

THE ESSENTIAL GUIDE FOR THE CARE OF PATIENTS WITH
GASTROENTEROLOGICAL AND HEPATOLOGICAL DISEASE

OXFORD HANDBOOK OF GASTROENTEROLOGY AND HEPATOLOGY

Stuart Bloom | George Webster | Daniel Marks

Thoroughly revised, now with a dedicated section on endoscopy, reflecting the many advances in this key area

Comprehensive A-Z of conditions allows fast access to focused key information about the range of conditions that may be encountered

Updated to highlight key current patient issues, including communication, palliative care, use of evidence, and patient-centred outcomes



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**Oxford Handbook of
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OXFORD HANDBOOK OF

Gastroenterology and Hepatology

THIRD EDITION

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Finally

So here's the result, and we hope you find this book of practical use, fun, and informative. We would welcome feedback, which can be directed to us via the OUP website www.oup.co.uk/academic/medicine/handbooks/ comments

Stuart Bloom and George Webster
University College London Hospitals
2006

Foreword

It is quite remarkable how much information is contained within this handbook, but the authors never forget its primary function—to provide clear and easily available evidence-based facts. It does not dwell on the evidence, always giving priority to clear management advice, but gives the reader the chance to pursue the background further with a few well-selected references.

The authors manage to make it relevant to all doctors confronted by patients with gastrointestinal symptoms. The handbook will instruct the medical student on the approach to the patient, guide the junior doctor on what do in the night, remind the registrars of their MRCP knowledge, and reassure the senior doctor that the principles of good patient care remain the same. It is nonetheless up to date in the latest therapies, which is important in a specialty with its fair share of ‘-mibs and -mabs’. In an era where there is often too much information available, it is good to have a resource that is tried, tested, up to date, and produced by gastroenterologists who have the respect of their peers.

Sir Ian Gilmore DL
Director, Liverpool Centre for Alcohol Research
Chairman, Alcohol Health Alliance, UK

Preface to the third edition

We were delighted to be approached by OUP to write a third edition of this text, which has given us an opportunity to take stock and reflect on developments in gastroenterology and hepatology over the past 8 years. It is not an overstatement that there have been transformational advances in both specialties: a profusion of new therapies for inflammatory GI diseases, the evolution of chronic viral hepatitides from often lifelong infections to be managed to potentially curable, and major updates across the board in cancer screening and management algorithms.

In this edition, we have comprehensively reviewed and updated the entire text. As part of this process, we have also:

- Written new Approaches on the management of patients with eating disorders, and post-liver transplant patients.
- Revised the Clinical Practice and Diagnostic section to highlight several patient issues that have come to increased prominence in recent years, including elements of communication, palliative care, and use of evidence, including patient-centred outcomes.
- Broken out the section on endoscopy into a dedicated chapter, which reflects the many advances since the previous edition.
- Comprehensively updated the A–Z section and the Drugs chapter, which now incorporates many new therapies as well as refined advice on how to select between options within a therapeutic class.
- Included additional topics in the Emergencies section on abdominal trauma, bowel obstruction, and major haemorrhage.

To achieve such a comprehensive update, we have been very grateful for the help and support of a number of subspecialty contributors. These include Drs Deepak Joshi, Louise China, Mathena Pavan, Bahman Shokouhi, Mark Samaan and David Graham, without whose input this edition would not have been possible. We are also extremely grateful for the advice and critical appraisal from a number of our colleagues including Dr Rami Sweis, Prof Robert Miller, Dr Karishma Sethi, and Dr Fran Bennett.

We hope that this has resulted in a portable text that remains a useful, up-to-date, and readable primer for clinicians of all grades working in Gastroenterology & Hepatology.

Stuart Bloom, George Webster, and Daniel Marks
University College London Hospital
2021

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Preface to the first edition

Why write another textbook?

There are many excellent textbooks of gastroenterology and hepatology, and many calls on our time. Apart from the fact that the commissioning editor, Alison Langton, asked us very nicely and persistently, a few considerations raised us from our naturally indolent state and gave us the energy to contemplate the task:

- The format and portability of the Oxford Handbooks is attractive and the series has not, to date, included a text on gastroenterology and hepatology. Even with white coats out of fashion, the Handbooks are easily transportable in rucksacks or handbags and do not induce herniae on opening.
- Gastroenterology and hepatology involve many organ systems. Most textbooks are organized anatomically (i.e. start at the mouth and move south), which often relates poorly to how patients present to doctors (e.g. the jaundiced patient—due to hepatitis A, gallstones, or pancreatic cancer?). This may lead to both repetition through the text, and a need for large complicated indexes to help search for relevant information.
- It seemed to us that there is a need for up-to-date information on how to approach both clinical scenarios (e.g. abnormal liver tests; lower GI bleeding) and specific conditions in GI and liver practice, both common and uncommon. This information needs to be organized in such a way that it can be easily obtained in the clinic, on the way to a ward to see a patient referred with an exotic or unfamiliar condition, or when telephoned for advice by a colleague—or a patient.

Who is it written for?

- This book is aimed at all those interested in the presentation and management of patients with gastrointestinal and liver disease. This includes some but not all medical students, most junior doctors training in hospital medicine and in general practice, and all those training in gastroenterology/hepatology, one of the most challenging and fast developing of the medical specialties.
- We hope it will also appeal to many senior doctors immersed in busy practice who may find it useful to be reminded of the salient points of commonly (and less commonly) encountered conditions and problems in the field.
- Finally we hope that in the age of multidisciplinary teams the book will be of value to those working in nursing and professions allied to medicine, particularly clinical nurse specialists and nurse consultants and those involved in pharmaceutical practice and dietetics.

How is it different from other textbooks?

We have organized the book into a series of sections. Underlinings represent an entry in the relevant section and will enable hyperlinking in the electronic version of the book (if it's successful).

- **⚠ Bold for emergencies ⚠** A section on GI emergencies offering help on acute management based on clinical priorities.
- **▶ Green for approaches to common clinical problems**
A section on the approach to various clinical problems and scenarios encountered in the clinic and on the wards.
- **⌚ Black for A to Z of topics**
Most of the book is dedicated to an A to Z of conditions and problems in gastroenterology and hepatology. This is (to our knowledge) a new way of organizing a text on the subject, but we hope it will enable readers in accessing information. Throughout this section, there are text links to other related topics, and to the emergencies and approaches section, highlighted as they are listed here.
- **→ SMALL CAPITALS FOR PARTICULAR DRUGS**
An index of drugs commonly used in gastroenterology and hepatology. This is not intended to duplicate or replace information in crucial and authoritative texts such as the *British National Formulary*, but rather to give key facts of dosage, methods of administration, and common cautions, side effects, and interactions. Practice points are also included, drawing on our combined experience in the specialty.

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Symbols and abbreviations

	caution	ANA	anti-nuclear antibody
	clinical practice and diagnostics	ANC	acute necrotic collection
	see <i>approaches</i> section	AP	acute pancreatitis
	see <i>emergencies</i> section	APC	adenomatous polyposis coli (gene) or argon plasma coagulation
	see <i>emergencies</i> section	apo-B	apolipoprotein B
	see <i>drugs</i> section	APTT	activated partial thromboplastin time
	raised	APUD	amine precursor uptake and decarboxylation (cells)
	lowered	ARR	absolute risk reduction
	online reference	ASA	American Society of Anesthesiology
	controversial topic	ASD	atrial septal defect
	therefore	ASM	anti-smooth muscle (antibodies)
α FP	alpha-fetoprotein	AST	aspartate aminotransaminase
γ GT	gamma-glutamyl transpeptidase	ATLS	Advanced Trauma Life Support
5-ASA	5-amino salicylate	AUDIT	Alcohol Use Disorders Identification Test
5-FU	fluorouracil	AV	arteriovenous
5-HIAA	5-hydroxyindoleacetic acid	AXR	abdominal X-ray
5-HT	5-hydroxytryptamine (serotonin)	AZA	azathioprine
AAD	antibiotic-associated diarrhoea	BAM	bile acid malabsorption
Ab	antibody	BCG	Bacillus Calmette-Guérin
ACE	angiotensin-converting enzyme or antegrade colonic enema	BCS	Budd-Chiari syndrome
ACTH	adrenocorticotrophic hormone	bd	twice a day
ADH	antidiuretic hormone	BDS	bile duct stones
AF	atrial fibrillation	β -HCG	beta human chorionic gonadotrophin
AFB	acid-fast bacillus	BMD	bone mineral density
AFLP	acute fatty liver of pregnancy	BMI	body mass index
AGA	American Gastroenterology Association	BMR	basal metabolic rate
AIDS	acquired immune deficiency syndrome	BMT	bone marrow transplant
AIH	autoimmune hepatitis	Bn	bilirubin
AIP	acute intermittent porphyria or autoimmune pancreatitis	BNF	British National Formulary
AKI	acute kidney injury	BP	blood pressure
ALA	amino-laevulinic acid or amoebic liver abscess	BSG	British Society of Gastroenterology
ALF	acute liver failure	Bx	biopsy
ALP	alkaline phosphatase	cAMP	cyclic adenosine monophosphate
ALT	alanine aminotransferase	CBD	common bile duct
AMA	anti-mitochondrial antibodies		
AMP	adenosine monophosphate		

CDAD	<i>Clostridioides difficile</i> -associated diarrhoea	DPL	diagnostic peritoneal lavage
CDAI	Crohn's disease activity index	DRE	digital rectal examination
CDC	Centers for Disease Control (US)	DRESS	drug reaction with eosinophilia and systemic symptoms
CDEIS	Crohn's disease endoscopic inflammation score	DS	Down syndrome
CE	capsule endoscopy	dsDNA	double-stranded DNA
CEA	carcinoembryonic antigen	DT	delirium tremens
CF	cystic fibrosis	DU	duodenal ulcer
CFTR	cystic fibrosis transmembrane conductance regulator	DVT	deep vein thrombosis
CGD	chronic granulomatous disease	EAggEC	entero-aggregatory <i>E. coli</i>
CHB	chronic hepatitis B	EBV	Epstein–Barr virus
CKD	chronic kidney disease	ECG	electrocardiogram
CLE	confocal laser endomicroscopy	EGC	early gastric cancer
CLO	<i>Campylobacter</i> -like organisms (test for)	EGF	epidermal growth factor
CMV	cytomegalovirus	eGFR	estimated glomerular filtration rate
CNS	central nervous system	EGG	electrogastrography
CO	carbon monoxide or cardiac output	EHEC	enterohaemorrhagic <i>E. coli</i>
COX	cyclo-oxygenase	EHL	electrohydraulic lithotripsy
CREST	calcinosis–Raynaud's–oesophageal dysmotility–sclerodactyly–telangiectasia (syndrome)	EIA	enzyme immunoassay
CRP	C-reactive protein	EIEC	enteroinvasive <i>E. coli</i>
CSF	cerebrospinal fluid	ELISA	enzyme-linked immunosorbent assay
CSU	catheter specimen of urine	EMR	endoscopic mucosal resection
CT	computed tomography	ENT	ear, nose, and throat
CTD	connective tissue disease	EPEC	enteropathogenic <i>E. coli</i>
CVA	cerebrovascular accident	EPO	erythropoietin
CVP	central venous pressure	ERCP	endoscopic retrograde cholangiopancreatography
CXR	chest X-ray	ESR	erythrocyte sedimentation rate
CYP	cytochrome P450	EST	endoscopic sclerotherapy
DAA	directly acting antiviral	ESWL	extracorporeal shock wave lithotripsy
DAEC	diffusely adhering <i>E. coli</i>	ETEC	enterotoxigenic <i>E. coli</i>
DBD	donors after brain death	EUA	examination under anaesthesia
DBE	double-balloon enteroscopy	EUS	endoscopic ultrasound
DCC	deleted in colorectal cancer (gene)	FAP	familial adenomatous polyposis
DEXA	dual energy X-ray absorptiometry	FAST	Focused Assessment with Sonography for Trauma
DF	discriminant function	FBC	full blood count
DIC	disseminated intravascular coagulation	FDG	2-fluoro-2-deoxy-D-glucose
DILI	drug-induced liver injury	FE1	faecal elastase type 1
DIOS	distal intestinal obstruction syndrome	FFP	fresh frozen plasma
DOAC	direct oral anticoagulant	FGP	fundal gastric polyp
		FIT	faecal immunochemical test
		FMF	familial Mediterranean fever
		FNA	fine-needle aspiration
		FNAC	fine needle aspiration cytology

FNH	focal nodular hyperplasia	HGD	high-grade dysplasia
FOBT	faecal occult blood test	HGV	hepatitis G virus
FSH	follicle-stimulating hormone	HHV	human herpes virus
G6PD	glucose 6-phosphate dehydrogenase	HIDA	hepatobiliary iminodiacetic acid (hepatobiliary scintigraphy)
GABA	γ -aminobutyric acid	HII	hepatic iron index
GAVE	gastric antral vascular ectasia	HIV	human immunodeficiency virus
GBS	Guillain–Barré syndrome	HNIG	human normal immunoglobulin
GCS	Glasgow Coma Scale	HNPPC	hereditary non-polyposis colorectal cancer
G-CSF	granulocyte colony-stimulating factor	HOCM	hypertrophic obstructive cardiomyopathy
GDA	gastroduodenal artery	HP	<i>Helicobacter pylori</i>
GH	genetic haemochromatosis	HPF	high-power field
GI	gastrointestinal (<i>also</i> glycaemic index)	HPV	human papillomavirus
GIST	gastrointestinal stromal tumours	HR	heart rate
Glu	glutamic acid	HRM	high resolution manometry
GMC	General Medical Council (UK)	HRQL	health-related quality of life
GMP	guanosine monophosphate	HRS	hepatorenal syndrome
GO	gastro-oesophageal	HRT	hormone replacement therapy
GOJ	gastro-oesophageal junction	HSV	herpes simplex virus
GORD	gastro-oesophageal reflux disease	HTLV	human T lymphotropic virus
GTN	glyceryl trinitrate	HUS	haemolytic uraemic syndrome
GU	gastric ulcer	HV	hepatic vein
GvHD	graft-versus-host disease	HVPG	hepatic venous pressure gradient
GWAS	genome-wide association study	IBD	inflammatory bowel disease
H&E	haematoxylin and eosin	IBS	irritable bowel syndrome
H ₂ RA	H ₂ -receptor antagonist	ICP	intracranial pressure
HAART	highly active antiretroviral therapy	IF	intrinsic factor
HAS	human albumin solution	IFAT	indirect fluorescent antibody test
HAV	hepatitis A virus	IFN	interferon
Hb	haemoglobin	IL	interleukin
HBCAg	hepatitis B core antigen	IM	intramuscular
HBeAg	hepatitis B envelope antigen	INR	international normalized ratio
HBsAg	hepatitis B surface antigen	IPAA	ileal pouch–anal anastomosis
HBV	hepatitis B virus	IPMT	intraductal papillary mucinous tumour
HCC	hepatocellular carcinoma	IPSID	immunoproliferative small intestinal disease (alpha-chain disease)
HCV	hepatitis C virus	IPVD	intrapulmonary vascular dilatation
HDL	high-density lipoprotein	IRIS	immune reconstitution inflammatory syndrome
HDU	high-dependency unit	ITU	intensive therapy unit
HDV	hepatitis D virus	IU	international units
HE	hepatic encephalopathy	IV	intravenous
HELLP	haemolysis–elevated liver enzymes–low platelets (syndrome)		
HEV	hepatitis E virus		

IVIG	intravenous immunoglobulins	MHA	Mental Health Act
JVP	jugular venous pressure	MHRA	Medicines and Healthcare Products Regulatory Agency
KS	Kaposi's sarcoma	MI	myocardial infarction
KSHV	Kaposi's sarcoma-associated herpes virus	MIBG	meta-iodobenzylguanidine
LARS	laparoscopic anti-reflux surgery	MMP	methylmercaptopurine
LBx	liver biopsy	MMR	measles, mumps, and rubella
LC	laparoscopic cholecystectomy	Mo	month
LCHAD	long-chain 3-hydroxyacyl coenzyme A dehydrogenase	MP	mercaptopurine
LCT	long-chain triglyceride	MRCP	magnetic resonance cholangiopancreatography
LDH	lactate dehydrogenase	MRI	magnetic resonance imaging
LDL	low-density lipoprotein	MS	multiple sclerosis
LFT	liver function test	MSM	men who have sex with men
LGD	low-grade dysplasia	MSU	mid-stream urine
LGV	lymphogranuloma venereum	MTB	<i>Mycobacterium tuberculosis</i>
LH	luteinizing hormone	MTTP	microsomal triglyceride transfer protein
LIF	left iliac fossa	NAC	acetylcysteine
LKM1	liver–kidney microsomes, type 1	NADPH	nicotinamide adenine dinucleotide phosphate (reduced form).
LLQ	left lower quadrant	NAFL	non-alcoholic fatty liver
LMWH	low molecular weight heparin	NAFLD	non-alcoholic fatty liver disease
LOS	lower oesophageal sphincter	NAPQI	acetyl-p-benzoquinone imine
LRLT	living-related liver transplant	NASH	non-alcoholic steatohepatitis
LS	liver stiffness	NBM	nil by mouth
LUQ	left upper quadrant	NBSR	National Bariatric Surgery Registry
MAC	<i>Mycobacterium avium complex</i>	NET	neuroendocrine tumours
MAHA	microangiopathic haemolytic anaemia	NF	neurofibromatosis
MAI	<i>Mycobacterium avium intracellulare</i>	NG	nasogastric (tube)
MALT	mucosa-associated lymphoid tissue	NHL	non-Hodgkin's lymphoma
MAP	mean arterial pressure	NHS	National Health System (UK)
MARS	molecular absorbance recirculation system	NICE	National Institute for Health and Care Excellence (UK)
MC&S	microscopy, culture and sensitivities	NJ	nasojejunal (tube)
MCH	mean corpuscular haemoglobin	NNT	number needed to treat (for one patient to benefit)
MCHC	mean corpuscular haemoglobin concentration	NOGCA	National Oesophago-Gastric Cancer Audit
MCN	mucinous cystic neoplasm	NRH	nodular regenerative hyperplasia
MCT	medium-chain triglyceride	NSAID	non-steroidal anti-inflammatory drug
MCTD	mixed connective tissue disease	NUD	non-ulcer dyspepsia
MCV	mean corpuscular volume	OATP	organic anion transporting polypeptide
MELD	model for end-stage liver disease (score)	OC	open cholecystectomy
MEN	multiple endocrine neoplasia (e.g. MEN-1)	OCA	obeticholic acid

OCP	oral contraceptive pill or ova, cysts & parasites	PTD	percutaneous transhepatic drainage
od	once a day	PTH	parathyroid hormone
OGD	oesophago-gastro-duodenoscopy	PTLD	post-transplant lymphoproliferative disorder
OLT	orthotopic liver transplantation	PUD	peptic ulcer disease
ORS	oral rehydration solution	PUO	pyrexia of unknown origin
PA	postero-anterior or pernicious anaemia	PV	by (per) vagina
PABA	para-aminobenzoic acid	PVT	portal vein thrombosis
PALS	patient advice and liaison service	qds	four times a day
PAN	polyarteritis nodosa	RA	rheumatoid arthritis
PAS	para-aminosalicylic acid or periodic acid-Schiff	RBC	red blood cell
PAT	parenteral antischistosomal therapy	RCT	randomized controlled trial
PBC	primary biliary cholangitis	RDW	red cell distribution width
PBG	porphobilinogen	RIBA	recombinant immunoblot assay
PCR	polymerase chain reaction	RIF	right iliac fossa
PCT	porphyria cutanea tarda	RIG	radiologically inserted gastrostomy
PDAI	pouchitis disease activity index	RUQ	right upper quadrant
PE	pulmonary embolism	SAAG	serum-to-ascites albumin gradient
PEG	percutaneous endoscopic gastrostomy or polyethylene glycol	SAMe	S-adenosylmethionine
PEJ	percutaneous endoscopic jejunostomy	SBP	spontaneous bacterial peritonitis
PET	positron emission tomography or pancreatic endocrine tumour	SBT	Sengstaken-Blakemore tube
PHG	portal hypertensive gastropathy	SC	subcutaneous
PICC	peripherally inserted central catheter	SCA	sickle cell anaemia
PMC	pseudomembranous colitis	SCC	squamous cell carcinoma
PN	parenteral nutrition	SCFA	short-chain fatty acid
PNS	peripheral nervous system	SD	standard deviation
PO	by mouth (<i>per os</i>)	SEDU	specialist eating disorder unit
POEM	peri-oral endoscopic myotomy	SeHCaT	selenium-75 labelled homotaurocholic acid test
PPI	proton pump inhibitor	SEMS	self-expanding mesh metal stent
ppm	parts per million	SIADH	syndrome of inappropriate antidiuretic hormone secretion
PPPD	pylorus-preserving pancreatico-duodenectomy	siRNA	small interfering ribonucleic acid
PR	by (<i>per</i>) rectum	SL	sublingual
prn	as required (<i>pro re nata</i>)	SLA	soluble liver antigen
PRO	patient-reported outcome	SLE	systemic lupus erythematosus
PSA	prostate-specific antigen	SMA	superior mesenteric artery
PSC	primary sclerosing cholangitis	SOD	sphincter of Oddi dysfunction
PT	prothrombin time	SOM	sphincter of Oddi manometry
		SOS	sinusoidal obstruction syndrome
		SPECT	single photon emission computed tomography
		SRS	somatostatin receptor scintigraphy

SSRI	selective serotonin-reuptake inhibitor	TSH	thyroid-stimulating hormone
stat	immediately (<i>statim</i>)	TTS	through-the-scope
SVC	superior vena cava	U&E	urea and electrolytes
SVR	sustained virological response <i>or</i> systemic vascular resistance	UC	ulcerative colitis
TACE	transcatheter chemoembolization	UDCA	ursodeoxycholic acid
TAE	transanal excision	UGT	uridine diphosphate glucuronyl transferase
TB	tuberculosis	UKELD	UK Model for End-stage Liver Disease
TDM	therapeutic drug monitoring	ULN	upper limit of normal
tds	three times a day	UO	urine output
TES	transanal endoscopic surgery	US	ultrasound
TG	triglyceride	UTI	urinary tract infection
TG(N)	thioguanine (nucleotide)	VBL	variceal band ligation
TGF	transforming growth factor	VCE	video capsule endoscopy
Th1	T helper cell type 1	VIP	vasoactive intestinal polypeptide
TIBC	total iron-binding capacity	VL	viral load
TIPSS	transjugular intrahepatic portosystemic shunt	VOD	veno-occlusive disease
TMP-SMX	trimethoprim–sulfamethoxazole (co-trimoxazole)	VTEC	verocytotoxin-producing <i>E. coli</i>
TNF	tumour necrosis factor	VZV	varicella zoster virus
TNM	tumour–node–metastasis (staging system for cancer)	WCC	white cell count
TOF	tracheo–oesophageal fistula	WDP	Wilson's disease protein
TPMT	thiopurine methyltransferase	WE	Wernicke's encephalopathy
TPN	total parenteral nutrition	WHO	World Health Organization
		wk	week
		WOPN	walled-off pancreatic necrosis
		ZES	Zollinger–Ellison syndrome



Plate 1 Brown macules on lips in patient with Peutz-Jeghers syndrome



Plate 2 Microstomia due to systemic sclerosis



Plate 3 Hereditary haemorrhagic telangiectasia

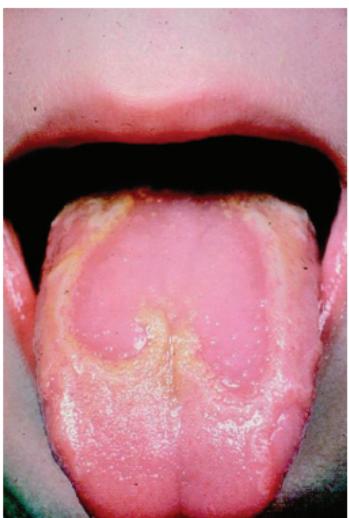


Plate 4 Geographic tongue



Plate 5 Glossitis



Plate 6 Wickham's striae: associated with lichen planus

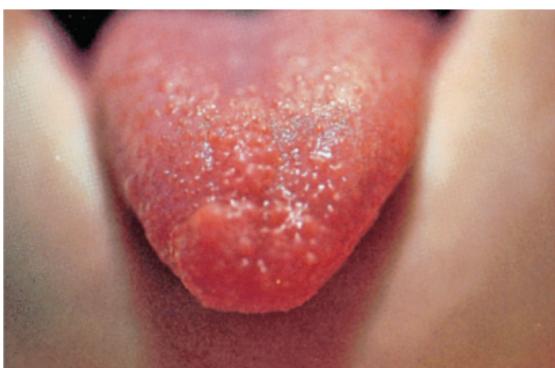


Plate 7 Cowden syndrome, with multiple lingual papillomata

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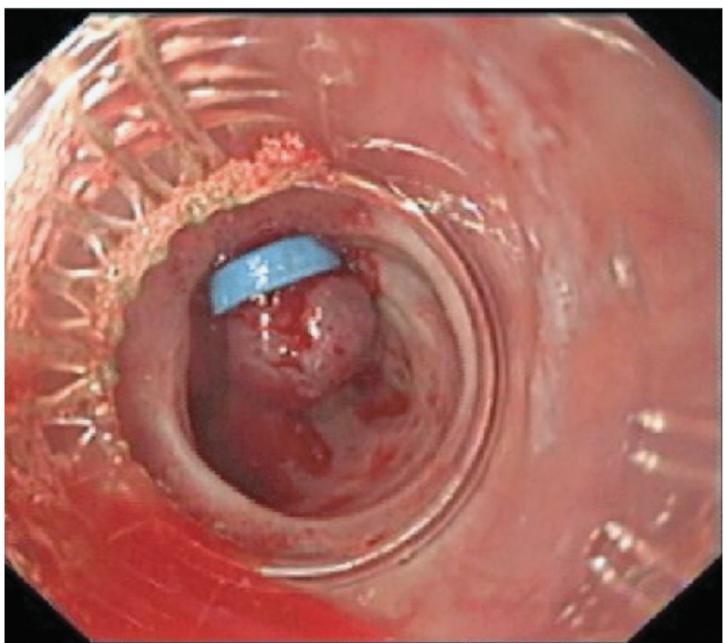


Plate 8 Variceal band ligation

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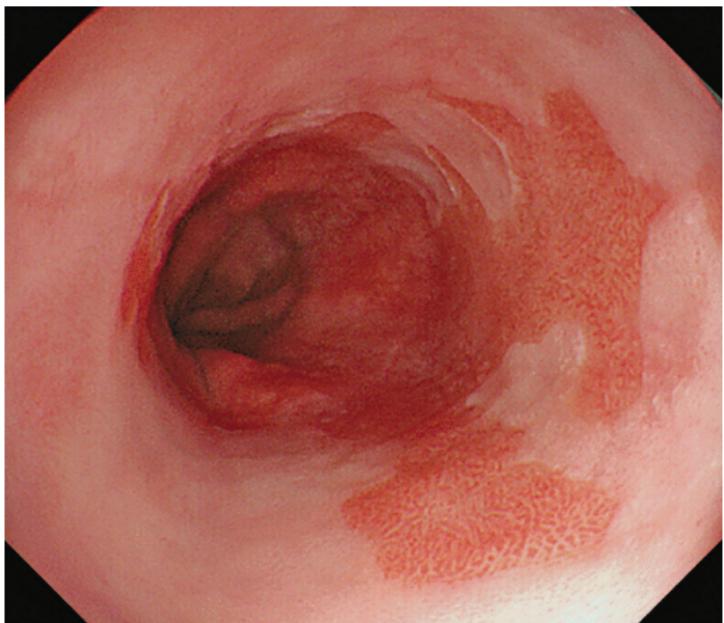


Plate 9 Barrett's oesophagus

Reproduced with permission from Rebecca C. Fitzgerald and Massimiliano di Pietro, *Oxford Textbook of Medicine*, Oxford University Press



Plate 10 Stenosing oesophageal carcinoma on a background of Barrett's oesophagus

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Plate 11 Oesophageal web on endoscopy



Plate 12 Eosinophilic oesophagitis

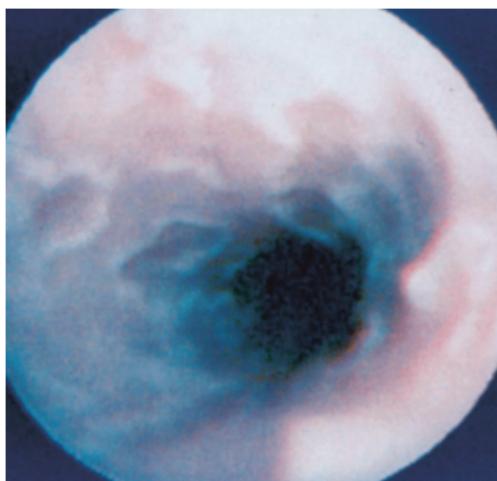


Plate 13 Herpes simplex oesophagitis

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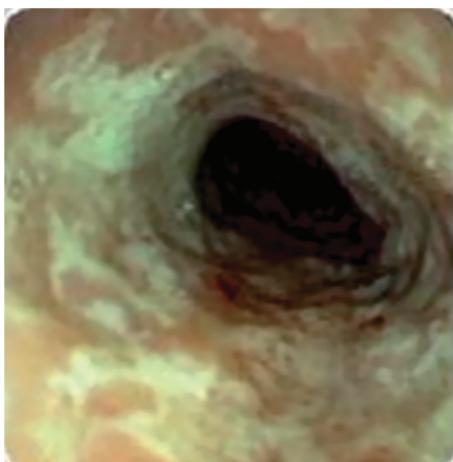


Plate 14 CMV oesophagitis

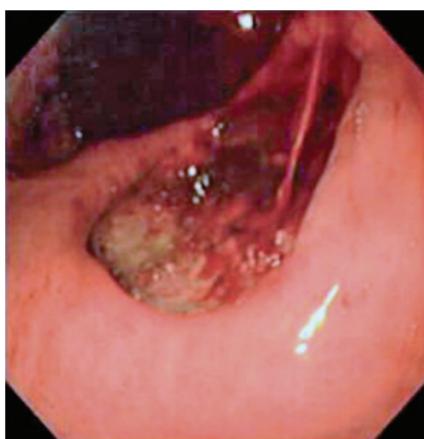


Plate 15 Endoscopic view of bleeding ulcer

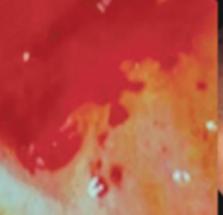
Ia	Ib	IIa
Spurting bleed	Oozing bleed	Non-bleeding visible vessel
		
IIb	IIc	III
Adherent clot	Flat spot in ulcer crater	Clean base ulcer
		

Plate 16 Forrest classification



Plate 17 Endoscopic image of spurting Dieulafoy lesion

Reproduced with permission from Klaus Mönkemüller and Walter Curioso, World Gastrointestinal Atlas of Endoscopy (www.giatlas.com)



Plate 18 Angiodysplasia



Plate 19 Duodenal ulcer



Plate 20 Duodenal familial adenomatous polyposis

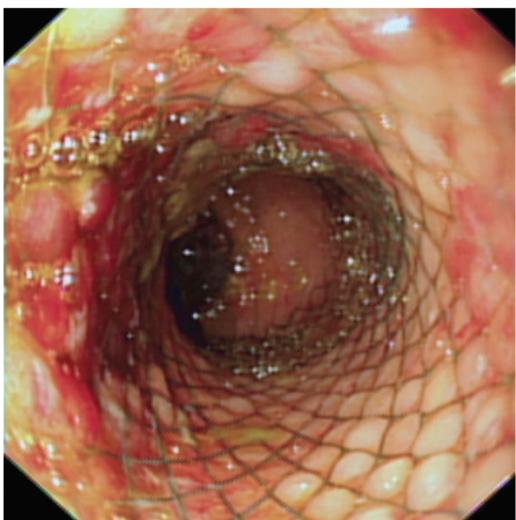


Plate 21 Duodenal mesh metal stent



Plate 22 Ulcerative colitis (illustrating the increasing grades of Mayo endoscopic subscore appearances; see Table 4.25)

Reproduced with permission from Samaan, M.A., et al. A Systematic Review of the Measurement of Endoscopic Healing in Ulcerative Colitis Clinical Trials: Recommendations and Implications for Future Research, *Inflammatory Bowel Diseases*, 20:8, 1465–1471, 2014

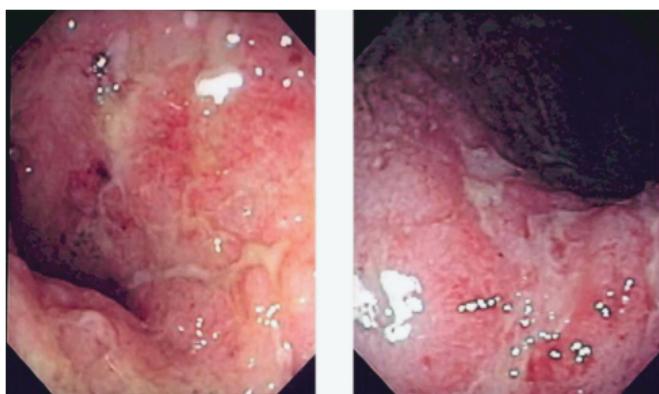


Plate 23 Crohn's disease. Aphthous and serpiginous ulceration

Reproduced with permission from Samaan M.A., D'Haens G. (2015) The Use of Endoscopy to Follow the Clinical Course of Crohn's Disease. In: Kozarek R., Chiorean M., Wallace M. (eds) Endoscopy in Inflammatory Bowel Disease. Springer, Cham



Plate 24 Crohn's disease. Cobblestone appearance of the mucosa

Reproduced with permission from Samaan M.A., D'Haens G. (2015) The Use of Endoscopy to Follow the Clinical Course of Crohn's Disease. In: Kozarek R., Chiorean M., Wallace M. (eds) Endoscopy in Inflammatory Bowel Disease. Springer, Cham

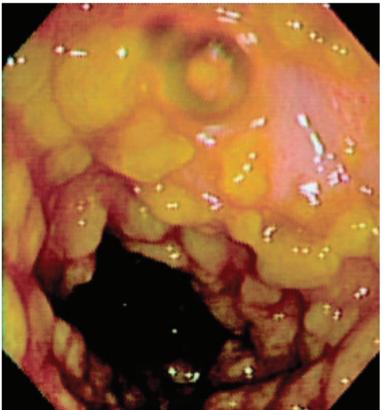


Plate 25 Endoscopic image of pseudomembranous colitis caused by *C. difficile*



Plate 26 Radiation colitis

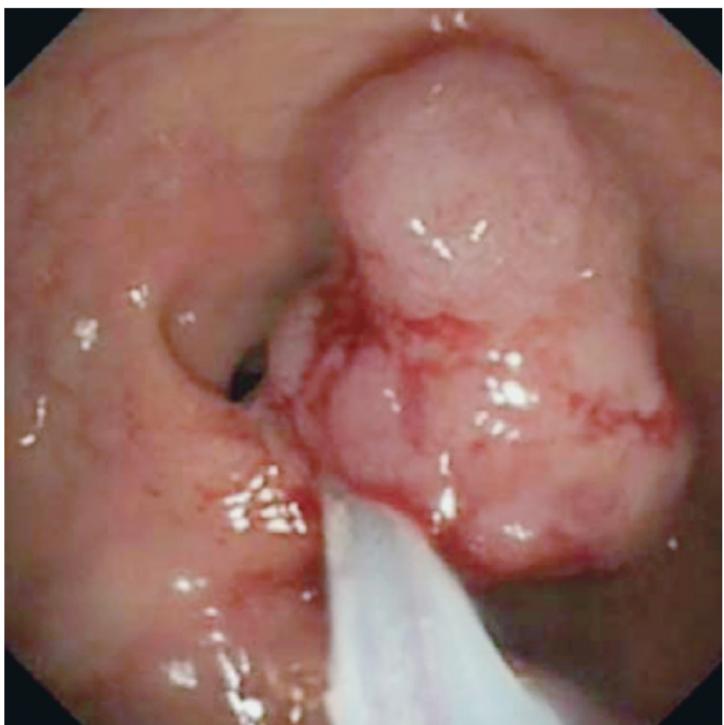


Plate 27 Colonic adenomatous polyp

Reproduced with permission from Matthew D. Gardiner and Neil R. Borley, Training in Surgery: The essential curriculum for the MRCS, Oxford University Press



Plate 28 Colon Cancer

Reproduced with permission from Daniel Marks and Marcus Harbord, Emergencies in Gastroenterology and Hepatology, Oxford University Press

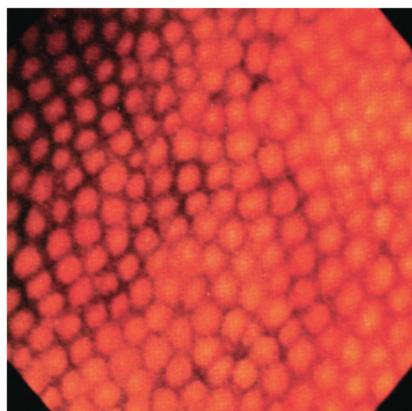


Plate 29 Kudo pit pattern: type 1 (round pits)

Reproduced with permission from Kudo, Shin-el, et al, Diagnosis of colorectal tumourous lesions by magnifying endoscopy, Gastrointestinal Endoscopy, 1996, American Society for Gastrointestinal Endoscopy

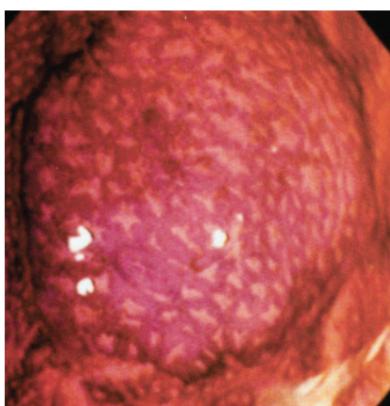


Plate 30 Kudo pit pattern: type 2 (stellar or papillary pits)

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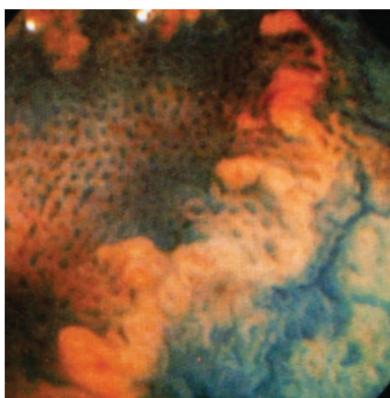


Plate 31 Kudo pit pattern: type 3s (small tubular or roundish pits)

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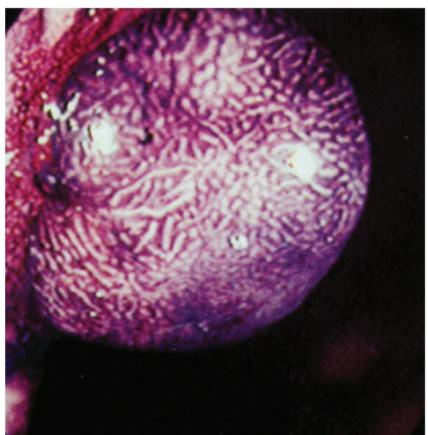


Plate 32 Kudo pit pattern: type 3L (large tubular or roundish pits)

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Plate 33 Kudo pit pattern: type 4 (branch-like or gyrus-like pits)

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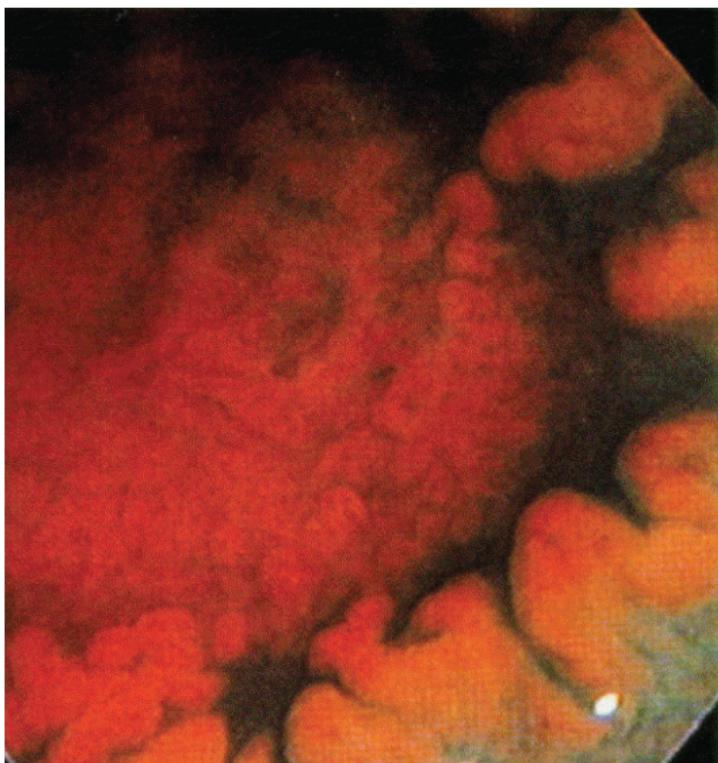


Plate 34 Kudo pit pattern: type 5 (non-structural pits)

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Plate 35 Melanosis coli

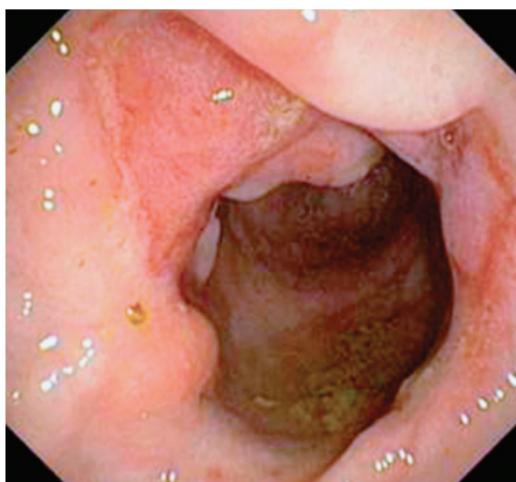


Plate 36 Solitary rectal ulcer

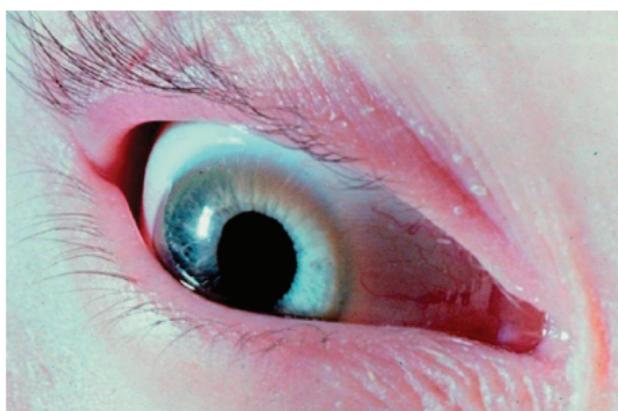


Plate 37 Kayser-Fleischer rings found round the edge of the iris

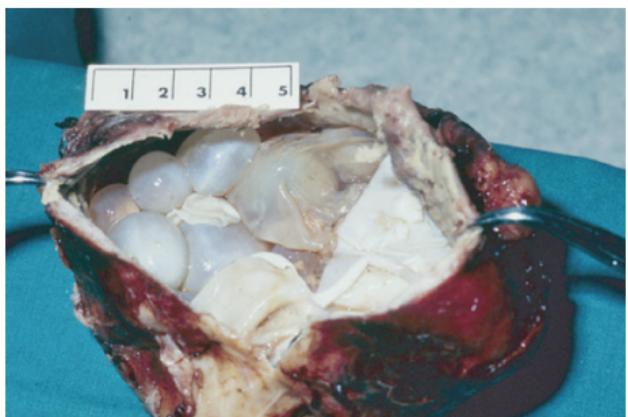


Plate 38 Hydatid cyst. Right hepatectomy specimen showing multiple daughter cysts

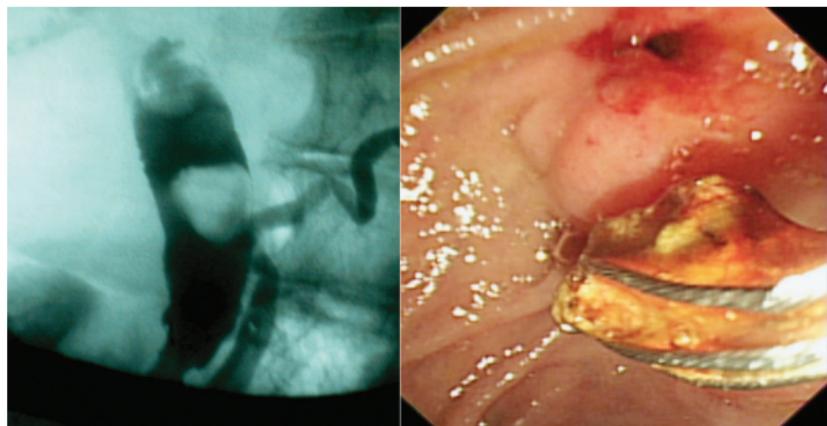


Plate 39 Common bile duct (CBD) stone (left) on cholangiogram at ERCP and (right) within the duodenum following removal with an endoscopic basket

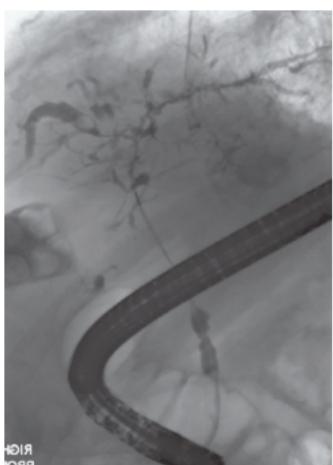


Plate 40 Primary sclerosing cholangitis

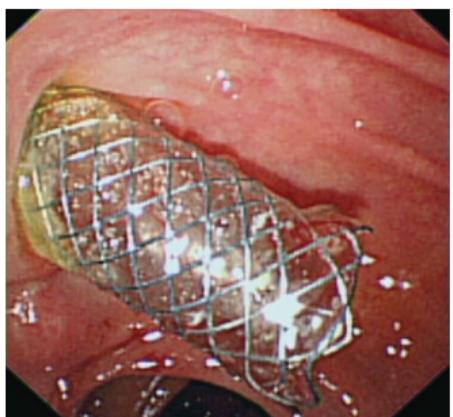


Plate 41 Biliary mesh metal stent

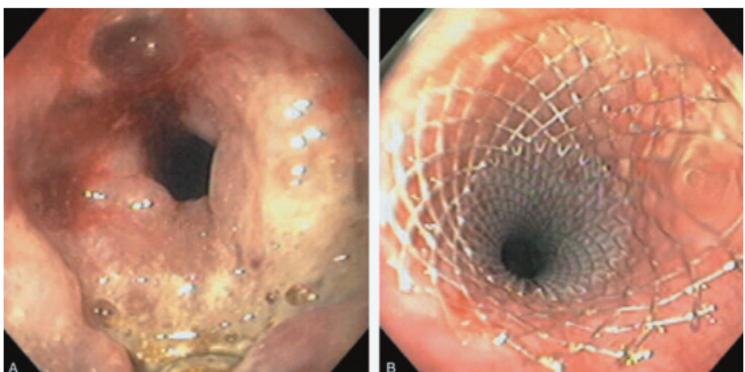


Plate 42 Endoscopically placed biliary and duodenal mesh metal stents in a patient with inoperable pancreatic cancer

Reproduced with permission from Feldman M, Friedman LS, and Sleisenger MH (2003). *Sleisenger and Fordtran's Gastrointestinal and Liver Disease*, Elsevier



Plate 43 Dermatitis herpetiformis



Plate 44 Erythema nodosum



Plate 45 Pyoderma gangrenosum



Plate 46 Henoch-Schönlein purpura

Reproduced with permission from Miguel A. González-Gay, Ricardo Blanco, and Trinitario Pina, *Oxford Textbook of Vasculitis*, Oxford University Press



Plate 47 Scrotal ulceration due to Behcet's disease



Plate 48 Ehlers Danlos



Plate 49 Keratoderma blenorrhagica, often seen as part of Reiters syndrome

Approaches to common clinical problems

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Acute diarrhoea

Most cases of acute diarrhoea are due to infections and are typically self-limiting, with intervention limited to oral rehydration. Diarrhoea lasting >14d is usually described as persistent (<30d duration) or chronic (>30d), and typically due to other causes (exceptions include  *Giardia* and  *Yersinia*): see ► [Approach to chronic diarrhoea](#).

Key questions in the history

- How long is the history?
- Are there systemic symptoms (fever, tachycardia) or vomiting?
- Is there recognizable blood in the stool?
- How frequent are the stools?
- Presence and location of any associated abdominal pain?
- Any contact with possible infected food or water?
- Recent travel history?
- Any contact with similarly ill people? Anyone in the family unwell?
- On examination, look for signs of dehydration and malnutrition.

Risk factors

- Age. After weaning, the protective effects of breast milk are lost. The elderly may have ↓ immune competence, but also ↓ acid secretion (e.g. due to *Helicobacter* infection, or drugs such as → PPIS).
- Immune deficiency. Includes patients with HIV (see  [HIV and the gut](#)), and those on anticancer chemotherapy.
- Medication. See also  [antibiotic-associated diarrhoea](#).
- Travel.
- Infected food and water: either a true infection (with ingestion of enteropathogens that multiply in gut), or ingestion of toxin in food contaminated with enterotoxin-producing microorganism.
- Known sensitivity to certain foods (see  [food allergy/intolerance](#)).

Classifying acute diarrhoea

Subdivide according to presence (Box 1.1) or absence (Box 1.2) of blood in stool, since the causes are largely different. Also consider whether the process involves mostly small or large intestine.

Box 1.1 Causes of acute diarrhoea with blood

- \ominus Shigella.
- Enterohaemorrhagic \ominus E. coli.
- \ominus Campylobacter.
- \ominus Salmonella.
- \ominus Yersinia.
- \ominus Amoebic dysentery.
- Antibiotic-associated colitis (see \ominus Clostridioides difficile).
- \ominus Schistosoma (*mansonii*, *intercalatum*, or *japonicum*) or *Trichuris*.
- Diverticulitis.
- Ischaemic colitis.

Box 1.2 Causes of acute diarrhoea without blood

- Viruses (\ominus rotavirus, norovirus, astrovirus, \ominus adenovirus, coronavirus).
- Bacteria:
 - Mild infection with \ominus Shigella, \ominus Salmonella, or \ominus Campylobacter.
 - \ominus E. coli (enterotoxigenic, enteropathogenic, enteroaggregative).
 - \ominus Cholera, \ominus Clostridia species.
- Protozoa: \ominus Giardia, cryptosporidiosis, Cyclospora.
- \ominus Strongyloides.
- Food toxins.
- Malaria.
- Systemic sepsis.
- Toxic shock syndrome.

Pathogens targeting small bowel include toxigenic bacteria, viruses, and *Giardia lamblia* (see \ominus giardiasis). These produce large volume, watery diarrhoea, and mid-abdominal pain. Blood and faecal leucocytes are rare. See Table 1.1.

Pathogens targeting large bowel are usually invasive. They produce lower abdominal or rectal pain, tenesmus, mucoid, or bloody diarrhoea with many faecal leucocytes, and inflamed rectal mucosa. See Table 1.2.

A few pathogens (e.g. \ominus Salmonella, \ominus Yersinia) infect the lower small bowel but can invade the colon as well. These can present on a spectrum from watery diarrhoea to colitis.

Table 1.1 Infectious agents targeting the small bowel

Agent	Source and incubation period
Viruses	Rotavirus, norovirus, calcivirus, torovirus, enteric adenovirus
Bacteria that colonize gut	<p><i>Vibrio cholerae</i> 2–144h. See cholera</p> <p><i>Vibrio parahaemolyticus</i> Raw fish or seafood, 2–48h. Usually a short illness</p> <p>Yersinia Principally invade lower small bowel but may invade colon. Clinical spectrum varies from watery diarrhoea to colitis</p> <p>Salmonella</p>
<i>E. coli</i> (ETEC, EPEC)	See Escherichia coli
<i>Giardia</i>	See giardiasis

Table 1.2 Infectious agents targeting large bowel

Shigella	Highly contagious. Spread usually faeco-oral but outbreaks can occur related to contaminated milk, ice-cream, or water. Toxigenic phase of fever, pain and diarrhoea starts early after infection
Campylobacter	Incubation period 24–72h. Usual source is infected animals. Most infections result from improperly cooked chicken (50–70% cases)
Salmonella	As <i>Campylobacter</i> . Toxic megacolon and perforation due to colitis can occur—most common when diarrhoea has lasted 10–15d
<i>E. coli</i> (EIEC, EHEC)	1–14d, mean 3d. See Escherichia coli
<i>Entamoeba histolytica</i>	See amoebiasis
<i>C. difficile</i>	See clostridial infections in GI tract

Investigations

Most attacks are self-limiting. In general, investigation is indicated in following circumstances:

- Course >2wk.
- Signs of systemic upset, including fever.
- Tenesmus or bloody diarrhoea.

- Special circumstances:
 - Outbreaks suggesting food poisoning.
 - MSM.
 - Immunocompromised host.
 - Ingestion of raw shellfish.
 - Antibiotic usage.

Stool culture is often requested, but few centres test for all pathogens; mixed infections are common, single stool cultures insufficient for some pathogens, and results often come back too late to influence management. In practice, apart from investigation of outbreaks and surveillance, stool culture in uncomplicated cases should be limited to exclusion of those pathogens for which antibiotic treatment is indicated (parasites, *Shigella*, *V. cholerae*) or where there are other possible causes of acute diarrhoea (e.g. inflammatory bowel disease).

Stool microscopy

- Ova, cysts, and parasites.
- Measurement of faecal leucocytes now rarely performed, or replaced by \triangleright faecal calprotectin. Will be positive in \ominus *Shigella*, \ominus *Campylobacter*, and EIEC & EHEC infections; variably so with \ominus *Salmonella*, \ominus *Yersinia*, and *C. difficile*; and negative in \ominus *cholera*, ETEC/EPEC, viral diarrhoea, and \ominus *giardiasis*.

Identifying microbial antigens

- ELISA for \ominus *Giardia* is more accurate than stool microscopy and should be ordered when there is an appropriate history.
- Serology/antibody testing are useful for \ominus *Yersinia enterocolitica*.
- ELISA kits are available for \ominus *Strongyloides* and \ominus *schistosomiasis*.

Imaging

AXR should be taken if patient toxic, to look for evidence of diffuse colitis, ileus, or \ominus toxic megacolon.

Treatment

Fluid replacement

- **Oral rehydration** nearly always preferred route, but if patient vomiting or intravascularly deplete (resting tachycardia with postural hypotension), **IV fluids** may be necessary.
- Unlike situation in patients with intestinal resection or jejunostomy, where sodium concentration of 90–120mM provides maximum salt and water absorption, optimal sodium concentration for rehydration in cases of mild–moderate acute diarrhoea probably \approx 50mM. Substitution of starch for rice, or cereal for glucose, associated with less diarrhoea and more rapid resolution.

Diet

Eating during an attack of acute diarrhoea can be uncomfortable because any food provides a stimulus to defaecation. No benefit to fasting, but dairy products should be avoided because of temporary \ominus lactose intolerance. Alcohol, caffeine, and fizzy drinks should be avoided.

Drugs

Antimotility agents can be very useful but should not be used if acute severe colitis because of risk of precipitating \ominus toxic megacolon. \rightarrow LOPERA-MIDE drug of choice.

Indication for antibiotics

- Reasonable to withhold empiric antibiotic therapy in most stable patients pending stool testing. Concerns about precipitating \ominus haemolytic–uraemic syndrome in patients with enterohaemorrhagic \ominus *E. coli*, but given most cases of bloody diarrhoea in adults not due to this pathogen, benefits of empiric treatment in symptomatic adults with severe bloody diarrhoea likely to outweigh risk.
- Community-acquired diarrhoea: >4 stools/d for >3d with ≥ 1 of pain, fever, vomiting, myalgia, and/or headache. Quinolone such as \rightarrow CIPROFLOXACIN 250–500mg bd. Optimal duration not known (although 3d suggested), but also single dose given early very effective.
- Traveller's diarrhoea in adults. Duration of diarrhoea \downarrow when quinolone such as \rightarrow CIPROFLOXACIN used.
- Isolation of specific pathogens: \ominus *Shigella*, \ominus *Vibrio cholerae*, \ominus *Salmonella typhi*, \ominus *Clostridiooides difficile*. For antibiotic selection for specific organisms, see relevant A-Z entry.
- *Giardia lamblia* (laboratory proven or clinical suspicion high).
- Laboratory-proven enteropathogenic \ominus *E. coli* infection, especially in very young or old. Antibiotic treatment of enterohaemorrhagic *E. coli* of no proven benefit, and theoretical risk of precipitating \ominus haemolytic–uraemic syndrome (HUS).

Diarrhoea in travellers

Around 30–50% of travellers to developing countries have an episode of infective diarrhoea, which is usually mild–moderate in severity and self-limiting. Investigation and treatment may be needed for bloody diarrhoea, when invasive organisms are involved, or when diarrhoea persists for >2wk.

Causal organisms

- Enterotoxigenic \ominus *E. coli* (ETEC) most common cause worldwide (also leading bacterial cause of gastroenteritis on cruise ships), but \ominus *Shigella* accounts for increasing proportion, and \ominus *Campylobacter* important in travellers to Asia.
- Other bacterial pathogens include *Aeromonas*, *Plesiomonas*, and *Vibrio*.
- Viruses (rotavirus, norovirus) responsible for up to 30% of cases.
- Parasitic causes uncommon, but *Giardia* found in 5%. \ominus *Cyclospora* seen occasionally. \ominus *Cryptosporidium* can be problem for immunocompromised.

- Consider \ominus amoebiasis in people with bloody stools.
- Geography affects likely cause. While ETEC and \ominus *Shigella* account for majority of isolates in Africa and Middle East, over 50% of people affected in Asia have \ominus *Campylobacter*.

Natural history, and mode of infection

- Most cases occur 5–15d after arrival. Malaise, anorexia, abdominal cramps, watery diarrhoea, and sometimes nausea with vomiting are hallmarks. Fever in ~50%. Most cases resolve in 6–10d.
- Gastric hypoacidity and immunosuppression ↑ risk, as does \ominus ulcerative colitis, \ominus Crohn's disease, and \ominus coeliac disease.
- Careful selection of food and drink to minimize infection ↓ but does not eliminate risk. Two other approaches are chemoprophylaxis or dispensing medication to be taken if diarrhoea develops.

Chemoprophylaxis

The Center for Disease Control (CDC; Atlanta, USA) does not recommend routine use of prophylactic antibiotics because of concerns about side effects and selection of resistant strains. Two settings where prophylactic antibiotics may be used are:

- Short-term travellers (2wk or less in endemic area) whose business or vacation schedule would be severely disrupted by an episode of diarrhoea.
- Patients with underlying medical conditions or immunocompromise.

Where ETEC, \ominus *Shigella*, or \ominus *Salmonella* predominate, a quinolone (ciprofloxacin 500mg od) is the drug of choice. For travellers to Asia, \ominus *Campylobacter* is common and frequently resistant to quinolones: azithromycin 500mg od should be used.

Self-medication with antibiotics A single dose of → CIPROFLOXACIN 500mg taken at 1st sensation of impending upset can ↓ duration and intensity of infection.

Other aspects of self-treatment Benefit of adding antidiarrhoeal agents such as loperamide (see → ANTIDIARRHOEAL AGENTS) to antibiotics unclear. Very important to ensure adequate fluid and electrolyte replacement using an oral rehydration solution, such as World Health Organization (WHO) rehydration solution.

Diagnostic approach to diarrhoea in the returning traveller

- Initial approach is the same as that for self-treatment of traveller's diarrhoea (3d of quinolone or azithromycin, ± loperamide, and adequate fluid/electrolyte replacement).
- Diarrhoea can be prominent symptom of **malaria**. Examine blood film for *Plasmodium* in travellers returning from malarial areas with fever and diarrhoea.
- Watery diarrhoea persisting >10d most commonly due to \ominus *giardiasis*. Send stool to be examined for *Giardia*, *Cryptosporidium*, *Cyclospora*, and *Isospora*.
- Empirical treatment with → METRONIDAZOLE or tinidazole for *Giardia* often reasonable. If fails to improve, further investigation with upper GI endoscopy and small bowel biopsy, sigmoidoscopy, and rectal biopsy required. If symptoms and biopsies consistent with \ominus tropical sprue, tetracycline with folic acid indicated.

Agitation and confusion in the GI patient

Background

'Disturbed consciousness' covers a wide range of clinical states, from mild disorientation and agitation, to drowsiness and coma. The midnight call to the ward to see a confused uncooperative 'liver patient' often represents a diagnostic and management challenge. The range of possible causes is wide (Box 1.3), but it is important to make the correct diagnosis, as treatment for one cause may be detrimental to another. Acute confusional states are usually due to organic cause, and rarely because of mental illness.

Box 1.3 Causes of disturbed consciousness in the GI patient

- ▲ Hepatic encephalopathy ▲.
- ⚡ Alcohol withdrawal/delirium tremens.
- ⚡ Wernicke's encephalopathy.
- GI bleed.
- Intracranial bleed (e.g. subdural).
- Seizure or post-ictal state.
- Sepsis.
- Intracranial infection (meningitis, encephalitis, abscess).
- Hypoglycaemia.
- Hyponatraemia.
- Illicit drug use/overdose.
- Hypoxia.
- Hypercapnia.
- Severe acute renal failure.
- Zinc deficiency.

Assessment

History

- Usually from family, friends, and medical and nursing staff.
- Find out about previous episodes of confusion, head injury, and psychiatric disease.
- Is there a history of alcohol excess, and when did patient last drink?
- Examine drug chart—any new sedatives/constipating agents?

Full general and neurological examination essential

- Review observation chart, including temperature. Ensure vital signs stable and airway protected.
- Is patient in pain (agitation is important manifestation of pain in patients with cognitive impairment).

- Specifically look for:
 - Signs of sepsis.
 - Evidence of malnutrition (\ominus Wernicke's encephalopathy).
 - Smell breath (for alcohol and foetor hepatis of encephalopathy).
 - Jaundice and signs of chronic liver disease or \ominus portal hypertension (e.g. splenomegaly, ascites).
 - Liver flap (\blacktriangle hepatic encephalopathy \blacktriangle).
 - Needle marks/tracks (drug overdose, sepsis, cerebral abscess).
 - Tremulousness, tachycardia, and sweating may relate to \ominus alcohol withdrawal (?stopped due to admission 48–72h previously).

Immediate investigations

- Finger prick for glucose BM.
- Pulse oximetry.
- Take blood for:
 - FBC, clotting.
 - U&Es, liver function tests (LFTs), CRP, glucose.
 - Ammonia (in patients with known or suspected chronic liver disease).
 ! However, caveats that ammonia levels are often chronically \uparrow in patients with liver disease and elevated readings should not deflect from searching for other causes of perturbed consciousness. In addition, normal value does not completely exclude diagnosis of encephalopathy (which is primarily clinical).
- Exclude sepsis (CXR, blood cultures, MSU/CSU, ascitic tap).
- Consider CT brain (especially if head injury or focal neurology).
- Consider blood and urine for alcohol/drug screen.

Management

- If patient agitated or aggressive, remove objects from around the bed with which the patient may harm themselves or others (e.g. glass vases).
- Nurse in a calm quiet environment, with as few people 'coming and going' as possible. Reasonable lighting helpful to \downarrow disorientation.
- Give Pabrinex 2 pairs IV/IM tds for 5d if any risk of \ominus Wernicke's encephalopathy.
- Use of midazolam 0.5–5mg PO/IM/IV (slow up-titration) or haloperidol 5–10mg PO/IM may be necessary in agitated patient, but should be avoided in patients with \blacktriangle hepatic encephalopathy \blacktriangle or \ominus alcohol withdrawal.
- Specific management depends on likely diagnosis (see \blacktriangle hepatic encephalopathy \blacktriangle , \ominus alcohol withdrawal, \ominus Wernicke's encephalopathy).

Anaemia and occult GI bleeding

Anaemia (Hb <120g/L in ♀, <130g/L in ♂) is common in GI practice, and a frequent reason for referral to gastroenterologists by other specialists. Often, gastroenterologists are asked for an opinion on the cause of a macrocytic or microcytic anaemia. Careful testing to identify various haematinic deficiencies is crucial (see Box 1.4). A classification of anaemia related to GI disease is shown in Table 1.3.

Table 1.3 Classification of anaemia related to GI disease

Cause	Type of anaemia
GI bleeding	Iron deficiency
↓ Red cell production	Haematinic deficiency: \ominus iron, \ominus vitamin B ₁₂ or \ominus folic acid (deficiency seen in pregnancy, ↑ cell turnover, inflammation) Marrow failure: aplastic anaemia, red cell aplasia, marrow infiltration
↑ Red cell destruction	Congenital (haemoglobinopathies, hereditary spherocytosis, red cell enzyme defects) Acquired (immune/non-immune)
Abnormal red cell maturation	Sideroblastic anaemia, myelodysplasia
Drug-related anaemia	See text. May be caused by bleeding (antiplatelets, non-steroidal anti-inflammatory drugs (NSAIDs), anticoagulants), drug-induced haemolysis, or marrow aplasia (e.g. mesalazine)
Extraintestinal effects of GI disease	Anaemia of chronic disease Liver, renal, endocrine disease

Haematinic deficiency

Most important are **iron, folic acid, and vitamin B₁₂**, but **copper and vitamins A, B₆, C, E, riboflavin, and nicotinic acid** also needed for erythropoiesis. Deficiency can arise through inadequate intake, malabsorption, ↑ need or use, or loss.

Box 1.4 Basic tests for haematinic deficiency

- FBC: Hb, red cell indices (MCV, MCHC, MCH, RDW), WCC and differential, platelets).
- Blood film examination.
- Reticulocyte count, haptoglobin, Coomb's test.
- Iron, total iron binding capacity (TIBC), transferrin saturation, ferritin.
- Vitamin B₁₂, and serum (\pm red cell) folate.
- U&Es.
- ➤ LFTs including albumin and γ GT.

Table 1.4 Causes of common haematinic deficiency in GI disease

	Iron	B ₁₂	Folate
Nutritional	Rarely sole cause	Vegans	Poor diet: elderly, alcohol misuse, institutionalized
Malabsorption			
Stomach	Anacidity: ➡ Atrophic gastritis ➤ Gastrectomy	➡ Pernicious anaemia ➡ Atrophic gastritis	➤ Gastrectomy
Small intestine	➡ Coeliac disease ➡ Tropical sprue	➡ Bacterial overgrowth Ileal resection ➡ Crohn's disease ➡ Coeliac disease ➡ Tropical sprue Fish ➡ tapeworm	➤ Gastric bypass ➡ Coeliac disease ➡ Tropical sprue ➡ Systemic sclerosis ➡ Amyloidosis ➡ Giardia Diabetic enteropathy ➡ Lymphoma ➡ Whipple's disease
Other		➡ Chronic pancreatitis	Alcohol
Loss or ↑ utilization	Bleeding		Liver disease ➡ Crohn's disease

For details of treatment of haematinic deficiencies and further details of individual causes, see ➡ iron, ➡ vitamin B₁₂, and ➡ folic acid.

Increased red cell destruction: haemolysis

Red cell destruction is mainly extravascular in liver, spleen, and bone marrow. Haem is metabolized to bilirubin, conjugated in liver, and excreted in faeces and urine.

Congenital causes

- Unconjugated hyperbilirubinaemia due to excess haemolysis seen in neonate as result of:
 - **Congenital spherocytosis** (in adult, spherocytosis usually indicates antibody-mediated red cell destruction), or
 - **Non-spherocytotic causes** such as inherited red cell enzyme defects (e.g. G6PD deficiency).
- **Haemoglobinopathies** These include structural haemoglobin variants such as sickle cell disease and disorders of globin chain synthesis (thalassaemias).

Acquired causes

- In adults can be seen in severe liver disease due to abnormal lipid composition of red cells.
- Disseminated cancers (e.g. arising from gastric or pancreatic primary) can cause disseminated intravascular coagulation and micro-angiopathic haemolytic anaemia (see Tables 1.4 and 1.5).

Diagnosis

Plasma haptoglobins bind to haemoglobin and are ↓ in intravascular haemolysis and in liver disease. Coomb's test will confirm autoimmune-mediated haemolysis. Haemolysis can result in pigment gallstones, which can be presenting feature of illness.

Drug-related anaemia

Think of the following:

- Upper GI irritation causing blood loss: → NSAIDS, aspirin. Combination of → NSAIDS and → CORTICOSTEROIDS associated with high risk of upper GI bleeding.
- Bleeding due to or exacerbated by specific drugs, e.g. clopidogrel, warfarin, heparin, direct oral anticoagulants (e.g. dabigatran, rivaroxaban, apixaban).
- Drug-induced haemolysis, e.g. oxidative haemolysis due to sulfasalazine, dapsone, or ribavirin.
- Production impairment (e.g. aplasia secondary to mesalazine).

Anaemia in liver disease

Table 1.5 Causes of anaemia in liver disease

Cause	Comment
Dilutional	↑ Plasma volume, splenomegaly.
Iron deficiency	Bleeding. Iron status can be difficult to establish. Ferritin may be ↑ as an acute phase protein. Transferrin, accounting for much of TIBC, often ↓. MCV may be normal or ↑ due to concomitant effects of chronic alcohol use or folate deficiency.
Vitamin B ₁₂ and folate	Liver stores B ₁₂ and folate. Folate often deficient in alcohol misuse due to poor nutrition and effect of alcohol in ↓ folate absorption.
Haemolysis	May be autoimmune in association with autoimmune hepatitis . Red cell lifespan ↓ due to abnormal membrane—if severe can produce 'spur cell' anaemia. Alcohol can cause sideroblastic anaemia. Haemolysis seen in Wilson's disease (probably due to copper toxicity to red cells). Zieve's syndrome .
Aplastic anaemia	Viral hepatitis: parvovirus, hepatitis A, B, C , EBV, CMV. Hepatitis often mild and marrow aplasia severe: damage may be immune-mediated. Alcohol may have direct marrow toxicity effects.

Iron-deficiency anaemia presumed to be due to occult GI blood loss

This is a common situation in gastroenterological practice, and a common reason for referral by non-gastroenterologists. Up to 100ml blood loss/d can still result in grossly normal looking stools. The source of bleeding is unidentified in ~5% of patients with GI bleeding.

► [Faecal occult blood testing](#) can be helpful, particularly if menorrhagia is suspected as a cause of anaemia in menstruating ♀. Iron deficiency diagnosed by either ↓ ferritin or ↓ transferrin saturation (ratio of [iron](#) to TIBC). Beware missing iron deficiency because of normal TIBC: this reflects mostly transferrin synthesis by liver, which can be impaired in chronic disease or inflammation.

Diagnosing the cause of iron-deficiency anaemia

History

- Focus on drugs that injure GI mucosa (e.g. aspirin, NSAIDs, bisphosphonates, potassium salts).
- Take a careful family history for bleeding disorders (e.g. unexpectedly heavy bleeding after relatively minor procedures, such as dental extractions).

Examination

Look for cutaneous stigmata of systemic diseases (\oplus dermatitis herpetiformis, neurofibromas, lip freckles suggestive of \ominus Peutz-Jeghers syndrome (Plate 1), mucosal telangiectasia in \oplus hereditary haemorrhagic telangiectasia (Plate 3), osteomas suggestive of \oplus Gardner's syndrome).

Investigations

Initial assessment may direct investigations to particular part of GI tract. For example:

- Dyspepsia or a clear history of NSAID or other irritant drug ingestion directs need for upper GI endoscopy, and a positive family history of \oplus colon cancer, change of bowel habit, or iron deficiency in elderly patient with aortic stenosis (suggesting possibility of \oplus angiodysplasia) will necessitate colonoscopy.
- In absence of clear symptoms, upper GI endoscopy and colonoscopy \uparrow at same session improves cost-effectiveness and results in significantly \uparrow diagnostic yield over either investigation alone.
- CT colonography appropriate where colonoscopy contraindicated. Sensitivity >90% for lesions >10mm.
- Screen for \oplus coeliac disease by testing serology, but if not performed, consider duodenal biopsy at the time of endoscopy.

Investigation of the patient with suspected occult GI bleeding or definite blood loss but normal upper GI endoscopy/colonoscopy

This is influenced by the briskness of bleeding.

- If there is any suggestion of an upper GI lesion, repeat upper GI endoscopy by a senior endoscopist using an enteroscope or paediatric colonoscope identifies lesions in substantial proportion of patients.
- Further imaging is probably not necessary in most patients unless there is inadequate response to iron therapy.
- In patients with inadequate response, \triangleright video capsule endoscopy (VCE) or \triangleright enteroscopy can detect lesions such as \oplus angiodysplasia, \oplus Crohn's disease, or small bowel neoplasia. VCE has a diagnostic yield of \approx 50%. Any symptom of intestinal obstruction or suggestion of luminal narrowing should prompt initial evaluation with a gelatine 'patency capsule', safe passage of which does much to minimize risks of impaction of the video capsule.
- In those with active bleeding, CT angiography can localize site of haemorrhage, but requires bleeding rate of \geq 2ml/min. Can be followed by direct selective angiography for therapeutic embolization. Scintigraphy with ^{99}Tc -labelled RBCs now rarely performed.
- \triangleright Double balloon enteroscopy permits visual inspection of the whole GI tract, along with diagnostic biopsy and therapeutic intervention, but involved procedure and not available everywhere.
- \ominus Meckel's scans may be helpful if no other bleeding source found.

Guidelines

BSG guidelines for the management of iron deficiency anaemia (2011).
 http://www.bsg.org.uk/images/stories/docs/clinical/guidelines/sbn/bsg_ida_2011.pdf.

Anorectal problems

Anal discomfort or pain and passage of bright red blood from the anus are common symptoms, often reported with some embarrassment and anxiety by patients. Many are frightened by thought of an anorectal examination. A definite diagnosis, with clear explanation of condition and available therapies, will make future visits less of an ordeal.

Clinical assessment

- Any bleeding must be carefully defined: spots of fresh blood on the paper suggest a perianal source, while darker blood or blood mixed in with stool suggest pathology higher up the colon.
- In cases of perianal pain, sepsis should always be looked for, but this can be difficult to detect in the clinic.
- Rigid sigmoidoscopy is frequently unsatisfactory, and now usually not done in clinic; ➤ flexible sigmoidoscopy is preferable. ➤ Endoanal US, ➤ examination under anaesthetic, and ➤ MRI are useful ancillary investigations.

Anal lesions

- Bleeding or prolapse of tissue through the anus is a common presentation of ➡ haemorrhoids. Diagnosis can be made on proctoscopy.
- Anal skin tags, fibroepithelial polyps, and thrombosed external piles are all relatively minor conditions that can cause major symptoms. Referral to a surgeon for excision may be needed.
- ➡ Rectal prolapse can be mistaken for prolapsing haemorrhoids. Diagnosis can usually be made by examining patient straining to pass stool. Unpleasant as it sounds, it is best to examine the patient sitting on lavatory rather than in left lateral position.
- ➡ Anal fissures can cause agonizing pain. May be diagnosed on history with careful examination of the anal canal, but sometimes examination under anaesthetic is needed. Treatment now often medical (e.g. with topical GTN or diltiazem ointment) rather than traditional lateral sphincterotomy or the discredited anal stretch. See ➡ anal fissure for details of medical management.
- ➡ Anorectal abscesses usually result from infection of anal glands along the dentate line. Acute infection may cause abscess and lead to chronic fistula. Abscess classified according to extent, and may be perianal, ischiorectal, intersphincteric, or supralevator. Causes and important differential diagnoses shown in Table 1.6.

Table 1.6 Causes and differential diagnosis of anorectal fistulae

Causes of anorectal fistulae	⌚ <u>Crohn's disease</u> , trauma, ⌚ <u>TB</u> , foreign bodies, anal surgery
Differential diagnosis	Pilonidal sinus, hidradenitis suppurativa, carcinoma, Bartholin's abscess, lymphoma

- While perianal abscess may be easy to diagnose, ischiorectal abscess can be much less obvious. Sepsis higher up the anal canal can present as rectal pain. Abscesses may communicate with anorectum: this may present as a fistulous tract.
- Assessing ⌚ anorectal fistulae traditionally involves examination under anaesthetic, but MRI and EUS have role in defining anatomy. Any discharging area or granulation tissue around anus should be assumed to communicate with anorectum until proven otherwise.
- Perianal itching (⌚ pruritus ani): most common site for intractable itch in the body). Many causes. Often managed by patients with variety of creams and lotions. Rarely help, and may make itching worse.
- Frequency of ⌚ perianal Crohn's disease varies from ≈15% in association with small bowel disease, to ≈35% in patients with ileocolitis or colitis alone. While management of associated sepsis may involve surgery or radiologically guided drainage, conservative approach is usually indicated and medical management often provides best chance of healing, especially with → anti-TNF monoclonal antibodies. Other medical approaches include antibiotics (→ METRONIDAZOLE, → CIPROFLOXACIN), and → AZATHIOPRINE.
- Sexually transmitted diseases (see Table 1.7).

Table 1.7 Sexually transmitted diseases with anorectal manifestations

Organism	Condition
Human papilloma virus	Perianal warts (condylomata accuminata)
⌚ <u>Herpes simplex virus</u>	Vesicles can occur around anus or in anal canal
<u>Treponema pallidum</u> (syphilis)	Primary or secondary lesions
Chlamydia	Can cause proctitis or even stricturing
Gonococcus	Can be asymptomatic

Rectal lesions

- Rectal discomfort or dissatisfaction, and passage of blood per rectum, are the most common symptoms of rectal disease. Digital examination and proctoscopy or sigmoidoscopy should allow exclusion of [rectal cancer](#), inflammation, or [solitary rectal ulcer](#). [Rectal prolapse](#) diagnosed from history and examining patient straining to pass stool.
- Outpatient rigid sigmoidoscopy often gives very limited views and most clinicians proceed straight to flexible sigmoidoscopy to define cause of rectal bleeding.
- Investigation of rectal discomfort may involve defaecating proctogram (see [defaecography studies](#)) to define mechanical problems with defaecation or [rectocoele](#). Endoanal US or pelvic MRI best tools to define perianal anatomy.
- Injury to anorectum from radiation therapy important cause of symptoms: up to 20% of patients receiving pelvic radiotherapy suffer radiation proctitis (see [radiation injury to the GI tract](#)).

Ascites

Intraperitoneal accumulation of fluid. Range of causes (see Table 1.8). In resource-rich countries, \textcircled{P} portal hypertension due to cirrhosis accounts for 80%, with intra-abdominal malignancy and heart failure making up most of rest. Note that ascites rarely occurs due to \textcircled{P} portal vein thrombosis in isolation, but may develop in setting of systemic sepsis or low serum albumin.

Table 1.8 Causes of fluid within the peritoneal cavity (i.e. ascites)

Mechanism	Causes
\textcircled{P} Portal hypertension	Parenchymal liver disease (e.g. \textcircled{P} cirrhosis, \textcircled{P} alcoholic hepatitis, \blacktriangle acute liver failure \blacktriangle), right heart failure, constrictive pericarditis, \textcircled{P} sinusoidal obstruction syndrome, \textcircled{P} Budd-Chiari syndrome, \textcircled{P} portal vein thrombosis
Peritoneal inflammation	\textcircled{P} Spontaneous bacterial peritonitis, malignant peritoneal deposits, \textcircled{P} TB, connective tissue disease (e.g. \textcircled{P} SLE, \textcircled{P} sarcoidosis, \textcircled{P} familial Mediterranean fever)
\downarrow Plasma oncotic pressure	Hypoalbuminaemic states (e.g. nephrotic syndrome, severe malnutrition, \textcircled{P} protein-losing enteropathy)
Impaired lymphatic drainage	Lymphatic obstruction (e.g. right heart failure, \textcircled{P} TB, lymphoproliferative disorders), lymphatic tear (e.g. trauma)
Other	Hypothyroidism, pancreatic ascites (ruptured pseudocyst or disrupted main duct)

Assessment of ascites

Always consider

- Is there unequivocal evidence of ascites (hospital admission and intensive investigation of portal hypertension rarely effective treatment for central obesity!)?
- What is the cause of ascites?
- What is the optimal management?

History

Full history essential, especially in those with recent-onset ascites. Focus on:

- Symptoms and risk factors for cirrhosis (see \blacktriangleright Approach to cirrhosis and chronic liver disease), \textcircled{P} portal hypertension, and cardiac disease.
- Internal malignancy (including recent weight loss and RUQ discomfort in cirrhotics, suggestive of \textcircled{P} hepatocellular carcinoma).
- Sepsis (including abdominal \textcircled{P} TB and \textcircled{P} spontaneous bacterial peritonitis).

Examination

Look for signs of:

- Chronic liver disease (see ► [Approach to GI examination](#)), ▲ **hepatic encephalopathy** ▲ (e.g. jaundice, liver flap).
- ↗ **Portal hypertension**: splenomegaly, dilated abdominal veins, caput medusa (superficial veins radiating out from umbilicus). Ascites due to portal hypertension usually occur in setting of hyperdynamic circulation (↑ HR, vasodilatation, ↓ mean arterial BP).
- Cardiac failure (cardiomegaly, ↑ JVP).

Investigation

- Bloods: FBC, U&Es, LFTs, ESR, CRP, clotting. Full assessment of causes of liver disease as appropriate (see ► [Approach to recent-onset jaundice](#)). Consider amylase (pancreatitis) and brain natriuretic peptide (heart failure), depending on suspected cause.
- Imaging. ► US and Doppler or contrast ► CT allow portal vein flow to be assessed, as well as intra-abdominal organs. 'Internal echoes' or 'septae' within ascites may suggest infection.
- Diagnostic ascitic tap essential in all cases, including in patients with known cirrhosis and ascites in hospital (who have high rate of ↗ spontaneous bacterial peritonitis). See ► [paracentesis](#). 20ml of fluid should be drawn, and assessed for:
 - **Colour** (see Fig. 1.1) Usually straw coloured. Blood suggests 'blood tap' or malignancy; white/milky suggests chylous ascites.
 - **White cell count** Normal <500 white cells/ μl , <250 neutrophils/ μl .
 - **Ascitic albumin** Allows calculation of serum-to-ascites albumin gradient (SAAG), which accurately differentiates ascites due to ↗ portal hypertension (SAAG >11g/L) from non-portal hypertension in >97% of cases.
 - **Microscopy and culture** Always inoculate into blood culture bottles. AFB positive in fluid of <20% of cases of peritoneal TB.
 - **Cytology** In suspected malignancy, providing larger volumes of fluid to the cytopathologist (e.g. >100ml) increases yield.
- Urinalysis (& 24h urine collection) if proteinuria.
- Further investigations tailored to results and clinical picture (e.g. ECG, CXR, echocardiogram if possible heart failure). Ascitic amylase >2,000IU/L suggests pancreatic ascites (e.g. following ↗ pancreatic pseudocyst rupture), and ascitic bilirubin > serum bilirubin supports diagnosis of biliary leak (e.g. ► [post-cholecystectomy](#)). Chylous ascites diagnosed by ascitic triglyceride (TG) level of >110mg/dl (and always with ascitic TG > plasma TG).

See Fig. 1.1 for diagnosis based on ascitic fluid analysis.

Management

Vital to treat underlying cause, not just manage ascites (see ➤ [Approach to cirrhosis and chronic liver disease](#)).

Portal hypertensive ascites

- **Salt restriction** No added salt to food should be specified, and a low-salt diet is preferable, but patient compliance with <1.5g/d (60mmol/d) is poor. However, salt restriction alone may lead to resolution of ascites in 20% of patients.
- **Restriction of fluid** to 1.5L is a standard component of management, but as fluid loss in ascites directly related to negative Na⁺ balance, fluid restriction rarely effective in absence of salt restriction.
- **Diuretics** A combination of spironolactone and furosemide usually required. Commence spironolactone 100mg/d and furosemide 40mg/d. Increase dosages every 4–5d to maximum spironolactone 400mg/d and furosemide 160mg/d, titrated against body weight (aim ↓0.5kg/d). Monitor U&Es for renal impairment, hyponatraemia and hyper/hypokalaemia.
- This approach does not work in 10%, defined as 'refractory ascites'. Treatment options then include large volume therapeutic ➤ [paracentesis](#), surgical shunting, ➡ [transjugular intrahepatic portosystemic shunt \(TIPSS\)](#), or ➡ [liver transplantation](#).
- Surgical portosystemic shunts and peritoneovenous shunts now rarely used as high complication rate and availability of alternatives.
- TIPSS effective at controlling ascites in most patients, but high occlusion rate (30–50% at 1y) and risk of ▲ **hepatic encephalopathy** ▲ (up to 30%), particularly in those with poor liver synthetic function (i.e. ↑ Bn, ↑ INR, ↓ serum albumin).
- ➡ [Liver transplantation](#) is definitive treatment for cirrhotic ascites, in patients who have 5y survival of 20% with medical therapy alone.

Non-portal hypertensive ascites

- Malignant ascites is usually refractory to diuretics, and requires repeated therapeutic ➤ [paracentesis](#). Generally very poor prognosis.
- Biliary peritonitis requires endoscopic or percutaneous biliary stenting & surgery, depending on cause.
- Similarly, management of pancreatic ascites depends on exact site and cause of pancreatic leak, with approaches including pancreatic rest (e.g. with NJ feeding), percutaneous drainage, endoscopic ➡ [pancreatic stent](#) insertion, ➤ [EUS-guided pancreatic pseudocyst](#) drainage, surgical pancreatic resection (e.g. ➤ [Whipple's procedure](#) or distal pancreatectomy), or → [OCTREOTIDE](#) (can ↓ pancreatic fluid output). Assess and manage in specialist centre.
- Tuberculous ascites treated with appropriate anti-TB therapy.
- Long-term tunneled ascitic drains may be appropriate in palliative cases to avoid repeated hospital admission.

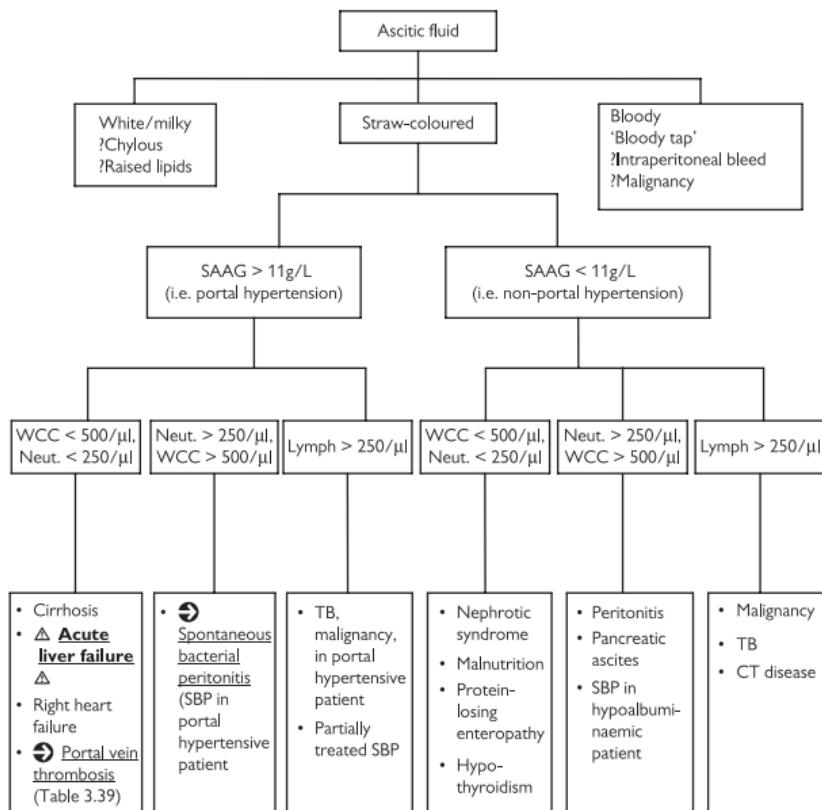


Fig. 1.1 Diagnosis of cause of ascites using SAAG and cell count. Although SAAG strongly predicts whether ascites is due to portal hypertension, interpretation of WCC necessitates incorporation of clinical information and other results (e.g. culture, cytology).

Bloating and wind

Excessive gas production is a common symptom causing patients to seek advice. Patients may attribute abdominal cramps, bloating, chest discomfort, audible bowel sounds, belching, and flatulence to gaseousness.

Composition and volume of intestinal gas

Main gases in flatus are oxygen and nitrogen (which come largely from swallowed air), and hydrogen, methane, and carbon dioxide (which come from intestinal lumen). Hydrogen and methane are largely products of bacterial metabolism; carbon dioxide can be derived from bacterial fermentation of dietary substances.

Excretion of flatus averages 600ml/d, and is no greater in patients complaining of gaseousness, suggesting heightened sensitivity to intestinal stretch or abnormal motility rather than ↑ volume, similar to observations in patients with \ominus irritable bowel syndrome.

Clinical assessment

History and examination

See Box 1.5.

Investigation

- FBC, U&Es, LFTs. Consider screening for \ominus coeliac and \ominus Giardia if history suggestive. Small intestinal \ominus bacterial overgrowth can be indicated by malabsorption of vitamins B₁₂ and D.
- Any blood in stool should prompt investigation of colon.
- Plain AXR.
- Consider upper and lower GI contrast examinations to exclude intestinal obstruction.

Therapy

- Air swallowing is common: reassurance and stopping gum chewing and smoking (including electronic cigarettes) can help.
- Belching often results from discomfort due to gastro-oesophageal reflux: acid suppression can be helpful.
- \ominus Bacterial overgrowth may contribute and need treating.
- Excessive flatus may respond to dietary modification (\downarrow intake of legumes, beans, fruits, and complex carbohydrates).
- Activated charcoal, taken orally before a meal, can \downarrow breath hydrogen.

- Some patients may have delayed intestinal transit and be constipated. Treatment with ↑ dietary fibre or non-stimulant osmotic laxatives (not lactulose, which is fermented in gut) can relieve constipation, but may initially cause ↑ bloating. Preliminary evidence that some probiotic bacteria (*Bifidobacter infantis*, present in VSL-3) may alleviate bloating in ☀ irritable bowel syndrome.

Box 1.5 Assessment of the gaseous patient

History

- **Diet** Legumes, beans, apples, prunes, raisins, and starches can all ferment, resulting in gas production.
- **Medications** Narcotics, analgesics, calcium channel blockers.
- **Surgery** 25–50% of patients experience gas bloating after Nissen fundoplication.
- **Psychiatric factors** such as anxiety or depression can be relevant.
- **Systemic diseases** ☀ Diabetes (gastroparesis due to autonomic neuropathy), ☀ systemic sclerosis (altered motility due to neuromuscular dysfunction), neuromuscular disorders such as muscular dystrophy, hypothyroidism.

Physical examination

- Examine for signs of weight loss, ascites, air swallowing, anxiety, and peritonitis. Look for succussion splash.

Chronic diarrhoea

Definition

Defined as diarrhoea >30d duration (if <14d, see ► [Approach to acute diarrhoea](#)). Patient's perception of diarrhoea needs to be clarified (\uparrow looseness of stools, \uparrow frequency of stools, urgency, abdominal discomfort, faecal incontinence). Stool weight ($>235\text{g/d}$ in ♂, $>175\text{g/d}$ in ♀) has been used to define diarrhoea, but weighing stool unpleasant and disliked by patient, nurse, and laboratory, and in any case stool weight $>\text{ULN}$ with normal consistency is not necessarily diarrhoea. Working definition of chronic diarrhoea is persistent abnormal passage of ≥ 3 loose stools/d.

Classification into **watery diarrhoea** (osmotic or secretory), **fatty diarrhoea** (steatorrhoea), or **inflammatory diarrhoea** is useful, but there may be considerable pathophysiological overlap. Investigation of steatorrhoea is described further in ► [Approach to malabsorption and steatorrhoea](#).

Pathophysiology and causes

Osmotic

Occurs due to presence in the gut of excess poorly absorbable, osmotically active solutes. Stool water content directly relates to faecal output of solutes exerting osmotic pressure across intestinal mucosa (electrolyte composition may vary according to electrical charge on poorly absorbed anions or cations, which is why measuring stool electrolytes is rarely useful). This explains two clinical hallmarks of osmotic diarrhoea:

- Diarrhoea stops when the patient fasts, or at least stops eating the poorly absorbed solute causing diarrhoea.
- Stool analysis, if necessary, will reveal an osmotic gap. That is, $\{2 \times [\text{Na}^+] + [\text{K}^+]\}$ (to account for anions) is $<$ faecal osmolality (usually assumed to be isotonic to plasma, i.e. 290mOsm/kg).

Secretory

Results from abnormal ion transport by intestinal epithelial cells. Four main categories of disease may be involved:

- Congenital defect in ion absorption.
- Intestinal resection.
- Diffuse mucosal disease, damaging/reducing epithelial cell numbers.
- Abnormal mediators (including neurotransmitters, bacterial toxins, hormones, and cathartics) that affect intestinal chloride and water secretion through changes in intracellular AMP and GMP.

Secretory diarrhoea is characterized by two features:

- Stool osmolality accounted for by $\text{Na}^+ + \text{K}^+$, and related anions, so the osmotic gap is small.
- Diarrhoea usually persists during a 48–72h fast.

Inflammatory (exudative)

Inflammation and ulceration may lead to loss of mucus, proteins, pus, or blood into bowel lumen. Diarrhoea accompanying intestinal inflammation may be due to impairment of normal colonic absorptive function.

Altered motility

Little experimental proof exists that ↑ motility causes diarrhoea, but has been implicated in:

- Diarrhoea of \hookrightarrow irritable bowel syndrome.
- Post-gastrectomy diarrhoea.
- \hookrightarrow Diabetic diarrhoea.
- \hookrightarrow Bile acid malabsorption-induced diarrhoea.
- Diarrhoea associated with hyperthyroidism.
- Drug-related diarrhoea (e.g. erythromycin as a motilin agonist, nicotine in electronic cigarettes).

Box 1.6 Causes of osmotic diarrhoea

Carbohydrate malabsorption

- Congenital:
 - Specific (disaccharidase deficiency, glucose–galactose malabsorption, fructose malabsorption).
 - Generalized (\hookrightarrow abetalipoproteinaemia, congenital \hookrightarrow lymphangiectasia, enterokinase deficiency, \hookrightarrow pancreatic insufficiency (e.g. due to \hookrightarrow cystic fibrosis)).
- Acquired:
 - Specific (e.g. post-enteritis disaccharidase deficiency).
 - Generalized malabsorption—see ► Approach to malabsorption and steatorrhoea (\hookrightarrow pancreatic insufficiency/biliary obstruction, \hookrightarrow bacterial overgrowth, \hookrightarrow coeliac disease, parasitic disease, \hookrightarrow short bowel syndromes, mucosal damage or disease, post-mucosal obstruction in lymphangiectasia, previous surgery including gastrectomy or intestinal resection leading to \hookrightarrow bile acid malabsorption).

Excess ingestion of poorly absorbed carbohydrate

- Lactulose therapy, sorbitol in elixirs or ‘sugar-free’ sweets, fructose in soft drinks or dried fruits, mannitol in sugar-free products, excess bran, or fibre.
- Magnesium-induced diarrhoea from antacids and laxatives.
- Laxatives containing poorly absorbed anions such as sodium sulphate, phosphate, or citrate.

Functional (IBS)

- Consider food hypersensitivity.

Box 1.7 Causes of secretory diarrhoea

- **Congenital** (microvillus inclusion disease, absent Cl/HCO₃ exchanger).
- **Acquired:**
 - Bacterial enterotoxins: ↗ cholera, ETEC, ↗ Campylobacter, ↗ Clostridium, S. aureus).
 - Hormones: VIPoma, medullary carcinoma of thyroid (calcitonin, prostaglandins), ↗ gastrinoma, villous adenoma, small bowel ↗ lymphoma.
 - Stimulant laxatives: phenolphthalein, anthraquinones, castor oil, cascara, senna.
 - Other drugs: antibiotics, diuretics, theophyllines, thyroxine, anticholinesterases, colchicine, prokinetics, ACE inhibitors, antidepressants (SSRIs), prostaglandins, gold.
 - Toxins: plants and fungi (Amanita), organophosphates.
 - Food products: caffeine, monosodium glutamate.

Box 1.8 Causes of inflammatory diarrhoea

- Infection: bacterial, viral, parasitic.
- Inflammatory bowel disease: ↗ ulcerative colitis, ↗ Crohn's disease, ulcerative jejunoileitis, ↗ microscopic colitis (often related to NSAIDs).
- Cytostatic agents: chemotherapy, radiotherapy.
- Hypersensitivity: ↗ eosinophilic gastroenteritis, nematodes, ↗ food allergy.
- Autoimmune: ↗ graft versus-host disease.
- ↗ Diverticular disease/diverticular colitis.
- Ischaemia.
- Radiation.
- Neoplasia (↗ colonic cancer, ↗ lymphoma).

Note: some causes of diarrhoea do not fit easily into this classification, e.g. ischaemic colitis (see ↗ intestinal ischaemia), ↗ amyloidosis).

History and examination (Fig. 1.2)

Taking a history of diarrhoea

- Clarify what the patient means by diarrhoea, and if acute or chronic.
- Aims of history are to:
 - Distinguish organic (e.g. duration <3mo, weight loss, nocturnal symptoms, continuous symptoms) from functional causes (absence of organic symptoms + long history and positive symptoms as defined by Rome criteria—see ↗ irritable bowel syndrome).
 - Distinguish malabsorptive diarrhoea (bulky, malodorous, difficult to flush, pale stools) from other causes (liquid/loose stools with blood or mucus).

Stool character and associated symptoms

- Consistently large volume diarrhoea likely to come from small bowel or proximal colon.
- Bloody diarrhoea indicates infectious, neoplastic, or inflammatory process; accompanying lethargy or anorexia may suggest mucosal cytokine release.
- Pale floating stools suggest steatorrhoea and is commonly due to pancreatic insufficiency (stools float because of gas content due to carbohydrate fermentation, not fat).

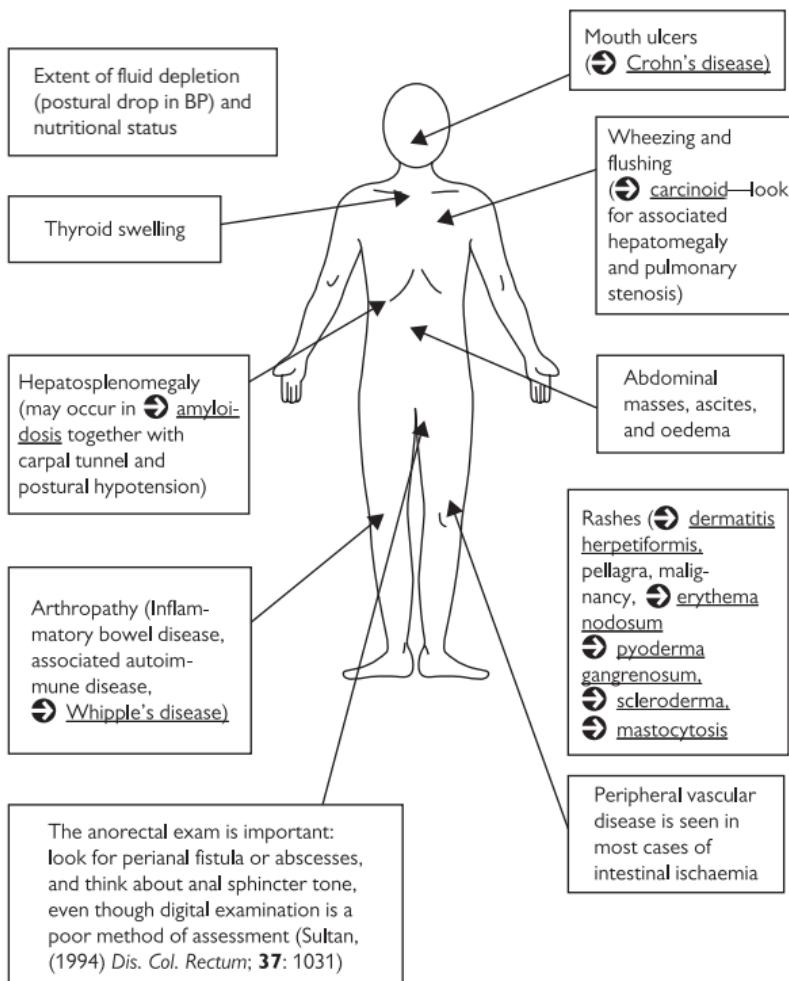


Fig. 1.2 Examining the patient with diarrhoea.

Assess for specific causes of diarrhoea

- Family history of inflammatory bowel disease, \ominus coeliac disease, \ominus colon cancer.
- Previous GI surgery leading to ↑ transit, \ominus bacterial overgrowth, or \ominus bile salt malabsorption.
- Systemic disease such as \ominus diabetes mellitus, thyroid disease (heat intolerance and palpitations may suggest hyperthyroidism), \ominus carcinoid (with associated flushing), \ominus systemic sclerosis.
- Drugs. See lists in text and Boxes 1.6–1.8—alcohol, caffeine, and non-absorbable carbohydrates such as sorbitol often missed. Don't forget surreptitious laxative abuse—factitious diarrhoea occurs in 4% of cases in general hospitals, but up to 20% in tertiary referral units.
- Foreign travel, exposure to contaminated water or potential pathogens (e.g. \ominus *Salmonella* in food handlers, *Brucella* on farms).
- Evidence of \ominus chronic pancreatitis.
- Sexual history is important. Anal intercourse is a risk factor for proctitis (causes include gonococcus, \ominus herpes simplex, chlamydia, \ominus amoebiasis), and oroanal transmission of \ominus giardia.
- Always ask about \ominus faecal incontinence: common (2% of population) and not always reported spontaneously. If present, take obstetric history in ♀ for perineal trauma and possible sphincter damage.
- Ask about diet and stress as aggravating factors. There is a link between physical/sexual abuse and functional bowel disease.
- Ask about illness in companions or family members.

Likely causes of diarrhoea in common clinical categories

- **Acute diarrhoea** See ▶ Approach to acute diarrhoea).
- **Chronic/recurrent diarrhoea, not previously investigated:**
 - \ominus Irritable bowel syndrome.
 - Inflammatory bowel disease (IBD): \ominus Crohn's disease, \ominus ulcerative colitis.
 - Parasitic or fungal infection.
 - Malabsorption.
 - Drugs or food additives.
 - \ominus Colonic cancer.
 - \ominus Diverticular disease.
 - Previous surgery.
 - Endocrine causes (e.g. thyroid disease).
 - Faecal impaction.
- **Chronic diarrhoea in previously investigated patients:**
 - Surreptitious \ominus laxative abuse.
 - \ominus Faecal incontinence.
 - \ominus Microscopic colitis.
 - Unrecognized malabsorption.
 - \ominus Neuroendocrine tumours.
 - \ominus Food allergy.

- **Nosocomial (hospital-acquired) diarrhoea** Diarrhoea is among the most common nosocomial illnesses (occurs in 30–50% of patients on ITU), and $\frac{1}{3}$ patients in chronic care facilities have at least 1 significant diarrhoeal illness/y. Two classes of patients need particular consideration.
 - **Diarrhoea in patients on ITU** Drugs, especially those containing magnesium and sorbitol, ↗ antibiotic-associated diarrhoea (↗ *C. difficile*, but also ↓ salvage of carbohydrate by colonic bacteria leading to osmotic diarrhoea), enteral feeding, intestinal ischaemia, pseudo-obstruction, faecal impaction, defective anal continence.
 - **Patients with cancer or on chemotherapy** Incidence of GI toxicity with chemotherapy or radiotherapy can approach 100% with some regimens. Radiation enterocolitis occurs at total body doses of $\geq 6\text{Gy}$ or pelvic irradiation of 3–4Gy (see ↗ radiation damage and the GI tract). Toxic chemotherapeutic agents include cytosine, daunorubicin, 5FU, methotrexate, 6-MP, irinotecan, and cisplatin. Some biological treatments (e.g. anti-IL-2 therapy) associated with watery diarrhoea, and the newer checkpoint inhibitors (e.g. anti-PD-1) can cause autoimmune colitis. ↗ *Typhlitis* (neutropenic enterocolitis) also potent cause of diarrhoea.
- **Diarrhoea in HIV-infected patients** *Cryptosporidium*, *Microsporidia*, *Isospora*, ↗ amoebiasis, ↗ *Giardia*, herpes, ↗ *CMV*, ↗ *adenovirus*, MAI, ↗ *Salmonella*, ↗ *Campylobacter*, *Cryptococcus*, *Histoplasma*, *Candida*, ↗ lymphoma, AIDS enteropathy (see ↗ HIV and the gut).
- **Diarrhoea in HIV-negative MSM** ↗ Amoebiasis, ↗ giardiasis, ↗ *Shigella*, ↗ *Campylobacter*, syphilis, gonorrhoea, *Chlamydia*, herpes simplex.

Diagnostic tests

Do not accept diagnosis of diarrhoea without some attempt to examine stool, even if only on glove after rectal exam, to look for blood, mucus, oil, or steatorrhoea.

- 75% of chronic diarrhoeas can be diagnosed by careful history and examination, coupled with basic haematology and biochemical tests, stool testing for infection and ➤ faecal calprotectin, and sigmoidoscopy with biopsy.
- In remainder, consider three further tests to get to definitive diagnosis:
 - Colonoscopy with biopsies.
 - Faecal elastase or quantitative stool fat.
 - Stool volume and osmotic gap in response to fasting.
- Indicators of functional rather than organic aetiology are long history ($>1\text{y}$), lack of significant weight loss, absence of nocturnal diarrhoea, and straining with defaecation. These indicators, taken together, $\approx 70\%$ specific for functional symptoms.

Basic investigations

- Send three stool samples for:
 - Culture.** Including ova, cysts, and parasites. Also consider testing for $\odot C. difficile$ if risk factors.
 - > Faecal calprotectin.** Alternatives depending on availability are faecal lactoferrin or \triangleright stool microscopy for faecal leucocytes. If present, suggests inflammatory diarrhoea.
- Toxicology. If you suspect factitious diarrhoea or laxative abuse, send stool and urine for laxative screen.
- Blood tests** FBC, ESR, CRP, iron, B₁₂, folate, thyroid function, glucose, U&Es, calcium, LFTs including albumin, coeliac serology.
- In most cases of diarrhoea where histology helps to make diagnosis, **sigmoidoscopy** is sufficient rather than full colonoscopy. The exception is when ileal histology is needed, or changes are patchy throughout the colon. Where there is significant weight loss or bleeding to suggest lower GI malignancy, full **colonoscopy** is needed.
- Radiological imaging** Plain AXR can show faecal impaction, pancreatic calcification, intestinal dilatation, or suggest colitis.

Stool fat

Historically a very useful test for fat malabsorption, but now often difficult to get done at all (many labs will refuse sample). Can be assessed qualitatively or quantitatively (see \triangleright 'Stool tests', p. 151), and if the latter, $>7\text{g/d}$ is abnormal. Largely replaced for assessment of pancreatic exocrine insufficiency by measurement of \triangleright faecal elastase.

Response to fasting and stool osmotic gap

Rarely of practical use in most cases, but may be useful in difficult cases.

- Steatorrhoeic stools are usually $>700\text{g}/24\text{h}$, and stool weight returns to normal on fasting. Inflammatory diarrhoeas respond variably to fasting but, like steatorrhoea, the stool osmotic gap is not usually helpful.
- Measuring stool electrolytes and osmotic gap may help classify chronic watery diarrhoeas. Analysis done on centrifuged sample, so results are possible from spot stool samples or 24–72h collections.
- Assume faecal osmolality = plasma (290mOsm/kg). This is true of freshly passed stool, but with time measured faecal osmolality can become falsely ↑ due to bacterial degradation of carbohydrate. Large measured deviations below 290mOsm/kg indicate contamination of stool with urine or water, gastrocolic fistula, or hypotonic fluid intake. In principle, stool sodium/potassium is high in secretory diarrhoea (unabsorbed electrolytes retain water in gut lumen) and low in osmotic diarrhoea (non-electrolytes retain water in gut lumen). Interpretation of stool osmotic gap and faecal electrolytes is shown in Table 1.9.

Table 1.9 Stool osmotic gap* and faecal electrolytes in the investigation of diarrhoea

Stool Na >90mM and osmotic gap <50mM	Secretory diarrhoea, or osmotic diarrhoea caused by sodium sulphate or phosphate ingestion
Stool Na <60 and osmotic gap >125mOsm/kg	Osmotic diarrhoea: if stool volume does not return to normal on fasting, suspect surreptitious magnesium ingestion
Stool Na >150 and stool osmolality >375–400mOsm/kg	Suspect contamination with urine
Stool osmolality <200–250mOsm/kg	Suspect contamination of stool with dilute urine or water

* Stool osmotic gap = plasma osmolality ($\sim 290\text{mOsm/kg}$) – $2 \times (\text{stool } [\text{Na}]^+ + \text{stool } [\text{K}^+])$

Other tests used in investigating diarrhoea

Specific tests for malabsorption (See also ► [Approach to malabsorption and steatorrhoea](#).)

- *Small bowel biopsy* Duodenal biopsy, which may be combined with small bowel aspirate for microbiological analysis, useful in diagnosing [Crohn's disease](#) (especially in children), [coeliac disease](#), [Whipple's disease](#), [giardiasis](#), [lymphoma](#), [eosinophilic gastroenteritis](#), [amyloidosis](#), [systemic mastocytosis](#), [lymphangiectasia](#), and various parasitic and fungal infections.
- *Small bowel imaging* Useful for fistulae, strictures, and previously undetected surgical bypasses.
- ► [Pancreatic function tests](#).
- ► [Breath tests](#) for fat, carbohydrate, and [bacterial overgrowth](#).
- SeHCAT test (see [bile acid malabsorption](#)).

Specific tests for watery diarrhoea

- Blood levels of certain hormones produced by  neuroendocrine tumours such as gastrin, VIP, somatostatin, pancreatic polypeptide, calcitonin, and glucagon may be useful. See ➤ gut hormone profile.
- Urine levels of 5-HIAA can help diagnose  carcinoid.

Specific tests for inflammatory diarrhoeas

- ➤ Faecal calprotectin usually raised.
- In addition to upper and lower GI endoscopy and small bowel studies, PET-MRI or ➤ indium-labelled leucocyte scanning may be useful, particularly in children.

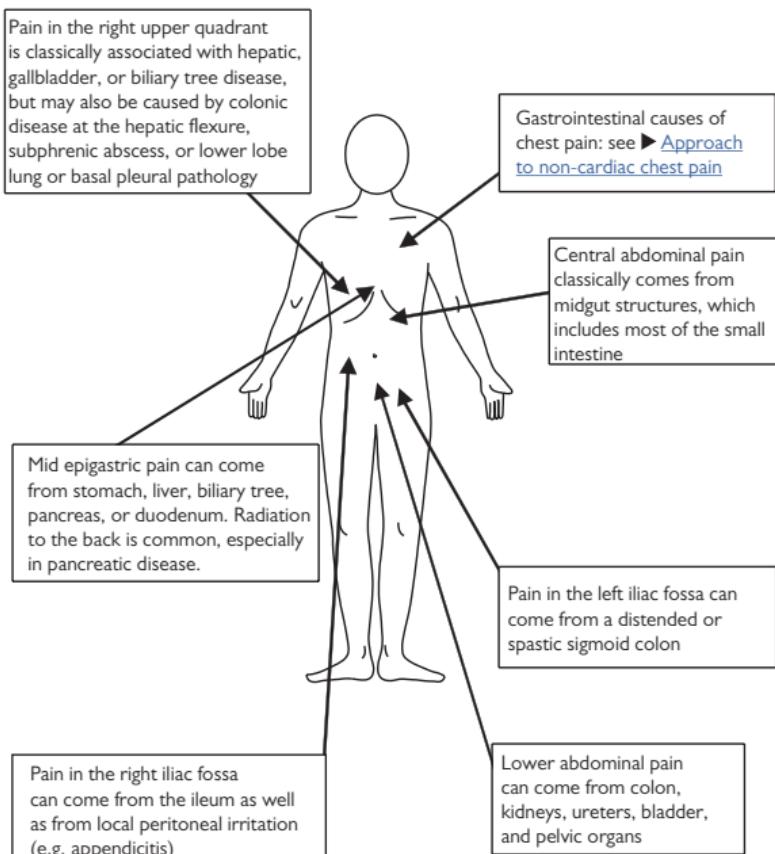
Antidiarrhoeal therapies

These can be divided into agents useful for mild-to-moderate diarrhoeas, and those for secretory or severe diarrhoeas. Most in current use work by ↓ motility rather than secretion. See → ANTIDIARRHOEAL AGENTS.

Chronic or recurrent abdominal pain

Abdominal pain is a very common cause of patients presenting to doctors. **Acute abdominal pain** usually has an organic cause and is dealt with elsewhere (see ▲ **Acute abdominal pain** ▲). While there are many pathological causes of **chronic abdominal pain**, it is commonly not due to organic disease and can thus be a source of worry, frustration, and confusion—to both doctor and patient alike. Diagnosis depends on interpreting the patient's experience into a medical model of disease. This can be difficult because of:

- The common innervation of many abdominal organs.
- The low concentration of nerve endings in the viscera.
- Patients' lack of prior experience of pain coming from these organs.
- The non-specific nature of the pain.



RUQ and LUQ pain can be attributed to lung or pleural pathology.

Fig. 1.3 Clinical approach to chronic or recurrent abdominal pain.

Types of abdominal pain

Distinguish between **visceral** pain (originates from noxious stimuli affecting abdominal viscous, and usually felt in midline); **parietal or somatic** pain (arising from stimulation of parietal peritoneum, usually localized to site of lesion); **referred** pain (felt in remote areas supplied by same neurosegment as diseased organ because of shared central pathways for afferent neurons from different sites); and **non-visceral** pain.

Critical features in assessing pain

- Site of pain, and where it radiates to (see Fig. 1.3).
- **Nature** of the pain. Ulcers ‘gnaw’, viscera ‘colic’, and ruptured aneurysms ‘tear’. Long duration of pain tends to correlate with non-organic cause, especially if not associated with weight loss (see ► [Approach to unintentional weight loss](#)) or other alarm symptoms. Estimating severity of pain is very unreliable.
- **Factors modifying pain** can be very helpful in diagnosis.
 - Aggravating foods, or more usually relationship of pain to eating, may be helpful. Alcohol can aggravate dyspepsia and intestinal spasm, cause pancreatitis, or worsen lymphoma pain.
 - Relief by bowel action or passing flatus suggests colonic source (see ➔ [irritable bowel syndrome](#)).
 - Pain related to menstruation suggests ➔ [endometriosis](#) or pelvic inflammatory disease.

Physical examination

- **Tachycardia, fever, and sweating** suggest infection, although can be absent in chronic infection. Frequent changes of position suggest visceral pain with no or little inflammation.
- **Inspect** For scars, hernias, and visible peristalsis.
- **Palpate** Rigidity or guarding suggests local peritonism. Palpable mass may result from organ enlargement, inflammation, or tumours.
- **Percussion** Tympany suggests excess air, either intraluminal or extraluminal. Light percussion, if painful, can suggest peritonism. Shifting dullness suggests ascites.
- **Auscultation** may reveal tinkling bowel sounds in intestinal obstruction, absent bowel sounds in ➔ [ileus](#), or bruits.
- Do rectal (PR) and, if necessary, vaginal (PV) examinations. Clear prior discussion of need for internal examination vital, and presence of chaperone important. Tenderness on PR or PV examination may not be appreciated by examining anterior abdominal wall.

Investigations

- FBC with MCV (iron studies, B₁₂, and folate if this is abnormal, or within normal range with ↑ RDW), ESR, and CRP.
- Check renal function and ➤ [LFTs](#).

- Examine urine for pyuria and haematuria, and send sample for MC&S. If appropriate, check ♀ of childbearing age for pregnancy.
- *Do not use inappropriate radiological tests.* ➤ Abdominal US can be highly informative and is non-invasive.
- Other tests depend on results of history and examination.

Non-visceral abdominal pain

When patients present with persistent or recurrent pain, it can be easy to overlook a non-visceral source. This may result in multiple unnecessary investigations, or application of a 'functional' or 'psychosomatic' label (with treatment directed accordingly). Pain may derive from:

- **Abdominal wall:**
 - Comprised of fat, aponeurosis, musculature, and skin. Somatic nerve supply from intercostal nerves T7–T12. Patients may have difficulty describing their pain clearly, as accuracy of cutaneous sensation ↓ through deeper tissues.
 - **Carnett's sign** may be helpful. Examine patient supine and identify site of maximum tenderness with examining finger. Ask patient to fold arms across chest and sit halfway up. If continued palpation at same point elicits similar or ↑ pain, this implies abdominal wall pathology. Myofascial trigger points also suggest musculoskeletal pathology.
 - Pain from shingles typically dermatomal and can precede rash.
- **Nerve entrapment:**
 - Rectus abdominis nerve entrapment syndrome causes point tenderness over the linea semilunaris of the rectus sheath.
 - Ilioinguinal or iliohypogastric nerve entrapment cause burning sensation in iliac fossa radiating to groin, with associated hyperesthesia and/or paraesthesia, generally made worse on movement (although hip flexion often provides some relief). Nerve at risk during appendicectomy, hernia repair, and Pfannenstiel incisions.
- **Postoperative incisional pain.**
- **Skeletal pain:**
 - Painful rib syndrome characterized by sharp pains followed by dull ache in lower costal margin, associated with ↑ mobility of anterior costal cartilages of 8th–11th ribs.
 - Precordial catch syndrome affects young patients, who experience abrupt sharp, stabbing chest pain, causing them to catch their breath.

Functional abdominal pain

Functional abdominal disorders account for ≈50% of all patients with abdominal pain seen by doctors, and almost all cases with abdominal pain lasting years. In most cases, diagnosis of  irritable bowel syndrome is possible from history (see Boxes 1.9 and 1.10). A small minority have intractable chronic pain; this may be associated with previous physical or sexual abuse, and onset may coincide with a bereavement.

Box 1.9 Rome IV criteria for irritable bowel syndrome

Recurrent abdominal pain on average at least 1d/wk in last 3mo associated with two or more of the following features:

- Related to defaecation.
- Associated with change in stool frequency.
- Associated with change in form (consistency) of stool.
- Symptoms must have started at least 6mo ago.

Symptoms supporting diagnosis of IBS:

- Abnormal stool frequency.
- Abnormal stool form.
- Difficulties in evacuation.
- Passage of mucus.
- Bloating or feelings of distension.

Box 1.10 Causes of chronic or recurrent abdominal pain

Generalized parietal pain due to peritonitis

- Bacterial peritonitis (including Θ spontaneous bacterial peritonitis).
- Ruptured cyst.
- Θ Familial Mediterranean fever.

Localized peritoneal pain

- Θ Appendicitis, Θ cholecystitis, Θ Crohn's disease, Θ endometriosis, chronic pelvic inflammation.
- Infiltration due to abdominal neoplasms.

Pain from increased tension in viscera

- \blacktriangle Bowel obstruction \blacktriangle .
- Biliary obstruction (Θ choledocholithiasis).
- Ureteric obstruction.

Ischaemia

- Θ Intestinal ischaemia (stenosis, embolism, vasculitis).
- Θ Henoch–Schönlein purpura.

Retroperitoneal causes

- Θ Chronic pancreatitis.

Extra-abdominal

- Neurological (neurogenic tumours, spinal degenerative disease, herpes zoster).
- Metabolic (diabetic ketoacidosis, Addisonian crisis, acute intermittent Θ porphyria).
- Haematological (Θ sickle cell anaemia).
- Toxic (lead).

Functional causes

- Θ Irritable bowel syndrome.
- Non-ulcer dyspepsia.
- Biliary pain (Θ sphincter of Oddi dysfunction).

Overinvestigation can result from lack of clinical knowledge or experience, or failure to spend time taking adequate history. This tends to sustain the disorder, as the patient recognizes the failure of the doctor to grasp the problem, and becomes increasingly frustrated by a succession of normal results. Time, if necessary spread over several visits, may have to be spent exploring emotional factors. A general approach outlined in Box 1.11.

Box 1.11 General approach to patient with functional abdominal pain

Establish rapport and trust Acknowledge symptoms as real and maintain non-judgemental attitude. Schedule brief but frequent appointments, and reassure when needed. Avoid temptation to do more diagnostic tests.

Set appropriate goals Do not expect cure: focus on adjustment, improvement in function, coping, and adaptation. Allow for setbacks.

Consider specialized referrals

- Pain clinic, relaxation training, clinical psychology, psychiatry.
- Dietician (for consideration of ↗ FODMAP diet or alternatives).

Drug treatment

- Analgesics, especially → OPIATES, often not helpful, and side effects such as constipation often compound problem.
- → ANTISPASMODICS can be useful if targeted to patients with cramping abdominal pain. Start with peppermint tea, oil, or capsules, then consider mebeverine 135–150mg PO tds or other similar agents.
- Low-dose antidepressants (e.g. amitriptyline 10–20mg PO nocte) can be beneficial, but patients often resistant to idea of taking antidepressants. Important to emphasize (in layman's terms) that at low doses these drugs have visceral analgesic effect rather than psychotropic actions.
- If available, non-pharmacological therapies (such as acupuncture or hypnotism) are often more effective than pharmacological therapies.

Cirrhosis and chronic liver disease

Background

- A diagnosis of chronic liver disease is usually made in patients under investigation for abnormal \blacktriangleright LFTs or with unexplained jaundice (see \blacktriangleright [Approaches to recent-onset jaundice](#), and \blacktriangleright [Approach to well patients with abnormal liver tests](#)), or rarely in those who present with \blacktriangle **hepatic encephalopathy** \blacktriangle .
- The most common causes in the UK are \ominus [alcoholic liver disease](#), \ominus [hepatitis C](#), and \ominus [non-alcoholic fatty liver disease \(NAFLD\)](#) (see Table 1.10).
- Cirrhosis is a histological diagnosis, characterized by diffuse hepatic fibrosis and nodule formation. Chronic non-cirrhotic liver disease and well-compensated cirrhosis can rarely be differentiated on clinical findings and biochemistry alone (LFTs may be normal, even in established cirrhosis).
- \ominus [Liver biopsy](#) should be considered in all cases of chronic liver disease. The exceptions may include patients with clear aetiology of liver disease who have clinically decompensated cirrhosis (e.g. small irregular liver on imaging, with markedly impaired liver function (\uparrow bilirubin, \downarrow albumin, ∇ prothrombin time) and evidence of \ominus [portal hypertension](#) (e.g. ascites, splenomegaly).
- Clinical distinction is often made between patients with compensated cirrhosis and those with decompensated cirrhosis. While distinction may not be absolute, clinical problems and management of these two patterns differ, and so are discussed separately here.

Table 1.10 Causes of cirrhosis and chronic liver disease

\ominus Alcoholic liver disease	\ominus Haemochromatosis
\ominus Hepatitis B	\ominus Autoimmune hepatitis
\ominus Hepatitis C	\ominus Wilson's disease
\ominus Primary biliary cholangitis	\ominus α_1-antitrypsin deficiency
\ominus Primary sclerosing cholangitis	\ominus Budd–Chiari syndrome
\ominus Drugs (e.g. methotrexate)	Secondary \ominus biliary cholangitis
\ominus Metabolic liver diseases	Cryptogenic ($\approx 15\%$)
\ominus Non-alcoholic fatty liver disease	

Compensated cirrhosis

The patient will have preserved liver synthetic function, without ascites or ▲ **hepatic encephalopathy** ▲. The focus of management is to prevent progression (decompensation) and avoid complications.

Management

Treat the cause A nihilistic approach to cirrhosis is not justified. Although the natural course is for progressive fibrosis and liver dysfunction, treatment of the underlying cause has been demonstrated to slow down, and even reverse, clinical progression in patients with established cirrhosis (e.g. ↗ haemochromatosis, ↗ hepatitis B and C). It is vital to address ↗ alcohol use disorder. Promising data are emerging on antifibrotic therapies reversing some effects of cirrhosis, but no agent has been approved yet.

- It is increasingly recognized that ↗ osteoporosis is strongly associated with cirrhosis, especially if cholestatic aetiology (e.g. ↗ primary biliary cholangitis) or on immunosuppression. ► Bone densitometry, p. 167) indicated. Calcium and vitamin D supplements slow progression, and bisphosphonates may be needed (though may cause side effects, including ↗ oesophagitis).
- Complications of ↗ portal hypertension may manifest as acute variceal bleeding (see ▲ acute upper GI bleeding ▲), ascites, or ▲ **hepatic encephalopathy** ▲ (i.e. 'decompensated'). After diagnosing cirrhosis, upper GI endoscopy should be considered, as finding gastro-oesophageal varices may merit primary prophylaxis (see ↗ portal hypertension).
- Risk of ↗ hepatocellular carcinoma (HCC) ↑ significantly once cirrhosis develops (e.g. annual incidence of HCC 1–4% in patients with cirrhosis due to ↗ hepatitis C). Evidence supports role for 6-monthly serum ► α FP and US.
- Additional liver insult may lead to decompensation in patients with cirrhosis. Those who may be at any risk of ↗ hepatitis A or B (e.g. frequent travellers to risk areas, drug users, multiple sexual partners) should be tested for immunity, and vaccinated as appropriate.
- Complications of cirrhosis are more common in malnourished patients. Give thiamine 100mg PO bd, encourage high calorie and protein intake, and refer for nutritional advice as necessary (see ► Approach to nutritional support). Note that patients with ↗ alcoholic liver disease may get a high proportion of daily calorie intake from alcohol. A night-time protein snack is therefore recommended.
- Prescribing medication in patients with cirrhosis may be complex, due to the risk of precipitating bleeding (e.g. NSAIDs), worsening liver function, ▲ **hepatic encephalopathy** ▲ (e.g. → OPIATES), or renal impairment (e.g. NSAIDs, aminoglycosides). See also ↗ drug-induced liver injury.
- Pregnancy may occur in cirrhotic patients, although 50% of premenopausal ♀ with cirrhosis have secondary amenorrhoea. Close liaison between patient, obstetrician, and hepatologist is essential. See ► Approach to liver problems in pregnancy.

Decompensated cirrhosis

- May be indicated by development of jaundice, ▲ **hepatic encephalopathy** ▲, or ascites. Jaundice and encephalopathy are much more commonly due to acutely deteriorating chronic liver disease than to ▲ **acute liver failure** ▲.
- Decompensation strongly predicts death, with 1 and 5y survival in patients with ↴ Child–Pugh score C of 42% and 21%, compared with 84% and 44% for Child–Pugh score A disease.

Assessment

- Careful history to identify causes of decompensation is vital (see Table 1.11 and Box 1.12). Ask about recent binge drinking (see ↴ **alcohol use disorder**), any new drugs, infections (common cause, but symptoms and signs of sepsis may be masked in cirrhosis), weight loss, or abdominal pain (e.g. ↴ **hepatocellular carcinoma**). Has there been any recent change in bowels (melaena, constipation) or haematemesis?
- As well as looking for signs of chronic liver disease (e.g. spider naevi, gynaecomastia—see ➤ **GI examination**, p. 130), are there signs of decompensation (jaundice, liver flap, ascites)? Assess grade of ▲ **hepatic encephalopathy** ▲. Full general examination to elicit source of possible sepsis (including urine dipstick), and rectal examination to exclude melaena or constipation necessary.

Investigations

- In all cases, blood should be sent for FBC, U&Es, LFTs, glucose, clotting profile, and blood cultures. See also ➤ **Approach to recent-onset jaundice**.
- Further investigations will depend on initial results and manifestation of decompensation, but must include a search for precipitant:
 - ➤ α FP.
 - Abdominal US with Doppler of hepatic and portal veins.
 - Culture of urine and sputum.
 - Diagnostic ascitic tap for cell count and culture (see ➤ **paracentesis**).
 - CXR.

Management

- Directed towards particular manifestation of hepatic decompensation (e.g. ascites) and treatment of precipitants. See other sections:
 - ➤ **Approach to recent-onset jaundice**.
 - ➤ **Approach to agitation and confusion in the GI patient**.
 - ➤ **Approach to ascites**.
 - ▲ **Acute upper GI bleeding** ▲.
 - ▲ **Hepatic encephalopathy** ▲.
 - ↴ **Hepatocellular carcinoma**.
 - ↴ **Hepatorenal syndrome**.
 - ➤ **Paracentesis**.
 - ↴ **Portal hypertension**.