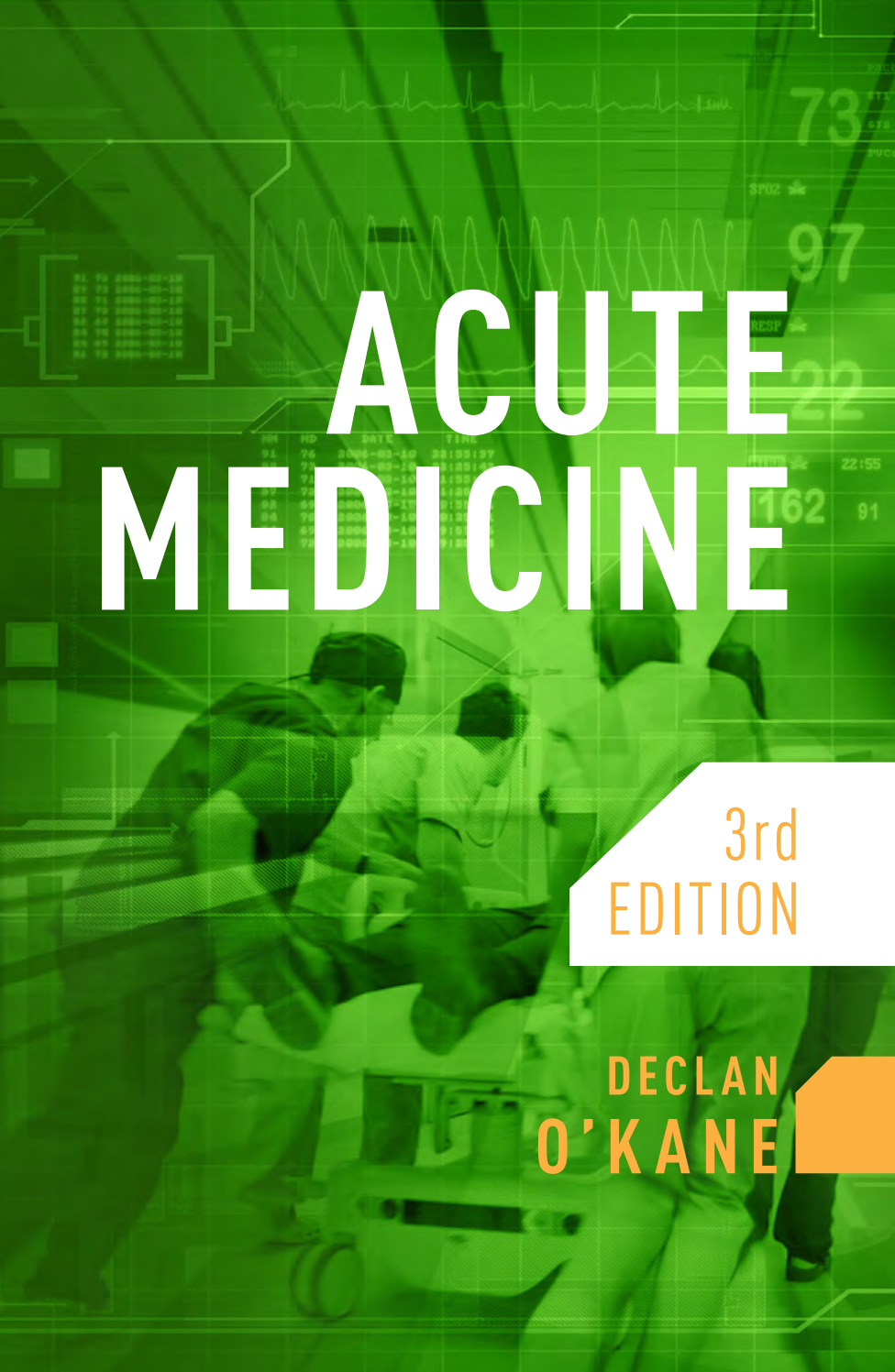
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Scion

ISBN 9781914961038

Second edition published in 2018 (ISBN 9781907904912)
First edition published in 2015

A CIP catalogue record for this book is available from the British Library.

Scion Publishing Limited
The Old Hayloft, Vantage Business Park, Bloxham Road, Banbury OX16 9UX, UK
www.scionpublishing.com

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Typeset by Medlar Publishing Solutions Pvt Ltd, India
Printed in the UK
Last digit is the print number: 10 9 8 7 6 5 4 3 2 1

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Preface

I wrote this book for my own needs to reference the questions that come up when dealing with acutely unwell medical patients. I was conscious that the answers I often needed could frequently not otherwise be found quickly and readily. I hope this will be a useful text for others at all levels, especially the on-call Medical SpR. Emergency department doctors and others may also find it useful. It is a quick reference of 'what and why' that covers common and not so common emergencies. It is compact and facts can be found quickly. I am very aware of the frailties of human memory and decision-making. A simple checklist at hand can hopefully enhance safety and clinical care. Included at the back is a quick emergency drug reference where drug information is consolidated to avoid repetition. This does not replace the *British National Formulary* (*BNF*) which has now been released as a free app and is the best source of prescribing information. Despite great care, we may have errors of omission or fact. This is not a cookbook to slavishly follow, but a guide to help the reader to analyse a difficult situation with a framework and some salient facts. Lastly, this is a book by a generalist. It is not intended to replace experts. All difficult cases benefit from early expert help – this book should aid the dialogue and identify key issues. To some the information will be new, and to others it is simply a reminder. It needs to be compact and concise so let us not waste further words or space.

Acknowledgments

I'd like to thank my wife and my two girls for their love, patience and support. This book is dedicated to the memory of my good friend, Jeremy Sherman FRCS. In my training I was fortunate to work for many wonderful hard-working clinicians. I am particularly indebted to Professor Jennifer Adgey CBE and the late Dr Seamus Coyle. I'd like to thank those who have read the manuscript and made helpful suggestions and additions including Dr Jacob F. de Wolff, Dr Andrew Solomon, Dr Pad Boovalingam, Dr Omar Kirresh, Dr Peter Rhead and Dr Christopher Miller, and Dr V Srinivasan and Dr Abdul Elmarimi for their kind help.

Updates to the 3rd edition

For this new edition almost all subjects have been edited and updated. We have Covid-19 and many other updates. I am grateful to Dr Omar Kirresh who is now a fellow colleague of mine here in Brighton. I'd also like to thank Dr Matthew Palethorpe who provided superb and detailed feedback and suggestions, and Simon Daley for his advice on ACS. In addition, I'd like to thank Dr Andrew Leonard, a fantastic colleague and first class acute medicine physician, for his leadership over what have been challenging times for all. Any remaining errors are mine. Finally, many thanks to Jonathan Ray and Clare Boomer at Scion for their wonderful support and encouragement.

If you have any comments, questions or suggestions, please write to me at drokane@gmail.com. Errata will be available on the page for the book at www.scionpublishing.com, on the Resources tab.

Declan O'Kane, 2023

Disclaimer

Every effort has been made in preparing this publication to provide accurate and up to date information in accordance with accepted standards and practice at the time of publication. The author can make no warranties that the information contained herein is totally free from error, not least because clinical standards are constantly changing. The author therefore disclaims all liability for direct or consequential damages resulting from the use of material within this publication. Readers are recommended to check all drug doses, indications and C/I and interactions used with the *BNF* or drug data-sheet prior to use. If a reader is unsure what to do then they should seek support from their senior medical adviser. Patients should seek help from their own doctor/healthcare provider.

Decision-making for the medical registrar

The first medical registrar year is tough and stressful, but with the years it gets easier and more enjoyable: you recognise the same patterns and problems like a chess puzzle and the solutions become easier to resolve in seconds, and you can solve other people's puzzles for them. Sometimes, however, a problem is completely new so you need to sit down and work it out from first principles and/or ask for help from someone who may have encountered the situation before. Referrals will come thick and fast – regard these as compliments to your skills in problem-solving. Get help once you have thought (time allowing) it through yourself and presented your plan. If you are unhappy or concerned call for advice. Share diagnostic dilemmas and don't sit on them. Don't go home without resolving your concerns. As consultants we constantly discuss interesting and difficult cases. Good medical practice is about reflection and seeking feedback. Good luck.

Abbreviations

5-HIAA	5-hydroxyindoleacetic acid
AAA	abdominal aortic aneurysm
ABC	airway, breathing and circulation
ABCDE	ABC + disability, exposure
ABG	arterial blood gas
ABU	asymptomatic bacteriuria
ACA	anterior cerebral artery
ACE	angiotensin-converting enzyme
ACEi	ACE inhibitor
Ach	acetylcholine
ACOMM	anterior communicating artery
ACS	acute coronary syndrome
ACTH	adrenocorticotrophic hormone
ADA	adenosine deaminase
ADEM	acute disseminated encephalomyelitis
ADLs	activities of daily living
ADR	adverse drug reaction
AED	automated external defibrillators *or* anti-epilepsy drug
AF	atrial fibrillation
AFB	acid-fast bacilli (TB)
AFLP	acute fatty liver of pregnancy
aHUS	atypical haemolytic uraemic syndrome
AIDP	acute inflammatory demyelinating polyneuropathy
AIDS	acquired immunodeficiency syndrome
AKI	acute kidney injury
ALA	alanine aminotransferase
ALF	acute liver failure
ALI	acute lung injury
ALP	alkaline phosphatase
ALS	advanced life support
ALT	alanine aminotransferase
AMAN	acute motor axonal neuropathy
AMTS	abbreviated mental test score
ANA	antinuclear antibody
ANCA	antineutrophil cytoplasmic antibody
ANP	atrial natriuretic peptide
APKD	adult polycystic kidney disease
APLS	antiphospholipid syndrome
APML	acute promyelocytic leukaemia
APTT	activated partial thromboplastin time
AR	aortic regurgitation
ARB	angiotensin-II receptor blocker
ARDS	acute/adult respiratory distress syndrome
ARF	acute respiratory failure
ART	antiretroviral therapy
ARVC	arrhythmogenic right ventricular cardiomyopathy
AS	aortic stenosis
ASD	atrial septal defect
ASO(T)	antistreptolysin O (titre)
AST	aspartate aminotransferase
ATN	acute tubular necrosis
AV	arteriovenous/atrioventricular
AVM	arteriovenous malformation
AVNRT	atrioventricular nodal re-entrant tachycardia
AVPU	awake, voice, pain, unresponsive
AVRT	atrioventricular re-entrant tachycardia
AXR	abdominal X-ray
BAL	bronchoalveolar lavage
BBB	bundle branch block
BD/bd	twice daily or 12-hourly
BE	base excess
BiPAP	bilevel positive airway pressure
BJP	Bence Jones protein
BMS	bare metal stents
BNP	B-type natriuretic peptide
BP	blood pressure
BUN	blood urea nitrogen
BVM	bag–valve mask
CABG	coronary artery bypass grafting
CAD	coronary artery disease
CBG	capillary blood glucose
CC	chest compression
CCB	calcium channel blocker
CCF	congestive cardiac failure
CEA	carcinoembryonic antigen *or* carotid endarterectomy
CFU	colony-forming units
CHB	complete heart block
C/I	contraindications

CI-AKI	contrast-induced acute kidney injury
CIDP	chronic inflammatory demyelinating polyneuropathy
CIS	clinically isolated syndrome
CK	creatine kinase
CKD	chronic kidney disease
CLO test	*Campylobacter*-like organism test (rapid urease test)
CMP	cardiomyopathy
CMV	cytomegalovirus
CO	cardiac output
COPD	chronic obstructive pulmonary disease
CPAP	continuous positive airway pressure
CPR	cardiopulmonary resuscitation
CRH	corticotropin-releasing hormone
CRP	C-reactive protein
CRT	cardiac resynchronisation therapy
CSF	cerebrospinal fluid
CSM	carotid sinus massage
CSU	catheter sample urine
CTG	cardiotocogram
CTPA	computed tomography pulmonary angiogram
CVP	central venous pressure
CVST	cerebral venous sinus thrombosis
CXR	chest X-ray
DAPT	dual antiplatelet therapy
DBP	diastolic blood pressure
DCM	dilated cardiomyopathy
DCR	damage control resuscitation
DES	drug-eluting stents
DHEA	dehydroepiandrosterone
DI	diabetes insipidus
DIC	disseminated intravascular coagulation
DKA	diabetic ketoacidosis
DM	diabetes mellitus
DNACPR	do not attempt cardiopulmonary resuscitation
DOAC	direct oral anticoagulant (previously NOAC)
DOB	date of birth
DPG	2,3-diphosphoglycerate
DRESS	drug rash with eosinophilia and systemic symptoms
DSA	digital subtraction angiography
DVT	deep vein thrombosis
DWI	diffusion weighted imaging
EBV	Epstein–Barr virus
ECG	electrocardiogram
ECMO	extracorporeal membrane oxygenation
EEG	electroencephalogram
EF	ejection fraction
ELISA	enzyme-linked immunosorbent assay
EMA	endomysial antibodies
EMG	electromyography
EPAP	expiratory positive airway pressure
EPO	erythropoietin
EPS	electrophysiological study
ERCP	endoscopic retrograde cholangiopancreatography
ESBL	extended-spectrum beta-lactamases
ESR	erythrocyte sedimentation rate
EST	exercise stress test
ESWL	extracorporeal shock wave lithotripsy
EVD	external ventricular drainage
EWS	early warning score
FBC	full blood count
FEV	forced expiratory volume
FFP	fresh frozen plasma
FMF	familial Mediterranean fever
FSH	follicle-stimulating hormone
FVC	forced vital capacity
G5W	5% glucose (dextrose)
GBM	glomerular basement membrane
GBS	Guillain–Barré syndrome *or* Glasgow–Blatchford Score
GCA	giant cell arteritis
GCS	Glasgow Coma Score
GFR	glomerular filtration rate
GGT	gamma-glutamyl transpeptidase
GH	growth hormone
GHB	gamma-hydroxybutyric acid
GI	gastrointestinal
GN	glomerulonephritis

GORD	gastro-oesophageal reflux disease
GRACE	Global Registry of Acute Coronary Events
GTN	glyceryl trinitrate
GTT	glucose tolerance test
GvHD	graft-versus-host disease
HAART	highly active antiretroviral therapy
HAP	hospital-acquired pneumonia
HAS	human albumin solution
HBV	hepatitis B virus
HCM	hypertrophic cardiomyopathy
HCV	hepatitis C virus
HDU	high dependency unit
HELLP	syndrome of haemolysis, elevated LFTs, low platelets
HF	heart failure
HHS	hyperosmolar hyperglycaemic state
HHT	hereditary haemorrhagic telangiectasia
HIT(T)	heparin-induced thrombocytopenia ± thrombosis
HIV	human immunodeficiency virus
HOCM	hypertrophic cardiomyopathy
HONK	hyperosmolar non-ketotic state
HPTHM	hyperparathyroidism
HR	heart rate (ventricular rate)
HRCT	high resolution CT
HRS	hepatorenal syndrome
HRT	hormone replacement therapy
HSC	haemopoietic stem cell
HSE	herpes simplex encephalitis
hsTn	high sensitivity troponin
HSV	*Herpes simplex* virus
HTIG	human tetanus immunoglobulin
HTLV	human T cell lymphotropic virus
HUS	haemolytic uraemic syndrome
IABP	intra-aortic balloon pump
IAH	impaired awareness of hypoglycaemia
IBD	inflammatory bowel disease
IBS	irritable bowel syndrome
ICA	internal carotid artery
ICD	implantable cardioverter–defibrillator
ICH	intracerebral haemorrhage
ICP	intracranial pressure
ICS	intercostal space
IGF-1	insulin-like growth factor 1
IHD	ischaemic heart disease
IJV	internal jugular vein
IM	intramuscular route
IMA	inferior mesenteric artery
INR	international normalised ratio
IP	incubation period
IPAP	inspiratory positive airway pressure
ITP	immune (idiopathic) thrombocytopenic purpura
IVC	inferior vena cava
IVDU	IV drug user
IVIg	intravenous immunoglobulin
IVII	intravenous insulin infusion
IVT	intravenous thrombolysis
IVU	intravenous urogram
Ix	investigations
JVP	jugular venous pressure
KUB	kidneys, ureter, bladder
LA	left atrium
LAD	left axis deviation *or* left anterior descending
LAFB	left anterior fascicular block
LBBB	left bundle branch block
LCA	left coronary artery
LCHAD	long-chain 3-hydroxyacyl-coA dehydrogenase
LDH	lactate dehydrogenase
LFT	liver function test
LIMA	left internal mammary artery
LMN	lower motor neuron
LMWH	low molecular weight heparin
LOC	loss of consciousness
LP	lumbar puncture
LPFB	left posterior fascicular block
LTOT	long-term oxygen therapy
LV	left ventricle
LVAD	LV assist device
LVEDP	LV end-diastolic pressure
LVEF	LV ejection fraction
LVF	left ventricular failure
LVH	left ventricular hypertrophy
LVOT	LV outflow tract
MAHA	microangiopathic haemolytic anaemia
MAOI	monoamine oxidase inhibitor

MAP mean systemic arterial pressure
MAT microscopic agglutination test *or* multifocal atrial tachycardia
MCA middle cerebral artery
MCH mean cell haemoglobin
MCV mean cell volume
MDAC multidose activated charcoal
MEN multiple endocrine neoplasia
MERS Middle Eastern respiratory syndrome
MG myasthenia gravis
MGUS monoclonal gammopathy of undetermined significance
MI myocardial infarction
MIC minimum inhibitory concentration
MLF medial longitudinal fasciculus
MND motor neurone disease
MODS multiple organ dysfunction syndrome
MPO myeloperoxidase
MR mitral regurgitation
MRCP magnetic resonance cholangiopancreatography
MRSA meticillin-resistant *Staphylococcus aureus*
MS multiple sclerosis *or* mitral stenosis
MSH melanocyte-stimulating hormone
MSU mid-stream urine *or* monosodium urate
MT mechanical thrombectomy
MTP massive transfusion protocol
MTS mental test score
MUMS migraine with unilateral motor symptoms
MVP mitral valve prolapse
Mx management
NAAT nucleic acid amplification test
NAC *N*-acetylcysteine
NBM nil by mouth
NC nasal cannula
NCS nerve conduction studies
NCSE non-convulsive status epilepticus
NDI nephrogenic diabetes insipidus
NEAD non-epileptic attack disorder
NEWS National Early Warning Score
NG nasogastric
NIH National Institute for Health
NIPPV non-invasive positive pressure ventilation
NIV non-invasive ventilation
NMO neuromyelitis optica
NMS neuroleptic malignant syndrome
NOAC new/novel oral anticoagulant (*see* DOAC)
NOS nitric oxide synthase
NRTI nucleoside reverse transcriptase inhibitors
NS 0.9% normal saline
NSAID non-steroidal anti-inflammatory drug
NSTEMI non-ST elevation MI
N&V nausea and vomiting
NVE native valve endocarditis
OCP oral contraceptive pill
OD overdose *or* once daily
OGD oesophagogastroduodenoscopy
OGTT oral glucose tolerance test
OPs organophosphates
PA pernicious anaemia *or* posterior–anterior
PAF paroxysmal atrial fibrillation
PAN polyarteritis nodosa
PAWP pulmonary artery wedge pressure
PBC primary biliary cirrhosis
PBG porphobilinogen
PCA posterior cerebral artery
PCC prothrombin complex concentrates
PCI percutaneous coronary intervention
PCOMM posterior communicating artery
PCP *Pneumocystis carinii* pneumonia
PCWP pulmonary capillary wedge pressure
PE pulmonary embolism
PEEP positive end-expiratory pressure
PEFR peak expiratory flow rate
PEG percutaneous endoscopic gastrostomy *or* polyethylene glycol
PEJ percutaneous endoscopic jejunostomy

PEP	post-exposure prophylaxis
PET	pre-eclamptic toxaemia *or* positron emission tomography
PFO	patent foramen ovale
PFTs	pulmonary function tests
PICA	posterior inferior cerebellar artery
PICC	peripherally inserted central catheter
PICH	primary intracerebral haemorrhage
PMC	primary motor cortex
PML	progressive multifocal leucoencephalopathy
PMR	polymyalgia rheumatica
PNH	paroxysmal nocturnal haemoglobinuria
POCUS	point-of-care ultrasound
POTS	postural orthostatic tachycardia syndrome
PPCI	primary percutaneous coronary intervention
PPD	purified protein derivative
PPE	plasma protein electrophoresis *or* personal protective equipment
PPI	proton pump inhibitor
PPM	permanent pacemaker
PRES	posterior reversible encephalopathy syndrome
PRL	prolactin level
PSA	prostate-specific antigen
PSC	primary sclerosing cholangitis
PSM	pansystolic murmur
PT	prothrombin time
PTH	parathyroid hormone
PTX	pneumothorax
PUD	peptic ulcer disease
PUO	pyrexia of unknown origin
PVD	peripheral vascular disease
PVE	prosthetic valve endocarditis
PVL	plasma viral load
Px	prevention or prophylaxis
QDS	four times a day or 6-hourly
RA	rheumatoid arthritis *or* right atrium
RAA	renin–angiotensin–aldosterone
RAD	right axis deviation
RAS	renal artery stenosis *or* reticular activating system
RAST	radioallergosorbent test
RBBB	right bundle branch block
RBC	red blood cell
RCA	right coronary artery
RCVS	reversible cerebral vasoconstriction syndrome
RF	respiratory failure *or* rheumatoid factor
RIF	right iliac fossa
ROSC	return of spontaneous circulation
RPGN	rapidly progressive glomerulonephritis
RR	respiratory rate
RRT	renal replacement therapy
RSV	respiratory syncytial virus
RTA	renal tubular acidosis *or* road traffic accident
RV	right ventricle
RVH	right ventricular hypertrophy
Rx	treatment
SACD	sub-acute combined cord degeneration
SAH	subarachnoid haemorrhage
SAN	sinoatrial node
SARS	severe acute respiratory syndrome
SBO	small bowel obstruction
SBP	systolic blood pressure *or* spontaneous bacterial peritonitis
SC	subcutaneous route *or* sickle cell
SCD	sudden cardiac death
SDH	subdural haematoma
SE	status epilepticus *or* side-effect
SIADH	syndrome of inappropriate ADH secretion
SIRS	systemic inflammatory response syndrome
SJS	Stevens–Johnson syndrome
SL	sublingual route
SLE	systemic lupus erythematosus
SMA	superior mesenteric artery
SMX	sulfamethoxazole
SOB	shortness of breath
SOFA	sepsis-related organ failure assessment
SOL	space-occupying lesion

SPECT	single-photon emission computed tomography
SR	sinus rhythm
SSP	secondary spontaneous pneumothorax
STEMI	ST-elevation MI
STI	sexually transmitted infection
SUDEP	sudden unexpected death in epilepsy
SUND	sudden unexpected nocturnal death
SVC	superior vena cava
SVR	systemic vascular resistance
SVT	supraventricular tachycardia
T1DM	type 1 diabetes mellitus
T2DM	type 2 diabetes mellitus
TAB	temporal artery biopsy
TACI	total anterior circulation infarct
TACO	transfusion-associated circulatory overload
TB	tuberculosis
TCA	tricyclic antidepressant
TdP	torsades de pointes
TDS	three times a day
TEN	toxic epidermal necrolysis
TF	typhoid fever
TFTs	thyroid function tests
TIA	transient ischaemic attack
TIBC	total iron-binding capacity
TIMI	thrombolysis in MI
TIPS	transjugular intrahepatic portosystemic shunt
TLOC	transient loss of consciousness
TMP	trimethoprim
TNF	tumour necrosis factor
TOE	transoesophageal echocardiogram
tPA	tissue plasminogen activator
TPHA	*Treponema pallidum* serology
TPN	total parenteral nutrition
TPO	thyroid peroxidase
TRAb	TSH receptor antibodies
TRALI	transfusion-associated lung injury
TSH	thyroid-stimulating hormone
TSS	toxic shock syndrome
TTE	transthoracic echocardiogram
TTG	tissue transglutaminase
TTP	thrombotic thrombocytopenic purpura
TVR	target vessel revascularisation
UA	unstable angina
U&E	urea/creatinine and electrolytes
UFH	unfractionated heparin
ULN	upper limit of normal
UMN	upper motor neuron
URTI	upper respiratory tract infection
USS	ultrasound scan
UTI	urinary tract infection
VATS	video-assisted thoracoscopic surgery
VB	variceal bleed
VBG	venous blood gas
VDRL	Venereal Disease Research Laboratory
VEGF	vascular endothelial growth factor
VF	ventricular fibrillation
VIHE	valproate-induced hyperammonaemic encephalopathy
VKA	vitamin K antagonist
V/Q	ventilation/perfusion
VRE	vancomycin-resistant enterococcus
VRIII	variable rate IV insulin infusion
VSD	ventricular septal defect
VT	ventricular tachycardia
VTE	venous thromboembolism
vWF	von Willebrand factor
VZV	varicella zoster virus
WBI	whole bowel irrigation
WCC	white cell count
WG	Wegener's granulomatosis/ granulomatosis with polyangiitis
WPW	Wolff–Parkinson–White syndrome
ZIG	zoster immune globulin

07 Liver disease

7.1 Jaundice

Pathophysiology

- Jaundice is due to excess circulating bilirubin in the tissues. It is a breakdown product of haem with blood levels >50 µmol/L when it becomes detectable clinically (normal <17 µmol/L). Seen most easily in pale skin in good light or in the scleral part of the eye. It may be seen in 3% of population as Gilbert's syndrome. It must be viewed in clinical context. It is included here as a sign of liver function. Is the patient toxic and unwell, is there pale stool and dark urine, wasting, cachexia and likely cancer? Bilirubin is conjugated with glucuronate within the liver so pre-hepatic is excess unconjugated form. Excreted in urine and faeces and gives them their distinctive yellow and brown colours, respectively. Look for IV drug use, alcohol, toxins, all drugs, history of gallstones, pregnancy. Most commonly the question is whether it is hepatic or post-hepatic and the most critical test is abdominal USS. Severe liver damage causes loss of synthetic function making procoagulant: fibrinogen, prothrombin, factors V, VII, IX, X and XIII. Anticoagulant proteins C and S. NOT gammaglobulins. Antithrombin, transferrin and caeruloplasmin. Albumin $t_{1/2}$ about 20 d. Glucose homeostasis – controlling blood sugar.

Causes of jaundice

- **Pre-hepatic haemolysis** with increased (unconjugated = indirect) bilirubin formation, raised reticulocytes, anaemia, high LDH. Gilbert's syndrome. LFTs are normal.
- **Hepatic:** alcoholic/non-alcoholic and other causes of cirrhosis, hepatitis A/B/C, toxins, drugs, anaesthetic agents, paracetamol, ALF, ischaemia, malignancy, severe right heart failure. Needs liver USS and usual work-up. Viral studies, cirrhosis work-up. Defined by aetiology. Raised ALT/AST, bilirubin. ALP may be elevated.
- **Post-hepatic:** pale stool, dark urine, abdominal pain, fever. Gallstones, worms, strictures, tumour, pancreatic cancer occluding CBD. Cholangitis. Elevated GGT and ALP. AST/ALT may also be raised. Obstruction seen on USS or MRCP. Needs mechanical release – ERCP/surgery.

7.2 Acute liver failure

- **About:** fulminant hepatic failure is where encephalopathy develops in under 2 weeks with a previously normal liver. Prothrombin time is a marker of synthetic function. Get good drug history and ask about over-the-counter and herbal and other natural remedies obtained from shops or internet.
- **Classification based on time from appearance of jaundice to developing encephalopathy.** Hyperacute <1 week: (paracetamol or viral). Massive necrosis. Acute <4 weeks: viral, drugs, others. Subacute 12 weeks: viral, drugs, others.

Causes	Details and notes
Infectious	**Viral hepatitis:** see below. **Bacterial:** leptospirosis, severe bacterial infections. **Protozoal:** amoebic infection.
Paracetamol overdose (1/2 of UK cases)	Within 4 h of presentation give activated charcoal just prior to starting *N*-acetylcysteine. NAC should be used promptly in all patients where paracetamol-induced liver injury is anticipated or there is concern of such and may be given acutely even if cause is unclear. ▶ Section 14.28 for paracetamol overdose protocol.
Other drugs and toxins	MAOIs, halothane, isoniazid, phenytoin, sulphonamides, amiodarone, propylthiouracil, Ecstasy, herbal remedies. *Amanita phylloides* mushroom, carbon tetrachloride. Enquire about all drugs taken, environmental toxins, herbal and natural remedies. Tetracycline, valproate and nucleoside reverse-transcriptase inhibitors can cause fatal liver disease. Many others so check all.
Inherited	**Wilson's disease:** autosomal recessive. Low serum Cu, low caeruloplasmin. Haemolysis. Raised urinary Cu. Treat with penicillamine. **Haemochromatosis:** AR. Iron overload, high ferritin. Transferrin saturation >50%. HFE gene mutation positive >95%. MRI ferriscan or liver biopsy. **Alpha-1 antitrypsin deficiency,** low alpha-1 antitrypsin.
Ischaemic	Circulatory failure and shock. Raised AST. Manage underlying cause.
Venous	**Venous thrombosis: Budd–Chiari syndrome:** acute ascites, USS diagnostic with thrombosed hepatic vein. Consider thrombolysis and TIPS. Hepatic failure is an indication for liver transplantation, provided underlying malignancy is excluded.
Pregnancy	Acute fatty liver of pregnancy, HELLP syndrome with haemolysis, raised AST/ALT and low platelet count. Expeditious delivery needed.
Reye's syndrome	Inhibition of beta-oxidation and uncoupling of oxidative phosphorylation in mitochondria. Acute encephalopathy with fatty infiltration of the liver. Precipitated by aspirin ingestion and viral infections.
Mushroom poisoning	ALF patients with known or suspected mushroom poisoning. Consider administration of **penicillin** G and **silymarin** (III) and should be considered for urgent orthoptic transplantation, the only life-saving option.
Autoimmune hepatitis	Patients with ALF (usually a biopsy is done) due to autoimmune hepatitis should be treated with corticosteroids (**prednisolone** 40–60 mg/d). In ALF patients with evidence of ischaemic injury, cardiovascular support is the treatment of choice.
Malignancy	Hepatoma: check USS and alpha-fetoprotein.
Miscellaneous	**Others:** idiopathic: viral, ischaemia: severe RHF, non-alcoholic steatohepatitis.

- **Clinical:** history of drug/toxin exposure key. Encephalopathy: flapping tremor, poor concentration. Reversal of day/night cycle, jaundice usually but not always – date when first appeared, bleeding and coagulopathy. Hypoglycaemia, fetor hepaticus, look for Kayser–Fleischer rings. RUQ tenderness, NO splenomegaly or ascites, exception is Budd–Chiari syndrome.

- **Identify likely precipitants of acute on chronic decompensation:** sepsis, spontaneous bacterial peritonitis, fluid overload, albumin. Transjugular intrahepatic porto-systemic shunt, renal failure, CNS suppressants. Electrolyte abnormalities, diuretic overuse, GI bleeding.
- **Clinical:** reversal of day/night sleeping, psychomotor dysfunction, impaired memory. Sensory abnormalities, poor concentration, disorientation, tremor, shuffling gait. Melaena, haematemesis. Fetor hepaticus, flapping tremor, asterixis. See Encephalopathy, ▸Section 7.11.
- **Investigations:** FBC: raised WCC, ESR and CRP, low platelets (alcohol, HELLP). Haemolysis in Wilson's disease: low Hb, raised reticulocytes, raised LDH. **Raised** prothrombin time. Raised bilirubin: elevated unconjugated. LFT: raised AST, raised ALT often >1000 (transaminases fall eventually). U&E: raised creatinine. Check paracetamol levels and salicylates. **VBG:** metabolic acidosis and raised arterial lactate and arterial ammonia. **Viral serology:** anti-HAV IgM, HBsAg, anti-HBc IgM, anti-HEV, EBV, CMV, HSV, HIV, anti-HCV (rare cause). **Others:** paracetamol level, caeruloplasmin and 24 h urine copper, ammonia levels. Autoimmune: ANA, anti-smooth muscle actin, anti-liver/kidney microsomal antibodies and immunoglobulins. **USS Doppler:** liver size and pathology, and hepatic veins for Budd–Chiari syndrome. **Miscellaneous:** pregnancy test. ANA, anti-smooth muscle, immunoglobulin, HIV status. **NB:** focal neurology not typical and suggests need for CT brain.
- **Management:** stop all potentially implicated drugs. Regard all as potentially hepatotoxic if no other evident cause. Consider *N*-acetylcysteine (NAC) infusion – possibly useful in both paracetamol and non-paracetamol ALF. **Supportive:** ABCs and O_2 to get and maintain sats >92% and admit to an HDU/ITU environment.
- **Hypovolaemia/**low **BP:** cross-match blood and transfuse if bleeding or anaemia. 4.5% human albumin solution is the colloid of choice to elevate CVP to 10 cmH_2O or until clinically euvolaemic. G5W if fluids needed (but can worsen hyponatraemia). Give 100 ml 20% human albumin solution per 2.5 L of ascites during paracentesis, or if SBP. Avoid NS (worsens fluid overload).
- **Hypoglycaemia:** stat dose 20 ml 50% IV **Glucose** and then 10% **Glucose** infusion as needed. **Glucagon** 1 mg IM/SC has limited effectiveness if no liver glycogen. ▸Section 5.2.
- **Low K, phosphate, magnesium:** replace as needed (▸Sections 5.4, 5.12, 5.14).
- **Hyponatraemia:** may need hypertonic 3% saline. ▸Section 5.10.
- **Pabrinex IV ×2** TDS for 1–2 d. Provide **thiamine** if alcoholic or malnourished. If suspected Wernicke's syndrome give for 7 d to prevent Korsakoff psychosis. Give before any nutrition/IV glucose. Long-term **Thiamine** 100 mg OD PO.
- **Cerebral oedema:** nurse at 20° head elevation. Consider mechanical hyperventilation to reduce PCO_2. **Mannitol** 200 ml of 20% (20 g/100 ml) IV over 20–30 min may repeat.
- **Stress ulcer prevention:** start IV PPI or **Ranitidine** 150 mg BD PO. PPI is a risk for *C. difficile* and SBP.
- **Antivirals: Aciclovir** for HSV or VZV and ganciclovir for CMV.
- **Antibiotics:** low threshold to treat any infection. Bacterial and fungal. Impaired immunity. Treat if encephalopathy. **Tazocin** 4.5 g 6–8 h IV is often 1st-line.
- **Coagulopathy: Vitamin K** 2–5 mg slow IV, 2–4 units FFP, platelets if $<50 \times 10^9$/L and bleeding. Vitamin K replaces any deficit, so any resulting coagulopathy is entirely due to reduced liver function. However, PT is not always a good indicator of bleed risk in ALF and giving FFP can lead to portal vein thrombosis so assess risk and benefits.

- **Hepatic encephalopathy:** avoid the use of FFP unless actively bleeding. FFP renders the PTT (a vital prognostic marker) less useful. Give **Lactulose** 20 ml BD ± enemas to ensure three bowel movements per day. Use phosphate enemas if unsuccessful. ▸Section 7.11.
- **Ascites and spontaneous bacterial peritonitis,** ▸Section 7.9.
- **Acidosis:** take expert advice and consider IV **$NaHCO_3$**. A pH <7.3 at >24 h after paracetamol overdose is a poor prognostic indicator.
- **Renal failure** and AKI common with ALF and may require haemofiltration or haemodialysis. ▸Section 10.4.

King's College criteria for liver transplant (discuss early)	
Discuss when	INR >3.0, hepatic encephalopathy, low BP despite resuscitation. Metabolic acidosis. Prothrombin time (seconds) > time from overdose (hours).
Transplant ALF due to paracetamol	pH <7.30 OR (INR >6.5 (PT >100 s) and serum creatinine >300 µmol/L (>3.4 mg/dl) in patients with grade 3 or 4 hepatic encephalopathy).
Transplant ALF due to other cause	INR >6.5 (PT >100 s), OR any 3 of the following: age <10 or >40 y; aetiology non-A, non-B hepatitis, or idiosyncratic drug reaction; duration of jaundice before hepatic encephalopathy >7 d; INR >3.5 (PT >50 s); serum bilirubin >300 µmol/L (>17.6 mg/dl).

7.3 Viral hepatitis

Causes	Details and management
A	Faeco-oral spread. Incubation 2–6 weeks. Malaise, jaundice. Usually self-limiting. 10% hospitalised. Prevent with vaccination. No chronicity. Check anti-HAV IgM.
B	Commonest viral cause of fulminant hepatitis. Sexual and maternal transmission (90% chronic). Blood, HBsAg, anti-HBcIgM. Incubation 6 weeks to 6 months. Currently no antiviral improves clinical outcome, some may advocate lamivudine. Infants born to HBsAg-positive mothers must receive hepatitis B immunoglobulin and be vaccinated within 12 h of birth. Fulminant hepatitis 1 in 1000.
C	Mild to severe illness. Sharing needles or from maternal route (6 out of 100), sexually rare. Malaise, fever, jaundice. Elevated ALT. Anti-HCV antibodies, HCV RNA. Nearly 10% prevalence in Egypt. Fulminant hepatic failure rare but is seen in HIV-positive men who have sex with men and has been reported sporadically in Asia. Acute infection treated with pegylated interferon.
D	Seen in those with hepatitis B. Prevent by hepatitis B vaccination.
E	Hepatitis E is generally mild unless pre-existing liver disease or pregnant. Causes acute and chronic disease. 4 genotypes. Faeco-oral transfer so need good hand hygiene. Flu-like illness, malaise, jaundice. Send anti-HEV IgM antibodies. Usually self-limiting. 1 in 20 may develop GBS.
Non- A/E	Acute hepatitis of presumed viral cause with negative serology. Due to unknown viruses or variants of hepatitis B.

Others	CMV, EBV, VZV, yellow fever, adenovirus, parvovirus. Patients with known or suspected HSV or VZV as the cause of ALF should be treated with **Aciclovir. Ganciclovir** for CMV.
General	Consider virus-specific therapy for HCV, all with acute viral hepatitis should avoid alcohol consumption and paracetamol. Sexual contact should be avoided if the partner is not immune. Those with sub-fulminant or fulminant hepatitis should be referred early for possible liver transplantation and supported in an ITU setting. The ALT level is not prognostic, but PT and bilirubin and lactate are prognostic.

7.4 Alcoholic hepatitis

- **About:** the aim of the liver clinician is to keep the patient alive long enough to allow them to benefit from alcohol cessation (Hazeldine *et al*., 2015).
- **Acute liver dysfunction** with jaundice in known alcoholic. Poor prognosis. Discriminant function >32 implies >50% mortality at 1 month. Reversible if patients are non-cirrhotic. The term hepatitis is a misnomer as transaminases (AST and ALT) are marginally elevated.
- **Causes:** acute exacerbation in known alcohol abuser. Look out for SBP. Quantity of alcohol ingested is not always directly proportional to risk of liver disease. Steatohepatitis (fat + hepatocellular injury + inflammation ± fibrosis). Loss of liver function.
- **Clinical:** pyrexia, raised HR, jaundice, encephalopathy, anorexia. Hepatomegaly (tender), abdominal discomfort, nausea, worsening ascites. Alcoholic neuropathy, cerebellar degeneration, cardiomyopathy, AF. Evidence of hepatitis B/C/HIV infection.
- **Aetiology:** polymorphs + necrosis in zone 3. Mallory bodies seen.
- **Investigations: FBC, U&E, LFT: raised** WCC, raised reticulocytes (haemolysis suggests Zieve's syndrome), raised CRP, raised bilirubin, AST, ALT (usually <200 rarely >400 U so not a severe biochemical 'hepatitis').
- **Abdominal USS:** hepatomegaly, coarse edge, increased echogenicity, free fluid.
- **Ascitic tap:** if spontaneous bacterial peritonitis suspected – neutrophil count >250 cells/mm^3. Infection seen in 10%. Transudate total protein <30 g/L, e.g. cirrhosis, CCF/RHF, nephrotic syndrome. Exudate has a total protein >30 g/L, e.g. cancer, infection, TB.
- **Specialist tests:** 'hepatic screen': immunoglobulins, anti-mitochondrial antibody, anti-smooth muscle antibody; ANA/dsDNA; ferritin (high in acute illness, check iron studies and transferrin saturation), caeruloplasmin (if <45 y); αFP; anti-HA IgM, HBsAg, anti-HCV ± EBV, CMV ± tumour markers (CA125, CA15-3, CA19-9, CEA, AFP) ± haptoglobin/LDH (haemolysis).
- **Liver biopsy:** histological confirmation is required where there is uncertainty about the diagnosis. 25% of presumed alcoholic hepatitis not confirmed on histology. Trans-jugular biopsy is required if coagulopathy.

Severity scorings to determine prognosis and need for abstention

- Several prognostic scores are available but the most practical one to assess severity is the Glasgow alcoholic hepatitis score (GAHS, see table below). This predicts 28-d and 3-month mortality and can be used as a guide for treatment with corticosteroids or pentoxifylline. It has an overall accuracy of 81% in predicting 28-d mortality.
- **Management:** supportive. Long-term abstinence from alcohol – refer to appropriate support on discharge. Management is supportive care to allow liver

regeneration without additional 'toxin' exposure. Nutrition must be maintained with enteral feeding if required.
- Manage alcohol withdrawal, complications of portal hypertension, ascites, encephalopathy, variceal haemorrhage. **Pabrinex** IV paired vials TDS for 1–2 d + IV **vitamin K.** Commence and continue **Thiamine** 200 mg PO OD. Signs of agitation of alcohol withdrawal consider **Chlordiazepoxide** PO or **Diazepam** PO.
- **Active treatment:** the role of steroids has been questioned by the STOPAH trial. However, some may consider in those with GAHS ≥9 (severe alcoholic hepatitis) either **Prednisolone** 40 mg OD for 28 days (reassess at Day 7) or **Pentoxifylline** 400 mg PO TDS for 28 days. Take local expert advice as some continue to use. If advice is to give steroids, ensure all infection is excluded/treated. NAC has also failed to improve 6-month survival. Reassess at Day 7 to decide on continuing steroid/pentoxifylline therapy.
- **Severe liver dysfunction: liver failure (INR >2, albumin <30, encephalopathy)** discuss with local or regional liver centre. In those with decompensated cirrhosis or alcoholic hepatitis then any rise in creatinine by 50% must be met with stopping diuretics and nephrotoxins with plasma expansion with albumin (▸Section 7.11) and renal advice. If signs of encephalopathy give **Lactulose** 20 ml 12 h ± enemas to ensure two bowel movements per day. ▸Section 7.11.
- **Best supportive care** involves access to 24 h endoscopy, expert fluid management, variceal banding and **Terlipressin** 2 mg 4 h for bleeding and early active management of sepsis – the commonest cause of death.
- **Antibiotics:** broad-spectrum antibiotics indicated for variceal bleeding. Prophylactic antibiotics after spontaneous bacterial peritonitis (SBP) such as **norfloxacin** or **ciprofloxacin** should be considered.
- **Early transplantation:** consider with severe alcoholic hepatitis because it reduces mortality, though some will go back to alcohol.
- **References:** European Association for the Study of the Liver (2010) EASL clinical practice guidelines. *J Hepatol*, 533:97. Hazeldine *et al.* (2015) Alcoholic liver disease – the extent of the problem and what you can do about it. *Clinical Medicine,* 15:179. O'Shea *et al.* (2010) Alcoholic liver disease. *Am J Gastroenterol*, 105:14.

Glasgow alcoholic hepatitis score (poor prognosis if score >9)			
Score	1	2	3
Age (y)	<50	≥50	
WCC ($\times 10^9$/L)	<15	≥15	
Urea (mmol/L)	<5	≥5	
Prothrombin ratio	<1.5	1.5–2.0	≥2
Bilirubin (μmol/L)	<125	125–250	>250

7.5 Alcoholic ketoacidosis

- **About:** seen with severe alcoholic liver dysfunction + alcohol and/or starvation. Exclude spontaneous bacterial peritonitis.
- **Clinical:** signs of advanced alcoholic liver disease, raised HR, dehydration. Jaundice, alcoholic hepatitis, ascites, coagulopathy, encephalopathy. Anorexia, N&V may be prominent. May follow 2–3 days after a binge. Ketones detectable in breath, Kussmaul's respiration.

- **Investigations:** FBC, U&E, LFT: low urea or AKI. Raised LFTs. Anaemia. Measure Mg, Ca, phosphate. **Glucose:** hypoglycaemia. Urine: ketones. **Venous blood gas:** raised AG **metabolic acidosis** with raised ketones (beta-hydroxybutyrate). Metabolic alkalosis if vomiting. **Ascites:** test as may have SBP – always aspirate.
- **Management:** supportive as for advanced alcoholic liver disease: IV fluids and IV **Glucose** and IV **Pabrinex** paired vials TDS for 1–2 d. Replace electrolytes and phosphate and magnesium as needed. Long-term abstinence from alcohol and refer to appropriate support on discharge. Alcoholic hepatitis, ▸Section 7.4.

7.6 Alcohol abuse

- **About:** alcohol is a colourless odourless liquid and liver toxin freely available for adults to consume in harmful amounts. Additives give the associated smell. It is a CNS depressant and sudden withdrawal can cause hyperexcitability, delirium and seizures. Alcohol misuse is common.
- **Alcohol history** from all patients. In those suspected of alcohol abuse start by suggesting one bottle of spirits a day and see what they say. Patients will often under report. Ask about the alcoholic life – what time they have their first and last drink, who gets the drink, falls, head injuries, violence, if children at risk involve social services, the central role alcohol takes, do they drink with someone, are they suicidal. What is their view, do they want to stop or simply cut back. Drinking is legal and a competent patient can self-discharge and go and you can do very little.
- **Recommended** limit of 14 units/week (males and females). 1 unit = 8 g alcohol = small glass of wine or half pint of beer. The liver effect of alcoholism is one facet compared to its effects on relationships, children, violence, unemployment, drink driving, hypertension, mental health issues.
- **Alcohol cessation:** sudden acute alcohol withdrawal can lead to DTs 1–3 days later and is potentially lethal. Patients should be encouraged to gradually reduce their alcohol intake over time.

CAGE questionnaire is recommended

Alcohol problem very likely if 2 or more positive answers to the following:

- Have you felt you should **C**UT down on drinking?
- Have you been **A**NGERED by suggestions you cut down?
- Have you felt **G**UILTY about drinking?
- Have you used alcohol as an **E**YE-opener in the morning?

Clinical presentations of alcohol abuse

- **Alcoholic hepatitis:** jaundiced, toxic, unwell, elevated ALT. ▸Section 7.4.
- **Liver failure:** jaundice, coagulopathy, encephalopathy, ascites. ▸Section 7.2.
- **Delirium tremens (DTs):** hyperactive delirium. Agitated, fever, sweating, picking at bedclothes (now is the time to treat), hallucinations, e.g. rats, terrified – can progress to acute seizure. ▸Section 7.8.
- **Suicide:** always ask about suicidal thoughts. Needs mental health review.
- **Trauma:** assaults, brain injury from falls and assaults, RTC.
- **Alcoholic cerebellar ataxia:** chronic cerebellar disease with ataxia.
- **Social:** spending one's life focused on obtaining and consuming alcohol leads to unemployment, divorce, homelessness, malnutrition, violence.
- **Cancer risk:** hepatoma, pancreatic cancer, oesophagus, head and neck.
- **Medical and social costs of alcoholism:** head injury, falls, assaults, road traffic accidents, seizures, overdoses, suicidal attempts, self-harm. Cerebral haemorrhage,

hypothermia, meningitis and chest infections, cardiomyopathy. Ketoacidosis, pneumococcal infections, low potassium, magnesium and calcium. Renal failure, Wernicke's and Korsakoff's psychosis and B_1 deficiency. Variceal haemorrhage and liver disease, peptic ulcer disease. Peripheral neuropathy, cerebellar degeneration, atrial fibrillation. Social and family break-up, abuse, divorce, poverty, violence.

- **Management:** alcohol-induced liver damage is silent often until a late stage when it presents in 80% as decompensated cirrhosis or alcoholic hepatitis. Long-term abstinence from alcohol is needed to allow liver regeneration. All attempts should be made to identify and change harmful behaviour early with information and coping strategies. A coordinated approach from primary and secondary care is needed as well as governmental and societal changes and attitudes to alcohol. Screening tools involve questionnaires in those at risk, GGT has a high predictive value in terms of liver disease and death. **Liver elastography** can assess fibrosis and is helpful. Various blood markers of fibrosis are being examined. See ▸Section 7.4 on alcoholic hepatitis for further information on acute presentation.

7.7 Zieve's syndrome

- **About:** rare, differential of bleeding in alcoholic liver disease.
- **Clinical:** jaundice, RUQ pain (alcoholic hepatitis), alcohol-related issues.
- **Investigations:** FBC: low Hb, raised reticulocytes, raised LDH, low haptoglobins. U&E/LFTs: raised bilirubin.
- **Blood film:** anaemia, spherocytosis due to haemolysis. Raised triglycerides.
- **Management:** supportive. Alcohol avoidance. Haematinics as needed.

7.8 Delirium tremens/alcohol withdrawal

- **About:** a cause of seizures and coma. Exclude SDH, pneumococcal bacterial meningitis, drugs. Best predictor is a past history of alcohol-related DTs.
- **Aetiology:** related to alcohol withdrawal. 1–4 days after last drink. Mortality is 15%. It is a central depressant. Withdrawal causes a hyperadrenergic state.
- **Clinical:** delirium, agitation, autonomic instability tachycardia, hypertension, low-grade fever, and diaphoresis. Develop seizures, aspiration, respiratory failure, arrhythmias. Fever, visual hallucinations and seizures occur after 24 h, peaking at 50 h. Signs of advanced alcoholic liver disease, dehydration. Jaundice, alcoholic hepatitis, ascites, coagulopathy, encephalopathy.
- **Differential:** opiate or cocaine use, hypoglycaemia, head injury (SDH/stroke/skull fracture). Sepsis, hepatic encephalopathy, psychotic illness. Encephalitis, non-convulsive status.
- **Investigations:** FBC, U&E and LFT. CRP: exclude infection and liver failure. **CXR:** exclude tumour, infection, TB, aspiration, perforation. **Sepsis screen:** chest, urine, aspirate ascites to exclude spontaneous bacterial peritonitis. ECG: exclude MI, AF. **Coagulation screen** if possible liver failure. **CT head:** if concerned about head injury or stroke or subdural haematoma, or some other pathology. Have a low threshold to scan if concerned. **LP:** if suspected meningitis (pneumococcal seen in alcoholics).
- **Management:** supportive: ABC, O_2 as per BTS guidelines. Manage in a well-lit area; involve family or known trusted carers to reduce anxiety. If significant sedation is needed then consider HDU/ITU environment for ABC. Monitor glucose, Mg and K and dehydration and treat accordingly. Agitated confused patient: start a

reducing dose regimen of **Chlordiazepoxide** or **Diazepam.** Determine when was last drink. Fits tend to classically occur about 48–96 h later. Titrate the dose to the level of agitation. Fixed dose schedule: (consider higher doses in very agitated and those with high body weight; watch for over-sedation): days 1–2: **Chlordiazepoxide** 10–30 mg 6 h. Days 3–4: **Chlordiazepoxide** 10 mg 8 h. Days 5–6: **Chlordiazepoxide** 10 mg 12 h and stop. Early discharge (>48 h) possible if asymptomatic and 24/7 supervision until days 5–6.

- **Seizures:** manage as status epilepticus (▸Section 11.15). Monitor GCS and ABCs. May need nasopharyngeal airway, recovery position and HDU bed or even ITU. Take advice if GCS <9. Low threshold to CT head if any concerns about head injury, SDH, meningitis, delirium, stroke. In the case that you are unable to convince the patient to take medications then **Lorazepam** 1–2 mg IV/IM or **Diazepam** IV/PO could be considered. **Avoid Haloperidol.** Identify early and sedate patients likely to 'go off' when they are compliant. Start as soon as any hyperactive features appear or high risk, e.g. a patient with previous delirium tremens and now off alcohol. Watch for over-sedation and precipitating encephalopathy. Consider HDU/ITU. Prophylactic anticonvulsants not usually recommended.
- **Wernicke–Korsakoff syndrome:** ataxia, ophthalmoplegia, nystagmus, low BP, memory disturbance, comatose, confusion, hypothermia. Give IV **Pabrinex** two sets of paired ampoules TDS for 3–5 d and then **Thiamine** 200 mg PO OD. ▸Section 15.16.

7.9 Cirrhosis, ascites and bacterial peritonitis

- **About:** decompensated cirrhosis is a medical emergency with a high mortality. Effective early interventions can save lives and reduce hospital stay. Complete checklist in all with decompensated cirrhosis within the first 6 h of admission.
- **Clinical:** jaundice, increasing ascites, hepatic encephalopathy, renal impairment, GI bleeding, signs of sepsis/hypovolaemia, occasionally signs may be minimal. May be mild to severe abdominal pain, ascites and generalised tenderness and signs of liver disease. Document current alcohol intake and other drugs.
- **Ascites grading:** grade 1 (mild) – detectable only by USS. Grade 2 (moderate) – moderate symmetrical distension of the abdomen. Grade 3 (large) – marked abdominal distension.
- **Precipitants:** GI bleeding (variceal and non-variceal), infection/sepsis (SBP, urine, chest, cholangitis, etc.), alcoholic hepatitis, acute portal vein thrombosis, development of hepatocellular carcinoma, drugs (alcohol, opiates, NSAIDs, etc.), ischaemic liver injury (sepsis or low BP), dehydration, constipation.

Investigations

- FBC, U&E, LFT, coag. screen, glucose, Ca/Mg/phosphate, blood cultures, urine dip/MSU and CXR for infection, CRP.
- **Liver USS:** liver size, coarse edge, increased echogenicity, free fluid throughout abdomen, hepatocellular carcinoma, portal vein or hepatic vein thrombosis, renal tract abnormalities.
- **Aspirate of ascites:** in all within 24 h (SBP can be clinically silent): a 10 ml aspirate with a blue/green needle in all unwell patients with ascites to exclude SBP: raised WCC and CRP. Neutrophil count >250 cells/mm^3 and low pH of ascitic fluid. Gram stain and aerobic and anaerobic culture. Measure ascitic protein because SBP more common with ascitic albumin <15 g/L and may need antibiotic prophylaxis.

Secondary peritonitis is likely if ascitic fluid shows >1200 cells/mm^3. Serum/ascites albumin gradient: >11 g/L suggests portal hypertension. Cirrhotic patients with low ascitic fluid protein concentration (<10–15 g/L) and/or high serum bilirubin levels are at high risk of SBP so consider prophylactic antibiotics.

- **Management: ABC, HDU** if worsening NEWS and liver failure. **Sodium restriction:** moderate restriction of salt intake to sodium of 80–120 mmol/d, which corresponds to 4.6–6.9 g of salt/d. No added salt diet. Avoid pre-prepared meals. Avoid IV NS. Alcohol ingestion then give IV **Pabrinex** 2 pairs of vials TDS for 1–2 d.

Managing ascites

- **Spontaneous bacterial peritonitis:** diagnostic paracentesis >250 polymorphs/mm^3 (0.25×10^9)/L. Treat with antibiotics, e.g. **Tazocin** 4.5 g TDS IV or **Ceftriaxone** 1–2 g IV OD for at least 5 d or as per local policy. EASL guidelines recommend **human albumin** (HAS) (day 1 give 1.5 g/kg and day 3 give 1 g/kg); reduced the incidence of hepatorenal syndrome from 30% to 10% and mortality from 29% to 10%. Following an episode of SBP patients should be considered for **Norfloxacin** 400 mg OD as prophylaxis. **Quinolones** have been used but increase risk of *C. difficile*. ▸Section 6.11.
- **Fluid/salt balance:** restrict dietary Na <90 mmol/d (5.2 g). Lowers diuretic requirement and increases resolution of ascites and shorter hospital stay.
- **Diuretics:** start **Spironolactone** 100 mg OD. There is a 3–5 day lag before natriuresis (urine Na > K) then add a loop diuretic, e.g. **Furosemide** 40–160 mg/d. Use spironolactone and furosemide in a ratio 50 mg to 20 mg, respectively. Spironolactone max dose 400 mg. Review diuretics and take advice if Na <125 mmol/L or serum creatinine rising >0% from baseline.
- **Steroids:** have been advocated for severe alcohol hepatitis but evidence is contentious. They increase risk of serious infections. Exclude/treat infection first. Use under expert guidance. Pentoxifylline has also been recommended but evidence again is not clear.
- **Therapeutic paracentesis:** recommended with large ascites. If renal function normal then administer **1 unit (100 ml) HAS 20%** following every 3 L drained or for every 2 L if there is impaired renal function. Failure to volume expand risks circulatory dysfunction + renal failure. Albumin better than artificial plasma expanders. Ascites recurs in 90% of patients if diuretics not begun and in 20% despite diuretics. **Do NOT leave drain *in situ* overnight or more than 6 h.** ▸Section 21.6.
- **Hyponatraemia:** ratio of Na >126 mmol/L, no need for H_2O restriction and continue diuretics if renal function stable. If Na <125 mmol/L consider stopping diuretics, especially if Na <121 mmol/L if creatinine rising (>150 µmol/L), volume expansion maintaining renal function is crucial. The maximum recommended weight loss during diuretic therapy should be 0.5 kg/d in patients without oedema and 1 kg/d in patients with oedema. ▸Section 5.10.
- **Prevent AKI:** increase in serum creatinine ≥26 µmol/L within 48 h, or ≥50% rise in serum creatinine over the last 7 d, or urine output <0.5 ml/kg/h for more than 6 h based on dry weight, or clinically dehydrated then suspend all diuretics and nephrotoxic drugs. Fluid resuscitates with 5% HAS or 0.9% NS (250 ml boluses with regular reassessment: 1–2 L will correct most losses). Monitor daily weights and aim for MAP >80 mmHg to achieve urine output >0.5 ml/kg/h based on dry weight. At 6 h, if target not achieved or EWS worsening then consider escalation to higher level of care. ▸Section 10.4.

- **GI bleed:** fluid resuscitate according to BP, pulse and venous pressure (aim for MAP >65 mmHg), suspected variceal bleed **Terlipressin** IV (caution if IHD or PVD; perform ECG in >65 y). If PT prolonged give IV **Vitamin K** 10 mg stat. If PT >20 s (or INR >2.0) – give FFP (2–4 units). If platelets <50 give IV platelets. Transfuse blood if Hb <7.0 g/L or massive bleeding (aim for Hb >8 g/L). Early endoscopy after resuscitation (ideally within 12 h). ▸Section 6.4.
- **Encephalopathy: lactulose** 30 ml QDS or phosphate enema (aiming for 2 soft stools/d). CT if SDH in differential. ▸Section 7.11.
- **Antibiotics:** sepsis start **Tazocin** 4.5 g TDS IV or **Ceftazidime** 1–2 g 8 h IV. Alternatives include **Ciprofloxacin** 500 mg BD PO/400 mg BD IV. Resolution is seen in 90%. Prophylaxis should also be considered.
- **Liver transplant:** those who survive an episode of SBP should be considered for liver transplantation.
- **Transjugular intrahepatic portosystemic shunt** (TIPS) for refractory ascites. 25% risk encephalopathy. Can cause heart failure.
- **VTE prophylaxis:** prescribe prophylactic LMWH (patients with liver disease are at a high risk of thromboembolism even with a prolonged PT; withhold if patient is actively bleeding or platelets <50).
- **References:** European Association for the Study of the Liver (2010) EASL clinical practice guidelines. *J Hepatol*, 533:97. Wiest *et al*. (2012) Spontaneous bacterial peritonitis: recent guidelines and beyond. *Gut*, 61:297.

7.10 Hepatorenal syndrome

- **About:** AKI with acute liver failure and cirrhosis – presents with oliguria. Exclude other causes of AKI first especially prerenal.
- **Aetiology:** splanchnic vasodilation with renal vasoconstriction, afferent renal vasoconstriction. Exclude prerenal failure by a trial of volume expansion.
- **Causes:** 40% of those with cirrhosis and ascites develop AKI. Causes are shock, diarrhoea, diuretics, sepsis, ATN, prerenal disease, drugs, paracentesis, obstruction or parenchymal renal disease. Exclude SBP as a cause.
- **Risk factors:** MAP <80 mmHg, dilutional hyponatraemia, urinary Na <5 mmol/L.
- **Differentials: prerenal failure, ATN,** nephrotoxic drugs, parenchymal renal disease (proteinuria/haematuria, abnormal renal USS), obstructive nephropathy, glomerulonephritis.
- **Classification. Type 1:** rapid AKI with oliguria. Creatinine quickly >350 µmol/L. Precipitated by spontaneous bacterial peritonitis (25% of patients), bleed or infection. Characterised by diuretic-resistant ascites, encephalopathy. Most die within 10 weeks. May respond to **terlipressin** which reduces splanchnic vasodilation (see below). **Type 2:** moderate and stable reduction in the GFR, median survival of 3–6 months. Slower. Creatinine rarely >180 µmol/L.
- **Criteria for diagnosis of hepatorenal syndrome in cirrhosis:** (1) cirrhosis with ascites + serum creatinine >133 µmol/L (1.5 mg/dl). (2) No sustained improvement of serum creatinine (to <133 µmol/L) despite 2 d of diuretic withdrawal and volume expansion with albumin (1 g/kg of body weight per day up to a maximum of 100 g/d). (3) Absence of shock. No current or recent nephrotoxic drugs, e.g. NSAIDs, etc. No parenchymal disease (no proteinuria >500 mg/d or microhaematuria (>50 RBC/high powered field)) and normal renal USS.
- **Clinical:** fatigue, malaise, progressive uraemia with oliguria without significant proteinuria. Chronic liver disease, ascites, jaundice, encephalopathy. Abdominal pain/ascites, e.g. SBP, ▸Section 7.9.

- **Investigations:** FBC, U&E, creatinine >130 µmol/L, creatinine clearance <40 ml/min. Check LFTs, PT. Urine culture and urinalysis: urine volume <500 ml/d. Proteinuria <500 mg/d. Urine Na <10 mmol/d. Urine osmolarity > plasma osmolarity. Urine RBC count <50 cells/high powered field.
- **Abdominal USS:** no renal parenchymal disease or obstruction to explain AKI, cirrhosis, ascites.
- **Sepsis screen:** diagnostic paracentesis for SBP, CXR, urinalysis, blood cultures.
- **Management:** specialist supportive care and nephrology review. Exclude other causes of AKI such as shock, ongoing infection or recent treatment with nephrotoxic drugs. Treat hypovolaemia with fluid challenge. Failure to respond suggests hepatorenal. Withdraw diuretics and other nephrotoxic drugs. Look for SBP and treat usually with **cefotaxime. In alcoholic hepatitis: pentoxifylline** 400 mg PO TDS may be used. **Vasopressin** and **noradrenaline** may be used but get specialist help. **Terlipressin,** a vasoconstrictor predominantly in the splanchnic circulation, is given as a dose of 0.5–2.0 mg IV QDS especially in type 1 in addition to day 1: 1 g HAS/kg; days 2–16: 20–40 g HAS/d. Diuretics are usually avoided. Continue until serum creatinine falls below 130 µmol/l. Where creatinine is rising despite treatment, 60 g HAS/d may be clinically indicated. As ever take expert guidance. **Octreotide** 100–200 mcg SC TDS may be used instead of **terlipressin.** Liver transplantation is usually indicated in types 1 and 2 and is the main definitive therapy. Transjugular intrahepatic porto-systemic shunting may be considered. Also see AKI, ▸Section 10.4.
- **References:** European Association for the Study of the Liver (2010) EASL clinical practice guidelines. *J Hepatol*, 533:97. Ginès & Schrier (2009) Renal failure in cirrhosis. *N Engl J Med*, 361:1279.

7.11 Hepatic encephalopathy

- **About:** potentially reversible neuropsychiatric disorder in those with liver failure. Exclude unrelated neurologic and/or metabolic abnormalities.
- **Aetiology:** associated with arterial NH_4 levels and other protein breakdown products crossing blood–brain barrier.
- **Identify likely precipitants: sepsis:** chest, urine, biliary, spontaneous bacterial peritonitis. **Metabolic:** fluid overload or electrolyte, e.g. low Na, low K, diuretic overuse. Transjugular intrahepatic porto-systemic shunt, renal failure. **Drugs:** sedatives, NSAIDs, CNS suppressants. **GI bleeding:** which may be variceal or non-variceal. Ischaemic liver injury: low BP, sepsis. **Acute portal vein thrombosis:** needs USS. Development of hepatocellular carcinoma continued alcohol intake.
- **Clinical:** reversal of day/night sleeping, psychomotor dysfunction, impaired memory. Sensory abnormalities, poor concentration, disorientation, tremor, shuffling gait. Melaena, haematemesis. Fetor hepaticus, flapping tremor, asterixis.

Grades of encephalopathy

- I: anxiety, mild confusion, reversed sleep/wake cycles, apathy, asterixis.
- II: + moderate confusion, disorientation, rigidity.
- III: + severe confusion, somnolence, incontinent, Babinski's sign.
- IV: + coma, decerebrate posturing.

Investigations

- **FBC, U&E and LFT:** raised WCC, AST/ALT, PT, alpha-fetoprotein.
- **Abdominal USS:** cholangitis, hepatocellular cancer, ascites, liver size.

- **Blood ammonia level:** raised due to GI bleeding, renal failure, hypovolaemia, urea cycle disorder, TPN, urosepsis, valproic acid.
- **CT head:** rules out acute bleeding.
- **Lumbar puncture:** if encephalitis suspected (check coag and plt first).
- **Diagnostic ascitic tap:** for spontaneous bacterial peritonitis.
- **EEG:** symmetrical slowing with (non-specific) triphasic waves.
- **Others:** exclude hypoxia, hypercarbia, uraemia, hypoglycaemia.
- **Ascitic tap always:** exclude spontaneous bacterial peritonitis.

Management

- **Supportive:** manage dietary input including adequate protein (1.5 g/kg/d) and calories (30 kcal/kg/d). Watch for re-feeding issues. Assessment by a dietitian with experience in liver disease is useful. Grade III or more encephalopathy consider intubation to protect airways and other supportive treatment often needed.
- **Drugs:** avoid opiates, NSAIDs, benzodiazepines. Check drugs for safety.
- **Precipitants:** look for and treat any cause, e.g. antibiotics for infection, paracetamol overdose, dehydration, manage bleeding, volume replace cautiously, avoid alcohol, diagnostic paracentesis for SBP and review all drugs.
- **Lactulose 20–50 ml BD** to give 3 loose stools per day. **Phosphate enema** BD may be needed. Lactulose is metabolised by bacteria in the colon to acetic and lactic acid, which reduces colonic pH, decreases survival of urease-producing bacteria in the gut, and aids conversion of ammonia (NH_3) to ammonium (NH_4), which is less readily absorbed by the gut.
- **Antibiotics: Ceftriaxone** 1–2 g/d. Consider **Rifaximin** 600 mg BD for 6 months, maintained remission from hepatic encephalopathy compared with placebo and significantly reduced hospitalisation (91% of the patients were using concomitant lactulose). **Metronidazole** 250 mg BD is also useful. Avoid neomycin.
- **L-ornithine L-aspartate** has a possible beneficial effect on mortality, hepatic encephalopathy, and serious adverse events in comparisons with placebo or no-intervention, but the quality of the evidence is very low.
- **References:** Bass *et al*. (2010) Rifaximin treatment in hepatic encephalopathy. *N Engl J Med*, 362:1071. Ginès & Schrier (2009) Renal failure in cirrhosis. *N Engl J Med,* 361:1279.

7.12 Chronic liver disease

- **About:** chronic liver disease (CLD) contrasts with ALF as management of declining liver function. Complications such as SBP, varices, acute decompensation need management. The aim is to preserve function long enough for transplant if possible.

Initial investigation for CLD of unknown aetiology

- FBC, LFTs, clotting screen, immunoglobulins – increased IgG in autoimmune, IgA in alcohol, IgM in PBC.
- Anti-mitochondrial (PBC), anti-smooth muscle, ANA in autoimmune hepatitis and renal failure in the presence of cryoglobulins (seen in viral disease specifically).
- Hepatitis viral/bacterial serology, alpha-1-antitrypsin, alpha-fetoprotein.
- Ferritin, copper, caeruloplasmin and urinary copper ± penicillamine challenge test (in patients <40 with unexplained CLD or seronegative hepatitis).
- Urinalysis and 24 h urine for creatinine clearance and protein, ECG, CXR, ultrasound and Doppler studies of abdomen, CT, MRI/MRCP studies may be needed.

Complications/associations of CLD

- Ascites in liver disease and spontaneous bacterial peritonitis (▸Section 7.9).
- Hepatic encephalopathy (▸Section 7.11).
- Coagulopathy: upper GI bleed and varices (▸Section 6.4).
- Renal impairment or hepatorenal syndrome (▸Section 7.10).

Assess mortality risk in cirrhosis: use Child–Pugh score	
Encephalopathy	None = +1, controlled/minimal = +2, advanced = +3.
Ascites	None = +1, mild = +2, moderate/severe = +3.
Bilirubin	(μmol/L): <34 = +1, 34–51 = +2, >51 = +3; in PSC/PBC the score levels are set higher: 68 = +1, and 170 = +2.
Albumin	(g/L): >35 = +1, 28–35 = +2, <28 = +3.
Prothrombin time (INR)	<4 s (INR 1.7) = +1, 4–6 s (INR 1.7–2.2) = +2, >6 s (INR >2.2) = +3.
Add scores	5–6: Class A has 100% 1 y survival 7–9: Class B has 81% 1 y survival 10–15: Class C has 45% 1 y survival

7.13 Liver abscess

- **Three types:** local bacteria, amoebic (*Entamoeba histolytica*), echinococcus (*E. granulosus*).
- **Clinical:** fever, abdominal pain, hepatomegaly, jaundice. Right pleural effusion, pleural rub. Occasionally abscesses are well tolerated and may present as PUO. Anaphylaxis (*E. granulosus*).
- **Investigations:** FBC: low Hb, raised neutrophil, raised CRP, raised ALP, raised B12. Serology can be useful – see below. CXR: raised right hemidiaphragm. Abdominal USS and CT diagnostic for liver abscess.
- **Differential:** liver cyst, hepatoma, metastases.
- **Management:** antibiotics are the 1st-line in therapy and then some require open or radiologically guided percutaneous drainage depending on the response (see below).

Causes

- **Pyogenic:** from appendicitis, cholecystitis, diverticulitis. Older patients. Multiple lesions, possible bowel malignancy. Diagnosis: USS, raised LFTs. Management: IV antibiotics and drainage. Foul smelling pus. Treat **Co-amoxiclav** 1.2 g 8 h or **Tazocin** 4.5 g TDS IV. Alternatives are **cefotaxime.** Consider adding **metronidazole** if causative organism unclear.
- **Amoebic:** see Amoebiasis, ▸Section 9.49.
- **Hydatid disease:** tapeworm infection. *E. granulosus* cysts in liver, lungs and bones usually asymptomatic and patients are well unless secondarily infected. Hydatid cyst rupture can lead to anaphylaxis. Hydatid serology 90% positive. Mortality is related to anaphylaxis and sudden death reported. Management: surgery remains the primary treatment and the only hope for complete cure. The puncture, aspiration, injection, and reaspiration (PAIR) technique is suggested with open surgery as a further option along with appropriate agents such as **albendazole** and **mebendazole** combination. Risk of anaphylaxis is, however, significant.

7.14 Gallstone disease and local complications

- **About:** commoner in women. Gallstones 10% of the population. Most are silent.
- **Risks:** mainly in females, middle age and beyond, obesity, those on octreotide. Liver disease, e.g. cirrhosis, rapid weight loss and fasting. Rare in black people other than sickle cell disease with haemolysis.
- **Aetiology:** lithogenic bile, raised insoluble cholesterol and insufficient bile acids. Obstruction of the gallbladder neck or cystic duct by a gallstone. Inflammation is more likely chemical rather than infective as bile is usually sterile.
- **Bacterial infection:** *E. coli*, *Klebsiella*, *Strep. faecalis*, and anaerobic organisms.

Pathophysiology and clinical presentations of gallstones	
Biliary colic	Gallstone stuck at cystic duct. Waves of RUQ or epigastric pain, N&V. Lasts 20 min then may return.
Acute cholecystitis	Inflamed gallbladder. Blocked cystic duct. May be bacterial infection and infected bile. Severe RUQ pain, fever. Murphy's positive pressure on RUQ catches patient on inspiration.
Emphysematous cholecystitis	Gas-producing bacteria in gallbladder. Blocked cystic duct. Classically male diabetics. Similar to cholecystitis. Toxic. Gas seen on AXR/CT.
Acalculous cholecystitis	Seen in critical care. Trauma or burns, those on TPN, etc. High mortality (see below). Possibly due to poor GB emptying.
Chronic cholecystitis	Ongoing inflamed gallbladder. Colic. May be asymptomatic. Develops 'porcelain gallbladder'.
Gallbladder perforation	Gallbladder perforates due to erosion and ischaemia. Stones pass into peritoneal cavity. Peritonitis. Fever, RUQ mass. High mortality.
Acute cholangitis	Fever, jaundice, rigors, sepsis (▶ Section 7.15).
Acute pancreatitis	With stones in common bile duct (▶ Section 7.16).

Investigations

- **Bloods:** FBC and U&E: raised WCC, CRP, creatinine, urea. LFT: bilirubin, ALP, GGT (esp. if common bile duct blocked), raised mild ALT and AST.
- **Abdominal USS:** gallstones, enlarged hydropic gallbladder with a thickened wall in the region of maximum tenderness. Gallstones in gallbladder and/or cystic duct or common bile duct. USS is more sensitive than CT for acute gallstone disease. USS can pick up stones as small as 2 mm. Identifies thickened wall gallbladder and gallbladder distension (>4 cm short axis) and pericholecystic fluid. Operator can also look for a positive Murphy's sign. Stones in common bile duct suggested if duct diameter >7 mm.
- **ERCP with cholangiogram** and sphincterotomy be needed for ductal stones.
- **Complications:** biliary sepsis, cholangitis, empyema (pus) of the gallbladder. Perforation and peritonitis, death occasionally.

Management

- ABC, O_2 as per BTS guidelines + IV access + NBM. NG tube if vomiting. **Fluids:** 1 L crystalloids (NS or Hartmann's) over 2–4 h and assess volume needs and replace.

- **Pain relief:** IM NSAIDs or **Morphine** 5 mg IV. Anti-emetics: **Cyclizine** 50 mg slow IV or **Ondansetron** 8 mg PO/IV BD. **Antibiotics: Tazocin** 4.5 g TDS IV for 10 d. Penicillin allergy **Cefuroxime** 1.5 g TDS IV + **Metronidazole** 500 mg TDS IV.
- **Surgical management:** a lap cholecystectomy is standard of care and should be carried out urgently within days of onset of symptoms unless frailty precludes it otherwise the patient is prone to further episodes. Early surgery has shorter stay, less pain and less mortality than open surgery. Those unfit for surgery may have temporary drainage. Commonest complication is bile leak which can be managed by ERCP and stenting. Conversion to open surgery is commoner in older, males, obesity, previous abdominal surgery. A fistula between GB and small bowel may result in a stone causing small bowel obstruction.
- **Biliary colic alone which settles within 6 h and no cholecystitis can go home with adequate pain control and have surgical review later.** Ask to return if worsens especially fever or worsening pain or severe vomiting. Murphy's negative.
- **Acalculous cholecystitis** can occur with no stones seen but a typical acute cholecystitis picture. Prognosis is worse. Seen with diabetes, fasting, TPN, sepsis, trauma, burns, opiates, IHD. Treat with antibiotics and supportive management. Gangrene and perforation are more common. Urgent cholecystectomy may be indicated. Other methods to treat chronic stones are oral bile acids (**Ursodeoxycholic acid**) or extracorporeal shock wave lithotripsy (ESWL).

7.15 Acute cholangitis

- **Aetiology:** bacterial infection of the biliary tree usually due to stones or impaired drainage within the common bile duct. Mortality 5–10%. Early ERCP and early antibiotic therapy.
- **Causes:** gallstones predominantly, strictures, sclerosing cholangitis, chronic pancreatitis, HIV-related cholangiopathy. **Rare:** clonorchis, ascarisis.
- **Clinical:** Charcot's triad of non-colicky RUQ pain to right shoulder, jaundice and fever. Biliary obstruction – dark urine and pale stool.
- **Investigations:** FBC, U&E, LFT: raised WCC, raised bilirubin, raised ALP, raised GGT, raised ALT. Blood cultures positive in half.
- **Abdominal USS:** enlarged hydropic gallbladder with a thickened wall and stones. Stones in common bile duct suggested if duct diameter >5–7 mm.
- **Abdominal CT:** can be useful to see obstruction and measure common bile duct. Can also exclude pancreatic carcinoma/other pathologies.
- **Magnetic resonance cholangiopancreatography (MRCP):** can visualise biliary tree anatomy and stones. Not possible if patient has non-compatible pacemaker, etc.
- **ERCP:** see stones in CBD and exclude tumour. Sphincterotomy can release impacted stones. Stenting if needed.

Management

- **Supportive:** IV fluids, crystalloids and basic ABC, O_2 as per BTS guidelines. NBM, NG if vomiting. Get abdominal USS as soon as possible.
- **Antibiotics: Tazocin** 4.5 g TDS IV for 7–10 d. Alternative consider **Cefuroxime** 1.5 g TDS IV + **Metronidazole** 500 mg TDS IV.
- **ERCP ± sphincterotomy:** allows bile drainage and passage of a stone ± spontaneously or pulled out with a basket device. If malignant lesion or stricture a stent can be placed.
- **Laparoscopic cholecystectomy** at 6–12 weeks for gallbladder stones.
- **Complications:** sepsis, ARDS, multi-organ failure.

7.16 Acute pancreatitis

- **About:** significant morbidity/mortality. Calculate Modified Glasgow Score.
- **Diagnosis:** needs 2/3 of typical abdominal pain, high amylase, high lipase and imaging. Admit under surgeons or gastroenterology.
- **Aetiology:** activation of trypsin, lipase and amylase and autodigestion leads to an inflamed oedematous/haemorrhagic pancreas. Ongoing tissue damage activates complement with a progressive systemic inflammatory response syndrome.

Causes

- **Gallstones (45%):** in ampulla of Vater allows bile reflux into pancreatic duct activating enzymes causing inflammation.
- **Alcohol (45%):** chronic alcohol for several years or occasional binge.
- **Hypertriglyceridaemia:** look at fundi for lipaemia retinalis.
- **Primary hyperparathyroidism,** hypercalcaemia: check Ca and PTH.
- **Cancer:** pancreatic cancer, biliary cancer.
- **Miscellaneous:** trauma, snakebite, HIV, CMV, EBV, sphincter of Oddi dysfunction.
- **Iatrogenic:** post ERCP reduce with IV hydration before.
- **Drugs:** steroids, thiazides, azathioprine, sulphonamide, octreotide, valproate.
- **Congenital:** pancreas divisum, familial non-X-linked dominant.

Clinical

- Raised HR, low BP, shock from sepsis, haemorrhagic pancreatitis. Severe epigastric pain to back eased with sitting up and forwards. Peritonitis with guarding, signs of causes, e.g. gallstones, alcoholism. Shocked, sepsis – generalised, pneumonia, low Hb.
- Bruising in flanks – Grey Turner's sign (associated 40% mortality). Peri-umbilical bruising – Cullen's sign (haemorrhagic pancreatitis). Coagulopathy from DIC. Cyanosed, dyspnoea from ARDS. Oliguria from AKI and/or hypovolaemia.

Diagnostic criteria for acute pancreatitis

- Requires two of the following three features: (1) abdominal pain consistent with acute pancreatitis (acute onset of a persistent, severe, epigastric pain often radiating to the back), (2) raised serum lipase activity (or amylase activity) >3× upper limit of normal (ULN), (3) characteristic findings on contrast-enhanced CT or MRI or USS.
- If clinical picture suggests acute pancreatitis, the serum amylase/lipase activity is <3× ULN (e.g. delayed presentation); imaging is needed to confirm the diagnosis otherwise the clinical picture + raised serum pancreatic enzyme activities suffices and a CT is not usually required for diagnosis acutely.

Investigations

- **FBC:** low Hb with haemorrhagic pancreatitis; raised MCV with alcohol. **U&E:** AKI, low Ca, raised triglycerides (familial hypertriglyceridaemia). **CRP:** >200 within first 4 days suggests acute severe attack – risk of complications, e.g. infection, pseudocyst, abscess formation.
- **Pancreatic lipase** raised (>3× ULN): more sensitive and specific than amylase. Elevated longer than amylase after disease presentation.
- **Amylase** (>3× ULN is diagnostic): usually >1000 IU/ml (levels up to 10,000 may be seen). Mild elevations >200 IU/ml not unique to pancreatitis but may also be seen in abdominal pain due to perforation of a viscus, small bowel obstruction, leaking AAA, ectopic pregnancy. A level of >1000 is more diagnostic, *but there is not a close*

correlation between amylase level and clinical severity. Very rarely a normal amylase suggests little remaining amylase-producing pancreatic tissue left. Amylase may be normal if alcohol-induced or high triglycerides. False positive serum amylase with macroamylasaemia – the level is constant.
- **Urinary trypsinogen-2** is now considered as a new test in development.
- **IL-6 and IL-8** may predict severity.
- **ABG:** low pH, low HCO_3, low PO_2 in severe cases, raised lactate.
- **Imaging: erect CXR/AXR:** exclude perforation, small bowel obstruction. Left pleural effusion may be seen. Look for calcification and sentinel loop. Bowel gas is seen in small bowel in centre of abdomen.
- **Contrast-enhanced CT/MRI abdomen:** reserved for patients in whom the diagnosis is unclear or who fail to improve clinically within the first 48–72 h after hospital admission or to evaluate complications. Best done at or after 3 days to support diagnosis and determine full extent of pancreatic necrosis and the presence of any fluid. CT may show fat-stranding surrounding the inflamed pancreas. Fluid may be aspirated to detect infection. Necrotic pancreas is identified by failure to opacify when CT with contrast is carried out. Gas bubbles may suggest infection. In a patient >40 y, look for a pancreatic tumour.
- **USS abdomen:** pancreatic mass, gallstones, pseudocyst, liver disease.
- **ERCP:** when aetiology unclear. May show a cause, e.g. ampullary tumour, stricture, gallstones, pancreas divisum and allow sphincterotomy. In those at high risk of pancreatitis post ERCP advise guidewire cannulation, pancreatic duct stents, rectal NSAIDs.

Severity scoring
- **Balthazar CT Severity Index: calculated on the basis of CT findings:** (A) normal pancreas +0, (B) focal or diffuse enlargement of the pancreas, contour irregularities, heterogeneous attenuation, no peripancreatic inflammation +1, (C) grade B plus peripancreatic inflammation +2, (D) grade C plus a single fluid collection +3, (E) grade C plus multiple fluid collections or gas +4. Percentage necrosis present on CT score: none +0, <33% +2, 33–50% +4, >50% +6. **Severe = score >6.**
- **Modified Glasgow Score:** ***P***aO_2 <60 mmHg; **A**ge >55 years; **N**eutrophils (WCC) >15 × 10^9/L; **C**alcium <2 mmol/L; **R**aised urea >16 mmol/L; **E**nzyme LDH >600 units/L; **A**lbumin <32 g/L; **S**ugar (glucose) >10 mmol/L. Note spells out PANCREAS. A score >3 suggests severe and ITU/HDU care should be considered (Moore (2000) A useful mnemonic for severity stratification in acute pancreatitis. *Ann R Coll Surg Engl* (2000); 82:16–17).

Local and systemic complications
- **Acute kidney injury:** multiple factors. Optimise fluid status, treat infection, stop nephrotoxins. AKI, ▸Section 10.4.
- **Pancreatic pseudocyst and fluid collections:** can form around the pancreatic mass and may need laparoscopic drainage.
- **Necrotising pancreatitis:** >50% of gland necrosed on imaging. Can lead to infection and abscess formation. Needs antibiotics ± surgery. May get walled-off necrosis. Can erode into retroperitoneal vessels, e.g. splenic artery with acute haemorrhage.
- **Pancreatic abscess:** CT shows a ring-enhancing fluid collection with gas. Surgical or percutaneous drainage. IV antibiotics.
- **Others:** exocrine: fat malabsorption (low faecal elastase), endocrine: secondary diabetes.

- **Systemic:** recurrent acute pancreatitis, ARDS, AKI, DIC, multi-organ failure, sepsis.
- **Chronic pancreatitis:** repeated episodes of pancreatic injury, often alcohol-related, and frequent admissions. Alcohol cessation is the key in those who drink. Symptoms mimic acute pancreatitis. Develops exocrine and later endocrine dysfunction with steatorrhoea and weight loss. **Diagnosis with CT/USS/ERCP.** Exclude gallstones. **Differential** is autoimmune pancreatitis, inherited causes that start in early adult life and pancreatic cancer. Treatment is alcohol avoidance, nutritional support, manage exocrine and endocrine needs. Acutely these patients may be seen for mainly pain relief and managing acute flares. Pancreatic duct stenting if local stenosis.
- **Portal vein/splenic thrombosis:** localised inflammation. Develop portal hypertension with splenomegaly and variceal bleeds.

Management

- **ABC** and O_2 as per BTS guidance. Give early aggressive hydration (250–500 ml/h depending on cardiac/renal status) with 0.9% NS or Hartmann's solution to give urine output >30 ml/h. Baseline volume loss is 4–6 L but assess case by case. Consider CVP monitoring, monitor urine output, and clinical assessments of hydration, oxygenation, etc. There may be significant '3rd space' losses, which will need to be accounted for. ITU/HDU admission with any signs of organ failure. Look for and correct any significant hypocalcaemia. Severe cases need CT at 3–7 d and assess severity with CT severity score.
- **Nutrition:** in mild/mod disease normal oral feeding can be considered if no significant gastroparesis and there are normal bowel sounds and no signs of ileus. Early feeding by naso/gastric/jejunal (NG/NJ) tube is advised if there is ongoing vomiting. Enteral feeding is preferred to TPN. However, those with severe disease may be initially NBM. Calcium and magnesium should be checked and replaced if needed and adequate hydration given.
- **Analgesia: tramadol** IV is preferred. **Morphine** 1–5 mg IV every 4 h is widely used. **Pethidine** 25–50 mg IV/SC/IM historically advocated as concerns that **morphine** increased sphincter of Oddi tone or caused spasm. Combine with anti-emetic **Ondansetron** 2–4 mg IV every 4–6 h when required.
- **Diabetes: may be new,** consider **variable rate insulin infusion** to control any hyperglycaemia.
- **Alcohol withdrawal:** consider **Chlordiazepoxide** or **Lorazepam** 1–2 mg PO/IV/IM 8 hourly and **Pabrinex** IV paired vials TDS for 1–2 d.
- **Antibiotics:** are given if evidence of specific infections. Advice now against prophylaxis. Fever often due to inflammatory nature of the disease. If infected necrosis suspected then either **Cefuroxime** 750 mg – 1.5 g TDS IV or **Tazocin** 4.5 g TDS IV or **Meropenem** 1 g TDS IV if penicillin allergic (choice of carbapenems, quinolones, metronidazole).
- **Nutrition:** can feed normally if mild, no N&V, and abdominal pain resolved. In moderate–severe disease try to continue enteral nutrition which may be by NG/NJ tube. Try to avoid parenteral nutrition unless the enteral route is not available, not tolerated, or insufficient for caloric requirements.
- **ERCP ± sphincterotomy** should be considered, usually within 24 h where there is a cholangitis or jaundice and a common duct stone, which requires removal. A sphincterotomy may be performed and/or stone removed. ERCP is not needed in most patients with gallstone pancreatitis without evidence of biliary obstruction. Manage gallstones with either cholecystectomy or ERCP; or ursodeoxycholic acid can be considered.

- **MRCP or endoscopic ultrasound** (EUS) rather than diagnostic ERCP should be used to screen for choledocholithiasis if highly suspected.
- **CT-guided FNA:** consider infected necrosis in those with pancreatic or extrapancreatic necrosis who deteriorate or fail to improve after 7–10 d; consider either CT-guided FNA for Gram stain and culture to guide antibiotic prescribing, or empiric use of antibiotics without CT FNA.
- **Respiratory support:** patient with severe upper abdominal pain can experience basal atelectasis and hypoventilation and develop respiratory failure and may need a mixture of analgesia with a trial of high FiO_2 with humidification, chest physiotherapy to help expectorate secretions, CPAP or even invasive ventilation on ITU.
- **Surgery** may be required where there is a **severe necrotising pancreatitis** or if there is an **abscess or pseudocyst.** Usually delayed about 4 weeks. A pancreatic necrosectomy involves removing dead pancreatic tissue, which may be done by laparoscopy. Minimally invasive methods are preferred to open necrosectomy. Consider cholecystectomy prior to discharge if gallstone pancreatitis. Asymptomatic pseudocysts may be observed and often resolve but some may need to be managed endoscopically.
- **Behaviour:** offer advice and help with good nutrition and in cessation of alcohol and smoking.
- **References:** Tenner *et al*. (2013) Management of acute pancreatitis. *Am J Gastroenterol*, 108:1400. UK Working Party on Acute Pancreatitis (2005) UK guidelines for the management of acute pancreatitis. *Gut*, 54(Suppl III):iii1. Banks *et al*. (2013) Classification of acute pancreatitis. *Gut*, 62:102.

7.17 Budd–Chiari syndrome

- **Introduction:** uncommon (1 in 100,000) condition characterised by obstruction of the hepatic venous outflow tract. Requires accurate, prompt diagnosis and aggressive therapy.
- **Causes:** hepatic vein thrombosis and post-sinusoidal portal hypertension. There may be hepatic thrombosis due to prothrombosis, stenosis or webs. Portal hypertension, liver congestion and centrilobular cell necrosis. Idiopathic. Prothrombosis, malignancy.
- **Clinical:** RUQ pain, asymptomatic to fulminant liver failure in days. Often with jaundice, renal failure and coagulopathy and encephalopathy.
- **Investigations:** FBC, U&E, LFTs, CRP. High AST/ALT/bilirubin and PT. Liver USS shows enlarged caudate lobe and hepatomegaly and regional echogenicity and ascites. CT/VT venography is also useful and MRI shows absence of blood flow in the occluded veins. If no local cause then needs a full thrombophilia screen. *JAK2* mutation. Catheter venography is considered the standard for the diagnosis of this condition.
- **Management:** medical, surgical and endovascular. Treat any cause. Best treated in tertiary care centres where liver transplantation is available. Endovascular interventions include angioplasty, stenting, catheter-directed mechanical thrombolysis, and creation of transjugular intrahepatic portosystemic shunts (TIPSS).