chest drain (see P920). The drain should be left unclamped and allowed to drain freely, the amount drained should be recorded.

Indications for specialist referral

- Traumatic haemothorax should be referred to the cardiothoracic surgeons.
- Haemothorax secondary to procedures should be referred if the patient is shocked and/or there is on-going significant blood loss requiring transfusion at a rate â‰¥1 unit every 4 hours (approx.).
- When in doubt discuss the case with the surgical team.

Practice point

- If there is decreased movement of one side of the chest, that is the side of pathology (eg fluid, infection, pneumothorax).

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Chronic massive effusion

A unilateral chronic effusion will usually have accumulated over weeks or perhaps even months. The commonest causes are malignancy, empyema, TB, autoimmune diseases (e.g. rheumatoid), and cirrhotic ascites with transdiaphragmatic movement.

Investigation

- Diagnostic aspiration: ideally, the chest should be scanned and marked by ultrasound prior to tapping the effusion as underlying collapse may cause significant elevation of the hemidiaphragm.
- A sample should then be withdrawn (50ml) and split into three for

â€¢ Biochemistry	Protein â‰¥30g/L implies an exudate
	Protein <30g/L implies a transudate

	LDH to assess Light's criteria (see opposite)
	pH <7.2 suggests a possible empyema
	Glucose <3.3mmol suggests a possible empyema (also seen in TB and autoimmune-related effusions)
	Amylase if acute pancreatitis suspected
	Triglycerides if chylothorax suspected
â€¢ Microscopy microbiology	Turbid fluid with neutrophils implies infection Blood-stained fluid implies malignancy but may be a haemothorax (check fluid haematocrit : if >1/2 blood haematocrit, suspect haemothorax) ZN staining for AFB (+ve in only 20% of pleural TB)
	Culture for TB and routine culture
â€¢ Cytology	For primary and secondary tumours. Positive in 60%, so negative does not exclude malignancy.

- Pleural biopsy should be performed if malignancy or TB is

suspected.

- Chest CT with contrast may help differentiate benign from malignant disease, pleural thickening, mesothelioma, or intrapulmonary pathology.

Management

The fluid may be drained by repeated aspirations of 1L/day until dry, or by the insertion of a small-bore intercostal drain (see P920), which should be clamped and released to drain 1.5L/day (this is the only instance when a chest drain may be clamped). Drainage of >1.5L/day may result in reperfusion pulmonary oedema. If the malignant effusion reaccumulates rapidly, consider chemical or surgical pleurodesis.

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Empyema

This is a serious complication of bacterial chest infection (P202). All effusions associated with a pneumonia (parapneumonic) should be tapped.

- To avoid long-term scarring and loculated infection the empyema requires urgent drainage by ultrasound guidance and usually the positioning of an intercostal drain.
- Frequently drainage fails as the empyema organizes with dense adhesions producing loculations. This can be assessed by ultrasound. Surgical drainage is the only option in this situation. The role of intrapleural thrombolytics remains unclear.
- Empyema should always be discussed with a respiratory physician or cardiothoracic surgeon.

Light's criteria for pleural fluid analysis

The pleural fluid is an exudate if one or more of the following criteria are met:

- Pleural fluid protein divided by serum protein >0.5
- Pleural fluid LDH divided by serum LDH >0.6

- Pleural fluid LDH more than two-thirds the upper limit of normal serum LDH level

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Acute upper airway obstruction: assessment

Presentation

- Stridor: inspiratory noise. Generated by the collapse of the extra-thoracic airway during inspiration
- Breathlessness
- Dysphagia
- Inability to swallow secretions (hunched forward, drooling)
- Cyanosis
- Collapse.

Ask colleagues to call a senior anaesthetist and ENT assistance immediately while you continue your assessment.

Identify the cause

(see table)

- History. Sudden onset, something in mouth or child playing with unsafe toy (foreign body), fever (epiglottitis, diphtheria, tonsillitis), hoarse voice (epiglottitis), sore throat (infective as listed), travel (Eastern Europeâ€”diphtheria), smoker + longer history + systemic

symptoms (?carcinoma), trauma.

- Examination. Where infective cause is suspected then examination of oropharynx must be undertaken in area where patient may be immediately intubated, with an anaesthetist standing by.
- Fever, drooling, stridor. Bull neck, lymphadenopathy, pseudomembrane over oropharynx (diphtheria). Swollen throat + epiglottis on direct/indirect laryngoscopy (epiglottitis).
- Investigations. Do not delay treatment if the patient is in distress. If the patient is relatively stable, perform a chest X-ray (foreign body), lateral neck X-ray (swollen epiglottis). FBC, U&E's, blood gases.

Indications for ITU/surgical referral

- Prior to examination of oropharynx if infective cause suspected
- Failure to maintain adequate airway or oxygenation
- Inability to swallow secretions
- Ventilatory failure (P_aO_2 â‰¤10kPa, P_aCO_2 â‰¥6kPa)
- Collapse
- Severe dyspnoea.

Management

- If severe, liaise immediately with ITU and ENT or general surgeons (potential for urgent tracheostomy).
- Priorities are
    - Stabilize the patient: ensure adequate airway

- Identify cause of obstruction
- Specific treatment measures.

Stabilize the patient

- Take arterial blood gases and give high percentage oxygen (â ‰¥60%)
- If clear cause of obstruction (foreign body, post-operative thyroid surgery), then take appropriate measures to gain patient airway (see below).

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- If patient is becoming increasingly exhausted or there is acute failure of ventilation then summon colleagues as above and be prepared to intubate or perform tracheostomy.

Causes of acute stridor

- Infective: acute epiglottitis, diphtheria, tonsillitis, or adenoiditis (children)
- Inhalation of foreign body
- Tumour of trachea or larynx
- Trauma
- Post-operatively (thyroid surgery)

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Acute upper airway obstruction

Foreign body

With total upper airway obstruction, perform Heimlich manoeuvre (stand behind patient, grip wrists across the patient's upper abdomen and tug sharply to raise intrathoracic pressure and expel foreign body). Otherwise perform chest X-ray, liaise with respiratory/ENT/cardiothoracic teams for retrieval under direct vision.

Epiglottitis

Usually *Haemophilus influenzae* type b, also *Strep. pneumoniae*. Treat with 3rd-generation cephalosporin, e.g. cefotaxime 2g tds (adults). Children more likely to require intubation, but if any concerns over airway then patient (adult or child) should be monitored on ITU after anaesthetic assessment.

Diphtheria

Uncommon in UK, occasionally seen in patients returning from abroad. Toxin-mediated problems include myocarditis and neuritis. Treat with diphtheria anti-toxin + antibiotic eradication of organism (consult microbiology).

Tumour obstruction

Unlikely to cause life-threatening obstruction without warning

symptoms over â‰¥ few days. If significant stridor present then administer 200mg hydrocortisone and thereafter prednisolone 40mg od po. If laryngeal origin liaise with ENT regarding tracheostomy. Lung cancer in trachea, or extrinsic cancer eroding into the trachea, will require urgent radiotherapy (or occasionally laser or cryotherapy via bronchoscope).

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Title: *Oxford Handbook of Acute Medicine, 2nd Edition*

Chapter 3
Shock

Shock

Shock is defined as inadequate perfusion of vital organs. Concurrent hypotension need not necessarily be present. The drop in blood pressure is a late finding, particularly in young, fit people, so resuscitation should ideally commence before this point is reached.

Priorities

- *If the blood pressure is unrecordable, call the cardiac arrest team* . Begin basic life support and establish venous access.
- Seek specialist help early.
- The cause of hypotension is often apparent. If it is not, then one can usually make a rapid clinical assessment of likely causes:
    - Cardiac pump failure
    - Hypovolaemia
    - Systemic vasodilatation
    - Anaphylaxis

- Obstruction (e.g. PE, tension pneumothorax, tamponade).

Differential diagnosis of shock

- Cardiac pump failure
  - Myocardial infarction (p12)
  - Dissection of thoracic aorta (p170)
  - Cardiac dysrhythmias (p62)
  - Acute valvular regurgitation or acute VSD (p34)
  - Drug overdose (cardiac depressants, see p792)
  - Myocarditis
- Hypovolaemia
  - Haemorrhage [GI tract (p608), aortic dissection or leaking AAA, post trauma (splenic rupture)]
  - Fluid losses (diarrhoea, vomiting, polyuria, or burns)
  - â€˜3rd spaceâ€™ fluid losses [acute pancreatitis (p670), ascites]
  - Adrenal failure (p584)
- Systemic vasodilatation
  - Sepsis (p266)
  - Liver failure (p658)
  - Drug overdose (calcium antagonists or other vasodilators, drugs causing multi-organ failure, e.g. paracetamol, paraquat)
  - Adrenal failure (may be both hypovolaemic and vasodilated)

- Anaphylaxis
    - Recent drug therapy
    - Food allergy (e.g. peanut)
    - Insect stings (p862)
- Obstruction
    - Cardiac tamponade (p184)
    - Pulmonary embolus (p146)
    - Tension pneumothorax (p242)

Shock: assessment

If the BP is unrecordable then call the cardiac arrest team . Begin basic life support (Airway, Breathing, and Circulation) and establish venous access.

If the cause of hypotension is not obvious, perform a rapid clinical examination looking specifically for the following.

- Check the airway is unobstructed physically and clear of vomit or blood. Give high-flow (60â€“100%) oxygen by mask (Â± reservoir bag) or ET tube if airway unprotected or breathing inadequate. Check both lungs are being ventilated (?tension pneumothorax).
- Note the respiratory rate (usually increased in acidaemia, pneumothorax, embolus, and cardiac failure, except at end stage).
- Check the cardiac rhythm and treat if abnormal (see pp62 â€“p106).
- Is the JVP elevated (see table)?
- Is the BP the same in both arms (thoracic aortic

dissection)?

- Are there any unusual cardiac murmurs? (Acute valvular lesion, flow murmurs may be heard in vasodilated patients.)
- Is the patient cold and clammy? This suggests cardiac pump failure or hypovolaemia; however patients with severe sepsis shock may also be peripherally shut down. Check for fever (NB: temperature may be sub-normal, especially in the elderly and children) and palpate the forearms (bounding pulses of proximal arterial vasodilatation).
- Is the patient warm and systemically vasodilated (feel finger pulp and feet). Palpate the forearm muscles for bounding pulses.
- Examine the abdomen. Is there a fullness or pulsatile mass in the abdomen (ruptured aneurysm)? Is there evidence of an acute abdomen (aneurysm, pancreatitis, perforated viscus)?
- Is the patient clinically dehydrated or hypovolaemic (skin turgor, mucous membranes, postural fall in BP)?
- Is there evidence of haematemesis (blood around mouth) or melaena (PR examination)?
- Is there any evidence of urticaria such as wheezing, soft tissue swelling (e.g. eyelids or lips) suggestive of anaphylaxis?
- Is conscious level impaired?

Investigations

â€¢ ECG
Acute MI , arrhythmias, PE (right heart strain with S1, Q3, T3)
â€¢ CXR
Pneumothorax, PE , dissection, tamponade, pleural effusion
â€¢ Blood tests

U&Es (renal impairment, adrenal failure), *FBC* (haemorrhage, â†‘ or â†“WBC in sepsis, â†“ platelets in liver disease and sepsis), *glucose* , *clotting studies* (liver disease, DIC), *LFTs* , *X-match*
â€¢ ABGs
Acidaemia (renal, lactic, ketoacidosis)
â€¢ Septic screen
Culture blood, urine, sputum
â€¢ Misc.
Where appropriate consider arterial blood lactate, Echo (suspected tamponade, dissection, valve dysfunction), LP , USS or CT abdomen Â± head

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Causes of hypotension with a raised CVP

- Pulmonary embolus (p146)
- Cardiac tamponade (p184)
- Cardiogenic shock (p44)
- Fluid overload in shocked vasodilated patients
- Right ventricular infarction (p28)
- Tension pneumothorax (p242)

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Shock: management

General measures

- Check the airway and give high-flow oxygen (60â€“100%) by face mask to optimize O_2 saturation. If conscious level is impaired (GCS <8), airway is unprotected, and/or breathing is inadequate, consider intubation.

- Lie the patient flat and raise the feet to try to restore BP.
- Insert 2 large-bore intravenous cannulae and commence infusion of colloid (e.g. HaemaccelÂ®) or blood. In most cases of shock, including cardiac causes, it is usually beneficial and safe to give colloid (200ml over 5â€“10 minutes) while a more detailed assessment is being carried out. If the fluid challenge brings improvement, consideration should be given to more challenges.
- Send blood for U&Es, glucose, FBC, X-match and blood cultures.
- Insert central venous line to monitor CVP, and for inotrope infusions if necessary. Insert arterial line for more accurate assessment of BP. Catheterize the bladder to monitor urine output.
- Titrate fluid replacement according to BP, CVP, and urine output. Over-enthusiastic fluid administration in patients with cardiac pump failure will precipitate pulmonary oedema with little gain or fall in stroke volume or cardiac output (see p282).
- Persistent hypotension in spite of adequate filling is an indication for inotropic support. The choice of first-line agent varies to some extent depending upon the underlying diagnosis.
- Treat the underlying condition and *enlist specialist help early* .
- Ensure someone takes time to talk to the relatives to explain the patient is seriously ill and may die. Discuss resuscitation status.

Cardiogenic shock (cardiac pump failure)

- Correct any cardiac arrhythmias and U&E imbalance.

- Optimize filling, guided by physical signs and response in stroke volume and filling pressures to fluid challenges.
- Possible concurrent hypovolaemia? iv fluids are the initial treatment. Give colloid challenges (100â€“200ml) and assess response.
- Adequate filling? If blood pressure allows, start a nitrate infusion (e.g. GTN 5mg/h). If very hypotensive, start an iv inotrope infusion. Commence epinephrine(adrenaline) (1â€“10Âµg/min) or dobutamine (5â€“20Âµg/kg/min), titrating the dose according to response (see p290 for details).
- A small amount of diamorphine (e.g. 2.5mg) is beneficial as it vasodilates, reduces anxiety, and lowers metabolic rate.
- Non-invasive or invasive ventilation should be considered in patients with severe heart failure as this decreases the work of breathing and provides beneficial effects on both left ventricular afterload and preload.
- If there is a potentially reversible cause for cardiogenic shock, consider intra-aortic balloon counterpulsation (p898).

Hypovolaemic shock

- Fluid replacement is the mainstay. There is no clear evidence to favour either colloids or crystalloids and in practice a mixture is used. Give blood to maintain Hb â‰¥8g/dl.
- Na^+ and K^+ abnormalities should be treated in the usual way. The metabolic acidosis usually responds to fluid replacement only.
- If the patient remains hypotensive in spite of fluids, consider other pathology (sepsis, tamponade, tension

pneumothorax, etc.). A reperfusion injury may occasionally manifest itself as a hypotensive, vasodilated circulation. If fluid replete, commence inotropes: adrenaline or dobutamine if a low cardiac output state is suspected, or norepinephrine if there is a high output, vasodilated circulation.

- If oliguria persists inspite of adequate resuscitation, frusemide (10â€“20mg iv) may be tried. The only aim here is to maintain a urine output as this makes fluid management much easier.

Practice point

- In one major study involving ~7000 patients, saline was equally effective as albumin for fluid resuscitation (Finfer *et al.* , *NEJM* , 2004, 350, 2294â€“6, SAFE Study).

Anaphylaxis

Atopic individuals are particularly at risk, but it may be a feature in some patients without any past history. Precipitants include

- Insect bites (especially wasp and bee stings, see p862)
- Foods and food additives (e.g. peanuts, fish, eggs)
- Drugs and intravenous infusions (blood products and intravenous immunoglobulin, vaccines, antibiotics, aspirin and other NSAIDs, iron injections, heparin).

Presentation

Cutaneous features include skin redness, urticaria, conjunctival injection, angioedema, and rhinitis. More severe manifestations

include laryngeal obstruction (choking sensation, cough, stridor), bronchospasm, tachycardia, hypotension, and shock.

Management

- *Secure the airway* : if respiratory obstruction is imminent, intubate, and ventilate or consider emergency cricothyroidotomy (see p914). A 14G needle and insufflation with 100% O_2 can temporize until the anaesthetist arrives.
- *Give 100% oxygen* : if there is refractory hypoxaemia, intubate, and ventilate.
- Lie the patient flat with head-down tilt if hypotensive.
- *Give intramuscular epinephrine 0.5â€“1mg* (0.5â€“1ml of 1 in 1000 adrenaline injection) and repeat every 10 minutes according to BP and pulse. Administer this *before* searching for intravenous access so as not to waste time.
- *If iv access is present, use small iv doses of epinephrine (0.1â€“0.2mg) then review response* . Subcutaneous epinephrine should not be given in anaphylactic shock due to variable absorption.
- Establish venous access and start iv fluids (colloid if hypotensive). Persistent hypotension requires a continuous epinephrine infusion titrated to a BP response.
- Give iv hydrocortisone 100â€“200mg and chlorpheniramine 10mg.
- Continue H_1 -antagonist (e.g. chlorpheniramine 4mg q4 â€“ 6h) for at least 24 â€“ 48 hours longer if urticaria and pruritis persist.
- Add an H_2 -antagonist (ranitidine 50mg iv tds).
- If the bronchospasm does not subside, treat as severe asthma (including salbutamol, nebulized or intratracheal epinephrine, aminophylline).

Angioneurotic oedema (C1-esterase inhibitor deficiency)

See p768 .

Shock with systemic vasodilatation 1

Patients should be monitored in either an ICU or HDU. Ideally, both an arterial line for continuous BP monitoring and intermittent blood sampling and a monitor for measuring cardiac output [e.g. oesophageal Doppler, pulmonary artery (Swanâ€“Ganz) catheter] should be used. A central venous catheter alone is often not adequate to monitor these patients.

Recent studies have cast doubt on the use of PA catheter monitoring of ICU patients and prospective trials are on-going. Whilst PA lines may be associated with increased mortality, the case against their use is not yet proven; if used diligently, with removal as soon as their usefulness has expired, we believe that central monitoring of haemodynamics can be useful in the management of such critically ill patients.

Oesophageal Doppler monitoring is a minimally invasive haemodynamic assessment tool, which provides the ability for on-going real-time haemodynamic assessment of the critically ill or compromised patient. This simple-to-use technology requires that a probe be inserted into the oesophagus to obtain measurement of blood flow in the descending aorta. Haemodynamic variables such as cardiac output, preload, afterload, and contractility are measured or derived from the oesophageal Doppler monitoring waveform.

Aims of management

- Correction of underlying cause

- Optimize organ perfusion
- Optimize oxygen delivery to tissues.

There have been several new developments over recent years that are believed to improve outcome in such patients:

- Early goal directed therapy (<6 hours) to obtain a CVP of 8â€“12mmHg, a MAP of >65mmHg, a urine output of >0.5ml/kg/h, and a central venous O_2 saturation ($ScvO_2$) >70%. This entails using more iv fluids and more inotropes early in critical illness; in one study it has been shown to decrease mortality from 47% to 31%.
- Intravenous hydrocortisone Many physicians are nervous about giving steroids to patients with septic shock. However, relative adrenal insufficiency occurs in 50â€“75% of such patients. One multi-centre study found that iv hydrocortisone (200mg/day) together with fludrocortisone (50Âµg/day) decreased mortality from 63% to 53% in patients with established refractory shock. The benefit was seen in non-responders to an ACTH stimulation (Synacthen) test.
- Activated protein C Severe sepsis is associated with a decrease in activated protein C (aPC). A recombinant aPC that has anti-inflammatory, anti-coagulant (including inactivation of factor V and VIIIA), and profibrinolytic properties, can be given with some outcome benefit.In one study, aPC (Drotrecogin Î±) decreased mortality from 31% to 25%, but doubled the risk of major bleeding from 1% to 2%.
- Low tidal volumes in ARDS Patients with ARDS were traditionally ventilated to a tidal volume of 10â€“15ml/kg ideal body weight. However, studies have shown that decreasing the tidal volume to 6â€“8ml/kg/ideal body weight results in a decrease in mortality from 40% to 31%.

Shock with systemic vasodilatation 2

It is important in the management of such critically ill patients *not* to lose sight of the needs of the patient. It is easy in an ICU setting not to examine patients but to look at charts. Always examine the patient at least twice a day and determine whether the clinical parameters match those on the ICU chart.

Ask yourself twice a day

- Fluid requirements (what is the fluid balance, is the patient clinically dry or oedematous?)
- Is the circulation adequate? Note the BP (and MAP), filling pressures, and cardiac output. Examine the peripheries (are they cool and shut down, or warm). Is the urine output satisfactory? Is there a marked swing on the arterial trace, which can suggest hypovolaemia? Is there a developing metabolic acidosis, which may indicate tissue hypoperfusion?
- Is gas exchange satisfactory? Watch closely for developing ARDS (p230). Examine the chest daily for deterioration that may be masked (on ABG) by adjustments of mechanical ventilation and do a CXR as appropriate.
- Are there signs of sepsis? Is there any new focus of infection?
- What do the tests show (U&Es, LFTs, Ca^{2+} , PO_4^{3-} , Mg^{2+} , CRP, cultures (blood, urine, sputum, line tips, etc.)?
- Is the patient receiving adequate nutrition (TPN or enteral)? Always give enteral nutrition if possible. Even enteral nutrition at 10ml/h will benefit the gut mucosa. Give with TPN if gut function is in doubt.

Optimizing oxygen delivery to tissues and oxygen consumption

- Aim for a MAP of at least 55â€“60mmHg. Such a pressure is usually required for good renal function. If the patient remains oliguric, especially in previously hypertensive patients, then consider raising the MAP by 10â€“20mmHg using vasopressor agents or inotropes (see below).
- Vasopressor and inotropic agents: if cardiac output is low, epinephrine (adrenaline) or dobutamine should be used, and if the patient is hypotensive with a high cardiac output (i.e. SVR is low), then norepinephrine (noradrenaline) should be used (this has relatively little inotropic effect). Alternatives that are favored in liver disease include terlipressin given as a bolus iv at 0.5mg, repeated every 30 minutes to a maximum of 2mg. Higher doses result in a much higher incidence of digital ischaemia.
- Note the effects any manoeuvre has on systemic haemodynamics and oxygen metabolism: e.g. infusion of noradrenaline may improve BP, but decrease oxygen extraction; increasing the PEEP on the ventilator may decrease cardiac output.
- Fluid replacement: expanding the circulation will often increase the cardiac output, but excessive fluid loading in the presence of â€˜leakyâ€™ pulmonary capillaries carries the potential risk of deterioration of gas exchange. If the patient is anaemic, use blood. Aim for a haemoglobin of â‰¥7g/dl, though possibly higher in patients with cardiorespiraotry compromise.

Sepsis syndrome and septic shock

Definitions

Bacteraemia
Positive blood cultures.
Sepsis
Evidence of infection *plus* systemic inflammatory response such as pyrexia or tachycardia.
Sepsis syndrome
Systemic response to infection *plus* evidence of organ dysfunction: confusion, hypoxia, oliguria, metabolic acidosis.
Septic shock
Sepsis syndrome *plus* hypotension refractory to volume replacement.

Presentation

General symptoms. Sweats, chills, or rigors. Breathlessness. Headache. Confusion in 10â€“30% of patients, especially the elderly. Nausea, vomiting, or diarrhoea may occur.

Examination. Hypotension (systolic BP <90mmHg or a 40mmHg fall from baseline), tachycardia, with peripheral vasodilatation (warm peripheries, bounding peripheral pulse, bounding pulses in forearm muscles) are the hallmarks of septic shock, but patients do become shut down eventually. SVR is reduced and cardiac output is increased initially but severe myocardial depression may occur. Other features include fever >38 Â°C or hypothermia <35.6Â°C (immunocompromised or elderly patients may not be able to mount a febrile response), tachypnoea and hypoxia, metabolic acidosis, oliguria. Focal physical signs may help to localize the site of infection.

Investigations

Blood tests
Blood cultures, U&Es , blood sugar, FBC , coagulation studies, LFTs, CRP , group and save serum, lactate, ABGs. Amylase, CK

and acute phase titres or antigen tests if appropriate.

Culture

Blood, sputum, urine, line-tips, wound swabs, throat swab, drain fluid, stool, CSF (as indicated).

Imaging

CXR , USS or CT brain, chest, abdomen, and pelvis for collections. Echo if endocarditis suspected.

Prognosis

The incidence of bacteraemia is 7/1000 admissions to hospital. Of these 20% develop septic shock and approximately 50% of these die.

Bacteraemia
15â€“20%
Bacteraemia plus shock
30â€“40%
Shock plus ARDS
40â€“60%

Mortality

Poor prognostic features in sepsis syndrome

- Age >60
- Multi-organ failure
- Renal failure
- Respiratory failure (ARDS)
- Hepatic failure
- Hypothermia or leukopenia
- Hospital-acquired infection

- Disseminated intravascular coagulation
- Underlying disease (e.g. immunocompromised, poor nutritional status, malignancy)

Sepsis syndrome: management 1

Patients with established shock require adequate haemodynamic monitoring and high-dependency facilities. The treatment is mainly supportive, trying to optimize blood pressure and tissue oxygenation and preserve vital organ perfusion until the infection is overcome by antibiotics and host defences. Successful management requires close liaison between several different teams (intensivists, physicians, surgeons, microbiologists, etc.).

Resuscitation

- Check the airway is clear. Give high-flow oxygen: if there is refractory hypoxia, intubate and ventilate. Treat respiratory failure (p224).
- Insert a large-bore peripheral venous cannula to begin fluid resuscitation. Insert central line and arterial line. Consider cardiac output measurement.
- Volume replacement is essential, and blood if haemoglobin is <7â€“10g/dl. Optimize filling pressures, watching gas exchange closely; worsening may suggest excess leakage from pulmonary capillaries. If this occurs, consider use of vasoconstricting inotropes (e.g. epinephrine, norepinephrine) if required to improve the circulation.
- Aim to keep mean arterial pressure >55â€“60mmHg. If cardiac output is low, epinephrine should be used and if cardiac output is high (and SVR low), then norepinephrine should be used. Suggested starting doses are

- Norepinephrine (noradrenaline) 1â€“12mg/min.
- Epinephrine (adrenalin) 1â€“12mg/min.

Alternatives include

- Terlipressin 0.5mg iv every 2â€“4 hours to a maximum of 2mg, though monitor closely for digital ischaemia and worsening acidosis (dobutamine may exacerbate vasodilatation in septic shock (or decompensated liver disease) and is generally best avoided.

Optimize haemodynamics and oxygen delivery

Conventional management involves trying to â€˜normalizeâ€™ the haemodynamic parameters (see below). However, it has been argued that in the setting of sepsis, as the oxygen extraction and utilization by the tissues are impaired, one should aim for â€˜supra-normalâ€™ circulation to try to improve oxygen delivery.

	Normal range	â€˜Idealâ€™ in sepsis
Cardiac index (L/min/m^2)	2.8â€“3.6	>4.5
SVR index (dynes/S/cm^5)	1760â€“2600	>1460
Oxygen delivery (*D* O_2 ml/min)	520â€“720	>800
Oxygen consumption (*V* O_2 ml/min)	110â€“140	>170

See p280 for formulae for haemodynamic calculations

Sepsis syndrome: management 2

Antibiotics

Antibiotic choice is dictated by the suspected site of infection and probable microbe, host factors such as age, immunosuppression, and hospitalization, and local antibiotic-resistance patterns. A suggested empiric regimen in patients with sepsis syndrome *and* the following source of infection is as follows:

Pneumonia
Community-acquired
Co-amoxiclav or Cefotaxime + clarithromycin
Hospital-acquired
Ceftazidime alone or Piperacillin + gentamicin NB: if *Staph. aureus* suspected, use teicoplanin or vancomycin (if MRSA), flucloxacillin (if MSSA)
Intra-abdominal sepsis
Cefotaxime + metronidazole or Piptazobactam Â± gentamicin
Biliary tract
Piptazobactam Â± gentamicin
Urinary tract
Community-acquired
Co-amoxiclav or cefotaxime
Hospital-acquired
Ceftazidime or Piptazobactam Â± gentamicin
Skin and soft tissue
Co-amoxiclav or Amoxycillin + flucloxacillin
Sore throat
Benzylpenicillin
Multiple organisms (anaerobes, *E. coli, Strep* .)
Vancomycin+ gentamicin + metronidazole or Clindamycin Â± gentamicin

Meningitis
Cefotaxime or (if pen. and cef. allergic) Vancomycin Â± rifampicin
Many now suggest chloramphenicol

NB: consult your microbiologists for local antibiotic policy.

Removal of infective foci

It is essential to identify and drain focal sites, e.g. obstructed urinary tract or biliary tree, drain abscesses, and resect dead tissue.

Causes of treatment failure

- Resistant or unusual infecting organism
- Undrained abscess
- Inflammatory response (raised CRP, raised WCC) may persist despite adequate anti-microbial therapy
- Advanced disease.

Toxic shock syndrome

- Distinct clinical illness caused by toxin-producing Gram-positive bacteria, usually staphylococci or streptococci.
- Infection is often localized and illness is manifest by the toxins.
- 85% of cases are female.
- Association with menstruation in females Â± the use of tampons.
- May occur with any focal infections due to a toxin-producing strain, including postoperative wound infections.

Clinical features

- Fever: >38.9Â°C
- Rash: diffuse macular (seen in â‰¥95%), mucous membrane involvement common. Desquamation 1â€“2 weeks later, palms and soles (consider drug reaction in differential diagnosis)
- Hypotension: systolic <90mmHg, or postural hypotension
- Diarrhoea frequent
- DIC and petechial rash
- Multi-organ failure may follow.

Laboratory findings

- Normochromic normocytic anaemia (50%) and leukocytosis (>80%)
- Renal/hepatic failure (20â€“30%)
- Elevated CPK is very common
- DIC
- Pyuria
- CSF pleiocytosis (sterile)
- Blood cultures rarely positive
- Vaginal swabs, throat swab, and wound swabs
- Toxin-producing *Staph. aureus* in 98% of menses-associated cases.

Therapy

- Limit toxin production/release
- Drain any focal collections and remove foreign bodies
- Anti-staphylococcal antibiotics (high-dose flucloxacillin or teicoplanin iv)
- Supportive care as for any patient with shock.

Lactic acidosis

Lactic acidosis is a metabolic acidosis due to excess production or reduced metabolism of lactic acid. It may be divided into two types, *type A* (due to tissue hypoxia) and *type B* (non-hypoxic).

Presentation

Patients are usually critically ill. Clinical features include

- Shock (often BP <80/40)
- Kussmaul respiration
- Tachypnoea
- Deteriorating conscious level
- Multi-organ failure including hepatic, cardiac, and renal failure
- Clinical signs of poor tissue perfusion (cold, cyanotic peripheries).

Investigations

- ABGs (pH <7.34, severe if pH <7.2)
- Serum electrolytes including bicarbonate and chloride to calculate anion gap, if lactate unavailable. Raised anion gap

>16mmol/L [anion gap = (Na^+ + K^+)-(Bicarbonate + chloride)]

- FBC (anaemia, neutrophilia)
- Blood glucose
- Blood lactate level >5mmol/L (use a fluoride tube)
- Screen for sepsis (blood cultures, CRP, MSU, etc.)
- Spot urine (50ml) for drug screen if cause unknown
- CXR looking for consolidation or signs of ARDS.

Assessment of severity

Severity is assessed by the blood lactate concentration and the degree of acidaemia. This may be confounded by the presence of acute renal failure. In the early stages, the arterial pH may be normal or even raised as elevated lactate levels in the CNS cause hyperventilation with a compensatory respiratory alkalosis. The best predictor of survival is the arterial pH. Patients presenting with a lactate of greater than 5mmol/L and a pH <7.35 have a mortality >50%.

Management

The principle of management is diagnosis and treatment of the cause, and amelioration of the underlying pathophysiology. All patients should be managed in a higher dependency area.

- Sepsis. Start broad-spectrum antibiotics (e.g. cefotaxime plus metronidazole, or amoxycillin, gentamicin, and metronidazole).
- Diabetic lactic acidosis. Insulin and fluids as appropriate (see p556).
- Shock. Consider invasive haemodynamic monitoring. Treat as on p262 .

- Renal failure. Treat by continuous haemofiltration. These patients are usually too unstable to tolerate haemodialysis. If haemodialysis is used, it is now conventional to use bicarbonate dialysis.
- Methanol. Infuse ethanol (competitive metabolism, see p824).
- Acidaemia. The role of bicarbonate is controversial as it may lower CSF pH and alter the oxygen dissociation curve unfavourably. There is no benefit of bicarbonate over equimolar saline in controlled trials.

Causes of lactic acidosis

Tissue hypoperfusion (shock)â€
Sepsis
Severe anaemia
Renal/hepatic failure
Severe hypoxia (same as â€)
Diabetes mellitus (uncontrolled)
Catecholamine excess (e.g. phaeocromocytoma or exogenous)
Malignancy (leukaemia, lymphoma)
Acute pancreatitis
Severe exercise
Paracetamol (acetaminophen) overdose
Drug-induced
(metformin, methanol, ethanol, salicylates, and cyanide)
Rare causes
Heriditary enzyme defects such as Glucose-6-phosphatase and fructose 1,6 diphosphatase deficiency

Type A Type B

Haemodynamic calculations

In general most systems these days calculate all the parameters that you require, and the formulae below should not be necessary. It is important to distinguish between indexed (modified for body surface area) and non-indexed values. Indexed values are signified by the letter I. Thus cardiac output (CO) becomes CI and systemic vascular resistance (SVR) becomes SVRI.

Mean arterial pressure (MAP)
MAP = Diastolic pressure + 1/3 (Systolic - Diastolic pressure)
e.g. BP 120/60 = MAP of 60 + 1/3 (120 - 60) = 80mmHg
R. atrial pressure
NR
1â€“7mmHg
R. ventr. systolic pressure
NR
15â€“25mmHg
R. ventr. diastolic pressure
NR
1â€“7mmHg
PA systolic pressure
NR
20â€“25mmHg
PA diastolic pressure
NR
3â€“12mmHg
Mean PA pressure
NR
9â€“16mmHg
Pulmonary artery wedge pressure
NR
3â€“12mmHg

The PAWP is increased in mitral regurgitation, and it may be difficult or impossible to obtain a typical â€˜wedgedâ€™ tracing.

Cardiac output (CO)

NR

4.0â€“6.2 L/min

Cardiac index (CI)

$$CI = \frac{\text{Cardiac output}}{\text{Body surface area}}$$

NR

2.8â€“3.6 L/min/m^2

Systemic vascular resistance (SVR) and SVRI

$$SVR = \frac{(MAP - RAP) \times 80}{CO}$$

NR

800â€“1500dyne/S/cm^5

$$SVRI = \frac{(MAP - RAP) \times 80}{CI}$$

NR

1760â€“2600dyne/S/cm^5 /m^2

Pulmonary vascular resistance (PVR)

$$PVR = \frac{(\text{Mean PA} - PAWP)}{CO}$$

NR

20â€“120dyne/S/cm^5

O_2 delivery

D O_2 = CO Ã— CaO_2

NR

900â€“1000ml/min

O_2 consumption:

V O_2 = (Ca O_2 -CvO_2) Ã— CO

NR

230â€“250 L/min

C aO_2 = oxygen content of arterial blood (measured by haemoglobinometer or derived from arterial gases)

C vO_2 = oxygen content of mixed venous blood (obtained from PA distal line)

Oxygen content = Hb (g/L) Ã— 1.34 Ã— oxygen sat.

Oxygen extraction ratio (OER)
OER = $V\ O_2\ /D\ O_2$
NR
0.22â€“0.3 (22â€“30%)

P.281

P.282

Appendices

Appendix 1: Understanding circulatory failure

Intelligent manipulation of the filling pressures and inotropic support of a patient with shock or heart failure requires a basic understanding of the way in which the left and right ventricles respond to changes in filling pressure and what effect different clinical conditions have on their function. The following is a somewhat simplified approach.

The stroke volumes of the right and left ventricles are identical but as the resistance of the pulmonary bed is much lower than that of the systemic bed, the right ventricle is able to do this at a lower filling pressure than the left ventricle. Raising the right atrial pressure with iv fluids will increase the stroke volume of the right ventricle. The left atrial pressure (and thus the LVEDP) will rise, keeping the stroke volume of both sides of the heart matched.

Sepsis, acidosis, â†‘K^+ , â†“Ca^{2+} , â†“Na^+ , MI or ischaemia, and certain drugs (e.g. Î²-blockers) are known to impair myocardial function. Inotropes will improve cardiac function.

Expanding the circulation with iv fluids becomes progressively less effective in increasing the stroke volume (and so cardiac output) as the function become more depressed, i.e. the increase in stroke volume per unit transfused becomes progressively less. Furthermore it increases the risks of

precipitating pulmonary oedema (see below).

Pulmonary oedema occurs when the hydrostatic pressure within the capillary overcomes the plasma oncotic pressure (the major determinant of which is the serum proteins and albumin). The critical PCWP for hydrostatic pulmonary oedema is approx. = *serum albumin (g/L)* Ã— *0.57* (i.e. with an albumin of 40g/L, critical PCWP = 22mmHg. The lungs will of course get â€˜stifferâ€™ as the PCWP rises and the patient may get breathless before this pressure is reached.

Thus, even in normal patients, continued iv transfusion will eventually raise the right- and left-sided filling pressures sufficiently to precipitate pulmonary oedema.

Circulation in sepsis

Sepsis produces a systemic inflammatory response that results in â€˜leakyâ€™ capillaries, in the lungs and elsewhere, as well as hypoalbuminaemia from a combination of impaired production and loss into extravascular spaces. Thus patients are at risk of pulmonary oedema at lower values of PCWP. Furthermore, the cardiac function is depressed so that iv fluids will produce less increase in stroke volume and cardiac output. It is more prudent to support the circulation with vasoconstricting inotropes (e.g. adrenaline) than fluids alone, remembering that when the capillaries are no longer leaky, the fluid deficit masked by adrenaline will need to be replaced as the adrenaline is turned down.

Appendix 2: inotrope support

Inotropes

General points

- Ensure all patients given inotropes have an adequate intravascular volume (CVP or Swan-Ganz catheter).
- The aim of inotropic support is to maximize tissue oxygenation (e.g. as assessed by plasma lactate and mixed venous oxygenation) and not cardiac output.
- The inotropes in widespread clinical use are catecholamines or their derivatives. Their haemodynamic effects are complex and reflect the relative importance of a and b adrenergic effects for each agent. They are summarized in the table below:

```
Isoprenaline
+++
-
+/-
+
Â±
Adrenaline
+
+
+
++
++
Dopamine
(low dose)
+
-
Â±
+
+
(high dose)
++
++
```

+ +
+ +
Â±
Dobutamine
+ +
-/+
+ +
+ +
Noradrenaline
-
+ +
+ +
-/+
-/+
Abbreviations : HR , heart rate; SVR , systemic vascular resistance; MAP , mean arterial pressure; CO , cardiac output; CP, coronary perfusion; +, increase; -, decrease; Â±, no change.

HR SVR MAP CO CP

Isoprenaline

Pharmacology

Isoprenaline is a synthetic Î²-adrenoceptor agonist ($Î²_1$ & $Î²_2$) with no activity on a-receptors. It is a bronchodilator, acts as a cardiac stimulant in heart block by stimulating the sino-atrial node, increasing conduction velocity and shortening the refractory period of the AV node. It has a positive inotropic effect. It also acts on skeletal muscle and blood vessels. It has a plasma half life of 5 minutes.

Drug interaction

- Tricyclic antidepressants enhance the effects

- Beta-blockers anatgonise the effects
- Sympathomimetic amines may produce an additive effect
- Anaesthetic gases sesnsitize the myocardium an may trigger arrhythmias
- Digoxin â€“ increased risk of tachyarrhythmias

Inotrope
Formulation
Volume to add to 500ml 5% Dextrose
Starting infusion rate
Maintenance dose
Adrenaline
1:1000 soln
2ml (2mg)
15ml/h (1Âµg/min)
15â€“180ml/h (1â€“12Âµg/min)
Dopamine
40mg/ml
20ml (800mg)
6ml/h (2.25Âµg/kg/min)
â€œRenalâ€• dose 25â€“13ml/h (1â€“5Âµg/kg/min)
â€œCardiacâ€• dose 13â€“26 ml/h (5â€“10 Âµg/kg/min)
Dobutamine
12.5mg/ml
40ml (500mg)
10 ml/h (2.5Âµg/kg/min)
10â€“60ml/h (2.5â€“15Âµg/kg/min)
Noradrenaline
2mg/ml
2ml (4mg)
15ml/hr (2Âµg/min)
7.5â€“90ml/h (1â€“12Âµg/min)
Isoprenaline
1mg/ml

5ml	(5mg)
3ml/h	(0.5Âµg/min)
3â€“60ml/h	(0.5â€“10Âµg/min)

Preparation of inotrope infusions for a typical 70kg patient

Adrenaline

Pharmacology

- Adrenaline is a $\hat{I}^2_2$ selective agonist (10-fold over $\hat{I}^2_1$) but makes little distinction between $\hat{I}\pm_1$ and $\hat{I}\pm_2$ receptors.
- It has generally little effect on MAP except in the presence of a non-selective $\hat{I}^2$-blocker, when the loss of $\hat{I}^2_2$ -mediated vasodilatation: converts adrenaline into an extremely potent pressor agent ($\hat{I}\pm_1$ selective blockers do not produce this effect).

Uses

- Anaphylactic shock angioedema and acute allergic reactions
- The use of adrenaline as an inotrope is largely restricted to septic shock were it may have advantages over dobutamine (see p688). It causes, however, a marked reduction in renal blood flow (up to 40%) and should only be used with a renal dose of dopamine.
- Cardiac arrest
- Open angle glaucoma
- Adjunctive with local anaestheic agents

Doses

- 0.2â€“1mg im for acute alleric reactions and anaphylaxis, respectively
- 1mg (10ml of 1:10,000, or 1ml of 1:1000) for cardiac arrest
- In shock infuse doses of 1â€“10Âµg/min.

Pharmacokinetics

It is extensively metabolized with 50% protein binding and a $t_{1/2}$ of 3 minutes, being metabolized by the liver and neuronal tissue.

Side-effects

- Cardiac arrhythmias
- Cerebral haemorrhage (overdose)
- Pulmonary oedema (overdose)
- Local ischaemic necrosis
- Anxiety, dyspnoea, palpitations, tremors, weakness, cold extremities

Drug interactions

- Tricylclic antidepressants
- Anaesthetic agents
- b-blockers
- Quinidine and dogoxin (cardiac dysrthmias more common)
- a-antagonists block the Î±-effects

Contraindications

- Hyperthyroidism
- Hypertension
- Ischaemic heart disease
- Closed angle glaucoma

Dopamine

Pharmacology

Dopamine acts on different receptors. At low doses D_1 and D_2 receptors are activated. D_1 receptors are found in vascular smooth muscle, and cause vasodilatation in the renal, mesenteric, cerebral, and coronary vascular beds. D_2 receptors are found on post ganglionic sympathetic nerve endings, and autonomic ganglia. At the next dose, $Î²_1$ receptors are activated with a postive chronotropic and inotropic effect, and at higher doses $Î±_1$ and $Î±_2$ receptors are also activated, which inhibit renal vasodilatation.

Uses

To increase renal blood flow in patients with impaired renal perfusion, usually in the setting of multi-organ failure. There is little evidence that dopamine affects clinical outcome.

Dosing

Dopamine at low infusion rates (0.5â€“2Âµg/kg/min) selectively vasodilates the renal (and mesenteric) vascular beds, increasing renal blood flow and GFR. At higher rates (2â€“5Âµg/kg/min) there is activation of $Î²_1$ and Î± receptors,

and subsequent decrease of renal blood flow.

Pharmacokinetics

Dopamine is rapidly distributed by active uptake into sympathetic nerves. The $t_{1/2}$ is 9 minutes with a V_d of 0.9 l/kg, but steady state is achieved within 10 minutes (i.e. more rapidly than predicted). It is metabolized by the liver.

Side-effects

- Cardiac arrhythmias rarely
- Hypertension if dosing too high
- Extravasation may cause skin necrosis. The antidote is infiltration of phentolamine in the ishaemic area
- Nausea, vomiting, headache, palpitations, and mydriasis
- Increased catabolism

Drug interactions

- Monoamine oxidase inhibitors
- Î±-blockers may exacerbate vasodilatation
- Î²-blockers may exacerbate hypertension
- Ergot alkaloids exacerbate peripheral vasoconstriction

Contraindications

- Phaeochromocytoma
- Tachyarrhythmias (untreated)

Dobutamine

Pharmacology

Dobutamine is an isoprenaline derivative acting on $\hat{I}^2_1$, $\hat{I}^2_2$, and $\hat{I}\pm_1$ receptors. It is used as a racemate with the d-isomer showing $\hat{I}^2_1$ (+$\hat{I}^2_2$) selectivity and the l-isomer $\hat{I}\pm_1$ selectivity. The $\hat{I}^2_2$ effects (vasodilation of mesenteric and skeletal muscle bed) and $\hat{I}\pm_1$ effects (vasoconstriction) tend to cancel each other out, so that it has little effect on bp unless high doses are used. It is less arrythmogenic than dopamine.

Uses

- Inotropic support for cardiac failure
- Inotropic support for septic shock and liver failure is controversial since it may cause vasodilatation.
- Pharmacological cardiac stress testing

Dosing

It is administered intravenously at a dose of 2.5â€“10 Âµg/kg/minute (rarely up to 40 Âµg/kg/min). The onset of action is within 2 minutes, with a peak effect at 10 minutes. In congestive cardiac failure it may increase PCWP, through an unknown mechanism.

Pharmacokinetics

The drug is extensively metabolized by the liver. It has a $t_{1/2}$ of 2.5 minutes, and V_d of 0.21/kg.

Side-effects

- Cardiac arrhthmias

- Myocardial ischaemia may occur if cardiac output increases
- Hypotension may be minimized by cocomitant use with dopamine at a dose to cause vasoconstriction. May occur in patients with sepsis or liver disease.
- Allergies are very rare
- Tissue necrosis at site of administration

Drug interactions

- Î±-antagonists may execerbate vasodilatation causing hypotension

Contraindications

- Low cardiac filling pressures
- Cardiac arrhythmias
- Cardiac tamponade
- Valvular heart disease (AS, ASTIP, MS, HOCM)
- Known hypersensitivity

Noradrenaline

Pharmacology

Noradrenaline has similar $\hat{I}\pm_1$ effects to adrenaline but it is slightly less potent on most $\hat{I}^2_1$ receptors, and has very little $\hat{I}^2_2$ activity. This lack of $\hat{I}^2_2$ -mediated vasodilatation makes it a much more potent pressor agent than adrenaline. It is sometimes employed in acute hypotension, but it has relatively little effect on cardiac output and the intense vasoconstriction

actually worsens tissue ischaemia (especially in kidney, skin, liver, and skeletal muscle).

If a noradrenaline infusion is used it should be never be stopped abruptly because of the risk of a sudden collapse of the bp.

Drug interactions

- Tricylic antidepressants (which block re-uptake into catecholamine nerve terminals) cause a 2â€“4-fold increase in sensitivity to adrenaline or noradrenaline infusions. MAO inhibitors (e.g. tranylcypromine and pargyline) markedly potentiate the effects of dopamine infusions which should be started at one-tenth the usual infusion rate, i.e. 0.2Âµg/kg/min.
- Dobutamine is *not* a substrate for MAO.

Milrinone

Milrinone is a potent inhibitor of phosphodiesterase (type III) and causes a concentration dependent increase in cellular cAMP. It acts as a positive inotrope and vasodilator, with little chronotropic activity. Its cardiac actions probably involve effects on calcium channels or fast entry sodium channels. The positive inotropic effects are enhanced by Î²-agonists. It has a $t_{1/2}$ of ~ 1h. It is used in the short term treatment of severe heart failure unresponsive to other therapy and acute heart failure following cardiac surgery.

Doses (for 70kg patient)

- Add 10mg to 40ml 5% dextrose (50ml final volume)
- Loading dose 17.5 ml (50Âµg/kg) over 10 minutes
- Maintenance dose 6â€“15ml/hr (0.3â€“0.8 Âµg/kg/min):

max 24mg/kg/day

Side-effects

- Hypotension and/or cardiovascular collapse in hypovolaemic patients

Enoximone

Enoximone is a potent inhibitor of phosphodiesterase (type IV) and causes a concentration dependent increase in cellular cAMP. It acts as a positive inotrope and vasodilator, with little chronotropic activity; these effects are not associated with increased myocardial oxygen consumption. It is over 20 times more potent than theophylline, and has a $t_{1/2}$ of ~ 1.5 hours. It is metabolised to an active metabolite which has 10% of potency and a half life of 15 hours. It is used in the treatment of congestive cardiac failure, and can be given either orally or intravenously.

Doses (for 70kg patient)

- Add 50mg to 40ml normal saline (50ml final volume)
- Loading dose 63ml (90Âµg/kg/min) over 10 minutes
- Infusion of 20â€“80ml/hr (5â€“20Âµg/kg/min): max. 24mg/kg/day

Side-effects

- Hypotension and/or cardiovascular collapse in hypovolaemic patients

Sodium bicarbonate

Pharmacology

Sodium bicarbonate is an important buffering mechanism *in vivo* . Its effects are short lived. The administration of sodium bicarbonate result in both a sodium load and generation of carbon dioxide. It causes intracellular acidosis, and is negatively inotropic, and for these reasons should be used cautiously. It may also produce a left shift in the oxygen dissociation curve, and decrease effective oxygen delivery. Mild acidosis also causes cerebral vasodilatation, and thus correction could compromise cerebral blood flow in those with cerebral oedema.

Uses

- Severe metabolic acidaemia (use in DKA is controversial)
- Severe hyperkalaemia
- Its use is best avoided in cardiac resuscitation, since adequate ventilataion and chest compression usually suffice.

Dosing

It is available as either an 8.4% solution (hypertonic, contains 1mmole HCO_3^{-2} /ml) or a 1.26 % solution (isotonic). It is usually administered as intermittent boluses of 50â€“100ml, and the effect on arterial pH and haemodynamics monitored. According to the UK Resuscitation Council Guidelines, the approximate dose of 8.4% solution required can be calculated as follows:-

$$\text{Dose in ml (mmoles)} = \frac{\text{Base excess} \times \text{Weight (kg)}}{3}$$

Thus a patient of 60kg with a base excess of -20, would require 400ml. of 8.4% bicarbonate to normalize the pH. This contains the equivalent of 400mmole of sodium. Our personal view is that this is too much, and one should try to correct the arterial pH to 7.0â€“7.1 by giving 50â€“100ml sodium bicarbonate followed by repeat arterial blood gases, and repeating the bicarbonate as necessary. This should buy enough time for more effective and safer measures to be employed to try to correct the underlying cause for the acidosis.

Side-effects

- Tissue extravasation causes severe necrosis. Give via a central line where possible.
- It precipitates in the line when given with calcium chloride, and can cause microemboli.

Drug interactions

- Precipitates with calcium salts

Contraindications

- Arterial pH >7.2

Editors: Ramrakha, Punit S.; Moore, Kevin P.
Title: *Oxford Handbook of Acute Medicine, 2nd Edition*

Chapter 4
Infectious diseases

Fever in a traveller 1

Assessment

- It is important to obtain a very accurate history of what countries what areas within those countries and the activities of the individu were there (i.e. visits to rural areas or urban travel only, camping hotels etc.) together with dates in relation to onset of illness, wha taken, and what were forgotten.
- Do not forget that although the patient has travelled they may hav infections such as pneumonia or pyelonephritis.

Initial investigations

See table .

Management

- The epidemiology and drug-resistance patterns of many tropical p constantly changing and expert advice can be easily obtained from infectious diseases unit. The telephone numbers of the schools of are given on p961 .

- *Patients should only be sent home if there is no evidence of seriou infection, they are afebrile, and a malaria film is negative. A single does not exclude malaria and the patient must be reviewed immed fever occurs* .
- *Isolation* . If there is a history of travel to rural West Africa (part Nigeria, Sierra Leone, Guinea, or Liberia) and the patient is febrile fever (p322). Discuss the case *immediately* with the regional infe unit. Only a malaria film and other immediately relevant blood tes performed after discussion with the on-site labs. Unless clearly suf haemorrhagic illness, the patient is kept on site until malaria has and then transferred to a supra-regional high-security infectious d capable of nursing patients with viral haemorrhagic fevers. If mala management can proceed as described on p354 . All other patients nursed in a side room until a diagnosis is established.
- Clinical *rabies* is rare in the UK but should be considered in travel encephalitis coming from a rabies-endemic area. A more common patients quite frequently present having suffered an animal bite w an endemic area. Post-bite prophylaxis can prevent rabies in virtu (see p328).
- *TB* should be considered when evaluating all patients, particularly subcontinent or Africa. TB is a frequent presenting illness in advar infection, especially in sub-Saharan African patients and may be (e.g. TB meningitis, miliary TB, abdominal TB). All patients with TB offered HIV testing. Consider drug-resistant TB especially if patien treated for TB or has been in prison in eastern Europe.

Investigations for febrile travellers

FBC
Look for anaemia (malaria, hookworm, malabsorption, leishmaniasis), (bacterial infections, amoebic liver abscess) or leucopoenia (malaria, fever, acute HIV seroconversion), eosinophilia (helminth/worm infecti thrombocytopenia (malaria, typhoid, dengue fever)
Blood films

Thin films should be examined by the haematologists for malaria. Thic be examined, but need expertise to interpret. Malaria antigen dipstick are now commercially available, quick, and require minimal training

U&Es

Renal failure may be seen with *P. falciparum* , viral haemorrhagic feve bacterial sepsis

LFTs

Jaundice and abnormal liver function are seen with hepatitis Aâ€“E, n leptospirosis, yellow fever, typhoid, liver abscesses, and many others

Clotting studies

Deranged with viral haemorrhagic fevers (p322), *P. falciparum* , bact hepatitis

Blood cultures

Mandatory for all febrile patients

Urinalysis

For blood and protein, and a specimen for culture

CXR

For pneumonia. Raised right hemidiaphragm in amoebic liver abscess

Other investigations to consider: serology (hepatitis Aâ€“E), CXR, Sputum MC&S

Fever in a traveller 2

Jaundice

Malaria, hepatitis Aâ€“E, leptospirosis, yellow fever, typhoid, liver abs

Splenomegaly

Malaria, leishmaniasis

Hepatosplenomegaly

Malaria, schistosomiasis, typhoid, brucellosis, leishmaniasis

Diarrhoea and vomiting

E. coli, Salmonella, Shigella, Campylobacter, Giardia, E. histolytica , *parahaemolyticus* , viral gastroenteritis

Skin lesions

Erythema nodosum (TB , leprosy, fungi, post-streptococcal infection)

Painful nodule with punctum (cutaneous myiasis, i.e. maggots) Derma
(onchocerciasis) Ulcers (syphilis, leprosy, leishmaniasis) Scabs, escha
anthrax) Erythema chronica migrans (Lyme disease)
Abdominal pain
With diarrhoea in dysentery, perforation of bowel (typhoid, dysentery)
Haematuria
Viral haemorrhagic fevers (p322), schistosomiasis, haemoglobinuria i
Meningism/confusion
Meningococcal and other bacterial meningitis, viral encephalitis
Bleeding tendency
Meningococcal septicaemia, haemorrhagic fevers, leptospirosis
RUQ pain, intercostal tenderness Â± R pleural effusion
Amoebic liver abscess
Pleural effusion
TB , liver abscess

Presenting feature Diagnosis to consider

P.299
P.300

Malaria: assessment

Malaria is a common cause of death from travel-acquired infection in t
this in all febrile patients returning from an endemic zone.

Organism

- *Plasmodium falciparum* is the causative agent of the most severe fatal or malignant form of malaria.
- *P. vivax, P. ovale* , and *P. malariae* may cause chronic, recurrent c not life-threatening.
- There are no reliable clinical guides to distinguish each type of in different species can be distinguished by their morphology on a blo may need expert interpretation. Malaria antigen blood dipstick tes differentiate reliably between *P. falciparum* and *P. vivax* . Mixed i occur. If in doubt therapy should be directed against *P. falciparum*

Symptoms

- Incubation period from 7 days minimum up to 1 year (but usually for *P. falciparum* , up to 2 years for *P. vivax* and *P. ovale* , up to 2 *malariae* .
- High fever, chills, and rigors followed by sweating. Alternate day f but many patients do not exhibit this.
- Headache is a very common symptom. If associated with impairme consciousness, behavioural change, or seizure activity, consider Cerebral malaria is defined as unrousable coma (GCS â‰¤ 9). Re haemorrhages, drowsiness, and other neurological signs may indic cerebral involvement, which may progress.
- Generalized flu-like symptoms, malaise, and myalgia.
- Abdominal symptoms: anorexia, pain, vomiting, and diarrhoea.

Examination

- No specific features
- Pyrexia in most, but not all cases, often up to 40Â°C during parox
- Splenomegaly
- Haemolytic jaundice.

Indicators of severity in P. falciparum m

- Neurological features (deep comas, seizures, decerebrate rigidity)
- Retinal haemorrhages
- Hypoglycaemia
- Parasitaemia >2%
- Schizonts on blood film

- Pulmonary oedema
- WCC >12 Ã— 10^9 /L
- Hb <7g/dl
- Coagulopathy (DIC)
- Renal failure (creatinine >250ÂµM)
- Lactic acidaemia (>6mmoYl)

P.301

P.302

Malaria: investigations

â€¢ FBC

Anaemia, non-immune haemolysis, leukopenia, and thrombo-cytopenia *falciparum* .

Blood films

Repeated blood samples over several hours should be examined by ar individual if the patient is unwell and malaria not found on the initial malaria antigen blood dipstick test for *P. falciparum* should also be pe as sensitive as a blood film read by an experienced microscopist and c speciation). If in doubt, treat for malaria and send the films to a refe for a definitive opinion. Thick films are more sensitive. Thin films ma easier and are used to calculate the parasitaemia.

Parasitaemia

Mild: <2% parasitaemia, temp. <39Â° C, and patient ambulant with severe: >2% parasitaemia or schizonts on film or complications.

G6PD status

Causes haemolysis in G6PD deficiency.

Glucose

Hypoglycaemia may occur with *P. falciparum* or iv quinine therapy, es pregnancy.

U&Es , LFTs

Acute renal failure and haemoglobinuria may occur in severe *P. falcipa* unconjugated bilirubin, AST , and LDH reflect haemolysis.

Blood cultures

Even if malaria is confirmed. Other infections such as a Gram-negativ may also be present.

Head CT scan and LP

May be required in suspected cerebral malaria to exclude other patho

ABG

Metabolic acidosis indicates severe malaria.

Malaria: management

General measures

- Admission is mandatory as rapid progression and death can occur
- Lower fever with tepid sponging and paracetamol.
- If severe malaria or cerebral malaria admit to HDU/ITU.
- Fits can be controlled with diazepam.
- In severe cases catheterize the bladder to monitor urine output and line to help manage fluid balance, as ARDS can easily be precipita patients. Renal support may be required.
- 2-hourly blood glucose estimations. Regular TPR, BP, urine output.
- Pre-treatment ECG required for iv quinine (causes QT prolongation
- In severe cases repeat blood films at least twice daily until paras falling and then perform daily. Daily U&Es, FBC, LFTs.
- Thrombocytopenia is usual and rarely needs support unless platelet 10^9 /L or bleeding.
- Discuss any severe or complicated malaria with ID unit early. *P. f* acquired on the Thai borders and in neighbouring countries may b resistant and need additional treatment with anti-malarials not g (e.g. parenteral artemether or artesunate).

Malaria: anti-malarial therapy[1]

P. falciparum

Uncomplicated, non-severe P. falciparum in

- Quinine orally, 600mg 8 hourly, reduced to 12 hourly if patient de cinchonism (nausea, tinnitus, deafness). For 5â€“7 days until afeb film negative *followed by* either a single dose of 3 tablets of Fansi (pyrimethamine and sulfadoxine) or, if FansidarÂ® resistant (parti East Africa) or FansidarÂ® allergic, give doxycycline 100mg bd for
- MalaroneÂ® (atovaquone/proguanil) and RiametÂ® (artemether/ have both been licensed for the treatment of non-severe *P. falcipa* for adults are MalaroneÂ®, 4 tablets once daily for 3 days; Riamet initially, followed by 5 further doses of 4 tablets each given at 8, 2 60 hours (total 24 tablets over 60 hours).

Complicated or severe P. falciparum in adult

- If parasitaemia >2% give quinine dihydrochloride iv 10mg/kg (max 250ml of normal saline over 4 hours. Repeat 12 hourly. Convert to above as soon as possible. (If severely ill or parasitaemia >5% m *first* dose of quinine dihydrochloride at 20mg/kg (max 1.4g) over 12 hourly by 10mg/kg. NB: use 10mg/kg first dose if recent mefl halofantrine, or RiametÂ® because of possible toxicity.) Quinine do 8 hourly, but need to watch carefully for toxicity (QT prolongation
- Mefloquine may also be effective but resistance is emerging and it contact a malaria expert for advice on the best regimenfor the cou
- Chloroquine resistance is now widespread and cannot be considere for *P. falciparum* in the UK.

Adjunctive therapy

- Steroids are not recommended for cerebral malaria.
- Exchange transfusion remains somewhat controversial but may be extreme parasitaemias (>10%). Seek specialist advice.
- Daily blood films until trophozoites cleared.
- Routine follow-up not indicated unless complications. Warn of smal and importance of repeating blood tests if further fever. Advise on prophylaxis.

Footnote

For advice in the UK phone London: 020 7387 9300 (treatment); 020 (travel prophylaxis). See BNF Section 5.4 for details of other centres.

P. vivax, P. ovale , and P. malariae

- Admission. If diagnosis secure and the patient is stable, admissio necessary, however many will require admission for short stay. G are as above.
- Acute therapy. Chloroquine remains the drug of choice with only resistance reported for *P. vivax* . Give chloroquine: 600mg (base) 300mg 6 hours later and 300mg daily for 2 days.
- Radical cure. Relapse due to persistent hepatic hypnozoite occurs and *P. ovale* . Primaquine given after course of chloroquine.
- Treatment is with primaquine 15mg daily for 14 days. Check G6PD giving primaquine as induces severe haemolysis in these patients,
- Patient advice. Avoid contact sports for 1 month because of the rupture.

Infections presenting with fever and rash

Rashes table: Features of the common ch exanthems

Varicella (chickpenpox)
Clear vesicles on erythematous base (5â€“12mm), evolving into pustu and crust
Lesions occur in crops, start on trunk and spread peripherally. Mucosa common
10â€“21 days
Pyrexia 1â€“2 days flu-like prodrome
Bacterial infection Varicella pneumonia Encephalitis Reactivates as he
Measles
Maculopapular, morbilliform
Starts on head and neck spreading peripherally
10â€“14 days
Coryza, conjunctivitis, cough, lymphadenopathy. Koplik's spots in late
Otitis media, bacterial pneumonia, measles pneumonia, encephalitis (1 deafness, sub-acute sclerosing panecephalitis (SSPE)
Rubella (German measles)
Pink macular
Progresses from trunk over 2â€“4 days, may be very mild or absent
14â€“21 days
Lymphadenopathy especially suboccipital
Arthritis in adults Encephalitis rare
Parvovirus (slapped cheek, erythema infectiosum, fifth disease)
Facial erythema in children. Macular or maculo- papular, morbilliform
Facial rash in children (slapped cheek) Generalized in adults
5â€“10 days
Lymphadenopathy Arthralgia
Arthritis in adults Foetal loss in pregnancy (hydrops) Anaemia in patie haemoglobinopathies Chronic infection in immunocompromised

Infection	Morphology	Distribution	Incubation	Associated features

Primary varicella infection (chickenpox)

The classical rash is described on p308 . Atypical presentations may oc immunocompromised host who may have fulminant cutaneous involver haemorrhagic chickenpox or conversely can develop systemic involvem rash.

Complications

Systemic complications are rare in the immunocompetent child but mc adults and the immunocompromised. In the UK chickenpox is responsib deaths per year in otherwise healthy adults.

- Secondary bacterial infections. Most frequent complication, 20â hospitalized adults, and responsible for approximately 50% of chi associated deaths. Super-infections with group A streptococcal sep children and staphylococcal skin infections (including toxic shock s bacterial pneumonia predominate.
- Viral pneumonia. Approximately 1 : 400 adult cases with 20% n Commoner in smokers. Characterized by cough, breathlessness, an diffuse pneumonitis on CXR.
- Hepatitis. Severe hepatitis rare except in severely immunocompr elevation in transaminases is usual.
- Encephalitis. Incidence of 0.1 % in adults, 20â€“30 % mortality.
- Cerebellar ataxia. 71 : 4000 cases in children, generally self-lim
- Reyes syndrome. Epidemiological association in childhood with aspirin use.

Management

Anti-viral and anti-microbial therapy

- Immunocompetent children. Anti-viral therapy not indicated. Ha

of suspicion for bacterial infection if ill enough to require hospital

- Immunocompetent adult moderately unwell. Within first 24 hc of rash may benefit from oral aciclovir 800mg five times per day v fever and number of lesions.
- Immunocompetent adult with evidence of pneumonitis. iv ac q8h and anti-staphylococcal and streptococcal antibiotic cover (e.
- Pregnancy. Aciclovir is not licensed for use in pregnancy, but app and non-teratogenic. Pregnant women are at increased risk of seve presenting within 24 hours of onset of rash, the use of aciclovir sh discussed with an expert.
- Immunocompromised adult or child. Aciclovir indicated in all ca disease and minimal immunosuppression, oral therapy with 800mg day may be sufficient. In more severe immunosuppression, e.g. pc any evidence of dissemination, treat with iv 10mg/kg q8h (adult c

Prophylaxis for high-risk susceptible pati

- *Hyperimmune immunoglobulin (VZIG)* is effective in preventing or varicella when given up to 10 days after exposure. VZIG should be susceptible (i.e. absent serum VZV IgG, result usually availale in 4 discussed with lab) immunocompromised individuals as soon as pc exposure to chickenpox or zoster. VZIG is indicated for VZV IgG-r women contacts and should also be given to newborn infants whos had primary varicella 7 days before to 7 days after the birth. Pro (taken from days 7â€“14 after exposure) is also effective in certair not licensed for this indication.
- VZIG supplies are limited and tightly controlled. Your consultant v microbiologist should be contacted in the first instance.
- Varicella vaccine is now licensed and can be considered for susce adults at risk and others felt to be at increased risk. It is a live va not be given to the immunocompromised.

Herpes zoster (shingles)

Reactivation from latent virus in the sensory root ganglia. Risk increas immunodeficiency. Vesicular rash developing in crops in a single derr dermatomes, or dissemination in immunocompromised (up to 20 diss are normal in the immunocompetent). Suspect immunodeficiency in re multi-dermatomal zoster.

Complications

These are more frequent in immunocompromised patients.

- Secondary bacterial infection.
- Post-herpetic neuralgia.
- Eye complications: keratitis occurs in 10% of patients with involve trigeminal nerve (ophthalmic zoster). Rarely there may be retinal
- Aseptic meningitis: CSF pleocytosis is common and generally asy
- Cerebral angiitis leading to a contra-lateral hemiparesis.
- Transverse myelitis: mainly in immunocompromised patients.
- Cutaneous dissemination: in excess of 20 vesicles outside of the a dermatome suggests a high risk of systemic dissemination.
- Systemic dissemination: lung, liver, and brain spread occurs, main immunocompromised patients.

Management

- Immunocompetent adult. Valaciclovir 1g tds, famciclovir 250mg aciclovir 800mg 5 times a day appears to reduce the duration of neuralgia if given within 48 hours of onset.
- Ophthalmic zoster. Stain cornea with fluoroscein to detect kerat ophthalmology opinion vital if decreased visual acuity or any evide involvement. If keratitis present treat with topical, aciclovir, or t ointment and iv aciclovir or oral valaciclovir or famciclovir.

- Uncomplicated zoster in immunocompromised. Give aciclovir f dissemination. Oral aciclovir, famciclovir, or valaciclovir for patient immunosuppression (e.g. on long-term steroid therapy). iv aciclovi for patients with severe immunosuppression.
- Disseminated zoster. Give iv aciclovir 10mg/kg q8h.

Varicella infection control

Chickenpox is infectious from 48 hours before the onset of the rash un after the onset. Patients should be nursed by immune staff using cont a neutral- or negative-pressure side room on a ward without immuno patients. Shingles is much less infectious unless it involves the face o part of the body.

Meningococcal infection: assessment

Rashes

Pupuric lesions are the hallmark of meningococcal disease but several patterns may be seen either separately or together.

- Petechial. Initially 1â€“2mm discrete lesions frequently on trunk, conjunctivae. Enlarge with disease progression and correlate with thrombocytopaenia and DIC, which are poor prognostic signs.
- Ecchymoses. The petechial lesions coalesce and enlarge to form purpura and ecchymoses particularly on the peripheries.
- Purpura fulminans. In extreme cases entire limbs or sections of purpuric and then necrotic due to the combination of DIC and vas
- Maculopapular. Non-purpuric and easily mistaken for a viral rash some patients. May look like flea bites.

Presentation

- Predominantly septicaemia. Symptoms and signs of septicaemia respiratory distress. May progress from first signs to death within a hours. Purpuric rash almost always develops but may be absent a Patient often not meningitic. Give antibiotics immediately after blo ICU immediately. Do not perform LP or CT scan.
- Predominantly meningitis. No shock, no respiratory distress. N predominate and rash may or may not be present.
- Bacteraemia without meningitis or sepsis. Non-specific flu-like or without rash. Positive blood cultures come as a surprise. Rash l present. May develop focal spread such as septic arthritis, pericar
- Chronic meningococcaemia. Low-grade fever, purpuric rash, and confused with gonococcaemia. Sepsis and meningitis do not develo may last for weeks unless recognized.
- Recurrent meningococcaemia. Suspect immunocompromise, pa complement deficiency.

Antibiotics

See p316 .

Investigations

- *Blood cultures.* Immediately. Also take EDTA blood sample for PCR FBC, U & Es, glucose, LFT, clotting.
- *Brain CT scan.* Should be performed prior to lumbar puncture in all predominantly meningitis with depressed consciousness or focal r (CGS <12 or fluctuating GCS, focal neurology, papilloedema, fits, hypertension). Give antibiotics before CT Scan. Do NOT delay trea *perform in patients with predominatly septicaemiaâ€"delays ICU c*

- *LP: Do not perform in patients with predominantly septicaemia* (de immediate management and may be dangerous if DIC). In general, is advisable in all patients with suspected meningitis prior to Lum

However, this introduces delays and recent guidelines from the B Society recommends that an LP can be performed without a head C with simple meningitis lie not septicaemic and no focal neurologica decrease in conscious level. Do NOT delay antibiotics beyond 30 r

Differential diagnosis of purpuric rash and

- Gonococcaemia
- Bacterial septicaemia with DIC
- Haematologic malignancy with sepsis
- Henochâ€“SchÃ¶nlein purpura
- In travellers consider

  Rocky mountain spotted fever (USA)

  Viral haemorrhagic fevers (see p322)

LP findings in meningococcal infections

Opening pr.
Often elevated
WBC
Elevated in almost 100%: median 1200 cell/Âµl, mainly PMN but may partially treated
Protein
Elevated in 90%
Glucose
Reduced in 75â€“80%
Gram-stain
Positive with a negative culture in 10â€“15%
Culture
Positive in 50â€“80% of meningitis
Antigen testing
Positive in 50% and correlates with gram-stain

Meningococcal infection: management

Antibiotic therapy

- Treatment must be started *immediately* if the diagnosis of *predom meningococcal septicaemia* is suspected. If the diagnosis is *predon meningitis* with no evidence of septicaemia, perform LP if no cont do not delay more than 30 minutes before antibiotics are given.
- If called by a GP then instruct the GP to administer penicillin 2miu a third-generation cephalosporin before arranging transfer to hosp

Treatment

- Cefotaxime 2g 4 hourly or ceftriaxone 2g bd.
- If the patient has had definite anaphylaxis or near anaphylaxis to chloramphenicol 25mg/kg 6 hourly (max 1g qds) may be consider
- If there is a possibility that the patient has pneumococcal meningi severely obtunded start dexamethasone 10mg 6 hourly for 4 days before the first dose of antibiotics: this has been shown to reduce substantially.

Prophylaxis

- Notify the case immediately to the local CCDC.
- CCDC will advise on antibiotic prophylaxis.
- Close contacts only, i.e. household, kissing contacts, close family contacts (if from a nursing home) etc. in previous 7â€“10 days.
- Staff members only if involved in resuscitation or endotracheal int suctioning without a mask on.
- Adults: Ciprofloxacin 500mg as a single dose (unlicensed indicatio

or rifampicin 600mg bd for 2 days

or ceftriaxone 250mg im stat.

- Children: Rifampicin 10mg/kg bd for 2 days.

Supportive therapy

- Intensive care monitoring is essential in any shocked patient or if impairment of consciousness.
- If shocked, urgent fluid replacement, aided by invasive monitoring Supportive care for septic shock is discussed on p270 .
- Treatment of DIC is supportive. Role of drotrecogin alfa (rAPC) is may be contraindicated because of thrombocytopenia, haemorrhag

Prognosis

- Meningitis without shock: mortality approximately 10%, neurologi uncommon. Coma is a poor prognostic sign.
- Fulminant meningococcaemia: mortality related to organ failure b 20â€“80%.

Enteric fever (typhoid) 1.

Presentation

- Non-specific symptoms, e.g. anorexia, myalgia, headache, malaise and sweats common. Remittent temperature gradually rising during to ~40Â°C with a relative bradycardia.
- Abdominal pain (30â€“40%), D&V (40â€“60%), or constipation (1C be seen. Acute abdomen occurs in later stages (perforation of bow

Splenomegaly (40â€“60%) and hepatomegaly (20â€“40%).

- Respiratory symptoms common including sore throat and cough.
- Neurological manifestations including encephalopathy, coma, meni seizures are seen in 5â€–10%.
- Rose spots are 2â€–4mm erythematous maculopapular lesions, bla pressure, and occur in crops of ~10 lesions on upper abdomen last hours. Present in 10â€–30% and easily missed.

A fulminant, toxaemic, form occurs in about 5â€–10% of cases with r in cardiovascular, renal, hepatic, and neurological function. In other p may be quite insidious. In the first 7â€–10 days after infection bacter seeding into the Peyer's patches of the gut leading to ulceration and 2â€–3).

Investigations

- Initial week of illness. Normal Hb, WCCâ†“ or â†‘, elevated hep Blood cultures positive in 80â€–90%.
- 2ndâ€–3rd weeks. dHb, â†“WCC, and â†“platelets due to marrov Blood cultures become negative, urine and stool cultures become culture positive. Abdominal X-rays and imaging is indicated if ther pain.
- Serology. Unhelpful at discriminating active infection from past e vaccination.

Complications

All uncommon with prompt diagnosis and therapy.

- Toxaemia. Acute complications include hyperpyrexia, renal and h dysfunction, bone marrow failure, and myocarditis.
- Gastrointestinal. Late complications due to breakdown in Peyer's including gastrointestinal haemorrhage and perforation.
- Metastases. Meningitis, endocarditis, osteomyelitis, liver/spleen.

- Chronic carriage. 1â€“3% beyond 1 year.

Enteric fever (typhoid) 2

Management

- Supportive care. If toxaemic admit to ITU. Urinary catheter and C Swanâ€“Ganz line to manage fluid balance. May need renal suppor
- Antibiotics. Multiple drug resistance has become a problem and a longer be used for empirical treatment. Quinolones, e.g. ciprofloxa orally for 14 days or 400mg bd iv, are currently the agents of cho has been described and ceftriaxone 2g od is an alternative until s known.
- Steroids. Indicated for the severe toxaemic form and have reduce although with a small increase in relapses. Give high-dose dexam followed by 1mg/kg 6 hourly for 8 doses.
- Surgery. Essential for bowel perforation (add metronidazole).
- Infection control. Notify the case to CCDC. Spread is faecal/oral should not prepare food until follow-up stool cultures (off antibioti

- *Salmonella enterica* serotype *typhi* and serotype *paratyphi* (less se widespread distribution including Africa, South America, and India
- Incubation period is 7â€“21 days and it is very rare >1 month afte endemic area
- Untreated mortality 10â€“15%; with adequate therapy mortality is the UK
- Relapse rate 1â€“7%
- Chronic carrier state: increased incidence in elderly, immunocomp with gall-stones. Ampicillin or amoxycillin (4â€“6g/day + probenici

ciprofloxacin (750mg bd) for 4 weeks will clear 80â€“90% of patie
20â€“50% if the patient has gall stones. Cholecystectomy may er
but not usually indicated if carriage is asymptomatic

Viral haemorrhagic fevers

Dengue fever
(serotypes Iâ€“IV) Tropical/sub-tropical zones, Americas, Caribbean, C
Africa *Transmission* : mosquitoâ€“man Huge epidemics *Incubation* : 3
(usually 4â€“7 days)
First exposure : high pyrexia, headache, joint pains, maculopapular ra
â†“WCC and â†“ platelets *Second exposure to different serotype* : Der
haemorrhagic shock in 15â€“25% cases
Isolation not required Mortality low in non-shock cases Treatment sup
Serological diagnosis (acute and convalescent sera) PCR useful in first
only
Yellow fever
Tropical Africa, Central and South America *Transmission* : mosquitoâ€
Incubation : 3â€“14 days
Severe cases: headache, myalgia, high fever, and vomiting 3â€“4 days
later symptoms return with jaundice, haemorrhage, and renal failure,
bradycardia, leukopenia, DIC , and abnormal liver function
Standard blood/body fluid isolation, advise staff on vaccination Case
Treatment supportive Diagnosis by PCR and serology
Lassa fever
Rural districts of West Africa (especially Sierra Leone, Guinea, Liberia
Transmission : rodentâ€“manâ€“man *Incubation* : 3â€“21 days Possibl
cases/year in West Africa
Fever, pharyngitis, retrosternal pain, and proteinuria Haemorrhagic c
20â€“30% of those admitted
Refer suspected cases to high-security isolation facility Mortality 1â€“2
15â€“20% in haemorrhagic cases Ribavirin effective treatment and p
Diagnosis by PCR and serology
Ebola virus

Rural areas of Central, East, (and possibly West) Africa in outbreaks a few hundred people *Transmission* : personâ€“person *Incubation* : 2â€ virus similar
Fever, headache, joint pains, sore throat, abdominal pain, and vomiti rash. Haemorrhagic manifestations common 3â€“4 days after onset
Refer suspected cases to high-security isolation facility Case fatality 5 supportive Diagnosis by PCR and serology

Disease Clinical features Outcome/management

Crimean-Congo haemorrhagic fever (CCHF)
Wide distribution, central Asia, southern Africa
Transmission : person-person, contact with blood of infected livestock, infected tick
Incubation: 1â€“12 days
Fever, malaise, irritability, headache, severe pains in the limbs and lo anorexia, nausea, vomiting, and abdominal pain Haemorrhagic manifes 4â€“5 of illness CNS involvement 10â€“25%
Refer suspected cases to high-security isolation facility Case fatality Treatment with ribavirin Diagnosis by PCR and serology

Disease Clinical features Outcome/management

- Dengue fever is commonly imported into the UK (estimated at 10 cases/year) and presents with fever, headache, and rash. Cases of haemorrhagic fevers are imported only once every few years
- Recognition is important because Lassa, Ebola, Marburg, and CCHF transmitted to health care workers of patients (including laborator suspected cases urgently with specialist high-security infectious d regarding investigation and possible transfer
- Suspected cases include patients with the onset of their fever withi leaving an endemic area, particularly if a malaria film is negative
- Limit local haematological investigations to an absolute minimum if four VHFs is suspected (but *always* perform malaria film first)

Rickettsial infections

These present with fever, headache, and rash and should be included diagnosis of febrile travellers. Recognition is important because the have significant mortality if left untreated. Isolation is not necessary. about 5â€“14 days.

R. conorii and *R. africae* are probably the two commonest of the group into the UK, usually from Africa, but *Rickettsiae* are widely distributed world.

Molecular and direct immunofluorescent diagnostic techniques are not so treatment has to be given on clinical suspicion. Serology is not pos second week of the illness at the earlierst and may take 3â€“4 weeks positive (and may be modified by treatment).

First-line treatment is with doxycycline 100mg bd Ã— up to 7 days (chlorampenicol, or quinolones have also been used).

Typhus group
Epidemic typhus: *Rickettsia prowazeki*
Fever, severe headaches, maculopapular rash on trunk spreading to
Complications include pneumonitis, encephalitis and myocarditis
Murine typhus: *Rickettsia typhi*
R. typhi less severe than *R. prowazekii*
Spotted fever group
Boutonneuse fever: *Rickettsia conorii*
Fever, severe headache, eschar (black scab with surrounding erythema) sparse papular rash
African tick typus: *Rickettsia africae* (plus others)
Rocky mountain spotted fever (N America): *Rickettsia rickettsiae*
Fever, headache, confusion and neck stiffness, joint pains, malaise. M at wrists and ankles spreading to trunk, may be petechial or purpuric. meningococcal sepicaemia. Mortality 30% untreated
Scrub typhus
SE Asia: *Orientia tsutugamishi*
Eschar, painful regional lymphadenopathy, fever, headache, malaise,

rash in 60%

Disease Clinical features

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Q fever

Coxiella burnetii is a disease of rural areas (reservoirs in sheep and c transmitted by inhalation of infectious particles in dust, contact with (e.g. in abattoirs) and by tickbites. *Presentation:* non-specific sympto myalgia, malaise, sweats; dry cough and features of atypical pneumo PUO and splenomegaly.

Investigations: Patchy CXR shadowing (lower lobes), hepatic granulor fixation tests identify antibodies to phase 1 antigens (chronic infectior endocarditis p122) and Phase 2 antigens (acute infection). *Treat* with (to try to prevent chronic infection) Â± co-trimoxazole, rifampicin, or

Human bites

- *Superficial abrasions* : Clean the wound. Re-dress the area daily.
- Give tetanus prophylaxis as needed. Check hepatitis B status and necessary (see p646). HIV counselling and urgent PEP if indicated HCV has also been transmitted by human bite, so appropriate follo (there is no HCV PEP).
- Have a low threshold for admission to hospital and iv antibiotic th mouth contains a number of aerobic and anaerobic organisms that aggressive necrotizing infection, particularly if the â€˜closedâ€™ s hand or feet are involved.
- *Antibiotic therapy* : All wounds that penetrate the dermis require Aerobic and anaerobic cultures should be taken prior to treatment A suggested regimen is co-amoxiclav 500/125mg tds po (or iv cef metronidazole). Consult your local microbiologists.
- *Facial bites* : Cosmetically significant bites should be referred toa

Puncture wounds should be cleaned thoroughly and treated with p
antibiotics (see above). Patients should be instructed to re-open th
express any purulent or bloody material 3â€“4 times a day for the

- *Hand bites* : Should be referred to the orthopaedic team; explorati
recommended. Clean the wound thoroughly. Give the first dose of
subsequent doses po unless there are signs of systemic upset.

Non-human mammalian bites

- General management is as for human bites (see above). Clean the
aerobic and anaerobic culture, tetanus prophylaxis as needed, and
antibiotics as above. Rabies prophylaxis (vaccine *plus* rabies-spec
immunoglobulin) should be considered in all cases if the bite occu
UK, or if the bite was from a bat *within* the UK or from an animal
facility. For up-to-date advice and supplies of vaccine and immun
the duty doctor, Virus Reference Division, Health Protection Agenc
London NW9 5HT (Tel. 020 8200 4400). See
http://www.hpa.org.uk/infections/default.htm
- *Rabies* is transmitted by infected saliva inoculated through the ski
of aerosolized virus (from infected bats). Presenting features are a
followed by parasthesiae and fasciculations. Agitation, confusion,
localized paralysis, and brainstem dysfunction follow. There is no
treatment once symptoms appear; prevention is essential.
- *Rabies vaccine* should be given prophylactically (in the deltoid) to
bites from infected animals (vets, animal handlers, field workers,
- Some Old World monkeys, particularly rhesus and cynomolgus mac
infected with herpes B virus (causes a similar illness in monkeys as
humans). It can be transmitted by bite and saliva and has caused
disseminated infection in humans. If the bite is from a macaque fr
of the virus, consider starting valaciclovir 1g tds Ã— 14 days penc
investigation.

Infections in intravenous drug users

In UK majority are HCV positive. Minority are HIV and HBsAg positive aureus bacteraemia and septicaemia is common. Patients with murmur echocardiography to investigate possibility of endocarditis. Multiple ro infiltrates are characteristic of tricuspid endocarditis with septic embo

Necrotizing fasciitis

- Patient usually extremely unwell
- Erythematous, exquisitely tender area, sometimes with underlying may show gas in subcutaneous tissues.
- Mainstay of treatment is *urgent* debridement of all necrotic tissue surgeon. Further imaging prior to theatre merely delays procedure providing further therapeutic information.
- Often polymicrobial.
- Clindamycin seems to be an important component of any antimicr One suggested treatment regime is ciprofloxacin 400mg bd iv, cli qds iv, benzylpenicillin 1.2â€“2.4g 4-hourly.
- Patients usually require daily debridement in theatre followed by surgery.

Severe acute respiratory syndrome (SARS

- This is a new coronavirus infection in man with a high transmissio respiratory contacts, particularly health care workers. Also probab by faeco-oral route and fomites. Causes fever, myalgia, and varia illness with rapid deterioration in second week of illness. Very low adolescents. High mortality in patients >60 years.
- Strict isolation and rigorous enforcement of infection control esse
- At the time of writing (July 2003), epidemic waning, but may reap

- Treatment as yet undefined. High-dose steroids may be of some b ill. Ribavirin is probably of no value.
- See http://www.who.int/csr/sars/en/index.html

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Bioterrorism

- There is increasing awareness of the possibility of a deliberate rel and chemical agents. Historically plague, *Salmonella* and anthrax used, as have nerve gases and biological toxins. The most recent releases have been Sarin gas (a nerve gas) on the Tokyo undergro anthrax spores (as white powder in the mail) in the USA in 2001.
- Releases are likely to be either airborne or food and water contan
- Clues that a deliberate release may have occurred would be the u appearance of an infection outside its normal range (e.g. anthrax i infection appearing in a patient unlikely to contract the disease or of patients with the same pattern of symptoms. â€˜White powder also continue to cause concern.
- Any suspicion of a deliberate release should be communicated urge consultant microbiologist and the CCDC (Consultant in Communica Control). Specific guidelines on diagnosis, management and prophy found on the HPA website http://www.hpa.org.uk/infections/topics_az/deliberate_release/me
- Current organisms of particular concern include smallpox, plague, melioidosis, botulism, glanders (an infectious disease caused by t *Burkholderia mallei*), and viral haemorrhagic fevers although othe involved.

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Smallpox
Initially macules, then deep vesicles predominantly on peripheries (of

superficial vesicles predominantly on trunk)
Yes
Supportive
Vaccination (post-exposure vaccination effective)
Plague
Likely to be pneumonic with severe sepsis in inhalational plague
Yes
Gentamicin, streptomycin, ciprofloxacin
Ciprofloxacin, doxycycline
Tularaemia
Likely to be flu-like or pneumonic with sepsis in inhalational tularaem
Very low possibility, but respiratory precautions advisable
Gentamicin, ciprofloxacin
Ciprofloxacin, doxycycline
Anthrax â€“ inhalational
Sepsis, haemorrhagic medistinitis (widened mediastinum), may be m
pneumonitis
Highly unlikely
Ciprofloxacin, doxycycline
Ciprofloxacin, doxycycline, vaccination
Anthrax â€“ cutaneous
Necrotic ulcer with marked surrounding oedema
Highly unlikely
Ciprofloxacin, doxycycline
Ciprofloxacin, doxycycline, vaccination
Anthrax â€“ white powder incident
If powder contains anthrax spores then highly infectious. Controlled
essential
Ciprofloxacin, doxycycline, vaccination
Melioidosis
Likely to present as septicaemic illness, but spectrum of illness
Ceftazidime, meropenem
Botulism
Multiple cranial nerve palsies, other palsies. No alteration in conscious
No
Antitoxin given on clinical suspicion
VHFs

Haemorrhagic illness with fever
Yes
Ribavirin for lassa and CCHF
Ribavirin for lassa and ?CCHF
Nerve gases
Anticholinesterase inhibitors, salivation, bronchorrhoea, sweating, br bradycardia, abdominal cramps, diarrhoea, meiosis, muscle fasciculati respiratory paralysis, tachycardia, hypertension, emotional lability, co convulsions, coma, central respiratory depression
Yesâ€”if clothing contaminated (transcutaneous absorption)
Supportive, atropine, pralidoxime, diazepam

Agent	Clinical	Person to person transmission risk	Treatmer

Editors: Ramrakha, Punit S.; Moore, Kevin P.
Title: *Oxford Handbook of Acute Medicine, 2nd Edition*

Chapter 5
Emergencies in HIV positive patients

Emergency presentations of HIV infection

Patients with human immunodeficiency virus (HIV) infection may present to acute medical services in a variety of circumstances:

- Patients with undiagnosed HIV infection presenting with HIV-related or -unrelated problems
- Patients with known HIV infection presenting with HIV-related or -unrelated problems
- Patients with HIV infection presenting with toxicity related to anti-HIV therapy [antiretroviral therapy; highly active antiretroviral therapy (HAART)]
- Patients presenting with primary HIV infection (seroconversion).

Clinicians providing acute medical care may be in a position to diagnose HIV infection in individuals in whom this has been previously unrecognized. In addition, clinicians providing emergency care may encounter individuals (healthcare workers and the general public) who may have been exposed to HIV and

in whom PEP may be considered.

The specific management issues for the above are considered in the following sections. Where there is local expertise in the management of HIV infection, it is recommended that care is provided in consultation with the appropriate team. This is particularly relevant where the prescribing of therapy may require consideration of co-prescribed antiretroviral therapies.

General principles

- The use of combination antiretroviral therapy has been extraordinarily successful in improving the prognosis for HIV-infected individuals, with HIV now considered a chronic manageable disease. Successful antiretroviral therapy significantly increases the CD4 count and reduces the risk of opportunistic complications. In over 95% HAART will reduce HIV RNA load to undetectable levels (e.g. <50copies/ml plasma).
- Patients with known or suspected HIV infection should therefore be investigated and managed aggressively, as the outlook may be far better than many clinicians may anticipate from historical experience.
- Unusual opportunistic infections and malignancies are often seen and can occur simultaneously or sequentially.
- Relapse is common.
- Toxicity from antiretroviral therapy may present to acute medical services.
- Drug interactions with antiretroviral therapy require consideration.
- Common diseases still affect HIV-positive individuals and may present atypically.

Examination of the mouth can reveal a great deal of information regarding the level of immunity (e.g. oral thrush, hairy leucoplakia suggests reduced immunity and increased risk of severe opportunistic infection; Kaposi sarcoma suggests increased risk of visceral KS).

Factors influencing presentation in HIV disease

Degree of immunosuppression

- The normal CD4 count is 500â€“1500 Ã— 10^6 cells/mm^3 and gradually decreases during the course of HIV infection.
- The CD4 count is used as a guide to a patient's susceptibility to complications of HIV infection (see figure). For example, *Pneumocystis jiroveci* (formerly known as *P. Carinii*) pneumonia (PCP) is uncommon with a CD4 count >200.

Patients (who are aware of their HIV status) are usually familiar with these measures and are likely to be aware of their most recent results.

Risk group and predisposition to different complications

HIV in the UK is predominantly seen in specific patient groups, and the incidence of HIV-related complications varies between these groups.

- Homosexual men have a higher incidence of Kaposi's sarcoma than other Caucasians.
- Injecting drug users are more likely to be co-infected with hepatitis C, and are more likely to experience sepsis related

to injecting.

- Individuals of African or Asian origin are more likely to present with TB (which may be atypical and/or extra-pulmonary in presentation).
- Individuals of African origin are more likely to experience cryptococcal infection.

Travel history

Many infections in the HIV-infected patient represent reactivation of latent pathogens and a comprehensive travel history is helpful in the differential diagnosis, particularly for individuals presenting with pyrexia.

- Histoplasmosis: travel to central America and the eastern USA.
- Coccidiomycosis: travel to the SW USA and parts of South America.
- Penicillinosis: travel to countries in SE Asia and Indonesia.
- Strongyloides hyperinfection: previous travel in the tropics.
- Leishmaniasis: travel in mediterranean and tropics.

Antiretroviral therapy

- Patients who are responding well to antiretroviral therapy (i.e. who are virologically suppressed and have achieved a significant increase in CD4 count) are much less at risk from opportunistic complications of HIV infection. General medical/surgical conditions should be considered in such patients (as in the untreated individual with HIV infection and a high CD4 count).
- However, toxicities of antiretroviral therapy may present to the emergency clinician (see p370), and caution should be

exercised when co-prescribing.

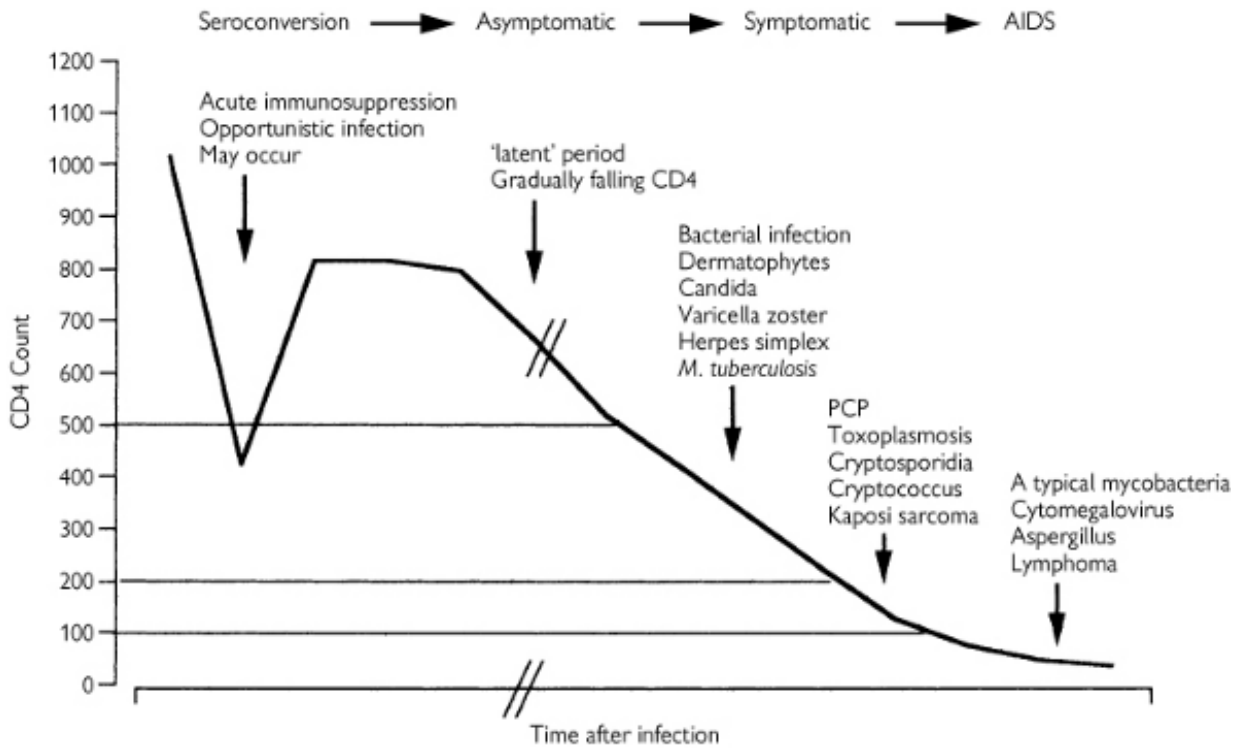

Figure. No caption available.

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HIV testing

In most situations, HIV testing should be carried out with informed consent and is usually undertaken in GUM/STI clinics, in primary care, or as part of routine antenatal care. However, the presentation of individuals with potentially HIV-related complications or at potential risk of previous HIV exposure to the emergency clinician may provide the opportunity to diagnose infection. Whilst many individuals may choose to have an HIV test within the confidential setting of a specific HIV-testing service, any healthcare provider should possess the essential skills for appropriate discussion of HIV testing.

Pre-test discussion

The following issues should be included in a â€˜pre-testâ€™ discussion

- Rationale for testing
- Benefits of knowing status
- When and by whom the result will be given
- â€˜Window periodâ€™ of infection (i.e. may take up to 3 months from exposure for HIV antibody test to become positive)
- Confidentiality (a negative test may not require disclosure to a GP and does not have implications for insurance/mortgages, etc.; a positive result does not necessarily need to be disclosed to third parties without consent but will have implications for insurance/mortgages).

Post-test discussion

The following principles should be followed in a â€˜post-testâ€™ discussion

- Giving a positive result should follow the normal principles of breaking bad news
- If a result is positive, early referral to an HIV clinician is recommended
- If a result is negative, the window period should be reinforced (particularly in situations where seroconversion is suspected: see below)
- If a result is negative, the opportunity for future risk reduction should be considered.

HIV testing without consent

It is rarely necessary to test for HIV infection without consent. However, this is justified in the following settings.

- Testing of organ transplantation donors.
- Testing of the unconscious/confused patient where HIV infection is suspected and the management of the patient will be materially changed by knowledge of their HIV status.
- Testing of the unconscious patient who is the â€˜donorâ€™ in a significant needlestick/splash injury. In this situation, testing is justified if the patient is unlikely to regain consciousness for 48 hours, but should only be performed on a blood specimen that has been previously taken for another purpose.
- Given the potential litigation arising from HIV testing without consent, it is advisable to seek a second opinion (preferably from a physician with HIV experience) that such testing is justified.

Primary HIV infection (PHI)

PHI (also known as HIV seroconversion illness) is easily overlooked. Intervention may help prevent further spread of HIV (individuals recently infected with HIV are thought to be highly infectious, particularly if unaware of their status).

Risk of recent infection

A significant history of exposure to a potential HIV source within the last 3 months (sexual, percutaneous, or mucocutaneous) in conjunction with any of the features below warrants performing specific diagnostic tests for PHI.

Symptoms and signs

- Typically within 2â€“4 weeks of exposure but can be up to 3

months

- Flu-like illness (fever, myalgia, headache, lymphadenopathy, retro-orbital pain)
- Maculopapular rash (differential diagnosis of secondary syphilis)
- Pharyngitis/oral ulceration
- Concomitant sexually transmitted infections (e.g. primary or secondary syphilis, gonorrhoea, genital ulcer disease).

Laboratory findings

- HIV antibody tests may be negative at the time of seroconversion and an HIV RNA viral load test may be required to confirm the diagnosis
- Lymphopaenia, thrombocytopaenia, and raised ALT/AST may occur.

Sequelae of acute immunosuppression

- CD4 count may transiently fall to <200 cells/mm^3 (therefore risk of opportunistic infections, particularly PCP)
- Candidiasis, viral warts, VZV.

Management

- The diagnosis of PHI will enable appropriate partner notification, screening for other sexually transmitted infections, and strategies to reduce onward transmission.
- The utility of antiretroviral therapy in this setting remains controversial and under study.
- Up to 25% of new infections may have primary resistance to

one or more antiretroviral agents: knowledge of local resistance rates is needed before initiating antiretroviral therapy.

- Early referral to an HIV specialist is recommended.

Acute neurological conditions in HIV positive patients: assessment

Opportunistic infections and malignancies, the direct effect of HIV itself, and antiretroviral drugs can all cause disease of the central or peripheral nervous system. The presenting features of different conditions are often varied and non-specific and tend to involve the same diagnostic approach and investigations.

Key symptoms and signs

- General. Look for evidence of advanced immunosuppression (see figure, p341).
- Unconsciousness. Assess and manage as on p406 .
- Seizure. Requires urgent contrast CT or preferably MRI head scan to detect SOL and, if none detected, suitability for diagnostic LP. Consider anti-epileptics but be aware of antiretroviral and other drug interactions (sodium valproate commonly recommended if receiving protease or non-nucleoside therapy).
- Headache. Elucidate symptoms of raised intracranial pressure suggestive of a SOL such as nausea, early morning headache, and increased intensity on coughing. Distinguish from facial pain caused by dental, sinus or herpetic neuralgia (check for herpetic rash).
- Meningism. May be reduced or absent due to reduced inflammatory response. Aseptic meningitis can occur during

primary HIV infection (seroconversion illness). With advancing immunosuppression, viral, bacterial, tuberculous, and fungal (cryptococcal) meningitides are more common and may not manifest typical signs of meningism.

- Paraparesis. Consider viral transverse myelitis (HIV, CMV, VZV, or HSV) or cord compression by infection or malignancy. Requires urgent MRI spine and subsequent LP if not contraindicated.
- Cognitive impairment. Wide differential. If associated with any focal neurological signs consider SOL, PML, HIV dementia, late syphilis.
- Psychiatric disturbances. An organic cause is often found. May be a result of antiretroviral drug interactions with anti-psychotic and recreational drugs. If aggressive, ensure patient has no access to contaminated sharps.
- Peripheral neuropathy. Typically of gradual onset and caused by certain antiretrovirals or HIV itself.
- Myopathy. Zidovudine (AZT) can cause myopathy or even rhabdomyolysis (check creatine kinase and renal function), arising from mitochondrial toxicity (see p370). It may also be due to the concomitant use of lipid-lowering agents.
- Rapid visual deterioration. Consider CMV-related retinitis (often apparent on fundoscopy), uveitis, endophthalmitis, and intracerebral causes. Retinal detachment may be a consequence of treatment. Immediate referral to ophthalmologist.

Acute neurological conditions in HIV positive patients: investigations

Blood tests

- Baseline (useful if already doneâ€”patient will often know results): CD4 cell count, HIV RNA viral load, serology for toxoplasma IgG (positive in >90% of patients with cerebral toxoplasmosis, indicative of risk of reactivation), CMV IgG, serological tests for syphilis (STS).
- Routine: FBC (low lymphocyte count may give a clue to CD4 depletion), U&Es, LFTs.
- Acute: inflammatory markers (CRP and ESR), STS, LDH (may be raised in lymphoma), blood cultures (bacterial, mycobacterial (4â€“6 weeks)). Consider CMV Direct Antigen Test (DAT) and cryptococcal antigen (CrAg) if CD4 count <200 cells/mm^3 (positive in >80% with cryptococcal meningitis).

Specific

- Stool, urine and throat cultures
- Chest X-ray. Consider TB at any CD4 count. Para-aortic and hilar lymphadenopathy might suggest MAI or lymphoma.
- Contrast CT or MRI scan of head
    - Contrast essential, MRI more sensitive than CT (risk of missing brainstem disease, *Toxoplasma* cysts and PML by CT).
    - Contrast enhancing SOL very likely to be either cerebral toxoplasmosis (typically multiple, with ring enhancement, associated with oedema, at the basal ganglia or grey-white matter interface) or cerebral lymphoma (typically fewer lesions, with irregular enhancement, associated with oedema, periventricular). Poor response to empirical toxoplasmosis treatment suggests lymphoma. Less commonly consider bacterial (e.g. streptococcus, nocardia), mycobacterial (e.g.

tuberculoma), or fungal (e.g. cryptococcoma) lesions. Mycobacterial disease is on the increase especially in â€˜high riskâ€™ populations e.g. patients from high prevalence TB areas.

- Meningeal enhancement and hydrocephalus can occur in tuberculous, cryptococcal or syphilitic meningitis.
- PML: non-enhancing, multifocal, subcortical white matter changes. No mass effect.
- HIV-associated dementia: non-enhancing, diffuse, deep white matter hyperintensities with prominent cerebral atrophy. No mass effect.
- Viral encephalitis (typically CMV, HSV, VZV) may display variably enhancing confluent changes but often normal.

- Brain biopsy. If disease stage and general prognosis fair, consider performing when no response to empirical treatment.
- EEG. Useful to confirm seizure activity and response to treatment but often non-specific for HIV encephalopathy and opportunistic infections.
- Contrast MRI of spine. The best modality for spinal cord and nerve root imaging.
- Nerve conduction studies/electromyogram. Useful if unusual or treatment-unresponsive sensory or motor symptoms and signs.

Lumbar puncture

- Arrange for contrast CT or MRI head before any LP and ensure that there are no clotting abnormalities
- Always measure opening pressure
- Collect 6â€“8ml of CSF and divide into 4 universal

containers and 1 fluoride tube for glucose (always take paired blood for glucose)

- Bottles 1 and 4 to microbiology for
    - RBC and WBC estimation
    - *Bacterial* : microscopy, culture, and sensitivity
    - *Mycobacterial:* Ziehlâ€“Nieelson microscopy, culture and consider PCR
    - *Viral:* PCR for CMV, HSV, VZV, JC virus (PML), EBV (lymphoma)
    - *Other:* Indian ink microscopy and CrAg (near 100% sensitivity and specificity for neurological cryptococcal disease), fungal culture, and STS
- Bottle 2 and both fluoride tubes to biochemistry for protein and paired glucose measurement
- Bottle 3 to cytology (rarely diagnostic) or immunology if indicated
- Raised CSF cell count and protein (upto 1g/L) can be an incidental finding in asymptomatic HIV infection; conversely, there may be little inflammatory response, e.g. in cryptococcal meningitis

Acute neurological conditions in HIV-infected patients: treatment

HIV
Encephalitis or aseptic meningitis
Diagnosis of exclusion
Highly active antiretroviral therapy (HAART)
Dementia/psychiatric presentation
Brain biopsy diagnostic but not performed for this reason

Seizures
Toxoplasmosis
SOL
90% anti-toxo antibody positive but do not discriminate active from inactive disease

- Sulphadiazine 1â€“2g iv/po qds + pyrimethamine 100mg po od on first day then 75mg po od + folinic acid 15mg po od for 4â€“6 weeks
- Clindamycin 1.2g po/iv qds + pyrimethamine 100mg po od on first day then 75mg po od folinic acid 15mg po od
- Atovaquone 750mg po tds for 21 days
- (consider use of dexamethasone to reduce cerebral oedema)

Seizures
Confusion
CT : ring enhancing lesions
Encephalitic illness
Brain biopsy gold standard, perform if no response to empirical therapy
Cryptococcosis
Headache Â± meningism
CSF : pleiocytosis with low glucose but may be normal in 20â€“30%. India ink stain, culture, and cryptococcal antigen

- Amphotericin 0.25mgâ€“1mg/kg iv od for up to 6 weeks Â± flucytosine 100mg/kg po/iv qds for 2 weeks (liposomal formulations may be used if concerns regarding nephrotoxicity
- Fluconazole 400mg bd

SOL (cryptococcoma)
Seizures
Confusion
Serum cryptococcal antigen positive 95%
Mycobacterium
Headache Â± meningism
CSF: pleiocytosis with low glucose in most cases ZN stain positive in only 10â€“20%. CSF culture takes 4â€“6 weeks

Obtain specialist microbiological advice; initiate therapy with at least 4 agents (preferably including those with CNS penetration, i.e. isoniazid + pyrazinamide) and consider steroids if fits or worsening neurological signs

Nocardia

Headache Â± meningism

Brain biopsy/culture

Combination of at least 2 of cotrimoxazole, amikacin, streptomycin, imipenem (or meropenem) and minocycline

SOL (tuberculoma)

Often co-existing pulmonary disease

Seizures

Confusion

Cytomegalovirus

Encephalitis

Viral detection in CSF or neural tissue. PCR , culture, or immunohistochemistry

- Ganciclovir 5mg/kg iv bd for 2â€“3 weeks
- Valganciclovir 900mg po bd
- Foscarnet 90mg/kg bd iv for 2â€“3 weeks

Transverse myelitis

Polyradiculitis

Varicella zoster

Encephalitis

Viral detection in CSF or neural tissue. Culture, immunohistochemistry, or PCR

- Aciclovir 10mg/kg iv tds for 10 days
- Aciclovir 800mg 5 times daily for 5â€“10 days
- Valaciclovir 1g po tds for 1 week

Transverse myelitis

Polyradiculitis

Herpes simplex

Encephalitis

Viral detection in CSF or neural tissue. Culture, immunohistochemistry, or PCR

- Aciclovir 5mg/kg iv tds for 10 days
- Aciclovir 200â€“400mg 5 times daily for 5â€“10 days
- Valaciclovir 500mg po bd for 5â€“10 days

Radiculitis
Seizures
PML (JC virus)
Motor dysfunction
CSF : anti-JC virus antibodies PCR
HAART
Cranial nerve palsies
Brain biopsy
Dementia
White matter MRI /CT changes
Lymphoma
SOL
CSF cytology
HAART + chemotherapy (treatment or palliative) + intracranial irradiation
Malignant meningitis Isolated nerve or spinal cord lesion
Brain biopsy
Check BNF for Contraindications, cautions, side-effects, and interactions

Condition	Possible presentations	Diagnostic tests	Treatment

Respiratory emergencies in HIV positive patients: assessment

Caution: HIV-infected patients presenting with cough warrant a high index of suspicion for *Mycobacterium tuberculosis* (TB) or multi-drug resistant TB. Such patients should wear a filter mask and be admitted to a side-room. If on a ward with other

immunocompromised patients, this should be with negative-pressure isolation facilities.

Key symptoms and signs

- General. Look for evidence of advanced immunosuppression and extra-pulmonary clues to aetiology (e.g. cutaneous KS, neurological signs due to cryptococcosis or retinitis due to CMV). Remember multiple pathologies can co-exist.
- Cough productive of sputum. Purulent sputum suggestive of bacterial or mycobacterial aetiology (incidence of *S. pneumoniae, H. influenzae* and TB up to 100-fold higher than in HIV-negative controls). Also consider *S. aureus* (in IVDUs), Gram-negative organisms (e.g. *P. aeruginosa*).
- Non-productive cough. In patients with CD4 cell count <200 cells/mm^3 the main concern is *Pneumocystis carinii* pneumonia (PCP, a fungus), which typically has a chronic, progressive history associated with breathlessness (see Table). PCP can occasionally occur in patients during primary HIV infection (seroconversion illness) and can be seen in patients despite good adherence to cotrimoxazole (SeptrinÂ®) prophylaxis. Other causes of non-productive cough include viral URTIs (any CD4 count), KS, lymphoma, and rarely lymphocytic interstitial pneumonitis (any CD4 count but typically raised CD8 cell count with SjÃ¶gren's symptoms).
- Haemoptysis. Suggestive of mycobacterial or fungal causes, pulmonary embolus, or KS.
- Breathlessness. If sudden onset, consider pneumothorax (secondary to PCP), pulmonary oedema, or pulmonary embolism. If gradual and progressive need to exclude PCP.
- Chest pain. More common in bacterial infections, KS, pneumothorax and pulmonary embolus. HIV-infected patients are more at risk of thromboembolic disease. Pneumothorax may complicate up to 10% of patients with PCP.

Clinical, laboratory, and CXR findings that may distinguish PCP from bacterial pneumonia

CD4 cell count
<200 cells/mm^3
Any
Symptoms
Non-productive cough
Productive cough
Purulent sputum
Symptom duration
A few weeks
3â€“5 days
Signs
Occasionally bilateral fine crackles (usually minimal signs)
Focal lung signs
Laboratory tests
WBC variable
WBC frequently elevated
Chest radiograph findings
Distribution
Diffuse > focal
Focal > diffuse
Location
Bilateral, Perihilar initially
Unilateral, segmental/lobar
Pattern
Diffuse, interstitial infiltrates
Often lobar or focal consolidation
Cysts
10â€“15%
5â€“10% (Klebsiella, Staphylococcal)
Pleural effusions

Very rare
25â€“30%

Findings Pneumocystis carinii Bacterial

Practice points

- Beware â€˜normalâ€™ CXR: respiratory history is the most important.
- If CD4 count <200 cells/mm^3 and history is compatible, consider PCP as the most likely respiratory infection and start empirical therapy. Diagnostic investigations can be deferred for several days until the patient is clinically stable.
- TB is on the increase in the UK.

Respiratory emergencies in HIV positive patients: investigations

Non-invasive investigations

NB: viral and fungal infections may cause few symptoms and signsâ€”if suspected, request viral PCR or culture and fungal microscopy and culture in addition to the investigations listed below.

- Baseline (useful if already done). CD4 cell count, HIV RNA viral load.
- Radiology. Chest X-ray (see table). Other radiology such as ultrasound, CT, or high-resolution CT performed as needed.
- FBC. Leucopenia suggests poor prognosis in bacterial infections and if pre-existing can guide choice of empirical

therapy.

- U&Es. Low Na^+ or renal impairment suggests poor prognosis.
- LFTs. Abnormalities suggest disseminated disease or other pathology.
- Serology . For *Legionella, Mycoplasma* , and other atypical pathogens.
- Cryptococcal antigen. A test with a >90% sensitivity and >95% specificity for systemic cryptococcaemia.
- ABGs. Hypoxia can occur in any pneumonic process but most characteristic of PCP.
- Heaf test (tuberculin skin testing). Results can be misleading or unhelpful as anergy is common. Only used in specific circumstances.
- Exercise oxygen saturation. Significant exercise desaturation very suggestive of a diffuse pneumonitis such as PCP. Useful in patients with â€˜normalâ€™ CXR and SaO_2 >93% at rest.
- Lung function tests. If available these may be useful as impaired gas transfer (KCO) has the same significance as oxygen desaturation.
- Blood cultures. Often positive in *S. pneumoniae* infections. Mycobacterial blood cultures may be useful (4â€“6 weeks).
- Sputum cultures. For microscopy and culture (bacterial and mycobacterial).
- Induced sputum. Nebulized hypertonic saline administered by specialist nurse or physiotherapist. Silver stain or immunofluorescence has a maximum of 85â€“90% sensitivity for PCP compared with gold standard fibre optic bronchoscopy (typically 50â€“60%). Also send samples for microscopy and culture (bacterial and mycobacterial). Do not perform on an open ward.

Invasive investigations

- Fibre optic bronchoscopy. Usually indicated if no response to treatment or second pathology suspected. Look carefully for KS lesions (transbronchial biopsies not routinely taken as risk of pneumothorax and haemorrhage). Send BAL samples for microscopy (including stains for pneumocystis) and culture (bacterial, fungal, and mycobacterial), viruses and PCR.
- Pleural aspiration. Cell count, protein, microscopy and culture (bacterial and mycobacterial), cytology, pleural biopsy of all significant effusions.
- Lung biopsy. transbronchial, percutaneous, or open lung biopsy. Seek specialist surgical advice.

CXR patterns in HIV-associated disease

Normal

- PCP , viral pneumonia (if hypoxic onexercise)

Focal infiltrate

- Bacterial (*S. pneumoniae, H. influenzae*)
- Mycobacteria (TB or MAI)
- Fungal organisms (cryptococcus, histoplasmosis, aspergillus, candida)
- Nocardia or *Rhodococcus equi* (rare)
- Pulmonary KS or lymphoma
- PCP (apical if on nebulized pentamidineprophylaxis)

Cavitating

- Bacterial (staphylococcal, streptococcal, nocardia,

anaerobes)
- Mycobacteria
- Fungal organisms
- PCP may produce thin-walled cysts (pneumatocoeles)

Pneumothorax

- PCP : occasionally when pneumatocoele ruptures
- TB

Diffuse infiltrate

- PCP , classical presentation
- Respiratory viruses (RSV , adenovirus, parainfluenza)
- CMV (often difficult to decide whether pathogenic role)
- Miliary tuberculosis
- Fungal organisms
- Toxoplasmosis
- Lymphocytic interstitial pneumonitis

Pleural effusion

- Bacterial (mainly *S. pneumoniae*)
- Mycobacteria (mainly TB)
- Lymphoma
- Heart failure
- KS

Mediastinal lymphadenopathy

- Not a feature of HIV-related lymphadenopathy
- Mycobacteria, fungal infection
- Lymphoma and KS

X-ray finding	Disease process

Respiratory emergencies in HIV

positive patients: management

General measures

- Monitor pulse, BP, and temperature regularly.
- Pulse oximetry should be used with supplementary oxygen to maintain saturations above 90%.

Assisted ventilation

Being HIV-infected is not in itself a contraindication to assisted ventilation or intensive care. Indeed, many acute respiratory infections requiring such support achieve excellent outcomes. It is the individual's stage of disease and general prognosis that deems such management appropriate or inappropriate, as well as the views of the patient and their next of kin.

Specific treatment of respiratory conditions:

Contact local microbiology services if uncertain.

Community-acquired pneumonia
(CD4 count >200 cells/mm^3)

- Co-amoxyclav 600mg tds iv/po *or* ceftriaxone 2g od iv for 7 days Â± azithromycin 500mg od iv/po for 3 days

Community-acquired pneumonia
(CD4 count <200 cells/mm^3)
If any suggestion of PCP treat as PCP +

- Azithromycin 500mg od/iv po for 3 days

Pneumocystis jiroveci pneumonia
(if PaO_2 <8kPa add prednisolone 75mg od po for 5 days, then 50mg od for 5 days, then 25mg od for 5 days)

Hospital-acquired pneumonia

- Cotrimoxazole 120mg/kg in 2â€“4 divided doses iv/po for 14â€“21 days. Reduce to 100mg/kg after 7 days if responsive (â†“ risk of toxicity)
- Clindamycin 600mgâ€“1.2g qds po/iv + primaquine 15â€“30mg od po for 14â€“21 days
- Pentamidine isetionate 4mg/kg od iv for 14â€“21 days + nebulized 600mg od for first 3 days
- Atovaquone 750mg po bd for 21 days
- Cefotaxime 1â€“2g tds iv *or* ciprofloxacin 500mg bd po/iv for 7 days +
- Azithromycin 500mg od iv/po for 3 days

Intravenous drug user
Cefotaxime 1â€“2g tds iv + flucloxacillin 1â€“2g qds po/iv for 7 days + azithromycin 500mg od iv/po for 3 days or ceftriazone + flucloxacillin
Neutropenic patient
(duration of treatment guided by microbiologist)
If any suggestion of PCP treat as PCP +

- Ceftazidime 1â€“2g tds iv for 7â€“14 days + azithromycin 500mg od iv/po
- Piperacillin 4g qds iv + gentamicin (2mg/kg iv loading dose then 3mg/kg iv in divided dose according to levels + azithromycin 500mg od
- Ciprofloxacin 500mgâ€“1g bd iv+ amoxycillin 2g tds iv + azithromycin 500mg od

Kaposi's sarcoma
HAART Â± chemotherapy
Lymphoma
HAART Â± chemotherapy

Condition Dosage, route, frequency, duration

Gastrointestinal (GI) presentations in HIV positive patients: assessment

Opportunistic infections, malignancies, and antiretroviral drug toxicity can all frequently manifest as symptoms/signs in the GI tract.

Key symptoms and signs

- General. Assess hydration, weight, and nutritional status.
- Diarrhoea. Can be caused by multiple pathogens: both common and opportunistic (see table p364), drug therapy, or advanced HIV *per se* . The presence of associated symptoms (fever, abdominal pain, blood, *per rectum*) should be established. An awareness of CD4 count will assist in directing management.
- Weight loss. Can be caused by advanced HIV infection, may be the result of chronic diarrhoea/malabsorption, may be the presenting symptom of underlying malignancy or opportunistic infection, or may represent toxicity to antiretroviral therapy (particularly subcutaneous fat loss).
- Abdominal pain. Can be a feature of GI infections (see p364), biliary tree disease, or pancreatitis (which may be drug induced, notably by nucleoside analogues, particularly ddI [didanosine]). Lactic acidosis and hepatic steatosis are rare complications of antiretroviral therapy that may present as vague abdominal pain.
- Loin pain/nephrolithiasis. A well-recognized side-effect of indinavir therapy. Stones are unlikely to be seen on plain X-rays and usually respond to conservative management with fluid input without need to discontinue the offending agent. With severe episodes (haematuria and confirmed calculi on renal tract investigation) change therapy as there is â†‘ risk of further episodes and progressive renal damage.

- Jaundice. May be the result of viral hepatitis (acute or chronic), biliary tract disease, drug-induced hepatitis, or hepatic involvement by other opportunistic infections or tumours.
- Dysphagia. Most commonly caused by candidal infection (oral *Candida* is usually present), and less commonly by ulceration secondary to HSV, VZV, CMV, or idiopathic (aphthous).
- Oral lesions. Oral C*andida* (usually in a pseudomembranous form, appearing as white plaques, but may be erythematous or hyperplastic) and oral hairy leucoplakia (white plaques on the side of the tongue) are common signs in individuals with HIV infection and may be the first presenting features of advancing infection. KS may present as red/purple macules on the palate or gingival margin.

Practice point

- There is an epidemic of acute hepatitis C and syphilis in sexually active gay males in the UK. Always test for these organisms if there are concerns or symptoms.

GI presentations in HIV positive patients: investigations

General investigations

- FBC, U&Es, LFTs. Check for evidence of anaemia, dehydration, hepatic dysfunction.
- Blood cultures. Bacterial GI infections are more likely to be accompanied by systemic infection in the

immunocompromised host. Mycobacterial blood cultures (particularly considering atypical mycobacteria in individuals with CD4 counts <100 cells/mm^3).

- Amylase. Check for pancreatitis in individuals presenting with abdominal pain.
- Uncuffed serum lactate. Consider the possibility of lactic acidosis in the unwell patient receiving antiretroviral therapy with non-specific abdominal symptoms. Send to a lab rapidly for an accurate result.
- Hepatitis serology. Consider acute hepatitis A/B in the jaundiced patient and chronic hepatitis B/C in patients with evidence of chronic liver disease. New onset of abnormal LFTs may be due to hepatitis C.

Specific investigations

- Stool specimens. Should be examined/cultured for bacteria and ova, cysts, and parasites. At least 3 stool specimens should be sent. *Clostridium difficile* toxin should be requested in individuals who have taken or are taking antibiotics. In an individual with severe immunosuppression (CD4 <100) and negative conventional stool analysis, examination for *Microsporidial* species should be performed.
- Abdominal X-ray. Look for evidence of toxic dilatation in the patient presenting with diarrhoea/abdominal pain. The major causes are CMV (with CD4 counts <100 cells/mm^3) and bacterial infections (*Salmonella, Shigella, Campylobacter*) at higher CD4 counts.
- Ultrasound scanning. Look for evidence of hepatic/biliary abnormality in patients with jaundice/abnormal LFTs, evidence of ascites in patients with abdominal distension, and abdominal masses/lymphadenopathy in individuals with opportunistic infections/tumours.
- CT scanning. Look for evidence of masses/lymphadenopathy

in individuals with abdominal pain, which may represent involvement by underlying opportunistic infections or tumours.

- Upper gastrointestinal endoscopy. Look for oesophageal lesions in patients with dysphagia, gastric lesions in patients with abdominal pain. Perform duodenal biopsies in individuals with chronic diarrhoea where no pathogen has been isolated.
- Sigmoidoscopy/colonoscopy. Look for evidence of involvement by opportunistic pathogens/tumours in patients with chronic diarrhoea or abdominal pain. Rectal/colonic biopsies should be performed in patients with chronic diarrhoea where no pathogen has been isolated.
- ERCP/MRCP. Should be considered in individuals with evidence of obstructive jaundice where no cause has been found, or in individuals with chronic abdominal pain looking for any evidence of ascending cholangitis.

GI presentations in HIV positive patients: Management

- General principles of rehydration, analgesia, and nutritional support should apply.
- Specific therapy should be directed towards the suspected/proven underlying cause (see table, p364). Consider empiric treatment with antibacterial agents (ciprofloxacin metronidazole) in the unwell patient with diarrhoea and additional anti-cytomegalovirus therapy (usually ganciclovir) if the CD4 count is <100 cells/mm^3 .
- Antiretroviral therapy should not be discontinued or modified without discussion with an experienced HIV clinician.

GI pathogens in HIV positive patients

Candida

- Oral: usually white plaques. Usually CD4 <350
- Oesophageal: dysphagia or odynophagia. Usually CD4 <200

- Usually based upon clinical appearance
- Can be confirmed by biopsy/culture

- Oral: usually with fluconazole (50mg Ã— 5 days) or 400mg stat
- Oesophageal: fluconazole 100mg od Ã— 14 days
- Higher doses of fluconazole or alternative agents may be recommended in cases of suspected/proven â€˜azoleâ€™ resistance

Salmonella

- Diarrhoea Â± fever, abdominal pain, and blood *per rectum* ; Colonic dilatation Â±. Any CD4 count

- Confirmed by stool (Â± blood) cultures
- Empiric treatment may be considered in the unwell patient

- Ciprofloxacin 500mg bd Ã— 7â€“14 days
- Cephalosporin if ciprofloxacin intolerant

Shigella

- Diarrhoea Â± fever, abdominal pain, and blood *per rectum* ; Colonic dilatation Â±. Any CD4 count

- Confirmed by stool (Â±blood) cultures
- Empiric treatment may be considered in the unwell patient

- Ciprofloxacin 500mg bd Ã— 7â€“14 days
- Trimethoprim if ciprofloxacin intolerant

Campylobacter

- Diarrhoea Â± fever, abdominal pain, and blood *per rectum* ; Colonic dilatation Â±. Any CD4 count
- Confirmed by stool (Â±blood) cultures
- Empiric treatment may be considered in the unwell patient
- Ciprofloxacin 500mg bd Ã— 7â€“14 days
- Erythromycin if ciprofloxacin intolerant

Crytosporidia

- May present acutely as â€˜travellers diarrhoeaâ€™ at any CD4 count which usually clears spontaneously, or chronically as watery diarrhoea with CD4 <100
- Demonstration of organism on stool analysis and/or biopsy
- No effective anti-microbial therapy (consider nitazoxanide). Acute crytosporidial infection usually resolves spontaneously; treat chronic infection with HAART

Microsporidia

- Watery diarrhoea in individuals with CD4 <100
- Demonstration of organisms by specific stool analysis or on biopsy/electron microscopy
- Albendazole is beneficial in some studies. Effective HIV treatment results in clinical improvement

Isospora

- Watery diarrhoea in individuals with CD4 <100
- AFB smear of stool
- Cotrimoxazole usually effective

Entamoeba histolytica

- Diarrhoea Â± blood and abdominal pain. Any CD4 count

- OC&P of stool
- Metronidazole 500mg tds or tinidazole then diloxanide

Giardia

- Watery diarrhoea. Any CD4 count
- OC&P of stool
- Metronidazole 250â€“500mg tds for 10 days or tinidazole

Cytomegalovirus

- Oesophageal: dysphagia with ulceration
- Gastric/upper GI : abdominal pain
- Colonic: diarrhoea Â± abdominal pain. Toxic dilatation may occur.
- CD4 <100
- Demonstration of organisms by immunocytochemistry of biopsy specimens
- Specific CMV therapy (usually ganciclovir 5mg/kg bd for 3â€“4 weeks).
- Effective anti-HIV therapy should reduce risk of recurrence/other end-organ disease

Herpes simplex
Herpes zoster
Mycobacterium avium complex

- Oesophageal ulceration, or proctitis/colitis
- Oesophageal ulceration
- Chronic, watery diarrhoea Â± abdominal pain. Usually systemic symptoms (fever, weight loss, pancytopaenia). CD4 <50
- Demonstration of organisms on biopsy/culture
- Demonstration of organisms on biopsy/culture
- Blood cultures (specific mycobacterial culture: may take several weeks), or demonstration of organisms on biopsy

- Aciclovir 200â€“800mg 5Ã—/day or 5mg/kg iv for 2â€“3 weeks
- Aciclovir 400â€“800mg 5Ã—/day or 5â€“10mg/kg iv for 2â€“3 weeks
- 3 agents (usually rifabutin, ethambutol, and clarithromycin or azithromycin)
- Effective anti-HIV therapy is associated with clinical response

Clostridium difficile

- Watery diarrhoea. History of antibiotics Any CD4 count
- Stool toxin assay
- Metronidazole 250â€“500mg qds Ã— 10â€“14 days
- Vancomycin 125mg qds Ã— 10â€“14 days

Pathogen Clinical presentation Diagnosis Treatment

Pyrexia of unknown origin

Assessment

- Look for signs/symptoms of focal infection
- Check for neutropenia
- Consider line sepsis if indwelling intravenous cannulae
- Consider drug-related fever (detailed drug history, including antiretroviral agents)
- Consider underlying lymphoma
- Detailed travel history essential.

Investigations

- Usual investigation of fever
- Cryptococcal antigen
- Mycobacterial blood cultures (MAI if CD4 <100)
- Consider
    - CT scan head
    - CT scan chest and abdomen
    - Lymph node biopsy (if significant lymphadenopathy)
    - Bone marrow examination
    - Gallium/white cell scan.

Treatment

- Unless clinically unwell, most clinicians would recommend withholding empiric antimicrobial therapy.
- Specific antimicrobial (or other) therapy should be directed against suspected underlying pathogen/process.

Dermatological presentations

- Consider drug-related causes (including antiretroviral agents), but do not discontinue antiretroviral agents (unless essential) without discussion with an HIV clinician.

  In particular, patients recently having commenced nevirapine therapy may be at risk of Stevens Johnson syndrome or toxic epidermal necrolysis, and patients having recently commenced abacavir may be at risk of a hypersensitivity syndrome (see, p370).
- Most dermatological complaints can behave atypically and

more severely in individuals with HIV infection.

- Shingles (*Varicella zoster*) may present with multi-dermatomal lesions and/or neurological involvement.
- Herpes simplex may present with more severe lesions and/or neurological involvement and requires higher doses of aciclovir than used in immunocompetent patients.
- Seborrhoeic dermatitis may present more aggressively in the HIV positive patient and may be recalcitrant to conventional therapy.
- Early syphilis should be considered in *any* HIV positive patient with dermatological lesions.

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Haematological presentations

Cytopaenias may be the result of HIV infection *per se* , antiretroviral (or other drug) toxicity, or bone marrow involvement by opportunistic infections or tumours.

- Mildâ€“moderate thrombocytopenia is a common finding in the HIV-infected patient; a severe ITP picture is well recognized. Usually responds to antiretroviral therapy, but steroids/immunoglobulin may be required in severe cases.
- Anaemia is a recognized side-effect of antiretroviral therapy [notably zidovudine (AZT) therapy].
- Neutropenia is a recognized side-effect of zidovudine (AZT), ganciclovir therapy and occurs more frequently in the HIV-infected patient receiving chemotherapy for malignancy. Standard management of neutropenia should apply.

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Antiretroviral toxicity 1

- Many clinicians are unfamiliar with the agents used to treat HIV infection. They are associated with multiple toxicities, some of which may present to the emergency clinician. Always consider discussing the case with a clinician experienced in use and toxicity of these drugs.
- The key principles of management are to recognize the possibility of iatrogenic illness and to exert caution in management. In order to minimize the risk of development of resistance and to preserve future treatment options, antiretroviral agents can be discontinued with discussion with an HIV clinician. If necessary, the toxic agent is switched and the withdrawal of one or two of a combination of agents (thus leaving an individual on suboptimal therapy) should be avoided.
- In individuals receiving antiretroviral therapy who present systemically unwell, the possibility of lactic acidosis should always be considered (see below).

Rash and hypersensitivity

- *Abacavir* hypersensitivity reaction (4%) can present as a fever or maculopapular rash (usually in first 2 months of treatment) often associated with one or more other symptoms or signs (fever; sore throat, GI or respiratory symptoms, laboratory abnormalities). If strongly suspected, abacavir should be discontinued and the patient *never* re-challenged (risk of fatal hypersensitivity reaction). This decision should be taken by an experienced HIV clinician.
- *Non-nucleoside reverse transcriptase inhibitors* (efavirenz and nevirapine): maculopapular rash (~10%) peaking at 2 weeks often associated with abnormal LFTs. Sometimes can be â€˜pushed throughâ€™ with antihistamines (cetirizine)

but needs close monitoring (associated severe or life-threatening hepatotoxicity not uncommon). Steven's Johnson syndrome and toxic epidermal necrolysis are well recognized but uncommon side-effects of nevirapine (â†‘ risk in women).

Mitochondrial toxicity

Usually attributed to the unwanted inhibition of mitochondrial DNA polymerase gamma by the nucleoside reverse transcriptase inhibitors (particularly stavudine and didanosine). Over months this can lead to mitochondrial dysfunction which can manifest as

- *Lactic acidosis/hepatic steatosis* resulting from general mitochondrial dysfunction. If suspected (general malaise, abdominal pain, metabolic acidosis, abnormal LFTs), an uncuffed blood sample should be sent for immediate lactate measurement and if high (>5mmol/L) with associated acidosis the offending drug(s) stopped. This condition can be rapidly fatal and admission to intensive care is occasionally required.
- *Acute pancreatitis:* particularly associated with didanosine (ddI) (also precipitated by alcohol, gallstones, pentamidine, and some OIs).
- *Myopathy* (muscle biopsy diagnostic): zidovudine (AZT).
- *Antiretroviral-induced peripheral neuropathy:* particularly associated with zalcitabine, stavudine, and didanosine.
- *Renal tubular acidosis/Fanconi's syndrome* have been rarely reported with tenofovir.

Practice point

- Always discuss treatment initiation/change with an

experienced HIV-clinician.

Antiretroviral toxicity 2

Metabolic disturbances

Hyperlipidaemia and glucose intolerance (including frank diabetes) have been associated with the use of antiretroviral therapy, particularly the protease inhibitors. The association with premature cardiovascular disease currently remains uncertain but is suggested by some cohort studies. The prescription of statins in this patient group should be made with care given the potential drugâ€“drug interactions; simvastatin is contraindicated in patients receiving protease inhibitors (pravastatin or atorvastatin are preferred).

Haematological toxicity

Nucleoside analogues [particularly zidovudine (AZT)] are associated with haematological toxicity especially anaemia and neutropenia which usually occurs during the first few weeks/months of therapy.

Hepatotoxicity

All of the available antiretroviral agents have been associated with hepatotoxicity, particularly in those individuals co-infected with hepatitis C/B. Nevirapine has been rarely associated with fulminant hepatitis (within the first 6 weeks of therapy). Hepatic steatosis (as part of a syndrome of mitochondrial dysfunctionâ€”as outlined above) is a well-recognized though rare complication of nucleoside analogue therapy. Most HIV physicians would closely monitor LFTs without discontinuation unless there is evidence of clinical hepatitis or an ALT/AST of >5â€“10 times the upper limit of normal.

Neurological toxicity

Efavirenz (and occasionally nevirapine) can cause significant neuropsychiatric disease. In the majority of patients this occurs in the first 4 weeks of therapy and can present as mood swings or depression. reatment is discontinued by 5â€“10% of individuals, though upto 50% will experience some symptoms of â€˜muzzy headâ€™ or nightmares.

Drug interactions with antiretroviral therapy

The protease inhibitors and non-nucleoside reverse transcriptase inhibitors are metabolized through the cytochrome p450 system and exhibit a wide variety of drug interactions, many of which have potentially serious consequences. It is recommended that co-administration of other P450-mediated agents should be with caution. Further information is available in the British National Formulary (BNF) or can be accessed via the Liverpool University website (http://www.hiv-druginteractions.org).

Post-exposure prophylaxis (PEP)

Evidence that PEP may be effective can be drawn from both animal and vertical transmission studies. The most compelling data are from a case-controlled study of healthcare workers where the administration of zidovudine (AZT) monotherapy was shown to be associated with approximately 80% reduction in HIV transmission.

Most hospitals/emergency departments will have established protocols for the management of PEP. However, the following general principles apply.

- The risk of HIV transmission is the product of the risk of the â€˜donorâ€™ being HIV and the risk of HIV infection from

the exposure.

- To estimate the risk of the donor being HIV positive, an understanding of the epidemiology of the â€˜risk groupâ€™ of the individual is helpfull.
    - For example, the risk of a homosexual man in the UK being HIV is estimated at 10â€“15% in London and 2.5% elsewhere.
    - The risk of an intravenous drug user being HIV is <5%. The risk of a heterosexual being HIV requires a knowledge of the HIV prevalence in the country in which they have been sexually active (as high as 20â€“50% in some sub-Saharan African countries).

Needlestick/Splash injury

The risk of HIV transmission from exposures has been estimated at

- Needlestick injury: 1 in 300
- Splash injury (to eyes or diseased skin): <1 in 1000.

Factors associated with increased risk include

- Donor: advanced HIV infection; high viral load
- Injury: hollow-bore needle; insertion of needle into artery or vein of patient; visible blood on device; deep injury.

Following assessment of the risk, consider PEP.

NB: Do not forget that optimal management of sharps injuries includes immediate wound management (bleeding and simple washing) and consideration of exposure to hepatitis B (assess

vaccination status and consider accelerated vaccination or immunoglobulin) and hepatitis C.

Sexual exposure

The risk of HIV transmission through sexual exposure is estimated as

- Unprotected vaginal sex (male to female): 1 in 1000
- Unprotected vaginal sex (female to male): 1 in 1000
- Unprotected anal sex (risk to insertive partner): 1 in 1000
- Unprotected anal sex (risk to receptive partner): 1 in 1000 to 1 in 30
- Oral sex with ejaculation: <1 in 25 000.

Given the potential opportunities for future risk reduction and concerns regarding PEP efficacy, HIV resistance, and drug toxicity in this setting, it is recommended that the decision to administer PEP after sexual exposure is taken in conjunction with clinicians experienced in GUM/HIV medicine.

PEP

A risk assessment should be carried out first. If the risk of infection is considered significant, PEP should be commenced as early as possible, ideally within 1 hour and certainly within 72 hours

Most hospitals recommend the administration of three agents:

- Zidovudine and lamivudine (co-administered as combivir, 1 tablet bd)
- A protease inhibitor (nelfinavir 1250mg bd or indinavir 800mg tds)

Notes

- The administration of PEP is associated with significant side-effects. The initial discussion and subsequent follow-up should be under the supervision of a clinician experienced in the use of these agents
- If the â€˜donorâ€™ is known to be HIV infected positive, ask about their antiretroviral therapy history, as this may alter the choice of PEP agents
- If the â€˜recipientâ€™ is pregnant or taking medications, be aware of the safety of these drugs in pregnancy and potential drugâ€“drug interactions
- Where possible, the â€˜donorâ€™ in such an injury should be encouraged to test for HIV to allow the discontinuation of PEP where possible. It is permissible to test such a donor for HIV without consent if they are deceased or unconscious (and unexpected to regain consciousness within 48 hours), though in the latter situation this should be performed on a previous blood specimen (see â€˜HIV testing â€™, p342)

Editors: Ramrakha, Punit S.; Moore, Kevin P.
Title: *Oxford Handbook of Acute Medicine, 2nd Edition*

Chapter 6
Renal emergencies

Acute renal failure (ARF)

Presentation

- Elevated creatinine (or urea) during biochemical screening
- Detection of oliguria by nursing staff.

Occasionally the patient may present to the A&E department with

- Malaise, confusion, seizures, or coma
- Nausea, anorexia, or vomiting
- Oliguria or abnormal urine colour
- Haematuria (pink rather than frank blood)
- Drug overdose (e.g. paracetamol)
- Constitutional symptoms (arthralgia, rhinitis, respiratory symptoms)
- Vasculitic rash
- Multi-organ failure.

In the majority of cases, their renal impairment can be resolved by adequate volume replacement, treatment of sepsis, and stopping nephrotoxic drugs. There are many causes of acute renal impairment, some of which, such as multi-system vasculitis or rhabdomyolysis, are important as their early diagnosis and treatment may have a profound effect on outcome (see table).

Assessment of severity

Patients with acute renal failure have a high mortality (~50%). The following history is important.

- History of fluid loss (D&V, diuretics, bleeding, fever). Diarrhoea may suggest haemolytic uraemic syndrome or hypovolaemia.
- History of sepsis (e.g. UTI, fever or hypothermia, bacterial endocarditis. Symptoms may be non-specific in elderly).
- Drug history NSAIDs, ACE-I, antibiotics in particular aminoglycosides and amphotericin, drugs for HIV disease.
- Non-specific symptoms (e.g. myalgia, arthralgia), neurological signs, ophthalmic complications, sinusitis, and skin rashes may suggest vasculitis.
- Past history of â†‘BP, DM, renovascular disease, prostatism, or haematuria.
- Patients with diabetes or myeloma have an increased risk of contrast induced renal impairment (avoid dehydration).
- Are there symptoms or signs of liver disease?
- Back ache may suggest pelvi-ureteric obstruction. Whilst this may affect a single kidney initially the other kidney is likely to become involved. Consider aortic aneurysm.
- Cholesterol emboli (aneurysms, absent pulses, rash).
- Post partum (HELLP syndrome, HUS, fatty liver, pre-eclampsia).

- Look for signs of fluid overload (dyspnoeic with signs of pulmonary oedema, high JVP or CVP, peripheral oedema, gallop rhythm) or dehydration (postural hypotension, â†“tissue turgor).

Poor prognostic features include

- Age >50 years
- Infection (esp. septicaemia)
- Burns (>70% surface area)
- Rising urea (>16mmol/24h)
- Oliguric for >2 weeks
- Multi-organ failure (>3)
- Jaundice.

The main priority is to try to prevent cardiovascular collapse and death, and to stabilize for transfer to a renal unit.

Assessment of patients with acute renal failure

- Is there life-threatening hyperkalaemia or pulmonary oedema?
- What is the likely cause?
- Is the patient still passing urine?
- Does it look normal?
- ECG
- Urgent U&Es + ABGs
- CXR

Pre-renal (75%)

- Check postural BP, HR
- Assess volume status, measure CVP
- Sepsis screen

Renal (20%)

- Urinalysis and microscopy for blood/casts
- Vasculitis screen
- Drug history
- CPK/myoglobin in urine

Post renal (5%)

- May have complete cessation of urine (anuria)

Acute renal failure: causes

Causes of acute renal failure

Pre renal

- Hypovolaemia
- Hypotension, shock (p258)
- Renal artery emboli
- Renal artery stenosis + ACEI
- Hepatorenal syndrome

Post renal(obstructive)

- Renal vein thrombosis
- Increased intra-abdominal pressure

- HIV drugs (indinavir)
- Intratubular (uric acid crystals)
- Ureteric
- Stones
- Retroperitoneal fibrosis/tumour
- Urethral
- Prostatic hypertrophy

Renal (parenchymal)

- Vasculitis (SLE, PAN)
- Glomerulonephritis
- Acute tubular necrosis
- Ischaemia (e.g. hypotension)
- Septicaemia
- Toxins (myoglobin, BJ proteins)
- Drugs (e.g. gentamicin), contrast
- Prolonged pre-renal oliguria
- Malaria
- Thrombotic microangiopathy
- Accelerated hypertension
- HUS/TTP (p704)
- Scleroderma crisis
- Sepsis

- Interstitial nephritis
- Drugs (NSAIDs, antibiotics)
- Infections (*Strep., Staph., Leptospirosis, Brucella*, G -ve sepsis, *Legionella*)
- Calcium, urate, oxalate overload
- Tumour lysis syndrome (p730)

Causes of immune-mediated ARF and vasculitis

- Microscopic polyangiitis
- Wegener's granulomatosis
- Churgâ€“Strauss syndrome
- Polyarteritis nodosa
- SLE
- Rheumatoid arthritis (and treatment)
- Goodpasture's syndrome
- Cryoglobulinaemia
- Henochâ€“SchÃ¶nlein purpura
- Acute proliferative glomerulonephritis
- Acute interstitial nephritis
- HIV
- Myeloma
- Leptospirosis (interstitial nephritis) or Hanta virus (pulmonaryâ€“renal syndrome)
- Infective endocarditis
- IgA nephropathy (rarely)

- Drugs (penicillamine or amphetamines)

Urgent investigations for patients with ARF

- U&Es
- FBC and blood film
- Coagulation studies (PT, APTT, TT, fibrinogen, FDPs)
- CPK, urinary myoglobin
- Haptoglobin
- Blood cultures
- Urine MC&S
- Urine Na^+ and osmolality
- ECG
- CXR
- USS kidneys (size of kidneys, obstruction)
- Consider other investigations to aid in diagnosis (see p382)

Acute renal failure: investigations

Blood tests

â€¢ U&Es	Urea is disproportionately raised in pre-renal uraemia, GI bleeds, catabolic states

â€¢ Ca^{2+}, PO_4^{3-}	Acidaemia increases ionized Ca^{2+}.
â€¢ FBC	Anaemia suggests chronic or acute on chronic renal failure. â†“platelets: liver disease, HELLP, sepsis. with MCV, blood film (HUS, myeloma, left shift). â†‘Platelets: vasculitis (e.g. Wegener's) eosinophilia, Churgâ€“Strauss syndrome, interstitial nephritis
â€¢ Coagulation	Abnormal in DIC, liver disease, SLE, HELLP syndrome, HUS
â€¢ LFTs	Acute hepatitis, paracetamol overdose, cirrhosis. Alkaline phosphatase often â†‘ in vasculitis
â€¢ LDH/HBD	Increased in HUS
â€¢ CPK	Very high in rhabdomyolysis
â€¢ Blood cultures	Should be taken from all patients with ARF
â€¢ Immunology	ANCA, anti-GBM, Igs, C3/C4, Rh factor, ANA, ENA, dsDNA, cryoglobulins, anti-cardiolipin and anti-Î²2-glycoprotein-1 antibodies (anti-phospholipid syndrome)

â€¢ ESR/CRP	CRP is often normal, ESR high in SLE
â€¢ Protein strip	For paraproteins (myeloma, light chain disease)
â€¢ HIV, HBsAg, HCVAb	Serology required for dialysis.

Urine

- Inspect the urine yourself. Contact the renal registrar or microbiology technician on call to arrange urgent microscopy. Save urine for cytology if haematuria is the dominant symptom.
- Send a specimen to microbiology for microscopy and culture.
- *RBC casts* suggest glomerulonephritis (refer to renal physician urgently), *pigment casts* suggest myoglobinuria, *WBC casts* suggest acute pyelonephritis. *Excess eosinophils* in the urine are associated with interstitial nephritis.
- Save a specimen for Benceâ€“Jones protein if myeloma is suspected.
- *Urine electrolytes and osmolality:* these may help but do not replace careful clinical examination and are unreliable when diuretics have been given. They may be less reliable in the elderly when sub-clinical renal impairment may be present. See table.

Other investigations

â€¢ USS	All patients with ARF should have an *urgent* ultrasound to exclude obstruction and to assess kidney size (small in acute-on-chronic failure), and blood flow on Doppler imaging.
CXR	Look at the heart size (dilated, pericardial effusion), pulmonary vasculature (pulmonary oedema, Kerley lines), lung fields (â€™fluffyâ€™ shadows: oedema, haemorrhage of Goodpasture's or Wegner's, infection).
ECG	Look for changes of hyperkalaemia (tented T-waves, QRS broadening) and signs of myocardial ischaemia or pericarditis.

Urinary electrolytes and osmolality in renal failure

	Pre-renal	Renal (ATN)
Urine Na^+ (mmol/l)	<10	>40
Urine/serum creatinine	>40	<20
Urine osmolality	>500	<350
Urine/serum osmolality	>1.2	<1.2

NB: The table above assumes that the patient is not taking diuretics.

Acute renal failure: management

Hyperkalaemia

In general terms the absolute K^+ concentration is less important than the effect on the cardiac conducting tissue (tented T-waves, broad QRS, flattened P-wave), but if the K^+ is >7mmol/L then treat urgently. If the hyperkalaemia is an unexpected isolated finding, and there are no ECG signs of hyperkalaemia, then repeat K^+ urgently.

If there are ECG changes or K^+ >7mmol/L, contact the renal team and arrange for urgent dialysis if appropriate. While this is being set-up

- Record 12-lead ECG, attach to cardiac monitor.
- Give *10ml of 10% calcium gluconate iv*, repeated every 10â€“20 minutes until ECG normalizes (patients may require up to 50ml). iv calcium does not lower the potassium level but reduces cardiac excitability.
- Give *nebulized salbutamol* (5â€“10mg) to drive K^+ intracellularly (use lower doses in patients with ischaemic heart disease).
- *50ml 50% dextrose with 10U actrapid insulin* over 15â€“30 minutes (monitor blood glucose); this should lower K^+ for several hours.
- *50â€“100ml 8.4% bicarbonate iv via central line over 30 minutes* (or 400ml 2.1% peripherally): represents a Na^+ load of 50â€“100mmol.
- 250mg *frusemide* or 5mg *bumetanide* iv over 1 hour.
- Polystyrene sulphonate resin enema (*calcium resonium*Â®) 30g increases gut losses of potassium. Follow with 15g po tds with regular lactulose. This takes 24 hours to work.

- Monitor serum K^+ frequently to assess response to treatment.

Fluid balance

- Manage on HDU or ITU
- Measure weight, BP (supine and sitting or upright), and pulse rate
- Assess hydration (central skin turgor, mucous membranes, and JVP)
- Insert central venous line and measure CVP. Monitor PCWP in patients who are hypoxic or severely compromised
- Examine fluid and weight charts, and operation notes if applicable.

If *volume depleted*

- If the patient has a low or normal CVP Â± postural hypotension give a trial of volume expansion (500ml of colloid or N saline) over 30 minutes. Monitor response of urine output and venous pressure. Continue fluids until CVP is 5â€“10cm at mid-clavicular line.
- When adequately filled (CVP >10 and/or PCWP >15) reassess urine output. If oliguric or anuric give frusemide 120mgâ€“250mg IVI (max. 4mg/min), followed by a frusemide infusion of 5â€“10mg/h. It is much easier to manage a patient passing urine than one who is oligo-anuric.
- If hypotension persists (MAP <60mmHg) in spite of adequate volume replacement (i.e CVP of >10cm), commence inotropic support (see p263).

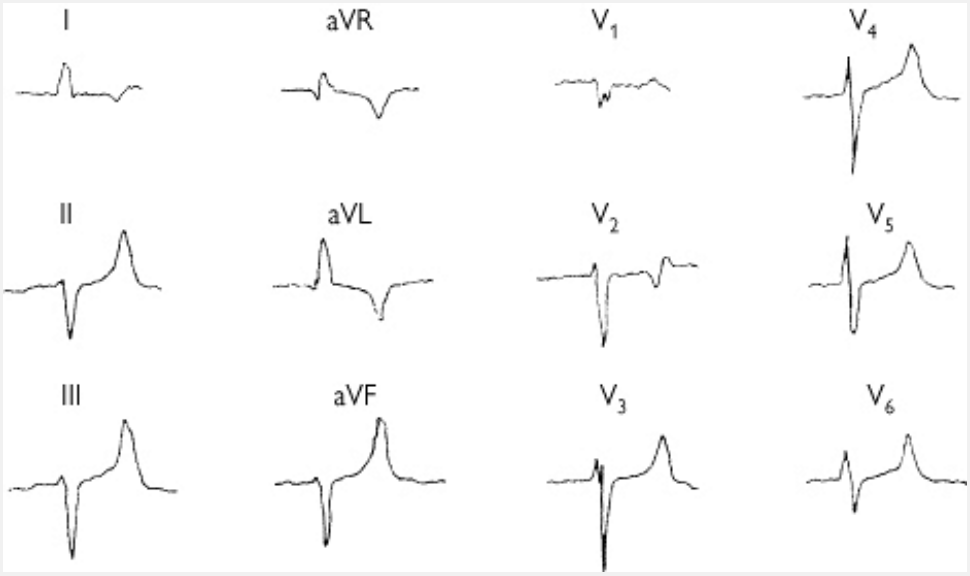
If *fluid overloaded*

- Consider urgent haemofiltration or dialysis. Consider venesection if there is a delay for dialysis; remove 250â€“500ml.
- Give oxygen to maintain SaO_2 >95%. Consider CPAP (p904).

- Start intravenous nitrates (e.g. GTN 2â€“10mg/h iv).
- Give iv frusemide: 120mgâ€“500mg, followed by infusion (5â€“10mg/h).
- Paracentesis if tense ascites is present (p926).
- Avoid opiates, although a single dose (e.g. 2.5mg diamorphine iv) may help relieve anxiety and the sensation of breathlessness.

Indications for dialysis

- Persistent hyperkalaemia (K^+ >7mmol/L)
- Fluid overload (e.g. refractory pulmonary oedema)
- Pericarditis (heralds the risk of tamponade, p178)
- Acidosis (arterial pH <7.1, bicarbonate <12mmol/L)
- Symptomatic uraemia (tremor, cognitive impairment, coma, fits, urea typically >45mmol/L)



ECG changes in hyperkalaemia

Acute renal failure: further management

Treatment of life-threatening hyperkalaemia, severe fluid overload, or dehydration take priority (p384).

Correct other abnormalities

- Acidaemia. Classically produces sighing respirations (Kussmaul's breathing) and may worsen hypotension (impaired cardiac function):
    - If pH is <7.2 give 100ml of 8.4% bicarbonate via central line over 15â€“30 minutes (or 400ml 2.1% bicarbonate peripherally)
    - Arrange urgent dialysis
    - Correction can cause symptomatic hypocalcaemia.

- Hyponatraemia. Usually dilutional (relative water excess). Management is discussed on p594.
- Hyperphosphataemia. If the product of $[Ca^{2+}]$ Ã— $[PO_4^{3-}]$ is >4.6 the risk of â€˜metastaticâ€™ precipitation is high. Aim to lower PO_4^{3-} to 0.6â€“1.4mmol/L. Give oral PO_4^{3-} binders (e.g. calcium carbonate 300â€“1200mg q8h po). The PO_4^{3-} usually falls with dialysis or haemofiltration. A new agent, Sevalemer, will also lower PO_4^{3-} concentrations (use 806mg tds).
- Nutrition. There is no role for protein restriction. Institute enteral or parenteral feeding early. In patients with diabetes, insulin requirements fall with renal impairment.
- Sepsis. Common precipitant/complication of ARF. Culture blood, urine, and specimens from other potential sites of infection. Treat with appropriate antibiotics remembering to adjust the daily dose in view of the renal impairment (septic shock is covered on p270).

Further measures

The causes of ARF are listed on p380. Most cases are multi-factorial with volume depletion or hypotension, sepsis, and drugs (e.g. injudicious use of ACE-I and NSAIDs), urinary tract obstruction and/or pre-existing chronic renal disease. It is essential to identify treatable conditions.

In practical terms it is probably most simplistic to divide patients into those with pre-renal, renal, and post-renal acute renal failure using *clinical assessment, filling pressures* (CVP, PCWP), and *USS*. Whilst sepsis is included as a renal cause, much of the early deleterious effects (i.e. hypotension) are potentially reversible with appropriate management. The principles of further management are as follows.

- *Optimize fluid balance*: there is no substitute for painstaking physical examination. Careful fluid balance

charts and daily weights guide replacement. Limit fluid intake to total fluid output plus 500ml/day. The best sign of intravascular volume depletion is postural drop in BP.

- *Intrinsic renal disease*: oliguria is reversed by restoration of circulating volume or blood pressure, but takes up to 8 hours to respond fully. It is important that fluid balance is optimized (CVP of 5â€“10cm, MAP of >75mmHg). If diuretics fail to improve urine output, ATN is likely to be established, and the patient will require renal support.

- Patients with severe portal hypertension and ascites may have marked oliguria (~250ml urine per day), and maintain a normal creatinine. Their urine is very concentrated and virtually devoid of sodium. They are usually resistant to diuretics, but may respond transiently to volume expansion. Beware of precipitating electrolyte or renal dysfunction by over-diuresis.

Anuria

Anuria implies that there is no urine output.

Causes

- Obstructed urinary tract (bilateral ureteric or bladder outflow)
- Renal infarction (e.g. prolonged hypotension in patients with atherosclerotic stenosis of renal arteries)
- Acute renal failure (p378).

Assessment

Assess as for ARF. However, also

- Ask specifically about symptoms of prostatism, or haematuria (tumour) and back ache (stones, aneurysm)
- Drug history (ACE inhibitors) as a possible cause of renal infarction, recent antibiotics, NSAIDs (interstitial nephritis)
- Recent renal angiography or angioplasty (renal infarction, contrast nephropathy)
- Constitutional symptoms suggestive of glomerulonephritis
- Has the patient previously lost a kidney?

Management

(see â€˜acute renal failureâ€™, p384)

If patient is anuric

- Examine for palpable bladder, enlarged prostate, or other pelvic masses. Insert urinary catheter to exclude retention
- If the bladder is empty, an urgent ultrasound is needed to exclude bilateral obstruction (or obstruction of solitary functioning system). Treat bilateral hydronephrosis with nephrostomies. Antegrade imaging can determine the level of obstruction
- If the USS is negative arrange a CT scan of the abdomen
- If obstruction is absent (one cannot exclude acute obstruction on USS) an isotope renogram will determine whether there is renal perfusion. If there is renal perfusion, then a retrograde ureterogram will determine whether there is obstruction. Absent renal perfusion suggests renal infarction.

Interstitial nephritis

This is caused by inflammatory cell infiltration of the renal parenchyma, usually induced by drugs (NSAIDs, penicillin, cephalosporins, sulphonamides, allopurinol, rifampicin, mesalazine, interferon), some infections (e.g. *Legionella, Leptospirosis*, viral), granulomatous interstitial nephritis (e.g. sarcoidosis). Other causes include DM, sickle cell disease, reflux nephropathy, renal transplant rejection.

Presentation. Acute renal failure, Â± fever, eosinophilia, and urinary eosinophils. Precipitating cause usually precedes renal impairment by a few days to 2 weeks (very variable).

Diagnosis. Renal biopsy.

Treatment. Stop offending drug. The use of steroids in this setting remains controversial.

Indications for renal biopsy

- Cause is unknown
- Heavy proteinuria (>2g/day)
- Features of systemic disease
- Active urinary sediment
- Immune mediated ARF
- Prolonged renal failure (>2 weeks)
- Suspected interstitial nephritis (drug induced)

Rhabdomyolysis

This is the development of ARF secondary to extensive muscle damage and release of myoglobin. Approx. 7% of all cases of ARF.

Presentation

- Most cases occur following muscle trauma (e.g. crush syndrome) or severe physical exertion [e.g. marathon running or military training (â€™squat jump syndromeâ€™)].
- Prolonged immobility (e.g. after drug overdose and coma) may result in pressure necrosis of the muscles.
- Symptoms include swollen tender muscles, dirty red-brown urine (like Coca-ColaÂ® mixed with urine) and/or oliguria.
- Malignant hyperthermia or malignant neuroleptic syndrome.
- Myoglobin is present in muscle as ferrous myoglobin (Fe^{2+}), and myoglobin is deposited in the kidney as ferric myoglobin (Fe^{3+}). Further oxidation of myoglobin by hydroperoxides generates a potent oxidizing species ferryl-myoglobin (Fe^{4+}) that causes renal injury. Alkalinization works by stabilizing the ferryl-myoglobin and making it less reactive.

Investigations

â€¢ U&Es	Typically â†‘â†‘K^+, â†‘creatinine : urea ratio
â€¢ Ca^{2+}, PO_4^{3-}	â†‘â†‘PO_4^{3-}, initial â†“Ca^{2+} (as it enters damaged muscle) followed by â€˜reboundâ€™ â†‘Ca^{2+}
â€¢ Urate	Usually â†‘â†‘ with tissue necrosis, also â†“ excretion

â€¢ LFTs	AST very high: from skeletal muscle
â€¢ CPK	Very high (up to 1 million u/L)
â€¢ ABG	Metabolic acidosis, hypoxic if here is associated acute lung injury (trauma) or infection
â€¢ Urine	The urine looks red-brown. Urinalysis is positive for blood (myoglobin tests positive), but no RBC seen on microscopy. Urinary myoglobin is diagnostic
â€¢ Misc.	aC, glucose, blood cultures, ESR, CRP, serum for toxicology Â± virology, plasma myoglobin, ECG. Serum looks clear (cf. haemolysis) as myoglobin does not bind haptoglobins and is rapidly cleared by kidneys.

Management

Patients are often febrile, dehydrated, and unwell. The priorities are

- Hyperkalaemia needs urgent treatment (see p384)
- Rehydration: in elderly patients or if the patient is oliguric, insert a central line and be guided by CVP. Watch for fluid overload
- Alkaline diuresis (see p834): alkalinization stabilizes the oxidizing form of myoglobin. It is usually effective within

the first 8 hours. Test urine regularly with pH strips to monitor treatment

- Analgesia: avoid NSAIDs: use opiate analgesia if required
- Avoid frusemide: this may precipitate myoglobin in the renal tubules
- Refer for a surgical opinion. Fasciotomies or debridement of necrotic tissue may be needed for compartment syndrome

- Avoid Ca^{2+} infusion to treat hypocalcaemia: it may cause metastatic calcification in damaged muscle and cause further tissue necrosis. However, iv Ca^{2+} is indicated for patients with severe hyperkalaemia
- Treat the underlying cause (see table)
- Dialysis or haemofiltration may be necessary for the short term but full recovery of renal function is likely.

Causes of rhabdomyolysis

- Crush injury
- Severe exertion, heat stroke
- Prolonged convulsions
- Prolonged immobility
- Polymyositis or viral myositis
- Malignant hyperpyrexia (p606)
- Acute alcoholic binge
- McArdle's syndrome
- Hypokalaemia
- CO poisoning (p802)
- Burns

- Diabetics ketoacidosis (p556)
- Ecstasy abuse (p810)
- Snakebite (p864)
- Electric shock (p854)
- Neuroleptic malignant syndrome

Hepatorenal syndrome

This is defined as the onset of renal failure in patients with severe liver disease in the absence of renal pathology. It may occur in either cirrhosis or acute liver failure. It may be characterized by a low urine sodium (<10mM), but this is *not* a criterion in the diagnosis.

Presentation

- Renal failure is most commonly found as incidental finding during biochemical screening of patients with ascites (cirrhosis), acute liver failure, or jaundice (most common in alcoholic hepatitis).
- Precipitants of hepatorenal syndrome in patients with advanced liver disease include injudicious diuretic use, paracentesis, porto-systemic shunt surgery, and contrast radiography (esp. biliary).

There are many causes of renal failure and liver disease which are *not* synonymous with hepatorenal syndrome. These include

- Hypovolaemia: caused by bleeding, over-diuresis, or post paracentesis circulatory dysfunction
- Sepsis
- Nephrotoxic drugs given to patients with liver disease (e.g.

gentamicin)

- Chronic viral hepatitis (HBV or HCV) causing glomerulonephritis
- Leptospirosis (marked hyperbilirubinaemia, other liver enzymes virtually normal)
- Paracetamol overdose.

Investigations

- See â€˜acute renal failureâ€™, p382.

Management

- Exclude other causes of renal failure in liver disease (see above).
- Insert a urinary catheter and monitor urine output.
- Volume challenge (500ml HaemaccelÂ® followed by 1L N saline over 2 hours. Stop all diuretics.
- Broad-spectrum antibiotics (e.g. cefotaxime + metronidazole, or ciprofloxacin + amoxycillin).
- If mean arterial pressure [diastolic pressure + (systolic - diastolic pressure) Ã· 3] is <75mmHg administer a vasopressor agent after volume expansion. The most appropriate agent is glypressin at 0.5â€“1mg iv bolus every 4â€“6 hours, or noradrenaline (1â€“10Âµg/min). Midodrine together with octreotide has also been used.
- N-acetylcysteine 100mg/kg bd by iv infusion may improve renal function if all else fails. Controlled trials are needed.
- If there is tense ascites, a total paracentesis will decrease the renal venous pressure and enhance renal blood flow (see p926).

- Haemofiltration or dialysis: patients tolerate haemofiltration better than haemodialysis. There is *no* value in dialysing a patient with end-stage cirrhosis and renal failure unless the patient is going to have a liver transplant. It is, however, reasonable to dialyse a patient with a reversible cause of liver failure (i.e. acute liver failure or acute alcoholic hepatitis).
- Hyperkalaemia and acidosis are rarely a problem.
- All patients should be discussed with a liver transplant centre. Hepatorenal syndrome can be reversed by liver transplantation, but the prognosis from liver transplantation is worse in this group.

Acute upper urinary tract infections

Infection of the upper urinary tract may result in acute pyelonephritis, renal abscess, pyonephrosis, or perinephric abscess (see figure). Infection with obstruction causes rapid tissue destruction unless the obstruction is relieved.

Predisposing factors

Either an ascending infection or haematogenous spread.

Organisms: *E. coli* 60%, *Proteus* 20%, *S. faecalis* 10%, *Klebsiella* 5%.

- Female (short urethra)
- Renal stones
- Bladder catheter
- Chronic liver disease
- Structural abnormality of renal tract
- Pregnancy

- Diabetes mellitus
- Intravenous drug abuse
- Infective endocarditis

Presentation

- Classical symptoms are loin pain, fever, and rigors.
- Non-specific symptoms may predominate: e.g. nausea, vomiting, anorexia, malaise, confusion, or weakness.
- Up to 75% have preceding lower urinary tract symptoms (frequency, dysuria). There may be associated haematuria.
- Severe, bilateral pyelonephritis or acute-on-chronic pyelonephritis may result in acute renal failure.
- A preceding history of intermittent loin pain may imply intermittent obstruction with pyonephrosis. Renal parenchymal abscesses are seen with iv drug use, endocarditis, or skin infections.
- Ask specifically about any predisposing factors (see above).
- Signs include fever, abdominal or loin tenderness, a palpable mass in the loin, and with severe infection, scoliosis concave towards the affected side, hypotension, and shock (septicaemia).
- The symptoms and signs may be difficult to distinguish from pneumonia (pleuritic pain and shallow breathing on affected side) or other causes of an acute abdomen (e.g. cholecystitis, diverticulitis).

Investigations

- Urinalysis commonly shows blood and protein. Urine nitrite is often positive. White cells, bacteria, WBC casts may be

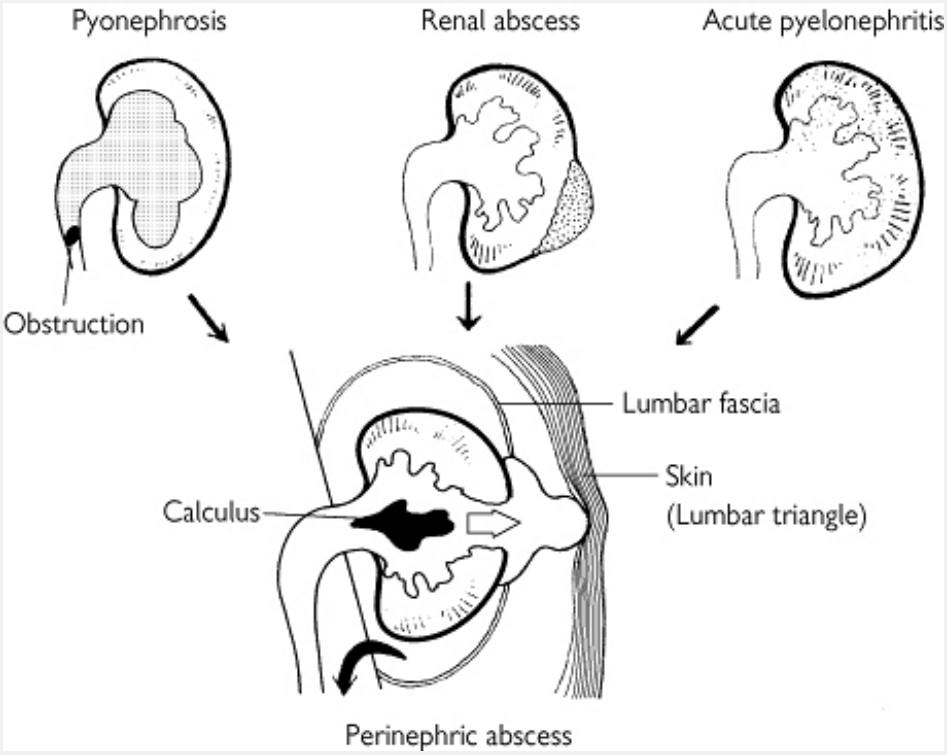
seen on microscopy. Culture may be negative in infections confined to the renal cortex.

- All patients should have U&Es (for renal dysfunctionâ€“dehydration, acute-on-chronic failure), glc, FBC (anaemia, leukocytosis) and blood cultures.
- AXR: stones, soft tissue mass, or loss of psoas line on affected side.
- USS to exclude obstruction and delineate renal and peri-renal collections. Arrange CT if surgery is planned.

Management

- Stabilize the patient: resuscitate severely ill patients with iv fluids Â± inotropes, guided by CVP and BP.
- Give iv antibiotics, e.g. cefuroxime 750mg tds and modify treatment in light of results of cultures. Continue antibiotics for total 7â€“14 days.

- Fluid balance: maintain high fluid intake (e.g. 3L/24h). Monitor fluid balance and urine output carefully for the first 48â€“72 hours.
- Analgesia: try NSAID if renal function is normal.(e.g. diclofenac sodium 75mg im). Alternatively try im pethidine 50â€–75mg q3h prn.
- Pyonephrosis, renal or perinephric abscess: requires urgent advice: contact the urologists. Remember to save a sample for MC&S.
- Investigate for any underlying cause: IVU, DMSA, and DTPA scans will determine anatomy, extent of renal damage, and remaining function.



Patterns of renal infections

Renal colic and renal stones

Spasmodic pain radiating from loin to groin usually due to stones or blood clots. ~2â€“3% of population have a stone in the upper urinary tract.

Presentation

- Pain: the site of the pain may vary, stones in the renal pelvis cause dull loin ache, ureteric stones produce severe colicky pain often of sudden onset radiating from loin to groin, bladder stones cause suprapubic and perineal or testicular ache and strangury.
- Haematuria (often frank) may be the only feature.

- With severe pain the patient will be restless, sweaty, pale, nauseated, and very distressed.
- Try to obtain a history of previous episodes, UTIs, fluid intake, occupation, periods of residence in hot climates, symptoms of hypercalcaemia, or family history of stone disease.
- On examination note any fever, abdominal tenderness (especially loin or subcostal), palpable kidneys. Do not miss a leaking abdominal aortic aneurysm that may be producing similar symptoms.

Investigations

Acutely, the tests required are

- Bloods: U&Es (for renal dysfunction) and glucose, FBC (for Hb, WCC)
- Urine: dipstick urinalysis for blood and formal microscopy for crystals, pyuria, and bacteria. Culture for infection
- AXR: the plain AXR film will detect >90% of stones
- CT scan or USS will show obstruction.

Other investigations to determine the underlying cause of the renal colic (stone formation, papillary necrosis, or clot) can usually be performed once the acute episode has been dealt with. Tests to consider include serum Ca^{2+} and urate (see p580 for investigation of hypercalcaemia) and 24-hour urine for Ca^{2+}, phosphate, oxalate, urate to detect a stone-forming metabolic defect.

Management of acute renal colic

- Analgesia: diclofenac sodium 75mg im repeated after 30 minutes. If needed pethidine 50â€“100mg im q4h prn with

an antiemetic.

- High fluid intake.
- Beware of infection above the stone and pyonephrosis (p397). If there is fever, bacturia, or obstruction treat empirically until culture results are known (e.g. cefuroxime 750mg iv tds) and decompress any obstruction.
- Large-sized stones with infection or obstruction require urological management such as ureteroscopic extraction or extracorporeal shock wave lithotripsy, or surgery.

Prognosis

~60% of all stones will pass (half of these within 48 hours). ~30% will require surgical removal. The risk of stone recurrence may be reduced by dietary advice (e.g. avoid high-oxalate foods such as rhubarb, spinach), a high fluid intake, controlling hypercalciuria (low-calcium diet, thiazide diuretics, bran), treating the cause if hypercalcaemic (p580), urinary alkalinization (hyperuricaemia, renal tubular acidosis, cystinuria), urinary acidification to pH <5.5 Â± urease inhibitors (struvite stones), allopurinol (urate stones) or d-penicillamine (cystine stones).

Causes of renal colic

Renal stones

Usually divided into *Radio-opaque (90%)*: contain Ca^{2+} or Mg^{2+}, e.g. calcium oxalate (hypercalciuria, hypercalcaemia, dehydration, renal tubular acidosis, medullary sponge kidney, hyperoxaluria), calcium phosphate (as before and UTIs), magnesium ammonium phosphate (UTIs with urease-positive organisms, e.g. *Proteus*). Cystine stones are â€˜semi-opaqueâ€™ due to their sulphur content

Lucent: (Urate or xanthine or rarely 2,8 dihydroxyadenine)

Indinavir crystal deposition (HIV drug)

Renal papillary necrosis

DM, sickle cell disease, analgesic nephropathy. Pain occurs when a papilla â€˜sloughsâ€™ into the ureter

Blood clots

Due to trauma, tumour (parenchymal or urothelial), bleeding diathesis, or polycystic kidney disease

Haematuria

History

Ask specifically about

- Severity of haematuria: pink urine, frank blood, or clots?
- The timing of haematuria: bleeding occurs at start or end of micturition suggests bladder neck, prostate, or urethral source. Blood mixed with the stream suggests a source higher in the urinary tract.
- History of trauma: even seemingly minor trauma can cause bleeding from congenital lesions of the urinary tract.
- Unilateral loin pain: consider calculi, tumour, cystic disease, or hydronephrosis. Painless haematuria suggests neoplasm.
- Disturbance of micturition: frequency, urgency, dysuria, hesitancy, poor stream, and dribbling suggest cystitis.

Bleeding and pain at the end of the stream is typical of a bladder stone.

- Constitutional symptoms: sore throats, arthralgia, malaise, and rash may indicate glomerulonephritis. AF is associated with renal emboli. Fever, dysuria, or abdominal pain may indicate infection. Bruising or other bleeding may indicate a bleeding diathesis.

Physical examination

- General examination. Hypertension (chronic or acute renal disease incl. polycystic disease), irregular pulse or heart murmurs (source of emboli), anaemia, bruising or purpura, oedema or pleural effusions.
- Urinary tract examination. Loin or abdominal tenderness, renal mass, pelvic mass, prostate enlargement, testes. Inspect the urine.

Investigations

â€¢ Urinalysis	Positive result seen with myoglobinuria (p392) and haemoglobinuria. Proteinuria suggests renal pathology
â€¢ Microscopy	RBC casts or dysmorphic red cells suggest glomerular origin. WBC casts suggest pyelonephritis. Other findings include crystals (stone disease), ova (schistosomiasis), and malignant cells
â€¢ FBC	Thrombocytopenia anaemia (haemolysis, leukemia), leukocytosis may indicate infection

â€¢ U&Es	For renal function
â€¢ Clotting	For coagulopathy
â€¢ G&S	If post traumatic or severe
â€¢ ASOT, Câ€™	If glomerulonephritis is suspected. Consider measuring autoantibodies. Refer to renal team
â€¢ Ultrasound	May diagnose polycystic disease, ureteric obstruction by stone or tumour, or gross renal abnormalities
â€¢ CT Scan	May demonstrate stones, hydronephrosis, renal injury or tumour, cystic disease, or urothelial tumour
â€¢ Cystoscopy	To exclude other causes of bleeding from the lower urinary tract.

Management

- Admit patients with
    - Post-traumatic haematuria (refer to urology)
    - Severe unexplained haematuria (incl. bleeding diathesis) esp. if there is clot retention. Insert a large (22G) triple lumen urinary catheter for continuous bladder irrigation to wash out clots

    - Haematuria and renal impairment (? glomerulonephritis). Arrange for urgent renal referral and biopsy
    - Severe infection, e.g. pyelonephritis. Commence antibiotics (e.g. cefuroxime Â± gentamicin) after taking appropriate cultures.
- Pain relief (pethidine 25â€“50mg iv with an anti-emetic). Pro-BanthineÂ® (propantheline bromide) 15mg tds po relieves painful bladder spasm of haemorrhagic cystitis and clot retention (may cause urinary retention).
- Correct any bleeding diathesis (FFP Â± Vit K for warfarin).

Causes of haematuria

Trauma	Blunt and penetrating injuries, iatrogenic (e.g. recent TURP, TURBT, or renal biopsy), severe exercise (â€™joggers haematuriaâ€™), foreign body
Stones	Renal, ureteric, or bladder
Infections	Pyelonephritis, haemorrhagic cystitis, acute prostatitis: bacterial, TB, or parasitic (e.g. schistosomiasis)
Tumours	Urothelial, renal parenchymal, prostatic
Bleeding diatheses	Haemophilia, thrombocytopenia

Renal pathology	Glomerulonephritis, renal arterial emboli, renal vein thrombosis
Drugs	Anti-coagulants, cyclophosphamide, d-penicillamine
Congenital	Polycystic disease, sickle cell disease (papillary necrosis), Alport's syndrome, hydronephrosis.

NB: Discoloured urine may also be due to beetroot, porphyria, rifampicin, co-danthramer, and vegetable dyes.

Renovascular disease

Renal artery stenosis may be atherosclerotic (common in the elderly and diabetics) or fibromuscular hyperplasia (generally younger patient without vascular disease elsewhere). It should be considered in all patients with

- Flash pulmonary oedema (sudden unexpected onset)
- Peripheral vascular disease, aortic dissection, type 2 diabetes
- Unequal kidneys on USS
- Impaired renal function in context of ACE inhibitor use
- Hypertension/coronary or carotid artery disease
- Complete anuria in a patient who has previously lost a kidney.

Investigations

- Ultrasound scan: to look as renal size and Doppler flow through the renal arteries.
- Isotope renogram: Done before and after giving an ACE inhibitor (captopril); GFR falls on the side with the stenosis.
- MRA is taking over from angiography as the gold standard investigation in some hospitals: be guided by your local radiologists. Ensure the patient is well hydrated pre, and maintains a good fluid intake post procedure.
- Digital subtraction angiography is sometimes used.

Management

- Optimize fluid status (see p384). There is often a fine balance between pulmonary oedema and pre-renal uraemia.
- Avoid ACE inhibitors and NSAIDs.
- Refer to a dedicated team of interventional radiologists and vascular surgeons. Generally speaking if the kidney is >8cm then salvage may be possible. If the kidney is small (<8cm), then intervention is probably hazardous and without benefit.
- Treatment may be by angioplasty, stenting, or bypass surgery. Remember BP control and treatment of other risk factors; the majority of patients with atheromatous renovascular disease die from their associated ischaemic heart disease.

Cholesterol embolism

Most commonly seen in arteriopaths after manipulation of vasculature (e.g. angiography) and is followed by acute renal

failure. Usually silent. There is partial occlusion of small- and medium-sized arteries resulting in ischaemic atrophy. More florid presentation includes widespread purpura, dusky and cyanotic peripheries with intact pedal pulses, GI bleeding, myalgia, and acute renal failure. It can be spontaneous or follow therapy with heparin or warfarin.

Diagnosis. Eosinophilia, renal impairment, hypocomplementaemia, ESR, ANCA negative. Urinary sediment is usually benign; mild proteinuria may be seen. Renal biopsy shows cholesterol clefts.

Management. The renal impairment is usually irreversible or only partially reversible (in contrast to ATN). Anti-coagulation is contraindicated. Treatment is supportive.

Contrast nephropathy

This is acute impairment of renal function, which follows exposure to radio-contrast materials. Incidence in an unselected population is 2â€“7% but this increases to 25% if renal function is already impaired. It results from a combination of afferent arteriolar vasoconstriction, interference with tubulo-glomerular feedback, tubular hypoxia, and direct nephrotoxicity of the contrast agent. Remember MRI scans do not employ toxic contrast agents.

Risk factors

- Pre-existing renal disease (incidence up to 60% if Cr >400ÂµM)
- Renovascular disease
- Proteinuria (increases risk 3 fold)
- DM (risk depends on renal function; incidence of ARF ~100% if Cr >400ÂµM)
- Congestive cardiac failure (incidence 7â€“8%)

- Multiple myeloma
- Pancreatitis
- Multiple contrast studies
- Dehydration
- Jaundice.

Management

There is no specific treatment. Prevention is the best policy.

- Monitor U&Es, creatinine.
- Try to ensure good hydration pre procedure (give patients who are at risk iv fluids if they are to be kept NBM for the procedure).
- Maintain high urine output. Stop nephrotoxic drugs (esp. NSAIDs) peri procedure.
- Outcome in one study: 68% regain normal renal function, 14% had partial recovery, 18% death, dialysis, or transplantation.
- N-acetylcysteine (50mg/kg bd by iv infusion peri procedure) may protect against contrast-induced nephropathy.

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Coma: assessment

Presentation

Coma is a â€˜state of *unarousable unresponsiveness*â€™.

- *No evidence of arousal:* there is no spontaneous eye opening, comprehensible speech, or voluntary limb movement.
- *Unresponsive* to external stimuli and surrounding environment, although abnormal postures may be adopted, eyes may open, or grunts may be elicited in response to pain.
- *Involuntary movements*, e.g. seizures or myoclonic jerks, may occur.
- GCS (P520) is a useful way of assessing and monitoring level of consciousness.
- *Signs of brain shift* (P526) may accompany decreasing level of consciousness.

Causes

For practical purposes, it is best to divide these into

• Metabolic • Toxic • Infective • Structural lesions	with or without	• Focal brainstem signs • Lateralizing cerebral signs • Meningeal irritation.

In general, toxic and metabolic causes usually do not produce focal signs (except rarely with hypoglycaemia, liver, or renal failure), whereas infections and structural lesions do. Meningism offers a very useful clue about the cause of coma (see below).

Coma without focal/lateralizing neurological signs

- Anoxia/hypoperfusion
- Metabolic: e.g. hypo-/hyperglycaemia, acidosis/alkalosis, hypo- or hypernatraemia, hypercalcaemia, hepatic or renal failure
- Intoxications: e.g. alcohol, opiates, benzodiazepines, tricyclics, neuroleptics, lithium, barbiturates, carbon monoxide
- Endocrine: hypothyroidism
- Hypo- or hyperthermia
- Epilepsy
- Hypertensive encephalopathy.

Coma with focal/lateralizing

neurological signs (due to brainstem or cerebral dysfunction)

- Vascular: cerebral haemorrhage or infarction
- Supra- or infratentorial space-occupying lesion: tumour, haematoma, abscess. In order to produce coma these either have to be within the brainstem or compress it by producing brain shift (P526).

Coma with meningism

- Meningitis, encephalitis
- Subarachnoid haemorrhage.

Assessment of severity

- GCS (P520)
- Signs of brain shift (P526) and/or brainstem compromise.

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Coma: immediate management

Priorities

- Stabilize the patient (airway, breathing, circulation). Give oxygen.
- Consider giving thiamine, dextrose, naloxone, or flumazenil.
- Examine patient. Is there meningism? Establish Glasgow Coma Scale score. Is there evidence of brainstem failure? Are there focal or lateralizing signs?
- Plan for further investigations.
- Observe for signs of deterioration and attempt to reverse them.

Stabilize the patient

- *Open the airway* by laying the patient on their side. Note the pattern of *breathing* (see signs of brain shift, P526). If there is apnoea or laboured or disturbed breathing, intubation and ventilation should be considered. Measure arterial blood gases.
- *Support the circulation*. Correct hypotension with colloid and/or inotropes. If prolonged therapy is required, both

require careful and frequent monitoring of central venous pressure and/or pulmonary artery wedge pressure. Search for any occult source of bleeding, e.g. intra-abdominal.

- *Treat seizures* with usual drugs (P472) but beware of over-sedation and hypotension.
- Take blood for *glucose, U&Es, calcium, liver enzymes, albumin, clotting screen, FBC, toxicology* (including urgent paracetamol and salicylate levels). Urine should be saved for *toxicology screen*.

Give thiamine, dextrose, naloxone, or flumazenil

- Check BM stix. There is a good argument for giving 50ml of 50% *dextrose* immediately for presumed hypoglycaemia because this will usually not cause any harm.
- The only concern is that glucose may precipitate Wernicke's encephalopathy in malnourished individuals. Some clinicians therefore favour giving a bolus of *thiamine* 100â€“200mg iv beforehand.
- *Naloxone* should only be given if opiate intoxication is likely (small pupils) and the patient is in coma or has a markedly reduced respiratory rate. In adults naloxone 0.8â€“2.0mg iv should be given at intervals of 2â€“3 minutes to a maximum of 10mg.
- *Flumazenil* should only be administered if benzodiazepine intoxication is likely; it is contraindicated in epileptics who have received prolonged benzodiazepine therapy. In adults flumazenil 200Âµg should be given over 15 seconds; further 100Âµg boluses may be given at 1-minute intervals (usual dose is 300â€“600Âµg maximum total dose outside intensive care setting is 1mg).
- Both naloxone and flumazenil may be given as intravenous

infusions if drowsiness recurs but intensive care monitoring is advisable.

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Coma: clues from examination 1

History

If available, the assessment may be made easier. Even if the history is not extensive, a witness may help to establish whether coma commenced suddenly (suggestive of a vascular event) or whether there was a gradual decline in level of consciousness over hours or even days. Individuals known to suffer from specific diseases may be wearing a Medicalert bracelet or carrying their regular medication. An enormous amount may be learned from a rapid but thorough examination.

General examination[1,2]

This should establish the following.

- Core temperature. A fever usually indicates infection but sometimes results from diencephalic lesions. Hypothermia is often forgotten as a cause for coma; the possibility of myxoedema should be considered.
- Heart rate and rhythm. May indicate a dysrhythmia as the reason for poor cerebral perfusion.
- Blood pressure. Prolonged hypotension of any cause will lead to anoxia and ischaemia. Apart from a cardiac cause, occult bleeding, a cause of sepsis, and drug intoxication

need to be considered.

- Respiratory pattern. Shallow, slow breathing should alert the examiner to the possibility of drug intoxication, e.g. opiates. Deep, rapid Kussmaul breathing suggests acidosis. Brainstem compromise can cause distinctive patterns of breathing (P525).
- Breath. Alcohol, ketones, hepatic, or uraemic foetor?
- Skin. There may be signs of trauma to the head. Bruising over the scalp or mastoids, blood in the nostrils, or external auditory meatus raises the possibility of a basal skull fracture. A rash suggests the possibility of meningitis. Look for signs of chronic liver disease or sallow discoloration of uraemia. Intravenous drug abuse may be suggested by needle tracks.
- Heart. Occasionally bacterial endocarditis or vasculitides associated with heart murmurs present with coma.
- Abdomen. Look for enlargement of organs which may give clues to the cause of coma. It is important not to miss an acute intra-abdominal event such as perforation of a viscus or a leaking aortic aneurysm.
- Fundi. Papilloedema indicates raised intracranial pressure but its absence does *not* exclude that possibility. Subhyaloid haemorrhages are pathognomonic of subarachnoid haemorrhage but are rare. Changes of diabetic or hypertensive retinopathy suggest the possibility of encephalopathy secondary to these conditions.

Is there meningism?

Neck stiffness should be assessed only if it is certain that there has been no trauma to the cervical spine. Increased stiffness suggests meningeal irritation, either because of inflammation or infiltrative processes affecting the meninges, or because of the presence of blood. Meningism raises the possibility of

meningitis, encephalitis, or subarachnoid haemorrhage. Start antibiotics immediately if meningitis is suspected.

Footnote

1

Plum F & Posner JB (1980) *The Diagnosis of Stupor and Coma*, 3rd edn; FA Davis, Philadelphia.

2

Bates (1993) *J Neurol Neurosurg Psychiat* 56: 589â€“598.

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Coma: clues from examination 2

Assess the GCS

This may reveal brainstem dysfunction or lateralizing signs. When testing the motor response decorticate or decerebrate posturing may become evident (P522). If there is a change in these signs, it may indicate brain shift (P526).

Look for evidence of brainstem dysfunction?

See P522 for details.

- Test and observe
    - Pupillary response
    - Corneal reflex
    - Resting position of eyes
    - Spontaneous eye movements
    - Oculocephalic response/Doll's head manoeuvre (if no C-spine injury)
    - Oculovestibular response/caloric stimulation
    - Swallowing

    - Respiratory pattern.
- There will be evidence of brainstem failure either because there is structural damage (intrinsic lesion or extrinsic compression due to brain shift, P526) or because of metabolic coma such as drug intoxication with diffuse, usually reversible, dysfunction.
- If there is focal brainstem dysfunction the cause is most likely structural or intrinsic brainstem disease.
- If there is rostro-caudal progression of brainstem signs consider a herniation syndrome (P526).
- If there appears to be diffuse brainstem dysfunction, it may not be easy to distinguish between structural and metabolic aetiologies. The most important clue is that in metabolic coma, irrespective of their size, the pupils continue to react except in very few exceptional cases (atropine, scopolamine, or glutethimide intoxication will depress brainstem function and produce pupillary abnormalities).

Are there lateralizing signs?

Testing of brainstem reflexes, assessing the GCS, and general examination may reveal facial asymmetry, and differences in muscle tone, reflexes, and plantar responses between the two sides. All these features point toward the possibility of a structural lesion, although occasionally metabolic coma is associated with focal neurological signs.

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Coma: management

Plan for further investigations

The history, physical examination, and/or laboratory studies may help make the diagnosis. Often, however, a diagnosis cannot be reached so rapidly. The practical approach is to divide patients according to the following scheme.

Brainstem function intact

Urgent CT head scan. This will reveal one of the following

- Operable lesions (e.g. subdural haematoma, subarachnoid or intracerebral haemorrhage); refer as appropriate.
- Inoperable lesions (e.g. bilateral cortical infarcts); treatment is supportive.
- Normal: a lumbar puncture should be performed. CSF analysis may suggest an infective process (e.g. meningitis, encephalitis) (P432). If the CSF is normal, the most likely diagnosis is a metabolic coma.

Brainstem function not intact

- Consider whether there are signs of brain shift (P526).
- If a herniation syndrome appears to be progressing rapidly,

mannitol should be given, hyperventilation commenced, and a surgeon contacted urgently (see â€˜raised ICPâ€™, P452).

- If the tempo of events is not so rapid, mannitol may be given and an urgent CT scan arranged.
- Even if the brainstem signs appear to be non-progressive, a CT scan should be arranged to exclude the possibility of an operable posterior fossa mass or haemorrhage (e.g. cerebellar haemorrhage).
- If the CT is normal, a lumbar puncture should be performed to exclude infection. If this too is normal the diagnostic possibilities are intrinsic brainstem disease not detected by CT, metabolic coma, or possibly infection, e.g. encephalitis, without leukocytic response.
- MRI is more sensitive in detecting intrinsic brainstem pathology.
- Lumbar puncture should be repeated the next day if there is no improvement in the patient's condition. Treatment is supportive.

Monitoring progress

- This requires regular observations of vital signs and neurological state (including GCS score).
- An important cause of deterioration in structural brain lesions is brain shift leading to herniation syndromes (P526). The emergency treatment of raised intracranial pressure is discussed on P454.
- Other reasons for deterioration are electrolyte or metabolic changes, hypovolaemia, or fluid overload. Plasma electrolytes and fluid balance need to be regularly assessed to avoid such problems.

Prognosis

In coma due to head injury, prognosis is clearly related to GCS score. Patients scoring 8 or less have a very poor prognosis. In non-traumatic coma, GCS alone is not a very good predictor. Patients with drug intoxications may have very low scores on admission but, in general, have good outcomes. Assessment of prognosis in non-traumatic coma is aided by simple features of the examination. For example, if after 24 hours it is still not possible to elicit pupillary responses, corneal reflexes, and oculovestibular response, survival is extremely unlikely.[1]

Footnote

1

Levy *et al.* (1981) *Arch Int Med* 94: 293â€“301.

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Limb weakness: assessment

History

The history should establish if there has been

- Sudden onset or gradual progression
- Weakness or incoordination
- Upper limb or facial weakness
- Asymmetrical or symmetrical weakness
- Associated sensory symptoms, e.g. paraesthesiae or numbness
- Difficulty with swallowing, speech, micturition, or defecation
- Back or neck pain
- Systemic symptoms, e.g. malaise, fever, diarrhoea and vomiting, arthralgia
- Recent trauma
- Previous medical history, e.g. hypertension, ischaemic heart disease, stroke, diabetes, connective tissue diseases, immunosuppression
- Drug history, e.g. phenytoin, isoniazid, vincristine, metronidazole.

Examination

- What is the pattern of weakness? Some common patterns, together with associated features, are illustrated on P418â€“19. This should help to localize the level of the lesion in the nervous system.
- Is the weakness upper or lower motor neurone/combination?
- If upper motor neurone, is it pyramidal? i.e. extensor more than flexor weakness in upper limbs; flexor greater than extensor weakness in lower limbs.
- Is there fatiguable weakness with repetitive effort? As in myasthenia.
- Are there any involuntary movements? Tremor, myoclonic jerks, or fits may be noted.
- What is the gait like? This is important to test if at all possible. It may demonstrate, for example, a hemiplegic gait, ataxia (cerebellar or sensory), a waddling (myopathic) gait, steppage (lower motor neurone) gait, festinating movements of the Parkinsonian patient.
- Is there any sensory loss? Where? Is there a â€˜sensory levelâ€™? Sensory changes are often the most difficult to elicit. Do not forget to test all modalities or to test the back of the legs up to the anal sphincter.
- What modalities of sensation are lost? Dorsal column loss produces a â€˜discriminatoryâ€™ loss with impaired two-point discrimination, joint-position and vibration loss, astereognosis, and sensory ataxia. Spinothalamic loss usually produces a lack of awareness of pain and temperature.

The history and examination should help to localize the lesion and, together with the patient's age, give an indication of the

likely pathological process involved.[1]

Footnote

[1]Adapted from
Lindsay KW, Bone I, and Callander R (1991) *Neurology and Neurosurgey Illustrated*, 2nd edn; pp.191â€“194; Churchill Livingstone, London.

Investigations

The initial investigation of choice depends upon the likely diagnosis. Investigations to consider are given in the table opposite.

Diagnoses not to miss

â€¢ Spinal cord compression	P508
â€¢Guillianâ€“BarrÃ© syndrome	P512
â€¢ Subdural haematoma	P464
â€¢ Stroke	P478

Diagnoses to consider

- Demyelination (multiple sclerosis, post infectious, etc.)
- Malignancy (carcinomatous meningitis, intracranial mass)
- Syringomyelia

- Motor neurone disease
- Vitamin deficiency (sub-acute combined degeneration-B_{12})
- Peripheral neuropathy (toxic, DM, autoimmune, amyloid, etc.)
- TB, syphilis

Investigations to consider

- Blood tests: FBC, U&Es, LFTs, ESR, CRP, prostate specific antigen, B_{12}/folate, protein strip, syphilis serology
- CT scan
- MRI brain Â± spine
- CSF analysis: protein, cells, oligoclonal bands
- Visual evoked potentials
- EMG
- NCS
- Tensilon test
- Muscle biopsy

Practice point

- A patient who can cycle easily, but only walk yards, usually has lumbar stenosis.

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Limb weakness: localizing the lesion

Monoplegia	Lesion site	Other features
Arm Â± face 	Contralateral cortex	• Visual field defect • Dysphasia (dominant hemisphere lesion) • Cortical sensory loss (â†“JPS and 2-point discrimination)
Leg only 	Contralateral cortex	• With ipsilateral sensory deficit
	Ipsilateral spinal lesion	• Contralateral pain and temperature loss • JPS lost on same side

Hemiplegia	Lesion site	Other features
Face + arm + leg 	Contralateral hemisphere	• UMN VII involvement • Impaired conciousness • Visual field defect • Dysphasia (if dominant hemisphere lesion)
	Contralateral internal capsule	• UMN VII involvement • Alert • No dysphasia (even with a dominant hemisphere lesion)
	Contralateral mid-brain lesion	• Contralateral IIIrd palsy • Impaired upgaze
Arm (Â± face) or leg alone 	Contralateral cortex	• VII unaffected • Visual field defect • Dysphasia (if dominant hemisphere lesion) • Cortical sensory loss (â†“JPS and 2-point discrimination)

	Contralateral medullary	• Ipsilateral pain and temperature loss • Contralateral Horner's syndrome • Contralateral palatal and tongue weakness
	Ipsilateral spinal lesion	• Pain and temperature loss in contralateral leg • Ipsilateral loss of JPS • Ipsilateral Horner's
Arm, leg, and opposite face 	Contralateral pons	• LMN face involvement on opposite side to weak limbs • Conjugate gaze deviation towards weak side

UMN = upper motor neurone; JPS = joint position sense

Hemiplegia	Lesion site	Other features

Arm and opposite leg 	Medullary lesion	• Palatal and tongue weakness on the side of arm weakness
Paraplegia	Lesion site	Other features
	Mid-line cortical lesion	• Cortical sensory loss (JPS and 2-point discrimination) • â€˜Frontalâ€™ incontinence • Normal pain and temperature
	Thoracic spine	• â€˜Sensory levelâ€™ • Acute urinary retention or hesitancy of micturition
Tetraplegia	Lesion site	Other features
Face and all four limbs involved 	Pontine lesion	• â€˜Locked-inâ€™ syndrome: only vertical eye movements possible
Face spared	Cervical	• No cranial nerve

	spine lesion	lesion • High lesions (C1â€“3) require ventilation • Lesions at C4 have intact diaphragmatic breathing
	Medullary lesion	• No palatal or tongue movement or speech but intact facial movements
Combined UMN and LMN signs		
		• The LMN signs point to the level of the lesion • Two lesions (e.g. cervical and lumbar spondylosis) may produce mixed signs in limbs
LMN limb weakness (Unilateral or Bilateral)		
		• Nerve root distribution? • Plexopathy? • Peripheral nerve distribution (mono- versus polyneuropathy) • Presence of reflexes suggests a myopathy (cf. neuropathy) • Specific distribution

		seen in e.g. fascioscapulohumoral dystrophy • Fatiguability suggests neuromuscular junction disease
LMN = Lower motor neurone		

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Acute dizziness: assessment

History

Determine whether

- *There is true vertigo*, i.e. a hallucination that either the patient or their environment is rotating.
- *Symptoms started acutely*, are progressively worsening, or are transient (see â€˜vertebrobasilar TIAsâ€™, P494). Vestibular neuritis typically begins over a period of a few hours, peaks in the first day, and then improves within days. Infarction causes a vestibular syndrome that typically has an abrupt onset. Transient ischaemic attacks often last for less than 30 minutes. Abrupt onset of vertigo for seconds after a change in head position is characteristic of benign positional vertigo.[1]
- *Symptoms worse with certain postures*. Vertigo is worse with certain head positions in benign position vertigo and some cases of central nystagmus (see below). Postural hypotension is frequently caused by drugs and can be caused by acute blood loss; uncommonly it is due to autonomic failure. Neck movements in cervical spondylosis or carotid sinus hypersensitivity may also lead to dizziness.
- *There is associated tinnitus* (as in MÃ©niÃ¨re's disease).
- *Hearing loss* is present in MÃ©niÃ¨re's disease,

cerebellopontine angle lesions, e.g. acoustic neuromas.

- *Ear discharge* may occur with middle ear disease.
- *Associated focal neurological symptoms*, e.g. unilateral weakness, clumsiness, paraesthesiae, or numbness.
- *Headache:* sudden onset in intracerebral haemorrhage; progressive with features of â†‘ICP in mass lesions (e.g. acoustic neuroma).
- *Any recent head injury*?
- *Systemic symptoms*, e.g. weakness and lethargy in anaemia.
- *Previous medical/psychiatric history*, e.g. hypertension, ischaemic heart disease, diabetes, risk factors for stroke or TIAs (P494), episodes of neurological disturbance, panic attacks, and anxiety.
- *Drug history* is pertinent to both true vertigo (e.g. phenytoin, gentamicin, frusemide) and dizziness (e.g. anti-hypertensives, anti-depressants, drugs for Parkinson's disease, hypoglycaemics).

Examination

Ear. Is there a discharge? Is the tympanic membrane normal?

Neurological examination should discover whether there are any focal signs due to brainstem or cerebellar disease (P522). Non-contiguous brainstem pathology may be due to patchy demyelination. Do not forget to assess the *corneal reflex*, the absence of which is one of the earliest signs of an ipsilateral acoustic neuroma. Observe the *gait* if possible; it may be ataxic. Examine *extraocular eye movements*. Is there an intranuclear ophthalmoplegia (vascular/demyelinating brainstem disease)? Examine carefully for *nystagmus* (see table). *Hallpike manoeuvre* involves positioning the patient's head over one side of the bed and watching for nystagmus.

Benign positional vertigo: nystagmus develops after a brief delay, but it fatigues and, with repetition, adapts. *Central nystagmus:* no initial delay, fatigueability, or adaptation. *Fundoscopy* may reveal papilloedema (suggestive of intracranial space-occupying lesion) or optic atrophy (which occurs with previous demyelination in multiple sclerosis).

General examination: measure BP (lying and standing). Postural hypotension is a common cause of dizziness.

Classification of nystagmus

- First degree nystagmus occurs only when the eyes are deviated to one side. If it occurs in the mid-line position as well, it is second degree. Nystagmus in all directions of gaze is termed third degree
- Vestibular nystagmus is due to dysfunction of the labyrinth or vestibular nerve. The slow phase is towards the lesion; the quick phase is away from the lesion. There may be rotatory nystagmus
- Central nystagmus is due to brainstem dysfunction (vestibular nuclei or their connections); there may no vertigo associated with this form of nystagmus. The nystagmus may be horizontal, vertical, or rotatory; sometimes it is present in one eye only. The quick phase is determined by direction of gaze: it is multi-directional
- Positional nystagmus may occur in benign positional vertigo but with repeated testing it adapts (see below). It may also occur with posterior fossa, e.g. cerebellar lesions (quick phase tends to be toward the lesion) in which there is no adaptation

Footnote

1

Hotson JR & Baloh RW (1998) *New Engl J Med* 339: 680â€“685.

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Acute dizziness: management

Investigations

These depend upon the likely diagnosis.

- Cerebellopontine angle lesions such as acoustic neuroma may be imaged by *CT with contrast* but, in general, posterior fossa and brainstem disease is better appraised by *MRI scanning*.
- *Pure tone audiometry* is a sensitive way of detecting sensorineural loss.
- *Cervical spine films* may reveal degenerative disease compromising vertebral artery circulation.
- Measure *blood sugar* and *FBC* if indicated.

Approach to dizziness/vertigo

True vertigo	Management
Acute labyrinthitis	• Bed rest • Consider cyclizine or prochlorperazine
Benign positional vertigo	• Avoid precipitating position • Epley manoeuvre or Cawthorneâ€“Cooksey exercises
MÃ©niÃ¨re's disease (sensorineural deafness and tinnitus)	• Bed rest • Consider cyclizine or prochlorperazine • Pure tone audiometry • ENT referral
Middle ear disease	â€¢ ENT referral
Brainstem/cerebellar disease (stroke, P478, demyelination, vertebrobasilar insufficiency, migraine, vasculitis)	â€¢ Consider CT/MRI
Cerebellopontine angle lesions (e.g. acoustic neuroma)	• Pure tone audiometry • CT, MRI scan

Dizziness but no true vertigo	Management
Hypotension	â€¢ Postural, cardiac, volume loss, or autonomic failure
Anaemia	â€¢ FBC, blood film, other investigations as necessary
Hypoglycaemia	â€¢ Diabetic on hypoglycaemics or insulin, insulinoma
Hyperventilation	â€¢ Attempt to reproduce symptoms. Explain
Cervical spondylosis	â€¢ A collar may be useful, if only to act as reminder
Carotid sinus hypersensitivity	â€¢ See P102

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Acute loss of vision

History

Determine whether

- *Visual loss is or was monocular or binocular, complete or incomplete*, e.g. hemianopia, central or peripheral loss, haziness or complete obscuration of vision.
- *Loss of acuity occurred instantly* as in amaurosis fugax.
- *Period for which it lasted*.
- *There were any other associated visual symptoms*, e.g. scintillations (â€˜flashing lights and shapesâ€™) occur in retinal migraine.
- *The eye is painful* Â± *red*.
- *Headache or facial pain:* unilateral or bilateral.
- *Associated focal neurological symptoms*, e.g. unilateral weakness, clumsiness, paraesthesiae, or numbness.
- *Any recent trauma?*
- *Systemic symptoms*, e.g. malaise, aches, and pains.
- *Previous medical history*, e.g. hypertension, ischaemic heart disease, diabetes, other risk factors for stroke or TIAs (P494), migraine, connective tissue diseases.

Examination

- *External appearance of the eye*. Is it red (P428)? Is there corneal clouding?
- *Visual acuity* should be measured for each eye with a Snellen chart. Near vision should be tested (with newsprint if necessary). If none of these are possible, the patient's acuity for counting number of fingers, or perceiving hand movement or light should be noted. Ideally, colour vision should also be examined with Ishihara plates.
- *Plot the visual fields*. Often careful bedside examnation is sufficient, although perimetry available in ophthalmological departments may be more sensitive. The loss of vision may be incomplete.
- *Is there an afferent pupillary defect?* (Swinging torch test.)
- *Fundoscopy* may reveal a retinal embolus, changes of central/branch retinal artery occlusion, swollen or pale optic nerve head, papilloedema, or hypertensive changes.
- *Is the temporal artery tender?* It need not be in temporal arteritis.
- *Complete neurological examination* is necessary to discover if there are any other associated signs.
- *Listen for carotid bruits* although they may not be present in patients with symptomatic carotid stenosis.
- *Assess heart rhythm (including ECG) and cardiovascular system* for possible cardiogenic source of embolus.
- *Measure BP (lying and standing) and blood sugar*. Hypotension in the presence of arteriosclerosis can lead to occipital lobe ischaemia. Hypertension and diabetes are risk factors for TIAs.

Investigations

See P480â€“2.

NB: An *ESR* should be performed in any patient aged >50 years who presents with monocular blindenss and unilateral headache. It is rarely normal in temporal arteritis. If the ESR is elevated and the presentation is compatible with temporal arteritis, high-dose corticosteroid therapy should be considered (initially 60mg/day orally) because the other eye is also at risk of anterior ischaemic optic neuropathy (see P760).

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Approach to acute/sub-acute visual loss

1 Monocular transient loss without prominent unilateral headache

- Amaurosis fugax (see â€˜TIAsâ€™, P494). In the elderly this may be due to embolism. In some younger patients it is probably due to vasospasm (a diagnosis of exclusion).
- Hyperviscosity syndrome (e.g. polycythaemia, myeloma, sickle cell anaemia), hypercoagulable state, vasculitis: blood film, protein electrophoresis, autoimmune screen, other haematological investigations as required (P728).
- Postural hypotension (may exacerbate vertebrobasilar ischaemia): stop any exacerbating drugs. Exclude autonomic neuropathy.

2 Monocular transient loss with prominent headache

- Migraine (usually there are positive phenomena, e.g. scintillations): observe, give analgesics/ergot derivative. Arrange neurological consultation.

3 Monocular sustained loss with red eye

- Acute glaucoma (dilated pupil and corneal clouding): urgent ophthalmology referral.
- Acute uveitis (inflammation of iris and ciliary body with small pupil), keratitis (corneal inflammation), endophthalmitis (involvent of vitreous, uvea, and retina with cellular debris/pus in anterior chamber), or ocular trauma. Urgent ophthalmic referral.

4 Monocular sustained loss without red eye

Central visual loss with relative afferent pupillary defect

- Optic neuritis Â± orbital pain exacerbated by eye movement. The commonest cause is demyelination but consider the possibility of mass lesions compressing the optic nerve (consider evoked potentials, CT orbit)
- Anterior ischaemic optic neuropathy due to presumed atherosclerosis of posterior ciliary arteries or to temporal arteritis (consider steroids, perform ESR, temporal artery biopsy).

Central scotoma without relative afferent pupillary defect

- Vitreous haemorrhage
- Macular disorder: macular degeneration, haemorrhage, or

exudate

- Branch retinal vein/artery occlusion.

Peripheral visual field loss

- Retinal detachment
- Chorioretinitis
- Intraocular tumour
- Retinal vascular occlusion.

5 Binocular sustained loss

- Field loss (e.g. quadrantonopia, hemianopia, bitemporal) â†’ CT scan
- Hypotension (e.g. cardiac failure) leading to posterior circulation insufficiency. Dysrhythmias or vertebrobasilar insufficiency may produce transient episodes of binocular visual loss. CT scan
- Toxic optic neuropathies (e.g. tobacco, alcohol, methanol).

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Painful red eye: assessment

History

This should establish if there has been

- *Ocular trauma or foreign body (including contact lens) in the eye* .
- *Sudden or gradual onset of symptoms, nature, and location of pain* soreness, or gritty sensations may occur with conjunctivitis but the severe in acute glaucoma.
- *Diminution of visual acuity* occurs with conditions affecting the co (variable reduction), iris (mild reduction), and glaucoma (severe r acuity).
- *Discharge* (not simply lacrimation) *from eyes* may be mucopurulen bacterial or chlamydial conjunctivitis. It may be mucid and stringy allergic conditions or dry eyes.
- *Headache or facial pain* is common with orbital cellulitis. It may p cavernous sinus thrombosis or herpes zoster ophthalmicus.
- *Photophobia* suggests corneal involvement or iritis.
- *Systemic symptoms* , e.g. malaise/fever, may occur with orbital c cavernous sinus thrombosis, vomiting is a feature of acute glauco arthralgia + urethral discharge suggests Reiter's or chlamydial in
- *Previous history* . Recurrent red eyes may occur with episcleritis, simplex corneal ulcer. Ask specifically about â†‘BP, heart disease, connective tissue diseases, and atopy.

Examination

What is red? The conjunctiva, iris, sclera, or episclera (which lies just conjunctiva and next to the sclera), eye lid, skin around orbit? Is ther haemorrhage, either sub-conjuctival or in the anterior chamber (hypha conjunctivitis there is â€˜injectionâ€™ or increased filling of existing vessels, with individual branches distinctly visible; the vessels can be the conjunctiva over the sclera. Ciliary or circumcorneal injection refers blueâ€“red discolouration, most conspicuous at the limbus (corneaâ€˜ border) and occurs in anterior uveitis or iritis and keratitis (corneal inflammation). Mixed injection (conjunctival + ciliary) also occurs in

Is there proptosis? Suggests a retro-orbital/intraoribtal mass or caver thrombosis in which it may become bilateral.

Is it pulsatile? As in a carotico-cavernous fistula, with an audible bruit

Is there ophthalmoplegia? Any mass lesion or cavenous sinus thrombo

Is visual acuity diminished? A Snellen chart should be used and near (with newsprint if necessary). In acute glaucoma, there is marked red acuity; in acute iritis or keratitis, acuity is only modestly diminished; conjunctivitis it is normal.

What is the size of the pupil? Fixed and dilated in acute glaucoma; sm reduced reaction to light in iritis; normal in conjunctivitis.

Is the red reflex normal? If it is, does the cornea appear normal? The may be impaired in keratitis, central corneal ulcer or oedema, anterio hyphaema (blood in anterior chamber after blunt trauma), anterior uv glaucoma, or endophthalmitis (involvent of vitreous, uvea, and retina debris/pus in anterior chamber). *Fundoscopy* may not be possible as v corneal clouding of acute glaucoma.

Are there any anterior chamber abnormalities? In acute anterior uveiti exudates in the anterior chamber.

Is there a rash or vesicles on the face, nose, or eyelid? Herpes zoster conjunctivitis, iritis, corneal ulceration, and 2Â° glaucoma.

Differential diagnosis of â€˜red-eyeâ€™

Acute glaucoma
Both ciliary and conjunctival vessels injected Entire eye is red
Injected
Dilated, fixed, oval
Steamy, hazy
Very slow
Very high

Iritis
Redness most marked around cornea Colour does not blanch on pressu
Injected
Small, fixed
Normal
Turgid
Normal

Conjunctivitis
Conjunctival vessels injected, greatest toward fornices Blanch on pres
over sclera
Normal
Normal
Normal
Normal
Normal

Subconjunctival haemorrhage
Bright red sclera with white rim around limbus
Normal
Normal

Normal
Normal
Normal

After RD Judge, GD Zuidema, FT Firzgerald 1989 *Clinical diagnosis* 5 e Brown, Boston.

Conjunctiva Iris Pupil Cornea Anterior chamber Intraocular A pressure

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Painful red eye: management

With a careful history and examination, the diagnosis may become clear. *Unless you are absolutely sure of the diagnosis, discuss the patient with an ophthalmologist*.

Diagnosis of painful red eye in non-traumatic cases

With prominent ocular discharge

- Viral/bacterial conjunctivitis (watery/mucopurolent discharge, normal red reflex, normal pupil)
- Bacterial/fungal keratitis (mucopurolent discharge, opaque cornea with impaired red reflex, normal or slightly reduced pupil)
- Keratoconjunctivitis sicca or atopic response (dry eye, mucoid strands).

Without prominent discharge and normal red reflex

Normal cornea

- Episcleritis, scleritis, or sub-conjunctival haemorrhage
- Orbital cellulitis (skin around orbit erythematous and tender)
- Carotico-cavernous fistula (dilated conjunctival vessels, forehead veins, and choroidal vessels because of â€˜arterializationâ€™, reduced acuity because of optic nerve ischaemia, pulsatile proptosis, and bruit)
- Cavernous sinus thrombosis [fever, acute onset painful ophthalmoplegia, conjunctival oedema and congestion, proptosis, oedema over mastoid (emissary vein) â†’ may progress to meningitis].

Abnormal cornea

- Corneal abrasion or ulcer (NB: herpes simplex and herpes zoster).

Without prominent discharge and impaired red reflex

- Acute glaucoma (severe pain, markedly reduced acuity, cloudy cornea, purple congestion at limbus, fixed dilated pupil, rockâ€“hard globe)
- Acute anterior uveitis (malaise, clear cornea, blueâ€“red congestion at limbus, anterior chamber exudate, iris muddy and injected, small pupil with reduced response to light)
- Endophthalmitis (reduced acuity, eyelid swelling, conjunctival injection, anterior chamber cellular debris, vitreous clouding, retinal haemorrhages)
- Keratitis (red congestion at limbus, pupil normal or reduced in size, cornea opaque)
- Central corneal ulcer.

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Acute bacterial meningitis: assessment

Presentation

- *Headache, fever, neck stiffness (absent in 18% of patients)*,[1] *photophobia* (often over hours to days).
- *Rash*. Meningococcal meningitis is most commonly associated with a macular rash progressing to petechiae or purpura (see P314) but other organisms may also cause a rash.
- *Confusion, psychiatric disturbance* (e.g. mania) or *altered level of consciousness*. In the elderly (especially those with diabetes mellitus or cardiopulmonary disease) and the immunocompromised or neutropenic, there may be little other than confusion.
- *Focal neurological signs* complicate meningitis in at least 15% cases. These can suggest cerebral damage (e.g. hemiparesis following venous infarction or arteritis) or indicate cranial nerve and brainstem involvement by basal exudation and inflammation (e.g. in *Listeria monocytogenes* meningitis). They can also indicate brain shift secondary to raised intracranial pressure (see P526). Consider the possibity of brain abscess or encephalitis if focal signs or seizures are prominent.[2] Papilloedema is uncommon (<1%) and should suggest an alternative diagnosis.

- *Seizures* are the presenting feature in up to 30%.

Predisposing factors

Usually none, but acute otitis media, mastoiditis, pneumonia, head injury, sickle cell disease, alcoholism, and immunocompromised states are all associated.

Causes in adults

Common	*Rarer*
â€¢ *Neisseria meningitidis*	â€¢ Gram negative bacilli (in elderly)
â€¢ *Strep. pneumoniae*	â€¢ *Listeria* (in elderly)

Assessment of severity

Mortality increases as consciousness decreases (~55% for adults in coma). *However*, meningitis can proceed with alarming rapidity even in the most alert patients.

Management

- Stabilize the patient (Airway, Breathing, Circulation); give oxygen.
- Commence antibiotics. It is *not* necessary to await CSF analysis.
- CT scan prior to lumbar puncture (this is the safest option).

- Make a definitive diagnosis with lumbar puncture.
- Reconsider antibiotic regimen after CSF analysis. Consider adjunctive corticosteroid therapy.
- Arrange for contacts (including medical/nursing staff) to have prophylaxis. Notify the public health service.
- Observe for and, if necessary, treat complications.

Footnote

1

Consensus Statement on Diagnosis, Investigation, Treatment and Prevention of Acute Bacterial Meningitis in Immunocompetent Adults (1999) *J Infect* 39: 1â€“15.

2

Anderson M (1993) *J Neurol Neurosurg Psychiat* 56: 1243â€“1258.

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Acute bacterial meningitis: immediate management

1 Antibiotic therapy: follow your hospital guidelines if available

- Adult patients with a typical meningococcal rash should be given iv *benzylpenicillin* 2.4g (4MU) every 4 hours. Adults between 18 and 50 without a rash should receive *cefotaxime* 2g q8h or *ceftriaxone* 2g every 12 hours. For adults over 50 without a rash consider addition of 2g ampicillin every 4 hours to cefotaxime or ceftriaxone as above (to cover *Listeria*). If the patient comes from an area of the world where penicillin and cephalosporin-resistant pneumococci are common (e.g. mediterranean countries) then add iv *vancomycin* 500mg every 6 hours. If the individual is allergic to penicillin, consider iv *chloramphenicol* 25mg/kg every 6 hours with *vancomycin* 500mg every 6 hours. Additional co-trimoxazole should be given in those over 50. Discuss the case with your microbiologist.[1]
- *Blood cultures* should be taken but it is dangerous to withold intravenous antibiotics until these are taken or lumbar puncture is performed. Most organisms will be diagnosed from blood cultures.
- Meningococcal infections are discussed on P316.

2 CT scan

- Our policy is that all patients should have a CT scan prior to lumbar puncture. Others suggest this need be performed only if there is decreased level of conciousness, focal signs, papilloedema (very unusual in meningitis), or signs suggesting impending cerebral herniation P526. You should discuss the patient with a senior member of your team.

3 Lumbar puncture

- *Measure opening pressure*. CSF pressure is often raised (>14cm CSF) in meningitis and there are only a few reports of cerebral herniation (coning) following the procedure. If the pressure is raised the patient must be observed closely at no less than 15-minute intervals. A CT scan is required to exclude a complication of meningitis or a space-occupying lesion, e.g. cerebral abscess.
- *Analysis of CSF see* table *opposite*

â€¢ CSF WCC	bacterial meningitis characteristically demonstrates a high (usually >1000/mm^3) WCC with predominance of neutrophils. A low CSF WCC (0â€“20/mm^3) with high bacterial count on Gram stain is associated with a poor prognosis
â€¢ CSF glucose	usually reduced (CSF : blood glucose ratio <0.31 in ~70%) but may be normal
â€¢ CSF protein	usually elevated (>1.0 g/l)

â€¢ Gram stain	is positive in 60â€“90% but may not be if there has been a delay between starting antibiotics and lumbar puncture. Also the yield of CSF culture falls to <50% from 70â€“85%.

This CSF profile may also occur with viral and TB meningitis in the early phase, but repeat CSF analysis shows transformation to a lymphocytic predominance. Patients with a CSF profile characteristic of bacterial meningitis should be treated as if they have this condition until proven otherwise.

CSF composition in meningitis

	Bacterial	Viral	TB meningitis
Appearance	Turbid	Clear	Clear
Cells (per mm^3)	5â€“2000	5â€“500	5â€“1000
Main cell type	Neutrophil	Lymphocyte	Lymphocyte
Glucose (mM)	Very low	Normal	Low
Protein (g/L)	Often >1.0	0.5â€“0.9	Often >1.0
Other tests	Gram stain	PCR	Ziehlâ€“Neelsen

	Bacterial antigen		Fluorescent test PCR

See P952 for reference intervals for CSF analysis

Footnote

1

Consensus Statement on Diagnosis, Investigation, Treatment and Prevention of Acute Bacterial Meningitis in Immunocompetent Adults (1999) *J Infect* 39: 1â€“15.

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Acute bacterial meningitis: continuing therapy

Reconsider antibiotics? Adjunctive steroids?

- *CSF lymphocytosis*. If the CSF pleocytosis is predominantly lymphocytic the diagnosis is unlikely to be bacterial meningitis. This is discussed further on P440.
- *CSF polymorphs >50 000/mm^3* suggests possibility of cerebral abscess. A CT brain scan should be performed.
- *CSF Gram stain:* if Gram -ve diplococci are visible continue with 2.4g *benzylpenicillin* iv every 4 hours or 2g *ampicillin* iv 4 hourly. Discuss the case with your microbiologist. If Gram +ve diplococci are visible give 2g *cefotaxime* iv 6 hourly and consider adding *vancomycin* 500mg iv 6 hourly. If Gram +ve cocco-bacilli suggestive of *Listeria monocytogenes* are visible give *ampicillin* 2g 4 hourly iv and *gentamicin* 5mg/kg/24h iv as a single daily dose or divided into 8 hourly doses.
- *Adjunctive corticosteroid therapy* has been shown to reduce the incidence of neurological sequelae in adults and children, especially in pneumococcal meningitis[1] and many neurologists now favour its use to reduce inflammation. In patients with raised ICP, stupor, or impaired mental status,

give 10mg dexamethasone iv loading dose, followed by 4â€“6mg po q6h.

Prophylaxis for contacts should be given immediately

- *Public health services* should be notified of any case of bacterial meningitis. They will be able to give advice on current prophylactic treatment and vaccination (possible with some strains of meningococcus); they will also assist in contact tracing. Patients with meningococcus are infectious and can spread organisms to others. Liaize with your local microbiologists.
- *Prophylaxis* should be given as soon as the diagnosis of bacterial meningitis is suspected. In the UK, for adult contacts, rifampicin 600mg bd for 2 days is recommended. The alternative for adults is ciprofloxacin 750mg as a single dose (for children older than 1 year: 10mg/kg bd for 2 days; for children 3 monthsâ€“1 year: 5mg/kg bd for 2 days).

Footnote

1

De Gans J *et al.* (2002) *New Engl J Med* 347: 1549â€“1556.
Van de Beek D *et al.* (2003) *Cochrane Database Syst Rev* 2003: CD004505.

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Acute bacterial meningitis: complications and their treatment

- *Raised intracranial pressure* may respond to steroids and, as discussed above, some neurologists give this routinely to reduce inflammatory reaction. In the acute situation, if there is evidence of brain shift or impending transtentorial herniation (P526) mannitol should be given 1g/kg over 10â€“15 minutes (~250ml of 20% solution for an average adult) and the head of the bed elevated to 30Â° (see P448). Oral glycerol has also been shown to be effective in some small trials.
- *Hydrocephalus* (diagnosed by CT) may require an intraventricular shunt and should be discussed urgently with neurologists. It can occur because of thickened meninges obstructing CSF flow or because of the adherence of the inflamed lining of the aqueduct of Sylvius or fourth ventricular outflow. Papilloedema may not be present.
- *Seizures* should be treated as seizures of any other aetiology (see P474).
- *Persistent pyrexia* suggests that there may be an occult source of infection. The patient should be carefully re-examined (including oral cavity and ears).
- *Focal neurological deficit* may occur because of arteritis or

venous infarction or space-occupying lesion, e.g. subdural empyema. Inflammatory reaction at the base of the skull may lead to cranial nerve palsies. A CT scan should be requested if it has not already been performed. Anti-coagulation is not of benefit for treatment of thromboses.

- *Subdural empyema* is a rare complication. Focal signs, seizures, and papilloedema suggest the diagnosis. It requires urgent surgical drainage.
- *Disseminated intravascular coagulation* is an ominous sign. Platelet and fresh frozen plasma may be required. The use of heparin should be discussed with a haematologist and neurologist.
- *Syndrome of inappropriate ADH* may occur. Fluid balance and electrolytes need to be checked regularly.

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Meningitis with lymphocytic CSF

Presentation

- Viral meningitis may be indistinguishable on clinical grounds from acute early bacterial meningitis but it is usually self-limiting.
- TB meningitis is usually preceded by a history of malaise and systemic illness for days to weeks before meningeal features develop. However, it may present very acutely. TB meningitis may be associated with basal archnoditis, vasculitis, and infarction leading to focal neurological signs, e.g. cranial nerve palsies, obstructive hydrocephalus with papilloedema.
- Cryptococcal or syphilitic meningitis in the immunocompromised present with features indistinguishable from TB meningitis.

Causes

Viral	*Non-viral*
â€¢ Coxsackie	â€¢ TB
â€¢ Echo	â€¢ Cryptococcus
â€¢ Mumps	â€¢ Leptospirosis
â€¢ Herpes simplex type 1	â€¢ Lyme disease
â€¢ Varicella zoster	â€¢ Syphilis
â€¢ HIV	â€¢ Brucellosis
â€¢ Lymphocytic choriomeningitis virus	â€¢ Paramenigeal infection with a CSF reaction

CSF findings

The CSF usually demonstrates a lymphocytosis but the CSF in viral meningitis may initially demonstrate predominantly neutrophils. It is important not to dismiss the possibility of TB meningitis if CSF glucose is normal; it may be in ~20% of cases and the tubercilin test may also be negative initially in a similar percentage. *M. tuberculosis* is seen in the initial CSF of approximately 40% of patients with tuberculous meningitis. Send CSF for viral and TB PCR.

Treatment regimens

- *Viral meningitis:* usually supportive treatment only.

- *TB meningitis:* pyrazinamide 30mg/kg/day and isoniazid 10mg/kg/day (up to a max of 600mg/day) achieve best CSF penetration. Give pyridoxine 10mg daily as prophylaxis against isoniazid neuropathy. For the first 3 months, add rifampicin (450mg/day if wt <50kg or 600mg/day if wt >50kg) and ethambutol (25mg/kg/day) if the patient is not unconscious. Thereafter, for the next 7â€“10 months, give isoniazid (at a lower dose of 300mg/day) and rifampicin. Consult your local respiratory/ID specialists for advice.
- There are several other regimens in use for *M. tuberculosis* meningitis; *M. avium intracellulare* requires a different combination of drugs.[1] *Corticosteroids* are often prescribed if there are focal signs, raised intracranial pressure, or very high levels of CSF protein (see â€˜adjunctive therapy for acute bacterial meningitisâ€™, P436).
- *Cryptococcal meningitis:* several regimens are used. Amphotericin B 0.6â€“1.0mg/kg/day alone or at a lower dose of 0.5mg/kg/day in conjunction with flucytosine 150mg/kg/day for 6 weeks appears effective. Fluconazole (400mg/day initially, then 200â€“400mg/day for 6â€“8 weeks) is an alternative which appears to be as effective in AIDS.

Footnote

1

Berger JR (1994) *Curr Opin Neurol* 7: 191â€“200.

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Acute viral encephalitis

Presentation

- *Change in personality*.
- *Confusion, psychiatric disturbance or altered level of consciousness*.
- *Headache, fever and some neck stiffness*. Meningism is usually not prominent: some individuals have a meningo-encephalitis.
- *Focal neurological signs*. Hemiparesis or memory loss (usually indicative of temporal lobe involvement) is not uncommon.
- *Seizures* are common; some are complex partial in nature.
- *Raised intracranial pressure* and signs of brain shift (P526).
- *Predisposing Factors:* immunocompromised patient.

Management

- Antibiotic therapy

  If there is any suspicion that the illness is meningitis, start antibiotics (P434). It is not necessary to await CSF analysis.

- Specific anti-viral therapies

  Acyclovir has dramatically reduced mortality and morbidity in HSV encephalitis. Most clinicians therefore give it in suspected encephalitis without waiting for confirmation that the pathogen is herpes simplex.

  - *Acyclovir* 10mg/kg iv (infused over 60 minutes) every 8 hours (reduced dose in renal insufficiency) is given for 10â€“14 days.
  - *Ganciclovir* 2.5â€“5.0mg/kg iv (infused over 60 minutes) every 8 hours should be given if cytomegalovirus is a possible pathogen (more likely in renal transplant patients or those with AIDS). Treatment is usually for 14â€–28 days depending upon response.

- CT scan: scan all patients prior to LP

  In a patient with focal neurological signs, focal seizures, or signs of brain shift a CT scan must be arranged urgently. CT may not demonstrate any abnormalities. In herpes simplex encephalitis there may be low attenuation areas, particularly in the temporal lobes, with surrounding oedema. MR imaging is more sensitive to these changes.

- Lumbar puncture

  - *Measure opening pressure*. CSF pressure may be raised (>14cm CSF) in which case the patient must be observed closely at 15-minute intervals.
  - *Analysis of CSF* usually reveals a lymphocytic leukocytosis (usually 5â€“500/mm^3) in viral encephalitis, but it may be entirely normal. The red cell count is usually elevated. PCR on CSF is sensitive and specific. CSF protein is only mildly elevated and glucose is normal.

- Further investigations

- *Serology:* save serum for viral titres (IgM and IgG). If infectious mononucleosis is suspected a monospot test should be performed.
- *EEG:* should be arranged even in those without seizures. There may be generalized slowing and, in herpes simplex encephalitis, there may be bursts of periodic high-voltage slow wave complexes over temporal cortex.

Complications

Neurological observations should be made regularly. Two complications may require urgent treatment.

- *Raised intracranial pressure* secondary to cerebral oedema may require treatment with dexamethasone (see â€˜intracranial space-occupying lesionâ€™, P458). There is some experimental evidence that steroids may potentiate spread of herpes virus, so dexamethasone should not be given prophylactically without a specific indication. In the acute situation, if there is evidence of brain shift, mannitol may be used (see â€˜raised intracranial pressureâ€™, P452). Another cause of raised ICP is hameorrhage within necrotic tissue. Perform a CT if there is any deterioration in the patient and discuss with neurosurgeons.
- *Seizures* may be difficult to control but are treated as seizures of any other aetiology.

Causes in UK

- Herpes simplex
- Varicella zoster
- Coxsackie

- Cytomegalovirus (in immunocompromised)
- Mumps
- Epsteinâ€“Barr virus
- Echovirus

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Head injury: presentation

- Varies from transient â€˜stunningâ€™ for a few seconds to coma.
- A fraction of patients who attend A&E need to be admitted for observation (indications for admission are given in on P449).

In the alert patient, determine the following.

- Circumstances surrounding injury. Was it caused by endogenous factors, e.g. loss of consciousness whilst driving? Or exogenous factors, e.g. another driver? Was there extracranial trauma?
- Period of loss of consciousness. This relates to severity of diffuse brain damage.
- Period of post-traumatic amnesia. The period of permanent memory loss after injury also reflects degree of damage (NB: period of retrograde amnesia or memory loss for events prior to injury does not correlate with severity of brain damage).
- Headache/vomiting. Common after head injury but if they persist raised intracranial pressure should be considered (P452).
- GCS score.

- Skull fracture present?
- Neurological signs. Are there any focal neurological signs?
- Extracranial injury. Is there evidence of occult blood loss?

The drowsy or unconscious patient needs the following.

- Urgent assistance from senior A&E staff and anaesthetists.
- Protection of airway. The patient who has deteriorating level of consciousness or is in coma should be intubated because hypocarbia and adequate oxygenation are effective means of reducing intracranial pressure rapidly. If the patient is neurologically stable and protecting their airway, intubation may not be necessary. Assume there is a cervical spine injury until an X-ray (of all seven cervical vertebrae) demonstrates otherwise.
- Hyperventilation. The pattern of breathing should be noted (P524). Hyperventilation of intubated patients with the aim of lowering P_aCO_2 is controversial: consult an intensivist.
- Support of circulation. Hypotension should be treated initially with colloid. If persistent or severe, exclude a cardiac cause (ECG) and occult haemorrhage (e.g. intra-abdominal).
- Treatment of seizures. Diazepam 5â€“10mg iv/rectally which may be repeated to a maximum of 20mg. If seizures continue, consider iv phenytoin (P474).
- Rapid survey of chest, abdomen, and limbs. Looking for a flail segment or haemo/pneumothorax, possible intra-abdominal bleeding (if there are any doubts peritoneal lavage may be required), limb lacerations, and long bone fractures.
- Brief history. Should be obtained from ambulance crew or relatives. The patient may have lost consciousness just

before the injury, e.g. due to subarcahnoid haemorrhage, seizure, or hypoglycaemia. The tempo of neurological deterioration should be established.

- Guidelines for performing skull X-rays and CT scans are on P446.

Symptoms following head injury

Symptoms associated with minor head injury

Headache, dizziness, fatigue, reduced concentration, memory deficit, irritability, anxiety, insomnia, hyperacusis, photophobia, depression, and general slowed information processing

Symptoms associated with moderate to severe head injury

As above, but also

Behavioural problems include irritability, impulsivity, egocentricity, emotional lability, impaired judgment, impatience, anxiety, depression, hyper- or hypo-sexuality, dependency, euphoria, aggressiveness, apathy, childishness, and disinhibition

Cognitive impairment includes deficits of memory, difficulty in abstract thinking, general slowed information processing, poor concentration, slow reaction time, impaired auditory comprehension, reduced verbal fluency, anomia, and difficulty planning or organizing

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Head injury: assessment

Examination

Rapid neurological assessment should take only a few minutes

- The level of consciousness must be noted with GCS score (P520).
- Note the size, shape, and reactions of pupils to bright light.
- Resting eye position and sponateous eye movements should be observed. If the latter are not full and the patient unresponsive, test oculocephalic and/or oculovestibular responses (P530).
- The doll's head manoeuvre should not be attempted if cervical spine injury has not been excluded.
- Test the corneal reflex (cranial nerves V and VII).
- Motor function should be assessed (see P520); any asymmetry should be noted.
- Look for features suggesting brain shift and herniation (P526).

Head and spine assessment

- The skull should be examined for a fracture. Extensive periorbatal haematomas, bruising behind the ear (Battle's sign), bleeding from the ear, and CSF rhinorrhoea/otorrhoea suggest a basal skull fracture. Look for facial (maxillary and mandibular) fractures.
- Only 1% of patients will have a skull fracture. This greatly increases the chances of an intracranial haematoma (from 1 : 1000 to 1 : 30 in alert patients; from 1 : 100 to 1 : 4 in confused/comatose patients). NB: potentially fatal injuries are not always associated with skull fracture.
- *Consider* the possibility of spinal cord trauma. â€˜Log-rollâ€™ the patient and examine the back for tenderness over the spinous processes, paraspinal swelling, or a gap between the spinous processes. The limbs may have been found to be flaccid and unresponive to pain during the neurological assessment. There may be painless retention of urine.

Indications for skull X-ray

- History of high-impact injury
- Decreased level of consciousness
- Amnesia
- Nausea/vomiting
- Neurological signs/symptoms
- CSF/blood from nose/ear
- Scalp bruising/swelling
- Suspected penetrating injury
- Difficulty in clinical assessment (e.g. alcohol, drugs, very young/elderly)
- Seizures

- *If GCS <12/15, arrange an urgent head CT*

Things to look for on skull X-rays

- Linear skull fracture (see above)
- Depressed skull fracture (requires elevation if depressed by more than the vault thickness)
- >3mm shift of a calcified pineal (if present)
- Integrity of craniocervical junction
- Fluid level in sphenoid sinus

Definite indications for CT scan[1]

- Skull fracture and persistent neurological dysfunction
- Depressed level of consciousness and/or neurological dysfunction (inc. seizures)
- Coma after resuscitation
- Suspected compound fracture of vault or base of skull (e.g. CSF leak)
- Skull fracture
- Confusion/neurological disturbance persisting >12 hours
- Seizure
- Significant head injury requiring general anaesthaesia

Things to look for on C-spine films

â€¢ Check all 7 C-spine vertebrae and C7-T1 junction are visible	
â€¢ Check alignment	â€¢ anterior and posterior of vertebral bodies
	â€¢ posterior margin of spinal canal
	â€¢ spinous processes

A step of >25% of vertebral body suggests facet joint dislocation

â€¢ Check contours	â€¢ outlines of vertebral bodies
	â€¢ outlines of spinous processes

Look for avulsion fractures, wedge fractures (>3mm height difference between anterior and posterior body height)

â€¢ Check odontoid	â€¢ open mouth and lateral views
â€¢ The distance between ant. arch C1 and odontoid should be <3mm disc spaceand odontoid	â€¢ disc spaces
â€¢ Check soft tissues	â€¢ space between anterior C3 and back pharyngeal shadow >5mm suggests retropharyngeal mass (e.g. abscess or haematoma from fracture of C2)

Footnote

[1]Adapted from
Report of the Working Party on the Management of with Head Injuries (1999) Royal College of Surgeons of England, London.

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Head injury: immediate management

- After resuscitation, *take blood* for *FBC, G&S, U&Es, arterial blood gases* and if the circumstances of injury are not clear or there is a suspicion of drug intoxication, *toxicology screen*.
- *Subsequent* management depends upon the pace of events and the clinical situation. >40% comatose patients with head injury have intracranial haematomas and it is not possible definitively to distinguish between these patients and those who have diffuse brain injury and swelling on clinical examination alone.
- *Urgent CT scan*. This is the next step in most patients who have depressed level of consciousness or focal signs (see table, P447). The speed with which this needs to be arranged depends upon the tempo of neurological detrioration (relative change in GCS score, P520) and/or the absolute level of consciousness (GCS <8). If CT scanning is not available at your hospital you must discuss with your regional neurosurgical centre.
- *Treatment of raised intracranial pressure* is discussed on P452; corticosteroids have no proven benefit. Discuss with your neurosurgical centre. In a rapidly deteriorating situation it may be necessary to proceed directly to surgery. It may be decided to hyperventilate and to give

mannitol (1g/kg over 10â€“15 minutes or ~250ml of 20% solution for an average adult) and frusemide (20â€“40mg iv) while obtaining an urgent CT scan.

- *Surgery* may be indicated for extradural (P460), subdural (P464), and possibly some intracerebral haemorrhages (P462) and complex head wounds such as compound depressed skull fractures.
    - A general rule is urgent evacuation is required of extradural haematomas which produce mid-line shift of 5mm or more and/or 25ml in calculated volume.
    - If the extraduaral haemorrhage is considered too small to warrant surgery on a CT scan performed within 6 hours of injury, the scan should be repeated after a few hours irrespective of whether there has been a deterioration in the patient's condition.
- *Non-operative management*. Brain contusion may be evident as areas of increased or decreased density but CT is not a sensitive way to detect primary diffuse brain injury. Effacement of the cavity of the third ventricle and of the perimesencephalic cisterns suggests raised intracranial pressure but the absence of these signs is not to be taken as an indicator or normal intracranial pressure. Many centres therefore proceed to intracranial pressure monitoring (P948) although this is a controversial subject.

Indications for admission following head injury

- Confusion
- Abnormal CT scan
- Decreased level of consciousness (<15/15)

- Clinical or radiological evidence of skull fracture
- Neurological signs or severe headache + vomiting
- Difficulty in assessment (e.g. alcohol, drugs, very young/elderly)
- Concurrent medical conditions (e.g. clotting disorders, diabetes)
- Poor social circumstances/living alone

NB: Very brief loss of consciousness or post-traumatic amnesia are not absolute indicators for admission but each patient needs to be assessed on their own merits.

If patients are discharged they should be sent home with

- A responsible adult who will be with them over the next 24 hours
- A head injury card which describes potential signs and symptoms(e.g. undue sleepiness, headache, vomiting, or dizziness) of delayedneurological dysfunction

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Head injury: further management

The aim of subsequent management is to minimize secondary injury to the brain other than intracranial haematomas (see table). Management may be better undertaken at a neurosurgical centre and if this is arranged the guidelines opposite should be followed for transfer.

The principles of management are

- *Regular and frequent neurological observation*. If there is deterioration consider whether there may be a secondary cause of brain injury contributing to this (see table). If there are new signs of raised intracranial pressure, declining level of consciousness, or signs of transtentorial herniation (P526), the patient requires intubation and hyperventilation if this has not already been performed. Mannitol may be started or a repeat bolus may need to be given (see P454) and repeat CT scanning may be necessary.
- *Regular monitoring of BP, blood gases, electrolytes, urinary output*. Pre-emptive treatment of a decline in any of these may prevent neurological deterioration. Hypotension is commonly due to sedative agents and/or hypovolaemia. But fluid therapy needs to be conducted with care because overgenerous administration may exacerbate raised intracranial pressure. Monitor CVP.

- *Prompt treatment of seizures* (P474).
- *Nasogastric tube* to administer nutrition and drugs including ranitidine 150mg bd for prophylaxis against gastric ulceration.
- *A bowel regimen* of stool softeners should be started.

Before transfer to Neurosurgical Unit[1]

- Assess clinically for respiratory insufficiency, shock, and internal injuries.
- Perform CXR, arterial blood gas estimation, cervical spine X-ray.
- Appropriate treatment might be to
    - intubate (e.g. if airway obstructed or threatened)
    - ventilate (e.g. cyanosis, P_aO_2 <7.9kPa, P_aCO_2 >5.9kPa)
    - commence iv fluids carefully
    - give mannitol, after consultation with neurosurgeon
    - apply cervical collar or cervical traction.
- Patient should be accompanied by personnel able to insert or to reposition endotracheal tube, to initiate or maintain ventilation, to administer oxygen and fluids, and to use suction.

Indications for neurosurgical referral (and/or urgent CT head scan) following head injury[1a]

- Recent intracranial lesion seen on CT

- Persisting coma (<9/15) after initial resuscitation
- Confusion which persists for >4 hours
- Progressive focal neurological signs
- Seizure without full recovery
- Depressed skull fracture
- Definite or suspected penetrating injury
- CSF leak or other sign of a basal skull fracture
- Urgent CT indicated but no local facilities available

Causes of secondary brain injury[2]

Systemic	Intracranial
Hypoxaemia	Haematoma (extradural, subdural, or intracerebral)
Hypotension	
Hypercarbia	Brain swelling/oedema
Severe hypocapnoea	Raised ICP
Pyrexia	Cerebral vasospasm
Hyponatraemia	Epilepsy
Anaemia	Intracranial infection
DIC	

Footnote

1

Mendelow AD & Teasdale G (1991) In Swash M & Oxbury J, ed. *Clinical Neurology*, Section 14, p. 698.

1a

Adapted from Report of the Working Party on the Management of with Head Injuries (1999) Royal College of Surgeons of England, London.

2

Miller JD (1993) *J Neurol Neurosurg Psychiat* 56: 440â€“447.

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Raised intracranial pressure (ICP)

Presentation

Normal ICP in adults is 0â€“10mmHg at rest. Treatment is required when it exceeds 15â€“20mmHg for >5 minutes. Symptoms and signs suggestive of raised ICP include

- *Headache and Vomiting* worse in mornings; exacerbated by bending.
- *Focal neurological signs* may occur if there is a space-occupying lesion and in some metabolic conditions (e.g. liver failure). But there may also be false localizing signs, e.g. VIth cranial nerve palsy.
- *Seizures* may occur with space-occupying lesions, CNS infection, or metabolic encephalopathies associated with raised ICP.
- *Papilloedema* is present only if there is CSF obstruction.
- *Impaired level of consciousness:* from mild confusion to coma.
- *Signs of brain shift*[1] may accompany decreasing level of consciousness. They are discussed with examination of brainstem function (P524).
- *Late signs: bradycardia and hypertension* (Cushing

response) probably results from direct medullary compression. Its clinical value is probably overemphasized in comparison to other signs of brain shift (P526).

Causes

- Head injury â†’ intracranial haematoma/brain swelling/contusion
- Stroke (haemorrhagic, major infarct, venous thrombosis)
- Metabolic (hepatic or renal failure, DKA, hyponatraemia, etc.)
- CNS infection (abscess, encephalitis, meningitis, malaria)
- CNS tumour
- Status epilepticus
- Hydrocephalus (of any cause)
- â€˜Benignâ€™ intracranial hypertension.

Assessment of severity

- GCS (P524)
- Signs of brain shift and brainstem compromise (P526).

Management

- Stabilize the patient
- Consider active means of reducing ICP
- Attempt to make a diagnosis
- Treat factors which may exacerbate raised ICP
- Observe for signs of deterioration and attempt to reverse

them

- Consider specific therapy.

What follows is the management for stabilizing a patient presenting acutely with raised ICP and may not be appropriate for many patients with a long progressive history of deterioration.

Practice point

- A morning occipital headache may indicate raised ICP or cervical spondylosis.[1a]

Footnote

1

Plum F & Posner JB (1980) *The Diagnosis of Stupor and Coma*, 3rd edn; FA Davis, Philadelphia.

1a

Hawkes C (2002) *Hosp Med* 63:732â€“42.

Editors: Ramrakha, Punit S.; Moore, Kevin P.
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Raised intracranial pressure: immediate management

Stabilize the patient

- *Open the airway* by laying the patient on their side. Give oxygen. Measure *arterial blood gases*. Intubation and mechanical ventilation may be necessary because of respiratory compromise. It may also be necessary to reduce ICP by hyperventilating the patient (see below) to keep P_aCO_2 between 3.3â€“4.0kPa (25â€“30mmHg).
- *Correct hypotension*. Volume expansion with colloids or infusions of inotropes needs to be conducted with careful and frequent monitoring of CVP and/or pulmonary artery wedge pressure. In general, patients with raised ICP should be fluid restricted to 1.5â€“2.0L/day. So if volume expansion is required it should be kept to the minimum required to restore BP.
- *Treat seizures* (P474).
- *Examine rapidly* for signs of head injury (P444). If the patient is hypotensive, examine carefully for any occult site of bleeding. If there is a rash, consider the possibility of meningococcal meningitis; take blood cultures and give antibiotics (P434).
- Take blood for *glucose* (this may be raised in diabetic

ketoacidosis or hyperosmolar non-ketotic states, it may be very low in liver failure), *U&Es* (biochemical assessment of dehydration and renal function, potassium for susceptibility to dysrhythmia, hyponatraemia from inappropriate ADH, or hypernatraemia from aggressive diuretic-induced dehydration), *LFTs, albumin, clotting studies and ammonium* (to assess liver function), *FBC*, and *blood culture*.

Measures to reduce ICP

The value of ICP monitoring is a controversial subject. Irrespective of whether or not your patient's ICP is monitored, the following interventions should be considered.

- *Elevate head of bed* to ~30Â° (once cervical spine injury has been excluded) to promote venous drainage.
- *Hyperventilation* so that P_aCO_2 is kept between 3.7â€“3.9kPa will promote cerebral vasoconstriction and lower cerebral blood volume: this requires intubation and paralysis. It will also lower the BP and may compromise cerebral circulation. In patients with liver failure this is no longer recommended. Discuss with your local ITU.
- *Mannitol:* 0.5â€“1g/kg over 10â€“15 minutes (~250ml of 20% solution for an average adult) reduces ICP within 20 minutes and its effects should last for 2â€“6 hours. *Frusemide* 20â€“40mg iv may be given with mannitol to potentiate its effect. If required further boluses of smaller doses of mannitol (0.25â€“0.5g/kg) may be given every few hours. U&Es and serum osmolality should be monitored as a profound diuresis may result. Serum osmolality should not be allowed to rise over 320mOsm/kg.
- *Corticosteroids* are of benefit in reducing oedema around space-occupying lesions (P458) but are not helpful in the treatment of stroke or head injury. Dexamathasone is given as a loading dose of 10mg iv. It may be followed by

4â€“6mg q6h po/via NG tube.

- *Fluid restriction* to 1.5â€“2.0L/day. U&Es must be checked frequently.
- *Cooling* to 35 Â°C reduces cerebral ischaemia.
- *Avoid/treat hyperglycaemia* because it exacerbates ischaemia.

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Raised intracranial pressure: further management

Attempt to make a diagnosis

Often the history makes the diagnosis obvious and usually raised ICP is a secondary diagnosis. If a history is not available, focal neurological signs or focal seizures suggest an underlying structural cerebral lesion (although such signs may occur with hepatic or renal failure). Meningism raises the possibility of subarachnoid haemorrhage or meningitis.

A CT scan should be performed in all patients suspected of having raised ICP before lumbar puncture is considered.

(Lumbar puncture should be discussed with a senior colleague and/or Neurologist.) Blood sent for analysis on admission may help to detect metabolic causes of raised ICP.

Benign intra-cranial hypertension

Benign intracranial hypertension (BIH) is a syndrome of raised intracranial pressure in the absence of an intracranial mass lesion or hydrocephalus. Although rarely life-threatening, BIH can cause permanent visual loss due to optic nerve damage. This disorder affects 1 in 100 000 of the population overall, but this increases to 1 : 5000 obese women of child-bearing age. There is a predominance in women over men (4 : 1), aged 17â€“45 years.

Presentation

- Constant but variable headaches
- Visual disturbances (incl. diplopia, visual obscurations, scotoma) Â± nausea
- Problems with balance, memory
- Tinnitus
- Neck and back pains
- The presence of focal neurology incl. epilepsy does NOT occur in BIH.
- Preservation of cerebral function distinguishes BIH from acute viral encephalitis or bacterial meningitis.
- Fundoscopy almost invariably shows papilloedema (maybe unilateral).

Associations

- Obesity is present in >90%
- Menstrual problems
- Drugs (tetracycline, isoretinoin and etretinate, nalidixic acid, nitrofurantoin, and lithium)
- Oral contraceptive pill
- Steroid withdrawal
- Increased spontaneous abortion

Investigations

- CT head scan or MRI are usually normal.
- Lumbar puncture reveals an elevated CSF pressure (>20cm,

but may increase in obesity anyway).

Treatments (seek advice)

- Losing weight
- Repeated therapeutic LP every 2â€“5 days
- Prednisolone (40â€“60mg/day) is effective in relieving the headache and visual obscuration due to papilloemea. However, steroids are to be avoided long term.
- acetazolamide +/- frusemide,
- surgical shunting (lumboperitoneal shunts).

Treat factors which exacerbate raised ICP[1]

- *Hypoxia/hypercapnia*. Arterial blood gases need to be measured regularly.
- *Inadequate analgesia, sedation, or muscle relaxation* lead to hypertension. NB: hypertension should not be treated aggressively. Pain, e.g. from urine retention, may be the cause. Rapid lowering of BP may lead to â€˜watershedâ€™/â€™border zoneâ€™ cerebral infarcts.
- *Seizures* are not always easy to identify in paralyzed patients.
- *Pyrexia* increases cerebral metabolism and, as a consequence, cerebral vasodilatation. It also appears to increase cerebral oedema. The cause of pyrexia should be sought but paracetamol (given rectally) and active cooling should be commenced.
- *Hypovolaemia*.

- *Hyponatraemia* is usually the result of fluid overload but may be caused by a syndrome of inappropriate ADH secretion. Treat with DDAVP 1â€“4Âµg iv daily (see P572).

Consider specific therapy

- Once a diagnosis is established it may be appropriate to consider surgery in order to decompress brain or insert a ventricular shunt to drain CSF.
- Intracranial infections need to be treated with the most suitable antibiotics.
- Hyperglycaemia (ketotic/non-ketotic) and liver or renal failure have their own specific management (see relevant sections).
- Often, however, there may not be a specific intervention that is appropriate, e.g. contusion following head injury, and management is confined to optimizing a patient's condition whilst awaiting recovery.

Footnote

1

Pickard JD & Czosnyka M (1993) *J Neurol Neurosurg Psychiat* 56: 845â€“858.

Editors: Ramrakha, Punit S.; Moore, Kevin P.
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Intracranial space-occupying lesion

Presentation

- *Symptoms of raised intracranial pressure*: headache, nausea, and vomiting (see P452).
- *Papilloedema* is present in the minority of cases.
- *Focal neurological symptoms and signs*. These depend upon location of the lesion, its extent and that of surrounding cerebral oedema, and compression of long tract fibres or cranial nerves. Some lesions, particularly those in the frontal lobe, are relatively â€˜silentâ€™ and may produce no signs or simply change in personality.
- *Seizures*.
- *Impaired level of consciousness* ranging from confusion to coma.
- *Signs of brain shift* (P526) may be present.
- *Fever* suggests an infection. There may be a recent history of ear ache/discharge, tooth ache, foreign travel, or immune compromise.
- *Acute onset of symptoms* suggests the possibility of a vascular event, either primary or bleeding into another type of lesion, e.g. tumour.

Management

Depends upon the diagnosis. In a comatose individual with known inoperable brain metastases it is usually not appropriate to intervene. On the other hand, if a patient presents for the first time with signs suggestive of a space-occupying lesion the diagnosis needs to be established.

- Assess severity
    - If comatose, protect the airway and manage as on P408.
    - If there are signs of brain shift which suggest impending transtentorial herniation (P526) give mannitol 0.5â€“1g/kg over 10â€“15 minutes (100â€“250ml of 20% solution for an average adult) and hyperventilate to keep P_aCO_2 between 3.7â€–3.9kPa. This may be followed by smaller doses of mannitol every few hours (P454).
    - If the patient is alert and stable it is best to await CT scan and in the interim make regular neurological observations.
- If the patient is *pyrexial* or the history is suggestive of *infection*, blood, sputum, and urine cultures should be sent. An urgent CT scan should be arranged for these cases; CSF analysis may be necessary but lumbar puncture should *not* be performed before the scan or discussion with neurologists/neurosurgeons.
- If a *vascular event* is suspected a CT should also be arranged urgently because decompression may be possible.
- *Seizures* should be treated. If they are recurrent, the patient may require loading with iv phenytoin. Many neurosurgeons, give oral phenytoin prophylactically to patients (300mg/day; therapeutic levels are not reached for

at least 5 days).

- *Steroid therapy* is given if it is thought that some of the symptoms/signs are due to tumour-related brain oedema. Give dexamethasone 10mg iv (loading dose), followed by 4â€“6mg po or ng q6h. This is a large dose of steroid (NB: dexamethasone 20mg/day equivalent to prednisolone 130mg/day) and urine/blood glucose should be monitored. Duration of therapy is guided by response to steroid and the patient's general condition.
- *Neurosurgery/radiotherapy* may be of some benefit in some individuals: discuss with your regional neurosurgical centre.

Common causes of intracranial space-occupying lesions

- Cerebral tumour (1Â°/2Â°)
- Subdural haematoma
- Intracerebral haemorrhage
- Tuberculoma
- Cerebral abscess
- Extradural haematoma
- Subdural empyema
- Toxoplasmosis (immunocompromised)

Practice point

- Hemi-sensory loss involving the trunk is likely to be due to a deep lesion involving the thalamus. Complete hemi-sensory loss may be seen in functional disorders, and can be distinguished by placing a tuning fork on each side of

> the forehead and the sternum. Patients with functional disease report that vibration is less on the affected side, which is anatomically not possible.[1]

Footnote

1

Hawkes C (2002) *Hosp Med* 63:732â€“42.

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Extradural haemorrhage

Presentation

There are no specific diagnostic features. Consider the diagnosis in any head-injured patient who fails to improve or continues to deteriorate.

- *Head injury* is almost invariable.
- *Skull fracture* present in over 90% of adult cases.
- *Headache and vomiting* may occur.
- *Impaired level of consciousness*. There may be an initial lucid interval following head injury but extradural haematomas may be present in patients who have been in coma continuously after the injury. Uncommonly, if the cause is a dural venous sinus tear (rather than shearing of a meningeal artery) lucid interval may extend for several days.
- *Seizures*.
- *Contralateral hemiparesis and extensor plantar* may be elicited.
- *Signs of brain shift* (P526).

Causes

Common	*Rare*
â€¢ Head injury â†’ tearing of meningeal artery (commonly middle menigeal)	â€¢ Head injury â†’ dural sinus tear
	â€¢ Intracranial infection (sinuses, middle ear, orbit)
	â€¢ Anti-coagulants/blood dyscrasia

Assessment of severity

Bilateral extensor plantars or spasticity, extensor response to painful stimuli, and coma are severe effects of an extradural haemorrhage.

Management

Depends upon tempo of presentation. Priorities are

- *Stabilize the patient:* protect the airway; give oxygen, support the breathing and circulation. Assume C-spine injury till excluded.
- *Treat seizures* (P474).
- *Urgent CT scan*
    - Haematomas with >5mm mid-line shift on CT and/or >25ml calculated volume require urgent evacuation.
    - If the extraduaral haemorrhage is considered too small to warrant surgery on a CT scan performed within 6

hours of injury, the scan should be repeated after a few hours irrespective of whether there has been a deterioration in the patient's condition.

- *Closely monitor neurological state* (inc. GCS)
    - If the patient slips into coma and signs of tentorial herniation (P526) are progressing rapidly, give 1g/kg of 20% mannitol as a bolus and inform on-call surgeons.
    - If there is evidence of brain shift, discuss with neurosurgeons: intracranial pressure should be reduced with mannitol (0.5â€“1.0g/kg 20% mannitol) and hyperventilation (P454).
- All patients must be *discussed with neurosurgeons*. Neurological impairment is potentially reversible if the extradural haematoma is treated early.

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Intracerebral haemorrhage

Presentation

- *Headache*, nausea, and vomiting of sudden onset is common.
- *Focal neurological deficit:* the nature of this depends upon location of haemorrhage. Putaminal haemorrhages (~30% of cases) or lobar bleeds (~30% of cases) may lead to contralateral hemiparesis and sensory loss, visual field disturbance, dysphasia (left hemisphere), or spatial neglect (more severe with right hemisphere lesions). In other words, they may present like a middle cerebral artery infarct (P488) but often there is a greater alteration in the level of consciousness. Thalamic haemorrhages (~10% cases) may result in eye signs (forced downgaze, upgaze paralysis, or skew deviation) as well as contralateral sensory loss and hemiparesis. Cerebeallar haemorrhage is dealt with on P492 and pontine bleeds on P490.
- *Seizures* may occur.
- *Global neurological deficit* with decreasing level of consciousness progressing to coma. There may be signs of brain shift (P526).
- *Hypertension*.

Common predisposing factors

- Hypertension (40â€“50%).
- Anti-coagulants.
- Metastatic neoplasm: bleeds may occur within lesion.
- Drug abuse (alcohol, cocaine, pseudoephedrine, amphetamines).

Assessment of severity

A low GCS (<9), a large-volume haematoma, and the presence of ventricular blood on the initial CT are factors that are predictive of a high mortality rate.

Management

Priorities are

- Stabilize the patient: protect the airway, give oxygen if required, support the circulation if necessary or appropriate, commence general measures for treating comatose patient (P408) if necessary. If there is evidence of raised intracranial pressure, it should be reduced (see P454).
- Correct bleeding tendency or effects of anti-coagulants.
- Make a definitive diagnosis with urgent CT scan. Liaize with regional neurosurgery unit early as surgical intervention may be of benefit. Whether aggressive intervention is appropriate should be decided early.
- If appropriate, intensive care/high dependency ward nursing observations are required for the drowsy or comatose patient if they are not transferred to neurosurgical centre immediately.
- Surgical decompression may be beneficial: usually for

accessible bleeds within the posterior fossa (see P492), putamen, or thalamus.

- Patients who have a seizure at the onset of the haemorrhage should receive iv anti-convulsants.
- Hypertension is common. If systolic BP >200 or diastolic >120mmHg following a haemorrhagic stroke, it probably should be treated to limit vasogenic oedema, but this is controversial[1],[2] *Sublingual* nifedipine is best avoided as it may cause a profound fall in BP. We recommend atenolol 25â€“50mg po if necessary.

Footnote

1

O'Connell JE & Gray C (1994) *BMJ* 308: 1523â€“1524.

2

Lavin P (1986) *Arch Int Med* 146: 66â€“68.

Editors: Ramrakha, Punit S.; Moore, Kevin P.
Title: *Oxford Handbook of Acute Medicine, 2nd Edition*

Subdural haematoma

Presentation

- This may present in one of two ways: acute or chronic. Both are usually the result of tearing of bridging veins (between cortical surface and venous sinuses).
- Acute haemorrhage into the subdural space follows head injury and can be impossible to distinguish on clinical grounds from extradural haemorrhage (P460).
- A chronic haematoma is also preceded in most cases by head injury but this is often so trivial that patients are unable to recollect it.
- Both types of patient may present with
    - *Skull fracture* (more common in acute cases)
    - *Headache*
    - *Impaired and fluctuating level of consciousness* ranging from mild confusion, through cognitive decline (e.g. impaired memory) to coma. The diagnosis should be considered in any individual, particularly elderly, who presents with intellectual deterioration or â€˜dementiaâ€™ of relatively recent onset
    - *Focal neurological signs* (hemiparesis, dysphasia, hemianopia, etc.)

- *Seizures* occur in a minority of patients
- *Signs of brain shift* (P526) or *papilloedema*.

Common predisposing factors

- Head injury: in young or old
- Old age: cortical atrophy stretches bridging veins.
- Long-standing alcohol abuse
- Anti-coagulant use.

Assessment of severity

The following are severe effects of an subdural haemorrhage

- Bilateral extensor plantars or spasticity
- Extensor response to painful stimuli
- Coma.

Management

Depends upon tempo of presentation.

- In suspected *chronic cases*, a CT scan is required less urgently unless there has been an acute deterioration on a background of steady neurological decline. Chronic haematomas become isodense with brain and are therefore sometimes difficult to distinguish; magnetic resonance imaging may be better.
- In *acute cases*, priorities are
    - Protection of airway, give oxygen, support the breathing and circulation as necessary.

- Liaison with neurosurgical team early.
- Close monitoring of neurological state (GCS).
- Consider methods to reduce intracranial pressure if raised (P454): if the patient slips into coma and signs of tentorial herniation (P526) are progressing rapidly, give 1g/kg of 20% mannitol as a bolus, inform on-call surgeon, and very urgent CT scan.
- Treat seizures (P474).

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Title: *Oxford Handbook of Acute Medicine, 2nd Edition*

Subarachnoid haemorrhage: assessment

Presentation

- *Headache*: classically sudden and severe (â€˜thunderclapâ€™), radiating behind the occiput with associated neck stiffness. Often, the time from onset to peak of headache is only a few seconds, but less dramatic presentations are common. Consider the diagnosis in any unusually severe headache, especially if the patient does not have a previous history of headaches and is over 40 years. Approx. 4% of aneurysmal bleeds occur at/after sexual intercourse, but most coital headaches are not subarachnoid haemorrhages. 10% of patients with subarachnoid bleeds are bending or lifting heavy objects at onset of symptoms.
- *Nausea, vomiting, dizziness* may be transient or protracted.
- *Impaired level of consciousness*: there may be initial transient loss of consciousness followed by variable impairment. Patients may present in coma.
- *Early focal neurological signs* may occur, especially if there has been a concomitant intracerebral haemorrhage. Third nerve palsy raises possibility of posterior communicating aneurysm.

- *Seizures* are uncommon, but subarachnoid haemorrhage in a person known to have fits suggests underlying AV malformation.
- *Herald bleed*: Between 20 and 50 % of patients with documented SAH report a distinct, unusually severe headache in the days or weeks before the index bleed.[1] These are often misdiagnosed as simple headaches or migraine, so a high degree of suspicion is required.
- Patients may present with secondary head injury following collapse. Blood seen on CT scanning may be attributed to trauma.

Causes

Common	*Rare*
â€¢ Aneurysm (70%)	â€¢ Clotting disorder/anti-coagulants
â€¢ AV malformation (5%)	â€¢ Tumour
â€¢ No known cause in up to 20%	â€¢ Vasculitis
	â€¢ Associated with polycystic kidney disease

Assessment of severity (prognostic features)

- *Hunt & Hess Scale* allows grading at presentation and

thereafter:

Grade 1	Asymptomatic or minimal headache + slight neck stiffness
Grade 2	Moderate or severe headache with neck stiffness, but no neurological deficit other than cranial nerve palsy
Grade 3	Drowsiness with confusion or mild focal neurology
Grade 4	Stupor with moderate to severe hemiparesis or mild decerebrate rigidity
Grade 5	Deeply comatose with severe decerebrate rigidity.

- â€¢ Prognosis is best in Grade 1 (mortality <5%), worst in Grade 5 (mortality 50â€“70%), and intermediate in between.
- â€¢ Neurological deterioration following presentation has a worse prognosis. Patients should be re-graded on the Hunt & Hess Scale.

Practice points

- First and worst headache in someone not prone to headaches should suggest vascular tumours or expanding aneurysm[1]
- Thunderclap headache may be due to a ruptured intra-

cranial aneurysm[1a]

- Patients who wake, often at the same time, with severe unilateral orbital pain will usually have cluster headache. Mostly middle-aged males.[1a]

Footnote

1

Edlow JA & Caplan LR (2000) *New Engl J Med* 342: 29â€“35.

1a

Hawkes C (2002) *Hosp Med* 63:732â€“42.

Editors: Ramrakha, Punit S.; Moore, Kevin P.
Title: *Oxford Handbook of Acute Medicine, 2nd Edition*

Subarachnoid haemorrhage: immediate management[1]

- Once the diagnosis is confirmed, discuss with regional neurosurgeons.
- Transfer Grade 1 and 2 patients as soon as possible. Surgery will prevent rebleeding and although optimal time for operation is debated (2 days versus 7â€“10 days post bleed), outcome is probably improved by early transfer.
- Surgery on poor prognosis patients is unrewarding; they are usually managed conservatively. However, suitability for surgery should be re-assessed if their condition improves.

Stabilize the patient

- *Protect the airway* by laying the drowsy patient in the recovery position. Give oxygen.
- Consider *measures to reduce intracranial pressure* if signs suggest it is raised (P452) but avoid dehydration and hypotension.
- *Treat seizures* with usual drugs (P474) but beware of over-sedation and hypotension.
- *Correct hypotension* if necessary with colloid or inotropes.
- *To avoid hypertension* the patient should be nursed in a

quiet room, sedatives may be required, and stool softeners should be given to avoid straining. Once the diagnosis is established, nimodipine is usually given to reduce vasospasm; it helps also to reduce blood pressure.

- *ECG monitoring* and *treat dysrhythmias* if they compromise blood pressure or threaten thromboembolism. Rarely subarachnoid haemorrhage is associated with (neurogenic) pulmonary oedema.
- Take blood for *clotting screen* (if bleeding diathesis suspected) and *U&Es* (biochemical assessment of dehydration, potassium for susceptibility to dysrhythmia, hyponatraemia from inappropriate ADH or hypernatraemia from aggressive diuretic-induced dehydration).

Confirm the diagnosis

- *Urgent high-resolution CT scanning* is required. This will clinch the diagnosis in 95% of patients scanned within 24 hours. Furthermore, it gives valuable information regarding possible location of aneurysm and may even demonstrate AV malformation. It may also display concomitant intracerebral and/or intraventricular bleeds.
- *Lumbar puncture* is *not* usually required, unless CT scan is normal but the history is highly suggestive. It is important to examine the CSF for blood under these circumstances; the presenting event may be a â€˜warning leakâ€™. Blood in the CSF may result from a traumatic tap. If this is the case there should be diminishing numbers of red cells in each successive tube of CSF (although this is not always reliable). If the blood has been present for >6 hours, the supernatant should be xanthochromic after centrifugation.

Footnote

1

Kopitnik TA & Samson DS (1993) *J Neurol Neurosurg Psychiat* 56: 947â€“959.

Editors: Ramrakha, Punit S.; Moore, Kevin P.
Title: *Oxford Handbook of Acute Medicine, 2nd Edition*

Subarachnoid haemorrhage: further management

Specific therapies

- *Nimodipine* is a calcium channel blocker which works preferentially on cerebral vessels to reduce vasospasm (and consequent cerebral ischaemia).[1] It has been shown to reduce morbidity and mortality following SAH. Give 60mg po (or in the comatose patient) every 4 hours; intravenous therapy is costly and requires central venous access.
- *Anti-fibrinolytics* were introduced to prevent lysis of clot and rebleeding. They have been associated with increased thrombotic complications and are not advised at present.
- Appropriate analgesia (codeine phosphate 30â€“60mg every 4 to 6 hours) and anti-emetics should be given for awake patients.[2]

Observe for deterioration. Attempt to reverse it

Neurological observations should be performed regularly. If there is a deterioration, e.g. lowering of the level of consciousness, a CT scan should be performed. There are several possible mechanisms for deterioration:

- *Cerebral ischaemia* is usually insidious and multi-focal. It may give rise to focal and/or global neurological deterioration. Volume expansion with colloid or induced hypertension with inotropes have been attempted but these procedures have not been properly studied.
- *Rebleeding* may be immediately fatal or lead to apnoea. It is reported that assisted ventilation for 1 hour may be all that is necessary for spontaneous breathing to return to the majority of apnoeic individuals.[3] Patients who rebleed are at high risk of further bleeding and should be considered for emergency aneurysm clipping.
- *Acute hydrocephalus* may be treated with ventricular drainage. This can lead to dramatic improvement in the patient's condition.

Refer for definitive treatment

Unless the patient has a poor prognosis (see Hunt & Hess scale, P466), they should be cared for at a neurosurgical centre. The complications listed above should be managed by clinicians experienced in treating them.

Footnote

1

Pickard JD *et al.* (1989) *BMJ* 298: 636â€“642.

2

Kirkpatrick PJ (2002) *J Neurol Neurosurg Psychiat* 73 (suppl. 1): i28â€“i33.

3

van Gijn J (1992) *Lancet* 339: 653â€“655.

Editors: Ramrakha, Punit S.; Moore, Kevin P.
Title: *Oxford Handbook of Acute Medicine, 2nd Edition*

Status epilepticus (tonicâ€“clonic) 1

Presentation

Generalized tonicâ€“clonic status epilepticus is either continuous tonicâ€“clonic convulsions (30 minutes or longer) or convulsions so frequent that each attack begins before the previous post-ictal period ends.

Causes

- Cerebral tumour (1Â°/1Â°)
- Intracranial infection
- Hypoglycaemia
- Head injury
- Electrolyte disturbance (low sodium, calcium, or magnesium)
- Drug overdose (e.g. tricyclics)
- Drug withdrawal (e.g. alcohol)
- Hypoxia (e.g. post cardiac arrest)
- Sequela of stroke
- Anti-epileptic non-compliance/withdrawal

NB: most episodes of status do not occur in known epileptic patients.

Management

Priorities

- Stabilize the patient. Give oxygen
- Anti-epileptic drug therapy
- Attempt to identify aetiology
- Identify and treat medical complications
- Initiate long-term maintenance therapy if appropriate.

Stabilize the patient

- *Open the airway* by laying the patient on side in a semiprone position with the head slightly lower to prevent aspiration. Usually an oral airway will suffice and endotracheal intubation is rarely necessary.
- *Give oxygen*.
- *Correct hypotension* with colloid if necessary. Obtain an ECG if the patient is hypotensive. CVP monitoring may be necessary.
- Take blood for *U&Es, glucose, calcium, magnesium, liver enzymes, FBC (inc. platelets)*; if relevant, blood should also be sent for *toxicology screen* (if drug overdose or abuse suspected) and *anti-convulsant levels*.
- *Thiamine 250mg* iv should be given if alcoholism or other malnourished states appear likely.
- If hypoglycaemia is suspected *50ml of 50% glucose* should be administered iv. Because glucose increases the risk of Wernicke's encephalopathy, thiamine 1â€“2mg/kg iv should

be administered beforehand in any patient suspected of alcohol excess.

Anti-epileptic drug therapy

A number of agents may be used:

- Benzodiazepines (diazepam, lorazepam)
- Phenytoin
- Fosphenytoin
- Miscellaneous (general anaesthesia, paraldehyde).

Practice point

- Intermittant olfactory hallucinations may indicate a malignant glioma of the anteromedial temporal lobe (uncus) leading to uncinate fits.[1]

Footnote

1

Hawkes C (2002) *Hosp Med* 63:732â€“42.

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Title: *Oxford Handbook of Acute Medicine, 2nd Edition*

Status epilepticus (tonicâ€“clonic) 2

Anti-epileptic drug therapy[1]

- *Diazepam* 10â€“20mg iv or rectally, repeated once 15 minutes later if necessary. Intravenous injection should not exceed 2â€“5mg/min. Diazepam is rapidly redistributed and therefore has a short duration of action. With repeated dosing, however, as peripheral lipid compartments become saturated, there is less redistribution and blood diazepam levels increase. When this happens there is a risk of sudden central nervous and respiratory depression as well as cardiorespiratory collapse. If seizures continue, give *lorazepam* 0.07mg/kg iv (usually 4mg bolus which may be repeated once after 10 minutes). Because lorazepam does not accumulate in lipid stores and has strong cerebral binding and a long duration of action, it has distinct advantages over diazepam in early status epilepticus.
- If seizures continue, give *phenobarbital* 10mg/kg iv at a rate of 100mg/min (i.e. about 70mg in an average adult over 7 minutes).
- If seizures continue 30 minutes after first administration of an anti-epileptic agent, start an infusion of *phenytoin* at 15â€“18mg/kg at a rate of 50mg/min (e.g. 1g over 20 minutes). NB: 5% dextrose is not compatible with

phenytoin. The patient should have ECG monitoring because phenytoin may induce cardiac dysrhythmias; pulse, BP, and respiratory rate should also be monitored. iv phenytoin is relatively contraindicated in patients with known heart disease, particularly those with conduction abnormalities.

- An alternative is *fosphenytoin* given as an infusion of 15mg PE (phenytoin equivalents) at a rate of 100mg PE/min (i.e. about 1000mg PE in an average adult over 10 minutes).
- In refractory status (seizures continuing for 60â€“90 minutes after initial therapy), the patient should be transferred to intensive care.
    - General anaesthesia with either *propofol* or *thiopentone* should be administered.
    - *Paraldehyde* (5â€“10ml im) is an alternative but requires glass syringes as it corrodes rubber and plastic.
    - *Treat raised intracranial pressure* (P452).
    - *EEG monitoring* should be commenced.
    - The anaesthetic agent should be continued for 12â€“24 hours after the last clinical or electrographic seizure; the dose should then be tapered down.

If treatment is failing to control seizures, consider whether

- Initial drug dose is adequate
- Maintenance therapy has been started and is adequate
- Underlying cause of status epilepticus has been correctly identified
- Complications of status adequately treated (see below)
- Co-existing conditions have been identified (e.g. hepatic failure)
- There has been a misdiagnosis: is this â€˜pseudo

statusâ€™?

Footnote

1

Shorvon SD (2001) *J Neurol Neurosurg Psychiat* 70 (suppl. 2): ii22â€“ii27.

Editors: Ramrakha, Punit S.; Moore, Kevin P.
Title: *Oxford Handbook of Acute Medicine, 2nd Edition*

Status epilepticus (tonicâ€“clonic) 3

Attempt to identify aetiology

- A history of previous anti-convulsant use, drug abuse/withdrawal (including alcohol), diabetes, trauma, or recent surgery (e.g. hypocalcaemia post thyroid or parathyroid surgery) is obviously helpful.
- Examine the patient for signs of head trauma, meningism, focal neurological deficit (the seizures may also have some focal characteristics), needle tracks, or insulin injection sites.
- Consider urgent CT scan if head injury may be a precipitant; a lumbar puncture may be necessary if CSF infection is likely.
- Although hypoglycaemia and hypocalcaemia should be corrected promptly, hyponatraemia should be reversed cautiously because of the possibility of precipitating pontine myelinosis.

Identify and treat medical complications of status

Treatment is required for

- Hypoxia
- Lactic acidosis
- Hypoglycaemia
- Dysrhythmias
- Rhabdomyolysis
- Electrolyte disturbance (especially hyponatraemia, hypo/hyperkalaemia)
- Hypotension/hypertension
- Raised intracranial pressure
- Hyperpyrexia
- Pulmonary oedema
- Disseminated intravascular coagulation

These complications are managed as in other contexts.

Initiate long-term therapy (if appropriate)

Some disorders, e.g. hypoglycaemia in a diabetic taking insulin, do not require long-term anti-convulsant therapy, but rather correction of the underlying problem. Other conditions may need anti-convulsant treatment for a short while, e.g. alcohol withdrawal, or indefinitely, e.g. repeated status epilepticus in multi-infarct dementia.

- *Sodium valproate* is now considered first-choice treatment, with *carbamazepine* as an alternative.[1] Initially, sodium valproate should be given 400â€“600mg/day orally in three divided doses (intravenous therapy can also be given). It should be increased by 200mg/day at 3â€–6-day intervals; the maintenance dose is 20â€–30mg/kg/day (usual adult dose is 1â€–2g/day). Carbamazepine should be started at

100â€“200mg 1â€“2 times daily; the maintenance dose is 7â€“15mg/kg/day divided in 2â€–3 doses (200â€–800mg/day for adults).

- *Phenytoin* may be continued after intravenous loading at daily dosages of 5mg/kg (about 300mg for an average adult) either orally or via a nasogastric tube or slow intravenous infusion. Dosage should be guided by phenytoin level measurements. Plasma concentration for optimum response is 10â€–20mg/L (40â€–80Âµmol/L). Phenytoin is disadvantageous because it requires monitoring.

Driving advice

In the UK, patients should inform the Driving and Vehicle Licensing Agency (Swansea). Driving licences are revoked until the patient has been free of daytime seizures for 1 year, treated or untreated. Drivers of large goods or passenger carrying vehicles usually have those licences revoked permanently.

For current medical standards of fitness to drive go to http://www.dvla.gov.uk/at_a_glance/content.htm

Footnote

1

Smith D & Chadwick D (2001) *J Neurol Neurosurg Psychiat* 70 (suppl. 2): ii15â€–ii21.

Editors: Ramrakha, Punit S.; Moore, Kevin P.
Title: *Oxford Handbook of Acute Medicine, 2nd Edition*

Stroke: overview

Presentation

- Sudden-onset focal deficit of cerebral function is the most common presentation.
- Alternative presentations include apparent confusion (e.g. due to dysphasia or visuospatial impairment), seizures, declining levels of consciousness or global loss of brain function and coma.
- If the symptoms last for >24 hours (or lead to death) and there is no apparent cause other than a vascular event, the diagnosis is most likely to be a stroke. If the symptoms last <24 hours and, after adequate investigation, are presumed to be due to thrombosis or embolism, the diagnosis is a TIA.

Causes

- Thrombosis or embolism causing cerebral infarction (~80% cases)
- Primary intracerebral haemorrhage (~15% cases)
- Subarachnoid haemorrhage (~5% cases)
- Cerebral venous thrombosis (1%).

Risk factors

See table.

Differential diagnosis

Many conditions may masquerade as a stroke:

- Cerebral tumour (1Â° or 2Â°)
- Brain abscess
- Demyelination
- Focal migraine
- Subdural haematoma
- Todd's paresis (post seizure)
- Hypoglycaemic attack
- Encephalitis.

An alternative diagnosis to stroke is more likely in

- Patients less than 45
- Presence of seizures
- Presence of papilloedema
- Prolonged and/or discontinuous evolution of symptoms.
- Absence of risk factors
- Fluctuating level of consciousness
- Pyrexia (at presentation)

In general, a stroke commences suddenly and the deficit is at its peak and established within 24 hours. If the evolution of symptoms is longer or progresses in a stuttering way over days or weeks, a space-occupying lesion must be suspected. If there

is a variable depression of consciousness, the diagnosis of a subdural haematoma should be entertained, and pyrexia at presentation should alert one to the possibility of a cerebral abscess.

Seizures occur in 5â€“10% of strokes at their onset although they are frequent sequelae. Papilloedema would be extremely unusual in arterial strokes but may occur in cerebral venous sinus thrombosis. Consider this diagnosis particularly in patients who may have become dehydrated and a young women (particularly during the puerperium) with headache and seizures Â± focal signs.

Dissection of the internal carotid or vertebral arteries should always be considered, particularly in younger patients who may have experienced only mild neck trauma. Often, however, there may be no clear history of preceding trauma. Carotid dissection may be accompanied by a Horner's syndrome; vertebral dissection presents with symptoms associated with brainstem stroke.

Risk factors for stroke

Global

- Increasing age
- Hypertension
- Diabetes
- Family history
- Increased lipids
- Homocysteinaemia

Lifestyle

- Drug abuse
- Smoking

- OCP
- HRT
- Diving (Caisson's disease)
- Neck trauma/manipulation

Cerebral

- Cerebrovascular disease
- Berry aneurysms
- Cerebral amyloid
- Cerebral AV malformation

Cardiac

- Atrial fibrillation
- Myocardial infarction
- Left ventricular aneurysm
- Ischaemic heart disease
- Cyanotic heart disease
- Patent foramen ovale
- Endocarditis

Peripheral vascular

- Carotid stenosis
- Pulmonary AV malformations
- Ehlers Danlos
- Type IV (carotid dissection)

Haematological

- Hypercoagulable states

- Polycythaemia
- Sickle cell disease
- Warfarin (haemorrhage)
- Thrombolysis

OCP = Oral contraceptive Pill

HRT = Hormone replacement therapy

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Stroke: haemorrhage or infarct?

Intracerebral haemorrhage often has an apoplectic onset with a combination of headache, neck stiffness, vomiting, and loss of consciousness of acute onset. Conscious level can be depressed for over 24 hours, there may be bilateral extensor plantar responses and the blood pressure is more likely to be raised 24 hours after admission. But although features such as these have been integrated into scoring systems, it is not possible with certainty to differentiate ischaemic from haemorrhagic stroke on clinical grounds alone. A CT scan is required.

When to scan?

All patients suspected of having a stroke should be scanned within 48 hours of onset. CT is the investigation of choice in the majority of cases because it is better at detecting haemorrhage in the early stages compared with MRI. After the first 24 hours, and in cases where the stroke is suspected to involve brainstem or cerebellum, MRI is superior. Where the CT scan is normal, diffusion-weighted MRI may reveal areas of cerebral ischaemia or infarction.

Urgent CT should be performed in the presence of

- Depressed level of consciousness

- History of anti-coagulant treatment or known coagulopathy
- No available history
- Features suggesting an alternative diagnosis requiring immediate action, in particular
    - Subarachnoid haemorrhage (severe headache, depressed level of consciousness, neck stiffness)
    - Subdural haemorrhage (headache, history of minor trauma, progressive or fluctuating signs and symptoms)
    - Space-occupying lesion (depressed level of consciousness, progressive signs, papilloedema)
    - Cerebral infection (headache, fever, neck stiffness, cranial nerve palsies)
- Indications for thrombolysis or early anti-coagulation.

Brain imaging should always be undertaken before anti-coagulant treatment is started.

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Stroke: other investigations

Apart from a CT scan, there are some basic tests that most patients suspected of having a stroke should have.

- *FBC*, to detect polycythaemia, thrombocythaemia, or thrombocytopenia.
- *ESR and CRP*, to screen for vasculitis, endocarditis, hyperviscosity.
- *Electrolytes and calcium* (neurological defect may be non-vascular and caused by hyponatraemia, hypercalcaemia, or renal failure).
- *Glucose* to exclude hypoglycaemia and non-ketotic hyperglycaemia (which can mimic stroke) and diabetes mellitus (a risk factor).
- *Cholesterol* (if taken within 12â€“24 hours of stroke).
- *Syphilis serology* (low yield but treatable condition). NB: VDRL (but not TPHA) may be positive in SLE and the primary anti-cardiolipin syndrome. TPHA (but not VDRL) is positive in patients previously exposed to non-syphilitic treponemes (e.g. yaws).
- *Prothrombin time/INR* if the patient is taking warfarin.
- *ECG* to determine cardiac rhythm and exclude acute myocardial infarction.

- *Carotid Doppler ultrasound* to exclude high-grade (>70%) stenosis or dissection. This should be performed in patients who would be suitable for carotid endarterectomy or angioplasty. A bruit need not be present!
- *Cardiac echocardiography* may demonstrate the presence of valvular disease or intracardiac clot or may detect some rare causes of stroke such as atrial myxoma or patent foramen ovale.

Some patients, particularly young ones without common risk factors (see above), should be investigated further. Possible tests include

- *Serum protein, electrophoresis, viscosity*. In hyperviscosity syndromes the ESR is usually raised but not always.
- *Autoantibody screen*. (particularly for SLE).
- *Haemostatic profile*. In haemorrhagic stroke not apparently secondary to hypertension, measurement of PT, APTT, bleeding time, and fibrin degradation products may be indicated. In cerebral infarcts, blood should be taken for protein S, C, anti-thrombin III, and anti-cardiolipin antibodies. APTT may be prolonged in anticardiolipin syndrome. Consider testing for sickle cell in black patients. The Factor V_{Leiden} mutation may be an important risk factor for the development of venous thrombosis.
- *Toxicology screen* on admission sample if drug abuse (e.g. cocaine, pseudoephedrine, or amphetamines) suspected.
- *Urine tests* may detect homocystinuria (without other clinical manifestations) or porphyria. If BP is labile consider phaeochromocytoma and measure urinary catecholamines.
- *CSF analysis* may be necessary if the diagnosis of stroke is not well established, e.g. normal CT scan and no risk factors.
- *Cerebral angiography* is also reserved for cases where the

diagnosis is not well established and in those in whom cerebral vasculitis or malformation is suspected.

- *MRI* is more sensitive at detecting small infarcts, cerebral venous thrombosis, and lesions in the posterior fossa. In expert hands magentic resonance angiography may be comparable to conventional angiography.

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Stroke: complications[1]

Cerebral complications

Further neurological deterioration may be caused by the following.

- *Transtentorial herniation* (P526) is the commonest cause of death within the first week and carries a mortality of 80%. It is due to raised intracranial pressure (P452) secondary to cerebral oedema, and in ischaemic stroke is commonest after large MCA infarcts. Corticosteroids do not improve outcome; mannitol and hyperventilation may be useful temporary measures (P454); surgical decompression may be indicated in large haemorrhages, particularly cerebellar ones.
- *Haemorrhagic transformation* occurs in ~30% of ischaemic strokes (and up to ~70% of cardioembolic strokes), usually 12 hours to 4 days after the event. Neurological deterioration, it is usually due to a mass effect.
- *Acute hydrocephalus* due to compression of the aqueduct of Sylvius by oedema or blood may occur. Ventricular shunting may be of value.
- *Seizures* complicate ~10% of infarcts and are commonest in large, haemorrhagic, and cortical strokes. They usually respond to monotherapy (e.g. phenytoin).

- *Inappropriate ADH secretion* occurs in 10â€“15% strokes. It may initiate or worsen cerebral oedema and is treated by fluid restriction.
- *Depression* occurs in ~50% and may require therapy if it persists.

Systemic complications

- *Aspiration* is common. Dysphagia occurs in at least half of all cases of stroke[2], the incidence is higher in those with brainstem involvement or pre-existing cerebrovascular disease. It is often undetected at bedside and usually leads to aspiration. Testing the gag reflex is not a sufficient assessment; swallowing must be observed and if there is any suspicion video-fluoroscopy may be used. Patients should generally be fed upright.
- *Infection* is a common cause of death following stroke. Pneumonia (including aspiration) and UTIs are the usual problems.
- *Fever* usually occurs as a result of infection or DVT. Occasionally, it is a direct result of cerebral damage.
- *Venous thromboembolism:* the incidence of DVT following stroke is comparable to that following hip or knee arthroplasty. Pulmonary embolism accounts for up to 25% of early deaths following stroke. The use of prophylactic anti-coagulants reduces the incidence of venous thromboembolism but it is associated with an increased risk of haemorrhagic transformation which may outweigh any benefit. Many physicians use prophylactic low molecular weight heparin, although the RCP guidelines recommend compression stocking only. In the absence of intracranial haemorrhage, sub-clinical or overt proximal DVT should be treated with standard therapy. Below-knee DVT should be managed with compression stockings and serial USS monitoring for evidence of proximal extension.

- *Pressure sores* occur easily unless patients are regularly turned.

Practice point: Hypertension post stroke

- Hypertension is apparent in 75% of patients at the time of admission[3]
- BP usually falls over the first week and stabilizes to reveal underlying hypertension in about half of all patients
- Although early hypertension (BP >180mmHg) appears to be associated with a poor outcome there is no evidence that lowering BP in the acute phase of stroke is of any benefit
- We recommend that patients should be treated if BP >180/120 to 240/130, there are signs of accelerated hypertension, or there are complicating medical problems requiring urgent treatment such as severe heart failure or aortic dissection
- Drugs that may lower BP *precipitously* (e.g. short-acting calcium antagonists) should be avoided
- Many neurologists do not treat hypertension aggressively in patients who are known to have a significant carotid or basilar artery stenosis as this may precipitate fresh cerebral infarction

Footnote

1

Oppenheimer S & Hachinski V (1992) *Lancet* 339: 721â€“724.

2

Perry L & Love CP (2001) *Dysphagia* 16: 7â€“18.

Bath (1992) *Br Med Bull* 56: 422â€“435.

Editors: Ramrakha, Punit S.; Moore, Kevin P.
Title: *Oxford Handbook of Acute Medicine, 2nd Edition*

Stroke: secondary prevention[1]

- Attempt to modify â€˜risk factorsâ€™. (See risk factors, P478). Target BP should be below 140/85 (lower in diabetics). There is little to choose between the different classes of drugs: all reduce the risk of further events. Consider statins, esp. in those with co-existing IHD.
- Anti-platelet drugs. Aspirin reduces recurrence of stroke and death from other causes. In the absence of absolute contraindications aspirin (300mg initially and 75â€“300mg od thereafter) should be given immediately after the onset of stroke symptoms if haemorrhage is considered unlikely; otherwise it should be delayed until brain imaging has been performed. Patients intolerant of aspirin should be treated with clopidogrel (75mg od), which may be more effective than aspirin, particularly in high-risk patients. Patients in whom ischaemic stroke has recurred despite aspirin should be treated with aspirin and clopidogrel in combination, or aspirin and dipyridamole in combination (although the latter is controverisal).
- Anti-coagulants. To prevent recurrence of ischaemic stroke, warfarin is superior to aspirin in valvular, non-valvular, and paroxysmal atrial fibrillation but it is associated with increased risk of major bleeding. The balance of benefit may depend on patient group but generally favours warfarin, particularly in valvular AF. Aim for an INR of 2â€“3 provided there are no contraindications

and regular checks of INR are practicable. There is no consensus on when to initiate warfarin and whether a repeat CT is required to rule out late haemorrhagic transformation. Current practice is to delay the warfarinization for 1â€“2 weeks after the event, and to repeat the scan where the infarct is very large, or where there is clinical suspicion of haemorrhagic transformation. There is no place for either unfractionated heparin or low molecular weight heparins. In such cases, it is best to discuss management with a senior colleague. Intravenous heparinization should be commenced immediately in patients with proven cerebral venous thrombosis (regardless of presence of haemorrhagic change on CT), and many neurologists would also do the same for carotid/basilar dissection.

- Carotid endarterectomy. Should be considered in all patients with >70% ipsilesional stenosis. The operation has an appreciable morbidity (including further stroke) and mortality but appears to improve overall prognosis in selected patients. In centres with experience of the procedure carotid angioplasty may be an alternative particularly in patients who are considered poor surgical candidates.
- Patent foramen ovale. Some advocate closure using an endovascular device but there is only anecdotal evidence of its effectiveness. Current prospective evidence suggests that stroke patients with PFOs treated with aspirin or warfarin only do not have an increased risk of recurrent stroke or death compared with controls.[2]
- HRT and the oral contraceptive pill. Combined HRT increases the risk of ischaemic stroke and should be stopped. The combined, but not the progestagen only, oral contraceptive pill also appears to be associated with an increased risk of stroke. Switch to a progestagen- only formulation, or alternative forms of contraception.

Footnote

1

Marshall RS & Mohr JP (1993) *J Neurol Neurosurg Psychiat* 56: 6â€“16.

2

Homma S *et al.* (2002) *Circulation* 105: 2625â€“2631.

Editors: Ramrakha, Punit S.; Moore, Kevin P.
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Cerebral infarction syndromes

Anterior (carotid territory) circulation

Middle cerebral artery syndrome

- Total occlusion of the middle cerebral artery (usually embolic) leads to contralateral hemiplegia, hemianaesthesia, homonymous hemianopia, and deviation of the head and eyes toward the side of the lesion.
- Left-sided lesions lead to global dysphasia; right-sided ones are more likely to lead to unilateral neglect of contralateral space.
- Branch occlusions of the middle cerebral artery are more common and lead to incomplete syndromes: e.g. occlusion of upper branches leads to Broca's (â€˜non-fluentâ€™ or expressive) dysphasia and contralateral lower face and arm weakness; lower branch occlusion, on the other hand, may cause Wernicke's (â€˜fluentâ€™ or receptive) dysphasia.

Anterior cerebral artery syndrome

Occlusion of this artery (often embolic) can lead to paralysis of the contralateral leg, gegenhalten rigidity, perseveration, alien

limb syndrome, grasp reflex in the opposite hand, and urinary incontinence.

Posterior circulation

Posterior cerebral artery syndrome

Occlusion by thrombus or embolus may lead to combinations of contralateral homonymous hemianopia/upper quadrantonopia, mild contralateral hemiparesis and/or hemisensory loss, dyslexia, and memory impairment.

Lacunar infarction

Infarcts in small penetrating vessels, often the consequence of hypertension, lead to a number of syndromes: pure motor stroke or pure sensory stroke, or pure sensorimotor stroke, ataxic hemiparesis (combined cerebellar and pyramidal signs in the same limb).

Prognostic significance[1]

The type of stroke appears to be a significant factor in a patient's prognosis.

- Total anterior circulation infarcts, i.e. infarcts in the carotid territory leading to motor and sensory deficit, hemianopia, and new disturbance of higher cerebral function have the worst prognosis in terms of death or disability.
- Posterior circulation infarcts, PACIs, and lacunar infarcts have better prognoses, although patients with PACI have a high risk of recurrent stroke within 3 months.

Footnote

1

Bamford *et al.* (1991) *Lancet* 337: 1521â€“1526.

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Brainstem stroke

Presentation

Sudden onset of

- *Headache*, nausea, vomiting, vertigo
- *Weakness*: bilateral or unilateral
- *Sensory symptoms* (e.g. paraesthesiae) may be confined to face and if unilateral, may be contralateral to weakness
- *Ophthalmoplegia, gaze deviation, or dysconjugate eye movements*. In unilateral pontine lesions conjugate gaze deviation is directed away from the lesion and toward the side of the hemiparesis if there is one. The reverse obtains for frontal cortical strokes
- *Horner's syndrome*
- *Ptosis* caused by a mid-brain infarct in the absence of an accompanying third nerve palsy or Horner's syndrome is always bilateral
- *Nystagmus*
- *Hearing loss* caused by damage to the VIIth nerve nucleus or fascicle
- *Dysarthria or dysphagia*
- *Ataxia* which may be uni- or bilateral due to dysfunction of

cerebellar connections

- *Impaired level of consciousness* ranges from transient loss of consciousness to coma
- *Altered pattern of respiration*.

Signs associated with brainstem dysfunction are explained on P522. They result because of damage either to the nuclei (including cranial nerve nuclei) within the brainstem, to the cranial nerves, or to the long tracts which traverse and/or decussate within the brainstem. *â€™Crossed signsâ€™* may occur in brainstem strokes, e.g. part of the lateral medullary/Wallenberg's syndrome consists of loss of pain and temperature sensation from the contralateral trunk and limbs (crossed spinothalamic) and ipsilateral loss of the same sensory modalities from the face (uncrossed trigeminal tract). There are a large number of other eponymous syndromes associated with damage to particular zones within the brainstem. Learning these is not particularly rewarding; better to concentrate on the principles of brainstem anatomy.[1]

Causes

Thrombosis, embolism, haemorrhage, or vertebral artery dissection (especially following neck manipulation).

Assessment of severity

- Reduced level of consciousness and coma carry worse prognosis
- Extent of brainstem dysfunction may be appreciated from systematic examination of brainstem function (P522)
- Basilar occlusion carries a very poor prognosis (approx 80% mortality).

Management

Consult a neurologist. The imaging modality of choice is MRI; this should be performed urgently to rule out other diagnoses. Some centres may consider intra-arterial thrombolysis in patients with basilar occlusion if the patient is referred swiftly. Urgent intervention is required for.

- Metabolic coma with brainstem depression, e.g. opiates (P826)
- Transtentorial herniation â†’ progressive brainstem compression (P526)
- Posterior fossa mass with tonsillar herniation â†’ brainstem compression
- Cerebellar haemorrhage with/without brainstem compression (P526).

Footnote

1

Rowland (1991) In Kandel, Schwartz, & Jessell, ed. *Principles of Neural Science*, pp. 711â€“730.

Editors: Ramrakha, Punit S.; Moore, Kevin P.
Title: *Oxford Handbook of Acute Medicine, 2nd Edition*

Cerebellar stroke

Presentation

Triad of headache, nausea/vomiting, and ataxia is the classical syndrome. But it occurs in <50% of cases and, of course, is common in a number of other conditions. Patients present with symptoms and signs[1,2] which are often attributed to brainstem or labyrithine causes. Always consider the possibility of a cerebellar stroke as a serious alternative diagnosis because surgical decompression can be life saving if there is a mass effect within the posterior fossa. If the diagnosis is a possibility, ask for an urgent CT scan, or better still, an MRI.

- Headache, nausea/vomiting. Sudden or progressive over hours to days. Location of headache varies widely
- Dizziness or true vertigo. Occurs in ~30% of cases
- Visual disturbance. Diplopia, blurred vision, or oscillopsia.
- Gait/limb ataxia. Most alert patients report or demonstrate this
- Nystagmus or gaze palsy
- Speech disturbance. Dysarthria or dysphonia in ~50% of alert patients
- Loss of consciousness. May be transient but many present in coma

- Hypertension.

Predisposing factors

- Hypertension (>50%)
- Anti-coagulants: there is a disproportionately higher risk of cerebellar haemorrhage (cf. intracerebral haemorrhage) in patients taking warfarin
- Metastatic neoplasm.

Assessment of severity

Patients who present in coma, or subsequently develop it, will die unless they receive surgical treatment. There is debate about the prognosis of those who remain alert.

Management

Make a definitive diagnosis with urgent CT scan. (Is there a haemorrhage/ infarct? Is there distortion of fourth ventricle and aqueduct with dilatation of lateral ventricles?) Liaise with regional neurosurgery unit early.

Priorities

- Stabilize the patient and protect the airway. *See* â€˜comaâ€™ P408
- Correct bleeding tendency or effects of anti-coagulants
- Intensive care/high dependency ward nursing observations if patient is not transferred to neurosurgical centre immediately
- Definitive surgical decompression if necessary and possible.

Footnote

1

Dunne JW *et al.* (1987) *Quart J Med* 64: 739â€“754.

2

Editorial (1988) *Lancet* i: 1031â€“1032.

Editors: Ramrakha, Punit S.; Moore, Kevin P.
Title: *Oxford Handbook of Acute Medicine, 2nd Edition*

Transient ischaemic attacks (TIAs)

Presentation

Sudden-onset focal deficit of cerebral function or monocular blindness resolving within 24 hours. The symptoms should have developed within a few seconds and if several parts of the body (e.g. face, arm, leg) are involved they should have been affected simultaneously without any â€˜marchâ€™ or progression.

- Symptoms of carotid TIA. Hemiparesis, dysphasia, or transient monocular blindness (amaurosis fugax). See â€˜anterior circulation strokesâ€™ (P488)
- Symptoms of posterior circulation/vertebrobasilar TIA. Bilateral or alternating hemiplegia or sensory symptoms, crossed motor/sensory signs (ipsilateral face, contralateral arm, trunk or leg deficit), quadriplegia. Sudden bilateral blindness. Two or more of vertigo, diplopia, dysphagia, ataxia, and drop attacks if they occur simultaneously.
- Symptoms of uncertain arterial territory origin. Hemianopia alone or dysarthria alone.
- Symptoms not acceptable as TIA. Syncope, loss of consciousness or confusion, convulsion, incontinence of

urine or faeces, dizziness, focal symptoms associated with migrainous headache, scintillating scotoma.

Causes

Thrombosis or embolism (see P478 for risk factors).

Differential diagnosis

Many conditions may appear at first to be a TIA, e.g.

- Cerebral tumour (1Â° or 2Â°)
- Brain abscess
- Demyelination
- Focal migraine
- Subdural haematoma
- Todd's paresis (post seizure)
- Hypoglycaemic attack
- Encephalitis.

Investigation

A CT scan should be performed as ~5% of patients will have an otherwise unsuspected cause (e.g. mass lesion). Otherwise, investigation is the same as ischaemic stroke (see P482).

Management

The objective is to prevent recurrence or complete stroke. The general principles of management are those used in treating ischaemic stroke (P480â€“8). Perhaps the only difference lies in treatment of recurrent TIAs not controlled by aspirin. In the acute situation, if major stroke is threatened by a â€˜crescendoâ€™ of recurring TIAs

- Give high-dose aspirin (300mg/day)
- Add clopidogrel (75mg od)
- Expedite investigations of underlying cause (carotid stenosis, cardiac emboli etc.)
- Consult a neurologist.

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Confusional states and delirium 1

Up to 10% of acute medical admissions are complicated by acute confusion or delirium. The hallmark of *acute confusional states* is disorientation in time and place, impaired short-term memory, and impaired consciousness level. Typically, the patient is drowsy with a poor attention span and slowed mentation. In *delerium*, there are, in addition, disorders of perception such as hallucinations (seeing or hearing things not there) or illusions (misinterpreting shadows seen or sounds heard) and these may produce restlessness, agitation, and hyperactivity.

The main priority is to identify the cause of any treatable or life-threatening condition. Only a small minority (<10%) of patients will have a primary neurological disorder and commonly there are multiple factors that may apply; these patients carry a good prognosis.

Assessment

- Assess the mental state: check for disorientation and memory impairment with the mini-mental test. An anxiety state can usually be distinguished by talking to the patient. Vivid hallucinations in the absence of history of mental illness suggests alcohol withdrawal.

- Review the patient's notes and try to obtain history from friends/relatives of previous mental state or episodes of confusion. Patients with dementia are prone to confusion with intercurrent illness.
- Review the drug chart: benzodiazepines and narcotics may cause acute confusion in the elderly. Other drugs that may be involved are steroids, NSAIDs, Î²-blockers, and psychotropic medications.
- Assess the patient for acute illness: exclude faecal impaction and urinary retention. Relevant investigations are listed in the table on P498.
- Examine for any focal neurological signs (pupils, limb power, reflexes, and plantar responses).
- In patients with prior high alcohol intake, examine for signs of liver disease, liver â€˜flapâ€™, and possible Wernicke's encephalopathy (nystagmus, ataxia, VI nerve palsy).

Mini-mental examination for the elderly

- Age
- Time (nearest hour)
- 42 West Street: address for recall at the end of the test (make the patient repeat the address to check)
- Year
- Place (name of hospital)
- Recognition of two people (doctor, nurse, etc.)
- Date of birth (day and month)
- Year of World War 1 (or 2)
- â€˜Who is on the throne at the moment?â€™

- Count backwards from 20 to 1

Each correct answer scores 1 point. Healthy elderly people score 8

Practice point

- Patients who repeatedly protrude their tongue have tardire dyskinesia.[1]

Footnote

1

Hawkes C (2002) *Hosp Med* 63:732â€“42.

Editors: Ramrakha, Punit S.; Moore, Kevin P.
Title: *Oxford Handbook of Acute Medicine, 2nd Edition*

Confusional states and delirium 2

Systemic disorder

Differential diagnosis

- Sepsis
- Alcohol withdrawal
- Metabolic disorder
    - â†“ or â†‘glc, Na, or Ca
    - Vitamin deficiency
    - Endocrine disease (thyroid, adrenal cortex)
- Myocardial ischaemia
- Organ failure (renal, respiratory, liver, cardiac)

Drug toxicity

CNS disorder

- Dementia
- CVA (esp. non-dominant parietal lobe)
- Intracranial bleed (SAH, subdural)
- Infection (encephalitis, meningitis)

- Trauma
- Malignancy (1Â° or 2Â°)
- Post ictal; non-convulsive status
- Cerebral vasculitis (SLE, PAN)

Malignancy

Investigations

- Check urine, blood cultures, WBC, CRP, chest X-ray, U&Es, glc, LFTs, Ca^{2+}, arterial gases, pH, ECG, cardiac enzymes
- Consider magnesium, amylase, porphyrins, thiamine, B_{12}, folate, TSH, free T4
- Check prescribed medication serum alcohol/drug screen
- Consider CT scan with contrast, lumbar puncture, EEG, blood cultures, CRP, syphilis serology, Lyme serology
- Check chest X-ray Â± CT chest, serum calcium, CT brain

Management

- Treat the cause. Nurse in a moderately lit room with repeated reassurance. See if a family member can stay with the patient.
- If the patient is agitated and aggressive, sedation may be necessary. Benzodiazepines may exacerbate confusion: use major tranquillizers (e.g. haloperidol 2â€“10mg im po or chlorpromazine 25â€“50mg im/po). Observe the effect on the patient for 15â€–20 minutes and repeat if necessary. In patients with cardiac or respiratory failure, correcting hypoxia may calm the patient by itself. Chlormethiazole is indicated for confusion due to alcohol withdrawal (see P500).

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Acute alcohol withdrawal

Minor symptoms may be managed at home by the GP but often a short admission is more effective and allows observation for complications and psychosocial assessment Â± rehabilitation.

Presentation

- Initial symptoms include anxiety and tremor, hyperactivity, sweating, nausea and retching, tachycardia, hypertension, and mild pyrexia. These symptoms peak at 12â€“30 hours and subside by 48 hours.
- Generalized tonicâ€“clonic seizures (â€˜rum fitsâ€™) may also occur during this period, but status epilepticus is unusual. Typically these do not show the EEG characteristics of epilepsy and may be precipitated by flickering lights or other photic stimulation.
- Delirium tremens (â€˜DTsâ€™) occurs in <5% of individuals, usually after 3â€“4 days of cessation of alcohol intake. It is associated with an untreated mortality of 15%. Features include
    - Coarse tremor, agitation, confusion, delusion, and hallucinations
    - Fever (occasionally severe), sweating, tachycardia
    - Rarely lactic acidosis or ketoacidosis

- Also look for hypoglycaemia, Wernickeâ€“Korsakoff psychosis, subdural haematoma, and hepatic encephalopathy.

Management

- *General measures*
  - Nurse in a well-lit room to prevent disorientation. Rehydrate (iv fluids if necessary; avoid saline in patients with known chronic liver, disease). Monitor urine output.
  - Vitamin supplements: iv therapy (e.g. ParbinexÂ® 2â€“3 pairs of amps. iv *slowly* 8 hourly; watch for signs of anaphylaxis) for 5 days or oral therapy [thiamine 100mg po bd, vitamin B tablets (compound strong) 2 tablets tds, and vitamin C 50mg po bd] for 1 week.
  - Monitor BMs for hypoglycaemia and treat if necessary.
  - Severe hypophosphataemia may complicate alcohol withdrawal and should be treated with intravenous phosphates (polyfusor phosphates) if serum phosphate is <0.6mM (see P582).
  - Exclude intercurrent infection (pneumonia, skin, urine).
- *Sedation*
  - Long-acting benzodiazepines such as chlordiazepoxide (LibriumÂ®) or diazepam (ValiumÂ®) are commonly used; lorazepam is not metabolized by the liver and may be used in liver disease.
  - Carbamazepine is as effective as benzodiazepines but side-effects limit its use. For severe agitation, haloperidol 10mg im may be used.
- *Wernickeâ€“Korsakoff syndrome*

- Wernicke's disease comprises the triad of ophthalmoplegia (nystagmus, VI nerve palsy), ataxia (cerebellar type), and confusional state. In Korsakoff's syndrome, confusion predominates, often with overt psychosis, amnesia (antegrade and retrograde), and confabulation. Withdrawal symptoms may also occur.
- Diagnosis: reduced red-cell transketolase activity.
- Treat with iv thiamine (see above) while waiting for results.

- *Seizures*
  - Withdrawal seizures are typically self-limiting; if needed, use iv diazepam (DiazemulsÂ®) 10mg over 5 minutes (see P474).
  - Treat the patient with chlordiazepoxide (rather than chlormethiazole or carbamazepine). Phenytoin is less effective but should be added if there is a history of epilepsy or recurrent seizures.
- *Follow-up*
  - Arrange referral to an alcohol dependence clinic.

Sedation regimens in delerium tremens: a guide

Chlordiazepoxide	30mg q6h for 2 days
then	20mg daily (divided doses) for 2 days
then	10mg daily (divided doses) for 2 days
then	5mg daily for 2 days.

Start women on 20mg (instead of 30mg) and taper as above. Reduce the dose in liver disease, in elderly, and in slight individuals.

Carbamazepine

As effective as benzodiazepines and no abuse potential.

Start with 200mg/day in divided doses increasing to 400mg/day over the next 2â€“3 days and taper off by day 8.

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Neuromuscular respiratory failure: assessment

Presentation

A number of disorders of peripheral nerve, neuromuscular junction, or muscle may present with hypercapnic (type II) respiratory failure, or impending failure. There are many differences between these conditions but consider the diagnosis in the presence of the following features.

- *Limb weakness* progressing over hours or days with diminished/no reflexes but no upper motor neurone signs
- *Muscular tenderness or pain* may be a feature
- *Facial weakness*
- *Ptosis*
- *Bulbar dysfunction* is a particularly ominous sign because it may lead to improper clearance of secretions and aspiration
- *Paradoxical abdominal movement:* if the diaphragm is paralysed it moves passively into the thorax with the fall in intrapleural pressure produced by expansion of the ribcage in inspiration. As a result, the anterior abdominal wall also moves in (rather than out) during inspiration
- *Dyspnoea* or *distress in supine position:* if the diaphragm is paralysed movement of abdominal contents towards the

thorax is more prominent when the patient lies flat because gravity no longer acts to counteract this passive movement. As a result, the volume of air inspired is reduced. This is a rare but important cause of orthopnoea

- *Sensory symptoms* may be present with or without glove-and-stocking sensory loss
- *Autonomic instability* may be a prominent feature of Guillainâ€“BarrÃ© syndrome and may lead to cardiac arrest
- *Pneumonia* in known neuromuscular disease
- *Respiratory arrest:* a common pitfall is to consider the degree of respiratory distress unimpressive. Peripheral weakness in combination with an expressionless â€˜myopathicâ€™ facies may lead to a false sense of well-being when the patient may in fact be confronting impending respiratory arrest.

Assessment of severity

- The measurement of forced vital capacity is *mandatory* (measured with Wright respirometer available from anaesthetic nurse or intensive care unit). Note that oxygen saturations, peak flow rate, and FEV1 *do not correlate* with the degree of neuromuscular impairment.
- Forced vital capacity <30ml/kg causes impaired clearance of secretions.
- Forced vital capacity <15ml/kg suggests ventilatory failure and is an indication for immediate intubation and ventilation regardless of other parameters of respiratory function.
- Arterial blood gases: hypercapnia occurs relatively late.
- CXR to determine extent of consolidation if there is concomitant aspiration or infective pneumonia. Subtle linear atelectasis is often seen as a direct result of reduced

lung volume.

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Neuromuscular respiratory failure 2

Investigations for neuromuscular respiratory failure

- FBC, U&Es, CPK, ESR, CRP
- Forced vital capacity
- Arterial blood gases
- Chest X-ray
- NCS
- EMG
- Anti-AChR antibody/TensilonÂ® test
- CT/MRI scan for brainstem pathology
- Nerve biopsy, muscle biopsy
- Urine/plasma toxin screen (see table)

Management

- Assess severity and measure FVC frequently.

- Consider intubation and ventilatory support if in adults FVC <1L or 15ml/kg. Do not use suxamethonium as a muscle relaxant. It may cause a sudden rise in potassium in patients with denervated muscles.
- Liaise with neurologist early. Consider transfer to regional neurology unit if the patient is well and FVC >25ml/kg and stable. If the patient is unwell and FVC <15ml/kg or falling precipitously from a higher level, intubate electively and then consider transfer. All patients should be accompanied by an anaesthetist.
- Investigations (see table). Most of these conditions will not come into the differential but it is advised that blood be taken for virology screen and autoimmune profile, and 20ml be saved for retrospective analysis if required.
- ECG monitoring and frequent observation of BP and pulse is required if Guillainâ€“BarrÃ© is suspected because there is a high incidence of autonomic instability.
- Consider specific therapies (see table) and

  Guillainâ€“BarrÃ©
  P512
  Myasthenia gravis
  P505
  Botulism
  P516
  Heavy metal intoxication
  P505
  Organophosphate exposure
  P505
  Porphyria
  P505
  Rhabdomyolysis
  P392 .
- Subcutaneous heparin prophylaxis for deep vein thrombosis.

- Enteral nutrition should be considered early.

Central nervous system disease
Brainstem disease

- MRI scan
- Reduce ICP
- Decompress

Spinal cord disease

- MRI scan
- Decompress

Peripheral neuropathies
GBS (see P512)

- NCS
- iv immunoglobulin
- Plasma exchange

Organophosphates

- Red cell cholinesterase
- Plasma pseudo-cholinesterase
- Atropine
- Pralidoxime

Heavy metals: lead, thallium, gold, arsenic

- Blood and urine levels
- Specific antidote (see p797)

Drugs (e.g. vincristine)

- Stop drug

Malignancy

- Nerve biopsy
- Cytotoxics

Vasculitis (e.g. SLE)

- Nerve biopsy
- Immunosuppressants

Metabolic (porphyria)

- Urinary porphyrins
- Avoid precipitants
- iv glc /haematin

Diphtheria

- Throat swab
- Antitoxin

Neuro-muscular junction disease
Myasthenia gravis

- Anti-AChR Ab
- TensilonÂ® test
- Steroids
- Plasma exchange

Anti-cholinesterase overdose

- -ve TensilonÂ® test
- Stop drug

Hypermagnesaemia

- Plasma Mg
- iv calcium

Botulism (see P516)

- Antitoxin

Muscle disease

Hypokalaemia

- Plasma K^+
- K^+ replacement

Hypophosphataemia

- Plasma PO^{3-}_4
- PO^{3-}_4 replacement

Polymyositis

- EMG
- Muscle biopsy
- Steroids

Acute rhabdomyolysis

- EMG
- iv hydration

(see P392)

- Muscle biopsy
- Urine alkalinization

Condition Investigation Specific treatments

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Myasthenic crises[1]

Presentation

- *Generalized weakness* usually worse proximally, and classically painless and fatiguable. There may be ptosis and diplopia. Reflexes and sensation are normal.
- *Dyspnoea*. The patient may not at first glance appear very distressed. An expressionless myopathic facies together with weak muscles of respiration may give a false sense of well-being.
- *Bulbar dysfunction* is potentially dangerous as it may lead to impaired clearance of secretions and aspiration pneumonia.
- *Exhaustion and ventilatory failure* leading to coma.
- *History* of penicillamine use (may cause a syndrome identical to idiopathic myasthenia gravis).

Common predisposing factors

- Infection, surgery, drugs (see table). NB: corticosteroids used to treat myasthenia can initially lead to an acute crisis.

Assessment of severity

- Vital capacity is the most useful indicator. Arterial blood gases are not sensitive enough and demonstrate hypercarbia late.
- Bulbar dysfunction.

Cholinergic crisis

It may not be possible on clinical evaluation to distinguish between worsening myasthenia and excessive anti-cholinesterase treatment (which leads to weakness by producing depolarization block). Consider withdrawing anti-cholinesterases only after consulting a neurologist. Note that cholinergic crisis is very rare compared to myasthenic crisis.

Management

- Stabilize the patient: protect the airway; intubate and ventilate if necessary. Ensure there are no electrolyte disturbances (â†“K^+, â†“Ca^{2+}, â†‘Mg^{2+}) or drugs prescribed which exacerbate weakness.
- Consider TensilonÂ® (edrophonium) test (see table). Anti-cholinesterase treatment may be helpful if cholinergic crisis is excluded. If there is no effect with TensilonÂ®, reconsider the diagnosis. Withhold all anti-cholinesterase medications for 72 hours. The TensilonÂ® may be repeated at intervals.
- Immunosuppression should be supervised by a neurologist: prednisolone 120mg/day on alternating days produces improvement after 10â€“12 days, but should be introduced with care because there may be initial worsening of weakness. High-dose steroids are given until remission occurs. Azathioprine (2.5mg/kg) has also been used for maintenance therapy but takes months to have an effect.
- Plasmapheresis is used to remove circulating antibody. It usually involves exchange of 50ml/kg/day over several days. Many centres now favour iv immunoglobulin therapy.

- Regular anti-cholinesterase inhibitor therapy should be directed by a neurologist. Therapy depends upon response but one initial strategy is to commence with pyridostigmine 60mg q4h. This can be given by NG-tube or, if necessary, im neostigmine can be used instead (1mg neostigmine should be given for every 60mg pyridostigmine).

Drugs which may exacerbate myasthenia

Antibiotics		
Gentamicin	Tetracycline	Streptomycin
Neomycin	Tobramycin	Kanamycin
Colistin	Clindamycin	Lincomycin
Cardiac drugs		
Quindine		Quinine
Propranolol		Procainamide
Local anaesthetics		
Lignocaine		Procaine
Anti-convulsants/psychotropic		

drugs		
Phenytoin		Barbiturates
Lithium Chlorpromazine		
Muscle relaxants		
Suxamethonium		Curare
Analgesics		
Pethidine		Morphine
Hormones		
Corticosteroids (initially)		Thyroxine
Others		
Magnesium salts		

TensilonÂ® (edrophonium) test

- A history of asthma or cardiac dysrhythmias are relative contraindications. Atropine should be drawn up prior to the test in case edrophonium (an inhibitor of acetylcholinesterase) produces a severe cholinergic reaction, e.g. symptomatic bradycardia.
- Prepare and label two 1ml syringes: one containing saline, the other 10mg of edrophonium.

- Select a muscle to observe for the test and ask a colleague to assess its strength prior to the test.
- Inject, in stages, the contents of either syringe, keeping both patient and colleague blinded to the contents of each syringe. Ask the observer to reassess muscle strength after the contents of each syringe have been injected.
- Edrophonium should first be given as a bolus of 2mg (0.2ml) and untoward cholinergic effects should be observed for. If it is tolerated the remaining 0.8ml can be given 1 minute later.
- Improvement in muscle strength following edrophonium suggests the patient is suffering a myasthenic, not cholinergic, crisis.

Footnote

[1] Thomas CE *et al.* (1997) *Neurology* 48: 1253â€“1260.

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Spinal cord compression: assessment

Presentation

- *Back pain* is usually the first symptom. It often starts weeks before other features and becomes progressively unremitting keeping the patient awake at night. There may also be *radicular pain* which is misinterpreted and leads to a long and unrewarding search for the cause of chest or abdominal pain.
- *Sensory symptoms* such as paraesthesiae or a sensation of limb heaviness or pulling may then occur.
- *Sensory loss* may be apparent as a sensory level on testing. It is wise to test for pin prick (spinothalamic function) and joint position sense/ vibration sense (dorsal column function): anterior or posterior portions of the cord may be selectively compressed. â€˜Sacral sparingâ€™ refers to preservation of sensation in (usually) S3â€“S5 dermatomes; it is a relatively reliable sign of an intramedullary lesion (see causes) which initially spares laterally placed spinothalamic tract fibres subserving sacral sensation. Note that a sensory level only indicates the lowest possible level of the lesion: it may well be several segments higher.
- *Weakness* is often first described as clumsiness but soon

progresses to clear loss of power.

- *Autonomic dysfunction:* if the sympathetic pathways are involved, especially in high thoracic or cervical lesions, hypotension, bradycardia, or sometimes cardiac arrest may occur. This may be triggered by noxious stimuli such as pain, urinary tract infection, or abdominal distension caused by constipation or bladder outflow obstruction.
- *Sphincter dysfunction* commences as hesitancy or urgency of micturition and may progress to painless urinary retention with overflow. Constipation is another consequence of cord compression.
- *Fever* should alert one to the possibility of an infectious cause.
- *Respiratory failure* occurs with high cervical cord compression and is one cause of acute neuromuscular respiratory paralysis (P502).
- *Conus medullaris lesions* compress the sacral segments of the cord and lead to relatively early disturbance of micturition and constipation, impotence, reduced perianal sensation and anal reflex; rectal and genital pain occurs later. Plantar responses are extensor.
- *Cauda equina lesion:* lesions at or below the first lumbar vertebral body may compress the spinal nerves of the cauda equina leading to a flaccid, areflexic, often asymmetric paraparesis. Lumbosacral pain occurs early; bladder and bowel dysfunction appear relatively late. A sensory level is found in a saddle distribution up to L1 (corresponding to roots carried in cauda equina).
- *Combined conus and cauda lesions* produce a combination of lower and upper motor neurone signs.
- *General examination*: remember that likeliest cause is malignant compression from metastatic disease. Perform a careful examination, including breast and thyroid if appropriate.

Assessment of severity

The degree of weakness, sensory loss, and sphincter dysfunction are useful indicators of severity.

P.509

Causes of non-traumatic spinal cord compression

Tumours

Primary: intradural + extramedullary: schwannoma, meningioma; intradural + intramedullary: astrocytoma, ependymoma.

Metastatic (usually extradural): breast, prostate, lung, thyroid, GI tract, lymphoma, myeloma

Infection: staphylococcal abscess, tuberculoma, infected dermoid

Prolapsed intervertebral disc (central)

Cyst: arachnoid, syringomyelia

Haemorrhage

Skeletal deformity: kyphoscoliosis, achondroplasia, spondylolisthesis

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Spinal cord compression: management

This depends on the diagnosis and the condition of the patient. If the diagnosis is unknown it is imperative to make it swiftly and discuss the case with the regional neurosurgical centre. If the patient is known to have neoplastic disease and malignant compression is very likely, urgent radiotherapy is first-line therapy in most but not all cases. In some patients with disseminated disease it may not be appropriate to make any intervention apart from analgesia. Always consult a senior oncologist.

- Plain X-rays of the spine should be obtained immediately. These may show vertebral collapse, lytic lesions, or sclerosis. Perform a CXR to look for malignancy.
- Magnetic resonance imaging or CT myelography is the next investigation of choice. This should be arranged urgently. If facilities are not available locally, discuss with regional neurosurgical Centre.
- The use of high-dose steroids is controversial: there is no definite evidence of benefit in malignancy and in some cases of high-grade lymphoma they may trigger a fatal tumour lysis syndrome. Discuss with your senior colleagues.
- If the cause of compression appears to be infective (fever,

neutrophilia, raised CRP, etc.), blood, sputum, and urine cultures should be sent.

- Monitor haemodynamics and watch for autonomic dysfunction. Control pain and act to prevent constipation.
- If there is bladder dysfunction, urinary catheterization may be necessary. If immobile, start prophylactic subcutaneous heparin (5000U tds).
- If there is high cervical compression or if ventilation appears to be compromised, FVC and arterial blood gases should be measured. The indications for intubation (if this is appropriate) are discussed in â€˜acute neuromuscular respiratory paralysisâ€™ (P502).
- If a diagnosis is not apparent and immediate neurosurgical action is not indicated discuss with radiology with a view to CT-guided biopsy.

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Guillainâ€“BarrÃ© Syndrome (GBS) 1

Presentation

- *Progressive weakness of more than one limb* in an individual who may recently have experienced a mild respiratory or gastrointestinal febrile illness. Weakness is as commonly proximal as distal. It is usually symmetrical but may be asymmetrical.
- *Diminished tendon reflexes/areflexia* is common.
- *Sensory symptoms*. Paraesthesiae often precede weakness. Sensory loss is not usually profound although there may be a glove-and-stocking distribution impairment of two-point discrimination, joint position, and vibration sense. If there is a sensory level, spinal cord compression (P510) should be the diagnosis until proved otherwise.
- *Limb or back pain* is a major symptom in ~30%.
- *Cranial nerve dysfunction* occurs in 50%. Bulbar function and muscles of mastication are affected in 30%; ocular muscles in 10% of patients.
- *Ventilatory failure*. See â€˜acute respiratory failureâ€™ (P502).
- *Autonomic dysfunction* is common: sweating, tachycardia,

sudden swings of BP, dysrhythmias, and cardiac arrest. Bladder or bowel dysfunction occurs but if it is present from the outset or if it is persistent, reconsider the diagnosis.

- *Millerâ€“Fisher variant:* ophthalmoplegia (giving rise to diplopia), ataxia, and areflexia without significant weakness or sensory signs. Associated with anti-GQ1b antibodies in the serum.

Causes

GBS probably represents an immune-mediated attack on peripheral nerves. Infections which may precede it include cytomegalovirus, *Campylobacter jejuni*, Epsteinâ€“Barr virus, hepatitis B, *Mycoplasma*, and herpes simplex virus.

Assessment of severity

Poor prognostic features on presentation include

- Rapid onset
- Requirement for ventilation (bulbar compromise, reducing VC, respiratory failure)
- Age >40
- Reduced amplitude of compound muscle action potential (<10% of control) and extensive spontaneous fibrillation in distal muscles suggesting denervation (NB: electrophysiological studies may be normal in early GBS)
- Presence of autonomic dysfunction
- Axonal variant (often with preceding *Campylobacter jejuni* infection).

A grading system has been devised to follow a patient's progress:

- Grade 1: Able to run

- Grade 2: Able to walk 5m but not to run
- Grade 3: Able to walk 5m with assistance
- Grade 4: Chair/bed bound
- Grade 5: Ventilated.

Practice point

- Acute onset of bilateral facial palsy is usually due to Guillain-BarrÃ© syndrome. Long-standing bilateral facial weakness is usually due to Sarcoid or Lyme disease.[1]

Footnote

1

Hawkes C (2002) *Hosp Med* 63:732â€“42.

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Guillainâ€“BarrÃ© syndrome 2

Management

It is important to appreciate that GBS is a diagnosis of exclusion with an extensive differential (see â€˜acute respiratory paralysisâ€™ P502). The pace at which alternative diagnoses need to be excluded depends upon the history and findings.

The management of the patient with GBS is that of any patient with neuromuscular paralysis (P502), although there are a few important specific measures:

- *Monitor FVC* twice daily
- *Autonomic instability* is a common feature, so ECG monitoring and frequent assessment of BP and pulse is advisable, particularly in any patient with bulbar or respiratory involvement (NB: tracheal suction may lead to bradycardia or asystole)
- *CSF analysis* may be required. CSF protein may be normal initially but characteristically rises markedly and peaks in 4â€“6 weeks
- *Steroids* are of no benefit in GBS
- *Plasma exchange* is currently the only treatment that is proven to be better than supportive treatment alone. *Intravenous immunoglobulin* (0.4g/kg for 5 days) has never

been adequately compared with placebo but appears to be as effective as plasma exchange and is currently the standard treatment. Therapy should not be commenced without prior discussion with a neurologist.

- *DVT prophylaxis*.

Prognosis

Around 65% are able to resume manual work, 8% die in the acute stage (usually from autonomic dysfunction or pulmonary embolism), and the remainder are left with residual disability. The prognosis is worse in those with more severe disease.

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Botulism

Presentation

Botulism is caused by exotoxins of *Clostridium botulinum*. There are three syndromes: food-borne, subcutaneous drug users wound, and infantile. The latter two causes are rare and will not be discussed here. The most common form of botulism is food-borne with outbreaks usually attributed to canned food. Patients present with symptoms usually within 18 hours of ingestion of the toxin:

- *Sore throat, fatigue, dizziness, blurred vision*
- *Nausea, vomiting, constipation*
- *Rapidly progressive weakness* often beginning in the extraocular and/or pharyngeal muscles and descending symmetrically in severe cases to give upper and lower limb paralysis and respiratory failure (see â€˜acute respiratory paralysisâ€™, P502)
- *Paraesthesiae* may occur but there are no sensory signs
- *Parasympathetic dysfunction* causes a dry mouth, ileus, and dilated non-reactive pupils in an alert patient. This pupillary response may help to distinguish botulism from other neuromuscular disorders; however, in most cases the pupils remain reactive.

Wound botulism is similar, except gastrointestinal upset does not occur.

Assessment of severity

Limb weakness and ventilatory failure are indicators of severe disease. Patients with these features have a worse prognosis, as do patients over 20 years, and those who have ingested type A toxin.

Management

- Assess severity, *measure FVC frequently*, and attempt to exclude other important causes of neuromuscular failure (see P502). In particular, a *TensilonÂ® test* should be performed to exclude myasthenia gravis (P507); *nerve conduction* should be normal but it is important to exclude Guillainâ€“BarrÃ© syndrome (P512); *electromyography* is frequently abnormal in botulism (decrement of compound muscle action potential at slow rates of repetitive stimulation of $3s^{-1}$ and facilitation of motor response at rapid rates of $50s^{-1}$). Serum and stool should be assayed for toxin and *C. botulinum*.
- *General management* is described elsewhere (P502).
- *Specific treatment:* if botulism is suspected 10 000 units of trivalent (A, B, E) anti-toxin should be administered iv immediately and at 4 hourly intervals. Approximately 20% patients have minor allergic reactions to this and require corticosteroid and anti-histamines as for anaphylaxis (for supplies outside normal working hours contact Department of Health Duty Officer, tel: 020 7210 3000).
- *Guanidine hydrochloride* (an acetylcholine agonist) may be of benefit in some patients (35â€“40mg/kg/day orally in divided doses).
- Gastric lavage, emetics, cathartics, and enemas may be

used with caution to accelerate elimination of toxin from the gastrointestinal tract. The first two interventions are contraindicated if bulbar weakness is present; magnesium-containing cathartics should not be used as there is a risk that magnesium may enhance toxin activity.

Pathophysiology of botulism

Preformed botulinum toxin is a potent presynaptic blocker of acetylcholine release at the neuromuscular junction, post-ganglionic parasympathetic terminals, and autonomic ganglia. There are 6 antigenically distinct toxins (Aâ€“F) but only A, B, and E appear to be associated with human illness.

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Tetanus

Presentation

Tetanus is caused by the effects of exotoxins produced by *Clostridium tetani*. It occurs after *C. tetani* spores have gained access to tissues. The wound may be very trivial and in 20% of cases there is no history or evidence of injury. Incubation of spores may take weeks but most patients present within 15 days with

- *Pain and stiffness of jaw*
- *Rigidity and difficulty in opening mouth:* trismus or â€˜lockjawâ€™
- *Generalized rigidity of facial muscles* leading to the classical risus sardonicus or clenched teeth expression
- *Rigidity of body musculature* leading to neck retraction and spinal extension
- *Reflex spasms* are painful spasms elicited by stimuli such as pressure or noise. These usually occur 1â€“3 days after the initial symptoms and are potentially very dangerous as they may endanger respiration and precipitate cardiorespiratory collapse
- *Convulsive seizures*
- *Autonomic dysfunction* with both sympathetic (sweating,

hypertension, tachycardia, dysrhythmias, hyperpyrexia) and parasympathetic (bradycardia, asystole) involvement.

Cause

Exotoxin blocks inhibitory pathways within the central nervous system.

Assessment of severity

Rapidly progressing features and the onset of spasms signify worse disease and prognosis.

Management

- *Assess severity*. In severe spasms/respiratory failure ventilation will be required. Otherwise patients should be nursed in a quiet, dark room (to reduce reflex spasms) under close observation. Sedation with diazepam may be necessary but beware of respiratory depression.
- *General management* as discussed on P502.
- *Specific treatment:* human hyperimmune globulin 3000â€“10 000 units iv or im should be given to neutralize circulating toxin. This will not ameliorate existing symptoms but will prevent further binding of toxin to CNS. Penicillin iv (1.2g qds), or alternatively tetracycline 500mg qds, should be prescribed to treat *C. tetani*.
- *Wound care and debridement as appropriate:* swabs should be sent for culture but often do not grow the organism.
- *Prophylaxis in patients who have previously been immunized:* for any wound, give a booster dose of tetanus toxoid if the patient has not received a booster in the last 10 years. If the wound appears dirty and infected, or the patient has never been immunized/cannot recall/unable to give history, give human antitoxin (250 units im) in

addition to toxoid.

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Glasgow Coma Scale (GCS)

Developed to assess depth and duration of impaired consciousness in a standard fashion. The total is out of 15 (see table); the worst possible score is 3 (which even the dead can achieve). The scale has a high rate of inter-observer agreement and GCS score is one useful way of monitoring conscious level.

Eye opening

- If spontaneous, indicates brainstem arousal mechanisms are probably intact, but the patient need not be aware of their surroundings.
- Eye opening to speech is not necessarily a response to a verbal command to open the eyes; any verbal approach, e.g. calling the name of the patient, may elicit this.
- Eye opening to pain is best tested by using a stimulus in the limbs because supra-orbital or styloid process pressure can lead to grimacing with eye closure.

Verbal responsiveness

- An orientated patient knows who they are, where they are, and why they are there; they can recollect the month and year.

- A confused patient will converse but their responses indicate varying degrees of disorientation and confusion.
- An individual with inappropriate speech cannot sustain a conversation; their utterances are exclamatory or random and may consist of shouting or swearing.
- Incomprehensible speech does not consist of any recognizable words but involves moaning and groaning.

Motor response

See figure.

- Patients who obey commands show the best possible motor response but be careful not to misinterpret postural adjustments or the grasp reflex.
- If there is no response to command, a painful stimulus may be applied initially by applying pressure to the fingernail bed. If this elicits flexion at the elbow, pressure may be applied to the styloid process, supra-orbital ridge, and trunk to see if there is localization.
- If pain at the nail bed elicits a rapid withdrawal with flexion of the elbow and abduction at the shoulder it is scored 4.
- If instead it produces a slower flexion of the elbow with adduction at the shoulder, it is considered an *abnormal flexion response* (sometimes called *decorticate posturing*).
- If pain elicits extension of the elbow, adduction, and internal rotation of the shoulder with pronation of the forearm, this is noted as an *extensor response* (sometimes called *decerebrate posturing*).

Prognosis

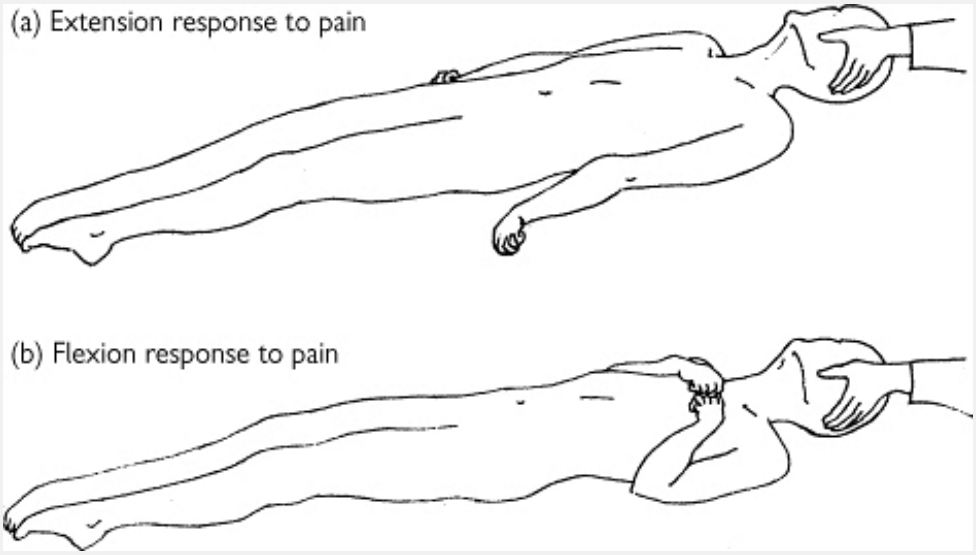
The GCS is a valuable tool in predicting likely outcome from coma, *but it has limitations* and should not be the only factor

used to assess prognosis. Patients with GCS 3â€“8 generally have far worse prognoses than those with >8. But the cause of coma is also an important predictor, e.g. metabolic coma (especially due to drug intoxication) generally has a better outlook than other causes, irrespective of GCS.

GCS

Eye opening	
Spontaneously	4
To speech	3
To painful stimulus	2
No response	1
Best verbal response	
Orientated	5
Disorientated	4
Inappropriate words	3
Incomprehensible sounds	2
No response	1

Best motor response	
Obeys verbal commands	6
Localizes painful stimuli	5
Withdrawal to pain	4
Flexion to pain	3
Extension to pain	2
No response	1



Posturing in coma

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Examination of brainstem function 1

Assessment of brainstem function is vital to the management of coma (P406), raised intracranial pressure (P452), brainstem strokes (P490), and brain death (P532). It is not necessary to have a detailed knowledge of brainstem anatomy. Some simple observations reveal a great deal about function at different levels of the brainstem.

Examination of the eyes

- Pupillary reactions. The size of the pupils and their reactions to bright light should be assessed. This tests the pathway from each eye (IInd cranial nerve) through the superior colliculus (mid-brain), its connection to the nearby Edingerâ€“Westphal IIIrd nerve nucleus (also in the mid-brain), and efferent parasympathetic outflow of the IIIrd nerve. The pupillary reflex is consensual so light in one eye should elicit constriction of both pupils. Thus observations of the pupillary response can interrogate brainstem function at the level of the mid-brain.
- Corneal reflex. This tests the integrity of the afferent pathway (Vth nerve) through to the efferent pathway (VIIth nerve). The corneal reflex is also a consensual reflex. This reflex allows one to interrogate brainstem function at the

level of the pons.

- Resting eye position. This may give a useful clue to asymmetric brainstem dysfunction. If the eyes are dysconjugate there must be a disorder of the nuclei of the IIIrd, IVth, or VIth nerves, their connections, or the nerves themselves. Note the IIIrd and IVth nuclei are located in the mid-brain, whereas the VIth nucleus is located in the pons.
- Spontaneous eye movements. If there are spontaneous fast (saccadic) horizontal and vertical conjugate eye movements the brainstem mechanism for generating saccades is intact and there is no need to test for the oculocephalic or oculovestibular response because
    - Horizontal saccades require the integrity of the paramedian pontine reticular formation (pons), the IIIrd nerve nucleus, the VIth nerve nucleus, and the medial longitudinal fasciculus connecting these.
    - Vertical saccades require the dorsal mid-brain to be intact.
    - Dysconjugate eye movements raise the possibility of unilateral damage to brainstem oculomotor nuclei, their connections, or cranial nerves innervating the extraocular muscles. In this case the resting position of the eyes may also be dysconjugate.
    - A number of oculomotor signs associated with brainstem dysfunction have been identified; none are absolutely specific but they may provide useful clues to site of lesion.[1]
- Oculocephalic response. The â€˜doll's head manoeuvreâ€™ (P530) should be performed only if cervical injury has been excluded. Both it and caloric stimulation assess the integrity of the vestibulo-ocular reflex which is a three-neurone arc from the semicircular canals via the vestibular nuclei to the IIIrd and VIth nerve nuclei.

- Oculovestibular response. Caloric stimulation (P530).

Footnote

1

Lewis & Topel (1992) In Weiner WJ, ed. *Emergent and Urgent Neurology*, pp. 1â€“25.

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Examination of brainstem function 2

The swallowing reflex

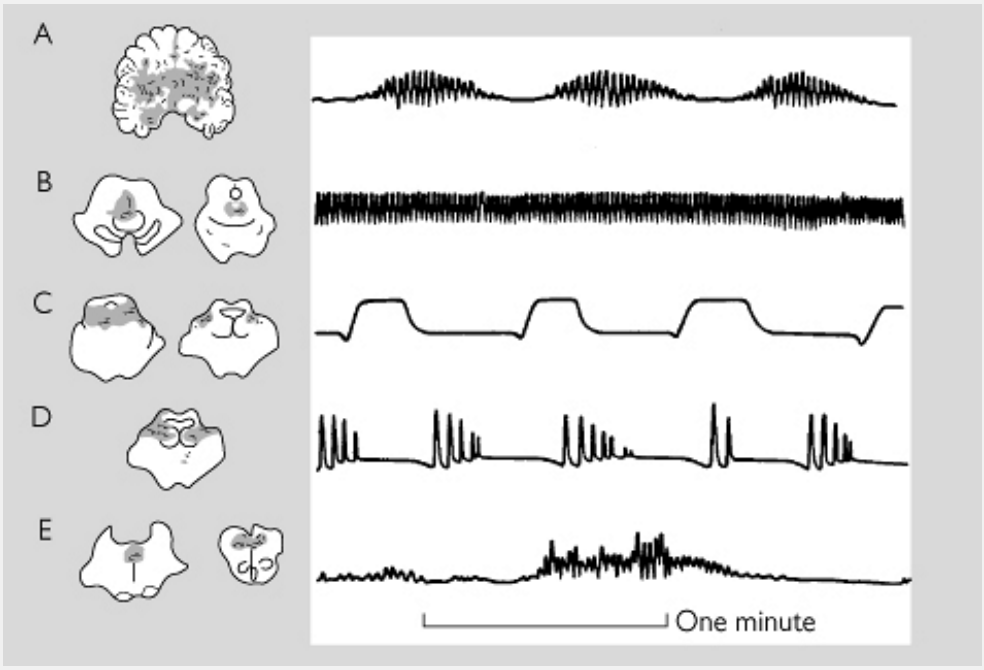
This may be tested by injecting 10ml of water in a syringe into the mouth of the patient. Reflex swallowing requires, amongst other things, that the swallowing centre in the reticular formation of the medulla, very close to the solitary nucleus, be intact.

Respiratory pattern

- This is sometimes useful in localization but often is not.
- *Central neurogenic hyperventilation*, for example, has no localization value. It is rapid, regular deep continuous breathing at ~25/min which is not produced by acidosis or hypoxaemia. Its usefulness is that increasing regularity of this pattern signifies increasing depth of coma and worsening prognosis.
- *Apneustic breathing* (prolonged inspiration followed by a period of apnoea), on the other hand, implies damage to the pons, as does *cluster breathing* (closely grouped respirations followed by a period of apnoea). Damage to the medullary respiratory centres is suggested by *ataxic breathing* and *gasping breathing* (Biot's respirations). The

former are characterized by a chaotic pattern of respiration; the latter consist of gasps followed by apnoeic periods of variable duration. Both are usually soon followed by respiratory arrest.

- Shallow, slow breathing may be due to medullary depression caused by drugs, e.g. opiates. *Cheyneâ€“Stokes respiration* may be caused by bilateral deep hemispheric and basal ganglia damage but is more usually due to non-neural causes, e.g. primary cardiovascular or respiratory dysfunction.
- *Long tract signs*. Finally, structural damage to the brainstem may produce long tract signs with dysfunction of descending pyramidal/extrapyramidal tracts or ascending sensory pathways. There may be â€˜crossed signsâ€™ because of decussation of pathways within the brainstem.



Abnormal respiratory patterns associated with pathologic lesions (shaded areas) at various levels of the brain. (a) Cheyne-Stokes respiration. (b) Central neurogenic hyperventilation. (c) Apneusis. (d) Cluster breathing (e)

Ataxic breathing. (From Plum F & Posner JB (1980) *The Diagnosis of Stupor and Coma* 3rd ed; FA Davis, Philadelphia, with permission.)

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Examination of brainstem function 3

Signs of brain shift[1]

Raised intracranial pressure may produce a number of distinct progressive brainstem syndromes associated with brain shift:

- Central herniation syndrome
- Lateral (uncal) herniation syndrome
- False localizing signs
- Tonsillar herniation.

Assessment involves

- Observation of respiratory pattern
- Pupillary reaction
- Oculocephalic/oculovestibular response (see above)
- Motor response at rest or to pain (see P520).

Central herniation syndrome

- Vertical displacement of the brainstem due to a supratentorial mass.

- The first sign is not of brainstem but rather *diencephalic* impairment. The patient becomes less alert and there may be Cheyneâ€“Stokes breathing. The pupils are small (perhaps due to hypothalamic sympathetic dysfunction) but reactive. There may initially have been unilateral hemiplegia due to the supratentorial mass. Characteristically in the early diencephalic stage, paratonic resistance (*gegenhalten*) develops in the contralateral limbs and both plantar responses become extensor. Eventually there is a decorticate response to pain (P520).
- *Mid-brainâ€“upper pontine* dysfunction becomes evident with fluctuations in temperature, onset of central neurogenic hyperventilation, apneustic or cluster breathing (see above), unreactive pupils which are â€˜mid-positionâ€™ and often irregular in shape, loss of vertical eye movements (which may be tested with the doll's head manoeuvre), increasing difficulty in eliciting horizontal oculocephalic and oculovestibular responses which may become dysconjugate (P530). Motor responses progress from decorticate (flexor) rigidity to decerebrate (extensor) rigidity in response to pain (P520).
- *Lower pontineâ€“upper medullary* compromise is revealed by often ataxic breathing, fixed mid-position pupils, and failure to elicit oculocephalic and oculovestibular responses. The patient is flaccid at rest; painful stimuli may not elicit any motor response except occasional flexor responses in the lower limbs.
- *Medullary dysfunction* is terminal. Breathing is ataxic or gasping. The *pulse rate may decrease and BP increase* (Cushing response). After a few gasps, breathing stops and pupils often dilate and become fixed.

Footnote

1

Plum F & Posner JB (1980) *The Diagnosis of Stupor and Coma*,

3rd edn; FA Davis, Philadelphia.

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Examination of brainstem function 4

Lateral (uncal) herniation syndrome

- Due to lesions in the lateral middle fossa or temporal lobe pushing the medial edge of the uncus and hippocampal gyrus over the free lateral edge of the tentorium.
- The first sign is a *unilaterally dilating pupil* (due to compression of the IIIrd nerve at the tentorial hiatus), which is initially sluggish in response to light. This may soon be followed by ptosis and a complete IIIrd nerve palsy with a fixed, dilated pupil. Oculocephalic and oculovestibular responses initially reveal only the palsy, but are otherwise intact.
- *Mid-brain* compression by the herniating uncus may follow rapidly (the diencephalic stage of central herniation is by-passed). The patient becomes progressively less alert and slips into coma. The oculocephalic and oculovestibular responses cannot be elicited. A hemiplegia ipsilateral to the expnading supratentorial lesion (due to the opposite cerebral peduncle being compressed at the tentorial edge) develops and soon progresses to bilateral extensor plantar responses. As compression continues both pupils become fixed in mid-position and central neurogenic hyperventilation commences.

- The rostrocaudal progression of signs associated with central herniation then follow with decerebrate/extensor rigidity etc. as above. Note decorticate/flexor response to pain is not usually seen in uncal herniation because the diencephalic stage is by-passed.

False localizing signs

As they expand, supratentorial lesions may distort intracranial structures and produce signs which appear to help in localising the primary lesion but are in fact due to traction â€˜at a distanceâ€™. The most common of these involve cranial nerves Vâ€“VIII.

Tonsillar herniation

Sub-tentorial expanding lesions cause herniation of the cerebellar tonsils through the foramen magnum and compress the pons and mid-brain directly. A degree of upward herniation through the tentorial hiatus may also occur and lead to compression of the upper mid-brain and diencephalon. It may be difficult to distinguish these effects from those produced by supratentorial lesions. One clue is that there is usually a lack of the rostrocaudal sequence of central herniation.

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Oculocephalic and oculovestibular responses

Background

Passive rotation of the head with respect to the trunk stimulates vestibular and neck receptors. In comatose patients with intact brainstems, this leads to reflexive *slow conjugate* eye movements in the direction opposite to head rotation. The contribution of neck proprioceptors (cervico-ocular reflex) is minimal; the most important reflex pathway in the brainstem extends from the semi-circular canals to the oculomotor nuclei (VOR). Ice water irrigation of a semi-circular canal â€˜switches offâ€™ its contribution to this pathway and leads to unopposed function of the contralateral semi-circular canal. The eyes then deviate toward the irrigated semi-circular canal. Both the doll's head manoeuvre and caloric tests check the integrity of the VOR; the latter is more sensitive.

Oculocephalic/doll's head response

- The doll's head manoeuvre should not be attempted if there is any possibility of cervical spine injury.
- The patient's head is first rotated laterally from one side to the other. Vertical movements may be elicited by flexion and extension of the head.

- â€˜Positiveâ€™ responses are noted if turning of the head elicits *slow conjugate* deviation of both eyes in the direction opposite to head movement (figure, opposite).
- Because there is much confusion about what constitutes positive or negative responses, it is best simply to describe what you see.

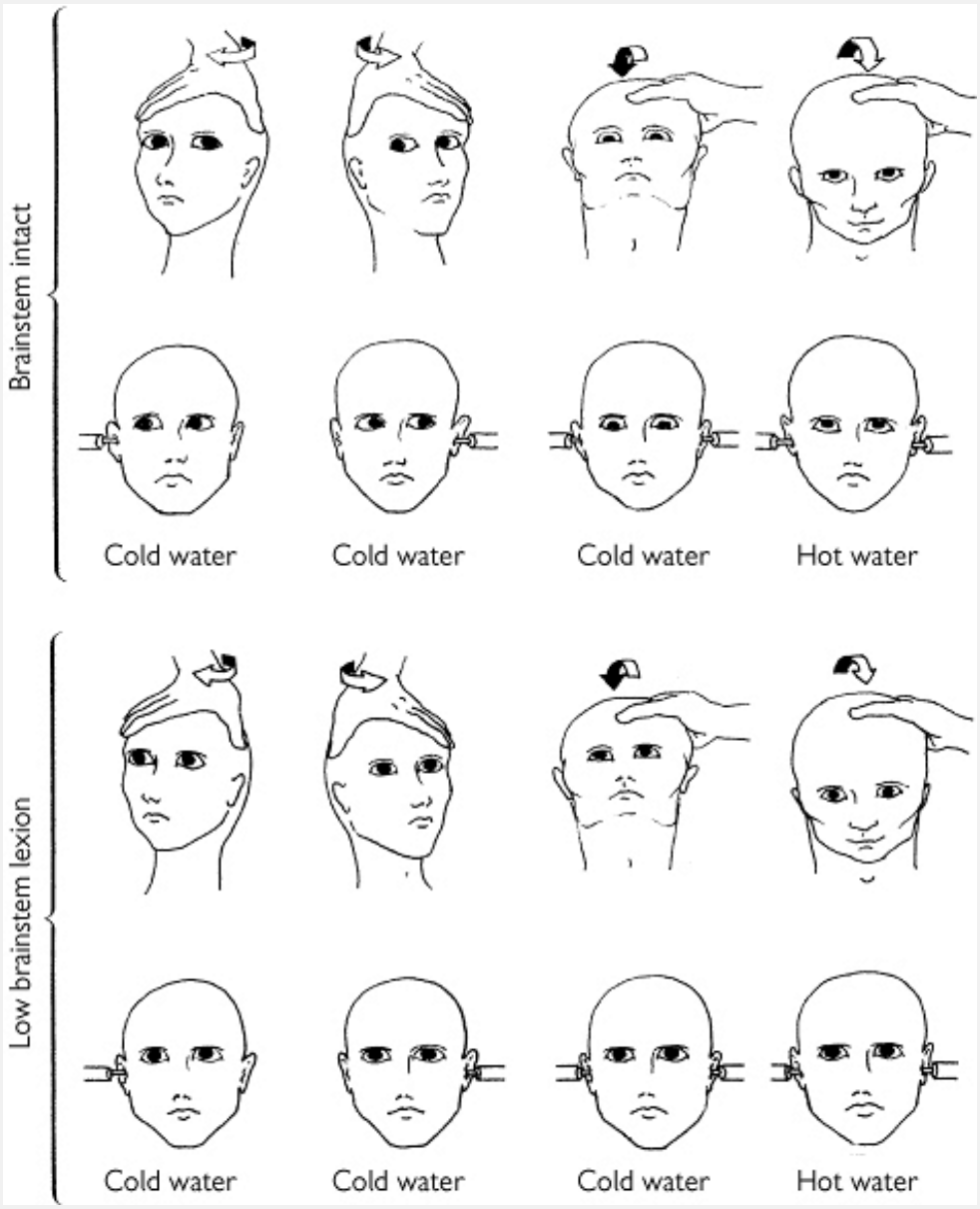
Oculovestibular/caloric response

- Caloric testing should be performed when the oculocephalic response is abnormal or cannot be performed (e.g. spine fracture).
- The head is then raised 30Â° above supine and 100ml of ice water is injected into the external auditory meatus using a thin polyethylene catheter.
- A â€˜positiveâ€™ response occurs when both eyes move toward the irrigated ear (figure, opposite). This may take up to a minute. Five minutes should elapse before the other ear is tested.

Significance of results

- If the VOR is intact, major brainstem pathology is unlikely.
- If the horizontal VOR is absent but the vertical one is present, there may be a lesion at the level of the pons.
- If both responses are absent, there is either a major structural brainstem lesion (figure, opposite) or there is a metabolic disturbance depressing brainstem function (e.g. opiates). Check pupil size and response to light; symmetrically, reactive pupils suggest metabolic coma. Only a few drugs such as atropine, scopolamine, and glutethimide depress brainstem function and produce pupillary abnormalities.

- If dysconjugate eye movements are elicited, a brainstem lesion is likely. Check to see if there is an internuclear ophthalmoplegia.
- It may not be possible to elicit a VOR using the doll's head manoeuvre because the patient has fast, roving saccadic eye movements. These suggest an intact brainstem.



Oculocephalic responses

Editors: Ramrakha, Punit S.; Moore, Kevin P.
Title: *Oxford Handbook of Acute Medicine, 2nd Edition*

Brain death

This is irreversible loss of the capacity for consciousness combined with irreversible loss of the capacity to breathe. Without the brainstem both these functions are lost. But patients with severe, irreversible brain damage who have no brainstem function may survive for weeks or months provided they have a normal circulation and are mechanically ventilated. Criteria for brain death have therefore been developed. It has been shown that patients who fulfil these, even if they are ventilated, will eventually develop cardiovascular collapse.

Preconditions

- There must be no doubt that the patient has irremediable structural brain damage which has been diagnosed with certainty. Usually, this a head injury or intracranial haemorrhage, but it may be anoxia post cardiac arrest when it is not always possible immediately to be certain that brain damage is irremediable.
- The patient must be in apnoeic coma (unresponsive to noxious stimuli and on a mechanical ventilator) with no spontaneous respiratory effort.
- There must be no possibility of drug intoxication and no paralysing or anaesthetic drugs should have been administered recently. Hypothermia must be excluded as a

cause of coma and the core temperature (rectal or external auditory meatus) should be >35Â°C.

- There must be no significant metabolic, endocrine, or electrolyte disturbance either causing or contributing to coma.

Tests for confirming brain death

All brainstem reflexes must be absent

- Pupils fixed and unresponsive to bright light (they need not be dilated). Paralytic eye drops, ocular injury, and lesions of the IInd/IIIrd cranial nerves may pose problems in this assessment.
- Absent corneal reflexes.
- Absent vestibulo-ocular reflexes on irrigation of each ear in turn with 20ml ice-cold water.
- No motor response within the cranial nerve distribution (eye, face, head) elicited by stimulation of any somatic area (nail bed, supraorbital and Achilles tendon pressure on each side). Purely spinal reflexes, e.g. deep tendon reflexes, may be retained.
- No reflex response to touching the pharynx (gag reflex), nor to a suction catheter passed into the trachea (cough reflex).

Apnoea

- No respiratory movements when the ventilator is disconnected and P_aCO_2 reaches 6.65kPa. (In order to avoid anoxia during this procedure, the patient should be

ventilated with 100% oxygen for 10 minutes beforehand; during disconnection, 6L/min 100% oxygen should be delivered via a tracheal catheter. If just prior to disconnection P_aCO_2 is <3.5kPa, give 5% CO_2 in oxygen via the ventilator until this level is reached, usually within 5 minutes.)

The tests must be performed by two experienced clinicians (one must be a consultant and the other a senior registrar or above) and all the above should be repeated after an interval which depends upon the clinical context.

NB: Consider the patient a potential organ donor. Discuss with relatives and contact the transplant co-ordinator for your area. Alternatively contact the duty officer for the UK Transplant Support Service (tel: 01179 757575).

Editors: Ramrakha, Punit S.; Moore, Kevin P.
Title: *Oxford Handbook of Acute Medicine, 2nd Edition*

Chapter 8
Psychiatric emergencies

Acute confusion: assessment

Acute confusional states, or â€˜*deliriumâ€™*, are relatively common: rates in excess of 30% in general hospital patients have been reported, and they are particularly common in care of the elderly, trauma, and orthopaedic wards. Acute confusion may occur on a background of chronic cognitive impairment (dementia), and may last for a prolonged period of days or even weeks. The cause of acute confusion is organic until proven otherwise.

Common features of acute confusion

- Rapid onset
- Fluctuation
- Clouding of consciousness
- Impaired recent and immediate memory
- Disorientation
- Perceptual disturbance, especially in visual or tactile modalities
- Psychomotor disturbance

- Altered sleepâ€“wake cycle
- Evidence of underlying cause.

Common causes of acute confusion

- Pain or discomfort (e.g. urinary retention, constipation)
- Hypoxia
- Metabolic derangement (renal failure, liver failure, acidosis, hypercalcaemia, hypoglycaemia) or endocrine derangement (thyrotoxicosis, Addison's disease, diabetes mellitus)
- Infection (systemic or localized)
- Cardiac (MI, CCF, endocarditis)
- Neurological (head injury, subdural haematoma, CNS infection, post-ictal states)
- Drugs (*prescribed:* benzodiazepines, opiates, digoxin, cimetidine, steroids, anti-parkinsonian drugs, anti-cholinergics, or *recreational*: especially stimulants)
- Alcohol or drug withdrawal.

Detection of acute confusion

- The presence or absence of cognitive impairment can help distinguish between organic and functional mental impairment.
- The 10-point Abbreviated Mental Test Score or the 30-point Mini Mental State Examination (see table) give a rapid estimate of key cognitive functions.
- History from friends and relatives helps determine whether or not the delirium is superimposed upon dementia.

Abbreviated Mental Test Score

Question	Score
What is your age?	1 for exact age
What is your date of birth?	1 for date and month correct (not year)
What year is it?	1 for current year only
What time of day is it?	1 for nearest hour
What address/place are we in?	1 for *exact* address or name of hospital (not just â€˜in hospitalâ€™)
Register 3-line address and recall at end of test	1 if correctly registered *and* recalled
Who is the King or Queen?	1 for current monarch
What year was World War 1?	1 for *either* first or last year
Count back from 20 to 1	1 if no mistakes/corrects
Identify two people (names/jobs)	self-spontaneously

(names/jobs)	1 if *both* recognized

Total score /10: less than 7 abnormal

Mini Mental State Examination

Time	Day, date, month, season, year	/ 5
Place	Country, county, town/city, building, floor	/ 5
Registration	3 objects (e.g. clock, table, umbrella)	/ 3
Attention and concentration	Spell *world* backwards or â€˜Serial 7sâ€™: 1 point for each correct letter/number	/ 5
Recall	Of the 3 objects listed above	/ 3
Naming	Show 2 objects: 1 point per correct name	/ 2
Repeating	Repeat â€˜No ifs, ands, or butsâ€™: correct if word perfect	/ 1
3-stage task	â€˜Take this paper in your right hand, fold it in half and drop it on the floorâ€™: 1 mark for each part done	/ 3

	correctly	
Reading	Write â€˜close your eyesâ€™: ask patient to obey this	/ 1
Writing	Ask patient to write a sentence: score if grammatically correct, not for a fragment	/ 1
Construction	Draw a pair of interlocking pentagons, ask patient to copy: score if approximately right and figures interlocking	/ 1
Total score /30	Usually 23 is the approximate cut-off for significant impairment in the elderly. Pre-morbid intelligence and culture can affect this	

Acute confusion: management

- It is often sufficient to treat the patient conservatively. Nurse in a welllit quiet room with familiar nursing staff or, better still, a familiar person such as a family member.
- Treat the cause. Always consider alcohol withdrawal (see below).
- Occasionally patients may refuse investigations or treatment. It may be important to go ahead with baseline investigations in order to rule out life-threatening causes for the confusion and this may need to be done under

common law (see below).

- If sedation is required, small amounts given orally are best. Offer liquid preparations if tablets are refused. Parenteral medication may be indicated if patients refuse or are particularly disturbed. See below for drugs and doses.
- Patients with on-going disturbance may require regular sedation (e.g. risperidone 0.25â€“0.5mg od/bd). Regular use of benzodiazepines may induce tolerance and dependence, so this is best avoided.

Sedation for acutely disturbed patients

- Start with atypical anti-psychotics such as *risperidone* 1â€“2mg or *olanzapine* 5â€“10mg (half doses in the elderly): both are available in rapidly dispersing tablets.
- If atypical anti-psychotics are unavailable, *haloperidol* 2.5â€“10mg or *chlorpromazine* 25â€“50mg may be used.
- If needed, add *lorazepam* 1â€“2mg (0.5â€“1mg in elderly) but remember that benzodiazepines may exacerbate confusion.
- Some patients, such as those with parkinsonism or those who are neuroleptic naÃ¯ve, are extremely sensitive to neuroleptics and may develop severe extra-pyramidal side-effects if these drugs are given. Use low doses if you are unsure and ensure that anti-cholinergic drugs such as procyclidine are available.
- If parenteral medications are required, use lorazepam and/or haloperidol (doses as above). im *diazepam* is sometimes used but is erratically absorbed and hence usually avoided.
- Reassess the patient after 15â€“20 minutes to assess the effects of the sedation.

- Patients given large amounts of sedation require vital signs monitoring every 5â€“10 minutes for the first hour then half-hourly until they are ambulatory.

Prognosis in acute confusion

Delirium and dementia both carry adverse prognosis. In particular, delirium increases length of hospital stay (by up to 10 days) and mortality and may produce residual cognitive impairment. It is important to ensure that cognitive assessment is repeated after the episode prior to discharge as residual deficits may go undetected otherwise.

Practice point

- Patients with visual hallucinations usually have organic behavioural disturbance.

Acute alcohol withdrawal

Also see p500.

Untreated, this carries a risk of seizures, permanent neurological complications, and death. It should be treated as a medical emergency.

Detection of alcohol withdrawal

Early clinical features include anxiety, restlessness, tremor, insomnia, sweating, tachycardia, ataxia, and pyrexia. Withdrawal may be complicated by seizures especially in those with known epilepsy. *Delirium tremens* can develop, and is characterized by confusion and disorientation, labile mood and irritability, hallucinations (auditory and visual), and fleeting delusions, often very frightening. Untreated, this condition

carries a significant risk of death.

Do not forget to screen for Wernickeâ€“Korsakoff syndrome, a complication of acute thiamine deficiency which may occur in chronic alcoholism. Wernicke's encephalopathy presents with acute confusion, ataxia, nystagmus, ophthalmoplegia, and peripheral neuropathy but not all of these symptoms need to be present. Untreated, a large number of these patients will develop long-term memory problems from Korsakoff syndrome.

Treatment of alcohol withdrawal

- Alcohol withdrawal patients can often be treated as out-patients. However, patients with a history of seizures or delirium tremens, or those with signs suggestive of delirium tremens, should be treated on a medical ward.
- Treatment of the withdrawal requires a long-acting benzodiazepine. The drug of choice is usually chlordiazepoxide. Oral chlormethiazole has been used in the past, but it is highly dependence inducing and dangerous if combined with alcohol. If an iv agent is needed use diazepam. A suggested reducing regime is suggested below.
- B-complex vitamins are required to prevent Wernickeâ€“Korsakoff syndrome (see above). In the first instance, parenteral therapy as pabrinex (ampoules 1 and 2, 1â€“2 pairs daily for 3â€“5 days iv or im) and thereafter oral vitamin supplements should be given.
- Other useful drugs may include
    - Î²-blockers for hypertension
    - Carbamazepine for seizures
    - Haloperidol for hallucinations: not usually required.

Withdrawal regime

See p500.

Aftercare

- Maintenance thiamine or multi-vitamin therapy is often indicated, at least in the initial period.
- Screen for residual cognitive impairment.
- Mobility and occupational therapy assessments before discharge may help if there are problems with the home environment.
- Identify the patient's local drug and alcohol service and encourage the patient to self-refer.
- Some hospitals have alcohol liaison nurses who may be able to assist with counselling or follow-up.

Practice point

- Sudden onset of confusion, delirium with sweating and shaking, particularly in patients recently hospitalized, may indicate alcohol withdrawal. Check the serum phosphate, as it may be very low (<0.4 mmol/l) in acute alcohol withdrawal.

Dealing with violent patients

Occasionally you may encounter violent patients in medical settings, and assaults on doctors and nurses do happen from time to time.

Predisposing factors

- Delirium
- Dementia
- Epilepsy
- Brain damage (especially temporal or frontal lobes)
- Alcohol intoxication *or* withdrawal
- Drugs (cocaine, crack, amphetamine, opiate, or sedative withdrawal)
- Functional mental illness (especially acute psychosis or acute mania)
- Personality disorder
- Previous violent behaviour in patients with such conditions may give an indication of future risk.

Management

Risks posed by violent patients may be minimized by following some simple rules.

- Do not see patients who may be violent in an isolated room, and do not see them on your own: ask a nurse or other professional to join you.
- Keep yourself between the patient and the door.
- If you are uncomfortable or afraid, end the interview and leave.
- It is usually sufficient to calm the patient down verbally and by avoiding confrontation.
- On occasion, it is necessary to sedate violent patients. Offer oral medication first, but give im if necessary. Haloperidol 5â€“10mg is the drug of choice, with lorazepam 1â€“2mg if additional sedation is required.
- Restraint may be required, particularly if sedation is to be

given: security and nursing staff may do this, or the police may be able tohelp if this is not possible.

- Liaise with the psychiatric team about current and on-going management. Nursing on a medical ward with a psychiatric nurse is always an option.

Deliberate self-harm

Deliberate self-harm (DSH) is a common presenting complaint to A&E and reason for admission. Severity of the sequelae of DSH vary greatly, from superficial cuts to serious overdoses requiring prolonged spells in hospital. Suicide is uncommon, but DSH increases the risk of subsequent suicide (1% of those who commit acts of DSH kill themselves in the next yearâ€”100x the general population risk) and 40â€“60% of suicides have a history of DSH. Assessment of patients who have harmed themselves is important in order to

- Detect those at risk of subsequent DSH or suicide
- Identify patients with significant mental health problems requiring treatment
- Plan aftercare in hospital or in the community.

Assessment by general medical staff

Assessment of DSH is normally done by a professional experienced in the field: a psychiatrist, specialist nurse, or social worker. However, it is important for *all* staff to be able to make a basic assessment of these patients, because patients may refuse to see a mental health worker or may attempt to leave the ward or department before a detailed assessment can be carried out.

What if a patient wants to leave before they are assessed by a mental health professional?

You have a duty of care to the patient that includes protecting them as best you can from on-going risk.

- Try to persuade the patient to stay for an assessment. If they agree, refer to the psychiatric team and ask the nursing staff to monitor the patient.
- If the patient refuses, then you will need to ask them to stay whilst you make your own assessment of risk.
- If they will not stay, and you are concerned, you will need to detain them under common law pending a formal psychiatric assessment.
- If they agree to stay, make your assessment. Do not forget to enquire about past episodes of self-harm and on-going psychiatric problems, as well as the questions above.
- If, after your assessment, you have concerns that require the patient to see a mental health professional, try to persuade them to stay. If they refuse, consider detaining them under common law pending urgent psychiatric assessment.
- If you are satisfied that the on-going risk is not of a magnitude that requires them to be detained, then allow them to be discharged but ensure that the GP is informed.
- Detaining patients who will not stay in hospital: see p548.
- Guidelines on treatment for patients who are refusing treatment: see p546.

Points to remember about DSH

- Risk assessment in older adults or children and adolescents requires specialist input. Always obtain advice in these cases.
- Staff attitudes towards patients who self-harm, especially if they do so frequently, can be very negative. Patients usually notice this. Try and maintain an empathic attitude and to understand what may motivate the behaviour, however difficult this may be.
- Some patients present repeatedly with DSH. These patients may have personality disorders with or without substance misuse, and may be very difficult to manage. Most A&E departments know their frequent attendees well and have strategies in place for particular individuals: always ask.

Questions to assess suicide risk after an act of self-harm

- Current mood and mood at time of act?
- Any forward planning, final acts, or suicide notes?
- Any precautions against being discovered?
- What was going through their mind at the time of the act?
- Did they mean to die?
- What is their view on having survived?
- What are their thoughts about the future now?
- Have they any feelings now that they wish to harm themselves? Have they made plans?

The Mental Health Act and common law

There is frequent confusion about one's legal rights around patients who may be mentally impaired.

The Mental Health Act 1983

Different rules apply in Scotland although the principles are the same: seek local advice.

This act allows for the compulsory detention and/or treatment of patients with mental illness and/or mental impairment of a nature and/or degree that requires in-patient treatment against their wishes. Thus patients who need to be in hospital because of a risk to their health and safety or that of others may be detained or brought into hospital if the appropriate people agree that this is necessary.

- *Section 2* allows a period of assessment and/or treatment for up to 28 days, and is usually applied to patients presenting for the first time or known patients with a new problem.
- *Section 3* (which may also follow a Section 2) allows detention for treatment for up to 6 months.
- Patients have the right to appeal against both Sections 2 and 3. Both sections require opinions from two appropriately qualified doctors and an approved social worker.
- *Section 4* allows patients to be brought into hospital with only one medical opinion and that of a social worker, and is only used in emergencies.
- *Sections 5(2) and 5(4)* apply to hospital in-patients and are described below.
- *Section 136* allows patients to be brought by the police to A&E (or another â€˜designated place of safetyâ€™) to be assessed by a doctor and a social worker who may make them informal or arrange for a Section 2 or 3.

People may be placed under a section either in the community or in hospital. It is possible to detain a patient on a medical ward and nurse them there if they require medical treatment (see below).

Common law

- This allows medical practitioners to act in the patient's best interests in emergency situations where they are unable to give consent (e.g. if they are unconscious, or conscious but lack capacity).
- If in an emergency, it is deemed necessary to detain a patient pending assessment or to treat a patient against their will then it is done so under common law.
- Treatment under common law is given in the best interests of the patient if it is carried out to save life or to ensure improvement or prevent deterioration of physical or mental health.

Always document in the notes that you are giving treatment in the patient's best interests under common law.

Treating patients against their will

The issue of how and whether to treat patients against their will arises surprisingly often. It is frequently presumed that this is due to mental illness although often this is not so.

What to do in this situation

The key to whether or not a patient is able to refuse treatment is whether or not they have *capacity* to do so. Psychiatrists are frequently asked to assess capacity, but in an emergency this is not always possible.

For a patient to have capacity, they must

- Be able to take in and retain the information relevant to making the decision and the consequences of refusal
- Believe this information
- Weigh up the information and arrive at a decision.

Remember

- Patients may have the capacity to make some decisions and not others
- Capacity in the same patient may fluctuate over time.

Mental illness or cognitive impairment *may* impair capacity, but *need not* do so: there are legal precedents where patients who are mentally unwell have been wrongfully treated against their will. Disagreeing with medical advice does not automatically constitute incapacity.

If a patient does not have capacity and requires emergency treatment, then this may be given against their will under common law (see p550).

The law on consent and capacity

- There is no such thing as proxy consent for adults in the UK: a third party cannot make a decision on a patient's behalf, though it is good practice to take their views into consideration.
- *The Mental Health Act 1983 does not allow doctors to treat mentally impaired patients against their will for physical problems.* Psychiatrists are occasionally asked to â€˜sectionâ€™ patients in order that they should be treated for a medical condition. This is illegal, even if the physical problem results from the mental problem (e.g. deliberate self-poisoning). The only exception would be where the

physical condition is the *cause* of the mental condition, e.g. detaining and treating a patient with severe confusion secondary to organic illness.

- Different rules apply to *children* and individuals with *advance directives*: you must always obtain specialist advice in such cases.
- Treating a patient who has capacity to refuse against their will can constitute a criminal offence. However, you are unlikely to be criticized for taking a decision to give life-saving treatment against a patient's will if you are unsure about capacity. Most people would acknowledge that it better to treat than not to treat in such situations.
- In any situation where you are unsure of what to do, obtain senior advice at an early stage. Many of the medical defence organizations offer legal advice on a 24-hour basis.

Patients who do not wish to stay in hospital

Sometimes patients do not wish to stay in hospital. Usually the problem can be discussed and an agreement can be reached between the patient and the medical team. From time to time this is impossible. If a patient is acutely confused, they may not be willing to stay and require physical restraint in order to keep them there. In the case of patients who have harmed themselves, teams may be concerned about the possible risks to the patient if they leave the ward.

What to do in this situation

- Assess the patient. What are the medical issues that require them to stay? Is their wish to leave part of an organic illness that may be treated?

- Is it possible to reason with the patient and persuade them to stay?
- If not, they may require psychiatric assessment regarding their capacity to decide to leave.
- If the patient tries to leave before psychiatric assessment, they may be detained under common law.
- If the wait for a psychiatric opinion is likely to take a long time (e.g. no psychiatric team on site), it may be necessary for them to be detained. Hospital in-patients may be detained by a nurse under Section 5(4), or by a single doctor under Section 5(2). Patients in A&E departments must be detained under common law.

Detaining a patient in an emergency

Common law

If you believe it is in the interests of the patient not to be allowed to leave, the security staff may be asked to prevent them from doing so. Document that you are doing this under common law. This should take place until a psychiatric opinion may be obtained.

Section 5(2)

- This section allows an in-patient on any ward to be prevented from leaving. It lasts a maximum of 72 hours and is only a holding measure pending a full Mental Health Act assessment by appropriate doctor(s) and a social worker.
- Any registered medical practitioner may use Section 5(2), not only a psychiatrist. It must be applied by the consultant

under whose care the patient currently is or their â€˜nominated deputyâ€™, i.e. a member of their team or whoever is covering their patients out of hours. It is actioned by filling in a Form 12 (these should be available on the ward) which should be delivered to the local Mental Health Act administration office as soon as it is practicable.

- The Section 5(2) expires once the patient has been seen by an appropriately qualified doctor and it is converted to a Section 2 or 3, or is rescinded. If a patient has been placed under Section 5(2), the duty psychiatry team should be informed, as should the mental health duty Social worker, to ensure that the patient is reassessed appropriately and quickly.
- Section 5(2) does not allow you to enforce medical treatment of any kind. *This would need to be given under common law if the patient is not consenting*.

Section 5(4)

- This section entitles a suitably qualified nurse to hold a patient for up to 6 hours pending the arrival of a doctor to assess the patient for Section 5(2). It is only used in situations where a doctor cannot arrive quickly, e.g. if they are off site.
- If the doctor decides that the patient needs to be held under Section 5(2), then the 72-hour duration of this latter section begins at the time the nurse imposed the Section 5(4). It ends once the patient has been assessed by appropriate mental health professionals regarding further detention or being made informal.

Sections 5(2) and 5(4) are only applicable to in-patients, not to patients A&E or out-patients. Patients in these areas are detained under common law pending psychiatric assessment.

Practice point

- It is best to detain people under common law if you don't think that they should leave the A&E dept. You are unlikely to be criticized for this, and you may ensure their safety in the short term.

Mentally ill patients in hospital

Patients with mental illnesses are subject to stigma from those working in the medical profession as well as society at large. Patients with chronic mental illnesses, such as schizophrenia, are at increased risk of ill health compared with the general population, and may from time to time require care from medical teams.

Guidelines for looking after patients with mental illness

- Hospital is frightening enough for the mentally well, let alone for the mentally ill. Mentally ill patients may require a lot of reassurance and explanation about what is happening to them.
- If people are on regular psychotropic medications, then *give them*. They will usually be able to tell you what they take and when. Remember that sudden discontinuation of certain medications, such as lithium and SSRIs, can precipitate mental health crises.
- Some patients are on depot injections, rather than tablets. Find when their next injection is due and, if this falls during their hospital stay, ensure that they receive it.
- If there is a medical reason for stopping a medication, or if you are at all unsure, then *ask for advice*. Ideally, this

should be from a psychiatrist who knows the patient, but otherwise the on-call or liaison psychiatrist will be able to help.

- It is good practice to communicate with the mental health team who know the patient, who will probably be based in the community. They will have a consultant and may have a social worker, community psychiatric nurse, or other keyworker who will appreciate knowing that their patient is in hospital.
- Communicate discharge plans to the community team: it may help you to speed the discharge up as community support may already be in place.

Remember, if you are ever unsure about a patient's mental state, it is best to talk to a psychiatrist about it and ask for them to be reviewed if necessary.

Sectioned patients on medical wards

Occasionally, patients who are in hospital under a section of the Mental Health Act 1983 become medically unwell. They may need to be transferred to and cared for on medical rather than psychiatric wards at these times. Please remember the following.

- Patients who are detained are likely to be seriously mentally unwell and therefore prone to becoming disturbed.
- It is acceptable for patients to be detained on a medical rather than a psychiatric ward under their section if that is where they need to be, but you should expect on-going input from the psychiatric team caring for the patient during their stay.
- Patients who are under a section should be nursed by a mental health nurse at all times, alongside the general ward nurses. If a patient presents particular risks or is very disturbed, more than one nurse may be required.

- Ensure that the psychiatric team looking after the patient are kept informed of the patient's progress, so that their transfer back to the psychiatric unit and their on-going medical care may be co-ordinated smoothly.
- Many psychiatric wards have neither the staff nor the equipment to perform even basic procedures (e.g. iv drips, monitoring). Patients going back to these wards need to be well stabilized medically before they return.

Practice points

- Always find out what medication a psychiatrically disturbed patient is taking. It is dangerous to stop certain psychotropic medications.
- New onset of confusion is organic until proved otherwise. Have a low threshold for starting acyclovir or other anti-viral therapy until herpes encephalitis is excluded.

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Editors: Ramrakha, Punit S.; Moore, Kevin P.
Title: *Oxford Handbook of Acute Medicine, 2nd Edition*

Diabetic ketoacidosis (DKA): assessment

DKA predominantly occurs in patients with insulin-dependent diabetes (type I). It does not usually occur in non-insulin-dependent diabetes. DKA is being increasingly recognized in some type II diabetics, esp. Afro-Caribbeans. Remember, patients may be prescribed insulin for poor diabetic control, and yet have non-insulin dependent diabetes.

Clinical features

These include

- Polyuria and polydipsia: patients become dehydrated over a few days
- Weight loss, weakness
- Hyperventilation or breathlessness: the acidosis causes Kussmaul's respiration (a deep sighing respiration)
- Abdominal pain: DKA may present as an â€˜acute abdomenâ€™
- Vomiting: exacerbates dehydration
- Confusion, coma occurs in 10%
- On examination assess state of hydration, ventilation rate, and smell for ketones.

Investigations

â€¢ Blood glucose	This need not be high. Severe acidaemia may be present with glucose values as low as 10mM (e.g. if the patient has recently taken insulin: this, alone, is insufficient to correct the acidaemia in the presence of dehydration)
â€¢ ABG	Assess the degree of acidaemia (pH and bic.)
â€¢ U&Es	Corrected
	$Na = Na^{+} + 1.6 \times \frac{[\text{plasma glc (mmol)} - 5.5]}{5.5}$
	Assess serum K^{+} and renal function
Urinalysis	Ketones strongly positive (ketones may be present in normal individuals after a period of starvation) NB: captopril and other sulphydryl drugs can give a false positive test for urinary ketones
â€¢ FBC	WBC may be elevated (neutrophilia): a leukaemoid reaction can occur in absence of infection
â€¢ Septic	Blood and urine cultures

screen	
â€¢ Plasma ketones	(see note below)
â€¢ CXR	Look specifically for any infection
â€¢ Amylase	May be high with abdominal pain Â± vomiting in absence of pancreatitis. Acute pancreatitis may occur in ~ 10% of patients with DKA.

Note

- Serum osmolality = 2 Ã— (Na^+ + K^+) + urea + glucose.
- Diagnosis of DKA requires positive urinary or plasma ketones and arterial pH â‰¤7.30 and/or serum bicarbonate â‰¤15mmol/L. Many labs do not measure plasma ketones.

- The elderly patient presenting with a high glucose, relatively normal acidâ€“base balance, and ketones in the urine does not have diabetic ketoacidosis, and may not be insulin dependent.
- Consider other causes of hyperglycaemia/acidosis, e.g. aspirin overdose, and in the elderly consider lactic acidosis.
- Plasma ketones can be estimated by diluting plasma 1:1 with N saline, and applying to a urine ketone dipstick. A result of +++ corresponds to a plasma ketone body concentration of 5mmol/L.

Common precipitants of DKA

â€¢ Infections	30%
â€¢ Non-compliance with treatment	20%
â€¢ Newly diagnosed diabetes	25%

Poor prognostic features in DKA

- pH <7.0
- Oliguria
- Serum osmolality >320
- Newly diagnosed diabetes

Editors: Ramrakha, Punit S.; Moore, Kevin P.
Title: *Oxford Handbook of Acute Medicine, 2nd Edition*

Diabetic ketoacidosis: management[1]

General measures

- Rehydration and insulin therapy are the mainstays of treatment.
- Site the iv cannula away from a major vein in the wrist. This may be required for an AV fistula in patients subsequently developing diabetic nephropathy. Start fluid replacement (see below).
- Insert a central line in patients with a history of cardiac disease/autonomic neuropathy or the elderly (see P866).
- Consider an arterial line to monitor ABGs and potassium.
- Nil by mouth for at least 6 hours (gastroparesis is common).
- Nasogastric tube: if there is impaired conscious level to prevent vomiting and aspiration.
- Urinary catheter if oliguria is present or serum creatinine is high.
- Broad-spectrum antibiotics if infection suspected.
- LMWH (e.g. enoxaparin) should be given as prophylaxis against DVTs, but is not standard clinical practice.

- The $t_{½}$ of insulin is short and continued replacement (iv or sc) is essential.

Fluid replacement

Use N saline Â± potassium until blood glucose is <12mmol/L. The average fluid loss in DKA is 3â€“6 litres. Aim to restore this over 24 hours.

(The following regime should be modified for patients with cardiac disease.)

- If hypotensive and oliguric, give iv colloids (Â± N saline) initially to restore BP; then
- 1 litre N saline over the first 30 minutes then
- 1 litre N saline with potassium (see table) 2 hourly for 8 hours then
- 1 litre N saline (with K^+, see table) 4 hourly until rehydrated (~24hours).
- The use of bicarbonate is controversial. If the pH <7.0, isotonic (1.26%) sodium bicarbonate given at a maximal rate of 500ml (i.e. 75mmol) over 1 hour is safe. Faster infusion rates cause a paradoxical intracellular acidosis. Add 10â€“20mEq K^+ per 500 ml. There is no evidence that the use of bicarbonate in DKA improves outcome.
- When blood glucose is <12mmol/L, commence a 5% dextrose infusion and continue insulin infusion. Continued insulin is required to inhibit ketoacid production.

Potassium replacement

See table. Total body potassium can be depleted by 1000mmol and the plasma K^+ falls rapidly as potassium shifts into the cells under the action of insulin. Use less potassium in patients with renal impairment or oliguria.

Insulin replacement

See table. Modify this regimen depending on the response to therapy.

- Aim for a fall in glucose of 5mmol/L per hour (and correction of acidosis and plasma bicarbonate).
- If the glucose or acidosis are not improving, increase the insulin infusion rate accordingly.
- Keep the blood glucose >10â€“14mmol/L for the first 24 hours or until the ketoacidosis resolves; maintain this with 5% dextrose infusion.

Plasma potassium (mmol/L)	Amount of K^+ (mmol) to add to each litre
<3.0	40
<4.0	30
<5.0	20

The sliding scale below is a guide and should be tailored to the patient and response to therapy.

- Add 50 units of actrapid to 50ml 0.9% saline and administer by intravenous infusion.
- Start the insulin infusion at 0.1U/kg/h initially. That is 7U/h for a 70kg person.
- If the blood glucose falls by >5mmol/L in 1 hour, then

decrease the rate of infusion to 0.05U/kg/h (i.e. reduce to half-dose).

- When the blood glucose is <12mmol/L, glucose should be infused instead of saline, and blood glucose stabilized according to the sliding scale below.
- *Do not stop insulin infusion until regular subcutaneous insulin is restarted*.

Blood glucose (mmol/L) (hourly)	Insulin infusion (units/hour)
0.0â€“2.0	Stop insulinâ€”call doctor
2.1â€“4.0	Call doctor
4.0â€“7.0	0.5 or 1
7.1â€–11.0	2
11.1â€–20.0	4
>20	7â€”call doctor

Footnote

1

Lebovitz HE (1996) *Lancet* 345: 767â€–772.

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Diabetic ketoacidosis: complications

Assessment during treatment

Remember rapid normalization of biochemistry can be detrimental in any patient. It is wiser to be cautious and sub-optimal than enthusiastic and dangerous.

- Blood glucose hourly with lab blood glucose 4 hourly.
- Plasma electrolytes 2 hours after start of treatment and then 4 hourly. The main risk is hypokalaemia.
- ABGs 4 hourly, until persistent improvement or normalized.
- Plasma osmolality 4 hourly.
- Some patients may require monitoring on an ECG for T-wave changes during treatment.
- Phosphate levels should be monitored daily during treatment (see below).
- Magnesium levels should be monitored daily (see below).
- The iv insulin infusion should be continued until 4 hours after the patient is commenced on subcutaneous insulin.

Complications

See table.

- Avoid *hypoglycaemia* from overzealous insulin replacement.
- *Cerebral oedema* occurs mainly in children. It may be precipitated by sudden shifts in plasma osmolality during treatment. Symptoms include drowsiness, severe headache, Â± confusion. Treat as on P454. Give iv mannitol 0.5g/kg body weight, repeated as necessary. Restrict iv fluids and move to ITU. Mortality is ~70%; recovery of normal function only 7â€“14%.
- *Serum phosphate* falls during treatment, as it moves intracellularly with potassium. If the phosphate level falls to below 0.4mmol/L, give phosphate iv (monobasic potassium phosphate infused at a maximum rate of 9mmol every 12 hours). Check preparations with your pharmacy.
- *Serum magnesium* may fall during insulin therapy. If magnesium levels fall <0.6 mmol/L, give 4â€“8mmol (2ml of 50%) magnesium sulphate over 15â€“30 minutes in 50ml N saline. Repeat as necessary.
- *Hyperchloraemic acidosis* (high anion gap acidosis in a well-hydrated patient) may be seen with excessive administration of saline and increased consumption of bicarbonate. No specific treatment is required.
- Tissue hypoperfusion results from dehydration and may trigger the coagulation cascade and result in *thromboembolism*. Consider using LWMH (e.g. enoxaparin sc) for prophylaxis in those at risk.

Complications of DKA

- Hypokalaemia
- Hypophosphataemia
- Hyperchloraemic acidosis

- Hypoglycaemia
- Cerebral oedema in children
- Thromboembolism

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Hyperosmolar non-ketotic coma (HONC)

HONC occurs in elderly patients with non-insulin-dependent diabetes. These patients are also at increased risk of venous and arterial thromboses. The mortality is very much higher than for ketoacidosis.

Presentation

- A history of diabetes is not usually known, and the patient is elderly
- Insidious onset of polyuria and polydipsia
- Severe dehydration
- Impaired conscious level: the degree correlates most with plasma osmolality. Coma is usually associated with an osmolality >440
- Respiration is usually normal
- The patient may rarely present with a CVA, seizures, or a MI.

Investigations

â€¢ Glucose	Usually very high (>50mmol/L)
â€¢ U&Es	Dehydration causes a greater rise in urea than creatinine (normal ratio of Cr:Ur up to 20:1 (ÂµM:mM). Significant hypernatraemia may be hidden by the high glucose.
	The hypernatraemia may appear to worsen as the glucose falls
	Relatively normal cf. DKA. A coexistent lactic acidosis considerably worsens the prognosis
â€¢ Plasma osm.	Calculate by [2 Ã— (Na^+ + K^+) + urea + glucose] needs to be >350mosm/kg for diagnosis
â€¢ FBC	Polycythaemia and leukocytosis may indicate dehydration or infection respectively
â€¢ ECG	Look for MI or ischaemia
â€¢ CXR	Look for signs of infection
â€¢ Urine	For urinalysis, MC&S. Remember that ketones may occur in any starved person, but the level will be below 5mM. Blood and protein on urinalysis may indicate UTI.

Management: general measures

- Rehydration and insulin therapy are the mainstays of treatment. Fluid replacement should be more cautious in the elderly. Give oxygen if hypoxic on air.
- Avoid fluid overload: monitor central venous pressure in all patients.
- Nil by mouth for at least 6 hours and insert an NG tube in patients with impaired conscious level to prevent vomiting and aspiration.
- Urinary catheter if oliguria is present, or serum creatinine is high.
- Anti-coagulate with LWMH (e.g. enoxaparin 40mg sc daily).

Fluid replacement

The average fluid lost is 8â€“10L. This should be replaced cautiously.

- 1 litre N saline over the first 60 minutes then
- 1 litre N saline with K^+ (see table, P559) every 2 hours for 4 hours then

- 1 litre N saline with K^+ (see table, P559) q6h until rehydrated (~48 hours).
- If the plasma Na is >160mM give 0.45% saline (0.5 N saline) for the first 3 litres. The Na^+ level is artificially lowered by the high glucose level (see below) and appears to climb as the blood glucose falls.
- When blood glucose <12mmol/L, commence a 5% dextrose infusion, and consider stopping insulin therapy and starting oral hypoglycaemic agents or diet alone.

Insulin regimen

This is similar to that for diabetic ketoacidotic coma (see table, P559), except that stopping insulin completely is less hazardous in the short term.

Practice points: hyperosmolar non-ketotic coma

- Severe hyperglycaemia can cause a technical error in the measurement of Na^+ concentrations. The corrected concentration can be calculated by*

$$\text{Corrected Na} = Na^+ + 1.6 \times \frac{[\text{plasma glc (mMl)} - 5.5]}{5.5}$$

- Treatment of severe hyperglycaemia causes an apparent increase in plasma Na^+ which in reality may not actually change
- Occasionally patients present with hyponatraemia which based on the above is a form of pseudohyponatraemia (see P574)

Footnote

*These formulae should be used with caution. Check with laboratory as some labs measure ionic Na^+.

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Hypoglycaemic coma: assessment

- All unconscious patients should be assumed to be hypoglycaemic until proved otherwise. *Always* check a blood glucose using a GlucostixÂ® (or BM stix) immediately, and *confirm* with a lab determination.
- The most common cause of coma in a patient with diabetes is hypoglycaemia due to drugs. The longer acting sulphonylureas such as glibenclamide are more prone to do this than the shorter acting ones.
- Patients who are *not* known to have diabetes, but who are hypoglycaemic, should have a laboratory blood glucose, and serum saved for insulin and C-peptide determination (insulinoma or factitious drug administration) *before* administration of glucose.

Presentation

Sympathetic overactivity (glc <3.6mmol/L)

- Tachycardia
- Palpitations
- Sweating
- Anxiety

- Pallor
- Tremor
- Cold extremities

Neuroglycopenia (glc <2.6mmol/L)

- Confusion
- Slurred speech
- Focal neurological defect (stroke-like syndromes)
- Coma

- Patients with well-controlled diabetes have more frequent episodes of hypoglycaemia, and can become desensitized to sympathetic activation. These patients may develop neuroglycopenia before sympathetic activation and complain of â€˜loss of warningâ€™.
- Î²-blockers blunt the symptoms of sympathetic activation and patients taking these drugs lose the early warning of hypoglycaemia.
- Patients with poorly controlled diabetes develop sympathetic signs early, and avoid these by running a high blood glucose. They may complain of â€˜being hypoâ€™ when their blood sugar is normal or high. They do not require glucose.
- Patients who have diabetes following a total pancreatectomy have more frequent and severe episodes of hypoglycaemia (â€˜brittle diabetesâ€™) because they lack glucagon producing (Î±) cells as well as Î² islet cells.

Investigations

- Blood glucose (BM stix and confirmed by lab glucose).
- U&Es (hypoglycaemia is more common in diabetic

nephropathy)

- Save serum, *prior* to giving glucose, for insulin and C-peptide levels (send ~20ml blood to the lab for immediate centrifugation if indicated).

Note

- A lab glucose of less than 2.2mmol/L is defined as a severe attack.
- Coma usually occurs with blood glucose <1.5mmol/L.
- Low C-peptide and high insulin level indicate exogenous insulin; high C-peptide and insulin level indicate endogenous insulin [e.g. surreptitious drug (sulphonylurea) ingestion or insulinoma].

Causes of hypoglycaemia

Drugs

- Insulin
- Sulphonylureas
- Alcohol
- Salicylates
- Prescription errors (e.g. chlorpropamide for chlorpromazine)
- Others

  Disopyramide

  Î²-blockers

  Pentamidine

  Quinine

Organ failure

- Hypopituitarism (esp. acute pituitary necrosis)
- Acute liver failure
- Adrenal failure
- Myxoedema
- Rarely CCF or CRF

Infections

- Sepsis syndrome
- Malaria

Tumours

- Insulinoma
- Retroperitoneal sarcoma

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Hypoglycaemic coma: management

Acute measures

- Remember to *take blood* prior to glucose administration (glucose, insulin, C-peptide). See P564.
- If there is a history of chronic alcohol intake or malnourishment, give iv *thiamine* 1â€“2mg/kg to avoid precipitating Wernicke's encephalopathy.
- If patient is conscious and co-operative, give 50g *oral glucose* or equivalent (e.g. LucozadeÂ®, or milk and sugar).
- Give 50ml of *50% dextrose* iv if patient is unable to take oral fluids.
- If iv access is impossible, give 1mg of *glucagon* im. Then give the patient some oral glucose to prevent recurrent hypoglycaemia. Glucagon is less effective in hypoglycaemia due to alcohol.
- Admit the patient if the cause is a long-acting sulphonylurea or a long-acting insulin, and commence a continuous infusion of 10% glucose (e.g. 1 litre 8 hourly) and check glucose hourly or 2 hourly.

Further management

- Patients should regain consciousness or become coherent within 10 minutes although complete cognitive recovery may lag by 30â€“45 minutes. Do not give further boluses of iv glucose without repeating the blood glucose. If the patient does not wake up after ~10 minutes, repeat the blood glucose and consider another cause of coma (e.g. head injury while hypoglycaemic, see P444).
- Prolonged severe hypoglycaemia (>4 hours) may result in permanent cerebral dysfunction.
- Patients on sulphonylureas may become hypoglycaemic following a CVA or other illness preventing adequate food intake.
- Recurrent hypoglycaemia may herald the onset of diabetic nephropathy, as this decreases insulin requirements: insulin is partly degraded by the kidney.
- Review patient's current medication, and inspect all tablets from home.
- Consider psychiatric review if self-inflicted.

Liver dysfunction and recurrent hypoglycaemia

- Hypoglycaemia is common in acute liver failure, when coma may occur (as a result of liver failure rather than hypoglycaemia). Severe hypoglycaemia is rare in chronic liver disease.
- In chronic alcoholics it is advisable to administer iv thiamine (1â€“2mg/kg) before iv dextrose to avoid precipitating neurological damage.
- An acute ingestion of alcohol can also suppress hepatic gluconeogenesis.

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Urgent surgery in patients with diabetes

Surgery requires patients to fast for several hours. In addition a general anaesthetic and surgery produce significant stresses on an individual. The hormonal response to stress involves a significant rise in counter-regulatory hormones to insulin, in particular cortisol and adrenaline. For this reason, patients with diabetes undergoing surgery will require an increased dose of insulin despite their fasting state.

Type I DM (insulin dependent)

- Try to put the patient first on the list. Inform the surgeon and anaesthetist early.
- Discontinue long-acting insulin the night before surgery if possible. If the patient has taken a long-acting insulin and requires emergency surgery, an infusion of 10% dextrose (10â€“100ml/h) can be used, together with an insulin sliding scale.
- Ensure iv access is available.
- When nil by mouth, start iv infusion of 5% dextrose with potassium (20mmol/L) at 100ml/h and continue until oral intake is adequate. Remember saline requirements (~100â€“150mmol Na/24h but increases post-operatively)

but do not stop dextrose infusion (risk of hypoglycaemia).

- Commence an iv insulin sliding scale (see table). Measure finger-prick glucose hourly and adjust the insulin infusion accordingly. Aim for 7â€“11mmol/L.
- Continue the insulin sliding scale until the second meal and restart the normal sc dose of insulin. As iv insulin has a very short half-life (3.5 min), this must be continued until the patient's subcutaneous insulin is being absorbed; an overlap of 4 hours is recommended.

Type II DM (non-insulin dependent)

- Discontinue glucose-lowering tablets or long-acting insulin the night before surgery if possible. If the patient has taken their oral hypoglycaemic or insulin and requires emergency surgery, start an infusion of 10% dextrose (10â€“100ml/h) with an insulin sliding scale.
- Check a fasting glucose: if >12mmol/L treat as above.
- If the patient's diabetes is normally managed with oral hypoglycaemic agents, these can be restarted once the patient is eating normally. The sliding scale can be tailed off 4 hours later.
- Diet-controlled diabetics often do not require a sliding scale at the time of surgery but may require iv insulin post operatively for a short period if blood glucose rises >12mmol/L. This may be tailed off, when eating normally.

Add 50 units of actrapid to 50ml 0.9% saline and administer by intravenous infusion. The sliding scale below is a guide only.

Blood glucose (mmol/L) (hourly)	Insulin infusion (units/hour)
0.0â€“2.0	Stop insulinâ€”call doctor
2.1â€“4.0	Call doctor
4.1â€“7.0	0.5 or 1
7.1â€“11.0	2
11.1â€“20.0	4
>20.0	Call doctor

- Adjust the scale according to the patient's usual requirement of insulin (e.g. a patient on MixtardÂ® 36U/24U requires 60U/24 h, i.e. 2.5 U/h normally).
- If blood glucose is persistently low (<4mmol/L) decrease all insulin infusion values by 0.5â€“1.0U/h.
- If blood glucose is persistently high (>13.0mmol/L) increase all insulin infusion values by 0.5â€“1.0U/h.

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Hyponatraemia: assessment

Presentation

- Mild hyponatraemia (Na^+ 130â€“135mmol/L) is common especially in patients taking thiazide diuretics and is usually asymptomatic. Moderate hyponatraemia (Na^+ 120â€“129mmol/L) is usually asymptomatic unless it has developed rapidly.
- Severe hyponatraemia (Na^+ <120mmol/L) may be associated with disturbed mental state, restlessness, confusion, and irritability. Seizures and coma prevail as the sodium approaches 110mmol/L.

History should focus on drugs, fluid losses (diarrhoea, frequency, sweating), symptoms of Addison's, symptoms or history of cardiac, lung, liver, or renal disease.

Examination should focus on careful assessment of volume status, and in particular should assess whether the patient is hypovolemic, normovolemic, and/or oedematous. Patients should therefore have an assessment of their lying and standing BP, HR, JVP Â± CVP, skin turgor, and the presence of oedema or ascites.

Patients who are hyponatraemic and hypovolemic are salt depleted.

Investigations

- In addition to U&Es, other tests should be aimed at excluding other causes of hyponatraemia (see table, P572).
- Measure serum osmolarity and compare it to the calculated osmolarity [2Ã—(Na^+ + K^+) + urea + glucose]: an increase in osmolar gap is with substances such as ethylene glycol, severe hyperglycaemia, mannitol, etc.
- Urine Na^+ combined with clinical assessment of fluid status may help determine the underlying cause:
    - Volume depletion from an extra-renal cause (see table, P572) is normally associated with a low urinary Na^+ (<10mmol/L)
    - Volume depletion with a high urinary Na^+ (>20mmol/L) suggests inappropriate renal salt-wasting (e.g. intrinsic renal disease, hypothyroidism, adrenal insufficiency, diuretics)
    - A low urine Na^+ (<10mmol/L) is seen in conditions such as CCF, cirrhosis, or nephrotic syndrome where there is sodium retention in response to poor renal perfusion
    - Euvolaemia with high urine Na^+ is seen with SIADH and rarely with severe myxoedema.

General principles

- Assessment of the patient's volume status (neck veins, orthostatic hypotension, cardiac signs of fluid overload, ascites skin turgor) will help in both diagnosis and subsequent treatment.
- Mild asymptomatic hyponatraemia will usually respond to treatment of the underlying cause and no specific therapy is necessary.

- Correction of hyponatraemia should be gradual to avoid volume overload and/or central pontine myelinolysis. Aim to restore the serum Na^+ to ~125mmol/L actively (iv fluids) and allow to rise gradually after that by treating the underlying cause.
- Seek expert help if serum Na^+ <120mmol/L Â± severely symptomatic.

- Patients with cirrhosis and ascites and severe hyponatraemia should have diuretics stopped, and be treated with volume expansion.
- SIADH or other conditions associated with plasma volume expansion can cause hypouricaemia (increased renal clearance).

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Hyponatraemia: causes

Decreased serum osmolarity

Hypovolaemia (hyponatraemia + hypovolaemia = salt depletion)

Renal losses (uNa >20mmol/L)	*Non-renal losses (uNa <20mmol/L)*
Diuretics	GI losses (diarrhoea, vomiting)
Addison's disease	Burns
Na-losing nephropathies	Fluid sequestration (e.g. peritonitis, pancreatitis)

Normovolaemic (normal or mildly increased ECV)

SIADH: urine osm. >100, serum osm. low (<260), urine Na^+ >40mmol/L

CNS disorders	*Malignancy*	*Pulmonary disease*
Trauma	Lung (oat cell)	Pneumonia
Stroke/SAH	Pancreas	TB
Malignancy (1Â°/2Â°)	Lymphoma or leukaemia	Lung abscess
Vasculitis (e.g. SLE)	Prostate	Cystic fibrosis
Infection (abscess or meningoencephalitis)	Urinary tract	Lung vasculitis
Drugs (via SIADH Â± â†'renal sensitivity to ADH or Na > H_2O loss)		
Opiates	Thioradizine	Chlorpropamide
Haloperidol	Carbamazepine	Thiazides
Amitriptyline	Clofibrate	
Cyclophosphamide		
Vasopressin	Oxytocin	Vincristine
Miscellaneous causes		
Severe myxoedema		

Psychogenic polydipsia		
Oedematous states		
Congestive cardiac failure	Cirrhosis with ascites	
Severe renal failure	Nephrotic syndrome	

Normal serum osmolarity

- Pseudo-hyponatreemia (e.g. lipaemic erum, paraprotein >10g/dl)
- Intracellular shift of Na^+ (e.g. hyperglycaemia, ethylene glycol)

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Hyponatraemia: management

- *Exclude pseudohyponatraemia:* lipaemic serum will be obvious (ask the biochemist). Calculate the osmolar gap to check there are no â€˜hiddenâ€™ osmoles (P572). Always exclude the possibility of artefactual â†“Na^+ from blood taken proximal to an iv infusion.
- *Asymptomatic hyponatraemia* should be corrected slowly so that serum sodium does not increase by >12mmol/L/day.
- *Symptomatic hyponatraemia* (e.g. seizures or coma) requires a more aggressive initial correction to increase serum sodium concentration by ~6mmol/L over 3â€“4 hours. Thereafter, correct serum sodium slowly, so that the overall increase is <12mmol/L per 24 hours. Seek expert help early. Start iv infusion of normal saline (150mmol/L) at 250â€“500ml/h watching carefully for fluid overload. As a guide, if 1 litre of N saline is infused instantaneously, it would increase serum sodium by 4â€“5 mmol/L. Alternatively, infuse 5% saline at 40â€“700mmol Na^+/h until serum sodium increases adequately.
- *If volume deplete (dehydrated)* start an iv infusion of normal saline (0.9% = 150mmol/L Na^+); insert a central venous line if indicated. Monitor fluid output: catheterize the bladder if there is renal impairment. Watch out for heart failure.
- *If not dehydrated:* for patients with moderate SIADH,

restrict fluid intake to 500/24h. Seek expert help.

Clinical manifestations of osmotic demyelination

- May be delayed 2â€“5 days
- Often irreversible or only partially reversible
- Dysarthria
- Dysphasia
- Paraparesis or quadriparesis
- Lethargy
- Coma or seizures.

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Hypernatraemia

Abnormalities in serum sodium are usually associated with changes in serum osmolality and ECV.

Presentation

Symptoms often relate to severe volume depletion: weakness, malaise, fatigue, altered mental status, confusion, delirium, or coma.

The way to determine the cause of abnormal serum Na^+ is by

- Careful assessment of the ECV (evaluation of neck veins, supine and standing BP, any cardiac signs of fluid overload (e.g. S3, oedema), and skin turgor), in association with
- Measuring the serum (Â± urine) osmolality. [Serum osmolality may be estimated by (2 Ã— (Na^+ + K^+) + urea + glucose) but this is inaccurate when there are other osmoles (e.g. ketones, ethanol, methanol, ethylene glycol, renal failure) that contribute.]

Serum Na^+ >145mmol/L is always associated with hyperosmolarity.

Causes of hypernatraemia

Normal or â†’extracellular volume (excessive Na^+ and

H_2O loss)

- Renal water losses *(urinary osm inappropriately low)*
  - Diabetes insipidus (central or nephrogenic)
  - Osmotic diuresis with water replacement only (e.g. DM)
- Non-renal water losses *(urinary osm >400mosmol/L)*
  - Hypotonic GI losses (e.g. diarrhoea)
  - Cutaneous losses (burns, heat shock, sweating, and high fever)
  - Chest infections with prolonged hyperventilation
- Salt overload (usually â€˜iatrogenicâ€™)
  - Concentrated $NaHCO_3$
  - Post-operatively when huge volumes of fluid used
  - In ITU when volume loaded with saline based fluids
  - Concentrated infant formula
  - Conn's syndrome (hypertension, hypokalaemia, alkalosis)

Management

- Avoid rapid and extreme changes in serum sodium concentration. It is safer to change serum sodium cautiously.
- If there is hypovolaemia, start fluid replacement. Normal saline (0.9%) contains elemental sodium at 150mmol/L. Use this initially to correct hypovolaemia if present, then change to 5% dextrose to replace water and slowly correct sodium concentration.
- If the patient is haemodynamically stable encourage oral

fluids.

- Monitor electrolytes twice daily initially.

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Acute hypocalcaemia

Presentation

- Abnormal neurological sensations and neuromuscular excitability
- Numbness around the mouth and paraesthesiae of the distal limbs
- Hyperreflexia
- Carpopedal spasm
- Tetanic contractions (may include laryngospasm)
- Focal or generalized seizures. Rarely extra-pyramidal signs or papilloedema
- Hypotension, bradycardia, arrhythmias, and CCF
- Chvostek's sign is elicited by tapping the facial nerve just anterior to the ear, causing contraction of the facial muscles (seen in 10% of normals)
- Trousseau's sign is elicited by inflating a blood pressure cuff for 3â€“5 minutes 10â€“20mmHg above the level of systolic blood pressure. This causes mild ischaemia, unmasks latent neuromuscular hyperexcitability, and carpal spasm is observed.

NB: Carpopedal spasm may occur during hyperventilation

induced respiratory alkalosis.

Investigations

- Plasma Ca^{2+}, PO^{3-}_4, and albumin
- Plasma Mg^{2+}
- U&Es
- ECG (Prolonged QT interval)
- Plasma PTH level
- SXR (intracranial calcification esp. hypoparathyroidism)

Management

- The aim of *acute* management is to ameliorate the acute manifestations of hypocalcaemia, and not necessarily to return the calcium to normal.
- For frank tetany, 10ml of 10% calcium gluconate (2.25mmol) can be given by slow iv injection over 10 minutes. *NB: 10ml of 10% calcium chloride (9 mmol) contains ~4-fold more calcium than calcium gluconate.* Calcium gluconate is preferred as it causes less tissue necrosis if it extravasates. iv calcium should never be given faster than this because of the risk of arrhythmia. Thereafter, an infusion of calcium (~0.025â€“0.05mmol/kg/h should be started). For a 70kg adult, add 50ml of 10% calcium gluconate or 10ml of 10% calcium chloride to 200ml N saline, and infuse at 50â€“80ml/h.
- Post parathyroidectomy, mild hypocalcaemia normally ensues, requiring observation only. In patients who have parathyroid bone disease however, â€˜hungry bonesâ€™ may cause profound hypocalcaemia shortly after the parathyroids are removed. This may cause a severe and

prolonged hypocalcaemia which requires prolonged treatment.

- Chronic hypocalcaemia is best managed with oral calcium together with either vitamin D, or, if the cause is hypoparathyroidism or an abnormality in vitamin D metabolism, a form of activated (hydroxylated) vitamin D such as alfacalcidol or calcitriol.
- If magnesium deficiency is present, add 20ml (~40mmol) of 50% magnesium sulphate solution to 230ml N saline (10g/250ml). Infuse 50ml of this (equivalent to 2g $MgSO_4$, 8 mmol) over 10 minutes, and at 25ml/h thereafter.

Causes of hypocalcemia

Vitamin D deficiency

- Asians
- Chronic renal failure

Loss of Ca^{2+} from circulation

- *Extra-vascular deposition*
  - Hyperphosphataemia (renal failure, tumour lysis)
  - Acute pancreatitis
  - Osteoblastic metastases (e.g. prostatic)

Intra-vascular binding

  - Citrate or blood products
  - Foscarnet (anti-CMV drug)
  - Acute respiratory alkalosis

Hypoparathyroidism

- Post parathyroid, thyroid, or neck surgery

- Idiopathic
- Pseudo-hypoparathyroidism
- Infiltration
- HIV infection

Disorders of Mg^{2+} metabolism

- Magnesium deficiency

Other

- Sepsis, burns
- Fluoride intoxication
- Chemotherapy (e.g. cisplatin)

Practice point

- If hypocalcaemia is difficult to correct, check for magnesium deficiency.

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Hypercalcaemia

- The free (ionic) plasma Ca^{2+} concentration is dependent on both arterial pH (â†‘ during acidaemia) and the plasma albumin.
- Ionized Ca^{2+} = measured Ca^{2+} + [40 - serum albumin(g/L)] Ã— 0.02. (e.g. If measured Ca^{2+} = 2.10mM and albumin = 30g/L, the corrected Ca^{2+} = 2.10 = [(40 - 30) Ã— 0.02] = 2.30mM).
- Most ITUs can now measure ionized calcium.

Presentation

- Routine biochemical screen in an asymptomatic patient
- *General:* depression (30â€“40%), weakness (30%), tiredness, and malaise
- *Gastrointestinal:* constipation, anorexia; vague abdominal symptoms (nauseas, vomiting), weight loss
- *Renal:* renal calculi (if long standing); nephrogenic diabetes insipidus (20%); type 1 RTA; pre-renal failure; chronic hypercalcaemic nephropathy, polyuria, polydipsia, or dehydration
- *Neuropsychiatric:* anxiety, depression, and cognitive dysfunction; coma or obtundation

- *Cardiac:* hypertension, cardiac dysrhythmias.

Urgent treatment is required if

- Calcium >3.5mmol/L
- Clouding of consciousness or confusion is present
- Hypotension
- Severe dehydration causing pre-renal failure.

Management

- *Rehydrate* patient with *iv N saline* (0.9%). Aim for about 3â€“6L/24h depending on fluid status (CVP), urine output and cardiac function.
- If patient does not pass urine for 4h, pass a urinary catheter, and a central venous line to monitor CVP.
- *Diuretics:* once patient is rehydrated, continue N saline infusion and add *frusemide* 40mg every 2â€“4hours. Continue monitoring CVP carefully to prevent either fluid overload or dehydration.
- Monitor electrolytes, especially K^+ and Mg^{2+} which may fall rapidly with rehydration and frusemide. Replace K^+ (20â€“40mmol/L of saline) and Mg^{2+} (upto 2 mmol/L saline) intravenously.
- If this fails to reduce plasma Ca^{2+} adequately (Ca^{2+} still >2.8mM) then the following measures should be considered:
- *Salmon calcitonin* 400IU q8h. This has a rapid onset of action (within hours) but its effect lasts only 2â€“3 days (tachyphylaxis).
- *Bisphosphonates* inhibit osteoclast activity thereby causing a fall in plasma Ca^{2+}. Administer *pamidronate* at 30â€“60

mg iv over 4â€“6 hours. (As a general rule give 30mg over 4h if Ca^{2+} is <3 mmol/L or for all patients with significant renal impairment, 60mg over 8h if Ca^{2+} is 3â€“4 mmol/L. Ca^{2+} levels begin to fall after 48 hours and remain suppressed for up to 14 days. *Zolendronate* has a shorter infusion time (15mins) and is said to more effective with a longer duration of action.

- *Steroids* (prednisolone 30â€“60mg po od): Most effective in hypercalcaemia due to sarcoidosis, myeloma or vitamin D intoxication.
- *Familial benign hypocalciuric hypercalcaemia:* â†'Ca^{2+}, N 24h urinary Ca^{2+}. This causes few symptoms (mild fatigue or lethargy). The PTH may be raised but the patients do not respond to parathyroidectomy.

Causes of hypercalcaemia

- Primary (or tertiary) hyperparathyroidism (85% of cases)
- Malignancy
  - Humoral hypercalcaemia
  - Local osteolytic hypercalcaemia (e.g. myeloma, metastases)
- Hyperthyroidism (present in 15â€“20% of patients)
- Granulomatous disorders (sarcoidosis)
- Drug related
  - Vitamin D intoxication
  - Theophylline toxicity
  - â€˜Milk-alkaliâ€™ syndrome
  - Thiazide diuretics

    - Lithium (mild, present in 50% patients on long-term lithium)
- Immobilization (Paget's disease)
- Benign familial hypocalciuric hypercalcaemia
- HTLV-1 infection may present with severe hypercalcaemia
- Phaeochromocytoma (part of MEA type II), acromegaly
- Adrenal failure
- Rhabdomyolysis (calcium may be high or low)
- Congenital lactase deficiency

Investigations for hypercalcaemia

- Plasma Ca^{2+}, PO^{3-}_4, and Mg^{2+}
- U&Es
- LFTs
- CXR
- Plasma PTH level
- 24h urinary Ca^{2+}
- Urinary cAMP

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Hypophosphataemia

Plasma phosphate is normally 0.8â€“1.4mmol/L.
Hypophosphataemia is common, and often unrecognized by clinicians. Most intracellular phosphate is present as creatine phosphate or adenine phosphates (e.g. ATP), and in RBC the predominant species is 2,3-diphopshoglycerate.
Hypophosphataemia does not necessarily indicate phosphate deficiency; similarly phosphate deficiency may be associated with normal or high plasma phosphate concentrations.

Causes of hypophosphataemia

Modest (0.4â€“0.75mmol/L)

- Decreased dietary intake
- Vitamin D deficiency
- Chronic liver disease
- Hyperparathyroidism
- Decreased absorption (vit D deficiency, steatorrhoea, phosphate binding antacids)
- Hungry bones syndrome (post parathyroidectomy, acute leukaemia)
- Lymphoma or the leukaemias syndrome
- Hyperaldosteronism

- Diuretics
- Fanconi syndrome

Severe (<0.4mmol/L)

- Respiratory alkalosis
- Treatment of diabetic ketoacidosis
- Alcohol withdrawal (esp. with ketoacidosis)
- Acute liver failure
- Hyperalimentation (i.e. feeding after starvation)
- Ventilation of chronic severe respiratory failure
- Neuroleptic malignant

Presentation

- Most cases of severe hypophosphataemia occur in very sick patients (often in an ITU). *Occasionally seen in asymptomatic patients*.
- Coincident Mg^{2+} deficiency exacerbates PO^{3-}_4, depletion and vice versa.
- Modest hypophosphataemia has no effect, but warrants investigation. Severe hypophosphataemia (<0.4mmol/L) may cause symptoms and requires treatment.

Manifestations of severe hypophosphataemia

- Myopathy (involving skeletal muscle and diaphragm)
- Rhabdomyolysis
- Cardiomyopathy

- Erythrocyte dysfunction
- Leukocyte dysfunction
- Metabolic acidosis
- CNS dysfunction (encephalopathy, irritability, seizures, paraesthesiae, coma)
- Respiratory failure
- Reduced platelet half-life
- Mineral mobilization

Treatment

- Phosphate repletion should generally be reserved for patients with sustained hypophosphataemia. Give oral effervescent Phosphate SandozÂ® 2 tabs tds or potassium phosphate iv (9â€“18mmol/24h).
- Excessive phosphate replacement may cause hypocalcaemia and metastatic calcification; monitor Ca^{2+}, PO_4^{3-}, K^+, and other electrolytes.

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Title: *Oxford Handbook of Acute Medicine, 2nd Edition*

Addisonian crisis: assessment

Adrenocortical insufficiency may be sub-clinical for days or months in otherwise well individuals. Stress, such as infection, trauma, or surgery, may precipitate an Addisonian crisis with cardiovascular collapse and death if the condition is not suspected. Crises may also occur in patients with known Addison's disease on replacement hydrocortisone if they fail to increase their steroid dose with infections.

Presentation

- Hypotension and cardiovascular collapse (shock)
- Faintness, particularly on standing (postural hypotension)
- Anorexia, nausea, vomiting, and abdominal pain
- Hyponatraemia
- Dehydration (thirst may not be apparent because of the low sodium)
- Diarrhoea in 20% of cases
- Symptoms of precipitant [fever, night sweats (infection); flank pain (haemorrhagic adrenal infarction); etc]. Note signs/symptoms of other endocrinopathies.
- Non-specific symptoms: weight loss, fatigue, weakness, myalgia.

- Hyperpigmentation suggests chronic hypoadrenalism.
- Psychiatric features are common and include asthenia, depression, apathy, and confusion (treatment with glucocorticoids reverses most psychiatric features).

Malignant secondaries

Present in the adrenals of a high percentage of patients with lung cancer, breast tumours, and malignant melanomas. Adrenal failure will only occur when over 90% of the gland is replaced by metastases.

Adrenal haemorrhage

This may complicate sepsis (meningococcal septicaemia, the Waterhouseâ€“Friderichsen syndrome), traumatic shock, coagulopathies, and ischaemic disorders.

- Severe stress substantially increases the arterial blood supply to the adrenals. However the adrenal gland has only one or two veins, making it vulnerable to venous thrombosis.
- Blood tests: a precipitous drop in haemoglobin, hyponatraemia, hyperkalaemia, acidosis, uraemia, and neutrophilia.
- The *Waterhouseâ€“Friderichsen syndrome* is the association of bilateral adrenal haemorrhage with fulminant meningococcaemia. Adrenal haemorrhage is also seen with other gram-negative endotoxaemias such as *Diplococcus pneumoniae, Haemophilus influenzae* B and DF-2 bacillus infections.

Hypopituitarism

As there is no mineralocorticoid deficiency, the salt and water

loss and shock are less profound than in primary Addison's disease.

Drugs

Rifampicin, phenytoin, and phenobarbitone accelerate the metabolism of cortisol and may precipitate Addisonian crisis in partially compromised individuals, or in those on a fixed replacement dose. Most adrenal crises precipitated by rifampicin occur within 2 weeks of initiating therapy.

Recognized causes of adrenal failure

- Autoimmune adrenalitis (70%)
- Tuberculosis of the adrenals (10â€“20%)
- Malignant secondaries in the adrenal glands
- Adrenal haemorrhage incl. meningococcal septicaemia
- Diseminated fungal infection (histoplasmosis, paracoccidioidomycosis)
- Hypopituitarism
- Drugs: metyrapone or aminoglutethimide can precipitate adrenal failure. Other drugs (see below) may cause relative adrenal insufficiency
- Congenital conditions
    - Adrenoleukodystrophy
    - Congenital adrenal hyperplasia
    - Familial glucorticoid deficiency

Causes of relative adrenal insufficiency

- Drugs
  - Metyrapone or aminoglutethimide
  - Ketoconazole
  - Etomidate
  - Rifampicin, phenytoin, and phenobarbitone
  - Trilostane
  - Megestrol acetate
  - Suramin
- HIV
- Severe sepsis
- Burns
- Acute or chronic liver failure

Practice points

- ~50% of patients with autoimmune adrenalitis have one or more other autoimmune disorders such as polyglandular autoimmune syndrome type 1 or 2.
- Never forget Addison's disease in a sick patient when the diagnosis is unclear.

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Addisonian crisis: management

Investigations

â€¢ U&Es	Hyponatraemia and hyperkalaemia (rarely greater than 6.0mM). High ur:cr ratio indicative of hypovolaemia
â€¢ FBC	Anaemia (normal MCV); moderate neutropenia Â± relative eosinophilia/lymphocytosis
â€¢ Glucose	Hypoglycaemia (rarely severe)
â€¢ Calcium	May be high
â€¢ Serum cortisol	Save for routine assay. Baseline <400nmol/L. Should be >1000nmol/L in â€˜sickâ€™ patients
â€¢ ABG	Metabolic acidosis, respiratory failure

â€¢ Urine	MC&S for infection; urinary Na excretion often high in spite of hypovolaemia
â€¢ CXR	Previous TB, bronchial carcinoma
â€¢ AXR	Adrenal calcification

Management

- Treatment may be required before the diagnosis is confirmed.
- General measures include oxygen, continuous ECG monitoring, CVP monitoring, urinary catheter (for fluid balance), and broad spectrum antibiotics (e.g. cefotaxime) for underlying infection.
- *Treat shock* (P260): give iv N saline or colloid (HaemaccelÂ®) for hypotension: 1L stat then hourly depending on response and clinical signs. Inotropic support may be necessary.
- Give iv *50% dextrose* (50ml) if hypoglycaemic.
- If adrenal crisis is suspected, the patient needs glucocorticoids urgently: use *dexamethasone* 8mg iv which will not interfere with the cortisol assay of a short SynacthenÂ® test. If dexamethasone is unavailable use hydrocortisone (can be stopped later). This single extra dose can do little harm and may be life saving.
- *Short SynacthenÂ® test* (omit if the patient is known to have Addison's disease): take baseline blood sample (serum) and administer tetracosactrin (SynacthenÂ®) 250Âµg im or iv. Take further samples at 30 and 60 minutes for cortisol assay.
- Continue steroid treatment as iv *hydrocortisone* (200mg

stat), then 100mg tds. Change to oral steroids after 72 hours.

- *Fludrocortisone* (100Âµg daily orally) when stabilized on oral replacement doses of hydrocortisone.

Prevention

- Patients on long-term steroid therapy and/or known adrenocortical failure should be instructed to increase steroid intake for predictable stresses (e.g. elective surgery, acute illnesses with fever >38Â°).
- For mild illnesses, if not vomiting, double the oral dose. Vomiting requires iv/im therapy (hydrocortisone 50mg tds).
- For minor operations or procedures (e.g. cystoscopy) give hydrocortisone 100mg iv/im as a single dose before the procedure.
- More serious illnesses require hydrocortisone 100mg q6â€“8h iv/im until recovered or for at least 72 hours.
- Double replacement doses when stabilized if on enzyme-inducing drugs.

Equivalent doses of glucocorticoids[1]

Drug	Equivalent dose (mg)
Dexamethasone	0.75
Methylprednisolone	4
Triamcinolone	4
Prednisolone	5
Hydrocortisone	20
Cortisone acetate	25

Footnote

1

British National Formulary (1995) Pharmaceutical Press, Royal Pharmaceutical Society of Great Britain, London: Section 6.3.2.

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Myxoedema coma

A common precipitant of coma is the use of sedatives, and subsequent hypothermia, in elderly female patients with undiagnosed hypothyroidism.

Presentation

- Altered mental status: disorientation, lethargy, frank psychosis
- Coma (symmetrical, slow-relaxing reflexes; ~25% have seizures)
- Hypothermia
- Bradycardia, hypotension (rare)
- Hypoventilation
- Hypoglycaemia.

Investigations

â€¢ U&Es	Hyponatraemia is common (50%)
â€¢ Glucose	Hypoglycaemia may occur
â€¢ FBC	Normocytic or macrocytic (Â± coexistent pernicious anaemia) anaemia
â€¢ Raised CPK	Often with a clinical myopathy
â€¢ Thyroid function	T4 and TSH
â€¢ Cortisol	To exclude co-existent Addison's disease, i.e. Schmidt's syndrome
â€¢ ABG	Hypoventilation with â†‘P_aCO_2, â†“P_aO_2 and acidosis
â€¢ Septic screen	Blood and urine cultures
â€¢ ECG	Small complexes with prolonged QT interval
â€¢ CXR	Pericardial effusion may occur.

Poor prognostic indicators

- Hypotension. Patients with hypothyroidism are usually

hypertensive. â†“BP indicates possible adrenal failure or cardiac disease. Response to inotropes is poor as patients are usually maximally vasoconstricted.

- Hypoventilation. This is the commonest cause of death in patients with myxoedema coma. The hypoxia responds poorly to oxygen therapy which tends to exacerbate hypercapnoea.

Management

- Transfer the patient to an intensive care unit. Mortality is up to 30%.
- Mechanical ventilation should be instituted for respiratory failure.
- CVP line. Patients are usually hypertensive and hypovolaemic as chronic myxoedema is compensated for by rising catecholamines.
- Broad-spectrum antimicrobials (e.g. cefotaxime). Bacterial infection is a common precipitant of myxoedema coma.
- Hypothermia should be treated as on P844: a space blanket is usually sufficient. Rapid external warming can cause inappropriate vasodilatation and cardiovascular collapse.
- Hydrocortisone (100mg iv tds) until Addison's is excluded.
- Institute replacement therapy before confirming the diagnosis.

- Ideally give 5â€“20Âµg iv (slow bolus) tri-iodothyronine (T3) twice daily for 3 days. After a few days treatment, commence oral thyroxine at 25â€“50Âµg/day or oral triodothyronine at 20Âµg bd. Some clinicians start thyroxine at a much higher dose, but this does carry a risk or precipitating cardiac ischaemia. T3 is preferable due to its short half-life and its effect disappears 24â€“48 hours

after it isstopped.

- If T3 is unavailable use thyroxine, 25â€“50Âµg po or via NG-tube daily.
- Myxoedema coma has a high mortality if inadequately treated.

Precipitants of myxoedema coma

- Drugs, including sedatives and tranquillizers
- Infection
- Cerebrovascular accident
- Trauma

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Title: *Oxford Handbook of Acute Medicine, 2nd Edition*

Thyrotoxic crisis: assessment

The term thyrotoxic crisis refers to a constellation of symptoms and signs which together imply a poor prognosis. Thyroid function tests provide no discrimination between simple thyrotoxicosis and thyrotoxic crisis. If the diagnosis has not been made, look for clues such as a goitre, or exophthalmic Graves' disease. The presentation may be confused with sepsis or malignant hyperthermia.

Presentation

Cardiovascular symptoms

- Palpitations
- Tachycardia/tachyarrhythmias
- Cardiac failure/oedema

CNS Symptoms

- Anxiety/agitation
- Violent outbursts
- Psychosis/delirium
- Fitting/coma

Gastrointestinal symptoms

- Diarrhoea
- Vomiting
- Jaundice

General symptoms

- Fever
- Hyperventilation
- Sweating
- Polyuria

Precipitants of thyrotoxic crisis

- Thyroid surgery/general surgery
- Withdrawal of anti-thyroid drug therapy/radioiodine therapy
- Thyroid palpation
- Iodinated contrast dyes
- Infection
- Cerebrovascular accident/pulmonary embolism
- Parturition
- Diabetic ketoacidosis
- Trauma or emotional stress.

Investigations

- Thyroid function tests (most labs can perform an urgent TSH/free T4 if needed)
- U&Es (?dehydration)
- Calcium (may be elevated)

- Glucose (may be low)
- FBC
- Liver function tests (?jaundice)
- Blood and urine cultures
- CXR (?pulmonary oedema or evidence of infection)
- ECG (rate, ?atrial fibrillation).

Assessment of severity

- The table opposite is used to assess the severity of a thyrotoxic crisis.
- Rarely, patients may present with an apathetic thyroid storm, and lapse into coma with few other signs of thyrotoxicosis.


```
Apyrexial
<99
Absent
Normal
Normal
0
>37.2
>99
Ankle oedema
â€”
â€”
5
>37.8
>110
Basal creps.
Agitation
Diarrhoea, vomiting
```

10
>38.3
>120
Pulmonary oedema
â€”
â€”
15
>38.9
>130
Delirium
Unexplained jaundice
20
>39.4
>140
â€”
â€”
25
>40
Coma, seizure
â€”
30

Temp (Â° C) Score	Pulse	Cardiac failure	CNS effects	GI symptoms

Assessment of severity of a thyrotoxic crisis

- Add the scores for each column.
- Add an extra 10 points if atrial fibrillation is present.
- Add 10 points if there is a definable precipitant.
- A total score of over 45 indicates thyroid crisis; a score of 25â€“44 indicates impending crisis.

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Thyrotoxic crisis: management

Patients with a thyrotoxic crisis or impending crisis

(score >25, P591)

- Admit the patient to intensive care.
- *Fluid balance*: CVP monitoring is essential to avoid precipitating or worsening cardiac failure. In patients with arrhythmias, the CVP will not accurately reflect left-sided pressures and Swanâ€“Ganz monitoring should be considered. Gastrointestinal and insensible (pyrexia and excessive sweating) fluid losses may exceed 5L/day and must be replaced.
- Fever should be treated with *paracetamol* and aggressive *peripheral cooling techniques*. Dantrolene has been occasionally used to control hyperthermia in thyrotoxic crisis. Do not use salicylates which will displace T4 from TBG and can hence worsen the storm.
- Î²-*block* the patient with propranolol 60â€“80mg q4h po or 1mg iv (repeated every 10min as necessary) with cardiac monitoring. Propranolol inhibits peripheral T4 â† T3 conversion. Fever, tachycardia, and tremor should respond immediately. An alternative is Esmolol (15â€“30mg as a bolus followed by 3â€“6mg/min).

If Î²-blockade is contra-indicated (e.g. asthma), guanethidine (30â€“40mg po 6 hourly) can be used.

- *Treat precipitating factors* such as infection (e.g. cefuroxime 750mg iv tds).
- High-dose *anti-thyroid drugs*. Propylthiouracil (1g loading dose then 200â€“300mg q4h po/ng) is more effective than carbimazole (20mg 4 hourly), at it inhibits peripheral T4 â†' T3 conversion.
- *Hydrocortisone* 300mg iv stat, then 100mg 6 hourly. This inhibits conversion of T4 to T3.
- Enoxaparin (clexane) 20mg/day sc should be given to very sick patients at risk of thromboembolism.
- Once organification of iodine has been blocked by anti-thyroid drugs, iodine can be used to inhibit thyroxine release from thyroid gland. *Lugol's iodine* contains 5% iodine and 10% potassium iodide in water. Give 1ml every 6 hours. *Do not give Lugol's iodine until at least 1 hour after the anti-thyroid drugs have been given*. Any iodine given prior to anti-thyroid medication may increase thyroid hormone stores. Continue iodine-containing preparations for a maximum of 2 weeks (lithium is an alternative to iodine in allergic patients).
- *Monitor glucose* levels 4 hourly and administer glucose 5â€“10% as required. Hepatic glycogen stores are readily depleted during thyroid storm.

Continuing treatment

- Response to treatment is gauged clinically and by serum T3 levels.
- Stop iodine/potassium iodide/lithium and Î²-blockers when controlled.
- Consider definitive treatment (e.g. surgery or radioactive

iodine).

- Treat atrial fibrillation in the usual way (P88). Higher doses of digoxin may be required as its metabolism is increased. Amiodarone inhibits peripheral T4 â†’ T3 conversion.

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Pituitary apoplexy

Presentation

Pituitary infarction may be *silent*. Apoplexy implies the presence of symptoms. The clinical manifestations may be due to leakage of blood/necrotic tissue into the sub-arachnoid space or rapid expansion of a suprasellar mass and pressure on local structures. This may be the presenting symptom of the pituitary tumour.

- Headache occurs in 95% of cases (sudden onset; variable intensity)
- Visual disturbance occurs in 70%, (usually bitemporal hemianopia)
- Ocular palsy (40%) causing diplopia. Unilateral or bilateral
- Nausea/vomiting
- Meningism (common)
- Hemiparesis or rarely seizures
- Fever, anosmia, CSF rhinorrhoea, and hypothalamic dysfunction (disturbed sympathetic autoregulation with abnormal BP control, respiration, and cardiac rhythm) are all described, but are rare
- Altered mental state, lethargy, delirium, or coma

- Symptoms of preceding pituitary tumour
- Acute hypopituitarism.

Clinically, pituitary apoplexy may be very difficult to distinguish from sub-arachnoid haemorrhage, bacterial meningitis, mid-brain infarction (basilar artery occlusion), or cavernous sinus thrombosis. Transient neurological symptoms are common in the preceding few days.

The clinical course is variable. Headache and mild visual disturbance may develop slowly and persist for several weeks. In its most fulminant form, apoplexy may cause blindness, haemodynamic instability, coma, and death. Residual endocrine disturbance (panhypopituitarism) invariably occurs.

Investigations

â€¢ U&Es	Hyper- or hyponatraemia may occur.
â€¢ Endocrine tests	Clotted blood for cortisol, thyroid function, prolactin, GH, and the gonadotrophic hormones.
â€¢ CT scan	Pituitary cuts, with administration of iv contrast, will reveal a tumour mass (or haemorrhage) within 24â€“48 hours.
â€¢ MRI scan	May be useful in the sub-acute setting.

Management

- Stabilize the patient (Airway, Breathing, Circulation).

- Hydrocortisone 100mg iv should be given if the diagnosis is suspected after the blood samples above have been collected.
- Monitor U&Es and urine output for evidence of diabetes insipidus.
- *Neurosurgical decompression* may be indicated (seek neurosurgical review). Obtundation and visual deterioration are absolute indications for neurosurgery. Patients without confusion or visual disturbance generally do well without surgery.
- Assess pituitary function once the acute illness has resolved and treat as necessary. A TSH in the normal range may be inappropriate if the T4 is low in pituitary disease, but this may occur in the sick euthyroid state characteristic of many seriously ill patients.

Causes of apoplexy in patients with pituitary adenomas

- Spontaneous haemorrhage (no obvious precipitant, the commonest)
- Anti-coagulant therapy
- Head trauma
- Radiation therapy
- Drugs (e.g. bromocriptine or oestrogen)
- Following tests of pituitary function.

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Hypopituitary coma

Hypopituitarism does not become evident until 75% of the adenohypophysis is destroyed, and at least 90% destruction is required for total loss of pituitary secretion. Complete loss of hormone secretion can rapidly become life threatening and requires immediate therapy. In a mild or incomplete form, hypopituitarism can remain unsuspected for years.

Presentation

In the absence of stress, patients with severe hypopituitarism may have few symptoms or signs. A general anaesthetic or infection may precipitate hypoglycaemia and coma, due to the combination of a lack of GH, cortisol, and thyroxine, all of which have a counter-regulatory effect on insulin.

Clues from the history include

- Known pituitary adenoma
- Recent difficult delivery: pituitary infarction following postpartum haemorrhage and vascular collapse is still the commonest cause of hypopituitarism. Features include failure of lactation (deficiency of prolactin Â± oxytocin), failure of menstruation (lack of gonadotrophins), non-specific features, e.g. tiredness, weakness, loss of body hair, and loss of libido (due to ACTH deficiency, hypothyroidism, and gonadotrophin deficiency)

- Men may give a history of impotence, lethargy, and loss of body hair
- Women report loss of menstruation.

Examination

- Examination of the comatose patient is discussed on P406â€“15
- Examine specifically for secondary sexual characteristics and physical signs of myxoedema
- Consider other causes for coma (P406).

Investigations

- General investigations for patients in coma are discussed on P408
- Take blood for baseline cortisol, ACTH, thyroid function, LH, FSH, prolactin, and GH
- Short synacthenÂ® test must be performed to test for adrenocortical reserve (P586)
- LHRH and TRH test can be performed at the same time as the short SynacthenÂ® test
- Defer formal pituitary function testing until the patient is stable
- CT scan of pituitary (tumour or empty sella)
- MRI scan may give additional information.

Management

- General measures are as for any patient in coma (P406)

- Give iv colloids Â± saline to restore BP if the patient is in shock
- Give glucose if the patient is hypoglycaemic
- Hydrocortisone 100mg iv should be administered if the diagnosis is suspected and continued (100mg iv tds, see P586)
- Start tri-iodothyronine (10Âµg bd) after hydrocortisone is started
- Investigate and treat any precipitating intercurrent infection

- If the patient fails to improve, consider other causes for coma (see P406)
- Long term, the patients will require replacement with hydrocortisone or prednisolone, thyroxine, testosterone, oestrogen/progesterone Â± GH.

Causes of panhypopituitarism

Pituitary

- Mass lesions (adenomata, cysts)
- Pituitary surgery or irradiation
- Infiltrative (haemochromatosis)
- Infarction (Sheehan's)
- Apoplexy (haemorrhage)
- Empty sella syndrome

Hypothalamic

- Mass lesions (metastases, e.g. breast, lung; craniopharyngiomas)
- Radiotherapy

- Infiltration (sarcoid, histiocytosis)
- Trauma, e.g. fractured skull base
- Infections (TB)

Editors: Ramrakha, Punit S.; Moore, Kevin P.
Title: *Oxford Handbook of Acute Medicine, 2nd Edition*

Phaeochromocytomas: assessment

- Phaeochromocytomas are catecholamine-producing tumours usually involving one or more adrenal glands. ~0% are bilateral, ~10% are extra-adrenal [usually around the sympathetic chain (paragangliomas)] and ~10% are malignant. They usually secrete AD or NA. A small proportion secrete DA, when hypotension may occur.
- Most are diagnosed during routine screening of hypertensive patients (they are found in only 0.1% of hypertensives). Pure AD-producing tumours may mimic septic shock due to AD-induced peripheral vasodilatation ($Î²_2$-receptors).

Presentation

- Classically a triad of episodic headaches, sweating, and tachycardia
- Hypertension (mild to severe sustained Â± uncontrolled paroxysmal, hypertensive episodes) and orthostatic hypotension (low plasma volume). 50% have sustained â†‘BP and 50% have paroxysmal â†‘BP
- Anxiety attacks, tremor, palpitations, cold extremities, and pallor

- Cardiac dysrhythmias (incl. AF and VF) and dilated cardiomyopathy
- Hypertensive crises may be precipitated by Î²-blockers, tricyclic anti-depressants, metoclopramide, and naloxone
- Unexplained lactic acidosis
- Triggers for hypertensive crises include surgery, opiates and contrast media.

Investigations

There are no tests which will diagnose a phaeochromocytoma acutely. Investigations are listed in the table opposite.

- Hypertensive patients with â†‘glc and â†“K^+ may have a phaeochromocytoma, but these are both non-specific features.
- *Urinary VMA* level (a catecholamine metabolite) is useful if markedly elevated (5â€“10Ã— upper limit of normal). Mild elevations are frequent (15%) in patients with essential hypertension, as VMA can be derived from dietary sources, including vanilla essence giving a false +ve test result. *Urinary catecholamines* (AD, NA, and DA) or metanephrines are more specific. Urine collections must be completed before pentolinium or clonidine tests as withdrawal of these compounds can give a false +ve result.
- *Plasma catecholamines* should be collected from an in-dwelling cannula placed over 30 minutes previously in a supine patient. Samples need to be taken directly to the lab (on ice) for centrifugation.
- *Pentolinium suppression test*. Take two baseline samples as above, then give 2.5mg pentolinium iv, and take blood again at 10 and 30 minutes. Plasma catecholamines decrease in normal subjects following ganglion blockade with pentolinium. If the response is borderline and no

hypotension occurs, then repeat with 5mg pentolinium.

- *Clonidine suppression test*. An alternative to the pentolinium suppression test employs clonidine. Following two baseline samples, give 0.3mg clonidine orally, and take blood hourly for 3 hours. Again if raised catecholamines are due to anxiety, they will suppress into the normal range with clonidine. Raised catecholamines from phaeochromocytoma will not be affected by clonidine.

- *MRI or CT* of the abdomen are useful to localize the tumour. Radiocontrast can lead to catecholamine release.
- *MIBG scan*. MIBG (^{131}I-metaiodobenzylguanidine) is taken up selectively by adrenal tissue. Useful to localize tumour or secondaries.
- *Selective venous sampling*: to localize extra-adrenal tumours.

Investigations for suspected phaeochromocytoma

- U&Es (â†“K^+, â†‘urea)
- Glucose (â†‘)
- Urinary VMA
- Urinary catecholamines (AD, NA, and DA), metanephrines
- Plasma catecholamines (AD, NA, and DA)
- Pentolinium suppression test
- Clonidine suppression test
- MRI or CT scan of adrenals
- MIBG scan for localization

Other causes of sympathetic overactivity

- Abrupt withdrawal of clonidine or Î²-blockers
- Autonomic dysfunction e.g. Guillainâ€“BarrÃ© syndrome or post spinal cord injury
- Stress response to surgery, pain, or panic
- Sympathomimetic drugs
    - Phenylpropanolamine (decongestant)
    - Cocaine
    - MAOI plus tyramine-containing foods (cheese, beer, wine, avocado, bananas, smoked or aged fish/meat)

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Title: *Oxford Handbook of Acute Medicine, 2nd Edition*

Phaeochromocytomas: management

Patients are usually volume depleted at presentation, and should be rehydrated prior to initiation of Î±-blockade, otherwise severe hypotension may occur. Î²-blockade alone may precipitate a hypertensive crisis, and must never be given prior to adequate Î±-blockade. Labetalol is predominantly a Î²-blocker and should not be used alone. Long acting Î±-blockers prevent escape episodes.

- Adequate fluid replacement with CVP monitoring.
- Acute hypertensive crises should be controlled with *phentolamine* (2â€“5mg iv bolus, repeated as necessary every 15â€“30 minutes). Alternatively start an infusion of nitroprusside (0.5â€“1.5Âµg/kg/min, typical dose 100Âµg/min, see P164).
- Preparation for surgery
    - Initiate oral Î±-blockade: *phenoxybenzamine* 10mg daily increasing gradually to 40mg tds. Monitor BP closely. Tumour Î²-stimulation may produce excessive vasodilatation and hypotension requiring inotropic support. Recent studies have shown that prazosin or doxazosin are equally effective and are being used increasingly

    - When the blood pressure is controlled with phenoxybenzamine, add propranolol 10â€“20mg tds
    - Invasive monitoring [pulmonary artery (Swanâ€“Ganz) catheter and arterial line] is mandatory.
- Hypotension commonly occurs intra-operatively when the tumour is removed, and this should be managed with blood, plasma expanders, and inotropes as required. Inotropes should only be used when the patient is appropriately fluid replete. Expansion of intravascular volume 12 hours before surgery significantly reduces the frequency and severity of post-operative hypotension. Angiotensin II should be available as an alternative inotrope for cases of resistant hypotension.

Autosomal dominant conditions with a high risk of developing phaeochromocytoma include

- *Von-Recklinghausen disease* [neurofibromata, cafÃ© au lait spots, Lisch nodules (iris hamartomas), and axillary freckling].
- *Von-Hippel Lindau disease* (cerebellar haemangioblastomas, retinal haemangiomas, and other neoplasms including hypernephroma).
- *Multiple endocrine neoplasia types 2a* (hyperparathyroidism and medullary thyroid carcinoma) *and 2b* (medullary thyroid carcinoma, bowel ganglioneuromatosis, and hypertrophied corneal nerves).

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Polyuria

Definition: >3 litres urine per day.

Presentation

- Confusion (hyponatraemia or dehydration)
- Coma
- Proteinuria on screening
- Depression or other psychiatric manifestations
- Renal stones.

Causes

- Excessive fluid intake
- Endocrine dysfunction (DM, diabetes insipidus, hypercalcaemia)
- Hypokalaemia
- Intrinsic renal disease (polycystic kidneys, analgesic nephropathy, medullary cystic disease, amyloidosis) or renal recovery from ATN. Post obstructive, e.g. after catheterization of patient in chronic retention. Post renal artery angioplasty

- Drugs (frusemide, alcohol, lithium, amphotericin B, vinblastine, demeclocycline, cisplatinum).

History

- Duration and severity (nocturia, frequency, water consumption at night)
- FH of diabetes mellitus, polycystic kidneys, renal calculi
- Drug history (diuretics, analgesics, lithium, etc., see above)
- Renal calculi (hypercalcaemia)
- Weakness (low potassium), depression (hypercalcaemia)
- Psychiatric history
- Endocrine history (menses, sexual function, lactation, pubic hair)
- Other significant pathology (e.g. causes of amyloid).

Investigations

- U&Es (renal disease, hypokalaemia)
- Glucose
- Calcium, phosphate, and alkaline phosphatase
- Plasma and urine osmolality [a U:P osmolality of <1.0 indicates diabetes insipidus, intrinsic renal disease (incl. â†“K^+), or hysterical drinking]
- AXR (nephrocalcinosis)
- Lithium levels if appropriate
- Dipstick protein and quantitation if indicated.

Management

- Assess fluid status (JVP, BP, postural drop, weight charts, CVP).
- Strict fluid balance and daily weights.
- Insert central line to monitor the CVP.
- Measure urinary sodium and potassium (random samples will give an indication of the loss of sodium or potassium initially, and if losses are great, accurate timed samples of <6 hours are possible).

- Replace fluid losses as appropriate to maintain a normal homeostasis, using combinations of saline and dextrose.
- Monitor potassium, calcium, phosphate, and magnesium daily or twice daily if necessary.
- If lithium toxicity is present, see P820.
- Avoid chasing fluids. At some point a clinical judgement has to be made to stop replacing urinary losses with iv fluids to allow the patient to reach their â€˜normal equilibriumâ€™. Once the patient is optimally hydrated then avoid replacing fluids iv to allow physiological homeostasis to occur.
- If diabetes insipidus suspected, arrange water deprivation test (see below).

Water deprivation test

- Stop all drugs the day before the test; no smoking or caffeine
- Supervise the patient carefully to prevent surreptitious drinking
- Empty the bladder after a light breakfast. No further fluids po

- Weigh the patient at time 0, 4, 5, 6, 7, 8 hours into the test (stop the test if >3% of body weight is lost)
- Measure serum osmolality at 30 minutes, 4 hours, and hourly till end of the test (check that the plasma osmolality rises to >290mosmol/kg to confirm an adequate stimulus for ADH release)
- Collect urine hourly and measure the volume and osmolality (the volume should decrease and the osmolality rise; stop test if urine osmolality >800mosmol/kg as DI is excluded)
- If polyuria continues, give desmopressin 20mcg intranasally at 8 hours
- Allow fluids po (water) after 8 hours. Continue to measure urine osmolality hourly for a further 4 hours

Interpretation

- *Normal response:* urine osmolality rises to >800mosmol/kg with a small rise after desmopressin
- *Cranial DI:* urine osmolality remains low (>400mosmol/kg) andincreases by >50% after desmopressin
- *Nephrogenic DI:* urine osmolality remains low (<400mosmol/kg) andonly rises a little (<45%) with desmopressin
- *Psychogenic polydipsia:* urine osmolality rises (>400mosmol/kg) but istypically less than the normal response

Editors: Ramrakha, Punit S.; Moore, Kevin P.
Title: *Oxford Handbook of Acute Medicine, 2nd Edition*

Malignant hyperthermia

Malignant hyperthermia is a drug- or stress-induced catabolic syndrome characterized by excessive muscular contractions, a sudden rise in body temperature, and cardiovascular collapse. The incidence is ~1:15 000, with a 30% mortality. The cause is unknown, but may involve abnormal calcium homeostasis in skeletal muscle cells. The condition seems to be inherited in an autosomal dominant manner with variable penetrance.

Drugs precipitating malignant hyperthermia

- Halothane
- Succinylcholine
- Methoxyflurane and enflurane
- Ketamine
- Phencyclidine
- Cyclopropane

Halothane and succinylcholine account for 80% of cases

Drugs considered safe in malignant

hyperthermia

- Barbiturates
- Nitrous oxide
- Diazepam
- Tubocurare
- Pancuronium
- Opiates

Diagnosis

- Malignant hyperthermia most commonly presents in the early 20s. The early signs are muscular rigidity, sinus tachcardia and SVTs, increased carbon dioxide production, and hypertension.
- Hyperthermia occurs late, and may be rapidly followed by hypotension, acidosis, and hyperkalaemia, which gives rise to ventricular tachycardia.
- The condition almost always occurs peri-operatively.
- The differential diagnosis includes phaeochromocytoma, thyrotoxic crisis, narcotic-induced hyperthermia in patients taking MAOIs, and drug-induced hyperthermia (caused by cocaine, phencyclidine, amphetamine, LSD, tricyclics, and aspirin), and certain injections such as malaria.
- Plasma CPK is high.

Treatment

The aim of therapy is to decrease thermogenesis, and promote heat loss.

- *Dantrolene:* 1â€“2.5mg/kg intravenously every 5â€“10

minutes to a maximum dose of 10mg/kg. The dantrolene should then be continued at a dose of 1â€“2 mg/kg (iv or orally every 6 hours for 2 days).

- Stop any anaesthetic agent.
- External cooling by submersion is helpful. All adminsitered fluids should be chilled.
- Procainamide should be given to all patients to prevent ventricular dysrhthmias (â†‘ uptake of calcium and may reduce hyperthermia).
- Hypotension should be treated with saline/colloids Â± isoprotenerol. Dopaminergic and Î±-adrenergic agonists reduce heat dissipation and should be avoided.
- Some authorities advocate prophyalctic anti-convulsants as seizures are common.

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Title: *Oxford Handbook of Acute Medicine, 2nd Edition*

Neurolepetic malignant syndrome

The neurolpetic malignant syndrome results from an imbalance of dopaminergic neurotransmitters following neuroleptic drug use. The incidence is ~0.5% in patients taking neuroleptic drugs. This syndrome is clinically distinct from malignant hyperthermia (P604); it is not an allergic reaction. The mean age of onset is 40 years. The mortality is ~10%.

Drugs associated with the neuroleptic malignant syndrome

- Haloperidol
- Phenothiazines
- Loxapine
- Thioxanthenes
- Dopamine-depleting drugs
    - metoclopramide
    - tetrabenazine
    - withdrawal of levadopa or amantadine

Clinical features

- Muscular rigidity incl. dysphagia, dysarthria early (96%)
- Extra-pyramidal signs (pseudo-parkinsonism), tremor (90%)
- Catatonia: muteness (95%)
- Altered consciousness Â± coma
- Increased serum CPK/AST (97%)
- Pyrexia (rarely >40Â°C) follows onset of rigidity.

The syndrome can occur within hours of initiating drug therapy, but typically takes ~1 week. It can also occur following a dosage increase of a well-established drug.

Complications

- Rhabdomyolysis (P392)
- Renal (15%) and hepatic failure
- Fitting is rare
- Cardiovascular collapse
- DIC
- Respiratory failure.

Differential diagnosis

- Malignant hyperthermia (P604)
- Heat stroke (P842)
- Other causes of catatonia
- Thyrotoxic crisis (P590)
- Phaeochromocytoma (P598)

- Drug-induced hyperthermia (caused by cocaine, LSD, phencyclidine, amphetamine, tricyclics, and aspirin).

Management

- Withdrawal of causative agent
- Dantrolene (1â€“2mg/kg every 6 hours up to a maximum 300mg/day)
- Paralysis and ventilation (curare, pancuronium)
- Bromocriptine, amantadine, levodopa (increase dopaminergic tone and reduce rigidity, thermogenesis, and extra-pyramidal symptoms).

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Title: *Oxford Handbook of Acute Medicine, 2nd Edition*

Acute upper gastrointestinal bleeding 1

Presentation

- Haematemesis (bright red, dark clots, coffee grounds)
- Melaena (black, sticky, smelly). This may arise from anywhere proximal to and including the caecum. Blood is cathartic and takes 4â€“6 hours to be passed. With massive bleeding (e.g. variceal) there may be dark clots in the stool. Other causes of dark stool include iron therapy, bismuth (present in De-NolÂ®), liquorice, or drinks such as red wine or Guinness
- Weakness/sweating and palpitations
- Postural dizziness and fainting
- Collapse or shock.

â€¢ Peptic ulcer
35â€“50%
â€¢ Gastroduodenal erosions
8â€“15%
â€¢ Oesophagitis
5â€“15%
â€¢ Varices
5â€“10%

â€¢ Mallory–Weiss tear
15%
â€¢ Upper GI malignancy
1%
â€¢ Vascular malformations
5%
â€¢ Rare miscellaneous
5% (e.g. Meckel's, Crohn's disease)

Causes Approx %

Assessment of severity

It is essential to categorize patients at the time of admission into high or low risk of death [see Rockall's Score (table)–*BSG Guidelines*]. Most deaths occur in the elderly with co-morbid disease.

In general high risk factors include the following

- Age >60 years (30% risk of death if >90years)
- Shock (BP <100mmHg systolic in patients <60 years or <120mmHg in patients >60 years. Measure postural change in BP in patients who are not shocked, and change in HR
- Inappropriate bradycardia or HR >120 per minute
- Chronic liver disease
- Other chronic disease (e.g. cardiac, respiratory, renal)
- Bleeding diathesis
- Decreased conscious level.

Management

Liaise with specialists early (on-call endoscopy team and surgeons). An experienced anaesthetist should be informed.

Most patients will have stopped bleeding by the time they are seen: however, all upper GI bleeds should be taken seriously as they may re-bleed in hospital, and the mortality following a re-bleed is high.

Priorities are

- Stabilize the patient: protect the airway, restore the circulating volume
- Identify the source of the bleeding
- Definitive treatment of the cause to stop the bleeding.

Age (years)
<60 years
60â€“79 years
>80 years

Shock
No shock
HR >100
SBP >100
HR >100
SBP <100
Co-morbidity
Nil

Cardiac
Liver
Renal
Malignancy
Diagnosis
Malloryâ€“Weiss
All other
GI tract malignancy

Stigmata of recent bleed
None or dark spot
Blood in upper GI tract
Adherent clot; spurter
Score <3 = excellent prognosis
Score >8 = high risk of death

Clinical variable	Points scored			
	0	1	2	3
Rockall's Score				

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Acute upper gastrointestinal bleeding 2

Initial management

- *Protect the airway:* position the patient on side.
- *iv access:* use 1â€“2 large bore (14Gâ€“16G) cannulae into peripheral vein for initial fluid resuscitation. If peripheral access is difficult, access via jugular, subclavian, or femoral vein may be necessary. CVP monitoring (see P866) allows early identification of bleeding, and is useful to prevent overfilling. It is essential in older patients or in those with massive haemorrhage. A fall of 5cm H_2O over 2 hours is suggestive of re-bleed.
- Take blood for *Hb and PCV* (does not fall until the plasma volume has been restored, but if low at presentation suggests massive blood loss or acute-on-chronic bleeding). *WCC* may be elevated but usually <15 000/mm^3. If WCC is elevated look for sepsis (sepsis predisposes to haemorrhage). *Platelet count*: if low suggests hypersplenism and chronic liver disease. *U&Es*: â†‘urea out of proportion to the creatinine indicates protein absorption by the gut. *Blood glucose*: may be low in patients with chronic liver disease. *PT and LFTs* if liver disease suspected, *Group and X-match* 4â€“8 units. Monitor *ABG* in severely ill patients.

- *Restore the circulating volume*
    - If there are no signs of haemodynamic compromise use a slow infusion of N saline (0.9%) to keep the iv line patent and for maintenance fluids.
    - Tachycardia, hypotension, or a postural fall in BP or a postural increase in HR (by > 30 bp)suggests a low intravascular volume. Give 500 mlâ€“1L colloid over 1 hour (e.g. HaemaccelÂ®) and then crystalloid and continue until blood is available. Stable BP takes precedence over body sodium balance.
    - Use compatible blood when it is ready (give 1unit/h) until volume is restored or CVP 5â€“10cm). If the rate of bleeding is slow, packed cells are preferred. If there is massive haemorrhage, ask for â€˜Oâ€™-negative blood which may be given without cross-matching. Save serum for retrospective cross-match.
- *Monitor urine output* and catheterize the patient if there are signs of haemodynamic compromise. Aim for >30ml/h. Prompt rescuscitation should restore urine output (see oliguria, P378).
- *Watch for the usual signs of overload* (raised JVP or CVP, pulmonary oedema, peripheral oedema). Too rapid transfusion may precipitate pulmonary oedema even before the total lost volume has been replaced.
- *Commence intravenous PPI*. After endoscopic treatment of bleeding ulcers, re-bleeding recurs in ~20% of patients. Intravenous omeprazole (80mg iv, followed by 8mg/h for 72 hours) decreases the risk of rebleeding from >20% to ~7% after endoscopic therapy. Many centres use iv pantoprazole.

- Consider passing an *NG tube*: this may help confirm â€˜coffee-groundsâ€™ or blood in the stomach and is useful in diagnosing re-bleeding. However NG tubes block easily, and are uncomfortable. They may predispose to

further bleeding, gastro-oesophageal reflux, and pulmonary aspiration.

- Keep the patient *nil by mouth* for the endoscopy.

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Acute upper gastrointestinal bleeding 3

Determine the source

- *History:* ask specifically about dyspepsia, alcohol, drug history (e.g. NSAIDs, anti-coagulants), risk factors for liver disease, normal vomit prior to haematemesis (Malloryâ€“Weiss tear, variceal bleed), previous GI bleeds, ulcers, or surgery.
- *Physical examination:* look for stigmata of chronic liver disease (including hepatomegaly and splenomegaly), scars of previous surgery, telangiectasia (Oslerâ€“Weberâ€“Rendu syndrome), abdominal bruit, bruises. Rectal examination may reveal melaena or semi-fresh blood.
- *Upper GI endoscopy* should be done within 12 hours of the bleed. It may be difficult to precisely locate the site of bleeding due to clots in the stomach but it is easy to exclude possible areas of bleeding which may help decide further management. Remember upper GI bleeding in patients with cirrhosis has a non-variceal origin in ~30% of cases.
- *Selective arteriography* of the coeliac axis, superior mesenteric or inferior mesenteric artery is of value when the bleeding site cannot be identified, usually after 2 or more negative endoscopies and bleeding is brisk

(0.5â€“1ml/min).

- *Barium studies* may be used to diagnose small bowel causes of melaena (e.g. Crohn's or tumour). *Labelled RBC scans* may also be useful. *Meckel's scan* may be useful in younger patients.
- *Capsule endoscopy* is being increasingly used in some centres.

General measures to stop the bleeding

- *Correct any coagulopathy*
  - Platelet count below 50 000/mm^3 should be treated with platelet support (6â€“12 units of platelets).
  - If the patient is on anti-coagulants, assess the need for anti-coagulation before reversal. If the patient may require re-anti-coagulation (e.g. prosthetic mitral valve) correct with fresh frozen plasma and/or a very low dose of vitamin K (0.5â€“1mg, iv). Otherwise give fresh frozen plasma (2â€“4 units) and iv vitamin K (5â€“10mg).
  - Cryoprecipitate may be required if the fibrinogen levels are low.
- *Serum calcium* may fall after several units of citrate-containing blood transfusion. Give 10 ml (4.5mEq) of calcium gluconate for every 3â€“4 units transfused. Supplement *magnesium* and *phosphate* as necessary (low in alcoholics).
- *Ulcer healing agents:* give an iv PPI such as pantoprazole (40mg iv daily) or omeprazole (80mg iv, followed by 8mg/h for 72 hours).
- *Tranexamic acid* (0.5â€“1.5g iv tds, or 1â€“1.5g tds po)

increases the levels of fibrinogen and may be helpful. Likewise *DDAVP* may be useful in patients with renal failure.

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Title: *Oxford Handbook of Acute Medicine, 2nd Edition*

Peptic ulcer disease

Bleeding peptic ulcers form the mainstay of upper GI bleeding, accounting for 60% of all cases, and one-third of these have been taking a NSAID. Patients may give a history of epigastric distress relieved by food but often there is no prior history.

- *Endoscopy* allows the bleeding site to be visualized. Identification of the bleeding vessel or adherent clot has prognostic significance: >80% of these patients will re-bleed, cf. <5% without these stigmata.
    - The bleeding point may be treated endoscopically by electro-coagulation, injection of adrenaline, alcohol or endoclips around the bleeding point and into the base, heat probe, or laser photocoagulation, depending on the local facilities
    - Keep the patient NBM for 6â€“8 hours post endoscopy in case a repeat endoscopy or surgery is needed.
- *Indications for surgery:* see table.
- *Medical management*
    - Treat with PPI for 4â€“8 weeks
    - Repeat endoscopy at 6â€–8 weeks to check the lesion has healed

    - A biopsy should be taken at the original endoscopy for the urease test for *Helicobacter pylori*. If positive add an *H. pylori* eradication regimen (see *BNF*).
- *Prognosis:* overall mortality is <10%. Mortality is reduced by early surgery in high-risk patients.

Practice point

- In one major study, intravenous PPI infusion was almost as effective as therapeutic endoscopy in bleeding peptic ulcer disease.

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Erosive gastritis/oesophagitis

These generally present as relatively minor bleeds but may be significant. Represent ~15% of upper GI bleeds, and are associated with prior use of aspirin or other NSAIDs in previously fit patients, or â€˜stressâ€™ in the critically ill patient.

- Management: at endoscopy there is commonly a generalized ooze of blood from the inflamed mucosa. Initial management is as before.
- Give PPI or sucralfate 1â€“2g q6h po or via NG-tube.
- PPIs are better than H_2-antagonists in healing oesophagitis and oesophageal ulcers.
- Correct any clotting disorder.
- If the lesions are too diffuse and the bleeding continues, partial gastric resection may be necessary.
- Prognosis: ~6% of patients with haemorrhagic gastritis require surgery. Overall mortality is <10%.

Relative indications for surgery

- Exanguinating haemorrhage (too fast to replace)
- Profuse bleeding

    - >6 units blood in initial resuscitation
    - continued bleeding at >1 unit per 8 hours
    - persistent hypotension
- Re-bleed in hospital
- Failed endoscopy therapy
- Rebleed after endoscopic therapy in patients >65 years
- Lesions which are at high risk of re-bleeding, e.g. posterior DU with visible vessel or giant gastric ulcer
- Special situations, e.g. patients with a rare blood group or patients refusing blood transfusion should be explored earlier

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Variceal haemorrhage: medical management

Oesophageal and gastric varices develop with portal hypertension of whatever cause. Bleeding from varices is typically vigorous and difficult to control and often occurs in the setting of abnormal clotting, thrombocytopenia, and sepsis.

Diagnosis

History and physical examination may raise the suspicion of a variceal source of bleeding but ~30% of cirrhotics have a non-variceal source of bleeding. The most reliable method is *upper GI endoscopy* which should be performed as soon as is feasible. Bleeding may occur from either gastric or oesophageal varices, or rarely portal hypertensive gastropathy.

Medical management

- Initial resuscitation is as described earlier (P610).
- Transfuse with blood, fresh frozen plasma, and platelets as necessary according to haematological parameters to try to stop the bleeding. Give vitamin K 10mg iv once only to exclude vitamin K deficiency. Avoid over-transfusion (may â†‘portal pressure and â†‘the risk of rebleeding).
- Give a bolus dose of metoclopramide 20mg iv. This

transiently increases the lower oesophageal pressure and decreases azygous blood flow.

- *Antibiotics*: take blood, urine, and ascitic cultures Â± microscopy. Start broad-spectrum antibiotics. Several studies have shown that variceal bleeding is associated with sepsis. Commence a third-generation cephalosporin or ciprofloxacin and amoxycillin. Treat for 5 days.
- *Terlipressin (glypressin)* (2mg initially, and then 1â€“2mg every 4â€“6 hours for up to 72 hours) is effective in controlling variceal bleeding by causing splanchnic vasoconstriction (relative reduction in mortality of ~34%). Serious side-effects occur in 4% and include cardiac ischaemia, peripheral vasoconstriction, which may produce significant hypertension, skin, and splanchnic ischaemia. *Nitrates* have been used to reduce the peripheral effects of vasopressin, but are not generally used with terlipressin. *Octreotide* is a synthetic analogue of somatostatin. It does not have the cardiac side-effects of the other agents and nitrates are not required. A recent Cochrane review found that octreotide had no effect on mortality, and had a minimal effect on transfusion requirements.
- *Endoscopic injection* of sclerosant into the varices or para-variceal can control the bleeding acutely. Side-effects (serious in 7%) include retrosternal pain and fever immediately post injection, mucosal ulceration, late oesophageal strictures. Emergency injection should be followed up by repeat injection sclerotherapy of varices until obliterated. Gastric varices are more difficult to inject, and thrombin should be used.
- *Band-ligation* of the varices is frequently used but is technically more difficult in the setting of acute haemorrhage.

- *Balloon tamponade* A Sengstakenâ€“Blakemore or Linton tube may be inserted (P928). Inflation of the gastric

balloon only usually suffices. This should not be left in place for more than 12 hours as ischaemic ulceration may occur, a risk increased by the co-administration of terlipressin.

- *Liver failure regimen* (P664): give lactulose 10â€“15ml q8h po or per NG tube to prevent encephalopathy and supplement with thiamine and multivitamins as necessary. Use magnesium or phosphate enemas for patients with severe encephalopathy.

Drugs to control variceal haemorrhage

Terlipessin (glypressin)	• Inject 2mg as an iv blous. • Inject 1â€“2mg every 4â€“6 hours • Stop at 72 hours
Vasopressin (used rarely)	• Add 120 units to 250ml 5% dextrose • Infuse 50ml (24 units) over 15 minutes then 50 ml/h (0.4U/min) for 12 hours • An infusion of nitrates or a transdermal GTN patch are sometimes used to minimize the cardiac side-effects of vasopressin
Octreotide	• 100Âµg iv bolus followed by a continuous infusion at 25â€“50Âµg/h (500Âµg in 50ml; 2.5â€“5ml/h). No effect on mortality

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Variceal haemorrhage: further management

Radiological management

TIPS is available in specialized units. Using a jugular or femoral approach, the hepatic veins are cannulated and an expandable stent is placed between the hepatic veins (low pressure) and the portal venous system (high pressure). The portal pressure should be decompressed to below 12mmHg.

Surgical management

This has been largely superseded by TIPS.

- *Emergency porto-caval shunting* is effective in controlling the bleed (>95%) but has a high operative mortality (>50%) and does not influence long-term survival. Few surgeons can do this now
- *Oesophageal transection* is used very rarely in the UK.

Prognosis

- Overall mortality is 30%. This is highest in those with severe liver disease (Child's Grade C, see table opposite).
- Success rates for cessation of acute bleeding varices

â€¢ Injection sclerotherapy or banding	~70â€“85%
â€¢ Balloon tamponade	~80%
â€¢ Terlipressin	~70%
â€¢ Octreotide	~70%
â€¢ Vasopressin + nitrates	~65%

Long-term management

- *Injection sclerotherapy* with 0.5â€“1ml sclerosant paravariceal or 1â€“5ml intravariceal at weekly intervals until the varices are obliterated (1 month); then at 3â€“6 monthly intervals.
- *Banding ligation* involves a similar regimen to injection therapy but achieves variceal obliteration more rapidly (39 days versus 72 days).
- *Propranolol* (80mg tds: aim for a 30â€“40% reduction in resting heart rate, but confirm reduction of portal pressure by measurement of wedged hepatic venous pressure gradient) reduces the rate of re-bleeding from varices and portal hypertensive gastropathy. It has not been shown to decrease mortality.
- *TIPS or shunt procedures* provide a more definite cure and bleeding tends to recur only when the shunt blocks, but there is an increased incidence of chronic hepatic encephalopathy.

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Malloryâ€“Weiss tear

This is a tear in the mucosa at the gastro-oesophageal junction following severe retching and is particularly common following large bouts of alcohol. The vomit is normal initially and becomes bright red.

Management

- Most stop bleeding spontaneously.
- Tamponade with a Sengstakenâ€“Blakemore tube may be used.
- Surgical over-sewing of bleeding point or selective arteriography and embolization of the feeding artery may be necessary.

Clinical or biochemical variable	Points scored		
	1	2	3
Encephalopathy grade	None	1â€“2	3â€“4
Ascites	Absent	Mild	Moderateâ€“severe
Bilirubin (Âµmol/L)	<35	36â€–60	>60
Albumin (g/L)	>35	28â€–35	<28
PT (seconds prolonged)	1â€–4	4â€–6	>6

The Childâ€“Pugh scoring system is a very effective way to get an index of the severity of liver disease in patients with cirrhosis. It is not directly applicable to patients with primary biliary cirrhosis or sclerosing cholangitis.

Childâ€“Pugh A	Score â‰¤ 6
Childâ€“Pugh B	Score 7â€–9
Childâ€“Pugh C	Score â‰¥10

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Acute gastroenteritis: assessment

Food-poisoning is an acute attack of abdominal pain, diarrhoea Â± vomiting 1â€“40 hours after ingesting contaminated foodstuffs and lasting 1â€“7 days. With the exception of an acute attack of inflammatory bowel disease and mesenteric ischaemia (see acute colitis) the majority of acute onset diarrhoea has an infective aetiology.

Differential diagnosis of acute diarrhoea

Common

- Gastro-enteritis (bacterial, viral, protozoal)
- *Clostridium difficile* diarrhoea (pseudomembranous colitis)
- Inflammatory bowel disease
- Food intolerance/allergy (e.g. lactase deficiency)
- Drugs (see table P630)
- Constipation with overflow

Less common

- Coeliac disease
- Tumour (benign or malignant)
- Carcinoid syndrome
- Bacterial overgrowth
- Pancreatic insufficiency
- Bile salt enteropathy
- Hyperthyroidism
- Autonomic neuropathy

Presenting features

Ask specifically about

- Recent eating habits esp. restaurants and food prepared by caterers. Anyone else (family/friends) with similar symptoms?
- Time interval between eating any suspicious substance and onset of symptoms. Early onset of vomiting or diarrhoea (6â€“12 hours) suggests ingestion of preformed toxin (e.g. *Staph*. exotoxin). Enterotoxin-producing organisms may take 1â€“3 days to produce symptoms.
- Recent travel (enterotoxogenic *E. coli*, *Salmonella*, *Giardia*, or amoeba)? Recent medication? Any antibiotics (*Cl. difficile*)?
- PMH, e.g. gastric surgery or immunosuppression (drugs or HIV).
- Anal intercourse increases the risk of amoebiasis, giardiasis, shigellosis, rectal syphilis, rectal gonorrhoea, *Chlamydia trachomatis*, HSV of rectum and perianal area (diarrhoea in HIV-infected patients is discussed on p358).
- The gross appearance of the diarrhoea may help: frankly

bloody stool, *Campylobacter* or *Shigella*; watery, â€˜rice-water stoolâ€™ classically secretory diarrhoea due to cholera, enterotoxogenic *E. coli*, or neuro-endocrine tumours. Typhoid produces greenish â€˜pea-soupâ€™ diarrhoea.

- Abdominal pain may be present usually cramp-like, or tenesmus.
- Fever: common with the severe bacterial diarrhoeas and acute exacerbations of Crohn's or UC.

Investigations

â€¢ FBC	â†‘WBC; â†‘haematocrit (dehydration)
â€¢ U&Es	â†‘Urea (dehydration); â†“K^+
â€¢ Blood cultures	Systemic infection may occur
â€¢ Stool cultures	Fresh samples, mandatory for wet mount microscopy for ova, cysts and parasites, culture, and antibiotic sensitivities. WBC in stool implies intestinal inflammation (mucosal invasion, toxin, inflammatory bowel disease, ischaemic colitis)
â€¢ *Clostridium difficile* toxin	Specifically request this for all patients who have recently taken antibiotics

â€¢ Sigmoidoscopy and rectal biopsy	Useful for persistent bloody diarrhoea (>4â€“5 days) without diagnosis or improvement.

General approach to treat acute diarrhoea

Severity of symptoms	Management
â€¢ Mild (1â€“3 stools/day)	Oral fluids only
â€¢ Moderate (3â€“5 stools/day)	Oral fluids, loperamide (ImodiumÂ®)
â€¢ Severe (>6 stools/day, fever)	Fluids (Â± ivi), anti-microbial agent

When to use antibiotics early

Unless shiga toxin-producing *E. coli* is suspected, it is reasonable to give speculative antibiotic treatment to all patients who have an increased risk of fatal or severe diarrhoea. These include frail elderly patients with achlorhydria (including patients on PPIs such as omeprazole), inflammatory bowel disease, poor haemodynamic reserve, or the immunocompromised.

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Bacterial gastroenteritis

Salmonella sp. may produce acute gastroenteritis (e.g. *S. enteritidis*, ~70â€“80% of cases), enteric fever (*S. typhi* and *S. typhimurium*, see P318), or asymptomatic carriage. Acute gastroenteritis often occurs in epidemics, and is derived from poultry, eggs or egg products, and occasionally pets (terrapins). *Symptoms:* 8â€“48 hours after ingestion with headache, vomiting (worse than either *Shigella* or *Campylobacter*), fever, and diarrhoea lasting 2â€“4 days (rarely bloody with mucus). Reactive arthritis may occur (in HLA-B27 +ve). enteric fever, see P318. *Management:* usually self-limiting after 2â€“5 days, and treatment is supportive for most cases. Some antibiotics can prolong carriage of the illness, and make clinical relapse more likely.

Clostridium perfringens (type A). 15â€“25% of cases of bacterial food poisoning. Spores are heat resistant and may germinate during reheating or slow cooking of meats. Enterotoxin is released when sporulation occurs in intestine. Incubation 8â€“22 hours *Symptoms:* diarrhoea, abdominal pain, nausea (rare to get vomiting). No fever. Lasts 12â€“24 hours. *Management:* Supportive.

Campylobacter infections are common (5â€“10% of patients with acute diarrhoea). The incubation period is 3â€“7 days, symptoms last for 1â€“2 weeks. Presentation often follows eating contaminated poultry. *Symptoms:* flu-like illness followed by headache, myalgia, abdominal pain (continuous

then colicky), diarrhoea, rectal bleeding occasionally. Rarely complicated by reactive arthritis (1â€“2%), Guillainâ€“BarrÃ© syndrome, or Reiter's syndrome. *Management:* Usually self-limiting <5 days. Treatment comprises either erythromycin or tetracycline. Anti-diarrhoeals are contraindicated.

Staph. aureus (2â€“5% of cases) can multiply at room temperature in foods rich in carbohydrates and salt (dairy products, cold meats, mayonnaise). A heat-stable exotoxin produces nausea, vomiting, and diarrhoea 1â€“6 hours after ingestion. Fever is uncommon. Treatment is supportive.

Bacillus cereus associated with slow-cooking foods and reheated rice (fastâ€“food takeaways). It produces an emetic toxin that results in vomiting in 1â€“5 hours, and diarrhoea 8â€–16 hours later. Treatment is supportive.

Vibrio parahaemolyticus produces epigastric pain (cf. those above), diarrhoea, vomiting, and fever 12â€–18 hours after ingestion of raw seafood (shellfish). May last up to 5 days. *Vibrio cholerae* is uncommon in the Western nations. It produces profuse secretory diarrhoea. The disease is usually self-limiting (5â€“7 days) but tetracyclines may be used.

Yersinia enterocolitica: incubation period 4â€–10 days after contact with infected animals, water, or ice cream. *Symptoms:* diarrhoea (80%), abdominal pain (80%), fever (40%), bloody stool in 10%, mesenteric adenitis, lymphadenopathy, reactive arthritis. Diagnosed by serology rather than culture. *Management:* Supportive.

Shiga toxin-producing *E. coli* (e.g. O157:H7). Infection is usually from contaminated meat/burgers. The incubation period is ~5 days. Stools rapidly become bloody over 24â€–48 hours, secondary to a diffuse colitis. Most patients resolve over 5â€–7 days without treatment. However, some, esp. children, may go to develop HUS with tiredness, microangiopathic anaemia, thrombocytopenia, renal failure Â± encephalopathy. Most recover with supportive care. Antibiotics are contraindicated, as certain antibiotics cause shiga toxin production and may

exacerbate or cause the development of HUS.

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Viral gastroenteritis

In addition to diarrhoea, URTI-like symptoms, abdominal cramps, headache, and fever may occur. The causative agent is usually not found but many viruses implicated (e.g. echovirus, Norwalk virus, and adenoviruses). Self-limiting illness (3â€“5 days). *Management:* oral fluids and restricting solid foods and dairy product intake usually suffice.

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Pseudomembranous colitis

This is produced by a necrolytic toxin produced by *Clostridium difficile*. Infection typically follows antibiotic therapy. Diarrhoea may occur during or up to 4 weeks following cessation of treatment.

Symptoms: diarrhoea is usually profuse, watery, and without blood (may be bloody in ~5%). It is commonly associated with abdominal cramps and tenderness, fever, and an elevated white cell count.

Diagnosis is based on detection of *Clostridium difficile* toxin in stool. Culture of the organism itself is unhelpful; ~5% of healthy adults carry the organism. Sigmoidoscopy is not diagnostic, but may show mucosal inflammation together with multiple yellow plaques.

Management: patients should be isolated and barrier nursed. Rehydrate and correct electrolyte abnormalities. Mild disease responds to oral metronidazole (500mg tds). Oral vancomycin 250mg qds for 7â€“14 days is an alternative. Severe disease requires iv therapy. Complications include toxic megacolon and colonic perforation.

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Giardiasis

Giardia lamblia is transmitted by the faeco-oral route. Risk factors include recent travel, immunosuppression, homosexuality, and achlorhydria. *Symptoms:* more chronic diarrhoeal illness with epigastric discomfort due to duodenal infestation. Malaise, bloating, flatulance, and occasionally malabsorption occur. Diagnosis is by stool microscopy for cysts or trophozoites or duodenal aspiration. If negative, consider blind therapeutic trial. *Management*: metronidazole is the treatment of choice, 2g daily for 3 days or 400mg tds for 5 days orally. Alternatives include tinidazole (2g single dose) or mepacrine hydrochloride 100mg tds for 5â€“7 days. Lactose intolerance post infection may persist for up to 6 weeks.

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Travellers' diarrhoea

Travel through developing countries is commonly associated with self-limiting acute diarrhoeal illness transmitted through food and water. The most frequent pathogen is enterotoxigenic *E. coli* (40% of cases). The illness lasts 3â€“5 days with nausea, watery diarrhoea, and abdominal cramps. Oral rehydration is usually sufficient. Antimotility agents (e.g. loperamide) may be used with caution. Antibiotic treatment (ciprofloxacin 500mg bd) may help patients with more protracted illness. Alternatives include doxycycline or co-trimoxazole. Diarrhoea that persists for more than 7 days requires further investigation including stool microscopy and culture, serology Â± sigmoidoscopy, and biopsy (see table). A 3â€“5-day course of a broad-spectrum antibiotic such as ciprofloxacin may terminate the illness.

Causes of travellers' diarrhoea

Bacterial

- Enterotoxigenic *E. coli* (40%)
- Shigellas and enteroinvasive
- *E. coli* (10%)
- *Salmonella* (5%)
- *Campylobacter* (3%)

- Aeromas/plesiomonas (5%)
- Vibrioparahaemolyticus (1%)

Not-identified (22%)

Viruses (10%)

- Norwalk
- Rotavirus

Protozoa (4%)

- *Giardia*
- *Entamoeba*
- *Cryptosporidium*
- *Microsporidium*

Causes of persistent diarrhoea in travellers

Protozoa

- *Giardia*
- *Lamblia*
- *Entamoeba histolytica*
- *Cyclospora cayetanensis*

Bacteria

- *Salmonella*
- *Campylobater*

Helminths

- Strongyloides

- Colonic schistosomiasis (rare)

Common drugs that may cause acute diarrhoea

Laxatives	Colchicine	Propranolol
Antacid (Mg^{2+}, Ca^{2+})	Quinidine	Aspirin
Lactulose	Digitalis	NSAIDs
Diuretics therapy	Theophyllines	Cytotoxic
Antibiotics	Cholinergic agents	Captopril

There are many drugs other than those listed above that can cause diarrhoea

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Bloody diarrhoea

Causes

- Acute infectious colitis
    - Bacillary dysentery (*Shigella* spp.)
    - Salmonellosis (P318)
    - *Campylobacter* (P626)
    - Haemorrhagic colitis (shiga-like toxin-producing *E. coli*)
    - Pseudomembranous colitis (P628)
- Inflammatory bowel disease (IBD, UC or Crohn's).

Presenting features

- Ask about duration of symptoms and recent eating habits. Others affected? Recent travel (enterotoxogenic *E. coli*, *Salmonella*, *Giardia*, or amoeba)? Recent medication? Any antibiotics (*Cl. difficile*)?
- The gross appearance of the stool may help. Inflammatory bowel disease may result in rectal bleeding (fresh red blood) in patients with disease largely confined to the rectum and sigmoid colon. Diffuse disease tends to be associated with diarrhoea. Infectious colitis results in

frankly bloody stool (*Campylobacter* or *Shigella*).

- Abdominal pain may be present: usually cramp-like, or tenesmus.
- Vomiting is uncommon in acute inflammatory bowel disease.
- Systemic features such as general malaise and lethargy, dehydration electrolyte imbalance, or fever are seen with the severe bacterial diarrhoeas and acute exacerbations of Crohn's or UC. Skin, joints, and eyes may be involved in either IBD or follow acute infection.
- Previous altered bowel habit, weight loss, smoking history, vascular disease (mesenteric infarction), mesenteric angina may be relevant.

Examination

Look for

- Fever, signs of dehydration (tachycardia, postural hypotension), abdominal distension. Abdominal tenderness or rebound over affected colon (IBD) may indicate colonic dilatation or perforation. An abdominal mass may indicate tumour or inflammatory mass.
- Mouth ulcers and perianal disease are common in active IBD.
- Erythema nodosum and pyoderma gangrenosum occur in inflammatory bowel disease; *Yersinia* may produce erythema nodosum. Rose spots indicate typhoid fever.
- Joint involvement (often an asymmetrical, non-deforming synovitis, involving large joints of the lower limbs) may occur in active IBD, but also in infectious colitis (e.g. *Campylobacter, Yersinia*).
- Uveitis is associated with both IBD and acute infectious

colitis.

Investigations

The priority is to exclude any infectious cause for the bloody diarrhoea and to monitor for complications.

Blood tests	FBC, U&Es, LFTs, CRP, ESR, coagulation studies
Microbiology	Stool MC&S, blood cultures, *Clostridium difficile* toxin
Sigmoidoscopy Â± biopsy	May help to distinguish between acute infectious colitis and inflammatory bowel disease (increased risk of perforation during colonoscopy)
Imaging	Plain AXR may help monitor colonic dilatation. Contrast studies are contraindicated acutely. Nuclear imaging studies (e.g. WBC scans) are used in IBD to demarcate extent of disease.

Practice point

- Always test for *C. difficile* in patients with new onset bloody diarrhoea.

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Bacterial dysentery

This is due to infection with *Shigella (S. dysenteriae, S. flexneri, S. boydii, S. sonnei)* or some shigella-like *E. coli* (0157:H7). Transmitted by the faeco-oral route, and clusters of cases are often found.

Symptoms

- It causes mild diarrhoea to a severe systemic illness between 1 and 7 days following exposure.
- Fever (usually resolves in 3â€“4 days).
- Abdominal cramps with tenesmus.
- Watery diarrhoea Â± nausea and vomiting (resolves by day 7). Bloody diarrhoea occurs later (after 24â€“72 hours) due to invasion of the mucosa.
- Diagnosed by stool culture. *E. coli* infections may be complicated by haemolytic uraemic syndrome.

Management

- Patients may require iv fluid replacement
- Antibiotics should be reserved for the most severe cases. Ampicillin (250mg po qds Ã— 5â€“10 days) is usually

effective, but in resistant cases co-trimoxazole or ciprofloxacin may be used.

- Anti-motility agents such as loperamide and codeine are contraindicated as they prolong carriage and worsen symptoms.

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Amoebic dysentery

Entamoeba histolytica can produce intermittent diarrhoea or a more severe illness that resembles inflammatory bowel disease. There is an increased risk in homosexuals, and in those with recent travel to third world countries. It is transmitted by the faeco-oral route.

Symptoms

- Diarrhoea or loose stool (Â± blood), abdominal discomfort, mild fever. In severe cases, liver abscess.
- Fulminant attacks present abruptly with high fever, cramping abdominal pain, and profuse bloody diarrhoea.
- Marked abdominal tenderness is present.
- Diagnosis is made by identifying amoebic cysts on stool microscopy.
- May be complicated by late development of amoebic liver abscess.

Treatment

- Aimed at replacement of fluid, electrolyte, and blood loss, and eradication of the organism.

- In acute-invasive intestinal amoebiasis oral metronidazole 800mg tds, for 5â€“10 days is the treatment of choice. Tinidazole (2g daily for 2â€“3 days) is also effective. This should be followed with oral diloxanide furoate 500mg tds for 10 days to destroy gut cysts.
- Metronidazole (or tinidazole) and diloxanide furoate are also effective for liver abscesses, and USS-guided aspiration may help improve penetration of the drugs and shorten illness.
- Diloxanide furoate is the treatment of choice for asymptomatic patients with *E. histolytica* cysts in the stool as metronidazole and tinidazole are relatively ineffective.

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Inflammatory bowel disease (IBD) 1

Inflammatory bowel disease includes Crohn's disease and UC. Crohn's disease is a chronic inflammatory disease of any part of the GIT, characterized by granulomatous inflammation. UC is a chronic inflammatory disease of the colon of unknown aetiology. It always affects the rectum, and extends proximally to a variable extent of the colon.

Ulcerative colitis

Presentation

- Gradual onset of symptoms, which are progressively more severe
- Diarrhoea is dependent on disease activity and extent. Nocturnal diarrhoea and urgency are common symptoms of severe UC
- Mucus and frank pus, or blood, is often mixed in with the stool
- Occasionally abdominal pain (not a prominent feature, though lower abdominal cramping pains relieved by defecation is common; severe abdominal pain suggests a severe attack with acute dilatation or perforation, or

ischaemic colitis)

- Urgency and tenesmus
- In severe disease there is severe (>6 motions/day) and nocturnal diarrhoea, anorexia, and weight loss. Blood may be altered in colour
- Aphthous ulcers (also present in Crohn's)
- Ask about recent cessation of smoking (precipitant).

Examination

Look for *fever*, signs of dehydration (tachycardia, postural hypotension), and abdominal distension. *Abdominal tenderness* or rebound over affected colon may indicate colonic dilatation or perforation. This may be masked if the patient is on steroids. An abdominal mass may indicate tumour or inflammatory mass. *Systemic features:* examine for extra-intestinal manifestations.

Crohn's disease

Presentation

- Diarrhoea 80%
- Abdominal pain 50% (colic and vomiting suggest ileal disease)
- Weight loss 70%
- Fever 40%
- Obstructive symptoms (colic, vomiting)
- Rectal bleeding 50% (commoner in colonic disease, but is present in 50% with ileal disease; colonic disease is associated with peri-anal disease in 30%)
- Extra-intestinal manifestations such as erythema nodosum

(5â€“10%), arthropathy (10%), or eye complications (5%) (see table P639)

- Symptoms of anaemia (iron, B12, or folate deficiency) or nutritional deficiencies.

Examination

Examine nutritional status and for evidence of malabsorption. Examine for evidence of intestinal obstruction (strictures). Fistulae may occur between the bowel and other organs (bladder, vagina). Toxic megacolon (>6cm on AXR) occurs but is much rarer than in UC. Bloody diarrhoea is occasionally massive.

Extra-intestinal manifestations of UC

Related to disease activity

- Aphthous ulcers
- Fatty liver
- Erythema nodosum
- Peripheral arthropathy
- Episcleritis
- Â± Pyoderma gangrenosum
- Â± Anterior uveitis

Unrelated to disease activity

- Sacroiliitis
- Ank. spondylitis
- Primary sclerosing cholangitis
- Cholangiocarcinoma (usually with PSC)

Extra-intestinal manifestations of Crohn's disease

Related to disease activity

- Aphthous ulceration (20%)
- Erythema nodosum (5%)
- Pyoderma gangrenosum (0.5%)
- Acute arthropathy (8%)
- Eye complications (5%)
    - Conjunctivitis
    - Episcleritis
    - Uveitis

Unrelated to disease activity

- Sacroiliitis (15%)
- Ank. spondylitis (4%)
- Liver disease (5%)
    - Gall stones common
    - Chronic active hepatitis (2%)
    - Cirrhosis (2%)
    - Fatty change (5%)

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Inflammatory bowel disease 2

Markers of a severe attack of IBD

- >6 bloody stools/day
- Systemically unwell: pyrexia and tachycardia
- Hb <10g/dl
- Albumin <30g/L
- Toxic dilatation (colon >6cm)

Although the presence of the above symptoms, signs, or findings indicate severe inflammatory bowel disease (UC or Crohn's), it should be noted that severe Crohn's disease may be present in the absence of any of the above.

Investigations

- Blood tests. Anaemia may be present if the colitis is acute and florid severe and iron-deficiency picture may be observed. â†‘WCC (neutrophilia) and â†‘platelets. â†“K^+ may follow severe diarrhoea. There may also be an element of pre-renal dehydration. In severe colitis albumin often falls to 20â€“30g/L. ESR and CRP reflect disease activity, though are often not elevated in distal (rectal) disease. They are useful to monitor therapy.

- Stool culture and microscopy
- Supine AXR Â± erect CXR. To look for wall thickening (moderateâ€“severe) and mucosal oedema, with loss of haustration and colonic dilatation (more severe cases). Colonic diameter >6cm indicates toxic dilatation, with risk of perforation. The extent of the disease can be indirectly assessed; distal colitis is often associated with proximal faecal loading. In the acute stages of a severe attack abdominal films should be performed daily, or twice daily if there is borderline toxic dilatation. Free air under the diaphragm on an erect CXR indicates perforation.
- White cell scan. ^{111}Indium-labelled WBC accumulate in areas of active inflammation, and are a useful adjunct to plain AXR to assess the extent of active disease. Crohn's typically shows patchy uptake and involvement of the small bowel while UC is commonly limited to colon.
- Sigmoidoscopy Â± colonoscopy. Bowel preparation is unnecessary and may cause reddening of the mucosa. Flexible sigmoidoscopy has a lower risk of bacteraemia and is easier than rigid sigmoidoscopy. Non-specific findings such as hyperaemia and contact or spontaneous bleeding are common. Ulceration suggests acute disease; pseudopolyps and atrophy of the bowel mucosa indicate chronic UC. Rectal biopsy from the posterior wall below 10cm should be taken from all patients (less risk of perforation).

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Inflammatory bowel disease 3

Management

- Rehydrate patient with iv fluids and correct any electrolyte imbalance (hypokalemia in particular). Inform and discuss the patient with surgical colleagues, especially if moderateâ€“severe.
- The differential diagnosis is wide (see above). Exclude infectious colitis (normal stool microscopy and culture) and systemic infections as far as possible.
- Avoid anti-motility opiate drugs (such as loperamide and codeine) and anti-spasmodics as they cause proximal constipation and may precipitate paralytic ileus and megacolon.
- Corticosteroids. Acute attacks of UC may respond to rectal steroids (e.g. PredfoamÂ® or PredsolÂ® enema, 20mg 1â€“2 times daily) especially if disease is confined to the rectum. However severe attacks require intravenous steroids (hydrocortisone 100mg qds iv) until remission is achieved. Crohn's disease is only treated if it is causing symptoms. Severe Crohn's disease should be treated with intravenous steroids (hydrocortisone 100mg qds iv or prednisolone 60â€“80mg iv daily.
- Aminosalicylates. In patients with UC, mesalazine should be started (800mg bd or tds orally) Â± mesalazine foam

enema (1g od pr) in addition to steroids: they help induce, and maintain, remission after steroids are tailed off. Use Pentasa for small bowel Crohn's.

- Elemental diets. Elemental diets are as effective as steroids for the treatment of Crohn's disease. However, it is difficult to get patients to comply.
- Other agents. *UC:* there are few data to support the use of azathioprine, cyclosporin, or methotrexate in acute attacks. Two trials have reported that nicotine patches significantly improve symptoms and help to induce remission of UC. *Crohn's* disease: each of these agents has been tried with variable success (they take up to 16 weeks to become effective). Azathioprine (2mg/kg daily) may be useful for maintenance of remission.
- Antibiotics. There is no evidence that broad-spectrum antibiotics are useful in UC. Metronidazole is useful in the treatment of perianal Crohn's fistulae. Ciprofloxacin may also be useful in Crohn's disease. Other antibiotics should only be used if specifically indicated and should be considered for patients developing toxic megacolon.
- Infliximab is being increasingly used (with success) for perianal and fistulating Crohn's disease.
- Nutrition. There is no evidence for keeping the patient â€˜nil by mouthâ€™. However a low residue and early institution of TPN may be of benefit, especially if the patient is likely to come to surgery. When the patient is recovering, stool-bulking agents (e.g. methylcellulose) may be used to adjust stool consistency.
- Smoking. Encourage patients who smoke to stop, as this enhances remission rates.

Differential diagnosis of

inflammatory bowel disease

Bacteria

- *Shigella*
- *Salmonella*
- *E. coli*
- *Camplyobacter*
- *Cl. difficile*
- *TB*
- *Gonococcus*
- *Chlamydia*
- *Yersinia*

Parasites

- Amoebiasis
- schistosomiasis

Miscellaneous

- Ischaemic colitis
- Lymphoma
- Trauma
- Radiation colitis

Indications for surgery

- Failure of symptoms to resolve after 5 days is an indication for proctocolectomy (7â€“10 days in some centres).
- Colonic perforation, uncontrollable bleeding, toxic megacolon, andfulminating disease requires *urgent*

proctocolectomy; ~30% of all patients with UC will require a colectomy at some stage.

- Toxic dilatation prior to treatment is not an indication for surgery(failure of the colonic diameter to decrease after 24 hours). Thedevelopment of dilatation *during* treatment is an indication for surgery.
- Surgery in Crohn's disease is not â€˜curativeâ€™ and is only indicated forperforation, obstruction, abscess formation, and fistulae (enterocutaneous or enterovesical). Recurrence rate after surgery is high.

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Jaundice: assessment

Jaundice requires urgent investigation and diagnosis. It may herald the onset of a severe hepatitis and acute liver (Â±renal) failure (see P658). It may indicate an obstructive jaundice which can be complicated by cholangitis and septicaemia (P654).

History

- Non-specific symptoms include anorexia, pruritus, malaise, lethargy, drowsiness, confusion, or coma. Dark urine and pale stools may be features of either obstructive jaundice or hepatitis.
- Colicky RUQ pain, previous biliary colic, or known gallstones suggests biliary colic (see P654). Fever, rigors, abdominal pain, and fluctuating jaundice should raise the suspicion of cholangitis. Painless jaundice and weight loss suggest pancreatic malignancy.
- Take a detailed drug history including homeopathic or proprietary preparations. Ask specifically about use of paracetamol and alcohol.
- Risk factors for infectious hepatitis: blood transfusion, iv drugs, homosexual, travel, ethnic origin, ingestion of shellfish.

Examination

- Note the degree of jaundice and look for stigmata of chronic liver disease (spider naevi or telangiectasia, palmar erythema, Dupuytren's contractures, etc.). Lymphadenopathy may reflect malignancy. Hepatic encephalopathy results in falling conscious level, and liver flap.
- Note the BP and the diastolic carefully: it falls with liver failure. Oliguria or shock may occur with acute liver failure (see P658). Examine for pleural effusions (may occur with ascites).
- Examine the abdomen for ascites, hepatomegaly, splenomegaly (portal hypertension or intravascular haemolysis), or masses.

Urgent investigations for jaundice (on the day of admission)

U&Es, LFTs	Exclude renal failure (hepatorenal syndrome P394)
Glucose	DM is common in haemochromatosis or pancreatic carcinoma; hypoglycaemia in acute liver failure
PT	â†‘in severe liver injury or DIC
FBC	â†“platelets (chronic liver disease with hypersplenism, malaria, or alcoholism, etc.); â†‘WBC (sepsis, alcoholic hepatitis)

Urinalysis and septic screen	Absence of bilirubin in the urine in a jaundiced patient (acholuric) indicates haemolysis or a conjugation defect (Gilbert's). Culture urine, blood, and ascitic fluid
CXR	Tumour or metastases, effusion assoc. with ascites
USS scan Â± CT scan	If patient is unwell or septic, exclude biliary obstruction which may require urgent decompression.
	Note spleen size and any masses in the liver
Paracetamol	If overdose is suspected or possible.

Non-urgent investigations for jaundice

Viral serology	Anti-HAIgM, HBsAg and anti-HBc, anti-HCV, Â±EBV or CMV serology.
Immunology	ANA, anti-SM, AMA and Igs (CAH, PBC)
Ferritin, iron, transferrin	â†‘ferritin is seen in any acute illness, but may indicate haemochromatosis (â†‘ in alcoholic liver hepatitis).

Causes of jaundice

- Viral hepatitis
- Alcoholic hepatitis Â± cirrhosis
- Drug-induced hepatitis (including paracetamol)
- End-stage cirrhosis (alcoholic, chronic viral hepatitis, haemochromatosis, Wilson's, cryptogenic cirrhosis, etc.)
- Haemolytic anaemia
- Gilbert's syndrome
- Biliary obstruction (stones or turnover)
- Intrahepatic cholestasis, post hepatitic (primary biliary cirrhosis, primary sclerosing cholangitis, sepsis, drugs)
- Autoimmune hepatitis
- Ischaemic hepatitis
- Sepsis

Note: EBV and CMV induced hepatitis/jaundice are rare in adults.

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Viral hepatitis

- Characterized by prodromal â€˜flu-likeâ€™ illness and very high transaminase (up to ~4000U/L) with little increase in ALP.
- If there is *no* coagulopathy, encephalopathy, or renal failure, send the patient home, and await virology results. Advise the patient to avoid alcohol. Arrange repeat LFTs and clotting after 2â€“3 days, and *see* the results (but not necessarily the patient). See the patient again within a week. Instruct the patient to return if increasingly unwell, or drowsy.
- For anti-HAV IgM positive patients no specific treatment is required but *all* household and school contacts should be immunized with HAV vaccine. This replaces previous guidelines that state that contacts should receive normal human immunoglobulins.
- For HBsAg positive patients, vaccinate family. Follow up for at least 6 months to ensure virus is cleared (HBsAg -ve, HBeAb +ve). Prophylactic-specific hepatitis B immunoglobulin (â€˜HBIGâ€™ 500 units im) is protective if given within 10 days of exposure to HBV: however only use for persons with clear exposure to HBsAg-contaminated material (needle-stick or sexual contacts who are HbsAb negative).
- For anti-HCV positive patients, try and determine source.

Check LFTs and HCV RNA for continued viral replication; seek specialist advice.

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Alcoholic hepatitis

- Acute hepatitis may be asymptomatic or present with nausea, vomiting, and anorexia, rarely RUQ pain. Fever may reflect severe liver damage but infection needs to be excluded. Most patients who present with alcoholic hepatitis have cirrhosis at presentation.
- The term alcoholic hepatitis is misnomer, as the transaminases rarely exceed 200U/L and are always <400U/L. The AST is always higher than the ALT (this is in contrast to most other liver diseases).
- Investigations: â†‘bilirubin may be up to 800ÂµM; albumin is often reduced; a prolonged PT usually signifies underlying cirrhosis; â†‘WBC with left shift may occur (even without infection), anaemia and thrombocytopenia suggests cirrhosis; renal failure (hepatorenal syndrome) may occur in severe alcoholic hepatitis.
- Screen for bacterial or fungal infections (blood, urine ascitic microscopy, and culture. If clinically suspected start broad-spectrum antibiotics (e.g. ciprofloxacin 750mg bd po and amoxycillin 1tds po Â± fluconazole (50â€“100mg iv daily) as prophylaxis against fungal infections.
- Admit most patients to hospital, unless mild (bilirubin <50ÂµM, normal PT) or patient in abstinent environment. Give thiamine (100â€“200mg/day), folic acid, and multivitamins. Monitor and correct K+, Mg^{2+}, PO_4^{3-} and

glucose. Start a high-calorie, high-protein diet. Low-protein diets are contraindicated.

- Delirium tremens or severe agitation may be managed with diazepam or chlordiazepoxide po (P501). Avoid iv chlormethiazole as this may cause respiratory depression. Treat seizures in the standard way (P472, 500).

- Calculate the discriminant index for alcoholic hepatitis:

$$\frac{\text{Bilirubin}}{17} + (\text{Prolongation of PT} \times 4.6)\ (40\%\ \text{mortality if} > 32)$$

[e.g. bilirubin = 340ÂµM, PT = 17s (control 12s) would score (340 Ã· 17) + (17-12) = 43]

- A value >32 should be treated with prednisolone 40mg/day for 4 weeks. The only practical contraindication is untreated sepsis. If there is doubt, then give broad-spectrum antibiotics for 24â€“48 hours prior to steroids.

Practice points

- The AST level is normally > the ALT and both are usually <200 U/L in alcoholic hepatitis. Never diagnose alcoholic hepatitis if the AST or ALT exceed 400 U/L
- Muscle injury or excessive exercise can increase both AST and ALT
- A very high AST or ALT (i.e >10,000 U/L) should suggest paracetamol (acetaminophen) overdose or ischemia.

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Drug-induced hepatitis

Patients with drug-induced jaundice should be monitored three times per week or admitted for observation, as many are serious and may not resolve. Withdraw suspected drug and observe. Look for rash and eosinophilia and exclude other causes (see table). (For paracetamol overdose, see P658). Drugs causing jaundice are listed in table opposite. Drugs causing a rise in transaminases, but rarely causing jaundice, are not listed. All drug-induced causes of jaundice should be reported to the CSM (yellow pages at the back of the *BNF*).

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Autoimmune hepatitis

This is characterized by elevated transaminases, up to a few thousand, usually <2000U/L, anti-smooth muscle antibody positive, ANA positive, and raised IgG (polyclonal). The total globulins (total protein-albumin) should be <35g/L in normals. Increased globulin (>45g/L) should always raise suspicion of autoimmune hepatitis. Confirm with liver biopsy. Treatment: steroids (prednisolone 30â€“40mg od) Â± azathioprine (1mg/kg) as a steroid-sparing agent once viral hepatitis has been excluded (i.e. HBsAg negative). If there is failure to respond in a young patient (<30 years), consider Wilson's disease.

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Acholuric jaundice

This is characterized by the absence of bilirubin in the urine. This may be caused by haemolytic anaemia (previous history, excess urinary urobilinogen, splenomegaly, reticulocytosis, etc.) or a congenital disorder of conjugation (Gilbert's syndrome, 2% of population). Fasting (<400 calories) for 48â€“72 hours (or iv nicotinic acid 50mg) will increase serum unconjugated bilirubin in patients with Gilbert's (bilirubin rarely >80ÂµM).

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Sepsis

Any severe infections may cause jaundice (incl. pneumonia). Most severe with intra-abdominal sepsis. LFTs may be cholestatic, or characterized by a predominant rise of the bilirubin only. Exclude other causes and treat infection with antibiotics Â± surgical drainage.

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Ischaemic hepatitis

Presentation

Occurs with significant hypotension or hepatic arterial occlusion. Predisposing factors include congestive cardiac failure Â± hypoxia. In its mildest form it manifests as mildly deranged LFTs (hepatitic picture, â†‘PT) in a patient with CCF and in its most severe form may present as acute liver

failure. Look for hypoxia, hypotension (may have normalized by the time of assessment), signs of arteriopathy (abdominal bruits from hepatic arterial occlusion), and signs of right ventricular failure. May cause confusion Â± encephalopathy. Exclude other causes of hepatitis (P644).

Management

Most will respond to correction of the underlying aetiology. Correct hypotension (see P257) and give oxygen to correct hypoxia. If hepatic artery or coeliac axis are occluded prognosis is poor, and depends on the extent of hepatic necrosis. Usually age and extent of disease preclude salvage surgery. Discuss with specialist centre. If signs of severe (acute) liver failure present, see P662 for guidance. Most patients are not fit enough for liver transplantation.

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Obstructive jaundice

See â€˜biliary obstructionâ€™, P654.

Common drugs that cause jaundice

Hepatitic	Cholestatic	Mixed
Paracetamol	Chlorpromazine	Sulphonamides
Rifampicin	Flucloxacillin	Sulphasalazine
Allopurinol	Azathioprine	Carbamazepine
NSAIDs	Captopril	Dapson
Halothane	Co-amoxiclav	Ranitidine
Methyldopa	Penicillamine	Amitriptyline
Hydralazine	Erythromycin	Nitrofurantoin
Isoniazid	Anabolic steroids	Co-amoxiclav

Phenytoin	Oral contraceptive	

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Gallstone disease

Gallstone disease affects 10â€“20% of the population. The stones may be predominantly cholesterol (>80%), pigment stones (<25% cholesterol; multiple, irregular, friable), or mixed (faceted, calcium containing). The majority are asymptomatic and diagnosed incidentally.

Complications of gallstones

- Biliary colic
- Cholecystitis Â± empyema and gangrene of gallbladder
- Acute pancreatitis (P479)
- GB fistula, gallstone ileus
- Obstructive jaundice
- Cholangitis Â± septicaemia or liver abscesses
- Perforation and peritonitis

Biliary colic

Presentation

Abdominal pain (RUQ) radiating to epigastrium, back, or shoulders associated with nausea and vomiting. Attacks

commonly follow a heavy meal and pass spontaneously. Differential diagnosis includes acute MI, leaking aortic aneurysm, peptic ulcer, intestinal obstruction or ischaemia, pancreatitis, renal colic, and pneumonia.

Investigations

USS to detect the stone and gallbladder distention. Urine microscopy, CXR, ECG will help exclude other conditions.

Management

- Pain relief (pethidine 50â€“100mg im q4h + prochlorperazine 12.5mg im q8h); avoid morphine.
- Laparascopic cholecystectomy in the longer term.

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Acute cholecystitis

Presentation

Sudden onset severe RUQ pain and symptoms similar to biliary colic with fever and persisting symptoms. Persistent vomiting suggests a bile duct stone. Physical signs include fever, tachycardia, sweating, RUQ tenderness, and peritonism, especially in inspiration (Murphy's sign) Â± palpable gallbladder. Jaundice (~33%) suggests obstruction of CBD. *Acalculous cholecystitis* is seen in elderly or patients with co-existing disease or trauma, in the ITU, and patients on TPN. Mortality is high (up to 50%) if not diagnosed early.

Investigations

â€¢ Blood tests	â†‘WCC is usual. LFTs show â†‘bilirubin, and cholestatic liver function tests; Â± â†‘amylase
â€¢ USS	Should demonstrate gallstones or biliary sludge Â± thickening of gallbladder wall
â€¢ AXR	Gallstones visble in ~10% of patients. Local peritonitis may produce a â€˜sentinal loopâ€™
â€¢ HIDA Scan	Using ^{99}Tc-label is usually diagnostic.

Management

- NBM and iv fluids; insert an NG-tube if there is severe vomiting.
- Antibiotics should cover enteric organisms and *Enterococcus* (e.g. cefuroxime 750mg iv q8h + metronidazole 500mg iv q8h).
- Early laparoscopic cholecystectomy is the treatment of choice.
- Complications include perforation, gallstone ileus, or fistula.

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Biliary obstruction

Biliary obstruction or apparent biliary obstruction will be associated with either a dilated or non-dilated biliary system and the patient may be either septic or aseptic. Biliary dilatation in patients with mechanical biliary obstruction may not always be apparent on USS.

Presentation

- Jaundice (painful or painless) Â± fluctuation
- RUQ pain Â± tenderness
- Fever (indicates infection or cholecystitis)
- Itching
- Dark urine Â± pale stools (not very useful in practice)
- Septic shock.

Investigations

â€¢ Blood tests	â†‘WCC indicates sepsis. U&Es may indicate renal failure or pre-renal uraemia. LFTs show â†‘bilirubin, â†‘â†‘ALP, and â†‘â†‘Î³-GT; â†‘amylase with concomitant pancreatitis; transient â†‘ALT, AST with passage of a stone and persistent in cholangitis (usually â‰¤400U/L; higher suggests hepatitis). Blood cultures and CRP mandatory.
â€¢ USS	This is mandatory, and should be performed within 12 hours if possible, to demonstrate the presence of dilated ducts Â± gall stones. Post cholecystectomy slight dilatation (~0.8cm) of CBD is normal.
â€¢ AXR	Aerobilia may indicate a gas-forming organism or recent instrumentation. There may be localized ileus.
â€¢ ERCP	Shows stones in CBD and allows examination of GI tract and ampulla to exclude other pathology. Give broad-spectrum antibiotics if intervention is planned.
â€¢ MRCP	Magnetic resonance cholangio panereatography is a very accurate noninvasive investigation.

Poor prognostic features

(depend on the cause)

- Elderly (>65 years)

- Shock
- Renal failure
- Cholangitis with cirrhosis, liver abscess, or high malignant stricture
- Cholangitis following transhepatic percutaneous cholangiography
- Acute pancreatitis.

Management

See algorithm.

- Analgesia (pethidine 50â€“100mg imq4h), NBM, iv fluids.
- Antibiotics (e.g. cefotaxime or ciprofloxacin + amoxycillin) if septic.
- Emergency decompression of the biliary system by
    - ERCP
    - Percutaneous drainage
    - Surgical decompression.
- Follow up with LFTs, CRP, and temperature.

- Repeat ERCP when well to exclude missed stones or further anatomic abnormality.
- Repeat USS or CT liver scan to look for hepatic abscesses.

Causes of biliary obstruction

Mechanical obstruction

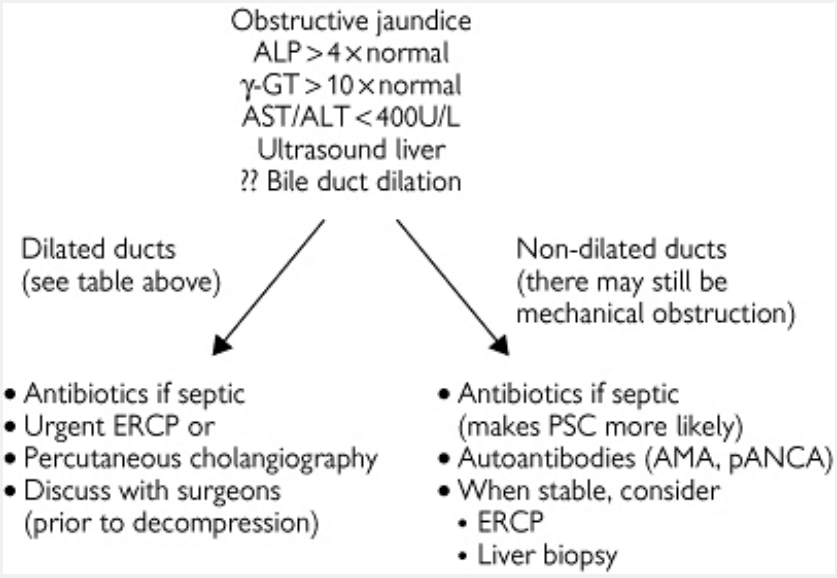
- Gallstones cholangitis
- Malignancy (pancreatic carcinoma, nodes, secondary

deposits, cholangiocarcinoma)

- Post-operative stricture
- Cavernous transformation of portal vein
- Parasitic infection (e.g. onchocerciasis)

Intra-hepatic Cholestasis

- Primary sclerosing
- Primary biliary cirrhosis
- Cholestatic drug reaction



Management algorithm for biliary obstruction NB: In cirrhosis there may be no duct dilatation with biliary obstruction.

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Ascites

Presentation

The patient may present with symptoms due to the fluid (abdominal distension, weight gain, abdominal pain), the underlying cause (jaundice, haematemesis, fever, or night sweats, frothy urine due to proteinuria), or complication of the ascites (dyspnoea, anorexia, reflux oesophagitis, herniae, pleural effusions, scrotal or leg oedema, peritonitis). Ask specifically about alcohol, risk factors for chronic liver disease, GI bleeding (portal hypertension), previous pancreatitis, risk factors for TB, cardiac history, exercise tolerance, and menstrual history (?ovarian malignancy).

Differential diagnosis

- Ovarian cyst
- Pregnancy
- Abdominal mass
- Obesity (simple or metabolic)

Investigations

â€¢ Blood tests	U&Es, glc, FBC, PT, LFTs, blood cultures. Amylase
â€¢ Ascitic tap (see P924)	An ascitic tap should be carried out in *all* patients unless a diagnosis of malignant ascites is certain. Inoculate blood culture bottles and send fluid in sterile pot for microscopy and WBC
â€¢ Imaging	Plain AXR shows a glass ground pattern with loss of psoas shadow. USS can detect as little as 30 ml. Note the size and texture of the liver and spleen, check patency of hepatic veins. CT scan may be required
â€¢ Urine	Urine sodium (cirrhotic ascites), 24 hour protein.

Management

Admit all patients with symptomatic ascites. Treat the underlying cause.

- *Cirrhotic ascites:* do not start diuretics if there is renal impairment. *Salt restrict* to 90mmol/day. *Paracentese* if tense or moderate ascites: drain *all* ascites as quickly as possible (maximum 25L in 5 hours), and then give 6â€“8g albumin per litre of ascites removed as 20% albumin. Start *spironolactone* upto 100mg/day increasing to 400mg/day. Add Frusenide 40mg/day if response is poor. If there is renal impairment (creatinine >140ÂµM) give an extra *colloid and crystalloid volume challenge* (e.g. 500ml gelofusine, over 1 hour followed by 1L N saline over 4

hours). There is no hurry to commence diuretics; start once settled after paracentesis. More harm than good is done by diuresing patients who are hypovolaemic.

- *Malignant ascites:* treatment is palliative, and may include total paracentesis to make the patient more comfortable. Specialist advice should be sought for future management of the malignancy.
- P*ancreatic ascites:* usually associated with a pancreatic pseudocyst and should be managed in consultation with surgical colleagues.

- *Spontaneous bacterial peritonitis* occurs in up to ~15% of patients admitted with cirrhotic ascites, and is frequently asymptomatic. It rarely, if ever, occurs in non-cirrhotic ascites. The risk is increased with low ascitic protein. >90% will yield +ve ascitic cultures if inoculated into blood culture bottles. All ascitic fluid should be inoculated into BC bottles at the bedside. Diagnosis: ascitic WCC >250PMN/mm^3. If culture +ve but acsitic WBC low, repeat tap for microscopy and treat if WBC >250PMN/mm^3. Treat with broad-spectrum antibiotic for enteric organisms and G +ve cocci (e.g. cefotaxime). Suspect TB ascites if there is a predominant lymphocytosis.

Causes of ascites

- Cirrhosis and portal hypertension
- Malignant ascites
- Congestive cardiac failure
- Pancreatic ascites
- Hepatic venous obstruction
- Nephrotic syndrome

- Hypothyroidism
- Infection (e.g. TB)

It does not occur with portal vein thrombosis, congenital hepatic fibrosis, or other causes of non-cirrhotic portal hypertension

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Acute liver failure: assessment

Acute liver failure (fulminant hepatic failure) is defined as a potentially reversible severe liver injury, with an onset of hepatic encephalopathy within 8 weeks of the appearance of the first symptoms and in the absence of pre-existing liver disease. A more recent classification is Hyper-acute liver failure: encephalopathy within 7 days of jaundice Acute liver failure: encephalopathy within 8â€“28 days of jaundice Sub-acute liver failure: encephalopathy within 29â€“84 days of jaundice.

Presentation

- The history may point to a cause (see table P660). Ask specifically about recent viral illnesses, paracetamol, alcohol, and drug history. Signs of chronic liver disease are typically not present (unless â€˜acute-on-chronicâ€™). Splenomegaly does not occur. If present consider an acute presentation of Wilson's disease, autoimmune chronic active hepatitis, or lymphoma. Frequently the presenting feature is a complication of liver failure. Patients with paracetamol overdose may present with severe abdominal pain and retching.
- Encephalopathy. Present in all cases (by definition) and conventionally divided into 4 grades (see table). Cerebral oedema is heralded by spikes of hypertension, dysconjugate

eye-movements, papilloedema is rare. Unless treated this progresses to decerebrate posturing (back, arms and legs rigid, hands in flexion, opisthonus), and brainstem coning.

Grades of hepatic encephalopathy

Grade 1	Drowsy but coherent; mood change
Grade 2	Drowsy, confused at times, inappropriate behavior
Grade 3	Very drowsy and stuparose but rousable; alternatively restless, screaming
Grade 4	Comatose, barely rousable

- Metabolic disturbances. Hypoglycaemia and hyponatraemia are common. Other abnormalities include â†“K^+, respiratory alkalosis, and severe hypophosphataemia. Lactic acidosis carries a poor prognosis.
- Cardiovascular abnormalities. Spikes of systolic hypertension may reflect cerebral oedema. The diastolic BP falls as disease progresses with a vasodilated hyperdynamic circulation (â†“SVR, â†‘cardiac output).
- Respiratory failure. Hypoxia is relatively common and may be worsened by localized infection, aspiration, or atelectasis. Non-cardiogenic pulmonary oedema is seen in ~10%.

- Renal failure. Indicates a worse prognosis with conservative treatment, and may be due to hepatorenal syndrome (see P394) or ATN (paracetamol).
- Bleeding problems. The PT is prolonged and reflects the progression of the disease. Low-grade DIC may occur with bleeding from the GI tract from gastritis or elsewhere. Sub-conjunctival haematoma is common in paracetamol-induced liver failure.
- Infections. Bacterial and fungal infections (septicaemia, pneumonia, peritonitis, UTIs) are more frequent due to impaired neutrophil function.

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Acute liver failure: investigations

Investigations

â€¢ Blood tests (daily)	U&Es, glucose (and 2 hourly BM stix), FBC, PT, LFTs (albumin is usually normal on admission unless â€˜acute-on chronicâ€™), phosphate, arterial blood gases. Blood group and crossmatch on admission.
â€¢ Blood tests (for diagnosis)	Viral serology (A IgM, HBsAg, HBcore Ab IgM, delta in HBsAg +ve, EBV, CMV, HSV), drug screen (esp. paracetamol), plasma caeruloplasmin (if <50 years Â± 24 hour urine copper).
â€¢ Bacteriology	Blood cultures, urine, and sputum MC&S daily (incl. fungal cultures). Throat and vaginal swabs.
â€¢ USS (liver)	To assess hepatic veins, portal vein patency, size (if possible), spleen

	size, nodes (lymphoma).
â€¢ ECG/CXR	Repeat CXR daily (infection/ARDS).
â€¢ EEG	May be helpful in the assessment of hepatic encephalopathy though not widely used.
â€¢ Liver biopsy	Rarely necessary but will exclude underlying malignant infiltration or cirrhosis where the diagnosis is in doubt. The trans-jugular approach is preferred as it carries lower risk of haemorrhage (P930).

Causes of acute liver failure in the UK

Drug-induced hepatitis (58%) (see P649)	Paracetamol OD (P828). Less commonly halothane, isoniazid, sulphonamides, NSAIDs, phenytoin, valproate, penicillins, MAOIs, ecstasy, sulphasalazine, disulphiram, ketoconazole
Viral hepatitis (36%) (see P646)	Hepatitis A, B, delta co-infection in HBsAg +ve carrier, NANB (*not* HCV in UK), E, less commonly CMV, EBV, and HSV
Toxins	*Amanita phalloides* (these mushrooms are available in the

	UK), herbal remedies, CCl_4
Malignancy Vascular	Lymphoma, malignant infiltration Buddâ€“Chiari syndrome, veno-occulive disease, ischaemic injury (shock and hypotension)
Miscellaneous	Wilson's (not strictly acute, as many are cirrhotic, but in all clinical respects similar), autoimmune hepatitis, malignant hyperthermia (incl. ecstasy), fatty liver of pregnancy, PET/HELLP syndrome, Reye's syndrome

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Acute liver failure: management

The mainstay of treatment is support until the acute insult resolves. If a patient fulfils criteria for liver transplantation (see table) on or during their admission they should be referred to a centre where liver transplantation is available (these are listed on P961).

It is vital to discuss all cases of severe liver injury with one of the regional liver transplant centres even though patients may not fulfil the criteria above, as it generally takes up to 48 hours to obtain an emergency graft, and delay in referral can result in failure to procure an adequate graft. All of these centres are also experienced in managing this serious illness. None of the known causes of acute liver failure respond well to medical therapy. Steroids may be of benefit in patients with lymphoma or autoimmune hepatitis, but by the time most patients present it is usually too late. All patients should be admitted to a high dependency or intensive therapy unit.

- Paracetamol overdose. Give N-acetylcysteine (see P828). The benefit of N-acetylcysteine may be evident up to 48 hours and possibly longer.
- General measures. Nurse supine (not 45Â° as often stated). Keep in a peaceful environment. Insert an arterial line and CVP line for monitoring and if possible a pulmonary

artery catheter (Swanâ€“Ganz) to optimize the haemodynamic status.

- Coagulopathy. The PT is the best indicator of liver function. Avoid giving FFP unless there is bleeding or unless undergoing surgical procedures or line insertion. Factor concentrates may precipitate DIC. The PT may rise and fall precipitously and should be measured twice daily if deteriorating. Give vitamin K 10mg once only iv. Give platelet support if thrombocytopenic and bleeding.
- Cerebral oedema. ICP monitoring is used in some centres. If signs of cerebral oedema are present then give mannitol (100ml of 20% mannitol); if in renal failure, watch for fluid overload. Hyperventilation decreases ICP at the expense of cerebral blood flow and should be avoided. Prostacyclin and N-acetylcysteine may decrease ICP. Hypertension is almost always secondary to raised ICP and should be treated with mannitol as above; antihypertensive drugs may precipitate brainstem coning. There is no evidence that giving lactulose or neomycin affects prognosis or prevents grade 3â€“4 encephalopathy. Flumazenil is reported to improve encephalopathy but does affect outcome. Seizures should be treated in the usual way (P472).
- Haemodynamic support. Correct hypovolaemia with colloid or blood but avoid fluid overload. Persistent hypotension may respond to noradrenaline or vasopressin infusion.
- Metabolic changes. Monitor *glucose* (BM stix) 2 hourly, and give 10% or 50% glucose to keep glc >3.5mM. Monitor serum *phosphate* (often very low), replace with iv (9â€“18mmol/24 hours) if less than 0.4mM. *Nutrition*: an ileus is usual present, so most feeding has to be parenteral.
- Renal failure. See P394. Monitor renal function (renal failure occurs in ~70% cases). Treat by haemodiafiltration rather than haemodialysis.

- Respiratory support. Monitor oxygen saturations continuously and give oxygen by mask if SaO_2 < 90%. Ventilate when grade 3 or 4 coma (avoid ET tube ties which compress the IJ veins).
- Infection. Start prophylactic antibiotics and anti-fungals (e.g. cefotaxime and fluconazole).
- Wilson's disease. Consider penicillamine and iv vitamin E.

Indications for liver transplantation

Paracetamol OD with arterial pH <7.3 (admission)

Grade 3 or 4 encephalopathy and PT >100s

or in the absence of above

ALL 3 of the following or

- PT >100s
- Creatinine >300ÂµM
- Grade 3â€“4 encephalopathy

Any 3 of the following

- PT >50s
- Jaundice to encephalopathy >7 days
- Age <10 years or >40 years
- Bilirubin >300ÂµM
- Unfavorable aetiology (i.e. non-paracetamol, not Hep A, not Hep B)

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â€˜Acute-on-chronicâ€™ liver failure

Patients with chronic liver disease from cirrhosis may present with acute decompensation due to a variety of causes (see table).

Clinical features

- Ask specifically for a history of previous hepatitis, jaundice, alcohol intake, previous drug history. Weight loss may point to a malignancy. Pruritis, pigmentation, and xanthelasma in a young woman may be due to primary biliary cirrhosis.
- Examine for evidence of long-standing liver dysfunction: leuconychia, palmar erythema, clubbing, spider naevi, gynaecomastia, and small testes. Splenomegaly and distended abdominal veins signify portal hypertension.
- Examine specifically for features of decompensation: encephalopathy (confusion, â€˜liver flapâ€™), ascites, oedema, jaundice, or fever.

Causes of acute decompensation of chronic liver disease

- Intercurrent infection
    - spontaneous bacterial peritonitis
    - pneumonia
    - skin infections
- Acute GI haemorrhage
- Additional hepatotoxic insult
    - alcoholic binge
    - acute viral hepatitis
    - hepatotoxic drugs
- Drugs
    - sedatives/narcotics
    - diuretics
- Metabolic derrangement
    - hypoglycaemia
    - electrolyte disturbance
- Major surgery
- Constipation
- Progression of disease

Investigations

Unless the cause for the decompensation and the diagnosis for the pre-existing liver disease are known the patient warrants full investigation (see P644).

Management

As for patients with acute liver failure, the mainstay of

treatment is supportive. The decision on how aggressively you manage the patient (i.e. admission to ICU, invasive monitoring, etc.) depends on the previous diagnosis, on a reversible element to the acute insult, and whether the patient is a candidate for liver transplantation. They have less capacity to regenerate their hepatocytes and prognosis of patients requiring mechanical ventilation and haemodynamic support is very poor without a transplant.

Sepsis

Start â€˜blindâ€™ treatment if there is a fever or increased WCC (e.g. cefotaxime) and be guided by culture results (e.g. a third-generation cephalosporin, bacterial peritonitis, see P657). Add iv fluconazole as an anti-fungal agent.

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Hepatic encephalopathy

Hepatic encephalopathy is a neuropsychiatric disturbance of cognitive function in a patient with acute-on-chronic liver disease (P664). It is said that patients with cirrhosis do *not* develop cerebral oedema, although we have seen extensor posturing in alcoholic cirrhotics following variceal haemorrhage.

Clinically there is usually altered conscious level, asterixis (liver flap), abnormal EEG, impaired psychometric tests, and an elevated arterial ammonia concentration. Patients may present with Parkinsonian features. However in patients with chronic liver disease, it may be sub-clinical with subtle changes in awareness or attention span. It is graded as on P658.

Treatment: the aim of treatment is to improve morbidity.

- Exclude other causes of confusion (see P496).
- Dietary restriction is controversial, and may be harmful in malnourished patients. Ensure adequate calorie intake.
- Give lactulose: this semi-synthetic disaccharide is poorly absorbed. It is digested in the large bowel and undergoes fermentation. This alters faecal pH and nitrogen utilization by bowel flora.
- Lactitol has a similar action to lactulose but has fewer side-effects.
- Phosphate enemas help to purge the large bowel. Most

useful in the context of an acute food load (e.g. GI bleeding).

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Liver abscesses

Presentation

- Commonly present with fever and night sweats, weight loss, or right upper quadrant or intercostal pain.
- The underlying cause (e.g. appendicitis) may be silent or barely noticed. Ask about recent abdominal pain, altered bowel habit, diarrhoea, biliary colic, blood PR, or inflammatory bowel disease.
- The travel history, occupation (farming is a risk factor for amoebiasis), or contact with infected persons (TB) may help.
- Examine for jaundice, hepatomegaly, pleural effusions (commonly right-sided), intercostal tenderness (characteristic of amoebic abscesses), abdominal masses (tumour or inflammatory mass), andlymphadenopathy. Perform a rectal examination for pelvic tumour.
- Severe infection may be associated with septic shock (P270).

Causes

- Pyogenic organisms (appendicitis, diverticulitis, carcinoma, biliary)

- Amoebic abscess (*Entamoeba histolytica*)
- Hydatid cyst (*Echinococcus granulosus*)
- TB (very rare)

Investigations

- U&Es (renal impairment with sepsis). LFTs (non-specific, tend to be cholestatic; may be normal with amoebic abscess).
- Prothrombin time may be prolonged with multiple abscesses.
- FBC (leucocytosis, eosinophilia, non-specific anaemia).
- Blood cultures, CRP, ESR.
- Amoebic and hydatid serology.
- Stool may contain amoebic cysts or vegetative forms.
- CXR (looking for effusion, or pulmonary TB).
- USS of liver, biliary tree, and abdomen (iliac fossae in particular) Â± CT scan with contrast, looking for masses. Both pyogenic and amoebic abscesses tend to be thick walled; hydatid cysts are thin walled and there may be daughter cysts. Solid tumours are echodense but may have necrotic hypodense centres.
- Gallium scan (or indium-111 labelled WBC scan) will show up pyogenic foci in the liver and elsewhere (e.g. terminal ileitis); amoebic abscesses do not take up the label.
- Aspirate any large abscesses and send for gram stain, and culture. If there is a suspicion of hydatid disease aspiration is contraindicated.

Management

- Aspirate any large abscesses under USS. It is pointless to try and drain multiple abscesses. If there is a continuing intra-abdominal source it is virtually impossible to eradicate liver abscesses without removing or dealing with that source (e.g. appendix).
- *Pyogenic abscess:* percutaneous aspiration of any large abscesses. Broad-spectrum antibiotics (e.g. cefotaxime and metronidazole).

- *Amoebic abscess:* see P636. Treat with metronidazole (or tinidazole) followed by diloxanide furoate. USS-guided aspiration may help improve penetration of the drugs and shorten illness. Secondary bacterial infection occurs in up to 20%.
- *Hydatid disease:* open surgical drainage is the treatment of choice. Albendazole may help reduce the risk of recurrence post surgery or be used in inoperable cases.
- Anti-tuberculous therapy for tuberculous abscesses.

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Acute pancreatitis: assessment

Acute pancreatitis is occasionally managed by physicians, particularly if it presents in an unusual way (e.g. chest pain).

Presentation

- Abdominal pain: epigastric or generalized, of rapid onset, but may occur anywhere (including chest); dull, constant, and boring. Radiation to the back or between the scapulae, often relieved by leaning forward (differential diagnosis is leaking aortic aneurysm).
- Nausea, vomiting, and dehydration Â± jaundice.
- Peritonitis with epigastric tenderness, localized rebound tenderness, or generalized abdominal rigidity. An abdominal mass may indicate a pancreatic pseudocyst or abscess. Bowel sounds usually absent.
- Tachycardia and hypotension; shock/collapse and respiratory failure in severe cases (especially in the elderly).
- Very rarely signs of bleeding in the pancreatic bed, Greyâ€“Turner's sign (ecchymosis in the flanks) or Cullen's sign (peri-umbilical bruising), tender red skin nodules (due to subcutaneous fat necrosis).
- Hypocalcaemic tetany.

Investigations

â€¢ Amylase	Elevated, but not specific (see table, P671), especially if only up to 4 Ã— upper limit of normal. A persistently raised amylase (several days to weeks) may indicate the development of a pseudocyst
â€¢ FBC	Raised haematocrit and leucocytosis
â€¢ U&E's	Urea may be raised with hypovolaemia
â€¢ Glucose	May be raised
â€¢ LFTs	AST and bilirubin often elevated especially in gallstone pancreatitis. Disproportionately elevated Î³-GT may indicate an alcohol aetiology
â€¢ Calcium	Hypocalcaemia (unless precipitant was â†“Ca^{2+})
â€¢ CRP	Elevated: used to monitor progression of the attack
â€¢ ABGs	Mandatory. Hypoxia Â± metabolic acidosis
â€¢ AXR	Generalized ileus or sentinel loops (dilated gas-filled loops in the region of the pancreas). Look for evidence of pancreatic calcification or biliary stone

â€¢ CXR	May show a pleural effusion, elevated diaphragm, or pulmonary infiltrates.
â€¢ USS	May confirm diagnosis and detect gallstones Â± biliary obstruction, pseudocysts, and abscesses
â€¢ CT abdomen	Dynamic contrast-enhanced is reliable at detection of pancreatic necrosis and grading severity.

Assessment of severity

- The severity of disease has *no* correlation with the elevation of serum amylase. Several prognostic indices have been published, but it takes 48 hours to fully appreciate disease severity. See table.
- The mortality from acute pancreatitis is approximately 10%, and rises to 40% in those developing a pancreatic abscess. The mortality is highest

in those with a first episode of pancreatitis. Around 15% of patients presenting with acute pancreatitis have recurrent disease.

Causes of abdominal pain and elevated serum amylase

- Acute pancreatitis
- Stomach or small bowel perforation
- Perforated peptic ulcer

- Mesenteric infarction
- Acute liver failure
- Acute cholecystitis or cholangitis
- Renal failure (modest elevation)
- Diabetic ketoacidosis

Markers of severity in acute pancreatitis[1]

At presentation

- Age >55 years
- WBC >16 Ã— 10^9/L
- Glucose >10mM (non-diabetic)
- LDH >350IU
- AST >250iu/L

During the first 48 hours

- Haematocrit fall >10%
- Urea rise >10mM
- Serum Ca^{2+} <2.0 mmol/L
- Base excess >4 mmol/L
- P_aO_2 <8 kPa
- Serum albumin <32g/L
- Estimated fluid sequestration >6L

Mortality: 0â€“2 criteria = 2%; 3â€“4 = 15%; 5â€“6 = 40%; >7 = 100%.

Practice point

- Severe acute abdominal pain is nearly always due to a surgical cause.

Footnote

1

Data compiled from Imrie CW *et al.* (1978) *Br. J. Surg.* 65: 37 and Ranson JH *et al.* (1974) *Surg. Gynaecol. Obstet.* 139:69.

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Acute pancreatitis: management

The principles of management are

- Liaise with surgeons
- Supportive measures: the majority will subside in 3â€“10 days
- Careful observation for the development of complications
- Identify the cause (see table P673).

Supportive treatment

- Establish iv access. If there is shock, markers of moderateâ€“severe pancreatitis, elderly patient, hypoxia not readily correcting with O_2 or other co-existent disease, insert a CVP line to help control fluid balance.
- Patients are usually severely volume depleted: give prompt fluid replacement with colloid (e.g. HaemaccelÂ®) or 0.9% saline. Monitor urine output and insert a urinary catheter if required.
- Oxygen should be given if there is hypoxia on air (use continuous pulse oximetry in severe cases and 6 hourly for the first 48 hours for rest, to monitor for respiratory

failure).

- Keep nil by mouth.
- The use of nasogastric suction has never been proven. There is an increasing vogue for the commencement of early enteral nutrition (nasojejunal), which is as effective as TPN in acute pancreatitis.
- Monitor blood glucose regularly and treat with insulin if high.
- Pethidine causes the least spasm of the sphincter of Oddi.
- Antibiotic prophylaxis with cefuroxime decreases secondary infections.
- Octreotide (somatostatin analogue): this suppresses pancreatic enzyme secretion but is of unproven benefit.
- Peritoneal lavage: there is no proven benefit.
- H_2-antagonists have not been shown to affect mortality.

Complications (seen in ~20%)

Local

- Abscess
- Pseudocyst Â± infection
- Biliary obstruction
- Ascites, pleural effusion
- Fistula
- Splenic, portal, or mesenteric vein obstruction

Systemic

- Electrolyte imbalance
- â†“Ca^{2+}, â†“Mg^{2+}

- Acute renal failure
- Shock
- Respiratory failure
- Sepsis

Septic complications

Sepsis is the most common cause of death. This should be suspected when there is a persistent fever, leucocytosis, pain/tenderness, or an overall clinical deterioration. These signs are an indication for multiple blood cultures and an abdominal CT. Pancreatic pseudocysts are more common in alcoholic pancreatitis (15% versus 3% in gallstone AP), but infection is more common in gallstone pancreatitis.

Biliary pancreatitis

Urgent ERCP within 72 hours of presentation reduces complications and mortality in patients with severe gallstone pancreatitis. The benefit has not been demonstrated in mild cases. There is a growing vogue for the use of MRCP (magnetic resonance cholangiopancreatogaphy) to diagnose biliary disease prior to ERCP.

Indications for surgery

Infected pancreatic necrosis or pancreatic abscess.
Radiologically guided percutaneous drainage is now preferred to surgery for pancreatic pseudocysts.

Causes of acute pancreatitis

Common (80%)

- Gallstones (including biliary microlithiasis or sludge) (60%)

- Alcohol (20%)

Rare (10%)

- Iatrogenic (ERCP or any form of abdominal surgery)
- Trauma (even seemingly minimal trauma, as pancreas is in a very vulnerable position, e.g. â€˜seat-belt signâ€™ or bicycle handle-bar injury)
- Infections

  Viral: mumps, rubella, coxsackie B, EBV, CMV, Hep A and B)

  Bacterial: mycoplasma

  Others: ascaris, flukes (*Clonorchis sinensis*)
- Systemic vasculitis (SLE, polyarteritis nodosa, etc.)
- Drugs (e.g. thiazides, frusemide, NSAIDs, sulphonamides, azathioprine, tetracyclines, and valproate; possibly steroids)
- Hypertriglyceridaemia (serum amylase falsely low)
- Hypercalcaemia or iv calcium infusions
- Hypothermia
- Pancreatic carcinoma (3% present with acute pancreatitis)
- Misc.: anatomical abnormalities (pancreas divisum, duodenal orperi-ampullary diverticulae), scorpion bites, cystic fibrosis

Unknown (10%)

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Blood transfusion reactions: assessment

Presentation	Causes	Timing
Shock (major haemolysis)	Red cell antibodies	Immediate (minutes/hours)
Lumbar pain, headache	ABO incompatibility	
Chest pain, SOB	Other antibodies	
Rigors, pyrexia		
Urticaria, flushing		
Hypotension		
Oliguria		
Haemoglobinuria		

Jaundice		
DIC		
Shock (septic)	Bacterial contamination	Immediate (minutes/hours)
Rigors, pyrexia		
Hypotension		
Oliguria		
DIC		
Fever	White cell antibodies	Early (30â€“90 minutes)
Isolated pyrexia	Recipient cytokines	
Rigors		
Allergic reactions	Donor plasma proteins (more common with plasma or platelets)	Early (minutes/hours)
Urticaria		
Pyrexia		
Rigors		
Facial oedema		

Dyspnoea		
Circulatory overload	Rapid transfusion	Early (hours)
Breathlessness		
Cough		
Transfusion-related acute lung injury (TRALI)	Donor white cell antibodies (rare)	Early (minutes/hours)
Non-cardiogenic pulmonary oedema		
Pyrexia		
Cough		
Breathlessness		
CXR changes		
Delayed haemolysis	Minor red cell antibodies	Late (7â€“10 days)
Pyrexia		
Anaemia		

Jaundice		
Delayed thrombocytopenia	Platelet antibody (commonly anti-PI^{A1})	Late (2â€“10 days)
Purpura		
Mucosal bleeding		
Infection	Hep. B, C, nonA/B/C CMV, EBV, HIV	Late (days/months)
	Toxoplasmosis	
	Malaria, syphilis	

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Blood transfusion reactions: management

The main problem encountered in practice is differentiating a (common) rise in temperature during a blood transfusion from (the rare but potentially lethal) major transfusion reactions. The common patterns of reactions are outlined on P676.

Pointers to a severe reaction include

- Symptoms: does the patient *feel* unwell?
- Pattern of temperature: a *rapid* rise in temperature to >38Â°C is common in minor reactions.
- Hypotension or tachycardia.

Management

â€¢ Isolated pyrexia	Slow transfusion
	Give paracetamol
	Finish transfusion if no progression of symptoms.

â€¢ Urticarial reaction	Slow transfusion
	Give chlorpheniramine 10mg iv/po
	Complete transfusion if no progression of symptoms
	Rarely, patients need hydrocortisone 100mg iv.
â€¢ Shock	Stop transfusion and give oxygen
Anaphylaxis	Give adrenaline 0.5â€“1mg sc and consider repeating every 10 minutes until improvement
ABO incompatibility	Contact duty anaesthetist and ITU
Septic shock	Give chlorpheniramine 10mg iv iv colloids (also consider crystalloid, inotropes, P257)
	Monitor fluid balance
	Take blood: FBC, U&Es; full coagulation screen (for DIC); repeat cross-match and Coomb's test; return donor blood

	Urine: bilirubin, free Hb.
â€¢ Circulatory overload (see p108)	Oxygen, frusemide iv (40â€“120mg)
	Nitrate infusion (0â€“10mg/h).
â€¢ TRALI	Life-threatening. Treat as ARDS (P230).
â€¢ Delayed haemolysis	Report to blood bank
	Repeat cross-match and Coomb's test
	Transfuse with freshly cross-matched blood.
â€¢ Thrombocytopenia	Immune mediated: treat with PI^{A1}-negative transfusions, high-dose iv IgG, steroids, and plasmapheresis (dilutional â†“platelets seen if >5 units transfused).

Report any serious or haemolytic reaction to haematologist.

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Sickle cell crisis: presentation

A small percentage of sufferers with sickle cell disease have recurrent crises, and repeated hospital admissions. There is an unwarranted tendency to attribute this to a low pain threshold, or to â€˜dependenceâ€™ on opiates, rather than to severity of disease. Analgesia should never be denied to patients. This group of patients has the *highest* rate of serious complications and mortality as a result of their severe disease.

Painful (vaso-occlusive) crisis

- This is the most common presentation in adults and children.
- Severe/excruciating pain is felt at one or more sites, especially long bones (small bones in children), back, ribs, sternum.
- There may be associated pyrexia (usually <38.5 Â°C), tenderness, local warmth and swelling, or there may be no objective features.
- Haemolysis may be increased (increased bilirubin, fall in Hb), but is not a good correlate.
- *There are no reliable clinical markers for severity of crisis*.

Chest crisis

- The commonest cause of mortality.
- Vaso-occlusion of pulmonary microvasculature results in reduced perfusion and local infarction.
- May be heralded by rib/sternal pain.
- Often precipitated by a chest infection.
- Symptoms (which may be minor initially) include pleuritic chest pain, breathlessness.
- Signs are minimal; usually reduced air entry at lung bases.
- CXR shows uni/bilateral consolidation, usually basal.
- P_aO_2 is often markedly reduced.

Cerebral infarction

- Usually in children <5 years, rare in adults.
- Presents as acute stroke.
- High risk of recurrence.

Splenic/hepatic sequestration

- Usually in children <5 years.
- RBCs trapped in spleen and/or liver, usually causing organomegaly.
- Causes severe anaemia; circulatory collapse.

Aplastic crisis

- Usually in children, young adults.

- Mainly caused by parvovirus infection, exacerbated by folate deficiency.
- Sudden fall in Hb, reduced reticulocyte count.

Haemolytic crisis

- Often accompanies painful crises.
- Fall in Hb; *increased* reticulocyte count.

Cholecystitis/cholangitis/biliary colic

- Pigment stones common due to haemolytic anaemia.
- Can be misinterpreted as vaso-occlusive crisis.

Priapism

- Prolonged, painful erections due to local vaso-occlusion.
- May result in permanent impotence.
- This is a urological emergency. On-call urologists should be informed on the patient's arrival in casualty.

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Sickle cell crisis: management

General measures

Control pain

- Oral analgesia (dihydrocodeine/NSAIDs) may be sufficient for minor crises.
- Usually parenteral opiates are necessary, often in high doses, e.g.
    - morphine 10â€“40mg im every 2 hours
    - diamorphine 10â€“25mg sc every 2 hours.
- Failure to control pain using these regimes usually indicates the need for a continuous opiate infusion, or a PCA pump. Some patients prefer pethidine but there is a risk of seizures as the drug metabolites accumulate.
- Supplementary analgesics, such as diclofenac 50mg tds po, may have a small additional benefit.

Ensure hydration

- iv crystalloids are preferred, but venous access may be a problem.

- Aim for an input of 3â€“4L/day.

Give oxygen

- Not of proven benefit (except in chest crises), but often provides symptomatic relief.
- In a severe chest crisis, CPAP/full ventilation may become necessary. Transfer to ITU early.

Give folic acid

Give 5mg po od (continue long term in all patients).

Give antibiotics

If an infective precipitant, or component, of the crisis is suspected, start â€˜blindâ€™ antibiotics (e.g. cefuroxime 750mg iv tds) after infection screen.

Investigations

â€¢ FBC	Hb (?fall from steady state)
	WCC (neutrophilia common)
â€¢ Reticulocytes	Raised in haemolysis, reduced in aplastic crisis
â€¢ HbS%	Can guide transfusion requirements
â€¢ Blood cultures	If pyrexial

â€¢ Stool cultures	If diarrhoea + bone pain (?salmonella osteomyelitis)
â€¢ CXR	Regardless of symptoms
â€¢ Pulse oximetry	Â± Arterial blood gases if hypoxic
â€¢ Bone X-ray	?osteomyelitis (persisting pain, pyrexia, or bacteraemia). ?avascular necrosis (chronic hip/shoulder pain)
â€¢ Viral serology	If aplastic crisis (?parvovirus)
â€¢ X-match	If transfusion/exchange indicated (see below).

Exchange transfusion

This is performed by venesection of 1â€“2 units, with fluid replacement (N saline, 1 litre over 2â€“4 hours) followed by transfusion of cross-matched blood. If a larger exchange is required, or fluid balance is precarious, the exchange can be performed on a cell separator. Aim for Hb between 7â€“9g/L in either case; *a higher Hb can increase blood viscosity and precipitate further sickling*. In severe crises, red cell exchange should be repeated until the HbS% is <40%.

Indications for urgent exchange transfusion

- Chest crisis
- Cerebral infarction
- Severe, persisting painful crisis
- Priapism

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Bleeding disorders: general approach

Presentation

- Normal haemostasis requires the interaction of platelets, fibrin from the clotting cascade, and the microvasculature. An abnormality of any of these components may present as easy bruising, purpura, or spontaneous or excessive bleeding.
- Muscle haematomas or haemarthroses suggests clotting factor deficiencies (e.g. haemophilia) whereas purpura or bruising suggests abnormalities of platelet function.
- Mucosal haemorrhage (acute GI bleed) may occur without any haemostatic abnormalities, e.g. due to peptic ulcer disease.
- If a coagulation or platelet abnormality is uncovered on â€˜routineâ€™ testing, examine the patient for occult bleeding (e.g. iron-deficient anaemia, fundal haemorrhages).

Causes

These can be divided into

- Coagulation abnormalities
- Platelet abnormalities (too few or dysfunctional)
- Microvascular abnormalities.

Investigations

All patients should have

- Coagulation screen (PT, APTT, TT)
- FBC and film
- U&Es
- LFTs
- X-match

Where appropriate consider

- Bleeding time
- Platelet function tests
- Bone marrow aspirate and trephine
- Autoantibody screen
- Anti-platelet antibodies
- Specific coagulation factor levels
- Acquired factor inhibitors

Management

General measures

- Avoid non-steroidal medications, especially aspirin.
- Never give intramuscular injections.
- Avoid arterial punctures.

- Enlist expert help with invasive procedures. Use internal jugular rather than subclavian route for central line insertion.
- Avoid automated blood pressure measurement devices as they may provoke bleeding into the upper arm.
- Examine skin, oral mucosa, and fundi for evidence of fresh bleeding.
- Restore circulatory volume with iv colloid if there is haemodynamic compromise and consider blood transfusion.

Specific therapy

- Look for any local cause for the bleeding (e.g. oesophageal varicies, vascular damage causing epistaxis, chest infection causing haemoptysis) that may be amenable to treatment.
- Stop any drug that may be exacerbating bleeding (table opposite).
- Correct coagulation abnormalities if appropriate (P688).
- Correct platelet abnormalities if appropriate (P692).

Drugs that may cause bleeding disorders

Coagulation abnormalities

Heparin

Wafarin

Asparaginase (dVitamin K-dependent factors)

Heparin analogues (argatroban, hirudin)

Thrombocytopenia

Immune	*Non-immune*
Heparin	Cytotoxic chemotherapy
Quinine	Chloramphenicol
Penicillin	Primaquine
H_2-receptor antagonists	Alcohol
Thiazide diuretics	

Abnormal platelet function

Aspirin, NSAIDs

Ticlopidine

Antibiotics (e.g. piperacillin, cefotaxime)

Dextran

Alcohol

Abnormal microvasculature

Corticosteroids

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Abnormal coagulation 1

Common causes

- Anti-coagulants
- Liver disease
- Vit. K deficiency
    - obstructive jaundice
    - small bowel disease
- DIC

Rarer causes

- Massive transfusion
- Haemophilia A, B
- von Willebrand's disease
- Acquired factor VIII inhibitors
- Amyloid (acquired Factor X deficiency)
- Î±$_2$-plasmin inhibitor deficiency

Diagnosis

Defect	Interpretation	Consider
â†‘PT	Extrinsic pathway defect	Warfarin, liver disease, vitamin K deficiency
â†‘APTT	Intrinsic pathway defect	Heparin, haemophilia, von Willebrand's disease, lupus anti-coagulant (anti-phospholipid syndrome)
â†‘PT and APTT	Multiple defects (usually acquired)	Liver disease, DIC, warfarin
â†‘TT	Abnormal fibrin production	Heparin effect, fibrinogen defect, excess FDPs (which interfere with reaction)
â†‘PT, APTT, TT	Multiple (acquired) defects	Deficient or abnormal fibrinogen or heparin.
		Reptilase time[1] will be normal if due to

		heparin
â†‘Fibrinogen	Excess consumption of clotting factors and fibrinogen	Consumptive coagulopathy (but not necessarily full DIC), severe liver disease
â†‘FDPs	â†‘Fibrin(ogen) degradation	The exact interpretation depends on the lab test used. Some do not distinguish between fibrin and FDPs. Some are more specific to fibrin degradation (e.g. D-Dimers) and are therefore suggestive of widespread clot formation and breakdown (i.e. DIC)
â†‘Bleeding time	Abnormal platelet function	von Willebrand's disease (â†‘APTT), congenital or acquired platelet dysfunction (see table P685). Consider platelet function studies

The lupus anticoagulant usually confers a pro-thrombotic rather

than a bleeding tendency.

Footnote

[1]Reptilase is a snake venom not inhibited by heparin. It converts fibrinogen to fibrin.

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Abnormal coagulation 2

Management

Options are

- *Fresh frozen plasma:* indicated for rapid warfarin reversal or treatment of acute DIC. Give approx. 15ml/kg i.e. 4â€“5 units (approx. 200 ml/unit). Watch for signs of fluid overload and give iv frusemide if necessary.
- *Vitamin K:* Phytomenadione 5â€“10mg iv slowly (daily for 3 days) if deficiency is suspected. 2â€“5mg iv/po will correct over-warfarinization in 6â€“12 hours. 0.5â€“1mg for minor adjustment.
- *Protamine sulphate* (1mg iv neutralizes 100iu heparin) is rarely used in practice. Stopping a heparin infusion will normalize an APTT in 2â€“4 hours.
- *Cryoprecipitate* should be considered if the fibrinogen is below 500g/L.
- *Factor concentrates* can be used in the treatment of isolated factor deficiencies, e.g. haemophilia. Concentrates of Factors II, VII, IX, and X are also available in some centres for specific reversal of warfarin effects (prothrombin complex concentrate).
- *Anti-fibrinolytics* are used occasionally for the treatment of life-threatening bleeds following thrombolytic therapy or

prostatectomy and in certain conditions associated with hyperplasminaemia (e.g. acute promyelocytic leukaemia, certain malignancies. Give *aprotonin* 50â€“100ml (0.5â€“1MU) slow iv followed by 20ml (200kU) every hour until bleeding stops; alternatively, *tranexamic acid* 0.5â€“1g slow iv injection tds.

- *Miscellaneous* DDAVP and oestrogens are occasionally used for haemophilia and renal failure.

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Circulating inhibitors of coagulation

Lupus anti-coagulant

- Causes prolonged APTT but predisposes to thrombosis, not bleeding (anti-phospholipid syndrome).

Acquired haemophilia

- Elderly patients presenting with severe bruising and prolonged APTT
- Discuss with haematologists.

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Abnormal platelets 1

Causes

Thrombocytopenia

Increased platelet consumption Immune

- Idiopathic (ITP)
- Drug induced
- SLE
- HIV related

Non-immune

- Massive transfusion
- Hypersplenism
- DIC, TTP

Reduced platelet production

- Myelosuppressant drugs, alcohol, viral infections
- Marrow infiltration/failure
- B_{12} or folate deficiency
- Inherited disorders (rare)

Abnormal platelet function

- Drugs (e.g. aspirin)
- Uraemia
- Liver disease
- Myeloproliferative disorders
- Myelodysplasia
- Dysproteinaemia (e.g. myeloma)
- Inherited disorders (rare)
    - Glanzman's disease (GP Ia deficiency)
    - Bernardâ€“Soulier (GP IIb/IIIa deficiency)
    - Chediakâ€“Higashi syndrome (abn. platelet granules)

Investigations

â€¢ Peripheral blood film	Evidence of haemolysis (?DIC ?TTP), or marrow infiltration
â€¢ Coagulation screen	?DIC
â€¢ Autoantibody screen	Associated autoimmune diseases
â€¢ Bone marrow aspirate	Increased megakaryocytes generally indicates peripheral consumption; decreased or abnormal

	megakaryocytes suggest a marrow problem
â€¢ Anti-platelet antibodies	Rarely indicated
â€¢ Platelet function tests	For bleeding in the presence of adequate platelet numbers on the blood film.

- Low platelets (<20 Ã— 10^9/L) may cause spontaneous bleeding and require platelet transfusion Â± treatment for the underlying cause.
- Moderately low counts (20â€“140 Ã— 10^9/L) will rarely cause spontaneous bleeding, unless there is an associated clotting abnormality (e.g. DIC) or a primary marrow defect, with production of defective platelets (e.g. myelodysplasia). Transfuse only if there is continued bleeding or in preparation for major surgery.
- High counts (500â€“1000 Ã— 10^9/L) may also indicate a primary production problem, with abnormal platelets (e.g. myeloproliferative disorders). (NB: moderately raised platelet count is a normal response to bleeding and is also seen in chronic inflammation.)

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Abnormal platelets 2

Management

This depends on the platelet count and severity of bleeding.

Immune-mediated thrombocytopenia

- Platelet transfusions are usually ineffective as sole therapy and rarely indicated.
- Prednisolone (1mg/kg od) is standard first-line treatment for adult ITP.
- Immunoglobulin 0.4g/kg/day iv infusion for 5 days (or 2g/kg/day for 1 day): this usually works quicker than steroids, but the effect only lasts 2â€“4 weeks. Start the infusion very slowly, as anaphylactic reactions (fever, urticaria, bronchospasm, and hypotension) are not uncommon.
- Pooled plasma product may be combined with the above.

Acute DIC/massive transfusion

Give platelet transfusions to maintain platelet count >50 Ã— 10^9/L (for chronic DIC, transfuse only for active bleeding).

Surgery

- Aim for platelet count >50 Ã— 10^9/L.
- For CNS surgery or multiple trauma, aim for count >100 Ã— 10^9/L.

Reduced platelet production (chronic, stable)

If no bleeding, transfuse if count <10 Ã— 10^9/L.

TTP/heparin induced thrombocytopenia

Platelet transfusions are contraindicated. Discuss all cases with the haematologists.

Platelet transfusion

- A single unit is either a pool of several buffy coats or platelets from a single donor from aphoresis.
- The number of platelets in a unit is <240 Ã— 10^9 which is sufficient for most indications unless there is on-going consumption (e.g. severe DIC).
- If no consumtpion, the platelets survive 2â€“5 days in circulation.

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Anti-coagulant therapy

Warfarin

- Warfarin overdose (accidental or deliberate self-harm) results in a prolonged PT (and thus INR).
- Risk factors for significant bleeding include poor control, local lesion (e.g. peptic ulcer, angiodysplasia of the colon), high level of anti-coagulation (INR >2.5), co-existent haematological abnormality (e.g. thrombocytopenia, myelodysplasia, etc.).

Management

- Moderate warfarin overdose (INR 5â€“8) without overt bleeding does not usually require specific treatment and patient may be managed as an outpatient provided they can attend for daily INR. Withhold warfarin until the INR falls to the therapeutic range. Try to identify the cause (incorrect tablets, alcohol binge, etc.).
- Asymptomatic patients with INR >8 should receive vitamin K as the risk of severe bleeding is high. Withhold warfarin and give 2mg of phytamenadione (iv preparation but absorbed well orally also) if INR <12, or 5mg phytamenadione if INR >12. Repeat INR the next day to

confirm reduction. Reintroduce warfarin when INR <5.

- Bleeding in patients on warfarin requires urgent correction of clotting. Give FFP 2â€“4 units iv and vitamin K 2â€“4mg iv (this dose does not usually interfere with re-anti-coagulation, whereas higher doses make subsequent anti-coagulation difficult). Identify and treat the local lesion from which the patient is bleeding. Consider giving prothrombin complex concentrate (purified Factors II, VII, IX, and X) for life-threatening bleeding (e.g. GI or CNS bleed). Discuss with the haematologists.

Heparin

Risk factors for bleeding include age, recent surgery or trauma, renal or liver failure, malignancy, APTT ratio >3, co-existent haematological abnormality.

Management

- Stop heparin: the APTT usually normalizes in 3â€“4 hours.
- Protamine sulphate (1mg iv neutralizes 100U heparin) may be used; halve the dose if heparin has been turned off 1 hour previously.
- *Low molecular weight heparins* are thought to have fewer bleeding complications. However, their plasma half-life is longer and they are less easily reversed with protamine. Treatment of overdose is as above, but with note that the APTT is normal on LMWH.
- *Heparin associated thrombocytopenia*: see P692.

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Bleeding with fibrinolytic therapy

Risk factors for bleeding with fibrinolytic therapy are given on P22. Severe haemorrhage should be managed with

- Supportive measures (colloid and blood transfusion)
- *Cryoprecipitate* transfusion as a source of fibrinogen
- *Aprotonin* 50â€“100ml (0.5â€“1MU) slow iv followed by 20ml (200kU) every hour until bleeding stops (alternatively, give tranexamic acid 0.5â€“1g slow iv injection tds).

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Bleeding in liver disease

The liver is involved in the synthesis of Factors II, III, IX, and X (the vitamin K-dependent factors) as well as the clearance of â€˜activatedâ€™ coagulation factors, fibrin molecules, and tPA. The abnormalities most commonly found are

Obstructive jaundice	Prolonged PT (vitamin K deficiency)
Acute liver failure	Prolonged PT and later prolonged APTT and TT (DIC)
Cirrhosis	Prolonged PT, APTT, and TT; low fibrinogen and/or dysfibrinogenaemia; raised FDPs, decreased clearance of tPA; low platelets (hypersplenism, DIC Â± marrow dysfunction).

Management

Treatment is required for active GI bleeding or as prophylaxis for surgery or liver biopsy.

- Give *vitamin K* 10mg iv slowly (single dose).
- *FFP transfusion* is more effective.
- Consider prothrombin complex concentrate (purified Factors II, VII, IX, and X) for life-threatening bleeding. Contact the haematologists.

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Bleeding in uraemia

Uraemia results in both platelet dysfunction (impaired aggregation, adhesion and activation) and endothelial dysfunction.

Management

- The treatment of choice is haemodialysis.
- Other measures that have been shown to be effective include
    - cyroprecipitate infusion
    - DDAVP (P698)
    - conjugated oestrogens
    - blood transfusion or erythropoietin to raise the haematocrit to >0.25.

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Massive transfusion/cardiopulmonary bypass

- Dilutional thrombocytopenia and coagulopathy usually occur once red cell concentrates equivalent to approximately two blood volumes have been transfused. With cardiopulmonary bypass, the extracorporeal circuit further damages the native platelets and depletes coagulation factors.
- Abnormalities include â†‘PT, â†‘APTT, â†‘FDPs, â†“fibrinogen.
- Post-transfusion thrombocytopenia is a distinct disorder seen 8â€“10 days following transfusion and is due to a platelet-specific antibody (see P678).

Management

Treatment should be discussed with the haematology team and involves platelet transfusion to keep platelet count >50 Ã— 10^9/L (or >100 Ã— 10^9/L for CNS lesions/multiple trauma), FFP (4â€“5 units) if PT or APTT >1.5 Ã— control, and cryoprecipitate (10â€“15 units) if fibrinogen <500g/L.

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Haemophilia and related disorders 1

Haemophilia A	X-linked recessive deficiency of Factor VIII (â†‘APTT; â†“Factor VIII activity)
Haemophilia B	X-linked recessive deficiency of Factor IX (â†‘APTT; â†“Factor IX activity)

Clinical presentation depends upon the degree of factor deficiency:

- Patients with <2% activity have a serious bleeding diathesis. Most are on home therapy
- Patients with 2â€“5% activity are moderately affected; they bleed rarely but should be treated as severe haemophiliacs when they do
- Patients with 5â€“40% factor activity rarely bleed spontaneously.

von Willebrand's Disease

- Autosomal dominant (Types I, IIa, and IIb) or recessive (Type III) with varying expression.
- Reduced levels of vW factor, which normally promotes platelet adhesion and protects factor VIII from destruction (hence â†“factor VIII activity; â†‘bleeding time; â†‘ or normal APTT).
- Less severe than the haemophilias, with haemarthroses and muscle bleeds being rare. Mucous membrane bleeding (esp. epistaxis) and post-traumatic bleeding are the main problems.

Acute presentations

- *Acute haemarthroses* often occur at sites of previous bleeding, particularly if this has led to degenerative joint disease. Ankles, knees, hips, elbows are the most common sites. Symptoms include local tenderness, warmth, and swelling, and may take days or weeks to resolve.
- *Intramuscular bleeds* can cause a compartment-type syndrome, leading to ischaemic necrosis and contracture. *Iliopsoas bleed* causes entrapment of femoral nerve and produces the triad of groin pain, hip flexion, and sensory loss over femoral nerve distribution. The pain may radiate to the abdomen, and mimic appendicitis.
- *Intracranial bleeding* is infrequent, but is still a common cause of mortality. It often follows minor head injury. Prognosis of intracerebral haemorrhage is generally poor. Extra-dural and sub-dural haemorrhage have a better prognosis.
- *Bleeding post-trauma:* classically there may be initial period of haemostasis; bleeding then becomes persistent or intermittent over days/weeks.

- *Haematuria/ureteric clot colic* is rare in haemophilia. Usually there is no detectable underlying abnormality of renal tracts.
- *Problems relating to co-existent HIV or hepatitis B/C infection* are now the commonest cause of mortality, due to infected Factor VIII administered during the 1980s.

Investigations

Generally, acute investigations are not necessary for simple joint and muscle bleeds in a known haemophiliac. Consider

- USS: for muscle haematomas (e.g. iliopsoas bleed)
- CT scan: history of head trauma, headache, abnormal neurology
- Factor VIII levels: if bleed is severe and treatment is necessary
- Factor VIII inhibitor titre: if refractory bleeds/history of inhibitor development.

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Haemophilia and related disorders 2

Most patients contact their haematologist directly unless they bleed when away from home. Be guided by your local haematologist.

General measures

- *Rest* of the affected part and ice packs may be of benefit.
- *Analgesia:* avoid NSAIDs and intramuscular injections. Oral analgesia (e.g. dihydrocodeine) for minor bleeds; iv injections or infusions of high-dose opiates may be necessary. *No im injections*.

Moderate or severe haemophiliac

- Treat with iv Factor VIII concentrate (minor bleeds, DDAVP).

Mild haemophiliac

- Factor VIII deficiency only: mild or moderate bleeds should be treated with DDAVP. Severe bleeds or those not

responding to DDAVP: treat with iv Factor VIII concentrate.

- Factor IX deficiency only: treat with Factor IX.

von Willebrand's disease

- *Mild and moderate bleeds*: Type I and IIaâ€”treat with DDAVP + tranexamic acid. Type IIbâ€”not DDAVP (risk of thrombocytopenia). Use Factor VIII.
- *Severe bleeds*: treat with Factor VIII concentrate and if bleeding continues, give cryoprecipitate and platelet transfusions.

NB: *All CNS and peri-spinal bleeds are regarded as severe.*

Factor VIII replacement

See table.

- Minor bleeds may respond to a single, slow, iv bolus of factor VIII.
- Major bleeds: 12 hourly treatments (8 hourly in severe bleeding) with frequent monitoring of Factor VIII levels, pre and post treatment.
- Patients with *Factor VIII inhibitors* present a particular problem. This can sometimes be circumvented by the use of alternative forms of factor VIII (human or porcine, depending on the type of inhibitor), or by the use of other products (e.g. FEIBA).

Factor IX replacement

See table.

- Plasma half-life is longer than Factor VIII, and once daily

administration is sufficient (twice daily in severe bleeds).

- Never give >3 doses (each a maximum of 50U/kg) of Factor IX in 36 hours as it is highly thrombogenic.

DDAVP

- *Indications:* Mildâ€“moderate haemophilia A, especially in children, von Willebrand's disease Type 1 and some Type II.
- *Dosage:* 0.4Âµg/kg in 100ml N saline iv over 20 minutes; may be repeated 8â€“12 hours later. Peak haemostatic effect in 60â€“90 minutes.
- Monitor pulse and BP every 5 minutes: side-effects include flushing, hypotension, tachycardia, headache, and nausea, rare reports of MI (caution in patients >40 years or with cardiac history).

Tranexamic acid

- Give with DDAVP in von willebrand's disease or mild Haemophilia A. Most useful in mucosal bleeds. Avoid in renal tact bleeding (may cause clots).
- *Dosage:* 1g po qds (adults). Mouthwash 4.8% q10 min for oral bleeding.

Cryoprecipitate

- Give for severe bleeding in von Willebrand's disease not responding to DDAVP and tranexamic acid.
- *Dosage:* 10â€“20 units (bags) for 70kg adult.

A rough guide for Factor VIII and IX replacement

Condition	Desired factor level (iu/dl)	Dose of Factor VIII (iu/kg)	Dose of Factor IX (iu/kg)
Mild/moderate bleeds	50	25	65 = benefix
			40 = replenine
Major/life-threatening bleeds	100	50	130 = benefix
			80 = replenine

e.g. A 70kg man with a minor bleed who is known to have haemophilia B and usually receives â€˜benefixâ€™ should receive 65 Ã— 70 = 4550 units (round to the nearest vial = 4500 units).

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Combined thrombotic and haemorrhagic disorders

A group of disorders in which the pathways of haemostasis become deregulated, leading to microthrombus formation, platelet consumption, and to a variable extent, clotting factor consumption. The exact pathogenesis varies, but in each case microthrombi cause organ damage, and thrombocytopenia results in bleeding. This co-existence of thrombosis and bleeding makes management very difficult.

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Disseminated intravascular coagulation (DIC)

An inappropriate activation of the coagulation pathways leading to

- Depletion of clotting factors, causing *prolongation of PT and APTT*
- Widespread thrombin activation, causing *increased TT and reduced fibrinogen*
- Formation of microthrombi, leading to *end-organ damage*
- Destruction of RBCs in fibrin mesh, causing *microangiopathic haemolysis*
- Consumption of platelets; *thrombocytopenia* increasing the bleeding tendency
- Activation of thrombolysis *(raised FDPs)* and further bleeding.

The â€˜full houseâ€™ of abnormalities does not need to be present initially, as the process is a progressive one.

Management

- *Treat the underlying cause* (60% have underlying sepsis).

- Supportive measures such as correction of shock, acidosis, and hypoxia may lead to an improvement in the coagulopathy.
- Transfuse blood to correct anaemia. Massive transfusion may exacerbate coagulopathy by dilution of coagulation factors and platelets.

Product replacement

- In acute DIC consider
    - FFP (15ml/kg, i.e. 4â€“5 units) if PT or APTT >1.5 Ã— control
    - 1 unit platelets if platelet count <50 Ã— 10^9/L or <100 Ã— 10^9/L and rapidly falling
    - Cryoprecipitate (10â€“15 units) if fibrinogen <500 g/L.
- Protein C concentrate has been used in non-randomized trials for severe sepsis and meningococcal septicaemia with some success, but is not yet widely available.
- Plasma exchange may also be considered.

Prognosis

In severe acute DIC overall mortality is high. Obstetric complications have the best prognosis if managed expediently. There is little evidence that measures to prevent thrombosis (heparin, antithrombin III) or prevent thrombolysis improve the general prognosis.

Causes of DIC

Common

- Gram -ve septicaemia
- *Staph. aureus* sepsis
- Meningococcal septicaemia
- Malaria (esp. *falciparum*)
- Disseminated malignancy
    - Mucinous adenocarcinomas
    - Prostatic carcinoma
- Liver failure

Rarer

- Incompatible blood transfusion
- Severe trauma/burns
- Acute promyelocytic leukaemia
    - Obstetric emergencies
    - Abruptio placentae
    - Amniotic fluid embolism
    - Retained dead foetus
    - Severe pre-eclampsia
- Anaphylaxis (e.g. snake bites)
- Hypoxia
- Haemangioma

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Thrombotic thrombocytopenic purpura (TTP) and haemolytic-uraemic syndrome (HUS)

The primary event appears to be endothelial damage, causing microthrombus formation, end-organ damage (esp. brain, kidneys), and platelet consumption. Patients with classic TTP have been found to have an antibody against a metalloproteinase (ADAMTS-13) which cleaves very large multimers of von Willebrand factor. These then accumulate and cause microthrombi and thrombocytopenia. The clinical picture tends to vary with age, renal abnormalities being more common in children and neurological problems in adults, but with considerable overlap.

Presentation

- Most commonly occurs suddenly in a young or middle-aged woman, or following a viral infection
- Fever
- Anaemia (haemolytic picture: associated with jaundice and haemoglobinuria)
- Thrombocytopenia with purpura and bleeding
- CNS (confusion, headache, meningitic symptoms, aphasia, visual disturbance, fits, coma, paralysis, psychosesâ€”often

fluctuating)

- Renal involvement (oliguria, anuria, haematuria) often mild initially
- HUS is often preceded by gastroenteritis or URTI.

Investigations

â€¢ FBC	Anaemia with thrombocytopenia. Moderate leukocytosis with left-shift
â€¢ Blood film	Fragmented RBCs, polychromasia, thrombocytopenia
â€¢ Clotting	Usually normal
â€¢ U&Es	In adults, creatinine slow to rise over a few days; rapid deterioration more common in children
â€¢ LFTs	â†‘Bili. (unconjugated). â†‘LDH (from haemolysis)
â€¢ Haptoglobins	Decreased
â€¢ Urinalysis	Proteinuria frequent; haematuria, haemoglobinuria
â€¢ Stool	Culture, especially for *E. coli* strains.

Associations of TTP and HUS

Recognized

- HIV infection
- SLE
- Normal pregnancy
- Drugs (OCP, cyclosporin)
- Gastroenteritis (esp. with *E. coli*, type 0157 : H7 in children)

Controversial

- Coxsackie B infection
- *Mycoplasma*
- Malignancies
- Bee stings
- Radiotherapy

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Microangiopathic haemolytic anaemia

Management of HUS and TTP

- Refer to specialist unit (renal and/or haematology).
- Give FFP while arranging urgent plasma exchange.
- Plasma exchange: aggressive regimen (65â€“140ml/kg/day) with FFP results in improvement (and possibly cure) of TTP in many patients. Tail only after remission obtained.
- Steroids used with plasma exchange may be effective.
- Dialysis (haemodialysis or peritoneal dialysis) is used for acute renal failure (usually children).
- Broad-spectrum antibiotics: unproven benefit, but seem sensible given infectious aetiology in some patients.
- Blood transfusion to correct anaemia.
- Platelet transfusion *contraindicated*; exacerbates thrombosis and may worsen the situation.
- Aspirin may be used once platelet count is >50 Ã— 10^9/L.
- Refractory TTP may respond to high-dose steroids, vincristine, or cyclosporin.

Prognosis

- Children/predominant HUS picture: 5â€“30% mortality. Renal impairment and hypertension is common in survivors.
- Adults/predominant TTP picture: 90% mortality if untreated; most die in first few days. With aggressive and early plasma exchange, mortality is now 710%, but relapses are frequent.

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Heparin-associated thrombocytopenia

- An idiosyncratic reaction seen in 1â€“2%. Much less common with low-molecular-weight heparins.
- It may be mild and transient in the first week, often resolving spontaneously with continued therapy.
- Late-onset thrombocytopenia is seen 10 days to 2 weeks after starting therapy and is caused by an IgG autoantibody that results in platelet activation, haemorrhage and, in 740%, thromboembolic events.
- Consider the diagnosis if the problem demanding heparinization does not resolve or worsens while the patient is on heparin (e.g. propagation of DVT) or a new thrombotic event takes place in a heparinized patient.

Management

As for heparin induced thrombocytopenia and thrombosis.

- Stop heparin immediately. Do not wait to see what happens to the platelet count.
- Consider heparin alternatives such as hirudin or danaporoid (discuss with your haematologists). Low-molecular-weight heparins can have a cross-over effect, and perpetuate the

problem. Switch to warfarin as soon as possible.

- Do not give platelets to treat thrombocytopenia, as this can lead to further platelet activation and thrombosis.

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Acute leukaemias: presentation

Types of acute leukaemia

Acute lymphoblastic leukaemia (ALL)

- Usually B-cell, occasionally T-cell in origin
- Mainly children and young adults.

Acute myeloid leukaemia (AML)

- Classified into types M1â€“M7 (â€˜FAB typesâ€™)
- Mainly adults, including elderly.

Both AML and ALL can develop by transformation of chronic myeloid leukaemia, or secondary to an underlying myelodysplastic syndrome, as well as occurring *de novo*.

Poor prognostic factors

- Increasing age
- High white cell count at presentation
- Underlying myelodysplastic syndrome
- Philadelphia chromosome positive acute leukaemia

- *Depends* upon sub-classification of leukaemia on basis of morphology, chromosomal abnormalities, and cell surface markers.

Presentation

Red cell problems

Anaemia: caused by suppression of erythropoiesis by leukaemia cells; also by bleeding due to low platelets or deranged clotting. The MCV is usually normal or high, unless blood loss is predominant.

White cell problems

- *High blast count*: may cause â€˜leucostasisâ€™ (crudely, sludging of white cells in small vessels), causing respiratory impairment, myocardial ischaemia/infarction, renal impairment, acute confusion, stroke, fits, migraine.
- *Leukaemia-related phenomena*: pyrexia, malaise, muscle and joint pains.
- *Neutropenia*: secondary to marrow infiltration by leukaemic cells.

Platelet problems

Thrombocytopenia due to myelosuppression by leukaemic infiltrate. Existing platelets may have sub-normal function. Risk of bleeding increases if platelets are <10 Ã— 10^9/L or <20 Ã— 10^9/L if there is concomitant sepsis or coagulation abnormality.

Coagulation problems

Range from a *prolongation of PT* to *DIC:* may be due to sepsis,

or the effects of leukaemia itself, esp. acute promyelocytic leukaemia (M3).

Priorities

- Stabilize the patient
- Treat immediate problems, e.g. bleeding, sepsis
- Confirm diagnosis
- Define treatment strategy.

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Acute leukaemias: management

Stabilize the patient

- Airway. Stridor may be secondary to mediastinal obstruction in certain cases of leukaemia, mainly T-ALL. If present, call anaesthetist immediately and arrange transfer to ITU.
- Breathing. Breathlessness may be due to infection (including atypical organisms), leucostasis (high WCC), severe anaemia, cardiac failure (leucostasis, severe sepsis), pulmonary haemorrhage. Give oxygen: where possible, use pulse oximeter to monitor oxygen saturation, avoiding arterial puncture with thrombocytopenia.
- Circulation. Shock is usually secondary to sepsis, but consider the possibility of blood loss if low platelets/clotting abnormalities, or cardiac failure from leucostasis.
    - Restore circulatory volume
    - Give broad-spectrum antibiotics immediately (after blood cultures) if sepsis suspected (see section on febrile neutropenia P718).
- Refer to a haematologist.

Treat immediate problems

- Infection. Until the blood film has been reviewed by a haematologist, assume the patient is neutropenic, and treat all infections aggressively. See section on febrile neutropenia (P718).
- Bleeding
    - Transfuse cross-matched blood (CMV-negative blood if available). Caution if high white cell counts
    - If platelets <20 Ã— 10^9/L, give 1 init of platelets. If there is active bleeding and platelet count <50 Ã— 10^9/L give platelets
    - If prothrombin time prolonged (>1.5 Ã— control), give 4â€“5 units FFP
    - If fibrinogen <500 g/L, consider cryoprecipitate in addition.

Transfusion in the presence of a high WCC is dangerous, and can precipitate the complications of leukostasis.

- High WCC. Discuss with haematologists. May require urgent leuko-pheresis, preferably in an ITU setting.

Confirmation of diagnosis

- Take a full history, looking for possible aetiological factors. Length of illness (was there a preceding chronic condition, e.g. myelodysplasia?). PMH (?Down's syndrome, radiation/chemotherapy exposure). Occupation (?exposure to irradiation, benzenes, other mutagens). Family history (rare familial syndromes, e.g. Fanconi's anaemia).
- Examine the patient, looking for accessory clues to diagnosis (?lymphadenopathy, hepatosplenomegaly, gum

hyperplasia) and identifying potential sites for infection (dental caries, skin lesions, etc.)

- Final confirmation then rests upon a bone marrow aspirate, with samples being sent for morphology, chromosome analysis, and cell surface markers.

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Acute leukaemias: treatment

The treatment of acute leukaemia depends upon the type of leukaemia, and involves several courses of chemotherapy, taking months or even years to complete. The prognosis has improved in recent years and depends upon the exact diagnosis. 80% of children with ALL are now cured whereas only around 30% of adults with AML are cured. The impact of the diagnosis on often young patients and their families is devastating, and extensive time is needed in discussion. Before embarking on chemotherapy, the following must be considered.

Sperm banking

Almost all forms of chemotherapy carry a high incidence of subsequent infertility. When desired by the patient, every attempt must be made to provide for banking of sperm collection prior to starting chemotherapy. Unfortunately in practice the presence of leukaemia itself often makes sperm non-viable, and the need to start treatment precludes repeated collections.

Discussion about side-effects

Patients need to be warned about hair loss, sterility, emesis (less of a problem with current anti-emetics, but varies with individual), infections, bleeding, mucositis, etc. Patient-orientated literature is available on acute leukaemia and

chemotherapy, and may be helpful.

Other considerations

- Lumbar puncture (?CNS involvement). Indicated in
    - Acute lymphoblastic leukaemia
    - AML if high WCC at presentation
    - Any neurological symptoms/signs.
- HLA typing of patient/siblings may be considered, with a view to possible bone marrow transplant in the future. This is usually, however, left to a later stage, once the patient has achieved clinical remission.
- CMV status should be determined, and CMV-negative products administered to CMV-negative patients throughout their treatment, especially if bone marrow transplantation is an option.

Prior to commencement of chemotherapy

- Commence allopurinol 24 hours in advance. Rasburicase is used if there is a high risk of tumour lysis syndrome (200mcg/kg iv od for 5â€“7 days).
- Prescribe regular antiseptic mouthwashes, to be used 4â€“5 Ã—/day in conjunction with anti-thrush prophylaxis (nystatin suspension, amphotericin lozenges, or oral fluconazole).
- Ensure adequate hydration aiming for 3L/day input.
- Give an antiemetic before chemotherapy, and at regular intervals during treatment with chemotherapy. Appropriate regimes include

- ondansetron 4â€“8mg iv/po bd
- metoclopramide 10â€“20mg iv/po plus dexamethasone 2â€“4mg iv/po 4â€–8 hourly.

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Early complications of bone marrow transplantation (BMT)

Always contact and refer the patient back to their BMT centre.

The morbidity and mortality following BMT (especially allogeneic BMT) is high, particularly within the first 100 days. The patients are very reliant on close medical and nursing surveillance to ensure that they do not perish from preventable/treatable causes. Patients may occasionally present outside on their transplant unit overnight or at weekends. They will be vulnerable to all kinds are infections: bacterial, viral, fungal, and protozoal. Even in the neutrophil count as normal, treat the patients as being neutropenic, and they will have poorly functioning lymphocytes and low antibody production. The following is a guide to some of the problems encountered.

Acute graft versus host disease

This causes skin rashes either localized (e.g. to palms) or widespread. The rash is typically non-itchy. There may be upper or lower GI symptoms (severe watery diarrhoea) and liver dysfunction (deranged LFTs). Mild GVHD of one site may be acceptable but consider early treatment (usually high-dose methyl-prednisolone) for widespread GVHD or diarrhoea. Discuss with the transplant centre.

Fever

See section on the neutropenic patient, P718.

Upper GI symptoms (mucositis, vomiting)

Symptomatic management including adequate analgesia (e.g. opiates) and H_2-antagonists or PPIs. Search for an infectious cause (mouthwash and swabs for HSV and *Candida*). Antiemetics usually required: lorazepam 1â€“2mg q8â€“12h, metoclopramide 10â€“20mg q6â€“8h, or ondansetron 4â€“8mg q12h.

Diarrhoea

Rehydrate. Monitor strict fluid balance. Stool culture (green watery diarrhoea suggests GVHD). May require early biopsy and steroids if large volume diarrhoea. Discuss with transplant centre.

Abnormal LFTs (drugs, GVHD, veno-occlusive disease)

Supportive measures: monitor fluid balance, coagulation tests, renal function; adjust drug doses accordingly. Search for an infectious aetiology. Veno-occlusive disease presents as hepatomegaly, jaundice, and weight gain. Liver ultrasound with doppler of the hepatic and portal veins (reversed hepatic-portal flow seen in veno-occlusive disease). Discuss with the transplant centre.

Interstitial shadowing on CXR

These may be diffuse or localized and associated with varying degrees of fever, breathlessness, and hypoxia.

Causes

Pulmonary oedema (fluid overload, cardiac failure due to chemo/radiotherapy, non-cardiac (ARDS)â€”related to sepsis or drug toxicity);

infection [bacterial, viral (esp. CMV), fungal, *Pneumocystis*]; thromboembolic; GVHD; pulmonary haemorrhage; idiopathic.

Management

Supportive treatment: oxygen, diuretics (if pulmonary oedema) and ventilatory support. CXR changes often minor if neutropenic. Cover for infectious causes with broad-spectrum antibiotics, anti-fungal agents, or occasionally anti-viral agents (if viral RTI is suspected). PCP is unusual if the patient is on co-trimoxazole prophylaxis. Consider bronchoscopy.

Early complications of BMT

- Skin rash
- GI complications
    - Nausea and vomiting
    - Mucositis
    - Diarrhoea
- Abnormal LFTs
- Haemorrhagic cystitis
- Interstitial shadowing on CXR
- Cardiovascular complications
    - Cardiac failure
    - Hypertension
    - Endocarditis

- Deteriorating renal function
- CNS complications

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Complications of bone marrow transplantation

Cardiac failure

- Cardiac toxicity may be secondary to high-dose cyclophosphamide, total body irradiation, and/or anthracycline exposure.
- Transient ST- and T-wave abnormalities and LV dysfunction on Echo are seen in up to 30% following conditioning prior to BMT.
- Overt cardiac failure may be seen with repeated high-dose steroid therapy that is required for episodes of GVHD.

Management

Standard therapy with diuretics and ACE-I.

Hypertension

Very common in the early days post BMT and due to cyclosporin therapy 9 renal impairment.

Treatment

Calcium antagonists (e.g. nifedipine SR, 10â€“20mg po bd).

Deteriorating renal function

Causes

- Drug therapy (cyclosporin A, amphotericin, aminoglycosides, chemotherapy, acyclovir, allopurinol)
- Pre-renal (dehydration, shock, bleeding)
- Tumour lysis syndrome (see P730).

Haemorrhagic cystitis

Frequency, dysuria, and haematuria; commonly related to cyclophosphamide (caused by acreolin, a metabolite), but also seen with anthracyclines, cytosine arabinoside, etoposide, adenovirus, and BK virus infection. Prevent with mesna (see data sheet for dose).

Management

Supportive therapy with blood and platelet transfusion and hydration is usually sufficient.

CNS complications

Symptoms

May include seizures, drowsiness/confusion, focal neurological signs, stroke.

Causes

- Metabolic (â†“Mg^{2+}, â†“Ca^{2+}, hypoxia, liver failure, renal failure)
- Infection [bacterial, viral (e.g. HSV), fungal (esp.

Aspergillus), *Toxoplasma*]

- Drug toxicity. Cyclosporin can cause tremor, confusion, and seizures
- Intracranial haemorrhage
- Cerebral infarction (embolic)
- Relapse of disease.

Investigations

CT scan, LP (after correcting clotting and platelets), blood cultures, serology, Mg^{2+} and Ca^{2+} levels, Echo.

Management

Specific therapy for underlying cause.

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The febrile neutropenic patient 1

- Neutropenia (in this context) may be defined as a total neutrophil count of <1 Ã— 10^9/L, regardless of total WCC.
- Significant infections are usually associated with a fever; and a â€˜spikeâ€™ to â‰¥38Â°C is regarded as warranting action. Severely ill patients may not, be able to mount a fever.
- The site of infection is not usually obvious; potential sites include chest, Hickman, or other central line (or inflammation around exit site of line), mouth, perianal area/perineum, urine, or skin.

Organisms

Common	*Other (10%)*
Gram-positive (60%)	*Staph. aureus*
Coagulase S -ve staphylococci	*Corynebacterium* JK
S. epidermis	*Acinetobacter* sp.
Streptococci	Mixed infections
viridans streptococci	Anaerobes
Gram-negative (30%)	Fungal infections
Escherichia coli	*Candida* sp.
Klebsiella spp.	*Aspergillus fumigatus*
Pseudomonas aeruginosa	Viral infections (VZV, CMV)
	Pneumocystis carinii

- A microbiological diagnosis is reached in only 740%.
- Coagulase -ve staphylococci: Hickman or other iv lines
- Viridans streptococci: mucositis 9 previous exposure to quinolones
- Fungal infections: occur after prolonged and profound neutropenia, previous antibiotic therapy, underlying lung

disease (pulmonary aspergillosis).

Basic microbiological investigations

- *Blood cultures* taken from Hickman line and by venepuncture. This allows line infections to be differentiated from bacteraemias.
- *Culture of urine and faeces* including stool for *C. difficile*.
- *Cultures from other suspected sites*, e.g. line exit sites, sputum, skin lesions, throat.
- *Viral serology*: less useful, as a rising titre is often necessary to diagnose infection. Viral antigen/particle detection (e.g. CMV DEAFF test), where possible, may be more helpful in an acute situation.
- *Line tips*: rush to laboratory. Do not allow to dry out on ward bench or insert into throat swab medium.

Important points

- *Antibiotic therapy should never be delayed to await further assessment of clinical progress, or lab results*.
- Neutropenic patients may not show a localized response to infection. The most common presentation is that of a fever of unknown origin.
- A pyrexia lasting >48 hours, despite iv antibiotics, usually requires some alteration to the anti-microbial regime.

- *Platelet requirements increase with sepsis*. Neutropenic patients are commonly also thrombocytopenic: keep platelet count above 20 Ã— 10^9/L.
- Thrombocytopenia also demands care with invasive procedures. Central lines and urinary catheters should be

inserted with platelet cover, and *arterial puncture is best avoided* (use pulse oximetry).

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The febrile neutropenic patient 2

Immediate management

Given the caveats on the previous page, the stabilization of a septic neutropenic patient is similar to that of any other septic patient.

- Oxygen, iv colloid, crystalloid, and inotropes should be administered as is appropriate to the patient's clinical condition.
- CVP readings may be taken from existing central lines to assess the patient's hydration status, but, with Hickman lines in particular, the readings are frequently not accurate, and should be interpreted in the context of the clinical assessment.

Anti-microbial regime

When in doubt, take microbiological advice; use hospital policy. Regimes for empirical therapy are based on broad-spectrum, bactericidal antibiotics. Monotherapy is hardly ever appropriate, even when an organism has been isolated: the patient may well have more than one infection. A typical policy is shown below.

Empirical antibiotic therapy for febrile neutropenia

1st line	*Tazocin* 4.5g iv tds (or *Meropenem* 500mg iv qds if penicillin allergic) plus
	Gentamicin 7mg/kg iv od (guided by levels)
2nd line	*Vancomycin* 1g iv bd (guided by levels) or *Teicoplanin* 400mg iv od (bd for first 24 hours) if line infection is suspected
3rd line	Consider *amphotericin* if fever is not settling after 72 hours especially in patients with long periods of neutropenia (e.g. AML or BMT patients). Discuss with local haematologists and microbiologists

Notes

- Doses of *vancomycin* and *gentamicin* will need to be adjusted according to serum levels.
- Add *metronidazole* 500mg iv q8h to 1st- or 2nd-line regimens if fever persists and anaerobic infection possible (mucositis).
- Add *amphotericin B* 200Âµg/kg/day iv increasing stepwise to 1mg/kg/day for 4 weeks for proven (or possible) fungal infection.
- The *change from 1st- to 2nd-line therapy* should be considered under the following circumstances

- Persistent pyrexia >48 hours (or less if the patient's condition markedly deteriorates)
- A new spike of temperature once the fever has settled on 1st-line antibiotics (suggesting emergence of another, resistant organism)
- Rising CRP in the face of apparently appropriate antibiotics.

- Choice of *3rd-line antibiotics* is often more arbitrary, and combinations should again be discussed with the microbiologists. Duration of neutropenia is an important factor, as fungal infections become more likely the longer the period of neutropenia.

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The febrile neutropenic patient 3

Particular situations

- *Infections of the mouth, perianal area, or elsewhere in the GI tract*: consider adding *metronidazole*.
- *Suspected line infections*: ensure good gram-positive cover (*vancomycin* or *teicoplanin*).
- *Diarrhoea after prolonged antibiotic therapy*: suspect *Clostridium difficile*; consider empirical oral *vancomycin* or *metronidazole* while awaiting stool culture results.
- Orophyrangeal mucositis due to *reactivation of herpes simplex virus* is common. It is effectively treated with *acyclovir*; the main complication is bacterial super infection.
- *Pyrexias associated with a normal CRP* virtually exclude bacterial or fungal infection as a cause of the fever.
- *Deteriorating renal function*: avoid nephrotoxic agents, particularly in combination (e.g. vancomycin, amphotericin, gentamicin).
- *Systemic candidiasis* may be manifest only as fever unresponsive to antibiotics: blood cultures are rarely positive; signs of local invasion, (e.g. endophthalmitis) are

seen in a minority. Have a high index of suspicion and treat aggressively with amphotericin or fluconazole.

- *Invasive aspergillosis* presents as fever, abnormal CXR and dyspnoea, or sinusitis (invasive disease of sinuses). There is extensive local tissue destruction with cavitating lung lesions or bone destruction of sinuses. Treat aggressively with iv amphotericin.
- *GCSF* may shorten a period of neutropenia and may be used for certain patients. Discuss with the haematologists.

When selecting an anti-microbial regime, it is worthwhile reviewing all recent microbiology results, including skin swabs (axilla, groin, perineal).

Causes of failure to respond to empirical antibiotics

- Wrong microbiological diagnosis Consider infection with fungi, viruses, protozoa, mycobacteria
- Line-associated fever
- Graft versus host disease (also possible with liver transplantation)
- Drug fever
- Inadequate antibiotic doses
- Underlying disease (e.g. relapse)

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Infections in the transplant patient

Infectious diseases are a major cause of mortality and morbidity following both solid organ and bone marrow transplantation, related to the immunosuppression (and in the case of BMT, the innate immuno-incompetence in the neutropenic and early engraftment phases).

Different pathogens are typically implicated in infections depending on the degree of immunocompetence of the patient:

- The neutropenic patient (see P718)
- The non-neutropenic transplant patient.

Cell-mediated immunity may be impaired for several months after bone marrow (and solid organ) transplantation. This predisposes to viral (CMV, HSV, adenovirus) and protozoal (*Pneumocystis carinii*, toxoplasmosis) infections.

- *Cytomegalovirus infections: see* P726.
- *Suspected Pneumocystis pneumonia*: treat with *high-dose septrin*; (0.96â€“1.44g q12h iv); consider urgent bronchoscopy/broncho-alveolar lavage.
- *Toxoplasmosis*: usually due to reactivation of latent infection. Presents as intra-cranial space-occupying lesion,

meningoencephalitis, or diffuse encephalopathy. Seizures and focal neurological signs are common. Treatment is with *pyrimethamine* and *sulphonamides*.

- *Other viral infections*
    - *HSV* commonly produces localized infection and dissemination is rare but recognized to produce encephalitis and pneumonia: Treat with *high-dose acyclovir* iv.
    - *VZV* reactivation is frequently seen and most infections are mild; encephalitis and pneumonitis are usually fatal. Treat with *high-dose acyclovir* (10mg/kg iv q8h).
    - *Adenovirus* infection produces an interstitial pneumonitis similar to CMV and may disseminate.

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Cytomegalovirus (CMV) infections in transplant patients

- Also see P351.
- May be acquired from the reactivation of previous CMV infection in recipient, due to immunosuppression.
- May be acquired from the bone marrow from a CMV-positive donor or CMV-positive blood products. (*All BMT recipients should receive CMV-negative blood products if they are CMV IgG negative prior to BMT*. CMV IgG-positive recipients can receive unscreened blood product).
- Do not usually occur until day 21 following BMT.
- Occur more commonly in allogenic and unrelated donor transplants, due to the greater immunosuppression.

Presentation of acute CMV infections

- Fever of unknown origin.
- Antigenaemia (detected by routine CMV-antigen testing, blood and urine).
- Graft failure/myelosuppression (anaemia, thrombocytopenia, leukopenia).

- Interstitial pneumonitis: deteriorating oxygen saturation, with widespread bilateral interstitial opacities on CXR.
- Enteritis (oesophagitis, gastritis, colitis): pyrexia, diarrhoea.
- Hepatitis.

Immediate management

- Ensure adequate respiration; consult anaesthetists and consider CPAP/ventilation early if oxygen requirements are increasing, or the patient is becoming exhausted.
- Inform haematologist responsible for patient's care.
- Take blood for CMV antigen, culture, and antibody testing.
- Send urine sample for CMV antigen.
- If CMV is strongly suspected, commence ganciclovir treatment immediately. Otherwise, consider
    - bronchoscopy/bronchoalveolar lavage if pulmonary infiltrate (send washings for CMV antigen)
    - upper GI endoscopy and biopsy.

Treatment

- *Ganciclovir* should be commenced at 2.5mg/kg iv tds.
- Side-effects of ganciclovir include nephrotoxicity, and myelosuppression/graft failure, which may be difficult to distinguish from the effects of CMV itself.

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Hyperviscosity syndrome

Causes

Increased cellularity	Raised plasma proteins
Polycythaemia (p or s)	Waldenstrom's macroglobulinaemia
â€¢ Haematocrit. 50â€“60% Leukocytosis (acute leukaemias)	â€¢ IgM paraprotein level >30g/L Myeloma usually IgA subtype
â€¢ WCC >50â€“100 Ã— 10^9/L	â€¢ Paraprotein level >80g/L

Presentation

Most patients develop symptoms when serum viscosity reached 5â€“6 centipoises (normal <1.8).

General features

- Muscle weakness
- Lethargy, headache
- Mental confusion, proceeding to coma
- Visual disturbance
- Congestive cardiac failure
- Fundoscopy
    - engorgement and sludging in the veins
    - haemorrhage, exudates
    - papilloedema.

Specific features

The predominant symptoms vary with the underlying cause.

- *Raised paraprotein*
    - Bleeding/purpura: platelet dysfunction and factor deficiency
    - Neuropathies
    - Renal impairment
    - Cardiac conduction abnormalities.
- *Leucostasis*
    - Myocardial ischaemia/infarction
    - Pulmonary infiltrates.
- *Polycythaemia*
    - Peripheral ischaemia
    - Transient ischaemic attacks/strokes
    - Myocardial infarction.

Management

Arrange urgent intervention (same day) depending on cause.

â€¢ Polycythaemia	Venesect 1â€“2 units
	Replace with N saline
â€¢ Leukaemia	Leucopheresis or chemotherapy
â€¢ High paraprotein	Plasmapheresis

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Tumour lysis syndrome

A syndrome of metabolic abnormalities and renal impairment that can occur within hours or days of commencing chemotherapy, due to rapid lysis of tumour cells. It is most likely to occur with bulky, highly chemosensitive disease (e.g. lymphomas, high blast-count leukaemias, germ-cell tumours).

Features

- Hyperuricaemia Â± urate nephropathy and oliguric renal failure.
- Hyperkalaemia (especially with progressive renal impairment).
- Hyperphosphataemia.
- Hypocalcaemia and hypomagnesaemia (due to rising phosphate).
- Cardiac arrhythmias (secondary to â†‘K^+, â†“Ca^{2+}, and â†“Mg^{2+}).
- Weakness, twitching, tetany (hypocalcaemia).
- Severe metabolic acidosis (renal failure).

Management

- Emergency treatment of hyperkalemia.
- Exclude bilateral ureteric obstruction by ultrasound.
- Alkalinize the urine (P834) if hyperuricaemia is present. Stop as soon as urate levels normal.
- Avoid calcium supplements except if there is neuromuscular irritability.
- Monitor U&Es, PO_4^{3-}, Ca^{2+}, and urate at least twice daily for the first few days of treatment.
- Strict fluid balance measurements, with urinary catheter if necessary.
- Indications for haemodialysis/intensive care
    - Rising K^+, creatinine, or PO_4 in spite of measures above
    - Metabolic acidosis
    - Fluid overload or oliguria in spite of diuretics.

Prevention

- Start *allopurinol* 300mg od (or bd) 48 hours prior to chemotherapy. Some units use rasburicase for high-risk patients (200mcg/kg iv od for 5â€“7 days).
- *Hyperhydrate* (iv fluids, 3â€“5 litres/24 hours) prior to chemotherapy. Urine alkalinization helps promote urate excretion.
- *Leucopherese* if high peripheral blast count.
- Continue iv fluids during therapy, giving frusemide to maintain diuresis.

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Hypercalcaemia of malignancy

See P580

- Urgent intervention required if Ca^{2+} >3mmol/L
- NB: true Ca^{2+} = measured Ca^{2+} + [(40 - albumin) Ã— 0.02].

Causes

- Bony metastases: probable local cytokine effect
- Myeloma: secretion of an osteoclast-activating factor
- Secretion of PTH-related peptide (non-small cell lung cancer).

Presentation

Nausea, vomiting, drowsiness, confusion, nocturia, polyuria, bone and abdominal pains, constipation.

Management

- Hydration: 3â€“4L over 24 hours, continuing for 4â€“5 days.

- Frusemide to maintain diuresis; has an additional Ca^{2+}-lowering effect.
- Following overnight hydration recheck Ca^{2+}, albumin.
- If symptoms persist, and/or Ca^{2+} remains >3mmol/L, give pamidronate disodium iv. A typical dosing regimen is

Ca^{2+} <3mmol/L	30mg over 4 hours
Ca^{2+} 3â€“4mmol/L	60mg over 8 hours
Ca^{2+} >4mmol/L	90mg over 24 hours.

- For myeloma, consider prednisolone 30â€“60mg po daily.

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Superior vena cava obstruction

Presentation

Awareness of fullness of head and tightness of collar, symptoms exacerbated by bending down, syncope, breathlessness, facial suffusion and oedema, engorgement of veins in neck, arms, and upper thorax.

Causes

- Usually bronchogenic carcinoma (9 secondary thrombosis of SVC)
- Other tumours, including lymphoma, more rarely.

Management

- FBC and film, U&Es, Ca^{2+}, albumin
- CXR, Doppler USS of neck veins if diagnosis uncertain
- Heparin, providing platelet count and clotting function are normal
- Arrange urgent radiotherapy (within 24 hours).

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Massive mediastinal mass

Presentation

Dry cough, stridor and dyspnoea, especially on lying flat.

Causes

- ALL (especially T-ALL with high WCC)
- High-grade non-Hodgkin's lymphoma
- Hodgkin's disease
- Germ cell tumour.

Management

- Histological diagnosis (or cytological from pleural effusion if present)
- General anaesthetic carries considerable risk
- Definitive treatment (radiotherapy or chemotherapy)
- Consider prednisolone 1mg/kg/day if urgent treatment is required.

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Chapter 12
Rheumatological emergencies

Acute monoarthritis: presentation

An acute monoarthritis should always be treated as septic arthritis until proved otherwise. Failure to treat septic arthritis is a medical disaster. 50% of cartilage proteoglycan is lost within 48 hours; bone loss is evident within 7 days; mortality of *Staph. aureus* arthritis is 10%.

Presentation

- Hot, swollen red joint
- Joint line tenderness
- Restricted range of movement
- Systemic features of fever and malaise.

Assessment

Look for any risk factors for infection:

- Diabetes mellitus
- Immunodeficiency state (monoarthritis is rare in AIDS)

- Underlying structural joint disease (e.g. rheumatoid arthritis or other deforming arthropathy, prosthesis)
- Sexual impropriety, intravenous drug abuse (predisposes to sacroileitis and acromioclavicular joint infection)
- Tuberculosis needs to be considered in at risk populations (e.g. Asians).

Ask for risk factors for gout:

- Alcohol
- High-purine diet (protein, e.g. meat)
- Drugs (e.g. thiazides, frusemide, ethambutol)
- High cell turnover states (e.g. lymphoma, polycythaemia, psoriasis).

Examine for evidence for multi-system disease:

- Rash
- Ocular involvement
- Oro-genital ulceration
- Gastrointestinal symptoms
- Renal involvement
- Pulmonary manifestations.

Conditions that mimic monoarthritis

- Bone pain or fracture close to a joint
- Tendinitis (especially at the wrist)
- Bursitis (commonly olecranon or pre-patellar bursae; no joint line tenderness)

- Neuropathic pain
- Soft tissue pain.

Differential diagnosis of a monoarthritis

Traumatic

- Traumatic synovitis
- Haemarthroses

- Fracture
- Haemophilia
- Ruptured anterior cruciate ligament

Non-traumatic

Infective

- *Staphylococcus aureus*
- *Neisseria gonococcus*
- *Staphylococcus albus*
- Streptococcal
- Gram negative rods

Crystals

- Uric acid (gout)
- *Calcium pyrophosphate (pseudogout)*
- Hydroxyapatite [usually a monoarthritis (shoulder) in elderly patients]

Monoarticular presentation of

- Rheumatoid arthritis
- Seronegative arthritis (e.g. Reiters, psoriasis)
- SLE

Miscellaneous

- Pigmented villonodular synovitis
- Secondary deposits
- Osteosarcoma

Practice point

- Always assume an unexplained monoarthritis is due to sepsis until proved otherwise.

Acute monoarthritis: investigations

1 *Synovial fluid analysis*: aspirate the joint to dryness (see p946) and send fluid for	
â€¢ WBC	Fluid may be placed in EDTA tube
â€¢ Microbiology	Fluid into sterile container and a sample into blood culture bottles and for AFBs

â€¢ Polarized microscopy	For crystals; fluid into sterile container.
2 *Take blood for*	
â€¢ Blood cultures	
â€¢ FBC	WBC high in infection and crystal arthritis
â€¢ CRP/ESR	Elevated with an inflammatory arthritis Elevated ESR and normal CRP suggest SLE
â€¢ U&Es, LFTs	May be impaired with sepsis
â€¢ Glucose	?Diabetic
â€¢ Uric acid	?Gout
â€¢ Clotting	Bleeding diathesis causing haemarthrosis
â€¢ Immunology	RF, ANA, anti-dsDNA, complement levels (?RA or SLE).
3 *X-ray the joint:* Chondrocalcinosis suggests pseudogout. But *not* helpful in the early diagnosis of a septic arthritis as the appearance may be unchanged for up to 2 weeks in infection.	

4 *Sepsis screen*: Cervical, rectal, and throat swabs.

Aspirate any cutaneous pustules for gram stain in patients with suspected gonococcal infection.

Indications for synovial fluid aspiration in casualty

- Suspected septic arthritis
- Suspected crystal arthritis
- Suspected haemarthrosis
- Relief of symptoms by removal of effusion in degenerative arthritis

Contraindications to joint aspiration

- Overlying sepsis
- Bleeding diathesis

P.739
P.740

Septic arthritis

The commonest pathogen in the UK is *Staph. aureus* (70%). *N. gonorrhoea* is a common cause in the young sexually active population. Other important causes include *Streptococci. H. influenzae* should be considered in children.

Management

- Admit and inform orthopaedic team.
- Aspirate the joint to dryness. Liaise with the orthopaedic team and consider early arthroscopy to facilitate effective joint washout especially if inflammatory markers are slow to fall.
- Strict rest for the joint (bed rest) and no weight bearing on infected joints.
- Analgesics (NSAIDs). Consider adding H_2-antagonist if history of dyspepsia.

Antibiotics

- Initially intravenous for 2 weeks, then oral for a further 4 weeks.
- Emperically start with *flucloxacillin* 1g q6h and *benzyl penicillin* 1.2g q4h. For penicillin allergy use *vancomycin* and *clindamycin*. In young children use cefotaxime to cover *H. Influenzae*.
- (NB: aminoglycosides are *not* effective in the acid pH of an infected joint; erythromycin penetrates the synovial fluid poorly.)
- Review antibiotics when microbiology available.
- For gonococcal arthritis, treat with i.v. *benzyl penicillin* 1.2g q4h for 7 days and then po *amoxycillin* 500mg tds for 10 days. Remember to trace and treat contacts (liase with GU medicine team).

Crystal arthropathy

Management

- May usually be managed as an out-patient.

- Bed rest.
- Analgesics. *NSAIDs*, e.g. diclofenac SR 75 mg bd (use cautiously in the elderly, patients with peptic ulceration, or patients with cardiac failure, renal, or liver disease).
- *Colchicine* is a good alternative if NSAIDs are contraindicated. Give 1mg initially followed by 500Âµg every 6 hours for the first 48 hours, maintenance dose 500Âµg bd.
- Give one dose of corticosteroid (*prednisolone* EC 30mg po) to help reduce the inflammation acutely and reduce symptoms. Do *not* give steroids if there is any possibility of septic arthritis.
- Rheumatology consultation if symptoms fail to settle; intra-articular corticosteroid may be given.
- Both allopurinol and probenecid are contraindicated during acute gout as both may prolong symptoms. They may be started for prophylaxis when the acute attack has settled if the patient has had more than three attacks of acute gout in 1 year, if tophi are present, or serum uric acid levels are high. Initiation of these drugs should be accompanied by either a NSAID or colchicine for the first 2 weeks.

Polyarthritis

Presentation

- Pain
- Stiffness (esp. early morning)
- Loss of function
- Joint inflammation

Differential diagnosis

Rheumatoid arthritis

Seronegative arthritis

- Psoriatic arthropathy
- Reactive arthritis
- Ankylosing spondylitis
- Enteropathic arthritis

Systemic lupus erythematosus

Crystal arthropathy

- Chondrocalcinosis
- Gout

Infections

- Viral
- Bacterial

Miscellaneous

- Sarcoid: associated with erythema nodosum (20%), and a transient RA like polyarthritis or acute monoarthritis.
- BehÃ§et's syndrome: polyarthritis (9 erythema nodosum) with painful orogenital ulceration and iritis.
- Familial mediterranean fever: occurs in middle eastern individuals with recurrent attacks of fever, arthritis (usually monoarticular), abdominal or chest pain (pleurisy).
- Transient polyarthritis may be associated with SLE, bacterial endocarditis (p120), para-infectious, Reiter's,

reactive arthritis, and Henochâ€“SchÃ¶nlein purpura.

Investigations

- Aspirate a large affected joint and analyse synovial fluid (see p946)
- Blood cultures if appropriate
- FBC with differential count
- CRP and/or ESR
- Biochemical profile (U&Es, LFTs, urate) and glucose
- Rheumatoid factor, ANA, anti-dsDNA (RA and SLE)
- Complement levels
- Viral serology
- X-rays (may show chondrocalcinosis typically knees and wrists, or early changes of rheumatoid arthritis with periarticular osteoporosis).

Management

General measures

- Bed rest: rest for the affected joints.
- NSAIDs, e.g. indomethacin 50mg tds adjusting dose according to symptoms and response (caution in elderly patients, patients with dyspepsia, asthmatics, and patients on anti-coagulants).
- Consider specific treatment of underlying condition (see above).
- Consider the need for physiotherapy and exercise regimens to reduce long-term disability.

Antibody	Association
Rheumatoid factor inflammatory	Rheumatoid arthritis and many disorders
ANA	SLE and many autoimmune disorders
Anti-dsDNA	SLE
ENA	Extractable nuclear antigen consists of
	RNP
	Ro (SSA)
	La (SSB)
	Anti-sm
	Anti-centromere
	SCL-70
	Jo-1
	Anti-cardiolipin
RNP	MCTD

	SLE
Ro (SSA)	Primary SjÃ¶grens, SLE
La (SSB)	Primary SjÃ¶grens
Anti-sm	SLE, chronic active hepatitis
Anti-centromere	Limited systemic sclerosis
SCL-70	Systemic sclerosis (diffuse)
Jo-1	Polymyositis
Anti-cardiolipin	SLE, anti-phospholipid syndrome

Rheumatoid arthritis

Clinical features

- Typically young women (F : M, 3 : 1).
- Symmetrical polyarthritis involving the small joints of the hands and feet.
- May present as a relapsing or persistent monoarthritis.
- All synovial joints are involved. Signs most common in hands, feet, knees but remember synovial joints of spine (and atlantoaxial joint/ligaments) and larynx (aryetenoid

joints).

- Extra-articular manifestations: vasculitis, subcutaneous nodules, lymphadenopathy, peripheral neuropathy, anaemia (normochromic normocytic, Fe deficiency, drug-induced aplasia, haemolytic), ocular involvement, pleurisy, pericarditis, pulmonary fibrosis.

Management

- General measures as before (p742).
- Early steroids reduce long-term joint destruction.
- Symptomatic treatment with NSAIDs.
- Long-term immunosuppressive therapy with methotrexate, gold, sulphasalazine, penicillamine, azathioprine, and hydroxychloroquine are all used.

Seronegative arthritides

Psoriatic arthropathy

Clinical features

- May present as an asymmetrical large or small joint oligoarthritis, symmetrical polyarthritis, or clinical picture similar to RA or AS. Joint destruction may be extensive (arthritis mutilans).
- Look for rash (scalp, behind ears, umbilicus, natal cleft), nail changes (pitting, onycholysis, ridging).

Management

- Treatment is as for rheumatoid arthritis with NSAIDs as the

mainstay.

- Avoid chloroquine as this precipitates psoriasis.

Reactive arthritis

Clinical features

- Typically young sexually active individual with oro-genital ulcers (painless), conjunctivitis (which may progress to iritis), rash (solesâ€”keratoderma blenorrhagica).
- May occur following non-specific urethritis or infection with *Shigella, Salmonella, Yersinia*, or *Campylobacter*.

Treatment

- NSAIDs are the main therapy.
- See p746 for Reiter's syndrome.

Practice point

- Marked morning joint pain or stiffness is most likely to be due to rheumatoid arthritis.

Reiter's syndrome

Clinical features

- Comprises a triad of seronegative arthritis, non-specific urethritis, and conjunctivitis.

- Skin lesions are psoriasiform (keratoderma blenorrhagicum) with brown macules progressing to pustules on the soles and palms.
- The arthritis begins 72 weeks after infection and the lower limb joints are most commonly affected (asymmetrical) and resolves over months; occasionally the skin lesions and arthritis progress to typical psoriatic arthropathy.
- It may be associated with a sterile urethral discharge and mild dysuria. Erosive lesions may affect the penis (circinate balanitis) or mouth.
- Rarely progresses to give aortic incompetence, heart block, pericarditis.

Treatment

NSAIDs, and sometimes steroids are the mainstay of therapy.

Ankylosing spondylitis

Clinical features

- Enquire about axial skeleton involvement (lower lumbar back pain with early morning stiffness).
- Peripheral joint involvement (740%), uveitis (p428), anaemia of chronic disease, and progressive immobility may be found.

Management

- NSAIDs for pain.
- Exercise to try to prevent progressive immobility.
- Sulphasalazine may be tried for joint disease.

- Refer to a rheumatologist for long-term management.

Enteropathic arthritis

- Large joint arthritis often coincides with active inflammatory bowel disease.
- Arthritis may predate the onset of intestinal symptoms; often there are other extra-intestinal manifestations (e.g. erythema nodosum and iritis).
- Treatment of colitis improves arthritic symptoms.

Infections

- *Viral*: rubella, parvovirus B19 (common, often presents with a generalized rash), and HIV seroconversion may present with polyarthritis.
- *Bacterial*: *Gonococcus* (rash, tenosynovitis, sexually active), *Staphylococcus* (immunosuppressed with septicaemia and seeding to several joints), infective endocarditis (vasculitic lesions, heart murmur).
- *Treatment*: see p295.

Vasculitis

The term vasculitis denotes an inflammatory reaction with destructive change of blood vessel walls. The vasculitides are classified into *primary* and *secondary* types.

Classification

Primary systemic vasculitis (simplistic classification)

	Primary	Secondary
Large arteries	Giant cell arteritis, Takayasu's arteritis	Aortitis 2Â° to RA or syphilis
Medium arteries	Polyarteritis nodosa, Kawasaki	Infection, e.g. HBV
Small and medium arteries	Churgâ€“Strauss, Wegener's, microscopic polyangiitis	Vasculitis 2Â° to RA, SLE, systemic sclerosis, drugs, or HIV
Small vessel	Henochâ€“Schonlein purpura, hypersensitivity vasculitis	Drugs, HCV or HBV infection

Causes of secondary vasculitis

- Infective endocarditis
- Malignancy
- Rheumatoid arthritis
- Systemic lupus erythematosus
- Cryoglobulinaemia (strongly associated with hepatitis C)
- Drug reaction

- Organ involvement varies with the type of vasculitis but commonlyincludes skin, joints, kidneys, lung, and nervous system

Presentation

- Arthralgia or arthritis, myalgia
- PUO
- Generalized systemic illness, e.g. weight loss, malaise
- Rashes: splinter haemorrhages, nail fold infarcts, purpura, livedo, nodules
- Renal disease: haematuria, proteinuria, hypertension, renal failure
- Lung disease: haemoptysis, cough, breathlessness, pulmonary infiltrates
- Neurological disease: mononeuritis multiplex, sensorimotor polyneuropathy, confusion, fits, hemiplegia, acute cerebral syndrome.

Causes of lung haemorrhage and renal failure

- Goodpasture's syndrome
- Wegener's granulomatosis
- Microscopic polyarteritis
- Systemic lupus erythematosus
- Leptospirosis

Causes of renal failure only (no lung haemorrhage)

- Anti-GBM disease
- Small vessel vasculitis
- Secondary vasculitis
- Medium vessel vasculitis (rare)

ANCA

c-ANCA (anti-neutrophil A-proteinase 3)

Wegener's granulomatosis

Microscopic polyarteritis

p-ANCA (anti-myeloperoxidase or elastase)

Microscopic polyarteritis

Churgâ€“Strauss syndrome

Atypical ANCA

Ulcerative colitis (also x-ANCA)

Sclerosing cholangitis

ANCA tests need to be interpreted in the clinical context. ANCA positive tests are seen in infection, malignancy, and a wide range of connective tissue disorders. A negative ANCA does not exclude any of the above.

Systemic lupus erythematosus (SLE): Assessment

This is a chronic autoimmune disorder characterized by the production of a wide range of autoantibodies against both

intracellular and cell surface antigens, though most often with ANA. It commonly affects young women (1 : 3 000 in the UK) and is ten times more common in West Indian blacks.

Patients with SLE may present to A&E in one of two ways:

- Known diagnosis of lupus having become acutely unwell. Clinically one has to determine whether their symptoms reflect disease activity, an underlying infection which may precipitate a flare up of the disease, or an unrelated condition.
- As a presenting diagnosis; the attending physician should be alert to the varied presentations of lupus.

Clinical features

Constitutional (90%)	Fever, malaise, weight loss
Musculoskeletal (90%)	Arthralgia, myalgia, myositis, deforming arthropathy (Jaccoud's) 2Â° to ligament and capsular laxity, aseptic necrosis 2Â° to steroid therapy
Cutaneous (80â€“90%)	Butterfly rash, photosensitive rash, discoid lupus, Raynaud's phenomenon, purpura, scarring alopecia, livedo reticularis, urticaria
Haematological (75%)	Thrombocytopenia, anaemia (normochromic normocytic, Coomb's +ve in 15%), leukopenia

	and lymphopenia
Neuropsychiatric (55%)	Depression, psychosis, fits, hemiplegia, cranial nerve lesions, ataxia, chorea, aseptic meningitis/encephalitis
Renal (50%)	Glomerulonephritis, nephritis or nephrotic syndrome, proteinuria, hypertension
CVS or RS (40%)	Pleurisy, pericarditis, pleural or pericardial effusion, Libmanâ€“Sacks endocarditis, shrinking lung syndrome
Aphthous ulcers (40%)	

Urgent investigations

â€¢ FBC	Anaemia, â†“WCC, and â†“plts (see above)
â€¢ U&Es, creatinine	Renal failure
â€¢ ESR	Elevated with disease activity
â€¢ CRP	Typically normal. â†‘ suggests infection
â€¢ APTT	Prolonged if there is an â€˜anti-cardiolipinâ€™ antibody (IgG or IgM)

â€¢ Blood cultures	Infection-induced flare-ups
â€¢ Urine	Dipstick for proteinuria or haematuria, microscopy for casts, culture for infection
â€¢ CXR	Infection or pleurisy
â€¢ ABG	Hypoxia with infection.

Practice point

- SLE in often characterized by a high ESR and a normal CRP.

Systemic lupus erythematosus: management

Other investigations

â€¢ Immunology	ANA, DNA, ENA, ACA, complement levels
â€¢ LFTs	Usually normal
â€¢ Viral	PCR for cytomegalovirus
â€¢ Urine	24 hour collection for creatinine clearance and protein excretion.

Points to note

- *Immunology*
    - >95% are ANA +ve (dsDNA antibody is almost pathognomonic of SLE)
    - Anti-dsDNA antibody titre may correlate with disease activity
    - Low complement levels correlate with disease activity (and renal involvement)
    - 40% are rheumatoid factor positive.
- Pneumococcal and meningococcal infections are more common in patients with SLE as a consequence of either hereditary or acquired deficiencies of the components of the complement pathway.
- Immunosuppressive therapy renders patients susceptible to the usual range of opportunistic infections including pneumocystis, cytomegalovirus, and mycobacteria.
- Chest and urine are the commonest sources of infection in clinical practice.

- Patients with disease activity classically have an elevated ESR but a relatively normal CRP.

An elevated CRP should alert you to look for an underlying infection.

Management

- *Prednisolone* 30â€“60mg od.
- Additional *immunosuppressive therapy* such as pulsed methyl prednisolone, azathioprine, or cyclophosphamide should be given on consultation with a rheumatologist.
- *Antibiotics* if infection is suspected (e.g. cefotaxime) which will treat most chest or urinary tract infections. If the source is known then anti-microbial therapy can be more rationally prescribed.
- *Hydroxychloroquine* (200mg/day) may be added if there is cutaneous or joint involvement.

Wegener's granulomatosis and microscopic polyarteritis nodosa (PAN) 1

- Both of these small vessel vasculitides may present to casualty with acute renal failure (rapidly progressive glomerulonephritis).
- Wegener's granulomatosis classically involves the upper and lower respiratory tracts and the kidneys.

Clinical features

â€¢ Systemic features	Fever, malaise, weight loss
â€¢ Upper respiratory	Nasal discharge, nose bleeds, sinusitis, collapse of the nasal bridge, deafness (all suggest a diagnosis of Wegener's)
â€¢ Lower respiratory	Shortness of breath, haemoptysis, cavitating lung lesions
â€¢ Kidneys	Nephritis with deranged renal function, haematuria, proteinuria, and active urinary sediment
â€¢ Musculoskeletal	Myalgia, arthralgia
â€¢ Neurological	Both peripheral and central
â€¢ Ask about smoking	Strongly associated with lung haemorrhage.

Urgent investigations

â€¢ FBC	Anaemia, neutrophil leukocytosis, thrombocytosis
â€¢ Renal function	Impaired renal function or acute renal failure

â€¢ LFTs	Low albumin (nephrotic syndrome). Elevated AST, ALT, and ALP with hepatitis
â€¢ CK and AST	Elevated due to myositis
â€¢ PT and APTT	Prolonged with widespread vasculitis and DIC
â€¢ ESR and CRP	Elevated
â€¢ Blood cultures	Sepsis
â€¢ ABG	Hypoxia (haemorrhage or infection), metabolic acidosis (renal failure)
â€¢ Urine	Dipstick for blood or protein, microscopy and culture 24 hour collection for creatinine clearance and protein excretion
â€¢ Sputum	Culture (infection often precipitates lung haemorrhage)
â€¢ Calcium/phosphate	Low corrected calcium and high phosphate suggest chronicity
â€¢ CXR	Shadowing seen in lung haemorrhage or infection; cavitating lesions typically occur in Wegener's granulomatosis

â€¢ USS of the kidneys	If in renal failure to exclude obstruction.

Wegener's granulomatosis and microscopic polyarteritis nodosa 2

Immunology

â€¢ c-ANCA	Positive (see below)
â€¢ ANA, anti-dsDNA	To exclude SLE
â€¢ RF	
â€¢ Complement levels	
â€¢ Anti-GBM antibody	A positive test suggests primary anti-GBM disease such as Goodpasture's syndrome, in which there is rapid progressive glomerulonephritis and lung haemorrhage
â€¢ Cryoglobulins	To exclude as a secondary cause of vasculitis

â€¢ Hepatitis serology	Hepatitis B and C.

Miscellaneous investigations

â€¢ ECG	Baseline Â± changes of hyperkalaemia if ARF is present
â€¢ Lung function tests	Measurement of KCO (increased with lung haemorrhage)
â€¢ Echo	To rule out unsuspected indolent infective endocarditis (secondary cause of vasculitis)
â€¢ X-ray sinuses	Commonly involved in Wegener's
â€¢ Renal biopsy	Histological diagnosis (light/immunofluorescence/EM).

Management

Involve specialists early, rheumatology and renal.

Emergency management

- Patients commonly die from hypoxia (pulmonary haemorrhage, pulmonary oedema), arrhythmias (secondary to electrolyte abnormalities), and concomitant infection.

- Ensure adequate *oxygenation* and consider ventilation if necessary.
- Assess *fluid balance* and monitor urine output carefully.
- Consider *invasive haemodynamic monitoring* (CVP, arterial line, Swanâ€“Ganz catheter).
- Patients with nephritis may be volume overloaded with *pulmonary oedema*. Treat with intravenous frusemide (80â€“120mg; high doses may be required), GTN infusion, venesection, or haemodialysis or haemofiltration.
- *Correct electrolyte abnormalities*: hyperkalaemia (see p384).
- Consider urgent haemodialysis or haemofiltration in patients with ARF or hyperkalaemia (consult renal physicians).
- Treat precipitating infections empirically with *cefotaxime* until a pathogen is identified.
- Treat underlying vasculitis
    - High-dose prednisolone (60mg/day)
    - Cyclophosphamide (only after renal or rheumatological opinion)
    - Plasmapheresis (renal units).

Points to note

- The ANCA test provides a rapid screening test and shows high sensitivity for patients with small vessel vasculitis.
- Patients with Wegener's granulomatosis are classically c-ANCA positive (cytoplasmic pattern of immunofluorescence, antibody against elastase I), whilst patients with microscopic polyarteritis may be either p-ANCA (perinuclear

pattern of immunofluorescence, antibody against myeloperoxidase) or c-ANCA positive. A negative ANCA does not however preclude the diagnosis of a small vessel vasculitis.

- Underlying infection especially infective endocarditis and chronic meningococcaemia should always enter the differential diagnosis of a patient with small vessel vasculitis.
- An infectious episode such as an upper respiratory tract infection often will precipitate the presentation of a small vessel vasculitis.

Cryoglobulinaemia

Cryoglobulins are immunoglobulins that precipitate at low temperatures and dissolve on re-warming. They precipitate in the superficial capillaries or outside vessels in the coldest part of the skin to produce microinfarcts or purpura.
Cryoglobulinaemia occurs in several conditions.

- Essential cryoglobulinaemia implies the absence of an identifiable cause.
- Renal disease is associated with all three types, and is thought to involve immune-complex pathways.
- Mean age, 42â€“59 years. M : F, 2 : 3.

Type 1 monoclonal

- Type 1 cryoglobulinaemia, or simple cryoglobulinaemia, is the result of a monoclonal immunoglobulin, usually IgM or IgG.
- Associated with myelo- or lymphoproliferative disease.

- Heavy proteinuria, haematuria, and renal failure may occur (membranoproliferative glomerulonephritis).
- Serum C4 and C1q are low.

Type 2 (mixed monoclonal) and type 3 (mixed polyclonal)

- Type 2 and type 3 cryoglobulinaemia (mixed cryoglobulinaemia) contain RFs (often IgM). These RFs form complexes with the fragment, crystallizable (Fc) portion of polyclonal IgG. The actual RF may be monoclonal (in type 2 cryoglobulinaemia) or polyclonal (in type 3 cryoglobulinaemia) immunoglobulin.
- Type 2 is associated with immune complex vasculitis and 50% have evidence of renal disease. Many cases are associated with HCV infection.
- Type 3 Mixed polyclonal is associated with SLE, and systemic infections (post-streptococcal nephritis, leprosy, and syphilis). Renal involvement is also seen.

Clinical features

- Renal involvement (haematuria, proteinuria, renal failure)
- Raynaud's phenomenon
- Purpura (esp. legs)
- Arthralgia and fever
- Confusion and weakness (2Â° to hyperviscosity)
- Hepatosplenomegaly (probably a manifestation of underlying aetiology).

Management

- There is no specific treatment.
- Plasmapheresis and immunosuppressive therapy may be tried.

P.759

P.760

Giant cell arteritis (temporal arteritis)

- The commonest type of primary large vessel vasculitis in clinical practice with an incidence of 1 : 10 000. This is typically a disorder of the elderly (mean age 70 years, with a F : M ratio of 2 : 1).
- The diagnosis is made clinically (see below) and is supported by an elevated acute phase response (ESR, CRP, and thrombocytosis), and temporal artery histology.
- The classical pathological description is of a segmental granulomatous pan-arteritis but in the early stage changes may be confined to thickening of the internal elastic lamina associated with a mononuclear cell infiltrate.

Clinical features

â€¢ Headache	90%
â€¢ Temporal artery tenderness	85%
â€¢ Scalp tenderness	75%
â€¢ Jaw claudication	70%
â€¢ Thickened/nodular temporal artery	35%
â€¢ Pulseless temporal artery	40%
â€¢ Visual symptoms (incl. blindness)	40%
â€¢ Polymyalgic symptoms	40% (see p762)
â€¢ Systemic features	40%
â€¢ CVA or MI	rare

Investigations

â€¢ FBC	Normochromic anaemia, thrombocytosis
â€¢ Biochemistry	Elevated alkaline phosphatase
â€¢ ESR	ESR >50mm in the first hour, 95% of cases
â€¢ CRP	Elevated
â€¢ Chest x-ray	Exclude underlying bronchial carcinoma
â€¢ Urinalysis	Exclude haematuria and proteinuria
â€¢ Temporal artery biopsy.	

Management

- Patients with suspected giant cell arteritis should be started on *high-dose prednisolone immediately*, as delay may result in blindness. For most patients 40mg od is sufficient but higher dosages 60â€“80mg may be used if the patient has visual symptoms.
- All patients should have a temporal artery biopsy performed within 48 hours of commencing steroids to try to confirm the diagnosis. A normal biopsy does not exclude the diagnosis because of the â€˜skipâ€™ nature of the disease.

Practice point

- Continuous headaches in patients .60 years may indicate cranial arthritis, but may be spondylitic.1

Footnote

1

Hawkes C (2002) *Hosp Med* 63: 732â€“42.

Polymyalgia rheumatica (PMR)

PMR is a clinical syndrome characterized by an acute phase response (high ESR or high CRP) which predominantly affects the elderly Caucasian population, median age of onset 70 years, females > males, annual incidence approximately 1 : 2500.

Clinical features

- Proximal muscle stiffness and pain without weakness or wasting.
- Systemic symptoms of malaise, fever, and weight loss.

Causes of proximal upper and lower girdle stiffness or pains

â€¢ Cervical spondylosis Â± adhesive capsulitis	No acute phase response, CPK (N)
â€¢ Lumbar spondylosis	
â€¢ Osteomalacia	
â€¢ Fibromyalgia	
â€¢ Hypothyroidism	No acute phase response, â†‘CPK
â€¢ Polymyositis/dermatomyositis	â†‘Acute phase response, â†‘CPK
â€¢ Inflammatory arthritis	â†‘Acute phase response

Investigations

â€¢ FBC	(Normochromic normocytic anaemia)
â€¢ U&Es, LFTs	[Elevated alkaline phosphatase is common (50%)]
â€¢ CPK	Normal (if high consider polymyositis or hypothyroidism)
â€¢ ESR	High (>40mm/h initially)
â€¢ CRP	High
â€¢ Rheumatoid factor	PMR may be the presenting feature of rheumatoid arthritis
â€¢ CXR	PMR symptoms may be the presenting feature of a neoplasm.

Treatment

- *Steroids*: prednisolone 20mg po od initially reducing to 5â€“10mg od over 2â€“3 months and very slow reduction thereafter. Some patients may require treatment for years.
- Monitor response with symptoms and ESR.

Points to note

- Polymyalgia rheumatica and giant cell arteritis form part of a clinical spectrum of disease and up to 40% of patients with biopsy-proven giant cell arteritis have polymyalgic

symptoms.

- Polymyalgic symptoms may be the presenting feature of an underlying neoplasm or connective tissue disease.
- Polymyalgic symptoms should respond dramatically to prednisolone. Failure to respond should alert the clinician to the possibility of an underlying neoplasm or connective tissue disease.

Practice point

- Never diagnose polymyalgia rheumatica in a patient, 50 years old.

Back pain: assessment

Approximately 5% of all medical consultations in the UK are for back or neck pain. In the majority of patients no definite anatomical diagnosis is made (non-specific back pain) but it is important not to miss the sinister causes of back pain.

Causes of back pain

Mechanical back pain

- Spondylolisthesis
- Spondylosis
- Intervertebral disc prolapse
- Spinal stenosis (claudication type pain)
- Apophyseal joint disease (exacerbated by lumbar extension, cervical or thoracic rotation)
- Non-specific back pain

- Trauma

Inflammatory back pain

- Rheumatoid arthritis
- Seronegative spondyloarthritides
    - Psoriatic
    - Ankylosing Spondylitis
    - Reiter's
    - Enteropathic
    - BehÃ§et's

Referred pain

- Aortic aneurysm
- Pyelonephritis, renal calculus
- Pancreatitis

Causes of â€˜sinisterâ€™ back pain

- Infection (discitis/epidural abscess)
- Malignancy
- Myeloma
- Osteoporotic crush fracture
- Paget's disease

History

Is pain likely to be mechanical, inflammatory, or sinister in origin?

- Mechanical back pain is exacerbated by prolonged sitting or standing, relieved by movement, and precipitated by trauma.
- Inflammatory back pain is characterized by prolonged early morning stiffness and is relieved by exercise.
- Sinister back pain (e.g. malignancy and infection) often lead to pain at night, constant pain, local bony tenderness, and may be accompanied by other systemic symptoms.
- Are there any sensory or motor symptoms? Ask specifically for any change in bowel or bladder function.

Examination

- General: look for evidence of malignancy.
- Spine (palpation for tenderness, muscle spasm, cervical spine flexion, extension, rotation and lateral flexion, thoracic spine rotation, lumbar spine flexion, extension, side flexion, compression of sacroiliac joints.
- Neurological examination looking specifically for absent ankle jerks (slipped disc) or long-tract signs in the legs. S1 nerve root signs and symptoms can be produced by a lesion in the region of the upper lumbar cord (central disc prolapse compressing the S1 nerve root).
- Always do a rectal examination and test perineal sensation.

Practice points

- Back pain at night suggests a sinister cause such as cancer or infection.
- Patients with acute onset of back pain and signs suggestive of a high lesion (eg L1- L3/4) may have weak thighs and

absent knee jerks, and are unlikely to have a disc lesion and may have a tumour.

Back pain: management

Investigations

Patients with back pain occurring at night and patients with neurological signs warrant investigation.

- X-rays of spine 9 CXR (?malignancy)
- FBC and ESR (elevated with sinister causes of pain)
- Biochemical profile (calcium, alkaline phosphatase, and phosphate)
- Immunoglobulins and protein electrophoresis (?myeloma)
- Acid phosphatase
- PSA
- Bence-Jones protein and urine protein electrophoresis.

Further imaging

- CT scan
- MRI scan (superior to CT for imaging the spinal cord and roots)
- Technetium bone scan (â€™hot-spotsâ€™ identify neoplastic or inflammatory lesions)
- Myelography
- Radiculography (to look for cord or root compression).

Management

- Analgesics
- Bed rest
- Physiotherapy
- Appropriate referral to a specialist.

Prolapsed intervertebral disc

Acute postero-lateral herniation of a lumbar disc, usually L4â€“L5 or L5â€“S1, is a common cause of acute incapacitating lower back pain. There is often a clear precipitating event (e.g. lifting) and pain may radiate in the distribution of the L5 or S1 nerve root.

Patients should be examined carefully for

- Paraspinal muscle spasm is often prominent
- Straight leg raising is typically reduced on the affected side
- Look for nerve root signs and test sacral and perineal sensation. Always do a rectal examination
- L5 lesion leads to weakness of extensor hallus longus, ankle dorsiflexion, and ankle eversion and altered sensation is perceived in the L5 dermatome
- S1 lesion leads to weakness of ankle plantar flexion, ankle eversion, and a diminished or lost ankle jerk and altered sensation is perceived in the S1 dermatome.

Treatment

- If the X-rays reveal a fracture, refer the patient to the orthopaedic team; severe pain from inflammatory arthritides should be referred to the rheumatologists.

- Majority of patients respond to conservative management.

- Bed rest until the acute pain subsides followed by mobilization and physiotherapy (patients may often be managed at home with instructions to return to the GP or doctor for review in 2â€“3 weeks).
- Non-steroidal anti-inflammatory agents.
- Physiotherapy.

Neurosurgical emergencies presenting as back pain

An acute disc prolapse at the L2/3 level may cause bilateral multiple root lesions and may affect bladder and bowel function (cauda equina syndrome).

This requires immediate investigation:

- Acute cauda equina compression (p508)
- Acute cord compression (p508)

C_1-esterase inhibitor deficiency (angioneurotic oedema)

This condition may be inherited or acquired, occurring approximately in 1 : 50 000 in the UK.

Hereditary

- Autosomal dominant inheritance
- Usually presents in the second decade
- Characterized by low serum concentrations of complement

components C2, C4, and C_1-inhibitor, but normal C1 and C3 levels.

Acquired

- Paraneoplastic syndrome: autoantibody against C_1-esterase inhibitor
- Characterized by low serum concentrations of complement components C1, C2, and C4.

Clinical features

- Laryngeal oedema (48% of attacks); may be life threatening
- Subcutaneous oedema (91% of attacks) affecting face, buttocks, genitals, and limbs. Usually non-itchy
- Abdominal symptoms: pain, vomiting, and diarrhoea.

Precipitating factors include

- Stress
- Infection
- Pre-menstrual
- Oestrogen-containing contraceptive pill
- Angiotensin-converting enzyme inhibitors.

Management

Acute severe attack

- C_1-esterase inhibitor plasma concentrate (an intravenous infusion of 1000 to 1500 units) usually effective in 30â€“60 minutes.
- Fresh frozen plasma 2â€“4 units may be given if C_1-esterase inhibitor plasma concentrate is not available.

Laryngeal oedema

- If a patient is admitted with laryngeal oedema 60% oxygen should be given immediately, blood gases should be checked, and a senior anaesthetist or ENT surgeon called as intubation or tracheostomy may be required (p914).
- Intramuscular adrenaline 0.5â€“1ml, 1 : 1000 (see p264).
- Hydrocortisone 200mg iv.
- Chlorpheniramine 10mg iv may be administered initially prior to the infusion of C_1-esterase inhibitor.

Prophylaxis

Those with greater than 1 attack per month:

- Tranexamic acid (1â€“1.5g 2â€“4 times daily). Effective in 28%.
- Attenuated androgens, e.g. danazol (unlicensed indication).

Editors: Ramrakha, Punit S.; Moore, Kevin P.
Title: *Oxford Handbook of Acute Medicine, 2nd Edition*

Chapter 13
Dermatological emergencies

Cutaneous drug reactions: presentation

- *Maculopapular erythema* with variable pruritus and scaling. Resolves over 2 weeks once the drug is stopped. 46% of cutaneous drug reactions.
- *Urticaria/angioedema:* accounts for ~25% of drug reactions. Sudden onset of individual pruritic erythematous lesions which resolve within 24 hours. Angioedema may involve mucous membranes and can be associated with life-threatening anaphylaxis (see p264). Aspirin, morphine, codeine act directly in mast cells to liberate histamine in sensitive individuals. Penicillin (and aspirin) can cause an IgE-mediated or IgG complement-fixing allergic reaction. Urticarial eruptions associated with serum sickness may be persistent and can be associated with systemic symptoms.
- *Fixed drug eruption:* characterized by a few well-demarcated painful erythematous lesions which frequently blister often involving the face, hands, forearms, and genitalia. Local hyperpigmentation persists after recovery. Rechallenge is associated with recurrent lesions in the

same location. Drugs implicated include sulphonamides, tetracyclines, barbiturates, salicylates, and dapsone. Represents 10% of cutaneous drug reactions.

- *Photosensitive drug eruptions:* cutaneous reaction limited to exposed sites with characteristic sparing of certain areas. May be due to either a photoallergic (immune-mediated, e.g. chlorpromazine, sulphanilamide, amiodarone) or phototoxic (non-immune, e.g. tetracyclines, sulphonamides, griseofulvin, naproxen, high-dose frusemide) reaction. Some drugs may induce photosensitive disorders suchas porphyria cutanea tarda or photo-onycholysis.
- *Erythema multiforme/Steven's Johnson syndrome:* associated with 10% of drug reactions. Sudden onset of erythematous lesions affecting the skin and mucous membranes. Acral sites are preferentially involved and individual lesions may have necrotic or targetoid appearances. Associated with fever, malaise, and sore throat due to mucous membrane involvement (Steven's Johnson syndrome) and rarely confluent epidermal necrolysis as seen in toxic epidermal necrolysis (see p786). Drugs implicated include salicylates, sulphonamides, penicillin, sulphonylureas, and barbiturates. Stop the drug; give steroids (prednisolone 30mg/day).
- *Exfoliative dermatitis:* presents as erythroderma. 4% of drug reactions. Causative drugs include barbiturates, salicylates, penicillin, sulphonamides, and sulphonylureas.
- *Toxic epidermal necrolysis:* there are two types. In adults it is an immunological disease provoked by drug hypersensitivity, but in babies it is due to the direct necrolytic effect of a *Staphylococcal* toxin. It may be caused by many different drugs including penicillins, sulphonamides and other antibiotics, blood products, NSAIDs, and anti-convulsants.

Cutaneous drug reactions: management

Points to note

- Usually develop within 1â€“2 weeks following initiation of therapy but occasionally reactions present later (due to cumulative toxicity).
- Development of extensive angioedema is associated with a risk of anaphylaxis and shock characterized by hypotension, bronchospasm, oropharyngeal irritation associated with angioedema, flushing, or urticaria and acral oedema.
- Patients who present with either erythema multiforme or Steven's Johnson syndrome may develop confluent areas of epidermal necrolysis as seen in toxic epidermal necrolysis (p786).
- Peripheral blood eosinophilia is rare.
- Intravenous routes of drug administration are more likely to be associated with anaphylaxis.
- Cutaneous drug reactions are common in treatment of HIV disease.

Management

- Severe angioedema and anaphylaxis require immediate treatment (see p264).
- Seek specialist advice for severe Steven's Johnson syndrome or toxic epidermal necrolysis.
- Stop any responsible drugs and prescribe an alternative if necessary. Hospitalized patients receiving numerous drugs should be assessed carefully and all non-essential therapy

discontinued.

- Prescribe oral non-sedating or sedating anti-histamines with simple emollients and medium-potency topical steroids. Short courses of systemic steroids may be required in erythema multiforme or Steven's Johnson syndrome.
- Pyrexia may occur with cutaneous drug reactions but underlying infection should always be excluded.
- There should be clinical improvement within a few days: persistent reactions should prompt a search for other causes.
- Although rechallenge with a suspected drug can provide a definitive diagnosis, reactions may be more severe and can lead to fatal anaphylaxis or severe toxic epidermal necrolysis.
- Specific RAST can be used to measure serum IgE antibody production in patients with penicillin allergy. However, a positive BPO-specific RAST for penicillin is only seen with the major antigenic determinants and a negative reaction does not exclude penicillin allergy.
- Skin biopsies can be useful for specific forms of cutaneous drug reactions such as fixed drug eruption and erythema multiforme.

Erythroderma

Presentation

- Erythroderma may be acute or chronic. Acute erythroderma is more likely to present as an emergency.
- There is generalized erythema associated with exfoliation.

- Scaling can be fine (pityriasiform) or coarse (psoriasiform).
- Patients may be febrile or hypothermic because of loss of temperature control mechanisms.
- Chronic erythroderma may be associated with nail dystrophy, diffuse hair loss, and ectropion. Palmo-plantar hyperkeratosis and peripheral lymphadenopathy may be prominent.

Causes

Common causes:	Eczema, psoriasis, drug reactions
Rare causes:	Cutaneous T-cell lymphoma, pityriasis rubra pilaris, toxic shock syndrome, Kawasaki disease, sarcoidosis

Investigations

- Monitor FBC, U&Es, albumin, calcium, and LFTs regularly.
- Blood cultures and skin swabs should be performed and sustained pyrexia, hypotension, or clinical deterioration should prompt a search for underlying sepsis.

Management

General measures

- Nurse in a warm room with regular monitoring of core

temperature and fluid balance. Patients should be nursed on a pressure-relieving mattress and/or LyofoamÂ® if necessary.

- Encourage oral fluids and high calorific food and protein supplements. Nasogastric feeding may be required. Avoid intravenous canulae because they can act as a potential source of infection.
- Monitor fluid balance closely: daily weights and clinical examination (as allowed by the exfoliation).

Specific therapy

- The skin should be treated at least four times daily with emollients such as 50% white soft paraffin/50% liquid paraffin or EpadermÂ®.
- A daily bath should be supplemented with emollients such as oilatum or balneum.
- Oral sedating anti-histamines such as hydroxyzine (10â€“100mg in divided doses) may be used and the dose adjusted according to severity and weight.
- Application of mild or potent topical steroids may be appropriate but liaise with specialist at early opportunity.
- In eczema, systemic treatment with prednisolone, azathioprine, or cyclosporin may be appropriate, and in psoriasis, acitretin, methotrexate or cyclosporin may be required. Liaise with specialist prior to embarking on this approach.

Complications

- Hypothermia

- Infection
- Hypoalbuminaemia
- High output cardiac failure.

Practice point

- Non-responsive or relapsing eczemic rash should suggest contact dermatitis.

Urticaria: assessment

Presentation

- Urticaria presents as erythematous pruritic evanescent areas of oedema involving the superficial dermis which may be small weals or larger plaques. Lesions present suddenly and will resolve within 24 hours, although new lesions may develop repeatedly.
- In severe urticaria systemic symptoms may predominate with the development of anaphylaxis characterized by histamine shock and collapse (see p264). Features include hypotension, bronchospasm, angioedema, and diffuse urticaria.
- Presence of extensive urticarial lesions does not imply anaphylaxis in the absence of systemic features. Drug sensitivities and reactions to radiographic contrast media are more likely to produce anaphylaxis.

Causes

- Bee/wasp stings, drug reactions (penicillin common, aspirin

and non-steroidal anti-inflammatory drugs), radiographic contrast media, blood products, food sensitivity such as nuts and shellfish.

- Physical causes of urticaria such as dermographism, pressure, vibration, cold, aquagenic, solar, and cholinergic (heat/exercise).
- Contact urticaria.
- Hereditary angioedema associated with a genetic deficiency of the enzyme C_1-esterase inhibitor (see p768).
- Malignancy and autoimmune disorders such as lupus associated with a functional deficiency of C_1-esterase inhibitor.
- Chronic idiopathic urticaria possibly due to autoantibodies produced against the low affinity IgE receptor.

Diagnostic points

- A family history may suggest hereditary angioedema.
- In patients with chronic urticaria, ask specifically about possible physical causes (e.g. induced by cold, exercise, water, pressure, heat, and rarely light and vibration. Dermographism is the most common form of physical urticaria; briskly stroking the skin with a firm object produces linear weals.
- Contact urticaria usually occurs within minutes after direct contact with various agents such as plants, aeroallergens, foods such as cheese, eggs, and fish and in healthcare workers after contact with latex. Contact sensitivity to latex products is also associated with a high incidence of anaphylaxis.
- If individual urticarial lesions persist for more than 24 hours a diagnosis of urticarial vasculitis is likely. Such lesions are tender and painful rather than pruritic and may

appear bruised. Unlike other forms of urticaria this diagnosis should be established by histology.

- Patch tests are not indicated in urticaria. Prick tests will indicate if individuals are atopic but rarely may also be useful in establishing a specific cause of contact urticaria (should only be carried out under medical supervision because of a risk of anaphylaxis). Total serum IgE levels may be elevated in atopic individuals. Specific IgE RAST may be used to identify potential sensitivities but can produce false negative/positive results.

Urticaria: management

- Anaphylactic reactions require immediate treatment (see p264).
    - Lay the patient flat.
    - Secure the airway and give oxygen.
    - Give intramuscular adrenaline 0.5mg (0.5ml of 1 in 1000 adrenaline injection) and repeat every 5 minutes according to BP, pulse, and respiratory function. iv adrenaline may be required if the patient is severely ill with poor circulation (see p264).
    - Start iv fluids if hypotensive.
    - Give iv hydrocortisone 100â€“300mg and chlorpheniramine 10â€“20mg. Continue H_1-antagonist (e.g. chlorpheniramine 4mg q4â€–6h) for at least 24â€–48 hours; longer if urticaria and pruritis persist.
    - If the patient continues to deteriorate, start iv aminophylline infusion (see p213). Patients on Î²-blockers may not respond to adrenaline injection and require iv salbutamol infusion.

- Hereditary angioedema may present with extensive urticaria and angioedema associated with systemic features including anaphylaxis. Management is discussed on p768.
- Severe acute urticaria with or without angioedema is usually not life threatening unless associated with systemic features of anaphylaxis.
    - Give oral anti-histamines such as hydroxyzine 25mg or chlorpheniramine 4mg.
    - A single dose of prednisolone 50mg orally may be prescribed but should not be continued indefinitely without specialist advice.
    - When the patient's condition has stabilized, they can be discharged on regular maintenance treatment with an oral non-sedating anti-histamine such as cetirizine 10 to 20mg daily, levocetrizine 5mg daily, desloratidine 5mg daily, or fexofenadine 180mg daily (sedative anti-histamines such as hydroxyzine or chlorpheniramine are usually not required for maintenance treatment of chronic urticaria).
- Patients with no specific identifiable cause of acute urticaria and all patients with chronic or physical forms of urticaria should be referred for specialist advice.
- Patients with contact sensitivity to latex should use alternatives such as AllergardÂ® gloves, vinyl gloves, or non-sterile copolymer gloves. Such individuals should be warned to use only non-latex polyurethane condoms.

Autoimmune bullous disease

Presentation

- Intact pruritic fluid-filled blisters
- Very itchy urticated erythematous plaques (pre-bullous eruption)
- Cutaneous and/or mucosal erosions.

Causes

- *Common:* bullous pemphigoid, pemphigus vulgaris
- *Rare:* pemphigoid gestationes (second/third trimester), dermatitis herpetiformis, pemphigus foliaceus, epidermolysis bullosa acquisita, bullous lupus erythematosus, linear IgA disease, paraneoplastic pemphigus.

Poor prognostic features

- Pemphigus (higher mortality than other autoimmune bullous disease)
- Age >60 years
- Extensive involvement.

Diagnosis

- Biopsy of a fresh blister for histology and a small fragment of perilesional skin should be sent for direct immunofluorescence studies.
- Serum should also be sent for indirect immunofluorescence studies.

Management

Liaise with specialist at an early opportunity.

General measures

- Intact blisters should be aspirated. Examine for new blisters daily.
- Patients should be bathed daily with emollients and if necessary chlorhexidine bath additive in order to prevent secondary bacterial infection. Use diluted potassium permanganate soaks for eroded and weeping areas with non-adherent dressings such as Jelonet or Mepitel under tubofast body suit/bandages. Avoid Fegaderm or other adhesive dressings. Nurse the patient on a ClinitronÂ® bed.
- Give oral sedating anti-histamines (e.g. hydroxyzine) for pruritis.
- Potent topical steroids (e.g. Dermovate cream) should be applied to individual lesions twice daily.
- Prescribe prophylactic sc heparin for immobile elderly patients.
- Monitor fluid balance carefully, FBC, U&Es, and LFTs regularly.

Specific systemic therapy

Liaise with specialists.

- Refer severe conjunctival disease to an ophthalmologist early.
- Pemphigus requires high-dose immunosuppression (prednisolone 80â€“100mg/day) but mild disease may be controlled with less.
- Bullous pemphigoid, when localized or mild, may respond to potent topical steroids alone (e.g. Dermovate cream) or can occasionally be controlled with nicotinamide 0.5â€“2.5g/day

and antibiotics (erythromycin or tetracyclines) Extensive disease will require immunosuppression. Prednisolone 30â€“60mg/day is usually required and the dosage gradually reduced according to response (i.e. once no new blisters are formed).

- Steroid sparing agents such as azathioprine 50â€“100mg/day should also be considered for extensive disease, where response to steroids is inadequate.
- For resistant disease consider methylprednisolone, cyclophosphamide, cyclosporin, mycophenolate, IrIgs, chlorambucil, and plasmapheresis.
- Mucosal disease requires regular DiflammÂ® and tetracycline mouth washes with CorlanÂ® lozenges (hydrocortisone 2.5mg) for painful erosions. 0.1% tacrolimus in orabate is currently experimental.
- If condition deteriorates consider secondary bacterial or viral infection of cutaneous or mucosal sites.

Pemphigus is characterized by *intraepidermal* separation and acantholysis of individual keratinocytes. In pemphigus vulgaris the split is suprabasal while in pemphigus foliaceus the separation is much higher in the epidermis. Penicillamine, captopril, rifampicin, and other drugs can rarely induce a pemphigus-like syndrome which is indistinguishable from pemphigus vulgaris. This accounts for <10% of all cases of pemphigus.

Bullous pemphigoid is characterized by a *sub-epidermal* split and an inflammatory infiltrate containing eosinophils. Specialist advice is required. Exclude other causes of bullous disease such as porphyrias, drugs (NSAIDs, barbiturates, frusemide), diabetes mellitus, and bullous amyloid. Also consider bullous insect bite reaction and bullous impetigo in the differential diagnosis particularly for localized blisters. Tense blisters on

the palms and soles may be due to endogenous eczema (pompholyx) or fungal infection (tinea).

Eczema herpeticum

Presentation

- Patients with atopic endogenous eczema are predisposed to secondary herpes simplex infection. This may occur as a primary infection following an episode of herpes labialis or after contact with an affected individual.
- Patients present with a sudden deterioration of their eczema characterized by widespread vesiculo-pustular lesions which are tender and gradually become necrotic. Resolution of the condition produces extensive crusting and exudation.
- Patients are usually pyrexial and toxic with a tachycardia. Cardiorespiratory collapse is unusual.

Management

- The condition can progress rapidly and therefore localized disease should be treated aggressively. Patients should be admitted and early specialist advice is required.
- Refer patients with ocular disease to an ophthalmologist urgently.
- Extensive mucosal disease may make oral nutrition difficult and patients may require intravenous fluids.
- Perform bacterial swabs daily: secondary bacterial infection is common and if present requires treatment with systemic antibiotics.
- Topical therapy

    - Do not use topical steroids
    - Use simple emollients such as aqueous cream
    - Chlorhexidine (topical antiseptic) and diluted potassium permanganate (1/10 000) (should be pale pink in colour or it is too strong) as a soak once or twice daily for brief periods to areas of excessive exudation.
- Give oral non-sedating anti-histamines.
- Start high-dose intravenous acyclovir at the earliest opportunity (maximum 10mg/kg/8 hourly). If intravenous therapy is not possible, give valaciclovir 1000mg tds for 7 days.
- Patients with severe atopic eczema should be advised about prompt treatment of herpes labialis and to avoid contact with herpes simplex.
- Adults with herpes labialis should be advised to avoid contact with children with atopic eczema.

Herpes zoster

See p312.

Generalized pustular psoriasis

Presentation

- Rapid onset of superficial pustules, usually in a patient with typical plaque psoriasis. Pustules may be confluent or pin-point and may be studded around the periphery of typical psoriatic plaques.
- Irritant topical therapies (e.g. potent topical steroids,

vitamin D analogues, coal-tar, and dithranol preparations) may precipitate generalized pustular psoriasis in patients with â€˜unstableâ€™ psoriasis (hot tender erythematous psoriatic plaques).

- Rarely patients develop generalized pustular psoriasis without a previous history, and similar presentations can occur in pregnancy.
- Pyrexia is often accompanied by systemic symptoms such as malaise, anorexia, and arthralgia. Cutaneous infection with *Staphylococcus aureus* is common and may result in septicaemia.
- Differential diagnosis includes bullous impetigo, toxic epidermal necrolysis, staphylococcal scalded skin syndrome, autoimmune bullous disorders, and in particular subcorneal pustular dermatosis, pustular vasculitis particularly due to herpes simplex infection or drugs, and eczema herpeticum.

Natural history

- There are repeated acute episodes of generalized pustulation associated with pyrexia and systemic symptoms resolving in 5â€“7 days to produce extensive superficial crusting. Episodes recur every 7â€“10 days.
- Patients with localized palmo-plantar pustular psoriasis have a mild chronic disease which is not associated with systemic abnormalities.
- Patients with generalized disease may develop ARDS and shock due to release of cytokines or the presence of septicaemia. Elderly patients with generalized pustular psoriasis (Von Zumbusch) have a worse prognosis.

Investigations

- Monitor FBC, U&Es, and LFTs regularly. A neutrophil leukocytosis is invariable. Abnormal LFTs and â†“Ca^{2+} may occur.
- Primary bacterial or viral infection should be excluded by appropriate bacterial and viral swabs. If febrile, take blood cultures.
- Perform ABGs in hypoxic patients or those with an abnormal CXR.

Management

Liaise with specialists at an early opportunity.

- Enforce bed rest; monitor temperature and fluid balance closely.
- Oral fluids with high calorie and high protein input/supplements.

Topical therapy

- The extensive crusting and exudation of the early phase of pustulation can be treated with topical potassium permanganate (1/10 000) soaks.
- For extensive disease, nurse on a ClinitronÂ® bed in a warm room.
- Bathe daily with emollients and antiseptic washes. Treat skin at least four times daily with emollients such as 50% WSP, 50% LP, Epaderm, or aqueous cream.
- Avoid topical steroids, vitamin D analogues, coal tar, and dithranol (may cause severe irritation and exacerbation of the disease).

Systemic therapy

- Give regular oral sedative anti-histamines (e.g. hydroxyzine).
- Bacterial infection should be treated with appropriate antibiotics.
- Severe generalized pustular psoriasis may require systemic treatment with retinoids, methotrexate, or cyclosporin: seek specialist advice.

Practice point

- Psoriasis rarely becomes secondarily infected.

Toxic epidermal necrolysis (TEN) 1

Presentation

Acute onset of morbilliform or confluent erythema associated with widespread blistering (necrolysis) and skin tenderness.

Diagnostic points

- Necrolysis is used to describe confluent blistering of the skin associated with epidermal separation rather like a large burn. It should be distinguished from discrete intact blisters which are characteristic of autoimmune bullous diseases.
- There may be clinical overlap between toxic epidermal necrolysis and erythema multiforme as seen in the Steven's Johnson syndrome. Mucocutaneous involvement is common and both oral and conjunctival erosions may be present.

- TEN should be distinguished from the *staphylococcal scalded skin syndrome (SSS)*. This usually occurs in children or immunosuppressed adults and is associated with the production of staphylococcal toxins. A skin biopsy is diagnostic: in TEN there is full thickness epidermal necrosis, sub-epidermal separation, and a sparse or absent dermal infiltrate while in SSS there is suprabasal epidermal separation with an intact basement membrane.

Causes

- Idiopathic
- Drug induced [sulphonamides and occasionally other antibiotics, anti-convulsants (not described with sodium valproate), NSAIDs].

Adverse prognostic factors

- Age greater than 60 years (25% overall mortality)
- Area of cutaneous involvement greater than 50%
- Blood urea greater than 17mmol/L
- Neutropenia (neutrophil count <1 Ã— 10^9/L)
- Idiopathic aetiology.

Management

The priorities are

- Try to identify the cause and treat. Stop drug
- Supportive care: fluid balance and nutrition
- Prevent complications

- Eye care
- Screening and treatment of sepsis.

Toxic epidermal necrolysis 2

1 Identify the cause

- A specific drug is unlikely to be responsible if treatment was started after the onset of erythema, necrolysis, or mucous membrane involvement.
- A drug aetiology should be considered if TEN develops 7â€“21 days after the first administration of a drug, or within 48 hours if the drug has caused an eruption in the past.
- If patients are on several different drugs, stop all that may be a cause.

2 General supportive care

- Patients should be nursed on an air fluid or ClinitronÂ® bed in a side room. A single designated nurse should attend the patient continuously and the room should be kept warm in order to prevent hypothermia.
- Core temperature should be continuously monitored via a rectal probe and a space blanket may be required if the patient becomes hypothermic because of cutaneous vasodilatation. However, patients frequently also develop hyperthermia which may necessitate temporary cooling of the room with fans.
- LyofoamÂ® dressings should be used between the patient and bedding in order to ease mobility and skin dressings.

Emollients should be applied every 2â€“4 hours to all areas or patients can be â€˜wrappedâ€™ to improve ease of handling and reduce sheer forces on the skin. This involves covering the skin with aqueous cream generously, then applying Jelonet, followed by Sofban then Coban bandages.

- Oral mucosal surfaces should be cleaned every 4â€“6 hours and sprayed with chlorhexidine and DiflammÂ®. Mucosal involvement may produce oral erosions or constrictions affecting the oral aperture or pharynx.
- Nasopharyngeal involvement may result in airway obstruction and necessitate ventilation.
- Mucous membrane involvement usually antedates skin necrolysis for several days before presentation. Gastrointestinal involvement may be characterized by bleeding and/or a protein losing enteropathy. The net result is a profound negative fluid and nitrogen balance.
- Monitor fluid balance closely, preferably by daily weights.
- If possible, fluids should be administered orally or via a nasogastric route. Avoid iv lines to reduce the risk of sepsis. 5â€“7 litres are usually required during the first 24 hours. A protein- and energy-rich nasogastric feed should be administered (1â€“1.5 L/day).
- Daily FBC, U&Es, LFTs, amylase(â†“), phosphate(â†“), and glucose (hyperglycaemia produces an osmotic diuresis aggravating dehydration),
- CXR should be performed regularly. Pulmonary oedema and ARDS are frequent complications. ABGs should be monitored and if there is deterioration, have a low threshold for admission to ITU and ventilation.
- Prophylactic anti-coagulation should be used (subcutaneous calcium heparin 5000 units tds or enoxaparin 40mg sc od).
- Patients are frequently terrified and in considerable pain. Adequate analgesia and tranquillizers should be

administered.

- Post-inflammatory pigmentary changes are common and will gradually resolve.

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Toxic epidermal necrolysis 3

1 Prevent complications: Infection

- Central venous lines should be avoided if possible. iv lines should be discontinued as soon as possible in order to reduce infection risk.
- Several cutaneous and mucous membrane sites should be swabbed daily. Culture sputum and urine daily. Intravenous and in-dwelling catheters should be changed frequently and tips sent for culture. Perform blood cultures daily if febrile. Remember that pyrexia is a feature of TEN and does not always indicate infection.
- Prophylactic antibiotics are only indicated if the risk of sepsis is extremely high such as severe neutropenia or a heavy single strain bacterial colonization of the skin.
- Antibiotics should be started if there is positive blood, urine, or sputum culture or indirect evidence of sepsis such as hypothermia, hypotension, fever, decreasing level of consciousness, reduced urinary output, or failure of gastric emptying.
- Weeping, crusted, and exudative areas of the skin should be treated by local application of potassium permanganate soaks (1 : 10 000).
- Necrotic epidermis should be carefully removed because it forms a focus for infection. Affected skin that has not become necrotic should not be removed. Topical *Flamazine*

should be avoided as this can cause neutropenia when applied to large surface areas.

2 Prevent complications: Ocular involvement

- Corneal scarring and blindness are the commonest sequelae of TEN.
- The cornea should be examined daily by an ophthalmologist and antibiotic or antiseptic eye drops should be applied every 1â€“2 hours.
- Synechiae form usually in the second week. These can be separated using a blunt instrument several times a day but this is controversial and the advice of an ophthalmologist is essential.
- Sicca syndrome and visual impairment due to corneal neovascularization may produce corneal scarring and blindness. Symptoms usually develop several weeks after the onset of TEN.

3 Specific systemic therapy

- There is no controlled evidence that any specific systemic therapy improves prognosis. In particular there is no evidence that systemic steroids are beneficial and adverse effects are numerous. Steroids should *not* be used as a standard therapy for TEN.
- Early treatment in first 12â€“24 hours with cyclosporin (3â€“4mg/kg/day) or cyclophosphamide (150â€–300mg per day) are beneficial but neither drug is established as a standard therapy in TEN and these drugs should not be prescribed without specialist advice.
- More recently good preliminary results have been obtained

with high-dose intravenous immunoglobulin therapy used in conjunction with pulsed methylprednisolone.
Plasmapheresis may be of benefit in some patients.

Editors: Ramrakha, Punit S.; Moore, Kevin P.
Title: *Oxford Handbook of Acute Medicine, 2nd Edition*

Chapter 14
Drug overdoses

Overdoses: general approach

- Overdoses account for 15% of acute medical emergencies.
- 65% of drugs involved belong to the patient, a relative, or friend.
- 30% of self-poisonings involve multiple drugs.
- 50% of patients will have taken alcohol as well.
- The history may be unreliable. Question any witnesses or family about where a patient was found and any possible access to drugs. Examination may reveal clues as to the likely poison (e.g. pinpoint pupils with opiates) and signs of solvent or ethanol abuse and iv drug use should be noted.

Management

- Priorities are
    - Resuscitate the patient
    - Reduce absorption of the drug if possible
    - Give specific antidote if available.

- Monitor their airway (place in the recovery position) and breathing, BP, temperature, acidâ€“base and electrolytes, and treat seizures or dysrhythmias. Intubate if GCS â‰¤8, and not reversible with naloxone or flumazenil.
- Take account of any active medical problems that the patient may have, e.g. iv drug users may have concurrent septicaemia, hepatitis, SBE, pulmonary hypertension, or HIV-related disease.
- Measures to reduce gut absorption include

    - *Gastric lavage* is only effective if used up to 1 hour post OD. It is contraindicated if corrosive substances or hydrocarbons have been ingested. Protect the airway with endotracheal intubation if conscious level is impaired.
    - *Activated charcoal* (50 g as a single dose) will absorb many drugs if given within 1 hour of ingestion although its effectiveness falls off rapidly thereafter. Drugs *not* absorbed by charcoal include iron, lithium, salts, alkalis, acids, ethanol, methanol, ethylene glycol, and organic solvents.
    - Repeated administration of activated charcoal (50g every 4 hours) may also accelerate whole body clearance of some drugs by interrupting enterohepatic cycling, e.g. phenobarbitone, phenytoin, carbamazepine, digoxin, paraquat, dapsone, quinine, and slow-release preparations such as theophylline. Charcoal is rather unpleasant to drink repeatedly and will be more reliably taken if given down a nasogastric tube.
    - *PEG bowel lavage:* in whole bowel irrigation, a solution of polyethylene glycol (not to be confused with ethylene glycol!!) is given orally or by NG tube at 2L/h in adults. It is continued until the rectal effluent becomes clear.

      Indications: ingestion of serious substances such as sustained-release or enteric-coated preparations. May be

used for lithium, iron, arsenic, lead oxide, or zinc sulphate.

Contraindications: bowel obstruction, perforation, ileus, or in patients seriously ill e.g. haemodynamic instability.

- *Ipecac-induced emesis* is *no* longer used.

Always seek advice from the local poisons unit (listed inside the front cover of the *BNF* and on p961).

Assessment of poisoning in the unconscious patient

Sign	Consider
Hypoventilation	Opiates, ethanol, benzodiazepines
Hyperventilation	Metabolic acidosis (aspirin, paracetamol), gastric aspiration, carbon monoxide
Pinpoint pupils	Opiates, organophosphates
Dilated pupils	Methanol, anticholinergics, tricyclics, LSD
Bradycardia	Î²-blockers, digoxin, opiates
Tachyarrhythmias	Tricyclics, anti-cholinergics, caffeine,

	theophylline, lithium, digoxin
Hyperthermia	Ecstasy, amphetamines, anti-cholinergics
Pyramidal signs, ataxia, hypotnia, hyper-reflexia and extensor plantars	Tricyclics or anti-cholinergic agents
Hypertension	Cocaine, amphetamines, ecstasy
NB: Occasionally patients present where poisoning is suspected but not known. Even where the history suggests self-poisoning be aware that serious underlying disease may be present. For example, patients who feel very ill will often self-medicate with aspirin and paracetamol.	

Drug overdoses and antidotes

Drug	Action	Antidote/Therapy
Anti-depressants	Activated charcoal	Diazepam for convulsions, cardiac monitoring

Aspirin		Alkaline diuresis, haemodialysis
Benzodiazepines	Protect airway	Flumazenil if severe
Î²-blockers	Check BP, HR, and breathing	Atropine (3 mg), glucagon 7mg im, consider pacing
Calcium antagonists	Calcium gluconate	Anti-cholinergics
Carbon monoxide	Give 100% oxygen	Treat cerebral oedema with mannitol, consider hyperbaric oxygen
Cyanide	Give 100% oxygen	Sodium thiosulphate, dicobalt edetate
Digoxin	Check K^+ and ECG	DigibindÂ® (digoxin-binding antibody)
Ethylene glycol	Gastric emptying	Infuse ethanol, 4-methyl pyrazole
Heavy metals	Gastric emptying	Dimercaprol, penicillamine, sodium calcium

		edetate
Iron tablets	Gastric emptying	Desferrioxamine
Lithium	Gastric emptying	Diuresis/dialysis
Mefenamic acid	Convulsions may occur. Treat with diazepam	None
Methanol	Monitor U&Es, glucose	Infuse ethanol, phenytoin for seizures, dialysis if severe
Organophosphorus insectides	Gastric emptying, remove clothes, and decontaminate	Atropine, pralidoxime
Opiates	Ensure breathing is adequate	Naloxone
Paracetamol	Gastric emptying if within 4 hours	N-acetylcysteine (or methionine)
Paraquat	Gastric emptying	Fuller's Earth (or bentonite or

		activated charcoal), intravenous vitamin E may be of benefit
Theophylline	Check plasma potassium urgently	repeat dose of activated charcoal

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Amphetamines

This agent (and its cogener methamphetamine) is widely abused for its effects on CNS arousal. A number of its methylenedioxy derivatives (e.g. â€˜ecstasyâ€™ or MDMA) are also available on an illicit basis and have additional hallucinogenic actions (LSD like).

Presentation

Sympathomimetic effects	*Central effects*
• Mydriasis • Hypertension • Tachycardia • Skin pallor	• Hyperexcitability • Agitation • Talkativeness • Paranoia (esp. with chronic use)

Complications

- Intracranial (and subarachnoid) haemorrhage: although attributed to its hypertensive effect this can occur after single dose.
- Vasospasm may be seen on angiography (â€˜string-of-beadsâ€™ sign).
- Ecstasy is associated with a heat-stroke-like syndrome (p604).

Poor prognostic features

- Hyperpyrexia (>42Â°C)
- Rhabdomyolysis
- Disseminated intravascular coagulation
- Acute renal failure
- Acute liver failure.

Management

- Sedate agitated patients with a benzodiazepine (e.g. 5â€“10mg diazepam iv or 1â€“2mg lorazepam im). Frankly psychotic patients may require haloperidol (5â€“10mg im). Haloperidol may decrease the seizure threshold.
- Monitor core temperature at least hourly initially.
- Seizures should be controlled with diazepam (5â€“10mg iv stat). New focal signs should prompt urgent CT scanning looking for evidence of intracranial bleeding.
- Significant hypertension (diastolic >120mmHg) may respond to sedation with diazepam. If not it should be controlled with labetalol, a combined Î±- and Î²-blocker: give 50 mg stat iv followed by an infusion of 1â€“2mg/min which should be stopped when the BP is controlled (selective Î²-blockers such

as atenolol may actually worsen the hypertension).

- Hyperpyrexia requires prompt cooling with tepid sponging or even chilled iv fluids as necessary to keep the rectal temperature <38.5Â°C. Chlorpromazine (25â€“50mg im) will decrease the core temperature but may cause sedation and hypotension. Dantrolene can decrease hyperpyrexia.
- Acidification of the urine can substantially increase drug elimination but can exacerbate electrolyte and pH disturbances. Avoid if rhabdomyolysis is present. It should only be used for severe overdose and where the patient can be closely monitored for response and adverse effects.

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Benzodiazepines

Deliberate overdose with this group of compounds is very common. Unless combined with other sedatives (e.g. alcohol or tricyclics) effects of overdosing are generally mild.

Presentation

- Drowsiness
- Slurred speech
- Nystagmus
- Hypotension (mild)
- Ataxia
- Coma
- Respiratory depression
- Cardiorespiratory arrest (with iv administration)

The elderly are generally more susceptible to cardiorespiratory depression with benzodiazepine overdose.

Management

- If patients present within 1 hour, empty the stomach by gastric lavage and give 50g activated charcoal. Activated charcoal may be given whilst lavage is being set up. Ensure the patient can protect their airway. No further intervention is usually required for mild to moderate overdoses.
- Severe overdose may require use of the benzodiazepine antagonist, flumazenil, e.g. comatose patients particularly where the diagnosis is uncertain and patients with significant cardiorespiratory depression. *Flumazenil* is given as an iv bolus of 0.2mg followed by a further bolus dose of 0.1mg every 2â€“3 minutes until the patient is rousable. Most benzodiazepines have a substantially longer duration of action than flumazenil and an IVI of 0.1â€“0.4mg/h will be needed to prevent early resedation.
- Avoid giving excess flumazenil to completely reverse the effect of a benzodiazepine. In chronic benzodiazepine abusers this can cause marked agitation and may precipitate seizures in patients who have taken an overdose of a combination of benzodiazepines and proconvulsants (e.g. dextropropoxyphene, theophyllines, and tricyclics).

Î²-blockers

These agents competitively antagonize the effects of endogenous catecholamines. They cause profound effects on atrioventricular conduction and myocardial contractility, and their effects are predictable based on their known pharmacology.

Presentation

- Sinus bradycardia
- Hypotension
- Cardiac failure
- Cardiac arrest (asystole or VF)
- Bronchospasm (rare in non-asthmatics)
- Drowsiness
- Hallucinations
- Fits (esp. with propranolol)
- Coma
- Hypoglycaemia (rare)

Prognostic features

- Subjects with pre-existing impaired myocardial contractility are less likely to tolerate even moderate overdoses of Î²-blockers.
- The ECG may provide some indication as to the dose ingested: mild overdose is suggested by first-degree heart block; widening of the QRS and prolongation of the corrected QT interval (particularly after sotalol) are associated with moderate to severe overdose.

Management

- Establish iv access.
- Check a 12-lead ECG and then monitor ECG continuously.
- Record BP regularly (at least every 15 minutes).
- *Gastric lavage* should be attempted if seen within 1 hour of ingestion. Give atropine (0.6â€“1.2 mg iv) *before* lavage to prevent vagal-induced cardiovascular collapse.

- *Hypotension:* treat with iv glucagon (50â€“150Âµg/kg followed by an infusion of 1â€“5mg/h). This peptide is able to exert an inotropic effect independent of Î²-receptor activation by raising myocardial cAMP levels.
- *Bradycardia:* may respond to atropine alone (0.6â€–1.2mg iv 6â€–8 hourly). Isoprenaline infusions (5â€–50Âµg/min) may be tried but are often ineffective. If the bradycardia persists and the patient is in cardiogenic shock a transvenous pacing wire should be inserted (see p878).
- *Convulsions:* treat in the standard way (p472). Give diazepam 5â€–10mg iv initially.
- *Bronchospasm:* treat initially with high-dose nebulized salbutamol (5â€–10mg) (higher doses may be needed). Nebulized ipratropium bromide (250â€–500Âµg) may be tried but it is unlikely to offer additional bronchodilatation in a fully atropinized subject. If nebulized bronchodilators are ineffective, an aminophylline infusion should be used (e.g. 0.5mg/kg/min).
- *Monitor blood glucose* regularly (hourly BMs). If hypoglycaemia develops give 50ml of 50% dextrose followed by an IVI infusion of 10% dextrose adjusting the rate as necessary.

Carbon monoxide

See â€˜smoke inhalationâ€™, p856. The commonest sources are smoke inhalation, poorly maintained domestic gas appliances and deliberate inhalation of car exhaust fumes. It causes intense tissue hypoxia by two mechanisms. Firstly, it interrupts electron transport in mitochondria. Secondly, it reduces oxygen delivery both by competing with O_2 for binding to Hb (its affinity for Hb is 220-fold that of O_2) and altering the shape of the HbO_2 dissociation curve (making it less sigmoidal).

Presentation

Patients present with signs of hypoxia without cyanosis. Skin and mucosal surfaces may appear â€˜cherry-redâ€™ (most obvious post mortem). Levels of COHb below 30% cause only headache and dizziness. 50â€“60% produces syncope, tachypnoea, tachycardia, and fits. Levels over 60%, cause increasing risk of cardiorespiratory failure and death.

Complications

These are the predictable result of local hypoxia. Sites at particular risk are CNS, affecting cerebral, cerebellar, or mid-brain function, e.g. Parkinsonism and akinetic-mutism; the myocardium with ischaemia and infarction; skeletal muscle causing rhabdomyolysis and myoglobinuria; skin involvement ranges from erythema to severe blistering.

Prognostic features

Anaemia, increased metabolic rate (e.g. children), and underlying ischaemic heart disease all increase susceptibility to CO. Neurological recovery depends on the duration of hypoxic coma; complete recovery has been reported in young subjects (under 50) after up to 21 hours, versus 11 hours in older subjects.

Management

- An arterial blood gas should be taken. Although P_aO_2 may be normal it is essential to measure the COHb concentration. Most ITUs have a carboxyhemoglobinometer.

  NB: monitoring O_2 saturation with a pulse oximeter is unhelpful since it will not distinguish HbO_2 and COHb (hence the apparent oxygen saturation will be falsely high).

- Apply a tight-fitting facemask and give 100% O_2. Check a

12-lead ECG and continuously monitor rhythm. Take blood for FBC, U&E, CPK, and cardiac enzymes.

- If the patient is comatose they should be intubated and ventilated with 100% FiO_2 (this reduces the half-life of COHb to 80 minutes cf. 320 minutes on room air). This should also be considered in patients who are severely acidotic or show evidence of myocardial ischaemia.
- Fits should be controlled with iv diazepam (5â€“10 mg). The metabolic acidosis does not generally require correction with iv $NaHCO_3$.
- Hyperbaric oxygen will shorten the washout of COHb but access and transfer times to a hyperbaric chamber can make this difficult. Consider if (1) the patients has been unconscious, (2) if COHb is >40%, and (3) if there are neurological or psychiatric signs.

Ensure medical follow-up as the neuropsychiatric sequelae may take many weeks to evolve.

Cocaine

Intoxication during its therapeutic use as a topical analgesic is extremely rare. It is rapidly absorbed, when applied intranasally (â€˜snortingâ€™) or smoked (free-basing â€˜crackâ€™). Occasionally it presents as massive overdosing when the swallowed packets of illicit, smuggled cocaine rupture. Its subjective and sympathomimetic actions are often indistinguishable from amphetamine.

Presentation

- Hypertension
- Tachycardia

- Skin pallor
- Ventricular arrhythmias
- Paranoid delusions (chronic use)
- Seizures (common), may occur in epileptics even at low doses
- CNS depression (with high doses) especially the medullary centres
- Cardiorespiratory failure

Complications

- Vasoconstrictor effects on the coronary circulation can cause myocardial ischaemia and infarction even in subjects with normal vessels.
- In the cerebral circulation the hypertension may precipitate stroke.
- Psychotic reactions (similar to amphetamine psychosis) may occur.

Prognostic features

- The lethal dose of cocaine is approximately 1200mg (regular users often tolerate doses considerably in excess of this).
- Cocaine can cause seizures in epileptics in â€˜recreationalâ€™ doses but for non-epileptics presentation in status epilepticus generally implies massive overdose and carries a poor prognosis.
- Rhabdomyolysis, hyperpyrexia, renal failure, severe liver dysfunction, and DIC have been reported and carry a high mortality.
- Patients with deficiency of serum pseudocholinesterase

appear to be at particular risk of life-threatening cocaine toxicity.

Management

- *General measures:* establish iv access taking blood for U&Es and CPK. Ensure the airway is clear. If GCS â‰¤8, consider intubation and mechanical ventilation. Agitation may require diazepam (5â€“10mg iv). Monitor ECG continuously for arrhythmias.
- *Ventricular arrhythmias:* treat with labetalol (50mg iv bolus and IVI of 1â€“2mg/min), provided the patient is conscious. Use lignocaine with caution as it may precipitate seizures. Phenytoin may be tried (250mg slow bolus over 5 minutes) particularly in patients with seizures.
- Monitor core temperature for evidence of *hyperpyrexia*. If necessary, start cooling measures (see p604), e.g. tepid sponging, or chilled iv fluids as necessary to keep the temperature below 38.5Â°C. Chlorpromazine 25â€“50mg im may be useful but sedation and hypotension may occur.
- *Significant hypertension* (diastolic >120mmHg) should be controlled initially with diazepam (5â€“10mg iv); if it remains high start labetalol (50mg stat iv, then an IVI of 1â€“2mg/min: stop when BP is controlled). Non-selective Î²-blockers (e.g. propranolol) may actually worsen the hypertension.
- *Seizures* should be controlled with diazepam (10â€“30mg iv stat and if necessary an IVI of up to 200mg/24h). Presentation with new focal seizures after cocaine ingestion usually implies ischaemic or haemorrhage stroke: arrange an urgent brain CT scan.

Cyanide

Poisoning is most commonly seen in victims of smoke inhalation (HCN is a combustion product of polyurethane foams). Cyanide derivatives are, however, widely employed in industrial processes and fertilizers. Children may also ingest amygdalin, a cyanogenic glycoside, contained in kernels of almonds and cherries. Cyanide acts by irreversibly blocking mitochondrial electron transport.

Presentation

HCN gas can lead to cardiorespiratory arrest and death within a few minutes. Onset of effects after ingestion or skin contamination is generally much slower (up to several hours). Early signs are dizziness, chest tightness, dyspnoea, confusion, and paralysis. Cardiovascular collapse, apnoea, and seizures follow. Cyanosis is not a feature. The classical smell of bitter almonds is unhelpful (it is genetically determined and 50% of observers cannot detect it). Pulmonary oedema and lactic acidosis are common in severe poisoning.

Prognostic features

- Ingestion of a few hundred mg of a cyanide salt is usually fatal in adults. Absorption is delayed by a full stomach and high gastric pH (e.g. antacids).
- Patients surviving to reach hospital after inhalation of HCN are unlikely to have suffered significant poisoning.
- Acidosis indicates severe poisoning.

Management

- Do *not* attempt mouth-to-mouth resuscitation. Give 100% O_2 by tight fitting face mask or ventilate via ET tube if necessary.

- Establish iv access.
- Check arterial blood gases. Acidosis indicates severe poisoning.
- Providing there are no signs of cyanide toxicity, ingested cyanide should be removed by gastric lavage (if <1h). Skin contamination requires thorough washing of the affected area with soap and water.
- If signs of cyanide toxicity are present, give 300mg of dicobalt edetate (KelocyanorÂ®) IV over 1 minute. If there is no response in 1 minute, repeat up to a max. of 900mg. Alternatively, give sodium nitrite (10ml of a 3% solution) and sodium thiosulphate (25ml of 50% solution).

Digoxin

Deliberate overdosing with digoxin is unusual. Significant toxicity is, however, a common adverse drug reaction in patients taking digoxin therapeutically (up to 25% of patients in some series). It is particularly common when renal impairment occurs (digoxin is almost totally cleared by the kidneys), and is exacerbated by hypokalaemia.

Presentation

- Nausea, vomiting, confusion, and diarrhoea.
- Visual disturbance (blurring, flashes, disturbed colour vision).
- Cardiac dysrhythmias (tachyarrhythmias or bradyarrhythmias).

Complications

- Hyperkalaemia.
- Cardiac dysrhythmias. The initial effect is usually a marked sinus bradycardia which is vagally mediated. This is followed by atrial tachyarrhythmias (with/without heart block), accelerated junctional rhythms, ventricular ectopy, and finally VT or VF.

Prognostic features

- Digoxin level >15ng/ml represents a severe overdose.
- Susceptibility to digoxin toxicity is increased by renal impairment, electrolyte disturbance (â†“K^+ or â†“Mg^{2+}), and hypothyroidism.

Management

- Take blood for a digoxin level and U&Es.
- Baseline 12-lead ECG and continuous ECG monitoring.
- *Gastric lavage* should be attempted if seen within 1 hour of overdose, followed by activated charcoal (50g stat). Activated charcoal (50g) should be repeated every 2 hours. Patients presenting >4 hours should be given cholestyramine orally (4g qds).
- Sinus bradyarrhythmias and AV block usually respond to atropine (0.6mg iv repeated to a total of 2.4mg). Asymptomatic ventricular ectopics do not require specific treatment.
- *Ventricular tachyarrhythmias* should be treated with phenytoin (250mg over 5 minutes). If this is not effective, give amiodarone (600mg over 1 hour) or lignocaine (100mg iv loading dose; then IVI of 1â€“4mg/min).
- Patients with haemodynamic instability, resistant ventricular

tachyarrhythmias, or high K^+ require treatment with *digoxin-binding antibody fragments* (Fab, DigibindÂ®). Dose: (no. of vials) = 1.67 Ã— amount ingested (mg). If latter unknown give 20 vials (infused over 30 minutes). Dose for patients intoxicated during chronic therapy: (no. of vials) = digoxin level (ng/ml) Ã— wt (kg) Ã— 0.01. Fab therapy will terminate VT in 20â€“40 minutes. The K^+ and free serum digoxin levels should be monitored for 24 hour after Fab therapy. A substantial hypokalaemia can develop and not infrequently there is a rebound in digoxin levels which may require administration of additional Fab. In patients with renal impairment this rebound is delayed and monitoring should be extended to 72 hours.

- Patients with severe renal failure are obviously unable to clear the Fabâ€“digoxin complexes. Plasmapheresis is indicated to clear the bound digoxin.
- If DigibindÂ® is not available, insert a transvenous pacing wire and try to control arrhythmias with a combination of overdrive pacing, DC shock, and drugs (see p884).

Ecstasy

Ecstasy, â€˜Eâ€™, and â€˜XTCâ€™ are street names for MDMA (methylenedioxy-metamphetamine). It produces a positive mood state with feelings of increased sensuality and euphoria. Side-effects with chronic use include anorexia, palpitations, jaw stiffness, grinding, of teeth, sweating, and insomnia. It can cause dehydration with hyperthermia, agitation, and fits. Other features include hyponatraemia, cerebral infarction, cerebral haemorrhage, and vasculitis. Most deaths from ecstasy result from disturbance of thermo- and osmoregulation leading to hyperthermia and increased plasma osmolality. MDMA also causes life-threatening, cardiac dysrhythmias, abnormal liver function tests, acute liver failure, and has been associated with

cerebral infarction and haemorrhage.

The hyperthermic syndrome occurs within hours of ingestion, and often follows intense physical activity. Features include core temperature >40Â°C, severe metabolic acidosis, muscle rigidity, DIC, and rhabdomyolysis.

Ecstasy may be combined with LSD, ketamine, caffeine, or sildenafil (â€˜sextasyâ€™). Ketamine causes pain-free floating sensations with vivid dreams.

Management

Consider other causes of hyperthermia (p604). Patients should be treated with dantrolene 1mg/kg up to a maximum of 5mg/kg. Dantrolene inhibits release of calcium from the SR in cells. Rhabdomyolysis should be treated in the usual way (p392).

Ethanol: acute intoxication

Patients may present either with acute intoxication (often on a background of chronic misuse), withdrawal syndromes, nutritional deficiency syndromes, or chronic toxicity (liver, CNS, peripheral neuromyopathy, etc).

Presentation

Ethanol initially results in disinhibition and euphoria, and with increasing serum levels, this progresses to incoordination, ataxia, stupor, and coma. Chronic alcoholics tend to require higher blood ethanol levels than â€˜socialâ€™ drinkers for intoxication. Try to obtain a history from friends or relatives. Examine the patient for signs of chronic liver disease, trauma, or signs of infection.

Complications

- Acute gastritis causes N&V, abdominal plain, and GI haemorrhage.
- Respiratory depression and arrest, inhalation of vomit (with ARDS Mendelson's syndrome), and hypothermia may accompany the profound sedation.
- Hypoglycaemia is common and should be excluded.
- Alcoholic ketoacidosis or lactic acidosis.
- Accidental injury, particularly head injury (subdural).
- Rhabdomyolysis and acute renal failure.
- Infection (septicaemia, meningitis).

Management

- Mild to modern intoxication usually requires no specific treatment: the need for admission for re-hydration and observation depends on the individual patient. Admit all patients with stupor or coma.
- Check the airway is clear of vomitus and the patient is able to protect it. Nurse in the recovery position.
- Ipecachuanha, gastric lavage, or charcoal are not indicated.
- Take blood for U&E, CPK, glucose, amylase, and ethanol (and methanol) levels, ABG (acidosis), lactate, ammonia. Analyse, urine (myoglobin, p294). Consider the possibility of other drug overdose.
- Monitor closely for respiratory depression, hypoxia, cardio arrhythmias, and hypotension and withdrawal syndromes (see p396).
- Check BM stix. In comatose patients, there is a good argument for giving 25â€“50ml of 50% dextrose immediately for presumed hypoglycaemia because this will usually not cause any harm. Follow with an IVI of 10% glucose if necessary.

- The only concern is that glucose may precipitate Wernicke's encephalopathy in malnourished individuals. Some clinicians therefore favour giving a bolus of thiamine 1â€“2mg/kjg iv beforehand.
- Rehydrate with intravenous fluids (avoid excessive use of saline in patients with signs of chronic liver disease); monitor urine output.
- Naloxone reduces the effects of alcohol toxicity but its use is not standard at present.
- Rarely, haemodialysis is used if intoxiciation is very severe or in the presence of acidosis.
- Watch for complications (see above) and treat as necessary.

- After recovery from the acute episode arrange for a psychiatric or medical assessment and follow-up and referral to an alcohol rehabilitation programme if appropriate.

Alchohol withdrawal and delirium tremens (DTs) see p500

Ethylene glycol

Ingestion may be deliberate but usually it is taken accidentally as an ethanol â€˜substituteâ€™; it is present in â€˜anti-freezeâ€™. EG toxicity is due to accumulation of toxic metabolites (aldehydes, glycolate, oxalates, and lactate). This metabolic route may be blocked by competitive antagonism with ethanol.

Presentation

- Impaired consciousness (â€˜inebriationâ€™ without alcohol on the breath).
- Seizures and focal neurological signs (e.g. ophthalmoplegias)

are seen in the first 24 hours.

- Loin pain, haematuria, and ATN occurs over the next 48 hours.

Prognostic features

- As little as 30ml of ethylene glycol can be fatal in adults.
- It is often taken with ethanol which is actually protective by blocking the metabolism of glycol to toxic metabolites.
- Renal failure can be averted if specific treatment is instituted early.
- Plasma levels of EG >500mg/L (8mmol/L) indicate severe overdose.
- The degree of acidosis is the best indicator of likely outcome.

Complications

- Oliguric renal failure (crystal nephropathy)
- Non-cardiogenic pulmonary oedema
- Cerebral oedema
- Cardiovascular collapse
- Myocarditis

Management

- Perform *gastric lavage* if presenting within 1 hour of ingestion. This will also enable confirmation that EG has been taken; commercial â€˜anti-freezeâ€™ often contains fluorescein which is easily detected with a UV light source (also detectable in urine).

- Establish iv access and take blood for U&Es, glucose, biochemical profile including Ca^{2+}, plasma osmolality, and ethanol and EG levels.
- Check arterial blood gases to assess degree of acidaemia. Calculate anion gap.
- Microscope a fresh urine sample looking for the needle-shaped crystals of calcium oxalate monohydrate which are pathognomonic.
- *4-methylpyrazole* (10â€“20mg/kg/day orally) is an inhibitor of alcohol dehydrogenase and has the advantage that unlike ethanol it does not cause CNS depression. It is now the drug of choice.
- The half-life of EG is short (3 hours). If 4-methylpyrazole is unavailable then an *ethanol infusion* should be started as soon as possible (detailed under â€˜methanolâ€™, p824). The infusion should be continued until plasma EG is undetectable. Infusion of ethanol will cause intoxication.

Indications for dialysis

Severe acidosis (declining vital signs or an EG level >500mg/L) or oliguria requires haemodialysis or peritoneal dialysis (the former is 2â€“3 fold more effective). Normal renal function is generally restored in 7â€“10 days although permanent impairment has been reported.

Flunitrazepam

Flunitrazepam (rohypnol) is sometimes referred to as the â€˜date rapeâ€™ drug. It is used as a short-term treatment for insomnia, as a sedative hypnotic, and a pre-anaesthetic. It has similar effects to ValiumÂ® (diazepam), but is ~10Ã— more potent.

Flunitrazepam intoxication leads to impaired judgment and impaired motor skills and can make a victim unable to resist a sexual attack. The combination of alcohol and flunitrazepam has a more marked effect than flunitrazepam alone. Effects begin within 30 minutes, peak by 2 hours, and can persist for up to 8 hours. It is commonly reported that persons who become intoxicated on a combination of alcohol and flunitrazepam have â€˜blackoutsâ€™ lasting 8â€“24 hours following ingestion. Adverse effects of flunitrazepam include decreased blood pressure, memory impairment, drowsiness, visual disturbances, confusion, dizziness, gastrointestinal disturbances, and urinary retention. Manage as for benzodiazepine over dose.

Gamma hydroxybutyric acid (GHB) or liquid ecstasy

This drug is dissolved in water and consumed until a high is reached. GHB increases intra-cerebral dopamine levels leading to drowsiness, seizures, hypoventilation, and unconsciousness. It acts synergistically with ethanol leading to CNS and respiratory depression.

Iron

Accidental ingestion is almost exclusively a problem in children. In overdose, iron binding mechanisms are rapidly saturated leading to high concentrations of free iron. The latter catalyses the widespread generation of free radicals which is the basis of the toxic manifestations of iron overdose.

Presentation

- Iron is extremely irritant and causes prominent abdominal pain, vomiting and diarrhoea, haematemesis, and rectal bleeding.

- Usually the initial GI symptoms subside before secondary signs develop 12â€“24 hours after ingestion. Hepatic failure, jaundice, fits, and coma are common.
- Very large overdose can cause early cardiovascular collapse and coma.
- In children, 1â€“2g of iron may prove fatal. Patients alive 72 hours after ingestion usually make a full recovery.
- Late sequelae of gastric fibrosis and pyloric obstruction have been occasionally reported.

Management

- The stomach should be emptied by *gastric lavage* (if <1h). The lavage fluid should contain 1% $NaHCO_3$. 50â€“100ml of a solution of 5â€“10g desferrioxamine in 50â€“100 ml water should be instilled and left in the stomach to prevent further absorption.
- A *plain AXR* may be useful to assess the number of tablets ingested.
- Establish iv access. Take blood for U&Es, LFTs, FBC, serum iron, % saturation.
- *Parenteral chelation therapy* is indicated if the serum Fe is >90Âµmol/L.
    - Desferrioxamine should be given im (2g for adults and 1g for children) every 6â€“12 hours (NB: 100mg of desferrioxamine binds 8.5mg of elemental Fe).
    - If the patient is hypotensive give desferrioxamine iv at a rate of 15mg/kg/h (recommended max daily dose is 80mg/kg; although if the patient tolerates it, and it is indicated by the serum Fe, higher doses may be given). The IVI is continued until the serum Fe falls below the TIBC.

- *Dialysis:* haemodialysis is indicated for very high serum iron levels that respond poorly to chelation therapy or if the urine output is not maintained during chelation therapy as the iron-chelate is only excreted in the urine.
- *Exchange transfusion* has also been used successfully for very severe intoxication.

Lithium

Lithium has a low therapeutic index and accidental toxicity can and does occur much more frequently than deliberate self-administration. Toxicity is commonly precipitated by administration of diuretics or intercurrent dehydration, e.g. following vomiting or a febrile illness.

Presentation

- Thirst, polyuria, diarrhoea, vomiting, and coarse tremor are common.
- In severe toxicity the effects on the CNS generally predominate, with impairment of consciousness, fine tremor, hypertonia, seizures, and focal neurological signs.
- Cardiac arrhythmia and hypotension are seen in very severe poisoning.

Prognostic features

Features of toxicity are usually associated with Li^+ levels of >1.5mmol/L. However, Li^+ enters cells relatively slowly so that the levels taken shortly after a large overdose may be very high with the patient showing few if any signs of toxicity. Levels >4mmol/L will probably require haemo- or peritoneal dialysis.

Management

- Patients presenting within 1 hour of ingestion should undergo gastric lavage. If slow-release preparations are involved whole bowel irrigation with PEG is useful. Activated charcoal is *not* useful.
- Check serum Li^+ level (ensure the tube used does not contain lithiumâ€“heparin anti-coagulant).
- Check U&Es: if hypernatraemia is present check serum osmolality.
- Any diuretic (especially thiazides) or other drug likely to alter renal handling of Li^+ (e.g. NSAIDs) should be stopped.
- Correct any fluid or electrolyte deficits. Forced diuresis using iv 0.9% saline e.g. 3â€“4litres/24 hours should be started if there are any signs of severe toxicity or levels >3mmol/L. (watch for fluid overload). The serum Na^+ and osmolality must be monitored daily as both are likely to rise.
- If levels are >4mmol/L or oliguria precludes diuresis then the patient should be haemodialysed. Although Li^+ can be effectively cleared from the extracellular compartment with dialysis, movement out of cells is much slower. Dialysis should be continued until Li^+ is not detected in the serum or dialysate. Levels should be measured daily for the next week in case Li^+ rebounds due to slow release from intracellular stores.

Lysergic acid diethylamide (LSD)

It is the prototypical psychedelic drug. Although its abuse was a feature of the 1960s and early 1970s it has reappeared in the last few years in increasing amounts. It is no longer manufactured for medicinal use but illicit sources are

surprisingly pure, i.e. free of adulterants. The preferred route is ingestion although it is occasionally injected and has been reported to be active if snorted.

Presentation

A typical dose of around 100Âµg causes

- Pupillary dilatation
- Sweating
- An acute anxiety state
- Tachycardia
- Depersonalization, visual illusions, and distortion of time

Large doses can cause convulsions, focal neurological deficit (due to vasospasm), and coma.

Complications

- Acute psychosis with visual hallucination, paranoia, or features of mania is well described.
- Very large overdoses have been associated with a mild bleeding disorder due to blockade of 5-HT-induced platelet aggregation.
- Rhabdomyolysis has been reported in the past but appears to have reflected the physical restraints used, i.e. â€˜straight-jacketsâ€™.
- Death from even large overdoses is unusual and usually reflects suicide or accidental trauma while under the psychedelic effects of LSD.

Management

- Absorption is likely to be complete by the time symptoms are manifest. Lavage may actually worsen the behavioural disturbance.
- Most patients will need a quiet side room and verbal reassurance only (â€˜talking downâ€™). The visual illusions fade in 4â€“8 hours.
- Very agitated patients can be sedated with diazepam (5â€“10mg iv) or im lorazepam (1â€“2mg) and/or im haloperidol 5â€“10mg.
- Seizures respond to diazepam iv (5â€“10mg bolus).
- The development of focal neurological signs should prompt a CT scan and probably cerebral angiography. Occasionally intense vasospasm is seen involving even the intracranial carotids.
- Comatose patients require full supportive care (p406) but generally recover fully in 24 hours. Aspiration appears to be a definite risk and protection of the airway is particularly important.
- There are no specific antidotes or methods for enhanced drug elimination.

Methanol

Poisoning usually follows ingestion of contaminated alcohol beverages or â€˜methylated spiritsâ€™. Intoxication in industrial settings follows absorption across the skin or lung. Alcohol dehydrogenase metabolizes it to formaldehyde which is oxidized to the toxic formic acid.

Presentation

- Significant ingestion causes nausea, vomiting, and abdominal

pain.

- Its effects on the CNS resemble those of ethanol although in low doses it does not have a euphoric effect.
- Visual symptoms present with falling visual acuity, photophobia, and the sensation of â€˜being in a snow stormâ€™.

Complications

- Up to 65% of patients have a raised amylase but this does not necessarily represent pancreatitis (usually salivary-gland amylase type). If pancreatitis is suspected clinically, measure serum lipase (haemorrhagic pancreatitis has been reported at post mortem).
- Seizures are seen in severe intoxication. CT scanning usually shows cerebral oedema or even necrosis in the basal ganglia.
- Patients with visual symptoms may develop irreversible visual impairment even with aggressive intervention.
- Rhabdomyolysis and acute renal failure.
- Hypoglycaemia.

Prognostic features

- 10ml of methanol can cause blindness and 30ml can be fatal.
- Peak plasma methanol is useful; >0.2g/L (6.25mmol/L) indicates significant ingestion and 0.5g/L (15.6mmol/L) is severe.
- Arterial pH correlates with formate levels; pH <7.2 is severe intoxication.

Management

- Take blood for U&E, CPK, glucose, amylase and ethanol/methanol levels, ABG (acidosis), anion gap, urine (myoglobin, p392).
- *Seizures* are probably best treated initially with diazepam (5â€“10 mg iv) followed by phenytoin (250mg iv over 5 minutes). Exclude hypoglycaemia.
- *4-methylpyrazole* (10â€“20mg/kg/day po) is an inhibitor of alcohol dehydrogenase and has the advantage that unlike ethanol it does not cause CNS depression. It is now the drug of choice. Give to all patients pending methanol levels, patients with methanol levels >0.2g/L (6.25mmol/L), acidotic patients, and anyone needing haemodialysis.
- *Ethanol infusion* should be used if 4-methylpyrazole is unavailable. Give iv as a 10% solution in 5% dextrose or N saline (i.e. take 50ml from a 500ml bag and replace with 50ml ethanol). A loading dose of 10ml/kg should be given followed by an IVI of 0.15ml/kg/h for non-drinkers (regular drinkers, 0.3ml/kg/h). Titrate to a plasma ethanol level of 1â€“1.5g/L (21.7â€“32.6mmol/L). Continue ethanol IVI for at least 48 hours.
- Metabolic acidosis should be corrected with iv $NaHCO_3$.
- *Haemodialysis* is reserved for those patients with renal failure, *any* visual impairment, or a plasma methanol level of >0.5g/L (15.6mmol/L). The ethanol infusion rate should be doubled during dialysis (or ethanol may be added directly to the dialysis fluid).

Isopropanol

Isopropanol is present in car screen wash. As a cause of poisoning with alcohols this is second after ethanol. It has twice the potency of ethanol on the CNS (its major metabolite,

acetone, compounds this) and isopropanol-induced coma can last >24 hours. Effects are seen within 30â€“60 minutes of ingestion and large overdoses cause coma and hypotension as the major effect. Haemodialysis is indicated if the hypotension fails to respond to iv fluids, vital signs decline, or blood levels are >4g/L (66.7 mmol/L). Monitor for hypoglycaemia and myoglobinuria.

Opiates

Overdosing with opiates usually occurs in regular drug users where the most commonly abused agent is diamorphine (heroin). It may taken intravenously, by skin-popping, smoked, or snorted. A number of other opiates have been similarly abused. Opiates such as dextropropoxyphene and dihydrocodeine (present in combination formulations with paracetamol) are often taken with alcohol by non-addicts with suicidal intent.

Presentation

Pinpoint pupils, severe respiratory depression Â± cyanosis, and coma are typical. The depressive effects are exacerbated by alcohol. BP may be low but is often surprisingly well maintained. Although some opiates, e.g. dextropropoxyphene and pethidine, increase muscle tone and cause fits in overdose in general opiates cause marked hypotonia.

Prognostic features

- Non-cardiogenic pulmonary oedema carries a poor prognosis.
- Patients with underlying ischaemic heart disease may be more susceptible to haemodynamic disturbance after naloxone is given.
- Renal impairment reduces the elimination of many opiates and prolongs their duration of action.

Management

- Monitor respiratory rate, depth of respiration, and pulse oximetry. Give oxygen by mask. Monitor ECG continuously for arrhythmias
- Establish iv access; take blood for U&Es and CPK. If paracetamol + opiate combinations have been ingested measure a paracetamol level (see p828).
- Any patient who is comatose or has respiratory signs requires a CXR (signs of infection, septic emboli, interstitial shadowing).
- The specific antidote is *naloxone* (a pure opiate antagonist) which should be given iv in boluses of 0.4mg at 2â€“3-minute intervals until the patient is rousable and any evidence of respiratory depression corrected. Doses of up to 2mg (and above) may be required but if no response is seen at this level then the diagnosis of opiate overdose should be revised.
- The duration of action of naloxone is shorter than many opiates hence an infusion should be started to avoid resedation (starting with 0.2mg/h

and increasing as necessary). In the case of overdose with long-acting opiates such as methadone infusion of naloxone may be necessary for 48â€“72 hours.
- Avoid giving sufficient naloxone to completely reverse the effect of opiates in an opiate-dependent subject. This is likely to precipitate an acute withdrawal reaction. If this occurs and hypertension is marked (diastolic >120mmHg) then give diazepam (5â€“10mg initially iv), and if it persists, commence iv labetalol (50mg stat followed by IVI until BP is controlled). NB: marked hypertension, acute pulmonary oedema and VT/VF have been observed in non-addicts given naloxone to reverse the effects of high therapeutic doses of opiates for pain.

- Convulsions which are opiate induced (usually pethidine or dextropropoxyphene) may respond to iv naloxone. Additional anti-convulsant therapy may be required.
- Pulmonary oedema present on admission requires oxygen, CPAP, or mechanical ventilation (p904). It does not respond to naloxone.
- Rhabdomyolysis and acute renal failure, see p392.

Complications

- All opiates can cause non-cardiogenic pulmonary oedema although it is most frequently seen with iv heroin.
- Rhabdomyolysis is common in opiate-induced coma and should be looked for in all cases.
- The substances used to dilute (â€˜cutâ€™) illicit opiates may also carry significant toxicity when injected (e.g. talc and quinine).
- iv drug users may develop right-sided endocarditis and septic pulmonary emboli (several localized infiltrates on CXR).
- Ingestion of paracetamol containing preparations (e.g. co-dydramol) may develop renal or hepatic failure.

Important points

- Dextropropoxyphene in combination with alcohol can cause marked CNS depression. Respiratory arrest can evolve rapidly within <30 minutes of ingestion. Give naloxone even if the patient is only mildly drowsy. Dextropropoxyphene also causes an acute cardiotoxicity with arrhythmias due to a membrane-stabilizing effect (naloxone ineffective).
- The respiratory depressant effects of buprenorphine are not fully reversed by naloxone. Doxapram has been used in

milder cases of buprenorphine overdose as a respiratory stimulant (1â€“4mg/min) although severe cases may require mechanical ventilation.

Paracetamol: assessment

In therapeutic doses, only a minor fraction is oxidized to the reactive/toxic species (NABQI) which is detoxified by conjugation with glutathione. In overdose, normal metabolic routes become saturated; therefore an increased fraction is metabolized via the cytochrome p450 system to toxic metabolites, whose detoxification rapidly depletes hepatic glutathione stores.

Presentation

- Apart from mild nausea, vomiting, and anorexia, patients presenting within 24 hours of ingestion are generally asymptomatic.
- Hepatic necrosis becomes apparent in 24â€“36 hours with right subchondral pain/tenderness, jaundice (and acute liver failure), vomiting, and symptoms of neuroglycopenia (confusion).
- Encephalopathy may worsen over the next 72 hours.
- Oliguria and renal failure.
- Lactic acidosis: either <12 hours (very rare) or late (10% of patients with ALF).

Complications

- Acute liver failure (ALF, see p658) with hypoglycaemia, cerebral oedema, and GI bleeding.
- Severe metabolic (lactic) acidosis.

- Pancreatitis (alone or with liver failure).
- Some 10% of patients develop acute renal failure from acute tubular necrosis which may be seen in the absence of liver failure.
- Very rarely patients with G6PD deficiency develop methaemoglobinaemia and haemolysis.

Investigations

â€¢ Paracetamol	Measure levels at least 4 hours post ingestion and plot on the graph in the figure on p831. If the time of overdose is not known, measure paracetamol 4 hours later, but commence N-acetylcysteine if in doubt.
â€¢ U&Es	Renal failure generally occurs on day 3.
â€¢ Glucose	May fall with progressive liver failure. Give iv dextrose (25â€“50ml of 50% dextrose) if necessary.
â€¢ FBC	In patients with severe overdoses and liver failure, thrombocytopenia is common and may be severe.
â€¢ LFTs	Transaminases rise early.
â€¢ PT	This may be normal despite high transaminases. The PT is the best indicator of the severity of liver failure.

â€¢ ABGs	To assess degree of acidosis.

Prognostic features

Fatal overdose may occur with <10g (usually in alcoholics, epileptics, or patients on enzyme-inducing drugs), but usually involves >30g. The cause of death is usually acute liver failure. Chronic alcoholics or patients on

phenobarbitone or phenytoin are more susceptible to developing hepatotoxicity and nephrotoxicity.

- Refer to a liver unit all patients with acidosis (pH <7.32) and coagulopathy (INR >1.5).
- If renal failure occurs in isolation (no coagulopathy but transaminase levels high), then refer to a renal unit.

Indications for liver transplantation in paracetamol overdose

- Late acidosis (>36 hours post overdose) with arterial pH <7.3
- PT >100s
- Serum creatinine >300ÂµM
- Grade 3 encephalopathy (confused, distressed, barely rousable)

Practice point

- Patients with paracetamol OD often develop sub-conjunctival haematoma due to vomiting, coagolopathy Â±

thrombocytopenia.

Paracetamol: management

- Patients presenting within 1 hour of ingestion should undergo *gastric lavage*.
- All patients with a large overdose of paracetamol (>10g) should be treated with NAC until levels are available.
- Allergic reactions to NAC occur in <5% of patients.
- Measure paracetamol levels at least 4 hours post ingestion and ideally 4 hours later, and plot on the graph in the figure on p831.
- All patients on or above the *â€˜normalâ€™ treatment line* (and presenting up to 24 hours after ingestion) should be given *NAC* (see table). Patients who are allergic to NAC may be treated with methionine, but this is less effective unless given early.
- Patients on enzyme-inducing drugs (e.g. phenytoin, carbamazepine, rifampicin, phenobarbitone) or with a history of high alcohol intake may develop toxicity at lower plasma levels and should be treated if the level is above the *â€˜high-riskâ€™ treatment line* (figure, p831).
- If the initial levels indicate no treatment is necessary, repeat the paracetamol levels 4 hours later. Occasionally there may be delayed absorption and treatment is inappropriately withheld.
- Give NAC to all severe overdoses (>10g) that present at 24â€“72 hours with symptoms or deranged investigations (LFTs, PT).
- *Monitor* U&Es, FBC, PT, LFTs, glucose, and arterial blood gases daily. Monitor glucose with BM stix at least 6 hourly.

- *Give vitamin K* iv 10mg (as a single dose, in case body stores are deficient) but *avoid giving FFP* unless there is active bleeding. The PT is the best indicator of the severity of liver failure; FFP may only make management decisions (e.g. liver transplantation) more difficult. All patients who are encephalopathic or have a rapidly rising PT must be referred to a liver unit.
- Management of *acute liver failure* is discussed on p658.

Specific treatment for paracetamol poisoning

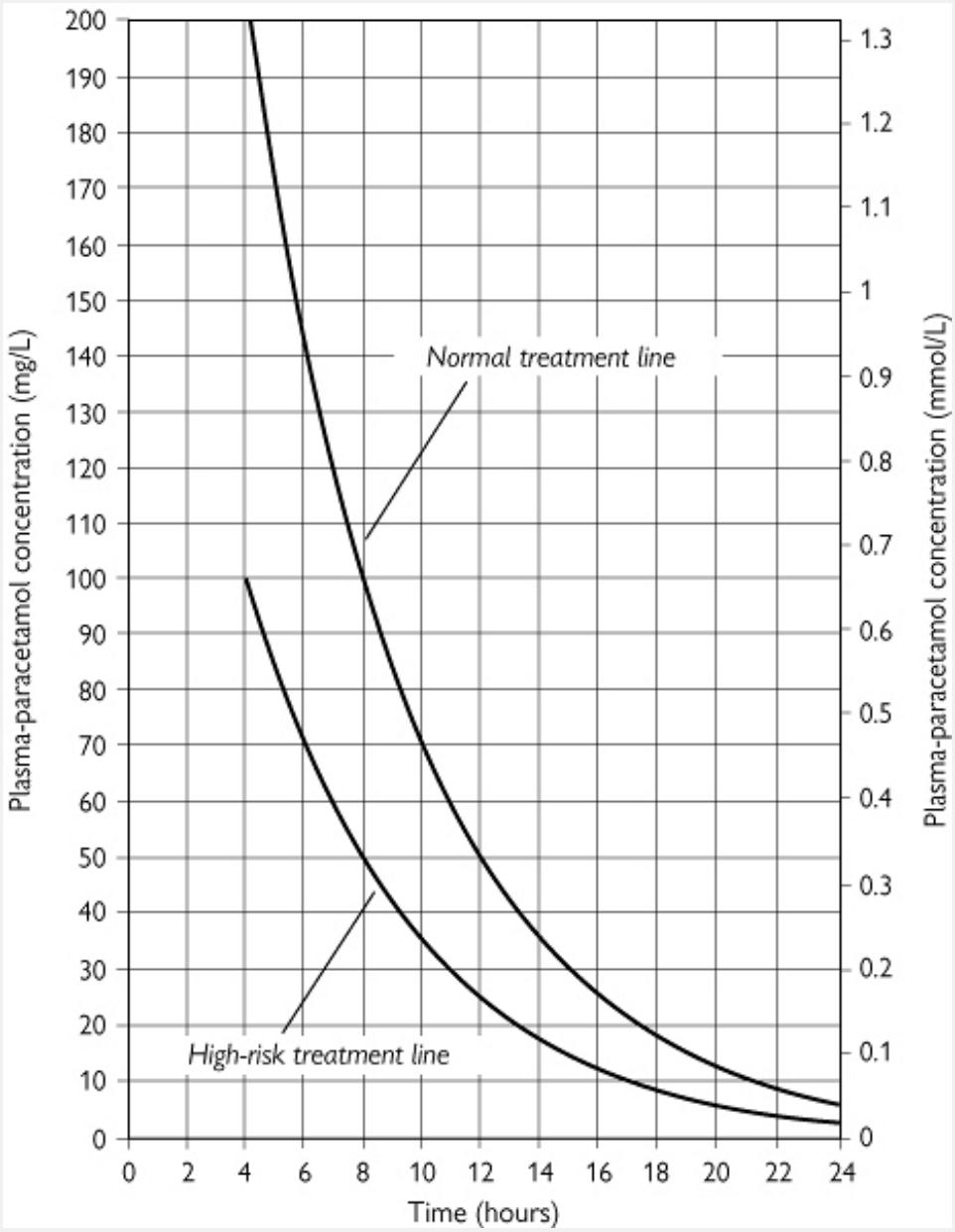
- NAC infusion

  150mg/kg in 200ml 5% dextrose over 15 minutes, followed by 50mg/kg in 500ml 5% dextrose over 4 hours, and finally 100mg/kg in 1L 5% dextrose over 16 hours.

  [Up to 10% of patients have a rash, bronchospasm, or hypotension during the infusion. Stop the IVI and give chlorpheniramine (10mg iv).]

- Oral methionine

  Only use if patient is allergic to NAC. Give 2.5g stat and 3 further doses of 2.5g every 4 hours



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P.831

P.832

Paraquat

This bipyridilium herbicide (GrammoxoneÂ® is a 20% solution cf. WeedolÂ® 2.5%) is notoriously toxic in overdose. Children

may drink it inadvertantly and horticulturists have occasionally been poisoned through skin splashing. Death is usually due to delayed pulmonary fibrosis and respiratory failure. The mechanism is thought to be due to the generation of cytotoxic oxygen radicals.

Presentation

- Nausea and vomiting are seen within a few hours of ingestion.
- Mouth and oesophageal ulceration are common.
- Oliguric renal failure develops with doses >2g within 12 hours of ingestion.
- Very high doses (e.g. 50â€“100ml 20% solution, i.e. >10g) may cause acute dyspnoea with an ARDS-like picture and rapid multi-organ failure.
- Insidious pulmonary fibrosis develops in the second week after exposure (often as the oliguria is resolving). This is not reversible and occasional survivors invariably have a severe handicap.
- Liver failure and myocarditis are also reported and thought to reflect the same free radical-mediated cell damage.

Prognostic features

- The dose ingested is a good predictor of outcome: death has been reported after only 10â€“15ml of the 20% solution (3g) of paraquat and is universal after 50ml (10g).
- Plasma levels of paraquat e.g. >2 mg/L at 4 hours or 0.1mg/L at 24 hours are associated with a poor prognosis.
- A low WBC on admission carries a poor prognosis.

Management

- Patients presenting within 6 hours of ingestion should *receive gastric lavage* with the instillation of a 30% solution of *Fuller's earth* (250ml) repeated 4 hourly. If the latter is not available then activated charcoal should be given (50â€“100g).
- Blood should be taken for FBC, U&E, LFT, and paraquat levels.
- Perform a baseline CXR and arterial blood gases.
- Monitor urine output (catheterize if necessary).
- iv fluids (but not a forced diuresis) are indicated when oesophageal ulceration is severe enough to produce dysphagia.
- The use of *haemoperfusion* or *haemofiltration* should be reserved for subjects whose outcome is borderline. It is only in these cases that the very small amounts of paraquat removed by either process (perhaps a few tens of mg) could conceivably affect outcome. Haemodialysis may of course be needed independently of drug elimination if renal failure develops.
- Attempts have been made to prevent or slow the process of pulmonary fibrosis and include radiotherapy to the lungs and immunosuppression with dexamethasone Â± cyclophosphamide. Neither has proved to be effective and cannot be recommended. A single report exists of acute lung transplantation to salvage a patient with terminal fibrosis but the patient subsequently died of a late paraquat-induced myopathy.

Salicylates

Aspirin is probably the commonest drug to be ingested deliberately in overdose. Occasionally poisoning follows the topical application of salicylic acid in keratolytics or ingestion of methyl salicylate (â€˜oil of wintergreenâ€™). Its primary toxic effect is to uncouple oxidative phosphorylation.

Presentation

- The typical features of moderate salicylate toxicity are sweating, vomiting, epigastric pain, tinnitus, and blurring of vision.
- In adults, there is also an early increase in respiratory rate causing an alkalosis that precedes the later development of a metabolic acidosis (children do not develop the early respiratory alkalosis).
- In severe overdose, the acidosis reduces the ionization of salicylic acid which enhances tissue penetration. In the CNS, this presents as agitation, tremor and fits, coma, and respiratory depression.

Complications

- Disturbance of electrolytes (hypokalaemia and either hyper- or hyponatraemia) and blood glucose (â†‘ or â†“) are common.
- Pulmonary oedema (non-cardiogenic, ARDS).
- Acute renal failure.
- Abnormal clotting due to hypoprothrombinaemia is very rare.
- Significant GI bleeds are surprisingly infrequent.

Prognostic features

- Therapeutic levels of salicylate are generally <300mg/L (2.2mmol/L). Levels of 500â€“750mg/L represent moderate OD and >750mg/L (5.4mmol/L) is severe.
- Severe metabolic acidosis is associated with a poor outcome.

Management

- Gastric lavage should be attempted where possible up to 12 hours after ingestion (or longer if there is evidence of continued absorption, as tablets may adhere to form large masses in the stomach).
- Take blood for U&Es, PT, salicylate, (and paracetamol) level on admission (ideally repeat 4 hours later to access continued absorption).
- Check arterial blood gases to assess degree of acidosis.
- Monitor blood glucose regularly (lab and/or BM stix every 2 hours).
- Mild or moderate salicylate overdose requires only oral or iv rehydration with particular attention to K^+ supplements.
- Marked signs/symptoms of salicylism or levels >750mg/L need specific elimination therapy (below, in order of use).
    - Activated charcoal should be given orally (50g 4 hourly).
    - Forced alkaline diuresis is no more effective than simple alkalinization of the urine, e.g. 1 litre 1.26% $NaHCO_3$ over 2 hours and repeat as necessary to keep the urinary pH >7.5).
    - Haemodialysis is indicated for levels >1000mg/L (7.25mmol/L), persistent or progressive acidosis, deteriorating level of consciousness.
- Pulmonary oedema may indicate either fluid overload or increased vascular permeability. Admit to ITU and insert a

pulmonary artery catheter for measuring wedge pressures. Non-cardiogenic pulmonary oedema may require CPAP or mechanical ventilation (p906).

P.835

P.836

Theophylline

Intoxication can be deliberate or iatrogenic due to the low therapeutic index of theophylline.

Presentation

- The features of acute ingestion reflect the local irritant GI effects of theophylline, i.e. nausea, vomiting, abdominal cramps, and diarrhoea. GI bleeding is also well recognized.
- Features of systemic toxicity include cardiac arrhythmias, hypotension, and seizures.

Complications

- Acidâ€“base disturbance: an initial respiratory alkalosis which gives way to a secondary metabolic acidosis.
- Marked hypokalaemia is common.
- Theophylline-induced fits carry a high mortality (up to 30%) and usually reflect serum theophylline levels of >50mg/L (0.28mmol/L).

Management

- Gastric lavage should be attempted if seen within 1â€“2 hours of ingestion. Activated charcoal should also be given both to prevent further absorption and to enhance systemic

clearance (50â€“100g stat then 50g 4 hourly), although this may not be practical in the presence of severe nausea and vomiting.

- Take blood for U&E and theophylline level.
- *Hypokalaemia* should be corrected aggressively with iv supplements (40â€“60mmol/h may be needed).
- Record a 12-lead ECG and then monitor ECG continuously for arrhythmias.
- Verapamil (10mg iv) and propranolol (2â€“5mg iv) are useful for treating supraventricular and ventricular *tachyarrhythmias* respectively. Lignocaine appears to have little effect on ventricular ectopy and should be avoided.
- *GI bleeding* should be managed in the usual way (p608). Avoid cimetidine which substantially inhibits theophylline metabolism (ranitidine is safe, e.g. 50mg iv tds).
- *Seizures* should be controlled with diazepam (10mg iv prn).
- *Haemoperfusion* (charcoal or resin) should be considered in severe overdoses particularly those with recurrent seizure activity or intractable vomiting. The latter represents direct stimulation of the area postrema and generally responds poorly to antiemetics, e.g. metoclopramide and prochlorperazine.

Tricyclic anti-depressants

First-generation agents (e.g. amitriptyline, imipramine, and desipramine) are the most likely to cause lethal intoxication. The newer second-generation tricylics (e.g. lofepramine) and tetracylics are generally much safer in overdose.

Presentation

- Anti-cholinergic features are prominent early on with dry mouth, dilated pupils, blurred vision, sinus tachycardia, urinary retention, myoclonic jerking, agitation, and even hallucinations.
- Cardiac arrhythmias from a quinidine-like (type Ia) effect on the heart, profound hypotension, convulsions, and coma follow.

Complications

- Severe intoxication causes deep coma with respiratory depression, hypoxia, and a metabolic acidosis.
- Neurological signs include a temporary loss of oculocephalic and oculovestibular reflexes, long tract signs, and internuclear ophthalmoplegia.
- Hypothermia, skin blistering (cf. barbiturates), and rhabdomyolysis are also reported.

Prognostic features

- Death may follow ingestion of as little as 1000mg of a tricyclic.
- Prolongation of the QRS >100ms suggests significant intoxication with a high risk of convulsion; a QRS >160ms is generally seen before ventricular arrhythmias develop. Patients with ischaemic heart disease (especially post MI) and conduction defects are particularly at risk.

Management

- Patients with CNS depression should be monitored closely, preferably on an ITU or high-dependency area.

- Gastric lavage should be attempted if seen within 12 hours of ingestion. Activated charcoal should be given orally (50â€“100g, single dose).
- Record a 12-lead ECG and monitor continuously for up to 48 hour.
- Respiratory failure may evolve rapidly, necessitating intubation and ventilation.
- Severe hypotension requires inotropic support (see p262).
- Severe acidosis should be corrected with iv $NaHCO_3$ (see p294).
- Control seizures with diazepam (5â€“10mg iv bolus prn).
- Sinus tachycardia and arrhythmias that do not compromise cardiac output do not need treatment. If output is failing then correct any acidosis or hypoxia before considering anti-arrhythmics.
- Most class I anti-arrhythmic agents are ineffective or worsen the conduction disturbance. Phenytoin (250mg iv over 5 minutes) or amiodarone (300mg IVI over 30 minutes) are the most useful for cardiac dysrhythmias.
- If all measures fail then an induced alkalosis (by hyperventilation or 50â€“100mmol $NaHCO_3$ over 15 minutes i.e. 50â€“100ml 8.4% $NaHCO_3$) may help by increasing binding of the tricyclic to plasma proteins.
- Tricyclic coma may last 24â€“48 hours. In many patients recovery is marked by profound agitation and florid visual and auditory hallucination (a â€˜central anticholinergic syndromeâ€™). Sedation may be necessary (e.g. po diazepam or chlormethiazole).

Editors: Ramrakha, Punit S.; Moore, Kevin P.
Title: *Oxford Handbook of Acute Medicine, 2nd Edition*

Chapter 15

Disorders due to physical agents

Disorders due to heat

- Patients exposed to heat present with a spectrum of disorders, from mild oedema/syncope (vasodilatation), though mild to moderate disorders (cramps and exhaustion) but with intact thermoregulation, to heat stroke where thermoregulation fails.
- *Predisposing factors*: obesity, strenuous exercise, alcohol, old age, anticholinergic drug ingestion, and hot climate.

Heat cramps

- Typically painful spasm of heavily exercising muscles (commonly in calves or feet) thought to be due to salt depletion.
- The diagnosis is clinical and further investigation rarely indicated.

Treatment

- Rest, massage of affected muscle and fluid replacement, either intravenously (N saline 1 litre over 2h repeated if necessary) or orally with 0.1% salt solution.
- Plain salt tablets may be usedâ€”take with copious amounts of water; in the stomach they will produce a hypertonic solution and may cause gastric irritation.
- Freshly squeezed orange juice (partly diluted with water) provides a simple way to replace salt, potassium, and water.
- Admission to hospital rarely indicated.

Heat exhaustion

- The symptoms reflect the effects of salt and water depletion, dehydration, and accumulation of metabolites.
- Predominant salt loss presents insidiously over days (cramps, nausea, weakness, postural dizziness, malaise), whereas mainly water loss presents more acutely with headache, nausea, and CNS symptoms (confusion, delirium, incoordination).
- *Examination*: Usually the patient is flushed and sweating with evidence of dehydration. Body temperature may be normal or mildly elevated (~38Â°C).
- *Investigations*: *U&E* may show hyper- or hypo-natraemia and pre-renal failure. *FBC* may show haemoconcentration. Mild elevations of *CK* and *LFTs* are common. Urine should be examined for myoglobinuria if the serum CK is markedly elevated >2000U/l (rhabdomyolysis).

Treatment

- Assess fluid deficit and replace with ivi if severe.
- Rest and fluid replacement are the mainstay.
- Young persons may just require aggressive oral rehydration [water, salt, commercially available rehydration preparations (e.g. *Dioralyte*Â®)] and may require 4â€“6 litres over 6â€“8 hours.
- Intravenous therapy should be guided by electrolytes (caution with â†“ or â†‘Na^+); a suggested regimen is N saline 1 litre over 30min followed by another over 1 hour, then alternating bags of 5% dextrose and N saline 2 hourly: be guided by the clinical state and U&E of the patient. The elderly will require more cautious fluid replacement, if indicated, guided by CVP.
- Recovery is usually rapid (12â€“24 hours).

Heat stroke

Excessive exposure to heat or strenuous exercise in a hot environment results in eventual failure of the thermoregulatory mechanisms, with rising body temperature and extensive multisystem damage.

Presentation

- Symptoms include headache, nausea, dizziness, parasthesiae in limbs, piloerection, confusion, delirium, seizures, and coma.
- Examination shows elevated body temperature (>40Â°C). There is profuse sweating unless the patient is severely dehydrated. Initially there is tachycardia and increased cardiac output which falls as cardiovascular collapse ensues. Neurological findings include muscle rigidity, dystonias, ataxia, seizures, and coma.

Investigations

â€¢ U&E	â†“ or â†‘K^+, dehydration, renal failure from ATN or rhabdomyolysis, â†“ or â†‘Na^+
â€¢ CK, AST, and LDH	Raised with rhabdomyolysis
â€¢ Glucose	Normal or low
â€¢ Ca^{2+}, PO_4^{3-}, Mg^{2+}	All usually low
â€¢ Clotting screen	Evidence of DIC
â€¢ FBC	Haemoconcentration, neutrophilia
â€¢ ABG	Initial respiratory alkalosis, then metabolic (lactic) acidosis
â€¢ Urine	Usually small volumes and concentrated. Test for myoglobin, tubular casts, protein
â€¢ ECG	Commonly shows non-specific ST and T wave changes and/or SVT

â€¢ AST	If >1000IU/litre in the first 24 hours, prognosis is poor with serious brain, kidney, and liver injury

Management

- *Stabilize the patient*
  - Ensure adequate airway and ventilation. Give oxygen.
  - Start peripheral iv fluids (crystalloid) promptly; insert CVP line Â± PA (Swan-Ganz) catheter to guide fluid replacement Â± inotropes.
  - Insert a urinary catheter and aim for an output of >30ml/h. If myoglobinuria is present consider alkaline diuresis (p392). Anuria and hyperkalaemia are indications for dialysis (p378).
  - Treat seizures with iv diazepam (p472); phenytoin has been reported to be ineffective.
  - Exclude hypoglycaemia.
- *Reduce body temperature promptly*
  - Begin external cooling with ice packs (in axillae, groin, and neck), tepid sponging and cooling fans; cold water immersion is inappropriate for unstable patients.
  - Violent shivering should be suppressed as it interferes with cooling; give chlorpromazine 10â€“25mg iv slowly.
  - Stop cooling when body temperature reaches 39Â°C; the temperature will fall further and hypothermia is to be avoided.
  - Dantrolene has been effective in some cases but needs further evaluation.

Hypothermia: assessment

This is defined as a core (rectal) temperature <35Â°C; it is designated mild (32â€“35Â°C), moderate (26â€“32Â°C), or severe (<26Â°C).

Risk factors

- Increasing age (impaired thermoregulation, reduced metabolism)
- Abnormal mental state
- Immobility (orthopaedic, Parkinsonism)
- Drugs (alcohol, barbiturate, major tranquillizers, antidepressants)
- Endocrine (hypothyroidism, hypoglycaemia, adrenal insufficiency, hypopituitarism)
- Autonomic neuropathy (DM, Parkinsonism)
- Malnutrition
- Renal failure
- Sepsis (excessive heat loss from vasodilatation)
- Exposure (inadequate clothing/heating, near-drowning).

Presentation

- Mild hypothermia presents as shivering which is maximal at 35Â°C and decreases thereafter, being absent at temperatures below 32Â°C. Other symptoms include mild confusion, weakness, fatigueability, lethargy, ataxia, and dysarthia.
- Progressive hypothermia is associated with delirium, coma, bradycardia and low respiratory rate, cardiac arrhythmias, dilated unresponsive pupils, and loss of reflexes. The EEG is â€˜flatâ€™ at, <20Â°C. Asystole occurs at <15Â° C.

- *Complications*: VF atrial tachy- and brady-arrhythmias, ARDS, aspiration pneumonia, pancreatitis, bowel ischaemia, acute renal failure, rhabdomyolysis, DIC.

Investigations

- Check the core temperature with a low reading rectal thermometer.

â€¢ Urgent bloods	*U&Es, CK* (dehydration, rhabdomyolysis).
	Glucose (usually high).
	Amylase (pancreatitis 2Â° to hypothermia).
â€¢ Routine bloods	FBC, phosphate (â†“), magnesium (â†“)
	Blood cultures
	Thyroid function
	Toxic screen
	Serum cortisol.

- ABG: The values obtained are abnormal â€“ an artefactual lower pH and higher P_aO_2 and P_aCO_2 â€“ as most ABG machines assume the sample was taken at 37Â°C. Some machines can be programmed with the patient's temperature to allow correction for the lower temperature

before the sample is analysed. Alternatively, to correct pH add 0.015 for every degree the patient's temperature is below 37Â°C. The P_aO_2 and P_aCO_2 need to be decreased by 7.2% and 4.4% respectively for every degree below 37Â°C.

- ECG: This may show bradycardia, tachycardia, AF and/or prolongation of PR and QTC intervals. â€˜Jâ€™-waves are seen with temperatures <30Â°C, as a hump in the interval between the QRS and T waves (best seen in V4â€“V6).
- Urine: MCS, dipstick (blood and protein), ?myoglobinuria.

Hypothermia: management

- *Stabilize the patient*
  - Ensure the airway is protected and give oxygen. Avoid hyperventilation as an acute fall in P_aCO_2 may trigger VF.
  - If the patient is unconscious, and injury suspected, immobilize the cervical spine until fracture can be excluded.
  - Establish venous access; exclude hypoglycaemia.
  - Start volume expansion with warm, iv crystalloid infusion if dehydrated (e.g. 5% dextrose 80â€“100ml/h) (fluid may be warmed in a â€˜blood-warmerâ€™ device). CVP monitoring and PA wedge pressure monitoring may help guide fluid replacement.
  - Insert a urinary catheter to monitor urine output (potential rhabdomyolysis).
  - Give iv thiamine 250mg if there is an alcohol history.
  - Severe metabolic acidosis (pH <7.1) should be treated with slow iv bicarbonate infusion (see p716) monitoring

ABG. Avoid rapid changes in pH. Milder degrees of acidosis are well tolerated and require no specific treatment.

- *Ventricular fibrillation* is common (precipitated by rapid changes in P_aCO_2 or pH, intubation without adequate pre-oxygenation, movement) and should be treated as normal (p6) while active rewarming proceeds (see below). Class 1 agents (lignocaine) may be ineffective at low temperatures; *bretylium tosylate* is more successful in cardioverting intractable VF. Atrial arrhythmias and ventricular ectopics without haemodynamic compromise do not require treatment.
- In the event of cardio-respiratory arrest, resuscitation should be continued until core temperature reaches at least 35 Â°C as the cold temperature may provide a degree of neuroprotection.

- *Rewarming*

  - Patients with mild hypothermia may be managed with passive external rewarming. Cover the patient, including scalp, in warm, dry blankets (â€˜space blanketâ€™ if available). Give warmed iv fluids to correct dehydration. Aim for a rise in temperature of 0.5â€“1Â°C/h and monitor closely for complications. Hypotension may be due to rapid vasodilatation; slow the rate of rewarming Â± iv fluids.
  - Moderate or severe hypothermia may require active re-warming, either external (heated blankets, water-bottles, warm bath) or internal [heated humidified oxygen, peritoneal dialysis with rapid exchange of warm fluids(~40Â°C), extra-corporeal blood warming techniques (e.g. haemodialysis, cardiopulmonary bypass]. This may result in vasodilatation, hypotension, and arrhythmias and should only be used in patients who are unstable or in cardiac arrest. Apply initially

only to the trunk to avoid excessive vasodilatation of extremities.

- *Other measures*
    - If the temperature is slow to correct, consider whether the patient is Addisonian or hypothyroid. If you suspect myxoedema, give liothyronine 20â€“40Âµg iv (T3) and hydrocortisone (HC) 200mg iv repeating as necessary. Always give HC with T3 in case there is underlying hypoadrenalism.

    - After septic screen, consider broad spectrum antibiotics for aspiration pneumonia or underlying sepsis as a precipitating factor. Give prophylactic antibiotics to patients with moderate-severe hypothermia (e.g. cefotaxime 1â€“2g q8h).

Hypothermia: localized injury

Chilblains (perniosis)

- *Presentation*: Painful, itching, dark red swellings, typically seen on the fingers or toes. Rarely the calves may be affected. Horse-riding in the winter months may result in chilblains on the upper, outer thighs, despite the riding trousers. More common in women.
- *Diagnosis* is easy; all inflammation is warm except chilblains which are cool to touch.
- *Treatment* is symptomatic and warmer covering. The lesions may recur every winter.

Trench foot

- *Presentation*: Usually occurs 12â€“24 hours after exposure to cold and damp. Initially the foot is cold and pale, with reduced sensation and pulses. This is followed by hyperaemia, painful swelling, sometimes with ulceration or gangrene if severe.
- *Treatment*: Conservative with elevation, rest, and strict attention to asepsis.

Frostbite

Presentation

- This results from freezing of the tissues and ischaemic necrosis due to vasospasm. Symptoms include numbness, stinging, or burning pain.
- Superficial frostbite (skin and sub-cutaneous tissues only) appears pale and has a somewhat soft and â€˜rubberyâ€™ feel.
- Deep frostbite involves deeper tissues, even bone, resulting in a hard, â€˜woodyâ€™ feel.

Treatment

- Treat any associated hypothermia (as above).
- If there is any possibility of refreezing, do not thaw (even if it means walking on frozen feet); refreezing increases tissue damage.
- *Rapid* rewarming is essential to minimize tissue necrosis; immerse in a water bath (40â€“42Â°C if tolerated) for several minutes.
- There is often considerable pain that may require iv/im analgesia.

- Clean the affected part and apply topical disinfectants (iodine 5â€“10%), bed rest, elevation. Debridement should be delayed until the limb has demarcated.
- Give tetanus prophylaxis if necessary.
- There is some evidence for the use prophylactic antibiotics (after appropriate swabs) in patients with deep frostbite (high dose penicillin).
- Heparin has not been shown to be useful.

Diving accidents

Decompression illness

Water pressure increases by 1 atmosphere for every 10m (33ft) below the surface. The increased pressure increases the amount of dissolved nitrogen in the plasma. Rapid ascent results in the formation of bubbles as the gas comes out of solution.

Symptoms

- Usually occur within the first hour of surfacing but may be delayed by up to 36 hours.
- â€˜Deepâ€™ muscle aches (â€˜the bendsâ€™).
- Skin symptoms: pain, parasthesiae, itching, and burning.
- â€˜The chokesâ€™: retrosternal pain, cough, breathlessness.
- Neurological symptoms: paraplegia, urinary retention, patchy spinal cord necrosis due to retrograde venous thombosis. Suspect all neurological symproms are due to decompression illness until proven otherwise.

Air embolism

If the breath is held on ascent (due to breath-holding or laryngospasm) the volume of gas in the lungs expands, and large pressure gradients are generated. Eventually alveoli rupture resulting in pneumothorax, pneumomediastinum, and sub-cutaneous emphysema. Ruptured pulmonary veins allow arterial air embolism (commonly into the carotid circulation).

- Symptoms vary from behaviour changes, confusion, focal neurological defects, seizures, coma, and death. A variety of other symptoms may occur depending on the arterial bed the emboli travel to and due to the free air in the thoracic cavity.

Treatment

- Give oxygen, analgesia, and intravenous fluids if dehydrated. Do not give nitrous oxide (*Entonox*Â®).
- If there is a possibility of air embolism lie on the left side with head-down tilt to collect air in the right atrium. Occasionally it may be possible to aspirate the air from the right atrium with a venous catheter.
- *Immediate recompression* is the only effective treatment. Contact your local poisons unit (see p854 for telephone numbers) who will be able to put you in contact with your nearest recompression chamber to your hospital and arrange urgent transfer.
- Never attempt recompression in water.

Pneumothorax

(see p236)

Near-drowning

- When immersed in water, a period of breath-holding is followed by involuntary inspiration. Aspiration of water, bacteria, and other particulate material follows.
- The distinction between fresh-water (hypotonic) and salt-water (hypertonic) drowning is only useful in that fresh-water inhalation results in marked haemolysis, electrolyte disturbances, intravascular volume overload, whereas salt-water ingestion may result in hypovolaemia and haemoconcentration. Their management is identical.
- In practice the volume of water aspirated is small; in 10â€“15%, laryngospasm results in â€˜dry drowningâ€™ and asphyxia.

Presentation

- Symptoms may range from none, to cough and mild breathlessness, to cardiorespiratory arrest and coma.
- Initial examination, blood gases, and CXR may be normal and do not predict subsequent clinical course.
- Examine specifically for trauma to cervical or thoracic spine.

Prognostic features

Survival is related to duration of submersion, extent and duration of hypoxia, water temperature, extent of hypothermia, presence of aspiration, adequacy of initial resuscitative efforts, age, and presence of co-existing medical conditions.

Management

- Asymptomatic patients should be observed for at least 6â€“12 hours. If examination, arterial gases, and CXR remain normal, they may be discharged.
- At the scene, manoeuvres to â€˜drain the lungsâ€™ are potentially dangerous and ineffective; aggressive mouth-to-mouth resuscitation and cardiac massage should be started if necessary.
- Give oxygen as soon as available. Intubate and ventilate if there is persistent hypoxia. 5â€“10cm H_2O PEEP may improve oxygenation.
- Patients with history of diving or evidence of head or spine trauma should be treated as having head/spine injury until proven otherwise.
- Hypothermia should be treated in the usual manner (p848). The low temperatures may provide a degree of neuro-protection and resuscitative efforts should not be stopped until the core temperature reaches >35Â°C.
- Metabolic acidosis is invariable; if pH <7.1, give iv bicarbonate 50ml 8.4% over 15â€“20 minutes (see lactic acidosis, p278).
- If there is clinical or radiological evidence of chest infection begin treatment with broad spectrum antibiotics (e.g. cefotaxime and metronidazole or amoxycillin, gentamicin and metronidazole).

Electric shock

- Damage is caused by a combination of thermal tissue injury and direct injury from the electric current passing though the tissue.
- The treatment is supportive.

Domestic electric shock

- Skin burns at the site of entry and exit of the current are common. These should be referred to a burns centre for specialist management.
- Cardiac damage may result in ST and T wave changes on ECG, VF, asystole, and other cardiac arrhythmias. Monitor for at least 24 hours, if the ECG is abnormal.
- Rhabdomyolysis with varying degrees of renal failure is common due to tetanic contraction and ischaemic necrosis of skeletal muscle (p392). There may be severe muscle burn injury even when there is minimal skin damage. If suspected, refer to a burns or plastic surgery unit.
- Neurological damage results in altered mental state, confusion, depersonalization, and patchy spinal cord demyelination.
- Heat may also be responsible for intravascular coagulation and ischaemic necrosis of other tissues. This is classically delayed by several hours. Treatment is supportive.
- Exclude co-existent fractures of spine and long bones.

Lightning injuries

- The voltage and current are several orders of magnitude greater than domestic electrical injuries (up to 10^5 A and 10^6 V) but exposure is extremely brief. Most of the current passes over the skin and deep tissue damage is less common.
- Skin entry burns have a â€˜fern-likeâ€™ pattern and are mainly superficial or partial thickness burns.
- Most patients survive without any significant arrhythmias. Ventricular fibrillation or asystole are occasionally seen.

Myocardial infarction, ECG abnormalities, and late arrhythmias have been reported.

- Dilated pupils may be the result of transient autonomic sympathetic discharge and should not deter active resuscitation.
- Direct injury to abdominal viscera, lungs, spinal cord, and tympanic membrane may be seen. Late complications include optic atrophyand cataracts.

Smoke inhalation

- This causes a combination of thermal and chemical injury to the lungs and varying degrees of systemic toxicity.
- The main cause of death in patients with smoke inhalation is cerebral hypoxia secondary to carbon monoxide exposure.
- Combustion of household materials can also generate a number of other toxic substances such as sulphur dioxide, nitrogen dioxide, acrolein (from wood and petroleum), hydrochloric acid (PVC), toluene diisocyanate (polyurethane), and hydrogen cyanide that may result in direct lung, skin, and conjunctival injury.

Presentation

- Common symptoms include cough, sore thoat, breathlessness, pleuritic retrosternal chest pain, headache, dizziness, nausea.
- Examination: Note the skin colour (normal, cyanotic). Look for perioral and perinasal burns, singeing of nasal hair, burns of oral mucosa (markers of significant, thermal,

respiratory-tract injury).

- Note cough and colour of sputum (?black), tachypnoea, wheeze, stridor and/or tachycardia. Assess mental state (? confused).

Initial investigations

â€¢ ABG	(Hypoxia, CO_2 retention)â€”note the *calculated* O_2 saturation from the machines is overestimated in the presence of significant COHb.
â€¢ Carboxy-Hb	(COHb) level from co-oximeter (available in some ITUs or contact duty biochemist). Non-smokers <1%, smokers 4â€“6%, >10% significant CO exposure, >50% coma, >70% fatal (see p802).
â€¢ CXR	May be normal. Progressive interstitial and alveolar shadowing mimicking cardiogenic pulmonary oedema (upper > lower lobes)
â€¢ ECG	Non-specific ST-T wave changes or signs of myocardial ischaemia.
â€¢ Pulse oximetry	Inaccurate; may only be normal in the presence of high levels of COHb.

Indications for admission

- History of significant smoke inhalation injury
- Clinical signs of significant lung injury (above)
- Confusion
- COHb level >15%,
- Hypoxia (P_aO_2 <10kPa on air)
- Raised P_aCO_2 on air.

Management

The initial ABG and CXR may be normal and do not predict subsequent clinical course.

- Resuscitate the patient (Airway, Breathing, Circulation).
- If the initial CXR and ABG are normal, observe the patient for 4â€“6 hours and if there is no clinical deterioration, discharge with instructions to return if they develop any respiratory symptoms.

- Give supplemental, humidified, cooled oxygen.
- Treat bronchospasm with inhaled and iv bronchodilators (see p213).
- Encourage deep breathing and cough to clear secretions; there may be copious sputum production. Send a specimen for culture.
- Start antibiotics if there is evidence of infection.
- *Indications for intubation and ventilation* include falling P_aO_2 despite maximal inspired oxygen, failure to clear secretions, or risk of upper airways obstruction (see ARDS, p230).

Carbon monoxide poisoning see p802.

Acute mountain sickness

- Usually seen within 24â€“36 hours of ascent.
- Symptoms include headache (most common), lethargy, irritability, difficulty concentrating, nausea, vomiting, palpitations, breathlessness, dizziness, and difficulty sleeping. Symptoms often worsen over the first 2â€“3 days then resolve completely by day 5â€“7.
- Examination and investigations are usually normal except for mild dehydration, alkalaemia, and bicarbonate diuresis if acclimatization has begun.
- The most effective treatment is descent to lower altitude and supplemental oxygen. Encourage bed rest and fluid intake. Sedatives may depress respiratory drive, exacerbating hypoxia, and mask signs of altered mental status.
- Dexamethasone is effective in reducing the symptoms of acute mountain sickness but does not reduce the objective manifestations of the illness or retard progression; it is only recommended if descent to lower altitude is not possible or delayed.
- Do not use diuretics acutely.

Acute high-altitude pulmonary oedema (HAPO)

- Non-cardiogenic pulmonary oedema occurs within 12â€“96 days of ascent.
- Type 1 HAPO is said to occur when an unacclimatized individual ascends to high altitude; Type 2 HAPO is said to occur when a high-altitude resident develops pulmonary oedema after returning from a visit to a lower altitude. The distinction is important as treatment differs (see below).

- Symptoms are as for acute mountain sickness (see above), but in addition there is low-grade fever, cough, and breathlessness at rest. Examination shows pulmonary oedema WITHOUT the usual signs of heart failure (elevated JVP, S3 gallop, cardiac enlargement).
- Investigations: ABG shows respiratory alkalosis and hypoxaemia; ECG may show sinus tachycardia with signs of right-heart strain. CXR may show patchy lung shadowing.

Treatment

- Mild type 1 and 2 HAPO may be treated with oxygen and bed rest; symptoms usually resolve in 1â€“2 days. Treatment with diuretics, digitalis, and steroids have not been shown to be useful.
- Moderate-severe type 1 HAPO may require intubation and ventilation with PEEP. Type 2 HAPO usually responds to bed rest and supplemental oxygen only.

High-altitude encephalopathy

- Usually occurs within 24 hours of ascent over 12 000 feet (~3600m).
- Initial symptoms of acute mountain sickness (see above) progress to papilloedema, retinal haemorrhages, ataxia, and focal neurological defects, seizures, and coma.
- Treatment is with oxygen and immediate descent to lower altitudes. High doses of dexamethasone may be beneficial but mannitol and diuretics are not routinely given.

Prevention

- Gradual ascent, adequate rest and fluids, and avoidance of

strenuous exercise reduce the incidence of high-altitude illness.

- Prophylactic acetazolamide (250mg po q8â€“12h) given the day before and for the first few days of ascent reduces the incidence and severity of acute mountain sickness.

Practice points: High altitude illness

- High altitude illness is usually seen when an unacclimatizedindividual travels to altitudes above ~7000 feet (2300m); theincidence and severity increases progressively with higher altitudesand with rapid rates of ascent.
- Acute symptoms occurs within 6â€“8 hours of ascent with markedindividual variation in tolerance to hypoxaemia at altitude.
- Commercial airlines cruising at altitudes of 29 000â€“37 000 have cabinpressures equivalent to an altitude of 6000â€“8000 feet; thus travellersmay be briefly exposed to conditions that may provoke mild high-altitude sickness!

Stings and insect bites

Acute presentation (within 2â€“3 hours)

History Ask specifically if reactions have occurred in the past and if there is any past history of angioedema, urticaria, bronchospasm, or anaphylaxis. Most patients developing anaphylaxis have no previous history of significant reaction.

Examine the wound for the â€˜stingerâ€™ and remove

carefully. Observe the patient carefully for 1â€“2 hours for any signs of evolving anaphylaxis (generalized urticaria and pruritus, bronchospasm, or oropharyngeal oedema). If present the patient requires urgent treatment (see below).

Management

- *Local reactions*
    - Clean the wound of any foreign material.
    - Apply an ice compress.
    - Give tetanus prophylaxis if appropriate.
    - Discharge with instructions to return if they develop breathlessness, wheeze, rash, oropharyngeal swelling, or generalized pruritus.
    - Some would advocate giving patients who may be potentially immunosupressed (e.g. diabetes, high-dose steroid therapy) prophylactic antibiotics (e.g. co-amoxiclav po) but there is little evidence this is of benefit.
    - Observe patients with prior history of systemic reactions closely.
- *Systemic reaction* (see p264, anaphylaxis)
    - Secure the airway: If respiratory obstruction is imminent, intubate and ventilate or consider emergency cricothyroidotomy (see p914). A 14 or 16G needle and insufflation with 100% O_2 can temporize until the anaesthetist arrives.
    - Give oxygen; if there is refractory hypoxia, intubate and ventilate.
    - Give intramuscular adrenaline 0.5â€“1mg (0.5â€“1ml of 1 in 1000 adrenaline injection) and repeat every 10 minutes according to bp and pulse.

Administer this *before* searching for intravenous access so as not to waste time.

- Establish venous access and start iv fluids (colloid if hypotensive). Persistent hypotension requires iv inotropes (see p262).
- Intravenous adrenaline may be required if the patient is severely ill with poor circulation. Give *slow* injection of 500 micrograms (5ml of the dilute 1 in 10 000 adrenaline injection) at 1mL/minute *stopping* when a response is obtained.
- If the patient continues to deteriorate, start intravenous aminophylline infusion. Patients on beta-blockers may not respond to adrenaline injection and require iv salbutamol infusion.
- Isolated bronchospasm may be treated with nebulized Î²-agonists (salbutamol). If there is prior history of systemic reactions, im adrenaline is the treatment of choice.
- Give iv hydrocortisone 100â€“300mg and chlorpheniramine 10â€“20mg.
- Continue H_1 antagonist (e.g. chlorpheniramine 4mg q4â€“6h) for at least 24â€–48h; longer if urticaria and pruritus persist.
- Do not forget local wound care as above.

- *Prevention*

Patients prone to serious reactions from stings should be provided with, and instructed on, the use of commercially available â€˜bee-stingâ€™ kits. [Available freely in the US and on a named-patient basis in the UK from the manufacturers (see BNF).] These contain pre-filled syringes of adrenaline for im injection and one also contains chewable tablets of chlorpheniramine.

Delayed presentation

- Due to local toxic reaction or infection, and rarely with serum sickness, vasculitis, Henoch-SchÃ¶nlein purpura, and haemolysis.
- Clean the wound and give tetanus prophylaxis if indicated as above.
- Practically, it is difficult to distinguish a local toxic reaction from infection. Treat with both an oral antihistamine and oral antibiotic (e.g. chlorpheniramine 4mg q4â€“6h and co-amoxiclav).
- Elevate if there is marked swelling and consider surgical drainage of fluctuant masses.

Snakebite

- The only indigenous venomous snake in the UK is the adder (*Vipera berus*) and acute envenomation is rare.

Presentation

- Local effects include pain, swelling, erythema, bruising, tender regional lymphadenopathy.
- Systemic effects such as hypotension and syncope, angioedema, abdominal colic, diarrhoea and vomiting, coagulopathy and spontaneous haemorrhage, ECG abnormalities, shock, ARDS, rhabdomyolysis, and renal failure are ominous, but *V. berus* bites are seldom fatal in adult humans.

Management

- Identify the snake if at all possible. The instinctive

response on being bitten is to give the snake a ritual beating, but this does not help in the identification.

- Non-poisonous bites should be cleaned, anti-tetanus prophylaxis given to the patient if needed, with prophylactic antibiotics as for animal bites (see p328).

Poisonous snake bites

First aid

- Immobilize the bitten part and keep below the level of the heart if possible.
- A veno-occlusive tourniquet should be placed immediately above the bite, taking care not to obstruct the arterial supply.
- Incision and suction of the wound is only indicated if the patient is seen within 15â€“20 minutes, the snake is large and identified as poisonous, the victim is young or elderly, and the nearest source of anti-venom is more than 2 hours away.
- The patient should be kept calm and quiet to avoid tachycardia and further vasodilatation and venom absorption.

In hospital

- All patients with bites from poisonous snakes should be admitted.
- Establish venous access and send blood for FBC, coagulation profile, U&E, group and X-match. Examine urine for myoglobin or haemoglobin.
- Treat hypotension and shock (p257).

- Watch for evolving compartment syndrome.
- All bites should be cultured and treated with antibiotics (see bites). Some authorities recommend high-dose hydrocortisone and antihistamine to reduce local inflammation and systemic symptoms.
- Indications for anti-venom treatment include systemic features (as above), coagulopathy, neutrophil leukocytosis, and if swelling extends to wrist/ankle within 4 hours of a bite on the hand/foot.
- *Contact your regional centres for details on identification, management and supply of anti-venom for adder and certain foreign snakes* (see p961).
- General measures: All bites should be swabbed for MC&S (see bites).

Editors: Ramrakha, Punit S.; Moore, Kevin P.
Title: *Oxford Handbook of Acute Medicine, 2nd Edition*

Chapter 16
Practical procedures

Central line insertion

You will need the following:

- Sterile dressing pack and gloves
- 10ml and 5ml syringe with green (21G) and orange (25G) needles
- Local anaesthetic (e.g. 2% lignocaine)
- Central line (e.g. 16G long AbbocathÂ® or Seldinger catheter)
- Saline flush
- Silk suture and needle
- No. 11 scalpel blade
- Sterile occlusive dressing (e.g. TegadermÂ®)

Risks

- Arterial puncture (remove and apply local pressure)
- Pneumothorax (insert chest drain or aspirate if required)

- Haemothorax
- Chylothorax (mainly left subclavian lines)
- Infection (local, septicaemia, bacterial endocarditis)
- Brachial plexus or cervical root damage (over enthusiastic infiltration with local anaesthetic)
- Arrhythmias

General procedure

- The basic technique is the same whatever vein is cannulated.
- Lie the patient supine (Â± head-down tilt).
- Turn the patient's head away from the side you wish to cannulate.
- Clean the skin with iodine or chlorhexidine: from the angle of the jaw to the clavicle for internal jugular vein (IJV) cannulation and from the mid-line to axilla for the subclavian approach.
- Use the drapes to isolate the sterile field.
- Flush the lumen of the central line with saline.
- Identify your landmarks (see p869 and p870).
- Infiltrate skin and sub-cutaneous tissue with local anaesthetic.
- Have the introducer needle and Seldinger guide-wire within easy reach so that you can reach them with one hand without having to release your other hand. Your fingers may be distorting the anatomy slightly making access to the vein easier and if released it may prove difficult to relocate the vein.
- With the introducer needle in the vein, check that you can aspirate blood freely. Use the hand that was on the pulse to

immobilize the needle relative to the skin and mandible or clavicle.

- Remove the syringe and pass the guide wire into the vein; it should pass freely. If there is resistance, remove the wire, check that the needle is still within the lumen, and try again.
- Remove the needle leaving the wire within the vein and use a sterile swab to maintain gentle pressure over the site of venepuncture to prevent excessive bleeding.
- With a No. 11 blade make a nick in the skin where the wire enters, to facilitate dilatation of the sub-cutaneous tissues. Pass the dilator over the wire and remove, leaving the wire *in situ*.

- Pass the central line over the wire into the vein. Remove the guide-wire, flush the lumen with fresh saline, and close off to air.
- Suture the line in place and cover the skin penetration site with a sterile occlusive dressing.

Measuring the CVPâ€”tips and pitfalls

- When asked to see a patient at night on the wards with an abnormal CVP reading, it is a good habit to always re-check the zero and thereading yourself.
- Always do measurements with the mid-axillary point as the zero reference. Sitting the patient up will drop the central filling pressure (pooling in the veins).
- Fill the manometer line, being careful not to soak the cotton ball stop. If this gets wet it limits the free-fall of saline or dextrose in the manometer line.
- Look at the rate and character of the venous pressure. It should fall to its value quickly and swing with respiration.

- If it fails to fall quickly consider whether the line is open (i.e. saline running in), blocked with blood clot, positional (up against vessel wall; ask patient to take some deep breaths), arterial blood (blood tracks back up the line). Raise the whole dripstand (if you are strong), and make sure that the level falls. If it falls when the whole stand is elevated it may be that the CVP is very high.
- It is easier, and safer, to cannulate a central vein with the patient supine or head down. There is an increased risk of air embolus if the patient is semi-recumbent.

Internal jugular vein cannulation

The internal jugular vein (IJV) runs just posterolateral to the carotid artery within the carotid sheath and lies medial to the SCM in the upper part of the neck, between the two heads of SCM in its medial portion and enters the subclavian vein near the medial border of the anterior scalene muscle (see figure). There are three basic approaches to IJV cannulation: medial to sternocleidomastoid (SCM), between the two heads of SCM, or lateral to SCM. The approach used varies and depends on the experience of the operator and the institution.

- Locate the carotid artery between the sternal and clavicular heads of SCM at the level of the thyroid cartilage; the IJV lies just lateral and parallel to it.
- Keeping the fingers of one hand on the carotid pulsation, infiltrate the skin with LA thoroughly, aiming just lateral to this and ensuring that you are not in a vein.
- Ideally, first locate the vein with a blue or green needle. Advance the needle at 45Â° to the skin, with gentle negative suction on the syringe, aiming for the ipsilateral nipple, lateral to the pulse.
- If you fail to find the vein, withdraw the needle slowly,

maintaining negative suction on the syringe (you may have inadvertently transfixed the vein). Aim slightly more medially and try again.

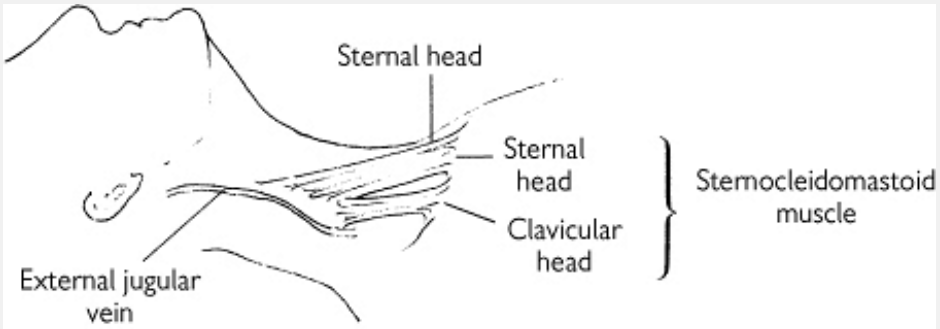
- Once you have identified the position of the vein, change to the syringe with the introducer needle, cannulate the vein, and pass the guide-wire into the vein (see p869).

Tips and pitfalls

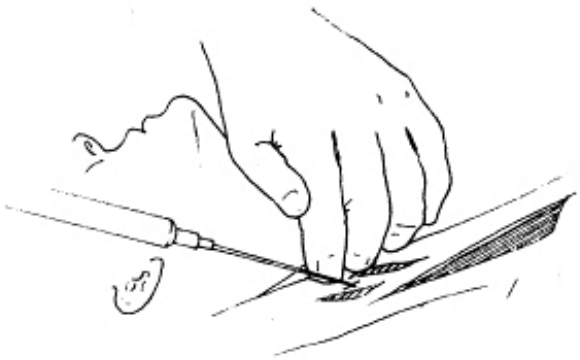
- Venous blood is dark, and arterial blood is pulsatile and bright red!
- Once you locate the vein, change to the syringe with the introducer needle, taking care not to release your fingers from the pulse; they may be distorting the anatomy slightly making access to the vein easier and if released it may prove difficult to relocate the vein.
- The guide-wire should pass freely down the needle and into the vein. With the left IJV approach, there are several acute bends that need to be negotiated. If the guide-wire keeps passing down the wrong route, ask your assistant to hold the patient's arms out at 90Â° to the bed, or even above the patient's head, to coax the guide-wire down the correct path.
- For patients who are intubated or requiring respiratory support it may be difficult to access the head of the bed. The anterior approach may be easier (see figure) and may be done from the side of the bed (the left-side of the bed for right-handed operators, using the left hand to locate the pulse and the right to cannulate the vein).
- The IJV may also be readily cannulated with a long AbbocathÂ®. No guide-wire is necessary, but, as a result, misplacement is commoner than with the Seldinger technique.
- When using an AbbocathÂ®, on cannulating the vein, remember to advance the sheath and needle a few mm to

allow the tip of the plastic sheath (~1mm behind the tip of the bevelled needle) to enter the vein. Holding the needle stationary, advance the sheath over it into the vein.

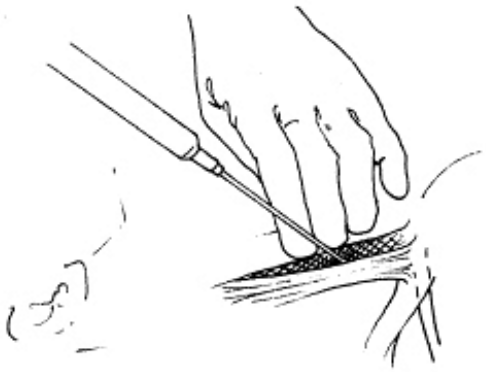
- Arrange for a CXR to confirm the position of the line.



(a) Surface anatomy of external and internal jugular veins



(b) Anterior approach: the chin is in the midline and the skin puncture is over the sternal head of SCM muscle

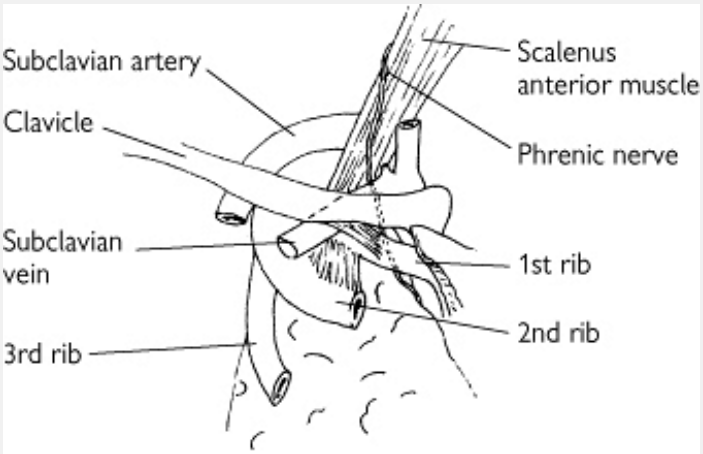


(c) Central approach: the chin is turned away and the skin puncture is between the two heads of SCM muscle

Internal jugular vein cannulation

Subclavian vein cannulation

The axillary vein becomes the subclavian vein (SCV) at the lateral border of the 1st rib and extends for 3â€“4cm just deep to the clavicle. It is joined by the ipsilateral IJV to become the brachiocephalic vein behind the sternoclavicular joint. The subclavian artery and brachial plexus lie posteriorly, separated from the vein by the scalenus anterior muscle. The phrenic nerve and the internal mammary artery lie behind the medial portion of the SCV and, on the left, lies the thoracic duct.



The subclavian vein and surrounding structures

- Select the point 1cm below the junction of the medial third and middle third of the clavicle. If possible place a bag of saline between the scapulae to extend the spine.
- Clean the skin with iodine or chlorhexidine.

- Infiltrate skin and sub-cutaneous tissue and periosteum of the inferior border of the clavicle with local anaesthetic up to the hilt of the green (21G) needle, ensuring that it is not in a vein.
- Insert the introducer needle with a 10ml syringe, guiding gently under the clavicle. It is safest to initially hit the clavicle, and â€˜walkâ€™ the needle under it until the inferior border is just cleared. In this way you keep the needle as superficial to the dome of the pleura as possible. Once it has just skimmed underneath the clavicle, advance it slowly towards the contralateral sternoclavicular joint, aspirating as you advance. Using this technique the risk of pneumothorax is small, and success is high.
- Once the venous blood is obtained, rotate the bevel of the needle towards the heart. This encourages the guide-wire to pass down the brachiocephalic rather than up the IJV.
- The wire should pass easily into the vein. If there is difficulty, try advancing during the inspiratory and expiratory phases of the respiratory cycle.
- Once the guide-wire is in place, remove the introducer needle, and pass the dilator over the wire. When removing the dilator, note the direction that it faces; it should be slightly curved downwards. If it is slightly curved upwards, then it is likely that the wire has passed up into the IJV. The wire may be manipulated into the brachiocephalic vein under fluoroscopic control but if not available it is safer to remove the wire and start again.

- After removing the dilator pass the central venous catheter over the guide-wire, remove the guide-wire, and secure as above.
- A chest X-ray is mandatory after subclavian line insertion to exclude a pneumothorax and to confirm satisfactory placement of the line, especially if fluoroscopy was not employed.

Ultrasound guided central venous catheterization

Traditional central venous catheterization methods rely on anatomical landmarks to predict vein position. However, the relationship between such landmarks and vein position varies significantly in â€˜normalâ€™ individuals. Failure and complication rates using landmark methods are significant and therefore serious complications may occur. Recent advances in portable ultrasound equipment have now made it possible to insert central venous catheters under 2D ultrasound guidance.

Advantages of this technique include:

- Identification of actual and relative vein position
- Identification of anatomical variations
- Confirmation of target vein patency.

Guidelines from the National Institute for Clinical Excellence (September 2002) state: â€˜*Two-dimensional imaging ultrasound guidance is recommended* as *the preferred method for insertion of central venous catheters into the inter-jugular vein (IJV) in adults and children in elective situations*â€™. However, training and equipment availability render such recommendations effectively useless in the UK at present.

Equipment/personnel needed

- Standard Seldinger-type kit or whatever is locally available
- An assistant is essential
- Ultrasound equipment:
    - Screen: displays 2D ultrasound image of anatomical

structures

- Sheaths: dedicated, sterile sheaths of PVC or latex long enough to cover probe and connecting cable (a rubber band secures the sheath to the probe)
- Probe: transducer which emits and receives ultrasound information to be processed for display. Marked with arrow or notch for orientation
- Power: battery or mains
- Sterile gel: transmits ultrasound and provides good interface between patient and probe.

Preparation

Perform a preliminary non-sterile scan to access each internal jugular vein for patency and size.

Patient

Sterile precautions should be taken with patient's head turned slightly away from the cannulation site. Head-down tilt (if tolerated) or leg elevation to increase filling and size of the internal jugular vein. Ensure adequate drapes to maintain a sterile field.

Excessive head rotation or extension may decrease the diameter of the vein.

Ultrasound equipment

- Ensure that the display can be seen
- Sheath is opened (operator) and gel squirted in (assistant)

A generous amount of gel ensures good contact and air-free coupling between probe tip and sheath. Too little may

compromise image quality.

- Probe and connecting cable are lowered into sheath (assistant) which is then unrolled along them (operator)
- Rubber band secures sheath to probe
- Sheath over probe tip is smoothed out (wrinkles will degrade image quality)
- Apply liberal amounts of gel to the sheathed probe tip for good ultrasound transmission and increased patient comfort during movement.

Scanning

The most popular scanning orientation for internal jugular vein central catheter placement is the transverse plane:

- Apply probe tip *gently* to neck lateral to the carotid pulse at the cricoid level or in the sternomastoid-clavicular triangle
- Keep probe perpendicular at all times with the tip flat against the skin
- Orient probe so that movement to the left ensures that the display looks to the left (and vice versa). Probes are usually marked to help orientation. By convention the mark should be to the patient's right (transverse plane) or to the head (longitudinal scan). The marked side appears on the screen as a bright dot
- If the vessels are not immediately visible, keep the probe perpendicular and gently glide medially or laterally until found

*When moving the probe watch the screen*â€”*not your hands*.

After identification of the internal

jugular vein (IJV)

- Position probe so that IJV is shown at the display's horizontal midpoint
- Keep probe immobile
- Direct needle (bevel towards probe) caudally under the marked midpoint of the probe tip at approximately 60Â° to the skin
- The needle bevel faces the probe to help direct the guide wire down the IJV later
- Advance the needle towards IJV

Needle passage causes a â€˜wavefrontâ€™ of tissue compression. This is used to judge the progress of the needle and position. Absence of visible tissue reaction indicates incorrect needle placement. Just before vessel entry â€˜tentingâ€™ of the vein is usually observed.

One of the most difficult aspects initially, when learning this technique, is the steep needle angulation required, but this ensures that the needle enters the IJV in the US beam and takes the shortest and most direct route through the tissues.

Needle pressure may oppose vein walls resulting in vein transfixion. Slow withdrawal of the needle with continuous aspiration can help result in lumen access.

Pass the guidewire into the jugular vein in the usual fashion.

Re-angling the needle from 60Â° to a more shallow angle, e.g. 45Â°, may help guidewire feeding. Scanning the vein in the longitudinal plane may demonstrate the catheter in the vessel but after securing and dressing the CVC, an x-ray should still be obtained to confirm the CVC position, and exclude pneumothorax.

Maintain sterility at all times, and secure the line so that it is comfortable for the patient.

The most common error in measurement of central venous pressure, particularly in CVP lines which have been in place for some time, is due to partial or complete line blockade. With the manometer connected, ensure that the line is free flowing, minor blockages can be removed by squeezing the rubber bung, with the line proximal being obliterated by acute angulation (ie, bend the tube proximal). Measure the CVP at the mid-axillary line with the patient supine. CVP falls with upright or semi up-right recumbency, regardless of the reference point. If the CVP is high, lift the stand that holds the manometer so that the apparent CVP falls by 10cm or so, and replace the CVP stand to ground level. If the saline or manometer reading rises to the same level, then the CVP reading is accurate. In other words, one ensures that the CVP manometer level both falls to and rises to the same level.

Pulmonary artery catheterization 1

Indications

PA catheters (Swanâ€“Ganz catheters) allow direct measurement of a number of haemodynamic parameters that aid clinical decision-making in critically ill patients (evaluate right and left ventricular function, guide treatment and provide prognostic information). The catheter itself has no therapeutic benefit and there have been a number of studies showing increased mortality (and morbidity) with their use. Consider inserting a PA catheter in any critically ill patient, after discussion with an experienced physician, if the measurements will influence decisions on therapy (and not just to reassure yourself). Careful and frequent clinical assessment of the patient should always accompany measurements and PA catherization should not delay treatment of the patient.

General indications (not a comprehensive list) include:

- Management of complicated myocardial infarction.
- Assessment and management of shock.
- Assessment and management of respiratory distress (cardiogenic vs non-cardiogenic pulmonary oedema).
- Evaluating effects of treatment in unstable patients (e.g. inotropes, vasodilators, mechanical ventilation, etc.).
- Delivering therapy (e.g. thrombolysis for pulmonary embolism, prostacyclin for pulmonary hypertension, etc.).
- Assessment of fluid requirements in critically ill patients.

Equipment required

- Full resuscitation facilities should be available and the patient's ECG should be continuously monitored.
- Bag of heparinized saline for flushing the catheter and transducer set for pressure monitoring. (Check that your assistant is experienced in setting up the transducer system BEFORE you start.)
- 8F introducer kit (pre-packaged kits contain the introducer sheath and all the equipment required for central venous cannulation).
- PA catheter: Commonly a triple lumen catheter, that allows simultaneous measurement of RA pressure (proximal port) and PA pressure (distal port) and incorporates a thermistor for measurement of cardiac output by thermodilution. Check your catheter before you start.
- Fluoroscopy is preferable, though not essential.

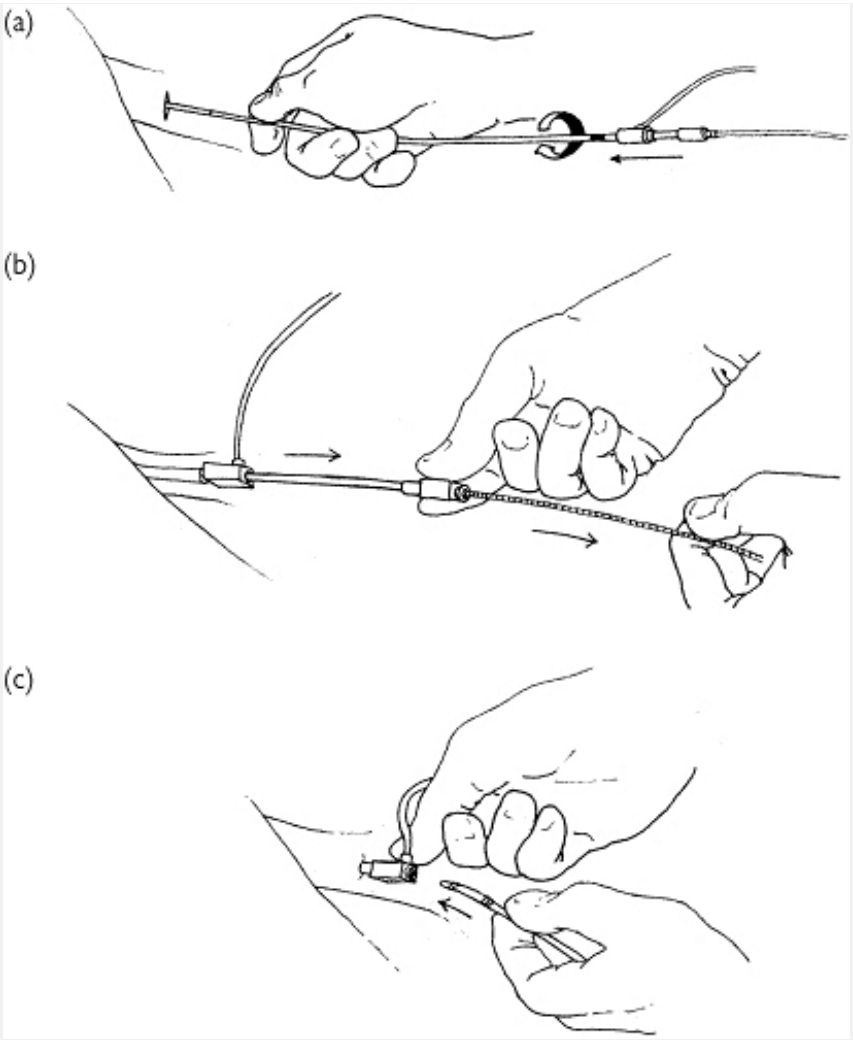
General technique

- Do not attempt this without supervision if you are

inexperienced.

- Observe strict aseptic technique using sterile drapes, etc.
- Insert the introducer sheath (at least 8F in size) into either the internal jugular or subclavian vein in the standard way (pp868â€“p70). Flush the sheath with saline and secure to the skin with sutures.
- Do not attach the plastic sterile expandable sheath to the introducer yet but keep it sterile for use later once the catheter is in position (the catheter is easier to manipulate without the plastic covering).

- Flush all the lumens of the PA catheter and attach the distal lumen to the pressure transducer. Check the transducer is zeroed (conventionally to the mid-axillary point). Check the integrity of the balloon by inflating it with the syringe provided (2ml air) and then deflate the balloon.
- The procedure is detailed on the following pages.



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Pulmonary artery catheterization

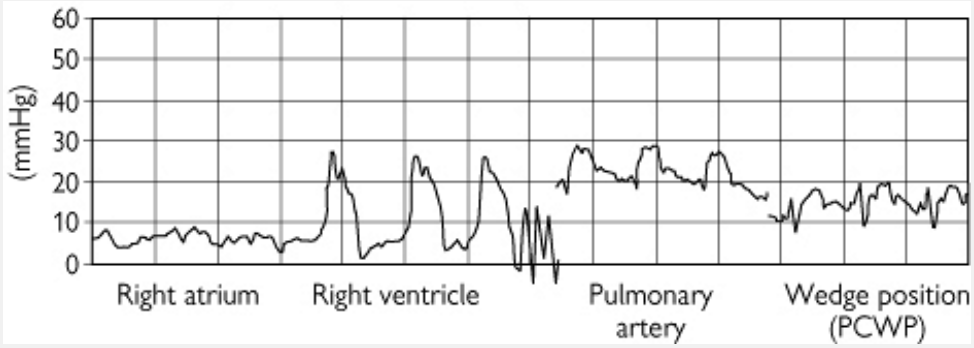
- The sheath and dilator are advanced into the vein over the guide-wire. A twisting motion makes insertion easier.
- The guide-wire and dilator are then removed. The sheath has a haemostatic valve at the end preventing leakage of blood.
- The PA catheter is then inserted through the introducer sheath into the vein (see above).

Pulmonary artery catheterization 2

Insertion technique

- Flush all the lumens of the PA catheter and attach the distal lumen to the pressure transducer. Check the transducer is zeroed (conventionally to the mid-axillary point). Check the integrity of the balloon by inflating it with the syringe provided (~2ml air) and then deflate the balloon.
- Pass the tip of the PA catheter through the plastic sheath, keeping the sheath compressed. The catheter is easier to manipulate without the sheath over it; once in position, extend the sheath over the catheter to keep it sterile.
- With the balloon deflated, advance the tip of the catheter to approx. 10â€“15cm from the right IJV or SCV, 15â€“20cm from the left (the markings on the side of the catheter are at 10cm intervals: 2 lines = 20cm). Check that the pressure tracing is typical of the right atrial pressure (see figure).
- Inflate the balloon and advance the catheter gently. The flow of blood will carry the balloon (and catheter) across the tricuspid valve, through the right ventricle and into the pulmonary artery.
- Watch the ECG tracing closely whilst the catheter is advanced. The catheter commonly triggers runs of VT when crossing the tricuspid valve and through the RV. The VT is usually self-limiting, but should not be ignored. Deflate the balloon, pull back, and try again.
- If more than 15cm of catheter is advanced into the RV without the tip entering the PA, this suggests the catheter is coiling in the RV. Deflate the balloon, withdraw the catheter into the RA, reinflate the balloon and try again using clockwise torque while advancing in the ventricle, or flushing the catheter with cold saline to stiffen the plastic. If this fails repeatedly, try under fluoroscopic guidance.

- As the tip passes into a distal branch of the PA, the balloon will impact and not pass further, the wedge position, and the pressure tracing will change (see figure).
- Deflate the balloon and check that a typical PA tracing is obtained. If not, try flushing the catheter lumen, and, if that fails, withdraw the catheter until the tip is within the PA and begin again.
- Reinflate the balloon slowly. If the PCW pressure is seen before the balloon is fully inflated, it suggests the tip has migrated further into the artery. Deflate the balloon and withdraw the catheter 1â€“2cm and try again.
- If the pressure tracing flattens and then continues to rise, you have â€˜overwedgedâ€™. Deflate the balloon, pull back the catheter 1â€“2cm, and start again.
- When a stable position has been achieved, extend the plastic sheath over the catheter and secure it to the introducer sheath. Clean any blood from the skin insertion site with antiseptic and secure a coil of the PA catheter to the patient's chest to avoid inadvertent removal.
- Obtain a CXR to check the position of the catheter. The tip of the catheter should ideally be no more than 3â€“5cm from the mid-line.



Pressure tracings during pulmonary artery catheterization

Normal values of right heart pressures and flows

Right atrial pressure	0â€“8mmHg
Right ventricle	
systolic	15â€“30mmHg
end diastolic	0â€“8mmHg
Pulmonary artery	
systolic/diastolic	15â€“30/4â€“12mmHg
mean	9â€“16mmHg

Pulmonary capillary wedge pr.	2â€“10mmHg
Cardiac index	2.8â€“4.2L/min/m^2)
(see p280 for haemodynamic formulae)	

Pulmonary artery catheterization 3

Tips and pitfalls

- Never withdraw the catheter with the balloon inflated.
- Never advance the catheter with the balloon deflated.
- Never inject liquid into the balloon.
- Never leave the catheter with the balloon inflated as pulmonary infarction may occur.
- The plastic of the catheter softens with time at body temperature and the tip of the catheter may migrate further into the PA branch. If the pressure tracing with the balloon deflated is â€˜partially wedgedâ€™ (and flushing the catheter does not improve this), withdraw the catheter 1â€“2cm and reposition.
- Sometimes it is impossible to obtain a wedged trace. In this situation one has to use the PA diastolic pressure as a guide. In health there is ~2â€“4mmHg difference between PA diastolic pressure and PCWP. Any condition which causes pulmonary hypertension (e.g. severe lung disease, ARDS, long-standing valvular disease) will alter this relationship.
- *Valvular lesions, VSDs, prosthetic valves, and pacemakers*: If these are present then seek advice from a cardiologist. The risk of SBE may be sufficiently great that the placement

of a PA catheter may be more detrimental than beneficial.

- PEEP (see p910). Measurement and interpretation if PCWP in patients on PEEP depends on the position of the catheter. Ensure the catheter is below the level of the left atrium on a lateral CXR. Removing PEEP during measurement causes marked fluctuations in haemodynamics and oxygenation and the pressures do not reflect the state once back on the ventilator.

Complications

- *Arrhythmias*: Watch the ECG tracing closely whilst the catheter is advanced. The catheter commonly triggers runs of VT when crossing the tricuspid valve and through the RV. If this happens, deflate the balloon, pull back, and try again. The VT is usually self-limiting, but should not be ignored.
- *Pulmonary artery rupture*: (~0.2% in one series). Damage may occur if the balloon is overinflated in a small branch. Risk factors include mitral valve disease (large v wave confused with poor wedging), pulmonary hypertension, multiple inflations, or hyperinflations of balloon. Haemoptysis is an early sign. It is safer to follow PA diastolic pressures if these correlate with the PCWP.
- Pulmonary infarction.
- *Knots*: Usually occur at the time of initial placement in patients where there has been difficulty in traversing the RV. Signs include loss of pressure tracing, persistent ectopy, resistance to catheter manipulation. If this is suspected or has occurred, stop manipulation and seek expert help.
- *Infection*: Risks increase with length of time the catheter is left *in situ*. Pressure transducer may occasionally be a source of infection. Remove the catheter and introducer and replace only if necessary.

- *Other complications*: Complications associated with central line insertion, thrombosis and embolism, balloon rupture, intracardiac damage.

P.881

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Indications for temporary pacing

1 Following acute myocardial infarction

- Asystole
- Symptomatic complete heart block (CHB) (any territory)
- Symptomatic 2Â° heart block (any territory)

â€¢ Trifascicular block	â€“ alternating LBBB and RBBB â€“ 1Â° heart block + RBBB + LAD â€“ new RBBB and left posterior hemiblock â€“ LBBB and long PR interval
â€¢ After anterior MI	â€“ asymptomatic CHB â€“ asymptomatic 2Â° (Mobitz II) block

- Symptomatic sinus bradycardia unresponsive to atropine
- Recurrent VT for atrial or ventricular overdrive pacing

2 Unrelated to myocardial infarction

- Symptomatic sinus or junctional bradycardia unresponsive to atropine (e.g. carotid sinus hypersensitivity)
- Symptomatic 2Â° heart block or sinus arrest
- Symptomatic complete heart block
- Torsades de pointes tachycardia
- Recurrent VT for atrial or ventricular overdrive pacing
- Bradycardia-dependent tachycardia
- Drug overdose (e.g. verapamil, beta-blockers, digoxin)
- Permanent pacemaker box change in a patient who is pacing dependent

3 Before general anaesthesia

- The same principles as for acute MI (see above)
- Sinoatrial disease, 2Â° (Wenckebach) heart block only need prophylactic pacing if there are symptoms of syncope or pre-syncope
- Complete heart block

Transvenous temporary pacing

- The technique of temporary wire insertion is described on p884.
- The most commonly used pacing mode and the mode of choice for life-threatening bradyarrhythmias is ventricular demand pacing (VVI) with a single bipolar wire positioned in the right ventricle: (see p886 for an explanation of common pacing modes).

- In critically ill patients with impaired cardiac pump function and symptomatic bradycardia (especially with right ventricular infarction), cardiac output may be increased by up to 20% by maintaining atrioventricular synchrony. This requires two pacing leads, one atrial and one ventricular, and a dual pacing box.

Epicardial temporary pacing

- Following cardiac surgery, patients may have *epicardial wires* (attached to the pericardial surface of the heart) left in for up to 1 week in case of post operative heart block or bradyarrhythmia. These may be used in the same way as the more familiar trans-venous pacing wires, but the threshold may be higher.

Atrio-ventricular sequential pacing

In critically ill patients with impaired cardiac pump function and symptomatic bradycardia (especially with right ventricular infarction), cardiac output may be increased by up to 20% by maintaining atrio-ventricular synchrony. This requires two pacing leads, one atrial and one ventricular, and a dual pacing box.

Patients most likely to benefit from AV sequential pacing

- Acute MI (especially RV infarction)
- â€˜Stiffâ€™ left ventricle: (aortic stenosis, HCM, hypertensive heart disease, amyloidosis)
- Low cardiac output states (cardiomyopathy)
- Recurrent atrial arrhythmias.

Temporary cardiac pacing 1

Ventricular pacing

- *Cannulate a central vein*: The wire is easiest to manipulate via the RIJ approach but is more comfortable for the patient via the right subclavian (SC) vein. The LIJ approach is best avoided as there are many acute bends to negotiate and a stable position is difficult to achieve. Avoid the left subclavicular area as this is the preferred area for permanent pacemaker insertion and should be kept â€˜virginâ€™ if possible. The femoral vein may be used but the incidence of DVT and infection is high.
- *Insert a sheath* (similar to that for PA catheterization) through which the pacing wire can be fed. Pacing wires are commonly 5F or 6F and a sheath at least one size larger is necessary. Most commercially available pacing wires are pre-packed with an introducer needle and plastic cannula similar to an AbbocathÂ® which may be used to position the pacing wire. However, the cannula does not have a haemostatic seal. The plastic cannula may be removed from the vein, leaving the bare wire entering the skin, once a stable position has been achieved. This reduces the risk of wire displacement but also makes repositioning of the wire more difficult should this be necessary, and the infection risk is higher.
- Pass the wire through the sterile plastic cover that accompanies the introducer sheath and advance into the upper right atrium (see figure p886) but do not unfurl the cover yet. The wire is much easier to manipulate with gloved hands without the additional hindrance of the plastic cover.
- Advance the wire with the tip pointing towards the right

ventricle; it may cross the tricuspid valve easily. If it fails to cross, point the tip to the lateral wall of the atrium and form a loop. Rotate the wire and the loop should fall across the tricuspid valve into the ventricle.

- Advance and rotate the wire so that the tip points inferiorly as close to the tip of the right ventricle (laterally) as possible.
- If the wire does not rotate down to the apex easily, it may be because you are in the coronary sinus rather than in the right ventricle. (The tip of the wire points to the left shoulder.) Withdraw the wire and re-cross the tricuspid valve.
- Leave some slack in the wire; the final appearance should be like the outline of a sock with the â€˜heelâ€™ in the right atrium, the â€˜archâ€™ over the tricuspid and the â€˜big toeâ€™ at the tip of the right ventricle.
- Connect the wire to the pacing box and check the threshold. Ventricular pacing thresholds should be <1.0 volts, but threshold up to 1.5V is acceptable if another stable position canot be achieved.
- Check for positional stability. With the box pacing at a rate higher than the intrinsic heart rate, ask the patient to take some deep breaths, cough forcefully, and sniff. Watch for failure of capture, and if so reposition the wire.
- Set the output to 3 volts and the box on â€˜demandâ€™. If the patient is in sinus rhythm and has an adequate blood pressure set the box rate to just below the patient's rate. If there is complete heart block or bradycardia set the rate at 70â€“80/min.

- Cover the wire with the plastic sheath and suture sheath and wire securely to the skin. Loop the rest of the wire and fix to the patient's skin with adhesive dressing.
- When the patient returns to the ward, obtain a CXR to

confirm satisfactory positioning of the wire and to exclude a pneumothorax.

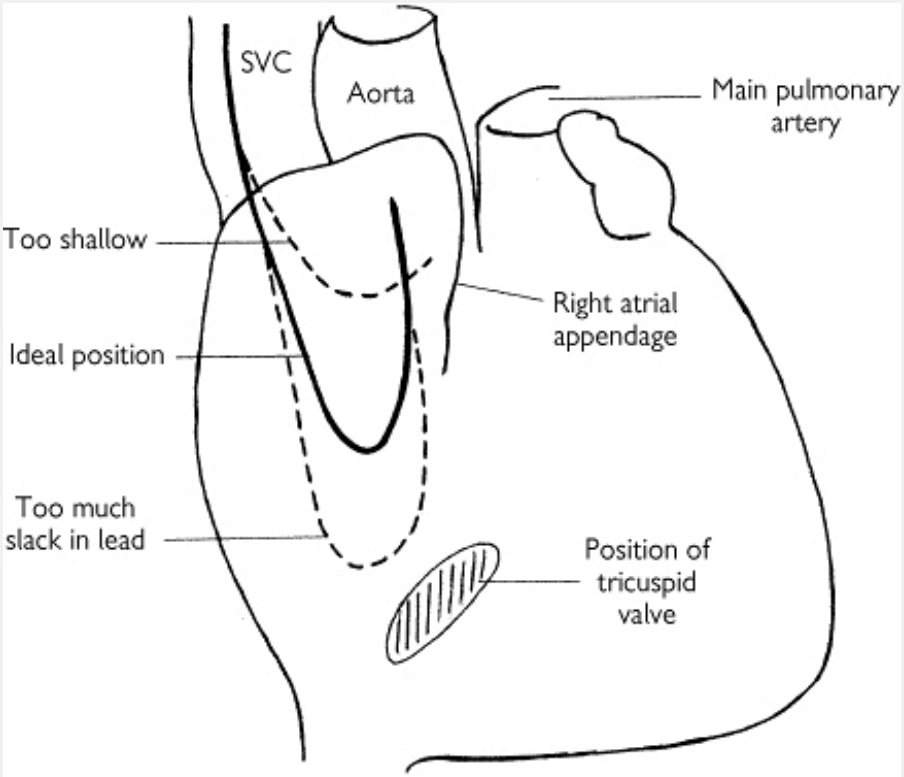
Complications of temporary pacing

- Complications associated with central line insertion
- Ventricular ectopics
- Non-sustained VT
- Perforation
- Pericarditis
- Diaphragmatic pacing
- Infection
- Pneumothorax
- Cardiac Tamponade

Temporary cardiac pacing 2

Atrial pacing

- The technique of inserting an atrial temporary wire is similar to that of ventricular pacing.
- Advance the atrial wire until the â€˜Jâ€™ is re-formed in the right atrium.
- Rotate the wire and withdraw slightly to position the tip in the right atrial appendage. Aim for a threshold of <1.5 volts.
- If atrial wires are not available, a ventricular pacing wire may be manipulated into a similar position or passed into the coronary sinus for left atrial pacing.



Positioning an artial wire for artial pacing

P.887

P.888

Temporary cardiac pacing 3

Complications

(see table)

1 Ventricular ectopics or VT

- Non-sustained VT is common as the wire crosses the tricuspid valve (especially in patients receiving an isoprenaline infusion) and does not require treatment.
- Try to avoid long runs of VT and if necessary withdraw the

wire into the atrium and wait until the rhythm has settled.

- If ectopics persist after the wire is positioned, try adjusting the amount of slack in the wire in the region of the tricuspid valve (either more or less).
- Pacing the right ventricular outflow tract can provoke runs of VT.

2 Failure to pace and/or sense

- It is difficult to get low pacing thresholds (<1.0V) in patients with extensive myocardial infarction (especially of the inferior wall), cardiomyopathy, or who have received class I anti-arrhythmic drugs. Accept a slightly higher value if the position is otherwise stable and satisfactory.
- If the position of the wire appears satisfactory and yet the pacing thresholds are high, the wire may be in a left hepatic vein. Pull the wire back into the atrium and try again, looking specifically for the ventricular ectopics as the wire crosses the tricuspid valve.
- The pacing threshold commonly doubles in the first few days due to endocardial oedema.
- If the pacemaker suddenly fails, the most common reason is usually wire displacement.
    - Increase the pacing output of the box.
    - Check all the connections of the wire and the battery of the box.
    - Try moving the patient to the left lateral position until arrangements can be made to reposition the wire.

3 Perforation

- A pericardial rub may be present in the absence of

perforation (especially post MI).

- *Presentation*: Pericardial chest pain, increasing breathlessness, falling blood pressure, enlarged cardiac silhouette on CXR, signs of cardiac tamponade, left diaphragmatic pacing at low output.
- *Management*
    - If there are signs of cardiac tamponade arrange for urgent ECHO and pericardial drainage (p890).
    - Reposition the wire.
    - Monitor the patient carefully over the next few days with repeat ECHOs to detect incipient cardiac tamponade.

4 Diaphragmatic pacing

- High output pacing (10V), even with satisfactory position of the ventricular lead may cause pacing of the left hemidiaphragm. At low voltages this suggests perforation (see above).

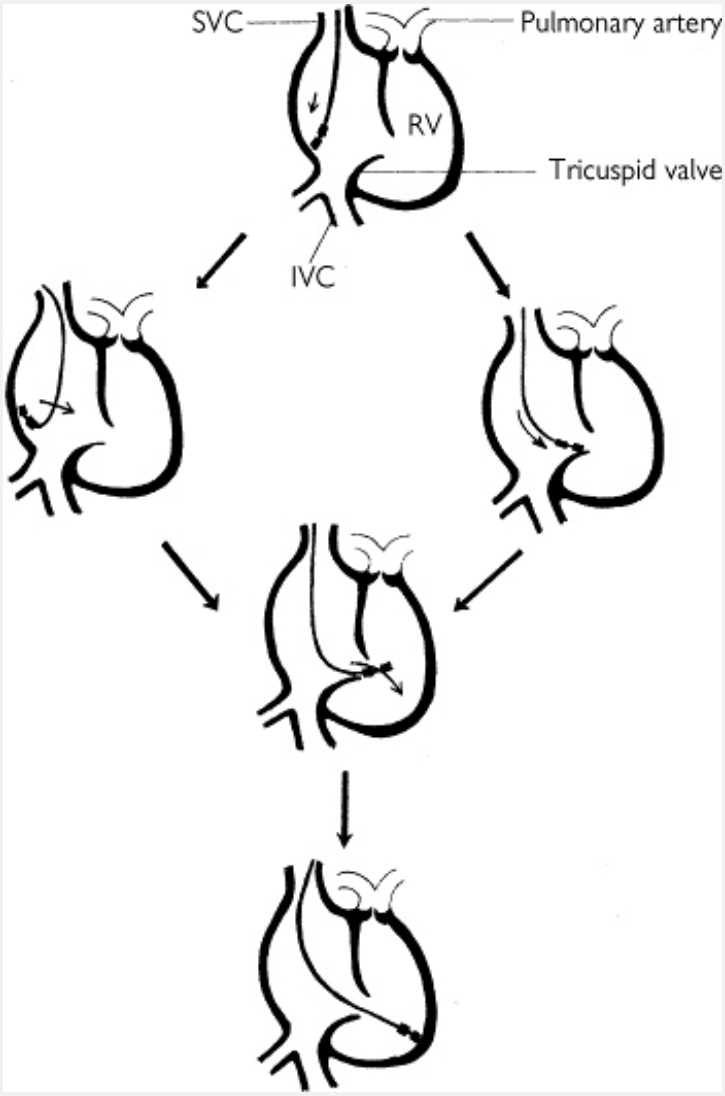
- Right hemidiaphragm pacing may be seen with atrial pacing and stimulation of the right phrenic nerve.
- Reposition the wire if symptomatic (painful twitching, dyspnoea).

Checklist for pacing wire insertion

- Check the screening equipment and defibrillator are working.
- Check the type of pacing wire: atrial wires have a pre-formed J that allows easy placement in the atrium or appendage and is very difficult to manipulate into a satisfactory position in the ventricle. Ventricular pacing

wires have a more open, gentle â€˜Jâ€™.

- Check the pacing box (single vs dual or sequential pacing box) and leads to attach to the wire(s). Familiarize yourself with the controls on the box: you may need to connect up in a hurry if the patient's intrinsic rhythm slows further.
- Remember to don the lead apron before wearing the sterile gown, mask, and gloves.



Insertion of a ventricular pacing wire (see text for details)

Pericardial aspiration 1

Equipment

Establish peripheral venous access and check that full facilities for resuscitation are available. Pre-prepared pericardiocentesis sets may be available. You will need:

- Trolley as for central line insertion, with iodine or chlorhexidine for skin, dressing pack, sterile drapes, local anaesthetic (lignocaine 2%), syringes (including a 50ml), needles (25G and 22G), No. 11 blade, and silk sutures
- Pericardiocentesis needle (15cm, 18G) or similar Wallace cannula
- J-guide wire (â‰¥80cm, 0.035 diameter)
- Dilators (up to 7 French)
- Pigtail catheter (â‰¥60cm with multiple sideholes, a large Seldinger-type CVP line can be used if no pigtail is available)
- Drainage bag and connectors
- Facilities for fluoroscopy or echocardiographic screening.

Technique

- Position the patient at ~30Â°. This allows the effusion to pool inferiorly within the pericardium.
- Sedate the patient lightly with midazolam (2.5â€“7.5mg iv) and fentanyl (50â€“200Âµg iv) if necessary. Use with caution as this may drop the bp in patients already compromised by the effusion.
- Wearing a sterile gown and gloves, clean the skin from mid-

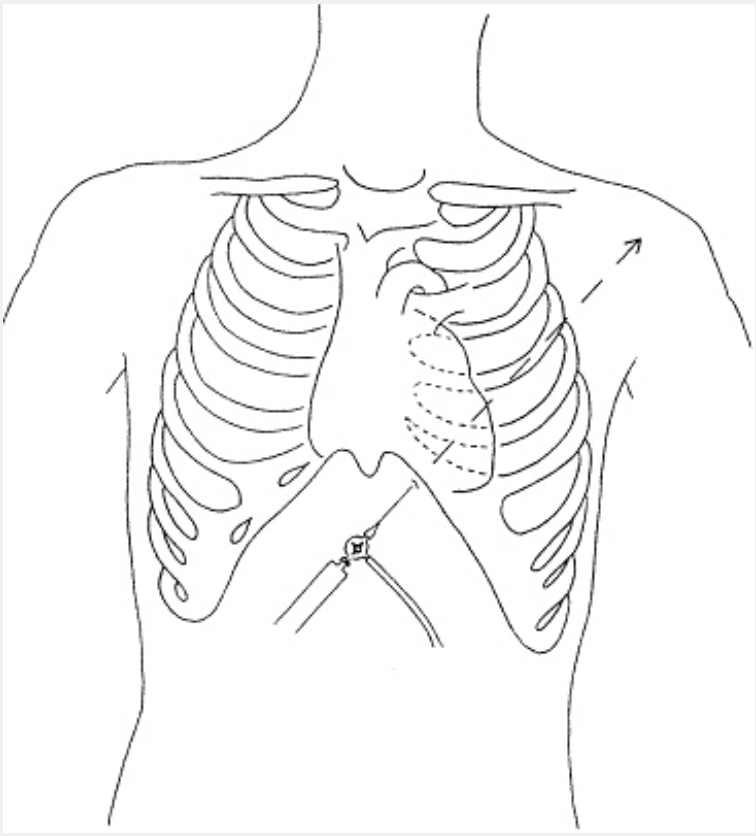
chest to mid-abdomen and put the sterile drapes on the patient.

- Infiltrate the skin and sub-cutaneous tissues with local anaesthetic starting 1â€“1.5cm below the xiphisternum and just to the left of mid-line, aiming for the left shoulder and staying as close to the inferior border of the rib cartilages as possible.
- The pericardiocentesis needle is introduced into the angle between the xiphisternum and the left costal margin angled at ~30Â°. Advance slowly aspirating gently and then injecting more lignocaine every few mm, aiming for the left shoulder.
- As the parietal pericardium is pierced, you may feel a â€˜giveâ€™ and fluid will be aspirated. Remove the syringe and introduce the guide-wire through the needle.
- Check the position of the guide-wire by screening. It should loop within the cardiac silhouette only and not advance into the SVC or pulmonary artery.
- Remove the needle leaving the wire in place. Enlarge the skin incision slightly using the blade and dilate the track.
- Insert the pigtail over the wire into the pericardial space and remove the wire.
- Take specimens for microscopy, culture (and inoculate a sample into blood culture bottles), cytology and haematocrit if blood stained (a FBC tube; ask the haematologists to run on the Coulter counter for rapid estimation of Hb).
- Aspirate to dryness watching the patient carefully. Symptoms and haemodynamics (tachycardia) often start to improve with removal of as little as 100ml of pericardial fluid.

- If the fluid is heavily blood stained, withdraw fluid cautiously; if the pigtail is in the right ventricle, withdrawal

of blood may cause cardiovascular collapse. Arrange for urgent Hb/haematocrit.

- Leave on free drainage and attached to the drainage bag.
- Suture the pigtail to the skin securely and cover with a sterile occlusive dressing.



Pericardial aspiration

Pericardial aspiration 2

Aftercare

- Closely observe the patient for recurrent tamponade

(obstruction of drain) and repeat ECHO.

- Discontinue anti-coagulants.
- Remove the drain after 24 hours or when the drainage stops.
- Consider the need for surgery (drainage, biopsy or pericardial window) or specific therapy (chemotherapy if malignant effusion, antimicrobials if bacterial, dialysis if renal failure, etc.).

Tips and pitfalls

- If the *needle touches the heart's epicardial surface*, you may feel a â€˜tickingâ€™ sensation transmitted down the needle: withdraw the needle a few mm, angulate the needle more superficially and try cautiously again, aspirating as you advance.
- *If you do not enter the effusion*, and the heart not encountered:
    - Withdraw the needle slightly and advance again, aiming slightly deeper, but still towards the left shoulder.
    - If this fails, try again aiming more medially (midclavicular point or even suprasternal notch).
    - Consider trying the apical approach (starting laterally at cardiac apex and aiming for right shoulder), if echo confirms sufficient fluid at the cardiac apex.
- If available, *intrathoracic ECG* can be monitored by a lead attached to the needle as it is advanced. This is seldom clinically useful in our experience. Penetration of the myocardium results in ST elevation, suggesting the needle has been advanced to far.
- *Difficulty in inserting the pigtail*
    - This may be because of insufficient dilatation of the

tract (use a larger dilator).

- Holding the wire taught (by gentle traction) while pushing the catheter may help; take care not to pull the wire out of the pericardium.

- *Haemorrhagic effusion vs blood*

  - Compare the Hb of the pericardial fluid to the venous blood Hb.
  - Place some of the fluid in a clean container; blood will clot whereas haemorrhagic effusion will not as the â€˜whippingâ€™ action of the heart tends to defibrinate it.
  - Confirm the position of the needle by first withdrawing some fluid and then injecting 10â€“20ml of contrast; using fluoroscopy, see if the contrast stays within the cardiac sillhouette.
  - Alternatively, if using ECHO guidance, inject 5â€“10ml saline into the needle looking for â€˜microbubble contrastâ€™ in the cavity containing the needle tip. Injecting 20ml saline rapidly into a peripheral vein will produce â€˜contrastâ€™ in the right atrium and ventricle and may allow them to be distinguised from the pericardial space.
  - Connect a pressure line to the needle; a characteristic waveform will confirm penetration of the right ventricle (see figure p879).

Complications of pericardiocentesis

- Penetration of a cardiac chamber (usually right ventricle)
- Laceration of an epicardial vessel
- Arrhythmia (atrial arrhythmias as the wire is advanced,

ventricular arrhythmias if the RV is penetrated)

- Pneumothorax
- Perforation of abdominal viscus (liver, stomach, colon)
- Ascending infection

DC cardioversion 1

Relative contraindications

- Digoxin toxicity
- Electrolyte disturbance (â†“Na^+, â†“K^+, â†“Ca^{2+}, â†“Mg^{2+}, acidosis)
- Inadequate anti-coagulation and chronic AF

Check list for DC cardioversion

â€¢ Defibrillator	Check this is functioning with a fully equipped arrest trolley to hand in case of arrest
â€¢ Informed consent	(Unless life-threatening emergency.)
â€¢ 12 lead ECG	AF, flutter, SVT, VT, signs of ischaemia or digoxin. If ventricular rate is slow have an external (transcutaneous) pacing system nearby in case of asystole

â€¢ Nil by mouth	For at least 4 hours
â€¢ Anti-coagulation	Does the patient require anti-coagulants? Is the INR >2.0 ? (Has it been so for >3 wks ?)
Potassium	Check this is >3.5mmol/L
Digoxin	Check there are no features of digoxin toxicity (see p808). If taking >250Âµg/day check that renal function and recent digoxin level are normal. If there are frequent ventricular ectopics, give iv Mg^{2+} 8mmol
â€¢ Thyroid function	Treat thyrotoxicosis or myxoedema first
â€¢ iv access	Peripheral venous cannula
â€¢ Sedation	Short general anaesthesia (propofol) is preferable to sedation with benzodiazepine and fentanyl. Bag the patient with 100% oxygen
â€¢ Select energy	(See table.)
â€¢ Synchronization	Check this is selected on the defibrillator for all shocks (unless the patient is in VF or haemo-dynamically unstable). Adjust the

	ECG gain so that the machine is only sensing QRS complexes and not P or T waves
â€¢ Paddle placement	Conductive gel pads should be placed between the paddles and the skin. Position one just to the right of the sternum and the other to the left of the left nipple (ant.-mid-axillary line), Alternatively, place one anteriorly just left of the sternum, and one posteriorly to the left of mid-line. There is no convincing evidence for superiority of one position over the other
â€¢ Cardioversion	Check no one is in contact with the patient or with the metal bed. Ensure your own legs are clear of the bed! Apply firm pressure on the paddles
â€¢ Unsuccessful	Double the energy level and repeat up to 360J. Consider changing paddle position (see above). If prolonged sinus pause or ventricular arrhythmia during an elective procedure, stop
â€¢ Successful	Repeat ECG. Place in recovery position until awake. Monitor for 2â€“4h and ensure effects of sedation have passed. Patients should be accompanied home by friend or relative if being discharged

Complications of DC cardioversion

- Asystole/bradycardias
- Ventricular fibrillation
- Thromboembolism
- Transient hypotension
- Skin burns
- Aspiration pneumonitis

Suggested initial energies for DC shock for elective cardioversion

â€¢ Sustained VT	200J	Synchronized
â€¢ Atrial fibrillation	50â€“100J	Synchronized
â€¢ Atrial flutter	50J	Synchronized
â€¢ Other SVTs	50J	Synchronized
â€¢ If the initial shock is unsuccessful, increase the energy (50, 100, 200,360J) and repeat.		
â€¢ If still unsuccessful consider changing paddle position and try 360 Joules again. It is inappropriate to persist further with elective DC cardioversion		

DC cardioversion 2

Notes

1 Anti-coagulation

The risk of thromboembolism in patients with chronic AF and dilated cardiomyopathy is 0â€“7% depending on the underlying risk factors.

Increased risk

- Prior embolic event
- Mechanical heart valve
- Mitral stenosis
- Dilated left atrium

Low risk

- Age <60 years
- No underlying heart disease
- Recent onset AF (<3 days)

Anti-coagulate patients at risk with warfarin for at least 3â€“4 weeks. For recent onset AF (1â€“3 days), anti-coagulate with iv heparin for at least 12â€–24 hours and, if possible, exclude intracardiac thrombus with a transoesophageal ECHO prior to DC shock. If there is thrombus, anti-coagulate with warfarin as above. For emergency cardioversion of AF (<24h), heparinize prior to shock.

The risk of systemic embolism with cardioversion of atrial flutter and other tachyarrhythmias is very low, provided there is no ventricular thrombus, since the co-ordinated atrial activity prevents formation of clot. Routine anti-coagulation with warfarin is not necessary but we would recommend heparin

before DC shock as the atria are often rendered mechanically stationary for several hours after shock even though there is co-ordinate electrical depolarization.

After successful cardioversion, if the patient is on warfarin, continue anti-coagulation for at least 3â€“4 weeks. Consider indefinite anti-coagulation if there is intrinsic cardiac disease (e.g. mitral stenosis) or recurrent AF.

2 Special situations

Pregnancy DC shock during pregnancy appears to be safe. Auscultate the fetal heart before and after cardioversion and if possible, fetal ECG should be monitored.

Pacemakers There is a danger of damage to the pacemaker generator box or the junction at the tip of the pacing wire(s) and endocardium. Position the paddles in the anteroposterior position as this is theoretically safer. Facilities for back-up pacing (external or transvenous) should be available. Check the pacemaker post cardioversionâ€”both early and late problems have been reported.

Intra-aortic balloon counterpulsation 1

Indications

- Cardiogenic shock post MI
- Acute severe mitral regurgitation
- Acute ventricular septal defect
- Pre-operative (ostial left coronary stenosis)
- Weaning from cardiopulmonary bypass

Rarely

- Treatment of ventricular arrhythmias post MI
- Unstable angina (as a bridge to CABG)

Contraindications

- Aortic regurgitation
- Aortic dissection
- Severe aorto-iliac atheroma
- Bleeding diathesis
- Dilated cardiomyopathy (if patient not a candidate for transplantation)

Complications

- Aortic dissection
- Arterial perforation
- Limb ischaemia
- Thrombocytopenia
- Peripheral embolism
- Balloon rupture

Principle

The device consists of a catheter with a balloon (40ml size) at its tip which is positioned in the descending thoracic aorta. The balloon inflation/deflation is synchronized to the ECG. The balloon should inflate just after the dicrotic notch (in diastole), thereby increasing pressure in the aortic root and increasing coronary perfusion. The balloon deflates just before ventricular

systole, thereby decreasing afterload and improving left ventricular performance (see below).

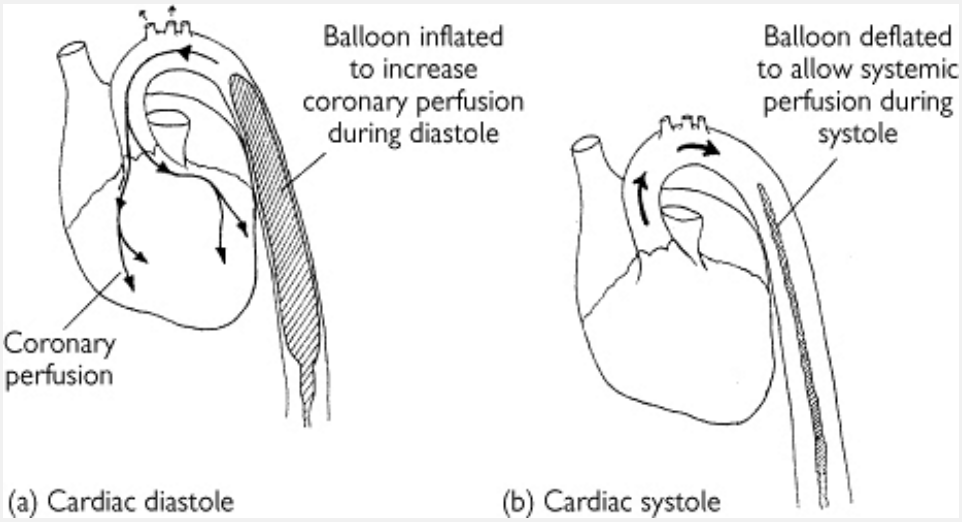


Figure. No caption available.

P.899

Counterpulsation has a number of beneficial effects on the circulation.

- Increased in coronary perfusion in diastole.
- Reduced LV end diastolic pressure.
- Reduced myocardial oxygen consumption.
- Increased cerebral and peripheral blood flow.

The IAB cannot assist the patient in asystole or VF; it requires a minimum cardiac index of 1.2â€“1.4L/min/m^2, often necessitating additional inotropes.

P.900

Intra-aortic balloon counterpulsation 2

Technique

Balloon insertion

Previous experience is essential. Formerly, a cut-down to the femoral artery was required, but newer balloons come equipped with a sheath which may be introduced percutaneously. Using fluoroscopy, the balloon is positioned in the descending thoracic aorta with the tip just below the origin of the left subclavian artery. Fully anti-coagulate the patient with iv heparin. Some units routinely give iv antibiotics (flucloxacillin) to cover against *Staph*. infection.

Triggering and timing

The balloon pump may be triggered either from the patient's ECG (R wave) or from the arterial pressure waveform. Slide switches on the pump allow precise timing of inflation and deflation during the cardiac cycle. Set the pump to 1 : 2 to allow you to see the effects of augmentation on alternate beats.

Trouble-shooting

- Seek help from an expert! There is usually an on-call cardiac perfusionist or technician, senior cardiac physician or surgeon.
- Counterpulsation is inefficient with heart rates over 130/min. Consider anti-arrhythmics or 1 : 2 augmentation instead.
- Triggering and timing: For ECG triggering, select a lead with most pronounced R wave; ensure that the pump is set to trigger from ECG not pressure; permanent pacemakers may interfere with triggering-select lead with negative and smallest pacing artefact. Alternatively, set the pump to be triggered from the external pacing device. A good arterial waveform is required for pressure triggering; the timing will vary slightly depending on the location of the arterial line

(slightly earlier for radial artery line, cf. femoral artery line). Be guided by the haemodynamic effects of balloon inflation and deflation rather than the precise value of delay.

- Limb ischaemia: Exacerbated by poor cardiac output, adrenaline, noradrenaline and peripheral vascular disease. Wean off and remove the balloon (see below).
- Thrombocytopenia: Commonly seen; does not require transfusion unless there is overt bleeding and returns to normal once the balloon is removed. Consider prostacyclin infusion if platelet counts fall below 100 Ã— 10^9/L.

IABP removal

- The patient may be progressively weaned by gradually reducing the counterpulsation ratio (1 : 2, 1 : 4, 1 : 8, etc.) and/or reducing the balloon volume and checking that the patient remains haemodynamically stable.
- Stop the heparin infusion and wait for the ACT (activated clotting time) to fall <150s (APTT <1.5 normal).
- Using a 50ml syringe, have an assistant apply negative pressure to the balloon.
- Pull the balloon down until it abuts the sheath; do not attempt to pull the balloon into the sheath.
- Withdraw both balloon and sheath and apply firm pressure on the femoral puncture site for at least 30 minutes or until the bleeding is controlled.

Principles of respiratory support 1

The aim of therapy is to relieve hypoxia and maintain or restore a normal P_aCO_2 for the individual. Relative indications for mechanical ventilation are discussed in the appropriate

chapters. This section discusses some of the principles involved.

Oxygen therapy

- Oxygen should be administered by a system that delivers a defined percentage, between 28% and 100% according to the patients requirements (e.g. via fixed percentage delivery masks such as Ventimask Mk iv).
- A Hudson mask or nasal cannulae give very variable F_iO_2 depending upon both flow rate of oxygen and the patients breathing pattern.
- Nasal prongs only deliver at F_iO_2 of 30% at flows of 2L/min, and become less efficient at higher flow rates (~35% at 3L/min with little further increase with increasing flow). Higher flow rates require humidification.
- A properly positioned, high flow oxygen mask, using oxygen at 6L/min, can provide an F_iO_2 of 60%.
- Combining nasal prongs and a high flow mask can achieve an F_iO_2 of ~80â€“90%.
- In practice it is rarely possible to consistently deliver >60% unless using CPAP or ventilation.
- Where sudden deterioration in oxygenation occurs always check the delivery system for empty cylinders, disconnected tubing, etc.

Indications

- Type I respiratory failure
- Type II respiratory failure (controlled therapy)
- Bronchial asthma
- Acute myocardial infarction
- Sickle cell crisis

- Carbon monoxide poisoning
- Cluster headaches

Complications

- Tracheobronchitis occurs with inhalation of â‰¥80% oxygen for over 12 hours and presents as retrosternal pain, cough, and dyspnoea.
- Parenchymal lung damage from oxygen occurs with F_iO_2 >60% for more than 48 hours without intermittent periods of breathing air.

Monitoring oxygen therapy

- The results of oxygen therapy should generally be measured by intermittent or continuous oximetry and intermittent arterial blood gases.
- Oximetry is an invaluable aid, but has limitations. In some situations (e.g. Guillainâ€“BarrÃ© syndrome) falling oximetry is a very late marker of impending respiratory failure, and CO_2 accumulation (e.g. in COAD) is clearly not monitored by oximetry.
- A S_aO_2 of 93% correlates very approximately with a P_aO_2 of 8kPa, and below 92% the P_aO_2 may fall disproportionately quickly.

Principles of respiratory support 2

Lung expansion techniques

- Periodic â€˜sighsâ€™ are a normal part of breathing and reverse microatelectasis. Lung expansion techniques are indicated for patients who cannot or will not take periodic large breaths (e.g. post abdominal or chest surgery, neuromuscular chest wall weakness).
- Post operative techniques used commonly by physiotherapists include incentive spirometry, coached maximal inspiration with cough, combined with postural drainage and chest percussion.
- Volume generating devices such as â€˜the BIRDâ€™ are triggered by the patient initiating inspiration, and deliver a pre-set tidal volume to augment the patient's breath. Liaise with your physiotherapist.
- â€˜Pressure-generatingâ€™ techniques (such as CPAP, NIPPV, and BiPAP) have the advantage that even if a leak develops around the mask, the ventilator is able to â€˜compensateâ€™ to provide the patient with the prescribed positive pressure (see below).
- For both volume and pressure generating techniques, the patients must be able to protect their airway and generate enough effort to trigger the machine.

Continuous positive airways pressure (CPAP)

- CPAP provides a constant positive pressure throughout the respiratory cycle.
- It acts to splint open collapsing alveoli which may be full of fluid (or a collapsing upper airway in obstructive sleep apnoea), increases functional residual capacity (FRC) and compliance, such that the work of breathing is reduced and gas exchange is improved.
- It allows a higher F_iO_2 (approaching 80â€“100%) to be

administered, cf. standard oxygen delivery masks.

- CPAP should usually be commenced after liaison with anaesthetists; in a patient for active management it should usually be started on the ITU.
- A standard starting pressure is 5cmH_2O; >10cmH_2O pressure is rarely used.

Indications

- Pulmonam oedema
- Acute respiratory failure (e.g. secondary to infection), where simple face mask oxygen is insufficient at treating hypoxamia.
- Acute resporatory failure where ventilation is either inappropriate or to be avoided if at all possible.
- Weaning from the ventilator.
- Obstructive sleep apnoea (OSA).
- In those for active management it is not a substitute for ventilation, and usually only buys a modest amount of time before intubation is required.
- Patient needs to:
    - be awake and alert
    - be able to protect the airway
    - possess adequate respiratory muscle strength
    - be haemodynamically stable.

Mechanical ventilation

Negative pressure ventilation (NPV)

- This works by â€˜suckingâ€™ out the chest wall and is used in chronic hypoventilation (e.g. polio, kyphoscoliosis, or muscle disease). Expiration is passive.
- The â€˜iron lungâ€™ or tank ventilator is the most well known; alternatives include thoracic cuirasses with a semi-rigid cage around the chest only and other devices which may be custom built.
- These techniques do not require tracheal intubation. However, access to the patient for nursing care is difficult, and positive pressure ventilation is the modality of choice in the acute setting; the patient may be extubated in a â€˜tank ventilatorâ€™ once the acute episode is over.
- Alternative devices such as rocking beds may be considered for stable patients requiring long term-ventilatory assistance.[1]

Intermittent positive pressure ventilation (IPPV)

Indications

Deteriorating gas exchange due to a potentially reversible cause of respiratory failure.

- Pneumonia
- Exaerbation of COAD
- Massive atelectasis
- Respiratory muscle weakness

  Myaesthenia gravis

  Acute infective polyneuritis

- Ventilation of the ill patient on the ITU is via either an ET tube or a tracheostomy. If ventilation is anticipated to be needed for >1 week, consider a tracheostomy.
- Head injury
- Cerebral hypoxia (e.g. post cardiac arrest)
- Intracranial bleed
- Raised intracranial pressure
- Major trauma or burns

There are two basic types of ventilator.

- Pressure cycled ventilators deliver gas into the lungs until a prescribed pressure is reached, when inspiratory flow stops and, after a short pause, expiration occurs by passive recoil. This has the advantage of reducing the peak airway pressures without impairing cardiac performance in situations such as ARDS. However, if the airway pressures increase or compliance decreases the tidal volume will fall, so patients need to be monitored closely to avoid hypoventilation.
- Volume cycled ventilators deliver a preset tidal volume into the lungs over a predetermined inspiratory time (usually ~30% of the breathing cycle), hold the breath in the lungs (for ~10% of the cycle), and then allow passive expiration as the lungs recoil.

Footnote

1

Hills NS (1986) *Chest* 90: 897.

Nasal ventilation

- Nasal intermittent positive pressure ventilation (NIPPV) delivers a positive pressure for a prescribed inspiratory time, when triggered by the patient initiating a breath, allowing the patient to exhale to atmospheric pressure.
- The positive pressure is supplied by a small machine via a tight-fitting nasal mask.
- It is generally used as a method of home nocturnal ventilation for patients with severe musculoskeletal chest wall disease (e.g. kyphoscoliosis) or with obstructive sleep apnoea (OSA).
- It has also been used with modest success as an alternative to formal ventilation via ET tube in patients where positive *expiratory* pressure is not desirable, e.g. acute asthma, COAD with CO_2 retention, and as a weaning aid in those in whom separation from a ventilator is proving difficult.
- The system is relatively easy to set up by experienced personnel, but some patients take to it better than others. It should not be commenced by inexperienced personnel.

Positive pressure ventilation 1

CMV (continuous mandatory ventilation)

- CMV acts on a preset cycle to deliver a given number of breaths per minute of a set volume. The duration of the cycle determines the breath frequency.

The *minute volume* is calculated by (*tidal volume* Ã—

frequency).

- The relative proportions of time spent in inspiration and expiration (I : E ratio) is normally set at 1 : 2, but may be altered, e.g. in acute asthma, where air trapping is a problem, a longer expiratory time is needed (p214); in ARDS, where the lung compliance is low, a longer inspiratory time is beneficial (inverse ratio ventilation, see p232)
- The patients should be fully sedated. Patients capable of spontaneous breaths who are ventilated on CMV can get â€˜stackingâ€™ of breaths, where the ventilator working on its preset cycle may give a breath on top of one which the patient has just taken, leading to over-inflation of the lungs, a high peak inspiratory pressure, and the risk of pneumothorax.
- Prolonged use of this mode will result in atrophy of the respiratory muscles; this may prove difficult in subsequent â€˜weaningâ€™, especially in combination with a proximal myopathy from steroids, e.g. in acute asthma.
- Ventilation may either be terminated abruptly or by gradual transfer of the ventilatory workload from the machine to the patient (â€™weaningâ€™).

SIMV (synchronized intermittent mandatory ventilation)

- SIMV modes allow the patient to breath spontaneously and be effectively ventilated and allows gradual transfer of the work of breathing on to the patient. This may be appropriate when weaning the patient whose respiratory muscles have wasted. It is inappropriate in acutely ill patients (e.g. acute severe asthma, ARDS); CMV with deep sedation reduces oxygen requirement and respiratory drive and allows more

effective ventilation.

- Exact details of the methods of synchronization vary between machines, but all act in a similar manner: the patient breathes spontaneously through the ventilator circuit. The ventilator is usually preset to ensure that the patient has a minimum number of breaths per minute, and if the number of spontaneous breaths falls below the preset level then a breath is delivered by the machine.
- Most SIMV modes of ventilation provide some form of positive pressure support to the patient's spontaneous breaths to reduce the work of breathing and ensure effective ventilation (see below).

Pressure support

- Positive pressure is added during inspiration to relieve part or all of the work of breathing.
- This may be done in conjunction with an SIMV mode of ventilation, or as a means of supporting entirely spontaneous patient-triggered ventilation during the process of weaning.
- It allows the patients to determine their own respiratory rate, and should ensure adequate inflation of the lungs and oxygenation. It is, however, only suitable for those whose lung function is reasonably adequate and who are not confused or exhausted.

Positive pressure ventilation 2

PEEP (positive end esxpiratory pressure)

- PEEP is a preset pressure added to the end of expiration only, to maintain the lung volume, prevent airway or alveolar collapse, and open up atelectic or fluid-filled lung (e.g. in ARDS or cardiogenic pulmonary oedema).
- It can significantly improve oxygenation by making more of the lung available for gas exchange. However, the trade-off is an increase in intrathoracic pressure which can significantly decrease venous return and hence cardiac output. There is also an increased risk of pneumothorax.
- â€˜Auto-PEEPâ€™ is seen if the patient's lungs do not fully empty before the next inflation (e.g. asthma).
- In general PEEP should be kept at a level of 5â€“10cm H_2O where required, and the level adjusted in 2â€“3 cm H_2O intervals every 20â€“30 minutes according to a balance between oxygenation and cardiac performance.
- Measurement and interpretation if PCWP in patients on PEEP depends on the position of the catheter. PCWP will always reflect pulmonary venous pressures if they are greater than PEEP. If the catheter is in an apical vessel where the PCWP is normally lower due to the effects of gravity, the pressure measured may be the alveolar (PEEP) pressure rather than the true PCWP; in a dependent area the pressures are more accurate. Removing PEEP during measurement causes marked fluctuations in haemodynamics and oxygenation and the pressures do not reflect the state once back on the ventilator.

Cricothyroidotomy

Indications

- To bypass upper airway obstruction (e.g. trauma, infections, neoplasms, post operative, burns and corrosives) when oral or nasotrachealintubation is contraindicated.
- In situations when endotracheal intubations fail (e.g. massive nasopharyngeal haemorrhage, structural deformities, obstruction due to foreign bodies, etc.)
- As an elective procedure in select patients to provide a route for suction of airway secretions (e.g. patients in neuromuscular disease). This should be converted to a tracheotomy if required for prolonged periods or if infection or inflammation occurs.

Procedure

This should not be attempted if you have not been taught it by an experienced physician/surgeon. Seek help.

- Locate the thyroid and cricoid cartilages.
- The cricothyoird space is just under 1cm in its vertical dimension. The cricothyroid artery runs across the mid-line in the upper portion.
- Clean the skin with iodine and isolate the area with sterile towels.
- Infiltrate the skin and the area around the cricothyroid space with local anaesthetic.
- Make a 3cm vertical mid-line incision through the skin, taking care not to cut the membrane.
- Palpate the cricothyroid membrane through the incision.
- Stabilize the larynx by holding between the index finger and thumb.
- Make a short transverse incision in the lower third of the cricothyroid membrane, just scraping over the upper part of the cricoid cartilage (preferably using the tip of a No. 11

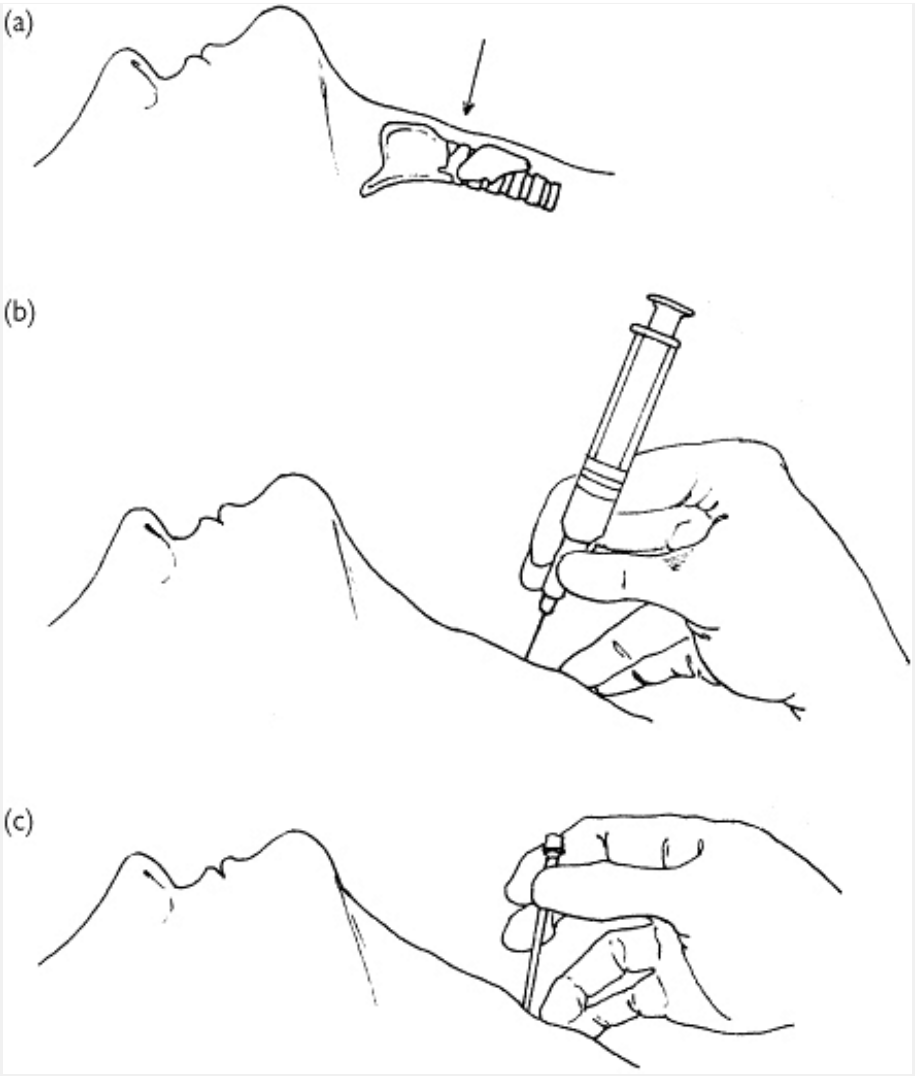
blade to go through the membrane). This minimizes the risk of cutting the cricothyroid artery.

- Dilate the membrane with forceps, insert the tracheotomy tube through the incision into the trachea, and secure.

Percutaneous cricothyrotomy using the Seldinger technique is quicker, may be performed by non-surgeons at the bedside, and is safer. See figure. After anaesthetizing the area, a needle is used to puncture the cricothyroid membrane and through this a guide-wire is introduced into the trachea. Over this a series of dilators and the tracheostomy tube can be safely positioned. P915

Complications of cricothyrotomy

- Haemorrhageâ€”usually due to damage to the cricothyroid artery
- Tube misplacement may occur in up to 15% of cases
- Subglottic stenosis
- Hoarseness
- Laryngotracheal-cutaneous fistula



Needle cricothyroidotomy

P.915

P.916

Endotracheal intubation

This is the best method for providing and maintaining a clear airway for ventilation, protection against aspiration, and suctioning and clearing lower respiratory tract secretions. The most common indication for urgent intubation by a physician is cardiac arrest. This is not a technique for the inexperienced: the description below is not intended as a substitute for practice

under supervision of a skilled anaesthetist.

You will need

- Laryngoscope, usually with a curved blade (Macintosh)
- Endotracheal tube (8â€“9mm internal diameter for men and 7â€“8mm for women) and appropriate adaptors
- Syringe for cuff inflation and clamp to prevent air escaping from the cuff once inflated
- Scissors and tape or bandage to secure the tube
- Lubricating jelly (e.g. KY jellyÂ®)
- Suction apparatus with rigid (Yankauer) and long flexible catheters.

Potential problems during intubation

- Certain anatomical variations (e.g. receding mandible, short neck, prominent incisors, high arched palate) as well as stiff neck or trismus may make intubation complicated; summon experienced help.
- Vomiting: suction if necessary. Cricoid pressure may be of use.
- Cervical spine injury: immobilize the head and neck in line with the body and try not to extend the head during intubation.
- Facial burns or trauma may make orotracheal intubation impossible. Consider cricothyroidotomy (see p915).

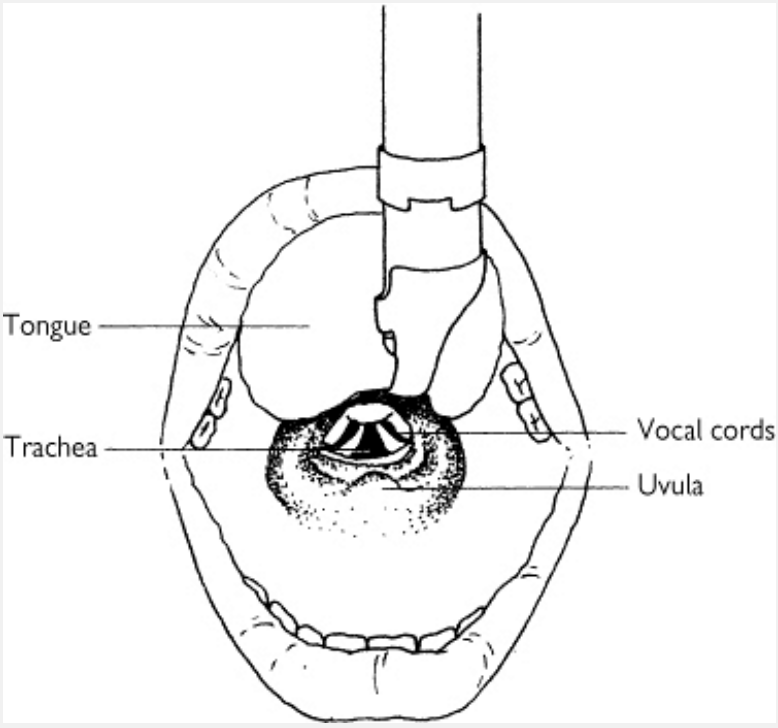
Procedure

- Place the patient with the neck slightly flexed and the head extended. Take care if cervical injury is suspected.

- Cricoid pressure: The oesophagus can be occluded by compressing the cricoid cartilage posteriorly against the body of C6. This prevents passive regurgitation into the trachea but not active vomiting. Ask your assistant to maintain pressure until the tube is in place and the cuff inflated.
- Pre-oxygenate the patient by hyperventilation with â‰¥85% oxygen for 15â€“30 seconds. Open the mouth and suction to clear the airway.
- With the laryngoscope in your left hand, insert the blade on right side of mouth. Advance to base of tongue, identifying the tonsillar fossa and the uvula. Push the blade to the left moving the tongue over. Advance the blade until the epiglottis comes into view.
- Insert the blade tip between the base of the tongue and the epiglottis (into the vallecula) and pull the whole blade (and larynx) upwards along the line of the handle of the laryngoscope to expose the vocal cords. Brief suction may be necessary to clear the view.
- Insert the ET tube between the vocal cords and advance it until the cuff is just below the cords and no further. Inflate the cuff with air.
- If the cords cannot be seen, do not poke at the epiglottis hoping for success, call for more skilled help and revert to basic airway management.

- Intubation must not take longer than 30 seconds; if there is any doubt about the position, remove the tube, reoxygenate, and try again.
- With the tube in place, listen to the chest during inflation to check that BOTH sides of the chest are ventilated. If the tube is in the oesophagus, chest expansion will be minimal though the stomach may inflate; air entry into the chest will be minimal.

- Tie the ET tube in place and secure to prevent it from slipping up or down the airway. Ventilate with high concentration oxygen.



Landmarks for endotracheal intubation.

Aspiration of a pneumothorax

If the pneumothorax is <75% and the patient is haemodynamically stable, it is reasonable to attempt aspiration of the pneumothorax in the first instance (p236).

You will need the following:

- 10ml and 50ml syringe with green (18G) and orange (25G) needles

- Dressing pack (swabs, sterile drapes, antiseptic) and sterile gloves
- 19G VenflonÂ® or alternative cannula
- Local anaesthetic (e.g. 2% lignocaine)
- Three-way tap

Procedure

- 1 assistant is required.
- Sit patient up, propped against pillows with hand behind his/her head; ensure you are comfortable and on a similar level.
- Select the space to aspirate, the 2nd intercostal space in the mid-clavicular line. Confirm with CXR that you are aspirating the correct side (a surprisingly common cause of disasters is aspirating the normal side).
- Clean the skin and use aseptic technique.
- Connect a 50ml syringe to a three-way tap in readiness, with the line which will be connected to the patient turned â€˜offâ€™ so that no air will enter the pleural cavity on connecting the apparatus.
- Infiltrate 5â€“10ml of lignocaine from skin to pleura, just above the upper border of the rib in the space you are using. Confirm the presence of air by aspirating approximately 5ml via a green needle.
- Insert a 16G or larger intravenous cannula into the pneumothorax, preferably whilst aspirating the cannula with a syringe, so that entry into the pleural space is confirmed. Allow the tip of the cannula to enter the space by approximately 1cm.
- Ask the patient to hold their breath and remove the needle. Swiftly connect the 3-way tap. Aspirate 50ml of air/fluid and

void it through the other lumen of the tap. Repeat.

- Aspiration should be stopped when resistance to suction is felt, the patient coughs excessively, or â‰¥2.5 litres of air has been aspirated.
- Withdraw the cannula and cover the site with a dressing plaster (e.g. Elastoplast or Band-aid)
- Check post procedure CXR. If there is significant residual pneumothorax insert a chest drain.

Aspiration of a pleural effusion

The basic procedure is similar to that for a pneumothoraxâ€”the site is different: one or two intercostal spaces posteriorly below the level at which dullness is detected. Ideally all cases should have an USS first to confirm the level of the effusion and ensure that the diaphragm is not higher than anticipated due to underlying pulmonary collapse.

- Position the patient leaning forward over the back of a chair or table. Clean the skin and infiltrate with local anaesthetic as above.
- Insert the cannula and aspirate the effusion with a 50ml syringe, voiding it through the 3-way tap. Repeat until resistance is felt and the tap is dry.
- Check a post procedure CXR.

Insertion of a chest drain 1

You will need the following:

- Dressing pack (sterile gauze, gloves, drapes, BetadineÂ®)

- Local anaesthetic (~20ml 1% lignocaine), 10ml syringe, green (18G) and orange (25G) needles
- Scalpel and No. 11 blade for skin incision; 2 packs silk sutures (1â€“0)
- 2 forceps (Kelly clamps), scissors, needle holder (often pre-packaged as a â€˜chest drain setâ€™)
- Where possible, use the new Seldinger-type chest tubes â€“ especially for pneumothorax
- Chest tubesâ€”a selection of 24, 28, 32, and 36Fr
- Chest drainage bottles, with sterile water for underwater seal
- 1 assistant.

Procedure

- Position the patient leaning forward over the back of a chair or table. If possible, premedicate the patient with an appropriate amount of opiate ~30 minutes before.
- Mark the space to be drained in the mid-axillary line; usually the 5th intercostal space for pneumothorax, below the level of the fluid for an effusion. Clean the skin.
- Select the chest tube: small (24Fr) for air alone, medium (28Fr) for serous fluid, or large (32â€“36Fr) for blood/pus. Remove the trocar. Check that the underwater seal bottles are ready.
- Infiltrate the skin with 15â€“20ml of lignocaine 1%. Make a short sub-cutaneous tunnel for the chest tube before it enters the pleural space (see figure). Anaesthetize the periosteum on the top of the rib. Check that you can aspirate air/fluid from the pleural space.
- Make a horizontal 2cm incision in the anaesthetized skin of the rib space. Use the forceps to blunt-dissect through the

fat and intercostal muscles to make a track large enough for your gloved finger down to the pleural space. Stay close to the upper border of the rib to avoid the neurovascular bundle.

- Check the length of the tube against the patient's chest to confirm how much needs to be inserted into the patient's chest. Aim to get the tip to the apex for a pneumothorax; keep the lowermost hole as low as possible (~2cm into the chest) to drain pleural fluid.
- Insert two sutures across the incision (or a purse-string, see figure). These will gently tighten around the tube once inserted to create an airtight seal but do not knotâ€”these sutures will be used to close the wound after drain removal.
- Remove the trocar. Clamp the end of the tube with the forceps and gently introduce the tube into the pleural space. Rotating the forceps 180Â° directs the tube to the apex (see figure). Condensation in the tube (or fluid) confirms the tube is within the pleural space. Check that all the holes are within the thorax and connect to the underwater seal. Tape these to the skin
- Gently tighten the skin sutures (see above) but do not knot. The drain should be secured with several other stitches and copious amounts of adhesive tape. They are very vulnerable to accidental traction. Wrap adhesive tape around the join between the drain and the connecting tubing.

- Prescribe adequate analgesia for the patient for when the anaesthetic wears off.
- Arrange for a CXR to check the position of the drain.
- Do not drain off more than 1 litre of pleural fluid/24 hours to avoid re-expansion pulmonary oedema.

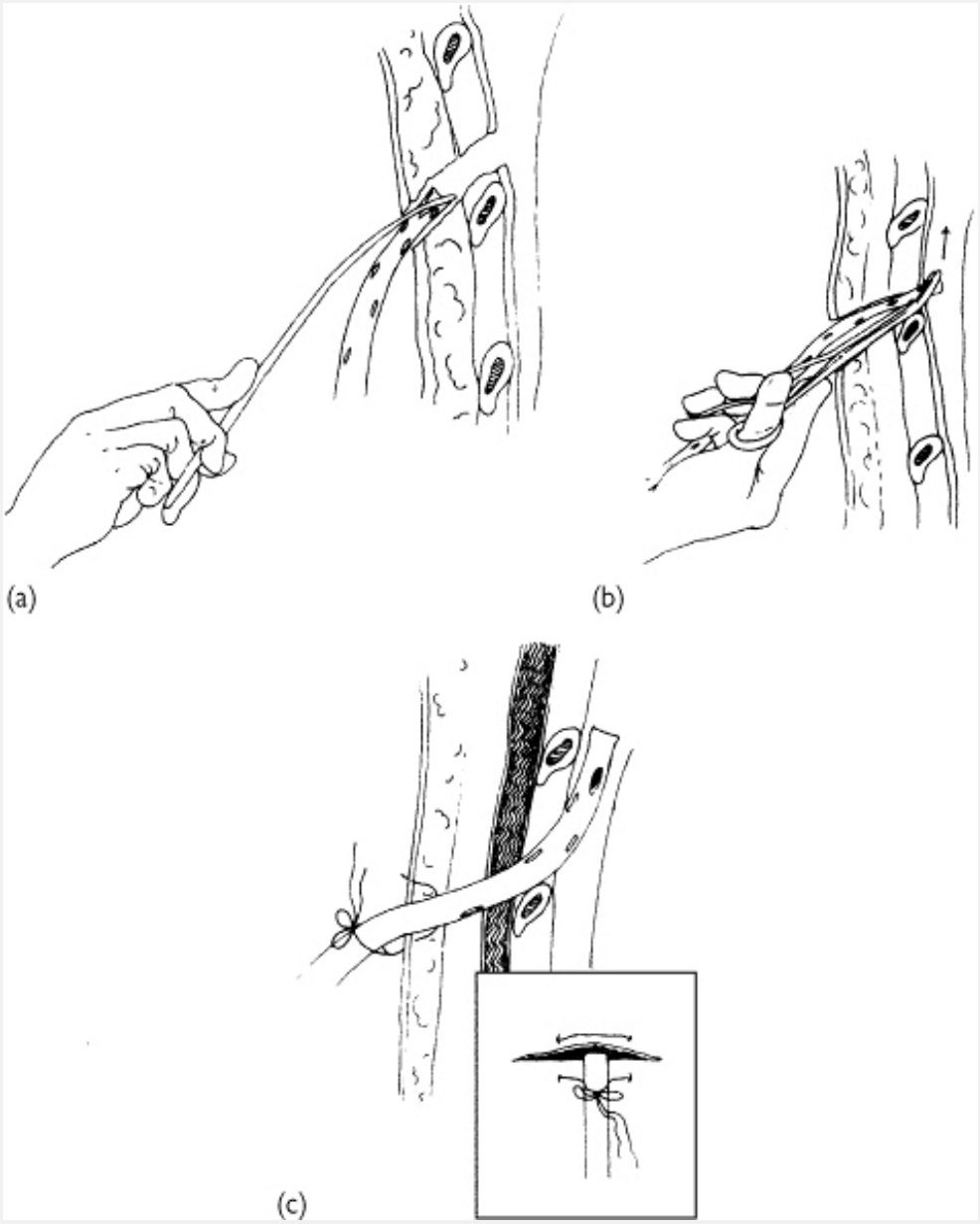


Figure. No caption available.

Insertion of a chest drain 2

Tips and pitfalls

- The chest drain should only be left in place while air or fluid

continue to drain. The risk of ascending infection increases with time. Prophylactic antibiotics are not usually indicated.

- Malpositioned tube: Obtain a CXR post procedure (and daily) to check the position of the drain and examine the lung fields.
    - If the drain is too far out, there will be an air leak and the patient may develop sub-cutaneous emphysema. Ideally, remove the drain and replace with a new drain at a new site; the risk of ascending infection is high if the â€˜non-sterileâ€™ portion of the tube is just pushed into the chest.
    - If the drain is too far in, it may be uncomfortable for the patient and impinge on vital structures (e.g. thoracic aorta). Pull the tube out the appropriate distance and re-suture.
- Obstructed tube: Check the water column in the chest drain bottle swings with respiration. This will stop if the tube is obstructed.
    - Check the drains and tubing are free of bends and kinks.
    - Blood clots or fibrin may block the tube and may be â€˜milkedâ€™ cautiously.
    - If the lung is still collapsed on CXR, replace the chest drain with a new tube at a new site.
- Lung fails to re-expand: This is either due to an obstructed system or persistent air leak (e.g. tracheobronchial fistula).
    - If the chest drain continues to bubble, apply suction to the drain to help expand the lung. Consider inserting further drains or surgical repair of leak.
    - If the chest drain is obstructed (see above), replace the drain.

- Removing the chest drain
    - DO NOT clamp the chest drain.
    - Remove the dressings and release the sutures holding the drain in place. Leave the skin incision sutures (purse-string) in position to close the wound once the drain is removed.
    - Remove the drain in a gentle motion, either in inspiration or in expiration with Valsalva.
    - Tighten the skin sutures. These should be removed after 3â€“4 days and a fresh dressing applied.
    - Any residual pneumothorax should be treated depending on the patient's symptoms, with a fresh chest drain if necessary.

Complications

- Bleeding (intercostal vessels, laceration of lung, spleen, liver)
- Pulmonary oedema (too rapid lung expansion)
- Empyema
- Sub-cutaneous emphysema
- Residual pneumothorax or effusion (malpositioned or obstructed chest drain)

Ascitic tap

Indications

- Diagnose or exclude spontaneous bacterial peritonitis (SBP)

- Ascitic protein and albumin
- Ascitic cytology may require 100ml fluid
- Ascitic amylase (pancreatic ascites)
- Stain and culture for AFBs; lymphocyte count (N <500 cells/mm^3)
- To drain cirrhotic or malignant ascites for patient comfort or fluid overload.

	Transudate	Exudate
Total protein	<30g/L	â‰¥30g/L
Ascitic protein: serum protein	<0.5	>0.5
Serum-ascitic albumin gradient	>11g/L	<11 g/L

Ascitic tap

- Lie patient supine, and tilted slightly to the left or right.
- Select the site (level with umbilicus, and 3â€“4cm lateral to a line passing to mid-inguinal point) and clean the area with iodine or equivalent. Ensure the bladder is empty and avoid any scars.
- Use a 20ml syringe with a 18G (green) needle. In obese patients use a longer needle (e.g. 18G AbbocathÂ®). If you plan to use a larger needle, infiltrate the area with local anaesthetic before proceeding.

- Insert the needle slowly into the abdomen whilst aspirating until fluid is obtained.
- Inoculate 5mls of the fluid into each bottle of a set of blood culture bottles (in cirrhotics for ?bacterial peritonitis) and send some in a sterilinÂ® or plain bottle for microscopy (5ml) and protein (1ml).
- Add 2ml ascites to EDTA tube â€“ send for blood count to haematology.
- Remove the needle and apply a sterile plaster over the puncture site.

Causes of transudative and exudative ascites

Transudative ascites	*Exudative ascites*
• Cirrhosis • Nephrotic syndrome	• Cirrhosis (rarely) • Pancreatic • Tuberculous peritonitis • Buddâ€“Chiari syndrome (hepatic vein thrombosis) • Malignancy • Cardiac ascites

NB: Most causes of transudates can also give rise to exudates and vice versa.

Total paracentesis

Daily small volume paracentesis is time-consuming, unnecessary, and increases the risk of infection and ascitic leakage. It is dangerous to leave a peritoneal tap catheter in place for more than a few hours. The risk of infection in our experience is great. It is safer to drain the ascites to dryness.

The rate of fluid drainage should be as fast as possible. During the first 3â€“6 hours of paracentesis, there is a significant increase in cardiac output, a decrease in systemic vascular resistance, and a modest fall in mean arterial pressure (by 5â€“10mmHg). In the presence of tense ascites the right atrial pressure (RAP) may be artificially elevated by transmitted intra-abdominal pressure, and RAP may fall acutely by ~3â€“5cm water. Thus fluid replacement is essentail.

- Use either a Kuss needle (if available), a large 14G long AbbocathÂ® (used for central lines), a peritoneal dialysis catheter or a Swanâ€“Ganz introducer (8.5F and rather large for the purpose).
- To avoid the catheter blocking due to omentum plugging the end, remove the metal introducer under strict aseptic conditions, and carefully make several perforations in the plastic of the catheter using a green or blue needle. Avoid holes close together and re-insert the metal introducer needle very carefully to avoid causing a tear in the cannula (this would increase the risk of the cannula breaking off in the abdomen). Noteâ€”the manufacturers do not recommend this; some companies produce special catheters with pre-formed side-holes. Always use these if available.
- Take a â€˜drip setâ€™ (iv fluid â€˜giving setâ€™) and, with a sterile blade, cut off the reservoir, leaving the tubing, luer locking device, and rate control mechanism. If a PD cannula or other device is used then some form of tubing needs to be attached to facilitate drainage.
- Position the patient supine and slightly tilted to one side. Select, clean, and infiltrate the site with 2% lignocaine as

for ascitic tap.

- Insert the cannula (attached to a 20ml syringe), aspirating as one advances the cannula. When ascitic fluid is obtained, advance the needle ~5mm more, then advance the plastic cannula holding the metal introducer, ready to prevent it going any deeper (as for inserting a VenflonÂ®).
- Remove the metal introducer and attach the drainage tube (modified â€˜giving setâ€™). Strap the introducer to the abdominal wall with elastoplast. It is not necessary to suture the cannula in place since it will be removed within 3â€“4 hours.
- Drain the ascites as rapidly as possible into an appropriate receptacle (have bucket to hand for emptying the contents).
- When the ascites stops draining or slows down, move the patient from side to side, and lie towards the drainage site.
- When drainage is complete, remove the catheter, apply plaster, and lie the patient with the drainage site uppermost for at least 4 hours.

Insertion of Sengstakenâ€“Blakemore or Minnesota tube

The Sengstakenâ€“Blakemore or Minnesota tube are inserted to control variceal bleeding when other measures (injection sclerotherapy, intravenous vasopressin, or octreotide) have failed. It should not be used as the primary therapy of bleeding varices since it is unpleasant, and increases the risk of oesophageal ulceration. If placed in the unintubated patient there is a very real risk of aspiration.

Seek experienced or specialist help early. Balloon tamponade is not a definitive procedure: make arrangements for variceal injection or oesophageal transection once the patient is stable.

Continue infusions of vasopressin or octreotide (pp488â€“90).

You will need the following

- Sengstaken or Minnesota tube
- Bladder syringe (for balloons)
- Sphygmomanometer
- X-ray contrast (diluted)

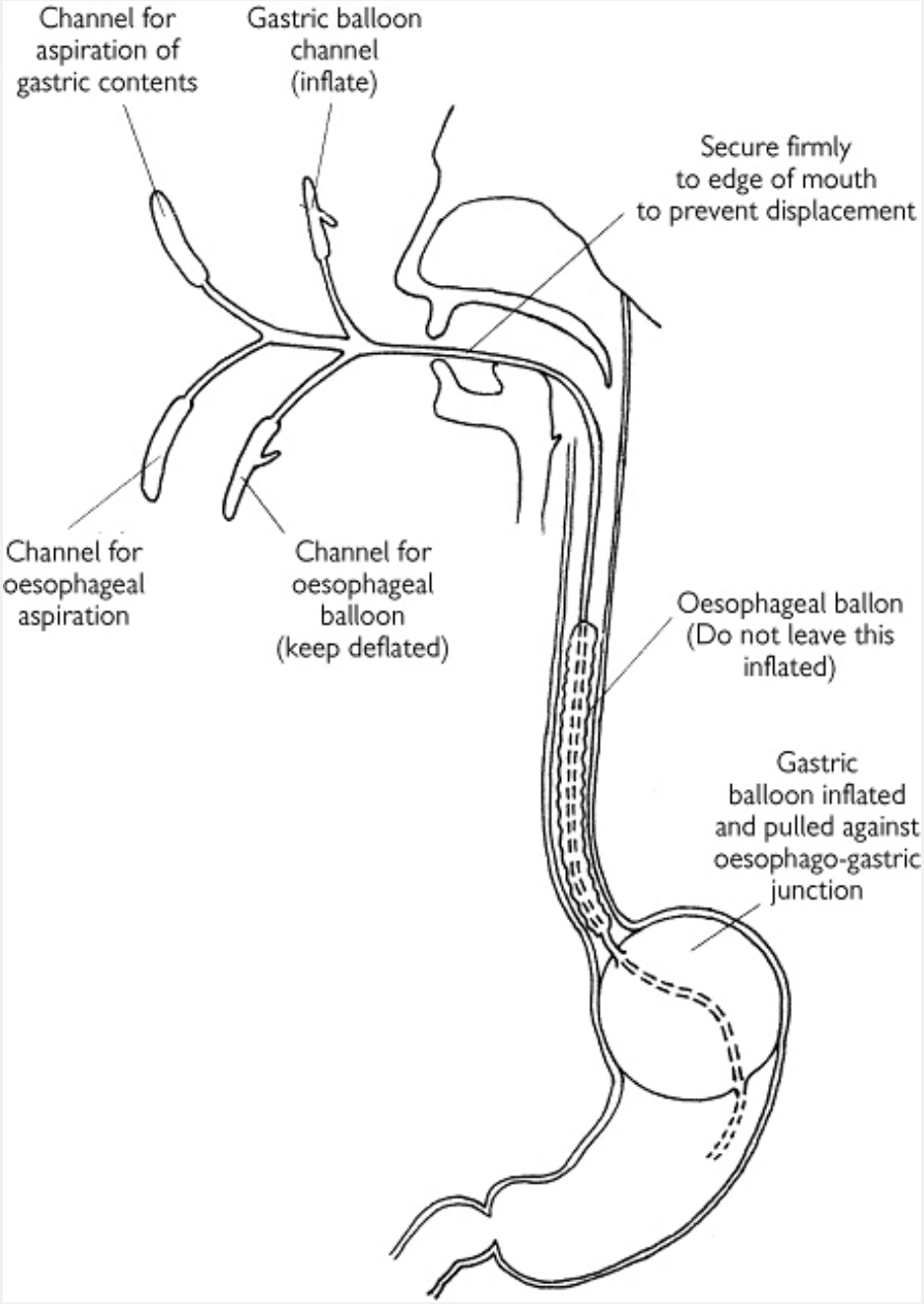
Procedure

- It is assumed that the patient is already being resuscitated, and is receiving intravenous glypressin (p618). The patient should ideally be intubated and ventilated. If not, there is an increased risk of aspiration. This risk may be reduced in the unintubated patient by injecting 10mg metoclopramide immediately before insertion. This can cause temporary cessation of haemorrhage and reduce the aspiration risk. Have a low threshold for sedation, endotracheal intubation, and ventilation.
- The SBT or Minnesota tube should be stored in the fridge (to maximize stiffness) and removed just before use. Familiarize yourself with the various parts before insertion if necessary. Check the integrity of the balloons before you insert the tube.
- Place an endoscope protection mouthguard in place (to prevent biting of the tube). Cover the end of the tube with KY jelly, and, with the patient in the left semi-prone position, push the tube down, asking the patient to swallow (if conscious). If the tube curls up in the mouth, try again or try another cooled tube.
- Insert at least 50cm, and start inflating the gastric balloon with 200ml water containing gastrografin (this enables the

balloon to be visualized on a CXR or AXR). Clamp the balloon channel. Then gently pull back on the tube until the gastric balloon abuts the gastro-oesophageal junction (resistance felt), then pull further until the patient is beginning to be tugged by pulling. Note the position at the edge of the mouth piece (mark with pen), and attach with elastoplast to the side of the face. Weight contraptions should not be necessary.

- In general the oesophageal balloon should never be used. Virtually all bleeding varices occur at the oesophagogastric junction and are controlled using this technique.
- If the bleeding continues, inflate the oesophageal balloon. Connect this to a sphygmomanometer via a 3-way tap to monitor the balloon pressure. Inflate to 40mmHg and close the 3-way tap. Check the pressure in this balloon every 1â€“2 hours. Do not deflate every hour.

- Do NOT leave the balloons inflated for more than 12 hours since this increases the risk of oesophageal ulceration.
- Obtain a CXR to check the position of the tube.
- The gastric channel should be aspirated continuously.
- If facilities for variceal injection are available, remove the SBT or MT immediately prior to endoscopy. If not, discuss the patient with your regional centre and transfer if appropriate.



Positioning of Sengstakenâ€“Blakemore tube for compression of oesophageal varices.

Transjugular liver biopsy

Indications

It is not without risk, and should not be applied merely to obtain histology for completeness.

- Bleeding diathesis contraindicating conventional biopsy techniques
- The biopsy will assist diagnosis and subsequent management.

Procedure

This is relatively straight-forward, and is based on the assumption that by taking the biopsy through the hepatic vein any bleeding will occur into circulation.

A large introducer is placed into the internal jugular vein or femoral vein. A catheter is introduced through this and manipulated into the hepatic vein. The catheter is removed leaving a guide wire *in situ*. A metal transjugular biopsy needle is passed over the wire and advanced into the hepatic vein. One has to avoid being too peripheral (risk of capsular puncture). The wire is removed, and the needle advanced whilst suction is applied. A biopsy is obtained by the â€˜Menghiniâ€™ technique. The biopsies obtained are much poorer than those obtained by conventional techniques.

Transjugular intrahepatic porto-systemic shunt (TIPSS)

Indications

- Uncontrolled or recurrent bleeding of oesophageal or gastric varices

- Diuretic resistant ascites

Principle

To lower the portal pressure acutely, a shunt is placed between a hepatic vein and portal vein tributary. Blood then flows from the high pressure portal system to the lower pressure hepatic venous system which drains into the IVC. The lowered portal pressure then makes bleeding from oesophageal varices less likely.

It is carried out in relatively few specialist centres and is technically quite difficult. Its advantage is that it does not require a general anaesthetic, the risk is lower than for a formal portacaval or mesocaval shunt procedure, and it does not hinder future liver transplantation. The centres carrying out most of these procedures in the UK are The Royal Free Hospital, London, Newcastle RI, Edinburgh RI, and Addenbrookes, Cambridge. Contact your regional centre if you feel this may be appropriate.

Method

The internal jugular vein is catheterized, and a cannula passed through the right atrium into the IVC, and into an hepatic vein. The portal vein is localized by USS, and a metal transjugular biopsy needle advanced through the liver substance into one of the portal vein tributaries (usually right portal vein). A wire is then passed into the portal vein and the metal needle withdrawn, leaving the wire joining the hepatic vein and portal vein. An expandable stent is then passed over the wire, and expanded by balloon inflation. A typical stent size is 8â€“12mm.

Complications

- The mortality is ~3%, usually from a capsular puncture.
- Hepatic encephalopathy occurs in ~20%.

- Failure to reduce portal pressure may occur if there are large extrahepatic shunts. These may need to be embolized.

Percutaneous liver biopsy

Procedure

- Obtain patient consent, warning of risk of bleeding, pneumothorax, gall-bladder puncture, and failed biopsy. Warn about shoulder tip pain, which may last several hours.
- Ensure prothrombin time is <3 seconds prolonged cf. control, and the platelet count is >80 Ã— 10^9/L, and that there is no other bleeding diathesis (e.g. severe renal failure in which platelet function is impaired). Other contraindications are ascites, and possibly tumour depending on planned management (risk of tumour seeding).
- If available always use ultrasound guidance, especially if the liver is small and cirrhotic.
- You will need a biopsy needle (Tru-cut or Menghini), 1% lignocaine, an orange (25G) and green (18G) needle, 5ml syringe, a No. 11 scalpel blade, iodine or equivalent, sterile towels, a plaster, sterile gloves, a dressing pack, and a bottle of formalin.
- Pre-medicate the patient with an appropriate amount of analgesia (e.g. 30â€“60mg dihydrocodeine) 15â€“30 minutes before the procedure.
- Lie the patient supine with the right hand behind their head. Percuss the upper border of the liver in expiration and mark with a pen. Select a site 2 intercostal space below the upper border, making sure it is not too close to the costal margin (and thence gall-bladder).

- Clean the skin with antiseptic and infiltrate with lignocaine as far as the capsule. Always go just above a rib, and make an incision with the scalpel to facilitate the larger biopsy needle passing through the skin. The capsule is felt as a grating feeling, and if the syringe is allowed to float on the palm of the hand will be seen to move with gentle respiration when the tip of the needle has penetrated the capsule. Do not prevent the needle from moving with respiration as this will increase the risk of capsular tear, and do NOT ask the patient to breathe deeply with the needle in this position.
- Remove the needle. Rehearse the patient asking them to breathe in, then out and stop (in expiration). It is imperative during the actual biopsy that they do not take a sudden gasp of breath. Rehearse it several times. We find it useful to keep saying â€˜stop, stopâ€™ etc. until the biopsy is complete. Avoid saying â€˜holdâ€™ since many patients will then breathe in at the crucial moment.
- Make a small skin incision with the scalpel and insert the biopsy needle when the patient is at end expiration.
- After the biopsy (do not attempt more than 2 passes), place a plaster over the site and ask the patient to lie on their right side for 4 hours.
- Nursing observations are pulse and bp every 15 minutes for 1 hour, every 30 minutes for 2 hours, hourly for 3 hours, 2 hourly for 8 hours. Avoid evening or late afternoon biopsies.

Plugged biopsy technique

This technique is used if there is a mild bleeding diathesis, and can be performed when the prothrombin time is up to 6 seconds prolonged with a platelet count of > 40 000mm^3. The biopsy is done through a sheath and the tract embolized using Gelfoam to try to prevent bleeding. Seek experienced help.

Acute peritoneal dialysis

Rarely used but does not require vascular access or anti-coagulation. Provides insufficient dialysis for the hypercatabolic patient. (Creatinine clearance rate of ~10ml/min may be achieved). This requires:

- Peritoneal dialysis catheter (may be inserted under LA on the ward)
- Intact peritoneal cavity free of infection, herniae, adhesions.

Complications of peritoneal dialysis

Peritonitis The commonest complication of CAPD: 0.8 episode/pt/yr. Infection occurs through the lumen of the catheter, along catheter tract, transmurally from GIT, or haematogenously (rare).

Assessment

- Common features are cloudy PD bag (99%), abdominal pain (95%), and abdominal tenderness (80%).
- Other features include fever (33%), nausea and vomiting (30%), leucocytosis (25%), diarrhoea or constipation (15%).
- Investigations: PD effluent cell count (peritonitis if >100 neutrophils/mm^3), culture PD fluid (inoculate a blood culture bottle), Gram stain PD fluid, FBC (for leukocytosis), blood cultures.

Management

- All patients require antibiotics, but may not require

admission. The antibiotics used depends on Gram stain and culture results. A typical protocol would be ciprofloxacin or vancomycin, plus metronidazole. Patients who have high fever with leukocytosis, and/or who are systemically unwell warrant IV antibiotics.

- Gram-negative infection, in particular *Pseudomonas*, is associated with more severe infection. Severe episodes may be accompanied by ileus, whatever the organism.
- If pain is prominent, give analgesia (opiate) and consider intermittent peritoneal dialysis (IPD) instead of PD.
- Patients may lose up to 25g protein/day in severe cases and should receive adequate nutritional support.
- If the infection is resistant to treatment, consider removal of Tenckhoff catheter and atypical organisms (e.g. fungi).
- Consider underlying gastrointestinal pathology especially if multibacterial, Gram-negative organisms, or other symptoms.

Fluid overload

Mild cases may respond to hypertonic exchanges (6.36% or 4.25% dextrose), fluid restriction (1 litre/day), and large doses of diuretics (e.g. frusemide 500mg bd). With pulmonary oedema, fluid removal is best achieved by rapid cycle IPD (4.25% dextrose, 60 min cycle time).

Poor exchanges

- Constipation may cause malposition of catheter
- Malpositioned catheter: The catheter should sit in pelvis, but occasionally flips upwards to lie against the diaphragm, causing shoulder tip pain and poor drainage. If the patient is constipated try laxatives, but may require surgical repositioning.

- Omentum wrapping around tip of catheter can be prevented by omentectomy at time of insertion.
- Fibrin debris blocking catheter seen as white deposits in effluent. Treat by addition of heparin (1000U/litre) to bags.

Hyperglycaemia

A significant amount of the dextrose in peritoneal dialysis solutions is absorbed (especially with â€˜heavyâ€™ 4.26% dextrose bags). Renal failure induces insulin resistance, so an elevated blood glucose may occur, as well as hypercholesterolaemia. Diabetic patients require special attention to insulin therapy.

Intermittent haemodialysis

A blood flow of ~250â€“300ml/min is needed across the dialysis membrane. The equivalent clearance obtained is approximately 20ml/min.

- Vascular access. Vascular access may be obtained by fashioning an AV shunt using the radial artery, or more commonly by using a Vascath which uses venous rather than arterial blood. This involves cannulation of the internal jugular, subclavian, or femoral vein.
- Anti-coagulation. Heparin is normally used. If contraindicated, e.g. recent haemorrhage, then prostacyclin may be used, but may cause hypotension and abdominal cramps.
- Haemodynamic stability. Patients with multi-organ failure commonly develop hypotension during haemodialysis. This may be ameliorated by high sodium dialysate, and priming the circuit with 4.5% human albumin solution.

Complications of haemodialysis

Hypotension Usually occurs within the first 15 minutes of commencing dialysis. It probably involves activation of circulating inflammatory cells by the membrane, osmotic shifts, and possibly loss of fluid. *Treatment*: Cautious fluid replacement and inotropes (watch for pulmonary oedema if over-transfused).

Risk factors or exacerbating factors for hypotension

- Multi-organ failure
- Autonomic neuropathy
- Valvular lesions (e.g. mitral regurgitation, aortic stenosis)
- Arrhythmias
- Pericardial tamponade
- MI or poor LV function
- Sepsis

Line infection Central lines are a common focus of infection. When a dialysis patient develops a fever of >38Â°C it should be assumed that the neck line is infected even if an alternative septic focus is known. *Management*: Take blood cultures both peripherally and from the neck line and replace the central line (avoid â€˜railroadingâ€™ over the previous line). Treat empirically with vancomycin 750mgâ€“1g iv in 100ml N saline over 1h at end of dialysis. Vancomycin should be given slowly or severe vasodilatation may give rise to the â€˜red man syndromeâ€™. An alternative is teicoplanin 400mg iv followed by 200mg iv daily. Both drugs are poorly removed by haemodialysis, a single dose will ensure therapeutic levels for several days. 90% will be due to *Staph. aureus or epidermidis*. Right-sided endocarditis may occur (p132).

Dialysis disequilibrium This occurs during the initial dialysis especially in patients with marked uraemia, and is more common in paatients with pre-existing neurological disease.

Clinical features: Headache, nausea and vomiting, fits, cerebral oedema. *Treatment*: Treat cerebral oedema as on p462. Short and slow initial dialyses may prevent this.

Dialyser reaction This is caused by an IgE or complement response against the ethylene oxide (sterilizing agent) or the cellulose component. Use of â€˜biocompatibleâ€™ membranes [e.g. polysulfone, polyacrylonitrile (PAN)] or dialysers sterilized by steam or Î³-irradiation may prevent further reactions.

The circuit should also be rinsed with N saline. *Clinical features* are of allergy: Itching, urticaria, cough and wheeze. Severe reactions may cause anaphylaxis. *Management*: Stop dialysis and treat anaphylaxis (see p258)â€”antihistamines (chlorpheniramine 10mg iv), hydrocortisone 100mg iv, bronchodilators (salbutamol 5mg by nebulizer), and, if severe, adrenaline (1mg im).

Air embolism Rare, potentially fatal. Symptoms may vary depending on patient's position. If sitting, air may pass directly to the cerebral veins causing coma, fits, death. If lying, air may pass to R ventricle and then to pulmonary vessels causing SOB, cough, and chest tightness. *If suspected*: Clamp dialysis lines, lie patient head-down on left side, administer 100% O_2 by mask. Aspiration of air with an intracardiac needle may be attempted in extreme circumstances.

Complications of haemodialysis

- Hypotension
- Line infection
- Dialysis disequilibrium
- Dialysis reaction (allergy)
- Cramps
- Air embolism

- Haemorrhage

Haemofiltration and haemodiafiltration

Continuous arteriovenous haemofiltration (CAVH) implies bulk solute transport across a membrane and replacement. Haemodiafiltration (CAVHD) involves the pumping of dialysate across the other side of the membrane. For both, arterial blood (driven by arterial pressure) is continuously filtered at a relatively low flow rate (50â€“100ml/min). Continuous venovenous haemofiltration involves pumping blood from a venous access to the dialysis membrane (150â€“200ml/min) (CVVH or CVVHD). The equivalent GFR obtained by these are approximately 15â€“30ml/min. These are used most commonly on ITU. Both of these methods cause less haemodynamic instability, and are particularly useful in patients with multi-organ failure.

Plasmapheresis

A therapy directed towards removal of circulating high molecular weight compounds not removed by dialysis. Particularly used in the removal of antibodies, or lipoproteins.

Indications

- Myasthenia gravis
- Guillainâ€“BarrÃ© syndrome
- Goodpasture's syndrome
- Thrombotic thrombocytopenic purpura (TTP)
- Haemolytic uraemic syndrome (HUS)
- Severe hyperlipidaemia

- Multi-system vasculitis
- Hyperviscosity syndrome (e.g. Waldenstrom's macroglobulinaemia)
- HLA antibody removal

Method

Requires central venous access with a large bore, dual lumen cannula. Usually five treatment sessions are given on consecutive days. Plasma is removed and replaced with, typically, 2 units FFP, 3 litres 4.5% albumin. iv calcium (10ml 10% calcium gluconate) should be given with the FFP. Febrile reactions may occur as with other blood products. Plasmapheresis has no effect on the underlying rate of antibody production, but is a useful treatment in acute situations such as Goodpasture's and myasthenia gravis.

- For HUS and TTP one must use fresh frozen plasma ONLY (preferably cryodepleted), usually a minumum of 3L/day (see p704).
- For hyperviscosity syndrome, a centrifugation system is required rather than a plasma filter (see p728).
- For lipopheresis there may be severe reactions if the patient is on an ACE inhibitor.
- An alternative to plasmapheresis is immunoabsorption in which 2 columns are used in parallel. This may be used in the removal of HLA antibodies, anti-GBM disease, or multi-system vasculitis.

Renal biopsy

Indications (see table)

Biopsy is now performed using real-time ultrasound guidance.

Contraindications

- Bleeding diathesisâ€”unless correctable prior to biopsy
- Solitary functioning kidney
- Uncontrolled hypertension, i.e. diastolic >100mmHg
- Urinary tract obstruction
- Small kidneys, since it is unlikely to reveal any treatable condition
- Patient unable to comply with procedure (? biopsy under GA)

Prior to biopsy

- Check Hb, clotting screen, G&S serum.
- Ensure IVU or ultrasound has been carried out to determine presence and size of two kidneys.
- Consent patient quoting ~1% risk of bleeding requiring transfusion.
- Do not attempt this if you have not been taught by an expert.

Technique

- You will need a Tru-Cut or other biopsy needle (e.g. BioptigunÂ®). Ensure you are familiar with the workings of the needle.
- Position patient prone on bed with pillows under abdomen.
- Visualize lower pole of either kidney with ultrasound (right

kidney lies more inferiorly and may be easier to image).

- Sterilize skin, drape with towels. Infiltrate local anaesthetic (10ml 2% lignocaine) under skin and to depth of kidney. Make a small skin incision with a scalpel to facilitate entry of biopsy needle.
- Insert biopsy needle as far as the renal capsule under US guidance.
- Ask patient to hold breath in at the end of inspiration (displaces kidney inferiorly) and take biopsy from lower pole.
- Apply sterile dressing.
- Bed rest for 24h to minimize risk of bleeding.
- Monitor bp and pulse half hourly for 2h, 1 hourly for 4h, then 4 hourly for 18h.
- Send renal biopsy tissue for light microscopy, immunofluorescence, and EM. Special stains (e.g. Congo red) if indicated.

Complications

- Bleeding: Microscopic haematuria is usual; macroscopic haematuria in 5â€“10%; bleeding requiring transfusion in 1%.
- Formation of an intrarenal AV fistula may occur, but is rarely of significance. If bleeding occurs from this, angiography and embolization may be needed.
- Loin pain if severe suggests bleeding.
- Pneumothorax is now rare.
- Ileus rarely.
- Laceration of liver, spleen, bowel rarely.

Renal transplant biopsy

Indications

- Decline in transplant function
- Primary non-function post transplant

Procedure

In principle the technique is similar to native renal biopsy, though the transplanted kidney lies more superficially in the iliac fossa. Ultrasound localization is useful. Biopsy may be taken from either upper or lower pole. Some centres find fine needle aspiration biopsy (FNAB) useful in diagnosis of transplant rejection.

Indications for renal biopsy

- Cause is unknown
- Heavy proteinuria (>2g/day)
- Features of systemic disease
- Active urinary sediment
- Immune-mediated ARF
- Prolonged renal failure (>2 weeks)
- Suspected interstitial nephritis (drug induced)

pH_i determination (gastric tonometer)

Patients in shock have reduced splanchnic perfusion and oxygen delivery. The resulting mucosal ischaemia may be difficult to diagnose clinically until it presents as GI bleeding or the sepsis

syndrome. The earliest change detectable following an ischaemic insult to the gut is a fall in intramucosal pH. Gastric mucosal pH parallels the changes in pH in other portions of the GI tract and monitoring this allows detection of gut ischaemia early.[1]

A tonometer is essentially an NG-tube with a second lumen leading to a balloon which lies within the mucosal folds of the stomach. The balloon is inflated with 0.9% saline for 30â€“90 minutes. This allows CO_2 from the mucosa to diffuse into the saline and equilibrate. The saline is then removed and analysed for pCO_2 with simultaneous arterial blood [HCO_3^-] measurement. pH_i is then calculated using a modification of the Henderson-Hasselbalch equation.

The correction factors and equations are supplied with the tonometer and you are advised to consult the literature that the tonometer is supplied with.

Footnote

1

Fiddian-Green RG, Baker S (1987) *Critical Care Med* 15: 153â€“156.

Joint aspiration

Many synovial joints can be safely aspirated by an experienced operator. Knee effusions are common and aseptic aspiration can be safely performed in casualty. The risk of inducing a septic arthritis is less than 1 in 10 000 aspirations, but certain rules should be followed.

- Anatomical landmarks are identified
- The skin is cleaned with alcohol or iodine

- A no touch technique is essential.

Indications for synovial fluid aspiration in casualty

- Suspected septic arthritis
- Suspected crystal arthritis
- Suspected haemarthrosis
- Relief of symptoms by removal of effusion in degenerative arthritis.

Contraindications to joint aspiration

- Overlying sepsis
- Bleeding diathesis

Knee joint Patient lies with knee slightly flexed and supported. The joint space behind the patella either medially or laterally is palpated, the skin cleaned, and a needle (18G, green) inserted horizontally between the patella and femur using a no-touch technique. There is a slight resistance as the needle goes through the synovial membrane. Aspirate on the syringe until fluid is obtained.

Elbow joint Flex the elbow to 90Â° and pass the needle between the proximal head of the radius (locate by rotating patients hand) and the lateral epicondyle; or the needle can be passed posteriorly between the lateral epicondyla and the olecranon.

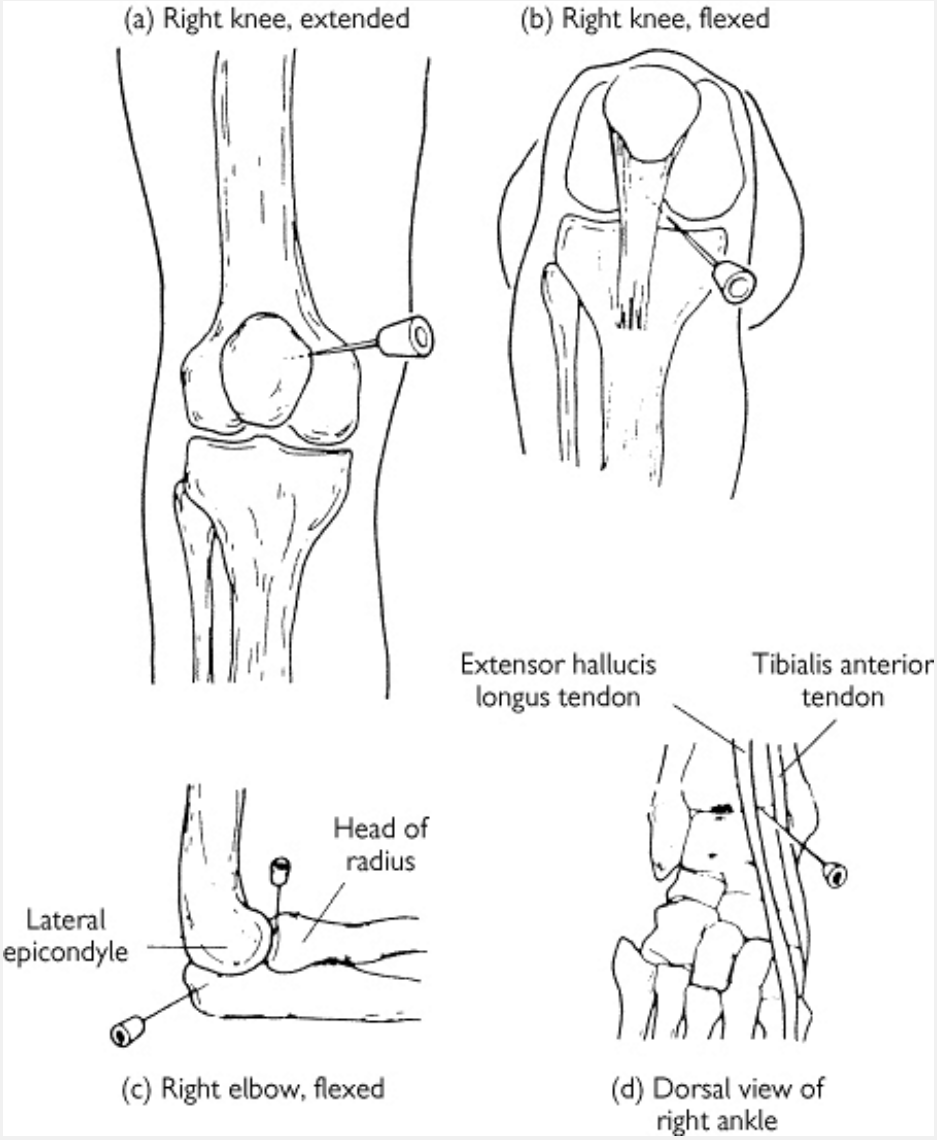
Ankle joint Plantarflex the foot slightly, palpate the joint margin between extensor hallucis longus (lateral) and tibialis anterior (medial) tendons just above tip of medial malleolus.

When synovial fluid is obtained:

- Note the color and assess viscosity
- Microscopy for cell count and crystals
- Gram stain and culture
- Synovial fluid glucose (â†“cf. blood glucose in sepsis).

Synovial fluid analysis

Condition	Viscosity	Opacity	Leukocyte count (per mm^3)
Normal	High	Clear	<200
Osteoarthritis	High	Clear	1000 (<50% PMN)
Rheumatoid	Low	Cloudy	1â€“50 000 PMN
Crystal	Low	Cloudy	5â€“50 000 PMN
Sepsis	Low	Cloudy	10â€“100 000 PMN



Approaches used for joint aspiration (after Crawley M (1974) *Br Hosp Med* 11: 747â€“55)

P.947

P.948

Intracranial pressure monitoring

Indications

- Cerebral trauma (GCS â‰¤8, compression of basal cistern on CT, mid-line shift >0.5mm on CT, raised ICP not requiring surgery)
- Acute liver failure (Grade 4 coma with signs â†‘ICP)
- Metabolic diseases with â†‘ICP (e.g. Reye's syndrome)
- Post-operative oedema (after neurosurgery)
- After intracranial haemorrhage (SAH or intracerebral).

ICP monitoring in patients who are at risk of unexpected rises in ICP should ideally be started before secondary brain injury has occurred, and where it would influence management of the patient. As facilities in neurosurgical centres may be limited, it has been suggested that these patients may be effectively managed in District Hospitals.[1]

Contraindications

- Uncorrectable coagulopathy
- Local infection near placement site or meningitis
- Septicaemia.

Method

- There are several types of devices available (subdural, extradural, parenchymal, or intraventricular); parenchymal and intraventricular monitors are more accurate but carry a higher risk than extradural monitors. They should be implanted by experienced persons only.
- There are pre-packaged kits available (e.g. the CodmanÂ® subdural bolt). This monitor is inserted in the pre-frontal region and the kit contains the necessary screws for creating a burr-hole, spinal needles to perforate the dura, etc.
- The ICP waveform obtained is a dynamic recording that

looks superficially very similar to the pulse waveform. It is due to pulsations of the cerebral blood vessels within the confined space of the cranium, with the effects of respiration superimposed.

- Cerebral perfusion pressure = mean arterial pressure-ICP.
- The normal resting mean ICP measured in a supine patient is less than 10mmHg (<1.3kPa).
- The level which requires treatment depends to some extent on the disease: in benign intracranial hypertension values of ~40mmHg may not be associated with neurological symptoms; in patients with cerebral trauma treatment should be initiated with mean ICP >25mmHg, though this value is debated.
- There are several types of pressure waves described of which the most significant are â€˜*A waves*â€™â€”sustained increases of the ICP lasting 10â€“20 minutes up to 50â€“100mmHg (6â€“13kPa). These are associated with a poor prognosis.
- The readings of the ICP monitors should always be accompanied by careful neurological examination.
- Treatment of raised ICP is discussed on p452.

Complications

- Infection (up to 5%)
- Bleeding (local, subdural, extradural, or intracerebral)
- CSF leak
- Seizures
- Misreading of ICP pressures.

Footnote

1

Goodwin J *et al.* (1993) *Clin Int Care* 4: 190â€“192.

Lumbar puncture 1

Contraindications

- Raised intracranial pressure (falling level of consciousness with falling pulse, rising bp, vomiting, focal signs, papilloedema). In general a CT scan should *always* be carried out prior to LP to exclude an obstructed CSF system or SOL (see p452).
- Coagulopathy or â†“ platelets (<50 Ã— 10^9/L).

You will need the following:

- Spinal needles.
- Dressing pack (sterile gauze, drapes, antiseptic, gloves, plaster).
- Local anaesthetic (e.g. 2% lignocaine), 5ml syringe, orange (25G) and blue (22G) needles.
- 3 sterile bottles for collecting CSF and glucose bottle.
- Manometer and 3-way tap for measuring the opening CSF pressure.

Procedure

For suspected meningitis, antibiotics should be given first (see p432).

- Explain the procedure to the patient.
- Spend time positioning the patient, this is crucial to success. Lie patient on their left side (or R side if you are left handed), with back on edge of bed, fully flexed (knees to chin), with a folded pillow between their legs, keeping the back perpendicular to the bed. Flexion separatesthe interspaces between the vertebrae.
- The safest site for LP is the L4â€“L5 interspace (the spinal cord ends at L1â€“L2). An imaginary line drawn between the iliac crests intersects the spine at the L4 process or L4â€“L5 space exactly. Mark the L4,5 intervertebral space (e.g. with a ballpoint pen).
- Clean the skin widely and place the sterile drapes over the patient.
- Inject 0.25â€“0.5ml 2% lignocaine under skin at pen mark with the 25G needle. Anaesthetize the deeper structures with the 22G needle. Use the anaesthetic sparingly: this may distort the anatomy making the procedure difficult and unnecessarily longer.
- Insert the spinal needle (stilette in place) in the mid-line, aiming slightly cranially (towards umbilicus), horizontal to the bed. Do not advance the needle without the stylet in place.
- With experience, you will feel the resistance of the spinal ligaments, and then the dura, followed by a â€˜giveâ€™ as the needle enters the subarachnoid space. Alternatively, periodically remove the stylet and look for escape of CSF. Replace the stylet before advancing.
- Measure CSF pressure with manometer and 3-way tap. Normal opening pressure is 7â€“20cm CSF with the patient in the lateral position. CSF pressure is increased with anxiety, SAH, infection, space occupying lesion, benign intracranial hypertension, CCF.
- Collect 0.5â€“1.5ml fluid in 3 serially numbered bottles and

remember to fill the glucose bottle.

- Send specimens promptly for microscopy, culture, protein, glucose (with a simultaneous plasma sample for comparison), and where appropriate, virology, syphilis serology, cytology for malignancy, AFB,

oligoclonal bands (multiple sclerosis), cryptococcal antigen testing, India ink stains, and fungal culture.

- Remove needle and place a plaster over the site.
- Patient should lie flat for at least 6h and have hourly neurological observation and bp measurement. Encourage fluid intake.

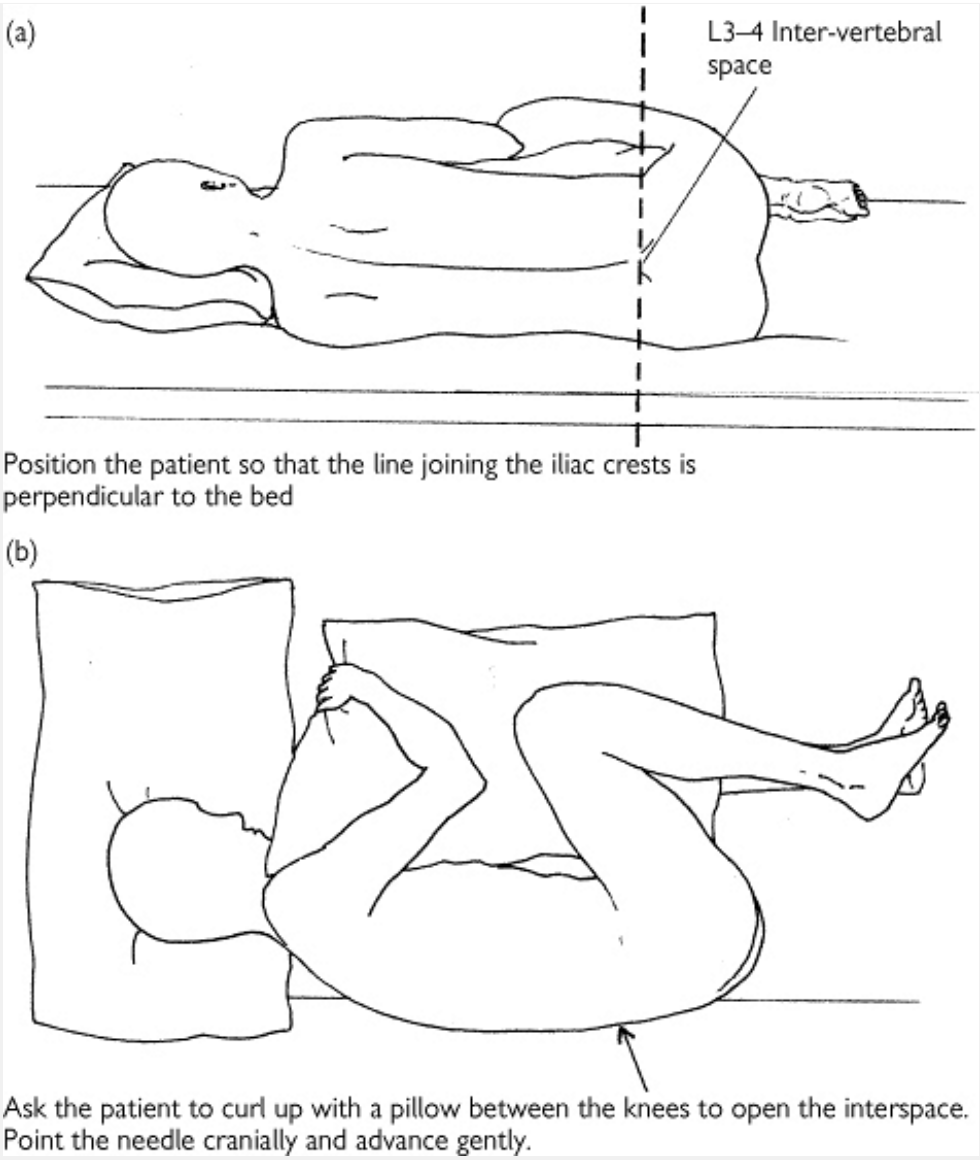


Figure. No caption available.

Lumbar puncture 2

Complications of lumbar puncture

- *Headache*: Common (up to 25%). Typically present when the patient is upright and better when supine. May last for days. Thought to be from intracranial traction due to CSF

depletion from a persistent leak from the LP site. May be prevented by using finer spinal needles, keeping the patient supine for 6â€“12 hours post LP, and encouraging fluid intake. Treat with simple analgesia, fluids, and reassurance.

- *Trauma to nerve roots*: Rarer but seen if the needle does not stay in the mid-line. The patient experiences sharp pains or parasthesiae down the leg. Withdraw the needle and if the symptoms persist, stop the procedure and seek expert help.
- *Bleeding*: Minor bleeding may occur with a â€˜traumatic tapâ€™ when a small spinal vein is nicked. The CSF appears bloody (see below) but the bleeding stops spontaneously and does not require specific therapy. Coagulopathy, severe liver disease, or thrombocytopenia carries the risk of subarachnoid/subdural bleeding and paralysis.
- *Coning*: Herniation of cerebellar tonsils with compression of the medulla is very rare unless the patient has raised ICP. Always get a CT brain scan prior to LP and review this yourself if possible. Mortality is high, but the patient may respond to standard measures for treating this (see p452).
- *Infection*: Rare if proper sterile technique used.

CSF analysis

â€¢ Normal values:	Lymphocytes <4/mm^3; polymorphs 0mm^3
	Protein <0.4g/L
	Glucose >2.2mmol/L (or >70% plasma level)
	Opening pressure <200mm CSF

	Bacterial	Viral	TB meningitis
Appearance	Turbid	Clear	Clear
Cells (mm^3)	5â€“2000	5â€“500	5â€“1000
Main cell type	Neutrophil	Lymphocyte	Lymphocyte
Glucose (mM)	Very low	Normal	Low
Protein (g/L)	Often >1.0	0.5â€“0.9	Often >1.0
Other tests	Gram stain Bacterial	PCR	Ziehl-Nieelson Fluorescent

	antigen		test PCR

- Bloody tap: Artefact is indicated by fewer red cells in successive bottles, no yellowing of CSF (xanthochromia). The true WBC count may be estimated by:

True CSF WBC = CSF WBC - Blood WBC Ã— CSF RBC/blood RBC

(i.e. if the patient's blood count is normal, subtract approx. one white cell for every 1000 RBC). To estimate the true protein level subtract 10mg/L

for every 1000 RBCs/mm^3 (be sure to do the count and protein estimation on the same bottle).

- Subarachnoid haemorrhage: (see p466) xanthochromia (yellow CSF). Red cells in equal numbers in all bottles. The RBCs will excite an inflammatory response (â†‘CSF WCC), most marked after 48h.
- â†‘â†‘CSF protein: Acoustic neuroma and spinal tumours; Guillainâ€“BarrÃ©; syndrome (p512).

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Reference intervals

Reference intervals: biochemistry (Always consult your local laboratory)

Substance	Reference interval
Acid phosphatase (total)	1â€“5IU/litre
Acid phosphatase (prostatic)	0â€“1IU/litre
ACTH	<80ng/litre
Alanine aminotransferase (ALT)	5â€“35IU/litre
Albumin	35â€–50g/litre

Aldosterone[1]	100â€“500pmol/litre
Alkaline phosphatase	30â€“300IU/litre (adults)
Î±-fetoprotein	<10kU/litre
Amylase	0â€“180 Somogyi U/dl
Angiotensin II[1]	5â€“35pmol/litre
Antidiuretic hormone (ADH)	0.9â€“4.6pmol/litre
Aspartate transaminase (AST)	5â€“35IU/litre
Bicarbonate	24â€“30mmol/litre
Bilirubin	3â€“17Âµmol/litre (0.25â€“1.5mg/dl)
Calcitonin	<0.1Âµg/litre
Calcium (ionized)	1.0â€“1.25mmol/litre
Calcium (total)	2.12â€“2.65mmol/litre
Chloride	95â€“105mmol/litre
[2]Cholesterol	3.9â€“5.5mmol/litre

LDL cholesterol	1.55â€“4.4mmol/litre
HDL cholesterol	0.9â€“1.93mmol/litre
Cortisol am midnight	450â€“700nmol/litre
	80â€“280nmol/litre
Creatine kinase (CK)	Men 25â€“195IU/litre
	Women 25â€“170 IU/litre
Creatinine	70â€“â ‰ ¤130Âµmol/litre
C-reactive protein (CRP)	0â€“10
Ferritin	12â€“200Âµg/litre
Folate	5â€“6.3 nmol/litre (2.1â€“2.8Âµg/L)
Î³-glutamyl transpeptidase (Î³-GT)	Men 11â€“51IU/litre
	Women 7â€“33IU/litre
Glucose (fasting)	3.5â€“5.5mmol/litre
Glycosylated haemoglobin (HbA_1C)	5â€“8%

Growth hormone	<20mU/litre
Iron	Men 14â€“31Âµmol/litre
	Women 7â€“33IU/litre
Lactate dehydrogenase (LDH)	70â€“250IU/litre
Magnesium	0.75â€“1.05mmol/litre
Osmolality	278â€“305mosmol/kg
Parathyroid hormone (PTH)	<0.8â€“8.5pmol/litre
Phosphate (inorganic)	0.8â€“1.45mmol/litre
Potassium (K^+)	3.5â€“5.0mmol/litre
Prolactin	Men <450 U/L; Women < 600U/L
Prostate specific antigen (PSA)	0â€“4ng/ml
Protein (total)	60â€“80g/litre
Red cell folate	0.36â€“1.44Âµmol/L (160â€“640Âµg/L)

Renin (erect/recumbent)[1]	2.8â€“4.5/1.1â€“2.7pmol/ml/h
Sodium (Na^+)	135â€“145mmol/litre
Thyroid stimulating hormone (TSH)	0.3â€“3.8mU/litre
Thyroxine (T4)	70â€“140nmol/litre
Thyroxine (free)	10.0â€“26.0pmol/litre
Total iron binding capacity (TIBC)	54â€“75Âµmol/litre
Triglyceride (fasting)	0.55â€“1.90mmol/litre
Tri-iodothyronine (T3)	1.2â€“3.0nmol/litre
Urea	2.5â€“6.7mmol/litre
Urate	Men 0.21â€“0.48mmol/litre
	Women 0.15â€“0.39mmol/litre
Vitamin B_{12}	0.13â€“0.68nmol/litre (>150ng/litre)

[1] The sample requires special handling: contact the lab.

[2] The level of cholesterol should be taken in clinical context.
Lowering levels above 5.5mmol/L reduces morbidity and mortality in primary and secondary prevention trials.

Reference intervals: urine

Substance	Reference interval
Adrenaline	0.03â€“0.10Âµmol/24h
Cortisol (free)	â ‰ ¤280nmol/24h
Dopamine	0.65â€“2.70Âµmol/24h
Hydroxyindole acetic acid (HIAA)	16â€“73Âµmol/24h
Hydroxymethylmandelic acid (HMMA, VMA)	16â€“48Âµmol/24h
Metanephrines	0.03â€“0.69Âµmol/mmol creatinine
Noradrenaline	0.12â€“0.5Âµmol/24h
Osmolality	350â€“1000mosmol/kg

Phosphate (inorganic)	15â€“50mmol/24h
Potassium	14â€“120mmol/24h
Sodium	100â€“250mmol/24h

Reference intervals: cerebrospinal fluid

see p952.

Reference intervals: ascitic fluid

see p657.

Reference intervals: haematology

Measurement		Reference interval
WBC (white blood cells)		3.2â€“11.0 Ã— 10^9/L
RBC (red blood cells)	Men	4.5â€“6.5 Ã— 10^{12}/L
	Women	3.9â€“5.6 Ã— 10^{12}/L
Haemoglobin (Hb)	Men	13.5â€“18.0g/dl
	Women	11.5â€“16.0g/dl

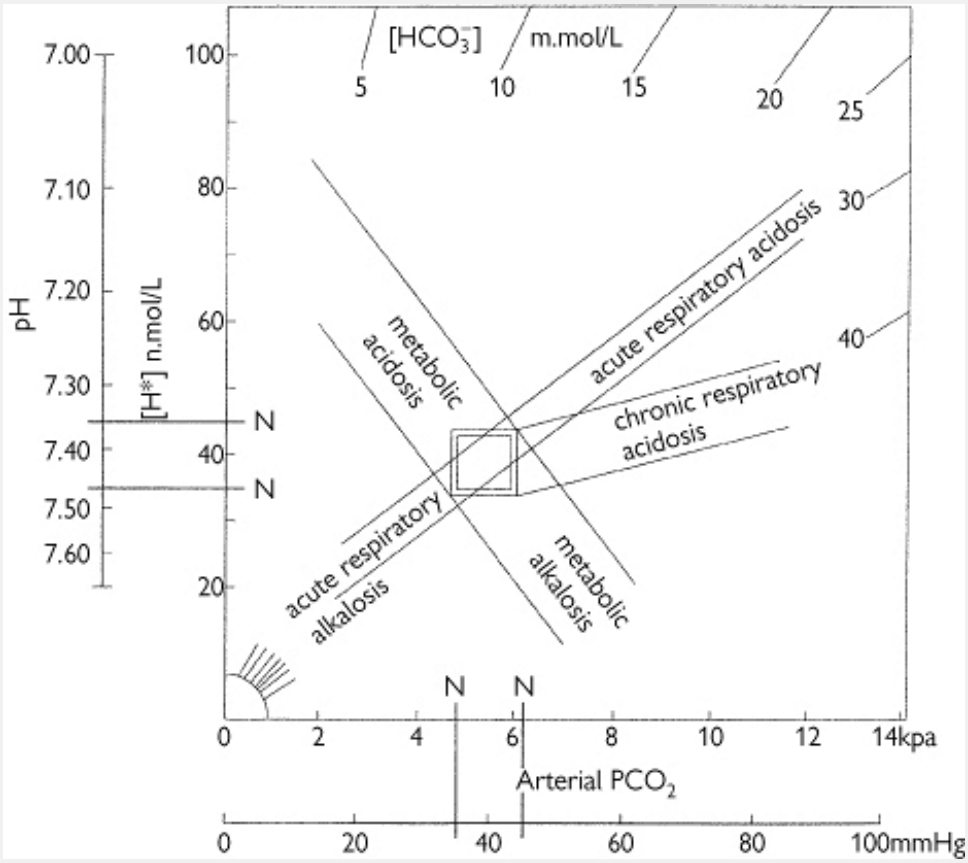
Haematocrit (HCT) or packed cell volume(PCV)	Men	0.4â€“0.54 l/L
	Women	0.37â€“0.47l/L
Mean cell volume (MCV)		82â€“98fl
Mean cell haemoglobin (MCH)		26.7â€“33.0pg
Mean cell haemoglobin concentration (MCHC)		31.4â€“35.0g/dl
Platelet count		120â€“400 Ã— 10^9/L
Neutrophils	%	40â€“75%
	Abs. no.	1.9â€“7.7 Ã— 10^9/L
Monocytes	%	3.0â€“11.0%
	Abs. no.	0.1â€“0.9 Ã— 10^9/L
Eosinophils	%	0.0â€“7.0 %
	Abs. no.	0.0â€“0.4 Ã— 10^9/L
Basophils	%	0.0â€“1.0 %

	Abs. no.	0.2â€“0.8 Ã— 10^9/L
Lymphocytes	%	20â€“45%
	Abs. no.	1.3â€“3.5 Ã— 10^9/L
Reticulocyte count[1]		0.8â€“2.0% (25â€“100Ã—10^9/L)
Erythrocyte sedimentation rate		depends on age (& â†‘ in anaemia)
(ESR)	Men	~ (age in years)-2
	Women	~ (age in years + 10)â€“2
Prothrombin time (PT)-factors II, VII, and X		10â€“14 seconds
Activated partial thromboplastin time (APTT)-factors VIII, IX, XI, and XII		35â€“45 seconds

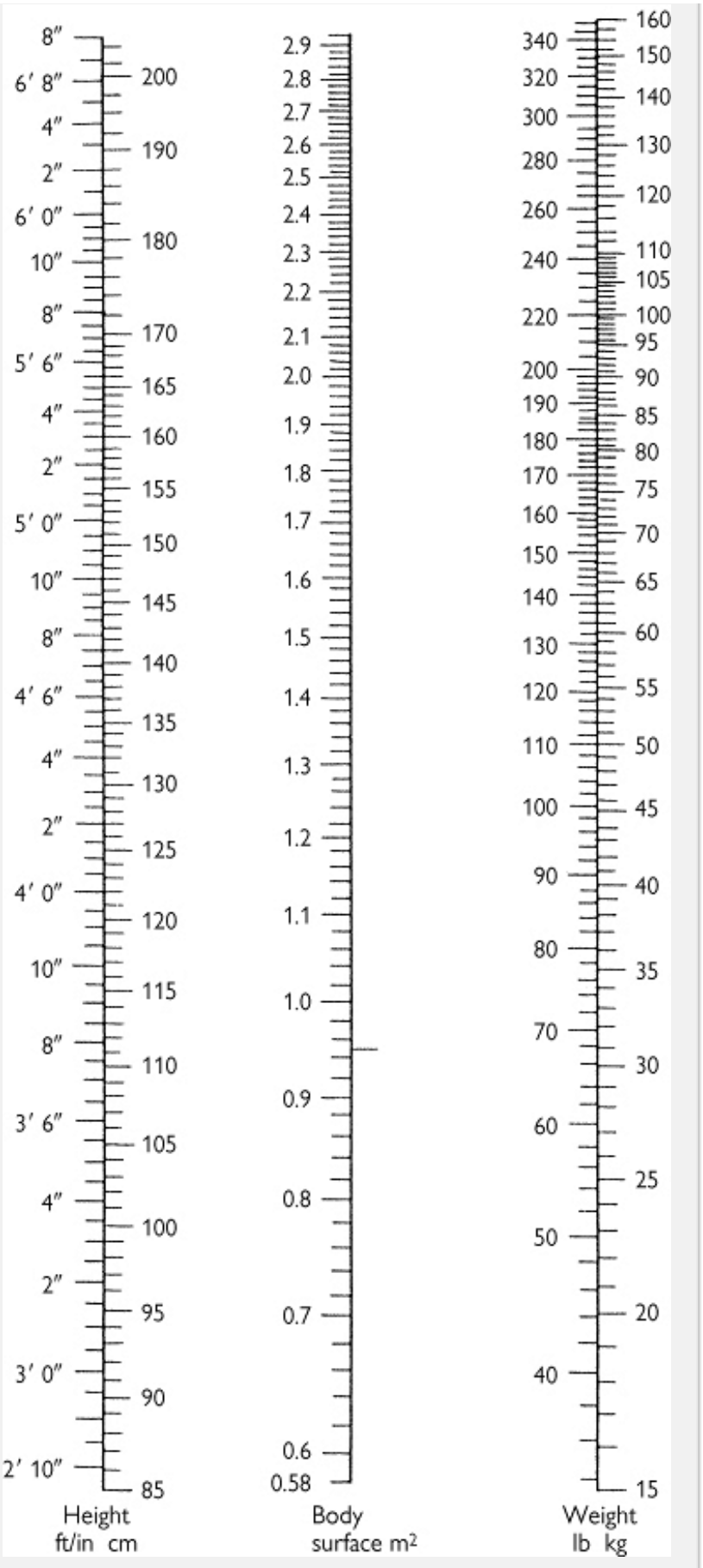
[1] Only use percentages if red cell count is normal; otherwise use absolute value.

Guidelines on oral anti-coagulation

International normalized ratio (INR)	Clinical condition
2.0â€“3.0	Treatment of DVT, PE, TIAs; chronic AF.
3.0â€“4.5	Recurrent DVTs and PEs; arterial grafts and arterial disease (including MI); prosthetic cardiac valves.



Acid base nomogram in the interpretation of arterial blood gases (after Flenley DC(1971) *Lancet* I: 270â€“3)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1.7
1.6
1.5
1.4
1.3
1.2
1.1
1.0
0.9
0.8
0.7
0.6
0.58
Body
surface m²
340
320
300
280
260
240
220
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
160
150
140
130
120
110
105
100
95
90
85
80
75
70
65
60
55
50
45
40
35
30
25
20
15
Weight
lb kg

Nomogram for body size

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Useful telephone numbers

Useful telephone numbers

Liver Units

Royal Free Hospital, London	0207 794 0500
Addenbrookes Hospital, Cambridge	01223 245 151
Freemans Hospital, Newcastle	0191 284 3111
Queen Elizabeth Hospital, Birmingham	0121 472 1311
St James Hospital, Leeds	0113 243 3144
Edinburgh Royal Infirmary, Edinburgh	0131 536 1000
Kings College Hospital, London	0207 737 4000

UKTS

United Kingdom Transplant Service	0117 975 7575

Poisons Units

National Helpline	0870 600 6266

National Teratology Unit

Drug & Chemical Exposure in Pregnancy	0191 232 5131

Tropical and Infectious Diseases

Hospital for Tropical Diseases, London	0207 387 4411
Northwick Park, London	0208 869 2831 (daytime)
	0208 864 3232 (out of hours, bleep infectious diseases registrar)
Liverpool	0151 708 9393
Glasgow	0141 211 1000

Anti-venom kits for snakebites

For information on identification and management contact:

Oxford (advice only)	01865 220 968
Liverpool	0151 708 9393
Liverpool (supply only)	0151 529 3226
London	0207 771 5394

Virus reference laboratory

Colindale, London	0208 200 4400

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Change in names of certain medicinal substances

Currently both British Approved Names (BANs) and recommended International Non-Proprietary Names (rINNs) are in use in the UK and for some substances these names differ, giving rise to confusion and the risk of medication error. Since 1 December 2003, where the names differ the rINN is the correct name.

Former BAN	New BAN
Acrosoxacin	Rosoxacin
Amethocaine	Tetracaine
Amoxycillin	Amoxicillin
Amylobarbitone	Amobarbital
Amylobarbitone Sodium	Amobarbital Sodium
Beclomethasone	Beclometasone

Bendrofluazide	Bendroflumethiazide
Benorylate	Benorilate
Benzhexol	Trihexyphenidyl
Benztropine	Benzatropine
Busulphan	Busulfan
Butobarbitone	Butobarbital
Carticaine	Articaine
Cephalexin	Cefalexin
Cephamandole Nafate	Cefamandole Nafate
Cephazolin	Cefazolin
Cephradine	Cefradine
Chloral betaine	Cloral betaine
Chlorbutol	Chlorobutanol
Chlormethiazole	Clomethiazole
Chlorpheniramine	Chlorphenamine
Chlorthalidone	Chlortalidone

Cholecalciferol	Colecalciferol
Cholestyramine	Colestyramine
Clomiphene	Clomifene
Colistin Sulphomethate Sodium	Colistimethate Sodium
Corticotrophin	Corticotropin
Cyclosporin	Ciclosporin
Cysteamine	Mercaptamine
Danthron	Dantron
Desoxymethasone	Desoximetasone
Dexamphetamine	Dexamfetamine
Dibromopropamidine	Dibrompropamidine
Dicyclomine	Dicycloverine
Dienoestrol	Dienestrol
Dimethicone (s)	Dimeticone
Dimethyl Sulphoxide	Dimethyl Sulfoxide

Dothiepin	Dosulepin
Doxycycline Hydrochloride (Hemihydrate Hemiethanolate)	Doxycycline Hyclate
Eformoterol	Formoterol
Ethamsylate	Etamsylate
Ethinyloestradiol	Ethinylestradiol
Ethynodiol	Etynodiol
Flumethasone	Flumetasone
Flupenthixol	Flupentixol
Flurandrenolone	Fludroxycortide
Frusemide	Furosemide
Gestronol	Gestonorone
Guaiphenesin	Guaifenesin
Hexachlorophane	Hexachlorophene
Hexamine Hippurate	Methenamine Hippurate
Hydroxyurea	Hydroxycarbamide

Indomethacin	Indometacin
Lignocaine	Lidocaine
Lysuride	Lisuride
Methimazole	Thiamazole
Methotrimeprazine	Levomepromazine
Methyl Cysteine	Mecysteine
Methylene Blue	Methylthioninium Chloride
Mitozantrone	Mitoxantrone
Mustine	Chlormethine
Nicoumalone	Acenocoumarol
Oestradiol	Estradiol
Oestriol	Estriol
Oestrone	Estrone
Oxpentifylline	Pentoxifylline
Phenobarbitone	Phenobarbital

Pipothiazine	Pipotiazine
Polyhexanide	Polihexanide
Potassium Clorazepate	Dipotassium Clorazepate
Pramoxine	Pramocaine
Procaine Penicillin	Procaine Benzylpenicillin
Prothionamide	Protionamide
Quinalbarbitone	Secobarbital
Riboflavine	Riboflavin
Salcatonin	Calcitonin (salmon)
Sodium Calciumedetate	Sodium Calcium Edetate
Sodium Cromoglycate	Sodium Cromoglicate
Sodium Ironedetate	Sodium Feredetate
Sodium Picosulphate	Sodium Picosulfate
Sorbitan Monostearate	Sorbitan Stearate
Stibocaptate	Sodium Stibocaptate
Stilboestrol	Diethylstilbestrol

Sulphacetamide	Sulfacetamide
Sulphadiazine	Sulfadiazine
Sulphamethoxazole	Sulfamethoxazole
Sulphapyridine	Sulfapyridine
Sulphasalazine	Sulfasalazine
Sulphathiazole	Sulfathiazole
Sulphinpyrazone	Sulfinpyrazone
Tetracosactrin	Tetracosactide
Thiabendazole	Tiabendazole
Thioguanine	Tioguanine
Thiopentone	Thiopental
Thymoxamine	Moxisylyte
Thyroxine Sodium	Levothyroxine Sodium
Tribavirin	Ribavirin
Trimeprazine	Alimemazine
Urofollitrophin	Urofollitropin

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ECG Ruler

Figure. No caption available.

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Color Plates

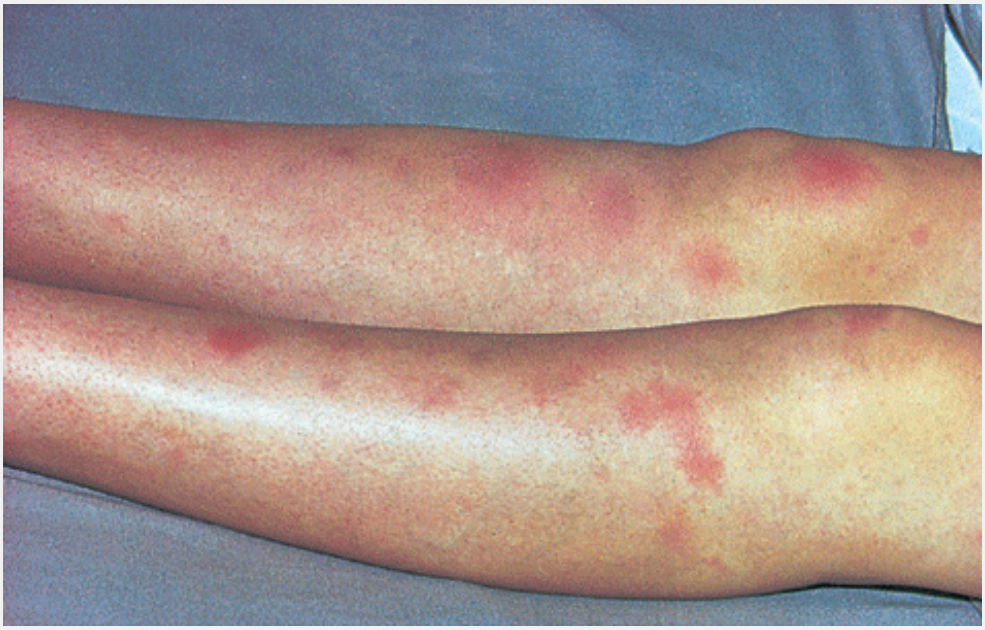

Plate 1: Erythema nodosum. The lesions can be very faint, but are indurated and painful on palpation.

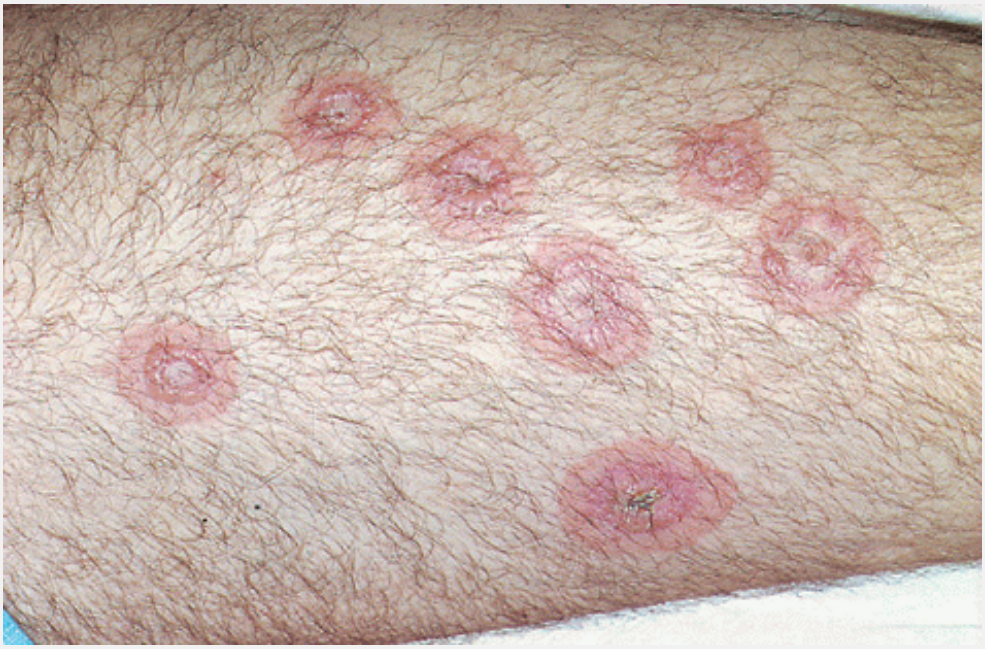

Plate 2: Blisters of bullous pemphigoid. Large, tense, raised lesions are seen on an erythematous eczematized base.

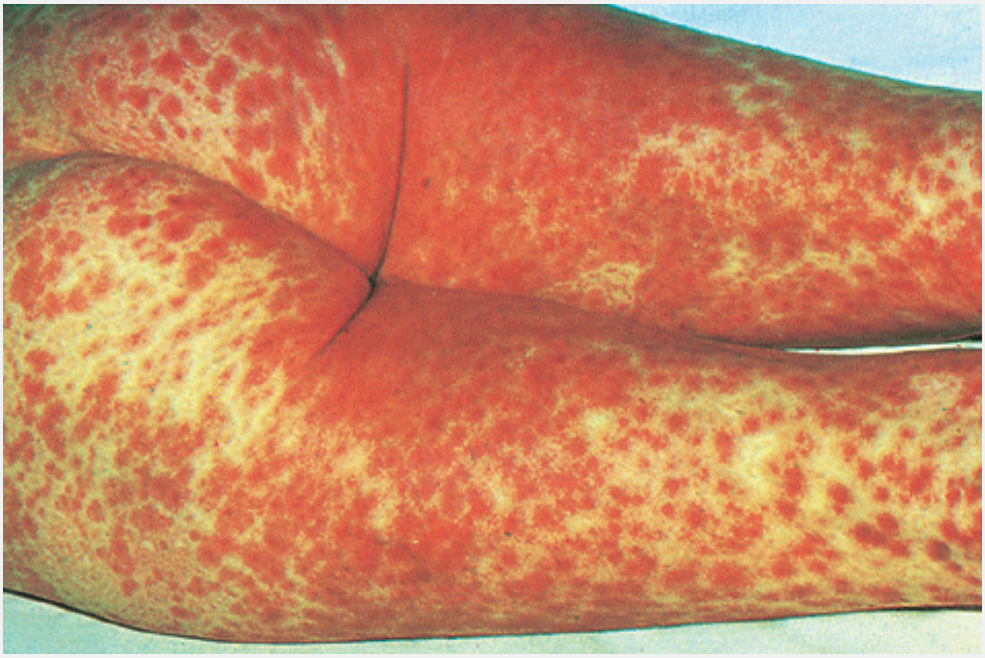

Plate 3: Erythema multiforme on the leg, note the presence of target lesions.

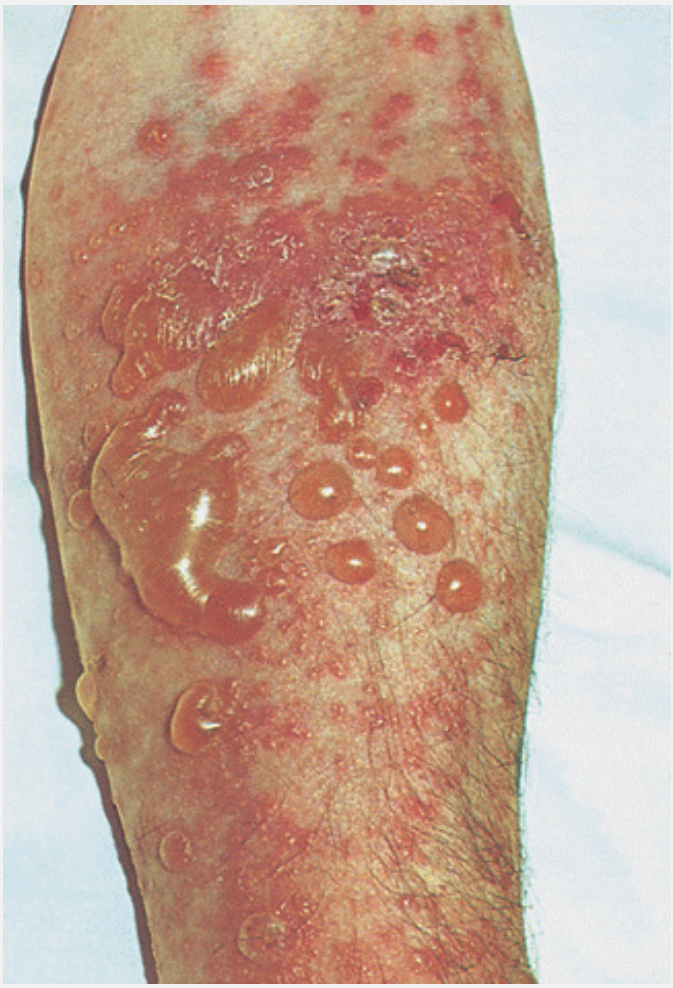

Plate 4: Morbilliform eruption caused by administration of ampicillin to a patient with infectious mononucleosis.

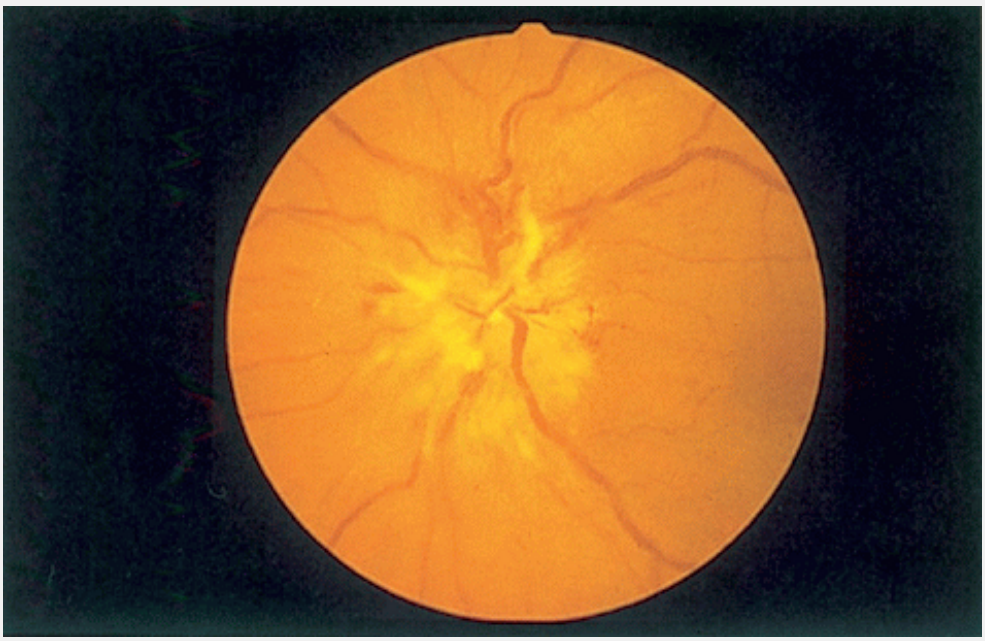

Plate 5: Acute papilloedema.

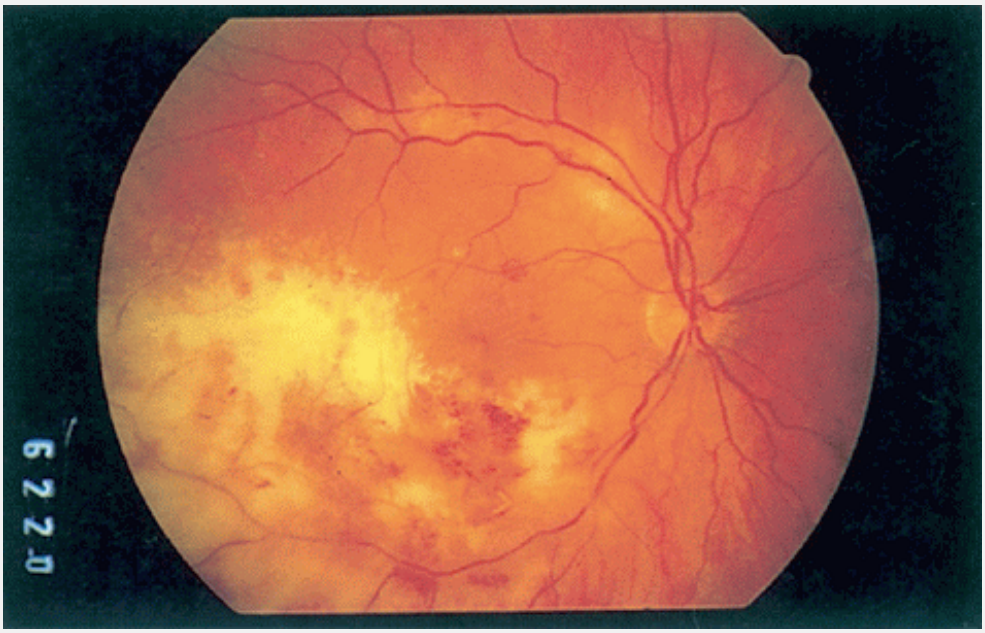

Plate 6: The typical appearance of cytomegalovirus retinitis in a patient with AIDS, characterized by retinal necrosis with an irregular granular border, patchy retinal

haemorrhage, and retinal inflammatory sheathing of the retinal vessels.

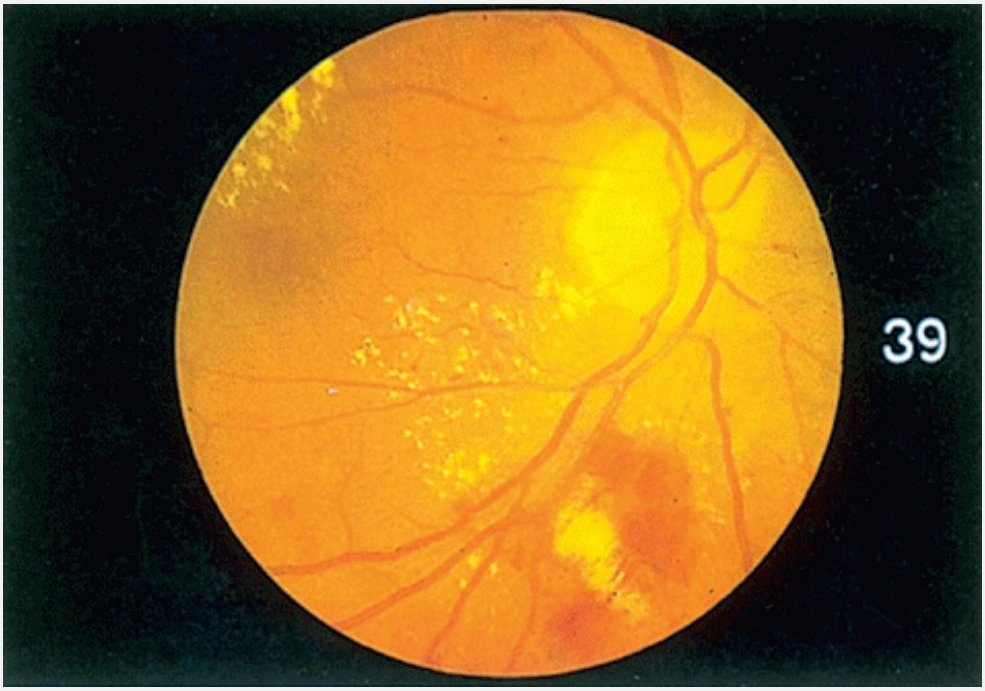

Plate 7: Hard exudates and cotton-wool spots in the right eye.

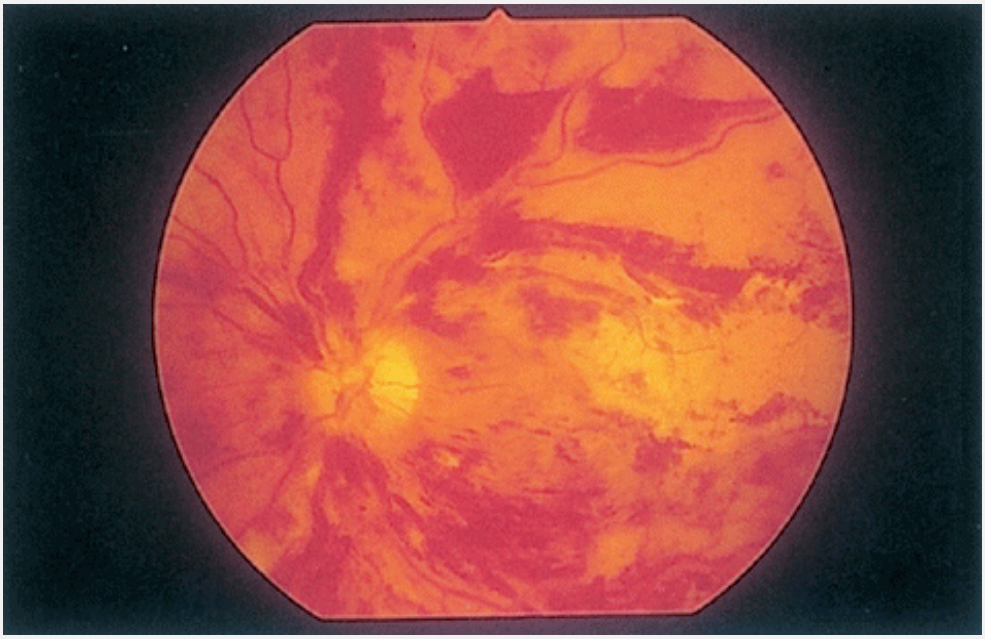

Plate 8: Central retinal vein occlusion with associated closure of the arterial circulation above the macula.

Footnote

The dermatology plates are taken from: Rona M MacKie (2003) *Clinical dermatology*, fifth edition. Oxford University Press, Oxford (with permission) The ophthalmology plates are taken from: David L Easty and John M Sparrow (eds) (1999) *Oxford Textbook of Ophthalmology*. Oxford University Press, Oxford (with permission).