Pass Finals
Pocket Essentials

Series Editors

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Pass Finals

Third Edition

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Medical students and doctors in training are expected to travel to different hospitals and community health centres as part of their education. Many books are too large to carry around, but the information they contain is often vital for the basic understanding of disease processes.

The Pocket Essentials series is designed to provide portable, pocket-sized companions for larger texts like our own Kumar and Clark’s Clinical Medicine. They are most useful for clinical practice, whether in hospital or the community, and for exam revision.

All the books in the series have the same helpful features:

- succinct text
- simple line drawings
- emergency and other boxes
- tables that summarise causes and clinical features of disease
- examination questions and answers

They contain core material for quick revision, easy reference and practical management. The modern format makes them easy to read, providing an indispensable ‘pocket essential’.

Parveen Kumar and Michael Clark
Series Editors
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In this new edition of *Pass Finals* we have brought the text up-to-date, aligning it with the 8th edition of Kumar and Clark’s *Clinical Medicine*. The example questions have been expanded and we have focused on clinical medicine and its assessment. The layout of the book has changed to make it more ‘pocketable’.

Our thanks go to Lynn Watt at Elsevier for her patience in the face of adversity and slipping deadlines, and our families for their tolerance as we spent our ‘free time’ in front of a computer screen.

As ever, good luck – and remember: they want to pass you, whatever it feels like on the day!

G.S.
E.C.
L.L.
June 2012

**Acknowledgements**

Our thanks go to Dr Nick Reading (Consultant Radiologist, Whipps Cross University Hospital) for supplying images for the radiology chapter.
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The range and depth of knowledge that medical students seem to be expected to retain grows continuously. This is despite the stated policy of many medical schools that the ‘information load’ should be reduced in undergraduate teaching. Over the last decade many traditional styles of examination have become less common, replaced by multiple-choice style examinations based on clinical scenarios and OSCE examinations, in place of long and short cases.

The advance of molecular medicine and the increasing links between basic sciences and clinical medicine have led us to include these topics in the text. Common radiological investigations are also included as they are becoming a key part of many examinations. The use of evidence-based medicine demands an understanding of statistics and trial design and these topics are, as a result, also included.

In this book we have tried to distil a core dataset in general and speciality medicine. The information is provided as bulleted lists and is supported by diagrams and self-assessment questions. By its nature, therefore, this is not a definitive textbook of clinical medicine and the page references to the 6th edition of Kumar and Clark’s *Clinical Medicine* are designed to point the reader towards a more in-depth explanation of the subject. We hope, however, that it will act as a source of rapid access information for the important disease processes and thereby act as a useful revision aid.

Finally we would like to thank those individuals that have supported our efforts – notably Ellen Green and Siân Jarman at Elsevier for their efforts and Sarah Russell for the design work. Also to Parveen Kumar and Michael Clark for their critique of the text and for writing *Clinical Medicine* in the first place, and to our families for support and coffee during the writing. Finally, we should thank the Good Samaritan for ongoing inspiration.

Good Luck!

G.S.
E.C.
L.L.
## Contents

1. How to pass medical finals ........................................... 1
2. Question types in medical finals .................................. 7
3. Objective Structured Clinical Examinations (OSCEs) ......... 17
4. Pharmacology and therapeutics .................................... 35
5. Radiology .................................................................... 51
6. Clinical chemistry .......................................................... 85
7. Infectious diseases ....................................................... 105
8. Respiratory medicine ..................................................... 133
9. Cardiology ................................................................... 159
10. Gastroenterology and hepatology .................................. 213
11. Rheumatology ............................................................... 263
12. Dermatology ................................................................. 289
13. Endocrinology ............................................................... 303
14. Renal medicine ............................................................ 335
15. Haematology ................................................................. 365
16. Oncology and genetic disease ......................................... 401
17. Neurology .................................................................. 419
18. Psychological medicine ................................................. 465
19. Statistics and evidence-based medicine ......................... 489

Appendix A. Answers to Multiple Choice Questions ............. 499
Appendix B. Answers to Extended Matching Questions .......... 501
Appendix C. Normal reference ranges:
- Normal values for laboratory tests .................................. 507

Index ............................................................................. 509
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There are, and always have been, several truisms about sitting final exams in medicine. At the end of the day, the vast majority of students pass their final exams and earn the right to call themselves ‘Doctor’. There are, however, tactics and techniques that you can use to make the process less painful.

**WRITTEN EXAMS**

Much of this sounds obvious, but ‘schoolchild errors’ are commonly made in the stress of final exams.

**Be prepared**

- Exam technique is a learned skill
- Know the distribution of marks for the paper
- Make sure you know the format of the exam
- Practise questions from past papers
- Practise keeping to time

**Directed learning**

- The vast majority of questions are about common and important areas of medicine
- Rare syndromes are very unlikely to come up
- Medical emergencies are often asked about
- Remember the classic pitfalls in medicine (Table 1.1)

**Read the instructions**

- Make sure you are quite clear on how many questions you have to answer and how much time you have for each one
- If need be, write the start and finish times for each section on the top of the paper and stick to them

**Answer the question asked**

- Read the question carefully – preferably twice
- Answer the question asked, not the one you want to answer – don’t just write down everything that you remember about the topic

**Answer all the questions**

- Attempt the correct number of questions
- If you are running out of time, try to put something down on paper, even if it is only an essay plan – you may get some credit

**Presentation**

- Clear, neat handwriting is easier to mark
- Structure your answer: headings and subheadings speed up marking
- Spell accurately
How to pass medical finals

**Table 1.1 The structured answer**

<table>
<thead>
<tr>
<th>For any disease, outline:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Incidence – common/rare</td>
</tr>
<tr>
<td>Distribution</td>
</tr>
<tr>
<td>Age</td>
</tr>
<tr>
<td>Sex</td>
</tr>
<tr>
<td>Geographical</td>
</tr>
<tr>
<td>Racial</td>
</tr>
<tr>
<td>Pathology</td>
</tr>
<tr>
<td>Aetiology</td>
</tr>
<tr>
<td>Clinical features</td>
</tr>
<tr>
<td>Associated conditions</td>
</tr>
<tr>
<td>Investigations</td>
</tr>
<tr>
<td>Therapeutic options</td>
</tr>
<tr>
<td>Outcome or prognosis</td>
</tr>
<tr>
<td>Complications</td>
</tr>
</tbody>
</table>

**Anonymous papers**

- Many exams require you to put a name or candidate number on each page – make sure you do

**MULTIPLE CHOICE PAPERS**

- Several different formats exist (see Ch. 2)
- Make sure that you know what question type is used
- Keep to time and answer all of the questions
- Do not spend long on a question you have no idea about – you can always go back to it
- Most questions have some obvious wrong answers – shortening the odds
- Practise as many questions as you can
- Questions are often re-used – do as many past papers as you can

**Negative marking**

- Rarely used
- Mark deducted for a wrong answer
- Aims to deter ‘wild guesses’
- Informed guesses are risky but on balance worth it

**CLINICAL EXAMS**

Clinical exams can be more nerve-racking than written papers. The ‘performance’ in front of examiners is stressful. Again, basic tactics will help you out.

**Dress code**

Go for smart, conservative and comfortable dress. Loud waistcoats and cartoon ties will not help.

**Equipment**

- The vast majority of the equipment you will need for a clinical examination will be provided
You will need:
- A stethoscope – make sure it is clean and working
- A pen – most important for long cases
- Ophthalmoscopes should be provided, but if you have your own and are comfortable using it, take it with you. Make sure the batteries are fresh
- Everything else is a luxury. Pockets bulging with equipment are uncomfortable and heavy

Three key aims
- Do not hurt or embarrass the patient
- Ensure the examiner sees you carry out all parts of the examination competently
- Synthesize a diagnosis, differential and management plan

The order of importance of the above depends upon the examiner and the case. If the diagnosis is straightforward, the examiner will want you to reach it without too much of a performance. If the diagnosis is difficult, he or she will want you to demonstrate your ability to elicit clinical signs, even if the underlying cause escapes you.

Examination technique
- Make sure that your examination technique is swift and professional
- Do what you are asked
  - ‘Examine the cardiovascular system’ means a full examination starting with the hands
  - ‘Listen to the heart’ means just auscultation
- Examiners should make it clear what they want

Dignity
- NEVER hurt or embarrass the patient
- ALWAYS introduce yourself
- ALWAYS ask permission to examine
- ALWAYS ask whether the area you are going to examine is painful or tender
- THANK the patient at the end of the examination

Scoring points
- A professional introduction, followed by an examination technique that is fluent and clearly well practised, is as important as reaching a diagnosis
- Even if the diagnosis eludes you, describe your findings
- Outline the positive findings at examination and the important negatives
- If you can, come up with a diagnosis and differential
- The longer you can talk, the fewer questions can be asked (although talking rubbish does not help)

VIVA VOCE EXAMS

Vivas or oral examinations still make up a part of final examinations in some medical schools. They may be routine for all candidates or used specifically to re-examine a borderline candidate. If you are called for a viva in the latter situation, remember that honours
students may be examined as well and that a selection of candidates across the whole range of marks will be examined to provide a standard range of scores.

In general, it is difficult to fail the whole exam because of a poor performance in a viva.

**Dress**
- Be smart and conservative

**Format**
- There are usually two examiners – one may be external
  You may be:

**Asked questions**
- e.g. What classes of drug are useful in the management of hypertension?

**Given a case scenario**
- e.g. Outline the management options for a 74-year-old woman who comes to see you with rheumatoid arthritis

**Asked about medical emergencies**
- e.g. A 55-year-old man is admitted with haematemesis and a blood pressure of 90/50. What would you do?

**Asked to report the results of an investigation**
- e.g. A chest X-ray, ECG or blood test results

**Identify an object**
- Pathological specimen
- Piece of equipment (e.g. nasogastric tube, urinary catheter)

**Tactics**
- ‘Engage your brain before your mouth’
- Structure your answer (Tables 1.1 and 1.2)
- Do not dig holes; if you realize that you are completely wrong, apologize and start again – the examiners expect you to be nervous
- When giving lists of causes, start with the commonest first
- When giving lists of investigations, start with the least invasive and explain how they help with the diagnosis
- Make sure the tests are appropriate; if you are going to mention a blood count, chest X-ray and so on, make sure you state why you are discussing them

**LAST-MINUTE REVISION**

**What to revise**
- Revising facts you already know is easier than learning new information in the weeks prior to the exam. Consistent learning throughout the course is the best preparation
- Target the revision to the exam. Base revision around past papers and the type of exam you are sitting
- In the last week, go over notes and take timed practice exams rather than trying to learn new data
How to revise

- Practise MCQs in a group. It is more fun and you will remember more.
- Outline essay plans and fill in the essential facts. You do not need to write out complete essays except to check timings.
- If your university offers mock or prize exams, sit them. They are good practice and will highlight weak areas.
- Use tools such as mind maps and revision aids. The more senses you use, the better the chance of the information sinking in. Jotting down lists and notes will help you absorb what you read.
- Remember to give yourself time to relax. Play sport, go out or meet your friends rather than burning the midnight oil. Learning when you are half-comatose is ineffective.
- Sleep and eat properly and avoid stimulants such as caffeine tablets.
- The night before the exam, do as little as possible. Find a way of relaxing and get a good (and sober) night’s sleep.
- And finally, do you really learn anything by frantically flicking through a book as you walk into the exam?

Table 1.2 Disease aetiology

For any clinical symptom or sign (e.g. diarrhoea\(^a\)), classify the causes into:

<table>
<thead>
<tr>
<th>Infective</th>
<th>Neoplastic</th>
</tr>
</thead>
<tbody>
<tr>
<td>Viruses</td>
<td>Colorectal cancer</td>
</tr>
<tr>
<td>Rotavirus</td>
<td>Autoimmune</td>
</tr>
<tr>
<td>Adenovirus</td>
<td>Coeliac disease</td>
</tr>
<tr>
<td>Bacteria</td>
<td>Metabolic</td>
</tr>
<tr>
<td>Staphylococcus aureus</td>
<td>Hypercalcaemia</td>
</tr>
<tr>
<td>Salmonella</td>
<td>Endocrine</td>
</tr>
<tr>
<td>Cholera</td>
<td>Thyrotoxicosis</td>
</tr>
<tr>
<td>Parasites</td>
<td>Neurological</td>
</tr>
<tr>
<td>Giardiasis</td>
<td>Autonomic neuropathy</td>
</tr>
<tr>
<td>Ascaris</td>
<td>Trauma/surgery</td>
</tr>
<tr>
<td></td>
<td>Post-gastrectomy</td>
</tr>
<tr>
<td></td>
<td>Iatrogenic</td>
</tr>
<tr>
<td></td>
<td>Drugs, e.g. laxatives</td>
</tr>
<tr>
<td></td>
<td>Idiopathic</td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Inflammatory bowel disease</td>
</tr>
</tbody>
</table>

\(^a\)List is not complete.
The ideal exam question, from the examiners’ point of view, is one that discriminates between different levels of knowledge or ability. A question that everybody gets right or wrong says little about an individual and is therefore a poor discriminator. Objective structured clinical examinations (OSCEs) are discussed in detail in Chapter 3.

**QUESTION TYPES IN WRITTEN EXAMS**

**Multiple choice questions (MCQs)**
- Questions usually comprise a stem that introduces the question, and five branches or options (Table 2.1)

**Single best answer questions (SBAs) AKA ‘Best of fives’**
- Choose the branch that provides the correct or best answer

---

**Table 2.1 MCQ styles**

1. Which of the following are true of aspirin?
   A. It may cause gastric ulceration
   B. It is associated with an increased risk of transient ischaemic attacks
   C. It is associated with renal dysfunction
   D. Its use is never indicated in acute myocardial infarction
   E. It may exacerbate inflammatory bowel disease

2. Which of the following are not true of paracetamol?
   A. It is an anti-inflammatory drug
   B. It results in hepatic necrosis in severe overdose
   C. It is metabolized in the liver
   D. It is usually given intravenously
   E. It is a non-steroidal anti-inflammatory drug

3. The following drugs are associated with the stated complication
   A. Flucloxacillin: jaundice
   B. Loperamide: diarrhoea
   C. Enalapril: cough
   D. Prednisolone: weight loss
   E. Metronidazole: nausea

**Answers:**
1. A, C, E
2. A, D, E
3. T, F, T, F, T
Example
Which one of the following is a cause of liver cirrhosis?
A. Cigarette smoking
B. Alcohol
C. Heroin
D. Cannabis
E. Methadone
*Answer: B*

True (T) or false (F) questions
- For each branch, decide whether the statement is true or false:

Example
The following are recognized causes of cirrhosis:
A. Alcohol
B. Autoimmune hepatitis
C. Hepatitis C
D. Haemochromatosis
E. Cystic fibrosis
*Answer: All are true*

Tips and tactics
- Always ensure that you know how to complete the question paper – read the instructions carefully
- For computer-scored papers, make sure that the marks you make on the paper are clear and confined to the correct part of the paper. Always use the pencil provided. Pens may not be detected properly by the computerized reader
- Keep an eye on the time. You may only have 2–3 minutes per question
- Going through the whole paper once, answering the questions you are sure of, then going back to those that need more time may ensure that you don’t miss any easy points
- Look for obvious incorrect answers. *Always* and *never* are rarely correct. Read the stem very carefully
- Check for negatives in the stem, e.g. Which of the following are *not* causes of abdominal pain? Getting this wrong could cost you 5 marks
- Even if you have no idea about the subject of a question, read the possible answers – there may be sections for which no specialist knowledge is required

Extended matching questions (EMQs)
- For a small set of questions, a common list of 15–30 options provides the list of possible answers:

Example Question 1 – Theme: Jaundice
A. Alcohol-related cirrhosis
B. Carcinoma of the pancreas
C. Hepatitis A
D. Hepatitis B
E. Hepatitis C  
F. Haemochromatosis  
G. Wilson’s disease  
H. Acute haemolysis  
I. Gilbert syndrome  
J. Primary sclerosing cholangitis  
K. Primary biliary cirrhosis  
L. Autoimmune hepatitis  
M. Budd-Chiari syndrome  
N. Cystic fibrosis  
O. Gallstone in the common bile duct

For each of the following questions, select the best answer from the list above:

I. A 28-year-old man notices that his eyes have a yellow tinge following a bad cough and cold. His liver function tests are normal apart from a bilirubin of 78 µmol/L  
II. A 76-year-old woman presents with jaundice and weight loss. She denies any abdominal pain. Her bilirubin is 280 µmol/L and the alkaline phosphatase 590 U/L. The alanine aminotransferase is 87 U/L. She has a family history of ischaemic heart disease. An ultrasound of her abdomen reveals a dilated common bile duct (Table 2.2)  
III. A 45-year-old man with known diabetes presents with jaundice. He is noted to have a deep tan and hepatomegaly. His ferritin is 1201 µg/L

Answers:  I, I, II. B, III. F

Example Question 2
A. Haemoglobin  
B. Myoglobin  
C. Albumin  
D. Ferritin  
E. Transferrin  
F. Alanine aminotransferase  
G. Collagen  
H. Fibrinogen  
I. Factor VIII  
J. Immunoglobulin  
K. Serotonin (5-hydroxytryptamine, 5 HT)  
L. Niacin  
M. Intrinsic factor  
N. Glucose-6-phosphatase  
O. Lactate dehydrogenase

Table 2.2 Picking out key facts

A 76-year-old woman presents with jaundice and weight loss. She denies any abdominal pain. Her bilirubin is 280 µmol/L and the alkaline phosphatase 590 U/L. The alanine aminotransferase is 87 U/L. She has a family history of ischaemic heart disease. An ultrasound of her abdomen reveals a dilated common bile duct. Here, the classical combination of painless jaundice and weight loss gives you the diagnosis of carcinoma of the pancreas.
For each of the following questions, select the best answer from the list above:

I. A peptide important in the absorption of vitamin B₁₂ (M)
II. An iron-containing protein derived from muscle (B)
III. A neurotransmitter released by carcinoid tumours (K)
IV. A helical structural connective tissue protein (G)
V. A protein to which bilirubin is bound in the blood (C)
VI. A protein capable of carrying oxygen in the circulation (A)
VII. A substance the deficiency of which results in pellagra (L)
VIII. A protein precursor of bilirubin (A)
IX. A protein released by injured hepatocytes (F)
X. A protein that exists in five subclasses (J)

• Note that any answer from the list may be appropriate for more than one question

A second type of EMQ

● This asks for more than one answer for each question:

Example

XI. State two molecules capable of carrying oxygen (A, B)
XII. State two proteins secreted into the intestine (J, M)
XIII. State three proteins found in erythrocytes or leucocytes (A, N, O)

Tips and tactics

● The examiner is usually looking for the best answer to the question; however, there may be other possible answers that will gain some marks

● Make an attempt at each part if you can, for the reasons given above. For each part of the question, underline the key facts and investigation results that may help you reach the correct answer

● Don’t be put off by diseases on the list of options that you know little about. They may well not be the answer to any of the questions posed

Short answers

● These questions ask you to write notes or a short summary on three or four related topics:

Example

1. Write short notes on each of the following:
   A. Thrombolysis in myocardial infarction
   B. Risk factors for ischaemic heart disease
   C. Aspirin in ischaemic heart disease

Patient management problems

● A description of a patient history and examination is given, followed by two or three questions. For each question there is a list of options and you are asked to grade the correctness of each option:

Example

A 55-year-old man, who works for a building company, is referred complaining of a cough. The cough has been present for 3 months and
on four occasions he has coughed up some blood. He now feels breathless after mild exertion. His wife has rheumatoid arthritis and he is her main carer. He has had a previous admission for angina and attends a diabetes clinic at his local GP’s. He is a smoker who drinks about 40 units of alcohol a week as beer. He is 180 cm tall and weighs 70 kg. He has some crackles at left midzone of his lungs but no other findings on examination.

Which four of the following would be most useful in making an immediate diagnosis?
1. ECG
2. Exercise ECG
3. CT of the chest
4. MRI of the lungs
5. Peak flow measurements
6. Lung function tests
7. Full blood count
8. Blood cultures
9. Arterial blood gases
10. Chest X-ray

*Answer: 1, 5, 8, 10*

A chest X-ray reveals calcified pleural lesions and increased lung markings, most notably in the bases. Based on this, what is the most likely diagnosis?
A. Carcinoma of the bronchus
B. Chronic congestive cardiac failure
C. Streptococcal pneumonia
D. Asbestosis
E. Rheumatoid lung disease

*Answer: D*

- The second variation of this question type asks for one-line answers to a series of questions about a case

**Example**

A 66-year-old man presents with chest pain. This started suddenly 2 hours previously. The pain is central and radiates to both shoulders. He is sweaty and feels very unwell. On examination, he is apyrexial and tachycardic with a blood pressure of 110/60.

1. What is the most likely diagnosis?

*Answer: Acute myocardial infarction*
2. What two investigations would be of immediate use?
   Answer: ECG and troponin

3. State four immediate therapeutic steps you would institute.
   Answer: High-flow oxygen, i.v. diamorphine, morphine, aspirin and consider thrombolysis or angioplasty

4. Suggest three possible complications of the therapies you suggest.
   Answer: Haemorrhage, gastrointestinal ulceration, respiratory depression

When answering these questions, remember that although your answers may be correct, there may be a better way of answering in order to show off your knowledge.

- Give a full answer – Acute myocardial infarction rather than Heart attack
- Give investigations of different modalities – ECG and troponin rather than Troponin and creatine kinase
- Give specific rather than general treatments with differing aims – High flow oxygen rather than Oxygen or i.v. access, diamorphine and aspirin rather than aspirin and clopidogrel

Essay questions

- These provide a title and sometimes some specific requirements for an essay:

Example

Outline the important considerations in palliation of a patient with an inoperable lung carcinoma. In your answer, outline the important therapies you would consider using.

Tips and tactics

- Read the question carefully and underline any ‘riders’ or specific instructions
- Spend a minute sketching an essay plan with section headings. This allows you to order your thoughts before committing them to paper
- Headings help the examiner as they speed up marking
- Answer the specific questions being asked; do not write a general essay on the subject in the hope of getting credit
- Always include the basics. The examiner may not assume that you know something even if it seems obvious
- Time the paper carefully. Writing two 30-minute essays instead of three 20-minute essays makes passing much harder
- Read through your answer:
  - Does it all make sense?
  - Does it answer the question?
  - Is the spelling correct?
  - Is it structured and easy to read?
- If you are running out of time, write out a structured essay plan with key facts about the subject. Most marking schemes will give you some credit for this
- If the examiners cannot read your writing, they cannot mark the essay!
CLINICAL EXAMS

Short cases

A series of patients are seen with the examiners who give you specific instructions
  • ‘Look at this patient – what is the diagnosis?’
  • ‘Examine this man’s chest’
  • ‘Listen to this woman’s heart’

You will then be expected to:
  • Introduce yourself
  • Carry out the appropriate examination
  • Present your findings and give a diagnosis, differential and management plan

Common topics for short cases

Cardiac
  • Heart sounds and murmurs
  • Cardiomegaly
  • Dextrocardia (rare)
  • Hypertensive retinopathy

Respiratory
  • Chronic obstructive pulmonary disease
  • Pulmonary fibrosis
  • Pleural effusions
  • Chest infections
  • Cystic fibrosis

Gastrointestinal
  • Chronic liver disease
  • Ileostomy/colostomy

General tips and tactics

• Be conscientious and see as many patients as possible – examiners can easily spot students who have limited experience with patients
• Practise your verbal communication skills to improve your bedside manner
• Look enthusiastic
• Speak clearly and confidently – the examiners cannot give marks for answers they cannot hear
• Always introduce yourself and do not embarrass or hurt the patient
• Look into the examiner’s eyes when you are answering
• Structure your answers sensibly, e.g. when asked for likely differential diagnosis, start with common things
• Avoid abbreviations and slang
• If you don’t understand the question ask for it to be repeated
• If you don’t know the answer, say so
• Don’t joke with the examiner (or patient) and never argue – even if you think you are correct there is little to gain and lots to lose.
• Fistulating Crohn’s disease
• Hepatosplenomegaly

**Renal**
• Transplanted kidney (right iliac fossa)
• Arteriovenous shunt for dialysis (left arm)
• Ileal urinary conduit (urine in the bag)
• Palpable kidneys (often polycystic kidney)

**Neurological**
• Multiple sclerosis
• Ophthalmoplegia
• Facial palsy
• Brachial plexus injury
• Ulnar or radial nerve damage
• Carpal tunnel syndrome
• Hemiparesis or paraparesis
• Charcot-Marie-Tooth
• Friedreich’s ataxia (check speech)
• Parkinson’s disease
• Cerebellar ataxia

**Endocrine**
• Thyroid status (Table 2.3)
• Acromegaly
• Diabetic retinopathy
• Diabetic sensory loss
• Hypopituitarism
• Cushing syndrome

**Rheumatological**
• Systemic sclerosis
• Rheumatoid arthritis
• Osteoarthritis
• Ankylosing spondylitis
• Paget’s disease of bone

**Long cases**
A prolonged period with a patient prior to presenting the case to an examiner. You may be taken back to the patient in order to assess a specific part of the examination technique.

### Table 2.3 ‘Examine this patient and assess her thyroid gland’

<table>
<thead>
<tr>
<th>Hypothyroidism</th>
<th>Hyperthyroidism</th>
</tr>
</thead>
<tbody>
<tr>
<td>Thick, rough, dry skin</td>
<td>Thin patient</td>
</tr>
<tr>
<td>Obesity</td>
<td>Sweaty</td>
</tr>
<tr>
<td>Bradycardia</td>
<td>Tachycardia ± atrial fibrillation</td>
</tr>
<tr>
<td>Slow relaxing reflexes</td>
<td>Exophthalmos with lid lag</td>
</tr>
<tr>
<td>Loss of outer third of the eyebrow</td>
<td>Tremor</td>
</tr>
</tbody>
</table>
Take a detailed history
With chronic disabling conditions, the social history is very important
Perform a thorough clinical examination
Keep an eye on the time and make legible notes. Divide the time into:
- History-taking
- Examination
- Reviewing your findings
- Going back to ask further questions
When presenting, adhere to the preferred format for your medical school
Give the positive and important negative findings
Outline a diagnosis and a differential
Outline the investigations that are appropriate
Outline treatment options, including long-term care needs if appropriate.
Objective Structured Clinical Examinations (OSCEs)

OSCEs are now the most common form of clinical examination. They allow for standardization of the examination for all candidates and a formalized and objective marking system. They are relatively expensive in terms of the number of examiners needed, but allow a large number of candidates to be assessed in a relatively short period of time. They are also fairer, as every candidate does the same stations.

**STRUCTURE**
- There is a ‘round robin’ of test stations
- The examiner stays at the station
- Each station lasts 5–10 minutes
- Stations may be paired, e.g. a clinical examination at one station and questions about the examination and diagnosis at the next
- Each station has a strict marking sheet (Fig. 3.1)
- A wide variety of stations can be included, allowing broad testing of skills and knowledge

**TYPES OF STATION**

**General**
- Taking a targeted history for a clinical scenario
- Examining a ‘patient’ (may be a simulated patient) – see speciality chapters
- Patient photographs
- X-rays – see Radiology, Chapter 5
- ECGs – see Cardiology, Chapter 9
- Laboratory test interpretation – see Clinical chemistry, Chapter 6

**Practical skills**
- Inserting a cannula
- Inserting a urinary catheter
- Taking blood
- Taking blood gases
- Administering i.v./i.m./s.c. injections
- Setting up an i.v. infusion
- Checking a blood transfusion
- Cardiopulmonary resuscitation
- Defibrillation
- Suturing
- Basic respiratory function tests
- Administration of a nebuliser
- Prescription and administration of oxygen therapy
- Breast/testes or rectal exam on a model
- Ophthalmoscopy
Candidate Name: Examination number:

Candidate instructions: Mrs Lewis has been referred having noticed blood in her stools. You have been asked by the consultant to take a focussed history of the presenting complaint. You do not need to ask about the past medical or social history, the drug history or to carry out a systems review. You do not need to present your findings to the examiner.

Examiner instructions: Please assess the candidate using the criteria listed.

<table>
<thead>
<tr>
<th>Criteria</th>
<th>adequate</th>
<th>inadequate</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Introduces self to patient, using own name, patient’s name, role and a greeting</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>States reason for the interview</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>Obtains consent to proceed</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>Asks patient's age</td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>Asks about occupation</td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>Obtains history of PR bleeding</td>
<td></td>
</tr>
</tbody>
</table>

Specific information points elicited

<table>
<thead>
<tr>
<th>Information points</th>
<th>Adequate</th>
<th>Inadequate</th>
</tr>
</thead>
<tbody>
<tr>
<td>7</td>
<td>Nature of bleeding (bright red, mixed with stool) both to score</td>
<td></td>
</tr>
<tr>
<td>8</td>
<td>Duration of symptoms</td>
<td></td>
</tr>
<tr>
<td>9</td>
<td>Frequency of bleeding</td>
<td></td>
</tr>
<tr>
<td>10</td>
<td>Previous episodes</td>
<td></td>
</tr>
<tr>
<td>11</td>
<td>Recent change in bowel habit</td>
<td></td>
</tr>
<tr>
<td>12</td>
<td>Normal bowel habit</td>
<td></td>
</tr>
<tr>
<td>13</td>
<td>Weight loss or anorexia (both to score)</td>
<td></td>
</tr>
<tr>
<td>14</td>
<td>Dietary changes</td>
<td></td>
</tr>
<tr>
<td>15</td>
<td>Shortness of breath</td>
<td></td>
</tr>
<tr>
<td>16</td>
<td>Medication history</td>
<td></td>
</tr>
<tr>
<td>17</td>
<td>Family history</td>
<td></td>
</tr>
<tr>
<td>18</td>
<td>Associated symptoms</td>
<td></td>
</tr>
</tbody>
</table>

Approach to patient

<table>
<thead>
<tr>
<th>Approach to patient</th>
<th>Adequate</th>
<th>Inadequate</th>
</tr>
</thead>
<tbody>
<tr>
<td>19</td>
<td>Active listening (verbal and non-verbal)</td>
<td></td>
</tr>
<tr>
<td>20</td>
<td>Clarifies and reviews</td>
<td></td>
</tr>
<tr>
<td>21</td>
<td>Avoids leading question</td>
<td></td>
</tr>
<tr>
<td>22</td>
<td>Avoids multiple questions</td>
<td></td>
</tr>
<tr>
<td>23</td>
<td>Does not use jargon or gives explanations</td>
<td></td>
</tr>
</tbody>
</table>

Examiner’s rating

<table>
<thead>
<tr>
<th>Examiner’s rating</th>
<th>4 good</th>
<th>3 pass</th>
<th>2 borderline</th>
<th>1 fail</th>
</tr>
</thead>
</table>

Fig. 3.1 Each station has a strict marking sheet.
Management questions

- Medical emergencies
- Writing a fluid chart
- Writing a prescription
- Reviewing a drug chart
- Writing a discharge summary

Communication

- Explaining a prescription to a patient
- Discussing a diagnosis with a patient
- Obtaining consent
- Describing a practical procedure
- Breaking bad news

Tips and tactics

- See General tips and tactics for clinical exams (Ch. 2)
- Make sure you are comfortable with the common procedures that crop up in OSCEs
- Practise the commonly needed practical skills in a clinical skills lab. These are easy marks to get
- Follow the (usually written) instructions
- At ‘patient-based’ stations, the examiner will have no verbal role. If you are expected to present findings, the instruction sheet will specifically tell you
- Even if a station has gone badly, you may have picked up some marks for professionalism, communication or rapport with the patient
- At the end of the station, forget it and clear your mind ready for the next one. Remember each station is a fresh start

EXAMPLE STATIONS

For each of the following stations, the key ‘point-scoring’ things that you should do are highlighted. There are general points for each type of station that are outlined at the beginning of each category. Don’t forget to confirm your examination number and name with the examiner before you start.

Clinical history

Remember to:

- Read the instructions and follow them exactly
- Introduce yourself (to the patient) using your and their name
- Explain who you are and ask permission to proceed
  - This doesn’t have to be too formal: ‘Would you mind if I asked you a few questions?’ will do
- Ask a couple of general questions, then rapidly target in on the key facts pertinent to the case
- Try not to lead the patient – ‘So where do you get the pain’, rather than ‘So you have chest pain?’
> Give the patient a chance to expand on the answer
> Ask if there is anything else they want to tell you
> Avoid going into a long discussion about your diagnosis – these stations are about you getting the appropriate history, not explaining the diagnosis to the patient
> During the patient interaction, try to ignore the examiner unless specific instructions are given or you are asked to present your findings
> Once the bell goes, thank the patient and leave

**Chest pain**

Mr Davis is a 57-year-old man who attended accident and emergency with chest pain. Take an appropriate history from him. The ‘patient’ will have some specific pain features indicating the cause of the pain. This is most commonly acute myocardial infarction or angina. Less commonly gastro-oesophageal reflux disease (p.218). Your history needs to elicit these. The key facts that you should ask about are:

- Duration of the pain
- Previous episodes
- Character of the pain
  - Heavy/crushing in acute MI
  - Dull/tight in angina
  - Continuous or varying
- Intensity (on a range from 1–10)
- Site
- Radiation – to neck or left arm in cardiac ischaemia

**Associated features**

- Nausea
- Sweating
- Dizziness/faintness
- Shortness of breath
- Inducing activities
  - Exercise
  - Cold, windy days
- Relieving activities
  - Rest
  - Taking glyceryl trinitrate
- Risk factors for ischaemic heart disease
  - Family history of heart disease, stroke, hypertension or diabetes
  - Smoking history
  - Diabetes mellitus
  - Hypertension
  - Previous history of ischaemic heart disease
  - Elevated cholesterol
- Medication history
- Allergies to medication
- Risk factors for treatment
  - Recent GI bleeding
  - Recent major surgery
  - Recent cerebrovascular accident
  - Blood coagulopathy
  - Diabetic eye disease
Shortness of breath without chest pain

Mrs Jones is a 78-year-old woman with increasing shortness of breath. Take an appropriate history from her.

The initial differential

- Congestive cardiac failure/acute pulmonary oedema
- ‘Silent’ ischaemic heart disease
- Pneumonia/lower respiratory tract infection
- Exacerbation of chronic obstructive pulmonary disease/asthma
- Bronchogenic carcinoma

Initial questions to determine the most likely cause

- New symptom or recurrence of previous symptom
- Duration and whether getting worse
- Associated symptoms
  - Cough
  - Sputum production and type – purulent/non-purulent/frothy
  - Presence of orthopnoea and paroxysmal nocturnal dyspnoea
- History of ischaemic heart disease
- Risk factors for ischaemic heart disease or COPD

Once the underlying cause is clear, you should target your history to the appropriate disease.

Silent ischaemic heart disease

- As for chest pain above

Congestive cardiac failure/pulmonary oedema

- Onset and severity
- Initiating, exacerbating and relieving factors
- Orthopnoea and paroxysmal nocturnal dyspnoea
- Cough/frothy sputum
- Ankle swelling
- Palpitations
- Chest pain
- Past history
  - Ischaemic heart disease
- Risk factors as for cardiac chest pain
- Medication history

Pneumonia/lower respiratory tract infection

- Cough
- Purulent sputum/colour of sputum
- Pleuritic chest pain
- Sweats/fevers
- Associated diarrhoea (atypical pneumonia)
- Risk factors
  - Smoking
  - Occupational exposure (dust/asbestos)
  - Animal exposure (birds)
  - Travel and contact history (TB)
  - HIV
**Objective Structured Clinical Examinations (OSCEs)**

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**Chronic obstructive pulmonary disease/asthma**
- Cough
- Sputum production
- Wheeze
- Acute or insidious onset
- Exposure to precipitant
- Usual peak flow
- Usual exercise tolerance
- Exercise tolerance at present
- Previous admissions
- Previous admissions to ITU
- Smoking history
- Use of steroids
- Domiciliary oxygen cylinders/concentrator
- Home nebulizer
- Indicators of infection
  - Fevers
  - Purulent sputum

**Shortness of breath with chest pain**

Peter Smith is a 25-year-old man who presents with severe left-sided chest pain and shortness of breath.

**Differential diagnosis**
- Pneumonia (see above)
- Pleurisy
- Ischaemic heart disease (see above)
- Pulmonary embolus
- Pneumothorax

**Pleurisy**
- Preceding cough/sputum
- Fever
- Flu-like illness
- Pleuritic chest pain (worse on deep breathing)

**Pulmonary embolus**
- Sudden onset
- Pleuritic chest pain
- Shortness of breath
- Haemoptysis
- Swollen calf
- Risk factors
  - Immobility (travel/surgery/other illness)
  - Smoking
  - Oral contraceptive pill
  - Pro-coagulopathy (family history)
  - Previous miscarriages
  - Inflammatory disease
  - Malignant disease
  - Previous DVT/PE

**Pneumothorax**
- Classically tall thin young man
- Sudden onset
- Chest wall injury
Short of breath with or without pain
No fever
No prodrome
Risk factors
- Asthma
- COPD
- Pulmonary fibrosis

**Abdominal pain**
Mr Flintoff is a 65-year-old man with abdominal pain. Take a history to ascertain the cause.

**Basic questions**

**Site**
- Epigastric – gastro-oesophageal reflux or dyspepsia
- Right subcostal – liver/biliary tree (e.g. gallstones)
- Left sided – diverticulosis/IBS/constipation
- Supra-pubic – bladder/pelvis
- Renal angles – renal stones/pyelonephritis

**Character**
- Constant
- Spasms/colicky

**Associated symptoms**
- Nausea
- Vomiting
- Diarrhoea
- Constipation
- Abdominal distension

**Exacerbating features**
- Eating
- Posture changes
- Deep breaths
- Specific foods, e.g. fatty foods (may suggest gallstones)

**Relieving features**
- Eating
- Vomiting
- Defaecation
- Antacids, other medications

**Gastro-oesophageal reflux**
- Central epigastric and retrosternal pain
- Burning/acidic in nature
- Worse with alcohol/caffeine/spicy foods
- Relieved by antacids
- Wakes from sleep at night
- Better when lying on left side
- Worse when bending over

**Biliary colic**
- Colicky pain (comes in waves)
- Right subcostal region
- Associated nausea/vomiting
- Associated jaundice
Objective Structured Clinical Examinations (OSCEs)

Pass Finals

24

- Dark urine
- Pale stools

Renal colic

- Loin pain radiating to iliac fossa/testes/labia
- Vomiting
- Very severe colicky pain
- Associated symptoms
  - Haematuria
  - Anuria
- Risk factors
  - Hot weather
  - Previous stones
  - Gout
  - Crohn’s disease
  - Urinary tract infections
  - Diuretics

Interpretation of results stations

Radiology

Radiology images in OSCEs tend to be simple investigations (chest X-rays, abdominal films, rarely CT scans of the head) with gross abnormalities and a short clinical history giving clues as to the diagnosis. They may also ask about the management of the abnormality. Chapter 5 covers all of the important films.

Chest X-rays

- Pneumothorax
- Tension pneumothorax
- Air under the diaphragm
- Pneumonia
- Pulmonary oedema
- Lung cancer

Abdominal films

- Renal stones
- Small bowel obstruction
- Sigmoid volvulus
- Toxic megacolon
- Pancreatic calcification

CT head

- Subdural/extradural/sub-arachnoid haemorrhage
- Mass lesions with oedema and midline shift
- Acoustic neuroma

Example A 67-year-old man is admitted with anorexia and a productive cough. He has been feeling unwell for about 2 weeks with a cough productive of bloodstained sputum. His chest X-ray is shown in Figure 3.2.

His temperature on admission is 36.7°C, oxygen saturation 93% on air

1. Describe the abnormality seen
   Answer: Cavitating lesion in right lung

2. Suggest three diagnoses in order of likelihood
   Answer: Lung abscess, bronchogenic carcinoma, pulmonary metastasis

3. Name two further appropriate investigations
Answer: High resolution CT scan of the chest; sputum microscopy and culture

**Example**  A 58-year-old woman is admitted for a CT-guided biopsy of a mass in the liver. List the important complications about which she should be advised and explain the procedure to her in order to gain informed consent

**Answer:** Complications about which she should be advised:

- Pain
- Bleeding
- Perforation of bowel
- Injury to right kidney
- Perforated gallbladder
- Pneumothorax

**Example**  A 76-year-old man presents with right loin pain and haematuria. His abdominal X-ray is shown in Figure 3.3.

1. Describe the abnormality seen.
   **Answer:** Calcified mass in the right lateral abdomen

2. Suggest two possible diagnoses
   **Answer:** Calcified (porcelain) gallbladder; renal calcification (nephrocalcinosis)

3. Suggest two useful radiological investigations
   **Answer:** Renal ultrasound CT abdomen

**Laboratory investigations**

Again, these tend to be simple investigations and ask for your interpretation and management (see Ch. 6)

**Example**  With reference to the following blood test results, answer the questions beneath:

- Hb 98 g/L WCC $7.2 \times 10^9$ /L platelets 198 MCV 101 fl
- Blood film: hypersegmented neutrophils

A. What is the haematological diagnosis?
   **Answer:** Macrocytic (megaloblastic) anaemia
B. List 3 possible causes of your diagnosis
   *Answer: Vitamin B<sub>12</sub> deficiency; folic acid deficiency; chronic liver disease*
C. Name two tests that would help you in determining the diagnosis
   *Answer: Liver biochemistry; serum haematinics*

**Practical procedure stations**

As with clinical stations, there will be a short clinical scenario followed by an instruction. As always, introduce yourself, explain the procedure, get verbal consent and give clear instructions to the patient. You may also be asked to list possible complications or comment on the result.

**Measuring peak flow**

Mrs Robinson has asthma and is breathless. Please measure the peak flow.

*Instructions for patient*
- Please follow the student’s instructions as they are given. Do not try to help or hinder the student but do try to do as they say.

*Instructions to examiner*
- The student introduces him/herself using his/her name and gains verbal consent
- Ensures a new disposable mouthpiece is attached
- Explains to the patient what to do, including
  - Asking the patient to take a deep breath in
  - Then blow out as hard and as fast as possible into the mouthpiece

![Fig. 3.3 Abdominal X-ray.](image-url)
Example stations

- Ensures that the patient understands the lips should be tight around the mouthpiece
- Ensures that the patient can hold the meter without obstructing the linear scale
- Measures the peak flow reading using the linear scale
- Remembers to assess the best of three measurements
- Encourages and thanks the patient

**Recording a 12-lead ECG**
- Ensure the patient is comfortable at rest, ideally lying flat
- Turn the machine off

**Limb leads**
- Right leg – Black
- Right arm – Red
- Left leg – Green
- Left arm – Yellow

**Chest leads**
- V1–4th intercostal space, right of sternum
- V2–4th intercostal space left of sternum
- V3 – Half way between V2 and V3
- V4 – Apex of the heart
- V5 – Same horizontal plane as V4, anterior axillary line
- V6 – Same horizontal plane as V4, mid axillary line
- Turn on the ECG machine, choose: Gain 10 mm/mV, speed 25 mm/second
- Select 12-lead ECG and press start

**Taking the blood pressure**
- Ensure the patient is at rest and comfortable
- Explain procedure
- Choose appropriate sized cuff
- Palpate brachial artery
- Place cuff around upper right arm with the inflation bag over the brachial artery (precise location usually marked with an arrow on the cuff)
- Inflate until the radial pulse is not palpable then increase by 20 mmHg
- Place diaphragm of stethoscope over brachial artery just below the cuff
- Gradually reduce pressure until first sound is heard (Korotkoff I = systolic blood pressure)
- Continue to reduce until silence (Korotkoff V = diastolic pressure)
- *Note:* the sounds may disappear (Korotkoff II) then reappear (Korotkoff III) before becoming muffled (Korotkoff IV)

**Urinary retention/catheterization**

**Instructions to student**
- This patient is complaining of difficulty passing urine and excruciating lower abdominal pain. He is unable to keep still easily because of pain. Please take a brief history and proceed as appropriate.

**Instructions to examiner**
- The student is presented with a male in acute urinary retention. No complicating features. Needs urgent catheterization
- The student introduces him/herself
- Obtains hx of urinary retention
Explain procedure of urethral catheter and gains consent
Administers prophylactic antibiotics after checking for allergies
Uses sterile technique
Uses local anaesthetic gel
Chooses appropriate size catheter
Inserts catheter
Obtains specimen of urine for analysis
Attaches bag
Documents procedure and leaves appropriate instructions for care of catheter

Taking blood cultures
An aseptic technique is vital to avoid skin contaminants
Repeat cultures from different sites at different times
Wear gloves for the procedure
Select an appropriate vein
Thoroughly clean the overlying skin
Do not touch the skin
Take 15–20 mL of blood
Open the tops of the culture bottles
Clean the top of the bottle with a sterile wipe
Place a fresh needle on the syringe and insert through the seal of each bottle, placing 8–10 mL of blood in each bottle
Clearly label the samples
Send to laboratory or place in incubator

Completion of microbiology request forms
In order to make an accurate diagnosis, the following information is vital:
Patient details
Clinical details: duration and type of illness, other related features
Antibiotic therapy: duration and type of treatment
History of foreign travel
Type of specimen
Requested investigation
Clinical risks – viral hepatitis/HIV

Specific clinical examination stations
Sometimes you will be asked to demonstrate a specific piece of history-taking or examination such as those below.

Examination of a patient with Parkinson’s disease
Instructions to student
Please examine this patient, paying particular attention to the power and tone of the upper limbs. Do not examine sensation. You may undertake any further examination of the neurological system you consider appropriate. You have 5 minutes, after which you will be asked to summarize the findings and come up with a diagnosis.

Instructions to examiner
The student introduces themselves and makes sure the patient is comfortable
Observation (tremor, muscle bulk, fasciculation, bradykinesia, mask-like facies, lack of blinking)
Asks about pain
Moves arms demonstrating cogwheel rigidity
Examines arms for power
Tests reflexes
Extra mark for: asking the patient to walk, glabellar tap, asking for example of handwriting, assessing function, e.g. buttons, knife and fork
Presentation of main features
Diagnosis

Examination of the thyroid gland and thyroid status
Mrs White has had palpitations and weight loss. Examine her thyroid gland.

- General inspection – look for signs of thyroid disease
- Examine the neck to look for a goitre
- Ask patient to take a sip of water and hold it in the mouth, then ask the patient to swallow while you watch the neck – look for movement of goitre with swallowing
- Stand behind the patient and gently feel the thyroid with both hands starting in the centre below the thyroid cartilage over the trachea, moving laterally to the two lobes which extend behind the sternomastoid muscle. Ask the patient to swallow again while you palpate. Assess the goitre for size, nodularity or diffuse enlargement, discrete nodules and firmness
- Palpate for lymph nodes
- Auscultate – listen over the thyroid for a bruit
- Pulse – count the rate and note presence or absence of atrial fibrillation
- Palms – warm and sweaty
- Tremor of fingers on outstretched arms
- Reflexes – slow relaxing in hypothyroidism, brisk in hyperthyroidism
- Examine the eyes for exophthalmus, lid retraction, lid lag
- Examine the reflexes for slow relaxation of in hypothyroidism

Deliberate self-harm assessment
Instructions for student
- This patient is recovering from a paracetamol overdose. Please assess her risk factors for suicide.

Instructions for patient
- Please answer the student’s instructions as they are asked. You have a previous history of depression and your brother killed himself by hanging. Your husband has recently left home and your daughter has an incurable cancer. Please act withdrawn and give answers slowly. Please ensure it is clear that you did not expect your suicide plan to be discovered.

Instructions to examiner
- The student introduces him/herself and gains verbal consent
- Performs suicide assessment
- Questions to be asked:
  - Was there a clear precipitant/cause for the attempt?
  - Was the act premeditated?
  - Did the patient leave a suicide note?
  - Had the patient taken pains not to be discovered?
  - Did the patient make the attempt in strange surroundings (i.e. away from home)?
  - Would the patient do it again?
  - Concern if any answer to the above is positive
Objective Structured Clinical Examinations (OSCEs)

- Also establish:
  - Has the precipitant/cause for the attempt resolved?
  - Is there continuing suicidal intent?
  - Does the patient have psychiatric symptoms?
  - What is the patient’s social support system?
  - Has the patient inflicted self-harm before?
  - Has anyone in the family ever taken their life?
  - Does the patient have a physical illness?

Communication with patients

- This may involve explaining a diagnosis, prescription or procedure, taking consent or breaking bad news
- Always use lay language rather than medical jargon
- Allow the patient time to speak and specifically ask if there are any questions

Explanation of the diagnosis of epilepsy

Instructions to student

- A 30-year-old mother of two has been referred by her GP with new tonic clonic seizures due to grand mal epilepsy. Please explain the diagnosis to the patient and give her appropriate advice on living with epilepsy and include suggestions to start therapy with any one of the first-line single agent therapies available. You have 10 minutes.

Instructions to the patient

- You have been referred to the hospital after having had two seizures which your GP thinks are epilepsy. Tests have confirmed the diagnosis. This doctor is going to explain the diagnosis and how to live with the condition and suggest treatment with tablets to reduce the number of fits.

Instructions to examiner

- The student introduces him/herself and makes sure the patient is comfortable
- Explains the diagnosis using lay terms and medical terms
- Checks understanding
- Explains options for treatment
- Explains likely benefits of drug therapy
- Gives information on side-effects of drugs
- Discusses driving regulations
- Makes time to listen to patient’s questions
- Gives extra back-up information to take home (e.g. leaflet, website address of epilepsy foundation, nurse specialist number, secretary’s number).

Corticosteroid prescription and dispensing

Instructions to student

- You are giving this patient a 6-week course of prednisolone, starting at 40 mg, to treat polymyalgia rheumatica. You are aiming to reduce the dose to half or less over 6 weeks. Please write a prescription and give it to the patient with appropriate advice.

Instructions to examiner

- The student introduces him/herself
- Checks patient’s details
- Asks about drug allergies
Issues accurate prescription: date, address, name, contact number, patient’s name and address and GP, legible accurate prescription and signature
Gives patient a steroid card
Explains to the patient that they must show this to any medical professional they see
Advice about side-effects (psychiatric symptoms, skin changes, weight changes and fat distribution, diabetes, bone loss, immunosuppression) is given
Warns patient not to stop the drug suddenly
Issues a prescription for bone protection (calcium and vitamin D or a bisphosphonate)

Diabetes: starting insulin
Mr Coleman is a 21-year-old man recently diagnosed as having insulin-requiring diabetes mellitus. Explain to him how to use insulin and self-administration.

Marking sheet
- Explanation of insulin regime
- Explains and demonstrates ‘stix’ testing of blood glucose using a pinprick
- Instruction and demonstration of sub-cut injection, watch patient attempt to give injection; give feedback on technique
- Explain importance of varying site of injection
- Warn about hypoglycaemic episodes
- Warn about other side-effects
- Warn about failure to take insulin increasing risk of ketoacidosis
- Explain importance of taking insulin when ill
- Check understanding, listen to questions
- Arrange follow-up appointment
- Give contact detail of responsible health professional (e.g. diabetes clinical nurse specialist)

Controlled drug prescriptions
Miss Madden is a 65-year-old woman with metastatic breast carcinoma who is taking morphine. Write a prescription for 10 mg of oral liquid morphine (Oramorph) 4 times a day for 1 month.
- Name/address/date of birth of patient
- Write out name of drug, dose regimen and total amount to be dispensed in words and numbers in indelible ink:
  - Morphine sulphate suspension ten (10) milligrams four (4) times a day for twenty-eight (28) days, total prescribed one thousand, one hundred and twenty (1120) milligrams
- Sign, print your name and date the prescription

Completion of death certificates
Personal details of the deceased
- Name
- Age – in completed years or if less than 1 year, in completed months
- Place of death – for hospital patients, this is the name of the hospital
- For patients at home, it is the private address
- For deaths elsewhere, the locality is recorded

Circumstances of certification
- Last seen alive by me – record the date that you last saw the patient alive
Information from post-mortem
- You should indicate here if the information you give takes account of a post-mortem
  - Ring option 1 if a post-mortem has been done
  - Ring option 2 if information from a post-mortem may be available later
  - Ring option 3 if a post-mortem is not being held

Seen after death
- Ring one option (a, b or c) only to indicate whether you or another medical practitioner saw the deceased after death

Cases reported to the coroner
Some cases are discussed with the coroner/procurator fiscal and a certificate is completed by the attending doctor after agreement with the coroner/procurator fiscal, e.g. patients dying within 24 hours of arrival at hospital but for whom the cause of death is known. If this is the case, then ring option 4 and tick box A on the back of the certificate. Remember for cases referred to the coroner for investigation, a certificate is not completed by the attending doctor (Table 3.1).

Cause of death statement
- Remember always avoid abbreviations
- This section of the certificate is divided into 2 parts:
  
  Part I
- Here the immediate cause of death and any underlying cause(s) are recorded
- It is vital that this section is completed accurately and fully with as specific details as possible, e.g. histological cell types for malignancies if known

Example A patient died from an intracerebral haemorrhage caused by cerebral metastases from a primary malignant neoplasm of the left main bronchus. This should be entered as follows:
- Disease or condition that led directly to death
  I (a) Intracerebral haemorrhage

<table>
<thead>
<tr>
<th>Table 3.1 Referral decisions</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>A death should be referred to the coroner/procurator fiscal for investigation if:</strong></td>
</tr>
<tr>
<td>The cause of death is unknown</td>
</tr>
<tr>
<td>The deceased was not seen by the certifying doctor either after death or within 14 days before death</td>
</tr>
<tr>
<td>The death was violent or unnatural or suspicious</td>
</tr>
<tr>
<td>The death may be due to an accident</td>
</tr>
<tr>
<td>The death may be due to self-neglect or neglect by others</td>
</tr>
<tr>
<td>The death may be due to industrial disease or related to the deceased’s employment</td>
</tr>
<tr>
<td>The death may be due to an abortion</td>
</tr>
<tr>
<td>The death occurred during an operation or before recovery from the effects of an anaesthetic</td>
</tr>
<tr>
<td>The death may be a suicide</td>
</tr>
<tr>
<td>The death occurred during or shortly after detention in police or prison custody</td>
</tr>
</tbody>
</table>
Intermediate cause of death
(b) Cerebral metastases

Underlying cause of death
(c) Squamous cell carcinoma of the left main bronchus
Occasionally, there are apparently two distinct conditions leading to
death. If there is no way of choosing between them they should be
entered on the same line and it should be indicated that they are joint
causes of death.

Do not use terms that imply a mode of dying rather than a cause of
death (Table 3.2).

Table 3.2 Terms implying a mode of death rather than a cause of death

<table>
<thead>
<tr>
<th>Disease or condition that led directly to death</th>
<th>Intermediate cause of death</th>
<th>Underlying cause of death</th>
</tr>
</thead>
<tbody>
<tr>
<td>(a) Intracerebral haemorrhage</td>
<td>(b) Cerebral metastases</td>
<td>(c) Squamous cell carcinoma of the left main bronchus</td>
</tr>
</tbody>
</table>

Other conditions contributing to death
II. Diabetes mellitus

Employment-related death
If you believe that the death may have been due to (or contributed to
by) employment followed at any time by the deceased, you should
indicate this by ticking the appropriate box on the front of the
certificate and report the death to the coroner/procurator fiscal
Signature of certifying doctor and name of the consultant
Sign the certificate and add your qualifications, address and the date
Print your name in block capitals also
If the death occurred in hospital, the name of the consultant
responsible for the care of the patient must also be recorded
Finally, complete the Notice to Informant section and the counterfoil of the certificate

**SUMMARY**

OSCE examinations can include any practical aspect of day-to-day medical practice. Use textbooks of clinical skills and clinical skills labs to get an idea of the techniques and procedures.

**Remember the cardinal rules**

- Use lay language
- Introduce yourself
- Seek consent
- Follow the instructions
- Develop a rapport with the patient
- Clear your mind between stations.
Pharmacology

- The study of the interaction between chemicals and the human body

Therapeutics

- The treatment of disease (any modality)

Pharmacodynamics

- The physiological and biochemical effects of a drug including their mechanism(s) of action

Pharmacokinetics

- The effect of physiological processes on drug concentrations and action

Cardinal features of therapeutics

- The right patient
- The right drug
- The right dose
- At an affordable cost

The right patient

- Clear diagnosis and/or clinical need (i.e. the drug will improve symptoms or outcome)
- Clear benefit in an asymptomatic/well patient (e.g. vaccination/primary prevention of disease or contraception)
- Absence of a contraindication due to co-morbidity (Table 4.1) or drug interaction (Tables 4.2–4.4)

The right drug

- Tolerability (e.g. side-effects)
- Efficacy (improved symptoms/prognosis demonstrated in trial data)
- Safety (efficacy balanced against risks of therapy)
- Therapeutic index (Fig. 4.1)
- Compliance and patient preference

The right dose

- Careful prescribing
- Careful dispensing and patient instructions
- Monitoring: Table 4.4 (drug levels, toxicity, early detection of adverse effects)

Affordability

- Pharmacoeconomics (value for money)
- Marketing (using generic vs branded drugs)
- Assessment by independent review (e.g. National Institute for Health and Clinical Excellence, NICE)
### Table 4.1 Common drug contraindications

<table>
<thead>
<tr>
<th>Co-morbidity</th>
<th>Drugs to avoid</th>
<th>Effect</th>
</tr>
</thead>
<tbody>
<tr>
<td>Asthma</td>
<td>Beta-blockers, Adenosine</td>
<td>Bronchospasm</td>
</tr>
<tr>
<td>Hypertension</td>
<td>Non-steroidal anti-inflammatories, COX-II inhibitors</td>
<td>Increased hypertension via sodium retention</td>
</tr>
<tr>
<td>Parkinson’s disease</td>
<td>Neuroleptics</td>
<td>Worsening symptoms</td>
</tr>
<tr>
<td>Respiratory failure</td>
<td>Opiates</td>
<td>Respiratory depression</td>
</tr>
<tr>
<td>Epilepsy</td>
<td>Tricyclic antidepressants, Anti-malarials, Anti-psychotics</td>
<td>Reduced seizure threshold</td>
</tr>
<tr>
<td>Atrioventricular block</td>
<td>Digoxin, Beta-blockers, Diltiazem</td>
<td>Heart block</td>
</tr>
<tr>
<td>Chronic liver disease</td>
<td>Warfarin</td>
<td>Increased sensitivity/bleeding</td>
</tr>
<tr>
<td>Renovascular disease</td>
<td>ACE inhibitors, Angiotensin II receptor antagonists</td>
<td>Reduced renal blood flow</td>
</tr>
</tbody>
</table>

### Table 4.2 Common pharmacokinetic drug interactions

<table>
<thead>
<tr>
<th>Drug 1</th>
<th>Drug 2</th>
<th>Interaction</th>
</tr>
</thead>
<tbody>
<tr>
<td>Warfarin</td>
<td>P450 inhibitors, Aspirin</td>
<td>Increased prothrombin time, Increased bleeding time</td>
</tr>
<tr>
<td>Theophylline</td>
<td>P450 inhibitors</td>
<td>Arrhythmia</td>
</tr>
<tr>
<td>Iron</td>
<td>Calcium salts (e.g. milk, antacids)</td>
<td>Reduced iron absorption</td>
</tr>
<tr>
<td>Digoxin</td>
<td>Quinidine</td>
<td>Displacement of drug from protein binding → bradycardia</td>
</tr>
<tr>
<td>Lithium</td>
<td>Thiazides, NSAIDs</td>
<td>Failure of excretion leading to seizures/ataxia</td>
</tr>
<tr>
<td>Oral contraceptive pill</td>
<td>Antibiotics, Anti-epileptics</td>
<td>Failure of contraception</td>
</tr>
<tr>
<td>Azathioprine</td>
<td>Allopurinol</td>
<td>Bone marrow suppression</td>
</tr>
</tbody>
</table>
**Pharmacodynamics**

**Drug–receptor interactions**

Biological effects of a drug will depend on several factors:

- **Affinity** – strength of binding to the target receptor
- **Efficacy** – effect by unit concentration
- **Potency** – dose of drug required for a given effect
- **Dose response** – effect plotted against dose
- **Drug – receptor interactions**
- **Agonists** – bind and activate receptor function
- **Partial agonists** – bind but cannot maximally activate a response
- **Antagonists** – block a receptor but no biological response – will inhibit physiological activation of the receptor

---

**Table 4.3 Common pharmacodynamic drug interactions**

<table>
<thead>
<tr>
<th>Drug 1</th>
<th>Drug 2</th>
<th>Interaction</th>
</tr>
</thead>
<tbody>
<tr>
<td>Beta-blockers (Atenolol)</td>
<td>Verapamil</td>
<td>Bradycardia/asystole</td>
</tr>
<tr>
<td></td>
<td>Diltiazem</td>
<td></td>
</tr>
<tr>
<td>ACE inhibitors</td>
<td>Loop diuretics</td>
<td>Hypotension</td>
</tr>
<tr>
<td>Digoxin</td>
<td>Amiodarone</td>
<td>Heart block</td>
</tr>
<tr>
<td></td>
<td>Verapamil</td>
<td>Heart block</td>
</tr>
<tr>
<td></td>
<td>Diuretics</td>
<td>Hypokalaemia → toxicity</td>
</tr>
<tr>
<td>Beta₂ agonists</td>
<td>Beta-blockers</td>
<td>Loss of effect/bronchospasm</td>
</tr>
<tr>
<td>(salbutamol)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Table 4.4 Drugs and the cytochrome P450 pathway**

<table>
<thead>
<tr>
<th>Drugs metabolized by the CyP450 pathway</th>
<th>Drugs that induce CyP450 activity</th>
<th>Drugs that inhibit CyP450</th>
</tr>
</thead>
<tbody>
<tr>
<td>Warfarin</td>
<td>Phenytoin</td>
<td>Omeprazole</td>
</tr>
<tr>
<td>Amitriptyline</td>
<td>Carbamazepine</td>
<td>Diltiazem</td>
</tr>
<tr>
<td>Ciclosporin</td>
<td>Barbiturates</td>
<td>Erythromycin</td>
</tr>
<tr>
<td>Statins</td>
<td>Rifampicin</td>
<td>Sodium valproate</td>
</tr>
<tr>
<td>Phenytoin</td>
<td>Alcohol</td>
<td>Isoniazid</td>
</tr>
<tr>
<td>Losartan</td>
<td>Allopurinol</td>
<td>Quinolones</td>
</tr>
<tr>
<td>Sertraline</td>
<td>Protease inhibitors</td>
<td>Grapefruit juice</td>
</tr>
<tr>
<td>Aminophylline</td>
<td>St John’s Wort</td>
<td></td>
</tr>
</tbody>
</table>

**Fig. 4.1** Definition of the therapeutic index.

**Pharmacology**

**Therapeutic index** = \[
\text{Lethal dose for 50\% of the population (LD}_{50}) / \text{Effective dose for 50\% of the population (ED}_{50})
\]
Competitive antagonists – reversibly block so high agonist concentrations their effect is reduced
Irreversible agonists – only lose effect once new receptors are formed

Mechanisms of action

Direct physiochemical effect:
- Alteration of pH (e.g. sodium bicarbonate, antacids)
- Osmotic diuretics (mannitol)
- Osmotic laxatives (lactulose)

Receptor antagonism:
- Beta-blockers (atenolol)
- Angiotensin II receptor antagonists (losartan)
  Direct binding to target compound:
- Infliximab: antibody that binds to tumour necrosis factor and stops its activity

Receptor agonism:
- β; receptors (salbutamol)
- Epinephrine

Transmembrane channel blockade:
- Calcium channel blockers (amlodipine)
- Na⁺/K⁺ ATPase blocker (Digoxin)
- Neurotransmitter reuptake inhibitors (Sertraline)

Enzyme inhibitors:
- Cyclo-oxygenase inhibitors (aspirin/NSAIDs)
- HMG CoA reductase inhibitors (statins)

Purine analogues → reduced DNA synthesis:
- Azathioprine

Antibacterials:
- Inhibition of bacterial cell wall formation (e.g. penicillins)
- Inhibition of bacterial genome replication (e.g. quinolones)
- Inhibition of bacterial RNA transcription (e.g. rifampicin)
- Inhibition of bacterial protein synthesis (e.g. aminoglycosides)
- Inhibition of folic acid metabolism (e.g. trimethoprim)

Hormones:
- Inhibition of hormone production (FSH/LH by the oral contraceptive pill)
- Increased secretion (insulin by sulphonylureas, e.g. gliclazide)
- Replacement (thyroxine, insulin)

Pharmacokinetics

Routes of administration

Oral/enteral
- Absorption via gastrointestinal tract
- Carried via portal vein via liver to peripheral circulation
- Therefore undergo first pass metabolism by liver
- Must be able to resist digestion (i.e. not protein based)
- May be altered by gut motility/presence or absence of food

Rectal/sublingual
- Allows delivery to site of action, e.g. mesalazine in ulcerative proctitis
- Rapid absorption
- Safe delivery in those who are nil-by-mouth
- Avoids first pass metabolism effect
**Intravenous**
- Direct administration into peripheral circulation. Peak plasma concentration achieved immediately

**Intramuscular/subcutaneous**
- Rapid delivery into circulation
- Formulation can delay absorption, e.g. depot injections

**Topical**
- Delivery to site of action (e.g. emollients for eczema, chloramphenicol eye drops)

**Inhaled**
- Direct action in pulmonary tissue (e.g. salbutamol)

**Transdermal**
- Absorption via skin
- Provides continuous, long duration therapy with predictable plasma drug levels
- e.g. nicotine replacement, fentanyl analgesia

**Intrathecal**
- Delivery directly into cerebrospinal fluid
- Allows bypassing of blood–brain barrier
- e.g. specific chemotherapies

**Absorption**
Depends on:
- Route of administration
- Degree of first pass metabolism
- Drugs that undergo significant first pass metabolism cannot be used orally
- Lipid solubility

**Volume of distribution (V_D)**
Determines final concentration of drug in target tissue and therefore dose effect
- Depends on:
  - Lipid solubility (ability to cross membranes into cells)
  - Protein binding (protein bound drugs may not be detectable/active)
  - Molecule size (ability to traverse endothelium into tissue fluid)
- Can be measured:
  - \( V_D < 5 \) litre: drug retained in vascular space only
  - \( V_D < 15 \) litre: drug confined to extravascular space only
  - \( V_D > 15 \) litre: drug distributed throughout total body water

**Metabolism**
Drug metabolism may be required for:
- Activation of a prodrug → active form (e.g. valaciclovir → acyclovir)
- Termination of function of a drug
- Conversion to a hydrophilic compound to allow renal excretion

**Phases of metabolism**
- I. Transformation to a polar metabolite, e.g. p450 oxidation
- II. Conjugation, e.g. acetylation, methylation

**Elimination**
The majority of drugs and their metabolites are eliminated by the kidneys
- Phase I and II metabolism required to facilitate excretion rate of elimination depends on glomerular filtration rate and tubular reabsorption dose adjustments may be required in renal impairment
Pharmacology and therapeutics

Biliary excretion:
- May be associated with enteral reabsorption (entero-hepatic circulation), e.g. metronidazole

Pharmacogenetics
Polymorphisms of metabolic enzymes can alter drug metabolism leading to:
- Reduced efficacy
- Increased toxicity, e.g. isoniazid acetylation, TPMT breakdown of azathioprine

Drug interactions
Important cause of morbidity due to iatrogenic injury:
- Pharmacokinetic: one drug alters the absorption, protein binding, metabolism or excretion of another (Table 4.2)
- Pharmacodynamic: The action of one drug alters the response to a second, e.g. enzyme inhibition (Tables 4.3, 4.4)
- Avoiding interactions:
  - Careful prescribing
  - Check for interactions (e.g. British National Formulary)
  - Avoid multiple drugs for the same indication where possible
  - Seek advice (e.g. pharmacist)

Drug monitoring (Table 4.5)
- Measurement of clinical effect or blood levels
- Assessment for side-effects/adverse effects
- Titration of dose to achieve therapeutic range/avoid sub-therapeutic or toxic doses
- Most important when the therapeutic index is small (Fig. 4.1)

Adverse drug reactions (ADRs)
Unforeseen event resulting from administration of a drug:
- Hypersensitivity – idiosyncratic/independent of dose (Table 4.6)
- Unexpected interaction – usually dose dependent (Tables 4.2–4.4)
- Side-effect – dose-dependent

<table>
<thead>
<tr>
<th>Table 4.5 Drugs requiring monitoring</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Drug</strong></td>
</tr>
<tr>
<td>Gentamicin</td>
</tr>
<tr>
<td>Azathioprine</td>
</tr>
<tr>
<td>Anti-epileptics</td>
</tr>
<tr>
<td>Tacrolimus</td>
</tr>
<tr>
<td>Lithium</td>
</tr>
</tbody>
</table>
Table 4.6 Hypersensitivity reactions

<table>
<thead>
<tr>
<th>Type</th>
<th>Pathology</th>
<th>Clinical signs</th>
<th>Example</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>Anaphylaxis: IgE mediated mast cell degranulation (\rightarrow) histamine response</td>
<td>Tachycardia, oedema, shock, urticarial rash</td>
<td>Penicillin</td>
</tr>
<tr>
<td>II</td>
<td>Humoral: antibody synthesis against the drug</td>
<td>Haemolytic anaemia</td>
<td>Metyldopa</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Loss of efficacy</td>
<td>Infliximab</td>
</tr>
<tr>
<td>III</td>
<td>Antibody – antigen complex formation with reduced capillary blood flow</td>
<td>Digital ischaemia, lupus-like reaction</td>
<td>Hydralazine</td>
</tr>
<tr>
<td>IV</td>
<td>Delayed: cell-mediated memory response</td>
<td>Contact dermatitis</td>
<td>Topical antibiotics</td>
</tr>
<tr>
<td>V</td>
<td>Autoimmune</td>
<td>Target organ damage</td>
<td>Not induced by drugs</td>
</tr>
</tbody>
</table>

Long-term effects
- Predictable from mechanism of action, e.g. osteoporosis with corticosteroids
- Unpredictable, e.g. pulmonary fibrosis with amiodarone

Reporting
- Informs other doctors of the risks of a drug
- Provides information of risk of adverse events
- UK: Medicine and Healthcare products Regulatory Agency (MHRA)
- ‘Yellow card’ system from the BNF or www.MHRA.gov.uk

POISONING

Causes
- Deliberate self-harm (e.g. paracetamol)
- Substance misuse (e.g. opiates, amphetamines)
- Accidental (e.g. analgesics)
- Criminal
- Iatrogenic (drug errors, duplicate prescribing)

Treatment
- Immediate assessment: airway/breathing/circulation/conscious level
- Seek information (patient/relatives; ambulance crew):
  - What was taken?
  - How long ago?
  - Mixed or single drug overdose?
  - Taken with alcohol?
Find out about the specific poison
- ToxBase (www.toxbase.org)
- Poisons unit help lines
- Local guidelines
- Senior advice

If taken within the last 4 hours, consider treatments to reduce absorption
- Gastric lavage within one hour (rarely used)
- Activated charcoal
- Induced vomiting (never use)
- Whole bowel lavage

Consider reversal agents/antidotes/antagonists (Table 4.7)

Management of specific drug overdoses

Paracetamol
- Used in UK in 45% of all deliberate self-harm related overdoses
- Toxic dose low (12 g/day or 150 mg/kg)
- Delayed toxicity, so may not present until late in clinical course

Mechanism of toxicity (Fig. 4.2)
- Saturation of glutathione metabolic pathway
- Accumulation of toxic metabolite
- Hepatic injury and necrosis

Clinical features
- Early: nonspecific nausea, vomiting, abdominal pain and malaise
- Late: 2 days–2 weeks: jaundice, coagulopathy, encephalopathy

Therapy (Fig. 4.3)
- Blood paracetamol levels
- Gastric lavage and charcoal in large amounts and within 4 hours
- If >24 g taken, treat straight away, DO NOT WAIT 4 HOURS
- If blood level on or above treatment line, give acetyl-cysteine (Table 4.8)

High risk groups
- Pre-existing glutathione depletion (AIDS, malnutrition, eating disorders)
- Chronic alcohol misuse

---

**Table 4.7 Treatments for common poisons/overdoses**

<table>
<thead>
<tr>
<th>Poison</th>
<th>Antidote</th>
<th>Mechanism of action</th>
</tr>
</thead>
<tbody>
<tr>
<td>Opiates</td>
<td>Naloxone</td>
<td>Opioid receptor antagonist</td>
</tr>
<tr>
<td>Benzodiazepines</td>
<td>Flumazenil</td>
<td>Receptor antagonist – use with care: can induce seizures</td>
</tr>
<tr>
<td>Paracetamol</td>
<td>Acetyl cysteine</td>
<td>Increases metabolism of drug</td>
</tr>
<tr>
<td>Methanol</td>
<td>Ethanol</td>
<td>Competes with metabolic pathway</td>
</tr>
<tr>
<td>Organophosphates</td>
<td>Atropine</td>
<td>Blocks effect of poison at cholinergic receptors</td>
</tr>
</tbody>
</table>

---
Fig. 4.2 Normal and toxic metabolic pathways for paracetamol.

Fig. 4.3 Normogram for the treatment of paracetamol overdose.
- CyP450 inducting drugs
- Staggered doses/inaccurate histories

**Indicators of high risk of liver failure – consider referral to specialist unit**
- ALT >1000 U/L
- Prothrombin time raised
- Worsening renal impairment
- Metabolic acidosis

**Aspirin**

Oral doses of:
- Less than 150 mg/kg – no toxicity to mild toxicity
- From 150–300 mg/kg – Mild-to-moderate toxicity
- From 301–500 mg/kg – Serious toxicity
- Greater than 500 mg/kg – Potentially lethal toxicity

**Mechanism of toxicity**
- Increased respiratory drive $\rightarrow$ respiratory alkalosis due to hyperventilation
- Combined metabolic acidosis (ketosis and lactic acidosis) with respiratory compensation

**Clinical features**
- Nausea and vomiting
- Tinnitus
- Hyperventilation
- Pyrexia, sweating, tachycardia
- Cerebral oedema $\rightarrow$ confusion, seizures, coma

**Management**
- Gastric lavage if within 12 hours as aspirin slows gastric emptying
- Activated charcoal
- Urine alkalinization
- If blood salicylate >700 mg/L consider haemodialysis

**Tricyclic antidepressants**

**Clinical features**
- Reduced level of consciousness
- Seizures
- Hyperreflexia and increased muscle tone
- Anticholinergic effects: dilated pupils, urinary retention, sinus tachycardia
- Ventricular arrhythmia/pulseless electrical activity, cardiac arrest

**Management**
- Gastric lavage and activated charcoal
- Assisted ventilation
- Cardiac monitoring
- Correction of acid-base imbalance
- Consider ITU care if airway compromised

---

**Table 4.8 N-acetylcysteine (NAC) treatment regime**

<table>
<thead>
<tr>
<th>Dosage</th>
<th>Solution</th>
<th>Administration Time</th>
</tr>
</thead>
<tbody>
<tr>
<td>150 mg/kg NAC</td>
<td>200 mL 5% dextrose</td>
<td>15 minutes</td>
</tr>
<tr>
<td>50 mg/kg NAC</td>
<td>500 mL 5% dextrose</td>
<td>4 hours</td>
</tr>
<tr>
<td>100 mg/kg NAC</td>
<td>1000 mL 5% dextrose</td>
<td>16 hours</td>
</tr>
</tbody>
</table>
**Opiates**
- Prescribed drugs: codeine/morphine
- Illegal drugs: heroin (diamorphine)

**Clinical features**
- Drowsiness
- Nausea and vomiting
- Respiratory depression
- Pinpoint pupils

**Management**
- Urine toxicology screen for other drugs
- Naloxone bolus (short-acting so may require repeated doses)
- Check for opiate patches on skin (inadvertent overdose)
- Monitor conscious level and respiratory rate

**Alcohol**
Common cause of reduced conscious level in emergency departments

**Clinical features**
- Associated with trauma/head injury
- Hypoglycaemia
- Respiratory depression
- Seizures
- Vomiting
- Aspiration pneumonitis

**Management**
- Supportive case: airway management and gastric lavage
- Monitor blood glucose and correct

---

**PRESCRIBING**

The following are requirements for a legal prescription:
- Written in ink
- Patient name
- Address or hospital identifier
- Date of birth
- Drug name (full spelling)
- Dose, frequency and route of administration
- Duration of course
- Prescriber’s name, signature and date

Consider:
- Generic vs trade names
- Generic drugs are just as safe and cheaper
- Trade names are sometimes useful for specific formulations (e.g. delayed release)
- Drug interactions (if in doubt check in the BNF at: http://bnf.org/bnf/index.htm)

**Controlled drugs (Box 4.1)**
- Hand written or produced by a secure computerized prescribing system
- Name, address and date of birth of the patient
- Name, preparation and strength of drug
- Total quantity to be dispensed in words and figures
- Dose and frequency
Prescribing in specialist groups

Prescribing in the elderly
- Compliance reduced:
  - Multiple medications (poly-pharmacy)
  - Reduced cognitive function
- Change in volume of distribution:
  - Reduction in body mass
  - Reduced cardiac output
  - Changes in body composition
- Increased sensitivity to drug action:
  - Increased gastrointestinal and psychomotor effects of drugs
  - Reduced ability to regulate blood pressure → postural hypotension
Therefore consider:
- Pragmatic prescribing – what is important and what is not
- Risk-benefit analysis: benefit of warfarin in AF vs risk of falls and haemorrhage
- Use scoring systems (e.g. CHADS2)
- Aim for once-a-day regimens
- Use Dosette boxes to improve compliance and avoid inadvertent overdose

Prescribing in pregnancy and breast-feeding
Medicine may:
- be teratogenic, e.g. ACE inhibitors, warfarin, anti-epileptics
- alter fetal growth
- alter physiology, e.g. NSAIDs → delayed closure of the ductus arteriosus
- alter maternal physiology, e.g. glucocorticoids → gestational diabetes
- have long-term risks to the child, e.g. diethylstilboestrol → vaginal carcinoma after puberty
Never assume a drug is safe – if in doubt do not prescribe.
Consider the benefits vs the risks of the drug for the individual and the pregnancy.

- Breast-feeding:
  - Doses in breast milk of most drugs are small
  - Risk–benefit should be discussed with the patient

### ADDITIONAL RESOURCES

British National Formulary – [www.bnf.org](http://www.bnf.org)
Medicines and Healthcare products Regulatory Agency –
[www.MHRA.gov.uk](http://www.MHRA.gov.uk)
ToxBase – [www.toxbase.org](http://www.toxbase.org)
National Institute for Health and Clinical Excellence – [www.nice.org.uk](http://www.nice.org.uk)
General Medical Council – [www.gmc-uk.org](http://www.gmc-uk.org)

### SELF-ASSESSMENT QUESTIONS

**Multiple choice questions (true or false)**

1. The following drugs exert their effect by binding to receptors:
   - A. Aspirin
   - B. Propranolol
   - C. Nifedipine
   - D. Cimetidine
   - E. Omeprazole

2. The following drugs are receptor agonists:
   - A. Salbutamol
   - B. Atenolol
   - C. Pilocarpine
   - D. Phenylephrine
   - E. Captopril

3. The following drugs undergo extensive first-pass metabolism:
   - A. Glyceryl trinitrate
   - B. Lidocaine (Lignocaine)
   - C. Insulin
   - D. Benzylpenicillin
   - E. Probenecid

4. The following drugs induce P450 enzymes:
   - A. Phenobarbital
   - B. Rifampicin
   - C. Cimetidine
   - D. Paroxetine
   - E. Carbamazepine

5. In paracetamol overdose:
   - A. Paracetamol levels are essential in planning treatment
   - B. Hepatic necrosis can occur up to 48 hours after ingestion
   - C. N-acetylcysteine prevents paracetamol absorption from the stomach
   - D. Rising INR is a poor prognostic indicator
   - E. Co-ingestion of alcohol enhances paracetamol toxicity

6. In salicylate overdose:
   - A. Aspirin delays gastric emptying
   - B. Respiratory alkalosis occurs in conjunction with metabolic acidosis
C. Acidifying the urine enhances aspirin excretion by the kidney
D. Activated charcoal may be useful up to 12 hours after ingestion
E. N-acetylcysteine improves prognosis in large overdoses

Multiple choice questions (single best answer)

7. A 67-year-old man with longstanding ulcerative colitis, who was taking azathioprine, was seen with a clinical diagnosis of gout. Which one of the following is most likely to increase the risk of azathioprine toxicity?
   A. Allopurinol
   B. Bendroflumethiazide
   C. Colchicine
   D. Ibuprofen
   E. Paracetamol

8. A 34-year-old man was admitted with severe shortness of breath and facial oedema after eating shellfish. He was given adrenaline, hydrocortisone and chlorphenamine. Which one of the following best describes the mechanism of action of chlorphenamine?
   A. Direct receptor antagonist
   B. Enzyme inhibitor
   C. IgE receptor blocker
   D. Mast cell membrane stabilizer
   E. Trans-membrane channel blocker

9. A 56-year-old woman developed a raised, itchy, erythematous rash on starting a course of amoxicillin for a chest infection. Which one of the following best describes the underlying physiological process?
   A. Antibody – antigen complexes resulting in microvascular insufficiency
   B. Development of auto-immune dermatitis
   C. IgE mediated mast cell degranulation and histamine release
   D. IgG mediated intravascular haemolysis
   E. T lymphocyte cell mediated reaction

10. Which of the following physiological processes is most important for the excretion of a drug through the kidneys?
    A. Conjugation to increase water solubility
    B. Enterohepatic recirculation
    C. Oxidation to reduce polarity
    D. Protein binding to decrease tubular reabsorption
    E. Urinary alkalization

11. A 32-year-old woman was admitted following an overdose. She was nauseated with abdominal pain. On examination, she was drowsy, her pupils were dilated and she had a heart rate of 140 beats per minute. What is the most likely medication that she has taken?
    A. Aspirin
    B. Codeine
    C. Diazepam
    D. Imipramine
    E. Paracetamol

12. A 23-year-old man was admitted unconscious. On examination, he was unrousable, with a respiratory rate of 6 per minute and oxygen saturations of 87% on room air.
What is the most appropriate initial management?
A. Intravenous flumazenil
B. Intravenous naloxone
C. Oral activated charcoal
D. Placement of an oropharyngeal airway
E. Urine toxicology screen

Extended matching questions

Question 1 Theme: Pharmacology
A. Allopurinol
B. Amoxicillin
C. Atenolol
D. Glyceryl trinitrate
E. Imipramine
F. Methotrexate
G. Ranitidine
H. Rofecoxib
I. Salbutamol
J. Thyroxine
K. Verapamil

For each of the following questions, select the best answer from the list above:
I. A drug that acts as a trans-membrane channel blocker
II. A drug that causes bronchodilatation
III. A drug that inhibits an enzyme required for the metabolism of azathioprine
IV. A drug that can cause hypertension
V. A drug that undergoes extensive first pass metabolism
VI. A drug that acts at the cell nucleus
VII. A drug that can cause tachycardia and tremor
Medical imaging remains a vital part of the diagnostic process. Diagnostic imaging is complemented by therapeutic procedures carried out by the radiologist. Interpretation of X-rays, CT and MRI scans, combined with the role of imaging in diagnosis and the risks of radiological procedures are important subjects in examinations.

Many radiological procedures involve exposure to ionizing radiation. They should only be used when indicated and will change the patient’s management. Care must be taken in women of childbearing age in order to avoid exposing the fetus.

**TYPES OF IMAGING**

**X-rays**
- Utilize electromagnetic radiation
- Commonest form of medical imaging
- Image illustrates the variations in radiodensity of tissues to X-rays

**Contrast studies**
- Introduction of radio-opaque contrast
- Outlines hollow organs, e.g. barium swallow
- Water-soluble contrast substances allow
  - Examination of vasculature containing the agent, e.g. angiography
  - Excretion of the contrast agent, e.g. intravenous urogram

**Computerized axial tomography (CT)**
- Utilizes X-rays
- Integrates large quantities of data
- Allows computerized reconstruction of cross-sectional images

**Ultrasound**
- Utilizes high-frequency sound
- Measures reflection of sound waves. Non-invasive and no radiation exposure
  - Obstetric ultrasound
  - Renal, hepatic and pancreatic imaging
  - Doppler studies of blood vessels

**Magnetic resonance imaging (MRI)**
- Magnetic fields used to induce ‘proton spin’
- No radiation exposure
- Data reconstruction allows detailed images
- Signal depends on water content of tissue
Nuclear medicine

- Use of isotopes in imaging
  - V/Q scan for pulmonary embolus
  - Renal function studies
  - White cell scans for occult infection
  - Bone scans for malignancy
  - PET scans

THE CHEST X-RAY (FIG. 5.1)

Order of analysis

Basic details

- State name and age of the patient
- Date of the X-ray
- Antero-posterior (AP) or postero-anterior (PA) (describes the direction of travel of the X-rays)
- Check left and right markers

Rotation of film

- Look at medial ends of the clavicle
- Symmetry either side of spinous processes
- Sternum and vertebral column should be in line

Pneumothorax

- Collapse of lung → free air in the pleural space
  - Simple (Fig. 5.2)
  - Lung collapse
  - No mediastinal shift
    - Tension
- Mediastinal shift away from the side of the pneumothorax
- Usually due to penetrating chest wall injury (Fig. 5.3)
- Is there air under the diaphragm?
- Black line immediately under diaphragm (Fig. 5.4)

Expansion

- Count posterior ribs visible in the lung field
- Normal is 6–7

Fig. 5.1 The normal chest X-ray.
The chest X-ray

Fig. 5.2 A large left-sided pneumothorax is seen.

Fig. 5.3 A left-sided pneumothorax is visible, with tracheal shift away from the left, suggesting a tension pneumothorax.

Fig. 5.4 Air under the diaphragm indicates an intra-abdominal perforation.
Trachea
- Is the trachea deviated? Mediastinal shift
- Is the carina splayed? Right atrial enlargement

Hilar shadows
- Look for mass lesions

Diaphragm
- Flattening – over-expansion
- Calcification – asbestosis

Lung fields
- Look at lung markings
- Dark areas
  - Loss of vascular markings (PE, emphysema)
  - Hyperinflation (chronic obstructive pulmonary disease, COPD – Fig. 5.5)
- White shadows
  - Collapse (loss of air volume)
  - Consolidation (infection) (Figs 5.6–5.8)
  - Mass lesion
  - Fluid in pleural space – pleural effusion
  - Alveolar fluid – pulmonary oedema
  - Calcification
  - Check the lung apices – fibrosis suggests old tuberculosis

Cardiac shadow
- Look at heart size
  - PA film only
  - Normal <50% thoracic diameter
- Shape of cardiac outline
The chest X-ray

Collapsed right upper lobe

Fig. 5.6 Lobar collapse.

Fig. 5.7 There is shadowing adjacent to the right heart border suggesting a right middle lobe pneumonia.

Right bronchopneumonia

Fig. 5.8 Right bronchopneumonia.
Fig. 5.9 Left lung abscess.

**Lung abscess with air fluid level**  
**Left base consolidation**

Rib deformity

Fig. 5.10 Tuberculosis.  
Old sites of infection appear as apical shadows.  
Thoracoplasty was a surgical deflation of the infected lobe used prior to antituberculous therapy.

Fig. 5.11 Apical fibrosis and volume loss suggests old tuberculosis.
• Presence of mechanical valves
• Double right heart shadow – enlarged right atrium

**Bones**
• Look for rib fractures
• Bone lesions, e.g. metastases

**Infections**

**Lobar pneumonia (Figs 5.6, 5.7)**
• White patches of consolidation in lung field
• Collapse of lobe → loss of lung volume → Local structures may be moved, e.g.
  • Elevated hemidiaphragm
  • Reduced rib spacing
• Bronchopneumonia (Fig. 5.8)
• Diffuse shadowing across more than one lobe

**Lung abscess (Fig. 5.9)**
• Circular lesion with air fluid level

**Tuberculosis (Figs 5.10, 5.11)**
• Apical shadowing or discrete lesion
• May show calcification
• Chest wall deformity due to thoracoplasty (removal of ribs)

**Miliary shadows (Fig. 5.12)**
• Miliary (blood-spread) tuberculosis
• Old chickenpox pneumonia
• Metastatic cancer, typically:
  • Renal
  • Prostatic
  • Breast
  • Bone
  • GI tract
  • Cervix
  • Ovary

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**Fig. 5.12** Miliary shadowing. This is classically seen after chickenpox pneumonia or miliary tuberculosis; however, it can also occur due to lung metastases.
**Fig. 5.13** Bronchogenic carcinoma.

Mass arising from right hilum

**Fig. 5.14** Mediastinal mass. Masses may be due to lymphadenopathy (malignancy, lymphomas or tuberculosis), tumours (thymomas, germ cell tumours) or large retrosternal goitres.

**Fig. 5.15** A single pulmonary metastasis.

Cannonball lesion in left midzone
Neoplasms

Bronchogenic carcinoma (Fig. 5.13)
- Dense white shadows in lung field
- Mediastinal lymphadenopathy
- Hilar enlargement

Lymphoma (Fig. 5.14)
- Mediastinal masses

Metastases (Fig. 5.15)
- Cannonball lesions – discrete masses

Bony infiltration (Figs 5.16, 5.17)
- Mottling or radiolucent areas in bones

Cardiac lesions

Mechanical valves
- Visible metal valve ring or cage

Cardiac surgery (Fig. 5.18)
- Midline sternotomy wires

Mottled shadowing of humerus

Fig. 5.16 Bony infiltration by tumour.

Fig. 5.17 Multiple lucent lesions in the skull suggestive of myeloma lytic lesions.
Fig. 5.18 Sternotomy wires from a previous coronary artery bypass graft are clearly visible. A large left pleural effusion can also be seen.

Fig. 5.19 Pulmonary oedema. The heart is enlarged, and the vascular engorgement is visible as increased upper zone vascular markings. The hila are also engorged.

Fig. 5.20 Pulmonary oedema. There are bilateral fluffy basal shadows and fluid in the horizontal fissure.
Enlarged heart (Fig. 5.19)
- Cardiothoracic ratio >50% (PA film)
- Loss of atrial appendage shadow
- Atrial enlargement
  - Splayed carina
  - Double right heart border

Abnormal cardiac outline
- Boot-shaped heart – tetralogy of Fallot
- Globular heart – pericardial effusion

Pulmonary oedema (Figs 5.19, 5.20)
- Fluid in the horizontal fissure
- Kerley B lines (interstitial oedema)
- Upper lobe pulmonary vascular filling
- Peribronchial cuffing
- Enlarged heart
- Pleural effusions

Thoracic aortic aneurysm (Fig. 5.21)
- Dilated aortic arch

Pleural effusions
- Loss of costophrenic angle
- Dense white shadow with no lung markings

Unilateral (Fig. 5.22)
- Pneumonia
- Malignancy
- Pulmonary embolus
- Cardiac failure

Bilateral
- Cardiac failure
- Vasculitis, e.g. rheumatoid arthritis
- Hypoalbuminaemia
**Fig. 5.22** Right pleural effusion.

**Fig. 5.23** Large hiatus hernia. A hiatus hernia may be seen as a hollow viscus with an air fluid level behind or to the left of the heart.

**Fig. 5.24** Dextrocardia. A right-sided cardiac shadow, sometimes as part of situs inversus. Always check the side markers on an X-ray.
Miscellaneous

**Hiatus hernia (Fig. 5.23)**
- Air fluid level in a viscus visible behind or left of the heart shadow

**Dextrocardia (Fig. 5.24)**
- A right-sided heart shadow may represent true dextrocardia or incorrectly placed side markers

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**THE PLAIN ABDOMINAL X-RAY (FIG. 5.25)**

**Order of analysis**

**Introduction**
- Patient’s name, age, date of X-ray
- Erect or supine

**Bones**
- Thoracic and lumbar spine

**Gas shadows**
- Gastric shadow – under left hemidiaphragm
- Small bowel loops – fold lines extend across the full width of the bowel
- Colonic shadow – haustral pattern does not extend across the full width of bowel

**Organ shadows**
- Liver (right upper quadrant)
- Gallbladder (if calcified gallstones present)
- Kidneys (and presence of calcification)
- Pancreatic calcification (chronic pancreatitis)

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*Fig. 5.25 Normal abdominal X-ray. Dotted line = liver edge.*
Fig. 5.26 Gastric dilatation. The stomach is grossly distended. There is accompanying small bowel distension.

Fig. 5.27 Small bowel obstruction with ileus. Multiple air fluid levels are seen in the small bowel (erect film).
Gastrointestinal abnormalities

Stomach
- Dilated stomach (Fig. 5.26)
  - Ileus
  - Pyloric stenosis
  - Diabetic gastroparesis

Small intestine
- Obstruction
  - Multiple air fluid levels (Fig. 5.27)
  - Dilatation (Fig. 5.28)
- Inflammation – separated bowel loops (due to thickened bowel wall)

Colon (Figs 5.29–5.32)
- Faeces – speckled appearance
- Toxic megacolon – dilated colon
- Volvulus – sigmoid dilatation (coffee bean sign)
- Colitis
  - Featureless colon
  - Ulceration
  - Mucosal islands

Liver
- Enlargement
- Gallstones
- Ascites – diffuse ground glass appearance

Pancreas
- Speckled calcification (chronic pancreatitis)

Fig. 5.28 Bowel distension due to obstruction. The loops are markedly dilated (arrow).
Fig. 5.29 The typical coffee bean shape shadow of a sigmoid volvulus on a plain film.

Fig. 5.30 Toxic megacolon. The transverse colon is dilated (arrow). Classically, the transverse colon is the site of the dilatation. This is a medical emergency as there is a high risk of perforation and peritonitis.
Fig. 5.31 Ulcerative colitis. The colon is smooth and featureless.

Fig. 5.32 Constipation. Faeces appear as a speckled pattern in the colon.
Urinary tract

Kidneys (Fig. 5.33)
- Calcification
- Staghorn calculi
- Stone in ureter

Bladder
- Stones
- Urinary catheter

Fig. 5.33 Staghorn renal calculus.

Fig. 5.34 Achalasia. This barium swallow shows the classical rat’s tail appearance of the distal oesophageal sphincter in achalasia.
Contrast (oral or rectal barium or intravenous water-soluble contrast) is used to define specific organs radiologically

**Barium studies**

**Barium swallow**
- Visualizes the pharynx and oesophagus
- Achalasia
  - Rat’s tail appearance of narrowed lower oesophageal stricture (Fig. 5.34)
  - Dilated oesophagus, often with food debris
- Strictures
  - Benign – short and smooth
  - Malignant – long and ragged (Fig. 5.35)

**Barium meal (rarely done now – gastroscopy has replaced)**
- Visualizes the stomach and duodenum
- Ulcer – discrete collections of barium
- Cancers – filling defects

![Fig. 5.35 Barium swallow showing a malignant oesophageal stricture.](image)
Barium follow-through (Fig. 5.36)
- Visualizes small bowel
- Strictures
- Inflammation
- Tumours
- Diverticulae – Meckel’s diverticulum

Barium enema (Figs 5.37–5.39) (rarely done now – colonoscopy has replaced)
- Visualizes colon
- Malignancy – apple-core lesions
- Diverticular disease
- Inflammatory colitis
- Polyps

Fig. 5.36 Barium meal and follow-through showing a terminal ileal stricture (the string sign of Kantor) in Crohn’s disease.

Fig. 5.37 Barium enema of a colonic carcinoma demonstrating an ‘apple-core’ stricture.
Fig. 5.38 Barium enema in ulcerative colitis. The colon is featureless with a loss of the normal haustral pattern.

Fig. 5.39 Diverticular disease on a barium enema.
Fig. 5.40 Ischaemic and haemorrhagic stroke. Fresh blood appears white; infarcts appear dark.

Fig. 5.41 Intracranial bleeds. (a) Extradural haematoma. (b) Subdural haematoma.

Fig. 5.42 Subarachnoid haemorrhage. Fresh blood appears white and is seen in the cortex and fissures.
**COMPUTED AXIAL TOMOGRAPHY (CT)**

Computerized axial tomography (CT or CAT scans) utilize computer-generated images captured using an array of X-ray beams. They have a high radiation dose. Intravenous contrast can be given to enhance vascular lesions. Oral contrast can be given to enhance the bowel.

**CT scans of the head**

**Cerebrovascular accidents (Fig. 5.40)**
- Ischaemic strokes may not be apparent for 48 hours; they appear as dark areas
- Haemorrhagic strokes appear as white areas

**Intracranial bleeds (Figs 5.41, 5.42)**
- Acutely blood appears white
- Extradural haemorrhages are biconvex
- Subdural haemorrhages are crescent-shaped
- Intracerebral bleeds are within the substance of the brain
- Subarachnoid bleeds appear as white areas in the ventricular system of the brain

**Mass lesions (Fig. 5.43)**
- Malignancies (primary or secondary)
- Local oedema appears black
- Look for midline shift

**CT scans of the body (Figs 5.44–5.47)**

CT scans of the body are useful for a very wide range of diseases. Staging of malignancy and location of occult malignancy are common uses. Variations in the scanning protocol allow for specific organs to be optimally imaged:
- CT pneumocolon for colonic cancer and polyps
- Pancreatic protocol for pancreatic tumours and pancreatitis
- CT KUB for urinary tract stones
- CT pulmonary angiogram for pulmonary embolus

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**Fig. 5.43 Intracerebral mass lesion (contrast-enhanced CT of the head).**
There is an enhancing mass with surrounding oedema and obliteration of the right lateral ventricle with midline shift.
Fig. 5.44 Normal CT appearances of the abdomen at the level of (a) the liver and (b) the kidneys.

Fig. 5.45 CT of the abdomen. There is a mass lesion in the liver.
Fig. 5.46 Calcified gallstones on abdominal CT.

Fig. 5.47 The CT shows a large mass in the liver.

ULTRASOUND

Ultrasound utilizes sound waves and their reflections in order to image structures. It is safe, quick and non-invasive. Boundaries between solids and fluids give strong signals, making ultrasound useful for identifying collections such as abscesses and pleural effusions.

Liver, pancreas and biliary tree (Fig. 5.48)

- Mass lesions in the liver
- Stones in the biliary tree
- Fatty change
- Biliary obstruction
- Carcinoma of the pancreas

Renal ultrasound

- Renal masses
- Hydronephrosis
- Renal stones
- Congenital renal abnormalities
Fig. 5.48 Hepatic ultrasound showing liver cysts.

Fig. 5.49 (a) Saggital and (b) coronal sections through a normal brain on MRI.
Vascular tree

- Doppler ultrasound of leg veins for deep vein thrombosis
- Carotid Dopplers for stenosis in cerebrovascular disease

MAGNETIC RESONANCE IMAGING (MRI)

MRI provides high-resolution imaging of internal structures based on the water content of the tissue. It is useful for accurate localization of pathology and its relationship to surrounding structures, notably in the central nervous system.

- Head (Fig. 5.49) and spinal cord to look for neurological disease
- Bones and joints to look for orthopaedic problems
- Small bowel – has replaced barium follow through in many centres
- Pelvis to stage malignancies, e.g. rectum or gynae
- Liver – to characterize mass lesions
- MRCP – to examine the biliary tree

INTRAVENTOUS CONTRAST STUDIES

Angiograms

- Outline vascular tree (Fig. 5.50)
- Coronary arteries for ischaemic heart disease
- Renal arteries for hypertension
- Cerebral arteries for subarachnoid haemorrhage

Digital subtraction angiography

- The digitized image prior to contrast is electronically subtracted from that with contrast, leaving just the contrast-outlined vascular bed
- Removes any overlying anatomical features

![Normal mesenteric angiogram.](image)
Fig. 5.51 A V/Q scan. The perfusion scan (a) shows a left mid-zone defect not seen on the ventilation scan (b), suggesting a pulmonary embolus.

Fig. 5.52 A PET scan demonstrating normal cardiac activity and a high signal mass in the lower oesophagus.

Fig. 5.53 White cell scans. The colon is outlined due to an acute pancolitis (ulcerative colitis).
Urograms

- Intravenous contrast excreted by kidneys
- Outlines the collecting ducts, renal pelvis, ureters and bladder
- Detects:
  - Non-functioning kidney
  - Hydronephrosis
  - Tumours
  - Calculi

NUCLEAR MEDICINE

Isotopes can be detected with photosensitive films or a gamma camera. The isotope is incorporated into a molecule designed to be picked up by a specific organ or excreted by the liver or kidney. Alternatively, blood cells can be labelled.

V/Q scans (Fig. 5.51)

- Ventilation and perfusion scans of lung fields
- A well ventilated area with no perfusion suggests a pulmonary embolus

PET (Fig. 5.52)

- Positron emission tomography
- Utilizes labelled glucose to identify tissues with a high metabolic rate
- Used in cancer detection and stage assessment

Red cell scan

- The patient’s erythrocytes are labelled and re-injected
- May detect a site of occult blood loss

White cell scan (Fig. 5.53)

- Labelled leucocytes are injected
- Localize at site of infection or inflammation, e.g. abscesses

Bone scan (Fig. 5.54)

- Shows sites of high bone turnover, e.g. bone metastases

Renal function scans

$[^{99}\text{Tc}]$DTPA scans

- Technetium diethylenetriaminepenta-acetic acid
- Measures glomerular filtration
- Each kidney measured separately

$[^{99}\text{Tc}]$DMSA scans

- Tc-labelled dimercaptosuccinic acid
- Measure renal tubular function

Captopril scans (Fig. 5.55)

- DTPA scan with captopril given
- May reveal renal artery stenosis
- Indicated by a delay in peak signal
Fig. 5.54 A bone scan showing multiple metastatic deposits in the skeleton.

Fig. 5.55 Renal scintigraphy. The strength of signal over the kidney is measured. A normal kidney reaches a peak signal at 10–12 minutes. With an obstructed kidney the count reaches a plateau rather than reducing, as the technetium does not pass into the bladder. Renal artery stenosis results in a delay in reaching a signal peak, with a lower peak. This is most marked after captopril is given.
INTERVENTIONAL RADIOLOGY

Interventional radiology allows therapeutic and diagnostic procedures to be carried out without the need for general anaesthetic and in a less invasive way than surgery, although haemorrhage and perforation of a viscus or a blood vessel are important risks. Vascular procedures carry the risk of arterial spasm or occlusion and therefore tissue ischaemia.

Directed biopsy

- Masses can be biopsied under CT or ultrasound control rather than requiring an open procedure under general anaesthetic

Vascular procedures

- Angioplasty of arterial stenosis
- Insertion of filters to prevent embolism
- Insertion of coils into berry aneurysms to prevent subarachnoid haemorrhage

Biliary stenting

- Insertion of a stent to overcome obstruction of the biliary tree, e.g. in cholangiocarcinoma
- Percutaneous transhepatic cholangiography (PTCA)

Drain insertion

- Nephrostomies to relieve hydronephrosis
- Insertion of drains into abscesses

SELF-ASSESSMENT QUESTIONS

Multiple choice questions (true or false)

1. The following are accepted risks of CT-guided biopsy:
   A. Haemorrhage
   B. Secondary tumours along the path of the biopsy needle
   C. Radiation mucositis
   D. Intestinal perforation
   E. Abscess formation

2. The following are true of CT scans of the head:
   A. A CT scan carried out within 24 hours of an ischaemic stroke is often normal
   B. Fresh blood appears dark on an unenhanced CT scan
   C. Acoustic neuromas are seen as masses arising from the pituitary fossa
   D. Oedema around mass lesions appears black
   E. Intravenous contrast is useful in the diagnosis of intracerebral mass lesions

Multiple choice questions (single best answer)

3. A 32-year-old man was admitted with severe colicky abdominal and loin pain and haematuria. Which of the following would be the most useful diagnostic test?
   A. Plain abdominal X-ray
   B. Ultrasound of the abdomen
   C. CT KUB
4. A 54-year-old woman with a long history of alcohol misuse was seen following a fall. She was drowsy and incoherent. Which one of the following would be most appropriate?
   A. Plain skull X-ray
   B. CT brain
   C. Ultrasound of the portal vein
   D. CT pancreas
   E. Plain chest X-ray

5. A 76-year-old man was referred with deteriorating renal function on blood tests following the prescription of lisinopril. Which of the following would be most appropriate to confirm the diagnosis of renal artery stenosis?
   A. CT KUB
   B. Ultrasound of the renal tract
   C. Captopril renogram
   D. Renal angiogram
   E. MRI both kidneys

6. A 16-year-old asthmatic man was admitted with worsening shortness of breath and chest pain. Which one of the following indicates a tension pneumothorax?
   A. Visible pleural shadow
   B. Loss of peripheral lung markings
   C. Tracheal shift towards the affected lung
   D. Tracheal shift away from the affected lung
   E. Visible air-fluid level

7. A 43-year-old woman was admitted with abdominal pain and vomiting. An erect chest X-ray demonstrates air under both hemidiaphragms. Which one of the following may result in this sign?
   A. Liver haematoma
   B. Splenic rupture
   C. Duodenal ulcer
   D. Acute pancreatitis
   E. Ectopic tubal pregnancy

8. A 76-year-old man is admitted with back pain and pain in his left thigh. He has had previous treatment for a renal cell carcinoma. Which of the following tests would be appropriate in his further investigation?
   A. Plain X-rays of the thoracic and lumbar spine
   B. Nucleotide bone scan
   C. CT scan of the abdomen
   D. Venogram of the left leg
   E. MRI scan of the spine

Extended matching questions

**Question 1 Theme: Radiology**

A. Plain PA chest X-ray
B. Plain AP chest X-ray
C. Plain abdominal X-ray
D. Plain skull X-ray
E. CT head
F. High resolution CT scan of the chest
G. CT pulmonary angiogram
For each of the following questions, select the best answer from the list above:

I. Which investigation would give the most accurate assessment of cardiac size?
II. Which investigation is most useful in assessing the stage of an oesophageal tumour?
III. Which investigation is most useful to determine the nature of liver cysts?
IV. Which investigation is most useful to detect multiple myeloma?
Throughout this chapter, the following simple abbreviations will be used:

- Sodium – Na⁺
- Potassium – K⁺

**FLUID AND ELECTROLYTE BALANCE**

**Water – Total body water**

- 50–60% of lean body weight ♂
- 45–50% of lean body weight ♀
- In a 70 kg male total body water is 42 litres
  - 28 litres intracellular
  - 9.4 litres interstitial
  - 4.6 litres plasma

**Distribution of water**

- Osmotic pressure is the primary determinant of water distribution between compartments
- In each compartment the following are responsible for osmotic pressure
  - Intracellular compartment – K⁺
  - Extracellular fluid compartment – Na⁺
  - Vascular compartment – proteins

**Distribution of 1 litre of standard intravenous replacement fluids**

- 5% glucose distributes equally across all three compartments
- 0.9% saline remains in the extracellular compartment
- Colloid stays in the vascular compartment

**Normal fluid and electrolyte requirements**

- Normal daily fluid requirement is 2–3 litres with 100 mmol Na⁺ and 70 mmol K⁺ which allows for urinary, faecal and insensible loss

**Sodium content of standard intravenous replacement fluids**

- 1 litre of 0.9% (physiological) saline contains 150 mmol Na⁺
- 1 litre of 5% glucose contains no Na⁺
- 1 litre of glucose saline contains 30 mmol Na⁺

**An example of a standard 24-hour fluid regime in a fasting patient**

- 1 litre 0.9% saline
- +2 litres 5% glucose
- Each with 20 mmol KCl added

All patients need assessment of volume status and recent electrolyte results before i.v. fluids can be safely prescribed.
When to decrease the above fluid regime
- Elderly patients – require less volume, particularly if in heart failure
- Acute kidney injury – replace fluids as the previous day’s urine output + 500 mL (remember these patients are often hyperkalaemic and may not require KCl supplements)
- Heart failure – reduce the volume
- Drugs – can alter water and electrolyte excretion, e.g. ACE inhibitors induce K⁺ retention

When to increase the above fluid regime
- Dehydration
- Shock
- Increased GI losses, diarrhoea, vomiting, NG aspiration – replace nasogastric losses with KCl supplemented 0.9% saline
- Increased insensible losses – fever/burns
- Pancreatitis
- Drugs – can alter water and electrolyte losses, e.g. diuretics increase Na⁺ and water loss

Regulation of extracellular fluid volume (Fig. 6.1)
- Extracellular fluid volume is regulated by Na⁺ excretion from the kidneys, which is dependent on the circulating blood volume
- Circulating volume is determined by neurohumoral mechanisms via
  - Volume receptors
  - Catecholamines
  - Atrial natriuretic peptide
  - Renin/angiotensin/aldosterone

Regulation of water homeostasis
- Water homeostasis is affected by thirst and the concentrating and diluting functions of the kidney via the effects of antidiuretic hormone (ADH)

Increased extracellular volume
Aetiology
- Heart failure
- Hypoalbuminaemia, e.g. nephrotic syndrome
- Cirrhosis
- Renal sodium retention
  - Acute nephritis
  - Chronic kidney disease
  - Oestrogens
  - Mineralocorticoids
  - NSAIDs

Clinical features
- Peripheral oedema
- Pulmonary oedema
- Pleural effusion
- Ascites
- Raised jugular venous pressure
- Raised blood pressure
- Third heart sound
Fig. 6.1 Regulation of extracellular fluid volume. (Reproduced from Kumar P, Clark M. Kumar and Clark’s Clinical Medicine, 8th edn. Edinburgh: Elsevier; 2012, with permission from Elsevier.)
Management
- Diuretics
- Treat underlying cause where possible

**Decreased extracellular volume**

**Aetiology**
- Haemorrhage
- Burns
  - Dehydration secondary to GI losses
  - Vomiting
  - Diarrhoea
  - Ileostomy
  - Ileus
- Renal losses
  - Polyuria
  - Diuretics
- Reduced renal tubular Na\(^+\) conservation
  - Reflux nephropathy
  - Papillary necrosis – NSAIDs, diabetes mellitus, sickle cell disease

**Clinical features**
- Postural hypotension – a fall in BP from lying to standing (normally the blood pressure rises on standing). May be due to reduced circulating volume, altered autonomic function or prolonged bed rest (Table 6.1)
- Low jugular venous pressure
- Peripheral vasoconstriction (cold skin and empty veins in the peripheries)
- Tachycardia
- Hypotension

**Management**
- Replacement of what is missing
  - Fluid/electrolytes lost (orally or intravenously)
  - Red cells
  - Plasma
- Treat underlying cause

---

**Table 6.1 Causes of postural hypotension**

<table>
<thead>
<tr>
<th>Hypovolaemia</th>
</tr>
</thead>
<tbody>
<tr>
<td>Autonomic failure</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
</tr>
<tr>
<td>Shy–Drager syndrome</td>
</tr>
<tr>
<td>Systemic amyloidosis</td>
</tr>
<tr>
<td>Drugs altering autonomic function</td>
</tr>
<tr>
<td>Ganglion blockers</td>
</tr>
<tr>
<td>Tricyclic antidepressants</td>
</tr>
<tr>
<td>Drugs altering peripheral vasoconstriction</td>
</tr>
<tr>
<td>Nitrates</td>
</tr>
<tr>
<td>Calcium channel blockers</td>
</tr>
<tr>
<td>α-blockers</td>
</tr>
<tr>
<td>Prolonged bed rest</td>
</tr>
</tbody>
</table>
Sodium

- Disorders of Na⁺ concentration are caused by disturbance of water balance.
- In all disorders of Na⁺ concentration, treatment should aim for slow changes in Na⁺ concentrations to avoid precipitating cerebral oedema.
- Plasma and urine osmolality are often useful measures to investigate the cause of altered sodium concentrations.
- Plasma osmolality can be estimated as:
  \[ 2[Na^+] + [\text{urea}] + [\text{glucose}] \]

Hyponatraemia

- May be associated with euvoalaemia, hypovolaemia or hypervolaemia.

Hyponatraemia with normal extracellular volume (euvolaemia)

Aetiology

- Abnormal ADH release
  - Syndrome of inappropriate antidiuretic hormone (ADH) (see Ch. 13).
  - Adrenal insufficiency, e.g. Addison’s disease.
  - Hypothyroidism.
  - Vagal neuropathy.
  - Stress.
  - Osmotically active substances causing ADH release, e.g. glucose, mannitol, alcohol, sickle cell syndrome.
- Psychiatric illness
  - Psychogenic polydipsia.
  - Tricyclic antidepressants.
- Drugs
  - Desmopressin.
  - Tolbutamide/chlorpropamide.

Clinical features

- Euvolaemia.
- Signs of underlying cause.

Management

- Treat underlying cause.
- Sometimes water restriction.

Salt-deficient hyponatraemia (hypovolaemic)

Aetiology

- GI losses
  - Vomiting.
  - Diarrhoea.
  - Haemorrhage.
- Renal losses
  - Osmotic diuresis (e.g. hyperglycaemia).
  - Diuretics.
  - Adrenocortical insufficiency.
  - Tubulo-interstitial renal disease.
  - Unilateral renal artery stenosis.
  - Recovery phase of acute tubular necrosis.
Clinical features
- Hypovolaemia (see above)

Management
- Replace lost fluid/electrolytes
- Treat underlying cause

Hyponatraemia due to water excess (hypervolaemic)

Aetiology
- Heart failure
- Liver failure
- Oliguric renal failure
- Hypoalbuminaemia
- Excess fluids (iatrogenic)

Clinical features
- Volume overload (see above)
- If severe, can cause drowsiness, convulsions and coma
- Signs of underlying disease

Management
- Fluid restriction
- Treat underlying cause

Pseudohyponatraemia
- Rarely hyperlipidaemia or hyperproteinaemia produces a spuriously low measured Na\(^+\) concentration
- Plasma osmolality is normal

Hypernatraemia
- Hypernatraemia nearly always indicates water deficiency
- In normal individuals with an intact thirst axis and free access to water, hypernatraemia is rare
- Thirst is frequently deficient in elderly patients, which makes them more prone to hypernatraemia

Aetiology
- Inadequate water intake PLUS
- ADH deficiency
  - Diabetes insipidus
- Insensitivity to ADH (nephrogenic diabetes insipidus)
  - Drugs (e.g. lithium, tetracyclines, amphotericin B)
  - Acute tubular necrosis
- Osmotic diuresis
  - Hyperosmolar diabetic coma
  - Total parenteral nutrition

Clinical features
- Volume depletion (see above)
- Confusion/convulsions
- Fever
- Features of underlying cause

Investigations
- Plasma osmolality will be high
- A low urine osmolality indicates diabetes insipidus
Fluid and electrolyte balance

Management
- Replace fluid
- Treat underlying cause (Table 6.2)

Potassium

Serum $K^+$ concentrations are determined by:
- Uptake of $K^+$ into cells (Fig. 6.2)
- Renal excretion (controlled by aldosterone)
- Extrarenal losses, e.g. gastrointestinal

**Table 6.2** Average concentrations and potential daily losses of water and electrolytes from the gut

<table>
<thead>
<tr>
<th></th>
<th>$\text{Na}^+$ mmol/L</th>
<th>$\text{K}^+$ mmol/L</th>
<th>$\text{Cl}^-$ mmol/L</th>
<th>Volume (mL in 24 hours)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stomach</td>
<td>50</td>
<td>10</td>
<td>110</td>
<td>2500</td>
</tr>
<tr>
<td>Small intestine</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Recent ileostomy</td>
<td>120</td>
<td>5</td>
<td>110</td>
<td>1500</td>
</tr>
<tr>
<td>Adapted ileostomy</td>
<td>50</td>
<td>4</td>
<td>25</td>
<td>500</td>
</tr>
<tr>
<td>Bile</td>
<td>140</td>
<td>5</td>
<td>105</td>
<td>500</td>
</tr>
<tr>
<td>Pancreatic juice</td>
<td>140</td>
<td>5</td>
<td>60</td>
<td>2000</td>
</tr>
<tr>
<td>Diarrhoea</td>
<td>130</td>
<td>10–30</td>
<td>95</td>
<td>1000–2000+</td>
</tr>
</tbody>
</table>

(Reproduced from Kumar P, Clark M. Kumar and Clark’s Clinical Medicine, 8th edn. Edinburgh: Elsevier; 2012, with permission from Elsevier.)

**Fig. 6.2** Regulation of uptake of potassium into cells.
## Hypokalaemia

### Aetiology
See Table 6.3.

### Clinical features
- If severe, muscle weakness
- Cardiac arrhythmias in abnormal hearts
- Potentiation of digoxin toxicity

### Management
- Give supplements
- Potassium-sparing drugs
- Treat underlying cause

---

**Table 6.3 Causes of hypokalaemia**

<table>
<thead>
<tr>
<th>Category</th>
<th>Causes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Increased renal excretion</td>
<td>Diuretics – thiazide and loop</td>
</tr>
<tr>
<td>Increased aldosterone secretion</td>
<td>Liver failure</td>
</tr>
<tr>
<td></td>
<td>Heart failure</td>
</tr>
<tr>
<td></td>
<td>Nephrotic syndrome</td>
</tr>
<tr>
<td></td>
<td>Cushing syndrome</td>
</tr>
<tr>
<td></td>
<td>Conn syndrome</td>
</tr>
<tr>
<td></td>
<td>Adrenocorticotropic hormone (ACTH) producing tumours</td>
</tr>
<tr>
<td>Exogenous mineralocorticoid</td>
<td>Corticosteroids</td>
</tr>
<tr>
<td></td>
<td>Carbenoxolone</td>
</tr>
<tr>
<td></td>
<td>Liquorice</td>
</tr>
<tr>
<td>Renal disease</td>
<td>Renal tubular acidosis types 1 and 2</td>
</tr>
<tr>
<td></td>
<td>Renal tubular damage</td>
</tr>
<tr>
<td></td>
<td>Acute leukaemia</td>
</tr>
<tr>
<td></td>
<td>Cytotoxics</td>
</tr>
<tr>
<td></td>
<td>Nephrotoxic drugs, e.g. gentamicin</td>
</tr>
<tr>
<td></td>
<td>Release of urinary tract obstruction</td>
</tr>
<tr>
<td>Severe dietary deficiency</td>
<td></td>
</tr>
<tr>
<td>Redistribution into cells</td>
<td>β-adrenergic stimulation</td>
</tr>
<tr>
<td></td>
<td>Acute myocardial infarct</td>
</tr>
<tr>
<td></td>
<td>β-agonists, e.g. salbutamol</td>
</tr>
<tr>
<td></td>
<td>Insulin, e.g. treatment of diabetic ketoacidosis</td>
</tr>
<tr>
<td></td>
<td>Correction of vitamin B\textsubscript{12} deficiency</td>
</tr>
<tr>
<td></td>
<td>Alkalosis</td>
</tr>
<tr>
<td>GI losses</td>
<td>Vomiting</td>
</tr>
<tr>
<td></td>
<td>Diarrhoea</td>
</tr>
<tr>
<td></td>
<td>Purgative abuse</td>
</tr>
<tr>
<td></td>
<td>Villous adenoma</td>
</tr>
<tr>
<td></td>
<td>Ileostomy</td>
</tr>
<tr>
<td></td>
<td>Fistulae</td>
</tr>
<tr>
<td></td>
<td>Ileus/intestinal obstruction</td>
</tr>
</tbody>
</table>
**Hyperkalaemia**

**Aetiology**
See Table 6.3.

**Clinical features**
- Cardiac arrhythmias
- Hypotension/bradycardia if severe
- Kussmaul breathing (associated acidosis)
- Widened QRS/tented T waves on ECG

**Management**
- See page 352 (Box 14.2) for emergency treatment
- Calcium resonium – exchange resin given orally or rectally
- Dialysis
- Treat cause

**Calcium**
Disorders of calcium metabolism are discussed in Chapter 11 (p. 263)

**Magnesium**
- Serum magnesium concentrations are determined by uptake in the small bowel and renal excretion
- Disordered magnesium concentrations occur in association with other electrolyte imbalance

**Hypomagnesaemia**

**Aetiology**
See Table 6.4.

**Clinical features**
- Inability to correct hypokalaemia
- Irritability
- Tremor
- Ataxia
- Carpopedal spasm
- Hyperreflexia
- Confusion/hallucinations
- Convulsions
- ECG shows prolonged QT interval, flat T waves

**Management**
- Give supplements
- Treat underlying cause

**Hypermagnesaemia**

**Aetiology**
See Table 6.5.

**Clinical features**
- Lethargy
- Muscle weakness
- Hyporeflexia
- Narcosis
- Respiratory paralysis
- Cardiac conduction defects
Calcium gluconate, dextrose and insulin
Dialysis
Remove cause

Phosphate
The regulation of phosphate concentrations is closely linked to that of calcium

Hypophosphataemia

Aetiology
See Table 6.6.

Clinical features
Diaphragmatic muscle weakness
Convulsions

Management
If mild, rarely requires treatment
If severe, give i.v. replacement slowly
Table 6.5 Causes of hypo/hypermagnesaemia

<table>
<thead>
<tr>
<th>Hypomagnesaemia</th>
<th>Hypermagnesaemia</th>
</tr>
</thead>
<tbody>
<tr>
<td>Decreased magnesium absorption</td>
<td>Impaired renal excretion</td>
</tr>
<tr>
<td>Malabsorption</td>
<td>Chronic kidney disease</td>
</tr>
<tr>
<td>Malnutrition</td>
<td>Acute kidney injury</td>
</tr>
<tr>
<td>Alcohol excess</td>
<td>Increased magnesium intake</td>
</tr>
<tr>
<td>Increased renal excretion</td>
<td>Purgatives</td>
</tr>
<tr>
<td>Drugs</td>
<td>Antacids</td>
</tr>
<tr>
<td>Diuretics – loop and thiazide</td>
<td></td>
</tr>
<tr>
<td>Digoxin</td>
<td></td>
</tr>
<tr>
<td>Diabetic ketoacidosis</td>
<td></td>
</tr>
<tr>
<td>Bartter syndrome</td>
<td></td>
</tr>
<tr>
<td>Alcohol excess</td>
<td></td>
</tr>
<tr>
<td>Hypercalciuria</td>
<td></td>
</tr>
<tr>
<td>Drug toxicity</td>
<td></td>
</tr>
<tr>
<td>Amphotericin</td>
<td></td>
</tr>
<tr>
<td>Aminoglycosides</td>
<td></td>
</tr>
<tr>
<td>Cisplatin</td>
<td></td>
</tr>
<tr>
<td>Ciclosporin</td>
<td></td>
</tr>
<tr>
<td>GI losses</td>
<td></td>
</tr>
<tr>
<td>Prolonged nasogastric suction</td>
<td></td>
</tr>
<tr>
<td>Excessive purgatives</td>
<td></td>
</tr>
<tr>
<td>GI/biliary fistulae</td>
<td></td>
</tr>
<tr>
<td>Severe diarrhoea</td>
<td></td>
</tr>
<tr>
<td>Acute pancreatitis</td>
<td></td>
</tr>
<tr>
<td>Hypomagnesaemia</td>
<td></td>
</tr>
<tr>
<td>Increased renal excretion</td>
<td></td>
</tr>
<tr>
<td>Drugs</td>
<td></td>
</tr>
<tr>
<td>Diuretics – loop and thiazide</td>
<td></td>
</tr>
<tr>
<td>Digoxin</td>
<td></td>
</tr>
<tr>
<td>Diabetic ketoacidosis</td>
<td></td>
</tr>
<tr>
<td>Bartter syndrome</td>
<td></td>
</tr>
<tr>
<td>Alcohol excess</td>
<td></td>
</tr>
<tr>
<td>Hypercalciuria</td>
<td></td>
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<tr>
<td>Drug toxicity</td>
<td></td>
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<tr>
<td>Amphotericin</td>
<td></td>
</tr>
<tr>
<td>Aminoglycosides</td>
<td></td>
</tr>
<tr>
<td>Cisplatin</td>
<td></td>
</tr>
<tr>
<td>Ciclosporin</td>
<td></td>
</tr>
<tr>
<td>GI losses</td>
<td></td>
</tr>
<tr>
<td>Prolonged nasogastric suction</td>
<td></td>
</tr>
<tr>
<td>Excessive purgatives</td>
<td></td>
</tr>
<tr>
<td>GI/biliary fistulae</td>
<td></td>
</tr>
<tr>
<td>Severe diarrhoea</td>
<td></td>
</tr>
<tr>
<td>Acute pancreatitis</td>
<td></td>
</tr>
<tr>
<td>Hypermagnesaemia</td>
<td></td>
</tr>
<tr>
<td>Impaired renal excretion</td>
<td></td>
</tr>
<tr>
<td>Chronic kidney disease</td>
<td></td>
</tr>
<tr>
<td>Acute kidney injury</td>
<td></td>
</tr>
<tr>
<td>Increased magnesium intake</td>
<td></td>
</tr>
<tr>
<td>Purgatives</td>
<td></td>
</tr>
<tr>
<td>Antacids</td>
<td></td>
</tr>
</tbody>
</table>

Hyperphosphataemia

Aetiology
See Table 6.6.

- Common in patients with chronic kidney disease

Management

- If acute, rarely requires treatment
- If chronic, give gut phosphate binders or dialyse

ACID–BASE DISORDERS

Acid–base balance is tightly buffered. The bicarbonate–carbonic acid buffer pair is the most clinically relevant due to variability of excretion of CO₂ by the lungs and bicarbonate and hydrogen ions by the kidneys:

\[
\text{H}^+ + \text{HCO}_3^- \leftrightarrow \text{H}_2\text{CO}_3 \overset{\text{Carbonic anhydrase}}{\rightarrow} \text{CO}_2 + \text{H}_2\text{O}
\]
Acid-base disturbance may be caused by:
- Abnormal carbon dioxide removal in the lungs (respiratory alkalosis/acidosis)
- Abnormalities of the regulation of bicarbonate and other buffers in the blood (metabolic alkalosis/acidosis)

Arterial blood gas analysis provides information on:
- \( \text{pH} \)
- Bicarbonate concentrations
- Partial pressures of oxygen and carbon dioxide

**Respiratory acidosis**
- Caused by retention of carbon dioxide
- Renal retention of bicarbonate may partly compensate (see Ch. 8)

**Respiratory alkalosis**
- Caused by increased removal of carbon dioxide as a result of hyperventilation (see Ch. 8)

**Metabolic acidosis**
- Caused by accumulation of acid
- Demonstrated by a fall in plasma bicarbonate
- Arises from:
  - Acid administration
  - Acid generation
  - Impaired acid excretion by kidneys
  - Bicarbonate losses from GI tract

### Table 6.6 Causes of hypo/hyperphosphataemia

<table>
<thead>
<tr>
<th>Hypophosphataemia</th>
<th>Hyperphosphataemia</th>
</tr>
</thead>
<tbody>
<tr>
<td>Redistribution</td>
<td>Chronic kidney disease</td>
</tr>
<tr>
<td>Respiratory alkalosis</td>
<td>Tumour lysis</td>
</tr>
<tr>
<td>Treatment of diabetic ketoacidosis</td>
<td>Rhabdomyolysis</td>
</tr>
<tr>
<td>Carbohydrate administration after starvation (re-feeding syndrome)</td>
<td>Old blood sample</td>
</tr>
<tr>
<td>Post-parathyroidectomy</td>
<td></td>
</tr>
<tr>
<td>Renal losses</td>
<td></td>
</tr>
<tr>
<td>Hyperparathyroidism, renal tubular defects, diuretics</td>
<td></td>
</tr>
<tr>
<td>Decreased intake/absorption</td>
<td></td>
</tr>
<tr>
<td>Dietary</td>
<td></td>
</tr>
<tr>
<td>Malabsorption</td>
<td></td>
</tr>
<tr>
<td>Vomiting</td>
<td></td>
</tr>
<tr>
<td>Gut phosphate binders, e.g. aluminium hydroxide</td>
<td></td>
</tr>
<tr>
<td>Vitamin D deficiency</td>
<td></td>
</tr>
<tr>
<td>Alcohol withdrawal</td>
<td></td>
</tr>
</tbody>
</table>

**Hypophosphataemia**
- Redistribution
- Respiratory alkalosis
- Treatment of diabetic ketoacidosis
- Carbohydrate administration after starvation (re-feeding syndrome)
- Post-parathyroidectomy
- Renal losses
  - Hyperparathyroidism, renal tubular defects, diuretics
- Decreased intake/absorption
  - Dietary
  - Malabsorption
  - Vomiting
  - Gut phosphate binders, e.g. aluminium hydroxide
  - Vitamin D deficiency
  - Alcohol withdrawal

**Hyperphosphataemia**
- Chronic kidney disease
- Tumour lysis
- Rhabdomyolysis
- Old blood sample
Anion gap (unmeasured anions) helps differentiate the causes
\[ \text{Anion gap} = ([\text{Na}^+] + [\text{K}^+]) - ([\text{HCO}_3^-] + [\text{Cl}^-]) \]

Normal anion gap = 10-18 mmol/L⁻¹

Note that albumin is a major unmeasured anion; a fall in albumin will reduce the anion gap

Metabolic acidosis with a normal anion gap

- Suggests that either hydrochloric acid is being generated or bicarbonate is being lost
- In all cases plasma bicarbonate is low and plasma chloride high

Aetiology

- Increased GI bicarbonate losses
  - Diarrhoea
  - Ileostomy
- Increased renal bicarbonate losses
  - Acetozolamide
  - Proximal (type 2) renal tubular acidosis
  - Hyperparathyroidism
  - Renal tubular damage – heavy metal poisoning, paraproteins, drugs
- Decreased renal hydrogen ion losses
  - Distal (type 1) renal tubular acidosis
  - Type 4 renal tubular acidosis

Metabolic acidosis with a high anion gap

- Suggests presence of unmeasured endogenous or exogenous anions

Aetiology

- Renal failure
- Lactic acidosis
- Ketoacidosis
- Exogenous acid such as salicylate (aspirin)

Metabolic alkalosis

- Causes
  - Chloride depletion – gastric losses, diuretics, diarrhoea, cystic fibrosis
  - Potassium depletion – mineralocorticoid excess, Conn syndrome, thiazide/loop diuretics
  - Exogenous alkalis, e.g. antacids plus one of the above

CARDIAC MARKERS

Biochemical markers of myocyte death can be used to stratify risk in acute coronary syndromes.

Cardiac troponin (troponin T and I)

Cardiac microfilament proteins which are sensitive markers for cardiac injury

- Not detectable in normal people
- Released early (2-4 hours) after injury and persist for up to 7 days
- If negative then repeat 9-12 hours after admission
- When elevated in patients presenting with chest pain can be very useful for determining prognosis
Creatine kinase (CK)

Sources
- Heart, skeletal muscle and brain (MM/MB/BB isoforms)

Raised in
- Myocardial infarction
- Muscle dystrophies
- Polymyositis
- Pulmonary embolus
- Postoperative period
- Myocarditis
- Muscle trauma, e.g. fits, injections, exercise

Aspartate aminotransferase (AST)

Sources
- Heart, liver, muscle and kidney

Raised in
- Myocardial infarction
- Liver disease (hepatitis of any cause)
- Haemolytic anaemia
- Muscle trauma, e.g. fits, injections, exercise

Lowered in
- Renal failure

Lactate dehydrogenase (LDH)

Sources
- All cells release LDH when damaged

Raised in
- Myocardial infarction
- Tissue necrosis of any cause
- Liver disease
- Kidney disease
- Haematological diseases, e.g. lymphoma haemolysis
- Muscle trauma, e.g. fits, injections, exercise

Liver function tests in the blood can be divided into three groups. Note that in severe disease, the first two groups can both be elevated and that drugs can induce liver enzymes (see Ch. 4)

- Tests suggesting bile duct obstruction (intra- or extra-hepatic)
  - Bilirubin
  - Alkaline phosphatase
  - γ-glutamyltranspeptidase
- Tests suggesting disease of hepatocytes
  - Aminotransferases ALT and AST
- Tests of liver synthetic function
  - Albumin
  - Prothrombin time

Further information is given in Chapter 10.
Bilirubin

**Sources**
- Mainly haemoglobin destruction

**Raised in**
- Bile duct obstruction of any cause
- Hepatitis of any cause
- Haemolytic anaemia
- Gilbert syndrome

Alkaline phosphatase

**Sources**
- Bile ducts, bone and placenta
- If source is the liver:
  - γ-glutamyl transpeptidase is elevated
- If source is bone:
  - γ-glutamyl transpeptidase is not elevated
  - Calcium/phosphate may be abnormal

**Raised in**
- Bile duct obstruction of any cause
- Liver malignancy/space-occupying lesion
- Bony metastases
- Hepatitis of any cause
- Osteomalacia
- Paget’s disease of bone
- Haematological malignancy, e.g. lymphoma
- Heart failure (liver congestion)
- Also normally higher in children and pregnancy

**Lowered in**
- Hypothyroidism

Gamma glutamyl transpeptidase (γ-GT)

**Sources**
- Bile ducts and kidney

**Raised in**
- Alcohol excess
- Bile duct obstruction of any cause including malignancy/space-occupying lesion
- Hepatitis of any cause if severe
- Renal carcinoma
- Induction by drugs

Alanine aminotransferase (ALT)

**Sources**
- Liver and heart

**Raised in**
- Hepatitis of any cause
- Bile duct obstruction of any cause
TESTS OF RENAL FUNCTION

Urea and creatinine are dependent on glomerular filtration rate (GFR). They do not rise above normal range until GFR is reduced by 50-60%.

Urea
- Plasma urea varies with protein intake, tissue catabolism and renal excretion

Raised in
- Renal disease of any cause
- Dehydration
- Upper GI bleeding
- Shock – infection, trauma (increased catabolism)
- Cardiac failure

Lowered in
- Liver failure
- Starvation, low protein diet
- Pregnancy
- Overhydration

Creatinine (and eGFR)

Levels alter with age, gender and muscle mass
- Retention of creatinine indicates glomerular insufficiency

Raised in
- Renal disease of any cause
- Old age

Lowered in
- Muscle-wasting
- Pregnancy

Urate
- End-product of protein metabolism
- Excreted by kidneys

Raised in
- Gout
- Eclampsia
- Leukaemia/myeloma/lymphoma
- Renal insufficiency
- Thiazide diuretic therapy

Lowered in
- Allopurinol therapy
- Acute hepatitis of any cause
- Salicylate therapy

ACUTE PHASE REACTANTS

- Nonspecific tests for inflammation/infection
- Include:
  - Erythrocyte sedimentation rate (ESR)
  - C-reactive protein (CRP)
SELF-ASSESSMENT QUESTIONS

Multiple choice questions (single best answer)

1. Persistent vomiting may result in:
   A. Respiratory acidosis
   B. Peripheral oedema
   C. Metabolic acidosis
   D. Hypokalaemia
   E. Hypercalcaemia

2. Hyperkalaemia may be a result of the use of which of the following diuretics:
   A. Furosemide
   B. Bendroflumethiazide
   C. Spironolactone
   D. Metolazone
   E. Bumetanide

3. Which of the following statements are correct for standard i.v. fluid solutions:
   A. 0.9% saline distributes to all three fluid compartments
   B. 5% dextrose remains in the vascular compartment
   C. Colloid is used in hypovolaemia
   D. 0.9% saline is indicated in most cases of hyponatraemia
   E. Hypertonic saline from 0.9% is useful i.v. fluid replacement therapy in patients with chronic liver disease

4. Which of these is a cause of a metabolic acidosis with a normal anion gap:
   A. Sepsis
   B. Diabetic ketoacidosis
   C. Aspirin overdose
   D. Acute kidney injury
   E. Type 4 renal tubular acidosis

5. Which of these is a cause of a metabolic acidosis with a high anion gap:
   A. Diabetic ketoacidosis
   B. Type 4 renal tubular acidosis
   C. Diarrhoea
   D. Lead poisoning
   E. Hyperparathyroidism

6. In which of the following situations is the pH likely to be lower than normal:
   A. Vomiting
   B. Hypokalaemia
   C. Conn syndrome
   D. Hyperventilating
   E. Hyperparathyroidism

7. An elevated troponin I occurs in the following circumstance:
   A. 12 hours after the onset of pain in an acute coronary syndrome
   B. Day 2 after hip replacement
   C. Following a tonic-clonic seizure
   D. Heart failure
   E. Rhabdomyolysis

8. Serum bilirubin would be normal in patients with:
   A. Gilbert syndrome
   B. A gallstone obstructing the common bile duct
Clinical chemistry

C. Gallstones in the gallbladder  
D. Autoimmune haemolytic anaemia  
E. Acute fulminant hepatitis A  

9. A low blood urea would be expected in:  
A. Pregnancy  
B. Upper GI bleeding  
C. Cardiac failure  
D. Acute kidney injury  
E. Dehydration

Extended matching questions

**Question 1 Theme: Abnormal blood test results**

A. Shock  
B. Cardiac failure  
C. Cardiac failure treated with loop diuretics  
D. Pneumonia  
E. Renal failure  
F. Nephrotic syndrome  
G. Renal tubular acidosis  
H. Diarrhoea  
I. High ileostomy volumes  

For each of the following questions, select the best answer from the list above:

I. An 84-year-old female presents with confusion and ankle oedema. Blood results show the following: Na⁺ 132, K⁺ 2.8, Urea 9.8, Creat 128. What is the most likely diagnosis?  
II. A 37-year-old patient with Crohn’s disease presents with malaise. Blood tests reveal the following: Na⁺ 132, K⁺ 2.8, Urea 10, Creat 60, Mg²⁺ 0.54 (low), Cl⁻ 105, pH 7.3, Bicarbonate 15. What is the most likely diagnosis?  
III. A 56-year-old male presents with fever and malaise. Blood tests reveal the following: Na⁺ 124, K⁺ 4.5, Urea 7.6, Creat 98, pH 7.54, PO₂ 8.2, PCO₂ 3.2. What is the most likely diagnosis?

**Question 2 Theme: Acid-base disturbance**

A. Acute kidney injury  
B. Acute liver failure  
C. Aspirin overdose  
D. Recurrent vomiting  
E. Renal tubular acidosis  
F. Diabetic ketoacidosis  
G. Respiratory alkalosis  
H. Type II respiratory failure  

For each of the following questions, select the best answer from the list above:

I. A 64-year-old female presents with confusion and breathlessness. Blood gas analysis shows the following: pH 7.3, PCO₂ 9.6, PO₂ 4.5, Bicarbonate 28. What is the most likely diagnosis?  
II. A 37-year-old patient with diabetes presents with a history of vomiting and confusion. Blood gas analysis shows the following: pH 7.15, PCO₂ 2.5, PO₂ 12.5, Bicarbonate 10. What is the most likely diagnosis?  
III. An 18-year-old male is found collapsed at home. There is no history available. Blood tests reveal the following: pH 7.25, PCO₂ 3.6, PO₂ 13.5, Bicarbonate 8, Na⁺ 135, K⁺ 4, Cl⁻ 101. What is the most likely diagnosis?
Question 3 Theme: Abnormal blood test results
A. Acute coronary syndrome  
B. Cardiac failure  
C. Polymyositis  
D. Hodgkin’s lymphoma  
E. Haemolytic anaemia  
F. Nephrotic syndrome  
G. Renal tubular acidosis

For each of the following questions, select the best answer from the list above:

I. A 74-year-old man presents with chest pains which he has had for 48 hours. Blood results show elevation of CK, AST and troponin I. What is the most likely diagnosis?

II. A 37-year-old patient presents with malaise. He has noticed a lump in his neck ever since he had an upper respiratory tract infection 2 weeks ago. Blood tests reveal the following: Haemoglobin 123 g/L, CK 70 U/L, LDH 637 U/L, troponin I not detected. What is the most likely diagnosis?

III. A 21-year-old male student presents with yellowness of the skin. He has recently been diagnosed with glandular fever. Blood tests reveal the following: Bilirubin 95 µmol, ALT 24 U/L, AST 31 U/L, haemoglobin 89 g/L. What is the most likely diagnosis?
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Infectious disease remains the most common cause of morbidity and mortality worldwide. In order for an infectious agent to propagate within the population, there must be a reservoir of infection and a mode of transmission. Thus, avoidance of infection starts with reduction of the reservoir and limiting or avoiding the transmission of an organism.

System-specific infections are discussed in the appropriate chapters.

**DIAGNOSIS OF INFECTIOUS DISEASE**

**History**
- Exposure to the causative agent
- Travel to a high-risk area or environmental exposure
- Contact with an infected individual
- Occupation and leisure activity history
- Animal exposure
- Sexual history
- Parenteral drug use
- Blood transfusion
- Vaccination history

**Examination**
- Presence of a fever (Table 7.1)
- Rashes
- Lymphadenopathy
- Hepatosplenomegaly
- Evidence of septic shock (hypotension, tachycardia, peripheral vasodilatation)
- Delirium (confusion, hallucination)

**Investigations**

**Full blood count and blood film**
- Neutrophilia suggests bacterial infection
- Lymphocytosis suggests viral infection
- Lymphopenia may suggest HIV infection
- Neutropenia may suggest viral infection
- Eosinophilia suggests parasitic infection

**Thrombocytopenia**
- Malaria or disseminated intravascular coagulation

**Cell fragments – haemolysis**
- Parasites on blood film, e.g. malaria

**Blood culture**
- Aerobic and anaerobic bottles
- Follow sterile procedure
- May require repeated samples
Infectious diseases

Liver function
- Elevated transferases liver enzymes in viral hepatitis

Microscopy, culture and sensitivity
- Can be performed on stool, urine, CSF, sputum, ascitic fluid, pleural fluid, joint aspirates
- Provides organism identification and antibiotic sensitivity

Immunological diagnosis
- Presence of antibodies against specific antigens
- Presence of specific antigens due to their reaction with a known antibody

Genetic diagnosis
- Detection of genome of organism, e.g. hepatitis C virus RNA
- Assessment of ‘viral load’ or replication, e.g. HIV, Hepatitis B

Histological examination
- Pathology of specific infections on tissue biopsy

Imaging
- Localization of an infection, e.g. by ultrasound or CT scanning
- Labelled white cell scanning localizes the source of an infection

TREATMENT OF INFECTION DISEASE

Antibacterial drugs (Fig. 7.1)

β-lactams

Penicillins
- Block cell wall growth
- Group 1: parenteral formulations
  - e.g. Benzylpenicillin
- Group 2: oral penicillin
  - e.g. Phenoxymethylpenicillin (penicillin V)
- Group 3: β-lactamase-stable penicillins
  - e.g. Flucloxacillin

Table 7.1 Causes of fever (pyrexia) of unknown origin (F(P)UO)

<table>
<thead>
<tr>
<th>Infections (20–40%)</th>
<th>Immune (15–20%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Abscess</td>
<td>Drugs</td>
</tr>
<tr>
<td>Tuberculosis</td>
<td>Autoimmune rheumatic disease</td>
</tr>
<tr>
<td>Urinary infection</td>
<td>Sarcoïdosis</td>
</tr>
<tr>
<td>Biliary infection</td>
<td>Other (10–25%)</td>
</tr>
<tr>
<td>Endocarditis</td>
<td>Thyrotoxicosis</td>
</tr>
<tr>
<td>Epstein–Barr or cytomegalovirus</td>
<td>Ulcerative colitis</td>
</tr>
<tr>
<td>Toxoplasmosis/Brucellosis/</td>
<td>Crohn’s disease</td>
</tr>
<tr>
<td>Lyme disease</td>
<td>Familial Mediterranean Fever</td>
</tr>
<tr>
<td>Primary HIV infection</td>
<td>Factitious</td>
</tr>
</tbody>
</table>

Malignancy (10–30%)
- Lymphomas
- Leukaemia
- Solid tumours, e.g. renal cell, hepatocellular

5–25% remain undiagnosed

Table 7.1 Causes of fever (pyrexia) of unknown origin (F(P)UO)
Fig. 7.1 Mechanism of action of antibacterial drugs.
Infectious diseases

- **Group 4**: extended spectrum
  - e.g. Amoxicillin, ampicillin
- **Group 5**: β-lactamase-resistant penicillin
  - e.g. Temocillin

**Cephalosporins**
- Inhibit cell wall synthesis
- Penicillinase-resistant
- Broader antibacterial range
- 10% of patients with penicillin allergy will have a reaction to cephalosporins

  **First generation**
  - Gram-positive cocci and Gram-negative
    - Cefalexin, cefradine
  
  **Second generation**
  - Gram-negative infections
    - Cefuroxime, cefaclor
  
  **Third generation**
  - Gram-negative infections
    - Ceftazidime, ceftriaxone, doripenem, ertapenem

  **Fourth and fifth generation now available**

**Monobactams**
- Aztreonam

**Carbapenems**
- Imipenem, meropenem, doripenem, ertapenem

**Aminoglycosides**
- Inhibit bacterial protein synthesis
- Gram negatives, e.g. *Pseudomonas*
- Gentamicin, neomycin
- **Note**: Renal and ototoxicity, therefore serum levels need monitoring

**Tetracyclines**
- Inhibit bacterial protein synthesis
- Atypical pneumonias, acne
- Tetracycline, doxycycline, tigecycline
- **Note**: Contraindicated in children and during pregnancy as they cause permanently stained teeth

**Macrolides**
- Inhibit bacterial protein synthesis
- Useful in atypical pneumonia
- Erythromycin, clarithromycin, azithromycin
- Gram-negative infection

**Chloramphenicol**
- Inhibits bacterial ribosome function
- Conjunctivitis (local therapy)

**Fusidic acid**
- Inhibits bacterial protein synthesis
- *Staphylococcus aureus* osteomyelitis

**Sulphonamides**
- Inhibit bacterial folic acid synthesis
- Used with trimethoprim in urinary tract and *Pneumocystis jiroveci* infection
**Quinolones**
- Inhibit DNA synthesis
- Gram-negative infections
- Ciprofloxacin, moxifloxacin

**Nitroimidazoles**
- Break bacterial DNA synthesis
- Anaerobic infections
- Metronidazole

**Glycopeptides**
- Inhibit cell wall synthesis
- Gram-positive bacteria
- Vancomycin, teicoplanin

**Side-effects of antibacterials**
- Sensitivity: rash/anaphylaxis
- Organism resistance, e.g. MRSA/VRE
- Disruption of normal gut flora → antibiotic related diarrhoea or pseudomembranous colitis

**Antifungal drugs**

**Polyenes**
- Disrupt fungal membranes
  - Amphotericin B – systemic disease
  - Nystatin – oral and enteric Candida

**Azoles**
- Broad-spectrum antifungals
  - Clotrimazole – ringworm
  - Ketoconazole – candidiasis

**Triazoles**
- Fluconazole – penetrates CSF
- Itraconazole

**Others**
- Terbinafine
- Griseofulvin
- Echinocandins

**Side-effects of antifungals**
- Itraconazole – fulminant hepatic failure and hepatic dysfunction
- Heart failure – avoid prescribing with calcium channel blockers

**Antiviral drugs**

**Aciclovir**
- Terminates viral DNA synthesis
- *Herpes simplex* and *varicella zoster* virus

**Ganciclovir**
- Cytomegalovirus infection

**Amantadine**
- Influenza virus

**Interferons**
- Hepatitis B and C
- Pegylated formulations are more effective and require less frequent dosing
**Ribavirin**
- Combination therapy (with interferon) for chronic hepatitis C

**Protease inhibitors**
- e.g. bocepravir for hepatitis C

**Antiretrovirals**
- See page 122.

**Nucleoside and nucleotide analogues**
- e.g. Lamivudine, tenofovir, used in combination therapy, e.g. for hepatitis B

**VACCINATION (TABLE 7.2)**

**Passive**
- Antibody raised against the infecting organism, e.g. tetanus immunoglobulin, diphtheria, rabies

**Active**
- Immunogenic antigen induces antibody production

**Live attenuated vaccines**
- Measles, mumps, rubella
- BCG

**Inactivated (killed) vaccines**
- Hepatitis A
- Pertussis (whooping cough)
- *Haemophilus influenzae b*
- Meningococcus A and C
- Pneumococcus
- Influenza
- Polio

---

**Table 7.2 UK Vaccination schedule**

<table>
<thead>
<tr>
<th>Age Range</th>
<th>Vaccines</th>
</tr>
</thead>
<tbody>
<tr>
<td>2, 3 and 4 months</td>
<td>Diphtheria, pertussis and tetanus &lt;br&gt; <em>Haemophilus influenzae b</em> &lt;br&gt; Oral polio &lt;br&gt; Meningococcus gp C &lt;br&gt; Tuberculosis (BCG) for infants at high risk</td>
</tr>
<tr>
<td>13 months</td>
<td>Measles &lt;br&gt; Mumps &lt;br&gt; Rubella &lt;br&gt; (MMR)</td>
</tr>
<tr>
<td>2, 14 and 12-13 months</td>
<td>Pneumococcal</td>
</tr>
<tr>
<td>By school entry</td>
<td>Diphtheria, pertussis, tetanus &lt;br&gt; MMR and oral polio</td>
</tr>
<tr>
<td>13–18 years</td>
<td>Diphtheria, tetanus and oral polio (plus human papilloma vaccine for girls)</td>
</tr>
</tbody>
</table>
Toxoids
- Tetanus
- Diphtheria

Recombinant vaccines
- Hepatitis B

**BACTERIAL INFECTION**

**Gram-positive cocci**

*Staphylococcus*
- *Staph. aureus*, epidermidis, saprophyticus (Fig. 7.2)
- Skin: cellulitis, impetigo, necrotizing fasciitis
- Lungs: pneumonia, abscesses
- Heart: endocarditis
- CNS: meningitis, abscesses
- Bones: osteomyelitis

![Diagram showing manifestations of Staphylococcal infection.](image)

**Fig. 7.2** Manifestations of *Staphylococcal* infection.
Infectious diseases

Gut: enterocolitis
- *Staph. aureus* produces a toxin, which may cause:
  - Food poisoning
  - Toxic shock syndrome
  - Scalded skin syndrome

**Management**
- Much community-acquired infection is penicillin-sensitive
- However, hospital spread of methicillin-resistant *Staph. aureus* (MRSA) is increasing

**Streptococcus**
- Majority of infections are due to β-haemolytic *Strep. pyogenes*
- Skin: impetigo, erysipelas
- Mouth: pharyngitis, tonsillitis
- Lungs: pneumonia – *Strep. pneumoniae*
- Other: endocarditis – *Strep. viridans*, scarlet fever, rheumatic fever

**Management**
- Majority are sensitive to penicillins

**Gram-negative cocci**

**Neisseria**
- *Neisseria meningitidis* → meningitis and septicaemia
- *Neisseria gonorrhoeae* → gonorrhoea

**Management**
- Penicillin or cefotaxime

**Gram-positive bacilli**

**Corynebacterium**
- *C. diphtheriae*
- Toxin-producing forms → diphtheria
- Nasal discharge
- Pharyngeal inflammation
- Laryngeal inflammation → husky voice
- Respiratory obstruction
- Myocarditis
- Neurological manifestations – cranial nerve palsies, polyneuropathy

**Management**
- Antitoxin + penicillin

**Listeria**
- *L. monocytogenes*
- → Abortions, meningitis or septicaemia

**Management**
- Ampicillin and gentamicin

**Clostridium**
- *C. botulinum, C. difficile* (see Ch. 10)
- *C. tetani* → tetanus
  - Infects puncture wounds and bites
  - Neurotoxin production
  - Neuromuscular blockade, lockjaw, muscle spasm, autonomic neuropathy

---

7 Pass Finals
**Management**
- Antitoxin, penicillin, ITU care

**B. anthracis (Bacillus group)**
- Anthrax
  - → Erythematous skin lesion that ulcerates
  - → Black central eschar
  - Pulmonary and GI tract involvement

**Management**
- Penicillin

**B. cereus (Bacillus group)**
- → Toxin mediated food poisoning

### Gram-negative bacilli

#### Brucella
- *B. abortus, melitensis, suis*
- Endotoxin → headache, fever, weakness
- Lymphadenopathy, hepatosplenomegaly
- Arthritis, encephalitis and endocarditis
- Contracted from non-pasteurized milk

**Management**
- Doxycycline

#### Bordetella
- *B. pertussis* – whooping cough
- Childhood disease
- Catarrhal phase – rhinorrhoea and conjunctivitis
- Paroxysmal phase – coughing attacks

**Management**
- Erythromycin in catarrhal phase

#### Haemophilus
- *H. influenzae, ducreyi, parainfluenzae*
- Increased risk of infection post-splenectomy
- Pneumonia, bronchitis
- Meningitis (*H. influenzae b*)
- Epiglottitis

**Management**
- Cefotaxime, cefuroxime

**Prevention**
- HiB vaccine

#### Cholera
- *Vibrio cholerae* (see Ch. 10)

### Enterobacteria
- *Escherichia coli*
- *Salmonella*
- *Campylobacter*
- *Shigella*
- *Helicobacter*
- *Yersinia* (see Ch. 10)
**Infectious diseases**

**MYCOBACTERIAL DISEASE**

*Mycobacterium tuberculosis*

- Acid-fast aerobic bacillus (Fig. 7.3)
- Droplet spread
- → Caseating granuloma
  - Lung
  - Adrenals
  - Terminal ileum
  - Lymph nodes
- → Cough, fever, weight loss, night sweats
- Immunosuppression → haematogenous spread (miliary TB)

**Complications**

- TB meningitis
- TB peritonitis

---

**Fig. 7.3 Manifestations of tuberculosis.**
- Arthritis and osteomyelitis
- Constrictive pericarditis

**Investigations**
- Imaging – X-ray/CT scan of the chest
- Microbiology – Ziehl-Neelson staining of sputum
- Bronchoscopy and washings
- Biopsy of solid lesions
- CSF examination in meningitis
- Early morning urine

**Management**
- Combination therapy (Table 7.3)

**Contact tracing**
- X-ray and tuberculin testing in close contacts

**Immunization**
- Bacille Calmette-Guérin (BCG)
- Bovine strain of TB with very low virulence after tuberculin testing

**Mycobacterium leprae**
- Leprosy (Hansen’s disease)
- Immune response determines disease type (there are two ends of a clinical spectrum)

**Tuberculoid**
- High cell-mediated immunity
- Hypopigmented skin patches
- Loss of sensation over patch
- Tender thickened nerves

**Lepromatous**
- Macules, papules or nodules in the skin
- Laryngitis and hoarse voice
- Collapse of nasal cartilage
- Leonine face

**Investigations**
- Impossible to culture organism
- Diagnosis is basically clinical

**Management**
- Dapsone, rifampicin and clofazimine for 2 years

### Table 7.3 Drug regimens for tuberculosis

<table>
<thead>
<tr>
<th>Disease</th>
<th>Regimen</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pulmonary TB</td>
<td>Rifampicin and isoniazid for 6 months, pyrazinamide and ethambutol for the first 2 months</td>
</tr>
<tr>
<td>TB meningitis and pericarditis</td>
<td>Rifampicin and isoniazid for 12 months, with pyrazinamide and ethambutol for the first 2 months and glucocorticoids</td>
</tr>
<tr>
<td>Drug resistance and HIV</td>
<td>Start standard therapy as above but alter based on sensitivities and known prevalence of resistance longer therapy and other agents e.g. quinolones may be needed</td>
</tr>
</tbody>
</table>
**SPIROCHAETES**

**Syphilis**

- *Treponema pallidum*

**Primary syphilis (10–90 days post-infection)**

- Painless ulcer (chancre) at infection site

**Secondary syphilis (4–10 weeks)**

- Lymphadenopathy
- Rash – papules or pustules
- Warty skin lesions (condylomata lata)
- Oral ‘snail track’ ulcers

**Tertiary syphilis**

- Granulomatous lesions
- Skin, bones, liver
- Aortic dilatation and valve regurgitation

*Fig. 7.4* Some manifestations of tertiary syphilis.
- Neurosyphilis – meningitis, cerebral gumma
- Tabes dorsalis – dorsal root demyelination (Fig. 7.4)

**Congenital syphilis**
- Hutchinson’s (notched) teeth
- Sabre tibia
- Long bone abnormalities
- Loss of nasal bridge

**Management**
- Procaine penicillin

**Leptospirosis (Weil's disease)**
- *Leptospira interrogans*
- Contact with animal reservoirs (rat’s urine)
- Headache, fever, myalgia
- Conjunctival suffusion
- Hepatosplenomegaly and lymphadenopathy

---

**Fig. 7.5** Manifestations of Lyme disease.
Infectious diseases

- May progress to:
  - Jaundice
  - Haemolytic anaemia
  - Renal failure

**Investigations**
- IgM antibodies
- *Leptospira* cultured in blood

**Management**
- Penicillins
- Erythromycin

**Lyme disease (Fig. 7.5)**
- *Borrelia burgdorferi*
- Carried by ixodid ticks (from deer and sheep)
- Erythema chronicum migrans
- Headache, fever and malaise
- Meningoencephalitis
- Cranial nerve palsies
- Cardiac arrhythmias, myocarditis
- Arthritis

**Investigations**
- IgM antibodies against organism

**Management**
- Amoxicillin/penicillin

**Viral Infections**
- Viral hepatitis is discussed in Chapter 10

**DNA viruses: Adenoviruses**
- Croup
- Gastroenteritis
- Mesenteric adenitis in children

**α-Herpesvirus**

*Herpes simplex-1 (HSV-1)*
- Stomatitis (primary infection)
- Cold sores
- Erythema multiforme

*Herpes simplex-2 (HSV-2)*
- Genital herpes

*Varicella zoster virus (VZV)*
- Chickenpox (primary infection)
- Shingles (see Ch. 12)

**β-Herpesvirus**

*Cytomegalovirus (CMV)*
- Retinitis
- Pneumonitis
- Gastrointestinal ulcers (in immunocompromised)

*Human herpes viruses 6 and 7*
- Roseola infantum (children)
Viral infections

**γ-Herpesvirus**

**Epstein–Barr virus (EBV)**
- Infectious mononucleosis
- Burkitt’s lymphoma
- Nasopharyngeal carcinoma
- Gastric carcinoma

**Human herpes virus 8**
- Kaposi’s sarcoma

**Erythrovirus B19**
- Erythema infectiosum in children (fifth disease/slapped cheek syndrome)
- Aplastic crisis in sickle cell disease
- Anaemia, leucopenia and thrombocytopenia

**Poxvirus**
- Smallpox (now eradicated worldwide)
- Molluscum contagiosum

**RNA viruses/PicoRNAviruses**

**Poliovirus**
- Poliomyelitis
- 95% asymptomatic
- 0.1% suffer paralytic poliomyelitis
- Asymmetric paralysis
- No sensory involvement

**Coxsackievirus**
- Hand, foot and mouth disease (vesicular rash)
- Meningitis and encephalitis
- Myocarditis and pericarditis

**Togaviruses**

**Rubella (German measles)**
- Conjunctivitis
- Lymphadenopathy
- Macular pink/red rash
- Fetal infection → cardiac defect, cataracts, mental retardation and deafness

**Flaviviruses**

**Yellow fever**
- Mosquito spread
- Africa and Asia
- High fever
- Bradycardia
- Jaundice
- Clotting abnormalities → bleeding

**Dengue**
- Spread by biting arthropod *A. aegypti* which lives in standing water in inner cities
- South America, Africa and Asia
### Infectious diseases

- High fever, malaise, headache, flushing, retrobulbar pain, backache
- Lymphadenopathy, petechiae on palate and skin rashes
- Haemorrhagic capillary leak syndrome
- Antibody testing for diagnosis
- Treatment is supportive

#### Orthomyxovirus

**Influenza**
- Type A → epidemics and pandemics
- Type B → localized outbreaks
- Type C → rarely produces disease

#### Paramyxovirus

**Measles (rubeola)**
- Incubation 8–14 days
- Malaise, fever, cough
- Koplik’s spots in the mouth
- Erythematous rash
- Complications
  - Pneumonia
  - Myocarditis
  - Encephalomyelitis
  - Subacute sclerosing panencephalitis

**Mumps**
- Incubation 18 days
- Fever, headache, anorexia
- Parotid gland swelling ± submandibular involvement
- Epididymo-orchitis after puberty

#### Rhabdovirus

**Rabies**
- Contracted in animal bites
- Anxiety, agitation, hydrophobia and aerophobia
- Hyperreflexia and muscle spasm
- Death at 10–14 days
- No effective treatment

### HUMAN IMMUNODEFICIENCY VIRUS (HIV) AND ACQUIRED IMMUNE DEFICIENCY SYNDROME (AIDS)

#### Epidemiology
- Young adults and children in developing world – heterosexual and vertical spread, breast-feeding
- Sexual intercourse (vaginal and anal)
- Blood spread (shared needles, transfusions)

#### HIV (Fig. 7.6)
- Two subtypes:
  - HIV1 Europe/America and South-East Asia
  - HIV2 Africa
- Retrovirus (reverse transcriptase allows DNA synthesis from RNA)
- Binds to CD4 lymphocyte surface marker
- Enters lymphocyte → viral synthesis
Clinical features
- Seroconversion illness 2 weeks after infection
- Fever, lymphadenopathy, headache

Investigations
- IgG against gp120
- IgG against p24
- Viral p24 antigen
- Viral culture
- Viral load (RNA copies/mL)

Clinical latency
- Median time of 10 years until clinical presentation of AIDS

Effects of HIV infection
- Infections due to low CD4 lymphocyte count
- Diagnosis based on low CD4 count and the presence of an AIDS-defining illness

Fig. 7.6 Manifestations of HIV.
Infectious diseases

Neurological disease
- HIV-related dementia
- Distal sensory polyneuropathy
- Autonomic neuropathy
- Progressive multifocal leucoencephalopathy
- Cryptococcal meningitis
- Cerebral lymphoma
- Cerebral toxoplasma

Eye disease
- CMV retinitis

Mucocutaneous disease
- Kaposi’s sarcoma
- Molluscum contagiosum
- Shingles
- Oral hairy leucoplakia (tongue)
- Oral/oesophageal candidiasis
- Squamous cell carcinomas

Haematological disease
- Low CD4 (<200)
- Anaemia
- Neutropenia
- Isolated thrombocytopenia

Gastrointestinal disease
- Weight loss
- HIV-related diarrhoea
  - Cryptosporidium
  - Microsporidium
  - HIV enteropathy
  - CMV colitis
  - Bacterial infection
  - Mycobacterium
- Sclerosing cholangitis
- Oesophageal candidiasis

Renal disease
- HIV associated nephropathy
- Focal glomerulonephritis

Respiratory disease
- Pneumonia
  - Pneumocystis jiroveci pneumonia (PCP)

Disease monitoring
- CD4 lymphocyte count
- HIV viral load (HIV RNA)

Management (Table 7.4)

Antiretroviral drugs
- HAART: highly active antiretroviral therapy–combination therapy that significantly reduces viral load and improves survival
- Nucleoside analogues, e.g. zidovudine/abacavir/lamivudine/didanosine/tenofovir
- Protease inhibitors, e.g. ritonavir/saquinavir/indinavir
Table 7.4 Post-exposure prophylaxis

<table>
<thead>
<tr>
<th>Post-needlestick injury</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blood from patient and injured person</td>
</tr>
<tr>
<td>Then 4 weeks of</td>
</tr>
<tr>
<td>Tenofovir and emtricitabine with polinavir and ritinavir</td>
</tr>
</tbody>
</table>

- Non-nucleoside reverse transcriptase inhibitors (only active against HIV1), e.g. nevirapine/efavirenz
- HIV cell fusion inhibitors, e.g. enfuvirtide

Complications of antiretroviral therapy
- Lipodystrophy syndrome (insulin resistance/dyslipidaemia/fat redistribution)

Early management of opportunistic infections
- Screening for infection, e.g. ophthalmoscopy for CMV retinitis

Prevention of infection
- Safe sex practices
- Needle exchanges
- Screening of blood transfusions

Fungal disease

Candidiasis
- *Candida albicans*
- Vaginal and oral thrush
- Oesophagitis
- Increased in the immunocompromised, e.g. antibiotics, steroids and in the elderly

Diagnosis
- Microscopy
- Clinical appearance

Management
- Nystatin for oral lesions
- Fluconazole/Amphotericin B

Histoplasmosis
- *Histoplasma capsulatum*
- TB-like disease
- Pulmonary focus
- Erythema nodosum and multiforme
- Treat with ketoconazole/itraconazole/amphotericin B

Aspergillosis

Bronchopulmonary allergic aspergillosis
- Mimics asthma
- Bronchiectasis and eosinophilia

Aspergilloma
- Fungus ball in cavity in lung
- Often in old TB focus
Infectious diseases

Invasive aspergillosis
- Immunocompromised patients
- Pneumonia
- Meningitis and intracerebral abscess

PROTOZOAL DISEASE

Leishmaniasis

Visceral leishmaniasis (kala-azar)
- Fever, cough, diarrhoea
- Pigmented rough skin
- Splenomegaly (often massive)
- Hypersplenism → pancytopenia
- Hepatomegaly

Cutaneous leishmaniasis
- Transmitted by sandfly
- Multiple painless nodules → ulceration

Trypanosomiasis

Sleeping sickness (African disease)
- Tsetse fly transmission
- Meningoencephalitis
- Apathy and somnolence

Chagas disease (American disease)
- Lymphadenopathy
- Hepatosplenomegaly
- Conjunctivitis
- GI motility disturbance
- Neurological complications

Toxoplasmosis

- Toxoplasma gondii
- Transmission by cats
- Lymphadenopathy
- Neck stiffness and headache
- Acute febrile illness

Malaria

Epidemiology
- 500 million people worldwide
- Hot humid countries

Aetiology
- Plasmodium – vivax, ovale, falciparum, malariae
- Transmitted by ♀ Anopheles mosquito

Clinical features
- High fever
- Splenomegaly
- Vivax, ovale and malariae → milder chronic disease
- Falciparum → more serious acute disease:
- Blackwater fever: haemolysis → black urine
- Cerebral malaria: convulsions, coma
Severe malaria: 1% erythrocytes infected (falciparum malaria) → Cerebral, renal and GI involvement
- Risk of splenic rupture
- Renal failure
- Haemolysis and thrombocytopenia
- Hypoglycaemia and acidosis

**Investigations**
- Thick and thin blood film shows parasites and allows identification
- Quantification of percentage of infected red cells
- Blood count, liver function tests, urea and electrolytes for complications

**Management**
- Falciparum: first line treatment is i.v. artesunate; if not available use i.v. quinine if severe malaria
- Other species: chloroquine

**Prevention**
See Table 7.5.

### NEMATODE, TREMATODE AND CESTODE INFECTIONS

**Nematodes Filariasis**
- Lymphangitis and elephantiasis

**Toxocara**
- Transmitted by dogs and cats
- Abdominal pain and hepatomegaly

**Intestinal infections**
See Chapter 10.

**Trematodes Schistosomiasis (Bilharzia)**

**S. japonicum/mansoni**
- Intestinal ulceration and fibrosis
- Granulomatous hepatitis
- Hepatosplenomegaly
- Portal hypertension

**S. haematobium**
- Dysuria and haematuria
- Bladder carcinoma

**Cestodes**
- Tapeworms
SEXUALLY TRANSMITTED DISEASES

Gonorrhoea

- *Neisseria gonorrhoeae*
- ♂ Urethritis and urethral discharge
- ♀ 50% asymptomatic
- Dysuria and vaginal discharge
- Conjunctival infection in the newborn
- Arthritis and rash in systemic disease

**Investigations**
- Nucleic acid amplification tests (NAATs) on urine. Microscopy and culture of urethral or vaginal swabs

**Management**
- Ceftriaxone and azithromycin

Chlamydia

- *Chlamydia trachomatis*
- ♂ Urethritis with discharge
- ♀ Acute salpingitis → subfertility
- Ophthalmic trachoma → blindness
- Reiter syndrome - oral ulcers, arthritis, conjunctivitis, urethritis

**Investigations**
- Nucleic acid amplification tests (NAATs) on urine. Serology (IgM) or antigen detection

---

**Table 7.6** Diseases notifiable under the Health Protection (notification) Regulations 2010

<table>
<thead>
<tr>
<th>Disease</th>
<th>Notifiable Disease</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acute encephalitis</td>
<td>Malaria</td>
</tr>
<tr>
<td>Acute infectious hepatitis</td>
<td>Measles</td>
</tr>
<tr>
<td>Acute meningitis</td>
<td>Meningococcal septicaemia</td>
</tr>
<tr>
<td>Acute poliomyelitis</td>
<td>Mumps</td>
</tr>
<tr>
<td>Anthrax</td>
<td>Plague</td>
</tr>
<tr>
<td>Botulism</td>
<td>Rabies</td>
</tr>
<tr>
<td>Brucellosis</td>
<td>Rubella</td>
</tr>
<tr>
<td>Cholera</td>
<td>SARS</td>
</tr>
<tr>
<td>Diphtheria</td>
<td>Scarlet fever</td>
</tr>
<tr>
<td>Enteric fever (typhoid or paratyphoid fever)</td>
<td>Smallpox</td>
</tr>
<tr>
<td>Food poisoning</td>
<td>Tetanus</td>
</tr>
<tr>
<td>Haemolytic uraemic syndrome (HUS)</td>
<td>Tuberculosis</td>
</tr>
<tr>
<td>Infectious bloody diarrhoea</td>
<td>Typhus</td>
</tr>
<tr>
<td>Invasive group A streptococcal disease</td>
<td>Viral haemorrhagic fever (VHF)</td>
</tr>
<tr>
<td>Legionnaires’ Disease</td>
<td>Whooping cough</td>
</tr>
<tr>
<td>Leprosy</td>
<td>Yellow fever</td>
</tr>
</tbody>
</table>

---
Management

- Doxycycline or azithromycin

Syphilis

See Spirochaetes, above.

HIV

See Viral infections, above.

Human papilloma virus (HPV)

- Sexual transmission
- Results in cervical dysplasia
- Cervical carcinoma
- Vaccine available

NOTIFIABLE DISEASES

See Table 7.6

SELF-ASSESSMENT QUESTIONS

Multiple choice questions (true or false)

1. The following diseases are paired with their correct mode of transmission:
   A. Leishmaniasis – sandfly bites
   B. Hepatitis A – intravenous drug use
   C. Giardiasis – faecal-oral spread
   D. Taenia solium – infected meat products
   E. Neisseria gonorrhoeae – sexual intercourse

2. The following antibiotics act by disrupting bacterial cell wall synthesis:
   A. Amoxicillin
   B. Metronidazole
   C. Cefuroxime
   D. Ciprofloxacin
   E. Gentamicin

3. The following are live attenuated vaccines:
   A. Oral polio vaccine
   B. Tetanus
   C. Bacille Calmette–Guérin (BCG)
   D. Haemophilus influenzae b
   E. Hepatitis B vaccine

4. The following are recognized side-effects of the named antibiotic:
   A. Ampicillin – rash in infectious mononucleosis
   B. Gentamicin – renal toxicity
   C. Flucloxacillin – ototoxicity
   D. Sulphonamides – erythema multiforme
   E. Fusidic acid – seronegative arthropathy

5. The following may result in atypical lymphocytes on a blood film:
   A. Epstein–Barr virus
   B. Cytomegalovirus
   C. Influenza A
   D. Toxoplasmosis
   E. Salmonellosis
6. The following are manifestations of staphylococcal disease:
   A. Osteomyelitis
   B. Scarlet fever
   C. Impetigo
   D. Infective endocarditis
   E. Cerebral abscesses

7. The following are true of *Mycobacterium tuberculosis*:
   A. It may cause a terminal ileitis
   B. Tuberculous meningitis results in a low protein and glucose in CSF
   C. Pyrazinamide is useful in eradicating organisms in macrophages
   D. Infection may cause lupus vulgaris
   E. Miliary infection results from haematogenous spread

8. The following organisms release a neurotoxin:
   A. *Clostridium botulinum*
   B. *Clostridium difficile*
   C. *Clostridium tetani*
   D. *Corynebacterium diphtheriae*
   E. *Yersinia*

9. The following belong to the herpesvirus family:
   A. Cytomegalovirus
   B. Epstein–Barr virus
   C. Coxsackievirus
   D. Varicella zoster virus
   E. Rhabdovirus

10. The following are of use in chronic viral hepatitis:
    A. Lamivudine
    B. Azathioprine
    C. Ribavirin
    D. Interferon-α
    E. Zidovudine

11. In the following diseases animal vectors constitute an important mode of transmission:
    A. Yellow fever (togavirus)
    B. Fifth disease (parvovirus B19)
    C. Rabies (rhabdovirus)
    D. Hand, foot and mouth disease (paramyxovirus)
    E. Molluscum contagiosum (pox virus)

12. The following are recognized complications of the named infection:
    A. Measles virus – subacute sclerosing panencephalitis
    B. Rabies – aerophobia
    C. Varicella – pneumonia
    D. Cytomegalovirus – retinitis
    E. Parvovirus B19 – aplastic anaemia

13. The following are causes of abnormal liver function tests in HIV infection:
    A. Zidovudine
    B. Lamivudine
    C. Sclerosing cholangitis
    D. Cytomegalovirus infection
    E. *Mycobacterium avium intracellulare*
14. The following drugs are paired with the appropriate mechanism of action:
   A. Ritonavir – protease inhibitor
   B. Zidovudine – nucleoside analogue
   C. Nevirapine – viral RNA inhibitor
   D. Lamivudine – inhibition of cell wall synthesis
   E. Saquinavir – protease inhibitor

15. The following increase the risk of systemic candidiasis:
   A. Diabetes mellitus
   B. Oral prednisolone
   C. Chronic kidney disease
   D. Acute viral hepatitis
   E. Intravenous cephalosporin therapy

16. The following are not features of falciparum malaria:
   A. Thrombocytopenia
   B. Intravascular haemolysis
   C. Bronchospasm
   D. Hyposplenism
   E. Hypoglycaemia

17. The following are indicators of severe malaria:
   A. Fever >38°C
   B. Parasitaemia >2%
   C. Dark urine
   D. Glucose-6-phosphate deficiency
   E. Convulsions

18. The following may cause conjunctivitis in the newborn babies of infected mothers:
   A. Syphilis
   B. Chlamydia
   C. Gonorrhoea
   D. HIV
   E. Rubella

19. The following are true of syphilis infection:
   A. Acute infection usually presents as a painless ulcer
   B. A rash involving the palms of the hands suggests a secondary streptococcal infection
   C. Neurological signs may be due to intracerebral abscesses
   D. Syphilis meningitis may complicate tertiary syphilis
   E. Congenital infection results in an internuclear ophthalmoplegia

20. The following may result in oral ulceration:
   A. Syphilis
   B. Ulcerative colitis
   C. Behçet syndrome
   D. Mumps infection
   E. *Toxoplasma gondii*

**Multiple choice questions (single best answer)**

21. The following are true of sexually transmitted disease:
   A. The incidence of nonspecific urethritis is falling
   B. Gonorrhoea infection is asymptomatic in 90% of infections in males
   C. Chlamydia is an important cause of male infertility
   D. Gonorrhoea may result in a pustular rash
   E. Reactive arthritis is not associated with chlamydia infection
22. Which one of the following is true of HIV infection:
   A. *Pneumocystis jiroveci* pneumonia is an AIDS-defining illness
   B. The CD4-positive lymphocyte count is a poor marker of immune status
   C. The median duration of infection prior to the development of AIDS is 2 years
   D. HIV dementia is due to a parvovirus infection
   E. Kaposi’s sarcoma is an indication of adenovirus infection

23. Which one of the following causes an acute hepatitic illness:
   A. Rhabdovirus
   B. Parvovirus B19
   C. Togaviruses
   D. Dane particle
   E. Epstein–Barr virus

24. Which one of the following is a Gram-positive organism?
   A. *Staphylococcus aureus*
   B. *Escherichia coli*
   C. *Helicobacter pylori*
   D. *Salmonella typhi*
   E. *Giardia lamblia*

25. A 23-year-old man presents with a cough, with rust-coloured sputum, peri-oral Herpes Simplex and findings of left lower lobe consolidation on chest X-ray. What is the most likely cause of his pneumonia?
   A. Staph. aureus
   B. Strep. pneumoniae
   C. H. influenzae
   D. *Pneumocystis jiroveci* pneumonia
   E. *M. tuberculosis*

26. A 76-year-old man presents with a fever, shortness of breath and a cough. On examination he has a pansystolic murmur that radiates to the axilla. On testing he has microscopic haematuria. What is the most likely diagnosis?
   A. Interstitial glomerulonephritis
   B. Pyelonephritis
   C. Bacterial endocarditis
   D. Cordae tendona rupture
   E. Mycoplasma pneumonia

27. A 43-year-old woman was referred with weight loss, sweats and a fever. Investigations revealed lymphopenia. A CD4 lymphocyte count was recorded as <100. What is the most likely underlying cause?
   A. Parvovirus B19
   B. Epstein–Barr virus
   C. Human immunodeficiency virus
   D. Human papilloma virus
   E. Cytomegalovirus

28. A 67-year-old man is being treated with steroids and antibiotics for an infective exacerbation of chronic obstructive pulmonary disease. He reports pain and difficulty in swallowing. What is the most likely diagnosis?
   A. Peptic oesophageal stricture
   B. *Helicobacter pylori* induced ulceration
   C. Oesophageal cytomegalovirus
D. Oesophageal candidiasis
E. Eosinophilic oesophagitis

29. A 14-year-old boy presents with a 3-day history of a non-productive cough, followed by the appearance of multiple erythematous spots on the torso, arms and legs. On examination he has white spots on the buccal mucosa. What is the most likely cause?
A. Chicken pox
B. Rubella
C. Erythema infectiosum
D. Scarlet fever
E. Measles

Extended matching questions

Question 1 Theme: Fever of unknown origin
A. Acute bronchopulmonary aspergillosis
B. *Pneumocystis jiroveci*
C. Staphylococcal pulmonary abscess
D. Aspergilloma
E. *Mycobacterium tuberculosis*
F. Falciparum malaria
G. Leishmaniasis
H. Liver abscess
I. Acute hepatitis A
J. *Streptococcus pneumoniae* pneumonia
K. *Mycoplasma* pneumonia
L. Schistosomiasis

For each of the following questions, select the best answer from the list above:
I. A 42-year-old Ugandan woman with known HIV infection and a CD4 lymphocyte count of 86 is admitted with a cough, haemoptysis, weight loss and cervical lymphadenopathy. A chest X-ray reveals diffuse apical shadowing of the left lung. What is the most likely diagnosis?

II. An 18-year-old man is admitted with a cough with rust-coloured sputum, anorexia, a temperature of 38.6°C and marked shortness of breath. On examination he is noted to have perioral herpes and coarse crackles at the right upper zone with some bronchial breathing. What is the most likely diagnosis?

III. A 28-year-old woman is admitted with a fever and jaundice. She has recently returned from India after visiting her family. She has a moderately enlarged liver and spleen. On full blood count she is noted to have a platelet count of 76. What is the most likely diagnosis?

Question 2 Theme: Investigation of pyrexia
A. Full blood count
B. Thick and thin blood film
C. Urea and electrolytes
D. Liver function tests
E. Serum calcium
F. Blood glucose
G. Blood cultures
H. Urine microscopy and culture
I. Sputum culture
For each of the following questions, select the best answer from the list above:

I. A 57-year-old woman is admitted with right upper quadrant pain, jaundice and a fever. On examination, she is tender in the right hypochondrium. What single investigation would be most useful in reaching a diagnosis?

II. A 28-year-old man returns from a trip to Kenya. He has a fever and is jaundiced. He has moderate splenomegaly. What single investigation would you choose to make the diagnosis?

III. A 76-year-old man develops a fever and cough with white frothy sputum a week after a mitral valve replacement. On examination he has fine crackles in both lung bases and a pansystolic murmur. Which investigation will be of most use in guiding treatment?
STRUCTURE AND FUNCTION

The structure of the respiratory system facilitates its role in extracting oxygen from the environment and disposing of waste gases (primarily carbon dioxide):

- The lungs provide a large surface area for gas exchange
- The alveolar walls present minimal resistance to gas exchange
- Efficient gas transfer is facilitated by matching ventilation to perfusion in the pulmonary capillary bed
- Host defences protect against inhaled gases, dusts and infectious agents

SMOKING

Cigarette smoke contains polycyclic aromatic hydrocarbons and nitrosamines which are potent carcinogens and mutagens. Smoking also causes release of enzymes from neutrophils and macrophages which destroy elastin leading to lung damage. Smoking is addictive. The dangers of smoking and the effects on the lungs are listed in Tables 8.1 and 8.2.

EXAMINING THE RESPIRATORY SYSTEM

Examination should contain all of the following and be done in roughly this order:

Look for:

- Clues around the bed
  - Oxygen
  - Inhalers
  - Nebulizers
  - Peak flow meter

Expose the chest

- Maintain the dignity of the patient. Act professionally
- Look for:
  - Cyanosis
  - Breathlessness/use of accessory muscles
  - Weight loss
  - Chest wall scars or deformity
  - Prominent veins on the chest wall (suggesting superior vena cava (SVC) obstruction)

Hands

- Flapping tremor of CO₂ retention – hold arms outstretched with wrists fully extended and fingers splayed and watch for movements of fingertips
### Table 8.1 The dangers of cigarette smoking

<table>
<thead>
<tr>
<th>General</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lung cancer</td>
</tr>
<tr>
<td>COPD</td>
</tr>
<tr>
<td>Carcinoma of the oesophagus</td>
</tr>
<tr>
<td>Ischaemic heart disease</td>
</tr>
<tr>
<td>Peripheral vascular disease</td>
</tr>
<tr>
<td>Bladder cancer</td>
</tr>
<tr>
<td>An increase in abnormal spermatozoa</td>
</tr>
<tr>
<td>Memory problems</td>
</tr>
<tr>
<td>Maternal smoking</td>
</tr>
<tr>
<td>Decreased infant birth weight</td>
</tr>
<tr>
<td>Increased fetal and neonatal mortality</td>
</tr>
<tr>
<td>Increase in asthma</td>
</tr>
<tr>
<td>Passive smoking</td>
</tr>
<tr>
<td>Risk of asthma, pneumonia and bronchitis in infants of smoking parents</td>
</tr>
<tr>
<td>An increase in cough and breathlessness in smokers and non-smokers with CPOD and asthma</td>
</tr>
<tr>
<td>Increased cancer risk</td>
</tr>
</tbody>
</table>

### Table 8.2 The effects of cigarette smoking on the lungs

<table>
<thead>
<tr>
<th>Large airways</th>
</tr>
</thead>
<tbody>
<tr>
<td>Increase in submucosal gland volume</td>
</tr>
<tr>
<td>Increase in number of goblet cells</td>
</tr>
<tr>
<td>Chronic inflammation</td>
</tr>
<tr>
<td>Metaplasia and dysplasia of the surface epithelium</td>
</tr>
<tr>
<td>Small airways</td>
</tr>
<tr>
<td>Increase in number and distribution of goblet cells</td>
</tr>
<tr>
<td>Airway inflammation and fibrosis</td>
</tr>
<tr>
<td>Epithelial metaplasia/dysplasia</td>
</tr>
<tr>
<td>Carcinoma</td>
</tr>
<tr>
<td>Parenchyma</td>
</tr>
<tr>
<td>Proximal acinar scarring</td>
</tr>
<tr>
<td>Increase in alveolar macrophage numbers</td>
</tr>
<tr>
<td>Emphysema (pan- and centri-acinar)</td>
</tr>
</tbody>
</table>

- Clubbing (Table 8.3)
- Peripheral cyanosis
- Nicotine staining

#### Face
- Anaemia
- Central cyanosis

#### Neck
- Examine JVP (remember a fixed distended JVP suggests SVC obstruction)
- Check for lymphadenopathy
Table 8.3 Some common causes of finger clubbing

<table>
<thead>
<tr>
<th>Category</th>
<th>Causes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Respiratory</td>
<td>Lung cancer</td>
</tr>
<tr>
<td></td>
<td>Fibrosis, e.g. idiopathic pulmonary fibrosis</td>
</tr>
<tr>
<td></td>
<td>Chronic lung sepsis</td>
</tr>
<tr>
<td></td>
<td>Bronchiectasis</td>
</tr>
<tr>
<td></td>
<td>Lung abscess</td>
</tr>
<tr>
<td></td>
<td>Empyema</td>
</tr>
<tr>
<td></td>
<td>Mesothelioma</td>
</tr>
<tr>
<td>Cardiovascular</td>
<td>Cyanotic heart disease</td>
</tr>
<tr>
<td></td>
<td>Infective endocarditis</td>
</tr>
<tr>
<td></td>
<td>Atrial myxoma</td>
</tr>
<tr>
<td>Gastrointestinal</td>
<td>Cirrhosis</td>
</tr>
<tr>
<td></td>
<td>Inflammatory bowel disease (IBD)</td>
</tr>
<tr>
<td>Others</td>
<td>Congenital</td>
</tr>
</tbody>
</table>

Thorax (Table 8.4)

- Locate tracheal position and apex beat
- Check for lymphadenopathy (axilla)

Assess chest expansion

**Anterior**
- Place hands on upper aspect of chest either side of sternum
- Ask patient to breathe in and out and watch your thumbs move laterally
- Do they move symmetrically?
- Repeat with your hands over lateral lower aspect of chest

**Posterior**
- Place hands over lateral lower aspect of chest and repeat the above

**Percussion**
- Compare left with right anteriorly and posteriorly
- Don’t forget apices and under arms

**Listen to breath sounds**
- Use diaphragm of stethoscope and again compare left with right
- Listen for added sounds (wheeze, crackles) (Table 8.5)

**Check for vocal resonance and fremitus**
- Ask patient to say 99 and listen with stethoscope (resonance) or palpate (vocal fremitus)

**Measure peak flow**
- See Chapter 3, page 26
- Normal values
  - 40-year-old – 175 cm tall $\delta = 620 \text{ L/min}$
  - 40-year-old – 155 cm tall $\varphi = 460 \text{ L/min}$
### Table 8.4 Physical signs of respiratory disease

<table>
<thead>
<tr>
<th>Pathology</th>
<th>Chest wall movement</th>
<th>Tracheal deviation</th>
<th>Percussion note</th>
<th>Breath sounds</th>
<th>Vocal resonance</th>
<th>Added sounds</th>
</tr>
</thead>
<tbody>
<tr>
<td>Consolidation (pneumonia)</td>
<td>Reduced on affected side</td>
<td>None</td>
<td>Dull</td>
<td>Bronchial</td>
<td>Increased</td>
<td>Crackles</td>
</tr>
<tr>
<td>Collapse (major bronchus)</td>
<td>Reduced on affected side</td>
<td>Towards lesion</td>
<td>Dull</td>
<td>Diminished/absent</td>
<td>Reduced/absent</td>
<td>None</td>
</tr>
<tr>
<td>Fibrosis (generalized)</td>
<td>Reduced</td>
<td>None</td>
<td>Normal</td>
<td>Vesicular</td>
<td>Increased</td>
<td>Crackles</td>
</tr>
<tr>
<td>Pleural effusion (&gt;500 mL)</td>
<td>Reduced</td>
<td>Away if massive</td>
<td>Stony dull</td>
<td>Diminished/absent</td>
<td>Reduced/absent</td>
<td>None</td>
</tr>
<tr>
<td>Pneumothorax (large)</td>
<td>Reduced</td>
<td>Away from lesion</td>
<td>Normal or hyper-resonant</td>
<td>Diminished/absent</td>
<td>Reduced/absent</td>
<td>None</td>
</tr>
<tr>
<td>Chronic obstructive pulmonary disease (COPD)</td>
<td>Reduced</td>
<td>None</td>
<td>Normal</td>
<td>Prolonged expiration</td>
<td>Normal</td>
<td>Expiratory wheeze</td>
</tr>
<tr>
<td>Asthma</td>
<td>Reduced</td>
<td>None</td>
<td>Normal</td>
<td>Prolonged expiration</td>
<td>Normal</td>
<td>Expiratory wheeze Crackles</td>
</tr>
</tbody>
</table>
Measuring respiratory function

### INVESTIGATIONS IN LUNG DISEASE

#### Imaging

- Chest X-ray (see Ch. 5)
- CT scan of the chest
  - Mass lesions
  - Interstitial lung disease
  - Bronchiectasis
  - Pulmonary embolism
- Ventilation perfusion (V/Q) scan
  - Diagnosis of pulmonary embolus
- PET (positron emission topography) scanning
  - Assessment of lymph node involvement and metastases in lung cancer

#### Endoscopy
- Bronchoscopy
  - Allows direct visualization of bronchi
  - Biopsies and cytology

#### MEASURING RESPIRATORY FUNCTION

### Peak flow rate

↓ in airflow limitation (used to monitor the condition and its treatment)

### Blood gas analysis (Table 8.6)

- Arterial blood sample (usually radial artery) measures partial pressure of $O_2$ and $CO_2$
- Essential to manage acute severe asthma and respiratory failure

---

**Table 8.5 Abnormal and additional breath sounds**

<table>
<thead>
<tr>
<th>Pathogenic process</th>
<th>Description of breath sounds</th>
<th>Auscultatory features</th>
</tr>
</thead>
<tbody>
<tr>
<td>Airways obstruction</td>
<td>Wheezes</td>
<td>High-pitched end-expiratory ‘squeaking’ noises</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Monophonic = single airway obstruction</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Polyphonic = many small airways obstruction</td>
</tr>
<tr>
<td>Consolidation</td>
<td>Bronchial breathing</td>
<td>Breath sounds in inspiration are the same as expiratory phase (similar to breath sounds heard over trachea)</td>
</tr>
<tr>
<td>Fibrosis</td>
<td>Fine crackles</td>
<td>Short-lived end-inspiratory high-pitched added sounds ‘like bubbles popping’</td>
</tr>
<tr>
<td>Fluid in alveoli (pulmonary oedema)</td>
<td>Pleural rub</td>
<td>Localized creaking/groaning added sounds</td>
</tr>
</tbody>
</table>

---

Pass Finals
Pulse oximetry
- Measures the difference in absorption of light by oxyhaemoglobin and deoxyhaemoglobin
- Used to assess and monitor arterial oxygen saturation

Spirometry
- Involves a maximum inspiration then forced expiration into a spirometer. Measures FEV1 and FVC
- Forced expiratory volume in 1 second (FEV₁) = volume of air expired in first second
- Forced vital capacity (FVC) = maximum volume of air expired
- The FEV₁:FVC ratio (normal >75) ↓ in airflow limitation, e.g. asthma
- Both FEV₁ and FVC ↓ in restrictive diseases, e.g. fibrosis

Transfer factor
- Measures transfer of gas across the alveolar-capillary membrane
- Decreased in alveolar disease/loss
  - Idiopathic pulmonary fibrosis
  - Sarcoidosis
  - Asbestosis
  - Emphysema
- Increased in pulmonary haemorrhage

**SAMPLING PLEURAL TISSUE**

**Pleural biopsy**
- Pleural lesions
  - Malignancy
  - Tuberculosis

**Pleural aspirate**
- Removing pleural effusion fluid
- Microscopy and culture in infection
- Protein content (transudate vs exudates)
- Cytology (malignancy)
- LDH

<table>
<thead>
<tr>
<th>Table 8.6 Abnormalities of blood gases in respiratory failure</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
</tr>
<tr>
<td><strong>Type I</strong></td>
</tr>
<tr>
<td>e.g. Severe asthma, pneumonia, acute respiratory distress syndrome (ARDS)</td>
</tr>
<tr>
<td><strong>Type II</strong></td>
</tr>
<tr>
<td>e.g. COPD, CNS depression (opiates), respiratory muscle weakness</td>
</tr>
</tbody>
</table>
**PULMONARY INFECTION**

**Pneumonia**
- Lung infections are classified by site (e.g. lobar pneumonia or bronchopneumonia) or by aetiology

**Aetiology (Table 8.7)**
- Bacterial
- Viral
- Opportunistic organisms
- Chemical (e.g. aspiration of vomit)
- Radiotherapy
- Allergic mechanisms

**Clinical features (Table 8.8)**
- Cough
- ± Purulent sputum
- Fever
- Pleuritic chest pain
- Breathlessness

<table>
<thead>
<tr>
<th>Infecting agent</th>
<th>(%)</th>
<th>Clinical circumstance</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>Streptococcus pneumoniae</em></td>
<td>&gt;50</td>
<td>Community pneumonia patients usually previously fit</td>
</tr>
<tr>
<td><em>Mycoplasma pneumoniae</em></td>
<td></td>
<td></td>
</tr>
<tr>
<td><em>Influenza A</em></td>
<td></td>
<td></td>
</tr>
<tr>
<td><em>Haemophilus influenzae</em></td>
<td>5</td>
<td>Pre-existing lung disease, e.g. COPD</td>
</tr>
<tr>
<td><em>Staphylococcus aureus</em></td>
<td>2</td>
<td>Children/i.v. drug users/flu outbreaks</td>
</tr>
<tr>
<td><em>Chlamydia pneumoniae</em></td>
<td>5</td>
<td>Community-acquired in institutions/families</td>
</tr>
<tr>
<td><em>Legionella pneumophila</em></td>
<td></td>
<td></td>
</tr>
<tr>
<td><em>Chlamydia psittaci</em></td>
<td>3</td>
<td>Contact with birds (not inevitable)</td>
</tr>
<tr>
<td><em>Pseudomonas aeruginosa</em></td>
<td>&lt;1</td>
<td>Cystic fibrosis</td>
</tr>
<tr>
<td><em>Pneumocystis carinii</em></td>
<td>&lt;1</td>
<td>AIDS/lymphomas/leukaemias/use of immunosuppressant drugs</td>
</tr>
<tr>
<td><em>Actinomyces israelii</em></td>
<td></td>
<td></td>
</tr>
<tr>
<td><em>Nocardia asteroides</em></td>
<td></td>
<td></td>
</tr>
<tr>
<td><em>Cytomegalovirus</em></td>
<td></td>
<td></td>
</tr>
<tr>
<td><em>Tuberculosis</em></td>
<td></td>
<td></td>
</tr>
<tr>
<td><em>Aspergillus fumigatus</em></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Anaerobic organisms</td>
<td>&lt;1</td>
<td>Inhalation pneumonia/alcohol excess/postoperative</td>
</tr>
<tr>
<td>None isolated</td>
<td>20</td>
<td></td>
</tr>
</tbody>
</table>
Specific features

Strep. pneumoniae
- Rust-coloured sputum
- Peri-oral HSV

Mycoplasma
- White cell count normal, cold agglutinins occur in 50%
- Extra-pulmonary complications, e.g. rash, myocarditis, pericarditis, haemolytic anaemia, myalgia, neurological abnormalities, abnormal liver function, diarrhoea

Staphylococcus aureus
- Abscesses – in lung and elsewhere

Coxiella burnetii
- Multiple lesions on chest X-ray

Investigations
- Chest X-ray
- Arterial blood gases or oxygen saturation
- Blood/sputum culture
- Microbiological: urine for pneumococcal or legionella antigen, serology in atypical cases

Management
- Antibiotics choice depends on severity and may vary according to local protocols (Table 8.8)
  - Mild: amoxicillin 500 mg three times a day (or clarithromycin if allergic)
  - Moderate: i.v. amoxicillin 500 mg three times a day and clarithromycin 500 mg twice a day
  - Severe: i.v. cefuroxime 1.5 g four times a day and clarithromycin 500 mg twice a day
  - Adjust as appropriate if particular organism suspected or known
- Oxygen
- Correct/prevent dehydration

Complications
- Respiratory failure
  - Type 1 – low \( P_{aO_2} \), low/normal \( P_{aCO_2} \)
- Lung abscess
  - Particularly aspiration pneumonia, staphylococcal or *Klebsiella* infection, bronchial obstruction (cancer or foreign body)
- Empyema
  - Pus in the pleural space

Table 8.8 CURB 65 score for community acquired pneumonia

<table>
<thead>
<tr>
<th>Each of the following scores 1:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Confusion (MTS &lt;9, new disorientation in time/person/place)</td>
</tr>
<tr>
<td>Urea &gt;7 mmol/L</td>
</tr>
<tr>
<td>Respiratory rate =30/minute</td>
</tr>
<tr>
<td>Blood pressure (SBP &lt;90 mmHg or DBP = 60 mmHg)</td>
</tr>
<tr>
<td>Age &gt;65 years</td>
</tr>
<tr>
<td>Score 0 or 1: Mortality low – could go home</td>
</tr>
<tr>
<td>Score 2: Mortality intermediate – admit to hospital</td>
</tr>
<tr>
<td>Score 3–5: Mortality high – consider HDU/ITU care</td>
</tr>
</tbody>
</table>

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- Blood pressure (SBP <90 mmHg or DBP = 60 mmHg)
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- Lung abscess
  - Particularly aspiration pneumonia, staphylococcal or *Klebsiella* infection, bronchial obstruction (cancer or foreign body)
- Empyema
  - Pus in the pleural space
Prognosis
- Overall 5% mortality for hospital inpatients
- >25% mortality for *Staph. aureus* pneumonia
- 50% mortality for severe community acquired pneumonia (Table 8.8)

Tuberculosis
- Caseating granulomatous infection due to *Mycobacterium tuberculosis* in the lung
- TB is a notifiable disease and contact tracing is important

Patients at risk
- Those from endemic areas
- Immunosuppressed patients
- HIV, steroids, malignancy
- Alcoholics/homeless people/people living in overcrowded conditions

Clinical features
- See Figure 8.1
- May be none
- Malaise and lethargy
- Anorexia/weight loss
- Fever
- Cough
- Haemoptysis
- Signs of
  - Pleural effusion
  - Pneumonia
  - Fibrosis

Investigations
- Chest X-ray
  - Affects upper zones particularly
  - ± Calcification
  - ± Cavitation
- Sputum microscopy (Ziehl–Neelsen stain) and culture
- Lung tissue microscopy and culture: bronchoscopy and washings or lung/pleural biopsies
- IGRA interferon gamma release assay: blood test which detects latent TB

Management
- 6 months of combination of antibiotics, usually
  - Rifampicin and isoniazid
  - + Pyrazinamide for first 2 months +
  - Add ethambutol if risk of drug resistance is increased
- Compliance is vital
- Multi-resistant TB occurs particularly in HIV, and may require more antibiotics (according to sensitivities) over a longer period

Side-effects of anti-TB drugs
Rifampicin
- Liver dysfunction
- Discoloration of body fluids
- Reduced effectiveness of oral contraceptives and other drugs
Fig. 8.1 Manifestations of primary and post-primary tuberculosis.

**Primary**
- Primary complex
- Small pleural effusion
- 3–8 weeks
  - Erythema nodosum
- Tuberculin test positive
- Calcification

**Post–primary immunity**
- Reactivation (or reinfection) usually years later due to:
  - Diabetes mellitus
  - Malnutrition
  - Immuno-suppression
  - Drugs, e.g. Cytotoxics
  - Steroids
  - Lymphoma
  - AIDS
- Adult post-primary pulmonary tuberculosis

**Incomplete immunity**
- Local spread
  - 6–12 months
    - Collapse and bronchiectasis
    - Pleural effusion
    - Pneumonia
    - Miliary tuberculosis
    - TB meningitis
- Blood–borne spread
  - Large number of bacilli
  - Tuberculosis affecting bones, joints, lymph nodes, kidneys and gastrointestinal tract
  - Small number of bacilli

- Tuberculosis occurring within 3 years
Isoniazid
- High doses cause polyneuropathy
- Pyridoxine is added to prevent this

Pyrazinamide
- Liver dysfunction

Ethambutol
- Retrolubular neuritis (patients need ophthalmology monitoring)

Streptomycin
- Vestibular nerve damage

Other mycobacteria
M. kansasii
- COPD and working in dusty conditions (e.g. miners)

M. avium intracellulare (MAI)
- Immunosuppressed patients, e.g. HIV

PULMONARY MALIGNANCY

Bronchial carcinoma
- Malignant tumour of bronchial tree

Epidemiology
- Most common malignancy 1.3 million cases per year worldwide
- Third most common cause of death in UK
- ♂ > ♀ (3:1)

Cell types
- Small cell (20–30%)
- Non-small cell
  - Squamous (40%)
  - Large cell (25%)
  - Adenocarcinoma (10%)
  - Bronchoalveolar cell (1–2%)

Aetiology
- Smoking (including passive)
- Asbestos

Clinical features
Symptoms See Table 8.9.

<table>
<thead>
<tr>
<th>Symptom</th>
<th>Frequency (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cough</td>
<td>41</td>
</tr>
<tr>
<td>Chest pain</td>
<td>22</td>
</tr>
<tr>
<td>Cough and pain</td>
<td>15</td>
</tr>
<tr>
<td>Haemoptysis</td>
<td>7</td>
</tr>
<tr>
<td>Chest infection</td>
<td>&lt;5</td>
</tr>
<tr>
<td>Others (malaise, breathlessness, etc.)</td>
<td>&lt;5</td>
</tr>
</tbody>
</table>
Signs
- Often none
- Clubbing
- Supraclavicular nodes (small cell)
- Signs of:
  - Pleural effusion or lung collapse
  - Chronic lung disease (e.g. asbestosis)

Spread of bronchial carcinoma
Direct
- Pleural effusion
- Erosion of ribs and involvement of chest wall structures in apical tumours (Pancoast’s tumour)
- Sympathetic ganglion (Horner syndrome – small pupil and ptosis)
- Recurrent laryngeal nerve palsy with unilateral vocal cord paralysis (hoarseness, bovine cough)
- Phrenic nerve palsy
- Oesophagus (dysphagia)
- Pericardial effusion
- SVC obstruction (headache, facial congestion, fixed distended veins)

Metastatic
- Bones (spinal cord compression can complicate)
- Liver
- Brain
- Adrenal glands (usually asymptomatic)

Non-metastatic extrapulmonary manifestations
- Weight loss
- Ectopic adrenocorticotropic hormone (ACTH), e.g. small cell
- Neurological, e.g. myasthenic (Eaton Lambert) syndrome
- Hypertrophic pulmonary osteoarthropathy (HPOA)

Investigations
- Chest X-ray
- CT scan and PET scanning for staging
- Bronchoscopy biopsy (proximal lesions) or percutaneous biopsy (peripheral lesions)

Management
- Multidisciplinary team approach

Surgery
- Only 5–10% of cases suitable
- For non-small cell

Radiotherapy
- Particularly for squamous cell
- Can be useful for symptom control
- Used for SVC obstruction

Chemotherapy
- Combination chemotherapy
  - Particularly useful for small cell
  - Also used for non-small cell

Prognosis
- 70% 5-year survival for those with local disease undergoing surgery
- Overall 20% at 1 year, 6–8% survival at 5 years
OBSTRUCTIVE LUNG DISEASE

Asthma

- Chronic inflammatory disease of the airways
- Three components
  - Reversible airflow limitation
  - Airway hyper-responsiveness to stimuli
  - Inflammation of the bronchi

Epidemiology

- Prevalence increasing, up to 15% population in UK

Aetiology and precipitating factors

- Atopy and allergy
- Increased airway responsiveness
- Cold air, exercise, pollution
- Occupational, e.g. isocyanates (paint-sprayers)
- Drugs, e.g. NSAIDs, beta-blockers

Clinical features

Episodes of:
- Cough
- Wheeze
- Breathlessness
- Chest tightness

Investigations

- Lung function tests
- Peak flow charts
- Skin testing of allergies

Management (Table 8.10)

- Self-management plan
- Avoid precipitants
- Stepwise drug treatments
- β₂-agonists (short- and long-acting)
- Antimuscarinics
- Anti-inflammatories, e.g. sodium cromoglycate
- Corticosteroids (inhaled or oral)
- Leukotriene antagonists (selected cases)

Chronic obstructive pulmonary disease (COPD)

- Progressive airflow limitation that is not fully reversible

Aetiology

- Smoking accounts for 90% of cases
  - 10–20% of heavy smokers develop COPD
- Rarely, α₁-antitrypsin deficiency

Clinical features

- Cough and sputum
- Wheeze
- Breathlessness
- Exacerbating factors
  - Upper respiratory tract infection
  - Cold/foggy weather
  - Pollution
Tachypnoea
Use of accessory muscles
Intercostal muscle recession on inspiration
Pursed lips on expiration
Reduced chest expansion
Hyperinflation
Cyanosis
Signs of respiratory failure:
- CO_2 retention (bounding pulse, peripheral vasodilatation, tremor, confusion, coma)
- Signs of cor pulmonale
  - Right ventricular failure (oedema, hepatomegaly \( \uparrow \) JVP)

**Investigations**
- Spirometry: FEV1:FVC ratio <70%
- Chest X-ray
- ECG (P pulmonale, right branch bundle block, right ventricular hypertrophy)
- \( \alpha_1 \)-antitrypsin level (in non-smokers)

**Management**
- Stop smoking
- Flu and pneumococcal vaccines
- \( \beta_2 \)-agonists
- Antimuscarinics, e.g. tiotropium

### Table 8.10 Acute severe asthma

<table>
<thead>
<tr>
<th>Clinical features</th>
<th>Life-threatening features</th>
<th>Very severe life-threatening features</th>
</tr>
</thead>
<tbody>
<tr>
<td>Inability to complete a sentence in one breath</td>
<td>Silent chest, cyanosis or feeble respiratory effort</td>
<td>A high ( P_aCO_2 ) &gt;6 kPa</td>
</tr>
<tr>
<td>Respiratory rate &gt; 25/min</td>
<td>Exhaustion, confusion or coma</td>
<td>A very low ( P_aO_2 ) &lt;8 kPa despite oxygen</td>
</tr>
<tr>
<td>Tachycardia &gt;110 beats/min</td>
<td>Bradycardia or hypotension</td>
<td>A low and falling arterial pH</td>
</tr>
<tr>
<td>Peak flow &lt;50% of predicted normal or best</td>
<td>Peak flow &lt;30% of predicted normal or best</td>
<td></td>
</tr>
</tbody>
</table>

**Management**
- Reassure the patient and monitor pulse oximetry and arterial blood gases
- Give oxygen 40–60%
- Nebulized \( \beta_2 \) agonist, e.g. salbutamol 5 mg and repeat if no improvement otherwise use 4-hourly
- Add nebulized anti-muscarinics, e.g. ipratropium bromide 0.5 mg
- Give i.v. steroids, e.g. hydrocortisone 200 mg i.v. every 4 hours
- Exclude pneumothorax on chest X-ray
- If no improvement, consider i.v. infusion of magnesium sulphate or salbutamol and ventilation
- Urgent referral to ITU
Obstructive lung disease

- Corticosteroids
- Prompt antibiotics if infection present
- Assisted ventilation with bilevel positive airway pressure ventilatory support – (BiPAP)
- Home oxygen (if meets recognized criteria for benefit)

**Surgery**
- Lung volume reduction in carefully selected patients

**Prognosis**
- 50% of patients with severe breathlessness die within 5 years
- Stopping smoking improves prognosis

**Obstructive sleep apnoea**

- Occurs in patients who are overweight
- 30% have other correctable factors, e.g. ENT problems, drugs (sedatives), alcohol, acromegaly

**Clinical features**
- Snoring/nocturnal choking
- Daytime sleepiness
- Unrefreshed or restless sleep
- Morning headaches or ‘drunkenness’
- Reduced libido
- Ankle swelling

**Investigations**
- Sleep study (measure oximetry, abdominal/thoracic movement and EEG during sleep)

**Management**
- Weight loss, ENT surgery, or correction of other factors listed above
- CPAP ventilation at night

**Bronchiectasis**

- Abnormal and permanently dilated airways

**Aetiology**

See Table 8.11.

**Clinical features**
- Cough and excessive sputum
- Recurrent chest infections
- Halitosis
- Haemoptysis
- Clubbing
- Coarse crackles in affected areas

**Investigations**
- Chest X-ray
- High-resolution CT of the lung
- Sputum examination
- Sinus X-rays
- Immunoglobulins
- Sweat electrolytes for cystic fibrosis

**Management**
- Postural drainage
- Antibiotics
**Table 8.11 Causes of bronchiectasis**

<table>
<thead>
<tr>
<th>Category</th>
<th>Causes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Congenital</td>
<td>Deficiency of bronchial wall elements</td>
</tr>
<tr>
<td></td>
<td>Pulmonary sequestration</td>
</tr>
<tr>
<td>Mechanical bronchial obstruction</td>
<td>Intrinsic</td>
</tr>
<tr>
<td></td>
<td>Extrinsic</td>
</tr>
<tr>
<td>Postinfective bronchial damage</td>
<td>Bacterial and viral pneumonia, including pertussis, measles and aspiration pneumonia</td>
</tr>
<tr>
<td>Granuloma and fibrosis</td>
<td>Tuberculosis, sarcoidosis and fibrosing alveolitis</td>
</tr>
<tr>
<td>Immunological over-response</td>
<td>Allergic bronchopulmonary aspergillosis</td>
</tr>
<tr>
<td>Immune deficiency</td>
<td>Post-lung transplant</td>
</tr>
<tr>
<td>Mucoiliary clearance defects</td>
<td>Genetic</td>
</tr>
<tr>
<td></td>
<td>Primary ciliary dyskinesia (Kartagener syndrome with dextrocardia and situs inversus)</td>
</tr>
<tr>
<td></td>
<td>Cystic fibrosis</td>
</tr>
<tr>
<td></td>
<td>Acquired</td>
</tr>
<tr>
<td></td>
<td>Young syndrome – azoospernia, sinusitis</td>
</tr>
</tbody>
</table>

- Bronchodilators if airflow limitation
- Steroids
- Heart/lung transplant

**Cystic fibrosis**

- Autosomal recessive disorder of the cystic fibrosis transmembrane conductance regulator (CFTR) which induces low salt and chloride excretion into airways leading to increased viscosity of airway secretions

**Clinical features**

**Respiratory**

- Recurrent chest infections
- Clubbing
- Sinusitis
- Haemoptysis
- Nasal polyps
- Spontaneous pneumothorax
- Respiratory failure
- Right ventricular failure

**Gastrointestinal**

- Steatorrhoea (pancreatic insufficiency)
- Meconium ileus
- Gallstones
- Cirrhosis

**Investigations**

- Sweat electrolyte test
- DNA analysis for genotype
Management
- Vaccinations (influenza, pneumococcus)
- Antibiotics
- Pancreatic/nutritional supplements
- Inhaled antibiotics, corticosteroids and recombinant human DNase
- CFTR gene therapy
- Lung transplant

Prognosis
- Median survival 40 years

OCCUPATIONAL LUNG DISEASE

Exposure to dusts, gases, vapours and fumes at work can lead to:
- Acute bronchitis and pulmonary oedema from irritants, e.g. SO₂, chlorine
- Pulmonary fibrosis due to mineral dust, e.g. coal
- Occupational asthma
- Hypersensitivity pneumonitis
- Bronchial carcinoma due to industrial agents, e.g. asbestos, radon

Coal-worker’s pneumoconiosis
- Patients may qualify for industrial injuries benefit

Aetiology
- Deposition of dust particles in small airways

Investigations
- Chest X-ray – fine micronodular shadowing
- Spirometry – mixed restrictive and obstructive pattern with reduced gas transfer

Complications
- Progressive massive fibrosis
  - Large round masses in upper lobes ± necrotic centres
  - May be associated with rheumatoid factor and antinuclear factor
  - Respiratory failure

Asbestosis
- Ubiquitous use of asbestos put many at risk
- Particular problems with roofers, shipyard workers, those making gas masks in the Second World War

Aetiology
- Deposition of inhaled blue fibres in airways
- Synergistic effect of smoking

Clinical features
- Breathlessness
- Cough
- Chest pain
Investigations
- Chest X-ray
  - Fine reticulonodular shadowing
  - Honeycomb lung
  - Pleural plaques/effusion
- Spirometry – restrictive ± ↓ gas transfer

Diseases caused by asbestos
- Pleural plaques
- Pleural effusion
- Bilateral diffuse pleural thickening*
- Mesothelioma* occurs 20–40 years after exposure to asbestos dust
- Asbestosis (restrictive fibrotic lung disease)*
- Carcinoma of the bronchus*

PULMONARY INFLAMMATION AND FIBROSIS

Sarcoidosis
- A multisystem granulomatous disorder presenting usually as
  - Bilateral hilar lymphadenopathy
  - Pulmonary infiltration
  - Skin/eye lesions

Epidemiology
- 19 in 100,000
- ♀ > ♂
- More severe in blacks than whites

Aetiology
- Unknown

Clinical features (Table 8.12)
- Commonly presents in third or fourth decade

Extrapulmonary features
- Skin
  - Erythema nodosum
  - Lupus pernio
- Eye
  - Uveitis
  - Conjunctivitis
  - Keratoconjunctivitis sicca

<table>
<thead>
<tr>
<th>Table 8.12 Presenting symptoms of sarcoid</th>
<th>(%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Respiratory symptoms/abnormal chest X-ray</td>
<td>50</td>
</tr>
<tr>
<td>Fatigue or weight loss</td>
<td>5</td>
</tr>
<tr>
<td>Peripheral lymphadenopathy</td>
<td>5</td>
</tr>
<tr>
<td>Fever</td>
<td>4</td>
</tr>
<tr>
<td>Normal chest X-ray</td>
<td>20</td>
</tr>
</tbody>
</table>

*Patients eligible for industrial injuries benefit
Pulmonary inflammation and fibrosis

- Face
  - Parotitis
  - Facial nerve palsy
- Metabolic
  - Hypercalcaemia (10%)
- CNS
  - Meningoencephalitis
  - Spinal cord disease
  - Myopathy
  - Polyneuropathy
- Gastrointestinal
  - Hepatosplenomegaly
- Cardiovascular
  - Cardiomyopathy

Investigations
- Chest X-ray
- CT chest
- Blood tests
  - FBC (normocytic anaemia)
  - ↑ ESR
  - ↑ Ca++
  - ↑ Serum angiotensin-converting enzyme (ACE)
- Transbronchial biopsy
- Spirometry
  - Restrictive defect
  - ↓ Gas transfer

Management
- Steroids

**Pulmonary involvement in systemic diseases**

**Rheumatoid arthritis (Fig. 8.2)**
- Rheumatoid factor always present
- Lung features may precede arthropathy

**Systemic lupus erythematosus**
- Pleurisy/pleural effusion

**Systemic sclerosis**
- Pulmonary fibrosis/honeycomb lung

**Granulomatosis with polyangiitis (Wegener’s granulomatosis)**
- Granulomatous vasculitis of small arteries
- Rhinorrhoea
- Nasal ulceration
- Nodular masses (± cavitation)
- Migratory pulmonary infiltrates
- Associated with antineutrophil cytoplasmic antibodies (ANCA)
- Treated with cyclophosphamide

**Churg–Strauss syndrome**
- Systemic vasculitis
- Asthma
- Rhinitis
- Eosinophilia
Goodpasture’s syndrome
- Disease associated with anti-glomerular basement membrane (GBM) antibodies which cross-react with the glomerulus and the lung
- Cough
- Haemoptysis (can be massive)
- Intrapulmonary haemorrhage
- Glomerulonephritis
- Treated with steroids

Pulmonary fibrosis and honeycomb lung
See Table 8.13.

<table>
<thead>
<tr>
<th>Localized</th>
<th>Diffuse</th>
</tr>
</thead>
<tbody>
<tr>
<td>Systemic sclerosis</td>
<td>Idiopathic pulmonary fibrosis</td>
</tr>
<tr>
<td>Sarcoidosis</td>
<td>Rheumatoid lung</td>
</tr>
<tr>
<td>Tuberculosis</td>
<td>Langerhans’ cell histiocytosis</td>
</tr>
<tr>
<td>Asbestosis</td>
<td>Tuberous sclerosis</td>
</tr>
<tr>
<td>Berylliosis</td>
<td>Neurofibromatosis</td>
</tr>
</tbody>
</table>
Cryptogenic fibrosing alveolitis (also known as usual interstitial pneumonia (UIP) and idiopathic pulmonary fibrosis

**Clinical features**
- Breathlessness
- Cyanosis
- Clubbing
- Bilateral fine inspiratory crackles
- Signs of:
  - Respiratory failure
  - Pulmonary hypertension
  - Right heart failure

**Disease associations**
- Autoimmune diseases

**Investigations**
- Chest X-ray – reticulonodular shadowing
- High-resolution CT
- Spirometry
  - Restrictive pattern with ↓ gas transfer
- Bronchoalveolar lavage – hypercellular
- Transbronchial biopsy

**Management**
- Oxygen
- Steroids
- Immunosuppressants, e.g. azathioprine
- Single lung transplant

**Complications**
- Respiratory failure

**Prognosis**
- Median survival 5 years

**Hypersensitivity pneumonitis**

**Aetiology**
- Inhalation of microbe spores e.g. farmer’s lung, bird fancier’s lung

**Clinical features**
- Fever
- Malaise
- Breathlessness
- Cough
- Tachypnoea
- Coarse inspiratory crackles
- Wheeze

**Investigations**
- Chest X-ray – fluffy nodular shadowing
- Precipitating antibodies (e.g. pigeon protein)
- Spirometry
  - Restrictive pattern with ↓ gas transfer
- Bronchoalveolar lavage – hypercellular

**Management**
- Avoid precipitant
- Steroids
PNEUMOTHORAX

- Air in the pleural space leading to lung deflation

Aetiology
- Spontaneous
- Chest trauma
- Intubation and ventilation

Clinical features
- See Table 8.4
- Pleuritic chest pain
- Breathlessness

Specific features
- Spontaneous pneumothorax: young patients: ♂ > ♀ 6:1, often tall and thin
- >40 years usually associated with COPD
- Rarely caused by asthma, carcinoma, lung abscess, severe pulmonary fibrosis
- If severe can present as tension pneumothorax (mediastinal shift and respiratory compromise)

Investigations
- Chest X-ray

Management
- Simple aspiration (second intercostal space mid-clavicular line)
- Intercostal drain if recurs after aspiration
- Surgery for recurrent pneumothorax

Complications
- Bronchopleural fistula

CARBON MONOXIDE POISONING

- Carbon monoxide combines readily with haemoglobin and prevents the formation of oxyhaemoglobin

Aetiology
- Gas appliances with poor ventilation

Clinical features
- Mental impairment
- Nausea and vomiting
- Headache
- Hallucinations
- Fits
- Drowsiness and coma
- Mild–moderate toxicity
  - Tachycardia
  - Tachypnoea
- Severe toxicity
  - Hypotension
  - Bradycardia
  - Myocardial damage
  - Respiratory distress
Investigations

- Blood carboxyhaemoglobin level

Management

- Remove the source
- High-flow oxygen
- Hyperbaric oxygen if:
  - Coma
  - Carboxyhaemoglobin level >10%

### SELF-ASSESSMENT QUESTIONS

#### Multiple choice questions (single best answer)

1. Clubbing is seen in:
   - A. Mesothelioma
   - B. Asthma
   - C. COPD
   - D. Diverticular disease
   - E. Pneumonia

2. The clinical findings of a pleural effusion are:
   - A. Hyper-resonant percussion note
   - B. Stony dull percussion note
   - C. Increased tactile vocal fremitus
   - D. Increased vocal resonance
   - E. Tracheal deviation even with small effusions

3. In asthma:
   - A. Peak flow rate is low during exacerbations
   - B. Patients always have reduced air entry on chest auscultation
   - C. FEV\textsubscript{1}:FVC ratio is normal
   - D. FVC is low
   - E. JVP is elevated

4. In pneumonia:
   - A. *Strep. pneumoniae* is an unusual cause
   - B. *Haemophilus influenzae* pneumonia usually occurs in patients with normal lungs
   - C. Pneumonia is only caused by bacteria
   - D. *Pneumocystis carinii* pneumonia occurs in patients who are immunosuppressed
   - E. Extrapulmonary abscesses do not occur in *Staph. aureus* pneumonia

5. In pneumonia:
   - A. *Coxiella Burnetti* is associated with contact with birds
   - B. Cold agglutinins are rare in *Mycoplasma* pneumonia
   - C. Patients with *Staph. aureus* pneumonia have a good prognosis
   - D. *Mycobacterium kansasii* usually presents in young adults
   - E. *Staph. aureus* is associated with recent influenza infection

6. Tuberculosis:
   - A. Treatment is with combination antibiotics
   - B. Prevalence is reducing
   - C. Mycobacteria are identified by haematoxylin and eosin stain
   - D. Pneumonia usually affects the lower zones of the lungs
   - E. Treatment with isoniazid causes eye problems
7. Lung cancer:
   A. Is the most common cause of malignancy-related death in the UK
   B. Most commonly is an adenocarcinoma
   C. Never occurs in non-smokers
   D. Patients usually present with haemoptysis
   E. Patients always have clinical signs

8. In lung cancer:
   A. A Pancoast’s tumour presents with pain in the chest
   B. Recurrent laryngeal nerve palsy is not a result of direct tumour spread
   C. Horner syndrome is associated with ptosis and a dilated pupil
   D. Spread to bone is uncommon
   E. Dermatomyositis may occur

9. In the treatment of lung cancer:
   A. Surgery is appropriate for most patients
   B. Radiotherapy is used for SVC obstruction
   C. Chemotherapy is most successful in adenocarcinoma
   D. A 20% 5-year survival is the norm for those with local disease only
   E. Radiotherapy is not used for palliation

10. In asthma:
    A. Airway hyper-responsiveness is a major feature
    B. Exacerbations are not precipitated by particular weather conditions
    C. Attacks can be precipitated by use of paracetamol
    D. Peak flow is elevated during exacerbations
    E. Intravenous magnesium sulphate is used for mild cases

11. In COPD:
    A. A common cause is α1-antitrypsin deficiency
    B. Disease occurs in smokers
    C. A small volume pulse suggests CO₂ retention
    D. Stopping smoking will not improve prognosis in severe cases
    E. Home oxygen is used in patients with PₐO₂ <12 kPa

12. Obstructive sleep apnoea:
    A. Is treated with inhaled steroids
    B. Can present with morning headaches
    C. Commonly affects people with a low body mass index
    D. ENT assessment is rarely necessary
    E. Is treated with single lung transplant

13. Pneumothorax:
    A. Can be a complication of mechanical ventilation
    B. Leads to a dull percussion note on the affected side
    C. Is usually treated with chest drain insertion
    D. Always requires chest drain insertion
    E. Usually presents with haemoptysis

14. In cryptogenic fibrosing alveolitis:
    A. Coarse crackles are heard on auscultation
    B. Spirometry shows a reduced FVC
    C. There is a good prognosis
    D. Clubbing is not a clinical feature
    E. There is an association with Crohn’s disease

15. Regarding occupational lung disease:
    A. In coal-worker’s pneumoconiosis large round opacities are usually seen on the chest X-ray
B. Patients may qualify for industrial injury benefits  
C. Mesothelioma usually occurs 5–10 years after exposure to asbestos fibres  
D. The risk of lung cancer is not increased  
E. Cigarette smoking in patients exposed to asbestosis only slightly increases the risk of bronchial adenocarcinoma

**Extended matching questions**

**Question 1 Theme: Breathlessness**

A. Adenocarcinoma of the lung  
B. Asthma  
C. Chronic obstructive pulmonary disease  
D. Extrinsic allergic alveolitis  
E. Cryptogenic fibrosing alveolitis  
F. Mesothelioma  
G. Heart failure  
H. Iron deficiency anaemia  
I. Pneumothorax

*For each of the following questions, select the best answer from the list above:*

I. A 23-year-old female has intermittent episodes of breathlessness and cough. She has a past history of eczema and her FEV₁:FVC ratio is reduced. What is the most likely diagnosis?  
II. A 50-year-old male smoker who works on a farm presents with progressive increasing breathlessness and weight loss over 6 months. He has finger clubbing. What is the most likely diagnosis?  
III. An 80-year-old female presents with episodes of breathlessness on exertion. She takes ibuprofen for joint pains and nifedipine for hypertension. She has normal pulmonary function tests and the PA chest X-ray is also normal. What is the most likely cause of her symptoms?

**Question 2 Theme: Pneumonia**

A. *Streptococcus pneumoniae*  
B. *Mycobacterium tuberculosis*  
C. *Haemophilus influenzae*  
D. *Mycoplasma pneumoniae*  
E. *Pneumocystis carinii*  
F. *Staphylococcus aureus*  
G. *Chlamydia psittaci*  
H. *Legionella pneumophila*  
I. *Coxiella burnetii*  
J. *Influenza A*

*For each of the following questions, select the best answer from the list above:*

I. A 28-year-old female who has previously been well and takes the oral contraceptive pill presents with a fever and a cough productive of rust-coloured sputum. A chest X-ray reveals a right middle lobe pneumonia. What is the most likely microbiological causal agent?  
II. A 50-year-old male who is known to have HIV with a low CD4 count presents with a history of fever and breathlessness. The chest X-ray looks normal and there are few clinical findings apart from marked hypoxia. What is the most likely microbiological causal agent?  
III. An 80-year-old female presents with fever and cough. She lives in an old people’s home where there has recently been a flu outbreak. A
chest X-ray shows right lower zone shadowing with an area suggesting a cavity. What is the most likely microbiological causal agent?

### Question 3 Theme: Abnormal chest X-rays

A. Sarcoid  
B. Goodpasture syndrome  
C. Cryptogenic fibrosing alveolitis  
D. Pneumothorax  
E. Pneumocystis pneumonia  
F. Extrinsic allergic alveolitis  
G. Cystic fibrosis  
H. Mesothelioma  
I. Asbestosis  
J. Tuberculosis

**For each of the following questions, select the best answer from the list above:**

I. A 20-year old student who has previously been well, takes a summer job on a local farm when she is travelling. Since she started working on the farm she has had a fever and malaise each afternoon but feels well again each morning. A chest X-ray shows fluffy nodular shadowing. What is the most likely diagnosis?

II. A 34-year-old female from South Africa who has been in the UK for 20 years saw her GP, with a troublesome cough. Her GP arranged a chest X-ray which has shown bilateral hilar lymphadenopathy. What is the most likely diagnosis?

III. An 82-year-old man presents with chest pain and cough. He lives in the East End of London and was exposed to asbestos during the war years. He has previously been told his chest X-ray is abnormal but not to be concerned. He completed a 4-week course of steroids for some arthralgia symptoms 1 week previously. A chest X-ray shows pleural plaques and a pleural effusion. What is the most likely diagnosis?
EXAMINING THE CARDIOVASCULAR SYSTEM

Position the patient:
- Position the patient at 30°–45° to the horizontal with the chest and upper body exposed. Remember to maintain the dignity of the patient.

General inspection
- Central cyanosis
- Cough or breathlessness
- Peripheral oedema
- Respiratory rate: 12–18 breaths per minute in adults
- Paraphernalia around the bed: ECGs/monitors/oxygen

Hands
- Peripheral cyanosis
- Nicotine stains
- Clubbing: congenital cyanotic heart disease, infective endocarditis
- Peripheral signs of infective endocarditis
  - Splinter haemorrhages and nail fold infarcts
  - Osler’s nodes: painful red raised lesions
  - Janeway lesions: small, non-tender red lesions on the palms

Face
- Central cyanosis: blue lips and tongue
- Malar flush: red flush on cheeks ± bridge of nose in mitral valve disease
- Pallor
- High arched palate – Marfan’s associated with aortic regurgitation

Chest
- Scars: sternotomy, pacemaker, mitral valvotomy
- Visible pulsations: ventricular heaves or apex beat

Radial pulse
- Heart rate – measure for at least 30 seconds

Rate
- Record the rate as beats per minute (be exact)
- Palpate both radial pulses (radio-radial delay – coarctation of the aorta or dissecting aortic aneurysm)
- Palpate radial and femoral pulse (radio-femoral delay – coarctation of the aorta)

Rhythm
- Irregular:
  - Atrial fibrillation (irregularly irregular – absolutely no pattern)
  - Multiple ventricular ectopics
  - Missed beats (heart block)
Fig. 9.1 The cardiac cycle and jugular venous pulse.

**Systole:**
- Aortic and pulmonary valves open, ventricles contract
- Mitral and tricuspid valves closed and atria fill (passive)

**Diastole:**
- Mitral and tricuspid valves open, atria contract and ventricles fill (active–atria contract)

**Opening snap:**
- Aortic valve opens (heard in aortic stenosis)
- Mitral valve opens (heard in mitral stenosis)

**Time:**
- x descent: end of atrial contraction
- y descent: tricuspid valve opens
- a wave: atrial systole
- c wave: increased ventricular pressure

**Jugular venous pressure:**
- x descent: end of atrial contraction
- v wave: Atrial filling

---

**Mitral/tricuspid regurgitation**

**Mitral/tricuspid stenosis**

---

**Mitral and tricuspid valves close**

**1st heart sound**

**Opening snap: aortic valve opens** (heard in aortic stenosis)

---

**Mitral and tricuspid valves open**

**2nd heart sound**

**Opening snap: mitral valve opens** (heard in mitral stenosis)

---

**Pulmonary valve closes**

**Aortic valve closes**
Character
(Table 9.1, Box 9.1)

Blood pressure
(Box 9.2)

Carotid pulse
• Feel each carotid artery separately
• Use fingertips along the line of the carotid

Jugular venous pulse (JVP)
See Fig. 9.1, Tables 9.2 and 9.3 and Box 9.3.

<table>
<thead>
<tr>
<th>Table 9.1 The radial pulse</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Character of radial pulse</strong></td>
</tr>
<tr>
<td>Low volume</td>
</tr>
<tr>
<td>Low volume and slow rising</td>
</tr>
<tr>
<td>Collapsing pulse</td>
</tr>
<tr>
<td>Pulsus alternans</td>
</tr>
<tr>
<td>Pulsus paradoxus</td>
</tr>
<tr>
<td>Pericardial effusion after asthma</td>
</tr>
</tbody>
</table>

**BOX 9.1. Collapsing pulse**
- Raise the arm above the level of the heart
- Palpate radial or brachial pulse
- *Normal*: The pulse is felt normally at the radial pulse, diminishing a little as the arm is raised
- *Abnormal* (Waterhammer): Strong tapping pulse hitting the fingers at the radial artery

**BOX 9.2. Blood pressure**
- Use an appropriately sized cuff
- Apply the cuff 25 mm above the antecubital fossa and palpate brachial artery. Inflate cuff until pulsation not palpable, place the diaphragm of the stethoscope over the artery, then deflate at a rate of 2–5 mmHg/second
- When a sound is heard with each pulse (Korotkoff 1) this is the systolic pressure
- The point at which the sound disappears (Korotkoff 5) represents the diastolic pressure
- Record each to the nearest 2 mmHg
### Table 9.2 Features which differentiate the jugular venous pulse from the carotid pulse

<table>
<thead>
<tr>
<th>Jugular venous pulse</th>
<th>Carotid pulse</th>
</tr>
</thead>
<tbody>
<tr>
<td>Double impulse</td>
<td>Single impulse</td>
</tr>
<tr>
<td>Falls on sitting and inspiration</td>
<td>No change with sitting and inspiration</td>
</tr>
<tr>
<td>Impalpable</td>
<td>Palpable</td>
</tr>
<tr>
<td>Fills from above if the internal jugular vein is occluded by light pressure at the base of the neck</td>
<td>Does not fill from above</td>
</tr>
<tr>
<td>Hepatojugular reflux – if pressure is put on the abdomen it increases venous return from the liver and the JVP becomes more prominent</td>
<td>No hepatojugular reflex</td>
</tr>
<tr>
<td>Obliterated by light pressure</td>
<td>Not obliterated by light pressure</td>
</tr>
</tbody>
</table>

### Table 9.3 Causes of an abnormal jugular venous pressure

- Right ventricular failure
- Fluid overload
- Tricuspid regurgitation (large V wave)
- Pericardial effusion or restrictive pericarditis
- Complete heart block (giant a waves (cannon wave) due to atrial contraction against a closed tricuspid valve)
- Superior vena caval obstruction (non-pulsatile)

### BOX 9.3. Jugular venous pulse

- With the patient at 45° turn the face to the left to relax the neck strap muscles
- Assess the internal jugular venous pulsation
- The height of the JVP is measured vertically from the sternal angle. Use a ruler or finger breadths to measure the height accurately
- The upper limit of normal is 4 cm

### Apex beat (Table 9.4)

- Position in terms of intercostal space and mid-clavicular line
  - Normal: 5th IC space, midclavicular line
- Record the most lateral and inferior position of palpable beat

### Reasons for failure to locate the apex beat

- Fat or muscular chest wall
- Left pneumothorax or pleural effusion
- Emphysema
- Pericardial effusion
- Dextrocardia
Examining the cardiovascular system

Precordium (Fig. 9.2)
- Palpate over each valvular area with the palm of the hand for thrills (palpable murmurs)
- Right ventricular hypertrophy may cause a sustained impulse (heave) at the left sternal edge
- Thrills – palpable heart murmurs (usually aortic stenosis)

Auscultation (Fig. 9.2 and Table 9.5)
- Listen with both the bell and the diaphragm to each valvular area
- Time any abnormal sounds with the carotid pulse

Heart sounds (Fig. 9.1)
- S1: Closure of mitral and tricuspid valves at the onset of systole

**Table 9.4 The apex beat**

<table>
<thead>
<tr>
<th>Quality</th>
<th>Haemodynamics</th>
<th>Causes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hyperdynamic (thrusting)</td>
<td>Volume overload</td>
<td>Aortic regurgitation Mitral regurgitation</td>
</tr>
<tr>
<td>Sustained (heaving)</td>
<td>Pressure overload</td>
<td>Aortic stenosis Hypertension</td>
</tr>
<tr>
<td>Tapping</td>
<td>Palpable first heart sound</td>
<td>Mitral stenosis</td>
</tr>
<tr>
<td>Dyskinetic segment</td>
<td></td>
<td>Left ventricular aneurysm</td>
</tr>
</tbody>
</table>

**Fig. 9.2 Valvular areas.**
Table 9.5 Cardiac auscultation

<table>
<thead>
<tr>
<th>High-pitched sounds (diaphragm)</th>
<th>Low-pitched sounds (bell)</th>
</tr>
</thead>
<tbody>
<tr>
<td>• S1 and S2</td>
<td>• S3 and S4</td>
</tr>
<tr>
<td>• Opening snap</td>
<td></td>
</tr>
<tr>
<td>• Ejection murmurs</td>
<td></td>
</tr>
<tr>
<td>• Early diastolic murmur of aortic regurgitation</td>
<td></td>
</tr>
<tr>
<td>• Mid-diastolic murmur of mitral stenosis</td>
<td></td>
</tr>
</tbody>
</table>

$S_2$ Closure of the aortic and pulmonary valves at the end of systole
- Aortic and pulmonary elements that may be separate:
  - Split $S_2$ normal in inspiration
  - Wide split $S_2$ in right bundle branch block and pulmonary stenosis
- Change in volume:
  - Loud $S_2$ in aortic stenosis
  - Obliterated $S_2$ in mitral regurgitation

$S_3$
- Occurs in early diastole and is due to rapid ventricular filling
- Normal in young people, or if the left ventricle is stiff
- Volume overload in mitral regurgitation, cardiac failure

$S_4$
- Occurs in late diastole due to ventricular filling in atrial systole
- Always abnormal due to reduced ventricular distensibility, e.g. aortic stenosis, acute myocardial infarction (MI)

Prosthetic valve sounds
- Mechanical valves make loud heart sounds often audible without a stethoscope
- Audible on closure:
  - Metallic aortic valve loudest at $S_2$
  - Metallic mitral valve loudest at $S_1$

Mitral valve
- Listen in the left axilla for radiation of mitral murmurs
- Turn the patient on to the left side and listen to the apex and axilla again in held expiration to accentuate quiet murmurs, e.g. mid-diastolic murmur of mitral stenosis
- If you suspect a mitral stenosis murmur, accentuate it with exercise (e.g. sit-ups)

Aortic valve
- Listen at the left sternal edge: sit the patient forward in held expiration to accentuate the early diastolic murmur of aortic regurgitation
- Listen for radiation of aortic murmurs to the carotids with the diaphragm followed by the bell for carotid bruits

Common murmurs
- Regurgitation murmurs occur when a closed valve leaks
- Stenosis murmurs occur when an open valve has a reduced luminal area
- Record grade of murmur (Table 9.6)
Table 9.6 Grades of cardiac murmur

<table>
<thead>
<tr>
<th>Grade</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>Not present</td>
</tr>
<tr>
<td>1</td>
<td>Barely audible. May be apparent is you are pre-warned that it is present and have ‘tuned-in’)</td>
</tr>
<tr>
<td>2</td>
<td>Quietly audible</td>
</tr>
<tr>
<td>3</td>
<td>Moderately well heard</td>
</tr>
<tr>
<td>4</td>
<td>Heard and thrill present</td>
</tr>
<tr>
<td>5</td>
<td>Loud, even if stethoscope partly off chest, with a thrill</td>
</tr>
<tr>
<td>6</td>
<td>Audible even if stethoscope is off the chest, with a thrill</td>
</tr>
</tbody>
</table>

Lung bases

- Sit the patient forward and listen at the lung bases for fine inspiratory crackles indicating pulmonary oedema

Abdomen

- Liver enlargement in right ventricular failure
- Pulsation of liver in tricuspid regurgitation
- Hepato-jugal reflux: pressure on the liver raises the height of the JVP
- Abdominal aortic aneurysm
- Aortic and renal bruits (auscultate in the midline and mid clavicular lines in the subcostal region)

Peripheral pulses

- Palpate:
  - Arm: Radial/brachial
  - Neck: Carotids (and listen for bruits)
  - Leg: Femoral/popliteal/posterior tibial (posterior to medial malleolus at the ankle) and dorsalis pedis (anterior aspect of the foot)

Peripheral oedema

- Check for dependent pitting oedema at ankles and sacrum

INVESTIGATIONS IN CARDIOLOGY

Chest X-ray (see Ch. 5)

- Heart size and shape
- Lung fields
  - Rib-notching in coarctation of aorta

Electrocardiography (Fig. 9.3 and Box 9.4)

- The electrocardiogram (ECG) is a recording of the electrical activity of the heart
- It is the vector sum of all the depolarization and repolarization potentials of all the myocardial cells
Fig. 9.3 The connections or directions that comprise the 12-lead ECG.
**BOX 9.4. Performing an ECG**

- Connect the ECG machine to a power point and switch on
- Connect the leads
- Limb leads
- Red to right arm
- Yellow to left arm
- Green to left leg
- Black (neutral) to right leg
- Chest leads
  - \( V_1 \): Fourth intercostal space just to right of sternum
  - \( V_2 \): Fourth intercostal space just to left of sternum
  - \( V_3 \): Halfway between \( V_2 \) and \( V_4 \)
  - \( V_4 \): Fifth intercostal space left of mid-clavicular line
  - \( V_5 \): On same horizontal as \( V_4 \) in anterior axillary line
  - \( V_6 \): On same horizontal as \( V_4 \) in mid-axillary line
- Check that there is paper and that the paper speed is correct (25 mm/s)
- Ask the patient to keep still
- Press record/acquire ECG
- Label the ECG with the patient’s name, and the date and time

**Limb leads**
- Six of the leads are obtained by recording from the limbs

**Chest leads**
- The other six leads record potentials between points on the chest wall and an average of the three limbs

**Aspects of the heart (Fig. 9.4)**
- \( V_1 \) and \( V_2 \) – right ventricle
- \( V_3 \) and \( V_4 \) – interventricular septum
- \( V_5 \) and \( V_6 \) – left ventricle
- Leads II, III and AVF – inferior aspect
- Leads I and AVL – lateral left ventricle

**ECG paper**
- Paper speed is 25 mm/s
- Therefore each small square = 0.04 s
- Each large square = 0.2 s

**Normal ECG waveform and intervals**
See Figures 9.5, 9.7.

**Axis (Fig. 9.6)**
- The normal axis of the heart is \(-30^\circ\) and \(+90^\circ\)
- Axis deviation can be identified by looking at the positive and negative deflections in leads I, II and III

**Exercise ECG (Box 9.5)**
- Assesses cardiac response to exercise
  - Treadmill or cycle ergometer
Fig. 9.4 Aspects of the ECG.
Fig. 9.5 Waves and intervals of the normal ECG.

**BOX 9.5. Procedure for exercise ECG**

- Continuous recording of pulse rate and 12-lead ECG and intermittent BP recordings (every 60 seconds)
- The patient walks on a treadmill or cycles an exercise bike, slowly on the flat at first then graduating to high-speed walking (or running or cycling) on a gradient until a predesignated target heart rate (according to age) is reached or until symptoms or ECG abnormalities prevent further exertion
- The ECG is analysed for ischaemic changes
Fig. 9.6 The cardiac axis. (a) The hexaxial reference system, illustrating the six leads in the frontal plane, e.g. lead I is 0°, lead II is +60°, lead III is +120°.
(b) Calculating the direction of the cardiac vector. In the first column, the QRS complex with zero net amplitude (i.e. when the positive and negative deflections are equal) is seen in lead III. The mean QRS vector is therefore perpendicular to lead III and is either −150° or +30°. Lead I is positive, so the axis must be +30°, which is normal. In left axis deviation (second column), the main deflection is positive (R wave) in lead I and negative (S wave) in lead III. In right axis deviation (third column), the main deflection is negative (S wave) in lead I and positive (R wave) in lead III. The frontal plane QRS axis is normal only if the QRS complexes in leads I and II are predominantly positive. (Reproduced from Kumar P, Clark M. Kumar and Clark’s Clinical Medicine, 8th edn. Edinburgh: Elsevier; 2012, with permission from Elsevier.)
• Detects myocardial ischaemia (ST depression and T wave changes) during exertion
• May be coupled with stress echocardiography

Indications
• Investigation of chest pain
  • Sensitivity and specificity 70%
• Risk assessment after MI

Contraindications
• Recent MI or troponin positive ACS (within 1 week)
• Dynamic ECG changes suggestive of severe ischaemia
• Aortic stenosis
• Hypertrophic obstructive cardiomyopathy

24-hour ambulatory taped ECG
• 24-hour recording of ECG via a portable recorder
• Records transient changes, e.g. paroxysmal tachycardias or rhythm pauses
• Event recording can link symptoms to changes in the ECG

Echocardiography
• Non-invasive ultrasound examination of the heart
• Records dynamic anatomy of the four chambers and the valves
  • Wall movement abnormalities (hypokinesia when ischaemic)
  • Valvular stenosis or regurgitation
  • Heart valve vegetations (endocarditis)
• Doppler echo gives information about
  • Blood flow
  • Ejection fraction
  • Pressure gradients
  • Trans-oesophageal echo – higher resolution assessment of heart valves
  • Stress echocardiography – uses inotropes to induce ischaemia
**Nuclear imaging (e.g. thallium scan, muga scan)**

- Used to measure myocardial function and perfusion defects and position
- Detects reversible ischaemia, e.g. resting or stress-induced, and irreversible ischaemia, e.g. MI
- Useful in those with impaired mobility

**Cardiac catheterization (Table 9.7)**

- Uses intraluminal catheter inserted via peripheral blood vessel to perform pressure measurements and contrast imaging from within the heart chambers, great vessels and coronary arteries

**Coronary angiography**

- X-ray contrast medium is injected directly into the main coronary arteries via an intracardiac catheter

**Indications**

- Primary percutaneous intervention for ACS, e.g. coronary artery stenting/angioplasty
- Troponin positive acute coronary syndrome (ACS)
- Angina refractory to medical therapy
- Strongly positive exercise test
- Angina after MI
- Chest pain where cause is unclear
- Cardiac MRI
- Non-invasive imaging of heart structure

**VALVULAR HEART DISEASE (TABLE 9.8)**

Lesions of the heart valves that lead to dysfunction (either regurgitation or stenosis)

**Mitral stenosis**

**Aetiology**

- Rheumatic fever
**Clinical features**

**Symptoms**  Only occur in moderate or severe stenosis.
- Progressive breathlessness
- Paroxysmal nocturnal dyspnoea
- Orthopnoea
- Haemoptysis
- Recurrent chest infections

Secondary to pulmonary venous hypertension

**Signs**
- Mitral facies (malar flush – a cyanotic purple discoloration over the upper cheeks)
- Small-volume pulse
- Atrial fibrillation
- Tapping apex beat
- Loud first heart sound unless calcific mitral stenosis
- Opening snap (OS)
- ‘Rumbling’ mid-diastolic murmur at apex with the patient on their left, with presystolic accentuation (if in sinus rhythm)
- Signs of right ventricular failure (raised JVP, peripheral oedema)

**Investigations**
- Chest X-ray
  - Small heart with large left atrium (widened carina)
  - Convex left heart border
- ECG
  - Bifid P wave (P mitrale) or atrial fibrillation
  - Right ventricular hypertrophy (right axis deviation and tall R waves in V1)
- Echocardiogram
  - Reduced lumen area (normal =5 cm², severe = 1 cm²)

**Management**

**Medical**
- Diuretics
- Digoxin for control of heart rate if in atrial fibrillation
- Anticoagulation if in atrial fibrillation

**Surgical**
- Non-responsive or severe disease
- Balloon valvotomy via femoral vein
- Closed valvotomy via the apex of the left ventricle
- Open surgical valvotomy

---

**Table 9.8** Typical ECG changes in acute MI

<table>
<thead>
<tr>
<th>STEMI</th>
<th>NSTEMI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Q waves</td>
<td>No Q waves</td>
</tr>
<tr>
<td>&gt;1 mm broad and 2 mm deep</td>
<td>Deep ST depression</td>
</tr>
<tr>
<td>Negative deflection at start of QRS complex</td>
<td>T wave inversion</td>
</tr>
<tr>
<td>Normal in AVR and V₁</td>
<td></td>
</tr>
<tr>
<td>ST elevation</td>
<td></td>
</tr>
<tr>
<td>T wave inversion</td>
<td></td>
</tr>
</tbody>
</table>
Mitrail valve replacement if:
- Mitral regurgitation also present
- Badly damaged valve leaflets
- Left atrial thrombus resistant to anticoagulation

Mitrail regurgitation

Aetiology
- Mitral valve prolapse
- Rheumatic heart disease (50% of all cases)
- Pre-existing aortic valve disease
- Acute rheumatic fever
- Infective endocarditis
- Ischaemic heart disease
  - Rupture of the cordae tendineae
  - Ischaemic cardiomyopathy
- Myocarditis/cardiomyopathy
  - HOCM
  - Dilated cardiomyopathy
- Autoimmune rheumatic disease
  - SLE
- Collagen synthesis disorders
  - Marfan syndrome
  - Ehlers-Danlos syndrome

Clinical features

Symptoms
- Palpitations secondary to increased stroke volume
- Pulmonary hypertension → dyspnoea and orthopnoea
- Reduced cardiac output → Fatigue and lethargy
- Right-sided heart failure

Signs
- Cardiac failure
- Apex: laterally displaced, hyperdynamic, systolic thrill

Heart sounds
- Soft first heart sound
- Loud pansystolic murmur at apex radiating to axilla
- Third heart sound

Investigations
- Chest X-ray
  - Left atrial and ventricular enlargement
  - Valve calcification
- Echocardiography
- Cardiac catheterization

Management
- Echocardiographic monitoring
- Endocarditis prophylaxis
- Surgery (valve replacement) if cardiac enlargement detected
- Symptomatic
  - ACE inhibitors, diuretics
Aortic stenosis

Aetiology
- Congenital (e.g. bicuspid valve)
- Rheumatic fever
- Calcific
- Non-valvular left ventricular outflow obstruction:
  - Hypertrophic obstructive cardiomyopathy (HOCM)
  - Congenital fibrous band above valve

Clinical features
Symptoms
- Often no symptoms until severe disease
- Exercise-induced angina, syncope, breathlessness
- Sudden death (usually within 3 years of symptom onset if not treated)

Signs
- Small-volume slow-rising pulse
- Sustained apex beat
- Systolic thrill in aortic area

Heart sounds
- Ejection systolic murmur in aortic area radiating to carotids
- Ejection click
- Soft second heart sound ± reversed split $S_2$
- Fourth heart sound

Investigations
- ECG – left ventricular hypertrophy/strain
  - Depressed ST segments and inverted T waves
  - Usually in I, AVL, V_5 and V_6
- Echocardiograph
  - Measures pressure gradient across valve
  - Gradient >50 mmHg suggests severe disease

Management
- Surgery – aortic valve replacement
- Avoid exercise
- Avoid vasodilators
- β-blockers for angina and palpitations

Aortic regurgitation

Aetiology
Acute
- Acute rheumatic fever
- Infective endocarditis
- Aortic dissection

Chronic
- Rheumatic heart disease
- Marfan syndrome
- Syphilitic aortitis
- Autoimmune rheumatic disease
  - Reiter syndrome
  - Ankylosing spondylitis
  - Rheumatoid arthritis
- Bicuspid aortic valve
- Severe hypertension
Clinical features
Symptoms
- No symptoms until left ventricular failure has occurred
- Palpitations
- Angina and dyspnoea

Signs
- Left ventricular failure
- Hyperdynamic circulation:
  - Pulsating nail beds (Quincke’s sign)
  - Head nodding (De Musset’s sign)
  - Collapsing/waterhammer pulse
  - Vigorous neck pulsation (Corrigan’s sign)
  - ‘Pistol shot’ sound on auscultation of the femorals
- Murmur over femorals (Duroziez’s sign)

Heart sounds
- Apex (displaced laterally, diffuse, hyperdynamic)
- Soft high-pitched early diastolic murmur at left sternal edge
- Ejection systolic aortic flow murmur
- Austin Flint (mid diastolic) murmur – from mitral valve leaflets in severe AR

Management
- Surgery – valve replacement – best done prior to onset of heart failure
- Medical – treat heart failure

Tricuspid regurgitation

Aetiology
- Functional TR secondary to right ventricular dilatation (e.g. cor pulmonale)
- Infective endocarditis in intravenous drug users
- Pulmonary hypertension
- Carcinoid syndrome

Clinical features
- Exertional breathlessness
- Gastrointestinal upset secondary to congestion
- Elevated JVP with giant v wave
- Enlarged pulsatile liver
- Peripheral oedema
- Ascites
- Pleural effusions
- Right ventricular impulse at left sternal edge

Heart sounds
- Pansystolic murmur at lower left sternal edge, louder in inspiration

Management
- Medical – treat right ventricular failure
- Surgical valve resection – for infective endocarditis
- Valve surgery
- Valve repair
  - Maintains anatomy of heart muscle
  - Avoids anticoagulation
### Tricuspid stenosis

**Aetiology**
- Rheumatic heart disease
- Women > men
- Carcinoid syndrome

**Clinical features**
- Almost always associated with another valve lesion
- Only when severe:
  - Hepatomegaly → abdominal pain
  - Ascites
  - Peripheral oedema

**Heart sounds**
- Low pitched mid-diastolic murmur

**Management**
- Diuretics
- Surgical valvotomy/replacement

### Pulmonary stenosis

**Aetiology**
- Usually congenital
- Rheumatic fever
- Carcinoid syndrome

**Clinical features**
- Right heart failure → peripheral oedema

**Heart sounds**
- Harsh mid-systolic murmur

**Management**
- Diuretics
- Balloon valvotomy

### ISCHAEMIC HEART DISEASE

Myocardial demand for oxygen/nutrients greater than delivery via coronary arteries.

**Aetiology**
- Occlusive coronary artery disease
  - Atherosclerosis
  - Thrombosis
  - Spasm
  - Embolus
  - Coronary arteritis, e.g. SLE
- Reduced oxygen delivery:
  - Anaemia
  - Hypotension
- Increased oxygen requirements
  - Thyrotoxicosis
  - Aortic stenosis

**Risk factors for coronary artery disease**
- Age
- Male sex (equalizes after the menopause)
- Family history
Hyperlipidaemia
Diet and obesity (30% of deaths are related to poor diet)
Smoking (risk returns to normal 10 years after stopping)
Hypertension (12–14% of deaths are HT related)
Diabetes mellitus
Hyperlipidaemia
Newer risk factors
- Sedentary lifestyle
- Stress/depression/lack of social support
- Binge alcohol consumption
- High lipoprotein (a)
- ACE gene deletion polymorphism
- COX-2 inhibitors (e.g. rofecoxib)

Risk stratification and prevention
Cardiovascular risk prediction
- Established cardiovascular or peripheral vascular disease
- Cholesterol >8 mmol/L
- LDL cholesterol >6 mmol/L
- BP >180/110 mmHg
- Diabetes
- Close relatives with early onset atherosclerosis

Angina
Clinical features
- Chest pain – heavy, tight, gripping
- Central, radiates to arms and jaw
- Breathlessness
- Usually no clinical signs

Exertional – relieved by rest

Investigations
- Resting ECG (Table 9.9)
  - Normal
  - Evidence of previous acute myocardial infarction
  - Transient ST segment depression, T inversion
- Exercise ECG (ST depression >1 mm during exercise which reverts to normal – Fig. 9.8)
- Stress echo or nuclear imaging
- Coronary angiography and intervention

Pathology
- Myocardial ischaemia with reversible myocardial injury

Management
- Eliminate risk factors
  - Stop smoking
  - Treat hypertension
  - Optimize diabetes treatment
  - Treat hyperlipidaemia
- Aspirin to prevent progression
- Nitrates to reduce peripheral resistance
- β-blockers to reduce myocardial oxygen requirements
- Calcium channel blockers, e.g. amlodipine
- Potassium channel blockers, e.g. nicorandil
**Table 9.9** The TIMI risk score in acute coronary syndrome (NSTEMI/UA)

<table>
<thead>
<tr>
<th>Risk factor</th>
<th>Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age &gt;65</td>
<td>1</td>
</tr>
<tr>
<td>More than three coronary artery disease risk factors – hypertension, hyperlipidaemia, family history, diabetes, smoking</td>
<td>1</td>
</tr>
<tr>
<td>Known coronary artery disease (coronary angiography stenosis &gt;50%)</td>
<td>1</td>
</tr>
<tr>
<td>Aspirin use in the last 7 days</td>
<td>1</td>
</tr>
<tr>
<td>Severe angina (more than two episodes of rest pain in 24 hours)</td>
<td>1</td>
</tr>
<tr>
<td>ST deviation on ECG (horizontal ST depression or transient ST elevation &gt;1 mm)</td>
<td>1</td>
</tr>
<tr>
<td>Elevated cardiac markers (CK-MB or troponin)</td>
<td>1</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Total score</th>
<th>Rate of death/MI in 14 days (%)</th>
<th>Rate of death/MI/urgent revascularization (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0–1</td>
<td>3</td>
<td>4.75</td>
</tr>
<tr>
<td>2</td>
<td>3</td>
<td>8.3</td>
</tr>
<tr>
<td>3</td>
<td>5</td>
<td>13.2</td>
</tr>
<tr>
<td>4</td>
<td>7</td>
<td>19.9</td>
</tr>
<tr>
<td>5</td>
<td>12</td>
<td>26.2</td>
</tr>
<tr>
<td>6–7</td>
<td>19</td>
<td>40.9</td>
</tr>
</tbody>
</table>

(Reproduced from Kumar P, Clark M. Kumar and Clark’s Clinical Medicine, 8th edn. Edinburgh: Elsevier; 2012, with permission from Elsevier.)

**Fig. 9.8** Twelve-lead ECG in angina showing ST depression and T wave inversion.
Acute coronary syndrome (Box 9.6)

- NSTEMI – non-ST elevation myocardial infarction
- STEMI – ST elevation myocardial infarction
- Unstable angina

Aetiology
- Coronary atheroma with overlying thrombus

Clinical features
- Chest pain
  - Severe
  - Sudden onset at rest
  - Persists several hours
- ‘Silent’ in 20%
- Sweating
- Breathlessness
- Nausea and vomiting
- Patient is pale, sweaty and grey
- Tachycardia

BOX 9.6. ACS – NSTEMI and unstable angina

Clinical features
- Pain at rest
- ‘Crescendo’ angina

Management
- Admission for bed rest with cardiac monitoring
- High-flow oxygen
- Aspirin 300 mg chewed stat then 75–150 mg daily

Pain relief
- Diamorphine 2.5–5 mg i.v. (plus antiemetic)

Anticoagulation
- Fondaparinux (Factor Xa inhibitor) or low molecular weight heparin subcutaneously to full anticoagulant dose, e.g. enoxaparin 1 mg/kg per day
- Continue aspirin 75 mg once a day and consider adding clopidogrel

Standard medical anti-anginal therapy
- β-blockers unless contraindicated
- Atenolol 50 mg orally
- Nitrates
- GTN i.v. infusion titrated to pain
- Isosorbide mononitrate 60 mg orally daily
- Consider – glycoprotein IIb/IIIa receptor inhibitors
- Prompt angiography and revascularization

Revascularization
- Percutaneous transluminal coronary angioplasty (PTCA)
- Intracoronary stents
- Coronary artery bypass grafting (CABG)
- Heart failure
- Hypotension

**Investigations**

**ECG** See Figures 9.9–9.11 and Table 9.8.

**Cardiac enzymes**
- Troponin I or T peaks at 24–48 hours
- Creatine kinase (CK) peaks 24 hours after ACS
- Aspartate aminotransferase (AST) and lactate dehydrogenase (LDH) rise 2–5 days after MI

![ECG Image](image)

**Fig. 9.9** Myocardial infarction. (a) Twelve-lead ECG showing full-thickness anterior MI with S–T elevation (STEMI). (b) Progressive ECG changes with time during an acute STEMI. ST elevation (I); Q waves (II); T inversion (III).

![ECG Image](image)

**Fig. 9.10** Twelve-lead ECG showing subendocardial infarct. Widespread T wave inversion, no Q waves (NSTEMI).
Fig. 9.11 Twelve-lead ECG showing inferior MI (S–T elevation) (STEMI).

BOX 9.7. Acute management of suspected MI

Clinical features
- Chest pain
- Sweating
- Breathlessness
- Vomiting
- Pale, sweaty, grey

ECG
See Figure 9.10.

Immediate treatment
- Fast track through A&E
- Continuous cardiac monitoring
- Oxygen 60% (if hypoxic)
- Diamorphine 2.5–5 mg i.v.
- Metoclopramide 10 mg i.v.
- Aspirin 300 mg chewed
- Emergency primary percutaneous transluminal coronary angioplasty

PTCA not available and no contraindications to thrombolysis
- Aim for rapid ‘door to needle time’
- Recombinant tissue plasminogen activator (rtPA) accelerated protocol OR
- Streptokinase 1.5 million units i.v. over 1 hour

Follow up with:
- Coronary care and monitoring for 48 hours
- Clopidogrel if coronary artery stents placed
Assessment of infarct site
See Figure 9.4.

Assessment of prognosis
- TIMI score (Table 9.9)

Acute management
See Box 9.7.

Aftercare

Ongoing pain after thrombolysis
- i.v. β-blocker or nitrate
- Emergency angiography and revascularization

Pain-free with signs of heart failure
- Nitrate ± diuretic
- ACE inhibitor long term

Pain-free with no complications
- β-blocker long-term
- Return to work in 2–3 months

All patients
- Aspirin 75–150 mg/day
- β-blocker if no contraindications (maintain heart rate <60 b.p.m.)
- Statin
- ACE inhibitor (improves myocardial remodelling)
- Risk factor stratification
- Exercise ECG ± angiography
- Structured rehabilitation
- No driving for 1 month

Complications

Early
- Arrhythmias (ventricular tachycardia/AF/heart block)
- Sudden death
- Pericarditis
- Heart failure
- Cardiogenic shock
- Ruptured papillary muscle or chordae tendineae → mitral regurgitation
- Ventricular septal defect (VSD)
- Cardiac dilatation/rupture

Late
- Deep venous thrombosis (DVT), pulmonary embolism (PE)
- Mural thrombus
- Cardiac aneurysm
- Dressler syndrome (fever, chest pain, pericarditis secondary to autoimmune carditis)

Sudden cardiac death and acute life support

Prognosis
- 50% die acutely
- 6–7% die in hospital
- 20% die within 2 years
- 30-day mortality depending on other risk factors 1–35%
Fig. 9.12 Basic life support.

Responsive?
- Check responsiveness
  - Shake and shout

Breathing?
- Open airway
  - Head tilt/chin lift/jaw thrust
  - If breathing: recovery position
- Check breathing
  - Look— for chest movement
  - Listen— for breath sounds
  - Feel— for expired air
  - Give 2 effective breaths
- Assess 10 seconds only
  - Signs of a circulation
  - Check circulation every minute
  - Circulation present continue rescue breathing

Signs of circulation?
- Only check carotid pulse if trained to do so. Take no more than 10 s
- Alternative signs: coughing any movement
- Start CPR?
  - Call for help
  - Mouth-to-mask ventilation
  - Ventilation: compression ratio 2:15

- No circulation
  - Compress chest
    - 100 per minute
    - 30:2 ratio

Send or go for help as soon as possible according to guidelines
Cardiac arrest

Basic Life Support if appropriate (see Fig. 9.12)

Precordial thump if appropriate

Attach defibrillator/monitor

Assess rhythm

VF/VT

Defibrillate x 3 as necessary

CPR 1 min

Non-VF/VT (Asystole, PEA)

CPR up to 3 min, (1 min if immediately after defibrillation)

During CPR correct reversible causes*

if not already:
• Check electrodes/paddle position and contact
• Attempt/verify: airway and O₂ i.v. access:
  • Give epinephrine (adrenaline) every 3 min
  • Correct reversible causes
  • Consider: amiodarone antiarrhythmics, atropine/pacing, buffers

*Potentially reversible causes:
• Hypoxia
• Hypovolaemia
• Hyper/hypokalaemia and metabolic disorders
• Hypothermia
• Tension pneumothorax
• Tamponade
• Toxic/therapeutic disturbances
• Thromboembolic/mechanical obstruction

Fig. 9.13 Universal advanced life support algorithm. CPR, cardiopulmonary resuscitation; PEA, pulseless electrical activity; VF/VT, ventricular fibrillation/ventricular tachycardia. (Copyright European Resuscitation Council www.erc.edu – 2012/042, with permission.)
HEART FAILURE

- Occurs when the heart is unable to maintain sufficient cardiac output to provide a physiologically normal circulation.

Pathophysiology
See Figure 9.14.

Aetiology
See Table 9.10.

Left heart failure

Aetiology
- Ischaemic heart disease (40%)
- Cardiomyopathy (35%)
- Hypertension (20%)
- Aortic/mitral valve disease
- Arrhythmias
- Congenital heart disease
- Pericardial disease

Clinical features
- Fatigue
- Exertional breathlessness
- Orthopnoea
- Paroxysmal nocturnal dyspnoea (PND)
- Pulmonary oedema → pink frothy sputum
- Distress
- Tachycardia
- Enlarged heart
- Gallop rhythm (triple fast rhythm due to third or fourth heart sound)
- Fine crackles at lung bases

Right heart failure

Aetiology
- Chronic lung disease = cor pulmonale
- Pulmonary emboli
- Pulmonary hypertension
- Left to right shunts
- Tricuspid regurgitation

Table 9.10 Causes of cardiac failure

<table>
<thead>
<tr>
<th>Cause</th>
<th>Pathological Change</th>
</tr>
</thead>
<tbody>
<tr>
<td>Myocardial dysfunction</td>
<td>High cardiac output</td>
</tr>
<tr>
<td>Ischaemic heart disease</td>
<td>Thyrotoxicosis</td>
</tr>
<tr>
<td>Cardiomyopathy</td>
<td>Anaemia</td>
</tr>
<tr>
<td>Hypertension</td>
<td>Paget’s disease</td>
</tr>
<tr>
<td>Volume overload</td>
<td>Left to right shunts</td>
</tr>
<tr>
<td>Valve disease</td>
<td>Compromised ventricular filling</td>
</tr>
<tr>
<td>Fluid overload</td>
<td>Constrictive pericarditis</td>
</tr>
<tr>
<td>Obstruction to flow</td>
<td>Pericardial tamponade</td>
</tr>
<tr>
<td>Aortic stenosis</td>
<td>Altered rhythm</td>
</tr>
<tr>
<td>Chronic lung disease</td>
<td>Atrial fibrillation</td>
</tr>
</tbody>
</table>
Clinical features
- Tiredness
- Anorexia, nausea
- Gastrointestinal upset
- Raised JVP
- Dependent pitting oedema
- Pleural effusions
- Hepatic enlargement
- Ascites
- Functional tricuspid regurgitation

Fig. 9.14 Pathophysiology of heart failure.
Investigation and treatment of cardiac failure

**Clinical features**
- Extreme breathlessness (often in middle of night)
- Wheeze
- Anxiety
- Cold sweat
- Cough with frothy pink sputum
- Grey and/or cyanosed
- Tachypnoea
- Peripherally shut down and cold
- Raised JVP
- Gallop rhythm
- Crackles and wheeze throughout chest
- Hypotension

**Immediate investigations**
- Chest X-ray – exclude pneumothorax
- Arterial blood gases – low $PO_2$, ± high $PCO_2$
- ECG – arrhythmia

**Immediate management**
- Sit up
- High-flow oxygen
- i.v. furosemide (frusemide) 40–80 mg
- i.v. diamorphine 2.5–5 mg (not if BP <80 systolic)
- i.v. metoclopramide 10 mg
- i.v. GTN (if not hypotensive)
- Nebulized salbutamol 2.5 mg if bronchospasm

**Investigations**
- Chest X-ray
- ECG
- Serum BNP (if normal excludes heart failure)
- Echocardiogram
  - Left ventricular ejection fraction <45%
- Cardiac catheter and coronary angiography
  For management of acute pulmonary oedema, see Box 9.8.

**Management**
- Identify and treat lifestyle causes or aggravating factors
- Drugs
  - Diuretics (spironolactone, furosemide)
  - ACE inhibitors (reduce mortality)
  - β-blockers (reduce mortality)
  - Digoxin
  - Nitrates
  - Anticoagulation
- Surgery
  - CABG
  - Valve replacement
  - Pacemaker
  - Heart transplant
HYPERTENSION

Primary ‘essential’ hypertension

Aetiology
- Genetic
- Fetal (low birth weight)
- Obesity ± sleep apnoea
- Alcohol
- Sodium intake
- Stress

Secondary hypertension

Aetiology
Renal
- Diabetic nephropathy
- Renovascular disease
- Adult polycystic disease
- Chronic glomerulonephritis
Endocrine
- Conn syndrome
- Adrenal hyperplasia
- Phaeochromocytoma
- Cushing syndrome
- Acromegaly
Cardiovascular drugs
- Coarctation of the aorta
- Oral contraceptive pill
- Steroids
- NSAIDs/COX-II inhibitors
Pregnancy
- Second half of pregnancy
- Pre-eclampsia
- Hypertension and proteinuria

Clinical features
- Usually no symptoms
- Features of underlying cause
- Headaches
- Nose bleeds
- Nocturia
- Complications (see below)
- Elevated blood pressure
- Renal artery bruit
- Radiofemoral delay (coarctation of the aorta)
- Left ventricular hypertrophy

Retinal changes
- Grade 1 – tortuosity of retinal arteries and ‘silver wiring’
- Grade 2 – grade 1 plus arteriovenous nipping
- Grade 3 – grade 2 plus flame haemorrhages and soft ‘cotton wool’ exudates
- Grade 4 – grade 3 plus papilloedema
Investigations
- Chest X-ray
- ECG (left ventricular hypertrophy and strain)
- Echocardiogram (left ventricular hypertrophy)
- Urinalysis for casts, protein and red cells
- Fasting blood glucose and lipids
- Serum urea, creatinine and electrolytes

Complications
- Cerebrovascular disease
- Coronary artery disease
- Retinopathy
- Renal disease

Management
General measures
- Weight loss
- Alcohol reduction

Younger (<55 years) and non-black

Older (≥55 years) or black

Step 1
A (or B*)

Step 2
A (or B*) + C or D

Step 3
A (or B*) + C + D

Step 4
Resistant hypertension
Add either α blocker or spironolactone or other diuretic

A: ACE inhibitor or angiotensin receptor blocker
B: β blocker
C: Calcium channel blocker
D: Diuretic (thiazide and thiazide-like)

* Combination therapy involving B and D may induce more new onset diabetes compared with other combination therapies

**Fig. 9.15** The British Hypertension Society Guidelines for combining blood pressure lowering drugs. (Adapted from Williams B, Poulter NR, Brown MJ et al. British Hypertension Society guidelines for hypertension management 2004 (BHS-IV): summary. BMJ 2004; 328:634–640.)
- Salt restriction
- Exercise
- Low fat diet
- Reassess after 6 months

**Drug therapy** See Figure 9.15 and Table 9.11.

### Malignant hypertension

#### Clinical features
- Diastolic BP >140 mmHg
- Progressive renal failure, proteinuria and haematuria
- Cerebral oedema or haemorrhage
- Grade 4 retinopathy
- Hypertensive encephalopathy

#### Management
- Aim to reduce diastolic BP to 100–110 mmHg over 24–48 hours
- Oral treatment is usual
- In urgent situations, e.g. aortic dissection
- i.v. sodium nitroprusside or β-blockers

### Table 9.11 Drug treatment of hypertension

<table>
<thead>
<tr>
<th>Class</th>
<th>Example</th>
<th>Side-effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>Thiazide diuretics</td>
<td>Bendroflumethiazide (bendrofluazide)</td>
<td>Hypokalaemia</td>
</tr>
<tr>
<td>Cardioselective β-blockers</td>
<td>Atenolol Bisoprolol</td>
<td>Bronchospasm Symptoms of hypoglycaemia</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Nightmares Cold peripheries Erectile dysfunction</td>
</tr>
<tr>
<td>ACE inhibitors</td>
<td>Enalapril Ramipril Lisinopril</td>
<td>Dry cough First-dose hypotension Renal function deterioration Hyperkalaemia</td>
</tr>
<tr>
<td>ACE II receptor antagonists</td>
<td>Losartan</td>
<td></td>
</tr>
<tr>
<td>Calcium channel blockers</td>
<td>Amlodipine</td>
<td>Erectile dysfunction</td>
</tr>
<tr>
<td>α-blockers</td>
<td></td>
<td>Hypotension</td>
</tr>
<tr>
<td></td>
<td>Doxazosin</td>
<td>Hypotension</td>
</tr>
<tr>
<td>Aldosterone antagonists</td>
<td>Spironolactone</td>
<td>Hyperkalaemia</td>
</tr>
</tbody>
</table>
CONGENITAL HEART DISEASE (Table 9.12)

- Affects 1% of live births $♂ > ♀$

Disease associations

- Maternal rubella infection
  - Patent ductus arteriosus
  - Pulmonary valve/artery stenosis
- Maternal drug/alcohol abuse
  - Septal defects
- Maternal radiation exposure
- Genetically inherited
  - Atrial septal defect
  - Congenital heart block
- Chromosomal abnormalities
  - Down syndrome $\rightarrow$ septal defects
  - Turner syndrome $\rightarrow$ coarctation of the aorta

Acyanotic – Left to right shunt

Ventricular septal defect (VSD)

- 1:500 live births

Clinical features

- Often no symptoms
- Fatigue
- Dyspnoea
- Loud pansystolic murmur at lower left sternal edge
- Thrill at lower left sternal edge
- Pulmonary hypertension

Table 9.12 Classification of congenital heart disease

<table>
<thead>
<tr>
<th>Acyanotic</th>
<th>Cyanotic</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal or increased blood flow through lungs</td>
<td>Reduced blood flow through lungs</td>
</tr>
</tbody>
</table>

With shunts

- Atrial septal defect
- Ventricular septal defect
- Patent ductus arteriosus
- Partial anomalous venous drainage
- Fallot’s tetralogy
  - Great vessel transposition
  - Epstein’s anomaly

Without shunts

- Coarctation of the aorta
- Congenital aortic stenosis
- Severe pulmonary stenosis
  - Tricuspid atresia
  - Pulmonary atresia
  - Hypoplastic left heart
Management
- Antibiotic prophylaxis for procedures
- Surgical closure

Complications
- Pulmonary hypertension
- Right ventricular hypertrophy
- Increased right sided pressures
- \( \rightarrow \) right to left shunt: Eisenmenger’s

Atrial septal defect (ASD)
Clinical features
- Usually none until adulthood
- Breathlessness
- Fatigue
- Right ventricular heave
- Loud pulmonary second sound
- Fixed splitting of second heart sound \( (A_2-P_2) \)
- Mid-diastolic murmur at left sternal edge

Management
- Angiographic transcatheter closure
- Surgical closure

Complications
- Pulmonary hypertension

Persistent ductus arteriosus
- Failure of closure of the ductus arteriosus
- \( \rightarrow \) Shunt from aorta to pulmonary artery

Aetiology
- Idiopathic
- Prematurity
- Maternal rubella

Clinical features
- Left heart failure
- Congestive heart failure
- Infective endocarditis
- Continuous ‘machinery’ murmur
- May develop pulmonary hypertension (Eisenmenger’s)

Management
- Surgical closure before pulmonary hypertension develops
- Angiographic ligation
- Aspirin
- Indomethacin in premature infants

Cyanotic – right to left shunt

Fallot’s tetralogy
- VSD
- Overriding aorta
- Right ventricular outflow obstruction
- Right ventricular hypertrophy

Clinical features
- Breathlessness
- Fatigue
- Hypoxia on exertion – cyanosis ± syncope
- Squatting – to improve venous return and reduce shunt
Cardiology

- Right parasternal heave
- Systolic ejection murmur
- Central cyanosis
- Finger clubbing
- Polycythaemia

Management
- Surgical correction
- Antibiotic prophylaxis

Eisenmenger syndrome
- Reversal of shunt in large VSD due to secondary pulmonary hypertension giving right to left shunt and cyanosis

No shunt

Coarctation of the aorta
- ♂ > ♀
- Turner syndrome
- Associated with bicuspid aortic valve and aortic stenosis

Clinical features
- Hypertension in upper limbs
- Radiofemoral delay
- Mid to late systolic murmur over the back

Investigations
- CXR
  - Dilated aorta
  - Rib notching (due to large collateral arteries eroding ribs)

Management
- Surgical excision

INFLAMMATORY AND INFECTIVE DISEASES OF THE HEART

Acute pericarditis
- Acute inflammation of the pericardium
- Associated with a pericardial effusion

Aetiology
- Infective
  - Viral: Coxsackie/mumps/HIV
  - Bacterial: *Staphylococcus/Strep. pneumonies*
  - Tuberculous
- Post-MI (acute in 20% of full-thickness anterior MI)
- Dressler syndrome (type 3 hypersensitivity 3 weeks after MI)
- Uraemic
- Malignant: metastatic > primary

Clinical features
- Chest pain
  - Substernal
  - Sharp
  - Worse on breathing
  - Relieved by sitting forward
  - Worse on lying flat
Inflammatory and infective diseases of the heart

- Fever
- Malaise
- Pericardial friction rub (sounds like ‘walking on snow’)

**Investigations**
- ECG (widespread ‘saddle-shaped’ ST elevation)

**Management**
- Anti-inflammatory drugs
- Rest
- Treat underlying cause
- 20% recur

**Pericardial effusion**

**Aetiology**

**Acute**
- MI with ventricular rupture
- Aortic dissection
- Post-cardiac surgery
- Post-transseptal puncture at cardiac catheterization

**Subacute and chronic**
- Metastatic malignant disease
- Tuberculous pericarditis
- Dressler syndrome

**Clinical features**
- Raised JVP
- Kussmaul’s sign (JVP elevates during inspiration)
- Pulsus paradoxus
- Failure to locate apex beat
- Quiet heart sounds

**Investigations**
- ECG (low-voltage complexes)
- Chest X-ray (large globular heart)
- Echocardiogram
- Pericardiocentesis for diagnosis and to treat incipient tamponade

**Constrictive pericarditis**
- Pericardial calcification or fibrosis

**Aetiology**
- Tuberculosis
- Haemopericardium
- Bacterial infection
- Rheumatic fever

**Clinical signs**
- Increased JVP during inspiration (Kussmaul’s)
- Fall in JVP during diastole (Freidreich’s)
- Fall is systolic BP during inspiration (pulsus paradoxus)
- Venous congestion → oedema/ascites/hepatomegaly

**Investigation**
- CXR: cardiac calcification in 50%/small heart
- ECG: low voltage QRS
- Echo
Myocarditis

Aetiology

- Viral
  - Coxsackie
  - Influenza
  - Rubella
  - Polio
- Protozoal
  - Trypanosoma cruzi (Chagas disease)
  - Toxoplasma gondii
- Toxins
  - Lead poisoning
  - Radiation injury
  - Drugs: methyl dopa, penicillins
- Bacterial infection
  - Diphtheria
  - Q fever
  - Coxiella burnetti
- Autoimmune disease

Clinical features

- Fatigue
- Palpitations
- Chest pain
- Acute cardiac failure
- Fever

Investigations

- Chest X-ray
- ECG
  - ST and T wave abnormalities
  - Arrhythmias
- Cardiac enzymes elevated
- Viral antibody titres
- Echocardiography
- Endomyocardial biopsy

Management

- Treat heart failure
- Treat underlying cause

Cardiomyopathy

Aetiology

- Dilated
  - Alcohol
  - Post-pregnancy
  - Hypertension
  - Valvular heart disease
- Hypertrophic
  - Familial/autosomal dominant
- Restrictive
  - Amyloid
  - Sarcoidosis
  - Endomyocardial fibrosis
  - Loeffler’s endocarditis
Rheumatic fever

Aetiology
- Group A streptococcal infection

Clinical features (Table 9.13)
- General
  - Fever
  - Malaise
- Carditis
  - New or changing murmurs
  - Cardiac failure
  - Pericardial effusion
- Arthritis
  - Fleeting polyarthritis of large joints
- Sydenham’s chorea (St Vitus’ dance)
  - Choreaathetoid movements
- Skin
  - Erythema marginatum
  - Subcutaneous nodules (painless)

Investigations
- Throat swab
- Antistreptolysin-O titre
- ESR
- CRP

Management
- Penicillin to eradicate streptococci
- Bed rest
- High-dose aspirin
- Corticosteroids (prednisolone 60–120 mg/day)

Infective endocarditis (Box 9.9)
- Sometimes acute. Usually insidious (subacute)
- Most commonly affects rheumatic or congenitally abnormal valves, VSD or patent ductus
- Prosthetic valves may also be affected

Table 9.13 Duckett Jones diagnostic criteria in rheumatic fever

<table>
<thead>
<tr>
<th>Major</th>
<th>Minor</th>
</tr>
</thead>
<tbody>
<tr>
<td>Carditis</td>
<td>Fever</td>
</tr>
<tr>
<td>Polyarthritis</td>
<td>Arthralgia</td>
</tr>
<tr>
<td>Chorea</td>
<td>Previous rheumatic fever</td>
</tr>
<tr>
<td>Erythema marginatum</td>
<td>Raised erythrocyte sedimentation rate (ESR)/C-reactive protein (CRP)</td>
</tr>
<tr>
<td>Subcutaneous nodules</td>
<td>Raised white cell count</td>
</tr>
<tr>
<td></td>
<td>Prolonged PR interval</td>
</tr>
</tbody>
</table>
Aetiology
- *Streptococcus viridans* (50% of cases)
- *Enterococcus faecalis*
- *Staphylococcus aureus*
  - Often acute
  - Associated with central venous catheters, temporary pacing wires and in i.v. drug users
  - Poor prognosis
- *Staphylococcus epidermidis*
  - i.v. drug users
  - Alcoholics
- *Coxiella burnetti* (Q fever)

Clinical features (Table 9.13)
- Seen in >50% of cases.
  - General
    - Malaise
    - Clubbing
  - Cardiac
    - Murmurs
    - Cardiac failure
  - Arthralgia
  - Pyrexia
  - Skin lesions
    - Osler’s nodes
    - Splinter haemorrhages
    - Janeway lesions
    - Petechiae

**BOX 9.9. Duke’s criteria for the diagnosis of infective endocarditis**

- Diagnosis can be made in the presence of:
  - 2 major criteria
  - 1 major and 3 minor
  - 5 minor criteria

<table>
<thead>
<tr>
<th>Major</th>
<th>Minor</th>
</tr>
</thead>
<tbody>
<tr>
<td>Positive blood culture:</td>
<td>Fever ≥38°C</td>
</tr>
<tr>
<td>Expected organism</td>
<td>Predisposing condition</td>
</tr>
<tr>
<td>Persistent positivity (3 of 3 or 4</td>
<td>Consistent but not diagnostic echo</td>
</tr>
<tr>
<td>cultures, separated by 12 hours)</td>
<td>Immunological phenomena present (Roth Spots/ Osler’s nodes/</td>
</tr>
<tr>
<td></td>
<td>glomerulonephritis/ rheumatoid)</td>
</tr>
<tr>
<td>Evidence of endocardial involvement:</td>
<td>Positive blood cultures</td>
</tr>
<tr>
<td>Echo: vegetation or abscess</td>
<td>Vascular phenomena (arterial emboli/mycotic aneurysm/</td>
</tr>
<tr>
<td>New valvular regurgitation</td>
<td>conjunctival haemorrhage/ Janeway lesions)</td>
</tr>
</tbody>
</table>
Eyes
• Roth spots
• Conjunctival haemorrhage
Splenomegaly
Neurological (cerebral emboli)
• Mycotic aneurysm
• Renal (haematuria”)

Investigations
Blood
• Anaemia
• Raised serum CRP and ESR
• Mildly abnormal liver biochemistry
• Raised total serum immunoglobulins
• Raised total complement and C3
Urinalysis
• Proteinuria with casts
• Microscopic haematuria
Blood cultures
• At least six sets from different veins at different times (positive in 75% of cases)
Echocardiography
• Trans-oesophageal echocardiography (TOE) is best for visualizing vegetations and is mandatory in non-native valves

Management
Antibiotics
• Bactericidal antibiotics chosen on the basis of blood culture results and sensitivities
• i.v. antibiotics for 2–6 weeks with back-titrations to confirm bactericidal serum levels

Indications for surgery
• Significant extensive valve damage
• Early infection of prosthetic valve
• Persistent infection with negative blood cultures
• Embolization
• Progressive cardiac failure
• Tricuspid valve infection in i.v. drug users

Prophylaxis

CARDIAC ARRHYTHMIAS

• Bradycardia – heart rate <60 b.p.m.
• Tachycardia – heart rate >100 b.p.m.

Sinus arrhythmia
• Due to normal changes in autonomic tone
• Heart rate increases in inspiration and falls in expiration

Sinus bradycardia
Aetiology
• Hypothermia
• Hypothyroidism
• Raised intracranial pressure
Fig. 9.16 Atrioventricular block. (a) ECG rhythm strip showing first-degree heart block with prolongation of the PR interval. (b) Complete heart block with dissociation of the P waves and QRS complexes.

Fig. 9.17 ECG rhythm strip showing second-degree ‘Wenckebach’ heart block, with prolongation of the PR interval and missed QRS.

Fig. 9.18 ECG rhythm strip showing second-degree ‘2:1’ heart block.
Cardiac arrhythmias

- Drugs (β-blockers, digoxin)
- Ischaemia

Sinus tachycardia

Aetiology
- Fever
- Exertion
- Emotion
- Pregnancy
- Anaemia
- Cardiac failure
- Thyrotoxicosis
- Drugs (sympathomimetics)

Sinus node disease (sick sinus syndrome)

Aetiology
- Ischaemia
- Infarction
- Degenerative disease

Clinical features
- Combinations of fast and slow supraventricular rhythms

Investigations
- ECG – long interval between P waves >2 seconds

Management
- Permanent pacemaker
- Antiarrhythmic drugs to combat tachycardia
- Anticoagulation

Atrioventricular block

First-degree
- Prolonged PR interval (Fig. 9.16)

Second-degree
- Some P waves conduct to ventricles
- Mobitz type 1 (‘Wenckebach’ – Fig. 9.17)
  - Progressive elongation of PR interval until failure to conduct
- Mobitz type 2
  - Dropped QRS conduction without progressive PR elongation
  - 2:1 or 3:1 block
  - Every second or third P wave conducts to ventricles (Fig. 9.18)

Third-degree (complete heart block)
- No P waves conduct
- Ventricular rhythm is maintained by spontaneous escape rhythm from ventricular myocardium with broad complexes

Aetiology
- Ischaemic heart disease
- Cardiac surgery
- Dilated cardiomyopathy
- Drugs

Clinical features
- May be no symptoms (first- and second-degree)
- Dizziness
• Syncope
• Blackouts (Stokes–Adams attacks) (third-degree)
• Cannon ‘a’ waves in JVP in third-degree

**Management**
• Permanent pacemaker for symptomatic bradycardias

**Bundle branch block**

**Aetiology**

**Right bundle branch block (RBBB – Fig. 9.19)**
• Congenital heart disease
• Cor pulmonale
• Pulmonary embolus
• Myocardial infarction
• Cardiomyopathy
• Hyperkalaemia
• Can be normal

**Left bundle branch block (LBBB – Fig. 9.20)**
• Aortic stenosis
• Hypertension
• Acute MI
• Severe coronary artery disease
• Cardiomyopathy

*Fig. 9.19* Twelve-lead ECG showing right bundle branch block and right axis deviation.

*Fig. 9.20* Twelve-lead ECG showing left bundle branch block.
Management
- Permanent pacemaker for symptomatic cases

Atrial tachyarrhythmias

Aetiology
- Ischaemic heart disease
- Rheumatic heart disease
- Thyrotoxicosis
- Cardiomyopathy
- Wolff–Parkinson–White syndrome
- Pneumonia
- Atrial septal defect
- Pericarditis
- Pulmonary embolus

Atrial flutter
- Atrial rate about 300/min with 2:1 or 3:1 AV conduction

Investigations
- ECG (Fig. 9.21) – sawtooth atrial flutter waves between QRS complexes

Management
- Electrical cardioversion
- Class III antiarrhythmic drugs
- Radiofrequency catheter ablation

Atrial fibrillation
- Uncoordinated rapid continuous activation of atria from multiple foci

Aetiology
See above.

Clinical features
- No symptoms
- Reduced exercise tolerance
- Palpitations
- Heart failure
- Embolic events
- Completely irregular pulse

Investigations
- ECG (Fig. 9.22)
  - No P waves
  - Irregular rapid QRS rhythm

Management
- Treat the cause
- Control ventricular rate
  - β-blockers
  - Digoxin
  - Verapamil

Fig. 9.21 ECG rhythm strip showing atrial flutter.
Cardioversion
- Electrical DC cardioversion
- Drugs (amiodarone, flecainide)
- Prophylaxis against thrombotic events
  - Warfarin
  - AV node ablation and permanent pacemaker insertion

Supraventricular tachycardia

Aetiology
- Provoked by
  - Exertion
  - Caffeine
  - Alcohol
  - β2-agonists
- Congenital (re-entry tachycardias)
  - Abnormal conduction from ventricle to atria:
    1. Wolff–Parkinson–White syndrome
    2. Lown–Ganong–Levine syndrome

Clinical features
- Palpitations
- Chest pain
- Breathlessness
- Syncope
- Polyuria
- Rapid regular pulse 140–280/min

Investigations (Fig. 9.23)
- ECG
  - Narrow complex QRS tachycardia
  - Occasionally broad complex when associated with interventricular conductance disturbances

Management (Fig. 9.24)
- Vagotonic manoeuvres
- Carotid sinus massage
- Ocular pressure
- Valsalva manoeuvre
Cardiac arrhythmias

**Drugs**
- Adenosine in increasing i.v. doses with continuous rhythm monitoring (avoid in asthma)
- Prophylaxis
- Accessory pathway ablation

**Ventricular tachyarrhythmias**

**Sustained ventricular tachycardia**
- Rapid ventricular rhythm at 120/minute for more than 30 seconds
Clinical features
- Palpitations
- Dizziness
- Syncope
- Angina

Investigations (Fig. 9.25)
- ECG – broad complex tachycardia

Acute management
See Figure 9.26.

Fig. 9.25 Twelve-lead ECG showing ventricular tachycardia.

Fig. 9.26 Management of broad complex tachycardia.
**Multiple choice questions**

**Pass Finals**

**Fig. 9.27** Four beats of sinus rhythm followed by a ventricular ectopic beat that initiates ventricular fibrillation. The ST segment during sinus rhythm is elevated owing to acute MI in this case.

---

**Long-term management**

- Drugs – class III antiarrhythmics
- Accessory pathway ablation
- Implantable cardioverter defibrillator (ICD)

**Torsades de pointes**

**Causes**

- Congenital long QT
- Electrolyte disturbances
- Drugs

**Investigations**

- ECG VT with alternating polarity
- Prolonged QT

**Management**

- ICD

**Ventricular fibrillation**

- See Figure 9.27
- Pulseless rapid irregular ventricular activity with no mechanical effect

---

**MULTIPLE CHOICE QUESTIONS**

**Multiple choice questions (single best answer)**

1. Which one of the following is a feature of aortic stenosis:
   - A. Collapsing pulse
   - B. Pan-systolic murmur
   - C. Syncope on exertion
   - D. Austin flint murmur
   - E. Opening snap

2. Which one of the following is a feature of mitral stenosis:
   - A. Atrial fibrillation
   - B. Thrusting apex beat
   - C. Early diastolic murmur
   - D. Loud second heart sound
   - E. Sudden death

3. In mitral regurgitation:
   - A. The pulse is characteristically collapsing
   - B. There is an apical pansystolic murmur radiating to the axilla
   - C. The ECG shows left ventricular hypertrophy
4. In tricuspid regurgitation:
   A. There is a pansystolic murmur radiating to the axilla
   B. Pulmonary hypertension is a cause
   C. There may be pulsatile splenomegaly
   D. Cannon waves are seen in the jugular venous pulse
   E. Complete heart block is common

5. In acute myocardial infarction:
   A. The ECG always shows raised ST segments
   B. The pain is characteristically left-sided and worse on inspiration
   C. Diamorphine is contraindicated
   D. Creatine kinase levels are maximally elevated 2–4 hours after the onset of pain
   E. Treatment with streptokinase reduces mortality

6. The following are signs of congestive cardiac failure:
   A. Raised jugular venous pressure
   B. Splinter haemorrhages
   C. Splenomegaly
   D. Papilloedema
   E. Lymphoedema

7. In unstable angina:
   A. The most common heart rhythm is atrial fibrillation
   B. The ECG shows ST depression and T wave inversion
   C. Creatine kinase is elevated
   D. Treatment of choice is anticoagulation with warfarin
   E. 30-day mortality is 50%

8. In systemic hypertension:
   A. The commonest cause is renal artery stenosis
   B. Complications include diabetes mellitus
   C. Effective treatment reduces the incidence of stroke
   D. Presents most commonly with headache
   E. The first-line treatment is methyldopa

9. The following are usual features of tetralogy of Fallot:
   A. Episodes of cyanosis
   B. Atrial septal defect
   C. Ebstein’s anomaly
   D. Normal life expectancy
   E. Right ventricular dilatation

10. The following are features of acute rheumatic fever:
    A. Recent staphylococcal throat infection
    B. Clubbing
    C. Roth spots
    D. Sydenham’s chorea
    E. Osler’s nodes

11. In acute pericarditis:
    A. The chest pain is characteristically crushing and radiates down the right arm
    B. The ECG shows widespread concave ST elevation
    C. There is usually pulsus paradoxus
    D. Viral infections are an uncommon cause
    E. High-dose prednisolone is the treatment of choice
12. The following are features of infective endocarditis:
   A. Spider naevi
   B. Osler’s nodes
   C. Huntington’s chorea
   D. Jaundice
   E. Past history of pulmonary TB

13. In patients with atrial fibrillation:
   A. The cardiac rhythm becomes more regular with exertion
   B. Common causes include rheumatoid arthritis and obstructive jaundice
   C. A fourth heart sound is always absent
   D. Digoxin should always be given
   E. Complications include stroke and mesenteric infarction

14. In supraventricular tachycardia:
   A. The onset is characteristically sudden
   B. The QT interval is prolonged
   C. Carotid sinus massage causes the heart rate to accelerate
   D. First-line treatment is atropine
   E. There is often underlying heart disease

15. The following are features of complete heart block:
   A. Syncopal attacks
   B. Giant V waves in the jugular venous pulse
   C. A delta wave on ECG
   D. It responds to an atrial pacemaker
   E. Shortened P–R interval on the ECG

16. Which one of the following criteria strongly supports the diagnosis of infective endocarditis?
   A. Positive Coxsackie virus serology
   B. Aortic sclerosis
   C. Temperature 37.5°C
   D. Positive blood cultures 12 hours apart
   E. Positional chest pain

17. A 56-year-old man was admitted with central chest pain. Which of the following is most effective in discounting ischaemic heart disease as a cause?
   A. Normal chest X-ray
   B. Normal ECG
   C. Normal creatine kinase
   D. Normal blood pressure
   E. Normal troponin I

18. A 66-year-old woman was seen with sudden onset central chest pain and widespread ST elevation on her ECG with a pulse rate of 50 b.p.m. What is the most appropriate management?
   A. Percutaneous coronary intervention
   B. Thrombolysis with alteplase
   C. Intravenous unfractionated heparin
   D. Oral indomethacin
   E. Oral atenolol

19. A 69-year-old man presents with an acute coronary syndrome. He is prescribed Fondaparinux. Which one of the following does fondaparinux?
   A. Glycoprotein IIb/IIIa
   B. Factor Xa
20. A 61-year-old man was found to have a blood pressure of 160/90 mmHg while being assessed for a colonoscopy. What is the most appropriate management?
A. Delay the procedure until the blood pressure is controlled
B. Carry out the procedure and advise him to consult his GP
C. Give a single dose of bisoprolol to cover the procedure
D. Start amlodipine orally
E. Commence i.v. fluids during the colonoscopy

**Extended matching questions**

**Question 1 Theme: Central chest pain**
A. Reflux oesophagitis
B. Angina
C. Acute coronary syndrome
D. Dissecting thoracic aortic aneurysm
E. Mitral valve prolapse
F. Costochondritis
G. Gallstones
H. Duodenal ulcer
I. Pneumothorax
J. Mesothelioma
K. Pulmonary embolus

*For each of the following questions, select the best answer from the list above:*

I. A 20-year-old male with Marfan syndrome presents with severe chest pain at rest associated with nausea and shortness of breath. Blood pressure is decreased in the right arm compared with the left arm. What is the most likely diagnosis?
II. A 55-year-old male smoker with diabetes presents with a history of self-limiting central chest pain lasting 2 minutes, associated with nausea and shortness of breath which starts every time he plays football with his grandson. What is the most likely diagnosis?
III. A 45-year-old obese female smoker presents with episodic burning chest pain, worse at night and after spicy foods. What is the most likely diagnosis?

**Question 2 Theme: Ankle swelling**
A. Left ventricular failure
B. Cardiomyopathy
C. Deep venous thrombosis
D. Nephrotic syndrome
E. Cellulitis
F. Ruptured Baker’s cyst
G. Liver failure
H. Gout
I. Charcot’s joints

*For each of the following questions, select the best answer from the list above:*

I. A 60-year-old male alcoholic present with a 3-month history of swelling of the abdomen and ankles, and shortness of breath on exertion. On examination there are no signs of chronic liver disease. His pulse is 120/minute with atrial fibrillation and the apex beat is
displaced laterally and inferiorly; he has ascites and ankle oedema. What is the most likely diagnosis?

II. A 70-year-old female with a history of myocardial infarction 10 years ago, and who returned from Australia 1 week ago, presents with swollen ankles, worse on the right, and shortness of breath on exertion. What is the most likely diagnosis?

III. A 50-year-old diabetic female on enalapril presents with a painful swollen right ankle which started 10 days ago. Examination reveals erythema and oedema, with a small painless ulcer on the right heel. What is the most likely diagnosis?

Question 3 Theme: Palpitations
A. Supraventricular tachycardia
B. Atrial fibrillation
C. Wolff–Parkinson–White syndrome
D. Anxiety
E. Thyrotoxicosis
F. Hypertension
G. Stokes–Adams attacks
H. Digoxin toxicity
I. β2-agonists
J. Cocaine abuse

For each of the following questions, select the best answer from the list above:

I. A 69-year-old female smoker being investigated for chest pains presents with sudden onset of rapid palpitations associated with dizziness and shortness of breath. Her pulse is irregular, rate 160/minute and BP is 90/60. The ECG shows no P waves. What is the most likely diagnosis?

II. A 68-year-old female recently saw her GP for wheeze and shortness of breath, and was prescribed some treatment. She now presents with episodes of dizziness, palpitations and tremor. On examination her pulse is regular, 130/min. The ECG shows a sinus tachycardia. What is the most likely diagnosis?

III. A 22-year-old law student presents with intermittent episodes of palpitations, shortness of breath and tingling in his fingers and round his lips. Examination is normal. Thyroid function tests a year ago (for similar symptoms) were normal. What is the most likely diagnosis?
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EXAMINING THE ABDOMEN

Examination should include all of the following and be done in the following order:

**Expose the abdomen**
- Lie the patient flat for abdominal examination
- Pay attention to the dignity of the patient and cover/uncover as needed

**General examination: hands/face/neck/thorax**

Look for:
- Jaundice (Table 10.1)
- Weight loss/malnutrition
- Anaemia
- Stigmata of chronic liver disease (Table 10.2)
- Spider naevi – demonstrate filling from the central arteriole by pressing in the centre
  - >5 in men or 7 in women pathological
- Koilonychia – iron deficiency anaemia – concave nails
- Leuconychia – hypoalbuminaemia – white nails
- Lymphadenopathy – supraclavicular fossae (a node in the left fossa may indicate oesophageal or gastric cancer)

<table>
<thead>
<tr>
<th>Table 10.1 Causes of jaundice</th>
</tr>
</thead>
</table>
| **Pre-hepatic** | Haemolysis | Autoimmune haemolytic anaemia  
Malaria |
| **Hepatic** | Abnormal bilirubin metabolism | Gilbert syndrome  
Benign recurrent idiopathic cholestasis (BRIC)  
Crigler–Najjar syndrome |
| **Hepatocellular dysfunction** | Viral hepatitis  
Drugs  
Alcohol  
Autoimmune  
Pregnancy  
Infiltrations |
| **Post-hepatic** | Cholestasis | Primary biliary cirrhosis |
| **Biliary obstruction** | Sclerosing cholangitis  
Gallstones  
Pancreatic carcinoma  
Cholangiocarcinoma |
### Table 10.2 Stigmata of chronic liver disease

<table>
<thead>
<tr>
<th><strong>Skin</strong></th>
<th><strong>Abdomen</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>Jaundice</td>
<td>Ascites</td>
</tr>
<tr>
<td>Spider naevi</td>
<td>Hepatomegaly</td>
</tr>
<tr>
<td>Caput medusae</td>
<td>Splenomegaly</td>
</tr>
<tr>
<td>Distended abdominal veins</td>
<td>Eyes</td>
</tr>
<tr>
<td>Bruising</td>
<td>Anaemia</td>
</tr>
<tr>
<td>Striae</td>
<td>Jaundice</td>
</tr>
<tr>
<td><strong>Hands</strong></td>
<td><strong>Mouth</strong></td>
</tr>
<tr>
<td>Liver flap</td>
<td>Fetur hepaticus</td>
</tr>
<tr>
<td>Leuconychia</td>
<td>Bleeding gums</td>
</tr>
<tr>
<td>Dupuytren’s contractures</td>
<td>Genitals/breasts</td>
</tr>
<tr>
<td>Palmar erythema</td>
<td>Gynaecomastia</td>
</tr>
<tr>
<td>Clubbing</td>
<td>Testicular atrophy/loss of body hair</td>
</tr>
<tr>
<td>Muscle wasting</td>
<td></td>
</tr>
</tbody>
</table>

### Abdomen

Look for:
- Shape of the abdomen and signs of distension
- Obvious masses
- Visible peristalsis
- Scratch marks due to obstructive jaundice
- Stretch marks
- Hernias (periumbilical, inguinal and femoral)
- Stomas
  - Bowel: ileostomy or colostomy
  - Urinary: ileal conduit
- Operation scars

### Palpation

- Ask if the abdomen is tender and, if so, where
- Start palpating away from this point; always look at the patient’s face during palpation
- Start gently, with the flat of the fingers, eliciting tenderness and obvious masses
- Palpate more deeply in an ordered way around the abdomen looking for deep masses
- Describe the location of findings as per the regions shown in Figure 10.1

---

**Fig. 10.1** Anatomical regions of the abdomen. EP, epigastrium; SC, subcostal; LN, loin; UM, umbilical; F, flank; SP, suprapubic; IF, iliac fossa.
Liver (Tables 10.3 and 10.4)

- The normal liver is only just palpable in slim people on inspiration
- Start from the right iliac fossa
- Use the pulps of the finger or the side of the index finger (with the hand flat)
- Ask the patient to take deep breaths in and out
- On inspiration the diaphragm flattens, pushing the liver down towards your fingers. Note the position of the lowest palpable point, e.g. ‘three finger breaths below the costal margin’
- The upper limit is defined by percussing in the mid-clavicular line from the nipple and noting the boundary between resonance and dullness (normally the sixth intercostal space)
- Note any tenderness or palpable texture

Spleen (Tables 10.4 and 10.5)

- Start from the right iliac fossa
- Palpate towards the left hypochondrium
- The normal spleen is not palpable
- Ask the patient to roll onto his or her right side to bring the spleen forward, making it easier to feel
- You will not be able to feel the upper margin
- An enlarged spleen moves down and medially on inspiration and is dull to percussion

### Table 10.3 Causes of hepatomegaly

<table>
<thead>
<tr>
<th>Infective</th>
<th>Metabolic</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acute viral hepatitis</td>
<td>Haemochromatosis</td>
</tr>
<tr>
<td>Epstein–Barr virus</td>
<td>Malignant</td>
</tr>
<tr>
<td>Malaria</td>
<td>Hepatocellular cancer</td>
</tr>
<tr>
<td>Kala-azar</td>
<td>Chronic leukaemia</td>
</tr>
<tr>
<td>Inflammatory</td>
<td>Secondary malignancy</td>
</tr>
<tr>
<td>Alcoholic liver disease</td>
<td>Cardiovascular</td>
</tr>
<tr>
<td>Primary biliary cirrhosis</td>
<td>Right ventricular failure</td>
</tr>
<tr>
<td>Infiltration</td>
<td>Tricuspid regurgitation</td>
</tr>
<tr>
<td>Amyloid fat</td>
<td></td>
</tr>
</tbody>
</table>

| Infiltration                               |                     |

### Table 10.4 Causes of hepatosplenomegaly

<table>
<thead>
<tr>
<th>Hepatic</th>
<th>Infection</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chronic liver disease</td>
<td>Viral hepatitis</td>
</tr>
<tr>
<td>with portal hypertension</td>
<td>Epstein–Barr infection</td>
</tr>
<tr>
<td>Malignancy</td>
<td>Schistosomiasis</td>
</tr>
<tr>
<td>Leukaemia</td>
<td>Infiltration</td>
</tr>
<tr>
<td>Lymphoma</td>
<td>Amyloid</td>
</tr>
<tr>
<td></td>
<td>Sarcoïd</td>
</tr>
</tbody>
</table>
### Table 10.5 Causes of splenomegaly

<table>
<thead>
<tr>
<th>Malignancy</th>
<th>Infective</th>
</tr>
</thead>
<tbody>
<tr>
<td>Myelofibrosis</td>
<td>Malaria</td>
</tr>
<tr>
<td>Lymphoma</td>
<td>Kala-azar</td>
</tr>
<tr>
<td>Chronic myeloid leukaemia</td>
<td>EBV</td>
</tr>
<tr>
<td>Infiltration</td>
<td>Chronic liver disease</td>
</tr>
<tr>
<td>Gaucher’s disease</td>
<td>Portal hypertension</td>
</tr>
<tr>
<td>Amyloid</td>
<td></td>
</tr>
</tbody>
</table>

### Table 10.6 Causes of enlarged kidneys

<table>
<thead>
<tr>
<th>Bilateral</th>
<th>Unilateral</th>
</tr>
</thead>
<tbody>
<tr>
<td>Polycystic kidney disease</td>
<td>Renal carcinoma</td>
</tr>
<tr>
<td>Hydronephrosis</td>
<td>Hydronephrosis</td>
</tr>
<tr>
<td>Amyloid</td>
<td>Large renal cyst</td>
</tr>
</tbody>
</table>

### Table 10.7 Causes of ascites

<table>
<thead>
<tr>
<th>Hepatic</th>
<th>Hypoalbuminaemia</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chronic liver disease (portal hypertension)</td>
<td>Nephrotic syndrome</td>
</tr>
<tr>
<td>Peritoneal</td>
<td>Protein-losing enteropathy</td>
</tr>
<tr>
<td>Peritoneal malignancy</td>
<td>Protein malnutrition</td>
</tr>
<tr>
<td>Infection</td>
<td>Vascular</td>
</tr>
<tr>
<td>Tuberculosis</td>
<td>Hepatic vein thrombosis</td>
</tr>
<tr>
<td></td>
<td>Budd–Chiari syndrome</td>
</tr>
</tbody>
</table>

### Kidneys (Table 10.6)

- Place your hand under the loin just below the level of the costal margin
- Use this hand to push the kidney up towards your other hand (balloting)
- If you are able to feel the kidney, just below the hypochondrium, it is enlarged
- You should be able to feel the upper pole of an enlarged kidney
- Always check for a transplanted kidney, usually in the right iliac fossa
- Check for an arteriovenous fistula (for haemodialysis) on the forearm

### Ascites (Table 10.7)

- Eliciting shifting dullness is the easiest and most appropriate test

#### Shifting dullness

- Percuss the abdomen from the umbilicus laterally until the boundary between resonance and dullness is apparent
- Position your hand so that this boundary is between the middle and ring fingers of your splayed hand
Gastrointestinal investigations

- Ask the patient to roll towards you keeping your hand on the abdomen
- Allow the fluid to settle (at least 15–20 seconds), then percuss again to demonstrate that the boundary has moved

**Fluid thrill**

*Do not do this in an exam unless asked to by the examiner.*

- Ask the examiner or the patient to place the lateral aspect of his or her hand firmly on the abdomen in the midline, then flick or tap the lateral aspect of the abdomen with one hand
- The other hand is placed on the opposite side to detect the vibration

**Hernial orifices**

- Palpate the hernial orifices
- Ask the patient to cough and feel for an impulse
- Repeat with the patient standing

**Tell the examiner**

- That you would like to examine the genitalia, test the urine and carry out a rectal exam

---

**GASTROINTESTINAL INVESTIGATIONS**

**Radiology**

See Chapter 5.

**Endoscopy**

Video endoscopes are used to examine the macroscopic appearances of the GI mucosa; samples can be taken for histopathology, cytology and microbiology. Therapeutic procedures can also be performed:

- Dilatation and stenting (inserting tubes used to bypass obstructions) of strictures
- Injection of bleeding lesions
- Polypectomy/excision of tissues
- Insertion of feeding tubes, e.g. percutaneous gastrostomy feeding tubes

**Gastroscopy**

- Examines the oesophagus, stomach and parts one and two of the duodenum

**Colonoscopy**

- Examines the rectum, colon and terminal ileum
- Used for patients with positive faecal occult blood tests during colorectal cancer screening

**Sigmoidoscopy**

- Examines the rectum and sigmoid colon

**Endoscopic retrograde cholangiopancreatography (ERCP)**

- Outlines the pancreatic duct and biliary tree
- Useful to examine dilated pancreatic and bile ducts
- Can be used to remove gallstones from the bile duct

**Enteroscopy**

- Examines the stomach and proximal small bowel
Video (wireless) capsule endoscopy

- Swallowed capsule incorporating camera, light source and transmitter
- Allows for examination of entire small bowel mucosa
  - Anaemia/obscure GI bleeding – if gastroscopy and colonoscopy normal
  - Detect small bowel Crohn’s disease
- Cannot be used to biopsy mucosa

Radioisotope studies

- \(^{13}\)C urea breath test for *Helicobacter pylori* infection
- SeHCAT scan for bile salt malabsorption
- Gastric emptying
- White cell scan to look for inflammation/collections
- Meckel’s scan
- Octreotide/MIBG scans to evaluate neuroendocrine tumours and metastases
- Red cell scan in obscure GI bleeding
- Hydrogen breath test for bacterial overgrowth

Stool tests

Microscopy and culture

- Infections

Faecal occult blood

- Used in population screening for colorectal malignancy

Faecal elastase

- Used to detect pancreatic insufficiency

Oesophageal Disease

Gastro-oesophageal reflux disease (GORD)

- Prolonged contact of gastric contents with the oesophageal mucosa
- Acid or bile causes mucosal irritation

Aetiology

See Figure 10.2.

Clinical features

- Retrosternal burning pain (heartburn)
- Can be worse during the night or when bending over
- Associated bitter taste in the mouth
- Sore throat/dysphonia
- Excessive salivation (water-brash)
- Nocturnal cough or bronchospasm (aspiration)
- Dysphagia (difficulty in swallowing)

Investigations

- Trial of antacid/proton pump inhibitor
- Upper GI endoscopy to look for oesophagitis
- Oesophageal pH studies and manometry (particularly if surgery to be considered)

Management

- Lifestyle changes: lose weight, reduce precipitants, e.g. smoking, alcohol
Over the counter meds (OTC)
- Antacids
- Histamine2-receptor blockers, e.g. ranitidine
- Proton pump inhibitors, e.g. omeprazole
- Prokinetics, e.g. domperidone
- (Laparoscopic) Nissen fundoplication

Complications
- Peptic oesophageal strictures
- Barrett’s oesophagus

Hiatus hernia
See Box 10.1 and Figure 10.2.

Barrett’s oesophagus
- Normal squamous mucosa is replaced with columnar epithelium with intestinal metaplasia as a consequence of severe GORD
- ♂ >> ♀
- 0.12–0.5% develop oesophageal adenocarcinoma per year
- Endoscopic screening/surveillance to detect dysplasia is controversial

Oesophageal carcinoma
- 40% squamous cell carcinomas
- 60% adenocarcinomas
- Prevalence: 10–15/100,000 and increasing

Clinical features
- Dysphagia: progressive: solids then liquids
- Weight loss
- Anorexia
- Lymphadenopathy
Investigations

- Upper GI endoscopy and biopsy
- CT scanning for staging
- Endoscopic ultrasound and PET scanning to stage, if CT shows lesion is not advanced

Management

- 10% 5-year survival
- Surgery gives best chance of cure but patients often present with advanced disease or poor performance status
- Neoadjuvant (preoperative) chemotherapy
- Chemoradiation (radiotherapy + chemotherapy)
- Radiotherapy for palliation
- Endoscopic palliation: oesophageal stents reduce dysphagia
- Palliative thermal ablation, e.g. laser

Achalasia

- Rare: 1:100,000 incidence
- Oesophageal aperistalsis and failure of relaxation of lower oesophageal sphincter
- → Dysphagia (intermittent to solids and liquids)

Investigations

- Barium swallow – shows the poor peristalsis and dilatation, swan neck deformity
- Endoscopy – to exclude malignancy
- Oesophageal manometry
  - Measurement of sphincter pressure (raised, non-relaxing)
  - Aperistalsis or non-propulsive contractions

Management

- Nifedipine or sidenafil can be tried but rarely give durable relief
- Endoscopic balloon dilatation of sphincter
- Injection of *Botulinium* toxin into sphincter
- Surgery (Heller’s procedure: division of muscle)
THE STOMACH

Dyspepsia
- Symptoms referable to the upper gastrointestinal tract
- Heartburn
- Epigastric pain
- Discomfort or ‘fullness’ after eating/bloating
- Nausea

Alarm signals
- Dysphagia
- Weight loss
- Vomiting
- Haematemesis, melaena or anaemia
- Anorexia
- Previous gastric ulcer or gastric surgery

Epidemiology
- 80% of population get symptoms at some time

Aetiology
- Non-ulcer (functional) dyspepsia
- GORD
- Gastritis (NSAIDs, *H. pylori*, bile)
- Peptic ulcer disease
- Gastric malignancy

Investigations
- $^{13}$C urea breath/serology/stool antigen test for *H. pylori*
- Upper GI endoscopy if alarm symptoms or if new symptoms over 45 years old

Management
- Treatment of cause, e.g. GORD, peptic ulcer
- Consider a trial of proton pump inhibitors if no alarm signals and age over 45

Peptic ulceration
- Breaches in the mucosa in the stomach or duodenum

Aetiology
- Gastric ulcers
  - *H. pylori* (60%)
  - NSAIDs and selective COX II inhibitors
  - Adenocarcinoma, lymphoma
  - Associated/worsened with steroids, bisphosphonates, chronic kidney disease, hypercalcaemia
- Duodenal ulcers
  - *H. pylori* (80%)
  - NSAIDs
  - Zollinger–Ellison syndrome

Clinical features
- Upper abdominal pain
- Pain at night or related to food
- Nausea
- GI haemorrhage (haematemesis or melaena)
Anaemia
Tender abdomen

Investigations
- Gastroscopy
- Testing for *H. pylori*
- Biopsy for histology (imperative for gastric ulcers to exclude malignancy)

Management
- *H. pylori* eradication therapy (proton pump inhibitor and two antibiotics for 7 days)
- Stop NSAIDs or other injurious agents
- Proton pump inhibitors for 8 weeks
- Follow-up gastroscopy at 6 weeks for gastric ulcer to ensure healing
- Non-healing ulcers should be treated surgically

Complications
- Haemorrhage → haematemesis/melaena
- Perforation → peritonism and air under diaphragm on chest X-ray
- Gastric outlet obstruction

Gastritis
- Inflammation of the gastric mucosa diagnosed histologically

Aetiology
- *H. pylori*
- NSAIDs
- Autoimmune (pernicious anaemia)
- Chemical, e.g. bile, alcohol

Management
- of cause e.g. *H. pylori* eradication, avoid NSAIDs

Upper GI bleeding

Aetiology
- Oesophageal or gastric varices
- Ulceration
- Mallory–Weiss tear (associated with vomiting)
- Malignancy

Clinical features
- Nausea
- Haematemesis
- Melaena
- Dizziness due to hypovolaemia
- Hypotension
- Tachycardia
- Stigmata of chronic liver disease
  - Splenomegaly
  - Ascites
  - Spider naevi
  - Caput medusae

Investigations
- Full blood count - low haemoglobin, high platelets
- Urea and electrolytes - high urea
Liver biochemistry – abnormal in liver disease
Coagulation – elevated prothrombin time
Group and cross-match blood
Gastroscopy to identify and treat cause

Management
See Box 10.2
80% will stop spontaneously
Gastroscopy
Therapy depends on cause (see below)

Varices
Endoscopic therapy
- Elasticated bands around varices
- Fibrin glue for gastric varices
Non-endoscopic therapy
- Vasopressin analogues, e.g. terlipressin
- Sengstaken tube
- Transjugular intrahepatic portosystemic shunt (TIPS)

Ulcers
Endoscopic:
- Adrenaline (epinephrine) injection
- Clipping of bleeding vessel
- Thermal coagulation
Intravenous PPI infusions reduce re-bleeding following endoscopy
Angiography and embolization of feeding vessel if endoscopy fails to find a source
Surgery for uncontrollable bleeding

Gastric tumours: Adenocarcinoma

Epidemiology
Incidence in men is twice that of women
15/100000 men/year in UK
Wide geographical variation, e.g. more common in Japan

Aetiology/associations
- H. pylori
- Smoking
Alcohol
- High dietary salt
- Mediterranean diet may be protective
- Family history
- Pernicious anaemia
- Previous gastric surgery

Clinical features
- May be asymptomatic
- Abdominal pain
- Early satiety
- Weight loss
- Nausea and vomiting
- Upper GI bleeding
- Palpable epigastric mass
- Left supraclavicular lymph node (Virchow’s)
- Enlarged liver due to metastases

Investigations
- Gastroscopy
- CT
- Laparoscopy
- Endoscopic ultrasound
- PET scanning

Management
- Surgery for low-stage tumours
- Palliation for high-stage tumours
- Palliative chemotherapy/radiotherapy
- 10% 5-year survival

Stromal tumours
- GI stromal tumours (GIST) can occur anywhere in gut but most common in stomach
- May ulcerate → bleeding
- Treated with surgery or imatinib (blocks the activated receptor tyrosine kinase activity of c-kit)

Malt lymphoma
- Mucosa-associated lymphoid tissue lymphoma of stomach
- Associated with *H. pylori*
- 80% are cured by eradication of *H. pylori*
- 90% 5-year survival

SMALL BOWEL DISEASE

Coeliac disease
- Hypersensitivity to gluten in wheat, barley, rye → small intestinal inflammation

Epidemiology
- England 1:300; Ireland 1:100, can occur at any age, peak diagnosis is in 5th decade
- Caucasians mainly
- Family history 10–15% of first-degree relatives affected
**Pathology**
- → Subtotal villous atrophy *(Table 10.8)*
  - Loss of villi
  - Crypt hyperplasia
- → Malabsorption *(Table 10.9)*

**Clinical features**
- Abdominal pain
- Diarrhoea
- Steatorrhoea/malabsorption
- Weight loss
- Symptoms of anaemia
- Mouth ulceration
- Anaemia → pale conjunctivae (50% iron deficiency)
- Dermatitis herpetiformis (blistering rash on extensor surfaces)

**Investigations**
- Anti-endomysial antibodies
- Tissue transglutaminase
- Endoscopy and duodenal biopsy is the diagnostic test
- Full blood count
  - Anaemia (macrocytic or microcytic)
  - Hyposplenism, Howell-Jolly bodies
- Dexa scan

**Disease associations**
- Thyroid disease
- Diabetes
- Inflammatory bowel disease
- Primary biliary cirrhosis
- Autoimmune hepatitis
- Sjögren syndrome

**Complications**
- Ulcerative jejunitis
- Unresponsive coeliac disease – associated with enteropathy-associated T cell lymphoma (EATCL)

---

**Table 10.8 Causes of villous atrophy**

<table>
<thead>
<tr>
<th>Disease</th>
<th>Condition</th>
</tr>
</thead>
<tbody>
<tr>
<td>Coeliac disease</td>
<td>Infection enteritis in children</td>
</tr>
<tr>
<td>Whipple’s disease</td>
<td>Kwashiorkor</td>
</tr>
<tr>
<td>Small bowel lymphoma</td>
<td>Cow’s milk protein intolerance</td>
</tr>
<tr>
<td>Primary hypogammaglobulinaemia</td>
<td>Zollinger–Ellison syndrome</td>
</tr>
</tbody>
</table>

**Table 10.9 Causes of small bowel malabsorption**

<table>
<thead>
<tr>
<th>Disease</th>
<th>Condition</th>
</tr>
</thead>
<tbody>
<tr>
<td>Coeliac disease</td>
<td>Crohn’s disease</td>
</tr>
<tr>
<td>Dermatitis herpetiformis</td>
<td>Whipple’s disease</td>
</tr>
<tr>
<td>Tropical sprue</td>
<td>Radiation enteritis</td>
</tr>
<tr>
<td>Bacterial overgrowth</td>
<td><em>Giardia intestinalis</em></td>
</tr>
<tr>
<td>Intestinal resection</td>
<td>Lymphoma</td>
</tr>
</tbody>
</table>
Oesophageal and small bowel carcinoma
Osteomalacia and osteoporosis

Management
- Gluten-free diet
- Iron/folate supplementation
- Treatment/prevention of osteoporosis

Bacterial overgrowth
- Bacterial colonization of the small bowel
- Commonly *Escherichia* or *Bacteroides*
- → Bacterial consumption of vitamin B₁₂
- → Breakdown of bile salts
- → Bacterial synthesis of folate

Aetiology
- Small bowel structural abnormalities, e.g. diverticulum
- Strictures

Clinical features
- Diarrhoea
- Steatorrhoea

Investigations
- Lactulose hydrogen breath tests
- Low vitamin B₁₂
- High folate

Management
- Correct structural cause if possible
- Rotating antibiotics, e.g. tetracycline, ciprofloxacin or metronidazole

Whipple’s disease
- Due to *Tropheryma whippleii*
- → Villous atrophy
- Diarrhoea and steatorrhoea
- Rare

Management
- Antibiotics

Small bowel tumours
- Lymphomas
- Adenocarcinomas (rare)
- Carcinoids

Carcinoid syndrome
- Occurs in only 5% of carcinoid tumours
- Due to serotonin (5-hydroxytryptamine, 5-HT), bradykinin and histamine secretion by liver metastases

Clinical features
- Flushing
- Diarrhoea
- Right heart failure
- Hepatomegaly
- Pulmonary valve stenosis
- Tricuspid regurgitation
Investigations
- 24-hour urinary 5-hydroxyindoleacetic acid (5-HIAA)
- CT or ultrasound of liver
- Octreotide-labelled scan

Management
- Octreotide to reduce symptoms
- Embolization of hepatic secondaries

INFLAMMATORY BOWEL DISEASE

Inflammatory diseases of the GI tract are of unknown aetiology. Both Crohn’s disease and ulcerative colitis demonstrate a defective mucosal immune system producing an inappropriate response to luminal antigens which results in uncontrolled inflammation.

Crohn’s disease

Epidemiology
- Prevalence = 50–60/100,000
- More common in Caucasian races
- Familial association
- Genetic predisposition

Pathology
- Any part of gut from mouth to anus
- Skip lesions – patchy disease with normal mucosa in between
- Commonly terminal ileum and ascending colon
- → Inflammation, ulceration, abscesses and fistulae
- Full bowel wall thickness involved
- Inflammatory infiltrates
- Non-caseating granulomata

Clinical features
- Depend on the area of bowel involved
- Mouth ulcers
- Diarrhoea
- Abdominal pain – colicky
- Nausea/vomiting
- Low-grade pyrexia
- Generally unwell, lethargy, weight loss
- Cutaneous fistulae (often perianal)

Disease associations (Fig. 10.3)
- Small joint arthritis
- Sacroiliitis
- Ankylosing spondylitis
- Iritis/uveitis/conjunctivitis
- Erythema nodosum – tender lower leg lesions
- Pyoderma gangrenosum – skin ulceration
- Sclerosing cholangitis

Investigations
- Blood tests: FBC, ESR, CRP, LFTs, Vitamin B12 and Red Cell folate
- Colonoscopy and terminal ileal biopsy
- Small bowel imaging – MRI, wireless capsule endoscopy or Barium follow through (involves radiation)
- Faecal calprotectin can be used to detect disease activity
Management

- **Induction of remission:**
  - i.v. or oral glucocorticoids
  - Enteral nutrition
  - Azathioprine or 6MP (usually with oral glucocorticoids for first few weeks)

- **Maintenance of remission:**
  - 5-aminosalicylic acid (5-ASA), e.g. mesalazine for colonic disease
  - Azathioprine/6MP

- **Treatment of therapy resistant disease:**
  - Anti-TNF-a antibodies (infliximab and adalimumab)
  - Other biologicals in clinical trials

- **Antibiotics for perianal disease**

- **Surgery for resistant disease but recurrence is inevitable**

---

**Fig. 10.3** Extra-gastrointestinal manifestations of inflammatory bowel disease (IBD).
Complications
- Vitamin B₁₂ deficiency
- Short bowel syndrome after surgery
- Toxic megacolon in colitis
- Kidney stones
- Gallstones
- Malnutrition
- Osteoporosis
- Colonic cancer
- Venous and arterial thromboembolism

Ulcerative colitis

Epidemiology
- Prevalence = 80–120/100000
- Uncommon in smokers

Pathology
- Limited to colon, inflammation spreads proximally from the rectum
- Mucosal inflammation → erythema, oedema and ulceration
- Microscopically → chronic inflammatory infiltrate, crypt abscesses, goblet cell depletion

Clinical features
- Diarrhoea
- Blood or mucus per rectum
- Mouth ulcers

Disease associations
- Uveitis/iritis/conjunctivitis
- Erythema nodosum/pyoderma gangrenosum
- Arthritis/sacroiliitis/ankylosing spondylitis
- Sclerosing cholangitis

Investigations
- Blood for inflammatory markers particularly CRP
- Stool cultures to exclude infection
- Plain abdominal X-ray for acute severe colitis to look for toxic megacolon
- Colonoscopy and biopsy

Indicators of acute severe colitis urgent treatment
- >Six stools per day with blood
- Fever >37.5°C
- Tachycardia >90 b.p.m.
- ESR>30 mm/h
- Haemoglobin <100 g/L
- Albumin <30 g/L

Management
- 5-ASA, e.g. mesalazine oral and topical, e.g. enemas or suppositories
- Steroids, e.g. prednisolone
- Azathioprine
- i.v. cyclosporin or infliximab for acute severe colitis
- Surgery for toxic megacolon, perforation, failure of medical therapy or malignancy
- Probiotics for pouchitis
Complications
- Toxic megacolon (Box 10.3)
- Iron deficiency anaemia
- Increased risk of colorectal cancer
- Thromboembolism

**COLONIC DISEASE**

**Colorectal cancer**

**Epidemiology**
- 1 in 27 of the population
- 10% are familial
- See Table 10.10 for other risk factors

**Aetiology**
- Genetic predisposition to promote accumulation of defects in growth regulating genes
  - *apc* gene mutation and loss
  - *K-ras* mutation
  - Smad2/4 loss
  - *p53* gene mutation and loss
- Microsatellite instability (failure of DNA repair)

**Pathology**

*Adenomatous polyps → adenocarcinoma*
- Most commonly in sigmoid colon or rectum

*Microsatellite instability tumours*
- Not associated with polyp formation
- More common in ascending colon and caecum

**Familial cancers**

*Familial adenomatous polyposis (FAP)*
- *apc* gene mutation
- → Multiple adenomatous polyps
- → Very high risk of malignant change

*Hereditary non-polyposis colorectal cancer (HNPCC)*
- Associated with microsatellite instability
- Associated increased risk of upper GI and gynaecological cancers
Colonic disease

Clinical features
- Change in bowel habit to diarrhoea
- Rectal blood/mucus
- Asymptomatic with iron deficiency anaemia
- Population FOB screening

Investigations
- Full blood count – iron deficiency anaemia
- Colonoscopy
- CT colonography for failed colonoscopy
- CT to stage the cancer (Table 10.11)
- MRI to stage and plan treatment for rectal cancers
- PET scanning with CT staging finds suspicious lesions

Management
- MDT approach
- Surgical resection
- Adjuvant chemotherapy
- Preop radiotherapy for rectal cancer

Complications
- Bowel obstruction
- Iron deficiency anaemia
- Hepatic metastases

Screening
- High-risk individuals (e.g. family history, previous polyps or cancer and ulcerative colitis)
- Population FOB screening

Diverticular disease
- Presence of mucosal pouches protruding outside the bowel
- Very common: 50% of those >50 years old

<table>
<thead>
<tr>
<th>Table 10.10 Risk factors in colorectal cancer</th>
</tr>
</thead>
<tbody>
<tr>
<td>Increased risk</td>
</tr>
<tr>
<td>Increasing age</td>
</tr>
<tr>
<td>Animal fat (saturated) and red meat consumption</td>
</tr>
<tr>
<td>Sugar consumption</td>
</tr>
<tr>
<td>Colorectal polyps</td>
</tr>
<tr>
<td>Family history of colon cancer or colonic polyps</td>
</tr>
<tr>
<td>Chronic inflammatory bowel disease</td>
</tr>
<tr>
<td>Obesity (body and abdominal)</td>
</tr>
<tr>
<td>Smoking</td>
</tr>
<tr>
<td>Acromegaly</td>
</tr>
<tr>
<td>Abdominal radiotherapy</td>
</tr>
<tr>
<td>Ureterosigmoidostomy</td>
</tr>
<tr>
<td>Decreased risk</td>
</tr>
<tr>
<td>Vegetable, garlic, milk, calcium consumption</td>
</tr>
<tr>
<td>Exercise (colon only)</td>
</tr>
<tr>
<td>Aspirin (including low dose) and other NSAIDs</td>
</tr>
</tbody>
</table>

(Reproduced from Kumar P, Clark M. Kumar & Clark’s Clinical Medicine, 8th edn. Edinburgh: Elsevier; 2012, with permission from Elsevier.)
Clinical features

- 95% asymptomatic, incidental finding
- Erratic in bowel habit
- Left iliac fossa pain
- Acute diverticulitis
  - Severe left iliac fossa pain
  - Fever and tachycardia
  - Abdominal tenderness, guarding ± mass

Investigations

- CT

Management

- High-fibre diet
- Antibiotics for diverticulitis
- Surgery for complications

Complications

- Diverticulitis – inflammation/infection
- Diverticular abscess
- Lower GI bleeding
- Perforation

Functional bowel disease

- GI symptoms without an identified pathology
- Irritable bowel syndrome

Clinical features

- Left iliac fossa pain
- Alternating diarrhoea and constipation
**BOX 10.4 Approaches to management of the irritable bowel syndrome (IBS)**

<table>
<thead>
<tr>
<th><strong>Action</strong></th>
<th><strong>End organ treatment</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>Explore dietary triggers</td>
<td>Refer to dietician</td>
</tr>
<tr>
<td>High-fibre diet ± fibre supplements for constipation</td>
<td>Refer to dietician</td>
</tr>
<tr>
<td>FODMAP diet for bloating</td>
<td></td>
</tr>
<tr>
<td>Anti-diarrhoeal drugs for bowel frequency</td>
<td>Loperamide, codeine phosphate, co-phenotrope</td>
</tr>
<tr>
<td>Constipation</td>
<td>5HT₄ receptor agonist, e.g. prucalopride</td>
</tr>
<tr>
<td>Smooth muscle relaxants for pain</td>
<td>Mebeverine hydrochloride, dicycloverine hydrochloride, peppermint oil</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th><strong>Central treatment</strong></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Explain physiology and symptoms</td>
<td>At consultation (leaflets with diagrams help)</td>
</tr>
<tr>
<td>Psychotherapy</td>
<td>Refer to clinical psychologist (see p. 1163)</td>
</tr>
<tr>
<td>Hypnotherapy</td>
<td></td>
</tr>
<tr>
<td>Cognitive behavioural therapy</td>
<td>Refer to psychiatrist</td>
</tr>
<tr>
<td>Antidepressants</td>
<td>Functional diarrhoea – clomipramine, diarrhoea-predominant IBS – tricyclic group, e.g. amitriptyline, constipation-predominant IBS – SSRI, e.g. paroxetine</td>
</tr>
<tr>
<td>Alter the microbiota</td>
<td>Rifaximin has shown short-term benefit in IBS patients without pre- and pre-biotics, constipation (Target I and II trials)</td>
</tr>
</tbody>
</table>

*(Reproduced from Kumar P, Clark M. Kumar & Clark’s Clinical Medicine, 8th edn. Edinburgh: Elsevier; 2012, with permission from Elsevier.)*

- Bloating
- Rabbit pellet stools
- Sensation of incomplete evacuation

**Investigations**
- Normal physical examination
- Rule out gynaecological problems
- Full blood count, CRP, TFTs and coeliac serology
- Gastroscopy and colonoscopy if atypical or alarm symptoms

**Management**
See Box 10.4.
CHANGE IN BOWEL HABIT

Diarrhoea (Fig. 10.4)

An increase in stool weight to >250 g/day, usually associated with an increase in stool frequency.

Osmotic diarrhoea

Non-absorbable hypertonic substances in the bowel lumen

- → Osmotic pressure draws water into the bowel

Aetiology

- Purgatives, e.g. magnesium sulphate
- Malabsorption → solutes in the bowel, e.g. glucose
- Absorptive defects, e.g. lactase deficiency
- Diarrhoea stops when the patient stops eating or taking the purgative
Secretory diarrhoea
- Increased secretion and decreased absorption of fluid and electrolytes

Aetiology
- Cholera toxin
- *E. coli* heat-labile and stable toxins
- Hormones, e.g. vasoactive intestinal peptides
- Bile salts and fatty acids following terminal ileal resection
- Some laxatives

Inflammatory diarrhoea
- Mucosal inflammation → loss of fluid and blood
- May also → absorptive failure
- e.g. Ulcerative colitis, Crohn’s disease, dysentery due to *Shigella*

Increased stool frequency: Abnormal GI tract motility
- Post-vagotomy
- Diabetic autonomic neuropathy
- Hyperthyroidism

Structural abnormalities
- Diverticular disease
- Colorectal carcinoma

Other
- Faecal impaction and overflow

Constipation

Aetiology
- Old age and immobility
- Low-volume/fibre diets
- Intestinal obstruction
- Colonic disease, e.g. colorectal carcinoma
- Hypothyroidism
- Hypercalcaemia
- Depression
- Parkinson’s disease
- Spinal cord lesions
- Drugs
  - Opiates
  - Iron
  - Antidepressants
  - Aluminium antacids

Management
- High fibre diet and adequate fluid intake
- Bulking laxatives – fibre/bran
- Stimulants – anthraquinones (senna), bisacodyl
- Osmotics – magnesium sulphate/macrogols
- Suppositories – bisacodyl
- Enemas – phosphate

GASTROINTESTINAL INFECTIONS
A very common cause of morbidity and mortality, notably in the developing world.
Viral infections

Aetiology
- More common in children than adults
- Rotavirus → epidemic diarrhoea in children
- Noroviruses → epidemic diarrhoea and vomiting in children (also involve adults)

Management
- Supportive

Bacterial infections

Cholera
- *Vibrio cholerae*
- Faecal–oral transmission
- ‘Ricewater’ high-volume stools
- Secretory diarrhoea due to cAMP activation
- Treat with oral rehydration therapy
- Ciprofloxacin or azithromycin if severe

Salmonella
- *Salmonella enteritidis* and *typhimurium*
- Eggs and poultry products
- 2–3 days of diarrhoea and malaise
- Rarely bloody diarrhoea
- Treat with oral rehydration
- Complications – cholecystitis and chronic carriage with re-infection

Staphylococcus
- *Staphylococcus aureus*
- Toxin-related gastroenteritis
- Short-lived diarrhoea and vomiting

Escherichia coli
- ETEC (enterotoxigenic) → watery diarrhoea
- EIEC (enteroinvasive) → dysentery
- EHEC (enterohaemorrhagic) → haemorrhagic colitis ± haemolytic uraemic syndrome, associated with serotype O157:H7

Yersinia
- *Yersinia enterocolitica* and *paratuberculosis*
- Enterocolitis, terminal ileitis
- → Fever, diarrhoea and abdominal pain
- → arthritis and Reiter syndrome

Campylobacter
- *Campylobacter jejuni*
- Mucosal ulcer and inflammation, colitis
- → Diarrhoea ± blood, fever
- Cramping abdominal pains
- Self-limiting, use azithromycin if severe
- Complications – Guillain–Barré syndrome

Shigellosis
- *Shigella dysenteriae, flexneri, sonnei*
- Usually affects children
- → Fever, abdominal pain, watery diarrhoea
Blood disorders

→ Haemorrhage
→ Anemia

Hypertension

→ Headaches
→ Nausea
→ Vision changes

Hypothyroidism

→ Fatigue
→ Constipation
→ Dry skin

Hyperthyroidism

→ Nervousness
→ Heat intolerance
→ Weight loss

Endocrine disorders

→ Diabetes
→ Cystic fibrosis

Malignant disease

→ Cancer
→ Multiple myeloma

Pancreatic disease

Acute pancreatitis

→ Acute inflammation of the pancreas

Aetiology

→ Alcohol
→ Gallstones

Bacillus cereus

→ Toxin-mediated
→ Short-lived vomiting
→ ‘Fried rice poisoning’

Clostridial infections

Clostridium perfringens

→ Spores in food
→ Watery diarrhoea and pain

Clostridium difficile

→ A and B toxins
→ Antibiotic associated diarrhoea, e.g. cephalosporins
→ Pseudo-membranous colitis → Bloody diarrhoea
→ Treat by stopping antibiotics; oral metronidazole or vancomycin

Protozoal infections

Amoeba

→ Entamoeba histolytica
→ Dysentery and colitis, liver abscess
→ Treat with metronidazole

Giardia

→ Giardia intestinalis
→ Diarrhoea and malabsorption (partial villous atrophy)
→ Treat with metronidazole

Cryptosporidium

→ Cryptosporidium parvum
→ Water-borne
→ Fever and diarrhoea
→ Self-limiting, in HIV can be severe and protracted

Helminths

Nematodes

→ Strongyloides stercoralis
→ Hookworm (Ancylostoma duodenale)
→ Roundworm (Ascaris lumbricoides)
→ Threadworm (Enterobius vermicularis)

Trematodes

→ Schistosomiasis

Cestodes

→ Tapeworms (Taenia saginata/solium)

PANCREATIC DISEASE

Acute pancreatitis

→ Acute inflammation of the pancreas

Aetiology

→ Alcohol
→ Gallstones
Infections, e.g. mumps, coxsackie B
Pancreatic tumours
Drugs, e.g. azathioprine, steroids, oral contraceptive
Iatrogenic, e.g. post-ERCP
Hyperlipidaemia
Other
• Trauma
• Cardiac surgery
• Scorpion bites
• Idiopathic

Clinical features
• Abdominal pain radiating to back
• Nausea and vomiting
• Abdominal tenderness and guarding
• Flank bruising (Cullen and Grey–Turner signs) if severe necrotizing

Investigations
• Amylase – elevated greater than 3 times (Table 10.12)
• Plain abdominal X-ray – pancreatic calcification suggests previous chronic disease
• CRP, full blood count, urea and electrolytes, liver function tests, calcium, glucose and blood gases for baseline and at 24 and 48 hours monitoring of severity
• Ultrasound – to diagnose gallstones
• CT at 72 hours to assess pancreatic necrosis for prognosis and look for complications
• MRI useful to see if a mass is solid or liquid

Management
• Oxygen requirements determined by ABGs
• i.v. fluids
• NG tube for suction if abdominal distension
• i.v. antibiotics
• Analgesia
• Feeding – usually enterally NG or NJ
• Early ERCP for obstructing gallstones

Complications
• Sepsis
• Multi-organ failure
Pancreatic disease

**Prognosis**

See Table 10.13.

**Chronic pancreatitis**

- Long-standing or repeated attacks of pancreatitis resulting in fibrosis

**Aetiology**

- Alcohol
- Autoimmune pancreatitis
- Hereditary, e.g. cystic fibrosis
- Tropical
- Hypercalcaemia

**Clinical features**

- Chronic abdominal pain
- Weight loss
- Exocrine or endocrine deficiency
- Steatorrhoea

**Investigations**

- Amylase is usually normal
- Plain abdominal X-ray or ultrasound shows pancreatic calcification
- Faecal elastase
- Blood sugar – elevated due to diabetes
- CT scan and MRCP

**Management**

- Analgesia
- Treatment of steatorrhoea with pancreatic enzymes
- Treatment of diabetes

**Pancreatic malignancy**

- Majority are adenocarcinomas
- Often present late and so have poor prognosis

---

**Table 10.13** Poor prognostic indicators in acute pancreatitis in the first 48 hours

<table>
<thead>
<tr>
<th>Indicator</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>&gt;55 years</td>
</tr>
<tr>
<td>WCC</td>
<td>&gt;15 × 10⁹/mL</td>
</tr>
<tr>
<td>Glucose</td>
<td>&gt;10 mmol/L</td>
</tr>
<tr>
<td>Urea</td>
<td>&gt;16 mmol/L</td>
</tr>
<tr>
<td>Albumin</td>
<td>&lt;30 g/L</td>
</tr>
<tr>
<td>ALT</td>
<td>&gt;200 U/L</td>
</tr>
<tr>
<td>Calcium</td>
<td>&lt;2 mmol/L</td>
</tr>
<tr>
<td>LDH</td>
<td>&gt;600 IU</td>
</tr>
<tr>
<td>P&lt;sub&gt;a&lt;/sub&gt;O₂</td>
<td>&lt;8 kPa</td>
</tr>
</tbody>
</table>
Clinical features
- Painless jaundice – bile duct compression
- Anorexia
- Weight loss

Investigations
- Ultrasound to assess biliary obstruction
- CT to stage for operability
- ERCP for cytology
- MRI/endoscopic ultrasound
- Percutaneous biopsy if not operable and chemotherapy possible

Management
- ERCP stenting to relieve jaundice
- Surgical resection of primary (only 20% cases operable)
- Chemotherapy 5FU and gemcitabine
- Palliative care

Pancreatic neuroendocrine tumours
- Gastrinomas and rarely other hormone-secreting tumours (e.g. insulinomas)
- Symptoms depend on hormone secreted

Zollinger–Ellison syndrome
- Gastrin-secreting tumour
- → High gastric acid secretion
- → Multiple gastroduodenal ulcers
- Diarrhoea

JAUNDICE

See Table 10.1 and Figure 10.5.

HEPATICITIS (TABLE 10.14)

Acute hepatocyte breakdown leading to release of aminotransferases (ALT, AST) and jaundice. Prolonged or severe damage results in synthetic failure, leading to a reduction in the synthesis of albumin and clotting factors (causing an elevated prothrombin time).

Causes
- Viral hepatitis
- Drugs (Table 10.14)
- Autoimmune hepatitis

Table 10.14 Causes of chronic hepatitis

<table>
<thead>
<tr>
<th>Viruses</th>
<th>Hereditary</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hepatitis B ± D</td>
<td>Haemochromatosis</td>
</tr>
<tr>
<td>Hepatitis C</td>
<td>α1-antitrypsin disease</td>
</tr>
<tr>
<td>Autoimmune hepatitis</td>
<td>Wilson’s disease</td>
</tr>
<tr>
<td>Drugs</td>
<td>Others</td>
</tr>
<tr>
<td>Methylidopa</td>
<td>Alcohol</td>
</tr>
<tr>
<td>Isoniazid</td>
<td></td>
</tr>
</tbody>
</table>

Table 10.14 Causes of chronic hepatitis
Alcohol
Haemochromatosis
Wilson’s disease

**Viral hepatitis**

**Hepatitis A (HAV) RNA virus**
- Faecal–oral spread (e.g. shellfish)
- Incubation 2–3 weeks
- No progression → chronic liver disease

**Clinical features**
- Nausea
- Anorexia
- Jaundice ± hepatomegaly/rash

Fig. 10.5 Bilirubin metabolism.
Investigations
- Anti-HAV IgM
- Elevated ALT/aspartate aminotransferase (AST)
- Elevated bilirubin (may be subclinical)

Management
- Supportive

Hepatitis B (HBV) DNA virus (Figs 10.6, 10.7)
- Blood/saliva/sexual/vertical spread
- Incubation 1–5 months
- 10–15% carriage in Africa and Far East

Clinical features
- Jaundice/malaise ± rash
- May be asymptomatic

Investigations (Fig. 10.6)
- Liver biochemistry – ALT elevated first then bilirubin
**Acute infection**
- Surface antigen (HBsAg) first marker
- e antigen (HBeAg)

**Seroconversion**
- Anti-HBs antibody
- Anti-HBe antibody
- Anti-HBc antibody (IgM)

**Successful clearance of virus or post-vaccine**
- Anti-HBs antibody

**Chronic carrier state**
- HBsAg (chronic infection)
- HBeAg (infectious carrier)
- Positive HBV DNA (active viral replication)

**Fig. 10.7** Clinical course of hepatitis B infection.
Management
- Treat symptoms in acute infection and monitor viral markers
- Antivirals for chronic infection: interferon, lamivudine, adefovir, entecavir and tenofovir

Complications
- Chronic infection → chronic liver disease
- Hepatocellular carcinoma
- 1% → fulminant acute hepatitis → death

Hepatitis D
- Only causes hepatitis when it co-infects with hepatitis B
- Commonest in i.v. drug abusers
- Diagnosis by detection of specific antibodies

Hepatitis C (HCV; Fig. 10.8)
- RNA virus
- Blood spread (rarely sex/saliva)
- Acute infection often asymptomatic
- 80% → chronic liver disease
- 30% of these → cirrhosis
- 5% of these → hepatocellular carcinoma

Investigations
- Anti-HCV antibodies
- HCV RNA in blood

Fig. 10.8 Clinical course of hepatitis C infection.
Abnormal liver function in chronic infection
Ultrasound and α-fetoprotein to detect hepatocellular carcinoma

Management
Antivirals, e.g. interferon and ribavirin to clear the virus
Newer antiviral agents have better efficacy, e.g. telaprevir, boceprevir
Efficacy depends on genotype
Liver transplantation is considered for those with decompensated cirrhosis

Others
Hepatitis E (1–2% mortality in pregnancy)
Epstein–Barr virus (EBV)
Cytomegalovirus (CMV)
Yellow fever

Autoimmune hepatitis

Epidemiology
♀ > ♂
Associated with other autoimmune disease, e.g. thyroid, diabetes

Clinical features
May be asymptomatic
Jaundice
Bruising
Signs of acute or chronic liver disease

Investigations
Antinuclear antibodies
Anti-smooth muscle antibodies Type I
Anti-soluble liver antigen antibodies
Anti-liver/kidney microsomal antibodies Type II

Management
Steroids/azathioprine

Fulminant hepatic failure

Aetiology
Hepatitis A B (D) and E
Drugs, e.g.
Paracetamol
Volatile liquid anaesthetics
Isoniazid
Ecstasy
Wilson’s disease
Pregnancy
Reye syndrome
Budd–Chiari
Autoimmune hepatitis

Clinical features
Jaundice
Encephalopathy
Drowsiness → coma
Hypoglycaemia
Low potassium or calcium
Coagulopathy and haemorrhage
Management
- Treat on a specialist unit
- Supportive therapy
- Liver transplant

CIRRHOSIS
Liver cell necrosis followed by nodular regeneration and fibrosis, resulting in increased resistance to blood flow and deranged liver function.

Aetiology
- Alcohol
- Hepatitis B or C
- Biliary cirrhosis
- Autoimmune hepatitis
- Haemochromatosis
- Wilson’s disease
- α1-antitrypsin disease
- Cystic fibrosis
- Non-alcoholic steatohepatitis (NASH)
- Hepatic venous congestion
- Budd–Chiari
- Drugs, e.g. methotrexate

Clinical features
Chronic liver dysfunction
- Jaundice
- Anaemia
- Bruising
- Palmar erythema
- Dupuytren’s contracture

Portal hypertension
- Splenomegaly
- Ascites
- Spider naevi
- Caput medusae
- Oesophageal/rectal varices

Investigations (Table 10.15)
- ALT/AST may be high or normal
- Alkaline phosphatase is usually high
- Bilirubin is usually high
- Albumin falls as cirrhosis worsens

Table 10.15 Liver function tests

<table>
<thead>
<tr>
<th>Hepatocellular damage (hepatitis)</th>
<th>Cholestasis (bile ducts)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aminotransferases (ALT/AST)</td>
<td>Bilirubin</td>
</tr>
<tr>
<td>γ-Glutamyl transpeptidase (γ-GT)</td>
<td>Alkaline phosphatase</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Synthetic function</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Albumin</td>
<td>Prothrombin time</td>
</tr>
</tbody>
</table>
Cirrhosis

- Prothrombin time often prolonged
- Sodium low in severe disease
- α-fetoprotein – hepatocellular carcinoma
- Ultrasound – liver may be large, normal or small; splenomegaly
- Endoscopy for oesophageal varices

Management
- Stop drinking
- Treat complications
- Transplantation

Complications (Table 10.16)
- Ascites
- Transudate (protein <30 g/L in fluid) (Table 10.17)
  Treatment:
  - Spironolactone + loop diuretics
  - Ascitic drainage
  - Venous shunt, e.g. TIPS
- Serum-ascites albumin gradient
  - >11 g suggests transudate
  - More sensitive than absolute protein
- Spontaneous bacterial peritonitis
  - Worsening of clinical state
  - Diagnosis: ascitic tap
  - Treatment: parenteral antibiotics
- Variceal bleeding
- Encephalopathy
- Hepatorenal syndrome
- Hepatocellular carcinoma

Table 10.16 Indicators of poor prognosis in cirrhosis

<table>
<thead>
<tr>
<th>Indicator</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Albumin &lt;25 g/L</td>
<td>Persistent jaundice</td>
</tr>
<tr>
<td>Sodium &lt;120 mmol/L</td>
<td>Ascites</td>
</tr>
<tr>
<td>Prolonged prothrombin time</td>
<td>Variceal bleeding</td>
</tr>
</tbody>
</table>

Table 10.17 Causes of ascites

<table>
<thead>
<tr>
<th>Transudate (protein &lt;30 g/L)</th>
<th>Exudate (protein &gt;30 g/L)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Portal hypertension</td>
<td>Infections</td>
</tr>
<tr>
<td>Cirrhosis of the liver</td>
<td>Peritoneal tuberculosis</td>
</tr>
<tr>
<td>Portal vein thrombosis</td>
<td>Malignancy</td>
</tr>
<tr>
<td>Low serum protein</td>
<td>Ovarian carcinoma</td>
</tr>
<tr>
<td>Liver disease</td>
<td>Peritoneal metastases</td>
</tr>
<tr>
<td>Nephrotic syndrome</td>
<td>Inflammatory</td>
</tr>
<tr>
<td>Malnutrition</td>
<td>Pancreatitis</td>
</tr>
<tr>
<td>Others</td>
<td></td>
</tr>
<tr>
<td>Right ventricular failure</td>
<td></td>
</tr>
<tr>
<td>Myxoedema</td>
<td></td>
</tr>
</tbody>
</table>
Primary biliary cirrhosis

- Chronic destruction of bile ducts
- ♀ > ♂

Clinical features
- Jaundice
- Itching
- Xanthelasma
- Hepatosplenomegaly

Investigations
- Antimitochondrial (M2) antibodies
- High alkaline phosphatase
- Relatively normal ALT
- Ultrasound
- Liver biopsy

Management
- Ursodeoxycholic acid may normalize liver biochemistry
- Supplement fat-soluble vitamins (A, D, E, K)
- Cholestyramine for itching
- Consider liver transplant when bilirubin >100 mmol/L

Hereditary haemochromatosis

- Autosomal recessive
- 1:400 homozygous
  - → Abnormalities of iron transportation
  - → Accumulation of iron in epithelial cells
- ♂ = ♀ but women less severely affected due to menstruation

Clinical features
- Heart: cardiomyopathy
- Pancreas: diabetes
- Pituitary hypogonadism
- Liver: hepatitis and cirrhosis, hepatocellular carcinoma
- Skin: pigmentation
- Calcium pyrophosphate deposition in joints – arthritis
- Testes: infertility

Investigations
- Ferritin >500 µg/L
- Serum iron >30 µmol/L
- Transferrin saturation >60%
- Liver biopsy
- HFE gene; also screen family

Management
- Venesection to normalize ferritin

Wilson's disease

- Autosomal recessive
- Defect of copper transport
  - → Failure of biliary copper excretion

Clinical features
- Liver: chronic hepatitis → cirrhosis
- Basal ganglia: tremor, dysarthria, dementia
Cirrhosis

- Kidneys: tubular degeneration
- Eyes: Kayser–Fleischer rings

**Investigations**
- Reduced serum copper and caeruloplasmin
- Elevated urinary copper
- Liver biopsy

**Management**
- Penicillamine – chelates copper

**α₁-antitrypsin deficiency**
- Inherited deficiency of α₁-antitrypsin
- Autosomal dominant
- Liver cirrhosis
- Early emphysema in smokers

**Alcohol-related liver disease and alcoholism**

**Pathology**
- Fatty change
- Alcoholic hepatitis
- Cirrhosis

**Clinical features**
- Those of the stage of liver disease (see above)

**Investigations**
- Abnormal liver function
- γ-GT elevation.
- AST: ALT >1
- Liver biopsy
- Ultrasound
- α-fetoprotein for hepatocellular carcinoma

**Management**
- Cessation of alcohol consumption
- Support during physical withdrawal (Table 10.18)
- Psychological support

**Complications**
- Hepatocellular carcinoma (10~15%)
- End-stage liver disease
- Wernicke–Korsakoff syndrome (see below)
- Encephalopathy
- Dementia
- Epilepsy (5~10%)

**Table 10.18** Withdrawal syndrome with benzodiazepines

<table>
<thead>
<tr>
<th>Insomnia</th>
<th>Perceptual distortions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anxiety</td>
<td>Hallucinations (which may be visual)</td>
</tr>
<tr>
<td>Tremulousness</td>
<td>Hypersensitivities (light, sound, touch)</td>
</tr>
<tr>
<td>Muscle twitchings</td>
<td>Convulsions</td>
</tr>
</tbody>
</table>

(Reproduced from Kumar P, Clark M. Kumar & Clark’s Clinical Medicine, 8th edn. Edinburgh: Elsevier; 2012, with permission from Elsevier)
Wernicke–Korsakoff syndrome
- Thiamine deficiency
  - → Acute Wernicke syndrome
    - Nystagmus, ataxia, confusion
  - → Chronic Korsakoff syndrome
    - Dementia, chronic amnesia, confabulation
- Investigations: red cell transketolase
- Management: parenteral thiamine

Hepatic encephalopathy
- Reversible neuropsychiatric deficit

Clinical features (Box 10.5)
- Flapping tremor of hands
- Decreased level of consciousness
- Personality changes
- Intellectual deterioration
- Slow, slurred speech
- Constructional apraxia – unable to copy a drawn five-pointed star
  - Worsened by:
    - Sepsis
    - Constipation, diarrhoea or vomiting
    - Diuretics
    - GI bleeding
    - Alcohol withdrawal

Investigations
- Urea and electrolytes
- Full blood count
- Liver function tests
- EEG
- Blood cultures to detect sepsis
- Ascitic tap for spontaneous bacterial peritonitis

Management
- Laxatives e.g. lactulose
- Treat sepsis

---

**BOX 10.5. Assessing hepatic encephalopathy**

**Presence of ‘liver flap’**
- Straight arms and hyperextended wrist with fingers splayed
- Slow wrist flexion

**Assessment of conscious level**
- Glasgow coma score

**Assessment of cognition**
- Mini-mental test

**Assessment of apraxia**
- Ask patient to copy a five-pointed star
- Repeat on a daily basis to demonstrate changes in encephalopathy
## Careful fluid balance
- Supportive treatment

### OTHER DISEASES OF THE LIVER

#### Liver abscess
- Single or multiple abscesses
- *E. coli*
- *Enterococcus faecalis*
- *Staphylococcus aureus*
- *Entamoeba histolytica* (amoeba)
- → Fever, rigors, vomiting, weight loss, shock

**Investigations**
- Blood count – anaemia and leucocytosis
- Blood cultures
- Amoeba serology
- Ultrasound and aspiration for culture and sensitivities

**Management**
- Broad-spectrum antibiotics
- Ultrasound-guided drainage
- Consider underlying bowel disease, e.g. colorectal cancer

#### Budd–Chiari syndrome
- Hepatic vein thrombosis
- → Hepatic failure
- Clinical ascites, abdominal pain and vomiting
- Hepatomegaly

#### Pregnancy related liver disease
- Fatty liver
- Hepatitis
- Cholestasis
- Eclampsia → hepatic necrosis
- HELLP syndrome (haemolysis, elevated liver enzymes, low platelets)

#### Hepatocellular carcinoma
- Common worldwide
- Alcohol, hepatitis B or C-related
- Investigations: ultrasound and α-fetoprotein
- Local treatment with surgery or radiofrequency ablation
- Transplantation if poor synthetic function

#### Hepatic metastases
- Commonest hepatic tumours
- GI tract, breast and lung carcinomas

#### Hepatic steatosis
- ‘Fatty liver’
- ALT usually elevated
- Commonly asymptomatic
- Commonly associated with alcohol
- Hyperlipidaemia
- Obesity
- Diabetes mellitus
Nash: Non-alcoholic steatohepatitis
- Fat deposition and inflammation in the liver
- Can progress to cirrhosis

Nafld: Non-alcoholic fatty liver disease
- Fat deposition
- Does not require inflammation for the diagnosis
- Excludes alcohol as a cause

**Table 10.19** Risk factors for gallstones

<table>
<thead>
<tr>
<th>Risk factor</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Increasing age</td>
<td>Weight loss</td>
</tr>
<tr>
<td>♂ &gt; ♀</td>
<td>Contraceptive pill</td>
</tr>
<tr>
<td>Multiparity</td>
<td>Ileal resection/disease</td>
</tr>
<tr>
<td>Obesity</td>
<td>Diabetes</td>
</tr>
<tr>
<td>Diet high in animal fat</td>
<td></td>
</tr>
</tbody>
</table>

**Table 10.20** Drugs and the liver

**Drugs causing hepatitis**
- Isoniazid
- Methylldopa
- Enalapril
- Nifedipine
- Ketoconazole
- Volatile anaesthetics
- Rifampicin
- Atenolol
- Verapamil
- Amiodarone
- Cytotoxics

**Drugs causing cholestasis**
- Oestrogens
- Ciclosporin
- Chlorpromazine
- Cimetidine
- Erythromycin
- Imipramine
- Azathioprine
- Haloperidol
- Ranitidine
- Nitrofurantoin
- Hypoglycaemics

**Hypersensitivity-mediated damage**
- Sulphonamides
- Penicillins
- Amoxicillin
- Flucloxacillin
- NSAIDs
- Salicylates
- Diclofenac
- Allopurinol
- Phenytoin
- Diltiazem
- Antithyroid
- Carbimazole
- Propylthiouracil
- Miscellaneous
- Necrosis
- Carbon tetrachloride
- Paracetamol
- Salicylates
- Cocaine
- Fibrosis
- Methotrexate
- Retinoids
- Tumours
- High-oestrogen OCP
- Chronic hepatitis
- Methylldopa
- Isoniazid
- Nitrofurantoin

DISEASES OF THE BILIARY TREE

Gallstones (Table 10.19)
- 10–20% of the population
- Often an incidental finding at ultrasound

Types
- Cholesterol stones
- Bile pigment stones

Clinical features
- 80% asymptomatic
- Acute cholecystitis – impacted stone leading to inflammation → right hypochondrial and shoulder tip pain, fever, vomiting ± jaundice
- Biliary obstruction by a gallstone → pain and jaundice; ERCP may be required to remove stone

Complications
- Pancreatitis
- Biliary – enteric fistula
- Gallstone ileus

Cholangiocarcinoma
- Primary tumour of bile ducts
- → Obstructive jaundice

Primary sclerosing cholangitis
- Multiple bile duct strictures
- Associated with ulcerative colitis
- Increased risk of cholangiocarcinoma
- Investigations: MRCP, liver biopsy and ERCP

---

**Fig. 10.9** Paracetamol metabolism.
DRUGS AND THE LIVER

The liver is responsible for the initial metabolism of oral drugs (first-pass metabolism) prior to the drug reaching the systemic circulation. Many drugs are also metabolized or excreted by the liver after reaching the systemic circulation. As a result, drugs can be responsible for hepatic disease (see Table 10.20, Fig. 10.9).

SELF-ASSESSMENT QUESTIONS

Multiple choice questions (single best answer)

1. Which of the following is the likeliest cause of jaundice in a 24-year-old man in the UK?
   A. Cancer of the head of the pancreas
   B. Sulphonamide antibiotics
   C. Malaria
   D. Iron deficiency anaemia
   E. Epstein–Barr virus

2. Exudative ascites occurs secondary to:
   A. Ovarian cancer
   B. Alcohol misuse
   C. Anaemia
   D. Coeliac disease
   E. Hypoalbuminaemia

3. Which of the following is the most sensitive method of diagnosing *Helicobacter pylori* infection?
   A. Blood urease test
   B. Endoscopy and biopsy
   C. *H. pylori* antigen in stool
   D. $^{13}$C urea breath test
   E. Serum *H. pylori* antibodies

4. Which one of the following is most likely to cause hepatomegaly?
   A. Portal vein thrombosis
   B. Carcinoma of the head of the pancreas
   C. Burkitt’s lymphoma
   D. Primary biliary cirrhosis
   E. Right heart failure

5. Which one of the following is a common complication of chronic gastro-oesophageal reflux disease?
   A. Bronchospasm
   B. Headache
   C. Gastric ulcer
   D. Achalasia
   E. Squamous metaplasia

6. Which one of the following increases the risk of oesophageal carcinoma?
   A. Omeprazole
   B. Aspirin
   C. Acid reflux
   D. Ascorbic acid
   E. *H. pylori*
7. Which one of the following is a characteristic finding in Barrett’s oesophagus?
   A. The presence of goblet cells
   B. Transitional cell metaplasia of the oesophageal mucosa
   C. Increased risk of oesophageal squamous cell carcinoma
   D. Villous formation
   E. Mucosal dysplasia

8. Which one of the following is associated with oesophageal varices?
   A. Hyposplenism
   B. Acute viral hepatitis
   C. Nodular regeneration and fibrosis of the liver
   D. Portal hypotension
   E. Increased risk of bleeding with propranolol

9. Which one of the following increases oesophageal sphincter tone?
   A. Alcohol
   B. Nifedipine
   C. Achalasia
   D. Isosorbide mononitrate
   E. Botulinum toxin

10. Which of the following is the commonest cause of gastric ulcer?
    A. Ibuprofen
    B. Proton pump inhibitors
    C. Gastric lymphoma
    D. *H. pylori*
    E. Alendronate

11. Which of the following is associated with gastritis?
    A. Salmonella enteritidis
    B. Chlorpromazine
    C. Pantoprazole
    D. Renal failure
    E. Thyrotoxicosis

12. Which one of the following is true of gastric MALT lymphoma?
    A. Is a tumour arising from basophils in the gastric mucosa
    B. May be effectively treated by omeprazole, clarithromycin and amoxicillin
    C. Frequently metastasizes
    D. Can arise anywhere in the gastrointestinal tract
    E. Is a Hodgkin’s lymphoma

13. Which one of the following is associated with a decreased risk of gastric adenocarcinoma?
    A. High dietary ascorbic acid
    B. Active *H. pylori* infection
    C. Gastric intestinal metaplasia
    D. Smoking
    E. Coeliac disease

14. Which one of the following is useful in the management of peptic duodenal ulcers?
    A. Omeprazole
    B. Aspirin
    C. Gluten free diet
    D. Iron sulphate
    E. Mesalazine
15. Which one of the following is associated with coeliac disease?
   A. Steatohepatitis
   B. Colon cancer
   C. Hypersplenism
   D. Dermatitis herpetiformis
   E. Thiamine deficiency

16. Which one of the following is characteristic of coeliac disease?
   A. Crypt shortening
   B. Decreased lamina propria lymphocytes
   C. Villus shortening
   D. Crypt abscesses
   E. Jejunal ulceration

17. Which one of the following is true of carcinoid syndrome?
   A. Lung metastases result in right-sided cardiac valve lesions
   B. Flushing and diarrhoea usually occurs
   C. Octreotide is of little therapeutic use
   D. The primary tumour is commonly in the liver
   E. Elevated Serum 5-HIAA is diagnostic

18. Which one of the following would favour the diagnosis of ulcerative colitis rather than Crohn’s disease?
   A. Non-caseating granulomata
   B. Crypt abscesses
   C. Enterovesical fistula formation
   D. Oral ulceration
   E. Failure to respond to oral methotrexate

19. Which one of the following is a recognized manifestation of Crohn’s disease?
   A. Retinitis pigmentosa
   B. Erythema multiforme
   C. Discoid lupus erythematosus
   D. Dermatitis herpetiformis
   E. Uveitis

20. Which one of the following is a risk factor for the development of colorectal cancer?
   A. NSAID consumption
   B. Chronic idiopathic constipation
   C. Alcohol consumption
   D. Ulcerative colitis
   E. Diverticulosis

21. A 28-year-old man presents with increased stool frequency and rectal mucus. What is the most likely diagnosis?
   A. Diverticular disease
   B. Irritable bowel syndrome
   C. Tubulovillous adenoma of the rectum
   D. Colorectal cancer
   E. Thyrotoxicosis

22. Which one of the following symptoms is more suggestive of colonic carcinoma than irritable bowel syndrome?
   A. Rectal bleeding
   B. Weight loss
   C. Alternating diarrhoea and constipation
   D. Sensation of incomplete evacuation of stool
   E. Bloating
23. Which one of the following is most useful in the management of irritable bowel?
   A. Mebeverine
   B. Ibuprofen
   C. Phenelzine
   D. Prednisolone
   E. Mesalazine

24. Which one of the following causes diarrhoea?
   A. Iron sulphate
   B. Octreotide
   C. Vasoactive intestinal peptide (VIP)
   D. Loperamide
   E. Hypothyroidism

25. Which one of the following may cause increased stool frequency?
   A. Vagotomy
   B. Diabetes insipidus
   C. Smoking
   D. Hypercalcaemia
   E. Hyperparathyroidism

26. The following are clinical features of cirrhosis of the liver except:
   A. Palmar erythema
   B. Caput medusae
   C. Macrocytosis
   D. Portal hypotension
   E. Bruising

27. Which one of the following drugs causes abnormalities of liver function?
   A. Ursodeoxycholic acid
   B. Flucloxacillin
   C. Folic acid
   D. Verapamil
   E. Thyroxine

Multiple choice questions (true or false)

28. The following organisms cause diarrhoea mainly via the mechanism given:
   A. Cholera – mucosal inflammation
   B. *E. coli* – enterotoxin production
   C. *Campylobacter* – mucosal inflammation
   D. *Bacillus cereus* – colonic ulceration
   E. *Giardia* – malabsorption of water

29. The following are true of pseudomembranous colitis:
   A. Diagnosis is based on the presence of *Clostridium difficile* in stool
   B. It is best treated with intravenous vancomycin
   C. Risk of the disease is increased by intravenous cephalosporins
   D. It may result in bloody diarrhoea
   E. The causal bacterium is a normal commensal gut organism

30. The following are recognized causes of acute pancreatitis:
   A. Gallstones
   B. Prednisolone
   C. Thyroxine
31. The following are indicators of poor prognosis in acute pancreatitis:
   A. Glucose < 6 mmol/L
   B. Hypocalcaemia
   C. Hypoxia
   D. Albumin > 30 g/L
   E. $P_{CO_2}$ < 5 kPa

32. The following favour a diagnosis of pancreatic carcinoma over acute viral hepatitis in painless jaundice:
   A. Weight loss
   B. Dilated bile ducts on ultrasound scanning
   C. Elevated alkaline phosphatase
   D. Unconjugated hyperbilirubinaemia
   E. Bilirubin > 300 µmol/L

33. The following are associated with an elevated serum gastrin:
   A. Omeprazole therapy
   B. Zollinger–Ellison syndrome
   C. Hyperchlorhydria
   D. Vagotomy
   E. Hypoglycaemia

34. The following are causes of a conjugated hyperbilirubinaemia:
   A. Gilbert syndrome
   B. Carcinoma of the head of the pancreas
   C. Cholangiocarcinoma
   D. Viral hepatitis
   E. Haemolytic anaemia

35. The following are associated with acute hepatitis A infection:
   A. Elevated alanine transaminase
   B. Nausea and vomiting
   C. Bilirubin level always greater than 100 µmol/L
   D. Progression to chronic hepatitis
   E. Food-related outbreaks

36. The following statements are correct in the interpretation of hepatitis B serology:
   A. HBs (surface) antibody positive – previous exposure to infection
   B. HBe antigen positive – high infectivity risk
   C. HBc (core) antibody positive – seroconversion
   D. HBs antigen positive – successful immunization
   E. HBe antibody positive – seroconversion after acute infection

37. The following are associated with hepatitis C infection:
   A. Cryoglobulinaemia
   B. Hepatocellular carcinoma
   C. Primary sclerosing cholangitis
   D. Hepatic cirrhosis
   E. Ascites

38. The following are causes of viral hepatitis:
   A. Epstein–Barr virus
   B. Isolated hepatitis D virus
   C. Cytomegalovirus in immunosuppressed patients
   D. Coxackie virus
   E. Adenovirus
39. The following are causes of fulminant hepatic failure:
   A. Paracetamol
   B. Hepatitis A
   C. Aspirin in childhood
   D. Halothane
   E. Haemochromatosis

40. The following are causes of transudative ascites:
   A. Right heart failure
   B. Peritoneal tuberculosis
   C. Ovarian malignancy
   D. Nephrotic syndrome
   E. Liver cirrhosis

Extended matching questions

Question 1 Theme: Diarrhoea

A. *E. coli*
B. Thyrotoxicosis
C. Hypercalcaemia
D. Autonomic neuropathy
E. Laxative abuse
F. Osmotic diarrhoea
G. Ulcerative colitis
H. Tubulovillous adenoma
I. Diverticular disease
J. Coeliac disease
K. Giardiasis
L. Pseudomembranous colitis

For each of the following questions, select the best answer from the list above:

I. A 65-year-old man with known diabetes mellitus is reviewed as he has worsening diarrhoea. Upper gastrointestinal endoscopy, duodenal biopsy and colonoscopy were all normal. Stool culture carried out on three occasions did not reveal any abnormality. Blood testing revealed normal urea and electrolytes, calcium and liver function. What is the most likely cause for his diarrhoea?

II. A 38-year-old man is admitted with profuse mucus per rectum and generalized weakness. His potassium is noted to be 2.9 mmol/L. What is the most likely diagnosis?

III. A 27-year-old woman is admitted with abdominal discomfort, profuse bloody diarrhoea and a low-grade fever. Investigations reveal an iron deficiency anaemia. What is the most likely reason for her diarrhoea?

Question 2 Theme: Abdominal pain

A. Sigmoid volvulus
B. Acute appendicitis
C. Cholecystitis
D. Duodenal ulceration
E. Bowel ischaemia
F. Diverticulosis
G. Crohn’s disease
H. Irritable bowel syndrome
I. Acute pancreatitis
J. Colorectal carcinoma
Gastroenterology and hepatology

Pass Finals

260

K. Carcinoid syndrome
L. Ovarian cysts
M. Ectopic pregnancy

For each of the following questions, select the best answer from the list above:

I. A 76-year-old man complains of pain in the abdomen after eating. This is associated with mild diarrhoea. In the past he has had a myocardial infarction and several episodes of angina. He has type II diabetes mellitus. He smokes 20 cigarettes a day and drinks 10 units of alcohol a week. Suggest a likely cause for his pain.

II. A 32-year-old woman is referred by her GP with abdominal pain, nausea, weight loss and diarrhoea. She is also complaining of a bruise-like rash on her lower legs and mild joint pains. On examination she has multiple oral aphthous ulcers and tender bruise-like lesions over her shins. What is the cause of her abdominal pain?

III. A 47-year-old woman is referred with left iliac fossa pain, bloating and alternating diarrhoea and constipation. Her weight is gradually increasing. The discomfort comes and goes but is relieved by defaecation. What is the most likely diagnosis?

Question 3 Theme: Malabsorption

A. Pernicious anaemia
B. Coeliac disease
C. Whipple’s disease
D. Primary biliary cirrhosis
E. Chronic pancreatitis
F. Cystic fibrosis
G. Bacterial overgrowth
H. Surgery for ileal Crohn’s disease
I. Partial gastrectomy
J. Chronic alcohol-related liver disease
K. Carcinoma of the head of the pancreas

For each of the following questions, select the best answer from the list above:

I. A 15-year-old man is referred with a 6-year history of abdominal pain, bloating and weight loss. He is 1.78 m (5 feet 2 inches) tall and weighs 47 kg (7 stones 6 pounds). He has diarrhoea 2–3 times a day. What is the most likely diagnosis?

II. A 56-year-old woman is noted to be vitamin B_{12}-deficient and anaemic. She has known autoimmune hypothyroidism but is otherwise well. What is causing her B_{12} deficiency?

III. A 49-year-old man with a long history of alcohol abuse is reviewed due to worsening diarrhoea and abdominal pain. The stools are reported as foul-smelling and difficult to flush. His liver function tests are mildly deranged. What is the cause of his symptoms?

Question 4 Theme: Intestinal bleeding

A. Oesophageal varices
B. Gastric ulcer
C. Duodenal ulcer
D. Coeliac disease
E. Small bowel angiodysplasia
F. Meckel’s diverticulum
G. Terminal ileal Crohn’s disease
H. Caecal carcinoma
I. Diverticular bleeding
J. Haemorrhoids

For each of the following questions, select the best answer from the list above:

I. A 56-year-old man was admitted with haematemesis, melaena, hypotension and a tachycardia. He had recently been taking indomethacin for joint pains. What is the likeliest cause for his symptoms?

II. A 76-year-old woman was seen with 3 months of diarrhoea and weight loss. What is the most likely diagnosis?

III. A 32-year-old woman was seen with bright red bleeding. What is the likeliest diagnosis?
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STRUCTURE AND FUNCTION

The muscular skeletal system comprises bones, joints and connective tissues.

Connective tissues

- Cartilage
- Tendons
- Ligaments

Extracellular matrix

- Macromolecule matrix contained in all connective tissues
- Components:
  - Collagens
  - Elastin
  - Glycoproteins
  - Proteoglycans

Joints

- Synovial
- Fibrocartilaginous
- Fibrous

Synovial joints (see Fig. 11.1 for the components)

- Ball and socket joints, e.g. hip joint
- Hinge joints, e.g. interphalangeal

Fibrocartilaginous joints

- Intervertebral discs
- Sacroiliac joints
- Pubic symphysis
- Costochondral joints

EXAMINING THE MUSCULOSKELETAL SYSTEM

Examination should include all of the following and be done in roughly this order:

Examination of individual joints

- Ask the patient if the joint is painful; proceed with care if it is
  Look for:
- Swelling
**Examination of the hands**

- Expose both arms to the shoulders
- Ask if they are painful
- Describe particular features of osteoarthritis or rheumatoid arthritis if present (Table 11.1 and Fig. 11.2)
- Then proceed as for individual joints above
- Also examine the nails and feel for nodules on the forearms

**Examination of the gait**

- Ask the patient to walk a short distance away from you, turn, walk towards you and stand still
Table 11.1 Some common particular features of osteoarthritis and rheumatoid arthritis in the hands

<table>
<thead>
<tr>
<th>Hand joints usually affected</th>
<th>Particular features</th>
</tr>
</thead>
<tbody>
<tr>
<td>Osteoarthritis</td>
<td></td>
</tr>
<tr>
<td>DIP joints (Heberden’s nodes)</td>
<td></td>
</tr>
<tr>
<td>PIP joints (Bouchard’s nodes)</td>
<td></td>
</tr>
<tr>
<td>Carpometacarpal joint</td>
<td>Square hand</td>
</tr>
<tr>
<td>Rheumatoid arthritis</td>
<td></td>
</tr>
<tr>
<td>PIP joints</td>
<td>Ulnar deviation</td>
</tr>
<tr>
<td>MCP joints</td>
<td>Palmar subluxation of MCP joints</td>
</tr>
<tr>
<td></td>
<td>Fixed flexion of PIP joints (Boutonnière deformity)</td>
</tr>
<tr>
<td></td>
<td>Fixed hyperextension of PIP joints (swan neck deformity)</td>
</tr>
</tbody>
</table>

Fig. 11.2 The hands in arthritis. (a) Nodal osteoarthritis. Heberden’s and Bouchard’s nodes and squaring of the thumb bases. The synovial joints are seen. (b) Rheumatoid arthritis.
### Table 11.2 Comparison of osteoarthritis and rheumatoid arthritis

<table>
<thead>
<tr>
<th>Description</th>
<th>Osteoarthritis (OA)</th>
<th>Rheumatoid arthritis (RA)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Description</td>
<td>Pain and disability associated with joint space narrowing; altered cartilage osteophyte formation</td>
<td>Systemic disease with chronic, symmetrical polyarthritis synovitis; non-articular features</td>
</tr>
<tr>
<td>Epidemiology</td>
<td>Most common type of arthritis</td>
<td>0.5–1% of the population (falling)</td>
</tr>
<tr>
<td></td>
<td>Prevalence increases with age</td>
<td>Presents at all ages</td>
</tr>
<tr>
<td></td>
<td>X-ray OA very common &gt;60 years</td>
<td>Commonly presents 30–50 years</td>
</tr>
<tr>
<td></td>
<td></td>
<td>♀ &gt; ♂ before menopause</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Familial or sporadic</td>
</tr>
<tr>
<td></td>
<td></td>
<td>HLA-DR4 in 50–70%</td>
</tr>
<tr>
<td>Aetiology</td>
<td>Primary idiopathic</td>
<td>Unexplained</td>
</tr>
<tr>
<td></td>
<td>Secondary:</td>
<td>T cell activation</td>
</tr>
<tr>
<td></td>
<td>Trauma, e.g. previous fracture</td>
<td>Presence of rheumatoid factors</td>
</tr>
<tr>
<td></td>
<td>Chondrocalcinosis</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Haemochromatosis</td>
<td></td>
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<tr>
<td></td>
<td>Acromegaly</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Haemophilia</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Avascular necrosis, e.g. steroids</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Sickle cell disease</td>
<td></td>
</tr>
<tr>
<td>Clinical features</td>
<td>Joint pain/swelling/instability</td>
<td>Slow onset but progressive</td>
</tr>
<tr>
<td></td>
<td>Morning stiffness</td>
<td>Symmetrical peripheral polyarthritis</td>
</tr>
<tr>
<td></td>
<td>Joint effusion and crepitus</td>
<td>Joint pain and morning stiffness</td>
</tr>
<tr>
<td></td>
<td>Bony swelling</td>
<td>Eased by gentle activity</td>
</tr>
<tr>
<td></td>
<td>Muscle wasting</td>
<td>Joints warm and tender</td>
</tr>
<tr>
<td></td>
<td>Limitation of movement and loss of function</td>
<td>Limitation of movement and deformity</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Joint effusion</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Muscle-wasting</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Lethargy, malaise</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Non-articular features (Fig. 11.3)</td>
</tr>
</tbody>
</table>
**Clinical subtypes**

**Nodal OA**
- Develops in late middle age
- Polyarticular involvement of the hand
- Particularly distal interphalangeal joints (Heberden’s nodes)
- Generally good long-term functional outcome
- Predisposes to OA of the knee, hip and spine
- X-ray – marginal osteophyte and joint space loss

**Erosive OA**
- Rare
- DIP and PIP joints
- Poor functional outcome
- X-ray – marked subchondral cysts
- May develop into rheumatoid arthritis

**Generalized OA**
- May occur in combination with nodal OA
- Hands, knees, first MTP joints and hips

---

**Fig. 11.3** Non-articular manifestations of rheumatoid arthritis.
Familial
♀ >> ♂
May be autoimmune
Large joint OA
Knees and hips

Crystal-associated OA (chondrocalcinosis)
- Calcium pyrophosphate crystal deposition
- Knees and wrists commonly affected
- X-ray – may show calcification in the cartilage

Investigations
- Inflammatory markers not elevated
- No autoantibodies
- X-rays abnormal if damage severe
- MRI can show early cartilage changes
- Arthroscopy – early fissuring and cartilage surface erosion

Management
- Treat symptoms and disability, not X-rays
- Explain diagnosis and reassure
- Weight loss and exercise
- Hydrotherapy (particularly lower limb joints)
- Heat/massage
- Analgesia
- Patients often use complementary medicine
- Joint replacements/other surgery

Rheumatoid arthritis

See Table 11.1 and 11.2 and Figures 11.2 and 11.3.

Clinical subtypes

Palindromic
- Monoarticular
- Progresses to other types

Transient
- Self-limiting
- Usually Rh factor-negative

Remitting
- Active for years then remits

Chronic persistent
- Most typical form
- Relapsing and remitting

Rapidly progressive
- Remorseless
- Progressive
- Rh factor-positive
- ACPA (anti-citrullinated peptide antibodies)-positive, are a better predictor for prognosis
- Associated with non-articular fractures

Investigations
- Anaemia
- ↑ inflammatory markers
- Rheumatoid factors (in 70%)
- X-rays – erosions
Management
- Explain diagnosis and reassure
- Multidisciplinary team approach
- NSAIDs and analgesics
- Disease-modifying antirheumatic drugs (DMARDs):
  - Sulphasalazine
  - Methotrexate
  - Leflunomide
- Anti-TNF drugs:
  - Etanercept
  - Infliximab
  - Adalimumab
- Corticosteroids (see Table 11.3 for side-effects)
- Less commonly used:
  - Gold
  - Penicillamine
  - Hydroxychloroquine
  - Azathioprine
  - Ciclosporin
  - Anakinra
  - Joint replacements/other surgery

Septic arthritis

Aetiology
- Direct injury
- Blood-borne infection
- → Susceptibility in
  - Chronically inflamed joints
  - Immunosuppressed patients
  - Artificial joints

Organisms
- *Staphylococcus aureus*
- *Streptococcus* and other *staphylococci*
- *Neisseria gonorrhoeae*
- *Haemophilus influenzae*
- Gram-negative organisms

Clinical features
- Joint pain
- Muscle spasm

**Table 11.3 Side-effects of steroids**

<table>
<thead>
<tr>
<th>General</th>
<th>Cardiovascular</th>
</tr>
</thead>
<tbody>
<tr>
<td>Weight gain</td>
<td>Hypertension</td>
</tr>
<tr>
<td>Fluid retention</td>
<td>Eyes</td>
</tr>
<tr>
<td>Skin</td>
<td>Cataracts</td>
</tr>
<tr>
<td>Acne</td>
<td>Bones</td>
</tr>
<tr>
<td>Thin skin with</td>
<td>Osteoporosis</td>
</tr>
<tr>
<td>easy bruising</td>
<td></td>
</tr>
<tr>
<td>Endocrine</td>
<td></td>
</tr>
<tr>
<td>Diabetes</td>
<td></td>
</tr>
<tr>
<td>Cushing syndrome</td>
<td></td>
</tr>
</tbody>
</table>
● Joint hot, red and swollen
● Signs of the source of infection

Investigations
● Urgent joint aspiration
  • Microscopy and culture/gram stain
● Elevated white cell count
● Blood cultures

Management
● Two i.v. antibiotics for 2 weeks (start antibiotics immediately diagnosis suspected)
● Followed by 6 weeks of oral antibiotics
● Initial immobilization of the joint
● Early physiotherapy
● Consider surgical drainage and washout

Seronegative spondyloarthropathies
● Conditions affecting the spine and peripheral joints which cluster in families and are associated with HLA-B27

Ankylosing spondylitis
● Episodic inflammation of spine and sacroiliac joints
● Asymmetrical large joint arthritis
● HLA-B27 in >90%
● Associated with uveitis and costochondritis
● Inflammatory markers elevated
● X-rays
  • Erosions and sclerosis of affected joints
  • Syndesmophytes
  • Bamboo spine
● Treated with preventative exercises and NSAIDs, TNF-α blocking drugs if severe

Psoriatic arthritis

Clinical features
● Arthritis in association with psoriasis
● May predate skin lesions
● DIP most common joints affected
● Dactylitis
● Erosions on X-rays (centre of joint unlike juxta-articular erosions in RA)
● 5% have arthritis mutilans
● Nail dystrophy in 85% of cases
● HLA-B27 in 50%

Management
● Treated with:
  • NSAIDs
  • Steroid injections to joints
  • Sulfasalazine
  • Methotrexate/ciclosporin
  • TNF-α blocking drugs, e.g. infliximab

Reactive arthritis
● Sterile synovitis following dysentery or a sexually acquired infection
Aetiology
- Trigger organism
  - *Salmonella*
  - *Shigella*
  - *Yersinia*
  - *Chlamydia*
  - *Ureaplasma*

Clinical features
- Acute asymmetrical lower limb arthritis
- ♂ > ♀
- Often also an enthesitis, e.g. plantar fasciitis
- Non-articular features
  - Acute anterior uveitis (see above)
  - Circinate balanitis
  - Keratoderma blenorrhagica
  - Nail dystrophy
  - Conjunctivitis
- Reiter’s disease = urethritis, arthritis and conjunctivitis

Management
- Treatment usually symptomatic with NSAIDs or steroid injections
- Treat underlying infection with antibiotics

**Inflammatory bowel disease (IBD)-associated arthritis**
- 10–15% of patients with IBD
- Lower limb joints
- In ulcerative colitis treatment of bowel disease may improve arthritis
- In Crohn’s disease, arthritis persists even when bowel is disease inactive
- 5% have sacroiliitis (independent of activity of IBD)
- Treatment with intra-articular steroids and sulfasalazine

Gout
- Inflammatory arthritis associated with hyperuricaemia and urate crystal deposition

Epidemiology
- 5% of population have hyperuricaemia
- 0.2% of population have gout
- ♂ > ♀
- Commonly presents between 30 and 50 years
- Rare in women before the menopause
- Familial or sporadic
- HLA-DR4 positive in 50–70%

Aetiology
- Causes of hyperuricaemia (Table 11.4)

Clinical features
- Acute onset
- Acute painful, red, swollen joint
- Often affects first MTP joint
- Precipitated by
  - Alcohol
  - Excess food
Dehydration
Diuretics

Investigations
- Joint fluid microscopy – needle-shaped crystals
- Serum urate
- Urea and electrolytes

Management
- NSAIDs
- Colchicine (particularly if NSAIDs cannot be used)
- If attacks are frequent give allopurinol to reduce urate 4–6 weeks after acute attack
- Lifestyle advice, e.g. diet, reduce alcohol intake

Chronic tophaceous gout
- Very high serum urate
- White urate deposits (tophi) in skin particularly ear lobes and around joints
- Associated with renal failure or use of diuretics

AUTOIMMUNE RHEUMATIC DISEASE

Systemic lupus erythematosus (SLE)
- Inflammatory multisystem disorder with arthralgia and rashes as common symptoms, and cerebral and renal disease as serious problems
Autoimmune rheumatic disease

Epidemiology
- ♂ > ♀
- Black > Caucasian
- Peak age of onset 20–40 years

Aetiology
- Familial
- ↑ HLA-B8 and DR3 in Caucasians
- Inherited deficiency of complement (C2 and 4)
- Related to female sex hormones
- Loss of immunological tolerance
- Environmental triggers
  - Drugs – hydralazine, isoniazid, methyldopa, oral contraceptive pill/HRT
  - Ultraviolet light

Clinical features
- The result of vasculitis (Fig. 11.4)

Fig. 11.4 Clinical features of systemic lupus erythematosus.
**Investigations**

**Blood tests**
- Normochromic normocytic anaemia
- Leucopenia
- Thrombocytopenia
- ± Autoimmune haemolytic anaemia
- ↑ ESR
- Normal CRP
- Antinuclear antibody (ANA) positive
- Double-stranded DNA positive in 50%, SLE-specific
- Low complement during attacks
- Rh factor-positive in 30–50%
- False positive syphilis serology
- Raised IgG and M

**Histology**
- e.g. Renal biopsy
- Characteristic histology and immunofluorescence

**CT/MRI**
- e.g. Brain, may show infarcts/haemorrhage

**Management**
- Explain diagnosis
- Avoid UV light if photosensitive
- NSAIDs for arthralgia
- Antimalarials (e.g. chloroquine) for skin and joint disease
- Steroids for active disease
- Immunosuppressants
  - Azathioprine/cyclophosphamide/mycophenolate if severe

**Course and prognosis**
- Episodic
- Periods of complete remission
- 10-year survival 90%

**Antiphospholipid syndrome**
- A syndrome associated with the presence of antibodies to phospholipids

**Clinical features**
- Arterial and venous thromboses
- Recurrent miscarriage
- Thrombocytopenia
- Chorea, migraine and epilepsy
- Valvular heart disease
- Skin disease, e.g. livedo reticularis
- A few patients will have SLE

**Investigation**
- Anticardiolipin antibodies
- Lupus anticoagulant antibodies
- ESR and ANA usually normal
- Prolonged APTT

**Management**
- Aggressive anticoagulation
  - Aspirin
  - Heparin/warfarin
Autoimmune rheumatic disease

Systemic sclerosis

- A rare multisystem disease with widespread obliterative damage to small blood vessels associated with fibrosis of the skin and internal organs

Clinical features

Raynaud’s phenomenon

- 97% of cases
- Arterial spasm of hands and feet
- Three phases
  - Pallor
  - Cyanosis
  - Erythema
- Numbness and pain

Skin

- Hands, face, feet, forearms
- Tight, waxy and tethered
- ‘Beaking’ of nose
- Microstomia
- Digital ulcers
- Telangiectasia
- Nail fold capillary loops

GI Tract

- Oesophagus
  - Reflux
  - Poor motility
  - Dilatation
- Small bowel
  - Bacterial overgrowth
  - Malabsorption

Renal

- Renal failure
- Malignant hypertension

Cardiorespiratory system

- Pulmonary fibrosis (common cause of death)
- Primary or secondary pulmonary hypertension
- Arrhythmias
- Conduction defects
- Pericarditis

Crest syndrome (Limited cutaneous scleroderma – LcSSc)

- Calciosisis (calcium deposits in skin and elsewhere)
- Raynaud’s phenomenon
- Oesophageal involvement
- Sclerodactyly
- Telangiectasia

Investigations

- Normocytic normochromic anaemia
- Urea and electrolytes and urinalysis including creatinine clearance
- Autoantibodies
  - Speckled/nucleolar/anticentromere – 79–80%
  - Rheumatoid factor – 30%
- Chest X-ray – reticulonodular shadowing
- Other tests according to organ involved
Management
- Education, counselling and family support
- Hand-warmers and vasodilators for Raynaud’s
- Proton pump inhibitors and motility agents
- Antibiotics and nutritional supplements
- Antihypertensives
- i.v. prostacyclin

**VASCULITIS**
- Inflammation of blood vessel walls (Table 11.5)

**BONE DISEASE (TABLE 11.6)**

**Osteoporosis**
- Low bone mass and micro-architectural deterioration of bone leading to bone fragility and increased fracture risk
- In osteoporosis the bone is mineralized normally but deficient in quantity and quality, including structural integrity

**Epidemiology**
- Common problem
- Lifetime risk of hip fracture in:
  - ♀ aged 50 years – 15%
  - ♂ aged 50 years – 5%

**Risk factors**
See Table 11.7.

**Clinical features**

**Vertebral crush fractures**
- Back pain
- Weight loss
- Kyphosis

**Fractures associated with falls**
- Colles’ fracture
- Fractured neck of femur

**Investigations**
- Ca**, PO₄ and alkaline phosphatase normal
- X-rays identify fractures
- DXA scanning
  - Measurement of bone density in lumbar spine and neck of femur
  - Osteoporosis is defined as bone density <2.5 SDs below the mean value of age-, sex- and race-matched controls
- Bone scan differentiates from bony metastases

**Management**
- Prevention
- Identification and monitoring of patients at risk

**Non-drug therapies**
- Diet rich in calcium and vitamin D
- Exercise
- Stopping smoking
- Reducing the risk of falls
<table>
<thead>
<tr>
<th>Name</th>
<th>Type of vessel</th>
<th>Clinical features</th>
<th>Diagnosis</th>
<th>Treatment</th>
</tr>
</thead>
</table>
| Giant cell arteritis (GCA) and polymyalgia rheumatica (PMR) | Large vessel (e.g. temporal artery) | >50 years  
GCA  
Headache  
Scalp tenderness  
Jaw claudication  
Malaise, tiredness  
Fever  
Sudden painless vision loss  
PMR  
Pain and stiffness in shoulders, neck, hips and spine  
Malaise  
Tiredness  
Fever  
Weight loss  
Depression  
Worse in mornings | Raised ESR  
Temporal artery biopsy (shows a giant cell arteritis) | Steroids |
| Polyarteritis nodosa | Medium-sized vessels | Middle-aged men usually  
Fever  
Malaise  
Weight loss  
Myalgia  
Neurological (mononeuritis multiplex)  
Abdominal (GI bleeding, infarction of viscera)  
Renal (hypertension and acute kidney injury)  
Cardiac (myocardial infarction and heart failure)  
Skin (gangrene, livedo reticularis) | Raised ESR  
Renal/hepatic/gut microaneurysms  
ANCA-usually negative | Steroids Azathioprine |
<table>
<thead>
<tr>
<th>Name</th>
<th>Type of vessel</th>
<th>Clinical features</th>
<th>Diagnosis</th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>ANCA-positive vasculitis</strong></td>
<td>Small vessels</td>
<td>Wegener’s (Granulomatosis with polyangiitis) and Churg–Strauss syndrome</td>
<td>ANCA</td>
<td>Steroids, Immunosuppressants</td>
</tr>
<tr>
<td>Wegener’s granulomatosis</td>
<td></td>
<td>Microscopic polyarteritis</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Churg–Strauss syndrome</td>
<td></td>
<td>Crescentic glomerulonephritis</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Microscopic polyangiitis</td>
<td></td>
<td>Associated with hepatitis B</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Non-ANCA vasculitis</strong></td>
<td>Small vessels</td>
<td>Henoeh-Schönlein purpura</td>
<td>Most self-limiting</td>
<td>Steroids if severe</td>
</tr>
<tr>
<td>Henoch-Schönlein purpura</td>
<td></td>
<td>Children mostly, after upper respiratory tract infection</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cryoglobulinaemic vasculitis</td>
<td></td>
<td>Purpura</td>
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<td></td>
<td></td>
<td>Polyarthritis</td>
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<td></td>
<td></td>
<td>Abdominal pain</td>
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<td></td>
<td></td>
<td>Glomerulonephritis</td>
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<td></td>
<td></td>
<td>Purpura</td>
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<tr>
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<td></td>
<td>Glomerulonephritis</td>
<td></td>
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<tr>
<td></td>
<td></td>
<td>Arthralgia, hepatitis C</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Behçet’s disease</strong></td>
<td>Small and large vessels</td>
<td>Japan, Turkey, Iran and countries bordering the Mediterranean</td>
<td>Pathergy reaction</td>
<td>Steroids, Ciclosporin, Colchicine, Thalidomide (not in pregnancy), Anti-TNF for severe cases</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Recurrent oral and genital ulceration</td>
<td></td>
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<tr>
<td></td>
<td></td>
<td>Uveitis</td>
<td></td>
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<tr>
<td></td>
<td></td>
<td>Erythema nodosum</td>
<td></td>
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</tr>
<tr>
<td></td>
<td></td>
<td>Papulopustular and pseudofolliculitis skin lesions</td>
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<tr>
<td></td>
<td></td>
<td>Arthritis</td>
<td></td>
<td></td>
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<tr>
<td></td>
<td></td>
<td>GI symptoms</td>
<td></td>
<td></td>
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<tr>
<td></td>
<td></td>
<td>Neurological symptoms</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Pathergy reaction</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Bone disease

**Drugs**
- Calcium and vitamin D supplements
- Bisphosphonates
- Raloxifene
- Recombinant human parathyroid hormone peptide 1–34
- Strontium
- Androgens in hypogonadal men

**Osteomalacia**
- Defective bone mineralization associated with low levels of vitamin D
- In children, the effects on the growth plates lead to rickets

**Aetiology**
See Table 11.8.

---

### Table 11.6 Biochemical abnormalities in common bone disorders

<table>
<thead>
<tr>
<th>Disease</th>
<th>Ca(^ {++})</th>
<th>PO(_4)</th>
<th>Alkaline phosphatase</th>
</tr>
</thead>
<tbody>
<tr>
<td>Osteoporosis</td>
<td>→</td>
<td>→</td>
<td>→</td>
</tr>
<tr>
<td>Osteomalacia</td>
<td>↓</td>
<td>↓</td>
<td>↑</td>
</tr>
<tr>
<td>Paget’s disease</td>
<td>→</td>
<td>→</td>
<td>↑</td>
</tr>
<tr>
<td>Bony secondary deposits</td>
<td>↑</td>
<td>↑ or →</td>
<td>↑</td>
</tr>
</tbody>
</table>

### Table 11.7 Osteoporosis risk factors, associated disease and drug therapies

<table>
<thead>
<tr>
<th>Risk factors</th>
<th>Disease</th>
</tr>
</thead>
<tbody>
<tr>
<td>Female sex</td>
<td>Endocrine</td>
</tr>
<tr>
<td>Increasing age</td>
<td>Cushing syndrome</td>
</tr>
<tr>
<td>Early menopause (including surgical)</td>
<td>Hyperparathyroidism</td>
</tr>
<tr>
<td>White race/Asian</td>
<td>Hypogonadism (including orchidectomy)</td>
</tr>
<tr>
<td>Slender habitus</td>
<td>Acromegaly</td>
</tr>
<tr>
<td>Lack of exercise/immobility</td>
<td>Type I diabetes mellitus</td>
</tr>
<tr>
<td>Smoking</td>
<td>Joints</td>
</tr>
<tr>
<td>Family history</td>
<td>Rheumatoid arthritis</td>
</tr>
<tr>
<td>Excess alcohol</td>
<td>Other</td>
</tr>
<tr>
<td>Nutrition (very low calcium diet, high protein intake for a long time)</td>
<td>Chronic kidney disease</td>
</tr>
<tr>
<td>Drug therapy</td>
<td>Chronic liver disease</td>
</tr>
<tr>
<td>Corticosteroids</td>
<td>Mastocytosis</td>
</tr>
<tr>
<td>Heparin</td>
<td>Anorexia nervosa</td>
</tr>
<tr>
<td>Ciclosporin</td>
<td>Inflammatory bowel disease</td>
</tr>
<tr>
<td>Cytotoxic therapy</td>
<td></td>
</tr>
</tbody>
</table>

---
Clinical features

Adults
- Bone/muscle pain and tenderness
- Subclinical fractures
- Proximal myopathy
- Tetany (low calcium)

Children
- Bowed legs
- ‘Rickety rosary’ costochondritis
- Myopathy

Investigations
- ↓ Ca++, ↓ PO₄, ↑ alkaline phosphatase
- ↓ 25-hydroxy vitamin D
- X-ray – defective mineralization
- ‘Looser’s zones’ on X-ray

Management
- Correction of cause
- Replacement of vitamin D

Paget’s disease
- Disorder of bone remodelling associated with excessive bone resorption and excess structurally abnormal new bone formation

Epidemiology
- Europe (especially northern England) » USA/Africa
- Patients >40 years
- Asymptomatic X-ray evidence very common
- Patients less commonly have symptoms
Aetiology
- Genetic component
- Geographical/ethnic clusters
- Viral aetiology has been suggested

Clinical features
- Commonly none
- Bone pain (spine/pelvis)
- Joint pain (near to involved bone)
- Deformities (tibia and skull)

Complications
- Nerve compression
  - VIIIth cranial nerve leads to deafness
  - Also IIInd, Vth and VIIth cranial nerves
- Increased bone blood flow
  - → High-output cardiac failure
- Pathological fractures
- Osteogenic sarcoma (<1%)

Investigations
- Normal Ca\(^{++}\) and PO\(_4\)\(^{-}\), ↑ alkaline phosphatase
- X-rays – excess abnormal bone

Management
- Simple analgesics for pain
- Bisphosphonates
- Surgery, e.g. joint replacement/osteotomy

DISORDERS OF CALCIUM METABOLISM

Hypercalcaemia

Aetiology
See Table 11.9.

Clinical features
- Tiredness
- Malaise
- Depression
- Renal stones
- Polyuria
- Bone pains
- Abdominal pain
- Peptic ulcer disease
- Ectopic calcification, e.g. corneal

Investigations
- Ca\(^{++}\), PO\(_4\)\(^{-}\), alkaline phosphatase
- Urea and electrolytes
- Chest X-ray
- Parathormone (PTH)
- Thyroid-stimulating hormone (TSH)
- Serum electrophoresis

Management
- Rectify cause
- i.v. Saline rehydration
- Bisphosphonates
Hypocalcaemia

**Aetiology**
See Table 11.9.

**Clinical features**
- Paraesthesiae
- Circumoral numbness
- Cramps
- Anxiety
- Tetany
- Fits
- Dystonia
- Psychosis
- Chvostek’s sign – tapping over the facial nerve produces twitching of facial muscles
- Trousseau’s sign – compression of the upper arm (e.g. with blood pressure cuff) produces tetany spasms of the hands

**Investigations**
- Ca++, PO4, alkaline phosphatase
- Urea and electrolytes
- X-rays

### Table 11.9 Causes of hypercalcaemia

<table>
<thead>
<tr>
<th>Cause</th>
<th>Description</th>
</tr>
</thead>
</table>
| Excessive parathormone (PTH) secretion | Primary hyperparathyroidism (commonest by far), adenoma, hyperplasia or carcinoma  
Tertiary hyperparathyroidism  
Ectopic PTH secretion (very rare indeed) |
| Excess action of vitamin D | Iatrogenic or self-administered excess  
Granulomatous diseases, e.g. sarcoidosis, TB  
Lymphoma |
| Excessive calcium intake | ‘Milk-alkali’ syndrome |
| Malignant disease (second commonest cause) | Secondary deposits in bone  
Production of osteoclastic factors by tumours  
PTH-related protein secretion  
Myeloma |
| Other endocrine disease (mild hypercalcaemia only) | Thyrotoxicosis  
Addison’s disease |
| Drugs | Thiazide diuretics  
Vitamin D analogues  
Lithium administration (chronic)  
Vitamin A |
| Miscellaneous | Long-term immobility  
Familial hypocalciuric hypercalcaemia |
Parathyroid hormone
- Vitamin D

Management
- Rectify cause
- Calcium/vitamin D

DISORDERS OF COLLAGEN
- Collagen is part of the extracellular matrix
- It consists of three polypeptide chains wound round one another in a triple helical conformation

Ehlers–Danlos syndrome
- Ten different types, mainly autosomal dominant
- Varying degrees of
  - Skin fragility
  - Skin hyperextensibility
  - Joint hypermobility

Clinical features
- Easy bruising
- Extensible velvety skin
- Hypermobile joints

Pseudoxanthoma elasticum
- Abnormal collagen and elastin

**Table 11.10 Causes of hypocalcaemia**

<table>
<thead>
<tr>
<th>Causes of hypocalcaemia</th>
</tr>
</thead>
<tbody>
<tr>
<td>Increased phosphate levels</td>
</tr>
<tr>
<td>Chronic kidney disease (common)</td>
</tr>
<tr>
<td>Phosphate therapy</td>
</tr>
<tr>
<td>Hypoparathyroidism</td>
</tr>
<tr>
<td>Surgical – after neck exploration (thyroidectomy parathyroidectomy – common)</td>
</tr>
<tr>
<td>Congenital deficiency (DiGeorge syndrome)</td>
</tr>
<tr>
<td>Idiopathic hypoparathyroidism (rare)</td>
</tr>
<tr>
<td>Severe hypomagnesaemia</td>
</tr>
<tr>
<td>Vitamin D deficiency</td>
</tr>
<tr>
<td>Osteomalacia</td>
</tr>
<tr>
<td>Vitamin D resistance</td>
</tr>
<tr>
<td>Resistance to PTH</td>
</tr>
<tr>
<td>Pseudohypoparathyroidism</td>
</tr>
<tr>
<td>Drugs</td>
</tr>
<tr>
<td>Calcitonin</td>
</tr>
<tr>
<td>Bisphosphonates</td>
</tr>
<tr>
<td>Miscellaneous</td>
</tr>
<tr>
<td>Acute pancreatitis (quite common)</td>
</tr>
<tr>
<td>Citrated blood in massive transfusion (not uncommon)</td>
</tr>
<tr>
<td>Malabsorption, e.g. coeliac disease</td>
</tr>
</tbody>
</table>
Clinical features
Skin
- Loose, lax, wrinkled (‘plucked chicken skin’)
- Particularly in the flexures

Other
- GI bleeding
- Angioid streaks in the eye
- Early myocardial infarction
- Claudication

Marfan syndrome
- Autosomal dominant
- Mutation of the collagen fibrillin
- Chromosome 15

Clinical features
- Tall stature
- Arachnodactyly (long thin digits)
- Long arm span
- High arched palate
- Recurrent joint dislocations
- Inguinal/femoral herniae
- Spontaneous pneumothorax
- Emphysema
- Aortic/mitral incompetence
- Aortic aneurysm
- Dislocation of the lens

SELF-ASSESSMENT QUESTIONS

Multiple choice questions (single best answer)

1. The following are features of osteoarthritis but not rheumatoid arthritis:
   A. Joint swelling
   B. Heberden’s nodes
   C. More common in women
   D. Negative rheumatoid factor
   E. Treatment may include joint replacements

2. In rheumatoid arthritis:
   A. 90% of patients have positive rheumatoid factors
   B. Infliximab is used as treatment in all patients
   C. HLA DR4 is present in 25%
   D. T cells are activated
   E. X-rays demonstrate the presence of osteophytes

3. In septic arthritis:
   A. Artificial joints are not affected
   B. Gram-positive organisms are usually the cause
   C. The joint is not usually swollen
   D. Immunosuppressants are used as treatment
   E. Treatment should wait for results of antibiotic sensitivities

4. Regarding autoantibodies:
   A. ANA occurs in 90% of cases of antiphospholipid syndrome
   B. Rheumatoid factor occurs in 40% of cases of systemic lupus erythematosus (SLE)
C. Rheumatoid factor occurs in 90% of cases of systemic sclerosis
D. Double-stranded DNA is specific for SLE
E. Anticentromere antibodies occur in 20% of cases of systemic sclerosis

5. Which of the following is seen in systemic sclerosis:
A. Butterfly skin rash
B. Pleural effusion
C. Thrombocytopenia
D. Hemiplegia
E. ‘Beaking’ of the nose

6. In systemic sclerosis:
A. Steroids are used
B. Malabsorption is caused by villous atrophy
C. Pulmonary fibrosis is a common cause of death
D. Raynaud’s phenomenon occurs in few cases
E. Hands are rarely affected

7. In osteoporosis:
A. Plasma calcium may be low
B. Diagnosis is made when bone density rises 2.5 SDs above the mean for sex- and race-matched controls
C. Fracture risk can be reduced by bisphosphonates
D. Men and women are equally affected
E. Calcaneal fractures are common

8. In polymyalgia rheumatica:
A. The ESR is usually low
B. There can be an association with giant cell arteritis
C. Disease is unresponsive to steroids
D. Weight loss makes the diagnosis unlikely
E. Symptoms are worse at night

9. Osteomalacia:
A. Is treated with steroids
B. Is associated with normal bone biochemistry
C. Does not cause myopathy
D. Can be caused by inadequate exposure to sunlight
E. Is rare in primary biliary cirrhosis

10. Causes of hypocalcaemia include:
A. Secondary deposits in bone
B. Addison’s disease
C. Hyperparathyroidism
D. Thiazide diuretics
E. Massive blood transfusion

11. In hypocalcaemia:
A. Tapping on the facial nerve may induce twitching of the facial muscles
B. Tetany does not occur
C. Treatment with bisphosphonates can be useful
D. Treatment with calcitonin can be useful
E. i.v. Calcium is contraindicated

12. In relation to serum bone biochemistry which statement is incorrect?
A. Calcium is normal and alkaline phosphatase elevated in Paget’s disease
B. Phosphate is high in hypocalcaemia associated with chronic kidney disease
C. Calcium is low and alkaline phosphatase elevated in osteomalacia  
D. Calcium is low in hyperparathyroidism  
E. Calcium is high and phosphate low in hyperparathyroidism

Extended matching questions

Question 1 Theme: Back pain
A. Osteoporosis  
B. Osteoarthritis  
C. Rheumatoid arthritis  
D. Ankylosing spondylitis  
E. Gout  
F. Reactive arthritis  
G. Systemic lupus erythematosus  
H. Osteomalacia  
I. Paget’s disease

For each of the following questions, select the best answer from the list above:

I. A 28-year-old male who has intermittent episodes of back pain has a raised ESR and is HLA-B27-positive. X-rays show syndesmophytes. What is the most likely diagnosis?  
II. A 60-year-old male smoker presents with progressive increasing episodes of back pain. His symptoms are worse in the mornings when he has stiffness. X-rays show no erosions. The ESR and alkaline phosphatase are normal. What is the most likely diagnosis?  
III. A 72-year-old female presents with an episode of severe back pain. She fractured her wrist recently during a fall and has a long history of asthma. She has normal alkaline phosphatase and calcium. What is the most likely diagnosis?

Question 2 Theme: Painful hands
A. Systemic sclerosis  
B. Osteoarthritis  
C. Rheumatoid arthritis  
D. Gout  
E. Reactive arthritis  
F. Systemic lupus erythematosus  
G. Septic arthritis  
H. Psoriatic arthritis

For each of the following questions, select the best answer from the list above:

I. A 56-year-old businessman has acute episodes of pain in the joints of his hands and feet. The episodes occur particularly in the distal and interphalangeal joints of the hands and first metatarsophalangeal joint of the great toe. His body mass index is 30 and the serum urate is elevated. What is the most likely diagnosis?  
II. A 35-year-old female presents with episodes of pain in the metacarpophalangeal joints of the hands. She has a fever and a rash on the face and the following blood results: rheumatoid factor positive, antinuclear antibody positive, ESR 15, CRP 145. What is the most likely diagnosis?  
III. A 72-year-old female presents with pains in the joints of her hands and her neck. On examination she has bony expansion of the distal interphalangeal joints of both hands. ESR is 35. What is the most likely diagnosis?
Question 3 Theme: Autoantibodies

A. Systemic sclerosis
B. Osteoarthritis
C. Rheumatoid arthritis
D. Gout
E. Reactive arthritis
F. Systemic lupus erythematosus
G. Septic arthritis
H. Antiphospholipid syndrome

For each of the following questions, select the best answers from the list above:

I. A 32-year-old female with a previous history of epilepsy presents with a history of recurrent miscarriage. She has a prolonged APTT and a positive anti-cardiolipin antibody. What is the most likely diagnosis?

II. A 35-year-old female presents with episodes of pain in the metacarpophalangeal joints of the hands. She has a fever. There are erosions on hand X-rays. Blood results show: rheumatoid factor negative, antinuclear antibody negative. What is the most likely diagnosis?

III. A 66-year-old retired schoolteacher has numbness and pain in her hands and feet. She has a positive-anticentromere antibody. What is the most likely diagnosis?
**FUNCTIONS OF THE SKIN**

- Physical barrier
- Protection against infection, chemicals and UV
- Prevention of excessive water loss or absorption
- UV-induced synthesis of vitamin D
- Temperature regulation
- Sensation
- Antigen presentation/immunological reactions and wound healing

**EXAMINATION OF THE SKIN**

**Look at the rash**
For useful terms, see Table 12.1.

**Note its distribution**
Useful terminology:
- Flexural/extensor (remember psoriasis is usually extensor and eczema is usually flexural)
- Localized/widespread
- Symmetrical/unilateral
- Facial
- Centripetal (trunk > limbs)
- Acral (hands and feet)
- Linear/annular
- Reticulate (lacy network)

**Feel the rash**
- Use gloves if necessary

**Examine**
- Nails
- Hair
- Mouth

**INFECTIONS**

**Bacterial infections**

**Impetigo**
- Weeping exudative areas with honey-coloured crust
- Highly infectious
- 90% due to *Staphylococcus aureus*

**Management**
- Topical/oral antibiotics

**Cellulitis**
- Hot tender area of confluent erythema
- Often on lower legs
Table 12.1 Useful terms to describe skin lesions

<table>
<thead>
<tr>
<th>Term</th>
<th>Meaning</th>
</tr>
</thead>
<tbody>
<tr>
<td>Atrophy</td>
<td>Thinning of skin</td>
</tr>
<tr>
<td>Bulla</td>
<td>Large fluid-filled blister</td>
</tr>
<tr>
<td>Crusted</td>
<td>Dried exudate</td>
</tr>
<tr>
<td>Ecchymosis</td>
<td>Large ‘bruise’</td>
</tr>
<tr>
<td>Erosion</td>
<td>Small denuded area of skin</td>
</tr>
<tr>
<td>Excoriation</td>
<td>Scratch mark</td>
</tr>
<tr>
<td>Fissure</td>
<td>Deep linear crack</td>
</tr>
<tr>
<td>Lichenified</td>
<td>Thickened skin with normal markings</td>
</tr>
<tr>
<td>Macule</td>
<td>Flat, circumscribed non-palpable lesion</td>
</tr>
<tr>
<td>Nodule</td>
<td>Large papule (&gt;0.5 cm)</td>
</tr>
<tr>
<td>Papule</td>
<td>Small palpable circumscribed lesion</td>
</tr>
<tr>
<td>Petechia</td>
<td>Pinpoint-sized macule of blood in the skin</td>
</tr>
<tr>
<td>Plaque</td>
<td>Large flat-topped palpable lesion</td>
</tr>
<tr>
<td>Purpura</td>
<td>Larger macule of blood in the skin which does not blanch on pressure</td>
</tr>
<tr>
<td>Pustule</td>
<td>Pus-filled lesion (white/yellow)</td>
</tr>
<tr>
<td>Scaly</td>
<td>Visible flakes/shedding of skin surface</td>
</tr>
<tr>
<td>Telangiectasia</td>
<td>Abnormal visible dilatation of blood vessels</td>
</tr>
<tr>
<td>Ulcer</td>
<td>Larger denuded area of skin</td>
</tr>
<tr>
<td>Vesicle</td>
<td>Small fluid-filled blister</td>
</tr>
<tr>
<td>Wheal</td>
<td>Raised erythematous swelling (dermal swelling)</td>
</tr>
</tbody>
</table>

- Can affect face (erysipelas)
- Caused by *streptococci*

**Management**
- Oral/i.v. antibiotics

**Viral infections**

**Herpes simplex**

**HSV Type 1 – direct contact, droplet infection**
- Vesicular lesions
- May be recurrent, e.g. cold sores

**Management**
- Topical aciclovir/oral valaciclovir

**HSV Type 2 – sexually transmitted**
- Affect genital area

**Herpes zoster (shingles)**

**Varicella zoster virus (VZV)**
- Reactivation of infection
- There may be a prodrome of tingling pain
Unilateral blistering eruption
- Single dermatomal distribution usually
- Otoscopy demonstrates vesicles in the external auditory meatus

Management
- Analgesia
- Oral valaciclovir/famciclovir or aciclovir

Complications
- Post-herpetic neuralgia (pain)
- Ocular involvement (ophthalmic nerve)

Fungal infections (mycoses)

Dermatophyte infections

Tinea corporis
- Body ringworm
- Slightly itchy asymmetrical scaly patch with central clearing and raised edge

Tinea cruris
- Groin ringworm

Tinea pedis
- Athlete’s foot

Tinea capitis
- Scalp ringworm

Management
- Antifungal cream
- Oral agents for feet/severe infections

Candida albicans
- Flexural areas
- Red areas with ragged edges
- Satellite lesions

Risk factors
- Immunosuppression including steroids
- Diabetes mellitus

Management
- Topical/oral antifungal agents

INFESTATIONS

Scabies
- *Sarcoptes scabiei*
- Itchy red papules
- Skin burrows visible in web spaces
- Diagnosis by skin scrapings

Treatment
- Malathion or permethrin
- Treat all skin below neck
- Treat all close contacts

ECZEMA (DERMATITIS) (TABLE 12.2)
- Acute – inflamed weeping skin with vesicles
- Subacute – erythema, dry/flaky skin, crusted
- Chronic – lichenified skin
### Epidemiology
- 40% of population have an episode associated with atopy
- Atopic individuals have a tendency to
  * Asthma
  * Eczema
  * Hay fever
  * Allergic rhinitis

### Atopic eczema

#### Aetiology
- Genetic – polygenic
- Environmental triggers
  * Detergents/chemicals
  * Infection
  * Stress/anxiety
  * Animal fur
  * Foods (dairy products in the very young)

#### Clinical features
- Itchy erythematous scaly patches
- Often flexural
- May be associated with nail pitting

#### Investigations
- May have raised IgE or eosinophils
- Skin-patch testing

#### Management
- Education and explanation
- Avoid irritants
- Emollients
- Bath oil or soap substitutes
- Topical steroids or immunomodulators (tacrolimus)
- Antibiotics for secondary infection
- Antihistamines
- Second-line agents
  * Phototherapy – Ultraviolet (UV) light
  * Oral steroids
  * Ciclosporin/azathioprine

---

<table>
<thead>
<tr>
<th><strong>Table 12.2</strong> Classification of eczema</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Endogenous</strong></td>
</tr>
<tr>
<td>Atopic eczema</td>
</tr>
<tr>
<td>Discoid eczema</td>
</tr>
<tr>
<td>Hand eczema</td>
</tr>
<tr>
<td>Seborrhoeic eczema</td>
</tr>
<tr>
<td>Venous (‘gravitational’) eczema</td>
</tr>
<tr>
<td>Asteatotic eczema</td>
</tr>
</tbody>
</table>
### PSORIASIS

- Common disorder characterized by red scaly plaques

### Epidemiology
- 2% of the population
- ♂ = ♀

### Aetiology
- T lymphocyte-driven
- Genetic – polygenic
- Environmental triggers
  - Infection
  - Drugs, e.g. lithium
  - UV light
  - Alcohol
  - Stress/anxiety

### Clinical features

#### Chronic plaque psoriasis
- Purplish/red scaly plaques, particularly on extensor surfaces
- Scalp frequently involved
- Can occur in areas of skin trauma (Köbner phenomenon)
- 50% associated with nail changes
  - Nail pitting
  - Distal separation of nail plate (onycholysis)
  - Yellow/brown discoloration
  - Subungual hyperkeratosis
  - If severe, loss of nail plate

#### Flexural psoriasis
- Occurs in older patients
- Patches in:
  - Groin
  - Natal cleft
  - Submammary areas

#### Guttae psoriasis
- Raindrop-like lesions on trunk
- Occurs in children/young adults 2 weeks after a streptococcal sore throat

### Arthritis associated with psoriasis
- See page 270

### Management
- Education and explanation
- Emollients
- Avoid irritants
- Topical steroids
- Calcipotriol (vitamin D₃ analogue)
- Coal tar
- Phototherapy, e.g. PUVA (psoralen + UVA)
- Methotrexate, TNF-α inhibitors if severe

### Complications
- Erythroderma – see below
Erythroderma

- Widespread inflammation of the skin

**Common causes**
- Atopic eczema
- Psoriasis
- Drugs, e.g. sulphonamides, gold
- Seborrhoic dermatitis

**Management**
- Bed rest
- Liberal i.v. fluids
- Keep warm
- Emollients
- Beware of sepsis
- Treat/remove the cause

**Complications**
- High-output cardiac failure
- Hypothermia
- Dehydration
- Hypoalbuminaemia
- Increased basal metabolic rate
- Capillary leak syndrome

**ACNE VULGARIS**

- Affects 85% of adolescents

**Cause**
- Follicular epidermal hyperproliferation
- Blockage of pilosebaceous unit
- Increased sebum production
- Infection with propionibacterium acnes

**Clinical features**
- Open comedones – blackheads
- Closed comedones – whiteheads
- Inflammatory papules
- Pustules

**Treatment**
- Reduce sebum production and reduce bacteria
- Topical retinoids and antibiotics
- Low dose oral antibiotics
- Oral retinoid drugs

**SKIN CANCER**

- There are three common types, see Table 12.3
- All are related to exposure to sunlight

**CUTANEOUS FEATURES OF SYSTEMIC DISEASE**

**Erythema nodosum**
- Painful dusky/purplish nodules
- Commonly on the shins
- Associations – see Table 12.4
### Table 12.3 Features of the three common skin cancers

<table>
<thead>
<tr>
<th>Type</th>
<th>Clinical features</th>
<th>Spread</th>
<th>Management</th>
</tr>
</thead>
<tbody>
<tr>
<td>Basal cell carcinoma</td>
<td>Occur in later life</td>
<td>No metastases</td>
<td>Surgical excision</td>
</tr>
<tr>
<td>(rodent ulcer)</td>
<td>Slow-growing nodule</td>
<td></td>
<td>Radiotherapy</td>
</tr>
<tr>
<td></td>
<td>May ulcerate</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Pearly edge</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Telangiectasia</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Can erode local structures</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Squamous cell carcinoma</td>
<td>Rapidly growing nodule which ulcerates</td>
<td>Metastases occur</td>
<td>Surgical excision</td>
</tr>
<tr>
<td></td>
<td>More common in immunosuppressed patients, e.g. renal transplant patients</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Also occurs in areas of chronic inflammation</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Malignant melanoma</td>
<td>Can occur in young patients</td>
<td>Early metastases</td>
<td>Wide excision</td>
</tr>
<tr>
<td></td>
<td>Transformation of ‘moles’</td>
<td></td>
<td>Radiotherapy</td>
</tr>
<tr>
<td></td>
<td>Consider in all bleeding pigmented lesions or ‘changing moles’</td>
<td></td>
<td>Immunotherapy</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Chemotherapy for metastases</td>
</tr>
</tbody>
</table>

### Table 12.4 Aetiology of erythema nodosum and erythema multiforme

**Erythema nodosum**
- Streptococcal infection
- Drugs (e.g. antibiotics, oral contraceptive pill)
- Tuberculosis
- Inflammatory bowel disease
- Sarcoid
- Leprosy
- Fungal infection, e.g. histoplasmosis
- Chlamydia infection
- Idiopathic

**Erythema multiforme**
- Herpes/Epstein–Barr virus infection
- Drugs (e.g. antibiotics, barbiturates)
- Mycoplasma infections
- Connective tissue disease, e.g. SLE HIV
- Carcinoma/lymphoma
Erythema multiforme

- Erythematous lesion with central pallor (target lesions)
- Symmetrical, particularly on limbs
- May blister
- Mucosal involvement = Stevens-Johnson syndrome
- Associations – see Table 12.4

Pyoderma gangrenosum

- Erythematous nodules with ulceration
- Large areas of ulceration
- Bluish/black edge
- Purulent surface
- Associations
  - Inflammatory bowel disease
  - Rheumatoid arthritis
  - Myeloma/leukaemia/lymphoma
  - Liver disease
  - Idiopathic

Management

- Topical/oral steroids
- Treatment of underlying condition
- Ciclosporin

Acanthosis nigricans

- Thickened hyperpigmented skin in the flexures, e.g. axilla
- Associations
  - Insulin resistance
  - Malignancy (particularly GI tract)

Chronic discoid lupus

- Red scaly atrophic plaques ± telangiectasia
- Face/exposed areas of skin
- May be associated with alopecia
- Triggered/exacerbated by UV light
- 30% antinuclear factor-positive
- 5% develop systemic lupus erythematosus (SLE)

Management

- Topical steroids
- Hydroxychloroquine
- Oral steroids/azathioprine/ciclosporin/thalidomide

Systemic lupus erythematosus (skin manifestations)

- Macular erythema on cheeks/nose/forehead (butterfly rash)

Pruritus (medical conditions associated with itching)

- Iron deficiency
- Malignancy, e.g. lymphoma
- Diabetes mellitus
- Chronic kidney disease
- Cholestasis
- Chronic liver disease
Thyroid disease
HIV
Polycythemia vera

**BULLOUS DISORDERS**

**Pemphigus vulgaris**
- Middle age
- ♀ > ♂

**Pathogenesis**
- Autoantibodies against desmosomal protein desmoglein 1 and 3

**Clinical features**
- Mouth ulcers 50%
- Flaccid blisters on trunk
- Rapidly denuding blisters

**Treatment**
- High dose corticosteroids

**Bullous pemphigoid**
- Age > 60 years
- Mucosal involvement rare
- Deep blisters
- Large tense bullae on hands and feet
- Itchy

**Treatment**
- Corticosteroids

**Dermatitis herpetiformis**
- Rare blistering disorder associated with gluten sensitive enteropathy (coeliac disease)
- Young adults
- ♀ > ♂

**Treatment**
- Gluten free diet
- Dapsone

**LEG ULCERS**

**Aetiology**
- Venous hypertension
- Arterial insufficiency
- Neuropathic (e.g. diabetes mellitus)
- Neoplastic (e.g. squamous cell carcinoma)
- Vasculitis

**Venous ulcers**
- Infection, e.g. syphilis
- Blood disorders, e.g. sickle cell disease
- Trauma
- Most common cause associated with venous hypertension or previous thrombosis
Dermatology

Pass Finals

- Often recurrent and chronic
- Usually painless
- Medial aspect of leg
- Exclude arterial insufficiency with Doppler

**Management**
- Topical therapy to ulcer
- Compression bandaging and elevation of legs
- Antibiotics for overt infection
- Diuretics for oedema
- Analgesia if painful
- Skin grafting if resistant to therapy

**Arterial ulcers**
- Punched out
- Painful
- Leg cold and pale
- Absent pulses
- History of hypertension, claudication, smoking, angina
- Investigate with Doppler studies/angiogram

**Management**
- Analgesia
- Topical treatment of ulcer
- Vascular reconstruction

**Neuropathic ulcers**
- Over pressure areas, e.g. metatarsal heads
- Result of trauma
- Polyneuropathy, e.g. diabetes mellitus
- Painless

**Management**
- Keep clean
- Avoid trauma including good foot care

**SELF-ASSESSMENT QUESTIONS**

**Multiple choice questions (single best answer)**

1. Which of the following is a risk factor for skin malignancy?
   A. Methotrexate
   B. Diabetes mellitus
   C. Steroids
   D. Phenytoin
   E. Sunlight exposure

2. In dermatology:
   A. A bulla is pus-filled
   B. Acral lesions affect the scalp
   C. An ecchymosis is a large bruise
   D. Purpura blanch on pressure
   E. Ringworm is a viral infection

3. In eczema:
   A. The rash is rarely itchy
   B. The rash is often on the extensor surfaces
   C. Stress can be a trigger factor
D. Ciclosporin is the usual treatment
E. 10% of the population experience the condition at some time in their lives

4. Psoriasis:
   A. Is more common in males
   B. Is not triggered by stress
   C. Most commonly affects extensor surfaces
   D. Is easily cured
   E. Is usually treated with topical antibiotics

5. Basal cell carcinoma:
   A. Is associated with early metastases
   B. May have telangiectasia
   C. Never ulcerates
   D. Is treated with chemotherapy
   E. Is most common in young adults

6. Malignant melanoma:
   A. Is not associated with early metastases
   B. Is rarely life-threatening in young people
   C. Is easily distinguished from benign moles
   D. Is treated by wide excision and adjuvant therapy
   E. Only occurs in the skin

7. Erythema nodosum:
   A. Often occurs on the arms
   B. Is not associated with Crohn’s disease
   C. Is associated with use of oral contraceptives
   D. Is common in tuberculosis
   E. Is most commonly associated with a viral infection

8. In erythema multiforme:
   A. Uniform red patches occur
   B. Lesions on the feet occur in Stevens–Johnson syndrome
   C. Is not caused by barbiturates
   D. Disease is less likely in immunosuppressed patients
   E. The rash is usually symmetrical

9. Leg ulcers:
   A. Are most commonly caused by arterial insufficiency
   B. Are always painful if venous
   C. Associated with neuropathy occur over metatarsal heads
   D. May need treatment with steroids
   E. Are rarely recurrent

10. Erythroderma:
    A. Is not a complication of eczema
    B. Is usually treated with fluid restriction
    C. Capillary leak syndrome may require intensive care
    D. Is treated with induced hypothermia
    E. Is localized to the legs

**Extended matching questions**

**Question 1 Theme: Erythematous rash**

A. Eczema
B. Psoriasis
C. Meningococcal septicaemia
D. Squamous cell carcinoma
E. Systemic lupus erythematosus
For each of the following questions, select the best answer from the list above:

I. A 39-year-old female presents with an erythematous rash on her legs. She has just returned from holiday in North Africa. The lesions are purplish, painful and warm to the touch. She has a medical history of Crohn’s disease and at present has a flare-up of her symptoms with diarrhoea. What is the most likely diagnosis?

II. A 12-year-old female presents with an erythematous rash on her arms. She has a history of asthma. She also says that she is having difficulty sleeping because of itching. The rash is flexural in distribution and she has nail pitting. What is the most likely diagnosis?

III. A 28-year-old male presents with a rash on his hands. It is weeping fluid and in parts has yellow crusting areas. His girlfriend has a similar rash. It responds to treatment with antibiotics. What is the most likely diagnosis?

Question 2 Theme: Skin ulcers

A. Venous ulcers
B. Squamous cell carcinoma
C. Malignant melanoma
D. Erythema multiforme
E. Erythema nodosum
F. Pyoderma gangrenosum
G. Impetigo
H. Erythrasma
I. Leprosy

For each of the following questions, select the best answer from the list above:

I. A 39-year-old female presents with an ulcer on her right shin. She recently injured this area while on holiday in Africa. She has a medical history of Crohn’s disease. She is worried that the ulcer is rapidly increasing in size. What is the most likely diagnosis?

II. An 82-year-old female presents with an ulcer just above the medial malleolus. She has been treated with dressings by the community nurses for 6 weeks without improvement. She has previously had surgery for varicose veins and is on aspirin for angina. The skin around the ulcer is pigmented and brownish. What is the most likely diagnosis?

III. A 48-year-old male presents with an ulcer on his ear. He is a keen gardener. He has had an area of crusting skin there for some time. There is an enlarged hard post-auricular lymph node. What is the most likely diagnosis?

Question 3 Theme: Pruritus

A. Iron deficiency
B. Squamous cell carcinoma
C. Diabetes mellitus
D. Erythema multiforme
E. Erythema nodosum
F. Cholestasis
G. HIV
H. Erythrasma
I. Polycythemia rubra vera

For each of the following questions, select the best answer from the list above:

I. A 39-year-old male presents with pruritus. A full blood count reveals that he has a low lymphocyte count. What is the most likely cause of his itching?

II. An 82-year-old female presents with itching, weight loss and abdominal pain. Her neighbours have told her that she looks yellow. She has recently been diagnosed with diabetes. An ultrasound suggests a mass in the head of the pancreas. What is the most likely cause of her itching?

III. A 48-year-old male presents with itching. He has also noted a change in his bowel habit and is awaiting colonoscopy. His full blood count shows a haemoglobin of 8.9 g/dL with an MCV of 69 fL. What is the most likely cause of his itching?
Hormones

- Chemical messengers
  - Polypeptide (e.g. insulin)
  - Lipid (e.g. cortisol)
  - Amine (e.g. tyrosine)
  - Glycoprotein (e.g. TSH)
- Signal between cells or organs
- Influence via:
  - Cell membrane receptors (e.g. insulin) → rapid effect
  - Intracellular receptors (e.g. thyroxine) → slow effect
- Allow adjustment to internal and external environment
- Transmitted via:
  - Blood (endocrine)
  - Directly to adjacent cells (paracrine)
- Secretion control
  - Usually negative feedback loop
  - Effect of hormone on release of secretion factor (e.g. thyroxine on TSH)
  - Effect of end substance on secretion (e.g. glucose on insulin)
  - Circadian rhythm (e.g. cortisol)

Endocrine disorders

- Common
  - Type 1 diabetes mellitus (10–30/100 000 per year)
  - Type 2 diabetes mellitus (2% of the population)
  - Thyroid disease (1.5–3 cases/1000 per year)
  - Subfertility (5–10% of all couples)
  - Menstrual disorders
  - Osteoporosis
  - Primary hyperparathyroidism (0.1%)
- Caused by abnormalities in hormone
  - Synthesis
  - Secretion
  - Control
  - Function
- Common disorders are shown in Table 13.1
- Rarer conditions provide classical cases for both written and clinical examinations and will be included in this chapter

Common pathologies

- Affect endocrine glands or their target organs
- Organ-specific autoimmune disorders
- Endocrine tumours
**Drugs affecting endocrine function**

- Direct induction (chlorpromazine → ↑ prolactin)
- Direct inhibition (amiodarone → hypothyroidism)
- Simulation (ACE inhibitors → hypoaldosteronism)
- Toxicity (chemotherapy → gonadal failure)
- Altered protein binding (anticonvulsants → ↓ T<sub>4</sub>)
- Exogenous hormones (steroids → Cushing syndrome)

**CLINICAL HISTORY IN ENDOCRINE DISEASE**

See Table 13.2.

**EXAMINING THE ENDOCRINE SYSTEM**

- Overall appearance (i.e. spot diagnosis), e.g. acromegaly, Graves’ disease, should be assessed
- All clinical ‘systems’ may be involved in endocrine disorders
- Full examination of all systems is expected (Box 13.1)
- Certain parts of the examination may be discriminatory in diagnosis

### Table 13.1 Common endocrine disorders

<table>
<thead>
<tr>
<th>Disorder</th>
<th>Disorder</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diabetes mellitus</td>
<td>Osteoporosis</td>
</tr>
<tr>
<td>Thyroid disease</td>
<td>Primary hyperparathyroidism</td>
</tr>
<tr>
<td>Subfertility</td>
<td>Short stature</td>
</tr>
<tr>
<td>Menstrual disorders</td>
<td>Delayed puberty</td>
</tr>
<tr>
<td>Excess hair growth</td>
<td></td>
</tr>
</tbody>
</table>

### Table 13.2 Points to note in taking an endocrine history

- **Past medical history**
  - Diabetes mellitus
  - Hypertension
  - Previous pregnancies/fertility
  - Previous surgery – thyroid/parathyroid, ovarian, testicular
  - Childhood milestones and development
  - Puberty
  - Previous radiation exposure – neck (thyroid), gonads
- **Family history**
  - Autoimmune disorders
  - Endocrine disorders
  - Diabetes mellitus
- **Social history**
  - Alcohol or drug abuse
  - Diet, e.g. salt/iodine intake
- **Drug history**
  - Details of all drugs taken at present and previous regular medications
  - Corticosteroids
  - Sex hormones, e.g. HRT, oral contraceptive pill
According to the given text, laboratory tests in endocrinology involve measuring hormones in blood, plasma, or urine. Markers of function include glucose in diabetes and calcium in hyperparathyroidism. Basal levels of hormones are useful for hormones with a long half-life, such as thyroxine (T\(_4\) and T\(_3\)). Dynamic tests are used to test the ability of a gland to respond appropriately to stimulation or suppression, such as in stimulant tests where normal adrenal response to a dose of synthetic ACTH is an increase in plasma cortisol levels.
**Suppression test – dexamethasone suppression test**
- Normal response to a dose of synthetic steroid is reduction in pituitary release of ACTH and subsequent fall in adrenal cortisol release and plasma levels
- Uncontrolled endogenous production of ACTH from a pituitary tumour or ectopic source leads to inadequate suppression of plasma cortisol level

**THYROID DISORDERS**

**Control of thryoxine secretion**
See Figure 13.1 and Table 13.3.

**Examination of thyroid gland and status**
See Box 13.2 and Chapter 3.

---

**Fig. 13.1** The hypothalamic-pituitary-thyroid axis. TRH, thyrotrophin releasing hormone. TSH, thyroid stimulating hormone.
Thyroid disorders

Table 13.3 Biochemistry of thyroid disorder

<table>
<thead>
<tr>
<th></th>
<th>Hormone levels</th>
<th>Dynamic and other tests</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>T4 and T3</td>
<td>TSH</td>
</tr>
<tr>
<td>Hyperthyroidism</td>
<td>↑</td>
<td>↓</td>
</tr>
<tr>
<td>Primary hypothyroidism</td>
<td>↓ ↑</td>
<td></td>
</tr>
<tr>
<td>Secondary hypothyroidism</td>
<td>↓ ↓ or normal</td>
<td></td>
</tr>
</tbody>
</table>

Box 13.2. Examination of thyroid gland and status

General inspection
• Look for signs of thyroid disease

Examine the neck
• Look for a goitre
• Ask the patient to take a sip of water and hold it in the mouth, then ask him or her to swallow while watching the neck – look for movement of goitre with swallowing
• Stand behind the patient and feel the thyroid with both hands, starting in the centre below the thyroid cartilage over the trachea, and moving laterally to the two lobes, which extend behind the sternomastoid muscle. Ask the patient to swallow while palpating. Assess the goitre for size, nodularity or diffuse enlargement, discrete nodules and firmness
• Palpate for lymph nodes
• Auscultate – listen over the thyroid for a bruit

Assess thyroid status
• Pulse – count the rate and note the presence or absence of atrial fibrillation
• Palms – warm and sweaty
• Tremor of outstretched arms

Examine the eyes
• Exophthalmos
• Lid retraction
• Lid lag

Examine the reflexes
• Slow relaxation in hypothyroidism

Goitre

Aetiology in a euthyroid patient
• Simple non-toxic goitre
• Iodine deficiency
• Treated Graves’ disease
• Puberty
• Solitary nodule
• Thyroid adenoma
• Thyroid cyst
• Thyroid carcinoma
Aetiology in a hypothyroid patient
- Hashimoto’s thyroiditis
- Radioiodine-treated Graves’ disease

Aetiology in a hyperthyroid patient
- Graves’ disease
- Toxic multinodular goitre

Hypothyroidism

Aetiology
- Atrophic (autoimmune – antithyroid antibodies)
- Hashimoto’s thyroiditis (thyroid peroxidase antibodies)
- Iodine deficiency
- Post radioiodine-treated hyperthyroidism
- Thyroidectomy

Clinical features
- Weight gain
- Tiredness
- Depression
- Patient feels the cold
- Constipation
- Poor appetite/libido
- Menstrual disturbances
- Myxoedema facies; thickened skin
- Dry, thin, brittle hair
- Periorbital puffiness
- Bradycardia and hypertension
- Slow relaxing reflexes

Investigations
- Biochemistry (Table 13.3)
- Haematology
  - Anaemia (usually normocytic/normochromic)
  - Macrocytosis (low T₄ or pernicious anaemia)
  - Microcytic (due to menorrhagia)
- Anti-thyroid antibodies
- Hypercholesterolaemia

Management
- Thyroxine replacement
- Caution in cardiac disease
- Monitor TSH

Hyperthyroidism

Common causes
- Graves’ disease (anti-TSH receptor antibodies mimic TSH)
- Toxic multinodular goitre
- Single toxic nodule
- Gestational
- Drugs (e.g. amiodarone)

Clinical features
- Heat intolerance
- Weight loss
- Increased appetite
Pituitary disorders

- Diarrhoea
- Irritability
- Sleeplessness, tiredness
- Exertional breathlessness
- Goitre
- Tachycardia/atrial fibrillation
- Tremor
- Hyperkinesia
- Proximal muscle wasting
- Cardiac failure
- Pretibial myxoedema

Eye signs (Graves' disease)
- Exophthalmos
- Lid lag
- Lid retraction
- Ophthalmoplegia

Investigations
- TSH suppressed
- Raised T<sub>3</sub> and/or T<sub>4</sub>

Management

Medical treatment
- Carbimazole (risk of agranulocytosis)
- Propylthiouracil (risk of agranulocytosis)
- β-blockers
- Radioiodine

Surgical treatment for
- Malignancy
- Pressure symptoms
- Failure of medical treatment

PITUITARY DISORDERS

Functions of the anterior pituitary

See Figure 13.2 and Table 13.4.

Control of growth hormone secretion

See Figure 13.3.

Acromegaly

Aetiology
- Pituitary tumour

Clinical features
- Often insidious nonspecific onset
- Headaches
- Polyuria
- Erectile dysfunction
- Visual field defects, e.g. bitemporal hemianopia
- Nerve compression, e.g. carpal tunnel syndrome
- Typical facies, e.g.
  - Thick greasy skin
  - Protrusion of lower jaw
  - Gaps between teeth
Fig. 13.2 The hypothalamic-pituitary axis. LHRH, luteinizing hormone releasing hormone; TSH, thyroid stimulating hormone; FSH, follicle stimulating hormone; CRH, corticotrophin releasing hormone; GHRH, growth hormone releasing hormone; ACTH, adrenocorticotropic hormone. TRH, thyrotrophin releasing hormone; ADH, antidiuretic hormone.

Table 13.4 Biochemistry of disorders of the hypothalamic-anterior pituitary axis

<table>
<thead>
<tr>
<th>Disorder</th>
<th>Hormone levels</th>
<th>Dynamic and other tests</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acromegaly</td>
<td>Growth hormone ↑</td>
<td>Oral glucose load (growth hormone (GH) fails to suppress)</td>
</tr>
<tr>
<td>Prolactinoma</td>
<td>Prolactin ↑</td>
<td></td>
</tr>
<tr>
<td>Panhypopituitarism</td>
<td>Luteinizing hormone (LH)/follicle stimulating hormone (FSH) ↓ GH ↓ TSH ↓ ACTH ↓</td>
<td>Luteinizing hormone releasing hormone (LHRH) test</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Insulin stress test</td>
</tr>
<tr>
<td></td>
<td></td>
<td>TRH test</td>
</tr>
<tr>
<td></td>
<td></td>
<td>SynACTHen test</td>
</tr>
</tbody>
</table>
Pituitary disorders

Large ‘spade-like’ hands
Cardiac failure
Diabetes mellitus
Hypertension

Investigations
- Glucose tolerance test – GH not suppressed by glucose
- Insulin like growth factor 1
- Visual fields (bitemporal hemianopia)
- MRI pituitary

Management
- GH antagonists (pegvisomant)
- Dopamine agonists (bromocriptine)
- Somatostatin analogues (octreotide)
- Pituitary radiotherapy (post-surgery)
- Trans-sphenoidal hypophysectomy

Hypopituitarism

Aetiology
Congenital
- Kallmann syndrome (hypogonadism)

Infective
- Basal meningitis (e.g. tuberculosis)
- Encephalitis
- Syphilis

Vascular
- Sheehan syndrome (postpartum necrosis)

Fig. 13.3 The growth axis. IGF-1, insulin-like growth factor 1.
Tumours
- Pituitary
- Hypothalamic
- Craniopharyngioma
- Meningioma
- Glioma
- Metastases (especially breast)
- Lymphoma

Infiltration
- Sarcoidosis
- Langerhans histiocytosis
- Haemochromatosis

Others
- Radiation
- Anorexia nervosa
- Trauma or previous surgery

Clinical features
- Due to progressive loss of anterior pituitary hormones (listed in order of frequency)

Growth hormone
- Growth failure
- Short stature

Prolactin
- Failure of lactation

Gonadotrophins
- Delayed puberty
- Infertility
- Amenorrhoea
- Loss of body hair

TSH
- Hypothyroidism

ACTH
- Adrenal failure (without pigmentation)

Investigations
- Determine hormone deficiencies
- Pituitary imaging, e.g. CT scan, MRI scan

Management
- Treat cause
- Hormone replacement

ADRENAL HORMONE ABNORMALITIES

Control of cortisol secretion
See Figure 13.4.

Cushing syndrome
- Overproduction of corticosteroids or excess corticosteroid treatment

Aetiology
ACTH-dependent (Cushing’s disease)
- Pituitary adenoma
- Ectopic ACTH-secreting tumours
Adrenal hormone abnormalities

Non-ACTH-dependent
- Adrenal adenoma
- Adrenal carcinoma
- Steroid treatment

Others
- Alcohol-induced pseudo-Cushing syndrome

Clinical features
- Weight gain
- Thin skin
- Striae
- Bruising
- Menstrual disturbances
- Psychosis
- Red face
- Central obesity
- Buffalo hump
- Hirsutism
- Proximal myopathy
- Hypertension
- Diabetes mellitus

Fig. 13.4 The hypothalamic–pituitary–adrenal axis.
Investigations

- Biochemistry (Table 13.5)
- Serum electrolytes
  - Sodium ↓
  - Potassium ↑
- Pituitary imaging
- Adrenal imaging
- Chest X-ray (ACTH secreting bronchogenic carcinoma)

Management

Pituitary-dependent

- Trans-sphenoidal resection of tumour

Adrenal adenomas

- Medical treatment with metyrapone, to induce remission before adrenalectomy

Ectopic ACTH

- Remove tumour if possible
- Control Cushing’s with metyrapone

Primary hypoadrenalism – Addison’s disease

- Destruction of adrenal cortex causing reduced production of glucocorticoid, mineralocorticoid and sex steroids

Aetiology

See Table 13.6.

Clinical features

- Tiredness
- Debility
- Nausea, vomiting
- Anorexia, weight loss
- Abdominal pain

Table 13.5 Biochemistry of disorders of the pituitary-adrenal axis

<table>
<thead>
<tr>
<th></th>
<th>Hormone levels</th>
<th>Dynamic and other tests</th>
</tr>
</thead>
<tbody>
<tr>
<td>ACTH-secreting pituitary adenoma (Cushing’s disease)</td>
<td>24-hour urine cortisol ↑  Midnight cortisol ↑</td>
<td>Dexamethasone suppression test</td>
</tr>
<tr>
<td>Ectopic ACTH secretion</td>
<td>24-hour urine cortisol ↑  Midnight cortisol ↑</td>
<td>Dexamethasone suppression test</td>
</tr>
<tr>
<td>Adrenal adenoma</td>
<td>24-hour urine cortisol ↑  Midnight cortisol ↑</td>
<td>Dexamethasone suppression test</td>
</tr>
<tr>
<td>Pituitary failure</td>
<td>9 a.m. cortisol ↓</td>
<td>Synacthen test (normal response)</td>
</tr>
<tr>
<td>Primary adrenal failure</td>
<td>9 a.m. cortisol ↓</td>
<td>Synacthen test (diminished response)</td>
</tr>
</tbody>
</table>
Diarrhoea
• Depression
• Menstrual disturbance
• Pigmentation – mouth, palmar creases
• Postural hypotension
• Dehydration
• Loss of body hair

Investigations
See Table 13.5.

Management
• Replacement of glucocorticoids and mineralocorticoids with oral hydrocortisone and fludrocortisone

PARATHYROIDS (SEE ALSO CH. 11)

Hyperparathyroidism

Aetiology
Primary
• Adenoma (80% solitary)
• Hyperplasia
• Carcinoma
Secondary
• Hyperplasia in hypocalcaemia
• Chronic kidney disease
• Osteomalacia
Tertiary
• Autonomous secretion after prolonged hypocalcaemia

Clinical features
• Abdominal pain
• Anorexia
• Constipation
• Pain
• Pathological fractures
• Polydipsia and polyuria
• Renal calculi

Due to hypercalcaemia

Investigations
See Table 13.7.
Management
- Treat underlying cause
- Parathyroidectomy if Ca\(^{++}\) >3 or symptoms
- Treat hypercalcaemia (p. 281)

Hypoparathyroidism

Aetiology
- Post-surgical
- Post-radiotherapy
- Autoimmune
- Pseudohyperparathyroidism = end organ resistance

Clinical features
- Cataracts
- Cramps
- Fits
- Paraesthesiae
- Tetany

Due to hypocalcaemia

Investigations
See Table 13.7.

Osteoporosis
- Reduction in bone density below normal for age and sex (p. 276)

SEX HORMONE AND REPRODUCTIVE DISORDERS

Amenorrhoea – primary or secondary

Aetiology

Pituitary causes
- Hyperprolactinaemia
- Hypopituitarism
- Thyrotoxicosis
- Anorexia nervosa

Ovarian causes (Table 13.8)
- Surgery
- Primary ovarian failure
- Polycystic ovary syndrome

Table 13.7 Biochemistry of disorders of calcium homeostasis

<table>
<thead>
<tr>
<th>Disorder</th>
<th>Hormone levels</th>
<th>Dynamic and other tests</th>
</tr>
</thead>
<tbody>
<tr>
<td>Osteoporosis</td>
<td>PTH normal</td>
<td></td>
</tr>
<tr>
<td>Primary hyperparathyroidism</td>
<td>PTH ↑</td>
<td>Serum calcium ↑ Serum phosphate ↓</td>
</tr>
<tr>
<td>Tertiary hyperparathyroidism</td>
<td>PTH ↑</td>
<td>Serum calcium ↑ Serum phosphate ↑</td>
</tr>
<tr>
<td>Primary hypoparathyroidism</td>
<td>PTH undetectable</td>
<td>Serum calcium ↓</td>
</tr>
<tr>
<td>Pseudohypoparathyroidism</td>
<td>PTH normal</td>
<td>Serum calcium ↓</td>
</tr>
</tbody>
</table>
Salt and water balance disorders

**Table 13.8 Biochemistry of ovarian disorders**

<table>
<thead>
<tr>
<th>Condition</th>
<th>Hormone levels</th>
<th>Dynamic and other tests</th>
</tr>
</thead>
<tbody>
<tr>
<td>Polycystic ovary syndrome</td>
<td>Androgens ↑</td>
<td></td>
</tr>
<tr>
<td>Primary ovarian failure</td>
<td>FSH ↑</td>
<td>LHRH test</td>
</tr>
<tr>
<td></td>
<td>LH ↑</td>
<td>Clomiphene stimulation test</td>
</tr>
<tr>
<td></td>
<td>Oestrogen ↓</td>
<td></td>
</tr>
</tbody>
</table>

- Congenital adrenal hyperplasia
  - Autosomal recessive
  - Enzyme deficiency in cortisol synthesis
  - → Sexual ambiguity/adrenal failure
- Chromosomal abnormalities
  - Turner syndrome (XO)

**SALT AND WATER BALANCE DISORDERS**

**Control of salt and water homeostasis**

See Box 13.3 and Figure 13.5.

**Diabetes insipidus**

- Deficiency of antidiuretic hormone (ADH) or insensitivity to its action

**Box 13.3. Water deprivation test**

- Free fluid overnight

**08:00 hours**

- No access to fluids
- Record hourly
  - Urine and plasma osmolality
  - Urine volume
  - Body weight
- Stop and allow fluid if body weight loss >3%

**16:00 hours**

- 2 µg desmopressin injection i.m.
- Continue fluid restriction according to urine output

**04:00 hours**

- Stop

**Normal**

- Normal plasma osmolality maintained up to urine concentration >800 mosm/kg

**Cranial DI**

- Urine fails to concentrate
- Plasma osmolality rises
- Abnormality is corrected with desmopressin

**Nephrogenic DI**

- As for cranial DI but not corrected by desmopressin
Aetiology
- Cranial causes
  - Idiopathic
  - Familial (DIDMOAD – diabetes insipidus, diabetes mellitus, optic atrophy, deafness)
  - Tumours, e.g. craniopharyngioma, glioma, metastases (breast)
  - Infiltration, e.g. sarcoidosis, histiocytosis
  - Sheehan syndrome (pituitary infarction following post- or antepartum haemorrhage)
- Nephrogenic causes
  - Idiopathic
  - Renal tubular acidosis
  - Hypokalaemia
  - Hypercalcaemia
  - Drugs, e.g. lithium, demeclocycline, glibenclamide

Clinical features
- Polyuria urine output (10–15 L/day)
- Thirst
- Nocturia
- Polydipsia
- Dehydration

Differential diagnosis
- Primary polydipsia (excessive water drinking/normal ADH secretion)
Salt and water balance disorders

**Investigations**
See Table 13.9.

**Management**
- Treat underlying cause
- Synthetic vasopressin analogue
- Desmopressin
- Carbamazepine
- Chlorpropamide

**Syndrome of inappropriate ADH secretion (SIADH)**
- Inappropriate ADH secretion → retention of water and hyponatraemia
- Low plasma osmolality with continued urinary sodium secretion

**Aetiology**

**Tumours**
- Small cell carcinoma of lung
- Prostate cancer
- Pancreatic cancer

**Lungs**
- Pneumonia
- TB

**CNS**
- Meningitis
- Tumours
- Head injury
- Chronic subdural haematoma
- SLE vasculitis

**Drugs**
- Chlorpropamide
- Carbamazepine
- Phenothiazines

**Clinical features**
- Confusion
- Nausea

---

**Table 13.9 Biochemistry of the hypothalamic-posterior pituitary axis**

<table>
<thead>
<tr>
<th>Hormone levels</th>
<th>Dynamic and other tests</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cranial diabetes insipidus</td>
<td>ADH ↓ (not measured routinely) Water deprivation test</td>
</tr>
<tr>
<td></td>
<td>High plasma osmolality Low urine osmolality Normal response</td>
</tr>
<tr>
<td></td>
<td>to desmopressin</td>
</tr>
<tr>
<td>Nephrogenic diabetes insipidus</td>
<td>ADH ↑ (not measured routinely) Water deprivation test</td>
</tr>
<tr>
<td></td>
<td>High plasma osmolality Low urine osmolality No response to</td>
</tr>
<tr>
<td></td>
<td>DDAVP</td>
</tr>
<tr>
<td>Inappropriate ADH</td>
<td>ADH ↑ (not measured routinely) Plasma osmolality low</td>
</tr>
<tr>
<td></td>
<td>Urine osmolality high</td>
</tr>
</tbody>
</table>
ENDOCRINE CAUSES OF HYPERTENSION

Control of the renin-angiotensin-aldosterone system

See Figure 13.6.

Primary hyperaldosteronism (Table 13.10)

- Rare (<1% of all hypertension)

Aetiology

- Conn syndrome (adrenal adenoma 60%)
- Bilateral adrenal hyperplasia (40%)

Table 13.10 Biochemistry of hyperaldosteronism

<table>
<thead>
<tr>
<th></th>
<th>Hormone levels</th>
<th>Dynamic and other tests</th>
</tr>
</thead>
<tbody>
<tr>
<td>Primary hyperaldosteronism (Conn syndrome)</td>
<td>Renin ↓ Aldosterone ↑</td>
<td>Serum K ↓ Aldosterone: renin ratio ↑ Metabolic alkalosis</td>
</tr>
<tr>
<td>Secondary hyperaldosteronism</td>
<td>Renin ↑ Aldosterone ↑</td>
<td>Serum K ↓ Metabolic alkalosis</td>
</tr>
</tbody>
</table>
Management
- Surgery for tumours
- Aldosterone antagonists, e.g. spironolactone

Phaeochromocytoma
- Very rare
- Tumour of the sympathetic nervous system (90% adrenal)
- Secretion of norepinephrine and epinephrine leading to
  - Peripheral vasoconstriction
  - Inotropic effects
  - Tachycardia
  - High blood pressure

Clinical features
- Anxiety, panic attacks
- Palpitations
- Tremor
- Sweating
- Headache
- Flushing
- GI upset
- Weight loss
- Hypertension (paroxysmal or continuous)
- Tachycardia
- Arrhythmias
- Fever

Investigations
- Raised 24-hour excretion of urinary catecholamines
- CT or MRI adrenal glands
- MIBG scan $^{131}$I metaiodobenzylguanidine is specifically taken up in sites of sympathetic activity
  - Positive in 90% of phaeochromocytomas

Management
- Remove tumour
- $\alpha$- and $\beta$-blockade ($\alpha$ first with phenoxybenzamine, then $\beta$ with propranolol) prior to surgery to prevent dangerous swings in blood pressure

Multiple endocrine neoplasia (MEN)
- Simultaneous or metachronous occurrence of tumours in a number of endocrine glands with autosomal dominant inheritance

Type 1
- 95% Parathyroid – adenomas, hyperplasia
- 70% Pituitary – adenomas
- 50% Pancreas – islet cell tumours (e.g. insulinoma), gastrinoma
- 40% Adrenal adenoma
- 20% Thyroid adenoma

Type 2a
- 95% Adrenal – phaeochromocytoma
- 90% Thyroid – medullary carcinoma
- 60% Parathyroid – adenomas, adenocarcinoma
Type 2b
- Type 2a plus Marfanoid phenotype plus visceral ganglioneuromas
- No hyperparathyroidism

**DIABETES MELLITUS**
- Syndrome characterized by chronic hyperglycaemia due to relative insulin deficiency or resistance or both

**WHO classification of diabetes**

**Type 1**
- β cell destruction usually leading to absolute insulin deficiency
- Autoimmune or idiopathic

**Type 2**
- Variable combination of insulin resistance and defects in insulin secretion

**Other specific types**

**Genetic defects**
- Defects of β cell function or insulin function
- Maturity onset diabetes of the young (MODY)
- DIDMOAD syndrome

**Endocrinopathies**
- Cushing syndrome
- Acromegaly

---

**Table 13.11 WHO criteria for the diagnosis of diabetes (glucose mmol/L)**

WHO criteria for the diagnosis of diabetes are:
- Fasting plasma glucose >7.0 mmol/L (126 mg/dL)
- Random plasma glucose >11.1 mmol/L (200 mg/dL)
- One abnormal laboratory value is diagnostic in symptomatic individuals; two values are needed in asymptomatic people.

The glucose tolerance test is only required for borderline cases and for diagnosis of gestational diabetes.
- HbA1c >6.5 (48 mmol/mol)

**The glucose tolerance test – WHO criteria**

<table>
<thead>
<tr>
<th>Normal</th>
<th>Impaired glucose tolerance</th>
<th>Diabetes mellitus</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fasting</td>
<td>&lt;7.0 mmol/L</td>
<td>&lt;7.0 mmol/L</td>
</tr>
<tr>
<td>2 h after glucose</td>
<td>&lt;7.8 mmol/L</td>
<td>7.8–11.0 mmol/L</td>
</tr>
</tbody>
</table>

- Adult: 75 g glucose in 300 mL water
- Child: 1.75 g glucose/kg bodyweight
- Only a fasting and a 120-min sample are needed
- Results are for venous plasma – whole blood values are lower.

**Note:** There is no such thing as mild diabetes. All patients who meet the criteria for diabetes are liable to disabling long-term complications.

(Reproduced from Kumar P, Clark M. Kumar & Clark’s Clinical Medicine, 8th edn. Edinburgh: Elsevier; 2012, with permission from Elsevier.)
Diabetes mellitus

Phaeochromocytoma
Hyperthyroidism

Diseases of the endocrine pancreas
- Trauma
- Pancreatectomy
- Chronic pancreatitis
- Fibrocalculous pancreatic diabetes
- Cystic fibrosis
- Haemochromatosis
- Cancer

Drug-induced
- Corticosteroids
- Thiazides

WHO criteria for diagnosis of diabetes

See Table 13.11 and Figure 13.7.

![Diagnostic algorithm for diabetes mellitus (glucose mmol/L).](image)

**Fig. 13.7** Diagnostic algorithm for diabetes mellitus (glucose mmol/L).
Fig. 13.8 Features of diabetic eye disease. (a) The normal macula (centre) and optic disc. (b) Dot and blot haemorrhages (early background retinopathy). (c) Hard exudates are present in addition in background retinopathy. (d) Multiple cotton-wool spots indicate pre-proliferative retinopathy requiring routine ophthalmic referral. (e) Multiple frond-like new vessels, the hallmark of proliferative retinopathy. White fibrous tissue is forming near the new vessels, a feature of advanced retinopathy. (This eye also illustrates multiple xenon arc laser burns superiorly.) (f) Exudates appearing within a disc width of the macula are a feature of an exudative maculopathy. (g, h) Central and cortical cataracts can be seen against the red reflex with the ophthalmoscope. (Reproduced from Kumar P, Clark M. Kumar and Clark’s Clinical Medicine, 7th edn. Edinburgh: Elsevier; 2009, with permission from Elsevier.)
Presenting clinical features

Due to hyperglycaemia
- Thirst
- Polyuria
- Weight loss
- Ketoacidosis
- Lack of energy
- Visual blurring
- Candida infections
- Asymptomatic, picked up on blood/urine testing

Due to complications
- Skin infections
- Retinopathy
- Polyneuropathy
- Erectile dysfunction
- Arterial disease
- Renal disease

Clinical features of complications

Macrovascular and microvascular disease
- Atheroma
- Strokes
- Myocardial ischaemia
- Renal disease
- Peripheral vascular disease
- Retinopathy

Eyes
See Figure 13.8.

Kidney
- Glomerulosclerosis
- Microalbuminuria
- Persistent proteinuria
- End-stage renal failure (associated with anaemia, raised ESR and hypertension)
- Ischaemia
- Ascending infection (pyelonephritis)

Neuropathy
- Peripheral polyneuropathy (loss of ankle jerks and malleolar vibration sense)
- Glove and stocking sensory neuropathy
- Mononeuritis multiplex
- Peripheral and cranial nerve
- Autonomic neuropathy:
  - Diarrhoea
  - Postural hypotension
  - Erectile dysfunction
  - Gastroparesis
- Diabetic amyotrophy – painful asymmetrical wasting of quadriceps
- Charcot’s joints

Diabetic foot (Table 13.12)
- Ischaemic and/or neuropathic ulcers
Infections
- Only increased in poor glycaemic control
- Skin sepsis, e.g. staphylococcal or candida
- Urinary tract infection
- Pneumonia
- TB

Management of diabetes mellitus
- Based on self-monitoring and management by the patient, helped and advised by specialists
- Requires good education and understanding of disease by the patient, including:
  • Monitoring blood sugar
  • Self-injection of insulin
  • Managing hypoglycaemic events

<table>
<thead>
<tr>
<th>Table 13.12 The diabetic foot</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Ischaemic</strong></td>
</tr>
<tr>
<td>Symptoms</td>
</tr>
<tr>
<td>Claudication</td>
</tr>
<tr>
<td>Rest pain</td>
</tr>
<tr>
<td>Signs</td>
</tr>
<tr>
<td>Trophic changes</td>
</tr>
<tr>
<td>Cold</td>
</tr>
<tr>
<td>Pulseless</td>
</tr>
<tr>
<td>Painful ulcers</td>
</tr>
<tr>
<td>Ulcers on heels and toes</td>
</tr>
</tbody>
</table>

Box 13.4. Hypoglycaemia

**Clinical features**
- Sweating
- Tremor
- Pounding heart
- Pallor
- Drowsiness
- Confusion
- Coma
- Fits

**Management**
- Mild
  - Oral rapidly absorbed carbohydrate, e.g. glucose drink, tea with sugar or sweets
- Severe
  - i.v. 50% glucose injection 20–50 mL (after taking blood to confirm hypoglycaemia but before waiting for result)
  - 1 mg i.m. glucagon injection
• How to recognize complications
• When to contact specialists for help

**Glycaemic control**

**Diet**
- All patients need education regarding a diabetic diet

**Drugs**
- Sulphonylureas, e.g. gliclazide
  - May cause hypoglycaemia (Box 13.4) and weight gain
- Biguanides, e.g. metformin; α-glucosidase inhibitors, e.g. acarbose
  - Do not cause hypoglycaemia
  - May aid weight loss
- Incretins, e.g. dipeptyl peptidase-4 inhibitors, e.g. sitagliptin, GLP-1 agonists, e.g. exenatide
- Insulin sensitizers, e.g. pioglitazone
  - May cause hepatotoxicity
  - May cause drop in haemoglobin

**Insulin formulations**
- Synthetic human insulins are almost exclusively used
- Insulin is given regularly by subcutaneous injection
- Insulin regimes are developed to suit individual patients and may be tailored according to specific needs for certain situations, e.g. missing meals, heavy exercise

**Soluble insulin**
- Fast-acting and short duration of action
- Good for fine control
- Needs frequent administration

**Prolonged acting insulin**
- Mixed in varying degrees with soluble insulin to give a prolonged duration of action but with less accuracy and slower onset of action

**Insulin analogues**

**Long acting**
- Insulin glargine; longer duration of action and less peaked concentration

**Short acting**
- Enter and leave circulation more rapidly

**Complications of insulin treatment**
- Lipoatrophy and lipohypertrophy at injection site
- Weight gain
- Hypoglycaemia

**Monitoring diabetic control**

**Home monitoring**
- Urine reagent strips – simple but not very accurate
- Blood glucose reagent strips – more immediately accurate

**Hospital blood tests**
- HbA1c (glycosylated haemoglobin)
- Fructosamine (glycosylated plasma protein)
- Both give an index of average blood glucose concentration over the past 6 weeks
Diabetes clinic check-up visits

- Every visit
  - Review self-monitoring
  - Review current treatment (including diet)
  - Ongoing patient education

**Box 13.5. Diabetic ketoacidosis**

### Clinical features

- Prostration
- Hyperventilation (Kussmaul’s breathing)
- Nausea and vomiting
- Abdominal pain
- Confusion
- Coma
- Dehydration
- Ketones on breath
- Hyperglycaemia
- Ketonuria or ketonaemia
- Acidosis

### Principles of management

- Replace fluid loss
- Replace electrolyte loss
- Restore acid-base balance (usually achieved by correcting circulating volume and stopping ketone production with insulin)
- Replace deficient insulin
- Continuous i.v. infusion of soluble insulin
- Monitor blood glucose
- i.v. glucose in i.v. fluids to prevent hypoglycaemia (Do not stop insulin)
- Seek underlying cause and treat appropriately

### Emergency treatment

- Insulin
  - Intravenous insulin 6 units stat then
  - 6 units/hour by continuous infusion with blood glucose monitoring
- Fluid
  - 0.9% saline
  - 1 L in 30 minutes then
  - 1 L in 1 hour then
  - 1 L in 2 hours then
  - 1 L in 4 hours then
  - 1 L every 6 hours for 24 hours
  - i.e. at least 4 L in first 24 hours
- Check serum potassium hourly initially and add 20 mmol/L of i.v. fluid when <4 mmol
- Monitor central venous pressure if shocked at presentation
- Insert urinary catheter if anuric for >2 hours
- Antibiotics if septic
- Subcutaneous heparin to prevent thrombosis
Annual review
- Weight
- Blood pressure
- Biochemical assessment of control
- Visual acuity and retinal examination
- Check feet for condition, pulses, sensation and ankle jerks
- Urinalysis for proteinuria
- Blood lipids
- Renal function

**Diabetic emergencies/diabetic ketoacidosis**
- Uncontrolled diabetes with acidosis and ketosis due to insulin deficiency (Box 13.5)

**Hyperglycaemic hyperosmolar state**
- Severe hyperglycaemia without ketosis usually in type 2 diabetes

**Clinical features**
- Severe dehydration
- Stupor
- Coma
- Underlying illness (e.g. pneumonia)

**Investigations**
- High plasma osmolarity
- High serum sodium
- Very high plasma glucose
- High urea
- Normal arterial pH

**Management**
- Treat underlying cause
- Intravenous insulin to correct hyperglycaemia
- 0.9% saline to correct fluid depletion – beware rapid changes of osmolality due to reducing plasma sodium or glucose levels too fast
- Subcutaneous prophylactic heparin
- Mortality is up to 25%

**SELF-ASSESSMENT QUESTIONS**

**Multiple choice questions (single best answer)**

1. TSH:
   A. Is produced by the parathyroid glands
   B. Is reduced in primary hypothyroidism
   C. Is a sensitive marker of under-treatment during thyroxine replacement
   D. Secretion should be inhibited in a normal TRH stimulation test
   E. Levels are high in Graves’ disease

2. The following are common features of Graves’ disease:
   A. Atrial fibrillation
   B. Multinodular goitre
   C. Oedema
   D. Anorexia
   E. Weight gain
3. The following are common features of hypothyroidism:
   A. Heat intolerance
   B. Pretibial myxoedema
   C. Hoarse voice
   D. Weight loss
   E. Suicide

4. The following statements about pituitary function are correct:
   A. Suspected diabetes insipidus is investigated with a fluid challenge
   B. Prolactin production, unlike that of other pituitary hormones, is principally controlled by a stimulatory factor
   C. ACTH and cortisol production display a circadian rhythm
   D. Sheehan syndrome is commoner in men than women
   E. TSH is secreted from the posterior pituitary

5. In patients with untreated active acromegaly:
   A. About 25% of patients have impaired glucose tolerance
   B. Arthritis is a common feature
   C. An oral glucose tolerance test is used to confirm the diagnosis
   D. The incidence of carcinoma of the colon is increased
   E. All of the above

6. The following are common features of panhypopituitarism:
   A. Diabetes mellitus
   B. Galactorrhoea
   C. Infertility
   D. Pigmentation
   E. Increased urinary catecholamines

7. The following biochemical findings are often seen in an acutely unwell patient presenting with an Addisonian crisis:
   A. Hypernatraemia
   B. Hyperkalaemia
   C. A low ACTH
   D. Hypocalcaemia
   E. A raised glucose

8. The following statements about Cushing syndrome are correct:
   A. The commonest cause is an ACTH-secreting tumour of the pituitary
   B. There is impaired glucose tolerance in 75% of cases
   C. Severe hypokalaemia may be indicative of ectopic ACTH production
   D. Proximal myopathy is a common feature
   E. C and D

9. The following are true of ectopic ACTH secretion:
   A. There is failure of suppression of cortisol secretion during a high-dose dexamethasone suppression test
   B. It may be caused by a bronchial carcinoma
   C. It may cause increased skin pigmentation
   D. It is associated with small atrophic adrenal glands
   E. A, B and C

10. The following are features of cranial diabetes insipidus:
    A. It may be associated with acanthosis nigricans
    B. It may be associated with postpartum haemorrhage
    C. It is caused by treatment with lithium
    D. It responds to treatment with DDT
    E. It is treated with fluid restriction
11. The following are causes of nephrogenic diabetes insipidus:
   A. Sheehan syndrome
   B. Pancreatic islet cell antibodies
   C. Excessive water drinking
   D. Hypocalcaemia
   E. Hypokalaemia

12. The following are features of SIADH:
   A. Hypernatraemia
   B. Low urine osmolality
   C. Diagnosis requires serum ADH measurement
   D. It often presents with fits
   E. Treatment includes fluid restriction

13. The following are true of phaeochromocytoma:
   A. It is the cause of 10% of all hypertension
   B. It is caused by a tumour of adrenal cortex in 90% of cases
   C. α- and β-Adrenergic blockers are used prior to surgery to prevent swings in blood pressure
   D. It is seen in MEN type 1
   E. It is associated with coarctation of the aorta

14. The following are seen in MEN type 2a:
   A. Marfanoid phenotype
   B. Phaeochromocytoma
   C. Pancreatic islet cell tumours
   D. Pituitary tumours
   E. Papillary carcinoma of the thyroid

15. The following statements about diabetes mellitus are correct:
   A. The diagnosis is made on the basis of a fasting glucose >7.8 mmol/L
   B. When it presents in pregnancy (gestational diabetes) it usually continues after delivery
   C. In patients with proliferative diabetic nephropathy, thrombolysis is contraindicated in the event of a myocardial infarction
   D. The glycated haemoglobin (HbA1c) level is used to diagnose diabetes
   E. The mortality following anterior myocardial infarction is twice as high in diabetic as in non-diabetic patients

16. Regarding type 2 diabetes:
   A. Treatment with metformin works by increasing pancreatic insulin production
   B. Retinopathy is much rarer than in type 1 diabetes
   C. The thiazolidinediones are a new class of drug for treatment
   D. It only affects adults over the age of 40
   E. The incidence in the UK is falling

17. In type 1 diabetes:
   A. Patients control their blood glucose by regular self-injection of i.m. insulin
   B. There is a strong genetic association with HLA-B27
   C. The average life expectancy is less than in type 2 diabetes
   D. There is an association with coeliac disease
   E. Patients on insulin are unable to hold a UK driving licence

18. The following statements about diabetic ketoacidosis are correct:
   A. It does not occur in patients with type 2 diabetes
   B. The plasma potassium is usually raised at presentation
C. When treatment is started the arterial pH falls  
D. The plasma anion gap is normal  
E. It can result in a low plasma phosphate level  

19. In diabetic ketoacidosis:  
A. Patients should be treated immediately with subcutaneous insulin  
B. Acid reflux usually corrects with insulin and fluid replacement  
C. Patients should eat normally as soon as possible  
D. A fast respiratory rate indicates concurrent pneumonia  
E. Insulin therapy is no longer needed when the blood glucose returns to normal  

**Extended matching questions**

**Question 1 Theme: Polyuria**
A. Diabetes mellitus  
B. Diabetes insipidus  
C. Chronic kidney disease  
D. Primary hyperparathyroidism  
E. Chronic hypokalaemia  
F. Urinary tract infection  
G. Diuretic therapy  
H. Compulsive water drinking  
I. Supraventricular tachycardia  

*For each of the following questions, select the best answer from the list above:*

I. A 48-year-old female with a previous Whipple’s operation (pancreatoduodenectomy) for Zollinger–Ellison syndrome presents with a 3-month history of polyuria and constipation. What is the most likely diagnosis?  
II. A 27-year-old female presents with polyuria 2 months after home delivery of a healthy 3.2 kg son. She needed urgent hospital admission after the birth for blood transfusion for postpartum haemorrhage. What is the most likely diagnosis?  
III. A 16-year-old male presents with a 4-week history of thirst, polyuria, malaise and loss of appetite. Serum urea and electrolytes are normal apart from $\text{HCO}_3 = 19$ mmol/L. What is the most likely diagnosis?  

**Question 2 Theme: Weight loss**
A. Thyrotoxicosis  
B. Coeliac disease  
C. Carcinoma of the stomach  
D. Diabetes mellitus  
E. Addison’s disease  
F. Anorexia nervosa  
G. Breast cancer  
H. Crohn’s disease  
I. Amphetamine abuse  

*For each of the following questions, select the best answer from the list above:*

I. A 57-year-old female on B12 injections for pernicious anaemia presents with anxiety, palpitations, intermittent diarrhoea and weight loss of 6 kg over 3 months. What is the most likely diagnosis?  
II. A 29-year-old male presents with night sweats, fever, abdominal pain and weight loss of 10 kg since he returned from Bangladesh 3
months ago. Examination shows increased pigmentation in the palmar creases and postural hypotension. What is the most likely diagnosis?

III. A 36-year-old female from Galway presents with a 6-month history of weight loss and abdominal cramps. Blood tests show iron deficiency and folate deficiency. What is the most likely diagnosis?

**Short answer questions**

1. Describe the clinical features of the following:
   A. Hyperthyroidism
   B. Acromegaly
   C. Primary hypoadrenalism

2. Write short notes on the following:
   A. Multiple endocrine neoplasia
   B. Phaeochromocytoma
   C. Goitre

3. Briefly discuss the causes of the following:
   A. Cushing syndrome
   B. Adrenal failure
   C. Diabetes insipidus

4. Write short notes on the following:
   A. Thyroid-related eye abnormalities
   B. SIADH
   C. Causes of polyuria

5. List the following:
   A. The hormones secreted by the anterior pituitary and their functions
   B. The causes of hypopituitarism
   C. The biochemical changes seen in primary hyperaldosteronism
FUNCTIONS OF THE KIDNEY

Excretory
- Waste products of metabolism

Regulatory
- Control of body fluid volume and composition

Endocrine
- Erythropoietin → haemoglobin synthesis
- Renin-angiotensin → blood pressure control

Autocrine
- Prostaglandins → renal blood flow
- Renal natriuretic peptide → sodium and chloride transport
- Nitric oxide → sodium excretion
- Protein catabolism

Metabolic
- Vitamin D → calcium metabolism

Functional structure

Cortex
- Glomerulus
  - Hydrostatic and oncotic pressure
  - Ultrafiltration of blood
  - 120 mL/min protein- and fat-free fluid
- Proximal convoluted tubule
  - Resorption of 60–80% water and Na⁺
  - Resorption of >99% K⁺/HCO₃⁻/glucose/amino acids
- Distal convoluted tubule
  - Water and NaCl control
  - Via action of ADH
  - K⁺ excretion

Medulla
- Loop of Henle
  - 15% long loops
  - Active transport of Na⁺/K⁺/Cl⁻
  - Interstitium is hypertonic (urea recycling)
    → Water resorption and urine concentration

EXAMINING THE RENAL SYSTEM
- All systems need to be examined but pay special attention to the following:
Kidneys (Box 14.1)

- Position
  - Usually impalpable
  - Usual location: superior tip level with 11th rib
  - Transplanted kidneys in the iliac fossae
- Size: Normally 3×6×11 cm
- Shape
- Scars from previous surgery
- Auscultate 5 cm above and lateral to umbilicus for renal artery stenosis

Urine

Urinalysis

- Chemical (Stix) testing
  - Blood
  - Protein
  - Glucose
  - Bacterial nitrites plus leucocyte esterases
  - pH
  - Specific gravity and osmolality

Microscopy

- White cells >10/mm³: inflammation or infection
- Red cells >10/mm³: bleeding
- Bacteria
- Casts: tubular deposits
  - Red cell casts always indicate disease
  - White cell casts in pyelonephritis
  - Coarse granular casts in proteinuria
  - Fine granular casts after exercise
  - Cell casts in acute tubular necrosis

Volume

- Oliguria
- Polyuria

INVESTIGATIONS IN NEPHROLOGY

Imaging: Plain X-rays

- Renal calcification
- Renal calculi
### Excretory urography
- Intravenous contrast excreted by kidneys
  - Anatomy of renal tract
  - Excretion of contrast

### Ultrasound
- Masses
- Cysts
- Dilatation of renal tract – obstruction
- Renal size
- Bladder emptying
- Renal vessel Doppler

### CT and MRI
- Detection of calculi/urography
- Renal masses
- Staging tumours
- Renal vessel imaging
- Retroperitoneal masses

### Arteriography
- Extrarenal arterial imaging

### Dynamic scintigraphy
- DPTA/MAG3/Hippuran – show perfusion
- Two phases:
  - Glomerular filtration
  - Outflow of urine from collecting system

### Static scintigraphy
- DMSA – uptake proportional to renal function
- Allows comparison of two kidneys
- Visualization of kidney

### Renal biopsy
- Transcutaneous under ultrasound control

### Indications
- Nephrotic syndrome
- Unexplained renal failure
- Diagnosis of systemic disease

### Contraindications
- Single kidney
- Small kidneys
- Haemorrhagic disorders
- Uncontrolled hypertension

### Biochemical renal function tests

#### Serum urea and creatinine
- Urea
  - Byproduct of hepatic protein metabolism
  - Rapidly reflects changes in renal perfusion and nephron function
Creatinine
- Byproduct of muscle function
- Synthesis constant over time
- Used to compare renal function over long time periods
- Increase when glomerular filtration rate (GFR) is reduced by 50–60%
  (i.e. may be normal in the presence of significant decrease in renal function)

Creatinine clearance
Estimates GFR = \( \frac{V \times U}{P} \times 100 \)
(eGFR can be estimated from a formula requiring serum creatinine only.)

Arterial blood gases
- Metabolic acidosis in renal failure due to failure to excrete fixed acid and to renal bicarbonate wasting

GLOMERULAR DISEASES

Glomerulopathy
- A group of disorders
  - With immunologically mediated injury to glomerulus
  - Involving both kidneys
  - With secondary injury after initial immune insult
  - May be part of generalized disease (e.g. SLE)
- Classification by histology
  - Focal: <75% glomeruli affected
  - Diffuse: >75% glomeruli affected
  - Segmental: only part of the glomerulus affected
  - Proliferative: glomerular cell hyperplasia
  - Crescents: lymphocyte infiltration of Bowman’s space
  - Membranous: Capillary wall thickening
- Classification by clinical features
  - Asymptomatic proteinuria ± microscopic haematuria
  - Acute nephritic syndrome (Fig. 14.1)
  - Nephrotic syndrome (Fig. 14.2)
  - Rapidly progressive glomerulonephritis

Pathogenesis
- Deposition of immune complexes
- Deposition of anti-glomerular basement membrane (anti-GBM) antibody

Aetiology

Immune complex nephritis
- Unknown antigen
- Viruses
  - Mumps
  - Measles
  - Hepatitis B and C
  - Epstein–Barr virus (EBV)
  - Coxsackie
  - Varicella
  - HIV
- Bacteria
  - Group A β-haemolytic streptococci
  - \textit{Streptococcus viridans}
Glomerular diseases

**Aetiology**
- Streptococcal throat infection or otitis media
- Systemic vasculitis
- Cryoglobulinaemia

**Comprises**
- Haematuria
- Proteinuria
- Hypertension
- Oedema
- Oliguria
- Uraemia

**Investigations**
- **General**
  - Urine microscopy for red cells and casts
  - Serum urea and creatinine (raised)
  - Creatinine clearance (low)
  - 24 hour urine protein (raised)
  - C3 and C4 (low)
  - Chest X-ray for pulmonary oedema
  - Renal imaging (usually normal)
- **Diagnostic**
  - Throat swab
  - Antistreptolysin O titre
  - ANCA
  - Anti-GBM antibody
  - Cryoglobulins

**Management**
- Daily weight checks
- Fluid balance chart
- Antihypertensive
- BP monitoring
- Salt restriction
- Fluid restriction
- Diuretics
- Dialysis if needed
- Antibiotics for post-streptococcal infections

**Complications**
- Hypertensive encephalopathy
- Pulmonary oedema
- Severe uraemia

**ACUTE NEPHRITIC SYNDROME**

Fig. 14.1 Acute nephritic syndrome.

- Staphylococci
- *Treponema pallidum*
- Gonococci
- Salmonellae
- Parasites
  - *Plasmodium malariae*
  - *Schistosoma*
  - Filariasis
- Host antigens
  - DNA (systemic lupus erythematosus – SLE)
  - Cryoglobulins
  - Malignant tumours
Fig. 14.2 Nephrotic syndrome.

Clinical features
- Oedema
  - Peri-orbital
  - Face
  - Arms
- Frothy urine
- Ascites
- Normal JVP

Comprises
- Proteinuria 3–5 g/day
- Hypoalbuminaemia
- Oedema
- Hypercholesterolaemia

Causes
- All types of glomerulonephritis
- Systemic vasculitides
- Diabetic glomerulosclerosis
- Amyloidosis
- Drugs
- Allergies

Clinical features
- Oedema
  - Peri-orbital
  - Face
  - Arms
- Frothy urine
- Ascites
- Normal JVP

Investigations
General
- 24 hour urine protein >3–5 g/day
- Serum albumin <30 g/L
- Serum urea and creatinine
- Creatinine clearance
- Chest X-ray for pulmonary oedema
- Renal imaging (usually normal)

Diagnostic
- Throat swab
- Antistreptolysin O titre
- ANCA
- Anti-GBM antibody
- Cryoglobulins
- Renal biopsy (except in young children with selective protein leak, long-standing diabetes or drug-induced disease)

Management
General
- Sodium restriction
- Diuretics
- ACE inhibitor

Specific (for minimal change glomerulonephritis)
- High-dose steroids
- Cyclophosphamide

Complications
- Deep venous thrombosis (requires long-term prophylactic anticoagulation)
- Sepsis
- Oliguric renal failure
- Lipid abnormalities
Glomerular diseases

- Drugs
  - Penicillamine
  - Hydralazine

Anti-GBM antibody
- Antibodies to type IV collagen

Secondary mechanisms
- Complement activation
- Fibrin deposition
- Platelet aggregation
- Neutrophil-driven inflammation
- Kinin activation

Clinical features
- GN presents in one of four ways (see above)

Investigations
- 24-hour urinary protein (measure twice)
  - Nephrotic >3.5 g/day
- Urine microscopy
  - Red cell casts/haematuria
- Renal function
- Autoantibodies
  - ANCA: vasculitis
  - ANA: SLE
  - Anti-glomerular basement membrane: Goodpasture’s
- Renal biopsy

Specific types of GN (Table 14.1)

**IgA nephropathy**

Pathology
- Focal proliferative GN
- Mesangial deposits of IgA

Clinical features
- Microscopic haematuria
- Children and young adults

Prognosis
- Usually good
- 20% eventually develop renal failure

**Henoch–Schönlein purpura**

Pathology
- Focal segmental GN

Clinical features
- Purpuric rash
- Abdominal colic ± GI bleeding
- Joint pain
- ♂ > ♀ (2:1)
- May follow recent respiratory infection

Prognosis
- Usually good

**Goodpasture syndrome**

Pathology
- Severe proliferative crescentic GN
Clinical features
- Lung involvement → haemoptysis
- Progressive renal failure

Prognosis
- Usually progresses to renal failure

**Acute nephritic syndrome**
Classically occurs 3 weeks after streptococcal throat infection or otitis media (see Fig. 14.1).

**Nephrotic syndrome**
See Figure 14.2.

### RENAL INVOLVEMENT IN SYSTEMIC DISEASE

#### Systemic vasculitis
- SLE – all types of glomerulonephritis
- Polyarteritis nodosa (PAN) – renal failure
- Microscopic polyarteritis – crescentic glomerulonephritis

---

**Table 14.1 Glomerulonephritis**

<table>
<thead>
<tr>
<th>Histology</th>
<th>Example of causes</th>
<th>Clinical presentation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Proliferative glomerulonephritis</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diffuse</td>
<td>Post-streptococcal</td>
<td>Acute nephritic syndrome</td>
</tr>
<tr>
<td>Focal segmental</td>
<td>SLE</td>
<td>Haematuria</td>
</tr>
<tr>
<td></td>
<td>Henoch–Schönlein purpura</td>
<td>Proteinuria</td>
</tr>
<tr>
<td>Crescentic</td>
<td>Wegener’s granulomatosis</td>
<td>Progressive renal failure</td>
</tr>
<tr>
<td></td>
<td>Goodpasture syndrome</td>
<td></td>
</tr>
<tr>
<td>Mesangiocapillary</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Type 1</td>
<td>Hepatitis B and C</td>
<td>Haematuria Proteinuria</td>
</tr>
<tr>
<td>Type 2</td>
<td>Measles</td>
<td>Nephrotic syndrome</td>
</tr>
<tr>
<td>Membranous</td>
<td>Unknown Malaria</td>
<td>Nephrotic syndrome</td>
</tr>
<tr>
<td>Minimal change</td>
<td>Unknown</td>
<td>Nephrotic syndrome (especially in children)</td>
</tr>
<tr>
<td>IgA nephropathy</td>
<td>Henoch–Schönlein purpura</td>
<td>Asymptomatic haematuria</td>
</tr>
<tr>
<td>Focal glomerulosclerosis</td>
<td>Diabetes mellitus</td>
<td>Proteinuria Nephrotic syndrome</td>
</tr>
</tbody>
</table>
Renal involvement in systemic disease

- Wegener’s granulomatosis – glomerulonephritis
- Antiphospholipid syndrome

Cryoglobulinemia

- Monoclonal or polyclonal expansion of abnormal immunoglobulins which precipitate reversibly in the cold (cryoglobulins)

Aetiology

- Viral infections, e.g. hepatitis B and C, cytomegalovirus (CMV), EBV
- Fungal infections
- Malaria
- Infective endocarditis
- Autoimmune diseases

Clinical features

- Glomerulonephritis
- Purpura
- Raynaud’s phenomenon
- Systemic vasculitis
- Polyneuropathy
- Hepatic involvement

Multiple myeloma

- 20–30% → acute kidney injury
  - Light chain deposition
  - AL amyloidosis
  - Hypercalcaemic nephropathy

Diabetes mellitus

See Chapter 13.

Amyloidosis

- A disorder of protein metabolism with extracellular deposition of insoluble fibrillar proteins in organs and tissues

Types

- AL amyloidosis
- Familial amyloidosis
- Secondary amyloidosis

AL amyloidosis

Pathology

- Plasma cell production of amyloidogenic immunoglobulin light chains (AL)
- AL chains are excreted in urine (Bence Jones proteins)
- Associated with myeloma and Waldenström’s macroglobulinaemia

Clinical features

- Nephrotic syndrome
- Cardiomyopathy
- Autonomic neuropathy
- Sensory neuropathy
- Carpal tunnel syndrome
- Hepatomegaly
- Splenomegaly
Familial amyloidosis

Pathology
- Autosomal dominant inherited mutant protein formation
- Mutant protein forms amyloid fibrils

Mutant proteins
- Transthyretin (commonest)
- Apolipoprotein A-1
- Fibrinogen
- Lysozyme

Clinical features
- Peripheral sensorimotor neuropathy
- Autonomic neuropathy
- Conduction defects in heart

Secondary amyloidosis

Pathology
- Amyloid is formed from acute phase protein serum amyloid A (SAA)

Aetiology
- Rheumatoid arthritis
- Inflammatory bowel disease
- Familial Mediterranean fever
- Tuberculosis
- Bronchiectasis
- Osteomyelitis

Clinical features
- Renal disease
- Hepatosplenomegaly

Diagnosis of amyloidosis
- Rectal or gum biopsy
- Amyloid stains with Congo red with green birefringence in polarized light

Management of amyloidosis
- Treat associated disorder
- Treat nephrotic syndrome or cardiac failure
- Chemotherapy for AL
- Liver transplant for transthyretin-associated amyloidosis

HIV-associated nephropathy (HIVAN)
- Focal glomerulosclerosis
  - Proteinuria $\rightarrow$ nephrotic syndrome
  - $\rightarrow$ Rapidly progressive renal failure
- 90% of patients are black
- HAART may slow/halt progression

Pre-eclampsia
- Proteinuria can $\rightarrow$ nephrotic syndrome – usually settles after delivery
Urinary tract infection

Haemolytic-uraemic syndrome (HUS)
- Follows gastroenteritis or respiratory tract infection, *E. coli* O157
- Comprises
  - Intravascular haemolysis
  - Thrombocytopenia
  - Acute kidney injury

Thrombotic thrombocytopenic purpura
- Microangiopathic haemolysis
- Renal failure
- Neurological disturbance

TUBULOINTERSTITIAL NEPHRITIS (TIN)

Acute TIN
- Drugs
  - Penicillin/cephalosporins
  - Sulphonamides
  - NSAIDs
  - Allopurinol
  - Phenytoin
  - Diuretics: furosemide
- Infections

Chronic TIN
- Drugs: NSAIDs
- Sickle cell disease/trait
- Reflux nephropathy
- Diabetes mellitus

HYPERTENSION AND THE KIDNEY
- Benign essential hypertension
  - Intimal thickening of small vessels
  - Reduction in kidney size
  - Increased glomerular damage → CRF
  - Requires careful control of BP <140/85
- Renal hypertension
  - Complicates bilateral renal disease
  - → Activation of renin-angiotensin system
  - → Salt and water retention → hypertension
- Renovascular disease
  - Renal artery stenosis → reduced renal blood flow
  - → Activation of renin-angiotensin system
  - → Salt and water retention → hypertension
  - May be exacerbated by ACE inhibitors

URINARY TRACT INFECTION
- 50000/million per year
- Common in women; 90% of attacks are isolated
- Uncommon in men
**Bacterial infections**

**Causative organisms**
- Usually from patient’s own bowel flora
- *E. coli* – 68%
- *Proteus mirabilis* – 12%
- *Staphylococcus saprophyticus* or *epidermidis* – 10%
- *Klebsiella aerogenes* – 4%
- *Enterococcus faecalis* – 6%

**Associated diseases**
- Diabetes mellitus
- Sickle cell disease or trait
- Analgesic misuse
- Stones
- Obstruction
- Polycystic kidneys
- Vesico-ureteric reflux

**Clinical features**
- Cystitis
  - Frequency of micturition
  - Dysuria
  - Suprapubic pain/tenderness
  - Haematuria
  - Smelly urine
- Pyelonephritis
  - Loin pain/tenderness
  - Fever
  - Systemic upset

**Investigations**
- Symptomatic women
  - Dipstix + for nitrites and leucocytes
  - >$10^2$ coliforms/mL + pyuria (>10WCC/mm³) or
  - >$10^3$ any pathogenic organism/mL or
  - Any growth from suprapubic bladder aspiration
- Symptomatic men
  - >$10^3$ pathogenic organisms/mL
- Asymptomatic patients
  - >$10^5$ pathogenic organisms/mL (on two occasions)
- Causes of sterile pyuria
  - *Chlamydia*
  - TB
  - Partially treated bacterial UTI

**Radiology**
- Excretory urography is now seldom performed; CT/MRI is more appropriate
  - Women with ≥3 attacks
  - All men
  - All children
- Abdominal X-ray and ultrasound
- Acute pyelonephritis

**Management**
- Oral antibiotics
  - Amoxicillin
  - Nitrofurantoin
• Trimethoprim
• Oral cephalosporin
• Intravenous antibiotics
  • For acute pyelonephritis with high fever, vomiting or systemic upset
  • Cefuroxime
  • Gentamicin
  • Ciprofloxacin

**Tuberculosis of the renal tract**
• Affects the renal cortex spreading to the papillae and into the urine, ureters and bladder
• May cause ureteric obstruction and hydronephrosis

**Investigations**
• Culture of acid-fast bacillae from early morning urine (EMU) samples

---

**RENAL CALCULI**

**Prevalence**
• 2% of UK population

**Types of urinary stone**
See Table 14.2.

**Aetiology**
• Dehydration
• Specific chemical abnormalities
  • Hypercalcaemia
  • Hypercalciuria
  • Hyperoxaluria
  • Hyperuricaemia
  • Cystinuria
• Infection
• Renal tubular acidosis
• Primary renal disease
• Drugs → calcium stones:
  • Loop diuretics
  • Vitamins D and E
  • Glucocorticoids
  • Antacids
• Drugs → uric acid stones
  • Thiazide diuretics
  • Salicylates

---

**Table 14.2 Types of urinary stone**

<table>
<thead>
<tr>
<th>Type</th>
<th>Frequency (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Calcium oxalate</td>
<td>65</td>
</tr>
<tr>
<td>Calcium phosphate</td>
<td>15</td>
</tr>
<tr>
<td>Magnesium ammonium phosphate</td>
<td>10–15</td>
</tr>
<tr>
<td>Uric acid</td>
<td>3–5</td>
</tr>
<tr>
<td>Cystine</td>
<td>1–2</td>
</tr>
</tbody>
</table>
Drugs that precipitate
- Indinavir

**Clinical features**
- Asymptomatic
- Renal colic
- Haematuria
- Urinary tract infection
- Obstruction

**Investigations**
- Midstream urine (MSU) and culture
- Serum urea and electrolytes, creatinine, eGFR
- Serum calcium
- Serum urate
- Plain abdominal X-ray
- Spiral CT
- Excretion urography
- Urinary calcium, oxalate and uric acid
- Sieve urine to trap stones for analysis

**Management**
- Analgesia (opiates, NSAIDs)
- High fluid intake
- Stones <0.5 cm pass spontaneously
- Stones >1 cm require intervention
- Obstruction or infection requires intervention

**Intervention**

**Percutaneous nephrolithotomy**
- Endoscopic extraction of renal pelvis stones through a percutaneous tract

**Extracorporeal shock-wave lithotripsy (ESWL)**
- Fragmentation of stones with shock waves focused in from an external source

---

**URINARY TRACT OBSTRUCTION**

See Table 14.3.

**Hydronephrosis**
- Dilatation of renal pelvis above obstruction

**Clinical features**
- Loin pain/tenderness
- Anuria – bilateral obstruction
- Polyuria
- Bladder outflow obstruction (hesitancy, poor stream, terminal dribbling)
- Palpable enlarged kidney(s)

**Investigations**
- Urea and electrolytes
- Ultrasound
- Excretion urography
- Cystoscopy
Management
- Relieve obstruction by temporary drainage via nephrostomy or urethral or suprapubic catheter
- Treat underlying cause
- Prevent and/or treat infection

Surgical drainage
- Urinary diversion
- Ureteric stents

ACUTE KIDNEY INJURY
- Abrupt deterioration in renal function which is usually reversible

Pre-renal uraemia
- Impaired perfusion of kidneys

Aetiology
- Hypovolaemia (acute blood loss, dehydration, sepsis)
- Hypotension
- Cardiac failure
- Renal artery stenosis (± ACE inhibitors)
- NSAIDs → reduced renal prostaglandins

Management
- Correct hypovolaemia or hypotension
- Monitor central venous pressure to maintain adequate vascular volume
- Stop causative agents

Acute uraemia due to renal causes

Aetiology
- Acute tubular necrosis (Fig. 14.3)
- Vasculitis
- Pre-eclampsia
- Haemolytic-uraemic syndrome
- Rhabdomyolysis

Post-renal uraemia
- Urinary tract obstruction

Table 14.3 Causes of urinary tract obstruction

<table>
<thead>
<tr>
<th>Within lumen</th>
<th>Neurogenic bladder</th>
</tr>
</thead>
<tbody>
<tr>
<td>Calculus</td>
<td>Urethral stricture</td>
</tr>
<tr>
<td>Blood clot</td>
<td>Calculus</td>
</tr>
<tr>
<td>Sloughed papilla</td>
<td>Gonococcal infection</td>
</tr>
<tr>
<td>Tumour</td>
<td>Outside pressure</td>
</tr>
<tr>
<td>Within wall</td>
<td>Tumours</td>
</tr>
<tr>
<td>Ureteric stricture</td>
<td>Aortic aneurysm</td>
</tr>
<tr>
<td>TB</td>
<td>Prostatic obstruction</td>
</tr>
<tr>
<td>Calculus</td>
<td>Retroperitoneal fibrosis</td>
</tr>
<tr>
<td>Post-surgical</td>
<td>Accidental ligation of ureter</td>
</tr>
<tr>
<td>Schistosomiasis</td>
<td>Phimosis</td>
</tr>
</tbody>
</table>
Investigations in acute kidney injury

**Determine whether pre-renal, renal or post-renal**
- Exclude bladder outflow obstruction – insert urinary catheter
- Ultrasound – to exclude upper urinary tract obstruction
- Fluid challenge – increased urine output will differentiate pre-renal from renal

**Urinalysis**
- Dipstick for protein and blood
- Myoglobin

**Serum biochemistry**
- Urea and electrolytes
  - Urea ↑, K+ ↑, Na+ ↓

**Causes** (renal ischaemia or direct renal toxins, e.g. gentamicin)
- Haemorrhage
- Burns
- Diarrhoea and vomiting
- Pancreatitis
- Diuretics
- Myocardial infarction
- Congestive cardiac failure
- Endotoxic shock
- Hepatorenal syndrome
- Contrast nephropathy
- Drugs
  - Aminoglycosides
  - NSAIDs
  - ACE inhibitors
- Pre-eclampsia

**Vulnerable situations**
- Cholestatic jaundice
- Disseminated intravascular coagulation (DIC)
- Pregnancy
- Liver failure

**Clinical features**
- Symptoms of uraemia
  - Anorexia
  - Nausea, vomiting
  - Pruritus
  - Drowsiness, fits
  - Epistaxis

**Biochemical features**
- Urea raised
- Potassium raised
- pH low
- Sodium low
- Calcium low
- Phosphate raised

**Fig. 14.3 Acute tubular necrosis.**
Acute kidney injury

Metabolic acidosis (pH ↓/HCO₃⁻ ↓/negative base excess)
Creatinine ↑, eGFR down
Calcium ↓ and phosphate ↑
Albumin
Alkaline phosphatase
Urate
Drug levels

Haematology
- Full blood count and blood film
  - Normal Hb
- ESR
- Coagulation studies

Microbiology
- Urine microscopy and culture
- Blood cultures

Management of acute uraemia

General management
- Admit to renal unit or ITU for support of all systems, with the aim of keeping the patient alive while waiting for renal function to recover

Diet
- Sodium and potassium restriction
- Protein restriction only if trying to avoid dialysis

Fluid balance
- Assessment of input–output chart
- Signs of fluid overload
- Serum electrolytes
- Daily weight check

Treat sepsis
- Avoid nephrotoxic drugs and alter dose for renally excreted drugs

Dialysis and haemofiltration in acute kidney injury

Indications
- Symptomatic uraemia
- Complications of uraemia, e.g. pericarditis
- Severe biochemical derangement
- Uncontrolled hyperkalaemia (Box 14.2)
- Pulmonary oedema
- Acidosis
- Removal of toxic drugs, e.g. aspirin overdose, gentamicin

Options
- Peritoneal dialysis
- Continuous haemofiltration

Prognosis
- Up to 50% mortality

Contrast nephropathy
- Caused by iodinated radiological contrast media
- Dose-dependent effect
Box 14.2. Hyperkalaemia

- Check result is compatible with patient’s clinical condition (if not repeat sample)
- ECG to look for changes of hyperkalaemia (peaked T waves, widened QRS complexes – Fig. 14.4) and put patient on cardiac monitor
- K⁺ >6.0 or with symptoms or ECG changes, give:
  - i.v. calcium gluconate 10 mL 10%
  - i.v. 50 mL 50% dextrose plus 10 units soluble rapid-acting insulin over 30 minutes, monitoring blood glucose for hypoglycaemia
  - Nebulized salbutamol 10 mg
  - Oral calcium resonium 15–30 g 2–3 times daily or
  - Rectal calcium resonium retention enema 50 g daily
  - Dialysis or haemofiltration if no correction

- Risk increased with
  - Pre-existing renal impairment
  - Hypovolaemia
  - Low cardiac output
  - Diabetes mellitus
  - Hyperviscosity
- Risk reduced by
  - n-Acetyl cysteine
  - Pre-hydration with saline

**CHRONIC KIDNEY DISEASE**

- Long-standing progressive impairment of renal function

**Prevalence**
- 600/million per year in UK
- End-stage renal failure – 200/million per year in UK

**Aetiology**
See Table 14.4.

**Clinical features**

**History**
- Duration of symptoms
- Drug ingestion, e.g. NSAIDs, analgesics and herbal therapies
- Past surgical history
- Previous chemotherapy
- Family history of renal disease

**Symptoms**
- Asymptomatic
- Malaise, loss of energy
- Insomnia
- Nocturia, polyuria
- Itching
- Nausea, vomiting, diarrhoea
- Paraesthesiae
- ‘Restless legs’ syndrome
Chronic kidney disease

Pass Finals 353

Fig. 14.4 The ECG in hyperkalaemia.

"tented" T wave

- Bone pain
- Peripheral or pulmonary oedema
- Anaemia
- Amenorrhoea and erectile dysfunction

**Signs**
- Short stature
- Anaemia
- Pigmentation on sun-exposed areas
- Brown nails
- Fluid overload
- Signs of underlying disease

**Investigations**

**Urine**
- Urinalysis
- Microscopy
- Culture
- 24-hour creatinine clearance or eGFR

**Table 14.4 Causes of chronic kidney disease**

<table>
<thead>
<tr>
<th>Congenital</th>
<th>Tubulo-interstitial disease</th>
</tr>
</thead>
<tbody>
<tr>
<td>Polycystic kidney disease</td>
<td>Nephritis</td>
</tr>
<tr>
<td>Glomerular disease</td>
<td>Idiopathic</td>
</tr>
<tr>
<td>Primary glomerulonephritis</td>
<td>Drugs</td>
</tr>
<tr>
<td>Secondary glomerulonephritis</td>
<td>Reflux nephropathy</td>
</tr>
<tr>
<td>(SLE, diabetes, amyloidosis)</td>
<td>TB</td>
</tr>
<tr>
<td>Vascular disease</td>
<td>Schistosomiasis</td>
</tr>
<tr>
<td>Atherosclerosis</td>
<td>Diabetes</td>
</tr>
<tr>
<td>Vasculitis</td>
<td></td>
</tr>
<tr>
<td>SLE</td>
<td>Obstruction</td>
</tr>
<tr>
<td>Hypertension</td>
<td>Stones</td>
</tr>
<tr>
<td></td>
<td>Prostate disease</td>
</tr>
<tr>
<td></td>
<td>Pelvic tumours</td>
</tr>
<tr>
<td></td>
<td>Retroperitoneal fibrosis</td>
</tr>
</tbody>
</table>
Biochemistry
- Urea and electrolytes
  - Urea ↑
  - Normal K⁺ or ↑
- Creatinine ↑ or eGFR ↓
- Calcium ↓ and phosphate ↑

Haematology
- Full blood count
  - Anaemia

Radiology
- Renal tract ultrasound
- Plain abdominal X-ray
- CT scan of abdomen and pelvis

Immunology
- Urinary Bence Jones proteins
- Serum electrophoresis and immunoglobulins
- Autoantibodies
- Complement levels

Microbiology
- Antistreptolysin O titre – post-Strep. infection
- Malaria film
- Hepatitis B and C serology

Histology
- Renal biopsy

Complications
- Anaemia (erythropoietin)
- Renal osteodystrophy (osteomalacia, rickets, hyperparathyroidism, osteoporosis, osteosclerosis)
- Pruritus
- Delayed gastric emptying
- Peptic ulceration (↑ gastrin)
- Pancreatitis
- Constipation
- Gout
- Hyperlipidaemia
- Hyperprolactinaemia
- Erectile dysfunction and male infertility
- Amenorrhoea and female infertility
- Short stature
- Cardiovascular disease
- Cardiac failure
- Sudden death
- Pericarditis
- Stroke

Management
General
- Treat underlying disease if possible
- Control hypertension
- Early referral to nephrologist when serum creatinine >350 µmol/L or in diabetics >250 µmol/L
Diet
- Calcium supplements
- Low phosphate diet
- Sodium and potassium restriction
- Protein restriction
- Fluid restriction

Anaemia
- Erythropoietin
- Iron therapy

RENAL REPLACEMENT THERAPY

Haemodialysis
- Blood from the patient is pumped through semipermeable membranes against a dialysate fluid allowing diffusion of molecules along concentration gradients
- Requires rapid blood flow through a large-bore double-lumen central venous catheter or arteriovenous fistula

Frequency
- Usually 4–5 hours 3 times per week

Complications
- Hypotension while on dialysis

Haemofiltration
- Removal of plasma water and dissolved electrolytes (potassium, sodium, urea and phosphate) by flow across a semipermeable membrane and replacement with a solution of desired biochemical composition
- Mostly used in acute kidney injury

Frequency
- Usually continuous

Peritoneal dialysis
- Uses peritoneum as semipermeable membrane
- Dialysis fluid is run into peritoneal cavity through a tube in the anterior abdominal wall
- Urea, creatinine and phosphate pass into the dialysate from the blood in peritoneal capillaries along a diffusion gradient
- Water and electrolytes go in through osmosis

Frequency
- Dialysis fluid is exchanged usually 3–5 times per day
- Fluid exchange takes about 40 minutes

Renal transplantation
- A kidney, explanted from either a cadaveric or living related donor, is anastomosed to the iliac vessels of the recipient
- The ureter is placed into the bladder
- Immunosuppression is required for the rest of the patient’s life

Prognosis
- 80% of grafts survive 5–10 years
- 60% of grafts survive for 10–30 years
CYSTIC RENAL DISEASES

- Solitary or multiple simple renal cysts are common, affecting 50% of the population >50 years old
- Usually asymptomatic

Autosomal dominant polycystic kidney disease

- Inherited disorder
- Presents in adulthood
- Multiple bilateral renal cysts
- Associated with hepatic cysts

Prevalence

- 1:400–1000

Responsible genes

- PKD 1 on chromosome 16
- PKD 2 on chromosome 4

Clinical features

- Acute loin pain ± haematuria (due to haemorrhage, infection or stone formation)
- Loin discomfort (due to large kidneys)
- Subarachnoid haemorrhage (secondary to berry aneurysm rupture)
- Hypertension
- Liver cysts
- Chronic kidney disease
- Large irregular palpable kidneys
- Hepatomegaly
- Ultrasound shows multiple renal cysts

Complications

- Progression to chronic kidney disease ~70% by age 70
- Pain
- Cyst infection
- Renal stones
- Hypertension
- Liver cysts
- Berry aneurysms (10%) → sub-arachnoid haemorrhage

Screening

- Children and siblings of patients should have renal ultrasound after age 20

TUMOURS OF THE UROGENITAL TRACT AND PROSTATE

Renal cell carcinoma

- Average age at presentation – 55 years
- ♂ > ♀ (2:1)

Clinical features

- Haematuria
- Loin pain
- Mass in flank
- Malaise
- Weight loss
- Polycythaemia (excess erythropoietin)
Investigations
- Ultrasound or CT
- MRI (for tumour staging)
- Raised ESR

Management
- Nephrectomy
- α-interferon/interleukin-2
- Tyrosine kinase inhibitors, e.g. sunitinib

Prognosis
- 60–70% 5-year survival for localized tumour
- 15–35% 5-year survival for lymph node involvement
- 5% 5-year survival for distant metastases

Urothelial tumours
- Transitional cell carcinoma, most common in the bladder
  - ♂ > ♀ (4:1)
  - Present most commonly after 40 years

Risk factors
- Cigarette smoking
- Industrial carcinogen exposure (β-naphthylamine, benzidine)
- Drugs (phenacetin, cyclophosphamide)
- Chronic inflammation (schistosomiasis causes squamous cell carcinoma)

Clinical features
- Painless haematuria
- Clot retention

Investigations
- Urine cytology
- CT/MRI
- Cystoscopy

Management
- Local tumour ablation – endoscopic diathermy
- Local tumour resection – endoscopic transurethral bladder tumour resection (TURBT)
- Cystectomy
- Radiotherapy
- Local or systemic chemotherapy

Prognosis
- 80% 5-year survival (T1 N0 M0)
- 5% 5-year survival (distant metastases)

Prostate cancer
- Sixth commonest cause of cancer death in men
- Malignant change in prostate gland is very common in older men
  - About 80% >80 years
  - Usually dormant or asymptomatic

Clinical features
- Bladder outflow obstruction
- Distant metastases to bone, lung or brain
Investigations
- Cystoscopy
- Transrectal ultrasound
- Prostatic biopsy
- Prostate-specific antigen (PSA)
- Bone scan

Management
Local disease
- Radical prostatectomy
- Radiotherapy

Metastatic disease
- Orchidectomy
- LHRH analogues (buserelin, goserelin)

Prognosis
- Variable

Testicular tumours
- Commonest in young men aged 30–35
- Seminomas 30%
- Teratomas 70%
- Higher risk in undescended testes and history of orchidopexy

Clinical features
- Testicular swelling (painless or painful)
- Distant metastases

Investigations
- Testicular ultrasound
- Surgical exploration and biopsy via the groin

Staging
- Chest X-ray
- α-fetoprotein
- β-human chorionic gonadotrophin
- Abdominal CT scan

Management
Seminomas
- Radiotherapy
- Chemotherapy

Teratomas
- Orchidectomy
- Chemotherapy

DISEASES OF THE PROSTATE

Benign prostatic enlargement
- Common over 60 years

Clinical features
- Bladder outflow obstruction
- Urinary tract infection
- Stones
- Acute urinary retention (Box 14.3)
- Chronic retention with overflow incontinence
- Bilateral hydronephrosis
- Smooth enlarged prostate on rectal exam
Investigations
- Urine culture
- Assessment of renal function
- PSA
- Cystoscopy

Management
- Observation

Medical
- \(\alpha\)-receptor blockers
- Finasteride

Surgical
- Transurethral resection of prostate (TURP)
- Prostatic stents

SELF-ASSESSMENT QUESTIONS

Multiple choice questions (single best answer)

1. IgA nephropathy:
   A. Is associated with carcinoma of the bronchus
   B. Presents after streptococcal infections
   C. Presents with a purpuric rash
   D. Is caused by anti-GBM antibody
   E. Usually progresses to chronic kidney disease

2. Goodpasture syndrome:
   A. May present with haemoptysis
   B. Is caused by immune complex deposition
   C. Causes membranous glomerulonephritis
   D. Rarely progresses to chronic kidney disease
   E. Is treated by nephrectomy

3. Acute nephritic syndrome:
   A. Occurs after \(E.\ coi\) infections
   B. Comprises oedema and low albumin
   C. Does not progress to acute kidney injury
   D. Urine microscopy shows red cell casts
   E. Is commonly complicated by hypercholesterolaemia

4. In nephrotic syndrome:
   A. Urine protein excretion is >3 g/day
   B. The renal lesion is always proliferative glomerulonephritis
   C. The urine may be fatty
D. The JVP is raised
E. Renal biopsy is contraindicated

5. Urinary tract infection:
   A. Is commoner in males
   B. Is always symptomatic
   C. Usually indicates an abnormal renal tract in females
   D. May be treated with oral gentamicin
   E. Is most commonly caused by \textit{E. coli} infection

6. Pyelonephritis:
   A. Is associated with a low urine leucocyte count
   B. Is usually secondary to urinary tract obstruction
   C. Is associated with diabetes insipidus
   D. Causes infertility
   E. May be complicated by septicaemia

7. Renal calculi:
   A. Are most commonly composed of uric acid
   B. May be asymptomatic
   C. May be caused by hyperkalaemia
   D. Are usually radiolucent
   E. Larger than 2 cm pass spontaneously

8. Management of bladder outflow obstruction should include:
   A. Fluid restriction
   B. External beam shock wave lithotripsy
   C. Ventriculo-peritoneal shunt
   D. Urethral catheter
   E. Orchidectomy

9. Pre-renal uraemia:
   A. Is caused by hypertension
   B. May be due to gastrointestinal bleeding
   C. Does not correct with fluid replacement
   D. Usually requires emergency dialysis
   E. Presents with pericarditis

10. Complications of acute kidney injury include:
   A. Subarachnoid haemorrhage
   B. Encephalitis
   C. Hypokalaemia
   D. Pericarditis
   E. Contrast nephropathy

11. Acute tubular necrosis:
   A. Is the renal lesion of amyloidosis
   B. May be part of multisystem failure
   C. May be caused by a reaction to oral radiological contrast
   D. Rarely requires dialysis
   F. Has a good overall prognosis

12. Causes of chronic kidney disease include:
   A. Paracetamol toxicity
   B. Sarcoidosis
   C. Cirrhosis of the liver
   D. Herbal therapies
   E. Gilbert syndrome

13. Management of chronic kidney disease commonly includes:
   A. Emergency urography
   B. Bone marrow transplant
C. Abdominal paracentesis
D. Total dental extraction
E. Phosphate restriction

14. Complications of chronic kidney disease commonly include:
   A. Anaemia
   B. Pseudogout
   C. Paget’s disease
   D. Haematuria
   E. AV fistula formation

15. A 66-year-old woman was found to be hypertensive and was commenced on ramipril. Ten days later she felt unwell and blood tests revealed: Urea 38 mmol/L (2.5–6.7), creatinine 420 µmol/L (79–118), potassium 6.9 mmol/L (3.5–5.0). What is the most likely underlying diagnosis?
   A. IgA nephropathy
   B. Chronic tubulointerstitial nephritis
   C. Chronic NSAID misuse
   D. Renal sarcoidosis
   E. Bilateral renal artery stenosis

16. A 77-year-old man was admitted with a pneumonia. His blood tests revealed: Urea 25 mmol/L (2.5–6.7), creatinine 280 µmol/L (79–118), potassium 7.2 mmol/L (3.5–5.0). What is the first step in his management?
   A. Oral calcium resonium
   B. Intravenous calcium gluconate
   C. Subcutaneous enoxaparin
   D. Intravenous insulin and dextrose
   E. Inhaled salbutamol

17. The glomerulus is responsible for the synthesis of an ultrafiltrate from blood. Which of the following is most important in this function?
   A. Na⁺/K⁺ transmembrane pump
   B. Capillary hydrostatic pressure
   C. Osmotic pressure in Bowman’s capsule
   D. Proximal loop amino acid resorption
   E. Urea recycling in the loop of Henle

18. A 64-year-old man presented with nocturia and hesitancy with a poor flow when urinating. What is the most likely diagnosis?
   A. Benign prostatic hypertrophy
   B. Bladder stone
   C. Transitional cell carcinoma of the bladder
   D. Prostatic adenocarcinoma
   E. Nonspecific urethritis

19. A 34-year-old woman is found to have multiple cysts on both kidneys and in the liver at ultrasound. A diagnosis of autosomal dominant polycystic kidney disease is made. What is the likelihood of her developing chronic kidney disease requiring renal replacement therapy?
   A. 5%
   B. 20%
   C. 50%
   D. 70%
   E. 90%
20. A 13-year-old girl was referred with peripheral oedema. Her urinary protein was 5 g/L. Which one of the following is most commonly associated with this diagnosis?
A. Hypokalaemia
B. Hyperamylasaemia
C. Achlorhydria
D. Hyperproteinaemia
E. Hypercholesterolaemia

Extended matching questions

**Question 1 Theme: Right-sided abdominal pain**
A. Pyelonephritis
B. Right ovarian cyst
C. Renal calculi
D. Appendicitis
E. Polycystic kidney disease
F. Crohn’s disease
G. Gallstones
H. Right lower lobe pneumonia
I. Pancreatitis
J. Renal cell carcinoma
K. Hydronephrosis
L. Hepatitis
M. Irritable bowel syndrome

For each of the following questions, select the best answer from the list above:
I. A 39-year-old advertising executive, who suffers with gout, presents with sudden onset of excruciating colicky pain in the right loin. On examination he is distressed and tender in the right flank. He is apyrexial. Urinalysis shows blood+++ and no nitrite. What is the most likely diagnosis?
II. A 49-year-old woman with chronic multiple sclerosis, confined to a wheelchair, presents with fever, confusion and vomiting. She is incontinent of urine with a permanent indwelling catheter. She is pyrexial with a temperature of 39°C. There is reduced air entry to the right lung base. Her PO₂ is 7.6 and urinalysis shows protein++, blood+, nitrite+. What is the most likely diagnosis?
III. A 39-year-old man presents with a 6-month history of a chronic dull ache in the right flank with a feeling of fullness on that side. Eighteen months ago he had emergency neurosurgical clipping of a berry aneurysm after suffering a subarachnoid haemorrhage. What is the most likely diagnosis?

**Question 2 Theme: Acute kidney injury**
A. Hepatorenal syndrome
B. Contrast nephropathy
C. Gentamicin toxicity
D. Acute GI haemorrhage
E. Hypertensive nephropathy
F. Haemolytic-uraemic syndrome
G. Goodpasture syndrome
H. Wegener’s granulomatosis
I. Prostatic obstruction
J. Retroperitoneal fibrosis
K. Renal artery stenosis
For each of the following questions, select the best answer from the list above:

I. A 48-year-old alcoholic cirrhotic female was admitted 2 days ago with constipation and confusion. She has become pyrexial with low blood pressure and oliguria. Her blood tests show acute kidney injury. What is the most likely diagnosis?

II. A 90-year-old man is admitted in a dehydrated, febrile and confused state. He was seen by his GP for a ‘stomach upset’ 2 days ago. His full blood count shows anaemia and thrombocytopenia with red-cell fragments on the blood film. His biochemistry shows acute kidney injury. What is the most likely diagnosis?

III. A 74-year-old male is admitted with symptoms of a urinary tract infection. In the past 2 days he has developed increasing abdominal pain, fever and anuria. On examination he has a mass in the pelvis which is tender and dull to percussion. His blood tests show acute kidney injury. What is the most likely diagnosis?
Haematology comprises the study of the components of the blood and the bone marrow, along with disorders of the lymphoreticular system. Common disorders include the anaemias and haematological malignancy.

**BASIC SCIENCE IN HAEMATOLOGY**

**Components of blood**

**Cellular**
- Erythrocytes (red cells)
- Reticulocytes (immature red cells)
- Leucocytes (white cells)
  - Lymphocytes
  - Monocytes
  - Eosinophils
  - Basophils
  - Neutrophils
- Platelets

**Non-cellular**

**Plasma**
- Liquid component of blood
- Includes
  - Fibrinogen
  - Clotting factors
  - Immunoglobulins
  - Albumin
  - Other plasma proteins
  - Electrolytes

**Serum**
- Fluid remaining after the formation of a fibrin clot (i.e. no fibrinogen)

**Stem cells**
- Progenitor cells for blood cells
- Proliferation and differentiation
- → Mature blood cells
- Self-renewal, so source cells not depleted (Fig. 15.1)

**Growth factors**
- Glycoproteins, e.g. granulocyte colony-stimulating factor (G-CSF)
- Regulate proliferation and differentiation of progenitor cells and mature cell functions
- Used to increase number of cell lines in response to stress, e.g. infection, blood loss, chemotherapy
Laboratory values (Table 15.1)

**Red cell indices**
- Size, number and haemoglobin content of erythrocytes
- Important in the classification of anaemia

**Erythrocyte sedimentation rate (ESR)**
- Rate of fall of red cells in a column of blood
- Measure of acute phase proteins and therefore of inflammation
- Increases with age
- ♀ > ♂
Plasma viscosity
- Measure of acute phase proteins
- No sex and little age variation

Reticulocyte count
- Immature red cells
- Measure of erythropoiesis
- Normally <2%
- Increased by high marrow activity, e.g.
  - After bleeding
  - Anaemia
  - Haemolysis

Haemoglobin

Structure
- Four globin (protein) chains
- Four haem (iron-containing) molecules
- Molecular weight 68000

Function
- Haem moiety binds and transports oxygen and CO₂

Genetics
- Adult Hb (HbA) consists of two α and two β globins
- HbA₂ consists of two α and two β globins (2% of adult Hb)
- Fetal Hb consists of two α and two γ globins

---

Table 15.1 Normal values for peripheral blood

<table>
<thead>
<tr>
<th></th>
<th>Male</th>
<th>Female</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hb (g/L)</td>
<td>135–175</td>
<td>115–160</td>
</tr>
<tr>
<td>PCV (haematocrit; L/L)</td>
<td>0.4–0.54</td>
<td>0.37–0.47</td>
</tr>
<tr>
<td>RCC (10¹²/L)</td>
<td>4.5–6.0</td>
<td>3.9–5.0</td>
</tr>
<tr>
<td>MCV (fL)</td>
<td>80–96</td>
<td></td>
</tr>
<tr>
<td>MCH (pg)</td>
<td>27–32</td>
<td></td>
</tr>
<tr>
<td>MCHC (g/L)</td>
<td>320–360</td>
<td></td>
</tr>
<tr>
<td>RDW (%)</td>
<td>11–15</td>
<td></td>
</tr>
<tr>
<td>WBC (10⁹/L)</td>
<td>4.0–11.0</td>
<td></td>
</tr>
<tr>
<td>Platelets (10⁹/L)</td>
<td>150–400</td>
<td></td>
</tr>
<tr>
<td>ESR (mm/h)</td>
<td>&lt;20</td>
<td></td>
</tr>
<tr>
<td>Reticulocytes</td>
<td>0.5–2.5% (50–100 × 10⁹/L)</td>
<td></td>
</tr>
</tbody>
</table>

ESR, erythrocyte sedimentation rate; Hb, haemoglobin; MCH, mean corpuscular haemoglobin; MCHC, mean corpuscular haemoglobin concentration; MCV, mean corpuscular volume of red cells; PCV, packed cell volume; RCC, red cell count; RDW, red blood cell distribution width; WBC, white blood count.

(Reproduced from Kumar P, Clark M. Kumar and Clark’s Clinical Medicine, 8th edn. Edinburgh: Elsevier; 2012, with permission from Elsevier.)
ANAEMIA

Anaemia (haemoglobin below the reference range) is not a diagnosis and a cause must be found.

Classification (Table 15.2)

- By erythrocyte volume (MCV)
  - Macrocytic – large red cells
    - B₁₂ deficiency
    - Folate deficiency
    - Chronic alcohol misuse
    - Chronic liver disease
    - ↑ Reticulocytes
    - Hypothyroidism
    - Drugs, e.g. azathioprine
  - Microcytic – small red cells
    - Iron deficiency
    - Thalassaemia
    - Sideroblastic anaemia
    - Anaemia of chronic disease
    - Myelodysplasia
  - Normocytic – normal red cells
    - Acute blood loss
    - Anaemia of chronic disease
    - Haemolysis
    - Infection
    - Pregnancy
    - Hypopituitarism
    - Hypothyroidism (may be macrocytic)
    - Renal failure

Clinical features

Symptoms

- Fatigue
- Headache \{ Common in normal population
- Faintness
- Breathlessness
- Angina
- Intermittent claudication
- Palpitations
Signs
- Pallor
- Tachycardia
- Systolic flow murmur
- Cardiac failure
- Koilonychia – spoon-shaped nails in iron deficiency
- Jaundice – haemolytic anaemia
- Bone deformity – thalassaemia major
- Leg ulcers – sickle cell disease

Investigations
- White cell count – if low, may be dilutional or bone marrow failure
- Reticulocyte count – measures bone marrow activity
- Blood film for erythrocyte morphology – may show dimorphic picture (both large and small red cells); seen in combined iron and folate deficiency

Iron deficiency anaemia

Iron metabolism
- Iron requirements
  -♂ 0.5–1 mg/day
  -♀ 1.2–1.7 mg/day (2–3 mg/day in pregnancy)
- Dietary iron 15–20 mg/day
- 10% absorbed
- Absorption is in duodenum and jejunum (Fig. 15.2)
- Transported in blood bound to transferrin
- Stored as ferritin and haemosiderin

Causes of iron deficiency
- Blood loss (commonly menstrual)
- Growth or pregnancy (↑ requirement)
- Decreased absorption (e.g. gastrectomy)
- Low dietary intake

Clinical features
- Koilonychia and brittle nails/hair
- Angular stomatitis
- Dysphagia
- Glossitis
- Plummer–Vinson or Paterson–Brown–Kelly syndrome

Investigations
- Blood count and film
- ↓ Serum ferritin
- ↓ Serum iron and ↑ iron-binding capacity ↓ transferrin saturation
- ↑ Serum soluble transferrin receptors

Management
- Identify and treat cause
- Oral iron – ferrous sulphate (first choice preparation) or gluconate
- Parenteral iron, severe malabsorption or chronic disease, e.g. inflammatory bowel disease if unable to tolerate oral

Anaemia of chronic disease

Aetiology
- Reduced erythropoiesis
- Reduced red cell survival
Fig. 15.2 Absorption of iron. (Reproduced from Kumar P, Clark M. Kumar and Clark’s Clinical Medicine, 8th edn. Edinburgh: Elsevier; 2012, with permission from Elsevier.)
Anaemia

Chronic infection
- Osteomyelitis
- Infective endocarditis
- TB

Chronic inflammation
- Rheumatoid arthritis
- Systemic lupus erythematosus (SLE)
- Polymyalgia rheumatica

Malignancy

Investigations
- Low iron and iron-binding capacity
- Normal or high ferritin
- Normal serum soluble transferrin receptors

Sideroblastic anaemia

Aetiology
- Abnormal haem metabolism
- Excess iron deposited in erythrocytes (ring sideroblasts)
- Inherited (X-linked) or acquired
  - Myelodysplastic syndrome, myeloproliferative disorders and myeloid leukaemia
  - Drugs, e.g. isoniazid
  - Alcohol/lead

Megaloblastic anaemia

Aetiology
- B12 deficiency (Fig. 15.3 and Table 15.3)
- Folate deficiency (Table 15.4)
- Myelodysplasia

Investigations
- ↑ MCV >96 fL (macrocytosis)
- Blood film – hypersegmented neutrophils
- Serum B12 and folate
- Red cell folate – better measure of tissue folate
- Look for underlying cause

Table 15.3 Causes of B12 deficiency anaemia

<table>
<thead>
<tr>
<th>Low dietary intake</th>
<th>Vegan diet – B12 high in meat, fish, eggs and milk</th>
</tr>
</thead>
</table>
| Impaired absorption (stomach) | Pernicious anaemia  
Gastrectomy  
Congenital lack of intrinsic factor |
| | Lack of intrinsic factor |
| Impaired absorption (small bowel) | Pancreatic insufficiency – failure to cleave off R-binders  
Terminal ileal disease – loss of absorption site  
Bacterial overgrowth – bacterial utilization of B12 |
| Abnormal metabolism | Transcobalamin II deficiency – congenital lack of B12 transporter |
Fig. 15.3 Absorption of vitamin B$_{12}$.
**Pernicious anaemia**

- → Megaloblastic anaemia

**Aetiology**
- Autoimmune disease
- Common (esp. in elderly)
- Anti-intrinsic factor antibodies in 50%
- Anti-parietal cell antibodies in 90%
- → Intrinsic factor deficiency due to autoimmune gastritis
- → B₁₂ malabsorption

**Disease associations**
- Autoimmune thyroid disease
- Addison’s disease
- Vitiligo
- Blond hair and blue eyes
- Blood group A
- Higher risk of gastric cancer in males

**Pathology**
- Gastric mucosal atrophy
- Achlorhydria (loss of gastric acid synthesis)

**Clinical features**
- Pallor and mild jaundice
- Glossitis (sore red tongue)
- Angular stomatitis
- Progressive polyneuropathy
  - Subacute combined degeneration of the cord
  - → Paraesthesia, weakness and ataxia
  - → Paraplegia
  - Rarely, optic atrophy or dementia

---

**Table 15.4 Causes of folate deficiency**

<table>
<thead>
<tr>
<th>Nutritional</th>
<th>Pathological</th>
</tr>
</thead>
<tbody>
<tr>
<td>Poor intake</td>
<td>Increased red cell synthesis, e.g.</td>
</tr>
<tr>
<td>Old age</td>
<td>haemolysis</td>
</tr>
<tr>
<td>Poor diet</td>
<td>Inhibited metabolism</td>
</tr>
<tr>
<td>Starvation</td>
<td>Drugs</td>
</tr>
<tr>
<td>Alcohol abuse</td>
<td>Anticonvulsants, e.g. phenytoin</td>
</tr>
<tr>
<td>Malabsorption</td>
<td>Methotrexate</td>
</tr>
<tr>
<td>Coeliac disease</td>
<td>Trimethoprim</td>
</tr>
<tr>
<td>Crohn’s disease</td>
<td>Increased cell turnover, e.g.</td>
</tr>
<tr>
<td>Anorexia</td>
<td>malignancy</td>
</tr>
<tr>
<td>Malignancy</td>
<td>Inflammatory disease</td>
</tr>
<tr>
<td>GI disease</td>
<td>Metabolic disease, e.g.</td>
</tr>
<tr>
<td>↑ Utilization</td>
<td>homocystinuria</td>
</tr>
<tr>
<td><strong>Physiological</strong></td>
<td>Haemodialysis</td>
</tr>
<tr>
<td>Pregnancy</td>
<td></td>
</tr>
<tr>
<td>Lactation</td>
<td></td>
</tr>
</tbody>
</table>
Management
- 1 mg vitamin B₁₂ per day for 7 days i.m.
- Then 1 mg every 3 months for life
- Oral high dose (e.g. 2 mg a day) vitamin B₁₂ can be prescribed as an alternative but requires good compliance

Folate deficiency
- → Megaloblastic anaemia

Folate absorption
- Found in spinach, broccoli, liver and kidney
- Cooking destroys folate
- Daily requirement 100 mg
- B₁₂ required for folate metabolism

Clinical features
- Anaemia
- Glossitis
- No neuropathy

Management
- Oral folate 5 mg/day

Prophylaxis
- Advised prior to and during pregnancy
- Reduces risk of neural tube defects

Sickle cell disease

Aetiology
- Mutation → abnormal β globin (HbS)
- → Sickle cell trait (heterozygote HbAS)
- Or sickle cell disease (homozygote HbSS)
- HbS is insoluble when deoxygenated
- → Hb forms crystals and deforms red cells
- → Sickle shape
- → Reduced red cell survival and microvascular obstruction

Epidemiology
- 25% of Africans carry abnormal gene
- Also India, Middle East and southern Europe

Precipitation of crisis
- Infection
  - Chest → hypoxia
  - Parvovirus → marrow aplasia → pancytopenia
  - Haemolysis due to sepsis
- Sequestration of red cells in liver and spleen
- Dehydration → increased plasma viscosity

Clinical features
- Onset after 6 months (as HbF level drops)
- Chronic haemolytic anaemia
- Recurrent painful crises
- Bone pain
- Chest – pleuritic pain (common cause of death – acute chest syndrome)
- Cerebral – fits, neurological signs
- Kidneys – papillary necrosis, inability to concentrate urine
Anaemia

- Spleen – splenic infarcts → hyposplenism
- Liver – pain and abnormal liver function
- Penis – priapism

**Long term**
- Hyposplenism → risk of infection
- Chronic leg ulcers
- Gallstones
- Necrosis of femoral heads
- Chronic kidney disease
- Chronic respiratory disease
- Stroke
- Retinopathy

**Investigations**
- Full blood count
  - Anaemia
  - Infection (leucocytosis)
- Blood film
  - Sickling
  - Hyposplenism
- Hb electrophoresis demonstrates HbS

**Management**

**Acute (Box 15.1)**
- i.v. fluids
- Oxygen
- Antibiotics if evidence of infection
- Adequate analgesia
- Exchange transfusions if severe crisis

**Long term**
- Pneumococcal and *Haemophilus influenzae* vaccines
- Folic acid
- Transfusions for clear indications and complications only
- Hydroxyurea increases Hb F production
- Bone marrow transplantation

**Thalassaemia**

**Aetiology**
- Inherited failure of synthesis of one globin type
- Accumulation of remaining globin type
- → Haemolysis and ineffective erythropoiesis

**β-thalassaemia**

**Minor (trait)**
- Carrier state (heterozygote)
- Asymptomatic
- Low MCV and MCH

**Major**
- Homozygote
- Severe anaemia requiring transfusions
- Onset 3–6 months old
- Infections
- Extramedullary haemopoiesis
  → Skull expansion and bossing
BOX 15.1. Management of acute painful crisis in opioid naive adults with sickle cell disease

**Morphine/diamorphine**
- 0.1 mg/kg i.v./s.c. every 20 minutes until pain controlled, then
- 0.05–0.1 mg/kg i.v./s.c. (or oral morphine) every 2–4 hours

**Patient controlled analgesia (PCA) (example for adults >50 kg)**

**Diamorphine**
- Continuous infusion: 0–10 mg/hour
- PCA bolus dose: 2–10 mg
- Dose duration: 1 minute
- Lockout time: 20–30 minutes

**Adjuvant oral analgesia**
- Paracetamol 1 g 6 hourly
- ± Ibuprofen\(^a\) 400 mg 8 hourly
- Or diclofenac\(^a\) 50 mg 8 hourly

**Laxatives (all patients)**
For example:
- Lactulose 10 ml×2 daily
- Senna 2–4 tablets daily
- Sodium docusate 100 mg×2 daily
- Macrogol 1 sachet daily
- Lubiprostone

**Other adjuvants**

**Anti-pruritics**
- Hydroxyzine 25 mg×2 as required

**Antiemetics**
- Prochlorperazine 5–10 mg×3 as required
- Cyclizine 50 mg×3 as required

**Anxiolytic**
- Haloperidol 1–3 mg oral/i.m.×2 as required

---

\(^a\)Caution advised with NSAIDs in renal impairment. (Adapted from Rees DC, Olujohungbe AD, Parker NE et al. Guidelines for the management of the acute painful crisis in sickle cell disease. Br J Haematol 2003; 120(5):744–752. Reproduced from Kumar P, Clark M, Kumar and Clark’s Clinical Medicine, 8th edn. Edinburgh: Elsevier; 2012, with permission from Elsevier.)

**Treatment**
- Folic acid
- Regular transfusions to suppress haemopoiesis and avoid deformity and anaemia
- Iron chelation to reduce overload
- Bone marrow transplantation

**α-thalassaemia**
- Deletion in one to four of the four α globin genes
- All four deleted → fetal death (hydrops fetalis)
- Three of four → moderate anaemia
- Two of four → carrier state, no anaemia
Haemolytic anaemia

- Anaemia due to the premature breakdown of erythrocytes, resulting in reduced red cell survival
- If haemolysis is acute, anaemia, jaundice and haemoglobinuria are seen

Aetiology

Inherited

- Sickle cell disease
- Thalassaemia
- Hereditary spherocytosis
- Hereditary elliptocytosis
- Glucose-6-phosphate dehydrogenase deficiency
  - X-linked recessive
  - → Haemolysis due to drugs, e.g. aspirin
  - Favism (fava beans → haemolysis)
  - Haemolysis due to infection
- Pyruvate kinase deficiency
  - Autosomal recessive
  - → Anaemia and splenomegaly

Acquired

- Autoimmune haemolytic anaemia (Table 15.5)
  - Autoantibodies against red cell membrane
  - Positive direct Coombs’ test (Fig. 15.4)
- Drug-induced autoimmune haemolysis
  - Quinine
  - Penicillin
  - Methyldopa
- Haemolytic disease of the newborn
  - Maternal anti-red cell IgG crosses placenta
  - → Fetal red cell destruction (Rhesus disease)
- Paroxysmal nocturnal haemoglobinuria
  - Red cell destruction by complement
  - → Haemolysis due to infection or surgery
  - → Early morning haemoglobinuria
  - Increased risk of venous thrombosis
- Mechanical haemolysis
  - Cardiac prosthetic valves
  - Marching
  - Microangiopathic haemolytic anaemia
- Others
  - Extensive burns
  - Renal and liver disease
  - Malaria

BLOOD GROUPS AND BLOOD TRANSFUSION

- Blood group of a particular patient is determined by red cell surface antigens
- The two common and most important groupings are ABO and Rhesus status
- The process of typing blood is based on a series of indirect Coombs’ tests to analyse the blood for the presence of these antigens
Cross-matching blood for transfusion is carried out by looking for agglutination when blood cells to be donated are mixed with the patient’s serum (Fig. 15.4).

**ABO blood group (Table 15.6)**
- Presence of A or B antigens on red cells
- Presence of anti-A or anti-B in serum
- Mixing incompatible blood → haemolysis

**Rh blood group**
- Presence or absence of D antigen
- Antibodies form if a D-negative patient is given D-positive blood

**Fetal Rhesus D syndrome**
- RhD-negative mother with a D-positive child will be sensitized at the first delivery
- Subsequent D-positive fetuses will be subjected to anti-D antibodies → hydrops fetalis
- Prophylaxis with anti-D antibodies given to the mother at each delivery suppresses the mother’s own antibody production, protecting future fetuses
Blood groups and blood transfusion

**Indirect antiglobulin test**

Normal cells sensitize *in vitro*
e.g. antibody screening, crossmatching

**Direct antiglobulin test**

Patient’s cells sensitized *in vivo*
e.g. autoimmune haemolytic anaemia, haemolytic transfusion reaction, HDN, drug-induced immune haemolytic anaemia

**Normal RBC**

**Patient’s serum/plasma**

**Anti-human globulin**

**Incubation *in vitro***

**Agglutination***

---

**Fig. 15.4 Coombs’ tests.** (Reproduced from Kumar P, Clark M. Kumar and Clark’s Clinical Medicine, 8th edn. Edinburgh: Elsevier; 2012, with permission from Elsevier.)

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**Table 15.6 The ABO and Rhesus blood groups**

<table>
<thead>
<tr>
<th>Group</th>
<th>Genotype antigens</th>
<th>Red cell</th>
<th>Antibodies</th>
<th>Frequency</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>O</td>
<td>OO</td>
<td>None</td>
<td>Anti-A and anti-B</td>
<td>44%</td>
<td>Universal donor</td>
</tr>
<tr>
<td>A</td>
<td>AO or AA</td>
<td>A</td>
<td>Anti-B</td>
<td>45%</td>
<td></td>
</tr>
<tr>
<td>B</td>
<td>BO or BB</td>
<td>B</td>
<td>Anti-B</td>
<td>8%</td>
<td></td>
</tr>
<tr>
<td>AB</td>
<td>AB</td>
<td>A and B</td>
<td>None</td>
<td>3%</td>
<td>Universal recipient</td>
</tr>
<tr>
<td>D +ve</td>
<td>C or D or E</td>
<td>D</td>
<td>None</td>
<td></td>
<td>Three genes determine genotype: C, D and E</td>
</tr>
<tr>
<td>D –ve</td>
<td>CDE</td>
<td>None</td>
<td>Anti-D&lt;sup&gt;a&lt;/sup&gt;</td>
<td></td>
<td>&lt;sup&gt;a&lt;/sup&gt;After exposure</td>
</tr>
</tbody>
</table>
Blood products

- Whole blood ~500 mL
- Packed cells – 250 mL of plasma removed
- Red cell concentrate – all plasma removed
- Platelet concentrates
- Granulocyte concentrates
- Fresh frozen plasma – replacement of clotting factors
- Cryoprecipitate – factor VIII, fibrinogen and von Willebrand factor
- Human albumin
- Normal immunoglobulin

Procedure for blood transfusion

- Type patient’s blood
- Cross-match donor blood with patient serum
- Donor blood is coded and labelled with the patient’s name; a record sheet with the unit number of the donor blood and the patient’s name and identification number is produced

When administering blood

- Two members of staff check the following:
  Between the patient and record sheet
  - Name of the patient
  - Date of birth of the patient
  - Identification number of the patient
  Between the blood and record sheet
  - Blood unit number
  - Blood group
  - Name, age and date of birth of the patient

Complications of blood transfusion

- Incompatibility → poor red cell survival

Transfusion reactions

- Usually ABO incompatibility
- Haemolysis and haemoglobinuria
- Rigors
- Dyspnoea
- Hypotension
- Renal failure
- Disseminated intravascular coagulation

Febrile transfusion reactions

- Mild fever and flushing
- Rarely due to haemolysis

Transmission of infection

- Viruses, parasites, bacteria and prions
- All blood screened for known infections

BLOOD COAGULATION (FIG. 15.5)

Vessel wall injury leads to:

- Vasoconstriction → reduced blood flow
- Platelet activation → serotonin and thromboxane
- Coagulation → fibrin clot formation
Fig. 15.5 Formation of the haemostatic plug. (Reproduced from Kumar P, Clark M. Kumar and Clark’s Clinical Medicine, 8th edn. Edinburgh: Elsevier; 2012, with permission from Elsevier.)
Platelet adhesion

- Adhesion to collagen exposed by vessel damage via glycoprotein Ia receptor on platelets and in combination with von Willebrand factor via glycoprotein Ib receptors
- Fibrinogen then binds to platelets, is converted to fibrin and forms cross-links, producing a platelet plug

Platelet prostaglandin

- Prostaglandin metabolism → thromboxane production
- → Vasoconstriction and platelet activation
- Process is inhibited by aspirin

Coagulation cascade (Fig. 15.5)

- Enzymatic reactions
- → Activation of coagulation proteins
- → Conversion of fibrinogen to fibrin

Coagulation factors

- Synthesized in the liver
- Enzyme precursors (XII, XI, X, IX)
- Enzyme co-factors (V, VIII)

Coagulation inhibitors

- Antithrombin inactivates clotting factors
- Activated protein C destroys factors V and VIII and initiates fibrinolysis
- Protein S – co-factor for protein C

Fibrinolysis (Fig. 15.6)

- Plasminogen converted to plasmin by tissue plasminogen activator (t-PA)
- Converts fibrin to fibrin degradation products and D-dimer fragments

Measurements of coagulation (Table 15.7)

- Prothrombin time (PT, normal 10-16 seconds)
  - Lengthened by factor VII, X, V or II abnormality
  - Increased by warfarin
- International normalized ratio (INR, normal = 1-1.3)
  - Comparison of prothrombin time to a known standard
  - Used to monitor warfarin
- Activated partial thromboplastin time (APTT, normal 23-31 seconds)
  - Abnormalities of factors XI, IX, VIII, X, V, II or I
  - Increased by heparin
- Thrombin time (TT, normal 12 seconds)
  - Prolonged by fibrinogen deficiencies and heparin
- Bleeding time
  - Standard cut made and time taken for bleeding to stop is measured

Correction tests – addition of normal plasma

- If this corrects an abnormal test, then a factor deficiency is the cause of the coagulopathy
- If no correction occurs, it suggests the presence of an inhibitor in the patient’s plasma
Blood coagulation

(A) Conversion of plasminogen to plasmin

Plasminogen → Plasmin

Plasminogen
\( \rightarrow \)
Plasmin

(B) Plasmin \( \alpha_2 \)-antiplasmin complex

\( \alpha_2 \)-antiplasmin

Fig. 15.6 Fibrinolysis. (Reproduced from Kumar P, Clark M. Kumar and Clark’s Clinical Medicine, 8th edn. Edinburgh: Elsevier; 2012, with permission from Elsevier.)

Table 15.7 Blood results in coagulopathy

<table>
<thead>
<tr>
<th></th>
<th>Prothrombin time (PT)</th>
<th>Activated partial thromboplastin time (APTT)</th>
<th>Bleeding time</th>
<th>Factor VIII: C level</th>
<th>Von Willebrand factor (vWF)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Platelet disorders</td>
<td>Normal</td>
<td>Normal</td>
<td>↑</td>
<td>Normal</td>
<td>Normal</td>
</tr>
<tr>
<td>Vitamin K deficiency</td>
<td>↑</td>
<td>↑</td>
<td>Normal</td>
<td>Normal</td>
<td>Normal</td>
</tr>
<tr>
<td>Haemophilia A and B</td>
<td>Normal</td>
<td>↑</td>
<td>Normal</td>
<td>↓</td>
<td>Normal</td>
</tr>
<tr>
<td>Von Willebrand’s disease</td>
<td>Normal</td>
<td>↑</td>
<td>↑</td>
<td>↓</td>
<td>↓</td>
</tr>
</tbody>
</table>

D-dimer assay
- Increased during fibrinolysis, e.g. after pulmonary embolus
- If negative, PE is very unlikely

Fibrin degradation products (FDPs)
- Increased by fibrinolysis, e.g. pulmonary embolus

Inherited coagulation defects: Haemophilia A
- X-linked inheritance found in 1:5000 men
- Factor VIII deficiency
Factor VIII <1% of normal
- Frequent spontaneous bleeding
- Joint bleeds → deformity

Factor VIII <5% of normal
- Severe bleeding after injury

Factor VIII >5% of normal
- Mild disease
- Prolonged bleeding after trauma

Investigations
See Table 15.7.

Management
- Factor VIII: Concentrate (C) i.v.
- Desmopressin intranasal spray (increases factor VIII:C levels)
- Minor bleeding – aim for 30% of normal
- Major bleeding – aim for 50% of normal
- Surgery – aim for 100% preoperatively

Complications of treatment
- Antibodies against factor VIII:C
- Complications of blood transfusion

Haemophilia B (Christmas disease)
- X-linked inheritance found in 1:30000 men
- Factor IX deficiency
- Clinically identical to haemophilia A

Management
- i.v. factor IX

Von Willebrand’s disease
- Three types (all chromosome 12)
  - Type 1: mild disease, autosomal dominant
  - Type 2: mild disease, autosomal dominant
  - Type 3: severe disease, autosomal recessive
- Bleeding follows trauma and surgery
- Spontaneous epistaxis
- Defect of platelet adhesion combined with factor VIII:C deficiency

Management
- Intranasal desmopressin
- Factor VIII/von Willebrand factor if required

Acquired coagulation defects: Vitamin K deficiency
- Failure of synthesis of vitamin K-dependent factors
- Reduced factors II, VII, IX and X
- Reduced protein C and S

Aetiology
- Inadequate stores (newborn children)
- Malabsorption (fat-soluble vitamin)
- Oral anticoagulants, e.g. warfarin

Investigations
- Elevated prothrombin time and APTT

Management
- Intravenous vitamin K
Chronic liver disease
- Vitamin K deficiency
- Reduced clotting factor synthesis
- Thrombocytopenia
- Abnormal platelet function

Disseminated intravascular coagulation (DIC)
- Uncontrolled fibrin production in blood vessels
  - Malignancy
  - Septicaemia
  - Transfusion reactions
  - Placental abruption and amniotic fluid embolism
  - Trauma, burns, surgery
  - Infections, e.g. Falciparum malaria
  - Liver disease
  - Snake bites

Investigations
- Elevated PT, APPT and TT if severe
- Low platelets and fragmented red cells
- Elevated FDPs and D-dimers

Clinical features
- Haemorrhage
- Shock
- Epistaxis, bleeding gums

Management
- Diagnose and treat cause
- Platelets
- Fresh frozen plasma (FFP)
- Cryoprecipitate
- Blood if required

Massive blood transfusion
- Lack of factors VIII and V in transfusion blood
- Few platelets
- Citrate in transfusions lowers serum calcium
- If giving >10 units, check clotting and platelets
- Consider platelets and fresh frozen plasma
- Calcium i.v.

Clotting factor autoantibodies
- 10% of haemophiliacs – antibodies against factor VIII
- SLE
- Post-childbirth

Anticoagulant drugs

Warfarin (Box 15.2)
- Oral vitamin K antagonist
- Increases prothrombin time

Heparin
- Parenteral administration
- Potentiates antithrombin III
- Elevates APTT
Low molecular weight heparin
- Subcutaneous administration
- Predictable anticoagulant effect dosed by weight

Fibrinolytics
- Activate plasmin
- Recombinant t-Pa
- Streptokinase

Anti-platelet drugs
- Aspirin
- Clopidogrel
- Dipyridamole
- Glycoprotein IIb/IIIa receptor antagonists
- Epoprostenol

New oral anticoagulants
- Direct thrombin inhibitors, e.g. dabigatran
- Factor Xa inhibitor, e.g. rivaroxaban

Thromboembolic disease
Thromboembolic disease is a very common cause of death; just under 50% of adult deaths result from its manifestations.
- Coronary artery thrombosis
- Cerebral artery thrombosis
- Pulmonary embolism (PE)

Thrombus
- Formation of solid clot in a vessel

Embolus
- Fragment of clot carried to a distant site
- → Obstruction of a vessel

Arterial thrombus
- Associated with atheroma
- → Platelet attachment
- → Propagation of thrombus

BOX 15.2. Uncontrolled bleeding due to anticoagulation with warfarin

Severe bleeding
- Stop warfarin immediately
- i.v. access
- Give 5 mg of i.v. vitamin K by slow infusion
- Prothrombin complex concentrate 50u/kg
- Blood transfusion if required

Less severe bleeding
- e.g. Epistaxis or haematuria or INR >8
- Withhold warfarin
- Consider vitamin K 0.5 mg i.v.
### Blood coagulation

**Venous thrombus**
- Occurs in normal vessels
- Commonly deep leg veins
- Risk factors (Table 15.8)

**Thrombophilia**
- Recurrent venous thrombosis
- Venous thrombosis under the age of 40
- Often a family history

**Aetiology**
- Factor V Leiden syndrome
- Antithrombin deficiency
- Protein C and S deficiency
- Antiphospholipid syndrome

**Deep vein thrombosis (DVT)**
Formation of thrombus in:
- Deep calf vein
- Axillary vein

---

**Table 15.8 Risk factors for venous thromboembolism**

<table>
<thead>
<tr>
<th>Patient factors</th>
<th>Disease or surgical procedure</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>Trauma or surgery, especially of pelvis, hip or lower limb</td>
</tr>
<tr>
<td>BMI &gt;30 kg/m²</td>
<td>Malignancy</td>
</tr>
<tr>
<td>Varicose veins</td>
<td>Cardiac or respiratory failure</td>
</tr>
<tr>
<td>Continuous travel more than 3 h in preceding 4 weeks</td>
<td>Recent myocardial infarction or stroke</td>
</tr>
<tr>
<td>Immobility (bed rest ≥3 days)</td>
<td>Acute medical illness/severe infection</td>
</tr>
<tr>
<td>Pregnancy and puerperium</td>
<td>Inflammatory bowel disease</td>
</tr>
<tr>
<td>Previous deep vein thrombosis or pulmonary embolism</td>
<td>Behçet’s disease</td>
</tr>
<tr>
<td>Thrombophilia</td>
<td>Nephrotic syndrome</td>
</tr>
<tr>
<td>Antithrombin deficiency</td>
<td>Myeloproliferative disorders</td>
</tr>
<tr>
<td>Protein C or S deficiency</td>
<td>Paroxysmal nocturnal haemoglobinuria</td>
</tr>
<tr>
<td>Factor V Leiden</td>
<td>Paraproteinaemia</td>
</tr>
<tr>
<td>Resistance to activated protein C (caused by factor V Leiden variant)</td>
<td>Sickle cell anaemia</td>
</tr>
<tr>
<td>Prothrombin gene variant</td>
<td>Central venous catheter in situ</td>
</tr>
<tr>
<td>Hyperhomocystinaemia</td>
<td></td>
</tr>
<tr>
<td>Antiphospholipid antibody/lupus anticoagulant</td>
<td></td>
</tr>
<tr>
<td>Oestrogen therapy including HRT</td>
<td></td>
</tr>
<tr>
<td>Dysfibrinogenaemia</td>
<td></td>
</tr>
<tr>
<td>Plasminogen deficiency</td>
<td></td>
</tr>
</tbody>
</table>

(Reproduced from Kumar P, Clark M. Kumar and Clark’s Clinical Medicine, 8th edn. Edinburgh: Elsevier; 2012, with permission from Elsevier.)
Clinical features
- Pain and tenderness
- Swelling of the limb
- Redness of overlying skin
- Pulmonary embolism

Investigations
- Doppler ultrasound of the vein
- Venography (intravenous contrast)

Management
- Low molecular weight heparin or IV heparin
- Warfarin
- Bed rest until anticoagulated
- Graduated pressure stockings

Complications
- Phlebitis
- Venous eczema

Pulmonary embolism
- Obstruction of a branch of the pulmonary artery by clot from a DVT

Clinical features
Small or medium PE
- Pleuritic chest pain
- Shortness of breath
- Haemoptysis in 30%
- Tachypnoea
- Pleural rub
- Coarse crackles
- Pleural effusion

Massive PE
- Collapse
- Shock
- Cardiac arrest electromechanical dissociation
- Elevated JVP (‘a’ wave)
- Gallop rhythm

Recurrent PE
- Breathlessness
- Weakness
- Syncope
- Gradual deterioration

Diagnosis
Clinical scoring to predict probability e.g., Wells or Geneva Score.

Investigations
- Chest X-ray – oligaemic area
- ECG often normal except for sinus tachycardia
  - S wave in lead I, Q wave and inverted T in lead III
  - Right axis deviation
  - Right bundle branch block
- Plasma D-dimers are elevated (high negative predictive value)
- CT pulmonary angiogram (first choice investigation)
• V/Q scan (see Fig. 5.51)
  • Radionucleotide scan
  • Demonstrates defects in perfusion of the lung in areas with normal ventilation
• Blood gases – hypoxia and low PaCO₂

Management
• High-flow oxygen
• Analgesia
• Low molecular weight heparin
• Warfarin
• Consider thrombolysis in massive PE

HAEMATOLOGICAL MALIGNANCY

These are malignant proliferations of:
• Lymphocytes
  • Hodgkin’s disease
  • Non-Hodgkin’s lymphoma
  • Chronic lymphocytic leukaemia
  • Myeloma (plasma cells)
• Immature lymphocytes
  • Acute lymphoblastic leukaemia
  • Hairy cell leukaemia
• Myeloid cells
  • Acute myelogenous leukaemia
  • Chronic myeloid leukaemia

Lymphomas: Hodgkin’s disease
• B cell malignant clone

Clinical features (Table 15.9)
• Lymphadenopathy
• B symptoms: fever, drenching sweats, weight loss
• Pruritis, fatigue
• Alcohol-induced pain
• Hepatomegaly
• Splenomegaly

Investigations
• Blood count – normal or anaemia, eosinophilia (Table 15.11)
• ESR ↑
• Uric acid sometimes ↑
• Chest X-ray – mediastinal mass or hilar lymph nodes
• CT scan
  • Lymphadenopathy
  • Liver or spleen enlargement or infiltration
• Lymph node biopsy and histology
• PET scan
• Bone marrow biopsy (shows Sternberg–Reed cells)

Management
• Depends on
  • Stage and histology
  • Site of tumour
  • Presence of B symptoms (Table 15.9)
**Haematology**

- Radiotherapy
- Chemotherapy
- Myeloablation and stem cell support

**Prognosis**
- 40–70% survival at 20 years
- Depends on stage of original tumour

---

### Table 15.9 Cotswolds modification of Ann Arbor staging classification

<table>
<thead>
<tr>
<th>Stage</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>Involvement of a single lymph-node region or lymphoid structure (e.g. spleen, thymus, Waldeyer’s ring) or involvement of a single extralymphatic site</td>
</tr>
<tr>
<td>II</td>
<td>Involvement of two or more lymph-node regions on the same side of the diaphragm (hilar nodes, when involved on both sides, constitute stage II disease); localized contiguous involvement of only one extranodal organ or site and lymph-node region(s) on the same side of the diaphragm (IIIE). The number of anatomic regions involved should be indicated by a subscript (e.g. II₃)</td>
</tr>
<tr>
<td>III</td>
<td>Involvement of lymph-node regions on both sides of the diaphragm (III), which may also be accompanied by involvement of the spleen (IIIS) or by localized involvement of only one extranodal organ site (IIIE) or both (IIISE)</td>
</tr>
<tr>
<td>III-1</td>
<td>With or without involvement of splenic, hilar, coeliac or portal nodes</td>
</tr>
<tr>
<td>III-2</td>
<td>With involvement of para-aortic, iliac and mesenteric nodes</td>
</tr>
<tr>
<td>IV</td>
<td>Diffuse or disseminated involvement of one or more extranodal organs or tissues, with or without associated lymph-node involvement</td>
</tr>
</tbody>
</table>

**Designations applicable to any disease state**

- **A** No symptoms
- **B** Fever (temperature >38°C), drenching night sweats, unexplained loss of more than 10% of body weight within the previous 6 months
- **X** Bulky disease (a widening of the mediastinum by more than one-third of the presence of a nodal mass with a maximal dimension greater than 10 cm)
- **E** Involvement of a single extranodal site that is contiguous or proximal to the known nodal site

Non-Hodgkin’s lymphoma

Aetiology
- 80% B cell
- Associated with EBV, HTLV and HIV infection

Clinical features
- Lymphadenopathy
- Symptoms due to site of tumour
- May involve GI tract, lungs, brain

Investigations
- Blood count
  - Anaemia
  - Thrombocytopenia
- Liver chemistry
- Chest X-ray
- CT scan of abdomen and thorax
- Bone marrow biopsy
- Lymph node biopsy

Management
- Depends on grade
- Radiotherapy
- Chemotherapy

Burkitt’s lymphoma

- Associated with Epstein–Barr virus
- Endemic in West Africa
- Jaw, abdominal and ovarian tumours
- Curable

Acute leukaemias

Aetiology
- Unknown in most cases
- T-cell leukaemia – retrovirus (HTLV-1)
- Specific genetic mutations
- Chromosome translocations, e.g. t (15; 17)
- Environmental factors
- Ionizing radiation

Clinical features
- Bone marrow failure
- → Weakness and tiredness due to anaemia
- → Bruising due to thrombocytopenia
- → Repeated infections

Investigations
- Blood count
- Blood film – leukaemic blast cells
- Bone marrow – blast cells

Management
- Correct anaemia and thrombocytopenia
- Treat any infection
- Chemotherapy to achieve remission
- Myeloablation with stem cell support to clear marrow of malignant cells
### Table 15.10 WHO classification of acute leukaemia

#### (a) Acute myeloid leukaemia

<table>
<thead>
<tr>
<th>Subtype</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>AML with recurrent genetic abnormalities</td>
<td>AML with t(8;21)(q22;q22) (RUNX1/RUNX1T1)</td>
</tr>
<tr>
<td></td>
<td>AML with inv(16)(p13q22) or t(16;16)(p13;q22) (CBFβ/MYH11)</td>
</tr>
<tr>
<td></td>
<td>Acute promyelocytic leukaemia with t(15;17)(q22;q12) PML/RAR-α and variants</td>
</tr>
<tr>
<td></td>
<td>AML with t(9;11)(p22;q23) (MLLT3/MLL)</td>
</tr>
<tr>
<td></td>
<td>AML with t(6;9)(p23;q34) (DEK/NUP214)</td>
</tr>
<tr>
<td></td>
<td>AML with inv(3)(q21q26) or t(3;3)(q21;q26) (RPN1/EVI1)</td>
</tr>
<tr>
<td></td>
<td>AML with CEBPA mutation</td>
</tr>
<tr>
<td></td>
<td>AML with NPM mutation</td>
</tr>
<tr>
<td></td>
<td>AML with MDS related changes</td>
</tr>
<tr>
<td></td>
<td>Therapy related myeloid neoplasm</td>
</tr>
<tr>
<td></td>
<td>Alkylating agent</td>
</tr>
<tr>
<td></td>
<td>Radiation-related type</td>
</tr>
<tr>
<td></td>
<td>Topoisomerase II inhibitor-related type</td>
</tr>
<tr>
<td></td>
<td>Other</td>
</tr>
<tr>
<td>AML, not otherwise categorized&lt;sup&gt;a&lt;/sup&gt;</td>
<td>AML, minimally differentiated</td>
</tr>
<tr>
<td></td>
<td>AML without maturation</td>
</tr>
<tr>
<td></td>
<td>AML with maturation</td>
</tr>
<tr>
<td></td>
<td>Acute myelomonocytic leukaemia</td>
</tr>
<tr>
<td></td>
<td>Acute monoblastic/acute monocytic leukaemia</td>
</tr>
<tr>
<td></td>
<td>Acute erythroid leukaemia (erythroid/myeloid and pure erythroleukaemia variants)</td>
</tr>
<tr>
<td></td>
<td>Acute megakaryoblastic leukaemia</td>
</tr>
<tr>
<td></td>
<td>Acute basophilic leukaemia</td>
</tr>
<tr>
<td></td>
<td>Acute panmyelosis with myelofibrosis</td>
</tr>
<tr>
<td></td>
<td>Myeloid sarcoma</td>
</tr>
</tbody>
</table>

#### (b) Acute lymphoid leukaemia – precursor lymphoid neoplasm

<table>
<thead>
<tr>
<th>Subtype</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>B-cell lymphoblastic leukaemia/lymphoma with recurrent genetic</td>
<td>t(9;22)(q34;q11) (BCR/ABL)</td>
</tr>
<tr>
<td>abnormality</td>
<td>t(v;11q23) (MLL rearranged)</td>
</tr>
<tr>
<td></td>
<td>t(1;19)(q23;p13) (E2A/PBX1)</td>
</tr>
<tr>
<td></td>
<td>t(12;21)(p13;q22) (TEL/RUNX1)</td>
</tr>
<tr>
<td>Hyperdiploidy</td>
<td>Hypodiploidy</td>
</tr>
<tr>
<td>B-cell lymphoblastic leukaemia/lymphoma not otherwise specified</td>
<td></td>
</tr>
<tr>
<td>T-cell lymphoblastic leukaemia/lymphoma</td>
<td></td>
</tr>
</tbody>
</table>

<sup>a</sup>The entities included in this group are defined almost identically to the corresponding entity in the French–American–British (FAB) classification.

(Modified from Jaffe ES, Harris NL, Stein H, Vardiman JW, eds. World Health Organization Classification of Tumours. Pathology and genetics of tumours of haematopoietic and lymphoid tissues. Lyon: IARC Press; 2008, with permission of the World Health Organization.)
Haematological malignancy

Acute myeloid leukaemia (AML)
- Classified by cell type (Table 15.10)
- 70% alive at 1 year → 30% alive at 5 years
- Treatment aims for complete remission
- Followed by bone marrow ablation

Acute lymphoblastic leukaemia (ALL)
- Predominantly a disease of children
- Cure rate 50–60% in children, 30% in adults
- Central nervous system involvement common
- → Prophylactic intrathecal chemotherapy

Chronic leukaemias
- Chronic leukaemias occur in older patients, most of whom die within 5 years of diagnosis
- Clinical course consists of a chronic illness lasting 3–4 years, followed by transformation into an acute leukaemia or sometimes myelofibrosis in the case of chronic myeloid leukaemia

Chronic myeloid leukaemia (CML)

Clinical features
- Anaemia
- Night sweats and fever
- Weight loss
- Splenomegaly → pain

Investigations
- Blood count – raised white count
- Multiple myeloid precursors
- Bone marrow biopsy
- Genetic testing for the Philadelphia chromosome (9:22 translocation) (positive in 90–95%)

Management
- Imatinib – tyrosine kinase inhibitor – 95% response rates
- Myeloablation with bone marrow transplant

Table 15.11 Causes of eosinophilia

<table>
<thead>
<tr>
<th>Causes</th>
<th>Lung disease</th>
</tr>
</thead>
<tbody>
<tr>
<td>Parasites</td>
<td></td>
</tr>
<tr>
<td><em>Ascaris</em></td>
<td>Asthma</td>
</tr>
<tr>
<td><em>Hookworm</em></td>
<td>Allergic bronchopulmonary aspergillosis</td>
</tr>
<tr>
<td><em>Strongyloides</em></td>
<td>Churg–Strauss syndrome</td>
</tr>
<tr>
<td>Allergy</td>
<td></td>
</tr>
<tr>
<td>Allergic rhinitis</td>
<td>Skin disorders</td>
</tr>
<tr>
<td>Drug reactions</td>
<td>Urticaria</td>
</tr>
<tr>
<td>Malignancy</td>
<td></td>
</tr>
<tr>
<td>Hodgkin’s disease</td>
<td>Pemphigus</td>
</tr>
<tr>
<td>Carcinoma</td>
<td>Eczema</td>
</tr>
<tr>
<td></td>
<td>Others</td>
</tr>
<tr>
<td></td>
<td>Sarcoidosis</td>
</tr>
</tbody>
</table>

Pass Finals
Chronic lymphocytic leukaemia (CLL)

Clinical features
- Often an incidental finding
- Infections due to neutropenia
- Anaemia (may be due to haemolysis)
- Lymphadenopathy
- Hepatosplenomegaly

Investigations
- Haemoglobin low or normal
- White count >15×10⁹/L
- 40% lymphocytes
- Platelets low or normal
- Serum immunoglobulins may be low

Management
- Nothing if asymptomatic
- Steroids for haemolysis
- Chemotherapy

Hairy cell leukaemia
- Rare
- Usually a B cell tumour
- Cells have filament-like projections
- Cladribine produces a 90% remission

Myeloproliferative disorders
- Uncontrolled proliferation of a blood cell line
- Can transform into acute leukaemias or from one myeloproliferation to another

Polycythaemia vera
- Red cell proliferation
- Patients usually >60 years old

Clinical features
- Tiredness
- Depression
- Tinnitus
- Vertigo
- Visual disturbance
- Itching after a hot bath
- Gout (due to increased cell turnover)
- Thrombosis or haemorrhage
- Plethora and cyanosis
- Splenomegaly

Investigations
- Haemoglobin raised
- Packed cell volume (haematocrit) ↑
- Acquired JAK2 genetic mutations in 95%
- 50% have ↑ platelets
- 75% have ↑ white cells
- Uric acid ↑
- Leucocyte alkaline phosphatase ↑
Management
- Venesection
- Chemotherapy
- Allopurinol to avoid gout, low dose aspirin for recurrent thrombosis

Prognosis
- 30% → myelofibrosis
- 5% → AML

**Essential thrombocythaemia**
- Platelet count >1000×10⁹/L
- → Bruising and bleeding (poor platelet function)
- Increased risk of thrombosis

**Myelofibrosis**
- Stem cell proliferation
- Bone marrow fibrosis

**Clinical features**
- Anaemia
- Weight
- Splenomegaly
- Bone pain
- Gout

**Investigations**
- Anaemia
- High platelets
- ‘Dry’ bone marrow aspirate
- High uric acid

**Management**
- Blood transfusion
- Folic acid, allopurinol, analgesia
- Chemotherapy and radiotherapy
- Splenectomy may be required

**Prognosis**
- 10–20% → AML

**Myelodysplasia**
- Stem cell defects
- → Bone marrow failure
- Abnormal red cells, leucocytes and platelets

**Management**
- Supportive therapy
- Chemotherapy

**Multiple myeloma and hyperglobulinaemia**
- Clonal expansion of plasma cells resulting in very high production of a single immunoglobulin (paraprotein) or an immunoglobulin component

**Myeloma**

**Clinical features**
- Elderly patients
- Bone lesions → pain and fractures
Haematology

- Hypercalcaemia
- Bone marrow infiltration
- → Anaemia, neutropenia
- Renal impairment
- Hyperviscosity syndrome (headache, stroke, retinal vein and artery occlusion)

Investigations
- Blood count (anaemia, low white cells)
- Elevated ESR and CRP
- Elevated calcium, urea and creatinine
- Protein electrophoresis – monoclonal band
- Skeletal X-ray survey – lytic lesions, e.g. skull (see Fig. 5.17)
- 24-hour urine for light chain proteins
- Bone marrow aspirate – plasma cells

Management
- Supportive treatment and treatment of complications, e.g. for fractures
- Steroids and radiotherapy for bone lesions
- Chemotherapy + stem cell transplantation

Waldenström’s macroglobulinaemia
- Older males
- IgM paraprotein
- → Hyperviscosity syndrome
- Lymphadenopathy
- Malaise and weight loss

PLATELET DISORDERS

Platelets, derived from megakaryocytes, are involved in the formation of clots.

Thrombocytopenia
- Low platelet count
- Low production in bone marrow
- High destruction in circulation
- Causes (Table 15.12)

Autoimmune thrombocytopenic purpura
- Follows viral infection in children (acute)
- Idiopathic in adult women (chronic)
- 60% have antiplatelet antibodies
- → Purpuric rash
- Epistaxis and menorrhagia
- Treat with steroids/splenectomy

Thrombocytosis
- High platelet count
- Haemorrhage
- Inflammation (any site)
- Essential thrombocythaemia
Table 15.12 Causes of thrombocytopenia

<table>
<thead>
<tr>
<th>Impaired production</th>
</tr>
</thead>
<tbody>
<tr>
<td>Selective megakaryocyte depression:</td>
</tr>
<tr>
<td>Rare congenital defects</td>
</tr>
<tr>
<td>Drugs, chemicals and viruses</td>
</tr>
<tr>
<td>As part of a general bone marrow failure:</td>
</tr>
<tr>
<td>Cytotoxic drugs and chemicals</td>
</tr>
<tr>
<td>Radiation</td>
</tr>
<tr>
<td>Megaloblastic anaemia</td>
</tr>
<tr>
<td>Leukaemia</td>
</tr>
<tr>
<td>Myelodysplastic syndromes</td>
</tr>
<tr>
<td>Myeloma</td>
</tr>
<tr>
<td>Myelofibrosis</td>
</tr>
<tr>
<td>Solid tumour infiltration</td>
</tr>
<tr>
<td>Aplastic anaemia</td>
</tr>
<tr>
<td>HIV infection</td>
</tr>
<tr>
<td>Excessive destruction or increased consumption</td>
</tr>
<tr>
<td>Immune</td>
</tr>
<tr>
<td>Active absorption requires the presence of intrinsic factor</td>
</tr>
<tr>
<td>Intrinsic factor is produced by gastric G cells</td>
</tr>
<tr>
<td>Active absorption takes place in the jejunum</td>
</tr>
</tbody>
</table>

(Reproduced from Kumar P, Clark M. Kumar and Clark’s Clinical Medicine, 8th edn. Edinburgh: Elsevier; 2012, with permission from Elsevier.)

SELF-ASSESSMENT QUESTIONS

Multiple choice questions (true or false)

1. Which of the following statements about haemoglobin are correct?
   A. Adult haemoglobin comprises two α and two γ chains
   B. Each haemoglobin molecule comprises four globin chains and one haem group
   C. Deoxyhaemoglobin is insoluble in water
   D. β-thalassaemia is an inherited inability to synthesize β globin chains
   E. Each haemoglobin molecule can carry four oxygen molecules

2. The following are true of vitamin B₁₂ absorption:
   A. Active absorption requires the presence of intrinsic factor
   B. Intrinsic factor is produced by gastric G cells
   C. Active absorption takes place in the jejunum
D. Chronic pancreatic insufficiency is a cause of vitamin $B_{12}$ deficiency  
E. Oral $B_{12}$ given once a month is useful in the treatment of pernicious anaemia

3. In autoimmune haemolytic anaemia:  
A. The direct Coombs’ (globulin) test will be positive  
B. The autoantibody is always IgG class  
C. Haemoglobinuria may occur  
D. *Mycoplasma* pneumonia is a recognized cause  
E. Jaundice is a recognized symptom

4. Regarding pernicious anaemia:  
A. Anti-parietal cell or anti-intrinsic factor antibodies are detectable  
B. Chronic hyperplastic gastritis results  
C. There is an increased risk of gastric cancer  
D. Oral intrinsic factor will reverse the vitamin $B_{12}$ deficiency  
E. Men are as commonly affected as women

5. The following are appropriate blood transfusion options:  
A. Group O donor to group A recipient  
B. Group A Rhesus-positive donor to group A Rhesus-negative recipient  
C. Group AB Rhesus-negative donor to group O Rhesus-negative recipient  
D. Group B Rhesus-positive donor to group A Rhesus-positive recipient  
E. Group A donor to group AB recipient

6. The following are recognized complications of blood transfusions:  
A. Urticarial rash  
B. Hepatitis C infection  
C. Fever  
D. Anaphylactic shock  
E. Disseminated intravascular coagulation

**Multiple choice questions (single best answer)**

7. A 36-year-old woman has the following full blood count: Hb 101 g/L, MCV 76 fl, MCH 24, WCC 9.4, platelets 187. Which one of the following is the most likely diagnosis?  
A. Megaloblastic anaemia  
B. Iron deficiency anaemia  
C. Aplastic anaemia  
D. Folate deficiency  
E. Polycythaemia rubra vera

8. A 25-year-old man presents with a fever, night sweats and abdominal pain. Which one of the following is the most likely diagnosis?  
A. Polycythaemia rubra vera  
B. Acute myeloid leukaemia  
C. Non-Hodgkin’s lymphoma  
D. Chronic lymphocytic leukaemia  
E. Acute lymphoblastic leukaemia

9. A 78-year-old man is found to have a white cell count of $32\times10^9/L$, 95% lymphocytes. What is the most likely diagnosis?  
A. Chronic myeloid leukaemia  
B. Chronic lymphocytic leukaemia
C. Acute lymphoblastic leukaemia  
D. Malignant myeloma  
E. Myelodysplasia  

10. Which one of the following is the best test for measuring the anticoagulant effect of warfarin?  
A. Activated partial thromboplastin time  
B. Bleeding time  
C. Prothrombin time  
D. Whole blood clotting time  
E. Thrombin time

Extended matching questions

Question 1  
A. Iron deficiency  
B. Vitamin B₁₂ deficiency  
C. Folic acid deficiency  
D. Sickle cell disease  
E. α-thalassaemia  
F. Hereditary spherocytosis  
G. Haemolytic anaemia  
H. Anaemia of chronic disease  
I. Acute haemorrhage  
J. Hypersplenism  

For each of the following select the most appropriate diagnosis from the list:  
I. A 43-year-old woman with a microcytic, hypochromic blood film  
II. A 17-year-old man with severe joint pain and abnormal red blood cells  
III. An 87-year-old woman with a macrocytosis following a gastrectomy

Question 2  
A. Erythrocytes  
B. Platelets  
C. Monocytes  
D. Neutrophils  
E. Basophils  
F. Eosinophils  
G. Lymphocytes  
H. Reticulocytes  
I. Megakaryocytes  
J. Plasma cells  

For each of the following choose the correct answer from the list above:  
I. The cell type from which platelets derive  
II. Cell type responsible for antibody production  
III. A nucleated cell that increases in numbers after acute blood loss

Question 3  
A. Blood group O  
B. Blood Group A  
C. Blood Group B  
D. Blood Group AD
E. D-Rhesus positive
F. D-Rhesus negative

*For each of the following choose the correct answer from the list above:

I. Blood group with a frequency of 8% in the population
II. Blood group characterized by the presence of anti-A and anti-B antibodies in the blood
III. Blood group of a mother whose fetus suffers Rhesus D syndrome
Oncology studies the management of ‘malignant disease’ illness arising from the uncontrolled proliferation of a cell clone. The clone characteristically is able to invade adjacent tissues (local spread) and seed to distant sites via the vascular or lymphatic circulation (metastasis). Malignancy is an important cause of death worldwide, most notably in the developed world (Fig. 16.1). Specific malignancies are discussed in the appropriate system chapter.

**CANCER EPIDEMIOLOGY**

**Sex differences (Table 16.1)**

- Sex-specific tumours (e.g. prostate)
- Risk factors (e.g. smoking, diet, alcohol intake)
- Genetic variation
- Hormonal variation (tumours dependent on hormones for growth)

**Age differences**

**Childhood cancers (age 3–13 years)**

- Hereditary, e.g. retinoblastoma
- Haematological, e.g. acute leukaemia

**Adult cancers**

- Frequency increases with age

**Geographical differences**

- Variation in population genotype distribution
- Variation in environmental factors, e.g.
  - Diet in gastric cancer (Fig. 16.2)
  - Hepatocellular carcinoma secondary to chronic viral hepatitis

**CANCER AETIOLOGY**

**Smoking**

- Associated with 30% of cancer deaths in the UK
- Implicated in several cancers
  - Lung carcinoma
  - Oral cavity cancers
  - Oesophageal carcinoma
  - Bladder (transitional cell carcinoma)

**Alcohol**

- Oral cavity cancers
- Oesophageal carcinoma
- Colorectal carcinoma
- Hepatocellular carcinoma
Fig. 16.1 (A) Causes of mortality by continent, demonstrating the relative importance of infection, malignancy and heart disease. Malignancy is responsible for roughly 13.5% of all male and 11.7% of all female deaths worldwide. (Data from the World Health Organization, 2008.) (B) CRC UK 2010 Cancer Mortality by tumour site.
Table 16.1 Age-standardized mortality for the 10 highest causes of malignancy-related death in the UK in 2000

<table>
<thead>
<tr>
<th>Rank</th>
<th>Male</th>
<th>Female</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Site</td>
<td>Mortality</td>
</tr>
<tr>
<td>1</td>
<td>Lung</td>
<td>48.6</td>
</tr>
<tr>
<td>2</td>
<td>Colon and rectum</td>
<td>18.7</td>
</tr>
<tr>
<td>3</td>
<td>Prostate</td>
<td>18.5</td>
</tr>
<tr>
<td>4</td>
<td>Stomach</td>
<td>10.1</td>
</tr>
<tr>
<td>5</td>
<td>Oesophagus</td>
<td>8.7</td>
</tr>
<tr>
<td>6</td>
<td>Bladder</td>
<td>7.0</td>
</tr>
<tr>
<td>7</td>
<td>Pancreas</td>
<td>6.6</td>
</tr>
<tr>
<td>8</td>
<td>Lymphoma</td>
<td>5.8</td>
</tr>
<tr>
<td>9</td>
<td>Leukaemia</td>
<td>4.9</td>
</tr>
<tr>
<td>10</td>
<td>Brain</td>
<td>4.5</td>
</tr>
</tbody>
</table>

*Lung cancer is now more common than breast cancer.


Fig. 16.2 Geographical variation in the mortality from gastric cancer. (Data from the World Health Organization, 1997.)
Environmental risks

Asbestos
- Mesothelioma
- Lung carcinoma

Hydrocarbons
- Lung carcinoma
- Skin cancers

UV light
- Melanoma
- Basal cell carcinoma
- Squamous cell carcinoma

Drugs

Oestrogens
- Vaginal carcinoma
- Endometrial carcinoma

Alkylating agents
- Acute myeloid leukaemia

Infections
- Viral hepatitis – hepatocellular carcinoma
- Schistosoma – bladder cancer
- Helicobacter pylori – gastric cancer
- Epstein–Barr virus – Burkitt’s lymphoma
- Papillomavirus – cervical cancer

CANCER GENETICS

- Malignancy results from genetic mutations that lead to uncontrolled proliferation of a cell clone
- These mutations and abnormalities can arise in several ways

Chromosome abnormalities
- Chronic myeloid leukaemia – 9:22 translocation (Philadelphia chromosome) positive in 95%
- Acute promyelocytic leukaemia – 15:17 translocation positive in >90%
- Burkitt’s lymphoma 8:14 translocation → myc gene over-expressed

Failure of DNA repair
- Mutation of DNA repair systems → hereditary cancer syndromes, e.g.
  - Xeroderma pigmentosum
  - Ataxia telangiectasia
  - BCRA 1 and 2 in breast cancer
  - Mismatch repair mutations in colon cancer

Tumour suppressors
- Mutation of tumour suppressor genes → over-expression of mutated gene product
- Failure of control of cell cycle → uncontrolled proliferation
- e.g. p53 mutations in GI cancers
Inherited cancers
- Specific mutations increase the risk of malignancy if inherited, e.g.
  - *apc* gene: familial adenomatous polyposis
  - *BCRA* genes: breast and ovarian cancer
  - *Rb* gene: hereditary retinoblastoma

Oncogenes
- Genes which, if activated inappropriately by a mutation, \(\rightarrow\) malignancy, e.g.
  - *C-Myc*: cervical cancer, Burkitt’s lymphoma, breast cancer
  - *K-Ras*: colorectal cancer
- The gene may have a cell cycle regulatory role
  - *bcl-2* expression \(\rightarrow\) resistance of apoptosis \(\rightarrow\) a proliferating clone that is open to further mutations \(\rightarrow\) malignant transformation

CANCER BIOLOGY

Cell proliferation
- Uncontrolled proliferation
- Often loss of cell differentiation
- \(\rightarrow\) Exponential growth curve
- ‘Doubling time’ describes the growth rate
- \(\rightarrow\) Very variable between tumour types
- As tumour enlarges, growth may slow due to:
  - Limitation of blood supply
  - Local production of growth inhibitors

Local invasion
- Penetration of malignant cells into other tissues
- Associated with loss of intercellular adhesion
- Increased production of proteolytic enzymes

Lymphatic spread
- Tumours seed to locally draining lymph nodes

Dissemination (Table 16.2)
- Invasion into blood vessels or lymphatics
- Allows seeding of cells to distant sites
- Metastases \(\rightarrow\) organs with a dense vasculature, e.g.
  - Liver
  - Lungs
  - Bone marrow
- Tumour cells express ligands for endothelial receptors
- \(\rightarrow\) Increased adhesion and invasion
- \(\rightarrow\) Specific metastatic patterns, e.g. breast cancer \(\rightarrow\) long bones

DIAGNOSIS OF CANCER

Clinical features
- Specific combinations of symptoms and signs can suggest particular malignancies
Oncology and genetic disease

For example, painless jaundice and weight loss → pancreatic cancer, dysphagia → oesophageal carcinoma

Personality change with complex focal neurology → intracerebral tumour

Cough, haemoptysis and weight loss → bronchogenic carcinoma

Characteristics of a palpable mass suggesting malignancy:
- Fixed to deep tissues
- Fixed to overlying skin
- Hard/‘craggy’ texture
- Overlying ulceration
- Lymphadenopathy

Family history of malignancy
- Colorectal carcinoma

Exposure to specific risks (see above)

Associated diseases that increase risk
- Hepatitis B or C (hepatocellular carcinoma)
- Pernicious anaemia (gastric cancer)
- Barrett’s oesophagus (oesophageal carcinoma)
- Asbestosis (bronchogenic carcinoma)

Imaging
- Can be highly suggestive of malignancy
- For example, chest X-ray in lung cancer

Tissue diagnosis
- Vital for confirmation of diagnosis and guiding treatment
- Tumour type
- Degree of differentiation (tumour grade)

Methods
- CT- or ultrasound-guided biopsy
- Endoscopic biopsy

### Table 16.2 Common sites of metastasis

<table>
<thead>
<tr>
<th>Site</th>
<th>Origin</th>
<th>Site</th>
<th>Origin</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bone</td>
<td>Breast</td>
<td>Liver</td>
<td>Gl tract</td>
</tr>
<tr>
<td></td>
<td>Bronchus</td>
<td>Breast</td>
<td></td>
</tr>
<tr>
<td>Thyroid</td>
<td></td>
<td>Bronchus</td>
<td></td>
</tr>
<tr>
<td>Prostate</td>
<td>Adrenal</td>
<td>Bronchus</td>
<td></td>
</tr>
<tr>
<td>Kidney</td>
<td>Lung</td>
<td>Kidney</td>
<td></td>
</tr>
<tr>
<td>Intracerebral</td>
<td>Bronchus</td>
<td>Prostate</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Breast</td>
<td>Breast</td>
<td></td>
</tr>
<tr>
<td>Stomach</td>
<td>Bone</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Prostate</td>
<td>Gl tract</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Thyroid</td>
<td>Cervix</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Kidney</td>
<td>Ovary</td>
<td></td>
<td>Testicular</td>
</tr>
</tbody>
</table>
Laparoscopic/open surgical biopsy
Fine needle aspiration (FNA) of subcutaneous mass

**Tumour staging (Table 16.3)**
- Assessment of distribution of tumour
- Classification varies with tumour
- Staging investigations required, e.g.
  - CT scanning
  - Lymph node sampling
  - PET
  - Laparoscopy

**Tumour markers**
- Serum markers for the presence of malignancy
- Useful in following response to treatment
- Can help demonstrate relapse post-therapy
- Rarely useful in initial diagnosis
- Examples:
  - Ca-125 – pancreatic/ovarian/GI cancer
  - Ca-19-9 – GI and pancreatic cancers
  - α-fetoprotein – hepatocellular carcinoma
  - β-human chorionic gonadotrophin (HCG) – choriocarcinomas, testicular carcinoma
  - Chorioembryonic antigen (CEA) – colorectal carcinoma

**Screening**
- Investigations used to detect premalignant tissue or malignancy in those in whom cancer has not been diagnosed
- Examples:
  - Mammograms for breast cancer
  - Smears for cervical cancer
  - Faecal occult blood and colonoscopy for colorectal carcinoma

**Surveillance**
- Investigations to detect recurrence of malignancy following treatment for a previous cancer
- Examples:
  - Mammography after breast cancer
  - Prostate-specific antigen (PSA) for progression of prostatic cancer

---

**Table 16.3 The TNM system**

<table>
<thead>
<tr>
<th></th>
<th>Extent of primary tumour</th>
</tr>
</thead>
<tbody>
<tr>
<td>T</td>
<td></td>
</tr>
<tr>
<td>N0</td>
<td>No involved lymph nodes</td>
</tr>
<tr>
<td>N1–4</td>
<td>Lymph node groups involved</td>
</tr>
<tr>
<td>M</td>
<td></td>
</tr>
<tr>
<td>M0</td>
<td>No metastases</td>
</tr>
<tr>
<td>M1</td>
<td>Metastases present</td>
</tr>
</tbody>
</table>
Surgical resection
- May be curative (complete tumour removal)
- May be palliative (symptomatic relief but not curative)

Radiotherapy
- High-energy electromagnetic radiation
- Targeted at specific site
- Useful adjuvant therapy to reduce relapse rate as well as curative intent

Chemotherapy
- Drug therapy aimed at killing tumour cells
- Also kills normal cells
- Given in cycles to allow normal cells to recover

Antimetabolites
- Block cell metabolism
  - Folic acid antagonists: methotrexate
  - Nucleic acid analogues: 5-fluorouracil

Plant alkaloids
- Inhibit microtubule formation
- \( \rightarrow \) Block cell replication
  - Vincristine

Taxanes
- Inhibit microtubule formation
- Useful in breast and ovarian cancers
  - Docetaxel

Cytotoxic antibiotics
- Block DNA replication
  - Doxorubicin

Platinum analogues
- Cross-link DNA strands
- \( \rightarrow \) Block DNA replication
  - Cisplatin

Alkylating agents
- Block DNA synthesis
  - Cyclophosphamide

Endocrine therapy
- Hormonal manipulation of tumour cells that express hormone receptors on their surface
  - Tamoxifen – blocks oestrogen receptor

Biological therapy
- Use of immunologically active substances
  - e.g. \( \alpha \)-interferon in melanoma/myeloma
- Targeted therapy, e.g. anti-TNFs

Adjuvant therapy
- Specific therapy after a primary therapy modality
- Used to treat undetected metastases
  - Breast and colon cancers
Neoadjuvant therapy
- Given before primary therapy to reduce the risk of metastasis

Myeloablation with stem cell support
- High-dose chemotherapy and radiotherapy
- Aims to kill all dividing cells
- Haemopoietic stem cells then given
  → Reverses resultant bone marrow failure
- Stem cells may be
  - Allogenic: from a matched donor
  - Autologous: taken from patient before therapy
- Collection of stem cells may be via
  - Bone marrow sampling
  - Peripheral blood sampling

COMPLICATIONS OF TREATMENT

Failure of therapy
- Incomplete surgical resection
- Tumour resistance to chemotherapy
- Failure of response to radiotherapy

Nausea and vomiting
- Common
- Treat with antiemetics (Fig. 16.3)
  - Metoclopramide
  - Domperidone
  - 5HT3 antagonists (ondansetron)

Hair loss
- Difficult to avoid, but regrows after therapy

Bone marrow suppression
- Dose-dependent effect of therapy

Neutropenia
- ↑ Bacteria, viral and fungal infection
- Treat with antibiotics
- Stem cell stimulating factors, e.g. GM-CSF

Thrombocytopenia
- → Bleeding
- Treat with platelet transfusion

Anaemia
- Treat with blood transfusion

Cardiotoxicity
- Dose-dependent effect of doxorubicin

Neurotoxicity
- Occurs with vincristine
- Must never be given intrathecally
**Sterility**
- Common with alkylating agents
- ♂ Sperm storage prior to therapy
- ♀ Ovum storage (still experimental)

**Mucositis**
- Mucosal inflammation – notably of the mouth and GI tract after radiotherapy

**PALLIATIVE CARE**
- Therapy aimed at reducing symptoms due to the malignancy

**Pain**
- Occurs in 70% of cancers
- → Step up analgesia until relief obtained (WHO analgesia ladder, Fig. 16.4)
• Paracetamol and non-steroidal anti-inflammatory drugs (NSAIDs)
• Weak opioids – codeine ± paracetamol
• Strong opioids – morphine or diamorphine

Specific analgesics
- Naproxen for bone pain
- Amitriptyline/gabapentin for pain due to nerve damage
- Carbamazepine/gabapentin for neuropathic pain

Continuous subcutaneous infusions
- Allow continuous delivery of analgesia, antiemetics and sometimes anxiolytics

Patient-controlled analgesia
- Continuous analgesia with the ability for the patient to give limited extra doses

Complications of analgesics
Opioids
- Constipation, nausea, vomiting
- Respiratory and CNS depression
- Drowsiness, hallucinations
NSAIDs
- GI ulceration
- GI bleeding
- Renal failure

Non-drug approaches
- Surgery to reduce tumour mass
- Radiotherapy
- Nerve blocks
- Steroids to reduce local inflammation

Fig. 16.4 The World Health Organization’s Analgesia Ladder.
**Gastrointestinal symptoms**

**Anorexia**  
- → Nasogastric feeding if appropriate

**Nausea and vomiting**  
- → Appropriate antiemetic therapy

**Bowel obstruction**  
- → Surgical bypass  
- Antispasmodics – hyoscine  
- Antiemetics  
- Nasogastric tube to reduce vomiting

**Psychological support**  
- Effective communication with the patient  
- Honesty about diagnosis and prognosis  
- Support for emotional crisis  
- Full explanations of symptoms  
- Human genetics and inherited disease

### HUMAN GENETICS

#### Chromosomal disorders

- Majority → spontaneous abortion

**Abnormal chromosome numbers**  
- Down syndrome: trisomy 21, 1:650 live births  
- Edward syndrome: trisomy 18, 1:3000  
- Patau syndrome: trisomy 13, 1:5000  
- Klinefelter syndrome: XXY, 1:1000 males  
- Turner syndrome: XO, 1:2500 girls

**Abnormal chromosome structure**  
- Deletion of chromosome segment  
  - Prader–Willi syndrome  
- Duplication of chromosome segment  
  - Charcot–Marie–Tooth syndrome

**Mitochondrial DNA abnormalities**  
- Inherited mitochondrial DNA mutations  
- Passed via maternal line (sperm do not donate mitochondria)  
- → Myopathies and neuropathies  
- e.g. DIDMOAD syndrome (diabetes insipidus, diabetes mellitus, optic atrophy and deafness)

**Gene defects (Table 16.4)**

- Result in abnormal protein being synthesized  
- Homozygous: both gene copies abnormal  
- Heterozygous: one gene copy abnormal

**Autosomal dominant disorders (Fig. 16.5)**

- One of the two gene copies is mutated  
- Normal gene not sufficient to compensate  
- Or mutated protein is toxic  
- Effect may vary in each generation
Varying penetrance
→ Disease skipping generations
New cases arise due to germ-line mutations

Autosomal recessive disorders (Fig. 16.6)
- Both gene copies have mutation (homozygous)
- No functioning protein synthesized
- Carrier state exists if only one copy affected (usually no clinical significance)
- → Inborn errors of metabolism

Sex-linked inheritance
- Mutations of genes on the X chromosome
- Vast majority are recessive (Fig. 16.7) but
  - Males only have one X chromosome, therefore are affected by mutation
  - Females act as carriers if heterozygotes

### Table 16.4 Autosomal dominant, autosomal recessive and X-linked recessive disorders

<table>
<thead>
<tr>
<th>Autosomal dominant</th>
<th>Autosomal recessive</th>
<th>X-linked recessive</th>
</tr>
</thead>
<tbody>
<tr>
<td>Achondroplasia</td>
<td>Albinism</td>
<td>Duchenne muscular dystrophy</td>
</tr>
<tr>
<td>Adult polycystic kidney disease</td>
<td>Cystic fibrosis</td>
<td>Haemophilia A</td>
</tr>
<tr>
<td>Familial Alzheimer’s disease</td>
<td>β-thalassaemia</td>
<td>Haemophilia B</td>
</tr>
<tr>
<td>Familial hypercholesterolaemia</td>
<td>Friedreich’s ataxia</td>
<td>Red–green colour blindness</td>
</tr>
<tr>
<td>Huntington’s chorea</td>
<td>Haemochromatosis</td>
<td>Wiskott–Aldrich syndrome</td>
</tr>
<tr>
<td>Marfan syndrome</td>
<td>Phenylketonuria</td>
<td></td>
</tr>
<tr>
<td>Neurofibromatosis type I</td>
<td>Sickle cell disease</td>
<td></td>
</tr>
<tr>
<td>Von Willebrand’s disease</td>
<td>Wilson’s disease</td>
<td></td>
</tr>
</tbody>
</table>

Fig. 16.5 Autosomal dominant inheritance.

One parent with one copy of abnormal gene

50% of offspring inherit abnormal gene
Fig. 16.6 Autosomal recessive inheritance.
**X-linked dominant**
- Heterozygote female has the disease
- Rare
- e.g. Vitamin D-resistant rickets

**Trinucleotide repeats**
- Multiple repeats of three nucleotides
- Severity of the disease α number of repeats
- Number of repeats increases with each generation
- Therefore severity increases with each generation = genetic anticipation
  - Myotonic dystrophy (CTG triplets)
  - Huntington’s chorea (CAG triplets)

**Genetic imprinting**
- Disease phenotype varies
- Depends on origin of mutant gene
- e.g. Deletion of long arm of chromosome 15
  - If inherited from mother → Prader–Willi syndrome
  - If inherited from father → Angelman syndrome

**Multifactorial inheritance**
- Encoded for by multiple genetic loci (polygenic)
  - Height
  - Hair colour
  - Hypertension
  - Pyloric stenosis
  - Ankylosing spondylitis

**Genetic screening and counselling**
Provision of information to prospective parents who are carriers of an inherited disease is vital for informed decisions to be made. Determination of these risks is important and requires screening.
Screening
- Detection of carrier of a mutation, e.g.
  - Thalassaemia
  - Sickle cell disease
  - Tay–Sachs disease
  - Haemophilia
  - Cystic fibrosis

Prenatal diagnosis

Maternal serum
- Maternal α-fetoprotein – neural tube defects
- Bart’s triple test on maternal serum assesses risk of fetal trisomy 21
  - α-fetoprotein (low)
  - β-human chorionic gonadotrophin (high)
  - Unconjugated oestriol (low)

Imaging
- Ultrasound for anatomical abnormalities
- Nuchal fold translucency for Down syndrome

Amniocentesis
- Sampling amniotic fluid for fetal cells
- α-fetoprotein and biochemical analysis
- Risk to fetus <1%

Chorionic villus sampling
- Chromosome/DNA analysis
- Risk to fetus 1–2%

Cordocentesis
- Fetal blood sampling
- Chromosome and DNA analysis
- Risk to fetus 1–2%

Counselling
- Risk of passing on genetic abnormality to child depends on inheritance and parental genome

SELF-ASSESSMENT QUESTIONS

Multiple choice questions (true or false)

1. Smoking has been associated with an increased risk of the following:
   A. Bronchial cancer
   B. Oesophageal cancer
   C. Transitional cell carcinoma
   D. Pharyngeal cancer
   E. Breast cancer

2. Regarding malignancy:
   A. A translocation between chromosomes 9 and 22 is seen in 10% of chronic myeloid leukaemia
   B. p53 mutations are common in gastrointestinal malignancy
   C. Helicobacter pylori is associated with a decreased risk of gastric cancer
   D. Kaposi’s sarcoma is only seen in immunocompromised patients
   E. Family history is important in determining the risk of breast cancer
3. The following are common sites of metastasis for the named primary cancer:
   A. Intracerebral: breast carcinoma
   B. Long bones: osteosarcoma
   C. Vertebral column: prostatic carcinoma
   D. Liver: bronchial carcinoma
   E. Liver: cutaneous basal cell carcinoma

4. The following are autosomal dominant:
   A. Haemophilia A
   B. Achondroplasia
   C. Haemochromatosis
   D. Red-green colour blindness
   E. Leprosy

5. The following genetic abnormalities result in the named condition:
   A. Trisomy 19 – Down syndrome
   B. XO – Turner syndrome
   C. XXY – Klinefelter syndrome
   D. Trisomy 21 – Patau syndrome
   E. XXO – Smith syndrome

6. The following are inherited in an X-linked recessive manner:
   A. Down syndrome
   B. Polycystic kidney disease
   C. Wiskott–Aldrich syndrome
   D. Haemophilia A
   E. Acute intermittent porphyria

Multiple choice questions (single best answer)

7. Which one of the following is a 5HT₃ antagonist antiemetic?
   A. Metoclopramide
   B. Cyclizine
   C. Granisetron
   D. Prochlorperazine
   E. Diazepam

8. A 55-year-old man presents with abdominal distension. He has a long history of chronic hepatitis C infection. Which one of the following is he at an increased risk of suffering?
   A. Pancreatic adenocarcinoma
   B. Cholangiocarcinoma
   C. Gallbladder carcinoma
   D. Hepatocellular carcinoma
   E. Gastric adenocarcinoma

9. A 29-year-old man requests information about his risk of colonic carcinoma. His father has just died of the disease at the age of 54. What is the man’s risk of developing a colonic carcinoma?
   A. 1 in 250
   B. 1 in 100
   C. 1 in 50
   D. 1 in 20
   E. 1 in 3

10. A 45-year-old woman was seen with a palpable mass in her left breast. What is the most appropriate way of confirming the diagnosis?
    A. Bilateral mammography
    B. Ultrasound guided fine needle aspiration
C. Breast lumpectomy  
D. Whole body PET scan  
E. Local lymph node excision

11. A 66-year-old man with a previous history of a bronchogenic carcinoma is admitted with confusion, nausea and diplopia. Which one of the following may provide most effective symptom control?  
A. Diazepam  
B. Metoclopramide  
C. Dexamethasone  
D. Odansetron  
E. Domperidone

12. In the treatment of malignancy:  
A. Surgery is always carried out with the aim of a cure  
B. Nausea is a rare side-effect of chemotherapy  
C. Combination chemotherapy is rarely more efficacious than single therapy  
D. Methotrexate is a folate metabolism antagonist  
E. Vincristine can be given intrathecally
EXAMINING THE NERVOUS SYSTEM

General rules

- Explain carefully to patients what you want them to do for each part of the examination and why
- Ask the patient to copy your actions, rather than trying to explain a complicated manoeuvre
- Always compare one side with the other
- Organize your examination into categories:
  - Mental state
  - Cranial nerves
  - Motor function
  - Reflexes
  - Coordination and gait
  - Sensation

Equipment

- Pen torch
- Snellen eye chart or pocket vision card
- Ophthalmoscope
- Tendon hammer
- 128 and 512 Hz tuning forks
- Cotton wool
- ‘Neuropins’
- Orange stick

Abbreviated mental test score

Ten questions give an indication of cerebral function, including orientation in time, place, long- and short-term memory; mark correct responses out of 10.

- Name?
- Age?
- Address?
- Where are you now?
- Name of the monarch?
- Name of the prime minister?
- Dates of the Second World War? (or another major event – relevant to the age of the patient)
- Remember the following address and repeat it when asked: 42 West Street, Edinburgh (ask the patient to recall this after asking the rest of the questions)
- What time of day is it now?
- Count backwards from 20 to 10
Cranial nerves

General observations suggesting nerve palsies:

- Ptosis (III)
- Facial droop or asymmetry (VII)
- Hoarse voice (X)
- Articulation of words, dysarthria (V, VII, X, XII)
- Abnormal eye position (III, IV, VI)
- Abnormal or asymmetrical pupils (II, III)

I Olfactory

- Supplies: sense of smell
- Ask the patient about changes in or absence of sense of smell
  - Use things that are close at hand, e.g. coffee/soap

II Optic

- Supplies: visual fields/acuity/field of vision
- Examine the fundi for:
  - Papilloedema
  - Optic atrophy
  - Maculopathy
  - Hypertensive or diabetic retinopathy

Test visual acuity

- Allow the patient to use glasses
- Ask the patient to read a Snellen eye chart with each eye
- Record the smallest line the patient can read for each eye
- Visual acuity is reported as a pair of numbers (20/20), where the first number represents how far the patient is from the chart and the second number is the distance from which the ‘normal’ eye can read a line of letters. For example, 20/40 means that at 20 feet, the patient can only read letters a ‘normal’ person can read from twice that distance

Test visual fields

- Position yourself at eye level, 1 metre or so in front of the patient and ask him/her to look into your eyes
- Hold your hands out to the sides halfway between you and the patient and wiggle a finger on both hands asking the patient to indicate which side he/she sees the finger move; if the patient only sees one side this indicates a lateral field defect or sensory neglect on that side
- Test the four quadrants of each eye while asking the patient to cover the opposite eye comparing with your own fields of vision for the appropriate eye

Test pupillary reactions

- Ask the patient to look into the distance
- Shine a bright light obliquely into each pupil in turn
- Look for both the direct (same eye) and consensual (other eye) reactions

III Oculomotor (tested with IV and VI)

- Supplies: superior, medial and inferior rectus and inferior oblique muscles, pupillary muscles, eye
Examining the nervous system

- Look for ptosis
- Test extraocular movements
  - Holding your finger about 1 metre in front of the patient, ask him/her to follow your finger with the eyes without moving the head
  - Check horizontal, vertical and oblique gaze using a cross or ‘H’ pattern; ask about diplopia
  - Pause during upward and lateral gaze to check for nystagmus
- Test pupillary reactions to light

IV Trochlear (superior oblique muscle)
- Inward and downward movement of eyes (see above)

VI Abducens (lateral rectus muscle)
- Lateral eye movement (see above)

V Trigeminal
- Motor
  - Ask the patient to first open the mouth and then clench the teeth
  - Palpate the temporal and masseter muscles as this is done
- Sensory
  - On both sides, use cotton wool to test
    - The forehead (olfactory division)
    - The cheeks (maxillary division)
    - The jaw (mandibular division)
- Corneal reflex
  - Ask the patient to look up and away
  - From the other side, touch the cornea (not sclera) lightly with a fine wisp of cotton wool
  - Look for the normal blink reaction of both eyes
  - Repeat on the other side

VII Facial
- Observe for any facial droop or asymmetry
- Ask the patient to do the following, noting any weakness or asymmetry
  - Raise eyebrows
  - Close both eyes tightly
  - Smile or show the teeth
  - Puff out the cheeks
- Upper vs lower motor neurone injury
  - With an upper motor neurone lesion (stroke), crossover of innervation means function is preserved over the upper part of the face (forehead, eyebrows, eyelids)
  - With a lower motor neurone lesion (Bell’s palsy), the entire side of the face is paralysed

VIII Vestibulocochlear
- Rub your fingers together next to one ear, while whispering a number in the other and ask the patient to tell you the number
- Repeat for the other side
- Weber’s test
  - Use a 512 Hz tuning fork
  - Place the base of the vibrating tuning fork firmly on top of the patient’s head
• Ask the patient where the sound appears to be coming from (normally in the midline)
  • In sensorineural deafness there will be deafness in the affected ear
  • In conductive deafness, the sound will be heard better in the deaf ear

**Rinne’s test (to compare air and bone conduction)**
• Use a 512 Hz tuning fork
• Place the base of the vibrating tuning fork against the mastoid bone behind the ear
• When the patient no longer hears the sound, hold the end of the fork near the patient’s ear and ask if he or she can hear it now (air conduction is normally greater than bone conduction)
  • In conductive deafness bone conduction is better than air conduction

**IX and X  Glossopharyngeal and vagus (tested together)**
• Ask the patient to swallow a sip of water, look for choking or dribbling
• Ask patient to say ‘Agh’, watching the movements of the soft palate and the pharynx. The uvula deviates away from the affected side
• Test the gag reflex (unconscious patient)
  • Touch the back of the throat on the soft palate with an orange stick on each side
  • It is normal to gag after each stimulus

**XI  Accessory**
• From behind, look for wasting of the trapezius muscles
• Ask the patient to shrug the shoulders against resistance
• Ask the patient to turn the head against resistance. Watch and palpate the sternomastoid muscle on the opposite side

**XII  Hypoglossal**
• Look at the tongue for wasting or fasciculation (lower motor neurone lesion)
• Ask the patient to
  • Protrude the tongue
  • Move the tongue from side to side
• The tongue moves towards the side of any lesion

**Motor function (corticospinal or pyramidal tracts)**

**Observation**
• Involuntary movements (e.g. tremor, tics, fasciculation)
• Wasting and asymmetry (pay particular attention to the hands, and shoulder and thigh girdles)

**Muscle tone**
• Ask the patient to relax
• Holding the patient’s hand, flex and extend his/her wrist and elbow
• Place both your hands on the thigh and gently roll the leg from side to side watching for corresponding movement of the foot
• There is normally a small, continuous resistance to passive movement
• Observe for decreased (flaccid) or increased (rigid/cogwheeling/spastic) tone
Power

Pronator drift
- This is a short screening test for muscle strength
- Ask the patient to hold both arms straight out in front, palms up and eyes closed
- With an upper motor neurone lesion, the patient will not be able to maintain extension and supination (and ‘drifts’ into pronation and flexion)

Muscle strength
- Test strength by asking the patient to move against your resistance
- Always compare one side to the other

Other tests of power
- Flexion (C5, C6, biceps) and extension (C6, C7, C8, triceps) at the elbow
- Extension at the wrist (C6, C7, C8, radial nerve)
- Squeeze two of your fingers as hard as possible (‘grip’, C7, C8, T1)
- Finger abduction (C8, T1, ulnar nerve)
- Opposition of the thumb (C8, T1, median nerve)
- Flexion (L2, L3, L4, iliopsoas) and extension at the hip (S1, gluteus maximus)
- Adduction (L2, L3, L4, adductors) and abduction at the hips (L4, L5, S1, gluteus medius and minimus)
- Extension (L2, L3, L4, quadriceps) and flexion (L4, L5, S1, S2, hamstrings) at the knee
- Dorsiflexion (L4, L5) and plantar flexion (S1) at the ankle
- Grade strength on a scale from 0 to 5 (Table 17.1)

Tendon reflexes
- Use a tendon hammer with as little force as needed to provoke a response
- Reinforcement
  - If the reflexes are not elicited as above then ask the patient to clench the teeth or grasp the hands together and then pull apart
  - Retest reflexes as this task is performed
- Reflexes should be graded on a 0 to 4 ‘plus’ scale (Table 17.2)

Biceps (C5, C6)
- Position the patient with the arms relaxed across the lap and partially flexed at the elbow with the palm down
- Place your thumb or finger on the biceps tendon

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**Table 17.1 Muscle strength grading scale**

<table>
<thead>
<tr>
<th>Grade</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>0/5</td>
<td>No muscle movement</td>
</tr>
<tr>
<td>1/5</td>
<td>Visible muscle movement, but no movement at the joint</td>
</tr>
<tr>
<td>2/5</td>
<td>Movement at the joint, but not against gravity</td>
</tr>
<tr>
<td>3/5</td>
<td>Movement against gravity, but not against added resistance</td>
</tr>
<tr>
<td>4/5</td>
<td>Movement against resistance, but less than normal</td>
</tr>
<tr>
<td>5/5</td>
<td>Normal strength</td>
</tr>
</tbody>
</table>
Neurology

Pass Finals

424

- Tap your finger with the reflex hammer
- Watch for flexion of the elbow

**Triceps (C6, C7)**
- Hold the patient’s hand across the chest
- Tap the triceps tendon above the elbow with the reflex hammer
- Watch for extension of the elbow

**Brachioradialis (C5, C6)**
- Rest the forearm on the abdomen or lap
- Tap the radius about 3–5 cm above the wrist
- Watch for flexion and supination of the forearm

**Knee (L2, L3, L4)**
- Hold your arm under the patient’s flexed knees, taking the weight of the legs on your forearm
- Tap the patellar tendon just below the patella
- Note contraction of the quadriceps and extension of the knee

**Ankle (S1, S2)**
- Dorsiflex the foot at the ankle with your hand, with the knee slightly bent and the leg rotated laterally
- Tap the Achilles tendon
- Watch and feel for plantar flexion at the ankle

**Clonus**
- Support the knee in a partly flexed position
- With the patient relaxed, quickly pull the foot into dorsiflexion
- Observe for sustained rhythmic beats of dorsiflexion

**Plantar response (Babinski)**
- Run a key or orange stick firmly along the lateral aspect of the sole of each foot
- Flexion of the big toe is normal
- Extension of the big toe with fanning of the other toes is abnormal and indicates an upper motor neurone lesion

**Coordination and gait (cerebellospinal connections)**

**Coordination**

**Rapid alternating movements (dys-diadochokinesis)**
- Ask the patient to tap the back of one hand with, alternately, the palmar and dorsal aspects of the other hand as accurately and quickly as possible

**Point-to-point movements (finger–nose and heel–shin)**
- Ask the patient to touch your index finger and his/her nose alternately several times. Move your finger about slowly as the

---

**Table 17.2 Tendon reflex grading scale**

<table>
<thead>
<tr>
<th>Grade</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>Absent</td>
</tr>
<tr>
<td>1+ or +</td>
<td>Hypoactive</td>
</tr>
<tr>
<td>2+ or ++</td>
<td>‘Normal’</td>
</tr>
<tr>
<td>3+ or +++</td>
<td>Hyperactive without clonus</td>
</tr>
<tr>
<td>4+ or ++++</td>
<td>Hyperactive with clonus</td>
</tr>
</tbody>
</table>
patient performs this task. Holding your finger still, ask the patient to touch his/her nose and then your finger with the eyes closed. Repeat for the other side

- Ask the patient to place one heel on the opposite knee and run it down the shin to the big toe and back again. Repeat with the patient’s eyes closed
- Look for past-pointing, intention tremor and clumsiness

**Romberg’s test (cerebellar connections and dorsal columns)**

- Ask the patient to stand with the feet together and eyes closed for 5–10 seconds without support (be prepared to catch the patient if unstable)
- The test is positive if the patient becomes unstable (indicating a vestibular or proprioceptive problem)

**Gait**

- Ask the patient to walk across the room, turn and come back and then walk heel-to-toe in a straight line

**Sensation**

**General**

- Compare symmetrical areas on the two sides of the body and distal and proximal areas of the extremities
- When you detect an area of sensory loss map out its boundaries in detail
- Test the following areas
  - Shoulders (C4)
  - Inner and outer aspects of the forearms (C6 and T1)
  - Thumbs and little fingers (C6 and C8)
  - Front of both thighs (L2)
  - Medial and lateral aspect of both calves (L4 and L5)
  - Little toes (S1)

**Light touch (dorsal columns)**

- Use a piece of cotton wool to touch the skin lightly
- Touch rather than brush the skin
- Ask the patient to respond whenever a touch is felt

**Pain (spinothalamic tracts)**

- Use a suitable sharp object (e.g. Neuropin) to test ‘sharp’ or ‘dull’ sensation

**Temperature (spinothalamic tracts)**

- This can be left out if pain sensation is normal
- Use a tuning fork heated or cooled by water and ask the patient to identify ‘hot’ or ‘cold’

**Vibration (dorsal columns)**

- Use a low-pitched tuning fork (128 Hz)
- Place the stem of the fork over the radial head or medial malleolus, and ask the patient to tell you if he/she feels the vibration

**Position sense (dorsal columns)**

- Hold the patient’s big toe away from the other toes with your fingers on each side of the toe
- Show the patient ‘up’ and ‘down’
- Ask the patient to close the eyes and to identify the direction in which you move the toe
- Test the fingers in a similar fashion

**Dermatomes** See Figure 17.1.
Fig. 17.1 Dermatomes of spinal roots and ophthalmic (V₁), maxillary (V₂) and mandibular (V₃) divisions of the trigeminal nerve.

NEUROLOGICAL INVESTIGATIONS

Routine investigations

See Table 17.3.

Neuroradiology

Skull X-ray
- Skull fracture
- Paget’s disease
- Myeloma
- Intracranial calcification
- Intrasellar tumour
### Table 17.3 Abnormalities in routine investigations and possible causes

<table>
<thead>
<tr>
<th>Test</th>
<th>Result</th>
<th>Potential cause/effect</th>
</tr>
</thead>
<tbody>
<tr>
<td>Urinalysis</td>
<td>Glycosuria</td>
<td>Diabetes → Polyneuropathy</td>
</tr>
<tr>
<td></td>
<td>Bence Jones protein</td>
<td>Myeloma → Cord compression</td>
</tr>
<tr>
<td>Blood count</td>
<td>Macrocytosis</td>
<td>Vitamin B&lt;sub&gt;12&lt;/sub&gt; deficiency Chronic liver disease Hypothyroidism</td>
</tr>
<tr>
<td>ESR</td>
<td>Elevated</td>
<td>Vasculitis</td>
</tr>
<tr>
<td>Serum electrolytes</td>
<td>Hypokalaemia</td>
<td>Muscle weakness</td>
</tr>
<tr>
<td></td>
<td>Hyponatraemia</td>
<td>Confusion/coma Central pontine demyelinolysis</td>
</tr>
<tr>
<td>Serum calcium</td>
<td>Hypocalcaemia</td>
<td>Tetany/spasms</td>
</tr>
<tr>
<td>Serum creatine phosphokinase (CPK)</td>
<td>Raised</td>
<td>Myositis</td>
</tr>
<tr>
<td>Chest X-ray</td>
<td>Tumour</td>
<td>Cerebral metastases Osmotic demyelination syndrome</td>
</tr>
<tr>
<td></td>
<td>COPD</td>
<td>CO&lt;sub&gt;2&lt;/sub&gt; retention</td>
</tr>
<tr>
<td>Thyroid function</td>
<td>Hypothyroidism</td>
<td>Confusion/dementia</td>
</tr>
<tr>
<td>Vitamin B&lt;sub&gt;12&lt;/sub&gt;</td>
<td>Low</td>
<td>Polyneuropathy Confusion/dementia Subacute combined degeneration of the cord</td>
</tr>
</tbody>
</table>

**Pituitary fossa X-ray**
- Enlargement with pituitary tumours

**Spinal X-rays**
- Fractures/vertebral collapse
- Metastases
- Spondylosis
- Tuberculosis

**Computed tomography (CT)**

**Brain**
- Cerebral tumours
- Intracranial haemorrhage
- Infarction
- Subarachnoid haemorrhage
- Midline shift (mass effect)
- Hydrocephalus
Cerebral atrophy
Pituitary lesions

Spine
Cord/bone lesions

Magnetic resonance imaging (MRI)
Greater resolution than CT for small lesions and does not require contrast injection
No radiation
High differentiation of white and grey matter
Contraindicated in patients with metal implants, e.g. aneurysm clips
Nerve root compression
Spinal cord lesions
Blood vessel imaging without contrast

Cerebral angiography (seldom used)
Intra-arterial or intravenous contrast is injected to demonstrate arterial or venous systems, e.g. berry aneurysms, arteriovenous malformations

Positron electron tomography (PET)
Maps function of specific areas of brain
Based on metabolic activity

Electroencephalography (EEG)
Records electrical brain activity from scalp electrodes on 16 channels
Used in:
  • Epilepsy (spikes or spike and wave abnormalities)
  • Diffuse brain disorders (slow waves, e.g. hepatic encephalopathy)

Electromyelography (EMG)
Demonstrates abnormal muscle innervation and myopathies

Nerve conduction studies
Neuropathies
Differentiate axonal and demyelinating pathologies

Visual evoked potentials (VEP)
Record time for visual stimulus to reach the visual cortex
Document previous retrobulbar neuritis

Lumbar puncture (LP) and cerebrospinal fluid (CSF) examination

Indications for lumbar puncture
Diagnosis of meningitis or encephalitis
Intrathecal injection of contrast or drugs
Diagnosis of subarachnoid haemorrhage
Measurement of CSF pressure (Table 17.4)
Therapeutic removal of CSF
Detection of CSF abnormalities, e.g. oligoclonal bands in MS
Cytology
**Table 17.4 Normal CSF**

<table>
<thead>
<tr>
<th>Appearance</th>
<th>Protein</th>
</tr>
</thead>
<tbody>
<tr>
<td>Crystal clear, colourless</td>
<td>0.2–0.4 g/L</td>
</tr>
<tr>
<td>Pressure</td>
<td>Glucose</td>
</tr>
<tr>
<td>60–150 mmH₂O</td>
<td>⅔–⅗ blood glucose level</td>
</tr>
<tr>
<td>Cell count</td>
<td>Microbiology</td>
</tr>
<tr>
<td>5/mm³</td>
<td>Sterile</td>
</tr>
<tr>
<td>No polymorphs</td>
<td></td>
</tr>
<tr>
<td>No red blood cells</td>
<td></td>
</tr>
</tbody>
</table>

**Contraindications for lumbar puncture**

- Raised intracranial pressure
- Suspected intracranial or spinal cord mass lesion
- *Note:* Unconscious patients and those with papilloedema *must* have a CT scan to exclude raised intracranial pressure or mass lesion before LP
- Platelet count <40×10⁹/L
- Abnormal coagulation

**Brain biopsy**

- Inflammatory and degenerative brain diseases
- CT-guided sampling of mass lesions

**UNCONSCIOUSNESS AND COMA**

- Coma is a state of unrousable unresponsiveness (*Box 17.1*)
- Consciousness is graded using the Glasgow Coma Scale (GCS, *Table 17.5*)

**Aetiology of coma (Table 17.6)**

- Diffuse brain dysfunction
- Brainstem lesion → damage of the lenticular activating system
- Brainstem compression/displacement through foramen magnum

**EPILEPSY**

- A continuing tendency to suffer epileptic seizures, a seizure being a convulsion or transient abnormal event resulting from paroxysmal discharge of cerebral neurones (*Box 17.2*)

**Prevalence**

- 2% of the population has two or more seizures
- 0.5% have ongoing seizures

**Classification**

- By clinical pattern of seizures (*Table 17.7*)
  - **Generalized**
    - Absence (petit mal)
    - Myoclonic
    - Tonic-clonic (grand mal)
    - Tonic
    - Akinetic
### BOX 17.1. Coma

- Check A B C D E (Airways, Breathing, Circulation, Disability, Exposure)
- Immobilize cervical spine if head or spinal injury suspected
- Look for warning cards/bracelets, etc., e.g. diabetics, epileptics

#### Examination
- Glasgow Coma Score
- Rectal temperature
- Smell breath for alcohol/ketones
- Blood pressure/pulse
- Pupils
  - Bilateral fixed dilated – brainstem death, barbiturates, hypothermia
  - Single fixed dilated – coning
  - Pinpoint – pontine lesions, opiates
- Fundi for papilloedema
- Eye movements
  - Doll’s head reflex
  - Fixed lateral gaze
- Lateralizing signs
  - Facial drooping
  - Muscle tone
  - Plantar responses
  - Tendon reflexes

#### Investigations
- Drug screen (urine or blood)
- Serum biochemistry and glucose
- Arterial blood gases
- Thyroid function tests
- Blood cultures
- ECG
- CT scan or MRI of brain
- LP and CSF examination (only after raised intracranial pressure excluded)
- EEG
- Serum cortisol

#### Immediate management
- Careful observation to detect changes in vital functions or depth of coma
- Protect airway
- Ventilate if necessary

#### Longer-term management
- Skin care
- Pressure area care
- Oral hygiene
- Nutrition (nasogastric feeding or percutaneous endoscopic gastrostomy tube)
- Eye care
- Urinary catheter only if essential
### Table 17.5 Glasgow Coma Scale

<table>
<thead>
<tr>
<th>Eye opening (E)</th>
<th>Motor function (M)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Spontaneous</td>
<td>Obeys commands</td>
</tr>
<tr>
<td>To speech</td>
<td>Localizes to pain</td>
</tr>
<tr>
<td>To pain</td>
<td>Withdraws</td>
</tr>
<tr>
<td>None</td>
<td>Flexion</td>
</tr>
<tr>
<td></td>
<td>Extension</td>
</tr>
<tr>
<td></td>
<td>None</td>
</tr>
<tr>
<td>Value: 4</td>
<td>6</td>
</tr>
<tr>
<td>Value: 3</td>
<td>5</td>
</tr>
<tr>
<td>Value: 2</td>
<td>4</td>
</tr>
<tr>
<td>Value: 1</td>
<td>3</td>
</tr>
</tbody>
</table>

Verbal function (V)

- Orientated: 5
- Confused conversation: 4
- Inappropriate words: 3
- Incomprehensible sounds: 2
- None: 1

### Table 17.6 Causes of diffuse brain dysfunction

- Drug overdose, alcohol: Adrenal failure
- Hypoglycaemia: Hyponatraemia
- Hyperglycaemia: Hypernatraemia
- Hypoxia: Metabolic acidosis
- Hypertensive encephalopathy: Hypothermia, hyperpyrexia
- Uraemia: Epilepsy
- Hepatic encephalopathy: Encephalitis
- CO₂ retention: Head injury
- Hypothyroidism: Subarachnoid haemorrhage

### BOX 17.2. Status epilepticus

**Definition**
- Seizures which follow each other without recovery of consciousness

**Management**
- Nurse the patient in an area with full ventilatory support available if required and with cardiac monitoring facilities
- Give oxygen and monitor pulse, O₂ saturation and BP
- Exclude hypoglycaemia
- Diazepam 10–20 mg i.v. at a rate of 2.5 mg/30 seconds until fitting stops (up to a maximum of 40 mg); beware of respiratory depression
- Loading dose of i.v. phenytoin, 15 mg/kg at a rate 50 mg/minute
- Maintenance phenytoin i.v. or oral depending on patient’s ability to take it
- If status continues unresponsive to treatment for more than 90 minutes, the patient needs to be anaesthetized with thiopental or propofol and ventilated
### Table 17.7 Clinical pattern of epileptic seizures

<table>
<thead>
<tr>
<th>Generalized tonic-clonic seizures</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Warning</strong> – vague</td>
</tr>
<tr>
<td><strong>Tonic phase</strong> – body becomes rigid before patient falls (often with a cry), biting the tongue and with urinary incontinence</td>
</tr>
<tr>
<td><strong>Clonic phase</strong> – a generalized convulsion with rhythmic jerking of muscles and frothing at the mouth</td>
</tr>
<tr>
<td><strong>Recovery</strong> – patient is drowsy or confused, or in a coma for several hours (post-ictal)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Absence seizures</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patient becomes still and staring and looks pale</td>
</tr>
<tr>
<td>Eyelids may twitch</td>
</tr>
<tr>
<td>Attack lasts a few seconds usually, during which the patient is unresponsive</td>
</tr>
<tr>
<td>No recollection of the event</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Partial (focal) seizures</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Aura</strong>, e.g. strange smell, tingling in a limb</td>
</tr>
<tr>
<td><strong>Motor (Jacksonian)</strong></td>
</tr>
<tr>
<td>Jerking movements begin at the angle of the mouth or in the hand, spreading to involve the limbs on the side opposite from the epileptic focus</td>
</tr>
<tr>
<td>Patient remains conscious</td>
</tr>
<tr>
<td>Paralysis of the affected limbs may follow for several hours (Todd’s paralysis)</td>
</tr>
<tr>
<td><strong>Temporal lobe epilepsy</strong></td>
</tr>
<tr>
<td>May be simple or complex</td>
</tr>
<tr>
<td>Feeling of unreality, often déjà-vu, associated with absence attacks, vertigo or visual hallucinations</td>
</tr>
</tbody>
</table>

**Partial**
- Simple (e.g. Jacksonian, no impairment of consciousness)
- Complex (impairment of consciousness)

**Aetiology**
- <30% have a clear underlying cause
- <2% Genetic
- Developmental abnormalities
- 2% Trauma
- Hypoxia
- Surgery (10% of neurosurgical operations)
- Pyrexia (in children, febrile convulsions)
- 3% Intracranial mass
- 15% Infarction (post stroke)
- 6% Alcohol/drug withdrawal
- Encephalitis
- Metabolic abnormalities, e.g. hyponatraemia, hypoglycaemia

**Investigations**
- EEG (abnormal during seizures, often normal in between)
- CT scan/MRI scan
• Serum biochemistry
• Chest X-ray

Management
During seizure
• Maintain airway and physical safety
• Rectal or i.v. diazepam 5–10 mg if seizure does not stop spontaneously

Prophylactic
• For recurrent seizures
• First-line drugs
  • Sodium valproate
  • Carbamazepine
  • Ethosuximide (petit mal)
• Second-line drugs
  • Phenytoin
  • Clobazam

Toxic drug effects
All drugs
• Ataxia
• Nystagmus
• Dysarthria
Phenytoin
• Gum hypertrophy
• Hypertrichosis
• Osteomalacia
• Folate deficiency
• Polyneuropathy

Driving
• It is illegal to drive if any form of seizure or unexplained loss of consciousness has occurred during the past year
• In the UK, it is essential that a doctor informs patients of the driving regulations; it is then the patient’s responsibility to inform the licensing authority

Pseudoseizures
• Often difficult to diagnose
• Prolactin normal (raises following a ‘true’ seizure)

Other causes of drop attacks, blackouts and episodes of disturbed consciousness
• Diagnosis can usually be determined from the history
• A witness account of an episode is especially valuable

Aetiology
• Syncope, e.g. simple, micturition, hyperventilation
• Transient ischaemic attack
• Panic attack
• Cardiac arrhythmia, e.g. Stokes–Adams attack
• Aortic stenosis
• Hypoglycaemia
• Vertigo
MOVEMENT DISORDERS

Parkinson’s disease

- Combination of tremor, rigidity and akinesia
- Gradual development over years

Prevalence

- Increases with age
- 1:200 over 70 years of age
- Less prevalent in smokers

Aetiology

- Idiopathic
- Drug-induced, e.g. phenothiazines
- MPTP (methylphenyltetrahypridine, impurity in illegally synthesized opiates)
- Encephalitis lethargica

Pathology

- Cell degeneration in the substantia nigra
- Loss of dopamine in the extrapyramidal nuclei

Clinical features

- Tremor: 4–7 Hz resting tremor (pill-rolling)
- Micrographia
- R rigidity: increased tone throughout the range of movement
- Cogwheel rigidity (stuttering rigid tone combined with tremor)
- Bradykinesia: poverty of movement
- Falls
- Mask-like facies
- Reduced blinking
- Stooping, shuffling gait (festinant)
- Poor arm swinging
- Monotonous speech, slurring dysarthria
- Normal power
- Brisk reflexes
- Downgoing plantars
- Cognitive function initially preserved; late dementia sometimes occurs

Investigations

- No diagnostic test; diagnosis made on clinical grounds

Management

- Levodopa plus dopa decarboxylase inhibitor, e.g. Sinemet or Madopar; start gradually increasing the dose until adequate response or limiting side-effects (see below)
- Dopaminergic agonists, e.g. bromocriptine/pergolide
- Entacapone – catechol-O-methyl transferase inhibitor
- Selegiline – monoamine oxidase B inhibitor
- Neurosurgery (occasionally for intractable tremor)
- Physiotherapy
- Physical aids

Side-effects of levodopa

Short term

- Nausea and vomiting
- Confusion
Movement disorders

- Visual hallucinations
- Chorea

**Long term**
- End-of-dose dyskinesia – On-off syndrome
- Chorea
- Dystonic movements

**Prognosis**
- Variable
- Usually worsens over 10–15 years with death from bronchopneumonia

**Benign essential tremor**
- Common, often autosomal dominant
- Upper limbs, head or trunk
- Alcohol/β-blockers may improve tremor

**Huntington’s disease**
- Autosomal dominant progressive chorea and dementia in middle life
- Mutation of Huntingtin gene (Ch. 4)
- Genetic anticipation: earlier onset with each generation

**Prevalence**
- 5:100,000

**Pathology**
- Cerebral atrophy
- Loss of neurones in caudate nucleus and putamen
- Depletion of γ-aminobutyric (GABA), angiotensin-converting enzyme (ACE) and met-enkephalin in substantia nigra
- High somatostatin levels

**Clinical features**
- Chorea (sudden involuntary jerky semi-purposeful movements, flitting from one part of the body to another)
- Progressive dementia

**Investigations**
- MRI or CT shows atrophy of caudate nucleus

**Management**
- Phenothiazines may reduce chorea

**Prognosis**
- Death 10–20 years after onset

**Screening**
- Mutation analysis is available for presymptomatic screening in families but no effective treatment is known to alter disease progression

**Other causes of chorea**
- Sydenham’s chorea (rheumatic fever)
- Drugs, e.g. phenytoin
- Thyrotoxicosis
- Stroke
- Systemic lupus erythematosus (SLE)
MULTIPLE SCLEROSIS

- Multiple plaques of demyelination in the brain and spinal cord disseminated in time and place
- Clinical diagnosis: two neurological events separated in time and neurological location

Prevalence

- Increases moving north from the Equator
- 60–100/100,000 in the UK

Aetiology

- 31% concordance among monozygotic twins
- HLA haplotype A3, B7, D2 and DR2 is more common
- Immigrants from low to high risk areas acquire the higher risk

Environmental

- ?Viral infection
- ?Dietary antigens

Pathology

- Plaques of demyelination particularly in
  - Optic nerves
  - Periventricular region
  - Brainstem and cerebellar connections
  - Cervical spinal cord
  - Corticospinal tracts
  - Posterior columns

Clinical patterns

- 80% Acute relapses/remitting
- 20% Chronic progressive

Optic neuropathy/neuritis

Clinical features

- Blurred vision in one eye
- Mild ocular pain
- Recovery within 1–2 months
- Optic disc swelling (optic neuritis)
- Normal disc (retrobulbar neuritis)
- Optic atrophy
- Relative afferent pupillary defect (dilatation of the affected eye when light is transferred from the good eye to the affected eye)

Brainstem demyelination

Clinical features

- Double vision
- Vertigo
- Facial numbness
- Weakness
- Dysphagia
- Pyramidal tract signs
- Nystagmus
- Ataxia
- Cranial nerve defects
- Internuclear ophthalmoplegia
Infections and inflammatory conditions of the nervous system

Spinal cord lesion

Clinical features
- Difficulty walking
- Sensory abnormalities
- Electric shock-like pains radiating down trunk and limbs caused by neck flexion (Lhermitte’s sign)
- Urinary symptoms (incontinence, retention)
- Spastic paraparesis
- Increased tone
- Weakness
- Brisk reflexes
- Up-going plantars
- Sensory level

Other presentations of MS
- Epilepsy
- Trigeminal neuralgia
- Tonic spasms of a hand
- Organic psychosis
- Dementia

Investigations

Imaging
- MRI brain and spinal cord (visualizes multiple plaques)

CSF
- Oligoclonal bands in 80%
- Raised mononuclear cell count 5–60 cells/mm³

Visual evoked responses
- Delayed following optic neuropathy

Management
- There is no cure but newer drugs can modify course
- Corticosteroids – i.v. methylprednisolone or ACTH may speed recovery in acute relapses
- β-interferon/glatiramer – reduces relapse rate but not long-term outcome. Oral fingolimod and teriflunomide and mono-clonal antibodies are being used.
- Physiotherapy
- Occupational therapy
  - Walking aids
  - Wheelchairs
  - Car/house conversions
- Speech therapy
- Counselling

Prognosis
- Unpredictable course ranging from grave disability to mild and benign

INFECTIONS AND INFLAMMATORY CONDITIONS OF THE NERVOUS SYSTEM

Meningitis

Aetiology
See Table 17.8.
Table 17.8 Causes of meningitis

<table>
<thead>
<tr>
<th>Bacteria</th>
<th>Fungi</th>
<th>Chronic inflammatory conditions</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>Neisseria meningitides</em></td>
<td><em>Cryptococcus neoformans</em></td>
<td>Sarcoidosis</td>
</tr>
<tr>
<td><em>Streptococcus pneumoniae</em></td>
<td><em>Candida</em></td>
<td>Behçet’s disease</td>
</tr>
<tr>
<td><em>Staphylococcus aureus</em></td>
<td></td>
<td>Syphilis</td>
</tr>
<tr>
<td><em>Listeria monocytogenes</em></td>
<td></td>
<td>Malignancy</td>
</tr>
<tr>
<td><em>Haemophilus influenzae</em></td>
<td></td>
<td>Blood</td>
</tr>
<tr>
<td><em>Mycobacterium tuberculosis</em></td>
<td></td>
<td>Following subarachnoid haemorrhage</td>
</tr>
<tr>
<td><em>Treponema pallidum</em></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

| Viruses                          |                           |                                 |
|----------------------------------|----------------------------|                                 |
| Enterovirus                      |                            |                                 |
| Echovirus                        |                            |                                 |
| Coxsackie virus                  |                            |                                 |
| Herpes simplex                   |                            |                                 |
| HIV                              |                            |                                 |
| Epstein–Barr virus (EBV)         |                            |                                 |

Table 17.9 Antibiotics in meningitis

<table>
<thead>
<tr>
<th>Suspected organism</th>
<th>Antibiotic</th>
</tr>
</thead>
<tbody>
<tr>
<td>Unknown</td>
<td>Cefotaxime</td>
</tr>
<tr>
<td>Meningococcus</td>
<td>Benzylpenicillin</td>
</tr>
<tr>
<td>Pneumococcus</td>
<td>Cefotaxime</td>
</tr>
<tr>
<td>TB</td>
<td>Rifampicin</td>
</tr>
</tbody>
</table>

Clinical features

- Headache
- Neck stiffness
- Fever
- Photophobia
- Vomiting
- Rigors
- Positive Kernig’s sign (worsening pain on knee extension when hip extended)
- Petechial/purpuric rash (meningococcal septicaemia)
- Drowsiness/focal signs (suggest complication, e.g. raised intracranial pressure/abscess)

Management

- Immediate treatment is vital – do not wait for tests
- Immediate parenteral antibiotics (Table 17.9)
- Further treatment depends on results of blood or CSF culture and sensitivities
- Viral meningitis requires no specific treatment
- i.v. steroids with first dose of antibiotics in adults with pneumococcal meningitis

Investigations

- CT of brain to exclude raised intracranial pressure
- Lumbar puncture (Table 17.10)
Infections and inflammatory conditions of the nervous system

Table 17.10 CSF findings in meningitis

<table>
<thead>
<tr>
<th>Appearance</th>
<th>Mononuclear cells (per mm³)</th>
<th>Polymorphs (per mm³)</th>
<th>Protein (g/L)</th>
<th>Glucose (% blood glucose)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal</td>
<td>Crystal clear</td>
<td>5</td>
<td>Nil</td>
<td>0.2–0.4</td>
</tr>
<tr>
<td>Viral</td>
<td>Clear/turbid</td>
<td>10–100</td>
<td>Nil</td>
<td>0.4–0.8</td>
</tr>
<tr>
<td>Pyogenic</td>
<td>Turbid/purulent</td>
<td>&lt;50</td>
<td>200–300</td>
<td>0.5–2</td>
</tr>
<tr>
<td>TB</td>
<td>Turbid/viscous</td>
<td>100–300</td>
<td>0–200</td>
<td>0.5–3</td>
</tr>
</tbody>
</table>

- Blood cultures
- Blood glucose
- Chest X-ray
- Skull X-ray (if trauma)
- Throat swab for *Neisseria meningitidis*

**Prophylaxis**
- Meningococcus is notifiable
- Family and very close contacts should be treated with ciprofloxacin or rifampicin to eradicate carriage
- Meningococcal vaccine to close contacts

**Tuberculous meningitis**
- More chronic course
- Difficult to diagnose
- May demonstrate multiple cranial nerve palsies
- Meningeal enhancement on MRI

**Acute viral encephalitis**

**Aetiology**
- Herpes simplex
- Echovirus
- Coxsackie virus
- Mumps
- EBV
- Adenovirus
- Varicella zoster
- Influenza
- Measles
- Rabies

**Clinical features**
- Often mild and self-limiting
- HSV-1 infection may be more serious
- Headache
- Fever
- Mood change
- Drowsiness
- Seizures
Focal signs
Coma

**Investigations**
- CT scan (may show diffuse oedema)
- EEG (characteristic slow wave changes in HSV)
- CSF (increased mononuclear cells, slightly raised protein)

**Management**
- i.v. aciclovir for suspected HSV-1

**Prognosis**
- 20% mortality in serious cases, with many others suffering long-term severe brain damage

Herpes zoster (shingles)
- Recrudescence of varicella zoster virus infection within a dorsal root ganglion

**Clinical features**
- Typical blistering rash and pain affecting dermatome supplied by the affected nerve root

Trigeminal nerve (ophthalmic division)
- Rash affects the eye and may cause corneal scarring

Facial nerve (Ramsay Hunt syndrome)
- Facial palsy
- Vesicles on ear lobe, external auditory meatus and fauces

**Treatment**
- Aciclovir

**Complications**
- Post-herpetic neuralgia

Neurosyphilis

**Meningovascular syphilis**

**Tabes dorsalis**
- Subacute meningitis with cranial nerve palsies or paraparesis
- Demyelination of dorsal roots
- Charcot’s joints (neuropathic)
- Ataxia
- Stamping gait
- Widespread sensory loss
- Argyll Robertson pupils (small irregular pupil, fixed to light, constricts to accommodation)
- Ptosis
- Optic atrophy

**Generalized paralysis of the insane (GPI)**
- Dementia
- Weakness
- Tremor
- Brisk reflexes
- Extensor plantars
- Argyll Robertson pupils

**Taboparesis**
- Congenital neurosyphilis
- Features of tabes dorsalis and GPI in childhood
Infections and inflammatory conditions of the nervous system

Management
- Parenteral penicillin for 2–3 weeks

Sporadic Creutzfeldt–Jakob disease (CJD)

Aetiology
- Prion disease (proteinaceous infectious particle)
- Can be passed on from surgical specimens, autopsy material (e.g. corneal grafts) and human pituitary hormones

Pathology
- Spongiform changes in brain

Clinical features
- Slowly progressive dementia develops after age 50

Variant CJD
- First noted in Britain in 1995

Aetiology
- Prion disease
- Linked to ingestion of meat from cattle infected with bovine spongiform encephalopathy (BSE)

Clinical features
- Younger patients
- Early neuropsychiatric symptoms
- Ataxia
- Dementia
- Myoclonus
- Chorea
- Death

Brain abscess
- A focal area of bacterial infection causing an expanding mass lesion in the cerebrum or cerebellum

Aetiology
- *Streptococcus milieri*
- *Bacteroides* spp
- *Staphylococcus* spp
- Fungi
- Parameningeal infection, e.g. ear, nose, paranasal sinuses
- Skull fracture
- Distant infection, e.g. pneumonia, infective endocarditis
- Immunosuppression, e.g. HIV infection

Clinical features
- Headache
- Fever
- Focal signs
- Seizures
- Vomiting
- Drowsiness
- Papilloedema

Investigations
- Imaging (mass lesion on CT or MRI ± hydrocephalus)
- Blood cultures
Neurology

- Raised ESR
- Raised white cell count
- Look for a local/distant focus of infection
- Lumbar puncture is contraindicated

Management
- Parenteral antibiotics
- Surgical decompression

Prognosis
- Mortality 25%
- Persistent epilepsy common in survivors

INTRACRANIAL TUMOURS (Table 17.11)

- Primary intracranial tumours account for about 10% of all neoplasms

Clinical features
- Direct mass effect on function, e.g. hemiparesis
- Raised intracranial pressure (Table 17.12)
- Seizures

Investigations
- CT or MRI scanning
- Brain biopsy

Table 17.11 Intracranial tumours

<table>
<thead>
<tr>
<th>Type</th>
<th>Prevalence (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Metastases</td>
<td></td>
</tr>
<tr>
<td>Bronchus</td>
<td></td>
</tr>
<tr>
<td>Breast</td>
<td></td>
</tr>
<tr>
<td>Stomach</td>
<td></td>
</tr>
<tr>
<td>Prostate</td>
<td></td>
</tr>
<tr>
<td>Thyroid</td>
<td></td>
</tr>
<tr>
<td>Kidney</td>
<td></td>
</tr>
<tr>
<td>Lymphoma (associated with AIDS)</td>
<td></td>
</tr>
<tr>
<td>Primary malignant</td>
<td>35</td>
</tr>
<tr>
<td>Astrocytoma</td>
<td></td>
</tr>
<tr>
<td>Oligodendroglioma</td>
<td></td>
</tr>
<tr>
<td>Lymphoma</td>
<td></td>
</tr>
<tr>
<td>Medulloblastoma</td>
<td></td>
</tr>
<tr>
<td>Benign</td>
<td>15</td>
</tr>
<tr>
<td>Meningioma</td>
<td></td>
</tr>
<tr>
<td>Neurofibroma</td>
<td></td>
</tr>
</tbody>
</table>

Table 17.12 Symptoms and signs of raised intracranial pressure

<table>
<thead>
<tr>
<th>Symptoms</th>
<th>Signs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Headache</td>
<td>Bradycardia</td>
</tr>
<tr>
<td>Vomiting</td>
<td>Decerebrate posturing (coning)</td>
</tr>
<tr>
<td>Papilloedema</td>
<td>False localizing signs</td>
</tr>
<tr>
<td>Impaired consciousness</td>
<td>VI nerve lesion</td>
</tr>
<tr>
<td>Respiratory depression</td>
<td>III nerve lesion</td>
</tr>
</tbody>
</table>
Management
- Reduce cerebral oedema using corticosteroids and/or i.v. mannitol
- Anticonvulsants
- Surgery
- Radiotherapy

Prognosis
- 50% survival at 2 years for high-grade malignant tumours

HYDROCEPHALUS
- Excessive CSF volume
  - Obstruction to CSF outflow
  - Increased CSF production
- Treated by ventriculo-peritoneal shunting or neurosurgical relief of obstruction

HEADACHE AND MIGRAINE

Tension headache
- The vast majority of chronic and recurrent headaches

Clinical features
- Throbbing headache
- Tight band sensation
- Pressure behind eyes

Management
- Avoid precipitating causes
- Simple analgesia (however recurrent analgesic use can induce cyclical headache)

Migraine
- Recurrent headaches associated with visual and gastrointestinal disturbance
- 12% of population report symptoms

Pathology
- Vasodilatation and oedema of blood vessels
- Release of vasoactive substances

Classical migraine

Clinical features
- Prodrome
  - Teichopsis (flashes)
  - Jagged lines
  - Unilateral patchy scotoma
  - Lasts 15 minutes to 1 hour
- Headache hemicranial or generalized
- Nausea and vomiting
- Generally irritable
- Preference for the dark
- Sleeping

Other patterns
- Migraine without aura
- Hemiplegic migraine
**Neurology**

**Differential diagnosis**
- Subarachnoid haemorrhage
- Transient ischaemic attack
- Partial seizures

**Management**
- Avoid precipitating features

**During attack**
- Paracetamol
- Antiemetics
- Sumatriptan (5HT₁ agonist)
- Ergotamine

**Prophylaxis**
- Pizotifen, methysergide (5HT₂ antagonists)
- Propranolol
- Amitriptyline (low-dose)

**Cluster headaches**
- Affect adults in third and fourth decades
- ♂ > ♀

**Clinical features**
- Recurrent bouts of excruciating pain centred around one eye
- Wakes patient at night
- Vomiting
- Watering and congestion of affected eye
- Transient ipsilateral Horner syndrome

**Management**
- Usually unhelpful
- Oxygen/sumatriptan during attack
- No analgesia effective for headache
- Verapamil/lithium for prophylaxis

**Other causes of headache**
- Subarachnoid haemorrhage
- Meningitis
- Sinusitis
- Brain tumours
- Temporal arteritis (see Ch. 7)
- Benign intracranial hypertension
- Head injury

---

**CEREBROVASCULAR DISEASE AND STROKE (TABLE 17.13)**

- Stroke is the third commonest cause of death in the UK
- A stroke is a focal neurological deficit due to a vascular lesion lasting >24 hours (if the patient survives)
- A transient ischaemic attack (TIA) is a brief episode of neurological dysfunction due to temporary ischaemia without infarction. NB The arbitrary time of 24hr is not longer used.

**Risk factors**
- Hypertension
- Smoking
- High alcohol intake
- Lack of regular exercise
Cerebrovascular disease and stroke

Table 17.13 Types of cerebrovascular disease

<table>
<thead>
<tr>
<th>Type of Cerebrovascular Disease</th>
</tr>
</thead>
<tbody>
<tr>
<td>Thromboembolic infarction</td>
</tr>
<tr>
<td>Cerebral and cerebellar haemorrhages</td>
</tr>
<tr>
<td>Dissection of carotid or vertebral arteries</td>
</tr>
<tr>
<td>Subarachnoid haemorrhage</td>
</tr>
<tr>
<td>Subdural and extradural haemorrhage</td>
</tr>
<tr>
<td>Cortical venous and dural sinus thrombosis</td>
</tr>
</tbody>
</table>

- Family history
- Hyperlipidaemia
- Afro-Caribbean race
- High-dose oral contraceptive pill

**Transient ischaemic attacks**

**Clinical features**
- Focal deficit depends on part of brain affected
- Usually due to microemboli

**Carotid system**
- Amaurosis fugax
  - Visual loss
- Aphasia (dominant side)
- Hemiparesis
- Hemianopic visual loss

**Vertebrobasilar system**
- Diplopia
- Vertigo
- Vomiting
- Dysarthria, choking
- Ataxia
- Transient global amnesia

**Evidence of source of embolus**
- Atrial fibrillation
- Carotid bruit
- Valvular heart disease
- Subclavian artery stenosis

**Investigations**
- Rapid investigation to identify reversible risks
  - Carotid Dopplers
  - Echocardiogram
  - CT scanning
- Immediate therapy to reduce acute and long-term risk
  - Anti-platelet drugs: aspirin/clopidogrel
  - Statins (irrespective of serum cholesterol)
  - Management of hypertension
- Carotid endarterectomy

**Cerebral infarction**

**Clinical features**
- Focal deficit depends on part of brain affected (see below)
- Initially flaccid areflexic weakness followed by spastic tone, brisk reflexes and extensor plantars
- See Figure 17.2 for arterial supply to the cerebral cortex
Dysphasia

- Dominance
  - Almost all right-handed and 50% of left-handed people have language function in the left hemisphere

- Expressive dysphasia
  - Lesion in Broca’s area in frontal lobe
  - Reduced fluency of speech
  - Failure to construct sentences
  - Comprehension preserved

- Receptive dysphasia
  - Lesion in Wernicke’s area in temporo-parietal region
  - Fluent speech with incorrect words
  - Use of jargon
  - Sounds like nonsense
  - Failure of comprehension

Fig. 17.2 Arterial supply to the cerebral cortex.
Middle cerebral/internal carotid artery (internal capsule stroke); posterior inferior cerebellar artery (brainstem stroke)
- Hemiparesis (limbs and face)
- Aphasia (dominant side)
- Hemianopic visual loss
- Dysarthria
- Coma, altered consciousness
- Vertigo
- Vomiting
- Dysphagia, choking
- Ataxia
- Contralateral loss of pain on face

Important parts of examination of patients with cerebrovascular disease
- Neurological signs
- Source of embolus (e.g. carotid bruit, atrial fibrillation)
- Blood pressure (in both arms)
- Optic fundi (hypertensive retinopathy, papilloedema)

Investigations
- CT/MRI imaging of brain (see Ch. 5)
  - Demonstrates site
  - Distinguishes between infarct or haemorrhage
- Carotid Doppler scanning
- Magnetic resonance angiography (for possible surgery)
- Blood count
- ESR
- Blood glucose, lipids
- Syphilis serology
- Chest X-ray
- ECG
- Echocardiogram

Management
- Assessment by a regional stroke team
- Thrombolysis in acute stroke (effective if given within 3 hours of onset)
- Aspirin 300 mg initially then 75 mg/day or other antiplatelet therapy
- Identify and treat risk factors where possible
- Antihypertensive therapy
- Anticoagulation (for atrial fibrillation)
- Surgery (internal carotid endarterectomy)

Rehabilitation
- Physiotherapy
- Speech therapy
- Occupational therapy
- Enteral nutrition if unsafe swallow (e.g. percutaneous endoscopic gastrostomy)

Prognosis
- 30–40% survival at 3 years (among initial survivors)
- 10% chance of further stroke within a year
Intracerebral haemorrhage

- Accounts for 10% of strokes

Aetiology
- Rupture of microaneurysms

Risk factors
- Hypertension

Clinical features
- Difficult to distinguish between haemorrhage and infarction
- Haemorrhage may be accompanied by headache and coma

Investigations
- CT head (see Fig. 5.40)

Management
- As for infarction, except avoid antiplatelet and anticoagulant drugs

Prognosis
- 70% death within 2 years

Subarachnoid haemorrhage

- Spontaneous arterial bleeding into subarachnoid space

Prevalence
- 6:100,000/year
- Accounts for 5% of strokes

Aetiology
- Saccular ‘berry’ aneurysms (70%)
- Arteriovenous malformation (AVM) (10%)
- No lesion (20%)

Clinical features
- Sudden onset of severe occipital headache
- Vomiting
- Loss of consciousness
- Neck stiffness
- Positive Kernig’s sign
- Papilloedema and retinal haemorrhages

Investigations
- CT scan
- Lumbar puncture (if CT undiagnostic) – red cells and/or xanthochromia in CSF
- CT/MR angiography

Management
Immediate
- Bed rest
- Treat hypertension
- Dexamethasone
- Nimodipine

Later
- Neurosurgical aneurysm clipping or coil insertion

Prognosis
- 50% mortality at presentation
- 10–20% more die in early weeks
Chronic subdural haematoma

- Accumulation of blood in subdural space following rupture of a vein after head injury (sometimes trivial)

Clinical features
- May be delayed
- Headache
- Drowsiness
- Confusion
- Focal deficits

Management
- Often conservative
- Usually resolve spontaneously without surgical drainage

DEGENERATIVE DISORDERS

Motor neurone disease

- Progressive degeneration of lower motor neurones and upper motor neurones of the cortex, cranial nerve nuclei and spinal cord

Incidence
- 2:100,000 per year
- Slight male predominance

Clinical patterns
- Progressive muscular atrophy – progressive weakness and wasting of arm and hand muscles
- Amyotrophic lateral sclerosis – progressive spastic tetraparesis or paraparesis with wasting and fasciculation
- Progressive bulbar palsy – degeneration of lower cranial nerve nuclei

Clinical features
- Muscle wasting
- Fasciculation
- Reflexes absent or exaggerated
- Dysarthria
- Dysphagia
- Nasal regurgitation of fluids
- Choking
- Bulbar and pseudobulbar palsy (see p. 455)
- Ocular movements are not affected
- Cerebellar or extrapyramidal signs do not occur
- Dementia is unusual
- Sphincter function is usually preserved
- No sensory signs

Investigations
- Diagnosis made on clinical grounds
- EMG – denervation of muscles with preserved motor conduction velocity

Prognosis
Relentlessly progressive course
- Death within 3 years
Management
- Riluzole (sodium channel blocker, inhibits glutamate release) slows progress
- No treatment affects outcome

Friedreich's ataxia
- Progressive degeneration of dorsal root ganglia, spinocerebellar tracts and corticospinal tracts

Aetiology
- Abnormal gene for frataxin (unknown function)
- Autosomal recessive

Clinical features
- Difficulty walking from about 12 years of age
- Ataxia of gait and trunk
- Nystagmus
- Dysarthria
- Absent reflexes in legs
- Optic atrophy
- Pes cavus
- Cardiomyopathy

NEUROPATHY
- A pathological process affecting peripheral nerves

Pathology
- Demyelination
- Axonal degeneration
- Wallerian degeneration (after nerve section)
- Compression
- Infarction
- Infiltration

Mononeuropathies
- Caused by peripheral nerve compression

Carpal tunnel syndrome
- Median nerve compression in carpal tunnel (at wrist)

Aetiology
- Idiopathic
- Hypothyroidism
- Diabetes mellitus
- Pregnancy
- Rheumatoid arthritis
- Obesity
- Acromegaly

Clinical features
- Tingling in fingers (especially at night)
- Weakness of thenar muscles
- Wasting of thenar eminence
- Weakness of abductor pollicis brevis (raising thumb away from palm)
- Weakness of opposition of thumb and little finger
Neuropathy

- Tinel’s sign (reproduction of tingling by tapping over carpal tunnel)
- Sensory loss of palm and radial three and a half fingers

Management
- Splint wrist
- Surgical decompression

Ulnar nerve compression
- Usually occurs after trauma at elbow

Clinical features
- Wasting and weakness of interossei and hypothenar muscles
- Sensory loss in the ulnar one and a half fingers

Radial nerve compression (‘Saturday night palsy’)
- Occurs after nerve is compressed against humerus when arm is draped over a hard chair for several hours

Clinical features
- Wrist drop
- Weakness of finger extension

Mononeuritis multiplex
- Multiple mononeuropathies

Aetiology
- Diabetes mellitus
- Leprosy
- Vasculitis
- Sarcoidosis
- Amyloidosis
- Malignancy
- Neurofibromatosis
- HIV infection

Polyneuropathies

Guillain–Barré syndrome
- Acute inflammatory post-infective polyneuropathy
- Follows 1–3 weeks after infection (often trivial, or *Campylobacter* infection)

Incidence
- 3/100000 per year

Clinical features
- Weakness of distal limb muscles ± numbness
- Weakness ascends over days for up to 3 weeks
- Can affect respiratory and facial muscles in 30%

Variants
- Autonomic neuropathy
- Miller–Fisher syndrome (affecting ocular muscles with ataxia)

Investigations
- Diagnosis is made on clinical grounds
- Nerve conduction studies (demyelinating neuropathy)
- CSF (cell count normal, protein raised 1–3 g/L)

Management
- Measurement of respiratory function (arterial blood gases, vital capacity, FEV₁)
Table 17.14 Other polyneuropathies

<table>
<thead>
<tr>
<th>Metabolic</th>
<th>Thalidomide</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diabetes mellitus</td>
<td>Vincristine</td>
</tr>
<tr>
<td>Uraemia</td>
<td>Cisplatin</td>
</tr>
<tr>
<td>Porphyria</td>
<td>Vitamin deficiencies</td>
</tr>
<tr>
<td>Amyloidosis</td>
<td>Thiamin (B₁)</td>
</tr>
<tr>
<td>Toxic</td>
<td>Pyridoxine (B₆)</td>
</tr>
<tr>
<td>Alcohol</td>
<td>Vitamin B₁₂</td>
</tr>
<tr>
<td>Drugs</td>
<td>Nicotinic acid</td>
</tr>
<tr>
<td>Phenytoin</td>
<td>Non-metastatic manifestation of malignancy</td>
</tr>
<tr>
<td>Isoniazid</td>
<td></td>
</tr>
<tr>
<td>Metronidazole</td>
<td></td>
</tr>
</tbody>
</table>

- Assisted ventilation if necessary
- High-dose i.v. γ-globulin
- Plasmapheresis
- Subcutaneous heparin for prevention of thromboembolism

**Prognosis**
- Spontaneous gradual recovery
- 15% disability or death

**Other polyneuropathies**

See Table 17.14

**Thiamin deficiency (Wernicke–Korsakoff syndrome)**

**Clinical features**
- Ocular signs
  - Nystagmus
  - Bilateral rectal palsy
  - Fixed pupils
- Ataxia
- Confusion (amnestic syndrome, with loss of short-term memory)

**Investigations**
- Reduced red cell transketolase

**Management**
- Parenteral thiamine

**Vitamin B₁₂ deficiency (subacute combined degeneration of the cord)**

**Aetiology**

See p. 371, Table 15.3.

**Clinical features**
- Distal sensory loss
  - Light touch
  - Vibration sense
  - Joint position sense
- Absent ankle jerks
- Extensor plantars
- Optic atrophy
- Dementia
Muscle disease

Investigations
- Reduced serum B$_{12}$
- Macrocytosis
- Megaloblastic bone marrow

Management
- Parenteral B$_{12}$

**Peroneal muscular atrophy (Charcot–Marie–Tooth disease)**
- Inherited sensorimotor neuropathy
- Several types: autosomal dominant and recessive

Clinical features
- Distal limb wasting and weakness
- Inverted ‘champagne bottle’ legs
- Pes cavus
- Clawing of toes
- Loss of sensation
- Loss of reflexes

**Autonomic neuropathy**

Aetiology
- Diabetes mellitus
- Guillain–Barré syndrome
- Amyloidosis

Clinical features
- Postural hypotension
- Retention of urine
- Erectile dysfunction
- Diarrhoea
- Diminished sweating
- Cardiac arrhythmias

**MUSCLE DISEASE**

Aetiology
See Table 17.15.

**Myasthenia gravis**
- Disorder of the neuromuscular junction

<table>
<thead>
<tr>
<th>Type</th>
<th>Example</th>
</tr>
</thead>
<tbody>
<tr>
<td>Inflammatory</td>
<td>Polymyositis</td>
</tr>
<tr>
<td>Metabolic</td>
<td>Cushing syndrome</td>
</tr>
<tr>
<td>Myasthenic</td>
<td>Myasthenia gravis</td>
</tr>
<tr>
<td>Hereditary</td>
<td>Duchenne muscular dystrophy</td>
</tr>
<tr>
<td>Myotonias</td>
<td>Myotonic dystrophy</td>
</tr>
<tr>
<td>Channelopathies</td>
<td>Periodic paralysis</td>
</tr>
</tbody>
</table>
Prevalence
- 4:100,000
-♀ > ♂ (2:1)
- Age of onset about 30 years

Aetiopathogenesis
- Unknown aetiology
- IgG antibodies to acetylcholine receptor
- Immune complex deposits on postsynaptic membrane
- Destruction of acetylcholine receptor
- Thymic hyperplasia in 70%
- Associated with
  - Thyroid disease
  - Rheumatoid arthritis
  - Pernicious anaemia
  - SLE

Clinical features
- Weakness and fatigability of muscles
  - Proximal limb
  - Extraocular
  - Speech
  - Facial expression
  - Mastication
- Ptosis
- Reflexes preserved but fatigable

Investigations
- Serum acetylcholine receptor antibodies (positive in 90%)
- Mediastinal imaging for thymoma (chest X-ray, CT, MRI)

Management
- Oral anticholinesterases, e.g. pyridostigmine
- Thymectomy (improves prognosis)
- Corticosteroids
- Azathioprine
- Plasmapheresis

Lambert–Eaton myasthenic-myopathic syndrome
- Non-metastatic manifestation of small cell carcinoma of the bronchus due to defective acetylcholine release at the neuromuscular junction

Clinical features
- Muscle weakness and absent reflexes which improve with contraction

Myotonic dystrophia
- Autosomal dominant inheritance

Clinical features
- Cataracts
- Frontal baldness
- Ptosis
- Facial weakness
- Progressive distal muscle weakness
- Mild intellectual impairment
CRANIAL NERVE DEFECTS

See Table 17.16.

Specific cranial nerve and brainstem defects

Optic pathway
See Figure 17.3.

Bell’s palsy
- Common acute, isolated facial nerve palsy

Aetiology
- Viral infection (often herpes simplex) causes swelling of nerve within petrous temporal bone

Clinical features
- Unilateral lower motor neurone facial weakness and droop
- Loss of taste on anterior two-thirds of tongue

Investigations
- Diagnosis made on clinical grounds

Management
- Prednisolone 60 mg reducing to zero over 10 days plus aciclovir
- Closure of eyelid to protect cornea

Prognosis
- Spontaneous improvement begins during second week
- Recovery takes up to 12 months
- Less than 10% have residual severe weakness

Bulbar palsy
- LMN weakness of cranial nerve nuclei within medulla (IX, X, XI, XII)

Aetiology
- Motor neurone disease
- Syringobulbia
- Poliomyelitis
- Myasthenia gravis

Clinical features
- Weakness of elevation of palate
- Loss of gag reflex
- Paralysed vocal cords
- Dysphagia
- Nasal regurgitation of fluids
- Choking

Pseudobulbar palsy
- Bilateral upper motor neurone lesion of lower cranial nerve nuclei

Aetiology
- Motor neurone disease
- Multiple sclerosis
- Multi-infarct dementia
- Severe head injury

Clinical features
- Stiff, slow, spastic tongue (not wasted)
- Dysarthria
<table>
<thead>
<tr>
<th>Nerve</th>
<th>Causes</th>
<th>Features</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>Head injury</td>
<td>Loss of smell (anosmia)</td>
</tr>
<tr>
<td>II</td>
<td>Optic neuritis, Optic nerve compression, Visual pathway lesion</td>
<td>See MS, Tunnel vision (if at chiasma), See Figure 17.3</td>
</tr>
<tr>
<td>III</td>
<td>Coning, Aneurysm of posterior inferior carotid artery, Diabetes</td>
<td>Ptosis, Eye points down and out, Fixed dilated pupil</td>
</tr>
<tr>
<td>IV</td>
<td>Rare</td>
<td>Diplopia looking away and down</td>
</tr>
<tr>
<td>V</td>
<td>Brainstem lesion, Acoustic neuroma, Cavernous sinus thrombosis</td>
<td>Sensory loss (face and tongue), Loss of corneal reflex, Deviation of jaw towards lesion</td>
</tr>
<tr>
<td>VI</td>
<td>MS, Glioma, Raised intracranial pressure</td>
<td>Convergent squint, Diplopia looking towards lesion</td>
</tr>
<tr>
<td>VII</td>
<td>Upper motor neurone lesion (infarction), Lower motor neurone lesion (Bell’s palsy, Ramsay Hunt syndrome, parotid gland disease)</td>
<td>Lower facial muscle weakness, Upper and lower facial weakness + Loss of taste on anterior two-thirds of tongue</td>
</tr>
<tr>
<td>VIII</td>
<td>Acoustic neuroma, Meningitis, Head injury, Drugs – gentamicin</td>
<td>Sensorineural deafness, Vertigo, Nystagmus</td>
</tr>
<tr>
<td>IX-X</td>
<td>Brainstem infarct, Motor neurone disease, Carcinoma of nasopharynx</td>
<td>Weakness of elevation of pharynx, Loss of gag reflex, Hoarseness, Dysphagia, Bulbar or pseudobulbar palsy</td>
</tr>
<tr>
<td>XI</td>
<td>Syringobulbia, Motor neurone disease, Carcinoma of nasopharynx</td>
<td>Weakness of sternomastoid and trapezius</td>
</tr>
<tr>
<td>XII</td>
<td>Brainstem infarct, Motor neurone disease, Carcinoma of nasopharynx</td>
<td>LMN lesion; unilateral wasting, weakness and fasciculation of tongue, UMN lesion; stiff, spastic tongue</td>
</tr>
</tbody>
</table>
Cranial nerve defects

**Fig. 17.3** Lesions of the visual pathway. (a) Optic nerve tracts and lesions.

- Dry gravelly voice
- Preserved gag reflex
- Exaggerated jaw jerk
- Emotional lability

**Horner syndrome**
- Lesion of the cervical sympathetic pathway

**Aetiology**
- Brainstem stroke
- Coning
- Syringomyelia
- Apical lung cancer (Pancoast’s tumour)
- Cervical rib
- Brachial plexus trauma

**Clinical features**
- Ptosis
- Myosis (constricted pupil)
- Enophthalmos
- Loss of sweating on side of face
Fig. 17.3—cont’d (b) Visual field defects caused by lesions in the optic pathway. Lesion 1: This is analogous to losing an eye. One eye is completely blacked out. Lesion 2: Here only inputs from the nasal retinas are cut, so peripheral vision is lost on both sides. This can be caused by a pituitary tumour. (The pituitary lies just under the optic chiasm.) Lesion 3: Homonymous hemianopia: loss of the left hemifield. Both eyes are blind to anything on the left side of the world (assuming the eyes are pointed straight ahead). Lesion 4: The lower optic radiations are carrying information from the upper visual world so vision is lost in the upper quadrants of the left hemifield. Lesion 5: Here the parietal portion of the optic radiations are cut, so the lower visual world is affected on one side. Lesion 6: When the cortex itself is lesioned, vision at the fovea is spared, perhaps because there is such a large representation of the fovea in the cortex, or perhaps due to overlapping blood supply. The loss of vision is not a complete hemifield, then, but a notched hemifield. This is called macular sparing.
**SPINAL CORD DISEASE**

**Spinal cord compression**

**Aetiology**
See Table 17.17.

**Clinical features**
- Radicular pain
- Spastic paraparesis or tetraparesis
- Sensory loss to level of compression
- Sphincter disturbance (retention of urine and incontinence)

**Investigations**
- Plain spinal X-rays
- Chest X-ray
- MRI
- Myelography

**Management**
- Surgical decompression if possible

**Syringomyelia and syringobulbia**
- A fluid-filled cavity (syrinx) within the cervical spinal cord (syringomyelia) or extending up into the brainstem (syringobulbia)

**Aetiology**
- Arnold–Chiari malformation
- Spina bifida
- Hydrocephalus
- Intrinsic cord tumours

**Pathology**
- The expanding cavity within the cord destroys spinothalamic neurones, anterior horn cells, lateral corticospinal tracts, sympathetic trunk, trigeminal, IX, X XI and XII nuclei

**Clinical features**
- Loss of pain and temperature sensation in upper limbs
- Painless burns
- Trophic changes
- Normal light touch sensation
- Loss of upper limb reflexes
- Wasting of small muscles of hands
- Spastic paraparesis

---

**Table 17.17 Causes of spinal cord compression**

<table>
<thead>
<tr>
<th>Within the cord</th>
<th>Outside the cord</th>
</tr>
</thead>
<tbody>
<tr>
<td>Spinal cord neoplasms</td>
<td>Vertebral neoplasms</td>
</tr>
<tr>
<td>Transverse myelitis</td>
<td>(metastases, myeloma)</td>
</tr>
<tr>
<td>In the meninges</td>
<td>Disc lesions</td>
</tr>
<tr>
<td>Epidural abscess</td>
<td>Vertebral collapse</td>
</tr>
<tr>
<td>Epidural haemorrhage</td>
<td></td>
</tr>
<tr>
<td>Ependymoma</td>
<td></td>
</tr>
<tr>
<td>Meningioma</td>
<td></td>
</tr>
</tbody>
</table>
Neuropathic joints
Brainstem signs, e.g. bulbar palsy, Horner syndrome

**Investigations**
- MRI

**Management**
- No effective treatment or surgery

**SELF-ASSESSMENT QUESTIONS**

**Multiple choice questions (single best answer)**

1. In epilepsy:
   - A. Generalized convulsions are characterized by maintenance of consciousness
   - B. Absence seizures are generalized
   - C. Absence seizures are commonest in adults
   - D. Temporal lobe seizures may affect the myocardium
   - E. Todd’s paralysis follows temporal lobe seizure

2. In epilepsy:
   - A. The EEG is usually diagnostic between fits
   - B. All generalized seizures should be treated immediately with intravenous diazepam
   - C. It is the doctor’s responsibility to inform the driving authorities when a patient is diagnosed with epilepsy
   - D. Ataxia usually signifies drug toxicity
   - E. Phenytoin causes alopecia

3. Which of the following statements is true in Parkinson’s disease?
   - A. Smoking predisposes to Parkinson’s disease
   - B. Males are more commonly affected
   - C. There is dopamine loss in the pyramidal nuclei
   - D. Incidence is 1:200 over 70 years of age
   - E. It may be caused by alcohol abuse

4. Common features of Parkinson’s disease:
   - A. Intention tremor
   - B. Cogwheel rigidity
   - C. Dementia
   - D. Characteristic findings on CT brain scan
   - E. Extensor plantar reflexes

5. Which of the following is true about Huntington’s disease?
   - A. It is inherited in an X-linked recessive manner
   - B. It is caused by a mutation on chromosome 5
   - C. It is associated with rheumatic fever
   - D. It is characterized by involuntary movements
   - E. It is associated with a higher than average IQ

6. The following are features of multiple sclerosis:
   - A. It may cause afferent pupillary defect
   - B. There is no concordance between monozygotic twins
   - C. The pathology is characterized by neurofibrillary tangles
   - D. Invariably leads to severe disability
   - E. Is associated with recent *Campylobacter* infection

7. The following are features of motor neurone disease:
   - A. Muscle hypertrophy
   - B. Ophthalmoplegia
C. Frontal balding
D. Cerebellar ataxia
E. Bulbar palsy

8. Causes of mononeuritis multiplex include:
   A. Diabetes mellitus
   B. Sarcoidosis
   C. Vitamin B₁₂ deficiency
   D. HIV infection
   E. All of the above

9. A 45-year-old man was seen with pain and numbness in his hands and feet. On examination there was sensory loss to touch in a glove and stocking distribution and wasting of the thigh muscles with reduced power. What is the most likely diagnosis?
   A. Acute intermittent porphyria
   B. Thalidomide therapy
   C. Thyrotoxicosis
   D. Chronic alcohol misuse
   E. Motor neurone disease

10. Which of the following is a characteristic of autonomic neuropathy?
    A. Hypertension
    B. Erectile dysfunction
    C. Polydipsia
    D. Diarrhoea
    E. Infertility

11. The following statements about cerebrospinal fluid (CSF) are correct:
    A. It normally contains 5–10 red cells
    B. In bacterial meningitis the lymphocyte count is raised
    C. In viral meningitis glucose is lower than one-third of blood glucose
    D. In subarachnoid haemorrhage, xanthochromia occurs after 18 hours
    E. In Guillain–Barré syndrome protein is normal with a raised cell count

12. Which of the following statements about CNS infections is true:
    A. Herpes zoster causes a symmetrical rash
    B. Prion diseases are transferred by droplet spread
    C. Acute viral encephalitis is commonly caused by rotavirus
    D. Meningococcal septicaemia causes a vesicular rash
    E. Tuberculous meningitis is associated with high CSF protein

13. The following statements about Creutzfeldt–Jakob disease (CJD) are true:
    A. It is caused by a herpes virus infection
    B. It can be acquired during prosthetic heart valve replacement
    C. New variant CJD is more common in vegetarians
    D. It causes spongiform changes in the brain
    E. It is treatable with antiretroviral drugs

14. The following are aetiologically linked with brain abscess:
    A. Glue ear
    B. Lumbar puncture
    C. Nasal bone fracture
    D. Bacterial meningitis
    E. Diabetes insipidus
15. The following are symptoms and signs of raised intracranial pressure:
   A. Headache
   B. Tachycardia
   C. Papilloedema
   D. Non-dominant hemiplegia
   E. Pronator drift

16. Which is the most important risk factor for cerebrovascular disease:
   A. Diabetes mellitus
   B. Hypertension
   C. Asian race
   D. Family history
   E. Hypothyroidism

17. Aetiological factors in transient ischaemic attacks include:
   A. Atrial fibrillation
   B. Deep venous thrombosis
   C. Aortic sclerosis
   D. Warfarin therapy
   E. Polycystic kidney disease

18. Chronic subdural haematoma:
   A. Is due to arteriovenous malformation in 10% of cases
   B. Is usually precipitated by severe head injury
   C. Is characterized by a classical ‘lucid period’
   D. Most often requires surgical drainage
   E. None of the above

19. A 69-year-old man was referred with a 2 hour history of left arm weakness. A CT scan of the head was normal. What is the most appropriate initial therapy?
   A. Oral streptokinase
   B. Intravenous clopidogrel
   C. Oral aspirin
   D. Oral simvastatin
   E. Subcutaneous fondaparinux

20. An 18-year-old woman was seen in the Emergency Department. She was reported to be drowsy. On examination she was not opening her eyes to verbal command or stimuli. She localized to painful. What is the best estimate of her Glasgow Coma Score?
   A. 3
   B. 5
   C. 7
   D. 12
   E. 15

21. A 26-year-old man was brought in by ambulance after having been found on the street unconscious. What is the most important first step in his management?
   A. Assess his airway, breathing and circulation
   B. BM Stix assessment of blood glucose
   C. Intravenous naloxone
   D. CT scan of the head
   E. Assessment of papillary reflexes
Extended matching questions

**Question 1 Theme: Difficulty walking/limb weakness**
A. Embolic stroke
B. Spinal cord compression
C. Guillain–Barré syndrome
D. Foot drop
E. Phenytoin toxicity
F. Motor neurone disease
G. Multiple sclerosis
H. Parkinson’s disease
I. Huntington’s disease
J. Friedreich’s ataxia
K. Hysteria

For each of the following questions, select the best answer from the list above:
I. A 34-year-old housewife presents with difficulty walking due to weakness in her legs, 2 weeks after recovering from a bout of food poisoning. Examination shows absent tendon reflexes and ½ power in both legs. What is the most likely diagnosis?
II. A 70-year-old right-handed hypertensive smoker presents with sudden onset of weakness in the left leg and difficulty speaking. What is the most likely diagnosis?
III. A 61-year-old solicitor presents with a 1-year history of increasing difficulty walking. His wife has noticed his hands shaking and his secretary finds his handwriting has become too small to read. What is the most likely diagnosis?

**Question 2 Theme: Headache**
A. Migraine
B. Temporal arteritis
C. Primary brain tumour
D. Hypertension
E. Subarachnoid haemorrhage
F. Meningitis
G. Encephalitis
H. Tension headache
I. Trigeminal neuralgia

For each of the following questions select the best answer from the list above:
I. A 24-year-old student presents with recent onset of flu-like symptoms, headache, vomiting, photophobia and neck stiffness. He is pyrexial (38.7°C), with a purpuric rash on the trunk. What is the most likely diagnosis?
II. A 32-year-old female legal secretary has a 6-month history of episodic throbbing right-sided headaches associated with nausea, often on Saturday mornings. What is the most likely diagnosis?
III. A 51-year-old Afro-Caribbean female with chronic kidney disease and diabetes presents with a 3-week history of headache and blurred vision. Fundoscopy reveals retinal haemorrhages and papilloedema. What is the most likely diagnosis?

**Question 3 Theme: Loss of consciousness/coma**
A. Grand mal epilepsy
B. Vasovagal faint
C. Hyperglycaemia
For each of the following questions select the best answer from the list above:

I. A 48-year-old female diabetic is found unconscious in bed. Her husband died recently and she was last seen arguing with her son the previous day. She visited her GP complaining of insomnia a week ago. What is the most likely diagnosis?

II. A 75-year-old female is found unconscious in bed and smells of urine. She is pyrexial (38.5°C) and a urine dipstick shows positive nitrites. What is the most likely diagnosis?

III. An 88-year-old female not seen for several days is found unrousable in her front room on New Year’s Day. On examination her pulse is 58 and regular, her BP is 90/60, there are no focal neurological signs but tendon reflexes are depressed. The ECG shows J waves. What is the most likely diagnosis?
Psychiatry is the study and management of disorders of mental function. Psychological medicine or liaison psychiatry is concerned with psychiatric and psychological disorders in patients who have physical conditions or complaints (Box 18.1).

THE PSYCHIATRIC HISTORY

The psychiatric history is different in some ways from standard history-taking. Corroboration and additional details should be sought from a relative or friend. The history should include the following:

Reason for referral
- Why and how the patient came to the attention of the doctor

Complaints
- As reported by the patient

Present illness
- Detailed account of the illness from its beginning to the present
- Include the degree of insight on the patient’s part

Family history
- Family atmosphere in childhood
- Early stresses (death or separation)
- Mental illness in family members

Personal history
- Short biography of childhood, school, jobs, marriage/divorce and children
- Present housing, social and financial situation

Personality
- Attitudes, beliefs, moral values and standards
- Leisure activities and interests
- Usual reaction to stress and setback

Medical history
- Health in childhood
- Menstrual and sexual history
- Previous mental health and past medical history
- Drug history, including use of alcohol, drugs and tobacco as well as over the counter and prescribed therapies
**Box 18.1. The approximate prevalence of psychiatric disorders in different populations**

<table>
<thead>
<tr>
<th></th>
<th>% (approx.)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Community</td>
<td>20</td>
</tr>
<tr>
<td>Neuroses</td>
<td>16</td>
</tr>
<tr>
<td>Psychoses</td>
<td>0.5</td>
</tr>
<tr>
<td>Alcohol misuse</td>
<td>5</td>
</tr>
<tr>
<td>Drug misuse (total in community 20% due to co-morbidity)</td>
<td>2 (an underestimate)</td>
</tr>
<tr>
<td>Primary care</td>
<td>25</td>
</tr>
<tr>
<td>General hospital outpatients</td>
<td>30</td>
</tr>
<tr>
<td>General hospital inpatients</td>
<td>40</td>
</tr>
</tbody>
</table>

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**Forensic history**
- Legal problems or contact with the police or courts
- Note any violent or sexual offences (risk assessment)

**EXAMINING THE MENTAL STATE**

**Appearance/general behaviour**
- Can give information about mood
- Facial appearance, eye contact, colour of clothes
- Posture
- Movement

**Speech**
- Disorders of thinking are recognized from speech

**Pressure of speech**
- Varied ideas arise in abundance
- Characteristic of mania
- Occurs in schizophrenia

**Poverty of speech**
- Patient reports lack/absence of thoughts
- Characteristic of depression
- Occurs in schizophrenia

**Thought blocking**
- Abrupt and complete interruption of stream
- Strongly suggests schizophrenia

**Disorders of form of thought**

**Flight of ideas**
- Quickly moving from topic to topic
- Distracted by clues in the immediate environment
- Clang associations (using words with similar sounds)
Examining the mental state

- Punning
- Rhyming

**Perseveration**
- Persistent and inappropriate repetition
- Occurs in dementia and other conditions

**Loosening of associations**
- Lack of clarity
- ‘Knight’s move’ thinking
- ‘Word salad’

**Mood**
- Affect/feeling/emotion

**Changes in nature of mood**
- Depression
- Anxiety
- Elation

**Changes in fluctuation of mood**
- Loss of emotion (apathy)
- Reduced variation in mood (blunted)
- Rapidly and excessively changeable mood (labile)

**Inappropriate mood**
- Incongruous mood such as laughing when describing death of close relative

**Thought content (worries and preoccupations)**

**Obsession**
- Recurrent persistent thoughts

**Compulsion**
- Repetitive, seemingly purposeful action
- Must be carried out
- Urge to resist

**Insight**
- Degree to which patient recognizes own illness

**Abnormal beliefs and interpretation of events (delusions)**
- Delusions are abnormal beliefs arising from distorted judgements
- They are:
  - False
  - Held with absolute conviction
  - Not modifiable by reason/experience
- Persecutory delusions – paranoid thoughts
- Delusions of worthlessness/grandeur
- Nihilism
- Thought insertion – the belief that thoughts are implanted from outside
- Thought withdrawal
- Thought broadcasting – the belief that unspoken thoughts are known to others
Abnormal experience referred to the environment, body or self

- Illusions
- Hallucinations
- Depersonalization – the patient feels ‘unreal’/detached/remote
- Derealization – the external environment feels unreal/remote

Cognitive state/memory

- Assessed using cognitive function testing (‘Folstein score’) (see Chapter 3)

ORGANIC MENTAL DISORDERS

Delirium/toxic confusional state

- Impairment of consciousness associated with abnormalities of perception and mood

Aetiology

See Table 18.1.

Clinical features

- Acute – clears within days
- Fluctuant with lucid periods
- Worse at night
- Visual hallucinations may occur
- Patient is frightened, suspicious, restless and uncooperative
- More common in elderly patients

Investigations

- To determine underlying cause
- Bloods
  - Full blood count (FBC)
  - Urea and electrolytes (U&E), glucose, liver function tests (LFTs), calcium
  - Vitamin $B_{12}$
  - Thyroid function tests

<table>
<thead>
<tr>
<th>Table 18.1 Causes of delirium</th>
</tr>
</thead>
<tbody>
<tr>
<td>Infection:</td>
</tr>
<tr>
<td>Any infection, particularly</td>
</tr>
<tr>
<td>if high fever</td>
</tr>
<tr>
<td>Metabolic disturbance:</td>
</tr>
<tr>
<td>Electrolyte upset</td>
</tr>
<tr>
<td>Hepatic/renal failure:</td>
</tr>
<tr>
<td>Hypoxia:</td>
</tr>
<tr>
<td>Endocrine:</td>
</tr>
<tr>
<td>Hypoglycaemia</td>
</tr>
<tr>
<td>Cushing syndrome:</td>
</tr>
<tr>
<td>Intracranial:</td>
</tr>
<tr>
<td>Trauma:</td>
</tr>
<tr>
<td>Tumour:</td>
</tr>
<tr>
<td>Abscess:</td>
</tr>
<tr>
<td>Subarachnoid haemorrhage:</td>
</tr>
<tr>
<td>Epilepsy:</td>
</tr>
</tbody>
</table>
● Blood and urine cultures
● ECG
● Chest X-ray
● CT of brain

Management
● Treat underlying cause
● Nurse carefully in a well-lit area
● Communicate clearly and concisely
● Give repeated information to orientate (family/carers can be useful for this)
● Ensure adequate hydration
● Sedate only if necessary, e.g. haloperidol i.m.
● Paracetamol if febrile
● Review all drugs and stop all but essential ones

Management of the agitated patient
● Agitated patient who is likely to harm him/herself or others

Emergency treatment
● Talk calmly to patient: if this fails, get help to restrain him/her
● Check blood sugar, oximetry, coma scale and for focal neurological deficit
● If not hypoglycaemic or hypoxic and has good coma scale with no focal neurology, then consider sedation with 5 mg i.m. haloperidol (repeat up to 20 mg if needed)
● If alcohol or benzodiazepine withdrawal likely, then use lorazepam 2 mg

Initial investigations
● Bloods – FBC, U&E, glucose, calcium, LFTs
● Blood and urine cultures if sepsis suggested
● Measure arterial blood gases
● ECG
● Chest X-ray

Dementia
● Progressive decline of cognitive function in the absence of clouded consciousness

Aetiology
See Table 18.2.

Differential diagnosis
● Depression

Investigations
● Blood
  ● FBC
  ● U&E, glucose, LFTs, calcium
  ● ESR, C-reactive protein
  ● Red cell folate, vitamin B₁₂
  ● Thyroid function tests
  ● Syphilis serology
  ● HIV antibodies if indicated and patient counselled
● Chest X-ray
● CT/MRI
Psychological medicine

### Table 18.2 Causes of dementia

<table>
<thead>
<tr>
<th>Degenerative</th>
<th>Intracranial</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alzheimer’s disease (65%)</td>
<td>Subdural haematoma</td>
</tr>
<tr>
<td>Dementia with Lewy bodies (25%)</td>
<td>Tumour</td>
</tr>
<tr>
<td>Frontotemporal dementia</td>
<td>Toxic</td>
</tr>
<tr>
<td>Huntington’s disease</td>
<td>Alcohol</td>
</tr>
<tr>
<td>Parkinson’s disease</td>
<td>Occupational</td>
</tr>
<tr>
<td>Normal pressure hydrocephalus</td>
<td>Lead or mercury poisoning</td>
</tr>
<tr>
<td>Primary progressive aphasia</td>
<td>Traumatic</td>
</tr>
<tr>
<td>Vascular</td>
<td>Box (punch drunk syndrome)</td>
</tr>
<tr>
<td>Cerebrovascular disease</td>
<td>Vitamin deficiency</td>
</tr>
<tr>
<td>Cerebral vasculitis/cranial arteritis</td>
<td>Thiamine</td>
</tr>
<tr>
<td>Metabolic</td>
<td>Vitamin B₁₂</td>
</tr>
<tr>
<td>Uraemia</td>
<td>Creutzfeldt–Jakob disease</td>
</tr>
<tr>
<td>Hepatic failure</td>
<td>HIV</td>
</tr>
<tr>
<td>Paraneoplastic syndromes</td>
<td>Syphilis</td>
</tr>
<tr>
<td>Endocrine</td>
<td>Whipple’s disease</td>
</tr>
<tr>
<td>Hypothyroidism</td>
<td>Psychiatrical</td>
</tr>
<tr>
<td>Hypocalcaemia</td>
<td>Pseudodementia</td>
</tr>
</tbody>
</table>

#### Alzheimer’s disease

**Neuropathology**
- Neuronal loss
- Neurofibrillary tangles
- Senile plaques
- Amyloid deposition

**Aetiology**
- Early onset – may be familial linkage to chromosomes 1, 14 and 21
- Late onset – apolipoprotein E gene

**Clinical features**
- Inability to learn new information or recall previously learnt information
- Decline in language, particularly names
- Apraxia – unable to carry out motor functions
- Agnosia – unable to identify/recognize objects
- Impairment of organizing/sequencing
- Behavioural change – wandering, agitation, aggression
- Paranoia and loss of insight

**Management**
- Cholinesterase inhibitors and drugs blocking glutamate transmission slow the rate of decline slightly but their use is clouded by complex cost–benefit arguments

#### Dementia with Lewy bodies

**Clinical features**
- Second commonest cause of dementia
- Fluctuating cognition with pronounced variation in attention/alertness
Schizophrenia

- Memory loss uncommon in early stages
- Sleep disorders, visual hallucinations, delusions and transient loss of consciousness

**Management**

- Avoid neuroleptic drugs

**Vascular dementia/multi-infarct dementia**

**Clinical features**

- History of transient ischaemic attacks or stroke
- Features depend on the site of ischaemic damage

**Management**

- Stroke prevention measures including antiplatelet drugs

---

**SCHIZOPHRENIA**

- Abnormal integration of emotional and cognitive functions

**Epidemiology**

- 2–4/1000 annual incidence
- 1% lifetime risk

**Aetiology**

- Genetic – lifetime risk in patients with a parent affected is 12%
- Altered neurotransmitters
  - ↑ Dopamine activity
  - Altered serotonin metabolism
- Environmental triggers
  - Cannabis use is a possible risk factor

**Clinical features**

- Peak onset early 20s
- ♀ = ♂

**Diagnosis**

- Based on presence of first-rank symptoms:
  - Auditory hallucinations
  - Thought withdrawal
  - Thought insertion
  - Thought broadcasting
  - Delusions
  - External controlled emotions
  - Somatic passivity and feelings (feeling that thoughts and acts are due to the influence of others)

**Subtypes**

**Positive schizophrenia**

- Acute onset
- Prominent delusions and hallucinations
- Good response to neuroleptics
- Better prognosis

**Negative schizophrenia**

- Insidious deterioration in personality
- Relative absence of acute symptoms
- Delusions and hallucinations absent
- Increasing apathy and eccentricity
Psychological medicine

- Slow withdrawal from society
- Poor response to neuroleptics

Management
- Combination of drug and social treatment delivered by multidisciplinary team

Drugs
- Antipsychotics/neuroleptics
  - Dopamine antagonists (chlorpromazine, haloperidol); unwanted side-effects are shown in Table 18.3
  - Atypical anti-psychotics (clozapine, risperidone, olanzapine) have less extrapyramidal side-effects

Psychological treatment
- Reassurance and support

Social treatment
- Structured work and social programme

MOOD (AFFECTIVE) DISORDERS

- Spectrum of disorders ranging from depression through to mania
- Patients who suffer attacks of both have bipolar disorder (Fig. 18.1)

Aetiology

Physical
- Genetic – monozygotic twin concordance 30–60%, higher in bipolar disorders

<table>
<thead>
<tr>
<th>Table 18.3 Unwanted effects of neuroleptic drugs</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Common effects</strong></td>
</tr>
<tr>
<td>Motor</td>
</tr>
<tr>
<td>Acute dystonia</td>
</tr>
<tr>
<td>Parkinsonism</td>
</tr>
<tr>
<td>Akathisia (restless, repetitive and irresistible need to move)</td>
</tr>
<tr>
<td>Tardive dyskinesia</td>
</tr>
<tr>
<td>(mouthing and smacking of the lips, grimaces and contortions of the face/neck)</td>
</tr>
<tr>
<td>Autonomic</td>
</tr>
<tr>
<td>Hypotension</td>
</tr>
<tr>
<td>Failure of ejaculation</td>
</tr>
<tr>
<td>Anticholinergic</td>
</tr>
<tr>
<td>Dry mouth</td>
</tr>
<tr>
<td>Urinary retention</td>
</tr>
<tr>
<td>Constipation</td>
</tr>
<tr>
<td>Blurred vision</td>
</tr>
<tr>
<td>Metabolic</td>
</tr>
<tr>
<td>Weight gain</td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td></td>
</tr>
</tbody>
</table>
Mood (affective) disorders

**Neurotransmitter imbalance** – downregulation of 5 HT receptors in depression

**Hormonal**
- Cortisol (Cushing syndrome) induces depression and corticosteroids alter mood, moreover hypercortisolaemia occurs in patients with depression
- Oral contraceptives/pregnancy/premenstrual

**CNS abnormalities** – brain MRI/PET studies show:
- Increased ventricular volume, frontal lobe atrophy and altered blood flow
- Volume reduction in the hippocampus

**Psychological**
- Maternal deprivation
- Learned helplessness

**Social**
- Stressful life events, e.g. divorce, unemployment
- Sexual abuse in childhood

**Clinical features**
- See Table 18.4
- Range of severity (Fig. 18.2)
  - Severe life-threatening disease
  - Minor forms

**Differential diagnosis**

**Mania**
- Drug-induced psychosis
  - Amphetamines/ecstasy/cocaine
  - Long-term cannabis use
  - Steroids
- Acute schizophrenia
- Hyperthyroidism/Cushing syndrome

**Depression**
- Malignancy
- Hypothyroidism/hyperparathyroidism
- Cushing syndrome
- Neurological diseases (multiple sclerosis, Parkinson’s)
- Cerebral ischaemia or tumour
- Heart failure
- Porphyria
Table 18.4 Clinical features of depression and mania

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Depression</th>
<th>Mania</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mood</td>
<td>Depressed</td>
<td>Elevated</td>
</tr>
<tr>
<td></td>
<td>Miserable</td>
<td>Labile</td>
</tr>
<tr>
<td></td>
<td>Unhappy</td>
<td>Irritable</td>
</tr>
<tr>
<td>Talk</td>
<td>Slow</td>
<td>Fast</td>
</tr>
<tr>
<td></td>
<td>Impoverished</td>
<td>Pressurized</td>
</tr>
<tr>
<td></td>
<td>Monotonous</td>
<td>Flight of ideas</td>
</tr>
<tr>
<td>Energy</td>
<td>Reduced apathetic/lethargic</td>
<td>Excessive</td>
</tr>
<tr>
<td>Ideation</td>
<td>Feelings of:</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Futility</td>
<td>Self-confident</td>
</tr>
<tr>
<td></td>
<td>Guilt</td>
<td>Delusions of:</td>
</tr>
<tr>
<td></td>
<td>Self-reproach</td>
<td>Wealth</td>
</tr>
<tr>
<td></td>
<td>Unworthiness</td>
<td>Power</td>
</tr>
<tr>
<td></td>
<td>Hypochondriasis</td>
<td>Influence</td>
</tr>
<tr>
<td></td>
<td>Worrying</td>
<td>Religious significance</td>
</tr>
<tr>
<td></td>
<td>Suicidal thoughts</td>
<td>Persecutory delusions</td>
</tr>
<tr>
<td></td>
<td>Delusions of guilt</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Nihilism</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Persecution</td>
<td></td>
</tr>
<tr>
<td>Cognition</td>
<td>Impaired learning</td>
<td>Disturbance of registration of memories</td>
</tr>
<tr>
<td></td>
<td>Pseudodementia if elderly</td>
<td></td>
</tr>
<tr>
<td>Physical</td>
<td>Early waking</td>
<td>Insomnia</td>
</tr>
<tr>
<td></td>
<td>Poor appetite</td>
<td>Weight loss</td>
</tr>
<tr>
<td></td>
<td>Weight loss</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Constipation</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Loss of libido</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Erectile dysfunction</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Fatigue</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Bodily aches and pains</td>
<td></td>
</tr>
<tr>
<td>Behaviour</td>
<td>Poverty of movement/</td>
<td>Disinhibition</td>
</tr>
<tr>
<td></td>
<td>expression</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Retardation/agitation</td>
<td>Increased sexual interest</td>
</tr>
<tr>
<td>Hallucinations</td>
<td>Auditory</td>
<td>Excessive drinking/</td>
</tr>
<tr>
<td></td>
<td></td>
<td>spending</td>
</tr>
<tr>
<td></td>
<td>Hostile</td>
<td>Fleeting auditory</td>
</tr>
<tr>
<td></td>
<td>Critical</td>
<td>Occasionally visual</td>
</tr>
</tbody>
</table>
Mood (affective) disorders

- Mania
- Hypomania
- Mild euphoria
- Cheery
- Hopeful
- Happy
- Gloomy
- Despondent
- Sad

**Fig. 18.2** Continuum of normal and abnormal mood.

---

**Table 18.5** Clinical features of normal grief reaction and depressive illness after bereavement (morbid grief reaction)

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Normal bereavement</th>
<th>Morbid grief reaction</th>
</tr>
</thead>
<tbody>
<tr>
<td>Onset</td>
<td>Immediately after loss</td>
<td>Delayed for weeks/months</td>
</tr>
<tr>
<td>Duration</td>
<td>Weeks</td>
<td>Months/years</td>
</tr>
<tr>
<td>Pattern</td>
<td>Slow acceptance and adjustment</td>
<td>Denial of loss and refusal to accept implications</td>
</tr>
<tr>
<td>Grief</td>
<td>Expressed openly</td>
<td>Expressed with difficulty</td>
</tr>
<tr>
<td>Guilt</td>
<td>Mild regret in early stage</td>
<td>Marked guilt often present</td>
</tr>
</tbody>
</table>

- Drugs
  - Steroids
- Psychiatric disorders
  - Schizophrenia
  - Alcohol/drug (e.g. amphetamines) misuse or withdrawal
  - Borderline personality disorder
  - Dementia
- Normal bereavement reaction ([Table 18.5](#))

**Management**

**Physical**

- Stop depressing drugs including alcohol
- Regular exercise (good for mild/moderate depression)
Depression (Fig. 18.3)

- Drugs – choice depends on side-effects and safety
  - Serotonin reuptake inhibitors, e.g. fluoxetine
  - Tricyclic antidepressants (TCAs), e.g. amitriptyline; see Table 18.6 for unwanted effects
  - New generation antidepressants, e.g. venlafaxine – serotonin and noradrenaline receptor blocker, mirtazapine increases both noradrenaline and selective serotonin transmission noradrenaline reuptake inhibitors, e.g. reboxetine
  - Monoamine oxidase inhibitors, e.g. phenelzine – used 2nd line
- Electroconvulsive therapy (ECT)
  - Used in life-threatening depression

Fig. 18.3 Sites of action of antidepressants with examples. (From Waller DG, Renwick A, Hiller K, (eds). Medical Pharmacology and Therapeutics. Edinburgh: Saunders; 2010, with permission)
Table 18.6 Unwanted effects of drugs used in affective disorders

<table>
<thead>
<tr>
<th>Tricyclic antidepressants</th>
<th>Lithium</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anticholinergic effects</td>
<td>GI symptoms</td>
</tr>
<tr>
<td>Dry mouth</td>
<td>Hypothyroidism</td>
</tr>
<tr>
<td>Constipation</td>
<td>Fine tremor</td>
</tr>
<tr>
<td>Tremor</td>
<td>Weight gain (increased appetite)</td>
</tr>
<tr>
<td>Blurred vision</td>
<td>Polyuria/polydipsia</td>
</tr>
<tr>
<td>Urinary retention</td>
<td>Toxic symptoms</td>
</tr>
<tr>
<td>Postural hypotension</td>
<td>Drowsiness</td>
</tr>
<tr>
<td>Cardiac effects</td>
<td>Blurred vision</td>
</tr>
<tr>
<td>ECG changes</td>
<td>Tremor</td>
</tr>
<tr>
<td>Arrhythmias</td>
<td>Ataxia</td>
</tr>
<tr>
<td>Lowered seizure threshold</td>
<td>Dysarthria</td>
</tr>
<tr>
<td>Weight gain</td>
<td>Convulsions</td>
</tr>
<tr>
<td>Sedation</td>
<td>Coma and death</td>
</tr>
<tr>
<td>Mania</td>
<td></td>
</tr>
</tbody>
</table>

Mania

Acute attacks
- Atypical antipsychotics
- Lithium – Table 18.6 lists unwanted effects
- Neuroleptic drugs for severe hyperactivity, e.g. haloperidol

Prophylaxis
- Lithium
  - Regular check on drug levels (narrow therapeutic window)
  - Regular check on renal function (renal excretion)
  - Regular check on thyroid function
- Carbamazepine
- Valproate

Psychological
- Psychotherapy
- Cognitive/behavioural therapy

Social
- Assistance with social problems
- Group support
- Stress management
- Family/carer support

PUERPERAL AFFECTIVE DISORDERS
- Childbirth has a higher relative risk of depression than life events or physical illness
- Treatment of these disorders is as for any other affective disorder

Maternity blues

Clinical features
- Brief episodes of emotional lability, irritability and tearfulness
- Occurs in 50% of women 2-3 days postpartum
- Resolves spontaneously
Postpartum psychosis

Clinical features
- 1 in 500–1000 births
- Onset usually within 2 weeks of birth
- Classical features of affective psychosis plus confusion and disorientation
- If severe, patient may have delusions that the child is deformed, evil or affected in another way which can lead to suicide or infanticide
- Responds well to treatment
- 20–30% recur in next puerperium

Postnatal depression

Clinical features
- Depression occurs in 10% of mothers in first postpartum year
- Clinically similar to other depressive illness
- Recovery after a few months

SUICIDE AND DELIBERATE SELF-HARM

Suicide

Risk factors
- Living alone
- Immigrant status
- Recent bereavement/separation/divorce
- Unemployment/retirement
- Male sex
- Older age
- Family or previous history of
  - Affective disorder
  - Suicide
  - Alcohol abuse

Table 18.7 For deliberate self-harm patients – indications for referral to psychiatrist

<table>
<thead>
<tr>
<th>Absolute indications</th>
<th>Relative indications</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clinical depression</td>
<td>Alcohol/drug abuse</td>
</tr>
<tr>
<td>Psychosis</td>
<td>Patients with risk factors for suicide (see above)</td>
</tr>
<tr>
<td>Clearly pre-planned suicide attempts</td>
<td>Patients with family history of suicide</td>
</tr>
<tr>
<td>Persistent suicidal intent</td>
<td>Patients with serious (particularly incurable) physical illnesses</td>
</tr>
<tr>
<td>Violent method used</td>
<td>Those in whom there is a major unresolved crisis</td>
</tr>
<tr>
<td></td>
<td>Persistent suicide attempts</td>
</tr>
<tr>
<td></td>
<td>Any patient giving concern</td>
</tr>
</tbody>
</table>
**Neuroses and stress-related/somatoform disorders**

- Previous suicide attempt
- Drug/alcohol addiction
- Severe depression/early dementia
- Incapacitating, painful physical illness

**Deliberate self-harm (DSH)**

- ♀ > ♂
- Most patients <35 years
- 90% involve self-poisoning
- Formal psychiatric disorder is unusual
- 1–2% kill themselves in the following year
- Assessment procedure (see Ch. 3)
- Indications for referral to psychiatric team (Table 18.7)

**NEUROSES AND STRESS-RELATED/SOMATOFORM DISORDERS**

**Anxiety disorder**

**Clinical features**
See Table 18.8.

**Differential diagnosis**

**Psychiatric disorders**

- Depression
- Obsessive compulsive disorder
- Schizophrenia
- Dementia
- Drug/alcohol dependence
- Benzodiazepine withdrawal

---

**Table 18.8 Clinical features of anxiety**

<table>
<thead>
<tr>
<th>Physical</th>
<th>Nervous system</th>
<th>Psychological</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gastrointestinal</td>
<td>Fatigue</td>
<td>Apprehension and fear</td>
</tr>
<tr>
<td>Dry mouth</td>
<td>Blurred vision</td>
<td>Irritability</td>
</tr>
<tr>
<td>Dysphagia</td>
<td>Dizziness</td>
<td>Difficulty concentrating</td>
</tr>
<tr>
<td>Epigastric pain</td>
<td>Headache</td>
<td>Distractibility</td>
</tr>
<tr>
<td>Flatulence/aerophagy</td>
<td>Sleep disturbance</td>
<td>Restlessness</td>
</tr>
<tr>
<td>Diarrhoea</td>
<td>Tremor</td>
<td>Sensitivity to noise</td>
</tr>
<tr>
<td>Respiratory</td>
<td></td>
<td>Depression</td>
</tr>
<tr>
<td>Sensation of chest</td>
<td></td>
<td>Depersonalization</td>
</tr>
<tr>
<td>constriction</td>
<td></td>
<td>Derealization</td>
</tr>
<tr>
<td>Difficulty inhaling</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Over-breathing</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cardiovascular</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Palpitations, awareness of</td>
<td></td>
<td></td>
</tr>
<tr>
<td>missed beat</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Chest pain</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Genitourinary</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Frequency</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Failure of erection</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lack of libido</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

---
Physical disorders
- Hyperthyroidism
- Hypoglycaemia
- Phaeochromocytoma

Management
Psychological
- Reassurance about physical symptoms
- Relaxation techniques
- Anxiety management training
- Biofeedback
- Behaviour therapies
- Cognitive behavioural therapy

Drugs
- Selective serotonin reuptake inhibitors (SSRIs)
- β-blockers for physical symptoms
- Short courses of benzodiazepines

Obsessive compulsive disorder
- Characterized by obsessional thinking and compulsive behaviour with varying degrees of anxiety/depression and depersonalization

Clinical features
- Persistent and intrusive obsessions/compulsions
- Functioning impeded
- Constant need to check
- Repetitive/superstitious actions

Management
- Behaviour therapy
  - Response prevention
  - Modelling
- Serotonin reuptake inhibitors (may need higher doses than those used in depression)

Dissociative (conversion) disorder (previously known as hysteria)
- Characterized by
  - Absence of physical pathology
  - Unconscious production
  - Triggered by an unresolved conflict or life event
  - Absence of sympathetic overactivity

Clinical features
- ♀ > ♂
- Rarely occurs in those >40 years
- See Table 18.9
- May confer advantage (secondary gain)
- Patients’ emotional distress is less than expected

Management
- Psychotherapy

Somatoform disorders
- Patients
  - Repeatedly present with physical problems
• Have repeatedly negative findings on clinical investigation
• Have no demonstrable physical cause

**Clinical features**

**Hypochondriasis**
- Preoccupation with ill health
- Disproportionate and unjustified concern

**Somatization disorder**
- Repeatedly present with a variety of medical symptoms
- Undergo repeated investigations/operations
- May have medical connections

**Management**
- Explain and reassure
- Explore psychological/social problems
- Avoid repeated investigations
- Graded exercise programmes
- Trial of an antidepressant

**Acute stress reaction and post-traumatic stress disorder**
- Occur in individuals in response to exceptional physical or psychological stress

**Acute stress reaction**
- Lasts a few hours/days
- Initial state of ‘daze’
- Then a phase of either
  - Withdrawal/stupor or
  - Agitation/over-activity
- Commonly associated with autonomic signs of anxiety

**Post-traumatic stress disorder**
- Delayed/protracted response to a stressful event
- ‘Flashbacks’
- Intense distress in/avoidance of situations resembling the event (including anniversaries)
- Emotional blunting/numbness
- Detachment from others
- Hypervigilance
- Insomnia

---

**Table 18.9 Common dissociative/conversion symptoms**

<table>
<thead>
<tr>
<th>Dissociative (mental)</th>
<th>Conversion (physical)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Amnesia</td>
<td>Paralysis</td>
</tr>
<tr>
<td>Fugue</td>
<td>Gait disorder</td>
</tr>
<tr>
<td>Pseudodementia</td>
<td>Tremor</td>
</tr>
<tr>
<td>Dissociative identity disorder</td>
<td>Aphonia</td>
</tr>
<tr>
<td>Psychosis</td>
<td>Mutism</td>
</tr>
<tr>
<td></td>
<td>Sensory symptoms</td>
</tr>
<tr>
<td></td>
<td>Globus hystericus</td>
</tr>
<tr>
<td></td>
<td>Hysterical fits</td>
</tr>
<tr>
<td></td>
<td>Blindness</td>
</tr>
</tbody>
</table>
Anxiety and depression
Occasionally suicide

Management
Counselling

**DRUG AND ALCOHOL MISUSE AND DEPENDENCE**

Current figures in the UK show 10% of women and 20% of men drink in excess of the recommended safety limits for long-term health risk

**Alcohol dependence syndrome**

**Clinical features**
- Compulsive need to drink
- Altered alcohol tolerance
- Stereotyped pattern of drinking
- Drinking takes primacy over other activities
- Repeated withdrawal symptoms
- Relief drinking to avoid withdrawal, e.g. early morning drinking
- Rapid relapse if patient drinks again following a period of abstinence

**Management**

Psychosocial support and group therapy
- Example: Alcoholics Anonymous

Drugs (effects are enhanced by combining them with counselling)
- Naltrexone reduces the risk of relapse into heavy drinking and the frequency of drinking
- Acamprosate alters neurotransmitters and reduces drinking frequency
- Disulfiram reacts with alcohol to form acetaldehyde which produces unpleasant symptoms to discourage drinking

**Drug misuse**

For commonly used illicit drugs the desired and adverse effects are shown in Table 18.10

**Management**
- Withdrawal programmes, e.g. using methadone
- Psychosocial support to help the addict live without drugs

**EATING DISORDERS**

**Anorexia nervosa**

**Aetiology**
- Genetic
- Childhood sexual abuse
- Dietary problems in early life
- Social factors
  - Higher social class
  - Occupation - ballet dancers/nurses

**Clinical features**
- BMI (body mass index) <17.5
- Intense wish to be thin
- Morbid fear of fatness
- Amenorrhoea in women
- ♀ >> ♂
<table>
<thead>
<tr>
<th>Drug</th>
<th>Desired effects</th>
<th>Adverse effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>Solvents (‘glue sniffing’)</td>
<td>Euphoria Floating sensation</td>
<td>Amnesia Visual hallucinations Inhalation of vomit Bone marrow/brain/liver/ kidney toxicity Tolerance</td>
</tr>
<tr>
<td>Amphetamines</td>
<td>Stimulant Euphoria</td>
<td>Psychological dependence Restlessness Over-activity Paranoid psychosis</td>
</tr>
<tr>
<td>Cocaine</td>
<td>Stimulant Hyperarousal</td>
<td>Dependence Paranoid ideation Fits Coronary artery spasm/ disease Perforation of nasal septum if inhaled</td>
</tr>
<tr>
<td>Cannabis</td>
<td>Exaggeration of pre-existing mood</td>
<td>No definite withdrawal syndrome or tolerance Psychosis</td>
</tr>
<tr>
<td>MDMA (‘Ecstasy’)</td>
<td>Psychedelic effects</td>
<td>Hyperpyrexia Acute hepatic/renal failure Possible chronic brain damage</td>
</tr>
<tr>
<td>Hypnotics (e.g. benzodiazepines)</td>
<td>Relaxation Sleep induction</td>
<td>Dependence Withdrawal syndrome Respiratory depression</td>
</tr>
<tr>
<td>Narcotics (morphine, heroin, codeine, methadone, pethidine)</td>
<td>Calm Slight euphoria Analgesia Flattening of emotions</td>
<td>Marked and rapid tolerance Withdrawal syndrome Respiratory depression Complications of injecting: Infection (e.g. HIV/ hepatitis B and C/ endocarditis) Vein thrombosis</td>
</tr>
</tbody>
</table>

- Onset in adolescence, rare >30 years
- Previous history of chubbiness/fatness
- Relentless pursuit of low body weight
- Distorted image of own body
- Eats little
- Avoids carbohydrates
- Vomiting/excess exercise/purging
- Loss of sexual interest
- Lanugo hair
Management
- Behaviour therapy – goal setting/reward for weight/dietary intake
- Psychotherapy
- Family therapy

Bulimia nervosa

Clinical features
- Binge eating
- Self-induced vomiting
- Laxative abuse
- Misuse of drugs, e.g. diuretics, thyroxine, anorectics
- $♀ >> ♂$
- Often associated with anorexia nervosa
- Premorbid personality – neurotic traits
- May be associated with
  - Depression
  - Alcohol dependence
- Fluctuation in body weight
- Periods irregular

Consequences of vomiting
- Cardiac arrhythmias
- Renal impairment secondary to low $K^+$
- Muscular paralysis
- Tetany – hypokalaemic alkalosis
- Swollen salivary glands
- Eroded dental enamel

Management
- Cognitive behaviour therapy
- SSRIs

Box 18.2. The basis of mental health laws for detention or commitment

1. The individual to be detained must be suffering from a defined mental illness.
2. Detention is for the purposes of observation and refinement of the diagnosis and/or to actively treat the disorder (i.e. detention is a means to an end).
3. Attempts to treat the individual on an outpatient basis have failed.
4. The offer of a voluntary admission to hospital has been refused or is impractical.
5. Treatment in hospital is necessary:
   - because it will benefit the outcome of the illness
   - to protect the patient from harm (in terms of physical health, mental health and abuse or manipulation at the hands of others)
   - to protect others from harm that the patient might cause them passively (neglect) or actively.
PSYCHIATRY AND THE LAW

Compulsory section under the Mental Health Act

Conditions
- For a patient to be held against his/her will under the Mental Health Act, he/she must be:
  - Suffering from a defined mental disorder
  - A risk to his/her and/or other people's health or safety
  - Unwilling to accept hospitalization voluntarily

Sections
See Box 18.2 for details.

SELF-ASSESSMENT QUESTIONS

Multiple choice questions (single best answer)

1. Of these first-rank symptoms of schizophrenia which also occurs in mania?
   A. Thought broadcasting
   B. Thought withdrawal
   C. Thought insertion
   D. Auditory hallucinations
   E. Persecutory delusions

2. In dementia the following is correct:
   A. Consciousness is clouded
   B. Multi-infarct dementia is the commonest cause
   C. Depression is a differential diagnosis
   D. Dementia with Lewy bodies accounts for 40%
   E. A CT scan is not indicated

3. The following management strategy in toxic confusional state may exacerbate the problem:
   A. Establish a corroborative history from a witness
   B. Nurse the patient in a darkened room
   C. Prescription of appropriate intravenous fluids if not drinking
   D. Minimize polypharmacy
   E. Prescription of antibiotics

4. In depression:
   A. Patients sleep well
   B. Patients usually have increased sexual interest
   C. Patients may have auditory hallucinations if disease is severe
   D. Monozygotic twin concordance is only 10% for unipolar depression
   E. Most patients are treated with psychotherapy alone

5. The following feature of mania may also be seen in thyrotoxicosis:
   A. Delusions of wealth
   B. Weight loss
   C. Excessive drinking
   D. Flight of ideas
   E. Critical hallucinations

6. Lithium:
   A. Is used to prevent depression
   B. 50% undergoes renal excretion
   C. Causes hyperthyroidism
D. Needs therapeutic drug level monitoring
E. Is used to treat acute attacks of depression

7. The following are factors that increase the risk of suicide:
   A. Female sex
   B. Young age
   C. No previous history of depression
   D. Living with a large extended family
   E. A family history of suicide

8. In deliberate self-harm:
   A. 75% is by self-poisoning
   B. There is often an associated psychiatric disorder
   C. Patients with depression should be referred to a psychiatrist
   D. A violent method makes suicide less likely
   E. Patients who planned to be discovered are at higher risk of suicide

9. The following are physical symptoms of anxiety disorder except:
   A. Chest pain
   B. Diarrhoea
   C. Erectile dysfunction
   D. Urinary frequency
   E. Jaundice

10. Anorexia nervosa:
    A. Patients often have a BMI of over 30
    B. Patients have usually been thin since childhood
    C. Is more common in higher social classes
    D. Amenorrhoea occurs late in the disease
    E. Patients think they are thin

11. Regarding the Sections of the Mental Health Act:
    A. Section 2 allows patients to be held for 6 months
    B. Section 3 is for psychiatric assessment only
    C. Section 5(2) relates to patients already in hospital
    D. Section 5(2) allows the patient to be detained for 6 hours
    E. Section 2 requires the signatures of one doctor and a social worker/relative

12. The following statements are correct:
    A. Obsessive compulsive disorder responds to low-dose serotonin reuptake inhibitors
    B. Paralysis is a common symptom of a conversion disorder
    C. Conversion disorder is produced consciously
    D. Post-traumatic stress disorder occurs immediately after a stressful event
    E. In acute stress reaction bradycardia is usual

13. The following are effects of illicit drugs:
    A. Cocaine causes hyperarousal
    B. Amphetamines induce sleep
    C. Cannabis use is associated with a withdrawal syndrome
    D. The development of tolerance to heroin is slow
    E. MDMA has no long-term side-effects

14. The following statements are correct about alcohol withdrawal:
    A. Delirium tremens occurs within hours of alcohol cessation
    B. Seizures can be treated as an outpatient
    C. Acamprosate will help tremor
D. Prevention with Disulfiram is usually effective
E. Drugs to prevent alcohol dependence are enhanced by combining them with counselling

15. Antidepressant drugs:
A. Are safe in overdose
B. SSRIs are used in all patients
C. Choice of drug depends on the side-effect profile
D. Tricyclic antidepressants are effective within a few days of starting treatment
E. Venlafaxine has no effect on serotonin

Extended matching questions

**Question 1 Theme: Agitation**
A. Acute confusional state
B. Acute mania
C. Puerperal psychosis
D. Schizophrenia
E. Obsessive compulsive disorder
F. Alzheimer’s disease
G. Anxiety disorder
H. Alcohol withdrawal syndrome
I. Cocaine abuse
J. Somatization disorder

*For each of the following questions, select the best answer from the list above:*

I. A 59-year-old female smoker who lives with her husband presents with agitation. On direct questioning she can remember details of the distant past but her short-term memory is poor. She has lost weight but there are no other physical signs or symptoms. What is the most likely diagnosis?

II. A 23-year-old female who was born in Jamaica but has lived in the UK since the age of 8 attends the A&E department alone; she is agitated. She appears to have threatening auditory hallucinations. She also says that she is having difficulty sleeping. The casualty records show a previous attendance at a psychiatric outpatient clinic 2 years ago. The limited physical examination she allows is normal. What is the most likely diagnosis?

III. A 48-year-old male presents with agitation. On direct questioning he admits to visual hallucinations. He has a previous history of gastrointestinal bleeding. On examination he is sweaty and the pulse rate is 110/min. Blood tests reveal the following: Hb 14.4, MCV 101. What is the most likely diagnosis?

**Question 2 Theme: Hallucinations**
A. Acute confusional state
B. Acute mania
C. Puerperal psychosis
D. Schizophrenia
E. Obsessive compulsive disorder
F. Alzheimer’s disease
G. Anxiety disorder
H. Alcohol withdrawal syndrome
I. Amphetamine abuse
J. Somatization disorder
For each of the following questions, select the best answer from the list above:

I. A 26-year-old man who lives with his mother presents with auditory hallucinations. He has recently been made redundant after he was said to be acting strangely at work. There are no physical signs or symptoms. He reports that he thinks people can hear his thoughts. On direct questioning his hallucinations are persecutory in nature. What is the most likely diagnosis?

II. A 33-year-old male attends the A&E department alone and agitated. He appears to have paranoid auditory hallucinations. He also says that he is having difficulty sleeping. The A&E records show a previous attendance 2 years ago with an overdose of benzodiazepines. He denies problems with alcohol use now or in the past. The physical examination shows a tachycardia and raised blood pressure. What is the most likely diagnosis?

III. A 45-year-old male presents with agitation and complaining that he cannot sleep. He has recently been dismissed from his job. His wife is very upset and is accusing him of spending huge amounts of money and of having an affair. On direct questioning he admits to fleeting auditory hallucinations. He has lost weight and reports increased libido. What is the most likely diagnosis?

Question 3 Theme: Psychiatric treatments

A. A tricyclic antidepressant
B. A selective serotonin reuptake inhibitor
C. ECT
D. Lithium
E. A monoamine oxidase inhibitor
F. Venlafaxine
G. Cognitive behavioural therapy
H. Carbamazepine
I. Chlorpromazine
J. Clozapine

For each of the following questions, select the best answer from the list above:

I. A 59-year-old female who lives with her husband presents with symptoms of depression. Her husband has just been diagnosed with lung cancer. She is overweight but there are no other physical signs or symptoms. What would be the most appropriate choice of treatment?

II. A 22-year-old female presents with an episode of hyperventilation. She describes panic attacks when trying to leave the house. The limited physical examination she allows is normal. You diagnose an anxiety disorder. She is not keen to take any drug treatment. What would be the most appropriate choice of treatment?

III. A 48-year-old man is known to have bipolar disorder. He had been on lithium but was recently found to be hypothyroid so the lithium had been stopped. He requires another drug for his returning symptoms of mania. What would be the most appropriate choice of treatment?
The epidemiology of a disease is a description of the demographics of the affected population and the environment from which they originate. Statistical analysis is the manipulation of data about a population sample designed to reveal similarities or differences between groups of differing patients or between treatment types. Statistical analysis is also used to describe details about a population.

**TYPES OF DATA**

**Nominal**
- Mutually exclusive groups
  - Male (♂) or female (♀)

**Ordinal**
- Ranked exclusive groups
  - Mild/moderate/severe

**Continuous**
- Numerical values that may be anywhere along a continuum
  - Age

**Descriptional statistics**
- A method of describing a population or a sample from that population

**Mean**
- The mathematical average of a set of numerical data

**Mode**
- The most commonly occurring value

**Median**
- The middle number when the dataset is arranged in numerical order
- If there is an even number of values it is the mean of the middle two

**Sample mean**
- The mathematical average of a variable measured in a sample

**Population mean**
- The mean calculated if the entire population under study were measured
  - Note: this is rarely achievable
Fig. 19.1 Gaussian or normal distribution. This is symmetrical about the mean. A total of 68% of all values in the dataset fall within ±1 standard deviation (SD), 95% between ±2 SD and 99% between ±3 SD. This is often described as the bell-shaped curve.

**Distribution**
- The pattern of spread of values
- Many biological values fit a ‘normal’ or Gaussian distribution, a bell-shaped curve

**Normal distribution**
- A symmetrical ‘bell-shaped’ curve distribution where the mean, mode and median are the same (Fig. 19.1)

**Skewed distribution**
- Very high or low values may result in an asymmetrical distribution leading to a positive (high value) or negative (low value) skew (Fig. 19.2)

**Variance**
- Describes the spread of values either side of a mean

**Standard deviation**
- Gives the range of values within which a certain proportion of the sample will lie
  - 68% will lie ±1 SD from the mean
  - 95% will lie ±2 SD from the mean
  - 99% will lie ±3 SD from the mean
Types of data

**Standard error**
- The range within which the population mean will lie based on the sample mean
- It allows an estimation of the range in which the true population mean will lie when a representative sample from that population is analysed.

**Comparative statistics**
- Allows data from two groups to be compared, with the aim of determining whether they originated from the same population or not, or, in the context of a trial, whether the differences between them are due to luck or really exist

**Hypothesis**
- The concept being tested

**Null hypothesis**
- That no difference exists between the two samples being analysed

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Fig. 19.2 Distributions. (a) Negative skew. (b) Positive skew. Representative sample from which population is analysed.
Bias

- Inequalities between the groups being compared that lead to incorrect conclusions being reached

Errors in experimental design that cause incorrect results

Type 1 error
- A false positive result
- A difference is found between two groups where one does not exist

Type 2 error
- A false negative result
- No difference is detected although one does exist

Parametric data

- Data values fit a ‘normal distribution’

Statistical tests

- Tests that provide a probability value
- The ‘p’ value is the probability that the two sets of data being compared are from the same population, i.e. that no difference exists between them
- Statistical significance is stated to be a probability of less than 1 in 20 that the two groups are the same (p<0.05)

Parametric tests

- Used on data following a normal distribution, e.g.
  - Student t-test
  - Paired t-test

Non-parametric tests

- Used on non-normally distributed data
  - Unpaired: Mann–Whitney
  - Paired: Wilcoxon

Nominal tests

- If data can be placed in a 2×2 square, e.g. the response to a treatment or placebo (Fig. 19.3) – then a Chi-squared test ($\chi^2$-test) can be used

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<tr>
<td>Placebo given</td>
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<td>50</td>
</tr>
<tr>
<td>Totals</td>
<td>48</td>
<td>52</td>
<td>100</td>
</tr>
</tbody>
</table>

Fig. 19.3 The 2×2 table. If you consider a disease for which a treatment is given, 100 patients enter a study and are randomized to receive the treatment or a placebo. The groups are mutually exclusive. An individual cannot be in more than one group. A 2×2 table can then be drawn up of the outcomes. In this example, 50 patients received the treatment and 41 were cured, as were 11 of those who received the placebo. Analysis of this data can be carried out using a Chi-squared test in order to determine whether the treatment is statistically better than the placebo.
95% confidence intervals

- The 95% confidence interval (CI) is the range of values around the mean within which the true population mean will lie in 95% of cases.
- It is calculated from the standard error. We can state that in 95% of cases, the population mean will lie ±2 standard errors from our sample mean.
- Data can therefore be expressed as a mean and 95% confidence interval, the values being the range provided by the mean ±2 standard errors.

Correlation and regression (Fig. 19.4)

Correlation coefficient

- Reports on the relationship between two variables.
- A value of 1 suggests a completely linear relationship.
- 0 suggests that no relationship exists between them.

Regression

- Allows calculation of the equation of a line drawn when two variables are plotted against each other.
- Once this equation is defined, the value of one variable can be calculated when the other is known.

Accuracy of test values

Normal range

- For any variable there is usually a range of normal values, usually defined as the mean value ±2 or 3 standard deviations.

Sensitivity

- The ability of a test to report an abnormal result when the disease is present.
- It reports on what proportion of patients with a disease will have a positive test.

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![Correlation and regression graph](Fig. 19.4 Correlation and regression. When two variables are plotted against each other, a scatter plot results. A line of best fit can then be drawn through these points and the accuracy of the relationship between the two variables can be calculated based on the variance between each data point and the best fit line. This is the correlation coefficient.)
Specificity
- The ability of a test to return a normal result when the disease is absent
- It reports on what proportion of patients without the disease will have a negative test

Positive predictive value (PPV)
- The proportion of positive tests where the disease is actually present
- A high PPV suggests that if the test is positive, then the disease is present, i.e. there are few false positives

CLINICAL TRIALS
- Designed to compare the effect of a therapy with either a placebo (i.e. an inactive substance) or another therapy

Power (calculation)
- A calculation of the numbers needed in a trial to confidently measure a stated difference between the two groups to ‘*p < 0.05’

Randomization
- Each patient entered into the trial has an equal chance of being in each of the therapy groups in the trial

Controlled trial
- Comparison of one therapy against another or a placebo

Blinded
- Patients do not know which therapy they are receiving

Double blind
- Neither the doctor nor the patient knows which therapy is being received

Bias
- Inequalities between the two groups other than the difference in therapy that they are receiving

Publication bias
- Failure of negative trials to be published, so only positive data about a therapy reaches the public domain

Intention to treat
- The analysis of the trial data includes all patients entered, irrespective of whether they completed the treatment course

Cross-over trials
- Each subject undergoes both types of therapy, one after the other
- A comparison can then be made for each individual patient

Endpoints
- Primary endpoint: the main measurement aim of the trial – this is used in the power calculation to determine the number of subjects
- Secondary endpoints: other measurements reported in the trial. The trial may not be sufficiently powered to test these without a type II error
**EVIDENCE-BASED MEDICINE**

**Definition**
- The conscientious, explicit and judicious use of current best evidence in making decisions about the care of individual patients

**Role**
- EBM leads to patient care guided by the best available data on therapies available, but it is specific to the patient; in other words it aims to take into account differences between individual patients
  - If a trial on hypertension were carried out in male Caucasians, its results may not be true of African women.

**Resources**

**Cochrane Collaboration**
- A collection of critical appraisals of trials on specific therapies

**Medline/Pubmed/Index Medicus**
- Databases of biomedical studies published worldwide

**Critical appraisal**
- The analysis of all the trials that have studied the same therapy in the same disease with a conclusion about the overall role of that therapy
- In general, only randomized controlled, preferably blinded trials are included and an intention to treat analysis is carried out

**Relative risk (RR)**
- The percentage change in the probability of an event occurring due to the therapy given
- If the chance of a stroke on aspirin is 2% and the chance off aspirin is 4%, the relative risk of a stroke on aspirin is 50% (the proportion of strokes that would have been avoided)
- A relative risk of 100% (≡1) suggests that the risk in each group is identical

**Absolute risk**
- The proportion of all patients who would benefit from the therapy
- In the above example, the chance of a stroke off aspirin is 4% while on aspirin it is 2%; therefore the absolute reduction in risk from taking aspirin is: 4% – 2% = 2%

**Number needed to treat**
- An estimation of the number of patients who would need to receive a therapy in order for a defined event to be avoided
- In the example, 2 in every 100 patients taking aspirin will be prevented from having a stroke; to avoid 1 stroke, therefore, 50 patients have to be given aspirin

**SCREENING AND SURVEILLANCE**

**Screening**
- The investigation of a population in order to identify those who have a specific disease
Surveillance

- The investigation of an individual in order to detect recurrence of a disease

Ransom’s criteria

- Criteria for an appropriate screening test
- That there is a safe and sensitive test for the disease with a high positive predictive value; the test should not have a high complication rate
- The yield of the test needs to be high enough to merit the cost of the test and the inconvenience and discomfort for both those in whom the disease is detected and those in whom it is not
- Earlier treatment of the disease has to have a benefit to the patient compared with late treatment; in other words, an effective therapy has to be available

Number needed to screen

- The number of individuals who have to be screened in order to prevent one death due to the disease

Lead time

- The time difference between detection of a disease by screening and the point at which it would have presented by causing symptoms

EPIDEMIOLOGY

- The study of disease and the way it is distributed within the population
- The risk of developing a specific disease can depend on a wide variety of factors

Genetic predisposition

- Genetic variation between individuals alters their susceptibility to a disease
  - HLA-B8 DR3 increases the risk of autoimmune disease

Exposure to causative agent

- Increased exposure to an infectious agent, carcinogen or other agent may be a function of geographical location, immediate personal contacts, work environment or personal habits such as diet, alcohol or smoking

Availability of healthcare

- Availability and utilization of healthcare resources impacts upon prevention of disease (e.g. vaccination) and the stage at which a disease presents; this may have a large impact on outcome

Social and cultural beliefs

- The response to disease is modified by an individual’s perceptions of illness and his or her society’s approach to disease management
Definitions in epidemiology

**Incidence**
- Number of new cases arising during a defined period of time
  - 300 per year

**Prevalence**
- Total number of cases in a population per unit time

**Prevalence rate**
- Prevalence per unit population

**Mortality**
- Death rate per unit time

**Mortality rate**
- Death rate per unit population per unit time

**Age-standardized mortality**
- Correction of the mortality rate for a disease for age

**Standardized mortality ratio**
- Ratio of deaths observed in a cohort to the number expected across the whole population
- For example the mortality in any specific age range in smokers is higher than that for the population as a whole

AUDIT AND GOVERNANCE

- Audit is a method of monitoring performance and standards in healthcare
- Governance is the mechanism by which standards are maintained

**Stages of audit**
- Describe the variable to be audited
- Choose an appropriate standard to be used as a benchmark for performance
- Collect the data on local performance
- Compare local results with the standard
- Identify ways of improving local performance
- Repeat audit after implementation of the new protocols in order to assess their effect

**Rules**
- Audit should be non-confrontational and non-judgemental
- Individuals should not be openly targeted
- However, an individual doctor who is under-performing should be encouraged to improve practice and supported in doing so

**Governance**
- The means by which organizations ensure the provision of quality clinical care by making individuals accountable for setting, maintaining and monitoring performance standards
- Involves individuals and groups of healthcare workers in identifying best practice and how it may be achieved
SELF-ASSESSMENT QUESTIONS

Multiple choice questions (single best answer)

1. A study of a pulse rate in an adult population of 500 people is carried out. Which one of the following would be the most appropriate method of describing the dataset that results?
   A. Mean and standard deviation
   B. Mode and range
   C. Median and interquartile range
   D. Mean and standard error
   E. Median and 95% confidence intervals

2. A clinical trial of a new drug is carried out and an ‘intention to treat’ analysis performed. What is the best description of this form of analysis?
   A. All patients who completed the trial are included
   B. All patients who were considered for the trial were included
   C. All patients who were randomized in the trial were included
   D. All patients who took the drug rather than placebo were included
   E. All patients who dropped out of the study were excluded from the analysis

3. A study looking at 1-year survival in patients randomized to one of two forms of drug treatment was carried out. What would be the most appropriate analysis tool to compare the treatments?
   A. Student t-test
   B. Mann–Whitney test
   C. Paired t-test
   D. Chi-squared test
   E. Regression analysis

4. Which one of the following is the best definition of ‘population screening’?
   A. Investigation of symptomatic patients for the underlying cause
   B. Assessment of a patient with a previous diagnosis for recurrence of the disease
   C. Assessment of patients with a disease for evidence of an associated condition
   D. Assessment of asymptomatic patients for a disease
   E. Random selection of a sample from a population for inclusion in a trial

5. Which one of the following defines prevalence?
   A. Number of patients with a disease seen in the hospital setting
   B. Number of patients with a disease expressed as a proportion of the total population
   C. Number of new patients presenting each year with a disease
   D. Number of new cases of the disease per 100000 people per year
   E. Total number of cases within the total population per year
## Appendix A

**Answers to MULTIPLE CHOICE QUESTIONS**

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Pass Finals

500

A

Answers to MULTIPLE CHOICE QUESTIONS

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18. Psychological medicine
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19. Statistics and evidence-based medicine
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Appendix B
Answers to EXTENDED MATCHING QUESTIONS

4. Pharmacology and therapeutics
   1. K
   2. I
   3. A
   4. H
   5. D
   6. J
   7. I

5. Radiology
   1. I. F. PA chest is the classical test but CT is more accurate.
   II. I.
   III. K. Much more sensitive than CT for liver lesions.
   IV. D. ‘Pepperpot’ skull lytic lesions are seen.

6. Clinical chemistry
   1. I. C. Confusion is nonspecific. Oedema suggests right heart failure. Hypokalaemia is an unwanted effect of loop diuretics. Renal failure could be secondary to heart failure or unwanted effect of diuretics.
   II. I. Hypokalaemia, hypomagnesaemia, dehydration and normal anion gap metabolic acidosis all result from electrolyte and water losses from high ileostomy outputs.
   III. D. Hypoxia and low $PCO_2$ suggests respiratory problem, fever suggests infection. Low sodium is a result of syndrome of inappropriate ADH (SIADH) and is associated with pneumonia.
   2. I. H. Hypercapnia and hypoxia suggest type II respiratory failure.
   II. F. Metabolic acidosis with respiratory compensation (low $PCO_2$) in a patient with diabetes who is unwell and vomiting is very suggestive of diabetic ketoacidosis.
   III. C. Metabolic acidosis with high anion gap is compatible with aspirin overdose.
   3. I. A. All three are markers of acute cardiac muscle damage.
   II. D. Lymphadenopathy and an elevated LDH give the diagnosis.
   III. E. Normal LFTs with a low Hb and elevated bilirubin point to this answer.

7. Infectious diseases
   1. I. E. There is evidence of immunocompromise and/or reactivated TB (chest X-ray, lymphadenopathy, fever).
   II. J. Rust-coloured sputum and peri-oral HSV are associated with *Strep. pneumoniae*.
   III. F. Hepatosplenomegaly, jaundice, a fever and low platelets are all characteristic of malaria.
2. I. L. Liver ultrasound would demonstrate cholecystitis (thickened inflamed gallbladder) and cholangitis (gas in biliary tree, stones or an obstructed biliary tree). CT would be the second choice.

II. B. The clinical picture is that of malaria.

III. G. The data suggest infective endocarditis. Multiple sets of blood cultures are needed to detect the organism and derive the antibiotic sensitivities.

8. Respiratory medicine

1. I. B. Eczema suggests atopy in a young woman. Spirometry results suggest an obstructive defect. These, together with history, make asthma very likely.

II. A. Breathlessness with clubbing and weight loss strongly suggest lung cancer, especially with progressive symptoms.

III. H. Normal chest X-ray and pulmonary function tests exclude many of the answers. NSAIDs (e.g. ibuprofen) cause GI ulceration and iron deficiency particularly in elderly patients.

2. I. A. *Strep. pneumoniae* is the commonest cause of pneumonia and is associated with rusty coloured sputum.

II. E. The marked hypoxia with normal chest X-ray suggests *Pneumocystis pneumonia* in this immunocompromised patient.

III. F. *Staph. aureus* pneumonia cavitates and is associated with flu outbreaks.

3. I. F. The clue is the fact that she gets better when she is away from the farm; extrinsic allergic alveolitis symptoms are worst at the time of antigen exposure.

II. A. Cough and bilateral lymphadenopathy is a common presentation of sarcoid.

III. H. His exposure to asbestos, the presence of chest pain and the chest X-ray findings make mesothelioma likely.

9. Cardiology

1. I. D. The presence of different blood pressures in each arm, interscapular pain and Marfan’s point to a dissected thoracic aorta.

II. B. This is exercise-induced angina in a patient with risk factors (diabetes mellitus and smoking).

III. A. The age and the relationship to food are suggestive of a gastrointestinal rather than cardiac cause.

2. I. B. The right heart failure and cardiomegaly in a drinker suggest alcoholic cardiomyopathy.

II. C. Deep vein thrombosis with a pulmonary embolus – recent travel with a swollen leg and breathlessness.

III. C. The history of diabetes and the presence of an ulcerated area could be cellulites or vascular insufficiency. The history favours the former.

3. I. B. The rate of 160 b.p.m. and no ‘P’ waves in a smoker suggest AF.

II. I. The tachycardia is due to the β-agonist (it also causes tremor). If the patient was not on inhalers consider thyrotoxicosis.

III. D. The symptoms are all due to anxiety-related hyperventilation – shortness of breath and tingling of the fingers and mouth.
10. Gastroenterology and hepatology
   1. I. D. Autonomic neuropathy due to diabetes mellitus links the symptoms.
      II. H. The mucus and low potassium suggest a tubulovillous adenoma. The mucus is very potassium rich and can be profuse.
      III. G. Ulcerative colitis (anaemia, fever and diarrhoea) all point to severe disease.
   2. I. E. The risk factors of diabetes and heart disease, combined with pain and diarrhoea after food, suggest mesenteric ischaemia.
      II. G. Ulcers, weight loss and anaemia, plus erythema nodosum, all point to inflammatory bowel disease and therefore Crohn’s in this question.
      III. H. Irritable bowel – the alternating bowel habit, bloating and left iliac fossa pain are suggestive and the weight gain discounts other pathologies.
   3. I. B. Growth failure with GI symptoms points towards coeliac disease, Crohn’s or cystic fibrosis. The latter is unlikely to present as late as this.
      II. A. Pernicious anaemia – the low vitamin B₁₂ and the history of autoimmune thyroid disease point to this.
      III. E. The history suggests chronic pancreatitis – steatorrhoea and chronic alcoholism.
   4. I. B. NSAIDs markedly increase the risk of gastric ulceration.
      II. H. The change in bowel habit and weight loss suggest that a carcinoma is the most important diagnosis to rule out.
      III. J. Bright red rectal bleeding suggests a rectal or anal cause, and in this age group haemorrhoids are the most likely.

11. Rheumatology
   1. I. D. Syndesmophytes are suggestive of ankylosing spondylitis and the ESR and HLA status support this.
      II. B. Osteoarthritis is a common cause of back pain. Normal bloods and no erosions on X-ray make the other diagnoses unlikely.
      III. A. Recent wrist fracture in a post-menopausal woman with normal bloods is highly suggestive of osteoporosis. She may have had steroids for her asthma, making osteoporosis more likely.
   2. I. D. Elevated urate suggests gout. The distribution of the joint symptoms is compatible with gout.
      II. F. Rash, joint pains and raised inflammatory markers with a positive ANA is strongly suggestive of SLE.
      III. B. Heberden’s nodes with normal ESR suggests osteoarthritis.
   3. I. H. Recurrent miscarriages are the key here.
      II. C. The MCP joint erosions and a systemic illness point to rheumatoid.
      III. A. Anticentromere antibodies are associated with systemic sclerosis.
12. Dermatology

1. I. I. Raised, purple, painful red areas on the legs suggest erythema nodosum, which is associated with Crohn’s disease.
   II. A. History of atopy. Distribution suggests eczema (flexural).
   III. F. Yellow crusts strongly suggest *Staph. aureus* infection.

2. I. F. An ulcer which is rapidly increasing in size in a patient with Crohn’s disease is highly suggestive of pyoderma gangrenosum.
   II. A. The pigmentation and brown colour suggest venous ulceration.
   III. B. Being a gardener suggests UV exposure. The appearance and hard node suggests SCC rather than malignant melanoma.

3. I. G. Infection with *Corynebacterium minutissimum*.
   II. F. Jaundice and itching = biliary obstruction.
   III. A. Iron deficiency is associated with itching.

13. Endocrinology

1. I. D. She has multiple endocrine neoplasia type I (a parathyroid adenoma causing hyperparathyroidism, associated with a pancreatic tumour). The high calcium resulting from this is causing the constipation and polyuria.
   II. B. She has Sheehan syndrome – a pituitary infarction following a postpartum haemorrhage – leading to diabetes insipidus. This is rare.
   III. A. There is a metabolic acidosis (low bicarbonate), thirst, polyuria and weight loss – classical early onset diabetes mellitus.

2. I. A. She has autoimmune disease already, so her risk of a further autoimmune disease is increased. Anxiety, palpitations, diarrhoea and weight loss are all pointing towards thyrotoxicosis.
   II. E. The palmar pigmentation, abdominal pain and postural hypotension suggest Addison’s disease (in this case due to adrenal tuberculosis suggested by sweats, weight loss and foreign travel).
   III. B. 50% of coeliac disease presents with iron deficiency. Weight loss and abdominal pain support this. The southern Irish origins increase the risk of coeliac.

14. Renal medicine

1. I. C. The history of gout increases the risk of renal stones. The colicky pain and sudden onset in the absence of indicators of infection support this.
   II. H. The chest signs point to a pneumonia. The urinary abnormalities may be due to an atypical pneumonia (e.g. mycoplasma or legionella).
   III. E. There is an association between polycystic kidney disease and berry aneurysms that result in subarachnoid haemorrhage. The pain is probably due to bleeding into one of the renal cysts.
Answers to EXTENDED MATCHING QUESTIONS

2. I. A. The presence of liver cirrhosis with new acute renal failure favours hepatorenal syndrome as the cause.
   II. F. Haemolytic-uraemic syndrome results from \textit{E. coli} O157 and occurs after food poisoning with this organism. The anaemia and thrombocytopenia are as a result of the haemolysis.
   III. I. The mass in his pelvis is his bladder. This is a classical presentation of acute retention due to prostatic enlargement.

15. Haematology
   1. I. A.
      II. D. Sickle results in sickled red cells and regional hypoxia causing severe pain.
      III. B. Although both B\textsubscript{12} and folic acid deficiency cause macrocytosis, only B\textsubscript{12} requires the stomach to be present to be absorbed.
   2. I. I.
      II. J.
      III. H. Both reticulocytes and platelets increase after blood loss but platelets do not have nuclei.
   3. I. C. O = 44\%, A = 45\%, B = 8\%, AB = 3\%.
      II. A.
      III. F. The mother must be RhD negative. A first RhD positive fetus induces anti-D antibodies. The second suffers the syndrome.

17. Neurology
   1. I. C. The distal progressive weakness and areflexia are typical of Guillain–Barré. The history of a recent GI infection supports this.
      II. A. The smoking and hypertension are key risk factors for ischaemic stroke. This is a non-dominant side event with dysphasia.
      III. H. The shuffling gait, micrographia and resting tremor all point to Parkinson’s.
   2. I. F. The rash, photophobia and fever all suggest meningitis (probably meningococcal).
      II. A. The combination of abdominal symptoms and unilateral headache, probably initiated by alcohol, points to migraine.
      III. D. The retinal changes suggest malignant hypertension, and are not features of diabetic retinopathy.
   3. I. G. All the elements are here for a benzodiazepine overdose, using drugs prescribed by the GP. She could be either ketoacidotic or hypoglycaemic but the history points to deliberate self-harm due to reactive depression.
      II. I. Septicaemia due to urinary sepsis.
      III. E. Hypotension, bradycardia and, in particular, J waves on the ECG all point to hypothermia.

18. Psychological medicine
   1. I. F. The pattern of memory loss is compatible with early dementia.
      II. D. She has first rank symptoms of schizophrenia. Her ethnicity increases the risk of this disease.
      III. H. High MCV suggests alcohol excess. Visual hallucinations, sweating and tachycardia occur in alcohol withdrawal syndrome.
2. I. D. Persecutory ideation and thought broadcasting suggest schizophrenia.
   II. I. Paranoia and agitation with a history of drug addiction points to amphetamines.
   III. B. Sleep loss, increased libido and spending beyond one’s means are suggestive of mania.

3. I. B. Tricyclics cause weight gain and so would be relatively contraindicated. SSRIs are useful in reactive depression.
   II. G. Anxiety disorders are usually effectively treated with CBT.
   III. H. Carbamazepine is a useful second-line drug in bipolar disorders.
Appendix C
Normal reference ranges:
Normal values for laboratory tests

These may vary from hospital to hospital.

<table>
<thead>
<tr>
<th>Test</th>
<th>Abbreviation</th>
<th>Normal range</th>
<th>Units</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Full blood count</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Haemoglobin</td>
<td>Hb</td>
<td>Males 13.5–17.7 Females 11.5–16.5</td>
<td>g/dL</td>
</tr>
<tr>
<td>Mean corpuscular volume</td>
<td>MCV</td>
<td>80–96</td>
<td>fL</td>
</tr>
<tr>
<td>Mean corpuscular haemoglobin</td>
<td>MCH</td>
<td>27–33</td>
<td>pg</td>
</tr>
<tr>
<td>Mean corpuscular haemoglobin concentration</td>
<td>MCHC</td>
<td>32–36</td>
<td>g/dL</td>
</tr>
<tr>
<td>Reticulocyte count</td>
<td>Retics</td>
<td>0.5–2.5%</td>
<td></td>
</tr>
<tr>
<td>Red cell count</td>
<td>RCC</td>
<td>Males: 4.5–6 Females: 3.9–5.0</td>
<td>×10¹²/L</td>
</tr>
<tr>
<td>White cell count</td>
<td>WCC</td>
<td>4–11</td>
<td>×10⁹/L</td>
</tr>
<tr>
<td>Basophils</td>
<td></td>
<td>0.01–0.1</td>
<td>×10⁹/L</td>
</tr>
<tr>
<td>Eosinophils</td>
<td></td>
<td>0.04–0.4</td>
<td>×10⁹/L</td>
</tr>
<tr>
<td>Lymphocytes</td>
<td></td>
<td>1.5–4.0</td>
<td>×10⁹/L</td>
</tr>
<tr>
<td>Monocytes</td>
<td></td>
<td>0.2–0.8</td>
<td>×10⁹/L</td>
</tr>
<tr>
<td>Neutrophils</td>
<td></td>
<td>2.0–7.5</td>
<td>×10⁹/L</td>
</tr>
<tr>
<td>Platelets</td>
<td></td>
<td>150–400</td>
<td>×10⁹/L</td>
</tr>
<tr>
<td><strong>Haematinics</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Serum B₁₂</td>
<td>B₁₂</td>
<td>160–925</td>
<td>ng/L</td>
</tr>
<tr>
<td>Serum folate</td>
<td></td>
<td>2.9–18</td>
<td>µg/L</td>
</tr>
<tr>
<td>Ferritin</td>
<td>Fe</td>
<td>Male: 20–260 Female: 6–110</td>
<td>µg/L</td>
</tr>
<tr>
<td>Iron</td>
<td></td>
<td>13–32</td>
<td>mmol/L</td>
</tr>
<tr>
<td>Total iron binding capacity</td>
<td>TIBC</td>
<td>42–80</td>
<td>mmol/L</td>
</tr>
<tr>
<td><strong>Other haematology</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Erythrocyte sedimentation rate</td>
<td>ESR</td>
<td>&lt;20</td>
<td>mm/hour</td>
</tr>
<tr>
<td><strong>Coagulation</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bleeding time</td>
<td></td>
<td>3–9</td>
<td>minutes</td>
</tr>
<tr>
<td>Active partial thromboplastin time</td>
<td>APTT</td>
<td>23–31</td>
<td>seconds</td>
</tr>
</tbody>
</table>

Continued
### Normal reference ranges: Normal values for laboratory tests

<table>
<thead>
<tr>
<th>Test</th>
<th>Abbreviation</th>
<th>Normal range</th>
<th>Units</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prothrombin time</td>
<td>PTPT</td>
<td>12–16</td>
<td>seconds</td>
</tr>
<tr>
<td>International normalized ratio</td>
<td>INR</td>
<td>1.0–1.3</td>
<td></td>
</tr>
</tbody>
</table>

#### Urea and electrolytes

<table>
<thead>
<tr>
<th>Test</th>
<th>Abbreviation</th>
<th>Normal range</th>
<th>Units</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sodium</td>
<td>Na⁺</td>
<td>135–146</td>
<td>mmol/L</td>
</tr>
<tr>
<td>Potassium</td>
<td>K⁺</td>
<td>3.5–5.0</td>
<td>mmol/L</td>
</tr>
<tr>
<td>Chloride</td>
<td>Cl⁻</td>
<td>95–106</td>
<td>mmol/L</td>
</tr>
<tr>
<td>Urea</td>
<td></td>
<td>2.5–6.7</td>
<td>mmol/L</td>
</tr>
<tr>
<td>Creatinine</td>
<td></td>
<td>79–118</td>
<td>µmol/L</td>
</tr>
</tbody>
</table>

#### Liver function tests

<table>
<thead>
<tr>
<th>Test</th>
<th>Abbreviation</th>
<th>Normal range</th>
<th>Units</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alanine aminotransferase</td>
<td>ALT</td>
<td>5–40</td>
<td>IU/L</td>
</tr>
<tr>
<td>Aspartate aminotransferase</td>
<td>AST</td>
<td>12–40</td>
<td>IU/L</td>
</tr>
<tr>
<td>Gamma glutaryl transpeptidase</td>
<td>gT</td>
<td>10–40</td>
<td>IU/L</td>
</tr>
<tr>
<td>Alkaline phosphatase</td>
<td>ALP</td>
<td>39–117</td>
<td>IU/L</td>
</tr>
<tr>
<td>Bilirubin</td>
<td>Bili</td>
<td>&lt;17</td>
<td>µmol/L</td>
</tr>
</tbody>
</table>

#### Other biochemistry

<table>
<thead>
<tr>
<th>Test</th>
<th>Abbreviation</th>
<th>Normal range</th>
<th>Units</th>
</tr>
</thead>
<tbody>
<tr>
<td>Glucose (fasting)</td>
<td></td>
<td>4.5–5.5</td>
<td>mmol/L</td>
</tr>
<tr>
<td>Glycosylated haemoglobin</td>
<td>HbA₁c</td>
<td>3.7–5.1</td>
<td></td>
</tr>
<tr>
<td>Calcium</td>
<td>Ca²⁺</td>
<td>2.20–2.67</td>
<td>mmol/L</td>
</tr>
<tr>
<td>Phosphate</td>
<td>PO₄³⁻</td>
<td>0.8–1.5</td>
<td>mmol/L</td>
</tr>
<tr>
<td>C reactive protein</td>
<td>CRP</td>
<td>&lt;10</td>
<td>mg/L</td>
</tr>
<tr>
<td>Urate</td>
<td></td>
<td>0.18–0.42</td>
<td>mmol/L</td>
</tr>
</tbody>
</table>

#### Lipids

<table>
<thead>
<tr>
<th>Test</th>
<th>Abbreviation</th>
<th>Normal range</th>
<th>Units</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cholesterol</td>
<td>Chol</td>
<td>3.5–6.5</td>
<td>mmol/L</td>
</tr>
<tr>
<td>HDL cholesterol</td>
<td>HDL</td>
<td>Male: 0.8–1.8 Female: 1.0–2.3</td>
<td>mmol/L/mmol/L</td>
</tr>
<tr>
<td>Triglycerides</td>
<td>Trig</td>
<td>Male: 0.7–2.1 Female: 0.5–1.7</td>
<td>mmol/L/mmol/L</td>
</tr>
</tbody>
</table>

#### Arterial blood gases

<table>
<thead>
<tr>
<th>Test</th>
<th>Abbreviation</th>
<th>Normal range</th>
<th>Units</th>
</tr>
</thead>
<tbody>
<tr>
<td>Arterial partial oxygen pressure</td>
<td>PₐO₂</td>
<td>10–13.3</td>
<td>kPa</td>
</tr>
<tr>
<td>Arterial partial carbon dioxide</td>
<td>PₐCO₂</td>
<td>4.8–6.1</td>
<td>kPa</td>
</tr>
<tr>
<td>pH</td>
<td>pH</td>
<td>7.35–7.45</td>
<td></td>
</tr>
<tr>
<td>Bicarbonate</td>
<td>HCO₃⁻</td>
<td>24–28</td>
<td>mmol</td>
</tr>
</tbody>
</table>
Illustrations are comprehensively referred to from the text; therefore, significant material in illustrations and tables have usually only been given a page reference in the absence of their concomitant mention in the text referring to that figure.

A
ABC (airway/breathing/circulation) in basic life support, 184f
abdomen
anatomical regions, 214f
examination, 213–217
cardiac patient, 165
pain, 23, 362
X-ray see X-ray
abducens nerve (CVI)
defects, 456t
testing, 420–421
ABO blood group, 377–378, 379t
abscess
brain, 441–442, 461
liver, 251
lung, 57, 140
absence seizures, 432
absolute risk, 495
absorption, drug, 39
acanthosis nigricans, 296
accessory nerve (CXI)
defects, 456t
testing, 422
accommodation, testing, 420
accuracy of test values, 493–494
ACE inhibitors see angiotensin-converting enzyme inhibitors
N-acetylcysteine, 42t, 44t
achalasia, 69, 220
aciclovir, 109
acid–base (pH) disorders, 95–97, 101–102
in respiratory failure, 138t
acidosis
metabolic see metabolic acidosis
respiratory, 96
acne vulgaris, 294–297
acquired immunodeficiency virus see human immunodeficiency virus
acromegaly, 309–311, 330
ACTH see adrenocorticotropic hormone
activated partial thromboplastin time, 382
acute coronary syndrome (ACS), 97, 172, 180–183, 180b, 209–210
TIMI risk score, 179t
acute leukaemias, 391, 393
acute phase reactants, 100
acyanotic congenital heart disease, 192–193, 192t
Addison’s disease (primary hypoadrenalism), 314–315
Addisonian crisis, 330
adenocarcinoma, gastric, 223–224, 255
adenoma
adrenal, 314, 314t, 320
pituitary, 314t
adenomatous polyposis, familial, 230, 405
adenoviruses, 118
ADH see antidiuretic hormone
adjuvant analgesics, sickle cell crises, 376
adjuvant therapy in cancer, 408
adrenal gland
congenital hyperplasia, 317
hormone abnormalities, 312–315
adrenocorticotropic hormone (ACTH)
Cushing disease and, 312
ectopic production, 312, 314, 314t, 330
synthetic, stimulation test using, 305
tumours secreting, 312, 314t
advanced life support, 185f
adverse drug reactions (and side-effects/toxicity), 40–41
antibacterials, 109, 127, 141–143
antidepressants, 477t
antiepileptics, 433
antifungals, 109
antipsychotics, 472t
illicit drugs, 483t
levodopa, 434–435
lithium, 477t
see also drug-induced disorders
affect see mood
affordability of drug, 35
African trypanosomiasis, 124
age, cancer and, 401
age-standardized mortality, 497
cancer and, 403t
agitation, 469, 487
agonists, 37, 47
AIDS see human immunodeficiency virus
airways
obstruction, breath sounds, 137t
see also lung, obstructive disease
smoking effects, 134t
see also ABC (airway/breathing/circulation)
AL amyloidosis, 343–344
alanine aminotransferase, 99
alcohol (ethanol), 482
abuse, 482
as antidote to methanol poisoning, 42t
cancer and, 401
dependency, 482
liver disease due to, 249–250 poisoning, 45
withdrawal symptoms, 481, 486–487
aldosterone
antagonists, 191t
oversecretion, 92, 320–321
alkaline phosphatase, 99
alkaloids, plant, 408
alkalosis
metabolic, 97
respiratory, 96
alkylating agents
causing cancer, 404
treating cancer, 408
allergic alveolitis, extrinsic, 153
allergic aspergillosis, bronchopulmonary, 123
alopecia (hair loss) in cancer therapy, 409
α-blockers, hypertension, 191t
α-herpesviruses, 118
alveolitis
cryptogenic fibrosing, 153, 156
extrinsic allergic, 153
Alzheimer's disease, 470
amantadine, 109
ambulatory ECG, 171
amenorrhoea, 316–317
American trypanosomiasis, 124
aminoglycosides, 108
amniocentesis, 416
amoebiasis, 237
amoxicillin, 48
amphetamine, 483t
amylose (serum), raised, 238t
amyloidosis, 343–344
diagnosis, 344
familial, 344
management, 344
secondary, 344
amyotrophic lateral sclerosis, 449
anaemia, 368–377
cancer treatment-induced, 409
pernicious, 373–374, 397
analgesics, 410–412
cancer, 410–411
complications, 411
sickle cell crises, 376b
ANCA-positive vasculitis, 277t–278t
aneurysm, thoracic aortic, 61
angina, 178–180
unstable (UA), 180b
TIMI risk score, 179t
see also acute coronary syndrome
angiography (incl. arteriography), 77
cerebral, 428
coronary, 172
renal, 337
angiotensin, 320f
angiotensin II receptor antagonists, 191t
angiotensin-converting enzyme (ACE) inhibitors, 191t
interactions, 37t
anion gap, 97
high, metabolic acidosis with, 97, 101
normal, metabolic acidosis with, 97, 101
ankle reflex, 424
swelling, 210–211
ankylosing spondylitis, 270
Ann Arbor staging classification of Hodgkin lymphoma, Cotswolds modification of, 390t
anonymous papers, 2
anorexia nervosa, 482–484, 486
antagonists, 37
antenatal (prenatal) diagnosis, 416
anthrax and B. anthracis, 113
antibiotics (antibacterial drugs), 106–109
adverse/side-effects, 109, 127, 141–143
endocarditis, 199
mechanisms of action, 106, 107f
pulmonary infections, 140
sensitivity tests, 106
septic arthritis, 270
tuberculosis, 115t, 141–143
urinary infections, 346–347
antibiotics (cytotoxic), 408
antibodies to blood group antigens, 379t
see also autoantibodies
anticoagulants, 385–386, 399
acute coronary syndrome, 180
anticonvulsants (anti-epileptics), 433
monitoring, 40t
prophylactic use, 433
status epilepticus, 431
toxicity, 433
antidepressants, 476, 487
in irritable bowel syndrome, 233b
tricyclic see tricyclic antidepressants
antidiuretic hormone (ADH; vasopressin), 86
disorders, 89–90
syndrome of inappropriate secretion, 319–320
antidotes, 42t
antiemetics, 417
cancer patients, 409
mechanisms of action, 408
antiepileptics see anticonvulsants
antifungals, 109
antiglobulin (Coombs’) test, 378t, 379f
antihypertensive drugs, 191t
combination therapy, 190f
antimetabolites, 408
antineutrophil cytoplasmic antibodies (ANCA)-positive vasculitis, 277t–278t
antiphospholipid syndrome, 274
antiplatelet drugs, 386
antipsychotics, 472
antiretroviral drugs, 122–123
α1-antitrypsin deficiency, 249
antiviral drugs, 109–110
hepatitis, 109–110, 128, 244
HIV (antiretrovirals), 122–123
mechanisms of action, 129
anxiety disorder, 479–480, 486
anxiolytic drugs, 480
aorta
aneurysm, thoracic, 61
coarctation, 194
aortic valve
regurgitation, 175–176
sounds, 164, 175–176
stenosis, 175, 207
apex beat of heart, 162
appearance, assessment, 466
arrhythmias, 199–207
arterial blood gas analysis see blood gas analysis
arterial thrombosis, 386
arterial ulcers, 298
arteriography see angiography
arthritis, 264–272
degenerative (osteoarthritis), 264–268, 265t
psoriatic, 270
reactive, 270–271
rheumatoid, 151, 263, 265t, 268–269, 284
septic, 269–270, 284
asbestos-related disease, 8–9, 149–150, 404
ascites
- causes, 216t, 247t, 254, 259
- examination, 216–217
aspartate aminotransferase, 98
aspergillosis, 124–125
aspiration, pleural, 138
aspirin
- overdose (and other salicylates), 44, 47–48
associations, loosening of, 467
asthma, 22, 145, 155–156
- drugs in, 145, 146t
- physical signs, 136t
ataxia, Friedreich’s, 450
atopic eczema, 292
atria
- fibrillation, 203–204, 209
- flutter, 203
- septal defect, 193
- tachyarrhythmia, 203
atrioventricular block, 201–202
- drugs contraindicated, 36t
atropine, 42t
audit, 497
auditory testing, 421–422
auscultation
- breath sounds, 135, 136t–137t, 287
- heart sounds and murmurs, 163–164
autoantibodies, 274–275, 284–285
- autoimmune haemolytic
  - anaemia (to red cells), 378t
  - clotting factors, 385
  - glomerulopathies, 338, 341
- autoimmune function, renal, 335
- autoimmune diseases
  - hepatic, 245
  - rheumatic, 272–276
- autoantibodies
- autoimmune haemolysis
  - anaemia of, 377, 378t, 398
  - drug-induced, 377
- autoimmune thrombocytopenic purpura, 396
autonomic neuropathy, 453, 461
diabetes mellitus, 325
avtosomal dominant disorders, 412–415, 413t, 417
polycystic kidney disease, 356, 361
autosomal recessive disorders, 413, 413t, 414f
azathioprine
- interactions, 36t
- monitoring, 40t
- toxicity, 48
azoles
- antibacterial, 109
- antifungal, 109
B
Babinski response, 424
baby (maternity) blues, 477
bacilli
- Gram-negative, 113
- Gram-positive, 112–113
Bacillus
- B. anthracis, 113
- B. cereus, 237
back pain, 286
bacterial antigens and immune complex nephritis, 338
bacterial infections, 111–118
- antibiotics see antibiotics
cutaneous, 289–290
gastrointestinal, 236
meningeal, 438
myocardial, 196
pneumonia due to, 139t, 140
sexually-transmitted, 126–127
urinary tract, 346–347
bacterial overgrowth in small bowel, 226
barium studies, 69–70
Barrett’s oesophagus, 219, 255
basal cell carcinoma, 295t, 299
basic life support, 184f
behaviour
- assessment, 466
- depression vs mania, 474t
Behçet’s disease, 277t–278t
beliefs
- abnormal, 467
- social and cultural, 496
Bell’s palsy, 455
benign essential tremor, 435
benzodiazepines
- overdose, 42t
- withdrawal syndrome, 213t
bereavement reactions, 475t
best answer questions, single, 7–8
β-agonist (beta-agonist)
- interactions, 37t
β-blockers (beta-blockers)
- hypertension, 191t
- interactions, 37t

β-herpesviruses, 118

β-lactams (beta-lactams), 106–108

bias, 492

β-blockers (beta-blockers)
- hypertension, 191t
- interactions, 37t

β-herpesviruses, 118

β-lactams (beta-lactams), 106–108

bias, 492

β-blockers (beta-blockers)
- hypertension, 191t
- interactions, 37t

β-herpesviruses, 118

β-lactams (beta-lactams), 106–108

bias, 492

β-blockers (beta-blockers)
- hypertension, 191t
- interactions, 37t

β-herpesviruses, 118

β-lactams (beta-lactams), 106–108

bias, 492

β-blockers (beta-blockers)
- hypertension, 191t
- interactions, 37t

β-herpesviruses, 118

β-lactams (beta-lactams), 106–108

bias, 492

bicarbonate (HCO₃) levels in respiratory failure, 138t

biceps reflex, 423–424

biguanides, 327

bilharzia, 125

biliary cirrhosis, primary, 248

biliary colic, 23–24

biliary tree/system, 253
- disorders, 253
- gallstones, 75f, 253
- obstruction, 213t, 253
- stents, 81
- ultrasound, 75

bilirubin, 99, 101–102

metabolism, 241f
- abnormalities, 213t, 258

biochemistry see chemistry

biological therapy see cancer

biopsy
- brain, 429
- directed/guided, 79, 81
- pleural, 138
- renal, 337

bipolar disorder, 472, 473f, 488
- mania
- blackouts, 433

bladder
- outflow obstruction, 348, 360
- X-rays, 68

bladder inflammation (cystitis), 346

bleeding time, 382
- coagulation;
- haemorrhage

blinded trials, 494

blistering (bullous) disorders, 297

blood
- coagulation see coagulation
- components incl. cells, 365
- faecal occult, 218
- hormone levels, assessment, 305
- products, 380
- transfusion see transfusion
- haematology
- count, full, 105
- cultures, 28, 105

blood films, 105, 127

blood gas analysis, 137, 338

blood groups, 377–380

blood pressure measurement, 27, 161b
- hypertension; hypotension

blood tests
- abnormal results (in general), 102–103
- sarcoidosis, 151

blues (maternity/baby), 477

bone(s), 276–281
- abdominal X-ray, 63
- chest X-ray, 57
- infiltrations from tumours, 59
- diseases, 276–281
- isotope, 79
- metastases (secondary deposits), 80f, 279t, 406t

serum biochemistry, 285–286

bone marrow ablation or suppression; see myeloablation;
- myelosuppression

Bordetella, 113

Borrelia burgdorferi and Lyme disease, 118

bowel habit changes, 234–235

bowel obstruction, cancer patients, 412
- colon; rectum; small intestine

brachioradialis reflex, 424

bradycardia, sinus, 199

brain (incl. cerebrum)
- abscess, 441–442, 461
- biopsy, 429
- diffuse dysfunction, causes, 431t

haemorrhage, 448

imaging see neuroradiology
infarction, 445–447

metastases, 406t

tumours, 442–443
- multiple sclerosis, 436

stroke, 447

breast cancer, 417–418
Index

breastfeeding and drug prescribing, 46–47
breath sounds, 135, 136t–137t, 165
see also ABC (airway/breathing/circulation)
breathlessness (dyspnoea)
chest pain with, 22–23
chest pain without, 21
bronchiectasis, 147–148
bronchogenic (bronchial) carcinoma, 59, 143–144, 418, 454
bronchopneumonia, 55f
bronchopulmonary allergic aspergillosis, 123
bronchoscopy, 137
Brucella, 113
Budd–Chiari syndrome, 251
bulbar palsy, 455
progressive, 449
bulimia nervosa, 484
bullous disorders, 297
bundle branch block, 202–203
Burkitt’s lymphoma, 391

C
calcium, homeostasis disturbances, 316t
see also hypercalcaemia; hypocalcaemia
calcium channel blockers, 191t
calcium pyrophosphate crystal deposition (chondrocalcinosis), 268
calculi (stones)
biliary tract (gallstones), 75f, 253
renal, 67f, 347–348, 360
Campylobacter, 236
cancer (malignancy), 401, 416–418
biliary, 253
brain, 442t
breast, 417–418
colorectal see colorectal cancer
cutaneous, 294, 295t, 298–299
UV light and, 404
gastric, 223–224, 255, 403f
general aspects
aetiology, 401
biology, 405
clinical features, 405–406
complications of treatment, 409–410
diagnosis, 405–407
epidemiology, 401
genetics, 404–405
palliative care, 410–412
staging, 407
treatment, 407–409, 418
haematological, 389–396
hepatic, 251
hepatomegaly due to, 215t
hepatosplenomegaly due to, 215t
hypercalcaemia in, 282t
lung see lung metastases
oesophageal, 69, 70f, 83, 219–220, 254
pancreatic, 239–240, 258
renal, 82
small bowel, 226–227
smoking and, 401, 416
splenomegaly due to, 216t
urogenital tract, 357–358
see also specific histological types (other than carcinoma)
candidiasis, 123, 129, 291
cannabis, 483t
captopril scans, 79
carbon monoxide poisoning, 154–155
carcinoid syndrome, 226–227, 256
carcinoma see cancer
cardiology see heart
cardiomyopathy, 196
cardiopulmonary resuscitation (CPR), 185f
cardiovascular system
anxiety effects, 479t
drugs
in acute coronary syndrome, 180b, 183
in heart failure, 188
in hypertension see antihypertensive drugs
hypertension due to, 189
examination, 159–165
systemic sclerosis-related disorders, 275
see also heart; vascular tree
carotid pulse, 161, 162t
carotid system
stroke, 447
transient ischaemic attack, 445
carpal tunnel syndrome, 450–451
cases
long, 14–15
scenario in viva voce exam, 4
short, 13
catheterization
cardiac, 172
urinary, 27–28
cellulitis, 289–290
central (cranial) diabetes insipidus (DI), 317t, 318, 319t, 330
central nervous system see brain;
nervous system
catheterization
cardiac, 172
urinary, 27–28
cellulitis, 289–290
central (cranial) diabetes insipidus (DI), 317t, 318, 319t, 330
central nervous system see brain;
nervous system
cellulitis, 289–290
central (cranial) diabetes insipidus (DI), 317t, 318, 319t, 330
central nervous system see brain;
cerebrovascular accidents, see also stroke
cerebrovascular disease, 444–449, 462
dementia, 471
cerebrum see brain
cestodes, 125, 237
Chagas disease, 124
Charcot–Marie–Tooth disease, 453
chemistry/biochemistry (clinical), 85–103
acute kidney injury, 350–351
bone, 285–286
calcium disturbances, 316t
chronic kidney disease, 354
hyperaldosteronism, 320t
hypothalamic–pituitary axis disorders
anterior pituitary, 310t
posterior pituitary, 319t
hypothalamic–pituitary–adrenal axis disorders, 314t
ovarian disorders, 317t
thyroid disorders, 307t
see also laboratory investigations
chemotherapy (cytotoxic drug), 408, 418
lung cancer, 144
chest (thorax)
ECG leads, 27, 167
wall movements in respiratory disease, 136t
X-ray, 24, 25f, 52–63, 158
cardiac patient see heart
chest examination
cardiovascular patient, 159
gastroenterological patient, 213
respiratory patient, 135
expansion, 135
exposure for, 133
chest pain, 11–12, 20
with breathlessness, 22–23
cardiac ischaemic see angina
central, 209–210
pericarditis (acute), 164
without breathlessness, 21
children
rickets, 280, 280t
vaccination schedules, 110t
Chlamydia, 126–127
chloramphenicol, 108
chlorphenamine, 48
cholangiocarcinoma, 253
cholangiopancreatography, endoscopic retrograde, 217
cholangitis, primary sclerosing, 253
cholera, 236
cholestasis, drug-induced, 252t
chondrocalcinosis, 268
chorea, non-Parkinson’s causes, 435
chorionic villus sampling, 416
Christmas disease (haemophilia B), 383t, 384
chromosome abnormalities
cancer cells, 404
disorders caused by, 412, 417
chronic disease, anaemia of, 368t, 369–371
chronic leukaemias, 393
chronic obstructive pulmonary disease (COPD), 22, 54f, 145–147, 156
Churg–Strauss syndrome, 151–152, 277t–278t
circulation see ABC (airway/breathing/circulation);
cardiocirculatory system
cirrhosis, 8, 246–251, 257
clinical chemistry see chemistry
Index

clinical examination see examination
clinical governance, 497
clinical history, 19–20
clinical trials, 494, 498
clonus test, 424
Clostridium, 112–113
  C. difficile, 217, 257
  C. perfringens, 217
  C. tetani, 112
clotting see coagulation
clipping of fingers, causes, 135t, 155
cluster headache, 444
CMV, 118
coaulation (clotting), 380–389
disorders, 383–389
drugs inhibiting see anticoagulants
factors, 382
  autoantibodies, 385
inhibitors, 382
measurements, 382–383
mechanism/pathways/physiology, 380, 382
coal-worker’s pneumoconiosis, 149
cocaine, 483t
cocci
  Gram-negative, 112
  Gram-positive, 111–112
Cochrane Collaboration, 495
colica sydrome, 224–226, 256
cognitive state, 468
depression vs mania, 474t
see also mental state examination
cold autoimmune haemolytic anaemia, 378t
colic
  biliary, 23–24
  renal, 24
colitis
  pseudomembranous, 237, 257
  ulcerative see ulcerative colitis
  collagen disorders, 283–284
colon, 230–233
  barium enema, 70
disease, 230–233
  malignant see colorectal cancer
  X-rays, 65
see also bowel obstruction
colonoscopy, 217
colorectal cancer (colon and/or rectal) cancer, 230–231, 256, 417
  barium enema, 70f
coma, 429, 463–464
see also Glasgow Coma Scale
communication, 19, 30–34
comparative statistics, 491
compression
  nerve
    median nerve at wrist, 450–451
    radial nerve, 451
    ulnar nerve, 451
    spinal cord, 459–460
compulsion, 467
see also obsessive compulsive disorder
compulsory section under Mental Health Act, 485
computerized axial tomography (CT), 51, 73
  biopsy guidance, 81
  body, 73
  kidney, 337
  head/skull/brain, 24–25, 73, 81, 427–428
spine, 428
confidence intervals, 493
confusion, toxic, 468–469, 485
congenital adrenal hyperplasia, 317
congenital heart disease, 192–194
congenital supraventricular tachyarrhythmia, 204
congenital syphilis, 117
cognermatible hyperbilirubinaemia, 258
conjunctivitis, 129
connective tissues, 263
consciousness
  disturbed, episodes of, 433
  grading, 429
  loss see coma; unconsciousness
consolidation, 136t–137t
constipation, 67f, 235
constrictive pericarditis, 195
continuous data, 489
continuous subcutaneous analgesia, cancer, 411
contraceptive pill interactions, 36t
contrast media
  excretion in urography, 337, 346
  nephropathy with, 351–352
contrast studies, 51, 69–70
  intravenous, 77–79
controlled drug prescribing, 31, 45
controlled trials, 494
conversion disorder, 480
convoluted tubules
  distal, 335
  proximal, 335
Coombs’ (antiglobulin) test, 378t, 379f
coordination tests, 424–425
cordocentesis, 416
corneal reflex, 421
coronary artery disease
  (occlusive), 177–183
  angiography, 172
  risk factors, 177–178
see also acute coronary syndrome
coronер, death referral to, 32t
correlation coefficient, 493
corticospinal tract testing, 422–424
corticosteroid prescribing/dispensing, 30–31
Corynebacterium, 112
cost affordability of drug, 35
Cotswolds modification of Ann Arbor staging classification, 390t
counselling, genetic, 416
Coxiella burnetii, 140, 198
coxackievirus, 119
cranial (giant cell) arteritis, 277t–278t, 330
cranial (neurogenic/central) diabetes insipidus (DI), 317t, 318, 319t
cranial nerves
  defects, 455–457
  examination, 420–422
creatinine, 100, 338
critical appraisal, 495
Crohn’s disease, 227–229, 256
  arthritis and, 271
  barium meal, 52, 70
cross-over trials, 494
cryptoglobinemia, 343
  vasculitis, 277t–278t
cryptogenic fibrosing alveolitis, 153, 156
Cryptosporidium, 237
crystal deposition
  calcium pyrophosphate (chondrocalcinosis), 268
  urate, 264, 272
cultural beliefs, 496
cultures (microbial), 106
  blood, 28, 105
  faecal, 218
Cushing syndrome, 312–314, 330
cutaneous... see skin
cyanotic congenital heart disease, 192t, 193–194
cyst(s), hepatic, 76f, 83
cystic fibrosis, 148–149
cystic renal diseases, 356, 361
cystitis, 346
cytotoxic drugs in cancer see chemotherapy

D
D-dimer assay, 383
data, types, 489–494
death (mortality)
cancer
  geographical variations, 402f–403f
  by site of tumour, 402f, 403t
  cardiac (sudden), 183
  myocardial infarction risk scores, 179t
certification, 31–34
  in epidemiological studies, 490–491
see also bereavement
deep venous thrombosis, 387–388
degenerative disease
  joints (osteoarthritis), 264–268, 265t.
  neurological, 449–450
deliberate self-harm, 29–30, 479, 486
Index

delirium, 468–469
delusions, 467, 474t
dementia, 469–471, 485
demyelination in multiple sclerosis, 436
dengue, 119–120
depression, 473–476, 474t, 485, 488
drugs see antidepressants postnatal, 478
dermatitis (eczema), 291–292, 298–299
dermatitis herpetiformis, 297
dermatology see skin
dermatomes, 425
dermatophyte infections, 291
descriptive statistics, 489
dexamethasone suppression test, 306
dextrocardia, 63
diabetes insipidus (DI), 317t, 330–331
diabetes mellitus, 322–329, 331–332
insulin, 31, 327
ketoacidosis, 328b, 329, 331–332
type 1/I, 322, 331

type 2/II, 322, 331
dialysis
acute kidney injury, 351–352
chronic kidney disease, 355
diamorphine, sickle cell crises, 376
diaphragm, X-ray, 54
diarrhoea, 234–235, 257, 259–260
HIV-related, 105
diet (nutrition)
folate deficiency due to, 373
management
acute kidney injury, 351
chronic kidney disease, 355
glycaemia, 327
digital subtraction angiography, 77
dignity in clinical examination, 3
digoxin interactions, 36t–37t
dilated cardiomyopathy, 196
diphtheria and C. diphtherium, 112
directed learning, 1
discoid lupus, chronic, 296
disseminated intravascular coagulation, 385
dissociative disorder, 480
distribution of data, 490
volume of (of drug), 39
water in body, 85
diverticular disease, 52, 231–232
DMSA (Tc-99) scans of renal function, 79
DNA
mitochondrial, abnormalities, 412
repair defects, and cancer, 404
DNA viruses, 118
dominant disorders
autosomal see autosomal dominant disorders
X-linked, 415
Doppler ultrasound
heart, 171
vascular tree, 77
dose, right, 35
double blind trials, 494
drain insertion, 81
dress code
clinical exam, 2
viva voce exams, 4
driving and epilepsy, 433
drop attacks, 433
drug(s) (therapeutic use), 35–49
acromegaly, 311
alcoholism, 482
arthropathies (incl. arthritis)
gout, 272
osteoarthritis, 269
psoriatic arthritis, 270
rheumatoid arthritis, 269
asthma see asthma cardiovascular, heart failure, 188
contraindications, 36t
diabetes mellitus, 327
hyperthyroidism, 309
inflammatory bowel disease
Crohn’s disease, 228
ulcerative colitis, 229–230
interactions, 36t–37t, 40
irritable bowel syndrome, 233b
liver and, 254, 257
mechanisms of action see mechanisms of drug action
migraine, 444
monitoring, 444, 40, 40t
multiple sclerosis, 437
osteoporosis, 279, 279t
overdose see overdose
Parkinson’s disease, 434
prescribing/dispensing, 45–47
controlled drugs, 31, 45
special patient groups, 46–47
steroids, 30–31
prostatic enlargement (benign), 359
psychiatric treatment see psychoactive drugs
pulmonary oedema, 188b
right, 35
sickle cell crises, 376b
side-effects/adverse reactions see adverse drug reactions;
drug-induced disorders
skin conditions
acne vulgaris, 294
atopic eczema, 292
psoriasis, 293
see also specific (types of) drugs
drug abuse, 482, 486
drug history, endocrine patient, 304t
drug-induced disorders
autoimmune haemolysis, 377
cancer, 404
constipation, 235
gastro-oesophageal reflux, 219
hepatic failure (fulminant), 245–246
hepatitis, 252t
hypercalcaemia, 282t
hyperkalaemia, 94
polyneuropathy, 452t
renal calculi, 347
see also adverse drug reactions
DTPA (Tc-99) scans of renal function, 79
Duckett Jones diagnostic criteria, rheumatic fever, 197t
ductus arteriosus, persistent, 193
Duke criteria for infective endocarditis diagnosis, 198b
Dukes’ classification, colorectal cancer, 232t
duodenum
barium meal, 69
ulcer, 221, 255
dynamic renal scintigraphy (functional scans), kidney, 79, 337
dysdiadochokinesis, 424
dyspepsia, 221
dysphasia (in stroke), 446
dyspnœa see breathlessness
dystrophia myotonica, 454–455
E
eating disorders, 468
EBV, 119
ECG see electrocardiography
echocardiography, 171
ectasy (MDMA), 483t
ectopic ACTH production, 312, 314, 314t, 330
eczema (dermatitis), 291–292, 298–299
EEG (electroencephalography), 428
Ehlers–Danlos syndrome, 283
Eisenmenger syndrome, 194
estase, faecal, 218
elderly, drug prescribing, 46–47
electrocardiography (ECG), 165–167
12-lead (normal), 27, 166f, 171f
24-hour ambulatory, 171
angina, 178
arrhythmias
atria fibrillation, 203
atrial flutter, 203
heart block, 200f, 202f
supraventricular tachyarrhythmia, 204
ventricular tachyarrhythmia, 206
exercise, 167–171
hyperkalaemia, 352, 353f
myocardial infarction, 159, 179f, 181f–182f
pulmonary embolus, 388
electroconvulsive therapy, 476
electroencephalography (EEG), 428
electrolytes
balance, 85–95
normal requirements, 85
electromyography (EMG), 85
elimination, drug, 39–40
see also excretion
embolism/embolus, 386
cerebral, 445
pulmonary, 22, 78f, 388–389
emergency (medical), 4
agitation, 469
diabetes mellitus, 328–329
emesis see vomiting
EMG (electromyography), 428
employment see occupation
encephalitis, acute viral, 439–440
encephalopathy, hepatic, 250–251, 250b
endocarditis, infective, 159, 197–199, 209
endocrine system, 303–333
disorders, 303–333
common, 303, 304t
short cases, 14
examination, 304
history-taking, 304t
laboratory tests, 305–306
renal endocrine function, 335
endocrine therapy, cancer, 408
endoscopic retrograde cholangiopancreatography, 217
endoscopy
bronchial, 137
gastrointestinal, 217
endpoints in trials, 494
Entamoeba histolytica, 237
enteral route of drug administration, 38
enterobacteria, 113
enteroscopy, 217
environmental factors, cancer, 401, 404
enzymes
cardiac, 98, 181
hepatic, 99
eosinophilia, causes, 393t
epidemiology, 496–497
epilepsy, 429–433, 460
communicating diagnosis, 30
drugs contraindicated, 36t
see also anticonvulsants
Epstein–Barr virus, 119
equipment for clinical examination, 2
neurological assessment, 419
erosive osteoarthritis, 267
error(s)
in experimental design causing incorrect results, 492
standard, 491
erythema (erythematous rash), 299–300
erythema multiforme, 295t, 296, 299
erythema nodosum, 294, 299
erythrocyes see red cells
erythroderma, 294, 299
Escherichia coli, 236
essay questions, 12
ethambutol side-effects, 143
ethanol, see also alcohol
euvolaemic hyponatraemia, 89
evidence-based medicine, 495
evoked potentials, visual, 428
examination (clinical exam), 2–3, 13–15
cardiovascular system, 159–165
cerebrovascular disease, 447
endocrine patient, 304
gastroenterological patient, 213–217
infections, 105
mental state see mental state examination
nervous system, 419–425
objective structured, 17–34
renal system, 216, 335–336
respiratory patient, 133–135
rheumatology patient, 263–264
skin disorders, 263
stations see stations examination
excretion, renal, 335
contrast media in urography, 337, 346
drugs, 39, 48
exercise ECG, 167–171
exposure to causative agent, 496
expressive dysphasia, 446
extended matching questions, 8–10
extracellular fluid volume
decreased see hypovolaemia
increased see hypervolaemia
normal, hyponatraemia with, 89
regulation, 86
extracellular matrix, 263
extracorporeal shock-wave lithotripsy, renal stones, 348
extradural haematoma, 72f
extrinsic allergic alveolitis, 153
exudative ascites, causes, 247t, 254
fingers
  clubbing, causes, 135t, 155
  nail changes in psoriasis, 293
  flaviviruses, 119–120
  flexural psoriasis, 293
  flight of ideas, 466–467
fluid
  balance, 85–95
  normal requirements, 85
  fluid collections causing swelling
  see oedema
fluid management
  diabetes mellitus, 328
  uraemia (acute), 351
fluid solutions, standard, 101
  fasting patient, 85–86
fluid thrill, 217
flumazenil, 42t
focal (partial) seizures, 432
folic acid deficiency, 373t, 374
fondaparinux, 209–210
foot, diabetic, 325, 326t
forensic history, psychological medicine, 466
fractures, osteoporotic, 276
fremitus, 135
Friedreich’s ataxia, 450
full blood count, 105, 398
  coeliac disease, 225
  sickle cell disease, 375
functional bowel disease, 232
fungal infections (mycoses), 123–124
  cutaneous, 291
drugs, 109
  meningeal, 438
  fusidic acid, 108

G

gait assessment, 264, 424–425
gallstones, 75f, 253
gamma-glutamyl transpeptidase, 99
γ-herpesviruses, 119
ganciclovir, 109
gas shadows, abdominal, 63
gastrin, elevated, 258
tumour-related, 240
gastritis, 222, 255
  see also stomach
gastrointestinal system, 213–261
  disorders, 213–261
  anxiety-related, 479t
cancer treatment-induced, 412

cystic fibrosis-related, 148

HIV-related, 122

short cases, 13–14

systemic sclerosis-related, 275

investigations, 217–218

barium studies, 69–70

X-rays, 65

magnesium losses, 95

potassium losses, 92

salt/sodium losses, 89

gastro-oesophageal reflux, 23, 218–219, 254

gastroscopy, 217

gender (sex) and cancer, 401, 403t

generalized paralysis of the insane, 420

generalized seizures, 429, 432

genetic associations and predisposition, 496

cancer, 404–405

collorectal, 230

diabetes mellitus, 322

see also familial disorders
genetic counselling, 416

genetic diagnosis of infectious agent, 106

genetic disorders, 412–417

blood

anaemias, 371, 374–377

cogulation disorders, 383–384

genetic imprinting, 415

genetic screening, 416

Huntington’s disease, 435
genentamicin monitoring, 40t
gonthary’s growth axis, 311f
growth factors in blood, 365
growth hormone (GH)

control of secretion, 309
deficiency (affecting and stature), 312

excess (causing acromegaly), 310t

Guillain–Barré syndrome, 451–452
guttata psoriasis, 293

H

haematology, 365–400

basic science, 365–367
disease, 365–400

HIV-related, 122

labatory values, 382, 398–399

haematoma, subdural see subdural haematoma

haemochromatosis, hereditary, 248
haemodialysis, chronic kidney disease, 355
haemofiltration
  acute kidney injury, 351–352
  chronic kidney disease, 355
haemoglobin, 367, 397
haemoglobinuria, paroxysmal nocturnal, 377
haemolysis, 105
haemolytic anaemia, 377
  autoimmune, 377, 378t, 398
haemolytic disease of the newborn, 377
haemolytic-uraemic syndrome, 345
haemophilia A, 383–384
haemophilia B, 383t, 384
Haemophilus, 113
haemopoiesis, 366f
  stem cells see stem cells
haemorrhage (bleeding)
  gastrointestinal, 222–223, 260–261
  intracranial, 73, 448
  with warfarin, uncontrolled, 386b
see also haematoma
haemorrhagic stroke, CT, 72f, 73
haemostatic plug formation, 381f
hair loss in cancer therapy, 409
hairy cell leukaemia, 394
hallucinations, 468, 487–488
  depression vs mania, 474t
hands
  examination
    cardiovascular patient, 159
    gastroenterological patient, 213
    respiratory patient, 133–134
    rheumatological patient, 264
    in liver disease (chronic),
      stigmata, 214t
    in osteoarthritis vs rheumatoid arthritis, 265t
    painful, 286
head, imaging see neuroradiology
headache, 443–444
healthcare availability, 496
hearing tests, 421–422
heart (cardiac…)
  apex beat, 162
  arrest, algorithm for management, 185f
arrhythmias, 199–207
  aspects on ECG, 167
  axis on ECG, 167, 170f
  block, 201–203, 209
  chemotherapeutic drug toxicity, 409
  congenital disease, 192–194
  cycle, 160f
  enzymes, 98, 181
  failure (congestive), 21, 186–188, 208
    left, 186
    right, 186–187
  inflammatory disease and infections, 194–199
  investigations, 165–172
  ischaemic disease see coronary artery disease; ischaemic heart disease
  myocyte death markers, 97–98
  outline abnormalities, 61
  short cases, 13
  size
    determination, 83
    enlargement, 61
  sounds see sounds
  surgery see surgery
  valves see valves
  X-rays, 59–61, 165
  shadows, 54–57
see also cardiovascular system
Helicobacter pylori, 218–219,
  221–223, 254
helminths (worms), 125, 237
Henle, loop of, 335
Henoch–Schönlein purpura, 277t–278t, 341
heparin, 385
  low molecular weight, 386
hepatitis, 240–246
  autoimmune, 245
  causes (in general), 240–241
  drug-induced, 252t
  viral, 130, 241–245, 258
    drug therapy, 109–110, 128, 244
    HAV, 241–242, 258
    HBV, 242–244, 258
    HCV, 244–245, 258, 417
    HDV, 244
  see also steatohepatitis
hepatocellular carcinoma, 251
hepatocellular dysfunction, 213t
hepatomegaly, causes, 215t, 254
hepatosplenomegaly, causes, 215t
hereditary non-polyposis colorectal cancer, 230
hernia
  examination for orifices, 217
  hiatus, 63, 219, 220b
herpes simplex 1 and 2, 118, 290–291
herpesviruses, 118–119, 128
HHV 6/7/8 (human herpes viruses), 118–119
hiatus hernia, 63, 219, 220b
hilar shadows, 54
histology, infections, 106
histoplasmosis, 123
history-taking, infections, 106
HIV see human immunodeficiency virus
Hodgkin lymphoma, 389–390
honeycomb lung, 152
hormone(s), 303–304
  laboratory tests, 305–306
  tumours secreting, 312
hormone therapy, cancer, 408
Horner syndrome, 457
HPV, 127
HSV 1 and 2, 118, 290
human herpes virus (HHV6/7/8), 118–119
human immunodeficiency virus disease and AIDS, 120–123, 128, 130
  nephropathy, 122, 344
human papilloma virus, 127
Huntington’s disease, 435, 460
hydrocarbons, carcinogenicity, 404
hydrocephalus, 443
hydronephrosis, 348–349
5-hydroxytryptamine (5-HT; serotonin)
  5-HT3 antagonists as antiemetics, 417
  reuptake inhibitors, 476, 480
hyperaldosteronism, 92, 320–321
hyperbilirubinaemia (raised bilirubin), 99
  conjugated, 258
hypercalcaemia, 281
hyperglobulinaemia, 395
hyperglycaemia in diabetes mellitus, 325
hyperglycaemic hyperosmolar state, 329
hyperkalaemia, 93, 101, 352b
hypermagnesaemia, 93–94
hypernaemia, 90–91
hyperparathyroidism (PTH excess secretion), 315–316
hypercalcaemia in, 282t
hyperphosphataemia, 95
hypersensitivity, drug, 40, 41t
  liver, 252t
hypersensitivity pneumonitis (extrinsic allergic alveolitis), 153
hypertension
  portal, 246
  systemic, 162, 208–209
  drugs contraindicated, 36t
  kidney and, 189, 345, 361
  malignant, 191
  primary/essential, 189, 345
  secondary, 189–191, 320–322
hyperthyroidism, 14t, 308–309
hypertrophic cardiomyopathy, 196
hyperuricaemia (raised urate), 100, 272t
hypervolaemia (increased extracellular fluid volume), 88
  hyponatraemia in, 90
hypnotic abuse, 483t
hypoadrenalism see Addison’s disease
hypocalcaemia, 282–283, 285
hypochondriasis, 481
hypoglossal nerve (CXII)
  defects, 456t
  testing, 422
hypoglycaemia in diabetes mellitus, 326b
hypokalaemia, 92
hypomagnesaemia, 93
hyponatraemia
  with decreased extracellular volume (hypovolaemia), 89
  with increased extracellular fluid volume (hypervolaemia), 90
Index

with normal extracellular volume, 89
see also pseudohyponatraemia

hypoparathyroidism (PTH deficient secretion), 316
hypoalbuminaemia, 94
hypopituitarism (incl. panhypopituitarism), 310t, 311–312, 330
hypotension, postural, 88
hypothalamic–pituitary axis, 310f
anterior pituitary, 310t
posterior pituitary, biochemistry of disorders of, 319t
hypothalamic–pituitary–adrenal axis, 313f
biochemistry of disorders of, 314t
hypothalamic–pituitary–thyroid axis, 306f
hypothesis, 491
hypothyroidism, 14t, 308, 330
hypouricaemia (lowered urate), 100
hypovolaemia (decreased extracellular fluid volume), 88
hyponatraemia in, 89–90
hysteria, 480

I
ideas
flight of, 466–467
generation (ideation) in depression vs mania, 474t

IgA nephropathy, 341, 342t, 359

imaging see radiology and specific modalities

immune complex nephritis, 338–341

immunization
active see vaccination
passive, 110–111

immunodiagnosis of infectious agent, 106

immunoglobulin A nephropathy, 341, 342t, 359
see also antibodies; autoantibodies; hyperglobulinaemia

immunology, chronic kidney disease, 354
see also autoantibodies

impetigo, 289
incidence, 497

Index Medicus, 495

infections, 105–132
in cancer causation, 404
cardiac, 194–199
diabetes mellitus, 326
diagnosis, 105–106
gastrointestinal, 235–237
hepatomegaly due to, 215t
hepatosplenomegaly due to, 215t
joint (septic arthritis), 269–270, 284
joint reactions following (reactive arthritis), 270–271
mode of transmission, 127
neurological/CNS, 437–442, 461
notifiable, 126t
respiratory tract see respiratory tract
sexually-transmitted, 126–127, 129
skin, 124, 289–291
splenomegaly due to, 216t
treatment, 106–110
urinary tract, 345–347, 360
see also abscess; microbiology and specific (types of) pathogens

infertility (sterility), cancer treatment-induced, 410

infestations, 291
inflammatory bowel disease, 227–230, 256
arthritis and, 271
inflammatory diarrhoea, 235
inflammatory disorders
heart, 194–199
liver see hepatitis
lung, 150–153
nervous system, 437–442

influenza, 120
inhaled drug administration, 39

inheritance see familial disorders and entries under genetic

injury, self-harming, 29–30, 479, 486

insight, degree of, 467
inspection and observation (look)
abdomen, 214
cardiovascular patient, 159
motor function, 422
rash, 289
respiratory patient, 133
insulin, 31, 327
insulin-sensitizing drugs, 327
intention to treat analysis, 494, 498
interferons, viral hepatitis, 109
international normalized ratio, 382
interpretations of results stations, 24–26
interstitial pneumonia, usual (cryptogenic fibrosing alveolitis), 153, 156
interventional radiology, 81
intestine see bowel habit changes;
bowel obstruction; colon; rectum; small intestine
intracerebral haemorrhage, 448
intracranial bleeds/haemorrhage, 73, 448
intracranial lesions
delirium caused by, 468t
masses, 73
tumours, 442–443
intracranial pressure, raised, 442t, 462
intramuscular drug administration, 39
intravenous contrast studies, 77–79
intravenous drug administration, 39
intrinsic factor, 372f
deficiency, 371t, 373
investigations
cardiac patient, 165–172
gastrointestinal see gastrointestinal system
infections, 105–106
lung disease, 137
neurological, 426–429
cerebrovascular disease, 447
renal see kidney
reporting results, 4
see also specific investigations and disorders
iron
absorption, 370f
deficiency
anaemia, 368t, 369
causes, 369
indices (in anaemias), 368t
metabolism, 369
irritable bowel syndrome, 232, 233b, 256–257
ischaemic attack, transient, 445, 462
ischaemic diabetic foot, 326t
ischaemic heart disease, 177–183, 209
risk factors, 20, 177–178
silent, 21
ischaemic stroke, CT, 72f, 73
isoniazid side-effects, 143
isotope scan see nuclear imaging;
sцинтиграфия
itching, 296–297, 300–301
J
jaundice, 8–9, 258
causes, 213t, 254, 258
joints, 263
examination, 263–264
fibrocartilaginous, 263
inflammation see arthritis
synovial, 263
jugular venous pulse, 161
K
kala-azar, 124
ketoacidosis, diabetic, 328b, 329, 331–332
kidney (renal…), 100, 335–363
carcinoma, 82
colic, 24
cystic diseases, 356, 361
disorders incl. nephropathies (in general), 335–363
diabetes insipidus (nephrogenic DI), 317–318, 319t, 331
diabetes mellitus-related, 325
HIV-related, 122, 344
hypertension and the, 189, 345, 361
hypokalaemia due to, 92
hyponatraemia due to, 89
osteomalacia and rickets due to, 280t
in systemic disease, 342–345
drug excretion, 39, 48
enlargement, causes, 216t
examination, 216, 336
failure
acute, 349–352, 360, 362–363
chronic, 352–355, 360–361
function, 335
dynamic scans, 79, 337
structure related to, 335
tests, 100, 337–338
imaging, 336–338
in chronic failure, 354
isotope scans/scintigraphy, 79, 80f, 337
ultrasound, 75, 337
X-rays, 68, 336
investigations, 336–338
radiological see imaging
(subheading above)
replacement therapy, 355
sodium retention, 86
stones/calculi, 67f, 347–348, 360
see also renovascular disease
knee reflex, 424
Korsakoff syndrome, 250, 452

laboratory investigations, 25–26
endocrine system, 305–306
haematology, 382, 398–399
renal function, 100, 337–338
see also chemistry
β-lactams, 106–108
lactate dehydrogenase, 98
Lambert–Eaton myasthenic-myopathic syndrome, 454
large intestine, see also colon; rectum
law, psychiatry, 485
laxatives, sickle cell crises, 376
lead time, 496
left bundle branch block, 202
left to right shunts, 192–193
leg ulcers, 297–300
legal issues in psychiatry, 485
leishmaniasis, 124
leprosy and M. leprae, 81
leptospirosis, 117–118
leucocytes see white cells
leukaemias
acute, 391, 393
chronic, 393
levodopa, 434
Lewy bodies, dementia with, 470–471
life support (acute), 183
advanced, 185f
basic, 184f
limb
ECG leads, 27, 167
weakness, 463
listening see auscultation
Listeria, 112
lithium, 477, 485–486
interactions, 36t
monitoring, 40t
unwanted effects, 465
liver
biochemistry, 98–99
chronic disease/dysfunction, 246, 385
drugs contraindicated, 36t
stigmata, 214t, 222
cirrhosis, 8, 246–251, 257
CT of mass lesions, 74f–76f
cyst, 76f, 83
drugs and the, 254, 257
enlargement see hepatomegaly;
hepatosplenomegaly
examination, 215
fulminant failure, 245–246, 259
functional tests, 98, 106, 246t
inflammation see hepatitis
ultrasound, 75, 76f
viral infections, 130
see also hepatitis
X-rays, 65
lobar collapse, 55f, 57
lobar pneumonia, X-rays, 57
long cases, 14–15
look see inspection
loop of Henle, 335
loosening of associations, 467
lumbar puncture, 428–429
meningitis, 438
see also cerebrospinal fluid
lung
abscess, 57, 140
cancer, 12, 59, 143–144, 156, 418
Lambert–Eaton myasthenic-myopathic syndrome, 454
secondary (metastases), 57, 59
consolidation, 136t–137t
fibrosis, 136t, 152
functional assessment, 137–138
honeycomb, 152
infection see respiratory tract
inflammatory disorder, 150–153
malabsorption, causes, 225t, 260
malaria, 124–125, 129
malignant hypertension, 191
malignant tumours see cancer
MALT lymphoma, 224, 255
management (patient), 10–12, 19
mania, 473, 477, 485
Marfan syndrome, 284
maternity blues, 477
MDMA, 483t
mean, 489
population, 489
sample, 489
measles, 120
mechanical haemolysis, 119
mechanical heart valves, 59, 159
mechanisms of drug action, 38
antibacterials, 106, 107f
antidepressants, 476f
antidotes to poisons, 42t
antiemetics, 410f
antivirals, 129
median, 489
median nerve compression at wrist, 450–451
mediastinal mass, X-ray, 58f
medical emergency, 4
medical history
endocrine patient, 304t
psychological medicine, 465
Medline, 495
megacolon, toxic, 66f, 230b
megaloblastic anaemia, 371
melanoma, malignant, 295t, 299
memory assessment, 468
see also mental state examination
meningitis, 437–439
meningovascular syphilis, 440
menstrual period, absence, 316–317
mental disorders see psychological
Mental Health Act, compulsory section, 485–486
mental state examination,
466–468
mesenteric angiogram, 77f
metabolic acidosis, 96–97, 101
in kidney disease, 338
metabolic alkalosis, 97
metabolic polyneuropathies, 452t
metabolism
drug, 39
renal, 335
metastases (disseminated tumour cells), 406t, 417

distant, 405, 406t

in bone, 80f, 279t, 406t
in liver, 251
in lung, 57, 59
from lung, 144
from prostate, 358

lymph node, 405

see also TNM classification

methanol poisoning, 42t

microbiology

acute kidney injury, 351
chronic kidney disease, 354
request forms, 28

microcytic anaemia, 368

microscopic polyangiitis, 277t–278t

microscopy

for pathogens, 106
faecal, 218
urine, 336

microvascular disease in diabetes mellitus, 325

migraine, 443–444

miliary shadows, 57

mononeuropathies, 450

mood (affect), 472–477

changes in fluctuation, 467
changes in nature, 467
continuum of normal/abnormal mood, 475f

disorders, 472–477

puerperal, 477–478

inappropriate, 467

morphine, sickle cell crises, 376

mortality see death

motility (GI) disorders, 235

motor function

antipsychotics affecting, 472

testing, 422–424
in Glasgow Coma Scale, 431t

motor neurone disease, 449–450, 460–461

motor neurone injury, upper vs lower, 421

mouth, ulcers, 297

movements

coordination tests, 424–425

disorders, 434–435

muco-cutaneous disease, HIV-related, 122

mucositis, radiotherapy-related, 410

MUGA scan, 172

multifactorial inheritance, 415

multi-gated acquisition (MUGA) scan, 172

multi-infarct dementia, 471

multiple choice questions, 2, 7

multiple endocrine neoplasia (MEN), 321–322
type 2a, 321, 331

multiple myeloma, 343, 395

multiple sclerosis, 436–437, 460

mumps, 120

murmurs, 164

muscle

atrophy

peroneal, 453

progressive, 449

disease (in general), 453–455

strength and power assessment, 423

tone assessment, 422

musculoskeletal system, 263–287

disorders (rheumatology), 263–287

short cases, 14

examination, 263–264

structure and function, 263

myasthenia gravis, 453–454

myasthenic-myopathic syndrome (of Lambert–Eaton), 454

Mycobacteria, 114–115

M. avium intracellulare, 143

M. kansasi, 143

M. leprae, and leprosy, 81

M. tuberculosis see tuberculosis

Mycoplasma pneumoniae, 140

mycoses see fungal infections

myeloablation and stem cell support in cancer therapy, 409

myelodysplasia, 395
myelofibrosis, 395
myeloid leukaemia (malignant
myeloid cell proliferations), 389
  acute, 393
  chronic, 393
myeloma, 59f, 395–396
  multiple, 343, 395
myeloproliferative disorders, 394
myelosuppression (bone marrow
suppression), cancer
treatment, 409
myocarditis, 196
myocardium
  infarction, 11–12, 208
  non-STEMI, 173t, 179t, 180,
  180b, 181f
  STEMI, 173t, 179t, 180,
  181f–182f
primary disease
  (cardiomyopathy), 196
myopathies, 453–455
myotonic dystrophy, 454–455
N
nail changes in psoriasis, 293
naloxone, 42t
narcotics see opioids
nausea, cancer patients, 409, 412
neck examination
gastroenterological patient, 213
respiratory patient, 134
thyroid disease, 307
negative marking, 2
Neisseria, 112
  N. gonorrhoeae, 126–127
nematodes, 125, 237
neoadjuvant therapy in cancer, 409
neonate (newborn), haemolytic
disease of the, 377
neoplasms see tumours
nephritic syndrome, acute, 339f,
342, 359
nephritis
  immune complex, 338–341
tubulointerstitial, 345
  see also glomerulonephritis;
  pyelonephritis
nephrogenic diabetes insipidus,
317–318, 319t, 331
nephrolithotomy, percutaneous, 348
nephrology and nephropathy see
kidney
nephrotic syndrome, 340f, 342,
359–360
nerve
  compression see compression
  conduction studies, 428
  cranial see cranial nerves
nervous system (incl. CNS),
419–464
degenerative, 449–450
disorders (=neurological
disorders), 319
ADH inappropriate secretion
(SIADH), 319, 331
anxiety-related, 479t
diabetes insipidus due to
(central DI), 317t, 318, 319t,
330
HIV-related, 122
sarcoïdosis, 151
short cases, 14
syphilis, 117, 440–441
examination, 421–422
investigations, 426–429
neurodegenerative disorders,
449–450
neuroleptics, 472
neurology see nervous system
neuromuscular junction disorders,
453–454
neuropathies (peripheral),
450–453, 461
diabetes mellitus, 325
leg ulcers associated with, 298
optic, in multiple sclerosis, 436
  see also polyneuropathies
neuroradiology (skull and internal
contents and spine),
426–427
CT, 24–25, 73, 81, 427–428
neuroses, 479–482
neurosyphilis, 117, 440–441
neurotoxicity of chemotherapeutic
drugs, 409
neutropenia with cancer
treatment, 409
newborn, haemolytic disease of the, 377 see also confidence
intervals
nitroimidazoles, 109
nodal osteoarthritis, 267
nodule, thyroid, solitary, 307
nominal data, 489
nominal tests, 492
non-Hodgkin lymphoma, 391
non-parametric tests, 492
non-ST elevation MI (NSTEMI), 173t, 179t, 180, 180b, 181f
non-steroidal anti-inflammatory drugs (NSAIDs), adverse effects/complications, 411
normal distribution, 490
notifiable diseases, 126t
NSAIDs, adverse effects/complications, 411
nuclear imaging/medicine, 52, 79
heart, 172
see also scintigraphy
nucleoside analogues, 110
HIV, 122
nucleotide analogues, 110
null hypothesis, 491
number needed to screen, 496
number needed to treat, 495
nutrition see diet

O
objective structured clinical examination, 17–34
observation see inspection and observation
obsession, 467
obsessive compulsive disorder, 480
obstructive lung disease see lung
obstructive sleep apnoea, 147, 156
occupation (employment) death relating to, 33–34
lung disease related to, 149–150
ocular problems see eyes
oculomotor nerve (CIII) defects, 456t
testing, 420–421
oedema (fluid collection)
peripheral, 165, 362
ankle, 210–211
pulmonary, 21, 61, 188b
oesophagus, 218–220
barium swallow, 69
Barrett’s, 219, 255
sphincter tone, 219f, 255
systemic sclerosis-related disorders, 275
tumour, 69, 70f, 83, 219–220, 254
varices, 255
oestrogens and cancer, 404
olfactory nerve (CI) defects, 456t
testing, 420
oncogenes, 405
oncology see cancer
ophthalmic branch of the trigeminal nerve, herpes zoster, 440
ophthalmology see eyes
opioids and opiates (narcotics) abuse, 483t
adverse effects/complications, 411, 483t
overdose, 42t, 45
sickle cell crises, 376b
optic nerve (CII) defects/lesions, 456t, 457f–458f
testing, 420
optic neuropathy/neuritis in multiple sclerosis, 436
optic tract lesions, 457f–458f
oral anticoagulants, 385–386
oral contraceptive interactions, 36t
oral route of drug administration, 38
oral ulcers, 297
ordinal data, 489
organ shadows, abdominal X-ray, 63
organic mental disorders, 468–471
organophosphate poisoning, 42t
orthomyxoviruses, 120
orthostatic (postural) hypotension, 88
osmotic diarrhoea, 234
osteoarthritis, 264–268, 265t
osteomalacia, 279–280, 279t, 285
osteoporosis, 276, 279t, 285, 316, 316t
ovarian causes of amenorrhoea, 316
overdose, 41–45, 47–48

P
P450 enzymes, 37t, 47
Paget’s disease, 279t, 280–281
pain
abdominal, 23, 338–341
back, 286
cancer, management, 410–412
chest see chest pain
hand, 286
sensation testing, 425
sickle cell crises, 374–375, 376b
see also analgesics; colic; headache
palliative care in cancer, 410–412
palpation, abdominal organs, 214–216
palpitations, 211
pancreas, 237–240
disorders, 237–240
endocrine pancreas, 323
malignant, 239–240, 258
ultrasound, 75
X-rays, 65
pancreatitis
acute, 237–239, 257–258
chronic, 239
panhypopituitarism (and hypopituitarism), 310t, 311–312, 330
paracetamol, 253f
overdose, 42–44, 47
parametric data, 492
parametric tests, 492
paramyxoviruses, 120
para-oesophageal hernia, 220
parasite antigens and immune complex nephritis, 339
parathyroid gland, 315–316
hormone secretion abnormalities see hyperparathyroidism; hypoparathyroidism
Parkinson’s disease, 28–29, 434–435, 460
drugs contraindicated, 36t
paroxysmal nocturnal haemoglobinuria, 377
partial seizures, 432
parvovirus B19, 119
patient communication with, 19, 30–34
management, 10–12, 19
right (in therapeutics), 35
patient-controlled analgesia
cancer, 411
sickle cell crisis, 376b
peak flow measurement, 26–27, 135, 137
pemphigoid, bullous, 297
pemphigus vulgaris, 297
penicillins, 106–108
peptic ulcer, 221–223, 255
perfusion, chest, 135, 136t
percutaneous nephrolithotomy, 348
pericardial effusions, 195
pericarditis acute, 194–195, 208
constrictive, 195
peripheral nerves see nerve; neuropathies; polyneuropathies
peripheral oedema see oedema
peritoneal dialysis, chronic kidney disease, 355
peritoneal fluid collections see ascites
peritonitis complicating cirrhosis, 247
pernicious anaemia, 373–374, 397
peroneal muscular atrophy, 453
perseveration, 466–467
personal appearance and behaviour, assessment, 466
personal history, psychological medicine, 465
personality, 465
pertussis (whooping cough) and B. pertussis, 113
PET scans, 79 see positron emission tomography
pH disturbances see acid–base disorders
phaeochromocytoma, 321, 331
pharmacodynamics, 37–38
definition, 35
interactions affecting, 37t
pharmacogenetics, 40
pharmacokinetics, 38–40
definition, 35
interactions affecting, 36t
pharmacology, 37–41
definition, 35
liver and, 254
in special patient groups, 46–47
pharynx, barium swallow, 69
phase I and II metabolism, 39
phenytoin adverse effects, 433
phosphate, 94
see also hyperphosphataemia; hypophosphataemia
phospholipids, antibodies to, 274
picorRNA viruses, 119
pituitary, 309–312
  disorders, 309–312
  amenorrhoea, 316
  function, 330
  see also hypothalamic–pituitary–
  adrenal axis; hypothalamic–
  pituitary–thyroid axis
pituitary fossa, X-ray, 427
plant alkaloids, 408
plantar response, 424
plasma
  in coagulation measurements, 382
  components, 375
  hormone levels, assessment, 305
  viscosity, 367
platelets
  adhesion, 382
  disorders, 383t, 396
  inhibitors (of aggregation/
  activation), 386
  prostaglandin, 382
  see also entries under thrombocyt-
platinum analogues, 408
pleura
  effusions, 61, 136t, 155
  tissue sampling, 138
pleurisy, 22
pneumoconiosis, coal-worker’s, 149
pneumonia, 21, 130, 155, 157–158, 361
  lobar, X-rays, 57
  physical signs, 136t
  usual interstitial (cryptogenic
  fibrosing alveolitis), 153, 156
pneumonitis, hypersensitivity
  (extrinsic allergic alveolitis), 153
pneumothorax, 22–23, 154, 156
  physical signs, 136t
  tension, 82
  X-ray, 52, 82
poisoning (incl. toxins), 41–45,
  47–48
  carbon monoxide, 154–155
  myocarditis due to, 196
  polioviruses, 119
  polyarteritis nodosa, 277t–278t
  polycystic kidney disease,
  autosomal dominant, 356, 361
polycythaemia vera, 394–395
polyenes, 109
polygenic (multifactorial)
  inheritance, 415
polymyalgia rheumatica,
  277t–278t, 285
polyneuropathies, 451–452, 452t
  in pernicious anaemia,
  progressive, 373
polyposis, familial adenomatous, 230, 405
polyuria, 332
population mean, 489
population screening see screening
portal hypertension, 246
position sense, 425
positive predictive value, 494
positron emission tomography
  (PET), 79
  brain, 428
postnatal (postpartum)
  psychological disorders,
  477–478
post-traumatic stress disorder,
  481–482
postural hypotension, 88
potassium, 91
  see also hyperkalaemia;
  hypokalaemia
power of trials, 494
poxvirus, 119
practical skills in OSCEs, 17, 26–28
precordium, 163
predictive value, positive, 494
pre-eclampsia, 344
pregnancy
  drug prescribing, 46–47
  hypertension, 189
  liver disease, 251
  pre-eclampsia, 344
  prenatal diagnosis, 416
  puerperal psychological
  disorders, 477–478
  Rhesus status and, 378
  prenatal diagnosis, 416
  prescription see drugs
  prevalence, 497–498
  prion disease, 441
  probability, 492
  procurator fiscal, death referral to,
  32t
  pronator drift, 423
prostaglandin, platelet, 382
prostate
  benign enlargement, 358–359
  cancer, 357–358
prothrombin time, 382
protozoal disease, 124–125
  gastrointestinal, 237
pruritus, 296–297, 300–301
pseudobulbar palsy, 455–457
pseudohyponatraemia, 90
pseudomembranous colitis, 237, 257
pseudoseizures, 433
psoriasis, 293–294, 299
  arthritis and, 270
psychoactive drugs, 488
  abuse, 482, 486
  see also specific (types of) drugs
psychological disorders
  (psychiatric disorders), 465–488
  history-taking, 465–466
  law, 485
  organic, 468–471
  treatments, 488
psychological support in cancer, 412
psychological treatment
  affective disorders, 477
  schizophrenia, 472
psychosis, postpartum, 478
publication bias, 494
Pubmed, 495
puerperal psychological disorders, 477–478
pulmonary embolus, 22, 65, 388–389
pulmonary non-vascular disorders
  see lung
pulmonary stenosis, 177
pulse (assessment), 159–161
  peripheral, 165
  pulse oximetry, 138
pupils
  in coma, 430
  testing reactions, 420
purine metabolism and
  hyperuricaemia, 272t
purpuria
  Henoch–Schönlein, 277t–278t, 341
thrombocytopenic see
  thrombocytopenic purpura
pyelonephritis, 346, 360
pyoderma gangrenosum, 296
pyogenic meningitis, 439t
pyramidal tract testing, 422–424
pyrazinamide side-effects, 143
pyrexia see fever
pyruvate kinase deficiency, 377
Q
  Q fever and Coxiella burnetii, 140, 198
questions, 7–15
  types, 7–15
  in written exams, 1, 7–12
quinolones, 109
R
  rabies, 120
  radial nerve compression, 451
  radial pulse, 159–161
  radioisotope scan see nuclear imaging; scintigraphy
  radiology (imaging), 51–83
  cancer, 406
  heart, 165, 171–172
  infections, 106
  urinary tract, 346
  interpretations of results stations, 24–25
  interventional, 81
  prenatal diagnosis using, 416
  respiratory system, 24, 52–63, 137
  types/modalities, 51–52
  urinary tract
    infections, 346
    kidney see kidney
  see also specific modalities
  radiotherapy, 408
  lung cancer, 144
  Ramsay Hunt syndrome, 440
  randomization in trials, 494
  Ransom’s criteria, 496
rash
  erythematous see erythema examination, 263
Raynaud’s phenomenon, 275
reactive arthritis, 270–271
receptive dysphasia, 446
receptor (for drugs), 37–38, 47–48
  agonists, 37
recessive disorders
  autosomal, 413, 413t, 414f
  sex/X-linked, 413, 413t, 417
rectum
cancer see colorectal cancer
route of drug administration, 38
red cells (erythrocytes)
  indices, 366
  isotope scan, 79
  sedimentation rate, 384
  volumes in anaemia, 365–367
reflexes
  corneal, 421
  tendon, 423–424
regression, 493
rehabilitation, stroke, 447
relative risk, 495
renal cell carcinoma, 356–357
renal organ/tissue see kidney
renin-angiotensin-aldosterone system, 320
renovascular disease, 345
drugs contraindicated, 36t
imaging, 82
reproductive system, sex
  hormone-related disorders, 316
reproductive toxicity of cancer treatments, 410
respiratory acidosis, 96
respiratory alkalosis, 96
respiratory failure, blood gases in, 138t
respiratory tract/system, 133–158
  anxiety effects, 479t
  cardiovascular system, systemic sclerosis-related disorders, 275
examination, 133–135
functional assessment, 137–138
HIV-related disorders, 122
imaging, 24, 52–63, 137
infection (lower incl. lung), 21, 139–143, 155
  X-rays, 57
short cases, 13
smoking and, 133
structure and function, 133
see also airways and specific regions
restrictive cardiomyopathy, 196
resuscitation, cardiopulmonary (CPR), 185f
reticulocyte scan, 367
retinal changes in hypertension, 189
retinopathy, diabetic, 324f
revision, 4–5
rhabdovirus, 120
Rhesus blood group, 377–378, 379t
rheumatic fever, 197, 208
rheumatoid arthritis, 151, 265t–266t, 268–269, 284
rheumatology see musculoskeletal system
ribavirin, 110
rickets, 280, 280t
rifampicin side-effects, 141
right bundle branch block, 202
right to left shunts, 193–194
ringworm (tinea), 291
Rinne’s test, 422
risk
  absolute, 495
  relative, 495
RNA viruses, 119
Romberg’s test, 425
routes of drug administration, 38–40
rubella, 119
rubeola (measles), 120
Salmonella, 236
salt, homeostasis, 317
salt-deficient hyponatraemia, 89–90
sample mean, 489
sarcoïdosis, 150–151
Sarcoptes scabiei and scabies, 291
scabies, 291
schistosomiasis, 125
schizophrenia, 471–472, 485
scintigraphy (isotope scan)
  bone, 79
gastrointestinal tract, 218
  pulmonary embolus, 78f, 137, 389
  renal, 79, 80f, 337
sclerosing cholangitis, primary, 253
screening, 495–496, 498
cancer, 407
genetic see genetic screening
Index

secretory diarrhoea, 235
seizure patterns, 432t
self-harming, 29–30, 479, 486
seminoma, 358
sensation, assessment, 425
sensitivity of tests, 493
sepsis in acute uraemia, 351
septic arthritis, 269–270, 284
seronegative
spondyloarthropathies, 270
serotonin see 5-hydroxytryptamine
sex (gender) and cancer, 401, 403t
sex hormone disorders, 316
sex-linked (X-linked) disorders, 413, 413t, 415, 415f, 417
sexually-transmitted diseases, 126–127, 129
shigellosis, 236–237
shingles (herpes zoster), 290–291, 423, 440
short answers, 10
short cases, 13
shunts (cardiac) in congenital heart disease, 192t
absence, 192t, 194
left to right, 192–193
sick sinus syndrome, 201
sickle cell disease, 374–375
sideroblastic anaemia, 371
sigmoidoscopy, 217
significance, statistical, 492
single best answer questions, 7–8
sinus arrhythmia, 199
sinus bradycardia, 199
sinus node disease, 201
sinus tachycardia, 201
skewed distribution, 490
skin (cutaneous…), 289–301
disorders (in general), 289–301
malignant see cancer
systemic see systemic disease examination, 289
functions, 289
leishmaniasis, 124
in liver disease (chronic),
stigmata, 214t
terminology for various lesions, 290t
skull, see also head;
neuroradiology
sleep apnoea, obstructive, 147, 156
sleeping sickness, 124
small intestine/bowel, 224–227
barium follow-through, 70
disorders, 224–227
endoscopy (enteroscopy), 217
systemic sclerosis-related disorders, 275
X-rays, 65
see also bowel obstruction
smoking
cancer and, 401, 416
respiratory effects, 133
social beliefs, 496
social history, endocrine patient, 304t
social treatment
affective disorders, 477
schizophrenia, 472
sodium, 89
content of standard iv. replacement fluids, 85
renal retention, 86
see also hypernatraemia; hyponatraemia
solvent abuse, 483t
somatoform disorders, 480–481
sounds
breath, 135, 136t–137t, 165
heart, 163–164
aortic regurgitation, 176
aortic stenosis, 175
mitral regurgitation, 174
mitral stenosis, 173
pulmonary stenosis, 177
tricuspid regurgitation, 176
tricuspid stenosis, 177
specificity of tests, 494
speech, assessing, 466
spinal accessory nerve see accessory nerve
spinal cord (lesions/disease), 459–460
in multiple sclerosis, 437
subacute combined degeneration, 452–453
spine
CT, 428
X-ray, 427
spinothalamic tract assessment, 425
spirochaetes, 116–118
spirometry, 138
spleen, examination, 216–217
splenomegaly
(hepatosplenomegaly),
causes, 215t
splenomegaly, causes, 216t
spondylitis, ankylosing, 270
spondyloarthropathies,
eronegative, 270
squamous cell carcinoma of skin,
295t
ST elevation MI (STEMI), 173t,
179t, 181f–182f
staghorn renal calculus, 67f
standard deviation, 490
standard error, 491
standardized mortality ratio, 497
Staphylococcus, 111–112, 128
S. aureus
endocarditis, 198
gastroenteritis, 236
pneumonia, 140
toxin, 112
S. epidermis, endocarditis, 198
stations (in OSCEs)
examples, 19–34
interpretations of results, 24–26
practical procedures/skills, 17,
26–28
specific, 28–30
types, 17–19
statistics, 489–498
status epilepticus, 431b
steatohepatitis, 252
steatosis, hepatic, 251–252
stem cells, haemopoietic, 365
support, after myeloablation, 409
stent, biliary, 81
sterility, cancer treatment-induced,
410
sternotomy wires, X-ray, 59, 60f
steroid prescribing/dispensing,
30–31
stomach, 221–224
barium meal, 69
cancer, 223–224, 255, 403f
doscopy, 217
ulcer, 221, 223, 255
X-rays, 65
see also gastritis
stones see calculi
stools (faeces)
increased frequency, 235,
256–257
tests, 218
Streptococcus, 112
S. pneumoniae, 140
streptomycin side-effects, 143
stress (psychological)-related
disorders, 481–482
stroke (cerebrovascular accidents),
444–449
CT, 73
stomal tumours, gastric, 224
subacute combined degeneration
of spinal cord, 452–453
subarachnoid haemorrhage, 72f,
448
subcutaneous drug
administration, 39
for continuous analgesia in
cancer, 411
subdural haematoma, 72f
chronic, 449, 462
sublingual drug administration,
38
substance (drug) abuse, 482, 486
suicide
risk assessment, 29
risk factors, 478–479, 486
sulphonamides, 108
sulphonylureas, 327
supraventricular tachyarrhythmia,
204–205, 209
surgery
cancer, 408
lung, 144
cardiac, 59
endocarditis, 199
heart failure, 188
mitral stenosis, 162
prostatic enlargement (benign),
359
surveillance, 496
cancer, 407
SynACTHen test, 305
synovial joints, 263
syphilis (and T. pallidum
infection), 116–117, 129
neurological involvement, 117,
440–441
syringobulbia, 459–460
syringomyelia, 459–460
systemic disease
 cutaneous involvement,
294–297
sarcoidosis, 150
systemic sclerosis, 275
pulmonary involvement, 151–152
renal involvement, 342–345
systemic lupus erythematosus, 151, 272–274, 296
systemic sclerosis, 275–276, 285
systemic vasculitis, 342–343

T

tabes dorsalis, 116f, 440
tachycardia (incl. tachyarrhythmia)
  atrial, 203
  sinus, 201
  supraventricular, 204–205, 209
  ventricular, 205–207
tacrolimus monitoring, 40t
tactile (touch) sensation, 425
taxanes, 408
technetium-99 scans of renal function, 79
temperature sensation, 425
temporal (giant cell) arteritis, 277t–278t
tendon reflexes, 423–424
tension headache, 443
tension pneumothorax, 82
teratoma, testicular, 358
test values, accuracy, 493–494
testicular tumours, 358
tetanus and C. tetani, 112
tetracyclines, 108
tetralogy of Fallot, 193–194, 208
thalassaemia, 375–376
thallium scan, 172
theophylline interactions, 36t
therapeutic index, 37f, 40
therapeutics
  cardinal features, 35
  definition, 35
thiamin(e) deficiency, 250, 452
thinking see thought
thirst axis, 318f
thoracic aortic aneurysm, 61
thorax see chest
thought (thinking)
  blocking, 466
  content disorders, 467
  form disorders, 466–467
thrombin time, 382
thrombocythaemia, essential, 395
thrombocytopenia, 105, 396
  cancer treatment-induced, 409
  causes, 397t
thrombocytopenic purpura
  autoimmune, 396
  thrombotic, 345
thrombocytosis, 396
thromboembolic disease, 386
  see also embolism; venous thrombosis
thrombolysis see fibrinolysis
thrombophilia, 387
thrombosis (thrombus), 386
  arterial, 386
  venous see venous thrombosis
thrombotic thrombocytopenic purpura, 345
thyroid gland, 306–309
  disorders, 306–309
  see also hyperthyroidism; hypothyroidism
  examination of gland and status, 14t, 29, 306, 307t
thyroid stimulating hormone (TSH), 307t, 329
TIMI risk score in acute coronary syndrome, 179t
tinea (ringworm), 291
TNF blockers, 269
TNM classification, 407t
  colorectal cancer, 232t
togavirus, 119
tonic-clonic seizures, generalized, 432
tophaceous gout, 272
topical drug administration, 39
torsades de pointes, 207
touch sensation, 425
toxic confusional state, 468–469, 485
toxic megacolon, 66f, 230b
toxicology see adverse drug reactions; overdose; poisoning
toxocara, 125
toxoids, 111
toxoplasmosis, 124
trachea
  deviation, 136t
  X-ray, 54
transfer factor, 138
transfusion (blood), 365, 398
  complications, 380, 398
  massive, 385
  procedure, 380
transient ischaemic attack, 445, 462
transplantation, renal, 355
transudative ascites, causes, 247t, 259
trematodes, 125, 237
tremor, benign essential, 435
  *Treponema pallidum* see syphilis
trials, clinical, 494, 498
triazoles, 109
triceps reflex, 424
tricuspid regurgitation, 176, 208
tricuspid stenosis, 177
tricyclic antidepressants, 476
  overdose, 44
  unwanted effects, 477t
trigeminal nerve (CV)
  defects, 456t
  ophthalmic division, herpes zoster, 440
  testing, 421
trinucleotide repeat disorders, 415
trochlear nerve (CIV)
  defects, 456t
  testing, 420–421
troponin I and T, 97, 101
trypanosomiasis, 124
tuberculoid leprosy, 115
tuberculosis and *M. tuberculosis*, 57, 114–115, 128, 141–143, 155
  meningeal, 439, 439t
  renal, 347
  acidosis, 97
  acute necrosis, 350f
  structure and function, 335
tubulointerstitial disease, 353t
  nephritis, 345
tumour(s) (neoplasms)
  gastric, 223–224, 403f
  hormone-secreting, 312, 321
  intracranial, 442–443
  lung, 59
  malignant see cancer; metastases in multiple endocrine neoplasia, 321
  oesophagus, 69, 70f, 83, 219–220, 254
  pancreatic, 239–240
  small bowel, 226–227
  urogenital tract, 356–358
  tumour markers, 407
  tumour necrosis factor (TNF)
    blockers, 269
  tumour suppressor genes, 404
  24-hour ambulatory ECG, 171
  type 1 and 2 error, 492
ulcer(s)
  cutaneous, 300
  leg, 297–300
  oral, 297
  peptic, 221–223, 255
  ulcerative colitis, 229–230, 256
  arthritis and, 271
  imaging, 67f, 78f
  ulnar nerve compression, 451
ultrasound, 51, 75–77
  Doppler see Doppler ultrasound
  prenatal, 416
  renal, 75, 337
  see also echocardiography
ultraviolet (UV) light and skin cancer, 404
unconsciousness (or partial loss of consciousness), 429, 462–464
urate (and uric acid), 100
  crystal deposition, 264, 272
  urea, 100, 102, 337
  uric acid see urate
urine
  investigations/tests (incl. urinalysis), 336, 427t
  in acute kidney injury, 350
  in chronic kidney disease, 353
  retention, acute, 27–28, 359b
urogram, 79
urography, excretory, 337, 346
urothelial tumours, 357
usual interstitial alveolitis
(cryptogenic fibrosing
alveolitis), 153, 156
UV and skin cancer, 404

V
V/Q scans see ventilation/
perfusion scans
vaccination (active immunization),
110–111
killed vaccines, 110
live attenuated vaccines, 110,
127
tuberculosis, 115
vagus nerve (CX)
defects, 456t
testing, 422
valves (heart), 172–177
disease, 172–177, 207–208
mechanical/prosthetic, 59, 164
variance, 490
varicella zoster virus (VZV), 118,
290–291, 440
varices
gastric, 223
oesophageal, 255
vascular dementia, 471
vascular tree/system
disorders (in general)
chronic kidney disease in, 353t
in diabetes mellitus, 325
Doppler ultrasound, 77
interventional radiology, 81
wall injury leading to clot
formation, 380
see also cardiovascular system;
cerebrovascular disease
vasculitis, 276, 277t–278t
systemic, 342–343
vasopressin see antidiuretic
hormone
venous thrombosis/
thromboembolism, 387
deep, 387–388
risk factors, 387t
venous ulcers, 297–298
ventilation/perfusion (V/Q)
scans, 79, 137
pulmonary embolus, 79, 137,
389
ventricles
fibrillation, 207
septal defect, 192–193
tachyarrhythmia, 205–207
verbal function in Glasgow Coma
Scale, 431t
vertebral osteoporotic fractures,
276
vertebrobasilar system and
temporary ischaemic attack, 445
vestibulocochlear nerve (CVIII)
defects, 456t
testing, 421–422
Vibrio cholerae and cholera, 236
vibration assessment, 425
video (wireless) capsule
endoscopy, 218
villous atrophy, 225
viral antigens and immune
complex nephritis, 338
viral infections, 118–120
cutaneous, 290–291
drugs see antiviral drugs
gastrointestinal, 232
liver (other than hepatitis), 245
myocardial, 196
neurological, 440
acute encephalitis, 439–440
meningitis, 438, 439t
sexually-transmitted, 127
visceral leishmaniasis, 124
visual acuity assessment, 420
visual evoked potentials, 428
visual field
assessment, 420
defects, 457f–458f
visual pathway lesions, 457f–458f
vitamin(s) (in general),
polyneuropathies with
various deficiencies, 452t
vitamin B12
absorption, 372f, 397–398
deficiency
anaemia, 371t
subacute combined
degeneration of spinal cord,
452–453
vitamin D
deficiency, 263, 280t
excess action, 282t
vitamin K deficiency, 280t, 384
viva voce exams, 3–4
vocal resonance, 135, 136t
volume of distribution, 39
volvulus, X-rays, 65
vomiting (emesis)
  bulimia nervosa, 484
  cancer patients, 409, 412
  persistent, 101
von Willebrand’s disease, 383t, 384
VZV (varicella zoster virus), 118, 290–291, 440

W
Waldenström’s macroglobulinaemia, 396
walking difficulty, 463
warfarin, 385–386, 399
  interactions, 36t
  international normalized ratio, 382
warm autoimmune haemolytic anaemia, 378t
water (body)
  diarrhoea and, 234f
  distribution, 85
  homeostasis, 317
  hyponatraemia due to excess of, 90
  total, 85
water deprivation test, 317b
Weber’s test, 421–422
Wegener’s granulomatosis, 151, 277t–278t
weight loss, 332–333
Weil’s disease, 117–118
Wenckebach block, 201, 202f
Wernicke–Korsakoff syndrome, 250, 452
Whipple’s disease, 226
white cells (leucocytes), 367
  elevated counts, 398
  isotope scan, 79
white shadows, 54
WHO see World Health Organization
whooping cough (pertussis) and B. pertussis, 113
Wilson’s disease, 248–249
withdrawal symptoms/syndromes
  alcohol, 481, 486–487
  benzodiazepines, 213t
work see occupation
World Health Organization (WHO)
  acute leukaemia classification, 392t
  analgesia ladder, 413t
  diabetes diagnostic criteria, 322t
  worms (helminths), 125, 237
written exams, 1–2
  questions, 1, 7–12
X
X-linked (sex-linked) disorders, 413, 413t, 415, 415f, 417
X-ray radiographs (plain films), 51
  abdominal, 24, 26f, 63–68
  kidney, X-rays, 68, 336
  chest see chest
  pituitary fossa, 427
  skull, 426
  spine, 427
Y
yellow fever, 119
Yersinia, 236
Z
Zollinger–Ellison syndrome, 218
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